



中华医学会 第六次细菌真菌感染学术会议

主办单位：中华医学会、中华医学会细菌感染与耐药防治分会

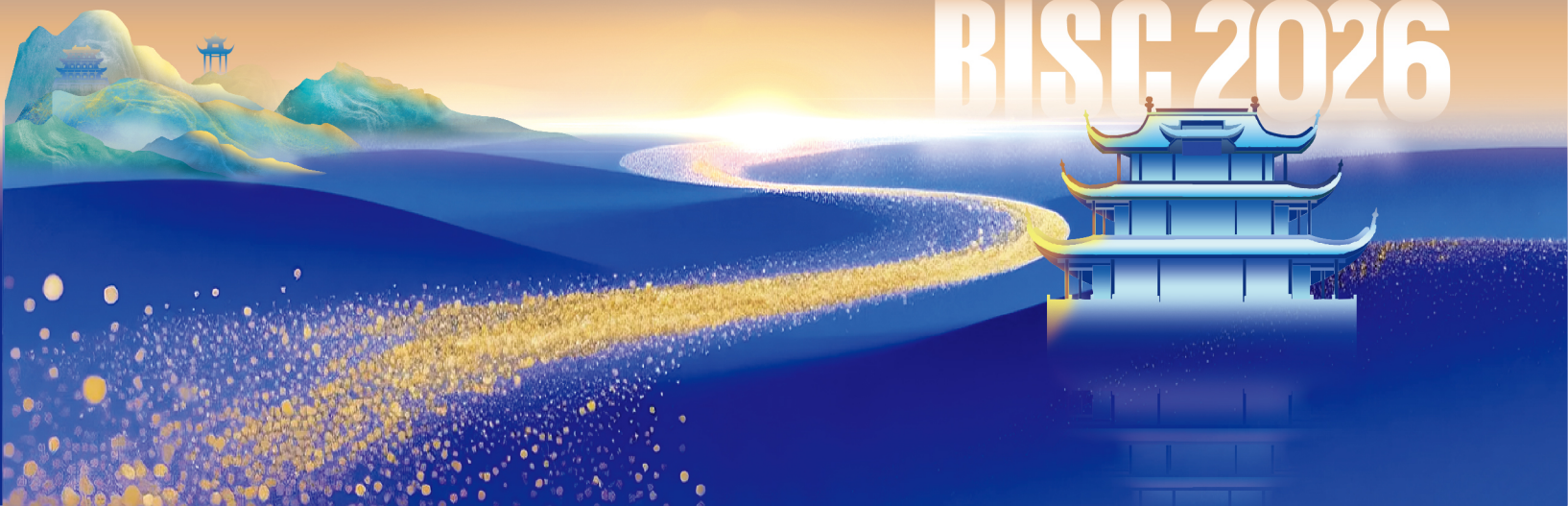
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论文汇编

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论文发言

细菌真菌感染的病原诊断技术

Ultra-Stable 2D Magneto-Fluorescent Probe-Mediated Multiplex Immunochromatographic Assay for Precise Bedside Detection of Sepsis

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Accurate bedside diagnosis of sepsis is essential for timely treatment and reducing mortality, yet technical limitations persist. Here, we present a multiplex-compatible lateral flow immunoassay (LFIA) that integrates a universal click-chemistry conjugation strategy with highly dispersible, film-like magnetic fluorescent probes (GFDQD@Si) to enable precise diagnosis through concurrent monitoring of pathogens and protein biomarkers. GFDQD@Si combines a two-dimensional high-area reactive interface; a magnetic interlayer for target enrichment and signal amplification; a multilayer quantum dots for fluorescence enhancement; and an outer silica shell that suppresses background fluorescence and confers superior flowability. This architecture overcomes the size disparity between bacteria and proteins, enabling efficient co-capture of multiple proteins/bacteria and achieving faster, more sensitive detection on an LFIA platform. The platform quantitatively detects two key sepsis biomarkers—procalcitonin (PCT) and interleukin-6 (IL6)—as well as the pathogen *Pseudomonas aeruginosa*, with limits of detection of $4.44 \text{ pg} \cdot \text{mL}^{-1}$ for PCT, $0.94 \text{ pg} \cdot \text{mL}^{-1}$ for IL6, and $7 \text{ CFU} \cdot \text{mL}^{-1}$ for bacteria. Validation in 75 clinical whole-blood samples demonstrated high sensitivity, ease of operation, and robustness, underscoring its potential for real-time bedside sepsis diagnosis. By simul-

taneously providing dual readouts of host-response biomarkers and pathogen detection, the GFDQD@Si-LFIA platform is expected to accelerate and improve clinical decision-making for sepsis.

细菌真菌耐药监测与耐药机制

外排泵 QacA 通过细胞膜脂质重编程促进金黄色葡萄球菌对万古霉素异质耐药形成

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背景 耐甲氧西林金黄色葡萄球菌(MRSA)中异质性万古霉素中介金黄色葡萄球菌(hVISA)表型,是导致万古霉素治疗失败的主要诱因。在流行的ST5型MRSA谱系中,外排泵基因qacA已被证实是hVISA形成的关键因素。但由于万古霉素并非典型的外排底物,其背后的分子机制目前仍尚不明确。

方法 将携带qacA基因的质粒转入临床ST5型万古霉素敏感金黄色葡萄球菌(VSSA)菌株,验证菌株是否发生hVISA表型转换;探究qacA对细菌细胞壁、生物膜及细胞膜的影响,并通过万古霉素探针定位观察其与菌体的结合情况。进一步采用定量脂质组学分析细胞膜脂质组分的变化,同时评估万古霉素能否与脂肪酸协同作用,逆转细菌的适应性脂质改变。

结果 本研究证实,qacA可不依赖药物直接外排、细胞壁增厚或生物膜形成,独立诱导VSSA向hVISA发生表型转换。细胞膜流动性检测及荧光漂白恢复(FRAP)分析表明,QacA蛋白的表达可显著提升细胞膜流动性、加快膜分子侧向扩散速率。共聚焦显微镜结果显示,携带qacA基因的菌株与万古霉素探针的结合能力明显下降。脂质组学分析进一步发现,qacA会引发细胞膜脂质重编程,特征为双不饱和甘油磷脂大量富集。此外,外源添加长链不饱和脂肪酸可与万古霉素产生协同杀菌作用。

结论 研究表明,qacA通过独特的脂质重编程途径驱动VSSA向hVISA表型转变;该过程形成高流动性细胞膜“熵屏障”,阻碍万古霉素与脂质II结合,而非通过直接转运药物产生耐药。本研究

结果颠覆了对消毒剂耐药因子的传统认知,同时揭示细菌细胞膜脂质组是提升万古霉素抗菌活性的一个关键的潜在靶点。

Class 1 DISARM System in Restriction of Conjugative Carbapenemase-encoding Plasmids in *Klebsiella Pneumoniae* Sequence Type 23

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Objectives Canonical hypervirulent *Klebsiella pneumoniae* sequence type 23 (ST23) causes severe infections while it generally maintains susceptibility to a broad spectrum of antimicrobials, yet the molecular basis of this phenotypic characteristic remains poorly understood. The purpose of this study was to investigate whether the presence of the DISARM system prevents antimicrobial-resistant plasmids invasion in *K. pneumoniae*

Methods Comparative genomic analysis was performed to detect the distribution of DISARM among *K. pneumoniae* lineages. PacBio single-molecule real-time sequencing was employed to identify DISARM-associated DNA methylation motifs. Transformation and conjugation assays were conducted to evaluate the impact of DISARM on plasmids defense

Results Class 1 DISARM system was selectively enriched in ST23 *K. pneumoniae* strains. The DISARM methylase modified host 5'-GRACRAC-3' motifs which were distributed in all conjugative plasmids in *K. pneumoniae*. The transformation efficiency

of plasmid pCOLADuet-MTmotif containing the methylation cognate site was reduced 2.9-fold compared with that of the plasmid pCOLADuet-1 in a ST23 DISARM-positive strain KP2613. Conjugation of carbapenemase-encoding plasmids (carrying blaKPC-2, blaNDM-1, and blaNDM-5) decreased 12- to 117-fold in KP2613 and 4.5- to 15.7-fold in *Escherichia coli* BL21-DISARM(+) compared with DISARM-negative strains KP2613 Δ DISARM and BL21-DISARM(-), respectively, indicating that Class 1 DISARM could effectively hinder the antimicrobial resistance plasmids invasion. Systematic deletion of individual DISARM genes revealed that disruption of any single gene did not fully abolish the DISARM-mediated defense or cause substantial growth defects

Conclusions Class 1 DISARM provides robust protection against antimicrobial-resistant plasmids, potentially contributing to the high antimicrobial susceptibility observed in ST23 hypervirulent *K. pneumoniae*

Heterogeneous Multicopy of BlaCTX-M Variants on The Same Plasmid Enhances Evolutionary Adaptability in Clinical *Klebsiella Pneumoniae*

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Pathogenic bacteria continually evolve under antimicrobial pressure through acquired resistance genes, making it crucial to understand their evolutionary strategies. We identify a clinical *Klebsiella pneumoniae* isolate resistant to ceftazidime/avibactam (CZA), harboring heterogeneous multicopy blaCTX-M, among which blaCTX-M-249 variant mediates CZA resistance. Both blaCTX-M-249 and its closely related allele blaCTX-M-65 are dominant within the clonal population and are located at two loci on the same plasmid, with their proportions shifting under antibiotic pressure. Using experimental and mathematical models, we demonstrate that the heterogeneous arrangement of blaCTX-M variants on the same plasmid confers greater stability and competitive advantage than that across separate plasmids, particularly during drug switching. Reanalysis of large genomic datasets supports the universality of this phenomenon. Our findings reveal an evolutionary strategy in which β lactamase genes, through multicopy heterogeneity on a single plasmid, ensure stable inheritance of resistance and enhance bacterial adaptability under fluctuating clinical antibiotic pressures.

Calcineurin-dependent Stress Adaptation Enables Caspofungin Heteroresistance Leading To Stable Resistance in *Candida Glabrata*

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Antifungal heteroresistance has emerged as a clinical challenge across diverse species. In *Candida glabrata*, however, it has rarely been reported. Here, we characterized heteroresistance in a multicenter collection of 156 *C. glabrata* isolates, revealing a 25% prevalence with caspofungin specificity and 37°C dependent phenotypes. Transcriptomic profiling of the heteroresistant subpopulation under escalating drug pressure revealed an adaptive program centered on cell cycle and cell wall integrity, including several members of calcineurin pathway. Mechanically, we identified the phenotype was abolished by pharmacological inhibition or Δ cnb1, Δ crz1 genetic deletion, confirming the regulator role of calcineurin. Crucially, heteroresistance func-

tioned as a reservoir for resistance, with in vitro descendant strains spanning a spectrum of MIC alterations. Mechanistically, we found the heteroresistance phenotype mostly independent of aneuploidy. In summary, our study established a stepwise model of heteroresistance in *C. glabrata*, wherein calcineurin serves as a master regulator that promotes a resistance reservoir, revealing a potential vulnerability that could be exploited to prevent treatment failure.

In Vivo Evolution of Tigecycline Resistance in ST540 Carbapenem-Resistant *Acinetobacter Baumannii*: Mechanisms and Global Epidemiological Perspective

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Carbapenem-resistant *Acinetobacter baumannii* (CRAB) is a persistent nosocomial pathogen, posing a major global health threat owing to limited treatment options. Although tigecycline is still effective against CRAB, resistance emergence has become a critical concern. This study aimed to elucidate the in vivo evolutionary mechanisms underlying tigecycline resistance in CRAB. A total of 11 STpas2-SToxf540 CRAB strains were recovered from rectal swabs, sputum samples, and the surrounding environmental specimens of an intensive care unit (ICU) hospitalized patient who had received tigecycline treatment. CgSNP analysis confirmed environment-to-patient transmission among these CRAB isolates. Comparative genomic analysis indicated that mutations in *adeS*, *pgaA*, and *gbsA* may be associated with tigecycline resistance. In situ mutagenesis and antimicrobial susceptibility testing verified that

the *adeS* N125S mutation mediates tigecycline resistance and collateral sensitivity to cefoperazone/sulbactam. Growth curve assays demonstrated that the *adeS* N125S mutation imposes a fitness cost on CRAB. Transcriptional analysis showed that the *adeS* N125S mutation drives the development of tigecycline resistance by upregulating the expression of the AdeABC efflux pump. By examining 45,377 publicly available global *A. baumannii* genome sequences, we characterized the molecular epidemiology of the STpas2-SToxf540 lineage and the distribution of *adeS* mutations. Our findings underscore the need to strengthen surveillance and rational antimicrobial use to prevent CRAB dissemination and antimicrobial resistance evolution, particularly in ICUs.

抗菌药物的药理药学研究与临床试验

Vancomycin Treatment Failures Support Machine Learning-based Identification of Heterogeneous Vancomycin-intermediate Staphylococcus Aureus Infections

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Objectives Heterogeneous vancomycin-intermediate *Staphylococcus aureus* (hVISA) infections remain underdiagnosed with unclear clinical impact. This multicenter study evaluated vancomycin treatment outcomes and developed a machine learning (ML)-based diagnostic model

Methods We prospectively enrolled 200 patients with MRSA infections from 20 Chinese hospitals between February 2012 and July 2021. Population analysis profile–area under the curve (PAP-AUC) testing was performed on all isolates to confirm hVISA phenotype, and confirmed strains underwent whole-genome sequencing. Vancomycin therapeutic drug monitoring and pharmacokinetic/pharmacodynamic (PK/PD) analysis was performed. A ML model was developed for hVISA prediction.

Results Of 200 MRSA-infected patients, 117 (58.5%) were identified with hVISA infections, including 98 (98/175, 56.0%) adult patients and 19 (19/25, 76.0%) pediatric patients. Despite higher vancomycin doses, adult patients with hVISA infection achieved lower PK/PD indices than vancomycin-susceptible *S. aureus* (VSSA). In adults receiving vancomycin monotherapy, hVISA infection was associated with significantly higher treatment failure than VSSA infection (34.6% vs. 5.0%, $P = 0.028$), with a PAP-AUC threshold

of ≥ 0.92 predictive of poor response. The predominant hVISA clones were ST5, ST239 and ST764, with ST5 and ST239 showing higher treatment failure rates than ST764. Among 10 ML models, LASSO-logistic regression performed best with AUC of 0.834 (95% CI 0.711–0.930) on test set, identifying vancomycin MIC, tracheal intubation, and prior penicillin use as key predictors.

Conclusion High prevalence of hVISA among MRSA isolates and its impact on vancomycin monotherapy warrant early identification. The ML model enables identification of high-risk patients, supporting a shift toward phenotype- and genotype-guided personalized dosing.

细菌真菌感染的流行病学

Emergence of Carbapenem-Resistant *Escherichia Coli* Coharboring blaCTX-M-199 and Penicillin-Binding Protein 3 Insertion Confering Increased Aztreonam/Avibactam Resistance in South China

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Background Infections caused by carbapenem-resistant *Escherichia coli* (CREC) pose a serious global public health threat due to limited therapeutic options. This study aimed to investigate the molecular epidemiology and the susceptibility to novel β -lactam/ β -lactamase inhibitor combinations in clinical CREC isolates

Methods Whole-genome sequencing analysis including multilocus sequence types, antimicrobial resistance genes, serotypes and phylogeny was conducted. Antimicrobial susceptibility testing was performed by the broth microdilution method. Filter mating assays were performed to evaluate the conjugation of the plasmid.

Results We identified an emerging extended-spectrum β -lactamase-encoding gene, blaCTX-M-199, in 8.9% (26/291) of CREC strains isolated in South China. Notably, 96.2% (25/26) of blaCTX-M-199-positive CREC strains exhibited aztreonam/avibactam (ATM/AVI) nonsusceptibility, with 38.5% (10/26) being fully resistant. All 26 blaCTX-M-199-positive strains harbored blaNDM-5 and YRIK/YRIN insertions of penicillin-binding protein 3, belonging to ST410 ($n = 10$) and ST167 ($n = 16$). Whole-genome sequencing revealed that blaCTX-M-199 can be located on the chromosome or on transferable plasmids. Transconjugants

exhibited a 2- to 4-fold increase in the minimum inhibitory concentration of ATM/AVI.

Conclusion These findings suggest that blaCTX-M-199 contributes to reduced ATM/AVI susceptibility and, in synergy with YRIK/YRIN insertions, likely confers significant ATM/AVI resistance. Notably, CREC strains coharboring blaCTX-M-199 and YRIK/YRIN insertions are emerging within international high-risk clones ST410 and ST167. Therefore, our study highlights the importance of monitoring the prevalence of blaCTX-M-199-harboring CREC and implementing its detection in clinical practice.

Keywords blaCTX-M-199; YRIK/YRIN insertions; ST167; ST410; aztreonam/avibactam resistance; carbapenem-resistant *Escherichia coli*

Recombination-driven Emergence of High-level Multidrug-resistant *Streptococcus Pseudopneumoniae*: A Retrospective Cross-sectional Genomic Epidemiology Study

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Background *Streptococcus pseudopneumoniae* has been overlooked in clinical practice. However, recent reports of severe invasive infections, together with our finding of high-level multidrug-resistant strains, highlight an escalating threat. Hence, we performed the first in-depth whole-genome analysis to elucidate the global resistance mechanisms of *S. pseudopneumoniae*.

Methods From 2009 to 2024, we collected 1,240 *Streptococcus pneumoniae* clinical isolates from eight institutions in Zhejiang, China. Whole-genome sequencing identified 32 as *S. pseudopneumoniae*. Broth microdilution was performed for representative macrolide and β -lactam antibiotics of these isolates. Global *S. pseudopneumoniae* next-generation sequencing data (n=99) were retrieved from the NCBI database. Whole genome analysis was performed to detect macrolide and β -lactam resistance determinants, investigate the transmission of resistance, and identify recombination hotspots associated with antimicrobial resistance. Pan-genomic analysis was used to identify specific sequences for the accurate detection of *S. pseudopneumoniae*.

Findings In Zhejiang Province, China, *S. pseudopneumoniae* exhibited high-level erythromycin resistance (MIC₉₀ >128 μ g/mL) at 87.1%, 67.7% resistance to tetracycline, and 74.2% non-susceptibility to penicillin. Globally, *S. pseudopneumoniae* is divided into three major phylogenetic clades, with resistant isolates predominantly clustered in Clade-II, which carries erm(B) and tet(M) resistance genes via transposons. PBP1a phylogeny suggests *S. pseudopneumoniae* originated from local *S. pneumoniae* and evolved independently. Top recombination-associated regions linked to β -lactams and aminoglycosides resistance genes and transposon transfer, highlighting the role of recombination in resistance development. Additionally, a novel, specific marker was identified, providing a reliable tool for accurate identification of *S. pseudopneumoniae*.

Coclusion Our study reveals a continuously escalating clinical threat posed by *S. pseudopneumoniae*, driven by the emergence of multidrug-resistant clones. The phylogenetic clustering of isolates within the resistant clones suggests a potential risk of global dissemination. Critically, recombination emerges as a key driver of resistance evolution. This study advances our understanding of *S. pseudopneumoniae*, offering critical insights to inform future clinical prevention.

肺炎克雷伯菌血流感染的临床及病原学特征——单中心回顾性临床研究

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目的 分析血流感染肺炎克雷伯菌 (*Klebsiella pneumoniae* bloodstream infection, KP-BSI) 的病原学特征及其对临床预后的影响, 为临床精准诊疗提供依据。

方法 回顾性分析 2021-2024 年复旦大学附属华山医院 KP-BSI 患者分离的 205 株非重复菌株及临床资料。通过微量肉汤法进行药敏试验, 利用二代测序分析序列分型 (Sequence Type, ST)、荚膜血清分型 (Capsular Locus, KL)、耐药及毒力基因。按特征将菌株分为高毒力组 (Hypervirulent *Klebsiella pneumoniae*, hvKP)、碳青霉烯耐药组 (Carbapenem-resistant *Klebsiella pneumoniae*, CRKP) 和敏感组 (CSKP), 比较不同病原学特征肺炎克雷伯菌引起血流感染的临床特征。

结果 205 株菌中 CRKP 占比达 61.0%, 对常用药物耐药率高, 但对替加环素和头孢他啶-阿维巴坦保持高度敏感。CRKP 组以 ST11-KL64 为绝对优势克隆 (74.4%), 且 *iucA* 和 *rmpA/A2* 毒力基因检出率均超 70%, 呈现向 hv-CRKP 演变的特征。hvKP 组以 ST23-KL1/KL2 为主。hvKP 组多为社区获得性

感染 (50%), 肝胆来源及临床侵袭综合征发生率显著高于他组, 糖尿病是其重要合并症; CRKP 组以医院获得性感染为主 (95%), 基础疾病负担最重, ICU 收治及侵入性操作比例最高; CSKP 组则以实体肿瘤及放化疗患者居多。CRKP 组的临床有效率 (63.3%) 最低, 其 7 天死亡率 (23.1%) 和 30 天死亡率 (33.9%) 均显著高于 CSKP 组和 hvKP 组 ($P<0.05$)。系统发育分析显示基因组进化与临床表型高度关联, ST11-KL64 克隆群是导致院内感染及不良预后的核心威胁。

结论 本院 KP-BSI 中 CRKP 检出率高且呈现高毒力特点, ST11-KL64 是主要的流行克隆。不同组别 KP-BSI 在基础疾病、感染来源及预后上存在显著临床异质性。CRKP 感染是早期及中期死亡的高危因素, 临床需警惕其高耐药与高毒力并存的传播风险。

Comparative Genomic, Phenotypic, and Clinical Characterization of ST11-KL25 and ST11-KL64 Hypervirulent Carbapenem-resistant *Klebsiella Pneumoniae* in A Tertiary Hospital, 2020–2023

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Hypervirulent carbapenem-resistant *Klebsiella pneumoniae* (hv-CRKP) poses a significant challenge in healthcare settings due to its combination of high virulence and multidrug resistance. In China, ST11 is the predominant lineage, with KL64 and the recently identified KL25 as key capsular subtypes. The clinical and genomic characteristics of ST11-KL25 remain insufficiently characterized. A total of 239 hv-CRKP isolates collected from 2020 to 2023 were analyzed. Molecular

typing, antimicrobial susceptibility testing, whole-genome sequencing, and phenotypic assays were used to compare the epidemiology, resistance mechanisms, and virulence traits of ST11-KL25 and ST11-KL64. Clinical data were reviewed to assess infection characteristics. ST11 accounted for 87.9% (210/239) of hv-CRKP isolates. Among ST11 isolates, KL64 (54.7%, 104/190) and KL25 (45.3%, 86/190) were the predominant capsular types. Phylogenetic analysis suggested that ST11-KL25 may have originated from KL64 through capsular switching, with increasing prevalence after 2021. Both sublineages exhibited extensive drug resistance; however, ST11-KL64 showed broader resistance, including higher rates of ceftazidimeavibactam and polymyxin resistance. Phenotypically, ST11-KL25 demonstrated greater competitive fitness and biofilm formation, while ST11-KL64 displayed higher *in vivo* virulence in the *Galleria mellonella* model. ST11-KL25 and ST11-KL64 exhibit distinct adaptation strategies within hv-CRKP. KL25 seems to be a stable, colonization-adapted subtype with consistent resistance and moderate virulence, while KL64 is more invasive, with broader resistance and higher virulence. Subtype-specific surveillance and intervention are essential to limit their spread and protect patient and public health.

细菌真菌感染的治疗

Butyrate Alleviates *Klebsiella Pneumoniae*-induced Sepsis by Regulating ABCF1-mediated Metabolic Reprogramming of Macrophages

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Sepsis, a life-threatening organ dysfunction caused by dysregulated host responses, remains a major global challenge with limited therapies options. Here, we show that the gut microbiota-derived metabolite butyrate protects against bacterial sepsis by reprogramming macrophage metabolism through the immune regulator ABCF1. In murine models of *Klebsiella pneumoniae* (*K. pn*) infection, antibiotic-induced microbiota depletion exacerbated inflammation and organ injury, whereas butyrate supplementation restored immune balance and improved survival. Butyrate reprogrammed macrophages toward an anti-inflammatory phenotype, suppressed glycolysis, enhanced oxidative phosphorylation, and reduced pro-inflammatory cytokines production. Furthermore, butyrate acted as a histone deacetylase inhibitor (HDACi) to modulate ABCF1 ubiquitination, stabilize its function, and sustain macrophage polarization. In septic patients, higher serum butyrate levels were associated with increased ABCF1 expression, reduced inflammation, less organ dysfunction, and improved outcomes. These findings identify microbiota-derived butyrate as an immunomodulatory metabolite that regulates macrophage function and underscore its potential relevance to host-microbiota interactions in sepsis.

Differentiating Patients with Disseminated Cryptococcosis From Pulmonary Cryptococcosis: The Role of Clinical Characteristics and Cryptococcus Antigen

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Background Cryptococcosis in non-human immunodeficiency virus (HIV)-infected populations is increasing, with disseminated cryptococcosis (DC) carrying a significantly higher mortality risk than localized pulmonary cryptococcosis (PC). Because management strategies for PC and DC diverge substantially, identifying robust indicators for systemic dissemination is critical for optimizing survival

Methods A retrospective study was conducted at a tertiary referral hospital in China (1999–2019), involving 475 pathologically confirmed non-HIV cryptococcosis patients. Clinical characteristics, radiographic findings, and serum cryptococcal antigen (CrAg) titers were compared between patients with PC (n=391) and those with DC (n=84)

Results **Host Factors and Symptoms:** Patients with DC were more likely to have received glucocorticoid therapy (16.7% vs 5.6%; $P = .001$) and had a higher prevalence of underlying autoimmune diseases (16.7% vs 6.1%; $P = .001$). Symptoms were present in 96.4% of DC patients compared to 47.6% in the PC group ($P < .001$). **Radiographic Features:** DC was significantly associated with more aggressive thoracic computed tomography (CT) findings, including patchy exudation (32.9% vs 15.3%; $P = .001$) and cavitation (14.3% vs 5.0%; $P = .009$). **CrAg Titer Dynamics:** High-level initial antigenemia (1:1280) was characteristic of DC, whereas titers $< 1:80$ were associated only with PC in this cohort. DC patients exhibited a protracted course of

antigenemia; at 24 months, the median CrAg titer in the DC group (1:40) remained fourfold higher than that of the PC group (1:10). **Outcomes:** DC patients had significantly higher mortality (9.5% vs 1.0%; $P < .001$) and lower cure rates (28.6% vs 74.7%; $P < .001$) despite more intensive induction regimens and longer treatment durations (median 18 vs 6 months)

Conclusions In non-HIV patients, glucocorticoid use, autoimmune disease, and aggressive CT manifestations (patchy exudation and cavitation) are key predictors of dissemination. A serum CrAg titer 1:1280 provides a robust indication for DC, necessitating urgent cerebrospinal fluid evaluation and intensive antifungal therapy

医院感染控制

Rising Difficult-to-Treat Resistance Amid Stable Carbapenem Resistance in *Pseudomonas Aeruginosa*, 2016–2025: A Retrospective Cohort Study in China

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Background Difficult-to-treat resistant *Pseudomonas aeruginosa* (DTR-PA) represents an emerging clinical threat, yet its epidemiological dynamics remain incompletely characterized in Asian healthcare settings

Methods We conducted a 10-year retrospective cohort study (2016–2025) analyzing 15,542 non-duplicate *P. aeruginosa*(PA) isolates from a 4,500-bed tertiary teaching hospital in China. Temporal trends in carbapenem-resistant PA (CR-PA) and DTR-PA detection rates were assessed using linear regression with annual percentage change (APC). The proportion of DTR-PA within CR-PA isolates was analyzed via binomial logistic regression. Cumulative detection rates across three study periods were estimated using Kaplan-Meier analysis.

Results While CR-PA detection rates remained stable (APC = 0.16%; $p = 0.653$), DTR-PA demonstrated a significant and sustained increase from 8.2% in 2016 to 12.8% in 2025 (APC = 0.81%; $p = 0.001$; $R^2 = 0.763$). The proportion of DTR-PA within CR-PA isolates increased progressively from 22.0% to 32.4%, with annual odds ratio of 1.12 (95% CI: 1.09–1.14; $p < 0.001$). Cumulative detection rates of DTR-PA accelerated across successive periods, with 2023–2025 showing earlier and higher detection rates than 2016–2019

(log-rank $p < 0.001$), particularly in ICU settings (day 90: 37.1% vs. 12.8%).

Conclusion DTR-PA constitutes an escalating threat masked by stable CR-PA rates. These findings necessitate institutionalizing DTR-PA as a distinct surveillance metric and reconsidering empirical therapy algorithms for suspected resistant *P. aeruginosa* infections.

Outbreak of *Klebsiella Grimontii* and *Klebsiella Michiganensis* in A Neonatal Intensive Care Unit

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Background The *Klebsiella oxytoca* complex (KoC) is an opportunistic pathogen capable of causing outbreaks in neonatal intensive care units (NICUs). We investigated an outbreak, caused by members of this complex, in a Chinese tertiary hospital NICU to elucidate its transmission route and underlying mechanisms

Methods The strains were isolated from rectal and oral swabs of infants. All strains underwent whole gene sequence, followed by multilocus sequence typing (MLST), single-nucleotide polymorphism (SNP) analysis, and phylogenetic tree construction. Virulence and resistance genes were annotated, and transmission pathways were inferred.

Results A total of 102 KoC isolates were obtained from 28 preterm, very-low-birth-weight infants. Among these infants, 21 developed clinical infections, including one case of bacteremia and two cases of necrotizing enterocolitis. The outbreak comprised two distinct clones: 86 *K. grimontii* (ST566, a novel sequence

type) and 16 *K. michiganensis* (15 ST35, 1 ST98). Isolates within each clone were nearly identical, differing by 0–2 SNPs. Analysis of global epidemiological data revealed that ST566 and ST35 are not prevalent sequence types worldwide, suggesting the outbreak may have been caused by a unique clone resulting from local evolution or a specific introduction. All outbreak strains harbored yersiniabactin siderophore genes (*ybtS*, *fyuA*, *entAB*) and the cytotoxins tilivalline/tilimycin, which were less frequent detected in adult fecal isolates. Spatiotemporal and bed-movement data suggested transmission via healthcare worker-mediated contact and potential environmental contamination. While most isolates were susceptible to the majority of antimicrobial agents tested, heteroresistance emerged in one patient.

Conclusion This NICU outbreak was caused by two genetically distinct KoC clones. Genomic and epidemiological evidence supports clonal spread, likely mediated by contact transmission. The high infection rate among colonized infants underscores the need for stringent infection control and surveillance in this vulnerable population.

Keywords *K. michiganensis*, *K. grimontii*, *Klebsiella oxytoca* complex, outbreak, infant

其他微生物及其感染

Carvacrol Suppresses Conjugative Transfer of Virulence Plasmid in Hypervirulent *Klebsiella Pneumoniae* by Disrupting Energy Supply and Pilus Assembly

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Horizontal virulence genes transfer through plasmid-mediated conjugation poses a major threat to global public health. Carvacrol is a plant extract and a widely used monoterpene phenol. Here, we report for the first time that carvacrol inhibits the conjugative transfer of a virulence plasmid, resulting in a decrease in virulence. We revealed the intrinsic mechanism by which carvacrol inhibits plasmid conjugative transfer by observing intercellular contact and pilus formation, as well as detecting changes in ROS and adenosine triphosphate (ATP) levels in the bacterium. We also conducted a transcriptome analysis. The inhibition of virulence plasmid conjugation was associated with decreased intercellular contact, reduced production of adhesive pilus, generation of extracellular free radicals, induction of oxidative stress, reduction of the ATP energy supply, suppression of the mating pair formation (Mpf) system gene, the DNA transfer and replication (Dtr) system gene. Our results revealed intracellular processes by which carvacrol inhibits conjugative transfer of the virulence plasmid, which would support the use of carvacrol to reduce the spread of virulence genes.

The VgrG2 Effector of *Acinetobacter Baumannii* Mediates Immune Evasion by Repressing Csu Pilus Assembly and Triggering Phagocyte Methuosis

wenzeng xu

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Summary *Acinetobacter baumannii* is a formidable nosocomial pathogen whose multidrug resistance and immune evasion capabilities present a major therapeutic challenge. This study identifies the type VI secretion system (T6SS) effector VgrG2 as a critical virulence regulator in *A. baumannii*. VgrG2 employs a two-pronged strategy to undermine host innate immunity. First, it transcriptionally represses the major adhesin Csu pilus, reducing bacterial recognition, phagocytic uptake, and neutrophils recruitment. Second, VgrG2 directly targets and hyperactivates the small GTPase Rac1 within phagocytes. This leads to actin cytoskeletal disarray, which drives excessive macropinocytosis, resulting in compromised phagocytosis and methuosis—a non-apoptotic, vacuole-dependent death specific to phagocytes. Thus, VgrG2 selectively eliminates key immune sentinels and alters pulmonary inflammation, promoting bacterial persistence and dissemination. These findings extend the role of T6SS effectors beyond inter-bacterial competition to include sophisticated eukaryotic-directed attacks, and highlight the VgrG2-Rac1 axis as a promising therapeutic target.

其他

Dynamic Immune Features for Predicting In-Hospital Mortality in ICU Elderly Patients with Sepsis: A Multicenter Prospective Cohort Study

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Objective We aimed to delineate dynamic immune trajectories in elderly ICU patients with sepsis (days 1, 4, and 7) and determine whether integrating longitudinal multidimensional immune and inflammatory markers can improve risk stratification and prognosis for in-hospital mortality beyond individual parameters.

Methods A total of 445 elderly patients with sepsis admitted to the ICUs of four hospitals in China from May 2023 to May 2024 were prospectively enrolled. We compared baseline and longitudinal immune/inflammatory profiles on ICU days 1, 4, and 7 between in-hospital survivors and non-survivors. Associations between biomarkers and in-hospital death were evaluated using multivariable logistic regression with stepwise confounder adjustment. Discrimination of individual markers and a derived composite model was assessed using time-point-specific ROC curves with DeLong tests. Model performance was further examined using bootstrap calibration and decision curve analysis, and was

subsequently visualized and implemented as a nomogram.

Results Among 445 elderly ICU patients with sepsis, 148 (33.26%) died during hospitalization, with a median time to death of 14.0 (8.0–22.5) days. The distributions of infection sites and causative pathogens were broadly similar between survivors and non-survivors, with upper respiratory tract infection (URTI) and Gram-negative bacterial infection being the most common in both groups. However, URTI was more frequent among non-survivors than survivors (127/148, 85.81% vs. 204/297, 68.69%), and Gram-negative bacterial infection was slightly more prevalent in non-survivors (78/148, 52.70% vs. 146/297, 49.16%). Across ICU days 1, 4, and 7, survivors consistently had higher total lymphocyte levels, driven mainly by persistently lower counts of total T cells, CD4⁺ T cells, and cytotoxic T lymphocytes (CTLs) in non-survivors, whereas B-cell counts were comparable. Non-survivors also showed higher IL6 and IL8 levels, with IL10 transiently elevated early (days 1 and 4). Individual immune markers had modest discrimination for in-hospital mortality (AUC ~0.49–0.64). A composite model integrating SOFA score, BUN, lymphocyte count, IL6, and CTL count independently predicted death and provided significantly better discrimination than any single immune marker at all time points (all $P < 0.05$), performing similarly to SOFA on days 1 and 4 (all $P < 0.05$) but outperforming SOFA on day 7 ($P > 0.05$).

Conclusion The integrated immune-feature composite model consistently demonstrated superior discrimination for in-hospital mortality across ICU days 1, 4, and 7 compared with any single immune parameter.

GPR65 调控 M2 样巨噬细胞在肺炎克雷伯菌肺炎中的保护机制研究

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目的 探究 GPR65 在肺炎克雷伯菌肺炎中发挥的功能及调控机制

方法 1. 收集临床重症肺炎克雷伯菌 (K. p.) 肺炎病人外周血, 检测 GPR65 表达及其与临床指标相关性; 2. 构建 K. p. 肺炎小鼠模型, 体内检测 Gpr65 表达及功能; 3. 单细胞组学检测小鼠肺组织 Gpr65 表达及差异基因功能富集; 4. 构建 Gpr65 髓系细胞条件性敲除小鼠 K. p. 感染模型, 体内验证巨噬细胞 Gpr65 功能; 5. 分离 WT 及 Gpr65^{-/-} BMDMs, 转录组学联合代谢组学体外检测 Gpr65 表达及差异基因改变, 探究巨噬细胞细胞代谢差异以及 Gpr65 下游信号转导机制; 6. 使用 Gpr65 激动剂 BT09089 体内验证 GPR65 在 K. p. 肺炎中的调控作用。

结果 1. 重症肺炎克雷伯菌肺炎患者外周血单核细胞 GPR65 蛋白表达降低且与 CRP、PCT 负相关; 2. 相比于 WT 组, Gpr65^{-/-} 小鼠生存率降低, 外周血及组织细菌负荷增加; 肺组织病理损伤加重、中性粒细胞浸润增加; 肺组织 TNF- α 、IL-6、IL-1 β 增加, IL-10 水平降低; 3. 单细胞组学证实小鼠肺组织中 Gpr65 主要表达于单核巨噬细胞; 4. 细胞转录组学及代谢组学结果表明, Gpr65^{-/-} 小鼠 BMDMs Arg-1 表达降低, 精氨酸代谢、胆固醇代谢以及 PPAR 信号通路表达降低; 花生四烯酸代谢、亚油酸代谢以及甘油磷脂代谢等脂代谢通路下调; 5. 相比于 Gpr65^{flox/flox} 组小鼠, Gpr65^{flox/flox}; Lyz2-Cre⁺ 组小鼠生存率降低, 外周血及组织细菌负荷增加, 肺组织病理损伤加重, 中性粒细胞浸润增高, 肺泡灌洗液蛋白浓度升高, 肺组织 TNF- α 、IL-6、IL-1 β 水平升高, IL-10 水平降低; 6. 相比于 WT 组 BMDMs, Gpr65^{-/-} 组 BMDMs 脂肪酸摄取能力降低, 脂代谢相关基因表达降低; 脂肪酸转运相关蛋白 Abca1 以及 PPAR γ 表达降低; 7. BT09089 促进肺

泡巨噬细胞胞内细胞因子 IL-10 表达以及 Arg-1 表达

结论 1.重症肺炎克雷伯菌肺炎患者单核细胞 GPR65 表达降低; 2. GPR65 在肺炎克雷伯菌肺炎中发挥保护作用; 3. GPR65 通过 cAMP-PKA-PPAR γ 通路促进 M2 样巨噬细胞极化, 参与肺炎后组织炎症消减; 4. GPR65 通过 PPAR γ -Abca1 促进巨噬细胞脂肪酸摄取参与脂代谢重编程。

关键词: 肺炎克雷伯菌/ 代谢重编程/ GPR65/ 巨噬细胞

Decoupling Infection From Replication: Intracellular Defense Systems and Ecological Context Jointly Shape Phage Dynamics

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Bacterial antiviral immunity is often inferred from efficiency of plating (EOP), assuming that susceptibility correlates with productive infection. Here, we challenge this assumption by showing that phage infectivity and replication output are frequently decoupled in *Pseudomonas aeruginosa*. By comparative genomic analysis of 1,500 genomes and quantitative phenotyping of 205 clinical isolates, we identify a widespread “plaque–production paradox,” whereby strains exhibiting similar susceptibility by EOP produce markedly divergent phage yields. Using the clinical isolate ZS-PA-35 as a model, we show that phage replication is constrained after adsorption by intracellular restriction within six defense islands. Systematic dissection further indicates that antiviral activity extends beyond annotated core

modules, with flanking genes contributing to overall defense capacity. Furthermore, we find that phage proliferation varies along two ecological axes: population density, represented by quorum sensing as a biotic axis, and temperature as an abiotic axis. Across these contexts, phage production changes markedly, with high-density cultures showing strong restriction linked to Island 5 and temperature shifts producing reproducible changes in viral output. Overall, these results indicate that plaque formation alone is a poor predictor of phage replication, and that phage production emerges from the interaction between intracellular defense potential and environmental state.

壁报交流

细菌真菌感染的病原诊断技术

A Single-tube RAA-CRISPR-Cas12a Diagnostic Platform for Rapid Detection of *Chlamydia Trachomatis*

null null

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Chlamydia trachomatis, a pathogen of global public health importance, is prioritized by the World Health Organization as a major sexually transmitted infection. Its continued worldwide spread poses persistent challenges to reproductive health and disease control systems, underscoring the urgent need for rapid and accurate diagnostic methods. While current clinical diagnosis primarily relies on nucleic acid amplification tests (NAATs), their dependence on expensive thermal cyclers, complex laboratory setups, and sophisticated procedures limits widespread use in low-resource settings. Recent advances in recombinase-aided amplification (RAA) combined with CRISPR-Cas12a have revolutionized molecular diagnostics. This study established an integrated one-tube CRISPR fluorescence detection system by combining rapid nucleic acid lysis, isothermal amplification, and CRISPR-Cas12a cleavage. The system is coupled with a portable palm-sized 4-channel fluorescence detector and a terminal app for visual readout. Experimental results demonstrated a detection limit of 10^1 copies/mL with no cross-reactivity to common reproductive tract pathogens including *Neisseria gonorrhoeae*, *Ureaplasma urealyticum*, *Candida albicans*, *Trichomonas vaginalis*, and *Gardnerella vaginalis*. Clinical validation against qPCR showed 100.00% sensitivity (95% CI: 87.66–100.00%), 98.31% specificity (95% CI: 90.91–99.96), 98.85% overall agreement (95% CI: 93.76–99.97), 96.55% positive predictive value (95%

CI: 80.04–99.49), and 100.00% negative predictive value (95% CI: 93.84–100.00%). This successfully developed CRISPR-Cas12a-based rapid detection method offers simple operation and fast results – complete within 30 min using rapid lysis (5 min nucleic acid release, 20 min RAA amplification, and 5 min CRISPR cleavage) – making it suitable for primary care and field screening, thereby providing a novel strategy for early diagnosis of *C. trachomatis* infection.

Explainable Machine Learning-Enhanced MALDI-TOF Mass Spectrometry for Rapid Detection of Carbapenem-Resistant *Klebsiella Pneumoniae* SHAP-Based Validation of A Multi-Biomarker Diagnostic Approach

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Purpose This study aims to develop a method combining MALDI-TOF mass spectrometry and interpretable machine learning for rapid detection of carbapenem-resistant *Klebsiella pneumoniae* (CRKP), providing biological explanations for model decisions through SHAP analysis

Methods We analyzed MALDI-TOF mass spectrometry data from 292 clinical *Klebsiella pneumoniae* isolates (145 CRKP strains, 147 carbapenem-susceptible strains). Four machine learning algorithms were evaluated, with the gradient-boosting model demonstrating optimal performance. The SHAP (SHapley Additive exPlanations) analysis framework was employed to enhance model interpretability and identify key biomarkers.

Results The gradient boosting model demonstrated excellent performance in CRKP detection, achieving an area under the curve (AUC) of 0.868 (95% CI: 0.812–0.924), with an accuracy of 81.4%, sensitivity of 79.3%, and specificity of 83.5%. SHAP analysis identified 15 key biomarkers, with the m/z 4518.00 Da feature exhibiting the highest importance (SHAP value: 1.2092). Key biomarkers primarily reside within the 4000–5000 Da range and correlate with known outer membrane pore proteins (OmpK35/OmpK36). This method reduces detection time to 15 minutes, significantly improving efficiency compared to conventional approaches (24–48 hours).

Conclusion The interpretable machine learning method established in this study not only enables rapid and accurate CRKP detection but also provides transparent decision-making rationale through SHAP analysis. The identified key biomarkers offer new insights into resistance mechanisms, supporting the translational application of MALDI-TOF technology in clinical drug resistance testing.

Neutrophil CD64 Index for Rapid Diagnosis of *Pneumocystis Jirovecii* Pneumonia in Malignancy Patients Requiring Mechanical Ventilation: A Retrospective Analysis

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Background *Pneumocystis jirovecii* pneumonia (PJP) incidence and associated mortality have risen significantly in non-HIV immunocompromised patients, highlighting the urgent need for rapid, non-invasive diagnostics. Current methods face limitations including

invasiveness, prolonged processing, or inadequate specificity. The neutrophil CD64 (nCD64) index emerges as a

promising novel biomarker. Here, we conducted this study to evaluate the diagnostic performance of nCD64 index for PJP and further assess the predictive value of its longitudinal changes for 28-day mortality.

Methods This retrospective cohort study (July 2022–March 2025) analyzed mechanically ventilated malignancy patients with unexplained diffuse pulmonary infiltrates at a tertiary intensive care unit (ICU). PJP diagnosis required predefined clinical, radiological, and bronchoalveolar lavage fluid metagenomic next-generation sequencing (BALF mNGS) criteria. The nCD64 index was measured via flow cytometry at ICU admission and serially after ≥ 3 days of antiPJP therapy. Diagnostic performance for PJP and prognostic value for 28-day mortality were assessed.

Results Among 28 PJP and 38 non-PJP patients, nCD64 index was significantly higher in PJP (13.33 vs. 2.84, $p < 0.001$). Receiver operating characteristic (ROC) curve analysis showed an area under the curve (AUC) of 0.846 (95% CI: 0.736–0.932) for PJP diagnosis, with sensitivity 89.3% and specificity 71.1% at cut-off ≥ 7 . Multivariate analysis confirmed nCD64 index as an independent PJP predictor (OR = 1.097, 95% CI: 1.026–1.173; $p = 0.007$). Post-therapy nCD64 index elevation predicted 28-day mortality with high sensitivity (81.8%) and specificity (86.7%).

Conclusion The nCD64 index functions as a dual-purpose biomarker for malignancy patients with respiratory failure requiring mechanical ventilation: it provides a rapid, non-invasive diagnostic tool for PJP and dynamically stratifies mortality risk. Moreover, dynamic tracking offers a real-time window into treatment response, guiding therapeutic decisions.

Magnetic SERS Nanozyme-Driven Trimodal Immunochromatography for Flexible, Accurate Detection of Gastrointestinal Infections

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直接探测粪便样本中的病原体对于确认胃肠道感染至关重要，但技术上依然具有挑战性。这里，我们报告了一个三峰态基于自组装磁性测定法（ICA）表面增强拉曼散射（SERS）纳米酶，使得通用的，高效磁富集目标细菌和病毒，并提供同时视觉（比色和催化放大的比色）以及超灵敏定量（SERS）读数显示在单一试纸上，因此能够快速且准确地检测粪便中的食源性病原体。多层 PtIr 的静电层层沉积将纳米颗粒和 40 nm Au 纳米星放置在 Fe₃O₄ 磁性核心上，显著增强了磁性过氧化物酶样活性 SERS 纳米酶并产生远超传统 SERS 标签，显著提升催化比色性能。该多模态 ICA 平台的放大和 SERS 检测灵敏度。该检测方法表现出极佳的分析性能：比色视觉 大肠杆菌（*E. coli*）O157 的检测极限（vLOD）诺如病毒（NoV）分别为 5×10^3 CFU/mL 和 0.05 ng/mL，且催化比色放大将这些限制降低 100 倍，差距为 2 倍。在 SERS 模式下，大肠杆菌 O157 和 NoV 的检测极限分别达到 8 CFU/mL 和 0.11 pg/mL。前往实现对病原体浓度的快速且准确的定量。我们建立了多维的自我优化浓度预测模型。特色融合神经网络。使用 116 份临床粪便样本进行验证。证明 MagTPI@AuNS-ICA 结合了便利性、快速性和准确性。结合 MDF-net 算法，ICA 平台实现了准确且快速的应用。样本中病原体浓度的预测，显示出极佳的一致性。采用 qPCR 检测。这些发现表明，这种三峰 ICA 具有一种可靠的，用户友好的现场食源性感染

快速检测平台 具有强大的临床转化潜力。

Single-Cell Raman Spectroscopy-Based Rapid Antifungal Susceptibility Testing of Clinically Prevalent and Rare Yeast Species: Validation Against The Sensititre YeastOne™ System

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Invasive fungal infections are associated with high mortality, and timely antifungal susceptibility testing (AST) is critical for guiding appropriate therapy. Conventional methods require 48 hours or more, creating an urgent need for rapid alternatives. In this study, we applied single-cell Raman spectroscopy (SCRS) combined with deuterium oxide (D₂O) metabolic labeling to perform rapid AST on seven clinically relevant yeast species, including *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida haemulonii*, *Cryptococcus neoformans*, *Saccharomyces cerevisiae*, and *Wickerhamomyces anomalus*, against four antifungal agents: fluconazole, voriconazole, micafungin, and amphotericin B. Minimum inhibitory concentrations (MICs) were determined by identifying the lowest drug concentration at which a statistically significant change in intracellular C–D signal intensity was observed relative to the drug-free control. Results were compared against those obtained using the Sensititre YeastOne™ reference system. SCRS-based MICs were within ± 1 concentration gradient of the reference MICs for all strain–drug combinations except one (*C. guilliermondii* against micafungin), with an overall categorical agreement of 96.8%. The total detection time was reduced

from 48 hours to 6–8 hours. Notably, distinct drug-class-specific metabolic signatures were identified: azoles consistently induced metabolic stimulation, whereas amphotericin B and micafungin produced metabolic suppression, reflecting their respective fungistatic and fungicidal mechanisms of action. These findings demonstrate that SCRS-based AST is a rapid and reliable approach for antifungal susceptibility determination across diverse yeast species, with potential for clinical translation.

Comparative Analysis of Influenza- and COVID-19-Associated Pulmonary Aspergillosis in Critically Ill Patients

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Objective Influenza-associated pulmonary aspergillosis (IAPA) and COVID-19-associated pulmonary aspergillosis (CAPA) are severe complications of viral pneumonia with high morbidity and mortality. This study aims to compare the demographic profiles, clinical characteristics, laboratory findings, radiological and bronchoscopic features, and outcomes of IAPA and CAPA in critically ill patients based on the latest international diagnostic criteria

Methods This retrospective single-center study enrolled 231 patients admitted to the ICU with influenza ($n = 91$) or COVID-19 ($n = 140$)-associated acute respiratory distress syndrome (ARDS) between March 2022 and June 2023. All patients underwent mycological testing of bronchoalveolar lavage fluid (BALF) or tracheal aspirates. IAPA and CAPA were defined according to expert consensus criteria (Verweij et al., 2020; Koehler et al., 2021). Demographic, clinical, laboratory,

radiological, and bronchoscopic data were collected and analyzed. Kaplan–Meier survival analysis was performed to assess 90-day mortality

Results A total of 101 patients (43.7%) met the criteria for pulmonary aspergillosis (IPA), including 35 IAPA (38.5%) and 66 CAPA (47.1%). CAPA patients were significantly older than IAPA patients (median age 71 vs. 63 years, $p = 0.003$). Chronic obstructive pulmonary disease was more prevalent in IAPA (31.4% vs. 9.1%, $p = 0.004$). Neutrophil counts and C-reactive protein levels were significantly higher in IAPA than CAPA ($p = 0.046$ and $p = 0.003$, respectively). CD4⁺ cell counts were lower in CAPA ($p = 0.019$). The median time from ICU admission to Aspergillus diagnosis was shorter in IAPA (3 days vs. 5 days, $p < 0.001$). Serum galactomannan (GM) positivity was higher in IAPA (71.4% vs. 39.4%, $p = 0.002$). Bronchial wall thickening and tree-in-bud signs were more frequent in IAPA on CT ($p < 0.001$ and $p = 0.039$). Bronchoscopy revealed more mucosal plaques in IAPA (40.0% vs. 12.1%, $p = 0.001$). Voriconazole trough concentrations were higher in CAPA ($p < 0.001$). Mortality was significantly higher in IPA patients than non-IPA patients ($p = 0.01$), but no difference was found between IAPA and CAPA

Conclusion IAPA and CAPA are associated with high mortality in critically ill patients. IAPA presents earlier, with more pronounced inflammatory responses and bronchoscopic abnormalities such as mucosal plaques. CAPA occurs in older patients and is associated with lower CD4⁺ counts and lower serum GM positivity. Enhanced awareness and early diagnostic strategies are essential to improve outcomes. Therapeutic drug monitoring is critical for optimizing antifungal therapy

Keywords COVID-19, influenza, pulmonary aspergillosis, CAPA, IAPA, bronchoscopy, voriconazole

皮肤炎患者多种诺卡菌合并蟾分枝杆菌混合性肺部感染 1 例

包丹妮

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目的 探讨免疫抑制状态下皮肤炎患者发生多重机会致病菌肺部感染的病原学动态演替特征，分析传统培养与靶向二代测序（tNGS）在复杂感染诊断中的互补价值。

方法 回顾性分析 1 例 72 岁皮肤炎男性患者的临床资料。患者在糖皮质激素联合他克莫司及托法替布长期免疫抑制治疗背景下出现肺部感染。通过连续痰培养、弱抗酸染色及基质辅助激光解吸电离飞行时间质谱（MALDI-TOF-MS）进行病原学鉴定，并结合多时点靶向二代测序（tNGS）及支气管肺泡灌洗液检测，对病原谱变化进行动态监测与综合分析。

结果 患者早期表现为肺部空洞性病变并伴曲霉 DNA 阳性，经验性抗真菌治疗无效。随后痰培养及 MALDI-TOF-MS 先后检出皮疽诺卡菌及非洲/新诺卡菌，首次 tNGS 仅检出皮疽诺卡菌序列，提示其对非洲/新诺卡菌覆盖不足。结合临床表现确诊诺卡菌肺部感染，经磺胺甲噁唑/甲氧苄啶联合亚胺培南及阿米卡星治疗后病情部分改善。随病程进展，影像学出现“部分吸收、部分进展”并伴新发病灶。进一步通过支气管肺泡灌洗液 tNGS 及分枝杆菌培养明确合并蟾分枝杆菌感染，其序列数由 1629 升至 36852。同时检出多重耐药鲍曼不动杆菌及耐药基因（blaOXA-23、sul1），提示继发感染及病原谱演替。在调整抗感染方案并优化免疫抑制治疗后，患者临床症状及影像学表现逐步改善。

结论 免疫抑制宿主肺部感染呈现明显的多病原动态演替特征，单一时间点检测难以全面反映感染状态。传统培养在病原确证及药敏分析中仍具关键作用，而 tNGS 在多病原检测及动态监测方面具有重要优势，但受探针覆盖及检测灵敏度等因素限制。二者联合应用可显著提高复杂感染的诊断准确

性，并为抗感染治疗策略的动态调整提供依据。

关键词： 皮肤炎；皮疽诺卡菌；非洲/新诺卡菌；蟾分枝杆菌；肺部感染；靶向二代测序

Comprehensive Performance Evaluation of A High-throughput Automated System for Pathogen Nucleic Acid Detection in Clinical Settings

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Objective This study evaluates the clinical performance of a high-throughput automated molecular detection system and proposes a comprehensive and standardized performance validation framework to address gaps in existing methodologies and provide a robust reference for future evaluations.

Methods Performance was validated for EBV DNA, HCMV DNA, and RSV RNA using clinical samples at various concentrations, along with WHO and national reference standards. The validation included concordance rate, accuracy, linearity, precision, limit of detection, interference testing, cross-reactivity, and carryover contamination.

Results The positive, negative, and overall concordance rates for EBV DNA, HCMV DNA, and RSV RNA were all 100%. Both intra-assay and inter-assay precision showed coefficients of variation (CV) below 5%. The linear correlation coefficient ($|r|$) for EBV DNA and HCMV DNA was ≥ 0.98 , demonstrating excellent linearity. The limits of detection (LoD) were 10 IU/mL for EBV DNA and HCMV DNA, and 200 copies/mL for RSV RNA. Both interference and cross-reactivity assessments met the CLSI EP07 standards, and no carryover contamination was observed.

Conclusion The system demonstrated excellent performance in terms of concordance, accuracy, precision, linearity, interference testing, and cross-reactivity. It is highly suited for large-scale pathogen screening and routine nucleic acid testing in clinical laboratories, both for qualitative and quantitative analyses. Additionally, this study introduces a comprehensive and standardized performance validation framework that addresses critical gaps in existing methodologies, offering a robust foundation for the rigorous evaluation of diagnostic systems and serving as a valuable reference for future research.

基于化学合成烟曲霉菌特异性糖表位的检测体系构建及临床应用研究

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烟曲霉 (*Aspergillus fumigatus*, AF) 是侵袭性曲霉病 (Invasive aspergillosis, IA) 的主要致病菌。然而现有诊断手段常在早期敏感性不足且多为属水平筛查, 难以实现既能早期发现又能达到种水平精准鉴别的检测。烟曲霉分泌的半乳甘露聚糖 (Galactomannan, GM) 是最早进入血液的抗原, 其半乳呋喃糖侧链在数量、分布和连接方式上的差异, 构成了烟曲霉相较于其他曲霉属的种特异性结构基础。

基于此, 本研究提出以烟曲霉 GM 寡糖的结构差异作为种特异性抗原表位, 通过精准化学合成结合单克隆抗体开发, 构建 GM/IgG/IgM 双通道抗原—抗体检测体系, 期望实现烟曲霉的早期且种水平的精准诊断。研究通过化学合成得到一系列不同构型的 GM 寡糖, 筛选优势表位并制备高特异性单克隆抗体, 建立抗原捕获与抗体分型联合检测方法, 并在临床样本中评估其诊断效能。

初步结果显示, 本研究成功合成了七种不同聚合度与连接方式的烟曲霉寡糖 (MGF-1 至 MGF-7), 并对其特异性结合能力及诱导巨噬细胞活化的潜能进行了检测。

结果表明, 七糖片段 MGF-5 和 MGF-6 不仅与商业化抗体表现出强结合力, 还能有效激活巨噬细胞, 增强其增殖与吞噬功能。这些发现支持 GM 寡糖作为种特异性抗原表位的可行性, 并为构建高灵敏、高特异的烟曲霉早期诊断方案提供了实验依据, 为临床精准诊断与治疗奠定了技术基础。

关键词: 烟曲霉菌, 寡糖片段, 化学合成, 抗原表位, 检测体系

Diagnostic Value of Plasma Cell-free DNA Metagenomic Next-generation Sequencing in Patients with Suspected Infections and Exploration of Clinical Scenarios—A Retrospective Study From A Single Center

null null

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Background Plasma cell-free DNA metagenomic next-generation sequencing (mNGS) has been applied as a non-invasive comprehensive method for the etiological diagnosis of various infectious diseases. However, research on the early diagnosis and real-world clinical impact of plasma mNGS in patients with suspected infection are still limited

Methods This study retrospectively included 140 patients with suspected infections who underwent early plasma mNGS and conventional culture testing. Referring to the clinical diagnosis of infectious diseases, the diagnostic performance of plasma mNGS and culture tests was compared, and the application scenarios and clinical effects of plasma mNGS were evaluated.

Results In our study, the positive rate of plasma mNGS was significantly higher than that of culture methods (55.71% vs 25.10%, $P < 0.001$) and blood cultures (55.71% vs 12.86%, $P < 0.001$). From the perspective of clinical diagnosis of infectious diseases, the sensitivity of plasma mNGS was significantly higher than that of culture (58.27% vs 37.80%, $P = 0.002$). When mNGS was combined with culture, it has higher detection sensitivity (69.29%), especially in patients with multi-site co-infections (73.68%) and patients with blood infections (73.17%). Plasma mNGS was more sensitive in detecting pathogens in patients with suspected infection when the procalcitonin (PCT) index > 5 ng/ml or the human neutrophil lipocalin (HNL) index > 200 ng/ml. In terms of treatment, a total of 69 patients (54.33%) benefited from plasma mNGS.

Conclusion Our study highlights the significant improvement in pathogen detection performance by combining conventional culture with plasma mNGS detection, especially in patients with multi-site co-infections and blood infections. Early use of plasma mNGS as an adjunct to culture can better guide clinicians to initiate appropriate anti-infective therapy.

感染性心内膜炎早期诊断与治疗的血浆与赘生物蛋白质组学研究

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目的 本研究旨在解析感染性心内膜炎 (Infective Endocarditis, IE) 患者的蛋白质组学特征, 构建基于血浆蛋白数据的机器学习模型, 用于高效区分 IE 与非 IE 个体, 发现潜在生物标志物, 服务于临床诊断与治疗。

方法 本研究纳入 2020 年 8 月至 2023 年 5 月

在广东省人民医院住院的心脏瓣膜病患者, 依据欧洲指南手术指征, 设立发现集 (238 例 IE、100 例非 IE) 和验证集 (各 92 例)。通过 LC-MS/MS 技术对血浆与赘生物样本进行非靶向蛋白质组学分析, 结合 Firmiana 平台、FragPipe 和 DIA-NN 完成肽段识别与定量。借助 XGBoost 进行机器学习建模, 结合 WGCNA、通路富集和单样本基因集富集分析, 辅以 ELISA 与免疫荧光等手段验证。

结果 共鉴定出 9,524 种血浆蛋白和 10,625 种赘生物蛋白, 筛选后分别纳入 2,314 种和 3,694 种用于分析。研究发现, NYHA IV 级患者中多种肝源蛋白 (如 APOA1、C4A、SERPINA6) 显著下调。结合蛋白组和血液指标构建的机器学习模型预测 NYHA IV 级的 AUC 达 0.85, 优于传统模型。即使缺乏病原学证据, 蛋白质组特征仍可反映感染严重程度。LRG1 在 IE 患者中显著上调, 与中性粒细胞胞外诱捕网 (NETs) 形成通路密切相关, 术后下调的 NDUF4 则可能为新型预后标志物。

结论 本研究基于系统蛋白质组学分析, 识别出与 IE 密切相关的差异蛋白和潜在生物标志物, 构建了准确高效的诊断模型, 为 IE 的早期识别和精准治疗提供了新思路与技术支撑。

Single-Cell and Transcriptomic Analysis Reveals Molecular Mechanisms Associated with Tuberculosis

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Objective This study aimed to explore the molecular mechanisms of tuberculosis (TB) by integrating single-cell RNA sequencing (scRNA-seq) and transcriptome analyses, identifying key immune response genes and regulatory networks, and developing diagnostic models and therapeutic insights

Methods A total of 198 blood samples were included: 83 TB patients, 51 individuals with latent TB infection (LTBI), and 64 healthy controls (HC). Seven scRNA-seq datasets and five GEO transcriptomic datasets were retrieved from NCBI BioProject and GEO. After quality control, cell clustering and annotation were performed using Seurat, and differentially expressed genes (DEGs) were identified via the Wilcoxon test. Cell-cell communication was analyzed by CellChat, while bulk RNA-seq DEGs were analyzed with the Limma package. A Lasso regression model was constructed to assess diagnostic performance, immune cell infiltration was analyzed, and potential drug targets were identified via DGIdb

Results Seventeen cell clusters were identified, including T cells, NK cells, monocytes, B cells, and platelets. Ten key genes were found to be differentially expressed between groups. CellChat revealed monocytes as central players in the TB immune response. A Lasso model distinguishing TB from LTBI achieved an AUC of 0.8889 in the validation set, indicating strong diagnostic potential. Immune profiling showed elevated neutrophil and monocyte levels and reduced T and B cells in TB, indicating immune imbalance. Genes such as LTBR and MMP9 were positively correlated with neutrophils, while NFATC1 and SRPRB correlated with T cells. Moreover, NFATC1 and TLR2 were significantly associated with known TB-related genes IFNGR1 and SLC11A1, suggesting regulatory involvement in disease progression. DGIdb identified five candidate therapeutic agents targeting these key genes

Conclusion This integrative analysis uncovered key immune cell subsets and molecular markers involved in TB pathogenesis, established a robust diagnostic model, and identified promising therapeutic targets, providing novel insights for TB diagnosis and treatment

感染性心内膜炎的分子早期诊断：探针捕获宏基因组测序新策略

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目的 感染性心内膜炎 (Infective Endocarditis, IE) 是一种临床死亡率和致残率均较高的严重感染性疾病,其早期诊断困难,部分病例因血培养阴性、抗生素预处理及特殊病原体存在而延误诊疗,导致预后不良。本研究旨在建立并评估一种基于探针捕获的宏基因组测序 (Probe-Capture Metagenomic Next-Generation Sequencing, PC-mNGS) 新策略,用于 IE 病原体的早期分子诊断,并探索耐药基因、毒力因子及潜在分子标志物,为临床精准用药与个体化治疗提供新思路。

方法 本研究纳入 2020 年 8 月至 2023 年 5 月在广东省人民医院住院的心脏瓣膜病患者,前瞻性入组疑似或确诊 IE 患者,并设置非感染性心脏病及健康人群对照。采集多类型样本 (外周血、血浆 cfDNA、术中瓣膜组织),经宿主序列去除及核酸建库后,应用定制化探针面板进行靶向捕获,涵盖常见及罕见病原体、耐药基因与毒力因子。随后进行高通量测序,并采用多步骤生物信息学流程进行质控、病原鉴定、丰度定量及背景污染判别。结合临床资料、改良 Duke 标准及影像学检查,评价诊断性能。

结果 初步显示,PC-mNGS 在病原检出率、灵敏度及特异度方面均优于传统血培养,尤其在血培养阴性和接受抗生素预处理的患者中表现突出。该方法不仅可快速获得病原体全谱,还能同时识别多重耐药基因 (如 *mecA*、*vanA*、ESBL 相关基因) 及毒力因子,从而揭示病原体的耐药机制与致病潜能。通过临床多维度整合,PC-mNGS 诊断结果与患者临床表现高度一致,在部分复杂或混合感染病例中提供了关键的病原学证据。进一步分析提示,该策略有望筛选出若干与 IE 相关的潜在分子标志物,为早

期诊断和疗效监测奠定基础。

结论 探针捕获宏基因组测序技术在感染性心内膜炎早期分子诊断中具有显著优势,能够弥补血培养阴性及低丰度感染病原检测的不足,提供病原体谱、耐药基因及毒力因子等多维度信息。该方法可在临床实践中为个体化抗感染治疗提供循证支持,提升早期诊断效率,改善患者预后,并为未来建立 IE 分子标志物数据库与临床决策支持系统提供可能。综上,本研究验证了 PC-mNGS 在 IE 早期诊断中的应用前景,具有重要的科学意义和临床转化价值。

Biomimetic Magnetic Virus-like Nanozyme-mediated Lateral Flow Immunoassay for Direct and Accurate Detection of Gastrointestinal Pathogens

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Rapid, direct, and highly sensitive detection of gastrointestinal pathogenic bacteria in real-world samples, continues to pose an unresolved challenge. Here, we propose an ultrasensitive and multiplex lateral flow immunoassay (LFA) capable of simultaneously identifying three gastrointestinal pathogens including *Helicobacter pylori*, *Salmonella typhimurium*, and *Escherichia coli* O157:H7, based on a "magnetic capture-catalytic enhancement" detection strategy. A magnetic virus-like nanozyme (Fe-Pt20-Au@Pt5) is biomimetically designed based on the structure of the coronavirus spike protein, by systematically assembling a layer of 20 nm urchin-like Pt nanoparticles (NPs) and a layer of 5 nm Au@Pt satellites onto 160 nm Fe₃O₄ particle, in which

Fe₃O₄ provides magnetic enrichment capability and peroxidase-like activity, while Pt and Au@Pt NPs work synergistically to enhance the colorimetric/catalytic activity of the nanozyme. The introduction of Fe-Pt20-Au@Pt5 into the LFA enables a triple signal amplification effect of "magnetic enrichment, synergistic enhancement, and multiple catalytic sites", thereby improving the sensitivity of detecting the three target pathogens to 4–9 CFU/mL, which is 1111–2500 times more sensitive than traditional AuNP-based LFA for bacterial detection. Furthermore, the proposed technique was validated for its on-site and clinical application potential by detecting 139 clinical stool samples, showcasing the significant potential of Fe-Pt20-Au@Pt5-LFA in real-time pathogen diagnostics.

肉汤纸片洗脱法 MIC₉₀特征与头孢他啶/阿维巴坦耐药肺炎克雷伯菌碳青霉烯酶类型及替代方案杀菌活性的相关性研究

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目的 评估肉汤纸片洗脱法 (BDE) 对头孢他啶/阿维巴坦 (CZA) 耐药肺炎克雷伯菌 (CRKP) 的耐药表型预测价值,探讨 BDE MIC₉₀特征与碳青霉烯酶类型、替代方案体外杀菌活性之间的相关性。

方法 收集 6 株 CZA 耐药 CRKP 临床菌株,采用二代基因组测序进行碳青霉烯酶基因分型。以微量肉汤稀释 (BMD) 法为标准,比较纸片扩散法 (K-B 法)、E-test 法和 BDE 法检测结果;采用液相色谱-串联质谱法 (LC-MS/MS) 验证 BDE 工作液中 CZA 实际浓度;以 BDE MIC₉₀为基础,设计时间-杀菌曲线实验,评估 CZA、氨曲南/阿维巴坦 (AZA) 及亚胺培南/瑞来巴坦 (IMR) 的杀菌活性。

结果 6 株菌株均经 BMD 确认为 CZA 耐药

(MIC 16/4~>256/4 $\mu\text{g/mL}$), 碳青霉烯酶基因型包括 KPC-2 (4 株)、KPC-6 (1 株) 及 NDM-4 合并 OXA-181 (1 株)。K-B 法与 BMD 一致; BDE 法则呈现出三种 MIC₉₀特征, 与碳青霉烯酶表型高度对应: ①MIC₉₀=6/4 $\mu\text{g/mL}$ (低 BMD MIC KPC-2 菌株), ②MIC₉₀=12/4 $\mu\text{g/mL}$ CLSI 折点间隙(高 BMD MIC KPC-2 及 KPC-6 菌株), ③MIC₉₀超出检测范围(NDM-4+OXA-181 菌株)。时间-杀菌曲线证实 BDE MIC₉₀模式与杀菌活性存在明确对应关系: ①菌株在 CZA 6/4 $\mu\text{g/mL}$ 下 24 h 维持持续杀菌活性; ②菌株中, CZA 8/4 $\mu\text{g/mL}$ 对 KPC-2 高 MIC 菌株完全无效, AZA 联合 IMR 实现协同杀菌; 对 KPC-6 菌株出现早期杀菌后 24 h 耐药反弹, 而 AZA 6/4 $\mu\text{g/mL}$ 维持持续杀菌; ③菌株对 CZA 完全无效, AZA 6/4 $\mu\text{g/mL}$ 可达完全杀菌。

结论 对于免疫功能低下患者, 维持持续杀菌活性具有重要临床意义, BDE MIC₉₀模式结合时间-杀菌曲线可为 CZA 耐药 CRKP 的个体化治疗决策提供实验室支持。

关键词: 肺炎克雷伯菌; 碳青霉烯耐药; 头孢他啶/阿维巴坦; 肉汤纸片洗脱法; 亚胺培南/瑞来巴坦; 氨曲南/阿维巴坦

靶向高通量测序在不明原因肺部感染患者中的诊断价值

侯素君

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目的 探讨靶向高通量测序(targeted next-generation sequencing, tNGS)技术在不明原因肺部感染患者支气管肺泡灌洗液(bronchoalveolar lavage fluid, BALF)中的病原学诊断价值, 以提高临床对该类患者的诊断和治疗水平。

方法 选取山东中医药大学附属日照市中医医院 2023 年 12 月-2024 年 12 月肺病科经初始经验性

抗感染治疗效果不佳的 448 例不明原因肺部感染患者, 进行回顾性分析。采集患者支气管肺泡灌洗液, 分别进行 tNGS 检测与传统病原学检测(包括灌洗液细菌培养、真菌培养、真菌涂片、抗酸杆菌涂片)。

结果 tNGS 检测阳性率为 99.11%, 高于传统病原学检测总阳性率 44.42%, 差异有统计学意义($P<0.001$)。检出细菌主要为铜绿假单胞菌、流感嗜血杆菌; 病毒主要为 EB 病毒、单纯疱疹病毒; 真菌主要为烟曲霉、白色念珠菌; 其他病原体包括分枝杆菌、诺卡菌、肺炎支原体。tNGS 检测细菌、分枝杆菌、病毒、肺炎支原体、诺卡菌的阳性率(35.93%、14.51%、45.76%、21.65%、1.56%), 均高于传统病原学检测的阳性率(21.43%、2.68%、0.00%、0.00%、0.22%), 差异有统计学意义(均 $P<0.05$)。此外, 相较于以单一感染为主的传统病原学检测, tNGS 对混合感染的检出率更具优势, 差异有统计学意义($P<0.001$)。

结论 tNGS 检测在不明原因肺部感染病原体阳性率、病原体种类检出率、不同感染类型检出率及混合感染检出率均优于传统病原学检测, 可作为传统检测的有效补充方法, 帮助临床医生早期识别病原体, 实施精准诊疗, 提升治疗效果。

关键词 tNGS; 肺部感染; 传统病原学检测; 病原体; 支气管肺泡灌洗液

血液透析患者灌洗液中分离吉拉迪贪铜菌的鉴定及耐药性分析

张建明 林玉玲 陈清

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目的 对血液透析患者灌洗液中分离的吉拉迪贪铜菌(*Cupriavidus gilardii*)进行鉴定及耐药性分析, 以为临床吉拉迪贪铜菌感染相关疾病的检测、鉴别、诊断和治疗提供参考。

方法 对灌洗液标本行革兰染色, 对分离菌株

依次行生化鉴定、质谱鉴定、16S rRNA 基因测序与药敏试验。

结果 吉拉迪贪铜菌在血平板上菌落为透明凸起、边缘规则、表面光滑、中等大小菌落；革兰氏染色可见短小革兰氏阴性杆菌；生化鉴定：氧化酶和过氧化氢酶呈阳性，脲酶阴性，不发酵葡萄糖和乳糖，不能还原硝酸盐，动力试验阳性；质谱鉴定为吉拉迪贪铜菌，分值达 2.35，并具有典型的质谱峰形态；16s rRNA 测序结果 BLAST 分析，与吉拉迪贪铜菌的同源性最高，达到 99%以上；药敏试验结果显示，分离菌株对氨苄西林、头孢唑林呈高水平的 MIC 值，同时对庆大霉素、哌拉西林/他唑巴坦、美罗培南和亚胺培南等耐药，对氨苄西林/舒巴坦、替加环素的 MIC 值低（分别为 $\leq 2/1 \mu\text{g/mL}$ 、 $\leq 0.5 \mu\text{g/mL}$ ），对头孢曲松、头孢吡肟、左氧氟沙星、头孢派酮/舒巴坦和复方磺胺等抗菌药物敏感，在治疗时可优先考虑选用。

结论 吉拉迪贪铜菌具有致病风险，免疫力低下患者感染居多，在临床诊疗过程中，应密切关注吉拉迪贪铜菌感染的发生，并根据药敏试验结果选择合适的抗生素进行治疗。

Small But Significant: Deciphering The Virulence and Pathogenesis of *Lancefieldella Parvula*

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Lancefieldella parvula (formerly known as *Atopobium parvulum*) is an opportunistic oral and intestinal anaerobe. Ectopic colonization via the mouth-to-intestine axis allows this bacterium to control the central hub of hydrogen sulfide (H_2S) producers, driving chronic inflammation and mucosal degradation. Crucially, *L. parvula* is linked to colorectal cancer (CRC) progression,

exhibiting an "early enrichment, late decline" dynamic that makes it a promising early biomarker. It also demonstrates synergistic pathogenicity in gynecological tumors and severe systemic infections. Given the clinical challenges of its fastidious growth and frequent misdiagnosis, this article reviews the taxonomic evolution, genomic traits, and pathogenic mechanisms of *L. parvula*, aiming to provide a foundational reference to promote precise clinical diagnosis, infection control, and early tumor screening.

Keywords *Lancefieldella parvula*, Colorectal cancer, Hydrogen sulfide, Taxonomy, Infection

宏基因组二代测序诊断惠普尔养障体致罕见重症肺炎 1 例病例报道

陈平

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目的 惠普尔养障体致罕见重症肺炎，其病情凶险，死亡率高且临床特征不典型。传统检测方法耗时且阳性率低，不易为临床提供及时有效的病原学依据，导致该病误诊率、漏诊率极高。目前，惠普尔养障体的早期诊断与精准治疗面临巨大挑战，近年随着检验技术的不断发展，尤其是宏基因组二代测序（mNGS）技术的蓬勃发展，可检测到传统检测方法无法检测到的罕见病原体，为惠普尔养障体致罕见重症肺炎的诊断提供了新思路。本文报道 1 例通过肺泡灌洗液 mNGS 成功确诊为惠普尔养障体致罕见重症肺炎的病例，其病情复杂、治疗过程曲折，以期该类患者诊治疗提供参考。

方法 患者，女，62 岁，体重 60 kg。因“呼吸困难、畏寒、发热 5 d”于 2025-02-10 就诊于我院，考虑肺部感染。第 1 天给予哌拉西林他唑巴坦抗感染但患者病情快速持续进展，第 2 天加用左氧氟沙星加强抗感染，并外送肺泡灌洗液 mNGS，第 3 天

mNGS 检出惠普尔养障体。综合患者既往健康状况（长期卧床、营养不良且贫血）以及临床症状，最终确诊为重症肺炎（惠普尔养障体感染），鉴于惠普尔养障体感染尚无标准治疗方案，且患者病情危重，最终决定采用头孢曲松联合复方磺胺甲噁唑 2 药加强抗感染，并实施全程治疗药物监测与不良反应预警管理。患者出院继续口服复方磺胺甲噁唑抗感染 12 个月。

结果 经头孢曲松联合复方磺胺甲噁唑 2 药加强抗感染 3 天后，患者临床症状显著改善（体温恢复正常，呼吸平稳），炎症值明显好转。持续强化抗感染治疗 11 天后，肺部感染得到有效控制，未发生药物相关不良反应，病情稳定予以出院。院外继续口服复方磺胺甲噁唑抗感染 12 个月，定期门诊随访，病情稳定无相关药物不良反应。

结论 惠普尔养障体引起的重症肺炎临床罕见，该病发病隐匿、临床表现缺乏特异性、病死率高，传统检测方法获得病原体耗时长且阳性率低，极易导致漏诊、误诊。早期快速诊断、选择合理抗生素可明显改善患者病情，减轻其医疗负担。mNGS 使惠普尔养障体致罕见重症肺炎的诊断率不断提高，这对患者早期诊治具有重要意义。因此，对于病情危重且病原学诊断不明的重症感染患者，在条件允许的情况下可考虑采用 mNGS 技术辅助诊断，并根据检测结果结合临床实际，制定个体化的抗感染治疗方案，以提高重症感染患者的救治率。

关键词：惠普尔养障体；重症肺部感染；宏基因组二代测序；个体化治疗

见微知著——一张涂片报告引发的思考

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这份临床案例报告通过一例右下肢外伤后严重感染的诊疗过程，系统展示了从病原学诊断到精准

治疗的完整链条，对复杂感染诊疗具有多重启示价值：

一、诊疗难点与突破

1.混合感染复杂性：

初始培养仅检出粘质沙雷菌（CRE 耐药株），但替加环素治疗无效，提示存在其他病原体

通过 NGS 技术发现厌氧菌（脆弱拟杆菌/大芬戈尔德菌），揭示多重微生物感染本质

2. 检测技术协同：

传统培养（需 48 小时）与快速 NGS（24 小时）互补

革兰染色发现"消失的革兰阳性杆菌"提示厌氧菌可能

质谱鉴定最终锁定产气荚膜梭菌

二、关键诊疗策略

1.抗感染方案优化：

四联方案：替加环素+亚胺培南+克林霉素+奥硝唑（覆盖需氧/厌氧菌及毒素抑制）

克林霉素的核心作用：抑制细菌蛋白合成，阻断毒素产生

2.外科干预时机：

6 次清创手术+VSD 负压引流

首次清创后 24 小时内即行筋膜切开减压术

三、临床启示

1.诊断维度：

对创伤后进展性感染需保持"三重怀疑"：

耐药菌（如 CRE）

厌氧菌（尤其产气荚膜梭菌）

混合感染生物膜形成

2.技术应用：

NGS 的局限：本例中未检出产气荚膜梭菌（因 tNGS 对 DNA 提取偏好性）

传统培养不可替代：厌氧培养 48 小时发现特征性双层溶血环

3.多学科协作：

微生物室-重症医学科-骨科的高频沟通机制

"涂片-NGS-培养"三重验证体系

四、核心经验

创伤后气性坏疽的"红色警报":

皮下捻发音+气泡溢出+快速进展性坏死

PCT 大幅升高, 伴凝血指标, 心肌损失标志物异常

2. 厌氧菌检测规范:

标本转运需<30 分钟

厌氧平板+厌氧袋培养

该案例印证了《临床微生物学手册》的核心观点: 对严重软组织感染, 微生物学证据需与临床表现实时互证, 任何技术都有其局限, 专业敏感度、责任心和临床判断力始终是诊疗决策的基石。

Rapid Molecular Identification of The Emerging Dermatophyte *Trichophyton indotineae* Via The Genomic Novel Marker

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Objective To develop and validate a practical molecular approach for specific identification of *Trichophyton indotineae*, an emerging dermatophyte associated with extensive inflammatory tinea and frequent terbinafine resistance, and to provide a useful tool for routine laboratory recognition, surveillance, and downstream resistance work-up

Methods Public ITS sequences in GenBank annotated as *Trichophyton mentagrophytes*, *T. interdigitale*, or *T. indotineae* were retrieved up to March 10, 2026, manually re-curated, and analysed within a shared 540 bp ITS region to assess the sequence-supported public distribution of *T. indotineae*. In parallel, 21 *Trichophyton* genomes were analysed by comparative genomics to identify lineage-specific single-copy targets. OG7443 was selected as the optimal marker, and two assays were developed: a duplex end-point PCR and a TaqMan real-time PCR. The duplex PCR was validated on 162 ITS-confirmed culture isolates from two centres,

and the TaqMan assay was validated on 213 samples from three centres, including 168 culture isolates and 45 direct skin-scraping specimens. Analytical sensitivity and per-sample consumable costs were also assessed

Results A total of 5,584 ITS records were retrieved, of which 4,744 were retained after re-curation. The exact type-associated haplotype H002 comprised 1,576 records, whereas a broader type-strain-anchored *T. indotineae* cluster included 1,698 records across 75 related haplotypes. India and Iran contributed the largest numbers of country-resolved records. Comparative genomic screening identified OG7443 as a *T. indotineae*-specific single-copy gene suitable for assay design. In the two-centre validation set, duplex PCR correctly identified all 58 *T. indotineae* isolates and all 104 non-*T. indotineae* isolates, yielding 100.0% sensitivity and 100.0% specificity. In the three-centre validation set, the TaqMan assay correctly identified all 53 positive and 160 negative samples, also yielding 100.0% sensitivity and 100.0% specificity. The analytical limit of detection was 7 copies/ μ L. Estimated consumable costs were approximately US\$0.39 per sample for duplex end-point PCR and US\$4.24 per sample for TaqMan real-time PCR

Conclusion OG7443 is a novel and reliable species-specific single-copy marker for *T. indotineae*. The duplex end-point PCR and TaqMan real-time PCR assays developed in this study showed excellent diagnostic performance in multicentre validation and can be deployed across different laboratory settings. The low-cost duplex PCR is especially suitable for resource-limited laboratories, whereas the TaqMan assay provides a higher-throughput option. These assays offer practical tools for routine identification, surveillance, and triage of specimens for subsequent antifungal resistance testing

Keywords *Trichophyton indotineae*; dermatophyte; OG7443; duplex PCR; TaqMan real-time PCR;

molecular diagnosis

全球首例 ST859 型副溶血弧菌致暴发性肢体坏疽：基于完整基因组的侵袭机制解析与救治复盘

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背景 副溶血弧菌 (*V. parahaemolyticus*) 通常被定义为自限性食源性病原体, 极少诱发深部组织侵袭性感染。但在特定易感宿主体内, 其致病表型可能发生从肠道定殖向暴发性坏死性筋膜炎 (NF) 的极端转换。本研究旨在通过完整基因组测序 (WGS) 解析罕见序列分型 ST859 的遗传特征, 并阐明其潜在的侵袭性机制。

方法 回顾性分析一例肝硬化患者感染副溶血弧菌后出现下肢暴发性 NF, 并迅速进展为难治性脓毒性休克及多器官功能障碍综合征 (MODS) 的救治过程。采集深部坏死组织行多重病原体靶向测序 (tNGS) 及传统培养; 利用 WGS 技术对分离株进行全基因组组装, 系统解析毒力基因簇 (VFDB)、分泌组规模、基因岛 (GIs) 及可移动遗传元件特征。

结果 1. 临床演进: 患者起病 16 h 内即进展为暴发性下肢坏疽, 合并难治性脓毒性休克 (大剂量血管活性药物依赖) 及多器官功能障碍综合征 (MODS), SOFA 评分峰值达 15 分, 肌红蛋白升至 10,728 ng/mL。医疗团队在病原学证据空窗期, 早期实施切开减压扩创, 并在后期精准识别了哌拉西林他唑巴坦诱导的免疫性血小板减少症 (DITP), 最终患者康复出院。

2. 基因组图谱: 分离株鉴定为罕见分型 ST859, 由双染色体及一个 118 kb 独立质粒组成。全基因组识别出 11 个基因岛, 且质粒插入序列 (IS) 元件密度显著高于染色体, 提示极高的遗传可塑性。菌株缺失肠道致病相关的 T3SS2, 但携带完整 T3SS1 毒

力簇及其效应子储备。

3. 侵袭机制：该菌株预测分泌蛋白占比高达15.19%。识别出编码钠驱动鞭毛马达的核心基因motX，提示其具备在组织水肿间隙极速渗透的生物物理基础。效应蛋白 VopQ/S 及 VPA0450 的协同作用介导了剧烈的细胞骨架瓦解与溶酶体稳态崩溃，从分子水平阐明了暴发性组织液化坏死的病理表型。

结论 本研究首次报道了由 ST859 型副溶血弧菌引发的致死性侵袭感染。该菌株凭借 motX 相关鞭毛系统驱动的高速扩散，以及 T3SS1 效应组的强细胞毒性，在肝硬化宿主中表现出类创伤弧菌的侵袭表型。这一发现挑战了临床对于海洋弧菌感染的经验性定势。在应对易感人群中出现的暴发性软组织感染时，应建立“临床表型权重优先于分类标签认知”的决策思维，通过早期分子诊断与前置外科干预，挽救患者生命。

关键词：副溶血弧菌；坏死性筋膜炎；完整基因组测序；ST859；III 型分泌系统；重症救治

宏基因组二代测序诊断小孢根霉致罕见脑脓肿 1 例病例报道

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目的 小孢根霉致罕见脑脓肿，其病情凶险，死亡率高且临床特征不典型。传统检测方法耗时长且阳性率低，不易为临床提供及时有效的病原学依据，导致该病误诊率、漏诊率极高。目前，小孢根霉感染的早期诊断与精准治疗面临巨大挑战，近年来随着检验技术的不断发展，尤其是宏基因组二代测序（mNGS）技术的蓬勃发展，可检测到传统检测方法无法检测到的罕见病原体，为小孢根霉致罕见脑脓肿的诊断提供了新思路。本文报道 1 例通过脑脊液 mNGS 成功确诊为小孢根霉致罕见脑脓肿的病例，其病情复杂、治疗过程曲折，以期该类患者诊治

疗提供参考。

方法 患者，男，55 岁，体重 45 kg，因“头晕、吐词不清 3 天”就诊于我院。入院第 2 天，患者出现高热，最高体温 39.2℃，脑积液常规+生化提示感染，头部 MRI 提示感染并脓肿形成？临床初步考虑颅内感染；脑脓肿？立即经验性的给予美罗培南联合万古霉素抗感染。入院第 4 天患者仍反复高热，最高体温可达 39.8℃，血培养、脑脊液培养均为阴性，考虑患者病情快速持续进展，于当日外送脑脊液 mNGS。第 5 天脑脊液 mNGS 检出小孢根霉。考虑患者（55 岁建筑工人常接触粉尘、泥土），患糖尿病 3 年未规律服用降糖药，存在感染小孢根霉的高风险因素，临床修订诊断为：脑脓肿（小孢根霉感染），立即改用注射用两性霉素 B、艾沙康唑 2 药联合抗真菌治疗并联合手术治疗。

结果 注射用两性霉素 B、硫酸艾沙康唑胶囊 2 药联合加强抗感染 30 天后，患者临床症状明显改善、脑脊液检查结果明显好转，颅内感染得到有效控制。继续持续抗感染 5 天后，患者病情平稳予以出院。出院后序贯口服硫酸艾沙康唑胶囊 11 月，持续门诊随访，病情稳定，未出现药物相关不良反应，患者对抗感染治疗结果表示满意。

结论 小孢根霉感染引起的脑脓肿临床罕见，该病发病隐匿、临床表现缺乏特异性、病死率高，传统检测方法获得病原体耗时长且阳性率低，极易导致漏诊、误诊。早期快速诊断、选择合理抗真菌药物可明显改善患者预后。mNGS 使小孢根霉致罕见脑脓肿的诊断率不断提高，这对患者早期诊治具有重要意义。因此，对于病情危重且病原学诊断不明的重症感染患者，在条件允许的情况下可考虑采用 mNGS 技术辅助诊断，并根据检测结果结合临床实际，制定个体化的抗感染治疗方案，以提高重症感染患者的救治率。

关键词：小孢根霉；脑脓肿；宏基因组二代测序；个体化抗感染

Optimizing Mycobacterial Diagnostics: Impact of Laboratory Process Optimization on Clinical Outcomes and Turnaround Time

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Objectives To evaluate the impact of an optimized laboratory workflow on diagnostic turnaround times, diagnostic performance, and clinical outcomes for mycobacterial infections

Methods We optimized the Mycobacterium diagnostic pathway at Peking Union Medical College Hospital by introducing centrifugation after biological inactivation of MGIT960-positive cultures. A comparative analysis of 66 pre-optimization (Jan-Apr 2024) and 90 post-optimization cases (May-Aug 2024) was performed using clinical, microbiological, and operational data from medical records.

Results The optimized workflow produced a cascading effect on efficiency. The initial acid-fast bacilli (AFB) smear positivity rate from MGIT960-positive cultures significantly increased from 42.42% to 93.33% ($P < 0.0001$), which was independently associated with the intervention ($OR = 22.64$, $P < 0.0001$). This led to substantial turnaround times reductions: the interval from MGIT positivity to final report decreased by 5.71 days, and the total processing time from specimen accession to final report shortened by 8.91 days (both $P < 0.0001$). Consequently, the median time to clinical follow-up was reduced by 26.7 days ($P = 0.032$) in the optimized cohort.

Conclusion A simple, low-cost optimization of the post-cultural diagnostic pathway markedly improved laboratory performance and accelerated clinical

decision-making. This strategy represents a highly effective and scalable solution for enhancing mycobacterial diagnosis, particularly in resource-limited settings.

基于宏基因组二代测序的肺癌化疗后下呼吸道感染病原谱特征及混合感染分析

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目的 肺癌化疗患者气道受损、粒细胞缺乏、免疫力低下，下呼吸道感染病原复杂、混合感染高发，传统检测阳性率有限。本研究采用宏基因组二代测序（mNGS），分析该人群下呼吸道感染病原谱与混合感染特点，评估 mNGS 的临床应用价值。

方法 回顾性选取 2024 年 1 月—2025 年 12 月宁夏医科大学总医院收治的 86 例肺癌化疗后疑似下呼吸道感染患者，均同步送检痰或支气管肺泡灌洗液（BALF）常规培养与 mNGS 检测。纳入标准：病理确诊原发性肺癌并完成至少 1 周期化疗；化疗后高热伴呼吸道症状，影像学见新发浸润影，排除肿瘤进展、放射性肺炎及免疫检查点抑制剂相关肺炎。排除标准：入院 48h 内使用广谱抗生素；合并其他非感染性肺部疾病。对比两种检测方式的病原阳性检出率、病原谱及混合感染占比，探讨 mNGS 对临床抗感染治疗方案的指导价值。

结果 86 例患者中，mNGS 病原总体阳性率 88.4%，显著高于常规培养的 41.9% ($\chi^2=39.74$, $p < 0.001$)。mNGS 共检出病原体 129 株，以细菌占比最高，其次为真菌、病毒及非典型病原体；优势致病菌为铜绿假单胞菌、肺炎克雷伯菌，真菌以曲霉属为主，病毒多见于巨细胞病毒与 EB 病毒。本组混合感染检出率 61.6%，以菌-真菌混合感染最多见，常规培养混合感染检出能力有限。依据 mNGS 结果，47.7% 患者优化抗感染方案，包括加用抗真菌、抗病

毒药物及更换抗生素。患者 30 天全因死亡率 14.0%，未调整方案组死亡率显著高于方案调整组 ($p=0.035$)。

结论 肺癌化疗后下呼吸道感染患者病原谱以铜绿假单胞菌、肺炎克雷伯菌及曲霉菌属为主，混合感染率高达 61.6%，以细菌及真菌双重感染最为常见，可能与肺癌患者气道定植及局部免疫功能紊乱相关。mNGS 较常规培养显著提高病原体检出率，对混合感染的识别具有独特优势，及时根据 mNGS 结果调整抗感染方案可改善肺癌化疗后感染患者的短期预后。

关键词：肺癌；化疗后感染；宏基因组二代测序；下呼吸道感染；混合感染

基于探针捕获法的靶向测序在疑似血流感染检测中的临床价值

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目的 评估基于探针捕获法的靶向测序 (targeted next-generation sequencing, tNGS) 在疑似血流感染 (Bloodstream Infection, BSI) 检测中的临床价值。

方法 回顾性分析 2025 年 4 月至 11 月徐州医科大学附属医院 399 例疑似 BSI 患者的临床资料，均同期接受探针捕获法 tNGS 与血培养检测。比较两种方法的病原体检出率、病原谱分布、诊断效能及 tNGS 结果对临床决策的影响。

结果 在 238 例确诊 BSI 患者中，tNGS 阳性检出率为 91.6% (218/238)，显著高于血培养的 32.4% (77/238) ($P<0.001$)。tNGS 检出的细菌和真菌谱更广，覆盖了恙虫病东方体、嗜肺军团菌、曲霉、耶氏肺孢子菌等血培养难以检出的苛养菌和胞内菌，并额外检出大量病毒及 1 例寄生虫。tNGS 诊断灵敏度显著高于血培养 (91.6% vs. 32.4%， $P<0.001$)，但特

异性低于血培养 (42.9% vs. 89.4%， $P<0.001$)；阴性预测值更高 (77.5% vs. 47.2%， $P<0.05$)，阳性预测值更低 (70.3% vs. 81.9%， $P<0.001$)。在血培养阴性的 147 例 tNGS 阳性患者中，89 例 (60.5%) 根据 tNGS 结果调整抗感染方案，主要为启动抗病毒治疗及覆盖难培养病原体。

结论 基于探针捕获法 tNGS 在血流感染病原检测中具有高灵敏度、广覆盖及指导临床治疗调整的优势，但其特异性较低，建议与血培养联合应用，以提升诊断准确性。

儿童脚癣病原学研究进展

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摘要 脚癣 (足癣) 是由皮肤癣菌引起的足部浅表真菌感染，主要累及足趾间、足底及足侧缘，是皮肤科最常见的真菌病之一。在成年人群中，脚癣是最常见的皮肤癣菌病，全球患病率可高达 20%~25%。长期以来，脚癣曾被认为是主要发生于成年人的疾病，儿童发病率相对较低。然而，近年来，儿童脚癣的发病率呈上升趋势，引起临床广泛关注。本文将从流行病学、主要病原菌、发病机制与易感因素以及诊断方法等方面，对儿童脚癣的病原学研究进展进行系统综述，旨在为儿童脚癣的病原学诊断和临床防治提供理论参考。流行病学方面，全球儿童脚癣患病率介于 0.03%至 15.6%之间，呈现显著的地域和人口学异质性。病原谱方面，皮肤癣菌占病原体的 96%以上，以红色毛癣菌和须癣毛癣菌为最主要的致病菌，不同地区和不同年龄段的病原分布存在差异。公共泳池、赤脚行走以及家养宠物等对于儿童脚癣来说是重要的环境因素。发病机制涉及病原菌的角蛋白酶系统、宿主免疫状态以及环境因素的综合作用。诊断方法包括传统的真菌镜检和培养以及新兴的分子生物学技术。未来的研究

方向应着力于以下几个方面：开展标准化、大样本的中国儿童足癣流行病学调查，明确患病率和病原谱；加强分子生物学技术在病原鉴定中的应用，探索基于 PCR 的快速诊断策略的临床推广；关注皮肤癣菌耐药性的演变趋势；以及整合病原学、免疫学和环境因素，深化对儿童脚癣发病机制的全面认识。

靶向二代测序诊断分析嗜肺军团菌所致重症肺炎 1 例

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摘要 患者男，58 岁，因“咳嗽、咳痰 3 天，发热 1d”于 2025 年 7 月 5 日于天津市第一中心医院门诊就诊。患者 3d 前淋雨后出现间断咳嗽、咳痰，于 7 月 4 日突发高热 39.3℃，伴嗜睡、纳差和胸闷。患者被诊断为社区获得性肺炎（CAP）予以厄他培南经验性治疗。由于患者持续发热，次日再次入院并收入该院呼吸与危重科进一步诊疗。7 月 10 日通过痰液进行靶向二代测序（tNGS）技术确诊嗜肺军团菌（LP）感染。给予左氧氟沙星联合利福平抗军团菌治疗 14d 后，PCR 复查军团菌核酸提示病原学转阴，患者发热、咳嗽和胸闷等临床表现均改善。LP 是导致 CAP 的非典型病原体，传统检测方法难以鉴别该病原菌导致临床极易出现误诊。tNGS 在重症 CAP 感染病原体早期鉴定及指导临床诊疗中发挥重要作用。本案例不仅强调了在传统微生物检测方法存在局限性的背景下，将 tNGS 整合于重症 CAP 精准诊疗流程中的重要性和迫切性，也对提高对军团菌肺炎的认知，掌握其诊治要点，提高其临床诊断率，降低病死率具有重要意义。因此，面对具有高危因素、病情进展迅速且伴有肺外症状的重症 CAP 患者，需要高度警惕军团菌感染的可能，并积极开展包括 tNGS 在内的先进分子诊断技术，助力临床及早精准诊疗，避免因诊断延迟导致的严重后果。

噬菌体免疫沉淀测序技术在感染性疾病中的应用进展

封怡梦

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噬菌体免疫沉淀测序（PhageImmunoPrecipitation Sequencing, PhIP-Seq）是一种基于噬菌体展示技术的高通量抗体检测方法，已成为感染性疾病研究的重要工具。该技术通过构建覆盖病原体蛋白质组的噬菌体展示肽库，与血清孵育后，利用免疫沉淀富集特异性结合的噬菌体，再通过高通量测序鉴定抗体识别的抗原肽段，从而全面绘制宿主的抗体应答图谱。PhIP-Seq 在感染性疾病研究中展现出多维度功能。在血清流行病学与病原监测方面，它能一次性筛查个体对海量病原的暴露史，精准识别既往感染并有效监测新发与再现病原。在诊断与预后生物标志物发掘领域，该技术可系统筛选与特定感染或疾病严重程度相关联的特异性抗体反应，为开发新型血清学检测方法提供关键靶点。此外，在宿主-病原互作机制研究上，PhIP-Seq 能够全面描绘针对不同病原乃至微生物群落的抗体响应全景图，揭示免疫反应的公共性和个体特异性，为理解感染免疫规律提供全新视角。尽管 PhIP-Seq 面临肽段长度有限、可能存在交叉反应以及依赖专业平台等挑战，但随着模型优化和测序成本的降低，其应用前景广阔。未来，该技术将进一步推动感染免疫图谱的绘制，并与传统诊断方法互补，为传染病的精准监测、诊断和防治提供有力支持。

基于数字 PCR 技术进行梅毒患者多类型临床标本的检测及分析

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目的 全球范围内梅毒发病率居高不下,传统血清学检测不仅存在窗口期漏检风险,而且无法实现病原体的绝对定量。微滴式数字 PCR (ddPCR) 具备绝对定量与低拷贝高灵敏检测优势。本研究拟建立并评价适用于血液、唾液、躯干病损部位拭子及脑脊液的苍白螺旋体 ddPCR 检测方法,并验证其临床应用价值。

方法 选择苍白螺旋体保守靶标基因 *polA*、*tpp47* 分别设计引物与探针,采用 Nichols 菌株 DNA 进行体系优化,建立从样本采集、核酸提取、液滴制备、扩增与多通道荧光读数分析的标准流程。将 ddPCR 结果与 qPCR 进行对照,比较梅毒不同分期中不同样本类型的检出率及拷贝数分布。

结果 建立的 ddPCR 方法在 1–105 copies/ μ L 范围内呈良好线性($R^2=0.9989$),最低检出限为 2.9(95% CI: 1.6–8.5)。对非目标病原未见交叉反应,特异性为 100%。在低载量样本检测中,针对 88 份血液与 19 份脑脊液,ddPCR 的检出率分别为 25.0%(22/88)、31.6%(6/19),高于 qPCR 的 15.9%(14/88)、0%(0/19); ddPCR 在 102 份唾液与 96 份病损拭子中检出率分别为 57.8%(59/102)、63.5%(61/96),高于 qPCR 的 45.1%(46/102)、58.3%(56/96)。值得注意的是,二期梅毒患者唾液 ddPCR 的检出率(86%, 43/50)显著高于一期(33.3%, 6/18)与早期潜伏梅毒(29.4%, 10/34);且拷贝数均值(300.6, Range: 0–2809.8)显著高于一期(3.3, Range: 0–15.4)与早期潜伏梅毒(27.0, Range: 0–838.5)。

结论 本研究建立的苍白螺旋体 ddPCR 检测体系适用于多类型临床样本,具有高灵敏度、高特异性与良好重复性,可作为血清学检测的重要补充,为早期诊断、神经梅毒分子诊断与病原负荷监测提供可靠工具。

关键词: 微滴式数字 PCR; 绝对定量; 梅毒螺旋体; 样本类型比较; 低载量检测; 诊断策略

基于 RPA-CRISPR/Cas12a 技术快速精准检测梅毒螺旋体

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目的 梅毒是由苍白螺旋体引起的慢性细菌感染,其早期诊断对于及时治疗和阻断传播至关重要。现有的血清学检测方法存在窗口期漏检和假阳性等局限,而 qPCR 等分子检测方法依赖昂贵设备和专业操作人员,难以满足即时检测(POCT)的需求。本研究旨在建立一种快速、灵敏且适用于 POCT 的梅毒螺旋体 CRISPR 检测方法。

方法 我们针对梅毒螺旋体 *tpp47* 基因设计了特异性 RPA 引物和 crRNA 序列,联合快速裂解技术,建立了一管法 RPA-CRISPR/Cas12a 检测体系。该方法使用 30 份唾液、20 份硬下疳拭子、30 份生殖器二期梅毒疹拭子进行验证。

结果 我们将 RPA 试剂、crRNA 和 ssDNA-FQ 集成于一管,37°C 加热 20min 后离心混入管盖位置的 Cas12a 核酸酶,使用 LC480II 在 37°C 下继续监测 30min。它省略了额外的开盖工艺,以避免样本交叉污染出现假阳性。该系统显示出 100% 的特异性,并且对于合成阳性质粒和临床样本的灵敏度均达到 10 拷贝/ μ L。值得注意的是,当使用 Cas12a 与 crRNA 的比例为 1:1.2 时,观察到最佳的荧光检测峰值。在样本验证中,一管法唾液、硬下疳拭子、生殖器二期梅毒疹拭子的阳性率分别为 83.3%(25/30)、90.0%(18/20)和 90.0%(27/30),优于 qPCR 的 66.7%(20/30)、85.0%(17/20)和 76.7%(23/30)。

结论 本研究建立了一种基于 RPA-CRISPR/Cas12a 技术的梅毒螺旋体 POCT 检测方法,适用于唾液、拭子等常规易采的无创性样本。只需一台恒温装置,无复杂操作,50 分钟即可获得检测结果,为梅毒的即时检测提供了一种简便、快速且可靠的新策略。

关键词: 梅毒螺旋体; CRISPR; Cas12a; POCT;
样本类型比较; 诊断策略; 临床验证

Analysis of High-Risk Factors for Mixed Infection with *Clostridioides Difficile* and Its Correlation with Recurrent *Clostridioides Difficile* Infection in Patients with Ulcerative Colitis

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Objective To explore the risk factors for mixed infection with *Clostridioides difficile* (CDI) in patients with ulcerative colitis (UC) and its correlation with recurrent CDI (R-CDI), providing evidence for clinical screening and individualized treatment.

Methods A total of 262 patients with CDI admitted to three hospitals in Sichuan Province from January 2020 to December 2024 were included. Mixed infection types (different genotypes of strains carried by the same host) were detected by PCR-ribotyping and multilocus sequence typing (MLST). The clinical characteristics, antibiotic heteroresistance rate, and biofilm formation ability of patients with mixed infection were analyzed, and the association between UC and the risk of mixed infection was evaluated using a logistic regression model.

Results Prevalence of Mixed Infection: Among the 262 CDI patients, 29 (11.1%) were found to have mixed infection, with the predominant MLST types being ST54, ST3, and ST42. Patients with UC had a significantly increased risk of mixed infection (odds ratio [OR] = 2.794, 95% confidence interval [CI] 1.632-7.649, $P = 0.001$). The heteroresistance rate of mixed

infection strains was 76.8%, with high resistance rates to levofloxacin, rifaximin, and tetracycline (19.8%, 23.4%, and 38.5%, respectively). Biofilm formation tended to favor the dominant strains in monoculture.

Conclusion UC, especially chronic recurrent UC, is an important risk factor for mixed infection with *C. difficile*. Mixed infection may increase the risk of R-CDI through the synergistic effects of high heteroresistance and biofilm formation. It is recommended to routinely screen patients with UC for CDI for mixed infection and optimize antibiotic selection to reduce the risk of recurrence and transmission of resistant bacteria.

常规鉴定技术与 16S rRNA 基因测序在临床菌株鉴定中的大规模比较分析

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目的 临床菌株的鉴定结果来源多样, 包括生化鉴定和 MALDI-TOF MS 等不同方法, 其鉴定一致性缺乏大规模验证。本研究旨在以 16S rRNA 测序为金标准, 系统评估某三甲医院近五年临床菌株鉴定结果的一致性, 明确鉴定不一致菌株的分布特征, 优化菌株鉴定流程。

方法 对 2021 年-2025 年从临床标本中分离出的致病菌进行回顾性分析。所有菌株均进行了 MALDI-TOF 或生化鉴定和 16S rRNA 基因测序, 当基因测序的一致性达到 99% 时, 认为鉴定是正确的。

结果 共纳入 1333 株临床分离菌, 其中革兰阴性菌 814 株 (61.1%)、革兰阳性菌 461 株 (34.6%)、真菌 58 株 (4.3%)。以 16S rRNA 基因测序 (真菌为 ITS 测序) 为参考方法, 种水平总体一致率为 68.49%, 其中真菌最高 (86.20%), 革兰阳性菌次之 (73.97%), 革兰阴性菌最低 (63.88%); 属水平总体一致率为 98.65%。

结论 临床菌株的常规鉴定在属水平上具有较高的鉴定准确率，但在种水平上存在一定的错误鉴定情况，尤其是对罕见菌及近缘物种群，但其对临床抗感染治疗决策影响有限；而属水平不一致多源于分类学更新或存在新物种等情况。建议常规微生物实验室定期更新本地数据库，对复合群内物种采用 16S rRNA、多基因座或全基因组测序复核，并加强菌株冻存库的质量控制与溯源管理，以进一步提高鉴定准确性。

Diagnostic Advantage of Droplet Digital PCR over Blood Culture in Sepsis: A Retrospective Study of 115 Patients

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Background Sepsis is a life-threatening condition that requires rapid and accurate identification of causative pathogens to guide timely antimicrobial therapy. Blood culture is the current diagnostic standard, but it suffers from low sensitivity and long turnaround times. Droplet digital polymerase chain reaction (ddPCR) has emerged as a promising molecular tool that may overcome these limitations. This study aimed to evaluate the diagnostic utility of ddPCR compared with conventional blood culture in patients with sepsis

Methods We performed a retrospective study of 115 patients admitted with sepsis to Tianjin First Central Hospital between October 2024 and June 2025. All patients underwent both blood culture and ddPCR testing on admission. Clinical characteristics, laboratory parameters, and infection outcomes were collected. Diagnostic performance, including sensitivity, specificity, positive predictive value, and negative predictive value, was calculated using blood culture as the reference

standard. Concordance between ddPCR, blood culture, and non-blood specimen cultures was analyzed. Statistical analysis was performed using descriptive statistics and agreement measures

Results Blood culture identified pathogens in 27.8% of patients, whereas ddPCR detected organisms in 53%. ddPCR revealed a broader microbial spectrum, particularly Gram-negative bacteria such as *Escherichia coli* and *Klebsiella pneumoniae*, and identified mixed infections frequently missed by culture. Within its detection panel, ddPCR demonstrated a sensitivity of 81.3% and specificity of 56.6%, with a high negative predictive value of 88.7%. ddPCR findings showed strong agreement with non-blood culture results in cases where blood cultures were negative, underscoring its clinical relevance. Early in the study, false-positive *Candida* results were observed but eliminated after stricter aseptic protocols were implemented

Conclusions Droplet digital polymerase chain reaction significantly outperformed blood culture in pathogen detection for sepsis, especially for Gram-negative and polymicrobial infections. Its high negative predictive value supports its use as a complementary tool to exclude bloodstream infections and guide early antimicrobial de-escalation. While positive findings must be interpreted with clinical context to avoid over-treatment, ddPCR offers substantial potential to accelerate pathogen identification, improve antimicrobial stewardship, and enhance outcomes in septic patients

靶向新一代测序技术 (tNGS) 在 HIV 合并肺部感染患者病原学诊断中的效能与临床价值

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目的 早期、快速且精准的病原学诊断，是临床确立诊断及优化治疗方案的重要依据。本研究旨在评估靶向新一代测序（tNGS）技术用于 HIV 合并肺部感染者的病原学诊断效能与临床价值。

方法 纳入 2023 年 11 月至 2025 年 10 月期间在广州医科大学附属市八医院住院治疗的 HIV 合并肺部感染患者作为研究对象。收集患者肺泡灌洗液（BALF）并同时常规病原学检查（CMT）与 tNGS 测序，评估 tNGS 的诊断效能及其对抗感染治疗方案调整的指导价值。

结果 共纳入 602 例患者，男性 498 例（82.7%），年龄中位数 52 岁。tNGS 与 CMT 病原体检出率分别为 99.0%（596/602）和 83.1%（500/602），双阳性 497 例，双阴性 3 例。tNGS 共鉴定 94 种病原体，涵盖 39 种病毒、38 种细菌、16 种真菌及 1 种支原体；传统培养法鉴定出结核与非结核分枝杆菌 10 种、马尔尼菲篮状菌 1 种及 36 种细菌。基于 tNGS 结果，临床治疗决策积极影响 389 例（64.6%），包含直接采纳 tNGS 诊断 233 例（38.7%）、tNGS 首次确认后采纳 149 例（24.8%）以及联合 tNGS 与常规诊断后采纳 7 例（1.2%），无影响 213 例（35.4%），包含常规方法首次确认后采纳 22 例（3.7%），仅采纳常规诊断 47 例（7.8%）以及两种方法均未采纳 144 例（23.9%）。

结论 研究证实 tNGS 在 HIV 合并肺部感染诊断中的关键作用，有助于实现早期检测并及时制定针对性抗感染治疗方案。

侵袭性曲霉病不同影像表型的转录组学研究

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目的 侵袭性曲霉病（IA）是临床致命的深

部真菌感染。依据胸部 CT 影像学特征，IA 主要分为气道侵袭（AIA）与血道侵袭（AGIA）两种具有不同预后的临床亚型。本研究旨在通过外周血白细胞转录组学技术，探索不同影像学亚型 IA 患者的全身免疫分子特征及底层致病机制，为临床精准诊疗提供理论依据。

方法 本研究构建了包含 123 例 IA 患者（含纵向随访样本）及 35 例健康对照（HC）的外周血专病队列。提取去红细胞后的白细胞总 RNA，进行高通量测序。运用 DESeq2 进行差异表达基因（DEGs）筛选，结合 GO 与 KEGG 数据库进行通路富集；利用 WGCNA 算法构建基因共表达网络，并运用 rMATS 分析可变剪切（AS）事件差异。

结果 测序数据质量良好，主成分分析（PCA）显示，AIA、AGIA 与 HC 组患者的白细胞转录组呈现显著的空间聚类分离，提示不同影像学表型对应着独特的全身免疫状态。差异分析成功鉴定出 AIA 与 AGIA 组间的大量 DEGs。KEGG 与 GO 富集分析表明，这些差异基因显著富集于中性粒细胞胞外诱捕网形成、代谢重塑及细胞因子受体活化等关键免疫及炎症通路。AGIA 组免疫炎症通路（TNF/NF- κ B、TLR 信号通路）激活更显著，代谢通路（氧化磷酸化、糖酵解）抑制更明显；AIA 组以轻度炎症反应为主要特征。

结论 侵袭性曲霉病气道侵袭与血道侵袭的影像学差异，本质上反映了宿主外周血免疫细胞不同的转录组学与转录后修饰特征。免疫炎症通路过度激活和能量代谢功能障碍是 AGIA 的关键病理特征，筛选的差异基因和核心通路为侵袭性曲霉病亚型鉴别及靶向治疗提供了新靶点。

外周血 mNGS 和血培养识别恶性血液病患者多重菌血症的诊断效能和预后价值对比

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目的 对比外周血 mNGS 和传统血培养 (BC) 在恶性血液病合并多重菌血症 (PBSI) 患者的诊断和指导预后的临床价值。

方法 单中心回顾分析经 mNGS 和 BC 同时确诊的恶性血液病合并菌血症患者临床资料和结局, 比较 mNGS 与 BC 对于 PBSI 的诊断效能和预后评估价值。

结果 共入组 175 名恶性血液病合并 mNGS 和 BC 双阳性菌血症患者, mNGS 检出 PBSI (48.6%) 明显高于 BC (30.3%)。mNGS 检出各类菌种数均较 BC 高, 尤其在检出厌氧菌、军团菌、芽孢杆菌、分枝杆菌等苛养菌和曲霉、毛霉菌等方面优势明显。mNGS 识别细菌合并真菌的 PBSI 阳性率 (19.43%) 较 BC (1.14%) 明显升高。mNGS 诊断 PBSI 的敏感性、阳性预测值、阴性预测值和 AUC 均高于 BC, 而周转时间明显减少。经 mNGS 分类的 PBSI 与单一菌血症 (MBSI) 患者在 30d 和 90d 的预后均有显著差异, 而经 BC 分类的 PBSI 与 MBSI 则在生存率方面无明显差异。多因素回归分析提示年龄、基线 SOFA 和 mNGS 鉴定的菌种类数是感染后 90d 内死亡的独立影响因素, 而 BC 报告的菌种类数则与预后无关。

结论 血 mNGS 在识别恶性血液病 PBSI 的诊断效能高于 BC, 且经 mNGS 鉴定的 PBSI 患者预后不佳。

Fishnet-like 2D Magnetic Nanozyme Probe Enables Ultrasensitive Bedside Immunodiagnosis of Bone Infection Pathogens

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Rapid, early, and accurate bedside diagnosis of

bone infections is an urgent clinical need that remains unmet. Here, we present a fishnet-like two-dimensional magnetic nanozyme (FGDAI) that integrates three functional modules: a monolayer graphene oxide substrate providing a large reaction interface; an Fe₃O₄ interlayer conferring efficient magnetic enrichment; and two dense layers of Au@Ir nanoparticles furnishing abundant catalytic sites that act synergistically with the Fe₃O₄ to enable cascade catalysis. This architecture delivers multiple signal amplification—"large reaction interface, magnetic enrichment, cascade catalysis"—within an immunochromatographic assay (ICA), effectively overcoming the sensitivity and robustness limitations of traditional colorimetric ICAs when challenged by complex clinical matrices. In addition, wheat germ agglutinin (WGA) was immobilized on the 2D FGDAI surface via lyophilization as a universal peptidoglycan recognition molecule, enabling efficient, broad-spectrum bacterial binding and thereby mediating ultrasensitive, simultaneous ICA detection of two important bone-infection pathogens (*Staphylococcus aureus* and *Pseudomonas aeruginosa*). FGDAI-WGA-ICA completes testing in under 25 min with a visual limit of detection of 10 cells/mL, exhibiting high sensitivity and specificity for the target pathogens. Moreover, validation in a cohort of 83 synovial fluid samples showed high concordance with clinical reference methods, supporting its potential for real-time, bedside diagnosis of bone infections.

Magnetofluorescent Immunoassay for Sepsis Monitoring: Silica Shell Protection and Click Reaction Conjugation Enable Ultrasensitive and Accurate Detection

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Rapid detection of inflammatory biomarkers from whole blood samples (such as fingertip blood) is crucial for early sepsis assessment and critical care intervention, yet great challenges remain. Here, we report an ultrasensitive lateral flow immunoassay (LFIA) that employs SiO₂ shell-protected magnetofluorescent probes, combined with click reaction for efficient antibody conjugation, enabling bedside, simultaneous detection of sepsis biomarkers interleukin-6 (IL-6) and procalcitonin (PCT). An ester-activated diyne linker enables universal functionalization of MagTQD@Si surface antibodies without the need for concurrent catalyst activation, while preserving high activity and stability of the nanoprobe. The MagTQD@Si probes enable rapid capture and ultrasensitive detection below the pg/mL level on LFIA, benefiting from magnetic enrichment and signal amplification provided by thousands of quantum dots. The SiO₂ shell not only stabilizes luminescence in whole blood but also improves chromatographic flow, thereby enhancing detection accuracy. The established MagTQD@Si-LFIA achieved detection limits of 0.73 pg mL⁻¹ for IL-6 and 2.32 pg mL⁻¹ for PCT, and provided quantitative analysis over an 4-order-of-magnitude dynamic range. Validation with 66 clinical samples showed concordance with ELISA results, with assay time reduced to only 20 min. Collectively, this platform enables direct, simultaneous multi-marker detection and holds promise for low-cost, bedside sepsis monitoring.

基于第三代纳米孔测序的病原快速检测算法构建与临床验证

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背景 下呼吸道感染病原体种类复杂、传统培养周期长、漏诊率高，临床亟需快速、精准、高通量的病原检测手段，以指导早期抗感染治疗。

方法 本研究构建覆盖细菌、真菌、寄生虫、病毒及抗生素耐药基因的整合核酸参考数据库，基于纳米孔测序数据开发优化生物信息学分析流程，提出新型综合评估参数 `all_ratio`，整合序列相似性、丰度、匹配数与匹配长度，实现病原高效鉴定。利用 40 例下呼吸道感染患者公共测序数据进行验证，并与传统培养及常规宏基因组流程进行对比。

结果 本方法在 40 例样本中与传统方法一致符合 23 例，额外检出 5 例常规方法未发现的病原体（含肺炎链球菌、阿氏肉芽肿等），12 例样本提示混合感染可能，对病毒病原体亦具有良好区分能力。相关算法已发表于 BMC Infectious Diseases（已发表），并建成一键式在线分析平台 PathoResistAI（预印

本 <https://www.biorxiv.org/content/10.64898/2026.02.12.705264v1>，投稿中），上传数据后约 30 分钟即可输出病原与耐药基因提示，适用于临床快速筛查场景。

结论 本研究建立的纳米孔测序病原检测方法灵敏度更高、速度更快、操作简便，可有效补充传统检测手段，为临床感染性疾病的快速诊断与精准用药提供可靠工具。

Plasma Versus Whole Blood Multiplex Droplet Digital PCR for Pathogen Detection in ICU Patients with Clinically Suspected Sepsis: A Prospective Multicenter Cohort Study

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Background Rapid pathogen identification remains challenging in critically ill patients with suspected sepsis. Droplet digital PCR (ddPCR) is a promising molecular diagnostic tool, but it is usually performed on plasma and may miss pathogen signals retained in cellular blood components. We therefore compared plasma and whole-blood ddPCR in ICU patients with clinically suspected sepsis

Methods In this prospective multicenter cohort study, ICU patients with clinically suspected sepsis underwent paired plasma and whole-blood ddPCR together with blood culture. Blood culture-negative/ddPCR-positive cases were interpreted using structured clinical adjudication

Results Among 223 patients, 62 (27.8%) had positive blood cultures. Both plasma and whole-blood ddPCR identified substantially more pathogens than blood culture alone and provided microbiological support for 38 and 46 adjudicated definite sepsis cases, respectively, among blood culture-negative patients. Overall performance was similar between matrices, but whole-blood ddPCR showed a higher detection rate for the *Candida* genus than plasma ddPCR (87.5% vs. 31.3%, $P = 0.03$). Concordant positivity in both matrices was associated with greater disease severity

Conclusions Both plasma and whole-blood ddPCR complement blood culture in ICU patients with clinically suspected sepsis. Although overall performance was similar, whole-blood ddPCR showed a selective advantage for *Candida* detection

Nanozyme-based Aptamer Platform for Detection of Bacterial Extracellular Vesicles in

Clinical BALF Samples

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Objective To develop a nanozyme-based aptamer sensing platform for rapid and reliable detection of bacterial extracellular vesicles (bEVs) and to evaluate its diagnostic performance in bronchoalveolar lavage fluid (BALF) samples from ICU patients

Methods A MOF-on-MOF nanozyme with dual enzyme-like activities was synthesized via a mild coordination strategy. An aptamer was functionalized onto the nanozyme through coordination between phosphate groups and Cu active sites, enabling target recognition and regulation of catalytic activity. Bacterial EVs were isolated from different species and characterized by transmission electron microscopy and nanoparticle tracking analysis. Lipopolysaccharide associated with Gram-negative bacterial bEVs was verified by silver staining. The sensing mechanism was investigated using inhibition experiments and electron spin resonance spectroscopy. The analytical performance of the platform was evaluated using bEVs as targets. Clinical BALF samples from ICU patients were further analyzed to assess diagnostic capability, and the results were compared with conventional inflammatory biomarkers using ROC curve analysis

Results The synthesized nanozyme exhibited both catechol oxidase-like and peroxidase-like activities, with good catalytic efficiency and stability. Mechanistic studies confirmed the involvement of hydroxyl radicals in the catalytic process. The platform successfully detected bEVs derived from multiple clinically relevant bacterial species. In clinical BALF samples, the bEV-based assay demonstrated a lower false-negative rate (8.7%) compared to routine laboratory testing (21.7%), and successfully identified missed infection cases. ROC

analysis showed superior diagnostic performance of the bEV-based method (AUC = 0.948) compared to conventional biomarkers, including white blood cell count, neutrophil count, C-reactive protein, and interleukin-6

Conclusion This study presents a nanozyme-based aptamer platform for bEVs detection that enables sensitive and reliable diagnosis of bacterial infections in complex ICU settings. By targeting pathogen-derived vesicles rather than host-response biomarkers, this approach provides improved diagnostic accuracy and demonstrates potential for clinical application

耶氏肺孢子菌定植与感染鉴别诊断模型的建立与评价：一项单中心回顾性研究

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目的 总结通过下一代测序 (NGS) 检测到耶氏肺孢子菌 DNA 患者感染与定植的情况, 形成诊断模型, 为 PJP 精确治疗与预防提供临床经验。

方法 单中心回顾性收集接受 mNGS 检查, 并检测到耶氏肺孢子菌 DNA 的患者。根据标准, 分为感染组和定植组。通过 LASSO 回归和单因素 logistic 回归确定独立危险因素, 进而形成诺莫图。

结果 本研究筛选了 2023 年 1 月至 2024 年 9 月行肺泡灌洗液 NGS 检查并检测到耶氏肺孢子菌 DNA 的患者共 593 名, 根据排除标准及诊断标准, 最终纳入 453 名患者, 分为 PJ 定植组和 PJ 感染组。与定植组相比, 感染组患者更年轻 (中位年龄, 59.0 vs. 63.0, $P=0.037$), 发热更常见 (68.4% VS 57.3%, $P=0.017$)。在影像学表现上, 感染组更多见磨玻璃表现 (71.5% VS 29.8%, $P<0.001$)、间质改变 (47.5% VS 31.6%, $P<0.001$), 而胸腔积液 (37.4% VS 26.2%, $P=0.012$)、实变征 (23.% VS 10.4%, $P<0.001$)、肺

不张 (3.5% VS 0.4%, $P=0.013$) 更多见于定植组。感染组患者有更多的基础疾病, 其中 HIV (14.9% VS 5.3%, $P=0.002$) 和器官移植 (22.3% VS 12.9%, $P=0.012$)、肾功能不全 (20.2% VS 7.6%, $p<0.001$) 两者存在统计学差异。而在定植组中, COPD 更为常见 (10.5% VS 3.2%, $P=0.001$)。感染组比定植组他克莫司 (15.2% VS 8.2%, $P=0.028$)、吗替麦考酚酯 (15.2% VS 4.7%, $P<0.001$) 使用频率更高。通过 LASSO 回归和 logistic 回归确定 10 个独立危险因素, 构建预测 PJP 概率的 nomogram 图。该模型的 AUC 为 0.865 (95%CI: 0.832-0.899), DCA 和 CIC 评估模型有很好的临床效用, 在加强 bootstrap 法的内部验证中, 高估值 (Optimism) 为 0.015, 内部验证中模型表现的 AUC 为 0.851。

结论 我们的 nomogram 模型为区分 PJ 感染与定植提供了简单、可靠的工具, 减少过度治疗带来的风险, 为临床提供更精准的治疗。

Keywords 耶氏肺孢子菌, mNGS, 定植, 感染, 预测模型

Whipples Disease with Multiple Serous Effusions As The Clinical Manifestation: A Case Report and Literature Review

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Background Whipple's disease, caused by *Tropheryma whipplei*, is a rare multisystem infectious disorder with diverse clinical manifestations. Typical symptoms include arthralgia, nausea, vomiting, diarrhoea, and weight loss, while nonspecific features such as fever, anaemia, and lymphadenopathy may also occur. Presentations with multiple serous effusions are exceedingly rare. Diagnosis remains particularly challenging

in resource-limited regions because of nonspecific symptoms and limited access to advanced diagnostic techniques

Case presentation: A 34-year-old male presented with fever, vomiting, diarrhoea, mild dry cough, and anorexia. Whole-body computed tomography revealed systemic inflammatory changes that mimicked vasculitis, including multiple serous effusions (pleural, peritoneal, pericardial, and pelvic) and omental thickening. Initial anti-infective therapy failed. Serological tests, pleural fluid analysis, and thorascopic pleural biopsy excluded systemic vasculitis and pleural malignancy. Given the diagnostic uncertainty, subsequently 18F-fluorodeoxyglucose positron emission tomography demonstrated diffuse peritoneal thickening accompanied by hypermetabolism, which prompted a biopsy. Definitive diagnosis was achieved via laparoscopic omental biopsy with histopathology, periodic acid-Schiff staining, and polymerase chain reaction. Despite receiving targeted antibiotic therapy for *T. whipplei*, the patient showed suboptimal clinical improvement. We speculated that the recurrence of the patient's condition was more likely attributable to immune reconstitution inflammatory syndrome. Combination therapy with doxycycline, hydroxychloroquine, and short-term glucocorticoids induced sustained remission. After more than two years of targeted anti-*T. whipplei* therapy, the patient demonstrated a favourable recovery

Conclusion Multiple serous effusions are uncommon clinical manifestations of Whipple's disease. Early identification of *T. whipplei* infection and timely targeted therapy are critical for improving patient prognosis.

Ultrasensitive and Rapid Detection of KPC-2-

producing Hypervirulent *Klebsiella Pneumoniae* Via A Centrifugal Microfluidic IMS-LAMP Biosensor

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Carbapenem-resistant hypervirulent *Klebsiella pneumoniae* (CR-hvKP), particularly strains producing KPC-2, pose serious clinical threats due to their high virulence, antibiotic resistance, and rapid transmissibility. Early and sensitive detection of hvKP producing KPC-2 is crucial to reducing mortality, but traditional detection techniques, such as culture and PCR, are time-consuming, labor-intensive, and instrument-dependent, making it difficult to achieve on-site high-throughput detection. Therefore, we first developed a microfluidic biosensor based on the integration of immunomagnetic separation (IMS) and loop-mediated isothermal amplification (LAMP) for the point-of-care detection of KPC-2-producing hvKP. The microfluidic chip integrates pathogen enrichment, nucleic acid extraction, and LAMP detection into a single workflow, significantly streamlining the workflow and realizing a one-step detection method. At the same time, based on magnetic separation technology to eliminate sample matrix interference and LAMP signal amplification, high-sensitivity detection in complex samples such as cerebrospinal fluid and blood is achieved, with detection limits of 101 CFU/mL and 102 CFU/mL respectively. Compared with conventional PCR, the platform achieves a 10-100 fold lower detection limit and reduces total assay time from >4 h to <2 h, enabling on-site diagnosis without specialized instrumentation. In addition, based on the multi-channel design, the microfluidic chip can detect 6 samples at the same time, improving the detection efficiency. Therefore, the microfluidic chip significantly

improves the speed, sensitivity and portability of detecting pathogens. The system is expected to become an alternative to technologies such as PCR, especially for resource-limited or bedside diagnostic environments.

An Extraction-free One-pot Assay for Rapid Detection of *Streptococcus Pneumoniae* by Combining Magnetic Separation and LAMP-AIE

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Objective *Streptococcus pneumoniae*, as the first pathogen of community-acquired pneumonia, can cause highly lethal and invasive diseases (such as meningitis and bacteremia), which are particularly threatening to the lives and health of children and the elderly. To address the limitations of traditional detection methods for *Streptococcus pneumoniae* (such as time-consuming culture, PCR relying on precision instruments) in grass-roots applications, as well as the diagnostic pitfalls of false-positive diagnosis triggered by a single target, this study innovatively established an extraction-free one-pot assay for rapid dual-gene detection of *Streptococcus pneumoniae* by combining magnetic separation and LAMP-AIE

Methods The method efficiently captures and enriches *Streptococcus pneumoniae* in samples by antibody-modified magnetic beads, and after lysis, directly targets *cpsA* and *lytA* using loop-mediated isothermal amplification (LAMP) at a constant temperature in a synchronized manner, which is combined with an aggregation-induced emission (AIE) materials to achieve real-time fluorescence in closed tubes or visual readout

by the naked eye

Results The dual-target combined detection avoids cross-reactions and has a specificity of 100%. Magnetic separation pre-enrichment increases the detection sensitivity of clinical samples to 10 CFU/mL, solving the problem of missed detection of low-load clinical samples

Time-Series Prediction-Powered LAMP-CRISPR/Cas12a Platform with Smartphone-Based Deep Learning Readout for Rapid Point-of-Care Identification and Virulence Stratification of *Streptococcus Pneumoniae*

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Streptococcus pneumoniae is a leading pathogen responsible for community-acquired pneumonia, septic meningitis, and sepsis globally. Rapid and accurate species identification combined with virulence stratification is critical for timely clinical intervention and infection control. Here, we developed a rapid, sensitive, and specific point-of-care diagnostic platform by integrating loop-mediated isothermal amplification (LAMP) and CRISPR/Cas12a, targeting two critical pneumococcal genes: the species-specific autolysin gene *lytA* and the capsule synthesis regulator gene *cpsA*. A smartphone-coupled deep learning framework was innovatively applied for automated lateral flow strip (LFS) readout based on reaction kinetic time series instead of conventional endpoint analysis. A hybrid convolutional neural network-long short-term memory (CNN-LSTM) model was constructed and trained using temporal kinetics of test/control (T/C) line ratios, enabling robust prediction of the final signal using only the initial 50% of reaction

progression. This predictive strategy shortened the total detection time to less than 5 min, in contrast to 15–30 min required for visual interpretation. The platform achieved limits of detection (LOD) of 10 fg/ μ L for LFS and 1 fg/ μ L for fluorescence detection, with 100% specificity against other common respiratory pathogens. Validation using 150 clinical isolates demonstrated 100% diagnostic sensitivity and specificity compared with culture and real-time PCR. The AI-predicted T/C ratio showed an excellent Pearson correlation coefficient of 0.982 with fluorescence-based quantification. This LAMP-CRISPR/Cas12a platform integrated with time-series deep learning provides a rapid, accurate, and field-deployable sample-to-answer solution for pneumococcal detection and virulence stratification in resource-limited settings, with high extensibility for other nucleic acid-based point-of-care diagnostics.

Pulmonary Coinfection with *Nocardia Cyriacigeorgica* and *Aspergillus* in A Patient with COPD: A Case Report Highlighting The Diagnostic Utility of MNGS

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Nocardia cyriacigeorgica is a significant opportunistic pathogen, but its co-infection with other pathogens like *Aspergillus* presents a profound diagnostic and therapeutic challenge. We report the case of a 67-year-old male with chronic obstructive pulmonary disease (COPD) on inhaled corticosteroids who presented with

septic shock and a large pulmonary abscess. While direct microscopy of bronchoalveolar lavage fluid (BALF) rapidly suggested *Nocardia*, the patient showed limited initial response to targeted antibacterial therapy. Subsequent metagenomic next-generation sequencing (mNGS) of the same BALF sample provided a crucial, comprehensive diagnosis by not only confirming *N. cyriacigeorgica* with a high read count but also identifying a significant co-infection with *Aspergillus fumigatus* and *Aspergillus flavus*. The addition of voriconazole to the regimen, guided by the mNGS result, led to marked clinical and radiological improvement. This case highlights that while conventional methods are vital for initial suspicion, mNGS is an invaluable complementary tool for uncovering complex mixed infections in critically ill, immunocompromised hosts. It underscores the importance of a comprehensive etiological diagnosis to guide appropriate, life-saving antimicrobial therapy.

军团菌致病性及其实验室诊断新技术

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【摘要】军团菌 (*legionellae*) 普遍存在于天然淡水和人工水系中或在原生动物的阿米巴

胞内寄居, 是引起军团病的重要病原体。本文就军团菌的致病性、实验室诊断新技术,

以及本实验室近 20 年来对军团菌与军团菌病研究所取得的科研成果, 结合国内外对军团菌实验室诊断新技术的发展趋向, 作一简要概述。

【关键词】军团菌; 致病性; 实验室诊断

Pathogen Spectrum of Aortic Graft Infections Uncovered by Combined Microbiologic Testing and In-situ Metagenomic Sequencing

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Background Aortic and graft-associated infections carry substantial morbidity and mortality. However, in-situ specimens are rarely obtainable, and blood-based tests are often misleading in identifying the true culprit pathogen. In-situ metagenomic next-generation sequencing (mNGS) is therefore needed to improve etiologic characterization in this highly challenging infection

Methods This cohort study included 107 patients evaluated for suspected aortic graft or endograft infections between March 2019 and November 2025 at Zhongshan Hospital, Fudan University, with diagnoses established according to the MAGIC (Management of Aortic Graft Infection Collaboration) criteria. Clinical characteristics and detailed microbiologic information—including conventional microbial tests and mNGS results—were systematically extracted for pathogen evaluation. Notably, a prospective subset of 16 patients had complete paired datasets and multi-site intraoperative specimens, including infected aneurysm, graft, and fistula samples. Statistical analyses were performed to delineate the pathogen spectrum and to compare the performance of blood versus on-site specimens and of mNGS versus conventional cultures

Results Using a multi-test microbial diagnostic strategy, microbiologic testing achieved a high overall positivity of 85%, with 61% of infections being monomicrobial and 24% polymicrobial. The pathogen spectrum was broad, dominated by *Salmonella*, *Staphylococcus* species, and gut flora-associated organisms, while several uncommon pathogens were also identified.

Thoracic and abdominal aortic infections showed differing trends, with abdominal cases more enriched for enteric and anaerobic organisms. In paired plasma and in-situ samples (101 organisms), mNGS identified many pathogens missed by culture, particularly anaerobes (mNGS-only: 68.8% in plasma; 25% in in-situ samples). Importantly, in-situ mNGS uniquely detected fastidious pathogens—including *Coxiella burnetii*, *Brucella*, and *Hungateella hathewayi*—consistently missed by blood tests and often undetected by in-situ culture. Biomass analysis across anatomical sites revealed clear site-specific dominance, with true pathogens peaking at the primary focus (e.g., graft/aneurysm for *Coxiella*; fistula for *Brucella*), underscoring the unique value of in-situ mNGS

Conclusions In-situ mNGS, when combined with conventional microbiologic testing, markedly improves pathogen identification in aortic graft infections—particularly for fastidious and site-specific organisms often missed by routine methods. These findings support in-situ mNGS as a valuable complementary tool for enhancing etiologic diagnosis in this highly challenging infection

Respiratory and Blood Samples Metagenomic Sequencing in Diagnosing Pulmonary Infections in Hematologic Patients

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Background Bacterial and fungal pulmonary infections (BFPI) are common in hematological patients

and pose significant diagnostic challenges. Metagenomic next-generation sequencing (mNGS) is valuable for diagnosing BFPI. However, for hematological patients with limited access to lower respiratory tract samples (LRTS), the clinical value of blood-mNGS compared to LRTS-mNGS requires further investigation

Methods A retrospective analysis was conducted on 160 cases with suspected pneumonia who underwent both blood-mNGS and LRTS-mNGS within one week. Diagnostic performance and impacts on antimicrobial adjustments were evaluated using clinical composite diagnosis (CCD) as the reference

Results Compared to CCD, LRTS-mNGS showed significantly higher positive percent agreement (PPA) than blood-mNGS [93.7% (119/127) vs. 34.6% (44/127), $P < 0.001$], with negative percent agreements (NPA) of 87.5% (21/24) and 91.7% (22/24), respectively. Blood-mNGS showed higher PPA in neutropenic than non-neutropenic patients [56.8% (21/37) vs. 25.6% (23/90), $P = 0.001$], with unique fungal detection advantages, identifying additional fungi in 7 cases: Mucorales (3), *Aspergillus* spp. (2), both Mucorales and *Aspergillus* spp. (1), and *Pneumocystis* spp. (1). Resistance genes were detected only by LRTS-mNGS. mNGS positively influenced antimicrobial adjustments in 54.3% (69/127) of cases, particularly for pathogens with low empirical coverage, such as *Legionella* spp. (0.0%, 0/7), *Pneumocystis* spp. (52.3%, 11/21), and Mucorales (55.6%, 5/9). Blood-mNGS detected these pathogens at rates of 71.4% (5/7), 77.8% (7/9), and 23.8% (5/21), respectively

Conclusion LRTS-mNGS outperformed blood-mNGS in diagnostic performance and resistance detection. Blood-mNGS identified pathogens in one-third of BFPI cases, with value for certain fungal infections, especially in hematologic patients with limited LRTS access

Metagenomic Sequencing-Based Diagnosis and Risk Factors of Legionnaires' Disease in Hematological Patients

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Background Legionnaires' disease (LD) is a severe pneumonia commonly caused by *Legionella pneumophila* and is associated with high mortality in patients with hematological diseases due to delayed diagnosis and treatment. This study aimed to investigate the clinical features, molecular diagnostic value, and independent risk factors for 28-day mortality in this population

Methods We retrospectively included hematological patients with pneumonia in whom *L. pneumophila* was detected by metagenomic next-generation sequencing (mNGS) and confirmed by *L. pneumophila* PCR. Clinical, imaging, laboratory, treatment, and outcome data were collected.

Results Fifty-four patients were included; 28 (51.9%) had severe LD, and 19 (35.2%) died within 28 days. The main manifestations were fever (100%) and respiratory symptoms (cough 92.6%, expectoration 79.6%, dyspnea 64.8%). Notably, 55.6% of patients presented with orange to reddish sputum, which may serve as a potential clinical clue for LD. Imaging showed mass-like consolidation as the predominant pattern (61.1%), a feature that may resemble invasive fungal pneumonia. Additional radiological features included air bronchogram (81.5%), reticulation sign (81.5%), and pleural effusion (59.3%). Multivariable Cox analysis showed elevated C-reactive protein (CRP) ($HR = 1.011$,

95% CI: 1.005-1.017, $P < 0.001$) and higher blood-mNGS Stringently Mapped Reads Number (SMRN) (HR = 2.787, 95% CI: 1.561-4.975, $P < 0.001$) as independent risk factors for 28-day mortality. Before mNGS detection of *L. pneumophila*, only seven patients (13.0%) received effective therapy.

Conclusion Hematological patients with LD may develop severe infection with high mortality. Elevated bacterial load in blood samples and increased CRP levels can identify high-risk patients who require more intensive treatment to improve prognosis.

基于 FTIR 光谱机器学习的肺炎克雷伯菌 KL 型别快速识别研究

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目的 肺炎克雷伯菌 (*Klebsiella pneumoniae*) 荚膜 KL 型别与其毒力特征、流行传播及临床风险密切相关。传统 KL 分型主要依赖分子生物学方法, 存在检测周期较长、成本较高等局限。本研究拟基于傅里叶变换红外光谱 (FTIR) 数据构建机器学习模型, 用于快速识别肺炎克雷伯菌 KL 型别, 并重点评估其对高毒力相关 KL1 型别的识别能力。

方法 本研究纳入 348 株肺炎克雷伯菌的 FTIR 光谱数据, 共获得 4100 条光谱记录。去除 KL 型别为 unknown 的样本后, 最终纳入 3687 条光谱记录, 来源于 313 个独立菌株, 覆盖 58 种 KL 型别。光谱分析聚焦于 900–1200 cm^{-1} 区间。采用 PCA 和层次聚类观察不同 KL 型别的光谱分布特征, 并构建 Random Forest、Support Vector Machine、Neural Network、Lasso Logistic Regression、PLS-DA 和 XGBoost 等监督分类模型。模型性能通过光谱水平内部验证、菌株水平分组验证及 KL1 专项分析进行综合评价。

结果 FTIR 光谱能够较好地地区分不同 KL 型别。在光谱水平内部验证中, Random Forest 和 Neural Network 均表现出较高的分类能力, 其中 Random Forest 的总体准确率达到 97.6%, 提示 FTIR 光谱中包含稳定的 KL 型别识别信息。在更接近实际应用场景的菌株水平分组验证中, Neural Network 仍保持较好的泛化性能, 整体准确率为 87.3%, macro-F1 为 0.824。针对高毒力相关 KL1 型别, 模型表现尤为突出: Random Forest 在光谱水平验证中的 KL1 recall 接近 100%, Neural Network 在菌株水平验证中的 KL1 F1-score 为 0.940, XGBoost 的 KL1 F1-score 为 0.947。KL1 vs non-KL1 分析中, 各模型 AUC 均约为 0.97–0.98, 提示 FTIR 结合机器学习具有较好的 KL1 快速筛查能力。

结论 本研究表明, 基于 900–1200 cm^{-1} FTIR 光谱并结合机器学习方法, 可实现肺炎克雷伯菌 KL 型别的快速识别。该方法在 KL1 型别筛查中表现良好, 有望作为传统分子分型方法的快速辅助工具, 为高毒力肺炎克雷伯菌的早期识别和临床风险评估提供参考。未来仍需扩大样本量, 并通过独立外部验证进一步评估其临床推广价值。

关键词: 红外光谱, 肺炎克雷伯菌

Analytical Performance of The Xpert Carba-R Assay for Direct Detection of Carbapenemase Genes in Respiratory Specimens From Hospitalized Patients: A Multicenter Evaluation in China

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Background Respiratory tract infections remain

the main sites of carbapenem-resistant Enterobacteriaceae (CRE) infections in China and limited information on enzyme genotypes and subtypes in China is available. In this study, we used whole-genome sequencing (WGS) and the Xpert Carba-R assay for the detection, genotyping and subtyping of CRE genes from respiratory specimens collected from Southeast (Zhejiang, Jiangxi and Fujian Provinces) and Northwest (Gansu Province) regions of China

Methods Respiratory specimens from hospitalized patients clinically diagnosed with pneumonia from seven tertiary hospitals in China from October 2022 to November 2023 were included. The CRE enzyme genes in specimens were directly detected and genotyped by using the Carba-R assay. Carbapenem resistance and genotypes were compared to a referee in combination of phenotypical and genotypical analyses of pure cultures recovered from the respiratory specimen. The CRE enzyme subtypes in isolates were determined by the WGS.

Results A total of 433 respiratory specimens were collected and tested in this study. The Carba-R assay detected 180 blaKPC (41.3%), 64 blaNDM (14.8%), 5 blaIMP (1.2%), 4 blaVIM (0.9%), and 4 blaOXA-48 (0.9%) genes. In comparison to the above referee, the sensitivity and specificity of the Carba-R assay for CRE detection were 100 and 90.4%. While there were no genotype distribution differences between the Southeast and Northwest regions, more KPC subtypes were identified in the Northwest ($n = 5$) than Southeast ($n = 2$) region.

Conclusion The Carba-R assay satisfactorily detected and identified carbapenemase genes directly in the respiratory specimens. A variety of CRE

enzyme genotypes and subtypes were identified in respiratory specimens especially the Northwest region of China.

Keywords

carbapenem-resistant Enterobacteriaceae, genotypes, respiratory specimens, the Xpert Carba-R assay, whole-genome sequencing (WGS)

基于多靶标特异性引物的非结核分枝杆菌快速分子诊断体系建立

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目的 非结核分枝杆菌 (NTM) 感染发病率逐年上升, 传统培养法耗时长 (2-4 周)、阳性率低, 难以满足早期精准诊断需求。本研究针对临床最常见致病的 4 种 NTM 物种——脓肿分枝杆菌脓肿亚种 (*Mycobacteroides abscessus* subsp. *abscessus*)、博莱亚种 (*M. abscessus* subsp. *bolletii*)、马赛亚种 (*M. abscessus* subsp. *massiliense*) 及鸟分枝杆菌复合群 (*Mycobacterium avium* complex, MAC), 设计并建立特异性引物快速分子诊断体系, 为 NTM 感染的早期病原学识别和精准治疗提供技术支撑。

方法 基于 4 种 NTM 物种的物种特异性基因序列, 设计并合成 4 组特异性 PCR 引物。以标准菌株及临床分离株验证引物的特异性与灵敏度。基于 4 种 NTM 物种的物种特异性管家基因及特征性序列差异位点, 运用 Primer Premier 6.0 及 NCBI BLAST 工具设计 4 组特异性 PCR 引物。以标准菌株 (ATCC 19977、ATCC 700686 等) 及实验室保存的临床分离株验证引物的特异性与灵敏度; 构建重组质粒标准品进行梯度稀释, 确定各引物对的检测下限; 以常见呼吸道定植菌及非分枝杆菌病原体 (铜绿假单胞菌、肺炎克雷伯菌、金黄色葡萄球菌、曲霉属等) 评估交叉反应性; 优化 PCR 反应体系及退火温度, 建立标准化检测流程。

结果 4 组引物对目标菌种均呈现单一特异性扩增条带, 与结核分枝杆菌复合群、常见非分枝杆菌呼吸道病原体 (如铜绿假单胞菌、肺炎克雷伯菌、

曲霉等)均无交叉反应,特异性达 100%;检测下限为 10^2 - 10^3 CFU/mL,灵敏度满足临床样本检测需求。

结论 本研究建立的基于 4 种特异性引物的 NTM 快速分子诊断体系,具有快速(2-4 小时)、特异(无交叉反应)、灵敏的优势,显著优于传统培养法。该方法适用于 NTM 感染的早期病原学诊断,尤其对术后迟发性切口感染、免疫低下患者播散性感染等疑难病例具有重要诊断价值,可为临床精准用药及医院感染聚集性事件的快速溯源提供关键技术支撑。

结核病人肺感染肺泡灌洗液中非结核分枝杆菌菌谱分析

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目的 对我院结核病人合并肺感染进行肺泡灌洗液菌种鉴定,了解其中非结核分枝杆菌的流行状况。

方法 回顾性分析天津市海河医院结核病住院病人 2024—2026 年间临床送检的肺泡灌洗液,采用基因芯片分型技术进行菌种鉴定,在送检保本中共检出 696 例非结核分枝杆菌(NTM),其中男性 360 例,女性 336 例,年龄分布在 15 岁-89 岁之间。

结果 3 年间共分离出 696 株非结核分枝杆菌,分别是胞内分枝杆菌、龟/脓肿分枝杆菌、堪萨斯分枝杆菌、偶然分枝杆菌、鸟分枝杆菌、浅黄分枝杆菌、戈登分枝杆菌、蟾蜍分枝杆菌、耻垢分枝杆菌。排在前三位的为胞内分枝杆菌 256 株(占 36.7%);龟/脓肿分枝杆菌 186 株(占 26.7%);堪萨斯分枝杆菌 116 株(占 16.7%)。其中男性多于女性;且年龄 ≥ 60 岁患者 441 例,占 63.3%。

结论 通过对 696 例病例的回顾性病例研究显示,咯血、支气管扩张、肺气肿、肺大泡是 NTM 肺病的独立预测因子,在疑似结核病人肺感染的肺泡

灌洗液中非结核分枝杆菌的菌种分布存在差异,建议临床医生在肺感染的诊断治疗中关注非结核菌的菌种鉴定和 60 岁以上有基础病的人群。同时关注病人免疫状况,由于 NTM 是条件致病菌,存在于环境和污染的水中,机体免疫防御功能受损是其发病的核心前提,另外注重与结核菌病的鉴别诊断,从而更加精准的治疗非结核菌引起的肺内感染性疾病。

The Last Diagnostic Line: Molecular Pathology Uncovers Missed Mycobacterial Infections

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Background Mycobacterial infections remain difficult to diagnose due to nonspecific clinical presentations and the limited sensitivity of traditional microbiological methods, particularly when fresh tissue is unavailable. Applying advanced molecular diagnostic technologies to formalin-fixed paraffin-embedded (FFPE) specimens offers a promising supplementary strategy to extend pathogen detection beyond routine workflows

Methods We present a detailed analysis of two illustrative cases.

Results In the first illustrative case, a non-tuberculous mycobacterial (NTM) infection was initially misdiagnosed as a malignant tumor, leading to surgical resection. The second case involved a patient initially presumed to have lung cancer with suspected metastatic lymphadenopathy, who developed a fever of unknown origin during antitumor therapy; tuberculosis was subsequently identified in the lymph nodes. In both cases, conventional microbiological testing was unavailable

due to the absence of fresh tissue; however, molecular testing of FFPE samples established the diagnosis, through FFPE-based MALDI-TOF MS in one case and FFPE-based PCR in the other.

Conclusion Molecular pathology techniques can serve as a valuable adjunct to routine mycobacterial diagnostics, particularly when fresh tissue is unavailable or culture-based methods are infeasible.

Burkholderia Pseudomallei-Induced Bone Infection: A Case Report and Literature Review

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Objective To improve the awareness of melioidosis among healthcare workers in non-endemic areas by analyzing a case of bone infection caused by *Burkholderia pseudomallei* in a non-endemic region and reviewing relevant literature.

Methods We report a case of lower extremity bone infection due to *B. pseudomallei* in a 71-year-old male farmer who presented with a one-month history of fever and swelling and pain in the left lower limb. The main predisposing factor was previously undiagnosed type 2 diabetes mellitus. Blood cultures at another hospital yielded *B. pseudomallei*, and the patient improved after receiving ceftazidime-avibactam combined with minocycline based on antimicrobial susceptibility results. Following admission, imaging examinations were completed, confirming the diagnoses of melioidosis septicemia and osteomyelitis. The patient continued anti-infective therapy with ceftazidime-avibactam and minocycline hydrochloride, underwent three surgical

interventions, and intraoperative pus specimens were collected for bacterial culture, antimicrobial susceptibility testing, and source tracing

Results Antimicrobial susceptibility testing revealed that the isolate was susceptible to imipenem, tetracycline, ceftazidime, doxycycline, and amoxicillin-clavulanic acid. Whole-genome sequencing confirmed the isolate as *B. pseudomallei*. Multilocus sequence typing (MLST) identified the isolate as sequence type 51 (ST51), and its genome sequence demonstrated close phylogenetic proximity to Asian strains. The patient was hospitalized for 20 days, during which the infection was substantially controlled. At a two-month follow-up visit, the patient remained afebrile without recurrent symptoms, and the lower limb wound exhibited favorable healing. Treatment and follow-up are currently ongoing

Conclusion With climate change and increasing population mobility, the endemic “map” of melioidosis may be expanding. As indicated by the literature review, bone infection is relatively uncommon among melioidosis cases, and diabetes mellitus constitutes the major risk factor for the disease. For patients with underlying conditions such as diabetes who present with atypical severe infections, proactive etiological investigation is essential, and genomic epidemiology can aid in tracing the source of infection. For bone infections caused by *B. pseudomallei*, surgical intervention combined with a full course of antibiotics is the cornerstone of successful management

关键字: *Burkholderia pseudomallei*; osteomyelitis; MLST typing; whole-genome sequencing.

真菌免疫荧光染色技术对多部位侵袭性真菌病病原学诊断价值的回顾性研究

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背景 侵袭性真菌病（IFD）因其高致死率及早期诊断困难而成为临床重大挑战。传统真菌培养法检测周期长、灵敏度不足，尤其在低载量样本及特殊真菌（如马尔尼菲篮状菌）的检测中表现欠佳，严重制约了患者的早期诊疗与预后改善。因此，亟需一种高效、便捷的病原学检测新策略。

方法 本研究采用回顾性分析方法，系统评估了真菌免疫荧光染色技术在多部位 IFD 快速筛查中的诊断价值。共纳入 258 例临床疑似 IFD 患者的各类标本，全面覆盖呼吸道（肺泡灌洗液 197 例、痰液 28 例、鼻拭子 15 例，合计 89.1%）、淋巴结（12 例）、消化道（6 例）、皮肤软组织（2 例）、中耳（1 例）及颅内（1 例）等不同感染部位，标本来源多样，具有良好的临床代表性。

结果 真菌免疫荧光染色技术成功检出了隐球菌、马尔尼菲篮状菌、曲霉菌及念珠菌等多种临床重要致病真菌。

结果 显示，不同部位标本的真菌检出特征存在显著差异，该技术不仅在呼吸道标本中检出稳定，在淋巴结、消化道等非呼吸道少见部位亦成功检出阳性致病菌。此外，不同感染部位呈现特异性菌谱分布，提示病原体具有明显的组织嗜性。

结论 真菌免疫荧光染色技术操作简便、检测快速（30 分钟内完成判读），灵敏度高且适用性广，可有效弥补传统培养法的不足，显著提升 IFD 的早期诊断效率，尤其对少见部位感染及特殊真菌的早期识别具有重要临床价值。未来结合分子诊断技术进一步优化流程，有望降低漏诊率、改善患者预后，具备广泛的临床推广前景。

Metagenomic Sequencing Reveals The Lung Microenvironment in Patients with Nontuberculous Mycobacterial Pulmonary Disease

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Objective To compare the pulmonary microbial community profiles between immunocompromised and immunocompetent patients with nontuberculous mycobacterial lung disease (NTM-PD), identify key microorganisms potentially implicated in co-pathogenesis, and explore the associations between their relative abundances and clinical immunological and inflammatory indices.

Methods A total of 111 sputum samples and 64 bronchoalveolar lavage fluid (BALF) samples were collected from 143 NTM pulmonary disease (NTM-PD) patients with varying immune statuses. Metagenomic next-generation sequencing (mNGS) was performed on these samples. Comprehensive bioinformatics analyses were conducted to characterize and compare the pulmonary microenvironment features of NTM-PD patients across different immune statuses.

Results The α -diversity in sputum samples from the immunocompromised group was significantly lower. Principal Coordinate Analysis (PCoA) of β -diversity for both sputum and BALF samples revealed significant differences between the groups. Linear discriminant analysis Effect Size (LEfSe) identified species enriched in the immunocompromised group. Co-occurrence network analysis indicated that, compared to the control group, the network structure in the immunocompromised group was more complex with more active connections. Mantel tests confirmed that the abundance of these enriched species correlated with the patients' clinical immune-inflammatory indices.

Conclusion Compared with immunocompetent

NTM hosts, immunocompromised patients exhibited reduced pulmonary microbial abundance and diversity. *Pseudomonas aeruginosa* emerges as a notable co-pathogen in immunocompromised NTM-PD patients, warranting further investigation into its interactions with NTM and the host.

Evaluation of MNGS for Antimicrobial Resistance Gene Detection in ICU Patients with Severe bacterial Infections

null null

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Background Given the escalating global health crisis posed by antimicrobial resistance, there is a pressing need for timely and targeted therapeutic approaches to ensure effective clinical treatment. Despite its established role in the culture-independent diagnosis of severe infections, the utility of metagenomic next-generation sequencing (mNGS) for predicting antimicrobial resistance (AMR) is poorly defined. Our study was designed to address this gap by systematically assessing the performance of mNGS for AMR prediction

Methods This retrospective analysis included 115 ICU patients with suspected severe infections treated at Zhongshan Hospital, Fudan University, between January and June 2025, yielding a total of 150 clinical samples. Patients were included if they were aged ≥ 18 years and had available clinical specimens that were processed concurrently by both conventional culture and metagenomic next-generation sequencing (mNGS). These specimens included lower respiratory tract samples, blood, and other sterile fluids. The concordance between antimicrobial resistance (AMR) genes identified by mNGS and phenotypic resistance

profiles from conventional antimicrobial susceptibility testing (AST) was assessed in the subset of samples with culture-confirmed bacterial pathogens and corresponding AST data ($n = 50$ pathogens from 44 patients).

Results When benchmarked against conventional antimicrobial susceptibility testing, mNGS demonstrated variable performance in antimicrobial resistance prediction across different pathogens, antibiotic classes, and sample Type analyzed. In gram-positive bacterial infections, mNGS testing showed a sensitivity of 45% (17–77%) with a specificity of 100% (48–100%). For gram-negative bacteria, the method achieved 49% sensitivity (33–65%) and 94% specificity (81–99%).

Conclusion mNGS demonstrated high specificity but moderate sensitivity for detecting antimicrobial resistance genes across both gram-positive and gram-negative bacteria. Due to this high specificity, a positive result is highly reliable for confirming the presence of a resistance mechanism. Conversely, the method's moderate sensitivity limits its power to rule out resistance, as negative results require confirmation by conventional methods. These findings position mNGS as a valuable complementary tool to traditional susceptibility testing. Furthermore, our study highlights that the current methodologies for detecting and interpreting antimicrobial resistance genes from mNGS data require further refinement.

细菌真菌耐药监测与耐药机制

Emergence of A Fusion Plasmid Carrying RND-type Efflux Pump Gene Cluster TmexCD2-toprJ2, blaNDM-1, and iuc3 in *Klebsiella Pneumoniae* Clinical Isolates

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Background Tigecycline-non-susceptible *Klebsiella pneumoniae* (TNSKP) is a significant global public health threat. The molecular epidemiological characteristics of the novel resistance mechanisms mediated by the mobile RND-type efflux pump gene cluster tmexCD-toprJ remain incompletely understood

Objective Our study aims to investigate the epidemiological characteristics and genetic traits of tmexCD-toprJ in TNSKP.

Methods We collected 980 KP isolates from a tertiary teaching hospital between 2020 and 2021, screening for TNSKP strains by microbroth dilution. Whole-genome sequencing was used to analyze the molecular epidemiological characteristics and resistance mechanisms of TNSKP and to resolve the genetic structure of the plasmid carrying tmexCD-toprJ.

Results We identified 25 TNSKP strains, including 17 CRKP and 8 non-CRKP strains. The tigecycline MIC values were 4 ug/ml (14 strains), 8 ug/ml (9 strains), and 16 ug/ml (2 strains). Multiple resistance mechanisms were detected, including AcrR, RamR, tet(A) mutations, and tmexCD-toprJ. The tmexCD-toprJ gene cluster was found in three strains: ST334 CRKP and ST39 CRKP (both carrying tmexCD2-toprJ2) and ST656 CRKP (carrying tmexCD1-toprJ1). ST39 CRKP also harbored blaNDM-1, tmexCD2-toprJ2, and iuc3 on IncFIB(K), IncU, and IncFII(K) plasmids, with a complete conjugation element.

Conclusion Our research identified multiple complex tigecycline resistance mechanisms in *K. pneumoniae*, including new ST types carrying tmexCD2-toprJ2. A fusion plasmid harboring virulence genes, carbapenem resistance genes, and tigecycline resistance genes was discovered. This study provides new insights into the tigecycline resistance mechanism of tmexCD-toprJ and offers potential therapeutic targets for TNSKP infections.

Keywords Carbapenem-resistant *Klebsiella pneumoniae*; tigecycline, resistance mechanisms, tmexCD-toprJ

Reveal The Expression Profile of SRNAs in CRKP Strains That Produce NDM-1, and Explore The Role of SRNA14 in The Development of This CRKP Resistance.

null null

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The problem of carbapenem antibiotic resistance caused by New Delhi metallo-beta-lactamase-1 (NDM-1) is a global challenge. According to incomplete statistics, the 30-day mortality rate of patients infected with NDM-1-producing *Klebsiella pneumoniae* and other Enterobacteriaceae bacteria is as high as 20-30%, and the detection rate is increasing year by year. Currently, the treatment for NDM-1-resistant infections in clinical practice mainly involves increasing the concentration of antibiotics and using combination therapy. The treatment effect is poor, and new drug resistance mutations are easily emerging. Therefore, in-depth analysis of the regulatory mechanism of NDM-1-related drug resistance, the search for new regulatory targets of drug resistance, and the development of targeted antibacterial

intervention strategies have important theoretical significance and clinical value. In recent years, non-coding small RNAs (sRNAs) have played a key role as important post-transcriptional regulatory factors in the bacterial gene expression regulatory network. More and more studies have shown that sRNAs can participate in various biological processes such as the formation of bacterial drug resistance, stress adaptation, and the expression of virulence factors by regulating the mRNA stability or translation efficiency of target genes. Therefore, exploring the regulatory role of sRNAs in NDM-1-mediated drug resistance is expected to provide a new research perspective for revealing the mechanism of drug resistance formation. In this study, we first used RNA-seq technology to conduct a systematic analysis of the transcriptome expression profiles of clinical isolates of NDM-1-producing *Klebsiella pneumoniae* and carbapenem-sensitive *Klebsiella pneumoniae*. A total of 5098 candidate genes related to NDM-1 resistance were identified, among which 781 were significantly differentially expressed in NDM-1-producing CRKP. These differentially expressed genes were mainly related to bacterial efflux pumps and transporters. Then, by analyzing the lengths and secondary structures of genes that did not match the reference genes and non-redundant protein databases, we obtained 297 sRNAs, among which 9 sRNAs were differentially expressed in NDM-1-producing CRKP. Based on the consistency of the results of RT-PCR experiments with the RNA-seq results, we selected sRNA14 as the key research object. By overexpressing sRNA14 and its predicted target gene *emrD* in the strain, we found that the increase in sRNA14 expression level could regulate the expression of the *emrD* gene, thereby affecting the drug resistance of NDM-1-producing *Klebsiella pneumoniae* to carbapenems. This study reveals a new mechanism of sRNA-mediated drug resistance regulation, providing new molecular evidence for in-depth understanding of

the NDM-1-related drug resistance regulatory network and potentially offering new targets for precise treatment strategies for CRKP infections in clinical practice.

河南某三甲医院耳念珠菌的临床特征、耐药机制及分子特点

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背景 耳念珠菌是一种新型多重耐药真菌病原体,具有高致死率并可引发医疗机构相关疫情,对全球公共卫生构成严重威胁。本研究回顾性分析某三甲医院 18 例耳念珠菌感染或定值患者的临床特征、耐药情况及分子流行病学特征。

方法 回顾性收集 18 例耳念珠菌感染或定值患者的临床资料,包括人口学特征、基础疾病、抗菌药物暴露史、侵入性操作及临床结局。采用微量肉汤稀释法测定耳念珠菌对 9 种抗真菌药物的最低抑菌浓度,并对 8 株菌株进行全基因组测序及单核苷酸多态性分析。

结果 18 株耳念珠菌中 9 株(50%)分离自血液标本,7 株(38.9%)分离自尿液标本。患者的中位年龄为 60 岁,女性占比 38.9%。中位住院时长为 41 天。合并症以高血压(38.9%)、神经系统疾病(38.9%)和心血管疾病(22.2%)为主。55.6% 的患者有既往抗真菌药物暴露史,38.9% 的患者临床结局不佳。药敏试验结果显示所有菌株均对氟康唑耐药(FLC, $MIC_{50/90} = 128/128 \mu g/mL$),8 株测序菌株中均检测到 *ERG11* 基因 Tyr132Phe 突变。一株菌株(5.6%)对两性霉素 B 耐药。所有分离株对 5-氟胞嘧啶、伊曲康唑、伏立康唑、卡泊芬净、米卡芬净、阿尼芬净和泊沙康唑保持较低的 MIC 值。系统发育分析表明耳念珠菌均聚类于东亚进化枝(Clade I)谱系。

结论 本研究中耳念珠菌感染以血流感染为主、半数以上患者具有抗真菌药物暴露史,菌株呈氟康唑全耐药,且属于同一谱系 Clade I,提示加强监测及针对性预防对于遏制耳念珠菌传播至关重要。

Genomic Features and Transmission Dynamics of Carbapenem-Resistant Hypervirulent *Klebsiella Pneumoniae*

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Background The convergence of carbapenem resistance and hypervirulence in *Klebsiella pneumoniae* (CR-HvKp) represents a critical threat to global health, combining the treatment challenges of multidrug resistance with the invasive pathogenicity of hypervirulent strains

Objective This study aimed to elucidate the molecular mechanisms underlying CR-HvKp emergence and to characterize its dissemination through distinct evolutionary trajectories.

Methods We conducted a comprehensive genomic epidemiological analysis of 127 CR-HvKp isolates from a tertiary hospital in China. Representative strains underwent long-read sequencing was employed to characterise plasmid structures. Bayesian phylogeography, integrated with global public data, was utilised to reconstruct evolutionary trajectories and transmission patterns across hosts and geographic locations.

Results The formation of 127 CR-HvKp was primarily driven by the coexistence of multiple plasmids facilitating phenotypic convergence. Carbapenem-resistant *Klebsiella pneumoniae* strains that acquired virulence (hv-CRKP) formation was dominated by ST11-KL64 CRKP lineages acquiring IncHI1B_pNDM-

MAR/repB_KLEB-type virulence plasmids alongside IncFII (pHN7A8)/IncR resistance plasmids. ST11-KL47 hv-CRKP exhibited similar resistance plasmid types but harbored a broader range of virulence determinants. ST11-KL64 hv-CRKP demonstrated strong dissemination potential, with evidence of inter-host and inter-regional spread.

Conclusion CR-HvKp emergence is driven mainly by the horizontal acquisition of virulence plasmids by carbapenem-resistant lineages. ST11-KL64 hv-CRKP represents the dominant clone, capable of cross-host and regional dissemination. Our findings underscore the necessity for integrated genomic surveillance within a One Health framework to curb the global spread of these high-risk bacteria.

Keywords Carbapenem-resistant hypervirulent *Klebsiella pneumoniae*; Evolutionary patterns; Formation mechanisms; Transmission

新生儿败血症合并化脓性脑膜炎的临床特征及危险因素分析

白朝辉

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目的 分析新生儿败血症合并化脓性脑膜炎的临床特征、实验室指标、病原学及危险因素。

方法 回顾性提取我院的败血症新生儿 109 例,将 82 例未合并化脓性脑膜炎新生儿设为 SWM 组,27 例合并化脓性脑膜炎新生儿设为 SPM 组。比较两组新生儿的一般资料,实验室指标,病原学,抗菌药物治疗和临床转归情况及危险因素。

结果 SPM 组新生儿出生时窒息、嗜睡、肌张力异常、前囟饱满、惊厥、发生率高于 SWM 组(均 $P < 0.05$)。SPM 组外周血 C 反应蛋白、脑脊液蛋白、脑脊液有核细胞数水平高于 SWM 组(均 $P < 0.05$)。

从 109 例新生儿中分离 116 株病原菌, SPM 组革兰阴性菌占比为 65.52%, 高于 SWM 组的 42.53% ($\chi^2=4.603$, $P=0.032$)。金黄色葡萄球菌和表皮葡萄球菌对青霉素、红霉素、克林霉素、苯唑西林耐药率均超过 50%; 大肠埃希菌和肺炎克雷伯杆菌对氨苄西林、头孢唑林、四环素、米诺环素、环丙沙星耐药率均超过 50%。SPM 组新生儿临床痊愈率 29.27%, 低于 SWM 组的 51.85% ($\chi^2=4.562$, $P=0.033$)。二分类 logistic 回归分析显示出生时窒息(OR=2.861, 95%CI: 1.018~8.045, $P=0.046$)、惊厥(OR=4.628, 95%CI: 1.392~15.377, $P=0.012$)、脑脊液蛋白 $\geq 600\text{mg/L}$ (OR=3.611, 95%CI: 1.272~10.243, $P=0.017$)、有核细胞数 $\geq 20\times 10^9/\text{L}$ (OR=2.863, 95%CI: 1.048~7.807, $P=0.040$)是新生儿败血症合并化脓性脑膜炎的独立危险因素。

结论 诊断为败血症的新生儿出生时窒息、惊厥、脑脊液蛋白和有核细胞数升高易继发化脓性脑膜炎。

2019-2025 年某院医院感染患者肺炎克雷伯菌的流行病学特征及耐药性分析

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目的 探讨医院感染患者中肺炎克雷伯菌(*Klebsiella pneumoniae*, KPN)的流行病学特征及耐药情况, 为临床合理用药和医院感染防控提供依据。

方法 回顾性收集 2019 年 1 月至 2025 年 12 月广东省人民医院临床患者分离的 KPN 菌株共 4706 株, 采用 VITEK MS 质谱系统及 VITEK 2 Compact 全自动微生物分析仪进行菌株鉴定和药敏试验。分析不同年份 KPN 分离率变化及其标本来源、科室分布和年龄特征, 并比较碳青霉烯耐药肺炎克雷伯菌(carbapenem-resistant *Klebsiella pneumoniae*, CRKP)

与碳青霉烯敏感肺炎克雷伯菌(carbapenem-sensitive *Klebsiella pneumoniae*, CSKP)的耐药差异。

结果 2019-2025 年共检出各类病原菌 45669 株, 其中 KPN 为 4706 株, 总体分离率为 10.30%, 且呈逐年上升趋势($P<0.001$)。菌株主要来源于呼吸道标本(1725 株, 52.36%), 其次为洁净中段尿标本(761 株, 16.17%)和血液标本(406 株, 8.63%)。患者主要分布于重症医学科及心脏重症医学科, >60 岁患者占 51.70%。KPN 对头孢菌素类、 β -内酰胺酶抑制剂及喹诺酮类药物耐药率较高, CRKP 对多数抗菌药物的耐药率显著高于 CSKP($P<0.001$), 呈现明显多重耐药特征。

结论 KPN 在医院感染中的流行水平呈上升趋势, 感染主要集中于呼吸系统、重症相关科室及中老年人群, CRKP 耐药形势严峻。应加强重点科室感染防控措施, 严格落实抗菌药物分级管理与耐药监测, 以遏制耐药菌传播。

关键词: 肺炎克雷伯菌; 医院感染; 碳青霉烯耐药; 耐药性; 流行病学特征

Genomic Insights Into A Multidrug-resistant *Pseudomonas Aeruginosa* ST463 Clinical Isolate Co-harboursing blaKPC-2 and blaNDM-9

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Objective Carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) is a critical pathogen in healthcare-associated infections. In this study, we characterize a clinical *P. aeruginosa* isolate from China that simultaneously harbours blaKPC-2 and blaNDM-9, two clinically important carbapenemase genes.

Methods Strain MZ67-2 was identified using the VITEK MS system, and antimicrobial susceptibility

testing was performed by broth microdilution. Whole-genome sequencing was conducted on the Illumina NovaSeq 6000 platform and assembled using Unicycler (v0.4.7). MLST and antimicrobial resistance gene identification were performed using BacWGSTdb. Phylogenetic relationships between MZ67-2 and other *P. aeruginosa* strains co-harboring blaKPC and blaNDM were inferred by SNP-based analysis and visualized using iTOL.

Results *P. aeruginosa* MZ67-2 was assigned to sequence type (ST) 463 and serotype O4. The isolate exhibited a multidrug-resistant phenotype, showing resistance to all tested antimicrobial agents except colistin. Whole-genome analysis identified a total of 17 antimicrobial resistance genes, including the carbapenemase-encoding genes blaKPC-2 and blaNDM-9. Analysis of the NCBI GenBank database indicates that *P. aeruginosa* strains carrying blaKPC or blaNDM alone are globally prevalent and may serve as reservoirs for the emergence of co-harboring strains. In contrast, isolates carrying both genes remain rare, with only seven cases reported worldwide to date (2020–2025), suggesting an evolutionary shift toward multi-carbapenemase carriage under the selective pressure of novel β -lactam/ β -lactamase inhibitor use.

Conclusion In summary, we report a clinical *P. aeruginosa* isolate from China co-harboring blaKPC-2 and blaNDM-9. The emergence of multi-carbapenemase-producing strains poses a serious threat to antimicrobial therapy, underscoring the need for continuous clinical surveillance.

Keywords *Pseudomonas aeruginosa*; carbapenem resistance; blaKPC; blaNDM; whole-genome sequencing

Genomic Epidemiology and Ceftazidime-avibactam Resistance Mechanism of KPC-3-producing *Pseudomonas Aeruginosa*: A Decade Retrospective Study in China

null null

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Carbapenem-resistant *Pseudomonas aeruginosa* (CRPA), especially KPC-producing *P. aeruginosa* (KPC-PA), is rapidly expanding and posing a serious public health threat. Here, we aim to characterise the epidemiology of KPC-3-producing *P. aeruginosa* in a tertiary hospital over a 10-year period and elucidate the mechanism of ceftazidime-avibactam (CZA) resistance driven by blaKPC-3 to blaKPC-267 mutations in CRPA, along with conducting a global phylogeographic analysis of KPC-3-producing *P. aeruginosa*. All 11 KPC-3-producing CRPA strains in this study belonged to ST1076 and were resistant to ceftazidime, cefepime, meropenem, and imipenem, displaying a multiple-drug resistance phenotype. The blaKPC-267-positive CZA-resistant strain SRMPA3523 was isolated from patient 1 after blaKPC-3-positive *P. aeruginosa* SRMPA1139 and SRMPA1630 were treated with CZA. Whole-genome sequencing indicated that blaKPC-3/267 was located on the Tn6296 transposon contained in the IncP-2 plasmid, which could be transferred into *P. aeruginosa* PAO1Rif. KPC-267 mediates resistance to CZA by reducing the inhibitory effect of avibactam and increasing affinity for ceftazidime. Global analysis indicated that blaKPC-3-carrying *P. aeruginosa* were predominantly in China, America, and Colombia, with ST1076 and ST111 as dominant clones. In conclusion, our study characterised the global phylogeography of blaKPC-3-carrying *P. aeruginosa* and first reported the KPC-267 variant, which converted from KPC-3. This finding highlighted the risk of developing CZA resistance in KPC-PA strains under

therapeutic pressure.

Genomic Epidemiology and Aztreonam-Avibactam Resistance Mechanisms of *Proteus Mirabilis* in China: An Eight-year Retrospective Study

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Background *Proteus mirabilis* has emerged as an important multidrug-resistant opportunistic pathogen, with the production of metallo- β -lactamases (MBLs) being a major contributor to its broad-spectrum resistance. Although the aztreonam-avibactam (ATM-AVI) combination represents a key therapeutic option against MBL-producing Enterobacteriaceae, the mechanisms underlying ATM-AVI resistance in *P. mirabilis* has not yet been reported

Methods A total of 176 multidrug-resistant *P. mirabilis* isolates were collected from a tertiary hospital in China (2017–2024). Antimicrobial susceptibility testing identified ATM-AVI-resistant isolates (MIC $\geq 8/4$ $\mu\text{g/mL}$). Whole-genome sequencing, gene cloning, RT-qPCR, and copy number analyses were used to determine resistance mechanisms. Growth rate assays evaluated fitness costs, and global phylogenetic analysis elucidated evolutionary and dissemination patterns.

Results Twelve isolates (6.8%, 12/176) were resistant to ATM-AVI, all carrying the blaPER-4 gene. Cloning experiments confirmed that blaPER-4 conferred significantly higher ATM-AVI resistance than blaPER-1. Increased resistance correlated with blaPER-4 overexpression and gene copy number amplification.

Whole-genome analysis showed that blaPER-4 was embedded in ISCR1-associated class 1 integrons located on both plasmids and chromosomes, with a strain carrying eight tandem chromosomal copies. These structures likely mediated gene amplification via rolling-circle replication and homologous recombination. Phylogenetic analysis revealed that blaPER-4-positive isolates were mainly associated with the ST135 lineage, suggesting transmission event within hospitals. Global data demonstrated that blaPER-4-carrying *P. mirabilis* strains were predominantly found in China (80%), while blaPER-1 strains were more common in the United States.

Conclusion The blaPER-4-carrying *P. mirabilis*, particularly the ST135 clone, represents a high-risk lineage associated with high-level ATM-AVI resistance mediated by gene overexpression and copy number amplification. This finding highlights a novel mechanism of ATM-AVI resistance and underscores the need for continuous genomic surveillance and rational antimicrobial stewardship to prevent its further dissemination.

Lipid A Modification Profiles of Polymyxin B-Resistant *Klebsiella Pneumoniae*, *Acinetobacter Baumannii*, and *Enterobacter Cloacae* Complex by MALDI-TOF MS

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Background Polymyxins are last-line antibiotics against multidrug-resistant Gram-negative bacteria. Resistance primarily arises from lipid A modifications (e.g., addition of phosphoethanolamine (pETN) or 4-

amino-4-deoxy-L-arabinose (L-Ara4N)), necessitating rapid and accurate detection methods. Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) enables direct analysis of these modifications

Methods A total of 58 non-duplicate, carbapenem-resistant and polymyxin B-resistant clinical isolates (51 *Klebsiella pneumoniae*, 4 *Acinetobacter baumannii*, and 3 *Enterobacter cloacae* complex) collected from Peking Union Medical College Hospital (2023-2024) were analyzed. Lipid A was extracted using an acetic acid-based method and analyzed by MALDI-TOF MS in negative ion mode to identify modification-specific mass shifts.

Results In *K. pneumoniae*, 47 isolates were polymyxin B-resistant and 4 were intermediate. Among the resistant isolates, 15 isolates exhibited modification by both pETN (mass shift +123 Da) and L-Ara4N (mass shift +131 Da). The remaining 32 resistant isolates displayed only L-Ara4N modification, which is chromosomally encoded. In *A. baumannii*, 2 isolates were polymyxin B-resistant and 2 were intermediate. Both of the two resistant isolates exhibited pETN modification. In *E. cloacae* complex, all 3 isolates were polymyxin B-resistant and exhibited L-Ara4N modification, which is chromosomally encoded.

Conclusion MALDI-TOF MS-based lipid A analysis rapidly and accurately identifies polymyxin B resistance mechanisms, revealing distinct, species-specific modification profiles. This method holds promise for enhancing clinical diagnostics and surveillance of resistant clones.

Machine Learning-Based Prediction of Carbapenemase Genotypes in *Klebsiella Pneu-*

moniae Using Routine Antimicrobial Susceptibility Profiles

null null

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Background Differentiating Serine from metallo- β -lactamase (MBL) producers in carbapenem-resistant *Klebsiella pneumoniae* (CRKP) is critical, as MBLs exhibit intrinsic resistance to salvage therapies like ceftazidime-avibactam. We developed a machine learning (ML) pipeline utilizing routine antimicrobial susceptibility testing (AST) data to predict CRKP genotypes and quantitatively investigate the "phenotypic masking" effect in dual-carbapenemase producers

Methods Minimum inhibitory concentration (MIC) profiles of 228 clinical CRKP isolates were analyzed. A dual-level strategy was designed: binary classification for rapid MBL screening and a multiclass strategy to explore phenotypic boundaries. Eight ML algorithms underwent 5-fold cross-validation on the training set (N=182). The top three performing models (Neural Network, Elastic Net, and Random Forest) were subsequently evaluated on an independent, unseen validation cohort (N=46)

Results In the independent validation cohort, all three top-tier models demonstrated highly consistent and robust performance, achieving Area Under the Curve (AUC) values >0.90 for both Serine and MBL prediction tasks. The Random Forest model (MBL AUC = 0.913) was designated as the final model due to its superior biological interpretability. The exploratory multiclass model achieved an overall accuracy of 78.3%. Confusion matrix analysis confirmed a significant "phenotypic masking" effect, where the profound resistance of Class A enzymes frequently obscured the phenotypic signatures of co-produced MBLs in Dual-positive isolates. Feature importance analysis revealed amikacin

and levofloxacin as the most pivotal predictors, reflecting underlying plasmid-mediated co-resistance networks rather than direct β -lactam resistance.

Conclusion ML models utilizing routine AST data serve as highly sensitive, zero-additional-cost screening tools for the early clinical triage of MBL-producing CRKP. However, the inherent phenotypic masking in co-producers establishes a biological ceiling, indicating that AI-based AST screening cannot entirely replace molecular diagnostics for resolving complex dual-carbapenemase genotypes.

四川省儿童碳青霉烯耐药革兰氏阴性菌的流行趋势与耐药性：一项回顾性研究(2021-2025)

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目的 抗菌药物耐药(Antimicrobial Resistance, AMR)是当今全球日益严重的健康威胁之一,通过分析四川省儿童碳青霉烯耐药革兰氏阴性菌(carbapenem-resistant Gram-negative bacteria, CRGNB)的分布情况和对抗菌药物的耐药模式,为本地区临床合理使用抗菌药物和医院感染防控提供依据。

方法 这是一项回顾性研究,采用2021-2025年四川省134家医疗单位的住院儿童(≤ 14 岁)分离到的非重复CRGNB菌株,按统一监测方案进行细菌鉴定、药敏试验。依据美国临床和实验室标准协会CLSI M100S34(2024),CRGNB定义为至少对一种碳青霉烯类(包括亚胺培南、美罗培南和厄他培南)表现为耐药的菌株,使用WHONET 5.6软件进行分析。

结果 共分离出CRGNB菌株2523株,其中男性患儿分离株占比为56.4%(1422/2523), $<28d \sim \leq 1y$ 年龄组分离率最高(41.8%, 1054/2523)。检出

率前5位的依次是肺炎克雷伯菌(41.8%, 1055/2523)、鲍曼不动杆菌(22.1%, 558/2523)、大肠埃希菌(10.0%, 252/2523)、阴沟肠杆菌(9.3%, 235/2523)和铜绿假单胞菌(6.4%, 162/2523),主要来源于呼吸道标本(59.6%, 1504/2523)。肠杆菌目菌株对替加环素、多黏菌素B敏感率超96%,肺炎克雷伯菌对头孢他啶/阿维巴坦敏感率达87.5%;鲍曼不动杆菌仅对多黏菌素B、替加环素耐药率较低(2.3%、2.5%),铜绿假单胞菌对头孢他啶/阿维巴坦、多黏菌素B敏感率为100%。

结论 四川省儿童CRGNB感染形势严峻且具有显著区域特征,婴儿为高危人群。多重耐药菌已对临床治疗构成严重挑战,需要密切关注。

云南省 HIV-1/AIDS 合并马尔尼菲篮状菌病患者抗真菌药敏试验 及临床预后细胞因子分析

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目的 通过体外药敏试验探索马尔尼菲篮状菌的抗真菌药物耐药折点以及判断药敏方法稳定性。

方法 选取我院2019~2023年5年间确诊的AIDS合并TM患者91例作为研究对象,将确诊患者根据预后情况分为预后好和预后差两组。1.对91例患者临床分离菌株进行体外药敏试验统计分析药敏折点。2.检测24例AIDS合并TM患者不同时间段(基线、两周、一个月)血清IL-6、IL-10、IL-2和TNF- α 炎症因子水平,比较与患者中性粒细胞的相关性和不同预后患者存在的差异。

结果 1.91例AIDS合并TM患者男性占比最高为71.43%(65/91);临床表征出现发热的患者最多,占81.32%(74/91)。2.两组患者在CD4+T细胞、AST、TP和ADA分布上差异皆有统计学意义($P<0.05$)。3.棘白菌素类药物ANI、CAS、MIF的

MIC 值相对较高,ANI 的范围是 0.015~4 μ g/mL,CAS 的范围是 0.015~2 μ g/mL, MIF 的范围是 <0.008~>8 μ g/mL;多烯类药物两性霉素 B 的范围是 0.12~1 μ g/mL;三唑类药物 ITR、FLU、VOR、POS 的 MIC 值除了 FLU 之外的 MIC 相对较低,ITR 的范围是 0.008~1 μ g/mL, VOR 的范围是 <0.03~0.12 μ g/mL,POS 的范围是 0.004~0.12 μ g/mL,FLU 的范围是 0.25~32 μ g/mL;FCT 的范围是 0.03~8 μ g/mL。4.24 例患者 IL-6、IL-2、TNF- α 和 IL-10 除 IL-6 预后不好组不同时间段变化差异有统计学意义($P=0.009$),其余细胞因子不同预后情况两组患者细胞因子浓度不同时间段变化和两组之间每个时间段浓度均无统计学差异($P>0.05$)。

结论 1.对于 CD4 计数小于 50 cells/ μ L 的患者,应高度警惕包括 TM 在内的机会性感染。预后差的患者相比预后好的患者 CD4 偏小、AST 偏大、TP 偏大、ADA 偏小,且预后差的患者伊曲康唑使用率低于预后好的患者,治疗时间不足的患者预后差,提示临床对上述指标异常的患者用药时加强对临床症状和实验室指标的监控,用伊曲康唑巩固治疗能显著提高患者预后。2.药敏结果提示艾滋病合并马尔尼菲篮状菌病患者使用两性霉素 B、伊曲康唑、伏立康唑、泊沙康唑、卡泊芬净进行抗真菌治疗,不易出现耐药。

2020-2024 年四川省老年患者血流感染病原菌的分布及耐药性

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目的 了解四川省 2020 年至 2024 年老年患者血流感染病原菌的分布特点及其对抗菌药物的耐药性。

方法 采用四川省 134 家医疗机构(三级医院 113 家,二级医院 21 家),老年患者(≥ 65 岁)血液

标本中分离的非重复病原菌,按统一监测方案进行细菌鉴定、药敏试验。所得结果依据美国临床和实验室标准协会(CLSI) M100 解释,使用 WHONET 5.6 软件进行分析。研究时段划分:2020—2022 年为新冠疫情流行期,2023—2024 年为后疫情时期,用于分析疫情对多重耐药菌(Multidrug-resistant organisms, MDR)及泛耐药菌(pan-drug-resistant organisms, PDR)流行的影响。

结果 2020 年至 2024 年,从老年患者血液标本中共分离到 65603 株菌,其中革兰阳性菌 23350 株(35.6%),革兰阴性菌 42253 株(64.4%)。检出率前五位的是大肠埃希菌(38.4%)、肺炎克雷伯菌(12.6%)、人葡萄球菌(6.6%)、表皮葡萄球菌(6.0%)和金黄色葡萄球菌(5.8%)。主要的肠杆菌目中,大肠埃希菌对厄他培南、亚胺培南、美罗培南耐药率分别为 0.8%、0.9%、0.9%,保持高度敏感,肺炎克雷伯菌对碳青霉烯类耐药率在 6.7%~8.4%之间;对头孢曲松耐药率分别为 49.3%、25.5%。铜绿假单胞菌对亚胺培南和美罗培南的耐药率分别为 9.8%和 8.6%;鲍曼不动杆菌对亚胺培南和美罗培南的耐药率分别为 54.5%和 60.2%。耐甲氧西林的金黄色葡萄球菌(MRSA)和凝固酶阴性葡萄球菌(MRCNS)检出率分别为 29.1%、70.8%,未发现万古霉素耐药的葡萄球菌。泛耐药菌(PDR)检出情况:检出泛耐药鲍曼不动杆菌(PDRAB)126 株,占比 11.2%(126/1124),未检出泛耐药肠杆菌目细菌与泛耐药铜绿假单胞菌。多重耐药菌的检出呈锯齿状分布,后疫情时期碳青霉烯耐药鲍曼不动杆菌(CRAB)、碳青霉烯耐药肺炎克雷伯菌(CRKP)检出率较疫情期显著上升($P<0.05$)。

结论 2020 年至 2024 年,四川省老年患者血液分离菌种类多样,新冠疫情后碳青霉烯类耐药菌负担有所上升,为 ICU 等重点科室带来防控与治疗挑战。各医疗机构应持续加强本地区细菌耐药监测,为临床合理选用抗菌药物提供依据,同时加强院内感染防控,以遏制耐药菌的扩散。

纹带棒杆菌临床分离株耐药-毒力耦联特征及 SrtA 介导生物膜形成促进协同致病的机制研究

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目的 纹带棒杆菌近年来已成为免疫功能低下患者及导管/植入物相关感染的重要条件致病菌，但其耐药分子谱、毒力因子分布及耐药-毒力协同增强机制尚不明确。本研究旨在系统解析纹带棒杆菌临床分离株的耐药表型与基因型特征、毒力因子谱及生物膜形成能力，并阐明 SrtA 在协同致病中的分子作用，为精准防控和靶向干预提供依据。

方法 收集 2022 年 1 月至 2025 年 6 月本院分离的非重复纹带棒杆菌 272 株，经 MALDI-TOF MS 联合 16S rRNA 测序鉴定。采用微量肉汤稀释法检测 12 种抗菌药物敏感性；全基因组测序分析耐药基因、毒力相关基因及 MLST 分型；结晶紫染色法评价生物膜形成能力，并通过细胞黏附/侵袭实验和巨噬细胞杀伤实验评估体外毒力；建立小鼠导管相关感染模型验证体内致病性。进一步构建 srtA 敲除株及回补株，结合转录组测序明确其调控机制。

结果 272 株纹带棒杆菌主要来源于痰液、血液、导管尖端和伤口分泌物，多重耐药率为 78.49%，对青霉素、氨苄西林和红霉素耐药率均超过 90%，对万古霉素、利奈唑胺和达托霉素均保持 100% 敏感。耐药表型与 erm(X)、blaCg、tet(W) 及 gyrA/parC QRDR 区突变高度一致，符合率达 95.35%。全基因组共检出 21 种毒力相关基因，其中 fimA、srtA、dlt 操纵子和 sitA 携带率均超过 80%；多重耐药株毒力基因携带率显著高于非多重耐药株 ($P < 0.001$)。72.09% 的菌株可形成生物膜，且强生物膜形成株的多重耐药率、黏附侵袭能力及小鼠体内定植负荷均显著高于弱/无生物膜株 (均 $P < 0.001$)。srtA 敲除后，菌株生物膜形成量下降 89.2%，黏附素表达及 β -内酰胺酶活性显著减弱，青霉素 MIC 下降 8~16 倍；回补

后上述表型部分恢复。转录组结果提示，SrtA 可能通过调控表面蛋白锚定、生物膜基质合成及药物应激响应网络，介导耐药与毒力的协同增强。

结论 纹带棒杆菌临床分离株具有显著的多重耐药特征及广泛的毒力因子携带背景，生物膜形成是其耐药与毒力协同增强的关键表型。SrtA 作为连接表面蛋白锚定、生物膜构建与协同致病的重要枢纽，可能成为该菌感染防治的新型靶点。本研究为纹带棒杆菌院内感染的精准防控及抗菌策略优化提供了实验依据。

关键词： 纹带棒杆菌；多重耐药；毒力因子；生物膜；SrtA；协同致病

A Long-stay Inpatient As A “hub” for Inter-species IncI2 Plasmid Transfer and Clonal Spread of The Mcr-1 Colistin Resistance Gene

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Background Infections caused by colistin-resistant bacteria have limited treatment options and high patient mortality. Bacteria carrying the mcr-1 gene are the major reservoirs of colistin resistance. The pathway by which mcr-1 transmits and spreads among hospitalized patients needs to be clarified to prevent its dissemination

Methods Consecutive Enterobacterales isolates were collected from a tertiary teaching hospital from 2016–2019, and the prevalence of Enterobacterales carrying mcr-1 was examined. Patient Z (long-stay on a multiple patient ward) was confirmed as a carrier of mcr-1-positive Enterobacterales. Clinical samples were

collected continuously to track transmission of *mcr-1*.

Results From February 2016–March 2019, 866 strains of Enterobacterales with a MIC for colistin ≥ 2 $\mu\text{g}/\text{mL}$ were collected, and 52 strains (*Escherichia coli*, $n=42$; *Klebsiella aerogenes*, $n=9$; *Klebsiella quasivariicola*, $n=1$) were *mcr-1* positive by PCR; of these, 37 strains were isolated from the patient Z. *E. coli* and *K. aerogenes* were ST2599 and ST56, respectively. The first *mcr-1*-positive *K. aerogenes* isolate was obtained from a sputum sample from patient Z at 29 days after her first admission, and *E. coli* and *K. quasivariicola* carrying *mcr-1* were isolated from a fecal sample 3 days later. All three strains carried a $\sim 66\text{-kb}$ IncI2 plasmid containing *mcr-1*; all plasmids were genetically identical. In addition, the plasmids were stable in recipients, suggesting interspecies transmission. Nine *E. coli* ST2599 strains from other patients carried the same *mcr-1* gene, indicating clonal transmission of *mcr-1*-positive bacteria within the ward. Genome sequencing revealed that the plasmid also contained the *stbAB* and *blaCTX-M-199* genes (*stbAB* is responsible for plasmid replication and segregation). Continuous administration of cefoperazone-sulbactam to patient Z during hospitalization might have promoted selection, maintenance, and transmission of the resistant IncI2 plasmid carrying *mcr-1*.

Conclusion A single inpatient can be a hub for either interspecies plasmid transmission or clonal spread of *mcr-1*-mediated colistin resistance, which could result in accelerated dissemination of resistance within a hospital. It is necessary to strengthen screening of *mcr-1*-positive strains, and to take appropriate infection control measures to tackle endemic colistin resistance

The Sensitivity of Ribosomal Central

Branches and Its Therapeutic Significance in RmtB-positive Carbapenem-resistant Klebsiella Pneumoniae

null null

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Background Plasmid-encoded 16S rRNA methyltransferase, particularly *rmtB*, has disseminated widely in carbapenem-resistant *Klebsiella pneumoniae* (CRKP), compromising the efficacy of aminoglycosides. Eravacycline (ERA), a novel synthetic tetracycline derivative, is designed to overcome classical tetracycline resistance; however, its evolutionary interplay with aminoglycoside susceptibility remains unclear

Objective This study aimed to investigate the collateral relationship between ERA resistance and aminoglycoside susceptibility in *rmtB*-positive CRKP and to elucidate the underlying molecular mechanisms and therapeutic potential of combination therapy.

Methods ERA-resistant derivatives were generated by stepwise induction. Collateral sensitivity (CS) was assessed in vitro and in vivo. Whole-genome sequencing, transcriptomics, and proteomics were integrated with *rmtB* gene manipulation. Molecular docking and kinetic simulations were performed to explore ribosome–drug interactions. Therapeutic efficacy was evaluated using time-kill assays and lung infection models in *Galleria mellonella* larvae and mice.

Results Acquisition of high-level ERA resistance restored aminoglycoside susceptibility in *rmtB*-positive CRKP, revealing a robust directional CS phenotype. ERA resistance was associated with enhanced virulence without apparent fitness cost. Multi-omics analysis identified *rmtB* as a regulatory hub, with reduced expression under increasing ERA pressure alongside reprogramming of efflux activity, iron metabolism, and energy pathways. Structural modeling suggested

that ERA-induced conformational remodeling of 16S rRNA may impair rmtB-mediated methylation, facilitating aminoglycoside re-entry. ERA combined with amikacin exhibited strong synergistic activity and improved survival in vivo.

Conclusion These findings uncover a ribosome-centered collateral sensitivity axis linking ERA resistance and aminoglycoside susceptibility, supporting evolution-guided combination strategies against high-level aminoglycoside-resistant CRKP.

Surveillance for Invasive Candidiasis in China (CHIF-NET 2018-2021): Rising Antifungal Resistance Observed in A Nationwide Longitudinal Study

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Background Invasive candidiasis (IC) is a severe infection primarily affecting immunocompromised patients and is associated with high mortality and substantial hospital costs. Accurate regional data on epidemiology and antifungal resistance of IC are crucial for effective clinical management

Methods The China Hospital Invasive Fungal Surveillance Net (CHIF-NET) study is a laboratory-based multicenter study initiated in August 2009. This report presented updated data from August 2017 to December 2021, involving 76 hospitals across 28 provincial regions in China, and included a 12-year longitudinal analysis. Isolates from patients with IC were assigned to species level by MALDI-TOF MS and ITS rDNA sequencing. Susceptibility testing was performed for nine antifungal agents using the broth microdilution method.

Results A total of 11679 *Candida* isolates were collected. *C. albicans* was the most common *Candida* species (46.0%), followed by *C. tropicalis* (17.6%), *C. parapsilosis sensu stricto* (15.6%), and *C. glabrata sensu stricto* (11.2%). Antifungal resistance rates showed notable variations among different *Candida* species, with the highest azole resistance observed in *C. tropicalis* isolates causing candidemia (42.5% to fluconazole and 38.9% to voriconazole). Cross- and multi-drug resistance to azoles and echinocandins was observed in all predominant *Candida* species.

Conclusion The species distribution of major *Candida* pathogens causing IC remained stable in China, while antifungal resistance increased, especially among non-*albicans* *Candida* species. Enhanced surveillance, accurate species identification, and strengthened antifungal stewardships are needed to address the growing challenge of antifungal resistance.

Assessment of Eravacycline Antimicrobial Susceptibility in China During The First Year Following Regulatory Approval (2023–2024): A Real-World Study

null null, Yi Li, Meng-Lan Zhou, Ran Jing, -Ya Lu,
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Eravacycline, a novel fluorocycline antimicrobial, was approved by China's National Medical Products Administration (NMPA) in March 2023; however, clinical breakpoints and real-world data on its use in China remain limited. We conducted a retrospective, questionnaire-based analysis of eravacycline use across 21 provinces in China during the first year after NMPA approval (September 2023–September 2024). Data from 3369

patients who received eravacycline were collected. We analyzed the distribution of pathogens and specimens, reported in vitro susceptibility to eravacycline, imipenem, meropenem, tigecycline, and polymyxins and evaluated microbiological outcomes. *Acinetobacter baumannii* (52.0%, 1259/2419) and *Klebsiella pneumoniae* (26.1%, 631/2419) were the most commonly reported pathogens. High levels of carbapenem resistance were observed: 704 of 771 (91.3%) for *A. baumannii* and 323 of 392 (82.4%) for *K. pneumoniae*. In contrast, susceptibility to eravacycline was 95.5% (737/772) and 92.5% (297/321), respectively. Microbiological outcomes suggested potential activity against these resistant isolates, though post-treatment culture data were limited. This study demonstrates that eravacycline exhibited potent in vitro activity against prevalent carbapenem-resistant Gram-negative pathogens in real-world Chinese clinical practice during its first-year post-approval. Continuous monitoring of eravacycline resistance trends, together with prospective studies that correlate microbiological and clinical outcomes in specific infection types, will be crucial for defining its long-term therapeutic utility and the risk of resistance emergence.

Global Epidemiological Survey and Genomic Analysis of Multiple Carbapenemases-producing *Citrobacter Freundii*

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Objectives Carbapenem-resistant *Citrobacter freundii* (CRCF) has emerged as a growing global health concern, as it is increasingly implicated in human infections and recognized as an important reservoir of clinically significant antimicrobial resistance determinants. Although *C. freundii* carrying single carbapenemase genes has been widely reported, systematic global analyses of isolates harboring multiple carbapenemase genes remain limited

Methods *Citrobacter* spp. isolates were recovered and antimicrobial susceptibility testing was determined using the broth microdilution method. We further conducted a comprehensive genomic analysis of multi-carbapenem-producing *C. freundii* (MCP-CF). Whole-genome sequencing data were used to characterize the carbapenemase gene profiles, multilocus sequence types (MLST), phylogenetic relationships, geographic distribution, and plasmid replicon compositions.

Results Through antimicrobial susceptibility testing, all MCP-CF isolates exhibited extensive resistance to β -lactams, with partial resistance to tigecycline but retained susceptibility to colistin. From the global perspective, MCP-CF isolates occurred at a low frequency but spanned multiple sequence types and geographic regions. Carbapenemase gene combinations predominantly comprised blaKPC and blaNDM and were associated with plasmids of heterogeneous replicon backgrounds. Phylogenetic analysis indicated that these isolates were phylogenetically dispersed rather than clonally related.

Conclusion Our findings demonstrate the capacity of *C. freundii* to acquire and disseminate multiple carbapenemase genes and reveal the widespread, yet under-recognized, distribution of these highly resistant strains. Continuous genomic surveillance and integrated

analyses of public genomic data are essential for improving early detection and informing effective infection control and antimicrobial stewardship strategies.

某中医院耐碳青霉烯类肺炎克雷伯菌感染的临床危险因素及基因组特征研究

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背景 耐碳青霉烯类肺炎克雷伯菌 (CRKP), 尤其是高毒力多重耐药菌株, 已成为医院获得性感染的重要病原菌, 且致死率较高。目前, 国内中医院 CRKP 感染的分子特征及死亡相关危险因素仍缺乏深入研究。

方法 对 2019-2022 年某三级中医院经微生物学确诊的 CRKP 感染患者开展回顾性研究, 采用多因素 logistic 回归分析院内死亡的独立危险因素。对 2022 年分离的 102 株 CRKP 菌株进行全基因组测序, 分析其耐药决定因子、毒力因子及系统发育关系。

结果 本研究共纳入 233 例 CRKP 感染患者 (死亡 76 例, 存活 157 例)。多因素分析显示, 院内死亡的 4 项独立预测因素为: 多器官功能障碍综合征 ($aOR=3.69$, 95% CI: 1.28~10.61; $P=0.015$)、脓毒症 ($aOR=3.04$, 95% CI: 1.30~7.12; $P=0.011$)、有创机械通气 ($aOR=5.95$, 95% CI: 2.78~12.75; $P<0.001$) 及入住 ICU ($aOR=4.10$, 95% CI: 1.55~10.84; $P=0.005$)。

基因组分析显示, 优势克隆株为 ST11-KL64 (55.9%) 和 ST15-KL19 (21.6%), 同时检出新型菌株 ST1658-KL60 与 ST3345-KL8。最常见质粒为 IncFIB (K) (85.3%), 其次为 IncHI1B (66.7%); IncFII (pHN7A8) (28.4%) 仅见于 ST11 型菌株。主要荚膜型为 KL64:O2a。碳青霉烯耐药主要由 blaKPC-2 介导 (92.2%, 94/102)。除优势野生型 blaKPC-2 外,

本研究还发现 2 种变异体: 1 株携带 blaKPC-33, 1 株携带新型 blaKPC-2 变异体, 其 Ω 环结构域存在 L169T (CTG→ACG) 氨基酸替换, 可介导头孢他啶 - 阿维巴坦耐药。82 株 (80.4%) 菌株为高毒力株 (毒力评分 4 分), 特征为同时携带气杆菌素 / 沙门菌素与耶尔森菌素 (以 ybt 9/ICEKp3 为主), 但不携带大肠菌素。

结论 本研究显示, 中医院内 CRKP 以 ST11-KL64 和 ST15-KL19 克隆株为优势流行型, blaKPC-2 为主要碳青霉烯耐药基因。高毒力与多重耐药为其普遍特征, 是导致高致死率的重要原因。上述结果提示, 中医院需制定针对性的感染防控与治疗策略。

关键词: 肺炎克雷伯菌; 死亡危险因素; 全基因组测序; 毒力因子; blaKPC-2 变异体

One Clone, Three Faces: Clonal ST11 Klebsiella Pneumoniae with Discordant Phenotypes Across Blood and Urine Isolates

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Background In recurrent infection, abrupt changes in colony morphology, carbapenemase testing, or antimicrobial susceptibility are often interpreted as evidence of strain replacement. In the setting of antimicrobial resistance, this assumption may misdirect both antimicrobial selection and infection prevention decisions

Case presentation We describe a long-term inpatient with recurrent infection from whom three sequential ST11 *Klebsiella pneumoniae* isolates were recovered from blood and urine. Over time, the isolates showed marked phenotype discordance: the first was

hypermucoviscous, string-test positive, Carba NP KPC-positive, and carbapenem resistant; the second was string-test negative, Carba NP negative, and showed a transient carbapenem susceptibility window; the third remained string-test negative but reverted to KPC positivity and carbapenem resistance. All isolates were identified by MALDI-TOF mass spectrometry, underwent repeat confirmation of decision-relevant susceptibility results, and were assessed by Carba NP. Core-genome SNP analysis supported clonality across episodes and argued against acquisition of an unrelated strain

Conclusion This case shows that major shifts in morphology, carbapenemase phenotype, and carbapenem susceptibility can occur within a single clonal ST11 *Klebsiella pneumoniae* lineage. For antimicrobial stewardship and infection prevention, recurrent isolates showing abrupt phenotype discordance should prompt repeat susceptibility confirmation, rapid carbapenemase testing, and, when clinically consequential, relatedness adjudication before reinfection is assumed.

Discordant Carbapenemase Mechanisms Detected within A Single BALF Specimen in Longitudinal CRKP Carriage: A Case Report

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Background Treatment of carbapenem-resistant *Klebsiella pneumoniae* (CRKP) is highly dependent on the underlying carbapenemase mechanism. In critically ill or long-term hospitalized patients, routine single-colony workflows may fail to detect within-specimen heterogeneity, potentially leading to misinterpretation of key therapeutic windows. We report a longitudinal

CRKP case in which discordant carbapenemase mechanisms were recovered from the same bronchoalveolar lavage fluid (BALF) specimen, challenging a previously reasonable mechanism-based treatment assumption

Case presentation An 82-year-old man with chronic obstructive pulmonary disease, cerebrovascular disease, severe hypertension, hypothyroidism, and Alzheimer's disease had been continuously hospitalized since April 2023 and experienced recurrent pulmonary infectious exacerbations with repeated antibiotic exposure. In January 2025, rectal screening yielded CRKP (KPRS-1, ST1326/KPC), which was susceptible to ceftazidime-avibactam (CAZ-AVI). In May, the same lineage was re-isolated from BALF (KPBAL-2, ST1326/KPC) with an identical susceptibility profile, supporting persistent carriage with cross-site re-detection. During a further relapse in November, BALF collected on the same day yielded two CRKP isolates with distinct mechanisms and lineages: KPBAL-3A (ST147/NDM) and KPBAL-3B (ST1326 with KPC+NDM features). Both were resistant to CAZ-AVI, indicating a clinically important shift in the presumed therapeutic window. Whole-genome relatedness analysis showed high clonality among the three ST1326 isolates (KPRS-1, KPBAL-2, and KPBAL-3B). The laboratory promptly communicated the discordant carbapenemase results and recommended multi-colony verification and repeat typing, prompting reassessment of the prior KPC-based therapeutic pathway

Conclusion This case shows that CRKP recovered from a single respiratory specimen may not reflect a single resistance mechanism. In high-risk settings such as intensive care, relapse, or poor clinical response, multi-colony verification combined with rapid carbapenemase typing can uncover clinically meaningful heterogeneity and prevent overestimation of CAZ-AVI activity. Mechanism-informed interpretive reporting

may help align antimicrobial decisions more closely with the true resistance profile.

RBT5 在白念珠菌生物膜耐药中的作用及靶向策略研究

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目的 白念珠菌极易形成高度耐药的生物膜，导致感染迁延反复，是临床治疗的重大挑战。RBT5 在菌丝形成过程中被激活，前期单细胞测序分析发现 RBT5 在白念珠菌生物膜中具有重要作用。本研究拟明确 RBT5 在生物膜形成中的作用，并以此为靶点筛选抗生物膜药物。

方法 单细胞测序分析 RBT5 在白念生物膜形成过程中的作用；构建 RBT5 缺失株，XTT 减低法评价 RBT5 缺失对生物膜唑类耐药性改变，转录组分析 RBT5 缺失后生物膜核心基因表达谱的改变，代谢组学分析 RBT5 缺失后生物膜核心代谢网络的改变，ICP-MS、压力平板试验、线粒体膜电位、ROS、ATP 含量检测等验证其作用机制；虚拟筛选、分子模拟及体内外验证明确靶药疗效。

结果

1、scRNA-seq 表明 RBT5 在生物膜晚期终末分化中具有关键作用（图 1）。

2、RBT5 缺失可逆转白念珠菌生物膜唑类耐药（表 1）。

3、RBT5 缺失驱动菌丝极性生长模式重塑，诱导形成过度延伸、机械稳定性显著降低的细长菌丝表型，使生物膜发育晚期出现网络架构疏松化的结构缺陷（图 2）。

4、RBT5 缺失破坏白念珠菌细胞内金属离子稳态，补充锌、铁可恢复其耐药性（表 2-4）。

5、转录组分析表明金属离子稳态、线粒体复合体组装、氧化应激、细胞壁功能、抗氧化能力等生

物学过程显著富集（图 3）。

6、RBT5 缺失降低白念珠菌线粒体膜电位及 ATP 含量，抑制线粒体功能，增加胞内 ROS 含量，降低其抗氧化能力（图 4）。

7、代谢组学揭示 RBT5 缺失驱动细胞内代谢重排，具体表现为糖酵解增强和 TCA 循环减弱（图 3）。

8、虚拟筛选及分子模拟明确靶药，体内外验证其靶向结合 Rbt5 逆转生物膜唑类耐药（图 5）。

结论 本研究揭示 RBT5 通过破坏白念珠菌金属离子稳态，抑制线粒体呼吸链功能，驱动生物膜能量代谢模式由氧化磷酸化向糖酵解转变，进而改变生物膜发育过程与结构架构成熟，并利用靶药结合 RBT5 逆转生物膜唑类耐药。研究结果为临床治疗白念珠菌生物膜相关感染提供新靶点与新策略。

关键词：RBT5；线粒体呼吸链；氟康唑耐药；代谢重编程；抗真菌靶点

Genomic Insights Into The Evolution of The IncP-2 Plasmid Harboring Multiple Antimicrobial Resistance Genes in XDR *Pseudomonas Aeruginosa* PAMS

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Objective Multidrug-resistant *Pseudomonas aeruginosa* (*P. aeruginosa*) poses a major threat to global public health, particularly strains carrying IncP-2 plasmids, which present significant challenges to clinical treatment. This study aims to elucidate the genetic basis of the extensively drug-resistant *P. aeruginosa* strain PAMS and the molecular evolution of the IncP-2 plasmid pPAMS

Methods An extensively drug-resistant *P. aeruginosa* strain, designated PAMS, was identified through antimicrobial susceptibility testing. Whole-genome sequencing revealed that PAMS carries an IncP-2 plasmid, designated pPAMS. Genetic structure analysis of this plasmid was performed, and its conjugative transfer ability was assessed through conjugation experiments. Additionally, the impact of plasmid pPAMS on bacterial virulence was investigated using a *Galleria mellonella* larval infection model

Results pPAMS contains two multidrug resistance integrons (In786 and In1237), an RND efflux pump gene cluster (**tmexCD3-toprJ3**), and a tetracycline resistance gene (*tet(C)*). The resistance region of pPAMS shares high similarity with the previously reported plasmids pPA1609-475 and pBM413, exhibiting an identical genetic structure but lacking the genetic element IS26-*tetR(C)*-*tetA(C)*-IS26. Furthermore, pPAMS possesses a unique ~20 kbp variable region, which may be associated with bacterial strain competitiveness. Conjugation experiments and antimicrobial susceptibility testing demonstrated that pPAMS could be transferred into *P. aeruginosa* PAO1, conferring a multidrug-resistant phenotype. Virulence assays indicated that plasmid pPAMS reduces bacterial pathogenicity

Conclusion This study elucidates the genetic basis of the extensively drug-resistant *P. aeruginosa* strain PAMS and the molecular evolution of plasmid pPAMS, suggesting that this plasmid may suppress the expression of virulence factors while mediating multidrug resistance

真菌性角膜炎致病菌谱与药敏变迁及那他霉素、两性霉素 B 滴眼液疗效对比分析

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目的 总结 2019-2024 年真菌性角膜炎致病菌分布及药敏试验结果,比较 2021-2024 年 5%那他霉素(NAT)与 0.1%两性霉素 B (AmB)滴眼液治疗真菌性角膜炎的临床疗效,分析抗菌药物有效率与药敏结果变化的关系。

方法 本研究采用双队列历史性研究设计。首先,回顾性收集 2019-2024 年在河南省立眼科医院诊治的真菌性角膜炎(FK)患者资料,包括眼前段照相+角膜荧光染色、共焦显微镜(IVCM)、角膜刮片、真菌的培养及鉴定、抗真菌药敏试验结果,以总结致病菌谱与体外药物敏感性变迁。其次,基于本中心 2021-2024 年临床诊疗数据库,构建历史性队列,纳入经裂隙灯显微镜、眼前段照相+角膜荧光染色、IVCM 及角膜刮片检查确诊且符合基线标准的 FK 患者,根据临床实际诊疗方案分为 NAT 组和 AmB 组。通过病历系统回顾性采集真菌的培养鉴定、药敏结果及随访资料。统计两种抗真菌药物疗效,比较不同年份间药物敏感性与有效率的变化,并分析二者的关联性。

结果 2019 年至 2024 年间,本中心共诊治 1784 例 FK 患者。致病菌属分布以镰刀菌属感染为首位,其次为曲霉菌属和链格孢菌属,其他菌属总计 32 株。药物敏感性方面,NAT 对常见致病真菌的年均最低抑菌浓度(MIC)由 3.05 μ g/mL 升高至 13.70 μ g/mL;而 AmB 的年均 MIC 从 15.17 μ g/mL 下降至 2.63 μ g/mL。历史性队列共纳入 2021 年至 2024 年期间于本中心诊治且符合标准的 559 例真菌性角膜炎患者。临床疗效分析表明,NAT 组有效率分别为 70.1%、63.1%、52.2%和 50.0%,总体疗效比较差异无统计学意义($\chi^2=7.532, p=0.057$),但线性趋势分析提示其疗效呈逐年下降趋势。与之相反,AmB 组有效率分别为 47.1%、62.2%、64.8%和 69.9%,总体疗效比较差异有统计学意义($\chi^2=8.538, p=0.036$),且其疗效呈现逐年上升趋势($\beta=0.300, p=0.007$)。相关性分析进一步显示,NAT 组有效率与其对应常见

病原菌的年均 MIC 值呈负相关($\beta=-0.099, p=0.008$)。同样, AmB 组有效率亦与其年均 MIC 值呈负相关($\beta=-0.084, p=0.004$)。

结论 真菌性角膜炎分离菌株对那他霉素敏感性降低, 对两性霉素 B 的敏感性升高, 体外药敏结果与临床疗效相关。

碳青霉烯耐药鲍曼不动杆菌的临床分布与耐药性分析

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目的 分析 2023 年 1 月至 2025 年 9 月本院碳青霉烯耐药鲍曼不动杆菌(CRAB)的临床分布、耐药性变迁及感染危险因素,为临床防控提供依据。

方法 采用回顾性研究方法,收集 2023 年 1 月至 2025 年 9 月临床分离的 1852 株鲍曼不动杆菌(AB),分析 CRAB 的检出率、人群分布、科室及标本来源特征,并进行药敏试验。采用单因素及多因素 Logistic 回归分析 CRAB 感染的独立危险因素。

结果 CRAB 总体检出率为 78.0%(1445/1852),各年度检出率均高于 75%,持续处于高位流行。感染主要集中于重症医学科(37.8%)、胃肠结直肠外科(14.4%)和呼吸内科(10.3%),其中呼吸内科 CRAB 构成比呈上升趋势(从 2023 年 6.9%升至 2025 年 16.0%)。标本以痰与肺泡灌洗液为主(75.6%)。药敏结果显示,CRAB 对多数 β -内酰胺类及氟喹诺酮类药物维持极高耐药率(>97%),对替加环素敏感率逐年上升至 78.1%,对黏菌素始终保持高度敏感(>98.6%)。单因素分析显示,CRAB 组在男性比例、痰与肺泡灌洗液、脓液及脑脊液标本来源,重症医学科、胃肠结直肠外科、创伤骨科及整形外科的科室分布,以及合并心脏疾病、肺部疾病、手术史、创伤骨科疾病和消化系统疾病的比例均显著高于碳青霉烯敏感的鲍曼不动杆菌 CSAB 组(均 $P<0.05$)。多因素分析显示,恶性肿瘤

是 CRAB 感染的独立危险因素($OR=3.009$)。

结论 本院 CRAB 流行形势严峻,耐药负担重,治疗选择有限。恶性肿瘤患者是 CRAB 感染的高危人群,应加强对重点科室的感染控制、规范抗菌药物使用并推进基于药敏的个体化治疗。

Clinical Relevance and Transmission Dynamics of KPC and NDM Co-producing Carbapenem-resistant *Klebsiella Pneumoniae* in China: A Multicentre Case-control and Genomic Epidemiological Study

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Background KPC and NDM co-producing carbapenem-resistant *Klebsiella pneumoniae* (KN-CRKP) is an escalating global health threat with limited treatment options

Methods Here, we conducted a multicentre retrospective case-control study on KN-CRKP in China (2020–2025), collecting 3012 non-duplicated CRKP isolates, of which 71 (2.4%) were KN-CRKP. For clinical analysis, 39 patients with KN-CRKP infections were identified from 71 isolates and matched in a 1:2 ratio with 78 patients infected by KPC-2-producing CRKP. For global analysis, we retrieved 100,141 genomes from GenBank, of which 662 non-redundant KN-CRKP sequences were combined with our 71 KN-CRKP isolates. Antimicrobial susceptibility testing, whole-genome sequencing (WGS), plasmid transfer and stability, fitness cost, transcriptomics and Bayesian phylogeography were used to investigate evolution mechanisms and molecular epidemiology of KN-CRKP strains

Findings Among the infected patients, hospital-acquired or ventilator-associated pneumonia was the

most common (41.0%, 16/39). Patients with KN-CRKP infections had a non-significantly higher 28-day mortality (38.5%, 15/39) than the KPC-CRKP control group (24.4%, 19/78; $p = 0.133$), but a significantly higher in-hospital mortality (46.2%, 18/39 vs. 25.6%, 20/78; $p = 0.036$). Independent risk factors included diabetes, a history of CRO (carbapenem-resistant gram-negative organism) infection treated with ceftazidime-avibactam (CZA) treatment, and recent use of β -lactam/ β -lactamase inhibitor combinations. All KN-CRKP isolates were resistant to carbapenems and CZA, but exhibited highly susceptible to colistin (98.6%), cefiderocol (94.4%), and aztreonam-avibactam (100%). The predominant KN-CRKP clones were ST11 (73.2%) and ST307 (15.5%). Global surveillance of 733 global KN-CRKP identified ST11 as a pandemic lineage diverging into China/Brazil subclusters, with emerging clones ST147/ST307 showing post-pandemic increases. Plasmid profiling revealed blaNDM mainly on IncX3/IncN plasmids and blaKPC on IncR/IncFII plasmids, with novel hybrid plasmids carrying both carbapenemases identified. blaNDM-carrying plasmids had higher transferability/stability than blaKPC-carrying ones. In vitro experiments confirmed blaNDM transfer from *Citrobacter freundii* to blaKPC-carrying *K. pneumoniae*, forming KN-CRKP.

基于“同源-异源”转录组学模型解析多重耐药鲍曼不动杆菌对依拉环素的非敏感机制

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目的 多重耐药鲍曼不动杆菌(MDRAB)对新四环素类药物依拉环素(ERV)的非敏感现象日益

引起临床关注。本研究旨在通过构建具备严格对照关系的“同源-异源”代表性菌株体系,精准剥离遗传噪音,初步解析MDRAB对ERV非敏感的分子机制。

方法 采用微量肉汤稀释法对29株临床分离MDRAB进行ERV敏感性筛查。结合多位点序列分型(MLST),选取ERV非敏感株Ab26(ST368)作为核心研究对象,并平行引入其同源敏感株AbH117(ST368)与异源敏感株AbH119(ST381),构建对照模型。运用全基因组测序(WGS)解析耐药与毒力本底;通过转录组测序(RNA-seq)执行多组交叉比对,筛选核心差异表达基因(DEGs),最后以RT-qPCR进行验证。

结果 表型与基因组特征分析显示,ERV对绝大多数受试株(96.6%)保持良好活性,仅Ab26表现出显著非敏感($MIC=4 \mu g/mL$)。WGS分析证实三株菌均携带blaOXA-23、armA等核心耐药基因,但Ab26相较于两株敏感菌并未表现出特异性获得性四环素耐药基因或经典外排泵的扩增,提示其非敏感表型主要源于转录调控。进一步的转录组比较通过三株菌交叉过滤,成功排除了株系特异性的遗传背景噪音,精确锁定了140个核心DEGs。功能与通路富集分析表明,与AbH117和AbH119两株敏感菌相比,Ab26发生了显著的代谢重编程:其跨膜转运系统、呼吸链及能量代谢相关通路整体下调,而氧化还原反应及外源物质代谢通路显著上调。随后,RT-qPCR结果确证了Ab26中外膜蛋白基因(ompA、carO)及16S rRNA甲基转移酶基因(rsmD)的表达量均显著高于同源株AbH117与异源株AbH119($P<0.05$)。其中,rsmD的异常高表达介导了核糖体30S小亚基靶点的甲基化修饰,显著降低了ERV的结合亲和力。

结论 本研究的“同源-异源”对照模型,有效克服了单一临床株比对的缺陷。研究表明,MDRAB对ERV的非敏感性并非依赖经典的外排泵过度激活,而是通过“代谢与转运抑制-膜结构代偿性稳定-核糖体靶点甲基化修饰”的多维协同实现。这一发现为突破新型四环素类抗生素耐药壁垒及优化多靶点

联合用药策略提供了分子依据。

Molecular Characterization of Two Conjugative Resistance Plasmids From A Clinical Multidrug-resistant ST15 *Klebsiella Pneumoniae* in China

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The increasing emergence of multidrug-resistant (MDR) *Klebsiella pneumoniae* strains has become a threat to public health, and it is important to understand the mechanisms underlying adaptive evolution. In this study, we characterized a clinical MDR isolate of *K. pneumoniae*, designated KPA1, which belongs to sequence type 15 (ST15), along with its two associated resistance plasmids, pKPA1-1 and pKPA1-2. Conjugation assays demonstrated that both plasmids were capable of self-transfer. Notably, pKPA1-1 could be transferred to both *K. pneumoniae* and *Escherichia coli*, while pKPA1-2 exhibited a restricted transfer capability, being transferable only to *K. pneumoniae*. Antimicrobial susceptibility testing, along with plasmid stability assays, indicated that the resistance spectrum of pKPA1-2 similar to that of pKPA1-1, and pKPA1-2 was more stable than pKPA1-1. In addition, virulence assays revealed that the acquisition of either plasmid resulted in a reduction in bacterial pathogenicity. This study elucidates the molecular characterization of conjugative resistance

plasmids pKPA1-1 and pKPA1-2. These findings shed light on the adaptive mechanisms underlying multidrug resistance in *K. pneumoniae*.

Suboptimal Ceftazidime-avibactam Exposure Drives Sequential blaKPC Mutations and Intra-host Coexistence of *Klebsiella Pneumoniae* Harboring Distinct Variants Leading To Persistent Infection

null null, Fu-Pin Hu

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Objectives KPC-producing *Klebsiella pneumoniae* infections are a rising global health threat. The factors driving blaKPC mutations during treatment and their contribution to infection persistence remain unclear. This study characterized blaKPC evolution under reduced-dose ceftazidime-avibactam therapy for renal impairment, using ten sequential *K. pneumoniae* isolates (showing resistance shifts) collected from a single patient during a persistent infection

Methods Antimicrobial susceptibility was determined by broth microdilution. Whole-genome sequencing was used to investigate blaKPC evolution. Time-kill assays assessed bactericidal and selective effects. Plasmid transformation and cloning assays validated blaKPC phenotypes. Molecular docking was used to investigate the binding affinity and structural changes of the KPC enzyme caused by different blaKPC variants

Results Four blaKPC subtypes (blaKPC-2, blaKPC-33, blaKPC-71, and blaKPC-145) were identified. Functional validation confirmed that blaKPC-2 conferred carbapenem resistance, while the three variants mediated ceftazidime-avibactam resistance. Trac-

ing their evolutionary trajectory revealed seven sequential mutation events during dose-adjusted ceftazidime-avibactam and carbapenem therapy, ultimately yielding the four observed subtypes. These mutations appeared to accumulate stepwise from blaKPC-2 to blaKPC-33 (D179Y) and blaKPC-145 (D179Y, T264A), which progressively increased ceftazidime-avibactam MICs. Molecular docking predicted variant-specific alterations in avibactam binding. Time-kill assays showed that 1×MIC/sub-MIC ceftazidime-avibactam suppressed but failed to eradicate the blaKPC-2-harboring isolate, potentially facilitating blaKPC-2 evolution. Multiple blaKPC variants coexisted within the same specimen, indicating intra-host heterogeneity. These reversible blaKPC mutations disappeared after eight days of combined imipenem and ceftazidime-avibactam therapy. Meropenem-vaborbactam, imipenem-relebactam, and aztreonam-avibactam showed in vitro activity against both KPC- and KPC variant-producing isolates

Conclusion In conclusion, suboptimal ceftazidime-avibactam exposure may promote sequential blaKPC-2 mutations and intra-host variants coexistence, driving persistent infection. These findings highlight the urgent need for improved therapeutic strategies against KPC/KPC variant-producing strains

Distinct Effects of GES Variants on Ceftazidime-avibactam and Imipenem-relebactam Resistance in Carbapenem-resistant *Pseudomonas Aeruginosa*: A Ten-year Retrospective Study

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Ceftazidime-avibactam (CZA) and imipenem-relebactam (IMR) are β -lactam/ β -lactamase inhibitor combinations active against carbapenem-resistant *Pseudomonas aeruginosa* (CRPA), yet resistance to these agents is increasingly reported. In this study, 916 CRPA isolates collected from 2016 to 2025 were screened for blaGES by PCR, and fifty isolates were identified as blaGES-positive. Five subtypes were detected, including GES-1 (68%), GES-5 (24%), GES-7 (2%), GES-15 (4%), and a novel variant, GES-69 (2%). Antimicrobial susceptibility testing by broth microdilution revealed distinct resistance patterns. Isolates carrying blaGES-1, blaGES-7, blaGES-15, and blaGES-69 showed elevated CZA MICs, whereas blaGES-5 was associated with increased IMR MICs. Cloning experiments and structural modeling suggested that substitutions at position 170, Ω -loop conformational changes, and alterations in residues such as E104 may affect substrate binding and inhibitor interactions. Whole-genome sequencing showed that blaGES variants were located on the chromosome within class 1 integrons embedded in Tn6485-like transposons. Analysis of publicly available genomes further indicated that blaGES-positive isolates were mainly associated with the high-risk clone ST235, were distributed across multiple Gram-negative species with *P. aeruginosa* as the predominant host and exhibited an expanding cross-species distribution. In summary, these findings demonstrate that subtype-specific variation in GES enzymes is likely to shape the activity of β -lactam/ β -lactamase inhibitor combinations within a conserved ST235 background.

Genomic Characterization of A Novel KPC-243-Producing Carbapenem-Resistant *Pseudomonas Aeruginosa* ST463 Strain

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Background Carbapenem-resistant *Pseudomonas aeruginosa* (CRPA), particularly the high-risk clone ST463, poses a serious threat in China. The emergence of ceftazidime-avibactam (CZA) resistance further limits therapeutic options. Novel KPC variants often drive CZA resistance, yet many restore carbapenem susceptibility. Here we characterize a new KPC variant, KPC-243, which confers dual resistance to carbapenems and CZA without losing carbapenemase activity

Methods A clinical CRPA isolate (CRPA3310) was obtained from a patient with prolonged CZA exposure. Antimicrobial susceptibility testing (AST) was performed by broth microdilution. Whole-genome sequencing (WGS) using Illumina and Nanopore platforms, followed by hybrid assembly and bioinformatic analysis, was used to identify resistance genes, plasmid features, and virulence determinants. Cloning experiments in *P. aeruginosa* PAO1 were conducted to assess the resistance phenotype conferred by blaKPC-243 compared to blaKPC-2.

Results CRPA3310 exhibited a multidrug-resistant profile, including resistance to meropenem (MIC ≥ 128 $\mu\text{g/mL}$), imipenem (≥ 128 $\mu\text{g/mL}$), and CZA (>128 $\mu\text{g/mL}$), while remaining susceptible only to colistin and amikacin. A novel blaKPC variant, designated blaKPC-243, was identified, showing 98.65% nucleotide identity to blaKPC-2. It encodes a tandem four-amino-acid insertion (Arg-Ala-Pro-Asn) at positions 269–272 of KPC-2, located within the Lys270 loop (a known mutational hotspot for CZA resistance). Cloning experiments confirmed that KPC-243 confers high-level CZA resistance (MIC >128 $\mu\text{g/mL}$, >128 -fold increase over KPC-2) while retaining resistance to mero-

penem (32 $\mu\text{g/mL}$) and imipenem (8 $\mu\text{g/mL}$). Multi-locus sequence typing assigned CRPA3310 to ST463. The blaKPC-243 gene was carried on a non-conjugative plasmid (pCRPA3310_KPC) within a Tn*6296* transposon structure. This plasmid showed high homology to prevalent blaKPC-2-harboring plasmids circulating in clinical ST463 isolates across China. Structural modeling suggests that the four-amino-acid insertion alters the Lys270 loop, likely impairing avibactam binding while preserving carbapenemase activity.

Conclusion This is the first report of a novel KPC variant, KPC-243, in a clinical CRPA ST463 isolate. KPC-243 confers dual resistance to carbapenems and CZA without regaining carbapenem susceptibility, a unique phenotype that severely restricts treatment options. The emergence of such a variant in a globally disseminated high-risk clone underscores the urgent need for enhanced molecular surveillance and new therapeutic strategies against evolving KPC enzymes.

Keywords Ceftazidime-avibactam; KPC-243; ST463; carbapenem-resistant *Pseudomonas aeruginosa*; dual resistance

Strain-specific Outer Membrane Vesicle-mediated Transfer of BlaOXA-24-like Plasmid in *Acinetobacter Baumannii* Restricts Cross-Species Dissemination

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The rapid rise of multidrug-resistant *Acinetobacter* spp. poses a major global health threat. In *Acinetobacter baumannii*, carbapenem resistance is frequently mediated by OXA-type carbapenemases encoded by

blaOXA-24-like genes, including blaOXA-72. Outer membrane vesicles (OMVs) are nanoscale proteoliposomes secreted by Gram-negative bacteria that can facilitate plasmid transfer, yet the mechanisms limiting their dissemination remain unclear. Nationwide screening of 2,880 *Acinetobacter* clinical isolates identified 10 strains carrying blaOXA-24 and blaOXA-72 plasmids across three species (*A. baumannii*, *A. pittii*, and *A. berziniae*). Sequencing revealed nine distinct plasmids, most bearing a Rep₃ C-module backbone with blaOXA-pdif resistance modules (9/10). Clinical strains produced significantly higher OMV protein levels than the laboratory strain ATCC 17978 ($P < 0.01$). OMVs from A2485 transferred the blaOXA-72 plasmid to ATCC 17978 at 1.9×10^{-7} per CFU, exceeding direct supernatant transfer (3.2×10^{-8} per CFU), and conferred resistance to meropenem, ceftazidime, and cefoperazone/sulbactam. Transfer was strictly donor-specific, with no transmission observed across 13 non-*A. baumannii* strains, and recipient strains failed to retransmit the plasmid, indicating a strong cross-species barrier and a non-reciprocal, donor-dependent process. Although all strains produced intact OMVs and encapsulated plasmid DNA, packaging efficiency varied considerably by host (~ 4.5 – 28.6 ng/ μ g). Strains with DNA loading (17978E/17978V: 28.62 and 23.98 ng/ μ g) equal to or exceeding that of donor A2485 (13.62 ng/ μ g) remained incapable of transfer. These findings demonstrate that dissemination is constrained by host-specific, post-packaging barriers rather than packaging efficiency, thereby limiting resistance spread to specific lineages while enabling localized adaptation.

Global Genomic Insights Into blaNDM-1 Dissemination and Plasmid Diversity in *Acineto-*

bacter Soli: A Retrospective Genomic Epidemiology Study

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Acinetobacter soli, traditionally regarded as an environmental bacterium, has increasingly emerged as a clinically relevant non-*baumannii* *Acinetobacter* species and a potential host for the dissemination of high-risk antimicrobial resistance genes. However, its role in blaNDM-1 dissemination remains poorly understood. We identified 35 blaNDM-1-positive *A. soli* isolates from 6,422 clinical *Acinetobacter* isolates collected from three hospitals in Zhejiang Province, China, and integrated them with global genomes and a public blaNDM-1-carrying plasmid database. Most isolates were recovered from urine samples (45.71%, 16/35) and showed high-level resistance to meropenem and imipenem ($\text{MIC}_{50} > 128$ mg/L). Phylogenetic analysis showed marked heterogeneity, with isolates distributed across multiple branches and six global clades, while low-SNP clusters (SNPs < 10) indicated local clonal expansion. Long-read sequencing identified five major blaNDM-1-carrying plasmid backbones, all harboring conserved Tn125-like transposons. These plasmid lineages accounted for 43.60% of blaNDM-1-carrying plasmids in *Acinetobacter*, with the pR4WN lineage increasing from 2019 to 2025. Only pSU1904NDM and pR4WN plasmids were transferable, and pR4WN showed higher transfer frequency, greater stability, and a more complex multidrug resistance structure. blaNDM-1 dissemination in *A. soli* is jointly driven by local clonal expansion and plasmid-mediated horizontal transfer, highlighting environmental *Acinetobacter* species as important reservoirs and vectors of carbapenem resistance. Continuous genomic surveillance of high-risk plasmid lineages across environmental and clinical

interfaces is warranted within a One Health framework.

高毒力耐碳青霉烯类肺炎克雷伯菌的耐药机制、毒力特征与感染防控研究进展

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目的 耐碳青霉烯类肺炎克雷伯菌 (CRKP) 与高毒力肺炎克雷伯菌 (hvKP) 曾是两条独立的威胁路径——前者以广泛的耐药性困扰临床, 后者可在健康人群中引发侵袭性感染。然而, 近年来两类菌株的“汇合”催生了兼具高毒力与碳青霉烯耐药性的高毒力耐碳青霉烯类肺炎克雷伯菌 (CR-hvKP), 这一被称为“超级细菌”的病原体对公共卫生构成了严峻挑战。传统观点认为毒力与耐药性之间存在进化权衡, 但 CR-hvKP 的出现打破了这一认知边界。本文旨在系统综述 CR-hvKP 的进化路径、耐药与毒力共存的分子机制、临床感染特征以及当前的防控策略, 为临床识别与感染控制提供参考。主要发现: CR-hvKP 主要通过三条进化路径形成: 一是高毒力菌株获得携带碳青霉烯酶基因的质粒; 二是耐药菌株获得携带毒力基因的质粒; 三是经典菌株同时获得携带耐药与毒力基因的融合质粒。在耐药机制方面, CR-hvKP 主要是产生碳青霉烯酶 (如 KPC、NDM、OXA-48 型等), 同时常伴有外膜孔蛋白缺失 (OmpK35/OmpK36) 及外排泵过表达, 导致对碳青霉烯类、头孢菌素类等多种抗生素的高度耐药。值得注意的是, 部分菌株已表现出对替加环素和多黏菌素这类药物的耐药性。在毒力方面, CR-hvKP 保留并强化了 hvKP 的核心毒力因子: 高黏表型主要由 *rmpA/rmpA2* 基因调控, 而气杆菌素 (由 *iuc* 基因簇编码) 和沙门菌素 (*iro* 基因簇) 等铁载体系统则是其高侵袭力的关键驱动因素。临床研究显示, CR-hvKP 感染与更高的死亡风险相关, 尤其在血流感染和 ICU 患者中更为突出, 但不同研究间因高毒力定

义标准 (表型拉丝试验与基因型检测) 的差异, 效应量估计存在显著异质性。在感染防控层面, 传统医院感染控制措施面临挑战, 噬菌体疗法、纳米颗粒等新型治疗策略仍处于探索阶段, 耐药风险尚未完全明确。

结论 CR-hvKP 的涌现标志着肺炎克雷伯菌已跨越“耐药”与“毒力”的进化边界, 形成了兼具二者优势的双重威胁病原体。当前对其进化动态和传播规律的认识仍不完整, 标准化诊断体系的缺失制约了精准防控。未来研究应聚焦于: 完善高毒力菌株的分子诊断标准以指导临床早期识别; 基于“全健康”理念加强医院与城市污水系统的联合监测; 探索新型抗菌药物及联合治疗方案。面对这一快速演化的病原体, 构建整合分子监测、精准诊断与分层防控的综合策略已刻不容缓。

A Cryptic Reservoir of Carbapenem Resistance: Plasmid-driven Emergence of A Novel Leclercia Lineage with A Highly Stable IncX3-blaNDM-1 Plasmid

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Background Leclercia is an under-recognised genus within Enterobacterales. Although NDM-type carbapenemases are widely disseminated, the role of Leclercia remains poorly defined

Methods A carbapenem-resistant Leclercia isolate (CRL4619) from a patient with lung cancer was characterised by antimicrobial susceptibility testing and whole-genome sequencing (WGS). The blaNDM-1-bearing plasmid was analysed using comparative genomics and phenotypic assays, including conjugation, stability, fitness, and biofilm formation. Publicly available Leclercia genomes were included for phylogenetic

and resistance ecology analyses.

Results CRL4619 was resistant to carbapenems and multiple β -lactams but remained susceptible to tigecycline (0.25 mg/L), colistin (<0.125 mg/L), ciprofloxacin (<0.125 mg/L), amikacin (8 mg/L), and aztreonam (2 mg/L). Although MALDI-TOF MS identified the isolate as *L. adecarboxylata*, genome-based analysis showed 84.4%–91.3% ANI and 26.7%–43.2% dDDH, supporting its classification as an undescribed lineage. The blaNDM-1 gene was located on a ~44.9-kb IncX3 plasmid (pCRL4619-NDM), identical to a plasmid identified in a *Citrobacter freundii* isolate from the same healthcare system in 2021 and closely related to IncX3-NDM plasmids reported internationally since 2013. The plasmid transferred efficiently to *Escherichia coli* J53 and remained fully stable after 10 days without antibiotic selection (150/150 colonies retained blaNDM-1), with no measurable fitness cost. CRL4619 exhibited limited biofilm-forming capacity. Analysis of 426 *Leclercia* genomes showed that the genus is predominantly environmental and carries diverse resistance determinants. Although blaNDM-1–IncX3 plasmids have been reported in a limited number of isolates within the major *L. adecarboxylata* lineage (Clade III), their occurrence in the newly identified Clade II lineage appears rare, suggesting cross-lineage dissemination of a conserved epidemic plasmid.

Conclusion This study reports, to our knowledge, the first identification of a blaNDM-1-carrying IncX3 plasmid in a clinical isolate belonging to an undescribed *Leclercia* lineage. This finding expands the distribution of the globally circulating IncX3-NDM platform across diverse genetic backgrounds and highlights *Leclercia* as a potential under-recognised reservoir of carbapenem resistance. Despite limited biofilm formation, infection in this case suggests that host susceptibility and healthcare exposure may outweigh classical virulence traits. Overall, these findings are more

consistent with a plasmid-mediated horizontal gene transfer-driven dissemination pattern, suggesting that resistance genes may circulate across diverse genetic backgrounds rather than being confined to specific clonal lineages.

Keywords *Leclercia*; blaNDM-1; IncX3; carbapenem resistance; horizontal gene transfer

Genomic Epidemiology and Mechanisms of Colistin Resistance in Carbapenem-resistant *Pseudomonas Aeruginosa*

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Objectives To determine the prevalence, clinical and molecular epidemiology, antimicrobial resistance determinants, and chromosomal mechanisms underlying colistin resistance in carbapenem-resistant *Pseudomonas aeruginosa* (CRPA), with particular emphasis on validating the contribution of mutations in two-component regulatory systems to colistin resistance

Methods A total of 557 non-duplicate CRPA isolates were collected and tested for colistin susceptibility by broth microdilution. Colistin-resistant CRPA (ColR-CRPA) isolates were further characterized by antimicrobial susceptibility testing, collection of clinical data, whole-genome short-read sequencing, phylogenetic analysis, multilocus sequence typing, serotyping, resistance gene profiling, and comparative analysis of mutations in resistance-associated chromosomal loci. Candidate mutations in *pmrA*, *pmrB*, *phoP*, and *phoQ* were introduced into *P. aeruginosa* PAO1 by allelic exchange, followed by MIC determination, disk diffusion testing, qPCR of lipid A modification-associated genes, and

time-kill assays

Results Among 557 CRPA isolates, 23 (4.1%) were colistin-resistant, with MICs ranging from 4 to 32 mg/L. These isolates exhibited multidrug resistance and high rates of resistance to ceftazidime and ceftazidime-avibactam (both 91.3%), whereas aminoglycosides retained the greatest in vitro activity. Most patients were from the ICU (56.5%), had prior exposure to carbapenems (78.3%) and colistin (56.5%), and showed poor outcomes, including a 30-day mortality of 47.8%. Genomic analysis revealed marked diversity, with 20 sequence types among 23 isolates; only ST235 and ST1236 showed low pairwise SNP distances suggestive of possible nosocomial transmission. All isolates carried multidrug-resistant determinants, including diverse β -lactamases and frequent disruptive mutations in *ampD*, *mexR/mexZ*, *nalC/nalD*, and *oprD*. No *mcr* genes were detected. Mutational analysis of colistin resistance-associated loci showed frequent substitutions in *pmrAB*, *parRS*, *phoQ*, and lipid A modification genes. Functional validation demonstrated that *pmrA* Q109K, *pmrB* L107P, and *phoQ* V260G increased the colistin MIC of PAO1 to 2–4 mg/L, while reversion of *pmrA* Q109K or *phoQ* V260G in clinical isolates reduced MICs from 32 to 4 mg/L. These mutations significantly upregulated *arnB* and *pmrA* expression and conferred reduced killing by colistin in time-kill assays

Conclusions Colistin resistance among CRPA was uncommon but clinically significant, being associated with multidrug resistance, substantial genetic heterogeneity, possible limited hospital transmission, and poor patient outcomes. In the absence of transferable *mcr* genes, colistin resistance was primarily driven by chromosomal mechanisms. Our findings identify *pmrA* Q109K, *pmrB* L107P, and *phoQ* V260G as functionally important mutations contributing to colistin resistance through activation of lipid A modification pathways in *P. aeruginosa*

Emergence of Cefiderocol Resistance Mediated by BlaAFM-1 Overexpression and FptA Mutations in Clinical Carbapenem-Resistant *Pseudomonas Aeruginosa* Isolates

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Objectives This study evaluated the in vitro activity of cefiderocol against clinical carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) isolates in China prior to its clinical introduction, and investigated the mechanisms underlying resistance

Methods A total of 557 non-duplicate CRPA isolates were collected from central China between 2021 and 2024. Antimicrobial susceptibility testing, whole-genome sequencing, transcriptional and functional assays, enzyme kinetics, molecular docking, and site-directed mutagenesis were performed to identify molecular determinants of cefiderocol resistance

Results Among the antibiotics tested, cefiderocol exhibited the highest in vitro activity against CRPA (99.10% susceptible), comparable to North America and Europe (99.23%). However, a modest rightward shift of MIC distribution was observed, with MIC ≥ 1 mg/L occurring more frequently in China (13.64% vs. 8.90%; $P = 0.0026$). MLST revealed extensive diversity (203 STs), with ST235 being the predominant lineage (19.93%). Notably, ST266 isolates displayed markedly reduced susceptibility compared to ST235 ($P < 0.001$) and uniquely co-harbored *blaAFM-1* and *blaIMP-45*. Functional assays indicated that *blaAFM-1* overexpression was a major driver of cefiderocol resistance, in-

creasing MICs to 16 mg/L. Long-read sequencing localized blaAFM-1 to an IncP-2 plasmid, and the elevated expression observed in cefiderocol-non-susceptible isolates was associated with increased gene copy number instead of promoter variation. Kinetic assays showed that AFM-1 exhibited higher catalytic efficiency against cefiderocol than NDM-1, and molecular docking predicted a strong binding affinity (-9.2 kcal/mol) between cefiderocol and AFM-1. Whole-genome sequencing of isolates with cefiderocol MICs ≥ 2 mg/L further revealed frequent alterations in iron-uptake systems, ampC, and efflux pump regulators. Reversion of the FptA G273R substitution restored cefiderocol susceptibility (MIC reduction from 16 to 4 mg/L) and reactivated iron-uptake pathways

Conclusions Cefiderocol remains highly active against CRPA in China; however, resistance can emerge through diverse mechanisms even without prior exposure. Early molecular surveillance will be crucial to ensure its rational use and sustained clinical efficacy

Keyword: *Pseudomonas aeruginosa*; cefiderocol; resistance; blaAFM-1; FptA.

临床分离 1 株具有侵袭性生长表型的特殊肺炎克雷伯菌分子特征研究

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背景 肺炎克雷伯菌 (*Klebsiella pneumoniae*, Kp) 的毒力表型演化具有多样性, 本研究针对一株分离自高龄多发伤合并糖尿病患者的特殊 Kp 菌株 (K1498) 进行研究, 该菌株在血平板上表现出独特的侵袭性生长特征。

方法 通过结晶紫法、刚果红实验评估其生物膜和胞外多糖合成能力; 利用大蜡螟及 CD1 小鼠模

型评价其体内致死力; 通过转录组测序及致病因子数据库 (VFDB) 对比, 分析其毒力基因特征。

结果 K1498 表现出独特的侵袭血平板生长且无法分离的表型, 其生物膜和胞外多糖产量均弱于标准高毒力菌株 NTUH-K2044。动物实验证实其毒力水平处于中等, 不属于典型高毒力菌株 (hvKp)。分子水平上, K1498 具有与 NTUH-K2044 不同的荚膜合成簇 (galF、wzi 等基因在 2044 中缺失), 且其 lpxC (TPM=10896)、SodB (TPM=6766) 和 OmpA (TPM=4071) 呈现超高水平表达。

结论 K1498 的侵袭性生长现象并非依赖其生物膜或胞外多糖合成, 而可能与其独特的荚膜组分及其高表达的粘附基因与应激适应相关基因的高表达有关, 这可能是由于该菌株在慢性病 (糖尿病) 宿主微环境下发生的特异性进化。

可调控双靶向配体-受体相互作用介导自聚集策略实现多重耐药细菌的广谱杀菌作用

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目的 多重耐药细菌感染已成为临床抗感染治疗中的重要挑战, 传统抗菌药物常面临抗菌谱受限、耐药快速产生以及对休眠菌和持留菌杀伤不足等问题。配体-受体相互作用介导的自聚集策略可通过受体识别诱导分子聚集, 放大局部多价相互作用, 从而增强杀菌活性并降低耐药发生风险。本研究旨在构建一种具有化学可调性的双靶向 LiRISA 抗菌平台, 使其同时识别革兰阴性菌外膜脂多糖 (LPS) 和细菌胞内 DNA, 从而实现对革兰阴性菌和革兰阳性菌的广谱、高效杀菌。

方法 以二精氨酸类肽模拟物 P1 为基础骨架, 对连接子和末端疏水区进行结构优化, 设计合成系列衍生物。采用等温滴定量热法评价化合物与 LPS、

DNA 的结合能力, 利用 Nile Red 探针、动态光散射和流式颗粒分析表征 DNA 或 LPS 诱导的自聚集行为, 并结合分子动力学模拟、核磁共振氢谱和透射电子显微镜解析其作用机制。进一步通过最低抑菌浓度、杀菌动力学、连续传代耐药诱导、细胞毒性、溶血实验及动物感染模型评价先导化合物的抗菌活性、安全性和体内治疗效果。

结果 经结构优化获得先导化合物 4a。与原始分子相比, 4a 对 LPS 的结合能力显著增强, 结合焓提高 211.5%, LPS 亲和力提高 3.9 倍, 同时保持良好的 DNA 结合能力和自组装性能。4a 可被 DNA 和 LPS 双重诱导发生自聚集, 其 DNA 诱导临界聚集浓度为 11.7 $\mu\text{g/mL}$, LPS 诱导临界聚集浓度为 10.5 $\mu\text{g/mL}$, 均明显低于其自身聚集浓度 46.0 $\mu\text{g/mL}$ 。体外抗菌结果显示, 4a 对多重耐药临床分离菌具有快速而强效的杀菌活性, 并能有效抑制耐药产生。机制研究表明, 4a 在革兰阴性菌表面可通过 LPS 诱导形成聚集体, 破坏外膜屏障并导致膜通透性增加、膜电位崩溃和胞质内容物泄漏; 在革兰阳性菌中则主要进入胞内并通过 DNA 诱导聚集发挥杀菌作用。4a 对哺乳动物细胞和红细胞毒性较低, 并在小鼠创面感染、单菌腹膜感染及革兰阳性/阴性混合腹膜感染模型中显著降低细菌负荷、改善生存率并促进创面愈合。

结论 本研究建立了一种可调控的双靶向 LiRISA 抗菌小分子平台。先导化合物 4a 通过 LPS 诱导的细菌表面聚集和 DNA 诱导的胞内聚集, 实现了对革兰阴性菌和革兰阳性菌的广谱杀菌, 并表现出抑制耐药、清除休眠菌和滞留菌以及良好体内安全性的综合优势。该策略为多重耐药细菌感染治疗提供了新的分子设计思路和潜在候选药物。

Combined Antimicrobial Susceptibility Testing Using Broth Disk Elution Method for BlaNDM-producing *Escherichia Coli* and *Klebsiella Pneumoniae*

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Objective This study aimed to establish and screen for multi-drug combination regimens with antimicrobial activity against blaNDM-producing strains, thereby providing alternative treatment options for clinical management of infections caused by such resistant bacteria.

Methods Twenty-one strains of blaNDM-producing *Escherichia coli* and 29 strains of blaNDM-producing *Klebsiella pneumoniae* (all of which were genotyped using PCR-based DNA sequencing) were selected from clinical isolates collected from 23 hospitals across 18 provinces and municipalities nationwide. Bacterial identification was performed using identified using MALDI-TOF. Referring to the 2026 edition of CLSI guidelines on aztreonam plus ceftazidime-avibactam broth disk elution method, we determined the susceptibility of the bacteria to aztreonam, ceftazidime-avibactam (or plus aztreonam), imipenem-relebactam (or plus aztreonam), meropenem-vaborbactam (or plus aztreonam).

Results The susceptibility rates of 50 strains to aztreonam, ceftazidime-avibactam, imipenem-relebactam and meropenem-vaborbactam were 16%, 2%, 4% and 0%, respectively; the susceptibility rates for ceftazidime-avibactam combined with aztreonam, imipenem-relebactam combined with aztreonam, and meropenem-vaborbactam combined with aztreonam were 98%, 46% and 74%, respectively. Eight strains were susceptible to aztreonam (including 4 strains of *E. coli* and 4 strains of *K. pneumoniae*) were not susceptible to ceftazidime-avibactam, imipenem-relebactam, or meropenem-vaborbactam, but were susceptible to all three of these agents in combination with aztreonam. Of the 27 strains resistant to meropenem-vaborbactam

combined with aztreonam, 96.3% were susceptible to ceftazidime-avibactam combined with aztreonam, and 51.8% were susceptible to imipenem-relebactam combined with aztreonam. Of the 13 strains resistant to imipenem-relebactam combined with aztreonam, 92.3% were susceptible to ceftazidime-avibactam in combination with aztreonam, but all strains were resistant to meropenem-vaborbactam in combination with aztreonam. One NDM-producing *E. coli* strain was non-susceptible to all tested antimicrobial agents, both as monotherapies and in combination.

Conclusion Compared with monotherapy, combinations of aztreonam with other antimicrobial agents demonstrated good antimicrobial activity against blaNDM-producing strains, with the combination of ceftazidime-avibactam and aztreonam exhibiting the strongest activity, followed by imipenem-relebactam plus aztreonam, and meropenem-vaborbactam plus aztreonam.

Epidemiological Characterization of Chromosome-mediated Colistin Resistance in Hypervirulent Carbapenem-resistant *Klebsiella Pneumoniae*

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Background Hypervirulent and carbapenem-resistant *Klebsiella pneumoniae* (hv-CRKP) poses a major clinical threat. Colistin is a last-resort agent against hv-CRKP, yet resistance driven by chromosomal mutations remains poorly characterized in its prevalence and functional impact

Methods From 2020 to 2023, 239 non-duplicate

clinical hv-CRKP isolates were collected from a tertiary hospital in China. Isolates were analyzed by multilocus sequence typing, antimicrobial susceptibility testing, conventional PCR screening, and targeted sequencing of *mcr*, *pmrAB*, *phoPQ*, *crrAB*, and *mgrB*. RT-qPCR assessed lipid A modification gene expression. Whole-genome sequencing was performed on colistin-resistant isolates. Functional roles of novel *pmrB* mutations were validated using CRISPR-Cas9 genome editing. Growth kinetics, competition assays, *Galleria mellonella* infection models, and transcriptomic profiling were conducted to assess fitness, virulence, and gene expression changes

Results Most isolates (210/239, 87.87%) belonged to ST11 lineage, and no *mcr* genes were detected. Mutations in *pmrB* were highly prevalent (232/239, 97.07%), with R256G representing a lineage-associated polymorphism, while specific variants (P95L, D150H, T157P, S203P) associated with elevated colistin MICs. *mgrB* alterations were identified in 6.28% (15/239) of isolates and were exclusively observed in colistin-resistant strains, whereas isolates carrying *crrB* variants (17/239, 7.11%) remained susceptible to colistin. Mutations in the HAMP and HisKA domains of *pmrB* were associated with increased colistin MICs and upregulation of lipid A modification genes. Functional validation using CRISPR-Cas9 confirmed that two novel *pmrB* variants (D150H and S203P) conferred resistance in ST11-KL25 isolates, as reversion restored colistin susceptibility and impaired bacterial growth under colistin pressure. Transcriptomic analysis demonstrated that reversion suppressed lipid A modification pathways (*arnA-D*, *eptA*). Despite fitness advantages

IncN 型 NDM-1 质粒通过共享 IV 型分泌系统协助 IncHI5 型 IMP-4 质粒的跨种播传播

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目的 分析同时携带 blaNDM-1 和 blaIMP-4 碳青霉烯酶基因的肺炎克雷伯菌临床分离株 KP1050 的基因组特征, 并探究耐药质粒水平传播的分子机制。

方法 微量肉汤稀释法测定 KP1050 对 12 种抗菌药物的最低抑菌浓度 (MIC)。结合 Illumina 短读长和 PacBio 长读长测序平台完成全基因组测序, 并进行 MLST 分型、质粒复制子分型及耐药基因鉴定。以大肠埃希菌 EC600 为受体菌, 滤膜法测定耐药质粒接合效率。利用同源重组技术敲除耐药质粒 IV 型分泌系统 (T4SS) 关键基因 (traD、traI), 探讨质粒协同传播机制。

结果 肺炎克雷伯菌 KP1050 对包括碳青霉烯在内多种抗菌药物耐药, 仅对阿米卡星、替加环素和多粘菌素敏感。该菌株携带的 blaNDM-1 和 blaIMP-4 碳青霉烯酶耐药基因分别位于 59 730 bp 的 IncN 型和 289 270 bp 的 IncHI5 型质粒上。IncN 和 IncHI5 型质粒均有完整的 IV 型分泌系统 (T4SS) 编码基因簇, 也均可接合至 EC600 受体菌。结合 GenBank 数据库对 IncHI5 质粒分析发现, 该类质粒骨架较为保守, 且主要分布于肺炎克雷伯菌, 存在显著的种属特异性。以携带 IncHI5 质粒的 EC600 接合子作为供体菌, 该质粒至肺炎克雷伯菌接合效率 (10-4) 显著高于大肠埃希菌 (10-7)。对质粒 T4SS 关键基因的敲除发现, IncHI5 型 IMP-4 质粒可在 IncN 型 NDM-1 质粒的协助下进行跨种水平传播, 存在共享 T4SS 的现象, 二者共存时 IncHI5 质粒至大肠埃希菌的接合效率出现显著提升。

结论 质粒间相互作用可促进碳青霉烯酶耐药基因的传播, blaNDM-1 在自身播散的同时可助力 blaIMP-4 的扩散。IncN 型 NDM-1 质粒可协助 IncHI5 型 IMP-4 质粒通过接合方式进行水平传播, 扩大 IncHI5 型耐药质粒宿主谱。

Decoding Resistance in *Diutina Catenulata* by Validating Clinically Relevant Erg11/Fks1 Mutations

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Objective To verify the causal relationship between specific mutations in the ERG11 and FKS1 genes and antifungal drug resistance in clinical isolates of *Diutina catenulata*.

Methods Recombinant plasmids expressing mutant alleles of ERG11 (F126L, K143R) or FKS1 (F621I, S1123G, I1348S, and the triple mutant S625L/S1123G/F1354L) were constructed and functionally validated in a *Saccharomyces cerevisiae* W303-1a model. Susceptibility testing was performed under different nutrient conditions (SD-Ura and YPD). Molecular docking analysis was conducted to elucidate the structural mechanisms of resistance.

Results Functional validation in *S. cerevisiae* confirmed that both ERG11 and FKS1 mutations conferred resistance in a nutrient-dependent manner. The ERG11-F126L mutation increased the fluconazole MIC

by 21-fold in SD-Ura compared to YPD. FKS1 mutations led to 1.4 to 2-fold increases in echinocandin MICs. Molecular docking revealed the mechanistic bases: ERG11-F126L expanded the ligand-binding cavity (DDG +1.2 kcal/mol), FKS1-F621I disrupted hydrophobic interactions, and compound mutations synergistically perturbed ATP binding domains.

Conclusion Specific mutations in ERG11 (F126L, K143R) and FKS1 (F621I and hotspot variants) are the primary drivers of the pronounced antifungal resistance observed in Chinese *D. catenulata* strains, with resistance phenotypes being modulated by nutrient availability. **KEYWORDS** amino acid substitution, *D. catenulata*, ERG11, FKS1, gene mutation, molecular docking, recombinant plasmid

Fulminant *Aeromonas Caviae* Bacteremia with Migratory Myalgia in An Immunocompetent Host: A Case Report of A CTX-M-3-producing Multidrug-resistant Strain

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Background *Aeromonas caviae* is an emerging waterborne pathogen of increasing clinical concern, particularly in the context of rising antimicrobial resistance. While the acquisition of extended-spectrum β -lactamase (ESBL) genes, such as the plasmid-mediated blaCTX-M, is well-documented in Enterobacterales, it remains uncommon in *A. caviae*. The emergence of such multidrug-resistant strains in environmental reservoirs poses a severe threat. Herein, we report a rare case of fulminant *A. caviae* bacteremia in an immunocompetent host, highlighted by atypical clinical manifestations

and a complex genomic resistome

Case presentation A 71-year-old fundamentally immunocompetent man presented with fulminant bacteremia that rapidly progressed to septic shock and unusual migratory myalgia following a minor injury in a paddy field. Initial empirical therapy with ertapenem was clinically ineffective. Blood cultures isolated *A. caviae*, and antimicrobial susceptibility testing revealed a multidrug-resistant phenotype. Whole-genome sequencing identified a sophisticated resistome, including the ESBL genes blaCTX-M-3, blaTEM-1B, and blaOXA-10, alongside the bifunctional aminoglycoside-fluoroquinolone resistance gene aac(6')-Ib-cr. Notably, the isolate remained susceptible to amikacin and specific carbapenems. Following antimicrobial susceptibility results, therapy was successfully transitioned to targeted biapenem, leading to rapid clinical recovery and microbiological clearance

Conclusion This case demonstrates that environmental *A. caviae* can act as a critical reservoir for clinically significant resistance determinants like blaCTX-M-3, capable of causing life-threatening, invasive infections even in previously healthy individuals. The clinical failure of initial empiric ertapenem therapy underscores the critical importance of susceptibility-guided antimicrobial interventions. Ultimately, these findings reinforce the urgent need for integrated One Health surveillance to monitor the horizontal flow of antimicrobial resistance genes between environmental ecosystems and human populations.

12 年全国多中心监测驱动的正常威克汉姆酵母流行病学与泛基因组学研究

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背景 异常威克汉姆酵母 (*Wickerhamomyces anomalus*) 是一种从环境分离的新兴机会性致病真菌, 可引起血流感染, 新生儿尤其是低出生体重儿为高危人群, 死亡率高达 16.7%-41%。然而, 目前缺乏大样本流行病学数据和基因组学研究。本研究旨在基于全国多中心收集菌株的分子分型和基因组学分析, 阐明该菌的流行病学特征、耐药现状、传播模式及泛基因组学特征。

方法 依托中国医院侵袭性真菌监测网 (CHIF-NET), 2009-2021 年前瞻性收集来自全国 23 个省份 44 家医院的 307 株非重复 *W. anomalus* 临床分离株。采用 CLSI 标准进行抗真菌药物敏感性试验; 微卫星分型分析菌株传播模式; 基于 350 株菌株 (306 株 CHIF-NET 菌株+44 株国际公开基因组) 构建首个 *W. anomalus* 泛基因组, 通过 PCA 和层次聚类分析群体结构, 并开展泛基因组全基因组关联分析 (pan-GWAS) 筛选耐药相关基因位点。

结果 *W. anomalus* 占有念珠菌临床分离株的 0.93%, 东北地区检出率最高 (4.6%), 华南地区仅 0.03%。新生儿组念珠菌血症占比高达 12.7%, 为其他年龄组的 20 倍; 81% 为血流感染。药敏结果显示 34.5% 菌株对氟康唑为非野生型 (NWT), 48.5% 对伏立康唑 NWT, 棘白菌素类和两性霉素 B 保持 >98% 野生型敏感性; 27% 耐药菌株无法用经典机制解释。微卫星分型鉴定出 118 种基因型, 其中 40 个院内克隆簇和 6 个跨机构基因型提示存在医院内传播。泛基因组分析显示, 在 ~100 株菌时达到饱和, 包含核心基因 (>80%)、软核心基因 (55-80%)、壳基因 (35-55%) 和云基因 (<35%)。基于基因存在-缺失矩阵的聚类揭示 5 个基因组簇, 其中簇 5 完全由中国临床分离株组成, 为国际基因组中未见的地域限制性谱系。泛基因组系统发育与临床表型显著相关: 簇 1 和簇 2 主要来源于新生儿, 多重唑类共耐药映射于特定系统发育分支。Pan-GWAS 发现耐药位点呈非随机多染色体分布, 7 号染色体为主要

枢纽; 大多数耐药相关位点位于标准参考基因组未组装的附属区域, 蛋白编码变异占主导。

结论 本研究首次基于全国多中心大样本揭示了 *W. anomalus* 的流行病学和泛基因组学全景。该菌具有高度可塑的泛基因组和具有临床预测价值的群体结构, 泛基因组框架可有效解码耐药功能机制。研究结果支持将全国敏感性监测与抗真菌药物管理政策相结合, 以早期识别高风险分离株。

Azole-induced In-host Microevolution of *Candida Parapsilosis* Drives MRR1-mediated Antifungal Resistance

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Candida parapsilosis is an important cause of candidemia and catheter-related bloodstream infection. Prolonged azole exposure may promote antifungal resistance during persistent infection, but how resistance emerges through in-host microevolution and whether it is accompanied by broader phenotypic remodeling remain unclear. In this study, we analyzed longitudinal *C. parapsilosis* bloodstream isolates from a patient with prolonged catheterization and azole therapy. Four representative isolates, PU17, PU110, PU123 and PU127, were selected for phenotypic, genomic, transcriptomic and functional analyses.

Antifungal susceptibility testing showed a step-wise increase in azole MICs in later isolates, especially PU123 and PU127. Genome-wide analysis demonstrated that the isolates were closely related and followed their order of recovery, supporting progressive

in-host microevolution rather than replacement by unrelated strains. This resistance trajectory was accompanied by reduced growth and altered colony and cellular morphology in later resistant isolates.

Transcriptomic analysis revealed clear separation between susceptible and resistant isolates. Differentially expressed genes were enriched in membrane-associated, transport-related and stress-response processes, suggesting broad transcriptional remodeling during azole resistance evolution. Consistently, spot assays showed altered responses under selected membrane- and cell wall-associated stress conditions. Resistant isolates also showed reduced biofilm metabolic activity, altered macrophage uptake, and lower early organ fungal burdens in a murine systemic infection model, indicating biological changes beyond antifungal susceptibility alone.

Because later resistant isolates carried an MRR1 T2957C point mutation corresponding to L986P, we evaluated its functional relevance by targeted point-mutation editing. Introduction of MRR1 T2957C into a susceptible background increased azole MICs, whereas reversion of this mutation in the resistant PU123 background reduced azole MICs. Targeted modification of this MRR1 point mutation was also accompanied by changes in growth, colony morphology, tissue fungal burden and expression of selected candidate genes.

Together, these findings support a model in which prolonged azole exposure selected for an MRR1-associated resistant state during persistent *C. parapsilosis* infection. Importantly, resistance emergence occurred together with phenotypic and transcriptional remodeling involving growth, morphology, biofilm activity, host-cell interaction and early in vivo colonization. This study provides longitudinal clinical evidence that azole resistance in *C. parapsilosis* may develop as part of a broader adaptive process rather than as an isolated change in antifungal susceptibility.

2021~2024 年四川省重症病区细菌耐药监测分析

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目的 了解 2021~2024 年四川省细菌耐药监测网成员单位重症病区分离的细菌种类及对临床常用抗菌药物的敏感性和耐药性, 为抗菌药物的合理使用提供依据。

方法 按照全国细菌耐药监测方案, 采用标准纸片扩散法或自动化仪器检测法, 测定监测药物对细菌的敏感性, 并参考 CLSI 标准, 使用 WHONET5.6 软件进行分析和总结。

结果 四年间共纳入数据分析的非重复细菌总数为 149393 株, 其中革兰阳性菌占 23.0% (34333/149393), 革兰阴性菌占 77.0% (115060/149393)。分离率排名前五位的是: 肺炎克雷伯菌、鲍曼不动杆菌、大肠埃希菌、铜绿假单胞菌和金黄色葡萄球菌。其分离率分别是 21.5%、13.0%、12.4%、9.2%和 6.8%。常见分离菌的耐药情况为肺炎克雷伯菌对头孢他啶、头孢噻肟、亚胺培南、左氧氟沙星的耐药率基本无变化。2023 年三代头孢菌素及碳青霉烯类耐药肺炎克雷伯菌的检出率最高分别为 35.0%和 20.3%。三代头孢菌素、喹诺酮类耐药大肠埃希菌的检出率在 2022 年时最低, 同年碳青霉烯类耐药大肠埃希菌的检出率最高 3.5%。鲍曼不动杆菌耐药率较低的前五位药物分别为: 多粘菌素 B、替加环素、米诺环素、头孢哌酮/舒巴坦和阿米卡星, 耐药率较 2014~2019 年度有所上升, 碳青霉烯类耐药鲍曼不动杆菌呈先下降再上升趋势。铜绿假单胞菌耐药率较低的前五名药物包括: 多粘菌素 B、阿米卡星、妥布霉素、庆大霉素和美罗培南, 2024 年新增监测药物头孢他啶/阿维巴坦, 耐药水平较低, 耐药率为 8.3%, 2022 年碳青霉烯类耐药铜绿假单胞菌的检出率最低 16.3%。未检出对利奈唑胺、万古霉

素、替考拉宁耐药的金黄色葡萄球菌, MRSA 的检出率无明显变化。

结论 四年间, 临床重症病区分离到细菌耐药率各不相同, 碳青霉烯耐药的革兰阴性杆菌检出率明显高于其他临床病区, 抗菌药物耐药形势较严峻, 需密切关注重症病区细菌耐药监测, 未临床治疗和多重耐药菌的防控提供依据。

Clinical Characteristics and Whole-Genome Sequencing Analysis of Carbapenem- and Colistin-Resistant Hypervirulent *Klebsiella Pneumoniae*

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Background Colistin-resistant hypervirulent carbapenem-resistant *Klebsiella pneumoniae* (ColR-hv-CRKP) has emerged as a critical clinical challenge, yet its clinical and genomic characteristics remain poorly understood

Methods From 2021 to 2024, 326 non-duplicate hv-CRKP isolates were collected from patients with confirmed clinical infections at a tertiary hospital in China. Antimicrobial susceptibility was determined by broth microdilution. Clinical data were retrospectively analyzed, and logistic regression identified risk factors for ColR-hv-CRKP infection. Whole-genome sequencing was performed to characterize molecular characteristics and colistin resistance-associated mutations.

Results Ninety-two isolates (92/326, 28.22%) were colistin-resistant by broth microdilution. Patients with ColR-hv-CRKP infection were more likely to have a history of ICU admission, prolonged hospitalization, and invasive procedures, were more likely to

have isolates recovered from sputum specimens, and had more frequent prior exposure to colistin (all $P < 0.05$). Multivariable analysis identified prior colistin administration (OR = 4.58, 95% CI 2.41-8.69) and sputum specimen source (OR = 2.44, 95% CI 1.35-4.42) as independent risk factors for ColR-hv-CRKP infection. Whole-genome sequencing revealed that most ColR-hv-CRKP isolates belonged to ST11 (90/92, 97.83%), mainly KL64 (52/92, 56.52%) or KL25 (36/92, 39.13%). Carbapenem resistance was primarily mediated by blaKPC-2 (91/92, 98.91%), while no mcr genes were detected. Whole-genome sequencing analysis showed that most ColR-hv-CRKP isolates (81/92, 88.04%) harbored colistin resistance-associated mutations. pmrB alterations were the most frequent, detected in 45.65% (42/92) of isolates, predominantly Thr157Pro (18/42) and Ser205Pro (8/42) substitutions. mgrB mutations occurred in 35.87% (33/92) of isolates, predominantly due to insertional inactivation (27/33, 81.82%) mediated by ISKpn26 and IS903B elements. Phylogenetic analysis revealed that all ST11-KL25 ColR-hv-CRKP isolates clustered into a highly homogeneous group with minimal intra-lineage diversity and displayed significantly smaller pairwise SNP distances than ST11-KL64/KL107 isolates ($P < 0.0001$).

Conclusion Colistin resistance in hv-CRKP was mainly associated with pmrB and mgrB mutations in the dominant ST11-KL25 and ST11-KL64 lineages. Prior colistin exposure was the key clinical risk factor, highlighting the selective pressure of colistin use and the urgent need for strengthened antimicrobial stewardship.

Keywords *Klebsiella pneumoniae*, colistin, resistance, whole-genome sequencing, clinical characteristics

Chromosomally Encoded blaNDM-1 Overexpression Drives Cefiderocol Heteroresistance in Difficult-to-treat Resistance *Pseudomonas Aeruginosa*

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Objective The emergence of cefiderocol heteroresistance poses a significant challenge to the management of difficult-to-treat *Pseudomonas aeruginosa* (DTR-PA) infections. This study investigated the underlying mechanism of cefiderocol heteroresistance in a DTR-PA strain that harbours both blaKPC-3 and blaNDM-1 and was isolated from a patient with no prior exposure to cefiderocol.

Methods Antimicrobial susceptibility was assessed using broth microdilution, disk diffusion, and MIC test strip methods. The genetic basis of resistance was elucidated through second- and third-generation whole-genome sequencing. Transcriptomic analysis was employed to quantify the expression of β -lactamase and efflux pump genes.

Results A heteroresistant subpopulation, *P. aeruginosa* HS2504 (MIC > 16 mg/mL), was isolated from the clinical DTR-PA isolate *P. aeruginosa* HS2526 (cefiderocol MIC = 1 mg/mL). Genomic analysis revealed that *P. aeruginosa* HS2526 and *P. aeruginosa* HS2504 both belonged to ST644 and differed by only five SNPs. They also shared an identical resistance gene profile, including blaKPC-3 and blaNDM-1. A key genetic difference was the deletion of an 11-copy IS-blaPME-1 unit located upstream of blaNDM-1 in *P. aeruginosa* HS2504. Notably, no mutations were identified in cefiderocol resistance-associated genes, such as TonB-dependent receptors and ftsI. RNA-seq and RT-PCR identified a fivefold upregulation of blaNDM-1 in

P. aeruginosa HS2504 as the sole significant change. Phenotypic confirmation was achieved by restoring cefiderocol susceptibility (the zone diameter increased from 6 mm to 24 mm) in *P. aeruginosa* HS2504 upon the addition of EDTA, a metallo- β -lactamase inhibitor.

Conclusion This study characterises the first reported cefiderocol-heteroresistant *P. aeruginosa* strain co-harbours blaKPC-3 and blaNDM-1 in China. We demonstrate that, while detectable by disk diffusion, heteroresistance is not detectable by broth microdilution and is primarily mediated by elevated blaNDM-1 expression rather than acquired mutations. These findings emphasise an unrecognised resistance mechanism that has significant implications for diagnostic practice and therapeutic outcomes.

携带 blaKPC 肺炎克雷伯菌院内克隆传播及突变进化分子机制研究

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关键词：肺炎克雷伯菌，头孢他啶-阿维巴坦，blaKPC 突变体，适应性进化，医院感染

目的 碳青霉烯耐药肺炎克雷伯菌已对全球公共卫生健康造成巨大挑战，头孢他啶-阿维巴坦作为最新 β -内酰胺- β -内酰胺酶抑制剂复方制剂是治疗产 KPC 酶肠杆菌目细菌的有效抗菌药物之一。但随着头孢他啶-阿维巴坦的广泛应用，blaKPC 基因发生突变导致耐药而治疗失败。

方法 收集病史资料及菌株，进行抗菌药物敏感性试验及全基因组测序进行肺炎克雷伯菌院内克隆传播轨迹分析；通过分子克隆与酶促反应动力学试验阐明 blaKPC 突变体介导头孢他啶-阿维巴坦耐药机制；通过质粒电转化试验、质粒测序明确耐药基因可转移性；通过菌株适应性竞争实验、生长曲

线、生物膜形成试验评估菌株在克隆传播过程中细菌发生的适应性进化。

结果 在 2020-2021 年, 复旦大学附属华山医院神经内科重症监护病房内的五位病人各分离到五株携带 blaKPC-76 肺炎克雷伯菌。通过全基因组测序分析显示, 五株肺炎克雷伯菌之间相差 SNP 数量小于 100, 提示存在克隆传播的可能。其中第一位检出 blaKPC-76 肺炎克雷伯菌的病人作为 index patient, 在这位病人体内可以观察到 blaKPC-2 到 blaKPC-79 到 blaKPC-76 的连续进化突变。与 blaKPC-2 相比, blaKPC-79 在 261A 和 262V 之间插入 7 个氨基酸 VYTRAPN; 而 blaKPC-76 在 blaKPC-79 的基础上增添了 D179Y 的突变。分子克隆表型显示, blaKPC-79 可介导头孢他啶-阿维巴坦 MIC 至 16mg/L, 而 blaKPC-76 可介导头孢他啶-阿维巴坦 MIC 至 128mg/L。酶促反应动力学数据表明, KPC-79 与 KPC-76 酶对头孢他啶的催化速率 (kcat/Km 降低) 降低, 阿维巴坦对 KPC-79 和 KPC-76 的抑制能力降低 (IC50 升高)。通过 blaKPC-2-blaKPC-79-blaKPC-76 共培养竞争实验发现, 头孢他啶-阿维巴坦浓度越高, KPC-76 肺炎克雷伯菌的竞争优势越大; 这也对应了 index patient 体内的 KPC 肺炎克雷伯菌的优势菌株选择。

结论 携带 blaKPC 新亚型肺炎克雷伯菌的多起克隆传播事件提示 blaKPC 新亚型已出现广泛传播的势头。而头孢他啶-阿维巴坦的使用施加的选择性压力可使 blaKPC 基因发生二次突变以适应更高浓度的抗生素暴露环境。

Development of Ceftazidime-avibactam Resistance Driven by Conversion of BlaKPC-2 To BlaKPC-78 During Treatment of ST463 Carbapenem-resistant *Pseudomonas Aeruginosa* Infection

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Background The emergence of ceftazidime-avibactam (CZA)-resistant carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) poses a major clinical challenge in contemporary clinical practice. In this study, we report the first identification of blaKPC-78 which driven by a mutation from blaKPC-2 in a clinical CRPA strain

Methods Six blaKPC-78 CRPA isolates, along with two blaKPC-2 strains from one patient, were subjected to antimicrobial susceptibility testing (AST), whole-genome sequencing (WGS), conjugation, and growth assays. Mechanistic investigations included structural modeling and docking, cloning experiments, efflux inhibition, and reverse transcription quantitative polymerase chain reaction (RT-qPCR).

Results The emergence of CZA resistance in CRPA isolates was driven by a mutation from blaKPC-2 to blaKPC-78 during CZA therapy. The AST results showed that all KPC-78-producing CRPA exhibited multidrug-resistant phenotype. WGS revealed that these strains belong to ST463 and blaKPC-78 gene was located in a type I plasmid and carried by Tn6296 transposon. Additionally, the co-occurrence of efflux pump overexpression and KPC-78 enzyme's stronger binding affinities for both ceftazidime and avibactam contributed to high-level resistance to CZA in CRPA. Moreover, despite the slower logarithmic growth of KPC-78-producing *P. aeruginosa* in monoculture, in vitro competitive co-culture experiments revealed that it conferred a competitive advantage over the KPC-2-producing strains.

Conclusion We report the first identification of blaKPC-78 in CRPA, delineate its evolutionary trajectory, and describe its genetic characteristics. The elevated hydrolytic activity of the KPC-78 producing

strain, along with the overexpression of efflux pumps, contributes to its high-level resistance to CZA. Considering the widespread of ST463 CRPA in China, it is imperative to enhance the surveillance of KPC-producing CRPA.

New Resistance Threat in Extensively Drug-resistant *Pseudomonas Aeruginosa* ST463 Co-producing KPC and IMP Carbapenemases: Plasmid Dynamics and Clinical Emergence

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Background Carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) ST463 is an important high-risk lineage in China, yet while the co-carriage of *Klebsiella pneumoniae* carbapenemase (KPC) and imipenemase (IMP) carbapenemases (KI-CRPA) within this lineage has been only sporadically reported, the evolutionary routes leading to the emergence of such dual-carbapenemase-producing strains remain poorly understood. Therefore, systematic investigation of KI-CRPA ST463 isolates is needed to elucidate their evolutionary origins and assess their potential clinical impact

Methods Six blaKPC/blaIMP co-harboring CRPA isolates were identified among 916 CRPA isolates collected at a tertiary teaching hospital in Hangzhou, China from 2016 to 2025. Antimicrobial susceptibility testing, short- and long-read whole-genome sequencing, comparative plasmid analysis, conjugation assays, growth assays, plasmid stability experiments, and pairwise competition assays were performed to characterize the genetic basis and biological consequences of dual-carbapenemase production. Global ep-

idemiology was analyzed using 57,536 publicly available genomes

Results All dual-carbapenemase isolates belonged to ST463 with limited core-genome diversity (pairwise single nucleotide polymorphism (SNP) distances ≤ 52). Two distinct plasmid configurations were identified: PAE0945 carried an approximately 470-kb IncP-2 blaIMP-45 plasmid plus an approximately 40-kb blaKPC-2 plasmid, whereas PAE1316 harbored a ~530-kb chimeric IncP-2 megaplasmid co-localizing both resistance genes with tandem blaIMP-45 copies. These findings support two evolutionary pathways: acquisition of an IMP plasmid in a KPC-positive background and recombination-driven megaplasmid formation. Dual-carbapenemase carriage imposed fitness costs including reduced growth rates and lower plasmid stability, yet competition assays demonstrated a concentration-dependent advantage under ceftazidime-avibactam pressure

Conclusions Our results show that ST463 dual-carbapenemase CRPA can emerge through multiple plasmid-mediated routes and may be maintained under antibiotic selection despite associated biological costs, posing significant clinical challenges for infection control

Dual RNA-seq Reveals QslA-mediated Quorum Sensing Inhibition in *Pseudomonas Aeruginosa*-*Acinetobacter Baumannii* Interaction and Dual-species Biofilm Formation

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Background *Acinetobacter baumannii* and *Pseudomonas aeruginosa* are opportunistic pathogens frequently co-isolated from polymicrobial infections. Interactions between them influence disease progression and therapeutic outcomes, yet the molecular mechanisms remain poorly understood

Methods *P. aeruginosa* and *A. baumannii* strains co-isolated from a pneumonia patient were examined. After 8-hour mono- and 1:10 (Pa:Ab) co-culture, total RNA was extracted and sequenced using Illumina NovaSeq 6000. Raw reads were aligned using STAR v2.7.11b, followed by sorting and indexing with Samtools v1.21, and quantified using featureCounts. Differentially expressed genes (DEGs) were identified using $|\log_2FC| \geq 1$ and $FDR < 0.05$. Functional validation was conducted using *P. aeruginosa* PAO1 transposon mutants. Biofilm was measured by crystal violet staining

Results In *P. aeruginosa*, 21 DEGs were identified during co-culture (10 upregulated, 11 downregulated). Notably, three QS-related DEGs: *qslA* ($\log_2FC$: 1.1), *rhlA* ($\log_2FC$: -1.1), and *gacS* ($\log_2FC$: -1.3), suggested suppression of QS signaling in *P. aeruginosa*. *qslA*, which encodes a QS anti-activator that represses QS-regulated gene expression, was upregulated, indicating a potential regulatory role in modulating interspecies interaction. In *A. baumannii*, 805 DEGs (23 upregulated, 782 downregulated) were identified, indicating broad transcriptional suppression, particularly in genes associated with membrane integrity, metabolism, and redox processes. Functional validation using PAO1 QS-related mutants (*rhlA*, *lasR*, *rhlI*, *phz*, *pqs*) revealed reduced inhibition zones against *A. baumannii*, supporting the involvement of QS in interspecies antagonism.

Furthermore, co-culture of a *qslA* mutant of PAO1 with a model strain of *A. baumannii*, AB5075, resulted in significantly diminished dual-species biofilm formation compared to the wild-type, highlighting the critical role of *qslA* in biofilm development in polymicrobial communities

Conclusions This study demonstrates a QS-related inhibitory mechanism employed by *P. aeruginosa* against *A. baumannii*, with *qslA* as a key regulatory factor in interspecies interactions. These findings advance our understanding of polymicrobial dynamics and highlight potential targets for treating co-infections

Global Epidemiological and Genetic Characteristics of Carbapenem-resistant *Escherichia Coli* Carrying *BlaIMP*

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Purpose Carbapenem-resistant *Escherichia coli* (CREC) is a serious global health threat. While *bla*NDM-positive and *bla*KPC-positive CRECs are well-characterized, the genomic and epidemiological features of *bla*IMP-positive CRECs remain poorly understood. This study provides a comprehensive analysis of *bla*IMP-positive CRECs by integrating local and global surveillance data

Methods A total of 94 CRECs were collected from four tertiary hospitals in Zhejiang Province during 2017-2024. Antimicrobial susceptibility testing, conjugation frequency assay, plasmid stability test, fitness cost analysis, and whole-genome sequencing were further performed for 9 *bla*IMP-positive CRECs. As of July 2025, statistical characteristics, phylogeographic

distribution, phylogenetic relationships, and MLST relationships of 340 IMP-producing *Escherichia coli* were further investigated from NCBI databases

Results All 9 IMP-positive CREC strains carried the blaIMP-4 gene and were multidrug-resistant but susceptible to colistin, tigecycline, and amikacin. Seven diverse sequence types (STs) were identified, with high-risk ST1193 clones being first detected. The isolates had similar blaIMP-carrying IncN plasmids with high conjugation frequencies (5.3×10^{-2} to 8.7×10^{-1}), 100% stability after 100 generations, and minimal fitness cost, facilitating regional dissemination. Furthermore, the genetic environments surrounding the blaIMP gene commonly featured a resistance transmission platform composed of integrons, insertion sequences, and transposons. Global analysis of 340 blaIMP-positive CRECs revealed high genetic diversity (82 STs), with ST131 predominant (36.18%). Clonal spread was observed for ST131 and ST216. Significant positive correlation existed between resistance genes and plasmid replicons ($r=0.5205$, $P<0.001$), highlighting plasmids' role in resistance transmission. China, Japan, Australia were the top three contributing countries, which also showed relatively diverse resistance genes but similar virulence factors

Conclusions This study revealed that in a local region of Zhejiang Province, IncN plasmids were effectively mediated the horizontal transfer of the blaIMP-4 gene among different clones, with first identification of high-risk ST1193. It further elucidated the important roles of other mobile genetic elements, such as class 1 integrons, IS26 and transposons, in the dissemination of the blaIMP gene. Globally, IMP-positive CREC show high genetic diversity with ST131 predominance. Regional evolution and dissemination of resistance genes were relatively independent among countries, and correlation analysis further confirmed the core role of plasmids. These findings emphasize the evolving risk of

blaIMP-positive CRECs and underscore the need for sustained genomic surveillance

Keywords blaIMP; IncN plasmid; carbapenem-resistant *Escherichia coli*; genomic epidemiology

KPC-33 and OmpK37 Mutations: Unraveling The Mechanism of Ceftazidime/avibactam Resistance in ST11 Carbapenem-resistant *Klebsiella Pneumoniae*

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Background Global surveillance indicates rising ceftazidime-avibactam resistance among carbapenem-resistant *Klebsiella pneumoniae* (CRKP), with sequence type 11 predominating in China. The contribution of blaKPC variants and porin alterations to high-level resistance remains significant

Methods We employed whole-genome sequencing and functional analyses to characterise a CZA-resistant ST11 CRKP isolate recovered from a patient without prior exposure to ceftazidime-avibactam or carbapenems.

Results The isolate harboured blaKPC-33 on a non-conjugative plasmid and multiple non-synonymous mutations in the porin gene ompK37, concomitant with high-level resistance to ceftazidime-avibactam and carbapenems while retaining susceptibility to tigecycline, polymyxin B and amikacin.

Conclusion blaKPC-33 coupled with OmpK37 alterations underpins dual resistance to ceftazidime-avibactam and carbapenems in ST11 CRKP, underscoring the need for genomic surveillance and rapid detection of this resistance mechanism.

The Antimicrobial and Antibiofilm Effects of Tetracycline-class Antimicrobials Toward Biofilms of *Staphylococcus Aureus* Isolated From Bone and Joint Infections.

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Objective To evaluate the in vitro susceptibility of *S. aureus* clinical isolates from bone and joint infections (BJIs) to tetracycline-class antibiotics and to analyze their molecular typing and tetracycline resistance gene profiles, thereby providing a scientific basis for clinical anti-infective therapy.

Methods A total of 222 non-duplicate *S. aureus* clinical isolates from BJI patients at the Third Hospital of Hebei Medical University were retrospectively collected. Minimum inhibitory concentrations (MICs) of conventional and novel tetracyclines were determined by broth microdilution. Molecular typing (MLST, spa typing, SCCmec typing, agr typing) and tetracycline resistance gene detection were performed via whole-genome sequencing. Thirty-four multidrug-resistant MRSA isolates were selected for biofilm assays. Biofilm-forming capacity was assessed by crystal violet staining, and minimum biofilm inhibitory concentrations (MBICs) and minimum biofilm eradication concentrations (MBECs) were determined. Checkerboard assays evaluated the fractional biofilm eradication concentration (FBEC) indices of linezolid, fosfomycin, levofloxacin, and rifampin combined with tetracyclines.

Results Among 222 isolates, 101 (44.86%) were MRSA. Demographic characteristics, infection types, and inflammatory markers did not differ significantly between MRSA and MSSA groups ($P > 0.05$). *S. aureus*

showed favorable susceptibility to minocycline and doxycycline, with resistance rates of 0% and 0.45%, respectively. For tigecycline, eravacycline, and omadacycline, MIC₅₀/MIC₉₀ values were 0.064/0.125, 0.25/0.5, and 0.25/0.5 µg/mL, with resistance rates of 0%, 6.07%, and 2.34%, respectively. ST59 was the predominant clone among MRSA, and ST22 among MSSA; agr group I was dominant. Among 42 tetracycline-resistant strains, tet(K) was the most prevalent resistance gene (66.67%). Novel tetracyclines effectively circumvented classical tetracycline resistance mechanisms. All 34 MDR-MRSA strains formed biofilms; MBIC and MBEC values markedly exceeded corresponding MICs. FBEC analysis revealed predominantly synergistic or additive interactions, with no antagonism. Combinations of linezolid with omadacycline or minocycline, and rifampin with eravacycline or omadacycline, exhibited relatively greater activity, whereas levofloxacin-based combinations showed weaker synergy.

Conclusion *S. aureus* isolates from BJIs demonstrated excellent in vitro susceptibility to novel tetracyclines. MDR-MRSA strains exhibited strong biofilm formation, with substantially elevated antimicrobial concentrations required against biofilm-associated bacteria. Novel tetracycline-based combinations, particularly those containing omadacycline, displayed synergistic or additive effects against mature biofilms. Given its intravenous and oral formulations, omadacycline is well suited for long-course sequential therapy and holds favorable clinical prospects in BJI management.

2 株非产酶碳青霉烯耐药肺炎克雷伯菌全基因组测序及耐药毒力特征研究

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目的 为明确本院非碳青霉烯酶产酶型碳青霉烯耐药肺炎克雷伯菌(non-CP-CRKP)的流行病学、耐药机制、毒力特征及基因组背景,为其临床检测、治疗及院感防控提供依据。

方法 本研究回顾性分析 2021 年 1—12 月本院 85 株碳青霉烯耐药肺炎克雷伯菌(CRKP),筛选 non-CP-CRKP 并收集临床资料;采用质谱仪鉴定、VITEK-2 系统联合纸片法行药敏试验,参照 CLSI 2023 版标准判定结果;通过 CTAB 法提 DNA 并完成 Illumina 二代全基因组测序,结合生物信息学数据库及工具分析菌株的耐药基因、毒力因子、基因突变、质粒类型,基于 SNP 构建系统发育树解析遗传进化特征。

结果 85 株 CRKP 中 non-CP-CRKP 共 2 株(占 2.35%),均分离自老年合并基础疾病患者的痰标本,2 株菌均为多重耐药表型,对青霉素类/ β -内酰胺酶抑制剂复合制剂、头孢菌素类、喹诺酮类及碳青霉烯类均耐药,仅对替加环素、头孢他啶/阿维巴坦敏感,其中 1 株额外对阿米卡星、复方新诺明敏感。2 株菌均携带 blaOXA 家族等耐药基因,acrR 基因突变与氟喹诺酮类耐药相关,ompK36、ompK37 基因突变与头孢菌素类、碳青霉烯类耐药相关;均携带菌毛合成、铁摄取等基础毒力基因,且菌株间毒力基因完备性存在差异。基因组分析显示,2 株菌为临床少见的 ST661 和 ST3083 型,遗传亲缘关系接近,质粒谱存在菌株差异。

结论 本院 non-CP-CRKP 已呈局部流行,其耐药由外膜蛋白突变与耐药基因共同介导,毒力特征存在菌株差异;临床需加强高危人群监测,合理使用抗菌药物,对碳青霉烯类耐药但碳青霉烯酶筛查阴性菌株需行基因检测明确诊断,治疗优先选用替加环素、头孢他啶/阿维巴坦并结合药敏制定个体化方案。

Convergence of Last-line Resistance Determinants in An XDR *Klebsiella Pneumoniae* Isolate Carrying blaNDM-5, Mcr-1.1, Mcr-8, and TmexCD1-toprJ1

null null

Sanmen People's Hospital

Background The emergence of multidrug-resistant *K. pneumoniae* carrying resistance to last-line antibiotics poses a growing clinical challenge. In particular, the convergence of carbapenem, colistin, and tigecycline resistance within a single isolate remains uncommon but is of increasing concern

Methods A clinical *K. pneumoniae* isolate (2023-1292) was recovered from a prostatic secretion sample and subjected to antimicrobial susceptibility testing. Whole-genome sequencing was performed using a hybrid approach combining Illumina and Oxford Nanopore platforms. Antimicrobial resistance genes, plasmid replicons, and genetic contexts were analyzed in silico. In addition, publicly available genomes co-harboring blaNDM, mcr, and tmexCD1-toprJ1 were retrieved for comparative genomic and phylogenetic analysis.

Results The isolate exhibited resistance to multiple antimicrobial classes, including carbapenems, ceftazidime/avibactam, tigecycline, and colistin. Genomic analysis identified 38 resistance genes distributed across seven plasmids and the chromosome. Notably, blaNDM-1 was located on an IncX3 plasmid, while mcr-1.1 and mcr-8 were carried on distinct plasmids. The tigecycline resistance-associated gene cluster tmexCD1-toprJ1 was co-localized with mcr-8 on a multidrug resistance plasmid. Comparative analysis of 53 related isolates revealed diverse sequence types and capsular types, with a predominance of strains from China. Among these, blaNDM-5 and mcr-8 were the

most frequently detected variants, and *tmexCD1-toprJ1* was widely distributed. A broader dataset ($n = 1,728$) further demonstrated that *tmexCD-toprJ* is present across multiple species and geographic regions.

Conclusion This study describes a *K. pneumoniae* isolate co-harboring *bla*NDM-1, *mcr* variants, and *tmexCD1-toprJ1*, with resistance determinants distributed across multiple plasmids. The co-occurrence of these genes highlights the ongoing accumulation of resistance to last-line agents and underscores the need for continued genomic surveillance.

插入序列介导的 *cirA* 基因失活协同驱动头孢地尔耐药与细菌适应性进化

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目的 头孢地尔(FDC)作为一种依赖细菌铁摄取系统进入细胞的铁载体头孢菌素,是治疗多重耐药革兰阴性菌感染的重要“最后防线”。然而,编码铁载体受体的 *cirA* 基因失活虽被认为是其耐药的重要机制,其是否同时赋予细菌适应性优势仍不明确。

方法 本研究从群体分布、分子机制及功能表型三个层面解析 *cirA* 失活的生物学意义。基于公共基因组数据库及多中心临床分离株开展基因组流行病学分析,以表征 *cirA* 变异的分布及演化特征。随后筛选代表性 *cirA* 失活菌株,并结合基因敲除与回补实验,评估 *cirA* 状态在头孢地尔耐药中的作用。进一步通过体外功能实验、巨噬细胞感染模型、转录组测序及小鼠肠道定植模型,从生长、竞争及宿主相关适应性等多个层面系统评估 *cirA* 失活的生物学效应。

结果 *cirA* 失活突变在肺炎克雷伯菌群体中总体发生率较低,但在中国来源菌株中呈上升趋势。

临床分离的 ST11-KL64 型 *cirA::IS903B* 突变株表现出头孢地尔高水平耐药,而基因回补可恢复其敏感性。进一步比较发现,IS903B 介导的 *cirA* 失活与简单基因敲除在表型上存在显著差异:前者在缺铁条件下表现出生长优势、竞争能力增强及质粒稳定性提高,而敲除株则表现出适应性缺陷。巨噬细胞感染模型及小鼠实验进一步证实, *cirA::IS903B* 可增强细菌在宿主环境中的生存能力及短期肠道定植能力。转录组分析提示该差异可能与代谢及转运相关通路的重编程有关。

结论 *cirA* 被 IS903B 破坏不仅与头孢地尔耐药相关,还伴随在铁限制环境中的适应性增强。与基因敲除不同,IS 介导的 *cirA* 失活呈现出不同的表型特征,提示其可能通过调控代谢及转运过程赋予菌株耐药性与适应性双重优势。该机制可能促进 MDR 克隆在临床环境中的持续传播,并为 FDC 耐药的监测与干预提供新的视角。

Emergence and Genomic Analysis of One Rare ST214Pas-ST2010Oxf Carbapenem Resistant *Acinetobacter Pittii* Strain, Co-producing Chromosomal NDM-1 and OXA-506

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Objectives To characterize a rare carbapenem-resistant *Acinetobacter pittii* strain co-producing chromosomal *bla*NDM-1 and *bla*OXA-506, and to investigate the genetic basis of carbapenem resistance

Methods A carbapenem-resistant *A. pittii* strain (ERTCM) was isolated from the wound of a 31-year-old female patient in China. Antimicrobial susceptibility testing, conjugation and stability assays were performed. Whole-genome sequencing (WGS, Illumina and Nanopore) was used for genomic analysis.

Results ERTCM belonged to ST214Pas/ST2010Oxf with KL38 and OCL6. The isolate was resistant to multiple antibiotics, including carbapenems and fluoroquinolones, but remained susceptible to amikacin, tobramycin, and colistin. WGS revealed one chromosome and three plasmids. Both blaNDM-1 and blaOXA-506 were located on the chromosome. blaNDM-1 was embedded in a Tn125 composite transposon flanked by ISAbal25 and 3 bp target site duplications, showing high similarity to plasmid-borne structures in *Acinetobacter baumannii*. Additional resistance genes, virulence factors, and two intact prophage regions were identified. blaNDM-1 was non-transferable and highly stable after serial passage.

Conclusion This study reports the first ST214Pas-ST2010Oxf *A. pittii* strain co-harboring chromosomal blaNDM-1 and blaOXA-506 in China, highlighting the role of Tn125-mediated chromosomal integration in carbapenem resistance dissemination.

Explainable Machine Learning Model for Predicting Carbapenem-Resistant *Pseudomonas Aeruginosa* Infections in Critically Ill Patients: A Retrospective Study Using The MIMIC-IV Database

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Background Carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) infections present substantial challenges in intensive care units (ICUs). Interpretable risk prediction models integrating routine clinical and laboratory variables are critical for early identification and targeted antimicrobial therapy

Methods This retrospective cohort study used

MIMIC-IV v3.1, including 1,317 ICU patients with *P. aeruginosa* infection (289 [21.94%] CRPA-positive, 1,028 carbapenem-susceptible). The cohort was split into training (80%) and test (20%) sets. Feature selection embedded in nested cross-validation (mutual information filtering + LASSO logistic regression) retained “stable” features (selected in $\geq 60\%$ of outer folds/top 20 frequent predictors). Seven machine learning models and a soft-voting ensemble were developed; performance was evaluated via ROC, Brier score, calibration curves, and DCA. SHAP analysis ensured interpretability.

Results Eleven stable predictors were identified: 30-day carbapenem/fluoroquinolone exposure, prior *Pseudomonas* isolation, polymicrobial infection, immunosuppressant use, SAPS II score, red cell distribution width, hematocrit, total calcium, base excess and age. SVM-RBF showed optimal discrimination-calibration balance (test set AUC-ROC 0.74 [95% CI 0.67–0.82], Brier score 0.144), with sensitivity 0.71 and specificity 0.65 at Youden’s threshold. DCA confirmed superior net benefit vs. “treat all/none” strategies. SHAP highlighted recent antibiotic exposure, prior *Pseudomonas* isolation, polymicrobial infection, and severity/physiological markers as key risk drivers.

Conclusion We developed and validated an interpretable SVM-RBF model for CRPA prediction in ICU patients with *P. aeruginosa* infection using nested cross-validation and stability-based feature selection. The model exhibits robust discrimination, calibration, and clinical utility, with SHAP providing biologically/clinically plausible explanations. External validation in diverse cohorts is needed for generalizability and clinical implementation.

Clinical Characteristics, Phylogenetic Analysis, and Antimicrobial Susceptibility of *Staphylococcus Aureus* Isolates From Bone and Joint Infections: A Single-Center Retrospective Study

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Objective To analyze clinical features, antimicrobial susceptibility, phylogeny, virulence genes and biofilm formation of *Staphylococcus aureus* isolates from bone and joint infections (BJIs), and explore lineage-specific characteristics associated with BJI subtypes.

Methods A retrospective study was conducted on 246 patients with microbiologically confirmed *S. aureus* BJIs at The Third Hospital of Hebei Medical University between March 2023 and March 2024. Clinical data were extracted from electronic medical records. Antimicrobial susceptibility testing was performed using broth microdilution according to CLSI guidelines. A total of 182 representative isolates were selected for whole-genome sequencing and multilocus sequence typing (MLST), and a core-genome SNP-based phylogenetic tree was constructed. All isolates were screened for 45 virulence-associated genes by PCR, including toxin genes, biofilm-associated genes, immune evasion genes, adhesin genes and enzyme genes. Differences in antimicrobial resistance, molecular typing, virulence genes and biofilm formation were compared between MSSA and MRSA groups and among different BJI subtypes.

Results Of 246 isolates, 43.50% were MRSA and 56.50% were MSSA. Males predominated in adults aged 19–79 years, and females dominated in those ≥ 80 years. All isolates were susceptible to vancomycin, teicoplanin and cotezolid. MRSA showed significantly

higher resistance to penicillin, oxacillin, macrolides, lincosamides and fluoroquinolones. Phylogenetic analysis revealed that MRSA was dominated by healthcare-associated CC5, CC8 and CC239, which were strongly associated with implant-related infections and exhibited stronger biofilm formation. MSSA showed high genetic diversity and higher PVL positivity, mainly related to native joint and vertebral infections.

Conclusion *S. aureus* BJIs present distinct demographic and genomic heterogeneity. MRSA is multi-drug-resistant but susceptible to glycopeptides and oxazolidinones, with CC5/CC8/CC239 as dominant clones linked to implant-related infections. MSSA is genetically diverse with high PVL carriage and correlates with native joint infections. Clonal background, virulence genes and biofilm capacity determine BJI clinical features and therapeutic complexity, supporting individualized clinical management.

Genomic and Phenotypic Characterization of Carbapenem-resistant *Acinetobacter Baumannii* Isolates From Patients and Trolleys and Their Potential Connections in An Intensive Care Unit

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Background Carbapenem-resistant *Acinetobacter baumannii* (CRAB) poses significant challenges in intensive care units (ICU) due to its multidrug resistance and environmental persistence. To date, most studies have focused on clinical isolates or patient-environment transmission. However, high-touch mobile surfaces have been less extensively characterized

Results We collected 49 CRAB isolates in 2019

and 2021 from ICU patients (n=32) and trolley surfaces (n=17). 91.84% (45/49) isolates belonged to ST2Pas and carried blaOXA-23. The capsular polysaccharide (K locus) and lipopolysaccharide (OC locus) types were predominantly KL7 and OCL1, respectively. Comparative genomic analysis revealed a high degree of genomic relatedness between patient and trolley associated isolates, including three clonal clusters (SNP differences <19). To further characterize environmental persistence, we assessed biofilm formation using Live/Dead staining and scanning electron microscopy (SEM), and evaluated disinfectant susceptibility across all isolates.

Conclusion These findings demonstrate the co-existence of closely related CRAB on patients and trolley surfaces within the same ICU and highlight the importance of considering high-touch mobile surfaces in infection prevention and control (IPC) strategies.

BlaNDM-1 阳性肺炎克雷伯菌临床分离株对美罗培南异质性耐药

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异质性耐药是指整体敏感菌株中, 存在一个或多个耐药水平高于主群体的亚群, 在暴露于抗菌药物后, 耐药亚群会迅速扩增, 使得细菌主群体对抗菌药物耐药。传统药敏检测方式可能严重低估其耐药风险, 导致临床抗菌药物治疗评价困难与治疗失败。研究显示, 碳青霉烯耐药肠杆菌目细菌对美罗培南的异质性耐药比例高达 52.9%, 其机制可能涉及碳青霉烯酶基因串联重复、外膜孔蛋白 OmpK36 突变或表达缺失等。然而, 现有研究主要关注基因组结构改变, 对其背后的调控机制及关联网络仍知之甚少。本研究旨在阐明 blaNDM-1 阳性肺炎克雷

伯菌对美罗培南异质性耐药的发生发展机制。

本研究共收集 708 株临床来源的碳青霉烯耐药肺炎克雷伯菌 (CRKP), 从中检出仅携带 blaNDM-1 型碳青霉烯酶菌株 38 株, 阳性率为 5.37%。不同省份 CRKP 群体中该类菌株的阳性率在 1.59%-40% 不等, 提示其流行存在地域差异。系统发育分析显示, 这些菌株主要分为 3 个簇, 具有一定遗传多样性。药敏试验结果显示, 38 株菌均对厄他培南耐药; 对美罗培南和亚胺培南的耐药率分别为 84.21% 和 55.26%。其中, 6 株菌呈现厄他培南单药耐药表型。对琼脂稀释法中表现为美罗培南高 MIC (16-128 mg/L) 及低 MIC (0.5-2 mg/L) 的菌株进行美罗培南 E-test 试验。

结果显示, E-test 与琼脂稀释法具有较好的一致性, 且在 6 株厄他培南单药耐药菌株的抑菌圈内均观察到克隆生长现象, 提示可能存在美罗培南异质性耐药表型。PAP 实验进一步显示, 6 株菌在各自最高不影响主群体生长药物浓度 ≥ 8 倍下, 存在频率 $\geq 1 \times 10^{-7}$ 的亚群生长, 且所能生长的最高药物浓度都达到或超过了 CLSI 规定的美罗培南临床耐药折点, 证实了 6 株 blaNDM-1 阳性肺炎克雷伯菌均对美罗培南异质性耐药, 且可能对临床治疗产生影响。与各自亲本菌株相比, 耐药亚群的美罗培南 MIC 上升了 4-64 倍, 且大部分亚群在无抗生素环境中传 50 代后仍能维持高 MIC 值不变, 表现为稳定型异质性耐药。

综上, 本研究发现 6 株厄他培南单药耐药的 blaNDM-1 阳性肺炎克雷伯菌均对美罗培南存在异质性耐药, 且以稳定型为主。这一发现揭示了传统药敏方法可能漏检的耐药风险。后续计划对筛选获得的耐药亚群进行全基因组测序与生物信息学分析, 深入探究其异质性耐药的具体分子机制。

Stepwise KPC Mutational Accumulation Confers High-Level Ceftazidime-Avibactam Resistance in ST11 Carbapenem-Resistant

Klebsiella Pneumoniae

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Ceftazidime-avibactam (CZA) has become an effective therapeutic option against carbapenem-resistant *Klebsiella pneumoniae* (CRKP). The emergence of *Klebsiella pneumoniae* carbapenemase (KPC) variants in CRKP is a major cause of CZA resistance. However, high-level CZA resistance conferred by accumulated KPC mutations was seldom reported. In this study, we observed that high-level ceftazidime-avibactam resistance was attributed to stepwise KPC mutational accumulation. A total of 21 KPC-producing *K. pneumoniae* isolates were collected from a single patient over one year, encompassing 17 harboring blaKPC-2, 2 harboring blaKPC-33, and 2 harboring blaKPC-275. The patient's treatment course indicated that prolonged CZA pressure likely drove the accumulation of mutations, leading to the sequential evolution from blaKPC-2 to blaKPC-33 and ultimately to blaKPC-275. Molecular docking revealed that the newly identified variant KPC-275 confers high-level CZA resistance, mediated by the cumulative effects of D179Y and T243P mutations, which enhance ceftazidime hydrolysis and diminish avibactam inhibitory activity. Antimicrobial susceptibility testing demonstrated that compared to blaKPC-2, expression of blaKPC-33 and blaKPC-275 in *E. coli* DH5 α elevated the MIC of CZA by 128-fold and 1024-fold, respectively. Moreover, unlike the individual D179Y or T243P mutations, the combination of both conferred high-level resistance to CZA but imposed a fitness cost. Whole-genome sequencing results demonstrated that these highly homologous ST11-type CRKP strains carried blaKPC within Tn6296 on IncFII/IncR plasmids. Additionally, the plasmid carrying blaKPC-275 integrated virulence-associated fragments via

IS5075, forming a hybrid virulence-resistance plasmid. Furthermore, global phylogeographic analysis of 928 KPC variant-producing *K. pneumoniae* isolates revealed pronounced geographical clustering and clone-driven dissemination, with Asia, particularly China, representing the largest reservoir and ST11 identified as the predominant lineage. In view of the widespread prevalence of KPC-KP strains, clinicians should be aware of the risk of treatment failure due to blaKPC mutation-mediated CZA resistance during therapy.

Functional and Structural Characterization of OXA-264 and OXA-895 Reveals Evolutionary Potential for Carbapenem Resistance

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Acinetobacter species are important opportunistic pathogens in healthcare-associated infections, with carbapenems remaining critical therapeutic antimicrobial. However, the emergence and evolution of OXA-type carbapenemases pose an increasingly serious threat to clinical treatment. In this study, we identified two chromosomally encoded OXA-type β -lactamases: OXA-264 from *Acinetobacter haemolyticus* and a novel OXA-230 variant from *Acinetobacter bereziniae*, named OXA-895. Antimicrobial susceptibility testing revealed that although the parent strains were susceptible to carbapenems, overexpression of blaOXA-264 and blaOXA-895 in *A. baumannii* ATCC 17978 conferred resistance to meropenem. Enzyme kinetics analysis demonstrated that both enzymes exhibited measurable carbapenemase activity, with OXA-895 showing reduced substrate affinity but increased catalytic turnover.

Structural modeling and covalent docking analysis indicated that a single amino acid substitution (D253N) in OXA-895 led to a rearrangement of the active site, altering substrate binding and catalytic rate. Together, these findings suggest that subtle sequence variations in chromosomally encoded OXA enzymes can lead to functional differences, highlighting the importance of intrinsic OXA variants in non-*A. baumannii* species as evolutionary reservoirs for carbapenem resistance.

Meropenem-driven Amplification of BlaAFM-1 Leads To High-level Cefiderocol Resistance in Difficult-to-treat *Pseudomonas Aeruginosa*

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Background Cefiderocol (FDC) is a novel siderophore cephalosporin for treating infections caused by carbapenem-resistant *Pseudomonas aeruginosa* (CRPA). However, the mechanisms underlying high-level FDC resistance in CRPA isolates from regions where FDC has not yet been clinically introduced remain unclear

Methods FDC susceptibility was assessed in 310 clinical CRPA isolates from eastern China. Enzyme inhibition assays, functional cloning, Nanopore sequencing, RT-qPCR, gene knockout, and in vitro induction experiments were performed to investigate resistance mechanisms.

Results Three ST266 difficult-to-treat resistant *P. aeruginosa* isolates carrying blaAFM-1 were identified, including one with low-level FDC resistance (MIC = 8 mg/L) and two with high-level resistance (MIC = 64 mg/L). AFM-1 was confirmed as the major determinant

of FDC resistance. In all isolates, blaAFM-1 was located on a conjugative IncP-2 megaplasmid. The low-level resistant isolate carried a single copy of blaAFM-1, whereas the high-level resistant isolates harbored multiple IntI1-mediated tandem copies. Nanopore sequencing and qPCR further confirmed that blaAFM-1 copy number and expression were markedly increased in the high-level resistant isolates, while the plasmid copy number remained unchanged. The amplification and resistance phenotype decreased after serial passage without antibiotics. Notably, blaAFM-1 amplification and elevated FDC MICs (up to 128 mg/L) were induced exclusively under meropenem selection pressure, and were abolished in an intI1 knockout mutant.

Conclusion Meropenem-driven, IntI1-mediated reversible amplification of blaAFM-1 represents a key mechanism underlying high-level FDC resistance in clinical *P. aeruginosa*. These findings highlight important implications for antimicrobial therapy and resistance surveillance.

From Low- To High-Level Resistance: Dynamic Transcriptional Adaptations and Efflux Pump Amplification in Cefiderocol-Stressed *Pseudomonas Aeruginosa*

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Pseudomonas aeruginosa is a bacterium with high antimicrobial resistance to several drugs including carbapenams. Recently, resistance to cefiderocol (FDC), a new siderophore cephalosporin, has been reported despite its rare use in clinical practice. Therefore, this

study aimed to investigate the dynamics of different resistance mechanisms in *P. aeruginosa* that evolve under FDC pressure, as well as the interactions between these mechanisms in evolutionary trajectories to guide clinical medication. *P. aeruginosa* ATCC 27853 was continuously induced with subinhibitory concentrations of cefiderocol in vitro to generate strains with different resistance levels. Phenotypic adaptability and molecular regulatory networks during the evolution of resistance were systematically elucidated using growth curves, pairwise competition assays, transcriptomics, and efflux inhibition assays. The minimum inhibitory concentration (MIC) of the induced FDC-resistant strain increased from 0.125 µg/mL to 64 µg/mL. Simultaneously, the growth rate and peak declined below those of the parental strain. The pairwise competition assay showed that the relative fitness of resistant strains versus parental strains was < 1 in LB and ID-CAMHB broths. Transcriptome analysis revealed that the MIC of the induced FDC-resistant strain was related to the dose of efflux pumps, together with a layer-by-layer regulation of gene expression, to adapt to environmental stress. In the initial resistant strain, efflux pumps were slightly upregulated, and energy metabolism was downregulated. Conversely, in the strain with a MIC of 64 µg/mL, efflux pumps were significantly up-regulated and drove bacterial reprogramming to induce resistance. Furthermore, in the presence of and efflux pump inhibitor phenyl-arginine β -naphthylamide (PA β N), the resistant strains exhibited significantly reduced MICs for FDC. In conclusion, these data indicate that multiple mechanisms of action are involved in the antibacterial activity of *P. aeruginosa* against FDC. Notably, the evolution of resistance was driven by the dose-dependent upregulation of core efflux pumps, complemented by stage-specific global physiological remodeling; however, it also came at a fitness cost.

Molecular Epidemiology of Carbapenemase-carrying *Klebsiella Pneumoniae* in China: Distribution of Carbapenemase Types, Capsular Serotypes, and Virulence Factors

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Abstract We conducted a large-scale genomic analysis of 9,082 carbapenemase-producing *Klebsiella pneumoniae* (CPKP) isolates originating from China and collected between 2005 and 2024, using genomes retrieved from the NCBI database. The aim was to characterize population structure, resistance determinants, capsular diversity, and virulence-associated loci at a national scale. The CPKP population exhibited substantial genetic diversity, encompassing 233 sequence types (STs), 109 capsular serotypes (KLs), and a wide range of carbapenemase genes. KPC-2-producing ST11 was the dominant epidemic lineage nationwide and remained prevalent throughout the study period. Within ST11, a temporal shift in capsular serotypes was observed, with KL47 predominating during 2013–2015 and KL64 becoming dominant from 2016 onward, while both serotypes persisted at substantial frequencies. In contrast, metallo- β -lactamases such as NDM-1, NDM-5, and IMP-4 showed heterogeneous clonal distributions without a single dominant lineage. Carbapenem-producing isolates belonging to hypervirulence-associated capsular serotypes (KL1 and KL2) were detected sporadically. KL1-type CPKP isolates were predominantly associated with ST23 and carried multiple classical virulence-associated loci, whereas KL2-type CPKP isolates were distributed across diverse

STs and exhibited more variable virulence gene carriage. Carbapenemase-producing KL1 and KL2 isolates were first detected in this dataset in 2013 in different regions of China. Virulence gene distribution was strongly structured by capsular serotype and clonal background. Classical hypervirulence-associated loci, including aerobactin, salmochelin, colibactin, and regulators of the mucoid phenotype (rmpADC), were largely confined to KL1 and a subset of KL2 lineages and were infrequently detected among the major carbapenem-producing clones, ST11 and ST15. In contrast, yersiniabactin was widespread among CPKP isolates but showed lineage-specific associations with distinct ICEKp elements. Resistance-associated plasmid backbones, including ColRNAI, IncFIB/IncHI1B, and IncFII, were commonly detected. Overall, this study provides a comprehensive population-level overview of CPKP in China and highlights the expansion of highly resistant clones alongside a limited and structured distribution of classical hypervirulence determinants.

Repeated Emergence and Fitness Heterogeneity of KPC-33 in ST11 *Klebsiella Pneumoniae* under Ceftazidime-avibactam Pressure

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Background Ceftazidime-avibactam (CZA) is an important drug for treating infections caused by KPC-producing *Klebsiella pneumoniae*. However, CZA exposure also selects for emergent KPC variants. Their in vivo evolutionary patterns, differences in fitness costs, and underlying molecular mechanisms remain unclear. **Methods:** We performed a longitudinal multi-omics analysis of 35 clonally related isolates from 8 patients

to define the within-host evolutionary trajectory of KPC variants and the basis of fitness heterogeneity in KPC-33. **Results:** Multiple KPC variants were identified during longitudinal follow-up, among which KPC-33 was the most frequently detected. KPC-33 arose independently in 5 CZA-treated patients and was also detected in 1 patient without documented CZA exposure, whereas other variants were only sporadically identified. KPC-33 consistently showed reduced *kcat* and *K_m* across different strain backgrounds, but the changes in catalytic efficiency were background-dependent. KPC-33 did not exhibit a uniform and pronounced fitness defect, but instead showed marked strain-dependent heterogeneity; Strains with higher competitive fitness generally showed only limited transcriptional changes, whereas those with lower fitness were accompanied by broader transcriptional remodeling. **Conclusion:** In this longitudinal cohort, KPC-33 was repeatedly detected, predominantly under CZA-associated selective conditions. Its fitness consequences were clearly strain background-dependent and may be associated with the extent of transcriptional remodeling. These findings provide new evidence for understanding the in vivo evolution of CZA resistance

TagN-mediated GroP-GalNAc Wall Teichoic Acid Glycosylation Maintains B-lactam Resistance in MRSA by Regulating PBP2a Membrane Localization

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Objective To investigate the role of TagN (α -GalNAc transferase) in β -lactam resistance of an unusual ST630 MRSA isolate (WH99,

tarP⁻/tarS⁻/tarM⁺/tagN⁺) and identify key functional residues of TagN.

Methods Deletion mutants of tagN and tarS were constructed. Resistance was tested by disk diffusion and MIC. WTA glycosylation was analyzed by native-PAGE and ion exchange chromatography. Cell wall structure was examined by TEM and autolysis. Gene expression was measured by RT-qPCR, and PBP2a localization by Western blot. Key residues were identified via truncation and site-directed mutagenesis.

Results Deletion of tagN (but not tarS) caused a 32-fold reduction in oxacillin MIC and loss of WTA GalNAc. The Δ tagN mutant showed thinner, looser cell walls (≈ 15 nm vs. 25 nm) and increased autolysis. Expression of pbp2, fntA, and WTA synthesis genes (tarO, tarA, tarG, tarH) was downregulated, while mecA transcription was unchanged. PBP2a total protein was unaffected, but its membrane localization was impaired. The C-terminal α -helix of TagN was essential; residues N823 and F830 (but not Y831) were critical for function. Double mutation N823A_F830A abolished both GalNAc modification and resistance.

Conclusion TagN is a novel MRSA resistance determinant independent of TarS/TarP. It maintains cell wall integrity via WTA GalNAc glycosylation and regulates PBP2a membrane localization. N823 and F830 in the C-terminal α -helix are core residues, providing a potential target against specific MRSA clones.

Transient AdeABC-mediated Eravacycline Resistance in Carbapenem-resistant *Acinetobacter Baumannii* ST2: A Mutation-independent Efflux Pump Adaptation

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Purpose This study evaluated the impact of sub-MIC eravacycline exposure on carbapenem-resistant *Acinetobacter baumannii* with tigecycline MIC ≥ 8 μ g/mL in clinical laboratory testing, and analyzed the resistance mechanisms

Methods 2144 *A. baumannii* isolates (2021–2024) from a Chinese tertiary hospital were analyzed for resistance trends. For 43 strains with tigecycline MIC ≥ 8 μ g/mL, we conducted: i) in vitro induction of resistance via serial sub-MIC eravacycline passage, ii) efflux pump inhibition assays using phenylalanine-arginine β -naphthylamide, iii) quantification of efflux pump gene expression (adeB, adeS), iv) genomic analysis of resistance-associated mutations.

Results Eravacycline exhibited MIC_{50/90} values that were 2–4-fold lower than those of tigecycline, demonstrating superior in vitro efficacy. Exposure to sub-MIC levels of eravacycline significantly increased resistance to eravacycline, tigecycline, minocycline, and polymyxin B, with PA β N reversing these effects. The expression of efflux pump-related genes adeB and adeS was upregulated, especially in eravacycline-induced strains. Although 88.37% of strains lacked mutations, eravacycline resistance demonstrated greater stability in adeB or adeS mutants. In 97.06% of strains with tigecycline MIC ≥ 4 μ g/mL, the induced eravacycline MICs exceeded achievable alveolar concentrations. Eravacycline resistance demonstrated a correlation with tigecycline. And its combination with polymyxin B showed no synergistic effect.

Conclusion Eravacycline exhibited superior in vitro antibacterial efficacy against *A. baumannii* compared to tigecycline, but it is necessary to be alert to the resistance caused by the rapid increase in efflux pump

expression. These findings highlight the need for cautious clinical use of eravacycline to mitigate resistance development.

Keywords Eravacycline, Tigecycline, Polymyxin B, Efflux pump, CRAB

Dynamic Balance of CRISPR-Cas Immunity and Antimicrobial Resistance Plasmid Anti-immunity Mediated by A Bi-functional Acr-Aca Protein AcrIE10

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Despite targeting by CRISPR-Cas system, antimicrobial resistance plasmids are prevalent in clinical isolates of carbapenem-resistant *Klebsiella pneumoniae* which represent a major public health threat. A stable co-existence of plasmids and CRISPR-Cas systems is mediated by anti-CRISPR (Acr) proteins. Here, we report that previously identified AcrIE10 encoded by a resistance plasmid combines two functions: it inhibits CRISPR immunity by directly binding Cas7* subunit through its Acr domain, and acts as an Acr-associated (Aca) protein that self-represses the transcription of Acr locus. AcrIE10 is a first example of an Aca protein that utilizes N-terminal ribbon-helix-helix (RHH) domain to specifically recognize the inverted repeat (IR) region in its own promoter. Crucially, a dimerization of AcrIE10 dimers is required for the effective binding to the IR and self-repression, while stoichiometry-dependent interaction with Cas7* facilitates transition to de-repressed state. These findings elucidate molecular mechanisms by which AcrIE10 operates as a dual-functional Acr-Aca protein to achieve a delicate balance between host

CRISPR-Cas immunity and plasmid anti-defence.

Molecular Epidemiology of Clinical Carbapenem-resistant *Citrobacter* Spp in China (2016–24)

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Background The global rise of carbapenem-resistant *Citrobacter* (CRC) has become a public health concern, but large-scale multicenter data from China remain limited

Methods From January 2016 to December 2024, 33,490 Gram-negative bacilli were isolated from patients with urinary tract, bloodstream, intra-abdominal, or respiratory tract infections across 23 hospitals in 17 Chinese provinces or municipalities. Among them, 379 *Citrobacter* isolates were identified, and 47 were confirmed as CRC. Antimicrobial susceptibility testing, whole-genome sequencing, and bioinformatics analysis were performed to characterize the molecular epidemiology of CRC

Findings CRC accounted for 12.4% (47/379) of *Citrobacter* isolates, with *Citrobacter freundii* being the predominant species. Provinces including Jiangsu, Liaoning, Yunnan, and Heilongjiang had CRC to *Citrobacter* ratios exceeding 20%, and urinary tract and intra-abdominal infections were the main sources. The CRC to *Citrobacter* ratio rose sharply from <10% to 20% during 2022–2024, peaking in 2024. Genomic characterization of 26 CRC strains (2021–2024) revealed that 24 were carbapenemase-producing *Citrobacter* (CPC), primarily carrying bla_{NDM}-1 or bla_{NDM}-5 (n=19). One *Citrobacter portucalensis* co-produced NDM-1 and KPC-2, and one *Citrobacter amalonaticus* carried mcr-

9. Multilocus sequence typing showed high genetic diversity, with at least 17 distinct sequence types (STs), among which ST116 was the most prevalent (n=4). Notably, ST22, a high-risk international clone, was not detected. Phylogenetic analysis revealed only two clonal transmission events (within the same hospital), indicating limited spread. CRC strains were highly resistant to β -lactams and their inhibitors; mono-KPC-producing strains remained susceptible to ceftazidime-avibactam, and all strains were susceptible to colistin. Genetic context analysis showed diverse blaNDM-carrying mobile elements, whereas blaKPC and blaVIM structures were stable.

Interpretation CRC in China is characterized by the predominance of *C. freundii*, NDM-type carbapenemases, high ST diversity, and the absence of the high-risk ST22 clone. Clonal transmission remains limited; however, the rapid increase in CRC proportion in recent years underscores the urgent need for enhanced national and global surveillance.

临床分离难治性耐药铜绿假单胞菌分子流行病学特征研究

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目的 探究临床分离难治性耐药铜绿假单胞菌 (DTR-PA) 的临床特征及分子流行病学特征。

方法 收集 2021-2025 年湘雅医院临床分离的非重复性 DTR-PA 菌株,并选取同期分离的非 DTR-PA 菌株进行比较分析其临床特征。采用纸片扩散法检测头孢他啶-阿维巴坦 (ceftazidime-avibactam, CZA) 和氨曲南-阿维巴坦 (aztreonam-avibactam, AZA) 对 DTR-PA 的敏感性,肉汤微量稀释法检测亚胺培南-瑞来巴坦 (imipenem-relebactam, IMR) 的

最低抑菌浓度 (minimum inhibitory concentration, MIC); 大蜡螟感染模型评估 DTR-PA 的毒力,并通过全基因组测序分析其耐药基因、毒力基因和序列分型。

结果 ①共收集到 44 株 DTR-PA,患者以男性和中老年患者为主,主要分布于 ICU 及呼吸内科 ICU; DTR-PA 患泌尿系统感染的几率显著高于非 DTR-PA。②44 株 DTR-PA 对三种新型抗菌药物的耐药率最低的是 CZA (38.6%, 17/44),其次是 AZA (59.1%, 26/44)、IMR (61.4%, 27/44)。③大蜡螟感染模型结果显示,39 株 DTR-PA 可导致幼虫最终死亡率达到 100%,说明本院 DTR-PA 整体毒力较强。④全基因组测序显示,44 株 DTR-PA 可分为 A~G 共 7 个类群,其中 Cluster A 为优势克隆群,ST463 为主要流行型别,碳青霉烯酶基因以 blaKPC-2 最常见,且 ST463 型菌株均携带 blaKPC-2; 毒力基因显示,44 株 DTR-PA 均携带 *exoT* 和 *exoY* 基因。

结论 本院临床分离 DTR-PA 主要分布于 ICU 及呼吸内科 ICU 等科室。患者多为中老年男性,且合并多种基础疾病,泌尿系统感染的几率显著高于非 DTR-PA。DTR-PA 对 CZA、AZA 和 IMR 的耐药率较高,因此,针对 DTR-PA 所致感染时,应谨慎选择此类抗菌药物。DTR-PA 中碳青霉烯酶基因的检出率非常高,以携带 blaKPC-2 为主,提示 blaKPC-2 在其耐药中发挥了重要作用。值得注意的是,本院临床分离 DTR-PA 的毒力较高。兼具高毒力和高耐药的携带 blaKPC-2 基因 ST463 的 DTR-PA 在本院 ICU 存在克隆传播,应监测其流行情况,并采取相应的措施防治其进一步播散。

2020-2024 年广东地区血液内科血流标本分离菌流行病学变迁分析

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目的 探讨 2020-2024 年广东省 56 家成员单位血液内科血液标本病原菌分布和常见抗菌药物耐药率和敏感率变迁, 比较性明晰血液内科血流感染的流行病学特征。

方法 对 2020-2024 年广东省 56 家成员单位血液内科、呼吸内科和重症监护病房血液标本的临床分离株分布构成比进行分析, 并对 5 年内检出率高的病原菌进行耐药性变化分析。分层抽取碳青霉烯耐药革兰阴性菌进行碳青霉烯酶型检测, 并检测新型抗菌药物体外药敏试验。

结果 5 年间, 广东省 56 家成员单位血液内科、呼吸内科和 ICU 血液标本分离菌株分别为 8968 株、6440 株和 25511 株, 三个科室病原菌分布构成比差异有统计学意义 ($P < 0.001$)。其中, 血液内科占比高的细菌分别是大肠埃希菌 (24.1%)、肺炎克雷伯菌 (17.5%)、铜绿假单胞菌 (11.7%)、凝固酶阴性葡萄球菌 (15.2%) 和金黄色葡萄球菌 (5.1%)。耐药分析发现, 大肠埃希菌和肺炎克雷伯菌对美罗培南耐药率分别从 2020 年 6.7% 和 5.8% 上升至 2024 年 14.0% 和 15.8%; 铜绿假单胞菌对美罗培南和亚胺培南耐药率从 2020 年 6.2% 和 10.2% 下降至 2024 年 1.9% 和 6.1%; 而鲍曼不动杆菌对常见抗菌药物耐药变迁呈现先下降再上升的趋势。金黄色葡萄球菌对常见抗菌药物敏感率整体比凝固酶阴性葡萄球菌高, 无糖肽类和利奈唑胺耐药株。屎肠球菌对万古霉素耐药率从 2020 年 0 上升至 2024 年 23.1%。主动监测 CRO 菌株的碳青霉烯酶表型, 80% 大肠埃希菌携带 blaNDM、90% 肺炎克雷伯菌携带 blaKPC、10% 铜绿假单胞菌携带 blaVIM 和 100.0% 鲍曼不动杆菌携带 blaOXA-23。针对 CRO 的药物敏感性显示, 碳青霉烯耐药大肠埃希菌对替加环素、多黏菌素和氨曲南/阿维巴坦耐药率为 0%, 碳青霉烯耐药肺炎克雷伯菌对氨曲南/阿维巴坦、头孢他啶/阿维巴坦和亚胺培南/瑞莱巴坦的耐药率为 0%。碳青霉烯耐药铜绿假单胞菌对阿米卡星和多黏菌素 B 敏感率达 95.0%, 对头孢他啶/阿维巴坦耐药率为 45.0%; 碳青霉烯耐药鲍

曼不动杆菌对舒巴坦/杜洛巴坦敏感率达 100.0%, MIC90 为 2 $\mu\text{g/ml}$, 对依拉环素 MIC50 和 MIC90 分别为 1 $\mu\text{g/ml}$ 和 2 $\mu\text{g/ml}$ 。

结论 血液内科血液标本分离菌构成与呼吸内科和 ICU 比较有显著差异。CRO 检出率呈升高趋势, 但对抗 CRO 的新型抗菌药保持高度敏感。

Diversity of *Optra* Genetic Structures in *Enterococcus Faecalis* From Retail Chicken and The Differential Biofilm-Forming Abilities of Isolates at Non-Frozen Temperatures

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Aims This study aimed to explore the diversity of *optrA* genetic structures in *Enterococcus faecalis* from retail chicken and the variance in their biofilm-forming capabilities at refrigerated and room temperatures. By comprehensively studying these two traits, we aim to fully understand the transmission and biofilm-forming capabilities at non-frozen temperatures of *optrA*-positive *E. faecalis*

Methods and results Analysis of Chinese-sourced *E. faecalis* genomes in the database indicated that 65.76% were *optrA*-positive, with animals as the predominant hosts. In 2020, 15 *optrA*-carrying strains were isolated from 96 retail chicken samples from four Chinese supermarkets. The *optrA* gene was situated on plasmids or chromosomes. A novel *optrA*-carrying plasmid structure was identified, resulting from IS1485-mediated structural changes. Tn6674-like and Tn558-like structures mediated inter-chromosomal transfer of *optrA*, while IS1216E and ISEnf1 promoted inter-plasmid transfer. Some isolates showed a greater tendency

for biofilm formation at refrigerated temperature, and others at room temperature

Conclusions In conclusion, this research reveals the genetic intricacy of *optrA*-positive *E. faecalis* and their temperature-associated biofilm-forming behaviors, highlighting the necessity of monitoring food-related microbial hazards

In Vitro Activity of Imipenem/relebactam and Ceftolozane/tazobactam Against *Pseudomonas Aeruginosa* Isolates in China: SMART 2020-2022

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Objective To delineate the in vitro susceptibility profiles of *Pseudomonas aeruginosa* (PsA) to ceftolozane/tazobactam (CT) and imipenem/relebactam (IMR) in China, with a focus on carbapenem-resistant (CR), multidrug-resistant (MDR), and difficult-to-treat resistant (DTR) PsA isolates, using data from the SMART surveillance program (2020–2022)

Methods A total of 1,350 PsA isolates were collected from 18 tertiary hospitals across China (2020–2022). Species confirmation and antimicrobial susceptibility testing were performed at a central laboratory. Minimum inhibitory concentrations (MICs) were determined by broth microdilution and interpreted per CLSI M100 (2024) and EUCAST 2024 criteria. Resistance phenotypes (CR, MDR, DTR) were defined using standard criteria. Quality control included reference strains *E. coli* ATCC 25922, PsA ATCC 27853, and *K. pneumoniae* ATCC 700603

Results Overall, 43.1% (582/1,350) of isolates were CR-PsA, 28.7% (388/1,350) MDR-PsA, and 14.3% (193/1,350) DTR-PsA. CT showed susceptibility rates of 87.1% (1,176/1,350) overall and 73.9% (430/582) against CR-PsA. IMR susceptibility was 45.5% (263/578) against CR-PsA, but higher against MDR-PsA (36.6%, 142/388) and DTR-PsA (16.6%, 32/193). Colistin exhibited the highest activity (>98% susceptibility across resistant subgroups). Regional and ICU vs. non-ICU variations were noted, with higher resistance in ICU settings. MIC distribution favored CT over ceftazidime/avibactam for resistant isolates

Conclusion CR-PsA, MDR-PsA, and DTR-PsA are highly prevalent in China. CT demonstrates superior in vitro activity against PsA, including CR-PsA, compared to IMR. These findings support CT as a valuable therapeutic option for suspected CR-PsA infections, but ongoing surveillance and judicious use are critical due to emerging resistance

Key Words : *Pseudomonas aeruginosa*; ceftolozane/tazobactam; imipenem/relebactam; carbapenem resistance; antimicrobial susceptibility; China

Fitness Costs and Underlying Mechanism of Tigecycline Resistance in *Escherichia Coli* Induced by Sub-minimal Inhibitory Concentrations of Tigecycline

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Background *Escherichia coli* strains resistant to tigecycline have been increasingly reported in recent decades and pose a serious threat to global public health

Objective The aim of this study was to investigate the fitness costs and underlying mechanism of tigecycline-induced resistance in *E. coli* strains with different resistance characteristics.

Methods Tigecycline-resistant *E. coli* strains were obtained via continuous in vitro induction with tigecycline concentrations below the minimal inhibitory concentration, and the cross-resistance and fitness costs of acquiring tigecycline resistance were investigated in all the induced resistant strains. The potential resistance mechanism was explored by proteomic profiling as well as qRT-PCR analysis.

Results Compared with those of the parent strains, the tigecycline MICs in the induced resistant strains were 8 to 32 times greater. The development of tigecycline resistance decreased the susceptibility of the strains to β -lactams and quinolones. The induced resistant strains also suffered fitness costs, with reduced growth rates, motility, competitiveness and biofilm formation ability. The expression analysis at molecular levels revealed the downregulation of genes encoding flagellum-mediated motility and outer membrane protein OmpF in an induced resistant strain and the upregulation of AcrAB-TolC efflux pump genes and its regulatory gene *marA*. In addition, tigecycline susceptibility increased when induced resistant strains were cocultured with the efflux pump inhibitor CCCP.

Conclusion This study revealed that the acquisition of tigecycline resistance led to a decrease in bacterial fitness, and the overproduction of efflux pump AcrAB-TolC and the downregulation of OmpF mediated by MarA might be the main mechanisms for the decreased susceptibility of *E. coli* to tigecycline and other antibiotics.

Combinatorial Effects of A Novel SHV-248

Variant, NDM-5, and OmpK35 Deficiency Drive High-level Cefiderocol Resistance in *Klebsiella Pneumoniae*

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ABSTRACT Cefiderocol holds significant therapeutic value against metallo- β -lactamase-producing Enterobacterales. However, reduced susceptibility to cefiderocol in NDM-producing strains is increasingly observed. This study elucidated the mechanism of high-level cefiderocol resistance in a clinical *Klebsiella pneumoniae* strain (KP5663, ST147-KL64) producing NDM-5, which emerged without prior drug exposure. Whole-genome sequencing identified, alongside blaNDM-5 and ompK35/ompK36 porin deficiencies, a novel β -lactamase gene variant, blaSHV-248. Functional characterization revealed that SHV-248 exhibited a moderately higher affinity for cefiderocol (binding energy: -5.15 kcal/mol) and a 1.6-fold greater hydrolytic activity against nitrocefin compared to SHV-12. Consistent with this, heterologous expression of blaSHV-248, but not blaSHV-12, increased the cefiderocol minimum inhibitory concentration (MIC) by fourfold, although the MIC remained within the susceptible range. Critically, genetic complementation demonstrated that restoring functional ompK35 alone reduced the cefiderocol MIC of KP5663 by 16-fold, whereas complementation with ompK36 had no effect. These findings define a novel synergistic triad wherein the combined, rather than individual, action of blaNDM-5, the novel variant blaSHV-248, and porin deficiency (primarily ompK35) is necessary and sufficient for high-level cefiderocol resistance.

IMPORTANCE This study identifies a novel SHV variant and, more importantly, delineates a distinct

“key determinant combination” model for cefiderocol resistance. This model does not rely on exceptional enzyme overproduction but on the convergence of three clinically relevant factors: a transmissible blaNDM-5, a chromosomally evolving SHV variant with incremental efficiency gains, and frequent porin loss. It underscores that, for NDM-producing *Klebsiella pneumoniae*, risk assessment must evolve to evaluate porin status alongside β -lactamase profiles, as even modestly more efficient enzymes like SHV-248 can become decisive factors within a permissive genetic background.

血培养阳性肉汤直接快速药敏试验性能评估

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目的 通过比较血培养阳性标本直接快速药敏试验(RAST)与常规药敏试验结果的符合率(CA),评估血培养直接快速药敏试验的临床应用价值,为实验室血流感染检测策略优化提供依据。

方法 收集 2025 年 1 月至 2025 年 6 月空军军医大学第二附属医院血培养阳性标本,参考美国临床和实验室标准化协会(CLSI)M100 S35 版对血培养阳性标本进行直接药敏试验和常规药敏试验,并按照 CLSI 折点标准进行结果判断。

结果 58 株大肠埃希菌中,美罗培南的符合率 CA%为 100% (58/58),头孢吡肟的 CA%为 93.1% (54/58),2 株出现极重大错误;环丙沙星的 CA%为 87.9% (51/58),出现 4 个重大错误;氨苄西林的 CA%为 91.4% (53/58);头孢他啶的 CA%为 89.7% (52/58),出现 2 个重大错误。32 株肺炎克雷伯菌中美罗培南的符合率 CA%为 100% (32/32);头孢吡肟的 CA%为 87.5% (28/32);环丙沙星的 CA%为 90.6% (29/32),出现 1 个极重大错误;复方新诺明

的 CA%为 93.8% (30/32),出现 1 个极重大错误。10 株铜绿假单胞菌中,美罗培南、头孢吡肟、环丙沙星和头孢他啶的符合率 CA%均为 100% (10/10);

结论 血培养直接快速药敏试验在常见肠杆菌和铜绿假单胞菌中能够准确、快速为临床提供初步药敏结果,特别是碳青霉烯类药物中,未出现重大错误。为临床开展快速抗感染精准治疗提供依据。

关键词: 血培养; 快速药敏; 性能评估;

2025 年甘肃省血液标本细菌分布及其耐药性分析

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目的 分析 2025 年甘肃省血液标本病原菌分布及耐药性特征,为血流感染临床诊疗和抗菌药物合理使用提供依据。

方法 收集甘肃省细菌耐药监测网 100 所医院 2025 年血液标本细菌监测数据,剔除重复菌株后采用药敏纸片扩散法、最低抑菌浓度法及全自动微生物检测系统进行药敏试验与统计分析。

结果 共纳入菌株 5702 株,革兰阳性菌占 39.9%,革兰阴性菌占 60.1%。革兰阳性菌以表皮葡萄球菌、金黄色葡萄球菌、人葡萄球菌、屎肠球菌和肺炎链球菌为主。MRSA 检出率 31.2%,MRCNS 检出率 78.4%,未检出万古霉素、替考拉宁耐药株。粪肠球菌对氨苄西林耐药率 5.6%,屎肠球菌对氨苄西林耐药率 79.3%;肺炎链球菌对红霉素耐药率 88.8%,对青霉素、左氧氟沙星耐药率较低。革兰阴性菌以大肠埃希菌、肺炎克雷伯菌、阴沟肠杆菌、鲍曼不动杆菌为主。大肠埃希菌对三代头孢、喹诺酮类耐药率分别为 50.5%、51.0%,碳青霉烯类耐药率

仅 0.4%。肺炎克雷伯菌碳青霉烯类耐药率 6.3%，阴沟肠杆菌对头孢他啶、头孢噻肟耐药率偏高。铜绿假单胞菌碳青霉烯类耐药率 17.1%，鲍曼不动杆菌碳青霉烯类耐药率高达 74.5%，多重耐药问题突出。嗜麦芽窄食单胞菌对常用药物整体敏感。

结论 2025 年甘肃省血液分离菌以革兰阴性菌为主，大肠埃希菌为优势菌株。不同菌种耐药差异明显，大肠埃希菌对三代头孢、喹诺酮类耐药率偏高，鲍曼不动杆菌碳青霉烯类耐药形势严峻。葡萄球菌、肠球菌、链球菌对万古霉素、利奈唑胺保持高度敏感。临床应结合本地区耐药监测结果，规范经验性抗感染治疗，加强多重耐药菌防控，促进抗菌药物合理应用。

关键词：血液；细菌分布；耐药性；血流感染；甘肃省

甘肃省细菌耐药监测网 2023—2025 年脑脊液标本分离细菌耐药性监测报告分析

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目的 了解甘肃省脑脊液标本分离细菌的种类分布特征及耐药性变迁趋势，为临床中枢神经系统感染的早期诊断及合理使用抗菌药物提供参考依据。

方法 收集 2023—2025 年甘肃省细菌耐药监测网各成员单位上报的脑脊液标本分离细菌数据，三年间分别有 83 所、89 所和 100 所医院的数据纳入最终分析。以保留同一患者相同细菌第一株的原则剔除重复菌株后，采用 WHONET 5.6 软件对病原菌分布及药敏结果进行统计分析。

结果 2023—2025 年共纳入脑脊液分离菌 838 株（依次为 218、344、276 株），革兰阳性菌连续三

年占主导（66.1%、66.0%、70.7%）。三年累计分离前 5 位依次为表皮葡萄球菌、人葡萄球菌、鲍曼不动杆菌、大肠埃希菌和肺炎克雷伯菌。耐甲氧西林凝固酶阴性葡萄球菌检出率持续处于高水平（70.5%~77.0%），耐甲氧西林金黄色葡萄球菌检出率逐年攀升，三年间均未发现对万古霉素及替考拉宁耐药株。屎肠球菌对氨苄西林耐药率（60.0%~86.7%）显著高于粪肠球菌，2025 年屎肠球菌对万古霉素耐药率达 13.3%，需警惕。肺炎链球菌对红霉素耐药率居高（88.2%~100.0%），但对左氧氟沙星保持完全敏感。革兰阴性菌中，三代头孢菌素耐药大肠埃希菌检出率呈上升趋势，碳青霉烯类耐药大肠埃希菌仅 2023 年检出（15.4%），后两年未见检出。肺炎克雷伯菌对碳青霉烯类耐药形势严峻，三年检出率分别为 30.8%、40.0%和 33.3%。鲍曼不动杆菌耐药情况极为恶劣，碳青霉烯类耐药率高达 75.0%~85.7%，但对多黏菌素 B 未见耐药，对米诺环素耐药率相对较低。

结论 2023—2025 年甘肃省脑脊液分离菌以凝固酶阴性葡萄球菌为主，整体耐药形势严峻且复杂。耐甲氧西林金黄色葡萄球菌检出率逐年升高、肺炎克雷伯菌对碳青霉烯类高度耐药及鲍曼不动杆菌严重多重耐药，均对临床治疗构成重大挑战。需持续开展本地区脑脊液耐药监测，以指导临床合理选用可透过血脑屏障的抗菌药物。

关键词：脑脊液；病原菌；耐药性；凝固酶阴性葡萄球菌；鲍曼不动杆菌；甘肃省细菌耐药监测网

2025 年甘肃省儿童细菌耐药监测分析

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目的 分析 2025 年甘肃省儿童及新生儿细菌感染和耐药现状,旨在指导儿科抗菌药物合理应用。

方法 菌株资料来源于 2025 年 1 月 1 日至 12 月 31 日甘肃省细菌耐药监测网 100 所成员单位细菌室,细菌抗菌药物敏感性试验按照全国细菌耐药监测网技术方案进行,结果判断采用美国临床实验室标准化委员会(CLSI)相关标准,利用 WHONET 5.6 软件对数据进行统计分析。

结果 2025 年甘肃省儿童及新生儿共分离临床菌株 20,685 株,革兰阳性菌和阴性菌分别占 41.6% 和 58.4%。痰液为最主要标本来源(53.9%),其次为脓液(4.1%)、尿液(3.8%)和血液(2.3%)。前 5 位分离株依次为金黄色葡萄球菌(24.6%)、流感嗜血杆菌(15.5%)、大肠埃希菌(14.0%)、肺炎链球菌(8.5%)和肺炎克雷伯菌(7.9%)。新生儿组与非新生儿组最主要分离株分别为大肠埃希菌(25.6%)和金黄色葡萄球菌(25.1%)。肺炎链球菌对红霉素高度耐药(97.0%),对青霉素和左氧氟沙星耐药率较低(分别为 0.5%和 0.8%),未检出万古霉素及利奈唑胺耐药株。耐甲氧西林金黄色葡萄球菌检出率新生儿组(47.9%)显著高于儿童组(33.3%),耐甲氧西林凝固酶阴性葡萄球菌检出率新生儿组(85.2%)亦高于儿童组(70.9%),两组均未发现万古霉素及替考拉宁耐药株。碳青霉烯类耐药肠杆菌目细菌(CRE)、碳青霉烯类耐药铜绿假单胞菌及碳青霉烯类耐药鲍曼不动杆菌检出率,新生儿组(7.6%、7.7%、32.0%)均高于儿童组(1.0%、3.1%、13.0%),提示新生儿面临更为严峻的多重耐药菌感染威胁。儿童组三代头孢菌素耐药大肠埃希菌检出率(46.7%)高于新生儿组(35.7%),而两组碳青霉烯类耐药大肠埃希菌检出率均处于低水平(儿童组 0.6%,新生儿组 0%)。

结论 2025 年甘肃省儿童分离菌以革兰阳性菌为主,新生儿组与儿童组在病原菌构成及耐药特征上存在明显差异。新生儿组耐甲氧西林葡萄球菌及碳青霉烯类耐药革兰阴性菌检出率均高于儿童组,整体耐药形势不容乐观。应重点加强新生儿病房多重耐药菌的主动筛查与持续监测,并规范儿科抗菌

药物的临床应用。

关键词: 细菌;耐药;儿童;新生儿;甘肃省

Emergence of Polymyxin Resistance Driven by A PhoQ Mutation in KPC-2-Producing *Klebsiella Pneumoniae*

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Background The emergence of polymyxin-resistant, carbapenem-resistant *Klebsiella pneumoniae* (CRKP) presents a critical challenge to clinical management. This study aimed to delineate the molecular mechanisms driving the acquisition of polymyxin resistance in CRKP

Methods We analyzed polymyxin-susceptible and polymyxin-resistant CRKP isolates obtained from a single patient. Antimicrobial susceptibility testing was performed to determine the minimum inhibitory concentrations. Whole genome sequencing was employed to identify variations in two-component systems and to screen for *mcr* genes, which were involved in polymyxin resistance. Differential gene expression was assessed using RNA sequencing and validated by quantitative real-time PCR. Furthermore, site-directed mutagenesis was utilized to confirm the causal role of specific mutations in conferring the resistant phenotype.

Results An L96P mutation in the PhoQ protein was found in the polymyxin-resistant CRKP isolate. Compared with the PhoQ wild-type, this mutation significantly upregulated expression of *phoP/Q*, *pmrD*, and *arnBCADTEF* operon-related genes. A corresponding L96P mutant was subsequently constructed in the polymyxin-susceptible ATCC 13883 strain via site-directed

mutagenesis. Antimicrobial susceptibility testing confirmed that the PhoQ L96P mutation elevates the minimal inhibitory concentrations of colistin and polymyxin B to 64 mg/L and >32 mg/L, respectively, from a baseline of 0.5 mg/L.

Conclusion The PhoQ L96P mutation is a pivotal driver of polymyxin resistance in CRKP, primarily mediated through the upregulation of the *arnBCADTEF* operon.

Integrated Clinical and Molecular Profiling Reveals Key Virulence–Resistance Mechanisms in *Klebsiella Pneumoniae* Bloodstream Infections

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Background The rising prevalence of hypervirulent *Klebsiella pneumoniae* (hvKP) and carbapenem-resistant *K. pneumoniae* (CRKP), alongside the emergence of carbapenem-resistant hvKP (CR-hvKP), poses increasing clinical challenges. However, interactions among virulence factors, resistance mechanisms, and organ injury in bloodstream infections (BSI) remain insufficiently understood, and integrated clinical–molecular analyses are limited. This study analysed the clinical features, antimicrobial resistance patterns, and virulence architectures of KP BSI isolates to support early risk stratification and precision therapy

Methods A cohort of 144 patients with KP BSI was analysed. Virulence and resistance genes were detected using polymerase chain reaction (PCR). Cohabiting patterns were assessed through hierarchical

clustering and correlation analysis, and associations between virulence modules and clinical indicators were evaluated using Pearson correlation, chi-square tests, and Mann–Whitney U tests

Results Virulence profiles differed markedly across strain types. A novel *aer*–*iroB*–*irp2* siderophore module was identified and was significantly associated with elevated total bilirubin (TBIL) and reduced estimated glomerular filtration rate (eGFR). Hs-CRP showed strong positive correlations with key siderophore genes, particularly *irp2*. A positive correlation between *rmpA* and *aer* suggested a potential capsule–iron acquisition pattern. In addition, *qnrA* showed significant positive correlation with *irp2*, indicating convergence between resistance and virulence traits

Conclusions Siderophore-driven inflammation, capsule–iron synergy, and resistance–virulence convergence were identified as key mechanisms in KP BSIs. The *aer*–*iroB*–*irp2* module and *rmpA*–*aer* pattern may serve as early markers of hypervirulence and organ involvement. These molecular signatures may support early risk stratification and guide the development of targeted therapies to mitigate organ injury

Keywords *Klebsiella pneumoniae*, Carbapenem resistance, Hypervirulent, Plasmid siderophore system, Resistance–virulence convergence

Genomic Characterization of A Multidrug-resistant *Empedobacter Falsenii*: Transposon-mediated Horizontal Transfer of A D Fola Gene Confers Resistance To Trimethoprim-sulfamethoxazole

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Background *Empedobacter falsenii* is an increasingly recognized opportunistic pathogen characterized by intrinsic multidrug resistance (MDR). This study characterizes an *E. falsenii* isolate exhibiting a complex resistance profile

Methods A bacterial strain (A7) was isolated from the ascites of an elderly female patient presenting with obstructive jaundice and multiple complications. Phenotypic identification and antimicrobial susceptibility testing were performed using the VITEK 2 system, followed by whole-genome sequencing (WGS) via the Illumina platform and comprehensive bioinformatic analyses

Results Strain A7 exhibited high-level resistance to carbapenems and trimethoprim-sulfamethoxazole (TMP-SMX). Although initially misidentified as *Mycobacteroides* spp. by biochemical assays, WGS definitively identified the isolate as *E. falsenii*. Genomic analysis revealed the presence of two distinct *folA* genes: a conserved wild-type and a truncated variant. Sequence and phylogenetic analyses demonstrated that the truncated *folA* originated from the phylum Firmicutes (*Bacillota*). Furthermore, the sequence region harboring this gene was accompanied by a Tn3 family transposase (TnAs3) and significant GC skew abnormalities, confirming the occurrence of horizontal gene transfer (HGT)

Conclusion This study confirms the cross-phylum horizontal transfer of a truncated *folA* gene driven by a transposon in *E. falsenii*. This novel mechanism

highlights the stealthy dissemination pathways of resistance genes in complex clinical environments

Structural and Sunctional Characterization of Novel KPC Subtypes in *Klebsiella Pneumoniae*: Implications for Ceftazidime-avibactam Resistance

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Carbapenem-resistant *Klebsiella pneumoniae* (CRKP) is a major clinical concern, with KPC-type carbapenemases as the primary resistance mechanism. The emergence of novel KPC subtypes has led to increased resistance to ceftazidime-avibactam, a key treatment for CRKP. This study explores the structural and functional properties of these novel KPC subtypes, their impact on resistance mechanisms, and their implications for treatment strategies.

Clinical ceftazidime-avibactam-resistant *K. pneumoniae* strains were collected from hospitals in China (2019-2022). Whole-genome sequencing identified mutations in the KPC gene. Enzyme assays tested the hydrolytic activity of purified KPC enzymes against β -lactams, with inhibition tests for β -lactamase inhibitors. Molecular dynamics simulations assessed enzyme conformational changes and drug interactions.

Novel KPC subtypes—especially KPC-33—mainly from *K. pneumoniae*, harbored key mutations in the Ω -loop (D179Y) and 270-loop (tandem repeats), altering resistance and virulence. Compared to KPC-2, most variants showed reduced catalytic efficiency and altered substrate affinity, though KPC-2-like ones (KPC-35, KPC-79, and KPC-93) retained partial activity. Vaborbactam inhibited all subtypes; avibactam

and relebactam were less effective. Crucially, structural simulations revealed that mutations near Trp105, the Ω -loop, and 270-loop caused significant conformational changes—particularly affecting Ser70 orientation and activity. Enzymes like KPC-33, KPC-76, KPC-123, and KPC-135 showed increased Ω -loop flexibility, displacing Ser70 and impairing hydrolysis. Though KPC-2-like enzymes had milder effects, all mutant enzymes displayed enhanced non-specific ligand binding and disrupted interaction with Ser70, undermining drug efficacy.

Mutations in KPC enzymes, particularly in the active site loops (Ω - and 270-loop), lead to significant structural alterations that affect drug binding and hydrolysis. These changes impact their binding affinity for β -lactamases and β -lactamase inhibitors, highlighting the urgent need for novel therapeutic strategies targeting the structural vulnerabilities of KPC enzymes.

Molecular Characterization of Mcr Genes and Chromosome-mediated Colistin Resistance in Clinical *Klebsiella Pneumoniae* Isolates

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Colistin is a critical antibiotic for treating carbapenem-resistant gram-negative bacterial infections. However, the issue of heteroresistance and the growing prevalence of colistin resistance have become increasingly severe. This study analyzed the resistance mechanisms of 50 colistin-resistant *Klebsiella pneumoniae* (ColR-Kpn) strains, with a focus on the molecular characteristics of five mcr-positive isolates. The most prev-

alent sequence type (ST)–K locus type (KL) combinations were ST11-KL47 (30%, 15/50), followed by ST15-KL19 (22%, 11/50) and ST48-KL62 (16%, 8/50). The MIC₅₀ and MIC₉₀ of colistin for the ColR-Kpn strains were 16 mg/L and 64 mg/L, respectively. Both mcr genes (mcr-1.1/mcr-8.2) and chromosomally mediated determinants—including mutations in two-component regulatory systems and the negative regulator mgrB—were identified among the ColR-Kpn strains. The five mcr-carrying ColR-Kpn strains belonged to four distinct STs—ST6092 (1), ST273 (1), ST1766 (1), and ST22 (2)—and harbored multiple resistance genes conferring resistance to aminoglycosides, β -lactams, quinolones, and other antimicrobials, showing a high concordance between genotypic resistance profiles and phenotypic susceptibility patterns. A synergistic effect between the mcr-1.1 gene and mutations in the regulator mgrB was observed, contributing to high-level colistin resistance in strain ColR-Kpn42 (MIC > 64 mg/L). Except for Kpn35, in which mcr-1.1 is located on the chromosome, the mcr-1.1/8.2 genes of the other four strains are located on IncX4, IncI2 and IncFII(K) plasmids and possess a relatively complete type IV secretion system, suggesting their potential for horizontal transfer. Our work documents the emergence of mcr-1.1/8.2 and chromosome-mediated colistin resistance clinical *K. pneumoniae* isolates from Jiangsu province, China. Continuous surveillance, antimicrobial stewardship, and control measures should be performed to prevent further dissemination.

上海市 92 所医院抗菌药物使用与耐药菌检出调查

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目的 调查上海市 92 所二级及以上医院抗菌药物使用及主要多重耐药菌检出情况, 比较二级与三级医院的差异, 探索抗菌药物使用与多重耐药菌检出关联, 分析不同级别医院耐药谱分化特征及驱动因素, 为精准化防控提供依据。

方法 采用网络填报的形式, 于 2023 年 2 月对上海市 92 所医院 2022 年 1 月 1 日-12 月 31 日患者抗菌药物使用及耐药菌的检出进行回顾性调查, 数据采用 SPSS 23.0 统计软件进行分析。

结果 共纳入 92 所医院, 其中二级医院 50 所, 三级医院 42 所, 二级医院的抗菌药物使用率高于三级医院 (46.06% vs. 38.86%, $P<0.05$)。二级医院的耐甲氧西林金黄色葡萄球菌 (53.00% vs. 45.29%)、耐万古霉素肠球菌 (0.68% vs. 0.09%) 和耐碳青霉烯大肠埃希菌 (3.29% vs. 2.84%) 检出率均高于三级医院 ($P<0.05$), 三级医院的耐碳青霉烯鲍曼不动杆菌、耐碳青霉烯肺炎克雷伯菌高于二级医院 ($P<0.05$)。抗菌药物使用增加, 耐万古霉素肠球菌的检出率增加 ($P<0.05$)。

结论 医院级别差异影响耐药谱特征, 加强抗菌药物的合理应用是控制多重耐药菌的关键, 应针对不同级别医院特点, 制定和实施精准的抗菌药物管理及感染防控措施。

First Functional Evidence of An Acquired FKS1 R638S Hotspot Mutation Causing High-level Micafungin Resistance in *Meyerozyma Guilliermondii*

null null

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Background Acquired echinocandin resistance has rarely been characterized in the *Meyerozyma guilliermondii* (formerly *Candida guilliermondii*) species complex, and hotspot FKS1 mutations have not previously been functionally confirmed in this species. During routine clinical surveillance, we identified three bloodstream isolates collected from the same hospital over a three-year period, all showing high-level micafungin resistance

Methods Antifungal susceptibility testing was performed using CLSI broth microdilution and gradient diffusion method. The full-length FKS1 gene of each isolate was sequenced to identify resistance-associated mutations, and PROVEAN was used to predict their functional impact. CRISPR-mediated homologous recombination was applied to introduce the same hotspot mutation into reference strain ATCC 6260. All engineered clones underwent complete Sanger sequencing of the FKS1 gene to confirm the presence of the targeted mutation and exclude off-target alterations

Results All three bloodstream isolates displayed high-level resistance to micafungin, with minimum inhibitory concentrations (MIC) values exceeding 8 ug/mL, whereas caspofungin and anidulafungin MICs were 2 ug/mL. In contrast, ATCC 6260 showed micafungin, caspofungin and anidulafungin MICs of 0.5, 0.25 and 1 ug/mL. Sequencing of full-length FKS1 revealed that all resistant isolates carried an identical hotspot R638S substitution, and PROVEAN predicted this amino-acid change to be deleterious. To verify its functional impact, we employed CRISPR-mediated homologous recombination to introduce R638S into ATCC 6260. All edited clones were confirmed by complete Sanger sequencing of FKS1, demonstrating the presence of only the intended substitution. The engineered R638S mutants reproduced the echinocandin

susceptibility profile of the clinical isolates, with micafungin MIC increasing from 0.5 ug/mL to more than 8 ug/mL and the Etest value rising from 0.094 ug/mL to greater than 32 ug/mL, accompanied by caspofungin and anidulafungin MICs of 2 ug/mL

Conclusions This study provides the first functional evidence that an acquired FKS1 R638S hotspot mutation mediates high-level micafungin resistance in *Meyerozyma guilliermondii*. These findings reveal an emerging echinocandin resistance mechanism in this rare species and underscore the need for continued molecular surveillance

抗菌药物的药理药学研究与临床试验

Establishment of Epidemiological Cut-off Values of Cefotaxime-sulbactam Against *Escherichia Coli*, *Klebsiella Pneumoniae*, *Enterobacter Cloacae*, *Proteus Mirabilis*, *Serratia Marcescens*, *Acinetobacter Baumannii* and *Staphylococcus Aureus*

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Objective To establish the epidemiological cut-off (ECOFF) value of cefotaxime-sulbactam against *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter cloacae*, *Proteus mirabilis*, *Serratia marcescens*, *Acinetobacter baumannii*, and *Staphylococcus aureus*.

Methods A total of 1,770 non-duplicate clinical isolates were collected from five laboratories across four cities in China. Minimum inhibitory concentrations (MICs) of cefotaxime-sulbactam were independently determined using the broth microdilution method according to EUCAST standards. ECOFFs were determined using ECOFFinder software and visual estimation following EUCAST principles

Results The ECOFF of *E. coli* and *K. pneumoniae* was 0.25/4 mg/L, the ECOFF of *E. cloacae* and *S. marcescens* was 0.5/4 and 1/4 mg/L, and the ECOFF of *P. mirabilis* was 0.06/4 mg/L. The ECOFF of *S. aureus* was 4/4 mg/L and the ECOFF of *A. baumannii* was 4/2mg/L.

Conclusion ECOFFs of cefotaxime-sulbactam were determined for seven clinically important bacterial species. These results provide essential reference values

for distinguishing wild-type from non-wild-type isolates and support more accurate interpretation of antimicrobial susceptibility testing.

Keywords ECOFF, epidemiological cut-off, cefotaxime-sulbactam

Effectiveness and Safety of Eravacycline for The Treatment of Various Infections: A Multi-center Real-World Retrospective Study in China

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Objective Eravacycline (ERV) is a novel synthetic fluorocycline antibiotic with broad-spectrum activity against a wide range of pathogens. This study aimed to evaluate the real-world effectiveness and safety of eravacycline in patients with various infections.

Methods This study was a multicenter, retrospective, real-world study. Adult patients who received eravacycline for at least 3 days and were followed for 30 days were included. Clinical outcomes were evaluated at day 3 of treatment, at the end of therapy, and on day 30. Microbiological effectiveness and safety were also evaluated. Use multivariate regression analysis and propensity score matching (PSM) to analyze the differential factors

Results In total of 3,369 patients from 21 provinces and cities were included. Pneumonia was the most common infection type, and ICU and hematology department was the most frequent source department. The most prevalent pathogens in the monomicrobial infection is *Acinetobacter baumannii*, followed by *Klebsiella*

pneumoniae. Overall, 94.6% patients received standard dosage of eravacycline (1 mg/kg intravenously every 12 hours). The mean duration of eravacycline therapy was 9.1 ± 5.0 days, with an effectiveness rate of 90.1% and an overall microbiological effectiveness rate of 90.7% at the end of therapy. The 30-day all-cause mortality rate was 11.8%. Adverse reactions were reported in 2.7% of patients, with nausea and vomiting being the most common events. Comparing the microbiological and clinical outcome between monomicrobial infection and polymicrobial infection at the end of therapy, polymicrobial infection, ICU admission and sepsis were identified as significant risk factors for unfavorable outcomes in multivariable logistic regression analysis. Compared to other infection type, diagnosis of pneumonia was associated with likelihood of treatment success.

Conclusion Eravacycline demonstrated favorable clinical and microbiological effectiveness across a wide range of infections in real-world settings and was well tolerated, supporting its potential role as an effective therapeutic option for severe bacterial infections.

Keywords eravacycline, safety, effectiveness

Development and Clinical Evaluation of An LC-MS/MS Method for The Determination of Isoniazid in Cerebrospinal Fluid From Tuberculous Meningitis

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Purpose Isoniazid (INH), a first-line anti-tuberculosis agent, exhibits variable cerebrospinal fluid (CSF)

penetration owing to NAT2 genetic polymorphisms. This study developed an LC-MS/MS method to quantify INH in the human CSF for therapeutic drug monitoring in patients with tuberculous meningitis

Methods The LC-MS/MS method developed and validated in this study includes linearity, sensitivity, accuracy, precision, extraction recovery, matrix effect, and stability evaluations, all of which meet the standards for bioanalytical method validation. This method was applied to a real-world prospective observational study to compare CSF trough concentrations of INH between patients receiving conventional anti-tuberculosis therapy and those receiving conventional therapy combined with intrathecal INH injection, and a pharmacokinetic study was conducted in one TBM patient.

Results The validated LC-MS/MS method achieved a total run time of 3.5 min, demonstrated linearity over the range of 5–4000 ng/mL, and had an LLOQ of 5 ng/mL, with all validation parameters meeting acceptance criteria. In the clinical cohort, the median CSF trough concentration of INH was significantly higher in the intrathecal therapy group (1130.00 ng/mL, $N=117$) than in the conventional therapy group (155.00 ng/mL, $N=45$, $P<0.001$). Target attainment rates at ≥ 120 ng/mL and ≥ 250 ng/mL were also significantly greater in the intrathecal group (84.62% and 77.78%, respectively) versus the conventional group (57.78% and 35.56%, both $P<0.001$). Pharmacokinetic analysis in a TBM patient after intrathecal INH administration revealed a T_{max} of 6 h, C_{max} of 2810 ng/mL, and an elimination half-life of approximately 14 h.

Conclusion A sensitive and reliable LC-MS/MS method was successfully developed and validated for quantification of INH in human CSF. This study confirms that intrathecal administration of INH can significantly increase drug concentrations in the CSF of TBM patients, providing methodological support and prelim-

inary clinical evidence for optimizing treatment strategies in TBM.

Keywords LC-MS/MS, isoniazid, cerebrospinal fluid, tuberculous meningitis

基于 PK/PD 靶标的老年医院获得性肺炎患者利奈唑胺给药策略优化研究

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目的 评估利奈唑胺治疗老年医院获得性肺炎 (hospital-acquired pneumonia, HAP) 患者的谷浓度达标情况、有效性和安全性, 阐明其在该人群中的药代动力学特征, 并探索最佳给药策略。

方法 纳入静脉使用利奈唑胺的老年 HAP 患者, 收集其人口学、临床特征、实验室指标、给药方案、药物浓度等信息, 评估稳态谷浓度达标率、临床与微生物学疗效及不良反应发生率。采用 Phoenix NLME®构建群体药动学 (population pharmacokinetics, PPK) 模型, 并通过蒙特卡洛模拟优化老年患者的给药策略。

结果 共纳入 126 例老年患者, 其中 87 例初次稳态谷浓度采样符合要求。以药代动力学/药效学 (pharmacokinetic and pharmacodynamic, PK/PD) 靶标为标准评估血药谷浓度的达标情况, 结果显示, 达标率 21.8%, 未达标率 8.1%, 超标率 70.1%。133 份呼吸道标本分离出耐药革兰阳性菌, 总体清除率 91.7%, 临床有效率 77.8%。44 例出现 ≥ 1 种不良反应, 血小板减少、贫血发生率分别为 27.0%、11.1%。共收集 147 个利奈唑胺浓度进行 PPK 分析, 清除率及表观分布容积群体典型值为 2.37 L/h、31.33 L, 年龄和肌酐清除率 (creatinine clearance, CrCL) 是影响清除率的协变量。若患者 60-69 岁且 CrCL 90-120 ml/min, 推荐 600 mg q12h; 若 60-69 岁且 CrCL 60-89 ml/min 或 70-79 岁且 CrCL 90-120 ml/min 者, 推

荐 400 mg q12h; 若 60-69 岁且 CrCL 15-59 ml/min、70-79 岁且 CrCL 30-89 ml/min 或 80-89 岁且 CrCL 90-120 ml/min 者, 推荐 300 mg q12h; 若 70-79 岁且 CrCL 15-29 ml/min、80-89 岁且 CrCL 15-89 ml/min 或 90-100 岁任何 CrCL 者, 推荐 200 mg q12h。

结论 老年患者使用利奈唑胺时具有较高的不良反应发生率和稳态谷浓度超标率, 凸显该人群优化给药的必要性。基于年龄和 CrCL 优化利奈唑胺给药方案可提高血药浓度的达标概率, 降低不良反应发生的风险。

Clinical Outcomes of Eravacycline in Chinese Patients with *Stenotrophomonas Maltophilia* Infections: A Multicentre Observational Study

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Objectives To evaluate the efficacy and safety of eravacycline (ERV) for treating *Stenotrophomonas maltophilia* infections in a real-world Chinese population

Methods This multicentre, retrospective, observational study analysed 125 adult patients treated with ERV (≥ 72 hours) for *S. maltophilia* infections from August 2023 to August 2024. Primary outcomes were overall clinical effectiveness at the end of treatment (EOT) and 30 days post-EOT. Secondary outcomes included patient prognosis, microbiological efficacy and adverse events (AEs).

Results The overall clinical effectiveness rate was 89.6% (112/125) at EOT and 85.6% (107/125) 30 days post-EOT, with 84.0% (105/125) of patients showing clinical improvement upon discharge. Microbiological effectiveness rate reached 90.4% (113/125), demonstrating concordance between microbiological and clinical responses in all but one case. Among these cases, single *S. maltophilia* infection accounted for 82.4% (103/125), predominantly affecting the pulmonary system (92/103, 89.3%), followed by bloodstream (14/103, 13.6%) and intra-abdominal infection (13/103, 12.6%). At EOT, clinical effectiveness rates were 89.1% (82/92) for pneumonia/pulmonary infections, 100% (14/14) for bloodstream infections, and 100% (13/13) for intra-abdominal infections; by day 30 post-EOT, these rates were 88.0% (81/92), 92.9% (13/14), and 100% (13/13), respectively. Adverse events were minimal (3.2%) and not severe.

Conclusion This large-scale real-world study supports ERV as an effective and safe therapeutic option for *S. maltophilia*, expanding the current treatment landscape for *S. maltophilia*.

Keywords *Stenotrophomonas maltophilia*; eravacycline; infection; clinical outcome; microbiological outcome; multidrug resistance

In Vitro Antimicrobial Susceptibility of Lefamulin Determined by Disk Diffusion Method: A Multicenter Study in China

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Objectives To evaluate the in vitro antimicrobial activity of lefamulin against common community-acquired pneumonia (CAP) pathogens using the standardized disk diffusion method, validate the reliability of this method and investigate age-specific susceptibility in clinical isolates

Methods A total of 1,250 clinical isolates, including 377 *Streptococcus pneumoniae*, 375 *Staphylococcus aureus*, 373 *Haemophilus influenzae*, and 125 *Moraxella catarrhalis*, were isolated from 25 tertiary hospitals in China between 2024 and 2025. The in vitro susceptibility of these isolates to Lefamulin was assessed using the disk diffusion method, following the interpretive criteria of the Clinical and Laboratory Standards Institute (CLSI). Age-stratified analysis was performed for pediatric (<18 years), adult (18–65 years), and elderly (>65 years) populations to assess potential age-related differences in susceptibility.

Results Lefamulin demonstrated consistently high susceptibility against all tested pathogens, with susceptibility rates of 100% for *S. pneumoniae*, 99.2% for *S. aureus*, 100% for *H. influenzae*, and 100% for *M. catarrhalis*. Age-stratified analysis revealed that Lefamulin exhibited uniformly high susceptibility across all groups.

Conclusion Lefamulin demonstrated broad-spectrum efficacy against common CAP pathogens, including resistant strains, with consistently high susceptibility across different age groups. The results of disk diffusion testing were consistent with data from the China Antimicrobial Resistance Surveillance Network, further confirming the reliability of disk diffusion for Lefamulin susceptibility testing. These findings highlight Lefamulin as an effective treatment option for CAP.

Keywords Lefamulin; disk diffusion; community-acquired pneumonia; antimicrobial susceptibility;

multicenter study

Population Pharmacokinetics and Exposure-response Analysis of Levofloxacin in Chinese Pediatric Patients with Severe Refractory *Mycoplasma Pneumoniae* Pneumonia

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Levofloxacin is recommended as an optional treatment for pediatric patients with severe refractory *Mycoplasma pneumoniae* pneumonia (SRMPP), but its use remains off-label due to limited pharmacokinetic/pharmacodynamic (PK/PD) data in this population. This study aimed to characterize the PK/PD properties of levofloxacin in pediatric SRMPP patients and define optimal dosing regimens. Scavenged blood samples from patients aged ≤ 18 years were collected using opportunistic sampling strategy to develop a population pharmacokinetic (PopPK) model of levofloxacin. The Cox proportional hazards model was applied to identify the optimal AUC_{ss,0–24h} cutoff associated with improved efficacy (shorter levofloxacin treatment duration and shorter cough resolution). Monte Carlo simulations were then performed to evaluate target attainment for this efficacy cutoff under guideline regimens (8–10 mg/kg q12 h for ages 1–5 years; 8–10 mg/kg q24 h for ages 5–16 years). A total of 191 pediatric patients (0.16–16 years) with SRMPP receiving intravenous levofloxacin were included in the PK analysis, and 161 patients were included in the exposure-response analysis. A two-compartment PopPK model was developed, identifying body weight as a significant covariate on clearance and central volume of distribution, and serum creatinine as

an additional covariate on clearance. Patients with $AUC_{0-24h} \geq 30.74 \text{ mg}\cdot\text{h/L}$ achieved shorter levofloxacin treatment duration ($P = 0.019$). Guideline-recommended dosing regimens result in overexposure in children <5 years and underexposure in those ≥ 5 years. Our model-based analysis suggests that 11 mg/kg q24 h or 5.5 mg/kg q12 h may provide more appropriate dosing regimens for children aged 1–16 years for the treatment of SRMPP.

液相色谱-串联质谱法同时测定人血清中总及游离两性霉素 B：方法验证及蛋白结合变异性的探究

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背景 两性霉素 B (Amphotericin B, AmB) 是临床指南推荐的一线抗真菌药物, 其具有血浆蛋白高度结合的特性, 其疗效与毒性主要受游离药物的影响。然而目前两性霉素 B 的治疗药物监测仍以检测总浓度为主, 而关于未结合 AmB 的临床数据较为匮乏, 其蛋白结合特性的影响因素尚未完全明确。

方法 建立快速、灵敏的液相色谱-串联质谱 (LC-MS/MS) 分析方法, 依据 ICH M10 指南完成方法学验证, 用于同时定量人血浆中两性霉素 B 的总浓度与未结合浓度。将该方法进一步应用于临床样品检测, 并探究两性霉素 B 的蛋白结合的关键影响因素。

结果 所建立的 LC-MS/MS 方法各项验证指标均符合 ICH M10 指南规定的验收标准, 成功应用于 26 例患者的 52 份血浆样品检测。斯皮尔曼相关性分析及局部加权散点图平滑 (LOWESS) 回归分析显示, 两性霉素 B 的蛋白结合率与多项生化指标及药物总浓度存在显著相关性。亚组分析进一步证实, 按 AmB 总浓度、血清白蛋白水平及估算肾小球

滤过率 (eGFR) 分组后, 不同亚组间 PBR 存在统计学显著差异。

结论 成功建立了一种简便、低样本量、稳定性好的 LC-MS/MS 方法, 可同时准确测定人血浆中两性霉素 B 的总浓度与游离浓度, 且适用于临床患者样品检测。该方法有望拓展至儿科人群, 为游离药代动力学研究及两性霉素 B 的个体化给药提供支持。

Impact of Estimated Glomerular Filtration Rate Equations on Vancomycin Dosing and Treatment Outcomes

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Background Vancomycin has a narrow therapeutic window and is primarily renally excreted. This study explored whether varied estimated glomerular filtration rate (eGFR) equations lead to differences in chronic kidney disease (CKD) staging and vancomycin dosage, and their impact on treatment outcomes

Methods This cross-sectional study retrospectively included adult patients receiving vancomycin for therapeutic purposes (empirical or targeted therapy) at Nanjing Drum Tower Hospital (2019–2023). Consistency of each of the metrics (eGFR values, CKD staging, dose staging, and staging recommendations) derived from different equations was compared. Incidences of distinct clinical outcomes were compared among patients receiving doses recommended by different eGFR equations. Logistic regression analyzed associations between inconsistent status and patient characteristics as well as clinical outcomes.

Results A total of 832 patients were identified. The Chinese population-adjusted creatinine (Cr)-based European Kidney Function Consortium equation (EKFC-eGFCr[CN]) had the smallest impact on dosing adjustments (3.4%), whereas the cystatin(Cys)-based Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation (CKD-EPI-eGFCys) had the largest impact (16.0%) and exhibited favorable performance in target vancomycin trough concentration (C_{min}) attainment and other clinical outcomes (except for target 24 h area under the concentrationtime curve [AUC_{0~24}]). Only staging discordance between the Xiangya equation and EKFC-eGFCr+Cys was associated with a reduced C_{min} attainment rate. When dosing recommendations disagreed with those from the Cockcroft-Gault (CG) equation, all eGFR equations except the Xiangya equation were associated with higher C_{min} attainment rates.

Conclusion Our study found that the CKD-EPI-eGFCys equation required the most dosing adjustments, while the EKFC-eGFCr(CN) equation required the fewest. Preferentially using the CKD-EPI-eGFCys was optimal for target attainment of key clinical outcomes.

Imipenem and Relebactam Pharmacokinetics in Peritoneal Fluid: Microdialysis Reveals Infection-Independent Penetration

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Objective To characterize the pharmacokinetics and peritoneal penetration of imipenem and relebactam, and to evaluate the impact of infection on their distribution and pharmacodynamic target attainment.

Methods A rat model of intra-abdominal infection was established, and microdialysis was used to dynamically measure unbound concentrations of imipenem (45 mg/kg) and relebactam (22.5 mg/kg) in plasma and peritoneal fluid following a single intravenous infusion. Pharmacokinetic parameters were estimated using noncompartmental and compartmental analyses. Peritoneal penetration was assessed by AUC ratios, and pharmacodynamic target attainment (PTA) was evaluated based on EUCAST PK/PD criteria.

Results Imipenem exposure in peritoneal fluid was significantly lower than in plasma, with AUC ratios of 0.29 (control) and 0.27 (infection), whereas relebactam showed high penetration (0.81 and 0.86, respectively). Both drugs reached peak concentrations at 30 min and exhibited rapid equilibrium without distribution delay. Model-derived partition coefficients were consistent with noncompartmental results. Infection increased the volume of distribution and clearance of relebactam but did not significantly affect peritoneal penetration for either drug. PTA analysis showed a marked decline at an MIC of 1 mg/L under updated EUCAST targets.

Conclusion Relebactam demonstrates favorable peritoneal penetration, whereas imipenem exposure is limited, leading to discordant distribution between the two agents. Infection does not significantly influence peritoneal permeability but alters systemic pharmacokinetics. Optimization of dosing strategies is required to ensure adequate peritoneal drug exposure and antimicrobial efficacy.

Keywords microdialysis; imipenem; relebactam; intra-abdominal infection; pharmacokinetics

Combined Antibactericidal Activity of

Imipenem-funobactam with Different Antibiotics Against Carbapenem-resistant Gram-negative Bacteria in China

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Objective Funobactam (FNB), a novel β -lactamase inhibitor, has shown potential capability to restore the activity of β -lactam antibiotics. However, the antibacterial activity of imipenem-funobactam (IPM-FNB) combined with other antibiotics remains insufficiently studied against imipenem-resistant gram-negative bacteria (CR-GNB).

Methods A total of 199 clinical CR-GNB isolates, including carbapenem-resistant *Escherichia coli* (CREC) (32 isolates), carbapenem-resistant *Klebsiella pneumoniae* (CRKP) (47 isolates), carbapenem-resistant *Acinetobacter baumannii* (CRAB) (58 isolates), and carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) (62 isolates), were collected across China from 26 medical centers. Antimicrobial susceptibility of IPM-FNB combined with aztreonam, ceftazidime, sulbactam, amikacin, ciprofloxacin, polymyxin B, or tigecycline was determined by broth microdilution with checkerboard assays, and the fractional inhibitory concentration index was calculated. Time-kill assays were performed for partial isolates.

Results When Against CREC and CRKP, IPM-FNB combined with aztreonam mainly exhibited synergistic effects (75.0% and 70.0%, respectively), with marked bactericidal activity against New Delhi metallo- β -lactamase (NDM)- and *Klebsiella pneumoniae* carbapenemase (KPC)-2-producing isolates. Against CRAB, IPM-FNB combined with sulbactam demonstrated the highest synergistic effect (68.8%) and showed rapid, sustained bactericidal activity in time-kill

assays. Against CRPA, most combinations showed additive effects, although IPM-FNB plus aztreonam achieved synergistic bactericidal activity in the tested isolate.

Conclusion IPM-FNB combined with sulbactam shows promising activity against CRAB. In addition, IPM-FNB combined with aztreonam is effective against CREC and CRKP, both KPC-2- and NDM-producing isolates. Additive activity are most common in IPM-FNB combinations against CRPA.

NF- κ B Inhibition Attenuates Polymyxin B Toxicity – A Network Toxicology and In Vivo Identified Therapeutic Approach

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Polymyxin B remains a first-line therapeutic option against Gram-negative bacterial infections; however, its clinical utility is substantially limited by dose-limiting toxicity, the mechanisms of which remain incompletely elucidated. Within a network toxicology framework, this study systematically investigated the potential toxic characteristics and underlying molecular mechanisms of Polymyxin B, with a specific focus on three key adverse effects: acute kidney injury, neurotoxicity, and skin pigmentation. Potential targets associated with Polymyxin B exposure and these toxicities were initially identified through integrated data mining of the SuperPred, SEA, GeneCards, and OMIM databases. A protein-protein interaction (PPI) network was subsequently constructed and analyzed using the STRING

database and Cytoscape software. Functional enrichment analyses, including Gene Ontology and Kyoto Encyclopedia of Genes and Genomes pathway analyses, were performed using Metascape. Furthermore, a compound-target-pathway network and Sankey diagram were generated to identify major active components, followed by molecular docking between these components and proteins encoded by the key targets. Molecular docking and molecular dynamics simulations confirmed strong binding affinities between Polymyxin B and core target proteins, namely STAT3, NF- κ B, PRKACA, and HIF1A. Notably, both PMB1 and PMB2 exhibited high binding affinity for NF- κ B. Consistent with these findings, in vivo studies in mice demonstrated that Polymyxin B treatment significantly enhanced the activation of the NF- κ B pathway in renal tissues. Conversely, co-administration of the NF- κ B pathway inhibitors PDTC and JSH-23 markedly attenuated Polymyxin B-induced nephrotoxicity. In conclusion, these experimental results indicate that hyperactivation of NF- κ B is a critical mechanism underlying Polymyxin B-induced renal toxicity.

基于前瞻性多中心临床观察性研究的去甲万古霉素群体药动学/药效学分析及给药方案评价

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背景 以万古霉素为代表的糖肽类药物是治疗 MRSA 感染的核心选择,但其治疗指数窗窄和毒性反应明确,指南推荐在治疗过程中监测血药浓度并及时调整给药方案,以提高疗效,降低不良反应。去甲万古霉素无疗效和安全性相关的目标治疗浓度,

目前临床基本参照万古霉素的治疗窗进行剂量调整,对临床疗效和安全性的影响尚不明确。因此,本研究开展了去甲万古霉素药物浓度的前瞻性、多中心临床观察性研究,为制定去甲万古霉素治疗革兰阳性菌感染的目标治疗浓度提供数据支持。

方法 纳入中国 20 家医院的确诊或拟诊革兰阳性菌感染患者建立群体药代动力学模型 (Population Pharmacokinetics, Pop PK) 模型,基于最终 Pop PK 模型采用经验贝叶斯估计,计算达稳态时每位患者的药动学 (Pharmacokinetics / Pharmacodynamics, PK/PD) 参数 (如 $AUC_{ss,24h}$ 、 $AUC_{ss,24h}/MIC$)。构建单因素 logistic 回归模型,通过回归系数筛选与疗效相关性最显著的 PK/PD 指数。采用列联表分析+卡方检验确定最终 PK/PD 靶值。基于最终 PK/PD 靶值,采用蒙特卡洛模拟对 10 种临床给药方案进行模拟,计算目标达成概率 (Probability of Target Attainment, PTA) 和累积响应分数 (Cumulative Fraction of Response, CFR)。

结果 共纳入 371 例患者和前期的 20 例健康受试者建立一级线性消除的二室药动学模型,可描述日剂量 200 mg - 2400 mg 范围内去甲万古霉素的 Pop PK 特征,各群体典型值(清除率 CL 为 4.54 L/h,中央室分布容积 V_c 为 17.7 L,外周室分布容积 V_p 为 23.0 L,室间清除率 Q 为 8.16 L/h。CL、 V_c 和 V_p 的个体间变异分别为 33.4%、39.4%和 44.4%。共纳入 190 例临床疗效可评价患者,最终确定 $AUC_{ss,24h} \geq 318$ 为去甲万古霉素的临床 PK/PD 靶值。模拟结果显示,临床常用剂量 800mg q12h 给药当 $MIC \leq 0.5 \mu g/mL$ 时, $PTA > 90\%$, $MIC = 1 \mu g/mL$ 时, PTA 为 62.1%,达标率偏低。

结论 初步获得了去甲万古霉素临床和微生物疗效相关的 PK/PD 靶值,进一步需在更多临床研究中验证。

关键词: 去甲万古霉素; 群体药代动力学; PK/PD 靶值; 给药方案评价

Coupled Hydrogen-Bond–Electrostatic Recognition of Phosphatidylglycerol Drives The Design of Resistance-Suppressing Miniature Peptidomimetics

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The emergence of multidrug-resistant (MDR) pathogens has urged us to find new antimicrobial strategies. Phosphatidylglycerol (PG) is an attractive bacterial-specific lipid target but is targeted by only one clinical agent, daptomycin. Yet daptomycin, like most reported PG binders, binds PG through an imprecise hydrophobic–electrostatic mode, necessitating a relatively large molecular size. This requirement, together with its strict Ca^{2+} dependence, significantly limits its efficacy. Here, we report bis-pyridinium amides (BisPAs), a rationally designed class of small molecules capable of precisely recognizing PG through amide–diol hydrogen bonding coupled with pyridinium–phosphate anionic– π interaction, independent of environmental conditions such as Ca^{2+} . The lead compound, BisPA14, with $\sim$ one-third the molecular weight of daptomycin, exhibits comparable PG-binding affinity, with $K_d(\text{BisPA14}) = 1.4 \times 10^{-6} \text{ M}$ versus $K_d(\text{daptomycin-Ca}^{2+}) = 0.9 \times 10^{-6} \text{ M}$. BisPA14 disrupts PG self-assembly and membrane integrity and simultaneously engages bacterial DNA as a secondary intracellular target. This dual-targeting mechanism enables BisPA14 to eradicate proliferating, tolerant, and persister bacterial populations while suppressing resistance evolution. It remains active in serum-containing environments, protects host cells from

bacterial damage, and demonstrates excellent biocompatibility and strong therapeutic efficacy in intraperitoneal, pulmonary, and bloodstream methicillin-resistant *Staphylococcus aureus* infection models. As a synthetically accessible small molecule that functionally mimics and improves upon daptomycin's lipid-targeting mechanism, this work establishes a secondary-bonding-driven PG-recognition paradigm for combating MDR bacterial infections.

利奈唑胺血药浓度影响因素及所致凝血障碍的回顾性分析

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徐州医科大学附属医院

目的 探究应用利奈唑胺患者血药谷浓度的影响因素，以及包括血药谷浓度在内的各项因素对患者凝血相关指标和所致凝血障碍的影响，为利奈唑胺的临床合理应用的有效性 & 安全性监测提供参考。

方法 回顾性收集、汇总、分析徐州医科大学附属医院 2023 年 2 月~2024 年 1 月期间应用利奈唑胺并进行了血药浓度监测，同时符合纳入标准的住院患者信息及相关指标数据，使用单变量分析与多元线性回归的方法探究影响患者利奈唑胺血药谷浓度的因素，以及探究血药谷浓度等因素与患者发生凝血障碍的相关性。结果 共纳入 48 例患者数据，单因素分析结果显示，肝功能、是否合并使用利尿剂、年龄与利奈唑胺血药谷浓度具有统计学相关性 ($P < 0.05$)，而多因素逐步分析仅保留肝功能 1 个变量作为独立危险因素。当利奈唑胺血药谷浓度超过 7 mg/L 时，患者在接受治疗后的 INR 和 APTT 水平相较于血药谷浓度在 2~7 mg/L 时呈现出明显上升 ($P < 0.05$)，同时出现凝血障碍的风险更大 (68.42% vs. 37.93%, $P = 0.039$)。此外，基础 PLT 值 ($\geq 200 \times 10^9/\text{L}$)、基础 ALT 值也是发生凝血障碍的独立危险因素

($P<0.05$)。结论 利奈唑胺血药谷浓度的影响因素较多,且超过 7 mg/L 时患者更易发生凝血障碍。通过监测患者的血药谷浓度来制定个性化给药方案,可能有助于减少利奈唑胺致凝血障碍不良反应发生风险。

【关键词】利奈唑胺;血药谷浓度;影响因素;凝血障碍;个体化用药

Pharmacokinetics, Safety and Population Pharmacokinetics/Pharmacodynamics Analysis of Meropenem-Vaborbactam in Chinese Healthy Participants

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Objective Meropenem-vaborbactam is a fixed-dose β -lactam/ β -lactamase inhibitor combination active against carbapenem-resistant Enterobacterales (CRE), especially KPC-producing CRE. This study evaluated its pharmacokinetics (PK), safety, and tolerability in Chinese participants, and performed pharmacokinetic/pharmacodynamic (PK/PD) analysis using in vitro data to assess the suitability of the standard dosing regimen for treating CRE infections in China.

Methods This single-center, open-label study included 20 healthy participants divided into two groups receiving meropenem-vaborbactam (1:1) at 1 g/1 g or 2 g/2 g via 3-hour infusion. Plasma and urine levels of meropenem, its open-ring metabolite, and vaborbactam were analyzed using a validated liquid chromatography-tandem mass spectrometry method. PK analysis was

conducted using WinNonlin. Monte Carlo simulations were used to evaluate four dosing regimens: 1 g/1 g every 8 hours administered via either a 3-hour or 4-hour intravenous infusion, and 2 g/2 g every 8 hours administered via either a 3-hour or 4-hour intravenous infusion.

Results Plasma concentrations of meropenem, its open-ring metabolite, and vaborbactam peaked immediately after infusion, with rapid distribution and elimination. Exposure increased proportionally with dose, and almost no accumulation was observed after repeated 8-hourly dosing. Most meropenem (68.5%-77.0%) and nearly all vaborbactam were excreted unchanged in urine. Both single and multiple doses were well tolerated, with no severe or serious adverse events. In addition, PK/PD analysis showed that the standard 2 g/2 g every 8 hours regimen with a 3-hour intravenous infusion achieved $\geq 90\%$ probability of target attainment for meropenem (45% fT > MIC) against CRE with MIC ≤ 8 mg/L. The corresponding cumulative fraction of response ranged from 98% to 100% for *Escherichia coli* and *Klebsiella pneumoniae* producing ESBLs and KPC-2, including blaKPC variants resistant to ceftazidime-avibactam.

Conclusion The standard meropenem-vaborbactam regimen (2 g/2 g every 8 hours, 3-hour infusion) demonstrated favorable PK and safety profiles, with PK/PD analyses supporting the appropriateness of the standard regimen in Chinese participants, consistent with global findings. These results support its use for treating CRE infections in the Chinese population. Extended infusions may offer additional benefit in critically ill patients or against pathogens with higher MICs.

Keywords Meropenem-vaborbactam, PK, PK/PD analysis, Monte Carlo simulation

Clinical Features, Risk Factors, and Individualized Management Strategies of Linezolid-Associated Lactic Acidosis: A Retrospective Cohort Study Based on 60 Cases

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Aims Linezolid, a key anti-Gram-positive antibiotic, can induce lactic acidosis, an uncommon but potentially fatal adverse event. Currently, its real-world clinical spectrum remains inadequately defined. This study aims to systematically characterize the full clinical spectrum of linezolid-associated lactic acidosis, explore factors associated with its severity, and propose a risk-stratified management framework, thereby informing its safe and precise use

Methods We retrospectively screened patients with lactate elevation (≥ 2.5 mmol/L) during linezolid therapy at a tertiary hospital (2018 to 2022). After excluding identifiable causes of hyperlactatemia (e.g., shock, hypoperfusion), cases were adjudicated for linezolid causality using standardized adverse drug reaction assessment, requiring temporal plausibility and lactate improvement following dose reduction or discontinuation. Sixty patients constituted the final cohort. Clinical, laboratory, and pharmacokinetic data were abstracted. Factors associated with severity were explored using univariate comparisons. Management strategies were categorized as dose reduction, discontinuation, or unchanged regimen

Results Among 60 patients, 61.7% were male; mean age was 55.2 years; 41.7% were ≥ 65 years. Hepatic impairment (cirrhosis or Child-Pugh B/C) was present in 25.0%; renal insufficiency (eGFR < 60 mL/min/1.73 m²) in 23.3%. Median treatment duration

was 18 days (range 2 to 115), with 20.0% receiving linezolid > 28 days. Nausea/vomiting, fatigue, and tachypnea were common. Median peak lactate was 3.4 mmol/L (2.5 to 16.5); 40.0% had pH < 7.35 . Prolonged treatment, cirrhosis, and reduced renal function were associated with more severe presentations. Trough concentrations (available in 42 patients) were elevated (> 10 mg/L) more frequently in patients with organ impairment, who also tended to have higher peak lactate. Dose reduction was the most common intervention (68.3%), followed by discontinuation (26.7%); 5.0% received no adjustment. Median time to lactate normalization was 7 days. All patients survived; no death was directly attributable to linezolid-associated lactic acidosis

Conclusion Linezolid-associated lactic acidosis is multifactorial, with prolonged therapy, advanced age, and hepatic or renal impairment as key predisposing factors. Baseline risk stratification and scheduled lactate monitoring are essential. Elevated trough concentrations in high-risk patients suggest a role for therapeutic drug monitoring, though this requires prospective validation. A graded intervention strategy appeared associated with favorable outcomes but warrants refinement through studies with systematic pharmacokinetic sampling

Efficacy, Safety, and Population Pharmacokinetics of Eravacycline for Carbapenem-Resistant Organism Infections in Immunocompromised Hosts: A Multicenter Prospective Cohort Study

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Objectives We aimed to evaluate the effectiveness, safety, and pharmacokinetics of eravacycline in treating carbapenem-resistant organism (CRO) infections in immunocompromised hosts (ICHs)

Methods A prospective study was conducted at five hospitals in China from January 2024 to July 2025. Patients with confirmed CRO infections who received intravenous eravacycline at a fixed, consecutive dose of 50 mg for at least 72 hours were included. Plasma concentrations were measured, and pharmacokinetic modeling was performed.

Results Among 177 patients (median age: 52 years; 44.1% transplant recipients), infection sites included the lungs (40.1%), intra-abdominal region (35.0%), bloodstream (6.2%), and multiple sites (18.6%). Microbiological clearance rates differed by infection site: intra-abdominal infections showed the highest clearance (80.6%, 50/62) and pulmonary infections the lowest (32.4%, 23/71), compared with the overall cohort clearance rate of 51.4% (91/177) ($P < 0.001$). The 28-day mortality rate was 35.6%. PPK modeling (one-compartment), based on plasma concentration data from 80 patients (54 transplant and 26 non-transplant), revealed reduced clearance in non-transplant patients with cirrhosis, with 45.7% lower clearance in Child-Pugh B and 86.3% lower clearance in Child-Pugh C. In transplant recipients, body weight (BW) exhibited a significant linear association with clearance, while the C-reactive protein level was inversely correlated with distribution volume, while moderate CYP3A4/5 inhibitor use increased the volume by 38.9%. Adverse events occurred in 13.6% of patients. Multivariable analysis identified older age and fungal co-infection as factors associated with mortality. A treatment duration of ≥ 5 days was associated with improved survival.

Conclusion Eravacycline monotherapy can

achieve favorable outcomes in ICHs with CRO infections and help in managing future CRO infections.

Keywords Eravacycline; Immunocompromised Host; Drug Resistance, Multiple, Bacterial

艾滋病合并非结核分枝杆菌及曲霉菌混合感染的抗感染方案优化与药学监护

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目的 探讨精准药学及药学监护对艾滋病合并混合感染患者提升疗效、降低不良反应的影响。

方法 药师以会诊为切入点,通过精准药学技术对一例艾滋病合并非结核分枝杆菌及曲霉菌混合感染患者的抗感染方案进行优化,并给予持续药学监护。

结果 60岁女性,因“间断咳嗽4月,加重半月”收入本院。患者4个月前查出胞内分枝杆菌阳性,给予“克拉霉素、利福布汀、西他沙星”抗NTM治疗。入院行纤支镜检查,肺泡灌洗液提示曲霉菌属阳性,药师建议行伏立康唑 CYP2C19 代谢基因检测,结果提示为中间代谢型(*1/*3)。药师根据基因检测结果,建议加用伏立康唑 200mg(首剂加倍) q12h 覆盖曲霉菌,同时为避免药物相互作用,降低利福布汀剂量至 0.15g qd,监测药物不良反应。后续药师又根据伏立康唑 TDM 检测结果,进一步调整伏立康唑剂量为 300mg q12h,1个月患者症状好转出院继续治疗。3个月后曲霉菌疗程足,停用伏立康唑。利福布汀恢复原剂量,继续抗胞内分枝杆菌治疗。

结论 在治疗团队中,药师通过精准药学技术协助医师优化药物治疗方案,监护药品不良反应,可以有效提高 HIV 患者的疗效和安全性。

Synergistic Action of Mitoxantrone Restores Tigecycline Activity and Combats Tet(X4)-mediated Resistance in Escherichia Coli

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This study focuses on addressing the challenge of tet(X4)-mediated multidrug resistance to tetracycline antibiotics, particularly tigecycline, through a drug repurposing strategy aimed at reversing the resistance phenotype. Utilizing the crystal structure of tet(X4) as a molecular target, we performed structure-based virtual screening of 2,137 FDA-approved drugs and identified mitoxantrone as a high-affinity candidate. Molecular docking and 100-ns molecular dynamics simulations demonstrated stable binding of mitoxantrone to the active site of tet(X4). In vitro assays showed that mitoxantrone significantly enhanced the antibacterial activity of tigecycline and other tetracyclines against tet(X4)-positive *E. coli*, with fractional inhibitory concentration index (FICI) values ≤ 0.5 , indicating strong synergy. Mitoxantrone also impaired bacterial efflux pump function and increased membrane permeability. In a murine peritonitis model, combination therapy markedly improved survival, reduced bacterial burdens in the liver and spleen, and suppressed pro-inflammatory cytokine levels, without inducing significant hepatic, renal, or hemolytic toxicity. Notably, mitoxantrone also decreased the mutation frequency associated with tigecycline resistance, suggesting its potential role in delaying resistance development. In brief, our findings offer a promising framework for developing adjunctive therapies targeting tet(X4)-mediated resistance.

苹果酸奈诺沙星胶囊对肺炎链球菌临床药敏折点的研究

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背景 抗菌药物临床折点是判断病原菌敏感性并指导感染治疗的重要依据。苹果酸奈诺沙星胶囊现行说明书中针对肺炎链球菌的药敏折点为敏感(S) $\leq 1 \mu\text{g/mL}$, 静脉制剂药敏参考流行病学界值(ECOFF)为 $0.5 \mu\text{g/mL}$ 。奈诺沙星针对肺炎链球菌尚缺乏PK/PD界值及整合临床研究数据形成的临床界值。

目的 基于奈诺沙星非临床PK/PD研究、群体药动学(PopPK)模拟及成人社区获得性肺炎(CAP)临床试验中疗效与MIC的相关性分析,探索并制定奈诺沙星对肺炎链球菌的药敏折点。

方法 结合奈诺沙星非临床PK/PD靶值与PopPK模拟获得的患者药物暴露量,采用蒙特卡洛模拟评价口服500/750 mg 每日1次、静脉滴注500 mg 每日1次及静脉-口服序贯7 d方案下的达标概率(PTA),确定PK/PD界值。整合4项奈诺沙星口服及静脉制剂II~III期临床研究,以临床和微生物学疗效为指标,开展剂量-暴露-效应相关性分析,并综合ECOFF、PK/PD界值和临床验证结果制定折点。

结果 共纳入412株肺炎链球菌, MIC₅₀和MIC₉₀分别为0.06、0.125 mg/L, ECOFF为0.5 mg/L。采用体外PK/PD靶值 $\text{fAUC}_{0-24\text{h}}/\text{MIC}=47.05$ 、 $\text{fCmax}/\text{MIC}=5.07$ 及小鼠肺部感染模型靶值 $\text{fAUC}_{0-24\text{h}}/\text{MIC}=44.4$ 模拟,当MIC $\leq 0.5 \text{ mg/L}$ 时,各给药方案PTA均 $\geq 90\%$,支持0.5 mg/L作为PK/PD界值。4项临床研究中,36例CAP患者基线分离得到肺炎链球菌;其中35例完成临床疗效评价,34例完成微生物学疗效评价,成功率分别为88.6%和91.2%。临床分离株MIC范围为0.015~0.25 mg/L,均不高于0.5 mg/L,且未见随MIC升高而疗效下降趋势。剂量-暴露-效应分析所得临床靶值高于非临床靶值,考

虑与奈诺沙星抗菌活性强、总体治愈率高及 MIC 分布范围窄有关, 现有数据尚不足以建立可靠的独立临床界值。进一步分析显示, 当 $MIC \leq 0.5$ mg/L 时, 各给药方案累积反应分数均为 100%。综合结果, 0.5 mg/L 可作为药敏折点制定的主要依据。

结论 奈诺沙星对肺炎链球菌的 ECOFF 及 PK/PD 界值均支持 0.5 mg/L; 临床分离株 MIC 均 ≤ 0.25 mg/L 且疗效良好。综上, 推荐奈诺沙星用于肺炎链球菌所致成人 CAP 时的药敏折点为: 敏感(S) $MIC \leq 0.5$ mg/L; 耐药(R) $MIC \geq 1$ mg/L。

Activity of Individual Drugs Against Biofilm in Hypervirulent *Klebsiella Pneumoniae*

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Aims biofilm is closely associated with persistent infection on medical devices implants, potentially resulting in antibiotic treatment failure due to the development of antibiotic tolerance. It is reported that hvKP produce more biofilm than cKP, and biofilm formation has been shown to promote intestinal colonization of hvKP. The objective of this study was to investigate the antibiofilm activities of ceftazidime (CAZ), piperacillin/tazobactam (PIP/TAZ) and amikacin (AMK) against hypervirulent *Klebsiella pneumoniae* (hvKP)

Methods Antibacterial susceptibility testing was conducted with CAZ, PIP/TAZ and AMK against biofilm-growing reference strain NTUH-K2044 and clinical strain KP20-350 using broth microdilution method. Further two strains were subjected to assess pharmacodynamic parameters including biofilm prevention concentration (BPC), minimal biofilm inhibitory concentration (MBIC), biofilm bactericidal concentration (BBC)

and the minimum biofilm eradication concentration (MBEC)

Results KP20-350 and NTUH-K2044 were all susceptible to CAZ, PIP/TAZ and AMK. The MIC values of CAZ, PIP/TAZ, and AMK against NTUH-K2044 were 0.25 mg/L, 4/4 mg/L, and 2 mg/L, respectively, while those against KP 20-350 were 0.125 mg/L, 4/4 mg/L, and 2 mg/L

Biofilm inhibition by individual drugs

For CAZ, BPC was determined to be $1/2 \times MIC$ and $1/16 \times MIC$ for NTUH-K2044 and KP 20-350 respectively. For PIP/TAZ, a concentration of $1 \times MIC$ was required to reach the BPC for both NTUH-K2044 and KP 20-350. Regarding AMK, the BPC was observed at $1 \times MIC$ for NTUH-K2044 and $1/8 \times MIC$ for KP 20-350. Furthermore, at sub-MIC concentrations of CAZ, PIP/TAZ, and AMK, an initial reduction in biofilm formation was followed by a slight increase.

Biofilm eradication by individual drugs

CAZ, PIP/TAZ and AMK showed effective biofilm eradication against NTUH-K2044 and 20-350. For CAZ, MBIC values were $1 \times MIC$ for both NTUH-K2044 and KP 20-350. For PIP/TAZ, MBIC values were $1/2 \times MIC$ and $1 \times MIC$ for NTUH-K2044 and KP 20-350. For AMK, MBIC values were $1 \times MIC$ and $4 \times MIC$ for NTUH-K2044 and KP 20-350. Compared to MBC of antibiotics, there are 16~128 fold and 256~512 fold increases in BBC value in CAZ and AMK. Regarding MBEC value, >1024 mg/L of CAZ, PIP/TAZ and AMK was required for complete viable cell eradication in biofilm matrix of NTUH-K2044 and KP 20-350.

Conclusions This study demonstrates that CAZ, PIP/TAZ, and AMK exhibit potent activity against hvKP biofilms, effectively inhibiting their formation and eradicating biofilms matrix. However, standard dosing regimens fail to achieve concentrations sufficient to eliminate all viable cells within established biofilms.

Therefore, in clinical settings with a risk of biofilm formation, early antimicrobial intervention and timely catheter removal improving the overall cure rate of hvKP related infection

肺炎克雷伯菌及鲍曼不动杆菌的抗菌活性，但铜绿假单胞菌除外。头孢哌酮-舒巴坦（1:1）对大肠埃希菌、肺炎克雷伯菌以及鲍曼不动杆菌 MIC 的降低以及敏感率的升高均优于头孢哌酮-舒巴坦（2:1）和头孢哌酮-舒巴坦（固定 8 mg/L）。

不同配比头孢哌酮-舒巴坦对革兰阴性杆菌的抗菌活性研究

黄湘宁

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目的 评估不同配比头孢哌酮-舒巴坦对临床常见革兰阴性杆菌的体外抗菌活性。

方法 采用肉汤微量棋盘法测定头孢哌酮、舒巴坦单药以及不同配比头孢哌酮-舒巴坦对 532 株革兰阴性杆菌的最低抑菌浓度（MIC）。

结果 头孢哌酮-舒巴坦（2:1）对大肠埃希菌的 MIC₅₀ 和 MIC₉₀ 分别为 16 和 64 mg/L，头孢哌酮-舒巴坦（1:1）的 MIC₅₀ 和 MIC₉₀ 分别为 8 和 32 mg/L，头孢哌酮-舒巴坦（固定 8 mg/L）的 MIC₅₀ 和 MIC₉₀ 分别为 8 mg/L 和 >128 mg/L。头孢哌酮-舒巴坦（2:1）对肺炎克雷伯菌的 MIC₅₀ 和 MIC₉₀ 分别为 16 和 >128 mg/L，头孢哌酮-舒巴坦（1:1）的 MIC₅₀ 和 MIC₉₀ 分别为 8 和 128 mg/L，头孢哌酮-舒巴坦（固定 8 mg/L）的 MIC₅₀ 和 MIC₉₀ 分别为 8 和 >128 mg/L（敏感率和耐药率分别为 53.1%、41.8%）。头孢哌酮-舒巴坦（2:1）对铜绿假单胞菌的 MIC₅₀ 和 MIC₉₀ 分别为 8 和 32 mg/L，头孢哌酮-舒巴坦（1:1）的 MIC₅₀ 和 MIC₉₀ 分别为 8 和 32 mg/L，头孢哌酮-舒巴坦（固定 8 mg/L）的 MIC₅₀ 和 MIC₉₀ 分别为 8 和 32 mg/L。头孢哌酮-舒巴坦（2:1）对鲍曼不动杆菌的 MIC₅₀ 和 MIC₉₀ 分别为 64 和 128 mg/L，头孢哌酮-舒巴坦（1:1）的 MIC₅₀ 和 MIC₉₀ 分别为 32 和 128 mg/L，头孢哌酮-舒巴坦（固定 8 mg/L）的 MIC₅₀ 和 MIC₉₀ 均为 >128 mg/L。

结论 舒巴坦明显增强头孢哌酮对大肠埃希菌、

细菌真菌感染的流行病学

The Genetic Diversity of Drug Resistance in Mycobacterium Tuberculosis Strains From The Tibetan Plateau

null null

The general hospital of Xizang Military Command

Objective This study aimed to characterize the genetic diversity of drug resistance in Mycobacterium tuberculosis (MTB) isolates from the Tibetan Plateau, elucidate the molecular epidemiological profile of tuberculosis (TB) in this high-altitude region, and offer a molecular basis to guide improved diagnostic, therapeutic, and preventive strategies.

Methods A total of 169 clinical MTB isolates were collected from the General Hospital of Xizang Military Command between January 2024 and April 2025. Drug resistance-associated mutations were identified via targeted gene sequencing.

Results Among the 169 isolates, the overall rate of genotypic resistance was 20.71 %, comprising mono-resistance (14.79 %), poly-resistance (1.78 %), and multidrug-resistance (MDR, 4.14 %). Retreated patients exhibited a higher resistance rate than newly treated cases (26.09 % vs. 14.29 %), with MDR exclusively identified in the retreatment group. Resistance to streptomycin was most prevalent (8.28 %), followed by isoniazid (7.69 %) and rifampicin (7.10 %). The predominant mutations observed were rpsL K43R and katG S315T. No mutations conferring resistance to second-line drugs were detected.

Conclusion The substantial burden of drug-resistant TB on the Tibetan Plateau—particularly streptomycin resistance—underscores the critical need for implementing precision diagnostics and optimizing therapeutic regimens.

Global Burden, Inequalities and Projections of Vancomycin-resistant Enterococcus Faecium and Enterococcus Faecalis, 1990–2050: A Systematic Global Analysis

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Background Vancomycin-resistant Enterococcus faecium (VREfm) and Enterococcus faecalis (VREfs) are major antimicrobial resistance threats. Previous assessments rarely distinguished species, limiting understanding of their epidemiology and control. To address this gap, we analysed trends from 1990 to 2021 and projected the burden through 2050 in order to assess the global burden, inequalities, and future patterns of VREfm and VREfs.

Methods We analysed deaths and disability-adjusted life years (DALYs) from Measuring Infectious Causes and Resistance Outcomes for Burden Estimation (MICROBE) across 204 countries from 1990 to 2021. Temporal trends were assessed using estimated annual percentage change (EAPC). Associations with the socio-demographic index (SDI), health inequalities, and decomposition of burden changes were examined. Future trends to 2050 were projected using a Bayesian age-period-cohort (BAPC) model.

Results In 2021, 11,021 deaths and 353,634 DALYs were attributable to VREfm worldwide, compared with 2991 deaths and 82,025 DALYs attributable to VREfs. Since 1990, VREfm has increased mainly in

higher-SDI regions, whereas VREfs has decreased in lower-SDI settings. Based on the BAPC model, VREfm burden is projected to continue rising across all indicators by 2050, while VREfs shows a sustained decline.

Conclusion This study demonstrates divergent species-specific trends, with an increasing burden of VREfm and a decline in VREfs. VREfm is concentrated in middle- to high-SDI regions, while VREfs is in lower-SDI regions. For both species, burden peaks in young children and older adults. These divergent patterns necessitate tailored strategies that prioritise young children and older adults, with a focus on hospital infection control and antimicrobial stewardship for VREfm in higher-SDI regions, and on community prevention and One Health approaches for VREfs in lower-SDI regions.

Genotypic Diversity of *Cryptococcus Neoformans* and Its Correlation with Clinical Characteristics and Prognosis of AIDS-Associated Cryptococcal Meningitis in Southern China

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This study investigated the genotypic characteristics of *Cryptococcus neoformans* (*C. neoformans*) isolates from HIV-associated cryptococcal meningitis (CM) patients in southern China and examined their associations with clinical features and outcomes. A total of 100 clinical isolates were identified by MALDI-TOF MS and genotyped by multilocus sequence typing. Antifungal susceptibility to five agents was assessed using the FUNGUS 3 system. Baseline demographic, clinical manifestations, radiological, and laboratory data were collected from the corresponding 100 patients, and outcomes were evaluated at weeks 4, 12, 24, and 48. Seven sequence types (STs) were identified: ST5 (83/100, 83.0%), ST4 (5/100, 5.0%), ST31 (3/100, 3.0%), ST43 (1/100, 1.0%), ST93 (4/100, 4.0%), ST395 (1/100, 1.0%), and a presumptive novel ST685 (3/100, 3.0%). Most patients were male (80.0%), and headache was the most common symptom (85.0%). Susceptibility rates for 5-flucytosine, amphotericin B, fluconazole, itraconazole, and voriconazole were respectively 98.9% (93/94), 71.9% (69/96), 82.3% (79/96), 59.4% (41/69), and 86.8% (59/68). Cumulative mortality reached 16%, 33%, 37%, and 39% at weeks 4, 12, 24, and 48. No significant differences were observed between 85 patients infected with ST5 and 15 ones with non-ST5 in clinical presentations or antifungal susceptibility. However, patients infected with ST5 exhibited consistently better survival rates across all time points, whereas those infected with ST93 showed the highest 12-week mortality. Accordingly, ST5 is the dominant genotype of *C. neoformans* in HIV-associated CM in Southern China; meanwhile, non-ST5 genotypes could have worse prognosis, indicating ST sequence typing of may act as a prognostic biomarker in patients with HIV-associated CM.

Genomic, Clinical, and Phenotypic Characterization of Multidrug-Resistant MRSA From A Tertiary Hospital in China, 2021-2024

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Background Methicillin-resistant *Staphylococcus aureus* (MRSA) continues to pose a major clinical threat, while multidrug-resistant (MDR) MRSA further limits available therapeutic interventions. This study aimed to characterize the genomic, clinical, and phenotypic profiles of MDR-MRSA collected from a tertiary hospital in China

Methods A total of 136 MDR-MRSA isolates were collected. WGS was used to determine molecular characteristics. Clinical data were analyzed to explore the associations between MDR-MRSA and patient outcomes. Antimicrobial susceptibility testing, biofilm formation assay, and hemolytic activity detection were conducted. The intracellular invasive capability was evaluated using immunofluorescence assay. The virulence characteristics were assessed via murine skin abscess and pneumonia models.

Results WGS of all MDR-MRSA isolates identified ST764-t002, ST5-t2480, ST59-t437 and ST764-t1084, as the predominant lineages. Core-genome SNP phylogenetic analysis identified six small transmission clusters within ST764. ST764 exhibited the broadest resistance profile and frequently carried *mupA*. Clinically, ST764 infection was associated with higher rates of bloodstream and pulmonary infection and higher 30-day mortality than non-ST764 MDR-MRSA. ST764-t002 displayed the strongest biofilm formation and the highest levels of adhesion to and invasion of BEAS-2B epithelial cells, whereas ST59-t437 and ST764-t1084 exhibited the greatest hemolytic activity. In murine skin

abscess and pneumonia models, ST764-t1084 and ST59-t437 caused the most severe disease.

Conclusion Our findings characterize the clinical features, genomic epidemiology, and virulence profiles of high-risk MDR-MRSA lineages in this hospital, particularly ST764, which exhibited broad antimicrobial resistance and was associated with poorer outcomes.

Keywords Methicillin-resistant *Staphylococcus aureus*, whole-genome sequencing, antimicrobial resistance, virulence

In Vitro Activity of Contezolid and Other Comparators Against Clinical Staphylococci and Enterococci: A Multicenter Study in China

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Objective To evaluate the in vitro activity of contezolid against clinical *Staphylococcus* and *Enterococcus* isolates from across China, and compare its performance with linezolid and other key agents.

Methods A total of 2510 non-duplicate Gram-positive cocci isolates were collected from 70 hospitals in seven Chinese regions. MICs were determined using broth microdilution per CLSI guidelines. MIC_{50/90} values, susceptibility rates, cumulative MIC curves, and MIC distribution agreement between contezolid and linezolid were assessed. Linezolid-resistant and NWT (MIC > 4 mg/L) contezolid isolates underwent whole-genome sequencing and resistance screening for *cfr*, *optrA*, *poxTA*, 23S rRNA mutations, and mutations in ribosomal proteins L3/L4/L22.

Results Contezolid exhibited potent in vitro activity, with >99% of isolates inhibited at ≤4 mg/L and

showed lower MIC_{50/90} than linezolid, with a consistently left-shifted cumulative MIC distribution. Cohen's kappa analysis supporting enhanced activity of contezolid. Notably, this study provides—to our knowledge—the first report of contezolid-resistant clinical isolates. Screening of 14 linezolid-resistant (including five contezolid NWT) isolates revealed universal *optrA*, *cfr* and *Cfr(D)* carriage with domain V 23S rRNA mutations (including G2576T, C2610G, T2504C, and G2528C), and no mutations in ribosomal proteins L3/L4/L22; these findings support class-linked cross-resistance.

Conclusion Contezolid demonstrated potent and consistent activity against drug-resistant Gram-positive cocci, supporting its potential as a therapeutic alternative to linezolid. Further studies are needed to confirm resistance mechanisms and clinical utility.

Ceftazidime/Avibactam-Resistant Carbapenem-Resistant *Klebsiella Pneumoniae* in China: A Nationwide Multicenter Study

Rongqi Lu

Peking union medical college hospital

Objective To define the epidemiology, antimicrobial resistance phenotypes, and genomic mechanisms of ceftazidime/avibactam (CZA) resistance among carbapenem-resistant *Klebsiella pneumoniae* (CRKP) across China.

Methods We conducted multicenter surveillance (2021–2024) across 26 tertiary hospitals in 19 provinces. Isolates underwent identification, broth microdilution AST, and whole-genome sequencing with genomic analyses. In KPC-2 only CZA-resistant isolates, *blaKPC-2* expression and copy number were quantified,

and porin/efflux mutations and expression were evaluated.

Results Among 4739 isolates, 101 (2.1%) were CZA-resistant CRKP, mainly older male inpatients with lower-respiratory infections. NDM predominated (55.4%); dual NDM+KPC producers showed the broadest, highest-level resistance. Tigecycline remained most active (3%), while resistance to other agents was generally $\geq 37\%$. Pediatric isolates—almost all NDM—had lower levofloxacin, aztreonam, and amikacin resistance than adults. Whole-genome analysis showed heavy ARG (mean 15.4) and plasmid (mean 5.6) burdens, with ST11 predominance (42.6%) concentrated in a major cluster (cluster 4; 43/44) enriched for KPC and NDM+KPC producers and linked to KL64/KL47 and IncF replicons. Canonical hypervirulent *K. pneumoniae* markers were absent. Among nine (8.9%) KPC-2-only CZA-resistant isolates, high-MIC strains showed significantly higher *blaKPC-2* expression and copy number than low-MIC counterparts. Most also carried *OmpK35* N-terminal truncation ($\Delta 1-38$), the *OmpK36* loop-3 GD insertion, and conserved *AcrA/AcrB* substitutions.

Conclusion CZA-resistant CRKP in China are uncommon but widely distributed, driven mainly by epidemic ST11-KL64/KL47 lineages with extensive multidrug resistance and no convergence with classical hypervirulence. In KPC-2-only CRKP, CZA resistance is associated with increased *blaKPC-2* gene dosage together with structural porin alterations and *AcrA/B* variants.

Diarrhoeal Disease Attributable To Enterotoxigenic *Escherichia Coli*: The Global Burden of Disease Study 1990–2021

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Background Enterotoxigenic *Escherichia coli* (ETEC) remains a leading cause of diarrhoeal morbidity and mortality, particularly among children in low-income regions. Global evidence on its long-term epidemiological trends and socioeconomic disparities is limited

Objective This study aimed to comprehensively evaluate the global, regional, and national burden of ETEC-related diarrheal diseases from 1990 to 2021 using the Global Burden of Disease (GBD) 2021 study. Furthermore, we applied Age-Period-Cohort (APC) models to analyze underlying temporal trends and utilized ARIMA models to forecast the ETEC burden through 2030, providing a scientific basis for targeted public health interventions and vaccine development strategies.

Methods We analyzed ETEC-attributable mortality and disability-adjusted life years (DALYs) from the Global Burden of Disease Study 1990-2021 across 204 countries. Age-standardized mortality rates (ASMR), incidence, and DALYs were estimated by sex, age, region, and Socio-demographic Index (SDI). Temporal patterns were assessed using joinpoint and age-period-cohort models, and mortality was projected to 2030 using time-series forecasting.

Results Globally, ETEC deaths declined from $\approx 430\,000$ (95% UI 270\,000-690\,000) in 1990 to $\approx 100\,000$ (58\,000-172\,000) in 2021, a 76.7% reduction ($p < 0.001$). In 2021, male and female ASMRs were 1.21 and 1.31 per 100\,000, respectively. Children < 5 years accounted for 46\,410 deaths (24\,780 males; 21\,630 females), a 77%

decline since 1990, whereas adults ≥ 70 years contributed 28\,020 deaths (-72% , $p < 0.001$). Sub-Saharan Africa and South Asia represented 68.4% of global deaths, with mortality rates of 4.53 and 3.89 per 100\,000. High-SDI regions reported < 0.06 per 100\,000 ($p < 0.001$). DALYs fell from 3.2 million (1.9-5.1 million) to 0.7 million (0.4-1.2 million). The largest annual percentage reduction occurred during 2000-2008 (EAPC-5.4%, 95% CI-6.1 to -4.7). Forecasts suggest continued but slower decline through 2030 (projected ASMR 0.78 per 100\,000, -22.4% vs 2021).

Conclusion ETEC-related mortality and DALYs have declined globally over three decades, yet substantial inequities persist, with young children in low-SDI regions remaining most affected. Strengthened vaccination, sanitation, and nutrition interventions are essential to sustain and accelerate progress toward global diarrhoeal-disease targets.

Prognostic Value of Objective Nutritional Indices (PNI, CO-NUT, and HALP) for In-Hospital Mortality in Surgically Treated Infective Endocarditis: A 14-Year Retrospective Study of Chinese Population

feng zang

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Objective Malnutrition is closely associated with poor clinical outcomes; however, its prognostic value in patients with infective endocarditis (IE) undergoing surgical treatment remains unclear. This study aims to investigate the association between three nutritional indices (PNI, CONUT, and HALP) and in-hospital mortality in patients with IE.

Methods In this retrospective study, we collected clinical data from 450 patients diagnosed with IE treated at Jiangsu Provincial People's Hospital over a 14-year period. The patients were categorized into two groups: the death group (n=42) and the control group (n=408). We utilized the PNI, CONUT, and HALP scores to assess nutritional status. Additionally, we employed stepwise adjusted multivariate logistic regression models and ROC curves to evaluate the independent predictive ability of various nutritional statuses concerning in-hospital mortality.

Results The overall in-hospital mortality rate in the cohort was 9.33%. Preoperative malnutrition was prevalent among patients with IE, with the prevalence of malnutrition based on the PNI and the CONUT scoring criteria being 44.00% and 75.11%, respectively. Compared to the control group, patients in the death group exhibited significantly poorer baseline nutritional status. After adjusting for confounding factors, a one-unit increase in the PNI was associated with a 7% reduction in the risk of in-hospital mortality (OR=0.93, 95%CI: 0.89–0.98, $p = 0.009$). Similarly, a one-unit increase in the HALP score was associated with a 4% reduction in the risk of in-hospital mortality (OR = 0.96, 95%CI: 0.93–0.98, $p = 0.001$). In contrast, a one-unit increase in the CONUT score was associated with a 16% increase in the risk of in-hospital mortality (OR=1.16, 95%CI:1.03–1.32, $p = 0.017$). A prognostic model incorporating these nutritional indicators demonstrated excellent discriminatory power (AUC=0.839) and calibration (Brier score=0.063).

Conclusion Preoperative malnutrition is highly prevalent among patients with IE undergoing surgery and serves as a strong independent predictor of postoperative in-hospital mortality. The routine application of objective scoring tools, such as the PNI, CONUT, and HALP, can significantly enhance preoperative risk stratification. Furthermore, interventions aimed at patients

at risk of moderate to severe malnutrition may lead to substantial clinical benefits.

中国 ICU 患者多重耐药细菌血流感染的特征研究：一项多中心前瞻性研究的事后分析

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目的 多耐药菌导致血流感染（MDR-BSI）是 ICU 患者发病率和死亡率高的主要原因之一。中国 ICU 患者 MDR-BSI 相关研究有限，本研究旨在评估导致 MDR-BSI 的危险因素、临床特征、治疗模式及其对 28 天死亡率的影响。

方法 基于 LDG NIS006108 多中心前瞻性观察数据集对中国 36 家三级医院 ICU 住院≥1 天且实验室确诊 BSI 的 1110 例成年患者做事后分析。主要终

点为 MDR-BSI 相关危险因素,次要终点为 28 天死亡率影响因素。分析患者特征、重症评分、药敏、治疗及 28 天死亡率等。统计分析均采用 R 软件描述性分析为主。MDR-BSI 相关因素及 28 天死亡风险采用单变量和多变量逻辑回归分析。

结果 1110 例 BSI 患者革兰阴性菌为 68.56%,主要有肺炎克雷伯菌(38.6%)、大肠埃希菌(22.9%)、鲍曼不动杆菌(14.3%)和铜绿假单胞菌(7.9%);阳性菌 27.57%。其中 837 例(75.4%)MDR-BSI,273 例非 MDR-BSI。多变量分析显示 MDR-BSI 的发生与 ICU 入住到发生 BSI 时间延长(OR=1.87,95% CI: 1.13~3.12, P=0.016)及尿路感染(OR=2.35,95% CI: 1.22~4.51, P=0.010)显著正相关(图 1)。单变量分析显示 MDR-BSI 患者入院到 LCBSI 发生的时间更长(OR=1.01,95% CI: 1.00~1.02, P=0.007)且更多机械通气(OR=1.36,95% CI: 1.03~1.80, P=0.028)。抗感染治疗中 MDR-BSI 患者更频繁使用碳青霉烯类、第三代头孢菌素、糖肽类和四环素类药物。总人群 28 天死亡率为 22.4%,多变量分析显示死亡患者 SOFA 评分较高(OR=2.33,95% CI: 1.42~3.83, P=0.006)、更多中心静脉导管(OR=1.55,95% CI: 1.05~2.3, P=0.029)由难治性耐药阴性菌导致感染(OR=2.21,95% CI: 1.40~3.54, P<0.001)比例更高。死亡患者在经验性恰当治疗中更常用碳青霉烯类、四环素类、多黏菌素和咪唑类;生存患者更常用其他 β -内酰胺类、三代头孢菌素和喹诺酮类(图 2)。

结论 中国 ICU 获得性 MDR-BSI 在重症患者中高发且病死率高,其发生与 ICU 入住到发生 BSI 时间延长、尿路感染呈正相关。临床管理需关注高危患者的耐药菌监测和抗菌策略。

基于黏液型的肺炎克雷伯菌感染患者的临床特征、基因型与药敏研究

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目的 明确 Kp 的黏液表型与毒力基因在患者感染的临床特征上有无差异。

方法 本研究回顾性收集 2024 年 5 月—2025 年 3 月山西医科大学第二医院的碳青霉烯类敏感肺炎克雷伯菌临床分离株,药敏试验采用纸片扩散法或微量肉汤稀释法进行。依据拉丝试验中单菌落的拉丝长度,划分为 hmKp(≥ 5 mm)、mKp(0~5 mm)和 cKp(0 mm)共 3 个队列。同时,检测这些菌株的 iucA、rmpA、rmpA2、iroB 和 peg-344 毒力基因后分组,并描述性分析基因的分布特点。结合基线特征,标本类型,糖尿病、肺气肿等基础疾病,入院时病情评估 NEWS 评分,常用血常规及生化指标,临床转归等临床资料进行单因素及多因素 Logistic 回归分析,比较并分析黏液表型分组及基因型分组之间的临床特征。同时并测定荚膜多糖含量,分析其与黏液表型和五个毒力基因各自的相关性。P<0.05 认为有统计学差异。

结果 共纳入了山西医科大学第二医院的 239 株碳青霉烯类敏感肺炎克雷伯菌临床分离株。根据黏液表型分组, hmKp 分离株 127 株、mKp65 株, cKp 分离株 47 株,不同黏液分型的患者在基线特征及临床转归结果无差别。单因素分析变量后, hmKp 队列的社区获得性感染率最高(77.95%, p=0.014),而慢性肝病(0.79%, p=0.011)等基础疾病较低。mKp 队列常伴有肺气肿(30.77%, p=0.018)和慢性肝病(10.77%, p=0.011)基础疾病,并且生化指标乳酸升高(43.08%, p=0.010)比例明显高于其他两组。与 cKp 组相比, hmKp 和 mKp 组患者的蛋白水平偏低,并在进一步的多因素分析结果显示低 ALB 水平是 hmKp 和 mKp 感染的独立危险因素。此外,碳青霉烯类敏感肺炎克雷伯菌临床分离株中 48.95% 的菌株同时携带 rmpA、rmpA2、iucA、iroB 和 peg-344 这 5 种毒力基因,除此之外还分布有其他 18 种基因型组合。hmKp 的 rmpA2 与 iucA 聚类为一簇,在 Kp 中具有一定的共现特征, CPS 含量与高黏液

表型显著相关($r=0.5$, $p<0.001$), 基因水平上 *rpmA2* 基因相较 *rpmA* 的调控作用更显著 ($r=0.24$, $p<0.001$)。

结论 Kp 的黏液表型与毒力基因与患者临床结局无显著关联。拉丝试验本身是 *hvkp* 的非特异性特征, 但其简便性仍有助于临床早期识别。

Global Phylogeography and Genomic Characterization of blaNDM-positive Enterobacter Cloacae Complex

null null

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Carbapenem resistant *Enterobacter cloacae* complex (CRECC) driven by the dissemination of blaNDM represents an increasing global threat, yet its phylogeographic characteristics and global population structure remain insufficiently understood. In this study, 39 blaNDM-positive CRECC clinical isolates collected from two hospitals in China during 2016-2024 were investigated using antimicrobial susceptibility testing, conjugation assays, whole genome sequencing, and fitness analysis. In our dataset, the spread of blaNDM was mediated by multiple plasmids, among which IncX3 was the predominant vehicle. Notably, a structure containing three tandem copies of blaNDM-1 was identified on an IncFII(Yp) plasmid. The repeat unit consisted of an ISCR1 associated genetic structure, suggesting that this element may contribute to local amplification of the resistance gene. In addition, a global genomic epidemiology analysis was performed using a total of 3,237 blaNDM-positive CRECC genomes, including genomes generated in this study and those retrieved

from the NCBI database (accessed on January 3, 2026). Conjugation frequencies differed markedly among plasmid types, with the IncX3 blaNDM-1 plasmid showing the highest transfer efficiency. Acquisition of blaNDM- or blaKPC-2-carrying plasmids also imposed measurable fitness costs on the recipient strain, although the extent of the effect varied across plasmid backbones. Phylogenetic and population structure analyses showed that ST171 is the predominant clone among global CRECC isolates. Further phylogenetic analysis indicated that blaNDM-1 and blaNDM-5 are the major NDM variants worldwide. Multiple NDM variants were detected in both China and the United States, with blaNDM-1 being the most prevalent. These findings provide insight into the resistance mechanisms and dissemination dynamics of CRECC and highlight the importance of strengthened genomic surveillance and improved infection control strategies to limit the spread of blaNDM carrying CRECC.

Genomic Epidemiology and Mechanisms of Clonal Succession in NDM-1-producing *Providencia* Spp.: A Focus on Evolutionary Fitness and Dominance

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Objective Carbapenem-resistant *Providencia* spp. (CRPs) are multidrug-resistant opportunistic pathogens posing a global threat. This study integrates epidemiological surveillance with multi-omics analysis to comprehensively characterize the evolutionary dynamics of CRPs in our hospital over the past decade

Methods CRPs isolates were consecutively collected from a tertiary hospital over eight years (2017–

2024). MICs were determined by broth microdilution per CLSI standards. Whole-genome sequencing (WGS) was performed for species identification and MLST. A core-genome SNP-based phylogenetic tree was constructed and integrated with Bayesian analysis. Phenotypic assays evaluated fitness and pathogenicity of dominant clones

Results A total of 162 non-duplicate NDM-1-producing CRPs were collected. WGS identified 116 (71.6%) as a novel species, *Providencia nosocomium* nov., all belonging to ST41 lineage. Temporal and genomic analyses revealed that since the first detection of ST41 carbapenem-resistant *P. nosocomium* (ST41-CRPN) in 2022, this clone rapidly caused a hospital outbreak (SNPs ≤ 84) and replaced the previously dominant ST346 carbapenem-resistant *P. huaxiensis* (ST346-CRPH) within two years. ST41-CRPN retained a multi-drug-resistant phenotype but with lower overall resistance than ST346-CRPH; aztreonam and cefiderocol maintained good in vitro activity. Phenotypic assays confirmed that, compared to ST346-CRPH, ST41-CRPN showed a 12.6% increased growth rate, a competitive index of 98:2, and significantly enhanced biofilm formation. In a *Galleria mellonella* infection model, its virulence was comparable to hypervirulent *Klebsiella pneumoniae* NTUH-K2044 ($p > 0.05$) and significantly higher than that of ST346-CRPH ($p = 0.0093$). Genomic analysis revealed key drivers: mobile genetic elements mediated chromosomal integration of the blaNDM-1 gene cluster, conferring resistance with minimal fitness cost; the clone harbors a complete T6SS-i2, enhancing interspecies competitiveness and host adaptability. BEAST indicated that this clone originated in Shandong, China (1922), expanded from coastal to inland cities, and established a global network across Asia, Africa, and North America in the 21st century

Conclusion Between 2017 and 2024, the dominant CRP clone in our hospital underwent replacement

from ST346-CRPH to ST41-CRPN. ST41-CRPN exhibits a profound evolutionary advantage by stably carrying resistance genes without fitness cost, coupled with robust environmental adaptability and high pathogenicity, securing an absolute competitive edge in clinical settings. This clone has breached multiple host barriers, spreading across many Chinese provinces with early signs of international dissemination. Targeted molecular surveillance and enhanced infection control strategies are urgently needed to curb its further global expansion

Keywords *Providencia nosocomium* nov.; NDM-1; ST41 clone; Clonal replacement; Adaptive evolution; T6SS

成人百日咳 12 例临床特征及误诊原因分析

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目的 近年来成人百日咳发病率呈上升趋势，但临床表现不典型，误诊率极高。本研究分析成人百日咳的临床特征及误诊原因，提高临床医生对该病的识别能力。

方法 回顾性分析 2023 年 1 月至 2025 年 12 月于宁夏医科大学总医院呼吸与危重症医学科确诊的成人百日咳患者 12 例。纳入标准：①年龄 ≥ 18 岁；②符合中国 CDC 百日咳诊断标准，鼻咽拭子百日咳鲍特菌 PCR 阳性；③临床资料完整。排除标准：①合并其他明确病原体感染；②慢性咳嗽病史 (> 8 周)。收集患者人口学资料、临床表现 (咳嗽特点、持续时间、有无鸡鸣样回声、咳嗽后呕吐、夜间加重)、外周血常规、C 反应蛋白、胸部影像学、首诊诊断、确诊时间及治疗转归。

结果 12 例患者中，男性 5 例 (41.7%)，女性 7 例 (58.3%)，年龄 19-62 岁，平均 38.5 ± 12.6 岁。

发病季节以夏秋季为主(9例, 75.0%)。临床特征: 阵发性咳嗽12例(100%), 咳嗽后呕吐7例(58.3%), 夜间加重9例(75.0%), 典型鸡鸣样回声3例(25.0%), 咳嗽期间歇期无症状10例(83.3%)。外周血白细胞升高6例(50.0%), 其中淋巴细胞比例升高8例(66.7%)。C反应蛋白正常或轻度升高(均 $<20\text{mg/L}$)。胸部影像学均无特异性改变, 3例(25.0%)显示肺纹理增粗, 余9例无异常。从发病到确诊中位时间为14天(范围: 6-42天)。首诊误诊11例(91.7%), 其中误诊为急性支气管炎6例(50.0%)、感染后咳嗽3例(25.0%)、咳嗽变异性哮喘2例(16.7%), 仅1例(8.3%)首诊考虑百日咳。所有患者接受阿奇霉素(500mg d1, 250mg d2-5)治疗, 治疗后5-7天咳嗽明显缓解10例(83.3%), 2例(16.7%)咳嗽持续至14天后逐渐缓解, 无严重并发症。

结论 成人百日咳临床表现不典型, 典型鸡鸣样回声少见, 以阵发性咳嗽伴呕吐、夜间加重为特征, 首诊误诊率高达91.7%。对于迁延性咳嗽(>2 周)伴阵发性特点、外周血淋巴细胞比例升高者应警惕百日咳可能, PCR检测有助于早期确诊。

关键词: 成人百日咳; 临床特征; 百日咳鲍特菌; 阵发性咳嗽; PCR诊断

慢性阻塞性肺疾病急性加重合并肺炎克雷伯菌感染的临床特征及其对短期预后的影响

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目的 探讨慢性阻塞性肺疾病急性加重(AECOPD)合并肺炎克雷伯菌感染的临床特征及其对短期预后的影响。

方法 回顾性纳入2020年1月至2024年12月我院AECOPD住院患者。依据痰培养或支气管肺泡

灌洗液病原学结果, 分为肺炎克雷伯菌(KP)感染组与非KP细菌感染组。收集一般资料、基础疾病、既往3个月抗生素暴露、炎症指标(白细胞计数、C反应蛋白、降钙素原)及血气分析。主要结局为住院期间治疗失败(定义为需升级抗生素、转入ICU或院内死亡)及30天再入院。采用多因素Logistic回归分析危险因素, 评估炎症指标预测效能。

结果 共纳入286例, KP感染组84例(29.4%), 非KP感染组202例(70.6%)。两组性别、吸烟史差异无统计学意义。KP组既往3个月抗生素暴露更常见(61.9% vs. 44.6%, $P=0.01$), 合并支气管扩张比例较高(28.6% vs. 17.8%, $P=0.04$)。KP组PCT升高更明显[0.92(0.38-2.41)ng/mL vs. 0.48(0.19-1.26)ng/mL, $P=0.02$], CRP及白细胞计数差异无统计学意义。KP组住院时间延长[10(7-15)天 vs. 8(6-13)天, $P=0.03$], 治疗失败率较高(32.1% vs. 20.8%, $P=0.048$), 30天再入院率差异无统计学意义(27.4% vs. 19.8%, $P=0.12$)。多因素Logistic回归显示, $\text{PCT} \geq 0.5\text{ ng/mL}$ ($\text{OR}=2.08$, 95%CI 1.18-3.66, $P=0.01$)及既往抗生素暴露($\text{OR}=1.86$, 95%CI 1.04-3.31, $P=0.036$)为治疗失败独立危险因素, KP感染本身未进入最终模型($\text{OR}=1.54$, 95%CI 0.89-2.67, $P=0.11$)。ROC分析显示PCT预测治疗失败AUC为0.70, 联合既往抗生素暴露后提高至0.75。

结论 AECOPD合并肺炎克雷伯菌感染患者既往抗生素暴露比例较高, 炎症反应以PCT升高为主要特征。治疗失败风险更多与炎症水平及既往抗生素使用相关, 而非单一病原本身。应重视炎症标志物与抗生素暴露史的综合评估, 以优化抗感染治疗策略。

关键词: 慢性阻塞性肺疾病急性加重; 肺炎克雷伯菌; 抗生素暴露

RICU机械通气患者呼吸机相关性肺炎病原谱变迁、耐药性特征及其与脱机成功率的关联

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目的 探讨呼吸重症监护病房(RICU)机械通气患者呼吸机相关性肺炎(VAP)的病原谱分布、时间变迁特征,并分析耐药菌感染对脱机成功率的影响。

方法 回顾性纳入2020年1月至2024年6月我院RICU收治的有创机械通气 ≥ 48 h且发生VAP的患者186例。根据VAP发生时间分为早发型(≤ 5 d, $n=72$)与晚发型(>5 d, $n=114$)。收集一般资料、基础疾病、抗生素暴露史、病原学及药敏数据。主要结局为28 d脱机成功。比较两组病原谱及耐药特征,采用多因素Logistic回归分析脱机失败相关因素,并行亚组交互分析。

结果 186例中早发型占38.7%,晚发型占61.3%。革兰阴性菌占78.5%。早发型以肺炎克雷伯菌(29.2%)和大肠埃希菌(18.1%)多见;晚发型铜绿假单胞菌(27.2%)与鲍曼不动杆菌(25.4%)比例升高($P<0.01$)。MDR总体检出率42.5%,晚发型高于早发型(52.6% vs. 26.4%, $P=0.001$)。CR-GNB检出率28.0%,集中于鲍曼不动杆菌及铜绿假单胞菌。2022—2024年铜绿假单胞菌检出率较2020—2021年呈上升趋势(26.7% vs. 18.9%, $P=0.080$)。28 d脱机成功率61.3%。MDR感染者脱机成功率低于非MDR组(50.6% vs. 68.9%, $P=0.020$),CR-GNB感染者进一步降低(45.1% vs. 67.8%, $P=0.010$)。多因素Logistic回归显示,MDR感染($OR=2.14$, 95%CI 1.12~4.08, $P=0.021$)及机械通气时间延长($OR=1.05$, 95%CI 1.01~1.09, $P=0.015$)为脱机失败的独立危险因素。交互作用提示,VAP发生时间对MDR感染效应存在修饰作用(P for interaction=0.030),晚发型合并MDR感染时脱机失败风险更高。

结论 RICU机械通气患者VAP病原以革兰阴性菌为主,晚发型非发酵菌比例及耐药率显著升高。MDR及CR-GNB感染与脱机成功率下降密切相关。

加强病原学监测及合理抗感染策略对改善预后具有重要意义。

关键词: 呼吸机相关性肺炎;病原谱;多重耐药菌;脱机成功率;重症监护

The HmuS Heme-degrading Enzyme of *Klebsiella Pneumoniae* Regulates Iron Homeostasis and Drives Virulence Heterogeneity in *Escherichia Coli* Through Modulating Bacterial Protein Synthesis.

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Objective To investigate the molecular mechanism by which the heme-degrading enzyme HmuS in hypervirulent *Klebsiella pneumoniae* (HvKP) of the K1-ST23 clone regulates colibactin synthesis through iron homeostasis, thereby driving intrastrain virulence heterogeneity

Methods Three K1-ST23 HvKP strains with PFGE homology $\geq 90\%$ were selected. Virulence differences were validated using *Galleria mellonella* larval infection model, mouse intraperitoneal infection model, and biofilm formation assay. Whole-genome sequencing and comparative genomics identified the differential gene *hmuS*. An *hmuS* knockout strain ($\Delta hmuS$) and complementation strain were constructed via homologous recombination. Siderophore production and intracellular iron content were measured using CAS plate assay, ICPMS, and ferrozine-based method. HmuS protein was expressed, purified, and its enzymatic activity was determined. Bacterial growth and intracellular ROS levels were assessed under oxidative stress (5 mM H_2O_2). Transcriptome sequencing (RNA-seq) and

RTqPCR were performed to analyze differentially expressed genes, focusing on the colibactin synthesis-associated *pks* gene cluster. In vivo virulence of Δ hmuS under different iron conditions was evaluated using a mouse pneumonia model, and bacterial load, histopathological damage, and inflammatory cytokines (IL6, TNF α , IL1 β) in lung tissues were measured

Results Significant virulence differences existed between high and low virulence strains; high virulence strains formed more biofilm ($P < 0.05$). Whole genome sequencing revealed a chromosomal deletion region (≈ 0.1 Mbp) containing *hmuS* in the low virulence strain. Under iron limited conditions, Δ hmuS produced significantly more siderophores than the wildtype (WT) strain but showed impaired growth; it failed to grow with hemin as the sole iron source, and growth was restored by FeSO₄ supplementation. Intracellular total iron and Fe²⁺ levels were markedly reduced in Δ hmuS ($P < 0.05$). Purified HmuS exhibited heme degrading activity (specific activity 56.1 nmol/min/mg). Under 5 mM H₂O₂, Δ hmuS displayed growth inhibition and elevated intracellular ROS. Transcriptome and RTqPCR analyses showed that the colibactin synthesis *pks* gene cluster (genes *clbB* to *clbP*) was significantly downregulated in Δ hmuS; iron limitation further suppressed its expression, while FeSO₄ partially restored it. In the mouse pneumonia model, the Δ hmuS group showed lower bacterial load, milder lung pathology, and reduced inflammatory cytokine levels compared with the WT group. Iron chelation (Δ hmuS+Dip) further attenuated virulence, whereas FeSO₄ supplementation partially restored virulence

Conclusion HmuS drives virulence heterogeneity in K1-ST23 HvKP by maintaining iron homeostasis to positively regulate colibactin synthesis, thereby influencing pathogenicity. This reveals a novel mechanism of virulence microevolution in homologous hypervirulent clones

Genomic Adaptation and Antimicrobial Resistance of *Pseudomonas Aeruginosa* in Non-cystic Fibrosis Bronchiectasis

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Objectives To investigate the genomic diversity, virulence characteristics, and antimicrobial resistance profiles of *Pseudomonas aeruginosa* isolates recovered from patients with non-cystic fibrosis bronchiectasis (NCFB)

Methods A total of 66 *P. aeruginosa* isolates from NCFB patients were characterized by whole-genome sequencing, core-genome phylogenetic analysis, multilocus sequence typing, O-serotyping, and pairwise SNP distance analysis. Loss-of-function mutations and virulence-associated genes were analyzed genomically. Antimicrobial susceptibility testing was performed for major antipseudomonal agents. To evaluate the role of alginate and iron transport-associated mutations in cefiderocol susceptibility, an *algD* deletion mutant and complementation strains were constructed

Results The 66 isolates showed substantial genomic heterogeneity, comprising 53 sequence types and diverse O-serotypes, with no dominant epidemic clone. Pairwise SNP analysis identified only three closely related isolate pairs, suggesting that most infections were sporadic rather than due to cross-transmission. Frequent loss-of-function mutations were observed in genes involved in chronic adaptation, including *mucA*, *algP*, *mexZ*, *oprD*, and *mexB*. *mucA* mutations were significantly more common in mucoid than non-mucoid isolates (93.8% vs 64.7%, $P = 0.02$), with frameshift mutations predominating. Virulence-associated genes were

broadly conserved, although considerable diversity was observed in pyoverdine receptor, motility, and selected secretion system-related genes. Resistance to carbapenems, ciprofloxacin, ceftazidime, and cefepime was common, whereas resistance to aminoglycosides, piperacillin/tazobactam, ceftazidime-avibactam, colistin, and cefiderocol was rare. Mucoid isolates exhibited significantly higher cefiderocol MICs than non-mucoid isolates (median, 0.25 vs 0.125 mg/L; $P = 0.0073$), enhanced biofilm formation, and reduced acute virulence in *G. mellonella*. Deletion of *algD* in a mucoid isolate reduced the cefiderocol MIC from 8 to 4 mg/L, while complementation restored the parental phenotype. High-cefiderocol-MIC isolates also carried mutations in iron transport-related genes; notably, complementation of *pirR* decreased cefiderocol MICs in three clinical isolates, and combined *algD* deletion plus *pirR* complementation further reduced the MIC to 1–2 mg/L.

Conclusions *P. aeruginosa* isolates from NCFB patients exhibit extensive genomic diversity and adaptive evolution, with frequent *mucA* inactivation and other loss-of-function mutations associated with chronic airway persistence. Mucoid isolates display increased biofilm formation, attenuated acute virulence, and reduced cefiderocol susceptibility. Decreased cefiderocol susceptibility appears to result from the combined effects of alginate overproduction and mutations in iron transport regulatory pathways, highlighting a multifactorial adaptive mechanism in NCFB-associated *P. aeruginosa*.

Bibliometric Analysis and Real-World Epidemiological Investigation of *Acinetobacter Baumannii* Research

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This study investigated global research trends on *Acinetobacter baumannii* and systematically characterized its clinical distribution, antimicrobial resistance, and molecular epidemiology in a single tertiary hospital in Hebei Province, China. A bibliometric analysis of original articles and reviews indexed in the Web of Science Core Collection from 2000 to 2025 identified 2,150 publications. China was the leading contributor (469 papers, 21.81%), followed by the United States (264, 12.28%), and Zhejiang University was the most productive institution (57 papers). For the clinical investigation, 4,028 *A. baumannii* isolates collected during 2014–2024 were retrospectively analyzed. Among them, 2,143 were carbapenem-resistant *A. baumannii* (CRAB), accounting for 53.2%; however, the CRAB proportion decreased from 63.0% in 2014 to 39.4% in 2024. Most isolates originated from the ICU (38%) and neurosurgery (11%), and sputum was the predominant specimen type (88%). Infection rates were significantly higher in patients aged ≥ 60 years ($p < 0.05$), and isolate numbers

showed marked seasonality, peaking in August and reaching a minimum in February. Antimicrobial susceptibility testing showed that CRAB exhibited near-universal resistance to multiple antibiotic classes, including β -lactams, fluoroquinolones, and tetracyclines, but remained highly susceptible to polymyxins, with a resistance rate of only 0.3%. Resistance rates for most antibiotics were broadly consistent with trends in defined daily doses (DDDs), and antibiotic resistance patterns correlated with antibiotic consumption intensity. PCR and agarose gel electrophoresis of 244 CRAB isolates revealed widespread co-carriage of resistance and virulence determinants: 84.0% (205/244) simultaneously harbored OXA-23 and OXA-51; 70.9% (173/244) co-carried the efflux pump genes *adeR*, *adeS*, *adeB*, and *adeJ*; and 75.8% carried all 10 biofilm-associated genes. Compared with the survival group, the death group had older age, lower serum albumin, lower platelet and lymphocyte counts, higher inflammatory markers (WBC, CRP, PCT, IL-6), and shorter hospital stay ($p < 0.05$). In conclusion, although the proportion of CRAB declined over time, its burden remains concentrated among elderly ICU patients with pneumonia. Strengthened antimicrobial stewardship and targeted interventions in key departments are essential to limit further spread.

Risk Factors, Nomogram, and Prognostic Value of Liver Function Trajectory in Sepsis-Related Liver Injury: A Three-Year Retrospective Cohort Study

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Background Sepsis-related liver injury (SRLI)

is a common and serious complication of sepsis, yet early prediction remains challenging and the prognostic significance of dynamic liver function recovery is not well characterized. This study aimed to develop a nomogram for early identification of SRLI and to evaluate the prognostic value of liver function trajectory in septic patients

Methods This three-year retrospective cohort study included 332 patients with sepsis admitted between December 2022 and December 2025. SRLI was defined as new-onset coagulopathy, hyperbilirubinemia, or transaminase elevation within 72 hours of sepsis diagnosis. LASSO regression and multivariable logistic regression were used to identify independent risk factors for SRLI, from which a nomogram was constructed and internally validated. Among patients who developed SRLI, a Day-14 landmark analysis was performed to assess the association between liver function trajectory and 30-day mortality using Kaplan–Meier survival analysis.

Results Of the 332 patients with sepsis, 121 (36.4%) developed SRLI, with an overall 30-day mortality of 38.0% (46/121). Eight independent predictors of SRLI were identified: cerebrovascular disease (OR = 2.647, 95% CI: 1.388–5.120, $P = 0.003$), source of abdominal infection (OR = 2.098, 95% CI: 1.122–3.966, $P = 0.021$), shock (OR = 1.807, 95% CI: 1.016–3.226, $P = 0.044$), SOFA score (OR = 1.134, 95% CI: 1.053–1.224, $P = 0.001$), APAR (OR = 1.158, 95% CI: 1.035–1.305, $P = 0.012$), lactate (OR = 1.199, 95% CI: 1.072–1.353, $P = 0.002$), and CRP (OR = 1.004, 95% CI: 1.001–1.007, $P = 0.021$); source of urinary tract infection was a protective factor (OR = 0.460, 95% CI: 0.205–0.976, $P = 0.049$). The nomogram demonstrated good discrimination (AUC = 0.788, 95% CI: 0.738–0.838) and calibration, with a bias-corrected AUC of 0.777 after bootstrap internal validation. In the Day-14 landmark analysis of 90 patients who survived to Day

14, those with a declining liver function trajectory had significantly lower 30-day mortality than those with a non-declining trajectory (4.2% vs. 63.2%, log-rank $P < 0.001$).

Conclusion This study developed a nomogram incorporating eight readily available clinical and laboratory variables for early prediction of SRLI. A declining liver function trajectory within the first 14 days was strongly associated with favorable 30-day prognosis. These findings may assist clinicians in early risk stratification and dynamic prognostic assessment of patients with sepsis.

化脓性肝脓肿患者的病原学、临床特征与继发脓毒症的危险因素分析

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目的 分析化脓性肝脓肿(PLA)患者的致病菌和临床特征,为临床诊疗提供参考。

方法 收集2021年2月至2025年09月期间就诊我院40例临床诊断为肝脓肿的患者,引流的脓液经过细菌培养、鉴定、药敏实验。记录患者的病原学特征及临床资料,进一步比较合并与不合并糖尿病患者及继发与未发生脓毒症患者的临床特征。

结果 PLA患者以男性患者最多见(67.5%, 27/40),主要位于右叶,占75.0%(30/40),最常见的合并症是糖尿病,占62.5%(25/40)。40例PLA患者中通过分离培养法检出40株细菌,肺炎克雷伯菌是PLA最主要的致病菌,占72.5%(29/40)。对肺炎克雷伯菌药物敏感性结果分析显示,对左氧氟沙星、头孢呋辛、头孢西丁敏感性下降,分别为75.86%、79.31%、82.76%,其余药物敏感性均超过90.00%以上。PLA合并糖尿病组患者的肺炎克雷伯菌感染率高于非糖尿病组($P < 0.05$),且进展为

脓毒血症比例较高,外周血白细胞计数水平更高,差异有统计学意义(均 $P < 0.05$)。PLA患者中有14例患者继发脓毒症,占35.0%,对PLA继发脓症患者进行Logistic多因素危险因素分析显示血清hs-CRP [OR值(95%CI), 1.012 (1.002 ~ 1.022), $P = 0.022$]是PLA继发脓毒症的独立危险因素。限制立方样条(RCS)分析发现当hs-CRP > 133 mg/L时,PLA进展为脓毒症的风险显著增加($P < 0.05$)

结论 糖尿病患者若出现不明原因发热、畏寒、寒战症状,需考虑PLA可能,需要尽早进行病原学检查。肺炎克雷伯菌是最主要的致病菌,感染后侵袭性强,当血清hs-CRP > 133 mg/L时,PLA进展为脓毒症的风险显著增加,需要临床医师提高警惕,选择合适的抗生素尽早开启治疗。

关键词: 化脓性肝脓肿;糖尿病;肺炎克雷伯菌;脓毒症

Efficacy and Safety of Fluconazole in The Treatment of Oral Candidiasis in Elderly Patients: A Systematic Review and Meta-analysis

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Objective With the accelerated aging of the population and the updates to global guidelines for the diagnosis and management of candidiasis, the standardized treatment of oral candidiasis in elderly patients has become increasingly significant. Fluconazole, the preferred systemic antifungal agent for treating oral candidiasis in elderly patients, has not yet undergone a

comprehensive evaluation of its efficacy and safety.. This study aims to systematically assess fluconazole's clinical efficacy and safety against other antifungals (nystatin, itraconazole, ketoconazole) in treating oral candidiasis in the elderly, providing evidence-based support for informed clinical and individualized treatment decisions

Methods A comprehensive literature search was performed in PubMed, Web of Science, The Cochrane Library, CNKI, VIP, and Wanfang databases to assess fluconazole for the treatment of oral candidiasis in elderly patients from database inception to March 2026. Fixed-effects or random-effects models were used to estimate pooled risk ratios (RR). Heterogeneity was assessed using Cochrane Q and I^2 statistics. Subgroup analysis were conducted based on different comparator drugs. Sensitivity analysis was execute by excluding studies one by one. Publication bias was assessed by Egger's test and funnel plots. Analyses were performed in the R software 4.2.3 using the 'meta' packages. The study was registered with PROSPERO, CRD420261381378

Results Of 9,501 studies identified, 13 randomized controlled trials (RCTs) involving 1,376 elderly patients with oral candidiasis were finally included in the meta-analysis. Meta-analysis results showed that the clinical cure rate in the fluconazole group was significantly higher than that in other antifungal agent groups ($RR = 1.17$, 95%CI: 1.08–1.27, $P < 0.01$), and the clinical efficacy rate in the fluconazole group was also significantly higher than that in the control group ($RR = 1.07$, 95%CI: 1.01–1.13, $P < 0.05$). In terms of safety, the incidence of adverse events in the fluconazole group was significantly lower than in the groups treated with other antifungal agents ($RR = 0.60$, 95%CI: 0.42–0.84, $P < 0.05$), and the disease recurrence rate was significantly lower than that in the control group ($RR = 0.90$, 95%CI: 0.42–0.84, $P < 0.01$). No significant publication

bias was detected by Egger's test or funnel plots. Sensitivity analysis by sequentially excluding each study revealed no substantial changes in the results, indicating low sensitivity and robust model estimates

Conclusions Our findings indicate that fluconazole effectively enhances treatment outcomes and lowers side effects and recurrence in elderly oral candidiasis patients, highlighting its safety and long-term benefits. Despite this, the studies reviewed were generally low quality, underscoring the need for large, well-designed randomized controlled trials to strengthen the evidence

Keywords Fluconazole; Oral candidiasis; Elderly; Meta-analysis

2021—2025 年四川地区儿童患者细菌耐药监测研究

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目的 分析 2021—2025 年四川省细菌耐药监测网各成员单位儿童患者 (≤ 14 岁) 的细菌耐药监测数据, 明确儿童感染性疾病的病原学分布特征及耐药现状, 为该地区医疗机构儿童抗菌药物的合理应用提供科学依据。

方法 依据全国细菌耐药监测网监测方案 (2024 版), 对 2021—2025 年四川省细菌耐药监测网成员单位儿童患者临床分离的各类标本进行细菌鉴定及药敏试验; 药敏结果参照 CLSI M100 第 35 版和 CLSI M45 第 3 版标准判读, 采用 WHONET 5.6 软件进行数据统计分析。

结果 本次研究共纳入 329708 株细菌, 其中革兰阴性菌 202915 株 (61.5%), 革兰阳性菌 126793 株 (38.5%)。分离率居前 5 位的病原菌依次为流感嗜血杆菌 (22.3%)、金黄色葡萄球菌 (16.0%)、肺

炎链球菌(16.0%)、卡他莫拉菌(14.9%)和大肠埃希菌(8.7%)。儿童患者分离细菌主要来源于呼吸道标本(80.4%)。药敏结果显示,流感嗜血杆菌对氨苄西林总耐药率高达82.2%,卡他莫拉菌对阿莫西林-克拉维酸总耐药率较低(<2.0%);耐青霉素非脑膜炎肺炎链球菌检出率在0.3%~0.6%间波动;耐甲氧西林金黄色葡萄球菌(MRSA)检出率在28.1%~29.6%间浮动;未检出耐万古霉素、替考拉宁和利奈唑胺的葡萄球菌。头孢噻肟/头孢曲松耐药大肠埃希菌(CTX/CRO-R-ECO)和肺炎克雷伯菌(CTX/CRO-R-KPN)检出率分布在43.2%~45.3%、26.4%~34.4%间浮动;而头孢噻肟/头孢曲松耐药沙门菌属检出率均呈逐年上升趋势,分别由23.6%、24.2%升至34.0%、33.7%。碳青霉烯耐药大肠埃希菌(CR-ECO)、肺炎克雷伯菌(CR-KPN)、鲍曼不动杆菌(CR-ABA)和铜绿假单胞菌(CR-PAE)检出率分别在0.7%~1.6%、4.8%~11.0%、9.8%~17.9%、2.7%~3.4%区间内上下起伏。

结论 2021—2025年四川省儿童患者临床分离菌以革兰阴性菌为主,主要耐药菌株(MRSA、CR-ECO、CR-KPN、CR-PAE、CR-ABA)检出率维持在一定范围,且未呈现下降趋势。本地区各级医疗机构应强化感染防控措施,完善儿童抗菌药物使用管理策略,以减少耐药菌株产生、延缓耐药性进展

Global Geographic and Genomic Epidemiology Analysis of Carbapenem-resistant *Escherichia Coli* Carrying blaNDM-9

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Carbapenem-resistant *Escherichia coli* (CREC), particularly strains producing New Delhi metallo- β -lactamase-9 (NDM-9), pose a growing threat as agents of nosocomial infections. Despite their emergence since

2013, a comprehensive global phylogeographic and genetic characterization of blaNDM-9-carrying CREC is lacking. Through 7 years (2018-2024) of surveillance of CREC strains in a tertiary hospital, we obtained seven blaNDM-9-carrying CREC. Antimicrobial susceptibility testing, conjugative transfer experiments, whole-genome sequencing (WGS), and fitness analysis were performed. Publicly available genomes of blaNDM-9-carrying CREC from NCBI (curated by July 2025) were integrated for global analysis. All seven blaNDM-9-carrying CREC exhibited resistance to most antimicrobials tested, except colistin. WGS revealed diverse blaNDM-9-carrying plasmid types (IncB/O/K/Z, IncHI2, IncFIB, and IncC) and sequence types of strains (ST156 predominant). Key mobile genetic elements IS26 and ISCR1 facilitated blaNDM-9 dissemination. Plasmid structural analysis traced the evolution of the IncB/O/K/Z plasmid, revealing potential intra-hospital persistence and spread. Carriage of blaNDM-9-carrying plasmid imposed a significant fitness cost. Global analysis ($n = 203$ isolates) demonstrated high genetic diversity (56 STs), with ST156 (20.1%) being the most prevalent. Spatially, isolates were concentrated in Asia (China: 85.2%). Primary isolation sources were humans (39.4%) and chickens (34.9%), with a notable shift toward human predominance since 2016. Our findings elucidate the critical role of specific mobile elements in transmission, highlight the significant burden in China, document a shift toward human-associated isolates, and identify ST156 as a globally prevalent lineage. We emphasized the necessity of intensified surveillance to track the dissemination of blaNDM-9-carrying CREC. **IMPORTANCE** This study provides the first integrative geographic and genomic epidemiology analysis of blaNDM-9-carrying carbapenem-resistant *Escherichia coli* (CREC). Our 7-year surveillance and genomic analysis revealed critical insights into the genetic

characteristics and transmission dynamics of CREC carrying blaNDM-9. The identification of mobile genetic elements, such as IS26 and ISCR1, underscores their role in the horizontal transfer of resistance genes, facilitating the spread of blaNDM-9. Furthermore, given the high frequency of blaNDM-9-carrying CREC in China and its likelihood of spreading clonally in hospitals, there is an immediate need to intensify surveillance efforts. Adopting a One Health perspective, our study highlights the interconnected antimicrobial resistance risks spanning human, animal, and environmental health domains, advocating for strengthened global phylogeographic and phylogenetic surveillance alongside clinical interventions to curb the spread of these high-risk epidemic clones.

爬宠类异宠来源真菌的种群构成及部分菌株体外抗真菌药物敏感性分析

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目的 了解爬宠类异宠来源真菌的种群构成、宿主分布特征及部分分离株对常用抗真菌药物的体外应答情况, 评估其潜在动物健康风险与公共卫生意义, 为爬宠类异宠真菌性疾病的监测、诊断及合理用药提供依据。

方法 于 2025 年 9 月至 2026 年 3 月采集广东省广州和中山地区社区、大学宿舍、养殖场及动物医院来源的爬宠类异宠样品 60 份, 宿主包括蛇类、蜥蜴类和龟类。采用沙氏葡萄糖琼脂培养基和念珠菌显色培养基进行真菌分离培养, 并结合 MALDI-TOF MS 进行鉴定; 选取部分代表性菌株, 进行体外抗真菌药物敏感性试验。

结果 共获得真菌分离株 103 株, 其中酵母样真菌 67 株, 占 65.05%, 丝状真菌 36 株, 占 34.95%。

阿萨希毛孢子为优势菌种, 共 26 株; 其次为光滑念珠菌 7 株、热带念珠菌 6 株。值得关注的是, 本研究分离到 5 株烟曲霉, 该菌具有较高的临床关注度, 提示爬宠类异宠可能携带具有潜在致病风险的真菌。不同宿主来源样本的优势真菌谱存在一定差异, 其中蛇类样本中阿萨希毛孢子分离最多, 蜥蜴来源样本的真菌多样性相对较高。药敏结果显示, 不同真菌对 6 种抗真菌药物的体外应答存在明显差异: 阿萨希毛孢子对酮康唑、氟康唑和伊曲康唑 MIC 整体较低, 但对米卡芬净天然耐药; 光滑念珠菌和热带念珠菌对米卡芬净及 5-氟胞嘧啶 MIC 较低, 而对部分唑类药物 MIC 存在升高; 烟曲霉对氟康唑体外活性较差, 而对伊曲康唑、两性霉素 B 和米卡芬净表现出较好的体外应答。

结论 爬宠类异宠可携带多种具有潜在临床意义的真菌, 其种群构成较为复杂, 不同宿主来源样本的优势真菌谱及不同菌种对抗真菌药物的体外应答均存在差异。上述结果提示, 爬宠类异宠不仅可能构成动物健康风险, 也可能具有一定的潜在公共卫生意义。临床诊疗中应重视病原学鉴定与药敏检测, 以提高抗真菌治疗的针对性和合理性。

关键词: 爬行动物; 异宠; 真菌; 流行病学调查; 药物敏感性; 体外抗真菌活性

Emerging Nosocomial Pathogen of Carbapenem-resistant *Acinetobacter Nosocomialis*: Global Genomic Landscape and Plasmid Structure Perspective

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Among members of the *Acinetobacter calcoaceticus*–*baumannii* (ACB) complex, carbapenem resistance in *Acinetobacter baumannii* has been extensively studied, whereas the genomic characteristics and plasmid features of *Acinetobacter nosocomialis* remain less well defined. This study aimed to characterize carbapenem-resistant *A. nosocomialis* (CRAN) isolates to elucidate their resistance mechanisms and assess their potential contribution to resistance dissemination. Twenty-six *A. nosocomialis* isolates were analyzed, among which three CRAN isolates were identified. Whole-genome sequencing revealed that carbapenem resistance genes were plasmid-borne, comprising blaNDM-1 (n=2) and blaOXA-23 (n=1). Comparative plasmid analysis showed that blaNDM-1 was associated with Tn125, while blaOXA-23 was located on Tn2006. Concurrently, global genomic analysis based on publicly available genomes revealed that *A. nosocomialis* shows a geographically imbalanced distribution, with a predominance of isolates from Asia (59.92%, n=287), followed by North America (25.26%, n=121); at the country level, China (34.66%, n=166) was the major contributor, followed by the United States (25.05% n=120) and Malaysia (7.93% n=38) and considerable sequence type diversity, with ST433 (10.44%, n=50), ST768 (9.81%, n=47), and ST410 (9.39%, n=45) representing the most frequently observed sequence type without clear dominance. This genetic diversity is supported by the absence of clear phylogenetic clustering among isolates. Overall, these findings provide important insights into the genomic characteristics and transmission potential of carbapenem resistance in *A. nosocomialis*.

The Nationwide Genomic Characteristics and Phylogenetic Evolution of ST23-K1 Hypervirulent *Klebsiella Pneumoniae* in Relation To

Virulence and Antimicrobial Resistance Acquisition

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Objective Hypervirulent *Klebsiella pneumoniae* (hvKp) ST23-K1 poses a global health threat due to its high virulence and increasing antimicrobial resistance. This study aimed to characterise the genomic feature and phylogenetic evolution of ST23-K1 in China

Methods Virulence was assessed using hypermucoviscosity phenotyping and a murine infection model. For ST23-K1 carrying acquired antimicrobial resistance genes (ARGs), the CRISPR/Cas system, protospacers, anti-CRISPR (Acr) genes, and plasmidome were characterised. Time-resolved phylogenetic analysis was performed using integrated locally generated and publicly available data

Results Among 400 K1 isolates, ST23 was the most prevalent sequence type, and its effective population size increased following CG23-I divergence. The CG23-I sub-lineage was widely distributed nationwide with limited evidence of clonal transmission. Isolates with an incomplete *cps* locus exhibited significantly reduced virulence compared with those carrying an intact locus. The prevalence of extended-spectrum β -lactamase-positive ST23-K1 isolates increased over time, whereas carbapenemase-producing isolates remained stable. Among acquired ARGs-positive ST23-K1 isolates, a conserved protospacer corresponding to a prevalent spacer was identified. This protospacer, together with *AcrIE* genes, was frequently co-located on IncFII-type plasmids

Conclusion ST23-K1 remains a hypervirulent

lineage undergoing ongoing evolutionary expansion. The presence of acquired ARGs in ST23-K1 may be associated with AcrIIE-harboring IncFII plasmids, and functional validation is required to clarify the underlying mechanisms. Continuous genomic surveillance is essential to monitor the evolution and antimicrobial resistance trends of ST23-K1

耐碳青霉烯肺炎克雷伯菌感染的临床危险因素与分子流行病学特征

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目的 探讨耐碳青霉烯类肺炎克雷伯菌 (Carbapenem-resistant *Klebsiella pneumoniae*, CRKP) 的分子流行病学特征、耐药机制和感染临床危险因素, 研究耐药性与毒力之间的交互关系, 为预防和临床干预提供科学依据。

方法 收集了 2016 年 11 月至 2023 年 10 月期间于青岛市市立医院住院患者中分离的肺炎克雷伯菌 (*Klebsiella pneumoniae*, KP) 菌株共 528 株及其对应的临床资料。根据药物敏感性试验结果, 确定 80 例 CRKP 感染患者作为 CRKP 组。以“分离日期前后 7 天 (± 7 天) 内分离出 CSKP 菌株”为条件, 为每例 CRKP 患者匹配分离出碳青霉烯敏感肺炎克雷伯菌 (Carbapenem-susceptible *Klebsiella pneumoniae*, CSKP) 菌株的患者; 若匹配不足, 则将时间窗口扩大至分离日期前后 1 个月 (± 30 天), 最终共匹配出 160 例患者构成 CSKP 组。收集所有入组菌株的临床资料并进行全基因组测序, 系统研究其分子流行病学特征和耐药、毒力基因谱; 采用多因素 logistic 回归模型筛选出 CRKP 感染的独立危险因素; 通过 Spearman 相关系数分析, 探索耐药性与毒力间的关系。

结果 多因素 logistic 回归分析显示, 感染前 30

天内抗菌药物使用史 (OR:4.411, 95% CI:1.749-11.128, Wald χ^2 值: 9.882, $p < 0.01$) 和感染前 30 天内进行腹部侵入性操作 (OR:6.846, 95% CI:3.141-14.922, Wald χ^2 值: 23.411, $p < 0.01$) 是 CRKP 感染的独立危险因素。CRKP 感染以 ST11 型 (80.0%) 为主; blaKPC-2 基因 (88.8%) 为主要耐药机制。CRKP 优势克隆 ST11 经历了从 ST11-K25/O5 向 ST11-K64/O2a 的血清型演变。整体层面耐药基因得分与毒力基因得分呈显著负相关 ($\rho = -0.321$, $p < 0.001$), 但亚组分析显示同一 ST11 克隆内部两者无相关性 ($\rho = 0.020$, $p = 0.872$)。ICU 是 CRKP 院内克隆传播的核心节点, 优势克隆可通过转科患者、医护人员或医疗器械向普通病房扩散, 形成跨科室传播链。

结论 感染前 30 天内抗菌药物使用史和感染前 30 天内进行腹部侵入性操作是其独立危险因素。CRKP 常携“捆绑式”耐药质粒呈广泛耐药。

侵袭性肺曲霉病患者肺微生物组多样性、特定类群及其预后价值

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目的 侵袭性肺曲霉病 (IPA) 是严重的机会性真菌感染, 多见于免疫低下或合并基础肺部疾病患者, 进展快、死亡率高, 临床诊疗难度大。目前对 IPA 患者肺部微生态环境的系统性研究仍较匮乏, 肺微生物组在其发生发展及预后中的作用尚未阐明。本研究旨在分析 IPA 患者肺微生物组的多样性、特征性菌群组成, 明确其与临床结局的关联, 为 IPA 的发病机制阐释、风险评估及靶向干预提供理论依据。

方法 采用回顾性队列研究设计, 纳入宁夏医科大学总医院 2020 年 8 月—2025 年 8 月收治的 189 例确诊 IPA 患者, 以 1:1 倾向得分匹配同

期 189 例年龄、性别匹配的非曲霉肺部感染患者为对照。收集痰液及支气管肺泡灌洗液标本, 通过传统培养、宏基因组二代测序、半乳甘露聚糖试验进行病原学检测, 比较两组患者肺微生物组 α 多样性与物种组成差异; 采用多因素 Logistic 回归分析 IPA 发生的独立影响因素, Cox 回归探讨肺微生物组特征与 28 天全因死亡率的关联。

结果 匹配后两组基线可比, 但 IPA 组合并糖尿病、慢性阻塞性肺疾病、心力衰竭及新冠肺炎的比例显著更高 ($P<0.05$), 28 天全因死亡率 (14.81%) 显著高于对照组 (6.88%, $P<0.05$)。IPA 患者气道细菌 α 多样性指数 (Shannon、Simpson、Chao1、Richness) 均显著升高 ($P<0.05$), 物种分析显示其以肺炎克雷伯菌、大肠埃希菌、不动杆菌、黏质沙雷菌等条件致病菌富集为特征, 对照组则以卡他莫拉菌、溶血嗜血杆菌为主。多因素 Logistic 回归显示, 假单胞菌属是 IPA 发生的独立危险因素 (OR=2.31, 95% CI: 1.52~3.51, $P<0.001$), 校正混杂因素后关联仍显著。Cox 回归未发现细菌整体多样性与 28 天全因死亡率存在显著关联 (HR=1.12, 95% CI: 0.76~1.65, $P=0.56$)。

结论 IPA 患者肺微生物组呈现多样性升高、条件致病菌富集的特征, 假单胞菌属可作为 IPA 风险评估的潜在生物标志物; 但气道细菌整体多样性并非 IPA 患者短期预后的可靠预测指标。本研究提示, IPA 患者肺部微生态失衡是曲霉感染与宿主免疫损伤、基础疾病、抗生素暴露等多因素共同作用的结果, 为 IPA 的微生态靶向干预提供了新思路。

关键词: 侵袭性肺曲霉病; 肺微生物组; 宏基因组二代测序; 多样性; 预后

Molecular Epidemiology and Persistence of Multidrug-Resistant *Acinetobacter Baumannii* in Zhejiang, China (2015–2020): Insights Into Resistance, Virulence, and Transmission Dynamics

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Background This study investigate the molecular epidemiology and population characteristics of 184 *Acinetobacter baumannii* clinical isolates collected in Zhejiang (2015–2020), shedding light on the persistence and success of ST208-KL2 lineage

Methods Whole-genome sequencing and bioinformatic analysis characterized the population structure and transmission dynamics of 184 *A. baumannii*. Plasmid analysis identified the surrounding structures of blaOXA-58 and blaNDM-1 genes. Serum inhibition assays and *Galleria mellonella* virulence experiments, combined with global epidemiological analysis, explored the persistence and dominance of ST208-KL2

Results Of the isolates, approximately 78.8% (145/184) exhibited carbapenem resistance, primarily driven by blaOXA-23, blaOXA-72, blaOXA-58, and blaNDM-1. The *A. baumannii* population was divided into 2 clusters, distinguished by differences in ST types and resistance islands profiles. Cluster2 accounted for 71 department-time transmission events, mainly involving long-term interdepartmental spread, particularly in the rehabilitation medicine department and intensive care unit. Recombination analysis revealed that recombination occurred mainly in capsular locus (KL) regions, prophage regions, and predicted protein regions. Phenotypic experiments found that ST208-KL2 isolates displayed increased virulence and greater resistance to serum inhibition compared to ST208-KL7 isolates. This finding likely explains its persistently higher prevalence throughout the study period, except in 2019

Conclusions Cluster2 isolates demonstrated significant advantages in ARG prevalence, resistance rates,

and transmission capacity. ST208-KL2, with its superior serum resistance and virulence compared to ST208-KL7, has emerged as a dominant lineage with global implications for infection control and public health

Dynamics of Clinical *Klebsiella Pneumoniae* Strains over The COVID-19 Pandemic in Qingdao, China

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Background Multidrug-resistant pathogens' dynamics under major societal and environmental disruptions are poorly understood. The COVID-19 pandemic, with its drastic changes in healthcare practices and antimicrobial usage, likely created unique selective pressures on hospital-based pathogens. This study aimed to investigate the genomic epidemiology of 528 *Klebsiella pneumoniae* (*K. pneumoniae*) clinical isolates collected from a tertiary hospital in Qingdao, China, to understand the population-level changes in response to the pandemic

Methods A total of 528 *K. pneumoniae* strains were collected between 2016-2023, covering the COVID-19 pandemic. All strains were subject to 2nd generation whole-genome sequencing. The sequence types were predicted with MLST and cgMLST methods. Antimicrobial resistance genes and virulence factors were predicted. Antimicrobial resistance phenotypes were determined. Co-occurrence network analysis was performed, identifying modular features of the networks.

Results SL258 and SL23 were the predominant sequence types, and K1 and O1 were the most frequent serotypes. A high level of virulence factors was found,

particularly for *ybt* genes, and their correlation with sequence- and sero-types were determined, leading to identification of connections between hypervirulent strain types with virulence factors. Comparison of strains pre-, during-, and post-pandemic led to several findings: 1) the most important multidrug-resistant SL258 strains and overall antimicrobial resistance levels increased during-pandemic and decreased post-pandemic; 2) a diversification of both multidrug-resistant and overall *K. pneumoniae* types occurred, with a decrease in community structure complexity during the pandemic followed by a drastic increase post-pandemic, characterized by the emergence and expansion of nine previously rare *K. pneumoniae* types (seven of which were multidrug-resistant); 3) a strain replacement event took place for SL258 strains, from K25/O5 type pre-pandemic to K64/O2a type post-pandemic.

Conclusion The COVID-19 pandemic led to rebalancing of *K. pneumoniae* community structure. This shift was primarily driven by the widespread empirical antibiotic use in hospitals, coupled with overburdened healthcare systems hindering effective infection control, and impaired patient immunity. These factors collectively promoted the spread and clonal expansion of resistant *K. pneumoniae* strains. Concurrently, social distancing and self-protective measures influenced bacterial transmission dynamics at the community level. This work looked into *K. pneumoniae* community dynamics caused by a full-scale disturbance, gaining insights into how social behaviors shape the pathogen landscapes.

Genomic Insights and Recent Epidemiology of A Multidrug-Resistant *Mycoplasma Hominis* Isolate in China: Implications for Clinical Management

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Mycoplasma hominis (*M. hominis*) is an opportunistic pathogen linked to urogenital and neonatal infections; however, limited genetic and epidemiological data are available. Extragenital infections in healthy adults are rare, and effective antibiotics are species-specific, complicating diagnosis and treatment. Hence, this study aimed to elucidate the clinical process, update the epidemiological characteristics, and investigate the genomic features of a multidrug-resistant *M. hominis* isolate from an immunocompetent pleuropneumonia patient in China. The *M. hominis* isolate ZY_MH01 was recovered from pleural fluid and was identified by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) and Whole Genome Sequencing (WGS). The completed genome was annotated using the Prodigal. Snippy v4.4.5 was utilized to conduct a core genome single nucleotide polymorphism (cgSNP) analysis between ZY_MH01 and 50 *M. hominis* strains from the NCBI GenBank database. Subsequently, phylogenies were constructed using IQtree v2.0.3 and visualized by iTOL. Antimicrobial resistance genes and susceptibility were identified by CARD RGI v6.0.3 and VITEK 2 Compact System. The antimicrobial resistance mutation in gene *parC* (S91I) was found in the genome. Phylogenetic analysis revealed that ZY_MH01 and strains from the NCBI database were epidemiologically related, with ZY_MH01's closest relatives being in the same city and sharing the same resistance and virulence genes. *M. hominis* should be considered a potential cause of pulmonary infection, particularly in patients unresponsive to broad-spectrum antibiotics. This study provides a detailed analysis of *M. hominis* epidemiology, highlighting regional evolutionary relationships among strains.

Keywords *Mycoplasma hominis*; pneumonia; immunocompetent; multidrug-resistance; cgSNP

Who Is at Risk? Clinical Features and A Predictive Model for 30- Day Mortality in Hematologic Patients with Enterococcal Bloodstream Infection

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Objective Given the high mortality and lack of a tailored prognostic model for hematologic patients with enterococcal bloodstream infection (EBSI), this study aimed to develop and internally validate a risk score to predict 30-day mortality

Methods We retrospectively analyzed 192 hematologic patients (≥ 14 years) with EBSI admitted between 2014 and 2024. Clinical features, microbiology, treatment, and outcomes were assessed. Candidate predictors for 30-day mortality were selected by LASSO and entered into multivariable logistic regression. A simplified risk score was derived from regression coefficients and internally validated by bootstrap resampling.

Results The median patient age was 43 years, and acute leukemia was the predominant underlying disease (72.4%). *Enterococcus faecium* was the leading

pathogen (71.4%), with low vancomycin resistance (1.6%). Most cases (71.9%) occurred as breakthrough infections, mainly during carbapenem therapy, and 72.9% met mucosal barrier injury laboratory-confirmed bloodstream infection criteria. The 14- and 30-day all-cause mortality rates were 13.5% and 22.4%, respectively. Independent predictors of 30-day mortality included age ≥ 50 years (aOR=2.29, $p=0.038$), severe graft-versus-host disease (aOR=6.06, $p=0.003$), septic shock (aOR=30.01, $p<0.001$). The final predictive model, incorporating these three factors along with pneumonia and high-risk hematologic disease, demonstrated optimal discrimination (AUROC 0.79, 95% CI 0.705–0.867) and calibration. A derived risk score stratified patients into low- (<2 points) and highrisk (≥ 2 points) groups, with markedly different 30-day mortality (11.3% vs. 39.0%, $P<0.001$).

Conclusion In hematologic patients, EBSIs commonly arise as breakthrough infections despite broad-spectrum antibiotic coverage, most often associated with mucosal barrier injury. Our parsimonious risk score enables early identification of patients at high risk of 30-day mortality to guide timely interventions.

Gamma-glutamyl Transferase As A Diagnostic and Prognostic Biomarker in Bloodstream Infection and Sepsis: A Retrospective Cohort Study

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Objective Bloodstream infection (BSI) and sepsis are life-threatening conditions with high mortality, and effective and easily accessible biomarkers are still limited. Gamma-glutamyl transferase (GGT), a routine

liver function parameter, is related to systemic inflammation and oxidative stress. This study aimed to investigate the association between GGT levels and BSI, and to evaluate the diagnostic and prognostic value of GGT in patients with sepsis

Methods A retrospective cohort study was conducted, enrolling 1193 hospitalized patients with positive blood cultures at the Third Hospital of Hebei Medical University between January 2021 and December 2024. Patients with acute viral hepatitis, alcoholic hepatitis, primary biliary cholangitis, biliary obstruction, immunosuppressant use or incomplete data were excluded. Demographic, clinical and laboratory data including GGT, IL-6, PCT, CRP and 30-day mortality were collected. Multivariate Cox regression, Kaplan-Meier survival analysis and ROC curve analysis were used to assess the independent prognostic value and predictive performance of GGT. Subgroup analyses were performed based on pathogen types and sepsis severity

Results Elevated GGT levels were significantly associated with BSI and sepsis severity. GGT levels peaked on the second day of hospitalization and remained higher in septic patients. Subgroup analysis showed higher GGT levels in Gram-negative infections than in Gram-positive infections, and the highest levels were found in fungal infections. Multivariate Cox regression revealed that elevated GGT and elevated PCT were independent risk factors for 30-day mortality. ROC analysis showed that the AUC of GGT for predicting 30-day mortality was 0.731, with an optimal cutoff of 82 U/L. The AUC of the combined model of GGT and PCT was 0.824, which was significantly higher than any single indicator. Kaplan-Meier analysis showed that patients with high GGT (≥ 82 U/L) had significantly lower 30-day survival rate than those with low GGT

Conclusion GGT is a readily available and low-cost biomarker that can assist in early diagnosis and risk

stratification of BSI and sepsis. Elevated GGT is an independent predictor of 30-day mortality in BSI patients. Dynamic monitoring of GGT helps evaluate disease severity and treatment response. The combination of GGT with PCT significantly improves prognostic accuracy, which is valuable for clinical practice especially in resource-limited settings

2014-2024 年儿童血液病患者血流感染病原体分布及耐药性分析

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目的 探究 2014-2024 年中国医学科学院血液病医院血液病患者发生血流感染 (BSI) 的流行病学特点, 以期更好指导血液病患者 BSI 治疗改善患儿预后。

方法 选择从 2014 年 1 月至 2024 年 12 月在中国医学科学院血液学研究所血液病医院住院的 14 岁以下血液病患者为研究对象, 对其临床资料、药敏数据进行回顾性分析。

结果与结论 共计 1050 名 (≤ 14 岁) 血液病患者发生 1401 例次 BSI, 患儿中位年龄 7.5 岁, 91.4% 的患儿原发病为恶性血液病, 其中以急性淋巴细胞白血病最为多见 (52.9%), 非恶性血液病以重型再生障碍性贫血最为多见 (80.0%)。革兰氏阳性菌的检出率高于革兰氏阴性菌的检出率 (53.0% vs 46.0%), 检出率整体位于前五位的病原微生物分别为草绿色链球菌 334 株、凝固酶阴性葡萄球菌 280 株、大肠埃希菌 223 株、肺炎克雷伯菌 176 株和铜绿假单胞菌 90 株。其中 89.9% 的 BSI 发生于患儿中性粒细胞缺乏期 (粒缺期), 粒缺患儿与非粒缺患儿的病原谱呈现显著差异性, 革兰阴性菌尤其是大肠埃希菌和肺炎克雷伯菌在粒缺患儿中检出率高于非粒缺患儿 (17.1% vs 5.7%, $P < 0.001$; 13.5% vs 4.3%,

$P = 0.002$), 而革兰阳性菌尤其是葡萄球菌在非粒缺患儿中检出率较高 (61.0% vs 21.8%, $P < 0.001$), 真菌在两组患儿中分布无显著差异。一半以上的患儿合并有其他部位感染, 其中合并呼吸道感染 (30.3%) 最为常见。合并不同部位感染的 BSI 患儿感染病原谱存在差异。伴呼吸道感染的患儿革兰氏阳性菌的检出率高于无呼吸道感染症状的患儿 (60.1% vs 49.8%, $P < 0.001$), 合并肛周感染的患儿革兰氏阴性菌检出率高于无肛周感染症状的患儿 (75.6% vs 44.3%, $P < 0.001$), 尤其是大肠埃希菌在合并肛周感染的患儿中检出率较高 (35.9% vs 14.7%, $P < 0.001$)。检出的主要革兰氏阴性菌普遍对美罗培南等碳青霉烯类抗生素和阿米卡星敏感, 耐药率分别低于 10.0% 和 5.0%。大部分革兰氏阳性菌对青霉素类、红霉素类以及四环素类抗生素耐药, MRSA (耐甲氧西林的金黄色葡萄球菌) 检出率为 21.0%。未检出对万古霉素耐药的葡萄球菌和肠球菌。不同病原微生物感染患儿预后存在明显差异, 真菌、嗜麦芽窄食单胞菌、肠球菌以及 CRO 感染显著增加了患儿的死亡风险。

2014-2024 年儿童与成人血液病患者血流感染病原体分布与耐药性分析对比

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目的 探究 2014-2024 年中国医学科学院血液病医院血液病患者成人血液病患者发生血流感染 (BSI) 感染病原谱及耐药性的差异, 以期为不同年龄段血液病患者提供早期抗生素选择及预后判断依据。

方法 选择从 2014 年 1 月至 2024 年 12 月在中国医学科学院血液学研究所血液病医院住院的发生血流感染的血液病患者为研究对象, 对其临床资料、药敏数据进行回顾性分析。

结果和结论 共计 1050 名 (≤ 14 岁) 血液病患

儿发生 1401 例次 BSI, 成人血液病患者共计发生 5828 例次 BSI。与成人 BSI 血液病患者相比, 血液病患儿发生 BSI 时革兰氏阳性菌的检出率较高(53.0% VS 20.1%, $P<0.001$), 革兰氏阴性菌的检出率较低(46.0% VS 78.1%, $P<0.001$), BSI 患儿葡萄球菌和链球菌的检出率高于成人患者, 分别为 25.8% vs 8.9% $p<0.001$ 、25.9% vs 7.5% $p<0.001$, BSI 患儿肠球菌的检出低于成人 BSI 患者为 1.0% vs 3.8% $p<0.001$ 。两者检出前三的革兰氏阴性菌均为大肠埃希菌、肺炎克雷伯菌和铜绿假单胞菌。真菌在 BSI 患儿中检出率较低(1.0% vs 1.8%, $p=0.034$)。在检出病原体的耐药性方面, 血液病患儿 BSI 检出的主要革兰氏阴性菌对主要抗生素的耐药率普遍低于成人患者, 尤其是 CRO 的检出率低于成人患者(8.3% vs 15.8%, $P<0.001$); 但患儿中检出的革兰氏阳性菌对除喹诺酮类抗生素以外的主要抗生素的耐药率普遍高于成人患者, 耐甲氧西林的葡萄球菌检出率高于成人患者(66.7% vs 51.0%, $P<0.001$)。

Emergence of Multidrug-resistant ST876 Serotype 14 *Streptococcus Pneumoniae* with Spontaneous Mutations Driving Pathogenesis: Genomic and Clinical Insights From Pneumococcal Pericarditis and Global Screening

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Background *Streptococcus pneumoniae* pericarditis is rare and lethal, yet how the pathogen evolves within the host during blood-to-pericardium spread remains unknown

Methods Two ST876 serotype 14 strains, hz23B (blood) and hz23P (pericardial effusion), were isolated

from one purulent pericarditis patient. We determined antimicrobial susceptibility test (AST) by broth micro-dilution, performed whole-genome sequencing and mutation detection, multi-locus sequencing typing, and phylogenetic analysis against 1429 global serotype 14 genomes, modeled protein structures for unique mutations, and quantified growth under anaerobic/low-nutrient conditions, plus adherence and invasion on nasopharyngeal and lung epithelial cell lines

Results Both isolates showed an identical AST profile, where a multidrug-resistant phenotype was observed. Genomes differed by only 36 SNPs, while hz23P acquired CiaH_W192L (transmembrane kinase loss) and FabT_E21A (DNA-binding reduction). These changes conferred hz23P's enhanced growth in THY and BSA+G under anaerobic stress ($p<0.0001$) but significantly reduced adherence ($p<0.0001$) and invasiveness ($p<0.01$) compared with hz23B. Global screening identified ST876 as a unique clone that carries pericarditis-linked mutations and successfully dominated China due to multidrug resistance

Conclusions We provide the first real-time evidence that ST876 serotype 14 pneumococci evolve within the host to survive the pericardial environment by attenuating virulence and energy. The global screen underscores the urgent need for surveillance targeting this multidrug-resistant and virulent clone

Keywords *Pneumococcus*; ST876; Serotype 14; Heart infection; Pericarditis; CiaH; FabT

2014-2023 年成人血液病患者血流感染流行病学特点及预后因素: 单中心结果分析

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目的 探讨 2014-2023 年间,中国医学科学院血液学研究所血液病医院成人血液病患者血流感染(BSI)的病原学分布、耐药变迁及发生 BSI 后 30 天内死亡的危险因素。

方法 回顾性分析 2014 年 1 月至 2023 年 12 月期间在本院住院的成人血液病患者(≥18 岁)并发 BSI 的临床资料及药敏试验数据。

结果 10 年间共计 3395 例成人血液病患者发生 4456 例次 BSI,共分离菌株 4703 株。其中,革兰阴性菌占 78.8%(3704 株),以大肠埃希菌、肺炎克雷伯菌及铜绿假单胞菌为主;革兰阳性菌占 19.1%(899 株),以草绿色链球菌、凝固酶阴性葡萄球菌及金黄色葡萄球菌为主;真菌占 2.1%(100 株),以热带念珠菌为主。趋势分析显示,大肠埃希菌检出率逐年下降,而铜绿假单胞菌、肺炎克雷伯菌、嗜麦芽窄食单胞菌及缓症链球菌等检出率呈上升趋势。BSI 发生时,86.9%的患者处于中性粒细胞缺乏期,64.5%伴有其他部位感染。病原谱在不同免疫状态及合并感染部位间存在显著差异:粒缺患者的革兰阴性菌感染率显著高于非粒缺患者;合并呼吸道感染者以非发酵菌(如嗜麦芽窄食单胞菌、不动杆菌)多见;合并腹腔感染者肠杆菌科及肠球菌属占比较高;合并肛周、口腔及皮肤软组织感染者分别以大肠埃希菌、铜绿假单胞菌及嗜麦芽窄食单胞菌为主。耐药方面,肠杆菌科细菌对三代头孢菌素及喹诺酮类药物耐药率较高;铜绿假单胞菌对碳青霉烯类药物的耐药率已超 20%;耐药菌(如 CREC、CRKP、CRPA)的发生率随年代增加。患者 30 天全因死亡率为 8.3%。多因素回归分析表明,高龄、合并糖尿病、严重粒缺、感染性休克、合并肺部/腹腔/皮肤及软组织感染,以及发生 CRO、真菌或肠球菌 BSI 是患者 30 天死亡的独立危险因素。

结论 成人血液病患者 BSI 病原菌分布广泛且具有临床异质性。不同免疫状态及合并感染部位患者的病原谱差异显著,且耐药菌株呈上升趋势。临床医师应结合患者临床特征,科学选择抗菌药物以改善预后。

关键词: 血流感染,血液病,病原学,耐药性,

危险因素

基于全基因组测序与 MALDI-TOF MS 技术的纹带棒状杆菌分子分型的流行病学研究

宋

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目的 通过分析河北省石家庄地区某三甲医院纹带棒状杆菌的耐药特征、分子分型及全基因组测序结果,了解本地区 *C. striatum* 的耐药表型及分子流行病学特征;探索以 7 个管家基因为靶点建立 *C. striatum* 多位点序列分型方法的可行性,并结合全基因组测序解析菌株的种群结构及系统发育关系,为该菌的流行病学监测及医院感染防控提供实验依据。

方法 收集石家庄某三甲医院临床分离的 80 株非重复 *C. striatum* 菌株。为提升研究的临床意义,筛选出 40 株来源于无菌体液及深部组织的菌株进行 MALDI-TOF MS 聚类分型,同时结合患者的临床资料进行统计分析。根据 MALDI-TOF MS 聚类分型筛选代表性菌株。针对 PubMLST 官网缺乏标准扩增方案的问题,本研究建立并优化了纹带棒状杆菌 MLST 的 PCR 扩增体系。随后通过 WGS 进一步解析菌株特征,利用 CARD 和 VFDB 数据库深度挖掘耐药决定簇及毒力因子分布,并整合遗传分型数据评估谱系间的亲缘关系。

结果 80 株 *C. striatum* 分离株标本来源主要为重症监护室、创伤急救科、呼吸科,感染人群以 60-69 岁男性中老年人群为主。MALDI-TOF MS 将 40 株 *C. striatum* 分为 3 个分支,各分支抗菌药物敏感性谱总体一致,仅庆大霉素存在轻度差异。32 株代表性菌株共鉴定出 26 种序列型(ST),呈现高度的遗传多样性特征。优势型别为 ST12、ST13 和 ST21(各占 9.38%)。48 株 *C. striatum* 全基因组分析显示: *rbpA* 基因高度保守性分布,而获得性耐药基因 *ermX* 在本地株中表现出明显的序列异质性(截短或

变异)。毒力谱分析提示核心调控与铁摄取系统基因具有高度保守性,而黏附因子 *spaD/F* 在不同来源菌株间存在分布差异。系统发育分析显示本地菌株呈现基因多系起源特征,但在整体深层分化的背景下,基于全基因组 SNP 遗传距离识别出 3 个高度一致的克隆聚集簇 (SNP<50)。

结论 MLST 分型提示本地区分离株具有较高的遗传多样性,群体结构呈现明显的多系起源特征。虽然整体遗传背景分化明显,但基于全基因组 SNP 分析识别出少数具有高度遗传一致性的菌株亚群。高分辨率 SNP 分析可有效弥补传统分型方法在监测精度上的不足,是识别特定谱系遗传特征及观察多重耐药菌演化规律的有效技术路径。

关键词: 纹带棒状杆菌, MALDI-TOF MS, MLST, 基因组测序, 核心基因组单核苷酸多态性

Phase-Specific Characteristics and Prediction of Mortality and Carbapenem-Resistant Gram-Negative Organisms in Allogeneic Hematopoietic Stem Cell Transplantation-Related Bloodstream Infection

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Background A systematic analysis stratifying bloodstream infection (BSI) by the conditioning (CP), post-infusion pre-engraftment (PIP), and post-engraftment (PE) phases of allogeneic hematopoietic stem cell transplantation (allo-HSCT) is limited

Methods Among 3119 consecutive allo-HSCT

patients (2013–2024), BSI episodes were classified as CP, PIP, or PE. We developed and validated two risk scores to predict carbapenem-resistant gram-negative organisms (CRO) BSI and 28-day mortality.

Results BSI incidence was 13.5% (420/3119). Gram-negative bacteria (GNB) predominated (76.0%), mainly *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*. For each patient's first BSI, aplastic anemia (AA) patients were more likely to develop BSI during CP, while myelodysplastic syndromes (MDS) patients were more susceptible starting from PIP. Among 128 patients with first BSI during CP after anti-thymocyte globulin (ATG), median onset was 4 days after the first dose; only 9 (7.0%) occurred within 24 hours. The 28-day mortality after first BSI was 8.6% (36/420). GNB (86.1% [31/36] of deaths), particularly CRO (36.6% [119/325] of GNB patients), were associated with increased early mortality. Two validated scores were established: a CRO BSI score—CRO colonization (3 points), carbapenem therapy (2), severe neutropenia >5 days (1); and a 28-day mortality score—sepsis/septic shock (2), PE-BSI (2), CRO BSI (1).

Conclusion AA patients warrant heightened vigilance for BSI during conditioning, and MDS patients after stem-cell infusion. BSI is unlikely within 24 hours of first-dose ATG. CRO colonization screening combined with our risk score may allow earlier identification and reduction of CRO BSI, thereby may reduce early mortality.

恶唑烷酮类耐药基因 *OprA* 在临床与畜牧业来源金黄色葡萄球菌中的传播特征研究

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背景 恶唑烷酮类抗菌药物，如利奈唑胺，是治疗革兰阳性病原菌感染的重要抗生素，尤其在甲氧西林耐药金黄色葡萄球菌等耐药菌感染的治疗中具有重要价值。*optrA* 基因是一种已知的利奈唑胺耐药基因，最初主要在肠球菌中被发现，而在金黄色葡萄球菌中的报道相对罕见。因此，明确 *optrA* 基因在金黄色葡萄球菌中的存在情况、遗传背景及其潜在传播途径，对于评估其公共卫生风险具有重要意义。

方法 本研究在中国 27 个省份 37 家医院收集的 1845 株金黄色葡萄球菌测序菌株中，鉴定到一株携带 *optrA* 基因的临床金黄色葡萄球菌分离株，编号为 18-W32-54。该菌株分离自四川省某三级医院皮肤科一名 29 岁女性患者的分泌物样本。研究首先通过抗菌药物敏感性试验评估该菌株对利奈唑胺的敏感性；随后采用全基因组测序和比较基因组学分析，进一步探究携带 *optrA* 的遗传元件在不同菌株和不同宿主来源中的分布情况及其潜在传播关系。此外，本研究还对 NCBI 数据库中公开可获得的 15520 株金黄色葡萄球菌基因组进行了筛查，以鉴定其中是否存在 *optrA* 基因。所有 *optrA* 阳性菌株均被纳入后续的系统发育分析和比较基因组学分析。

结果 临床分离株 18-W32-54 被鉴定为 ST398 型金黄色葡萄球菌，并携带多种耐药基因，包括 *optrA*、*fexA*、*blaZ*、*ermB* 和 *tet(L)*。其中，*optrA* 基因位于整合于染色体中的转座子 Tn6823 上。比较基因组分析显示，该 Tn6823 相关结构不仅存在于畜牧业来源的金黄色葡萄球菌中，还可见于屎肠球菌、粪肠球菌以及松鼠葡萄球菌等不同菌种中，提示该遗传结构可能在相关环境中发生了跨菌种传播。在对 15520 株金葡萄基因组的筛查中，共发现 13 株携带 *optrA* 基因的菌株，占比为 0.08%。这些菌株均来源于中国黑龙江省和广东省，分离自畜牧业、食品或相关环境样本。它们属于不同的序列型，包括 ST398、ST2308 和 ST6423，说明 *optrA* 基因已在多个金黄色葡萄球菌谱系中出现和扩散。

结论 本研究表明 *optrA* 基因已经在不同金黄色葡萄球菌谱系中发生传播，并进一步出现向临床菌株传播的迹象。该发现从“同一健康”视角提示，畜牧业、食品、环境与临床之间可能存在耐药基因流动的潜在通道。未来有必要持续加强对临床金黄色葡萄球菌中 *optrA* 基因的监测，结合基因组流行病学手段追踪其传播路径，从而更好地理解其扩散机制，并制定相应的防控策略。

The Prevalence and Transmission Dynamics of The Global NDM-producing Carbapenem-resistant *Acinetobacter Baumannii* Populations

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Background *Acinetobacter baumannii* is an important hospital-acquired pathogen, and the sustained prevalence of carbapenem-resistant *A. baumannii* (CRAB) has become a major challenge in clinical therapy. Although CRAB carrying New Delhi metallo- β -lactamase (NDM) remains relatively uncommon, its transmission potential warrants attention. This study investigated the epidemiology of clinical NDM-CRAB in China and, together with global genomic data, explored its population structure, transmission patterns, and resistance characteristics

Methods A total of 541 clinical CRAB isolates were collected in 2023 from 12 tertiary hospitals across China. blaNDM was screened by PCR and confirmed by Sanger sequencing. Positive isolates underwent antimicrobial susceptibility testing and whole-genome sequencing. Publicly available *A. baumannii* genomes were retrieved from the NCBI Pathogen Detection data-

base, and blaNDM-positive isolates were identified using ResFinder. Oxford MLST, core genome SNP analysis, phylogenetic reconstruction, plasmid profiling, and comparative resistome analysis were performed.

Results Eight of 541 clinical CRAB isolates were blaNDM-positive, yielding a detection rate of 1.5%. All NDM-CRAB isolates exhibited multidrug resistance but remained susceptible to polymyxins, cefiderocol, eravacycline, and tigecycline. A total of 2,763 global NDM-CRAB isolates were included, revealing a pronounced clonal population structure. ST1697, ST1418, ST1604, and ST2164 were the predominant sequence types, with marked geographic variation. Phylogenetic analysis showed distinct major clades and clustered clonal transmission within lineages. blaNDM was associated with multiple plasmid types, supporting plasmid-mediated horizontal transfer. Notably, within major sequence types, blaNDM-positive isolates showed heterogeneous phylogenetic distributions and variable associations with ARG burden.

Conclusion NDM-CRAB remains uncommon among clinical CRAB isolates in China, but multiple high-risk lineages have already emerged globally. Its dissemination is driven by clonal expansion and plasmid-mediated horizontal transfer, with lineage-specific differences observed across genetic backgrounds.

Global Burdens of Acute Hepatitis E in Older Adults From 1992 To 2021 and Projections until 2044

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Introduction As the global population ages, acute hepatitis E (AHE) in older adults has become a significant public health issue internationally. Nonetheless, detailed information on its global impact and changing patterns is limited. This study aimed to delineate the temporal trends and project future incidence of AHE in older adults, providing insights crucial for targeted prevention and control strategies.

Methods Estimates and 95% uncertainty intervals (UIs) for acute hepatitis E incidence and mortality across seven age brackets (65–69, 70–74, 75–79, 80–84, 85–89, 90–94, ≥95 years) were sourced from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2021. The age-standardized incidence and mortality rates for acute hepatitis E in these older adults were calculated using the direct method of age standardization. Joinpoint regression analysis was utilized to examine the evolution of age-standardized incidence and mortality rates from 1992 to 2021. The age-period-cohort (APC) model was applied to analyze the distinct impacts of age, period, and birth cohorts. Additionally, the Bayesian APC model was applied to forecast the global epidemiological trends through 2044.

Results In 2021, the estimated global age-standardized incidence and mortality rates of AHE among older adults were 85.20 (95% confidence interval (CI): 59.10 to 118.00) and 7.97 (95% CI: 6.84 to 9.41), respectively. The highest disease burden of incidence and mortality existed in Eastern Europe. From 1992 to 2021, the estimated global age-standardized incidence and mortality rates of AHE among older adults (AAPC: -0.57%, 95% CI: -0.59% to -0.55%, $P < 0.001$; AAPC: -0.45%, 95% CI: -0.66% to -0.25%, $P < 0.001$) both demonstrated significant declining trends. The changing trends varied significantly across different regions and 204 countries, with an increased trend of age-standardized incidence rates in the lower Socio-demographic In-

dex (SDI) regions. The age-period-cohort analysis results showed that the relative risk of incidence and mortality generally showed unfavorable trends over time in low-middle and low SDI regions. In addition, the age-standardized incidence and mortality rates were predicted to decrease annually, while the case number of these metrics was predicted to keep increasing until 2044

Conclusions Global patterns in the incidence and mortality rates of AHE among older adults have largely demonstrated a downward trend, though with notable variability. This suggests that while the global handling of pancreatitis has been effective, it remains inconsistent. Such trends are crucial for the appropriate distribution of healthcare resources and for developing relevant policies aimed at managing AHE among older adults effectively

脓肿分枝杆菌复合群耐药机制、群体结构及毒力特征的基因组学研究

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目的 针对脓肿分枝杆菌复合群(MABC)高度耐药及临床治疗困难的困境,本研究从病原体展开系统分析。通过整合河北地区临床分离株与北京地区公开基因组数据,系统解析中国北方MABC的耐药机制、基因组特征及分子流行病学特征;同时纳入博莱亚种公共基因组数据,对不同亚种间毒力因子谱进行比较分析,旨在为MABC感染的精准诊疗提供分子依据。

方法 对河北地区临床分离株进行全基因组测序(WGS),并整合北京地区81株MABC公开基因组数据及BV-BRC数据库中博莱亚种的基因组数据,

分析耐药基因、多位点序列分型(MLST)、优势克隆群(DCC)、系统发育关系及毒力因子图谱。

结果 1. 河北地区临床分离株体外物敏感性试验显示,大环内酯类药物在第14天的延长培养读中呈现亚种异质性:脓肿亚种多由敏感转为耐药(95.5%),马赛亚种则均保持敏感。WGS分析该现象与erm(41)基因多态性高度一致:脓肿亚种多携带完整的T28等位型,而马赛亚种则表现为erm(41)基因部分缺失。NZ61株(脓肿亚种)因携带C28变异亦未出现诱导耐药。氨基糖苷类耐药评估中检出部分菌株携带rrs A1408G突变,但个别菌株存在基因型-表型不一致现象。

2. 群体进化分析显示,河北地区以ST46和ST77为主要流行型,而北京地区菌株的ST型别表现出更高的多样性;并检出DCC1和DCC6全球优势克隆。系统发育树表明,京冀两地菌株呈现交错分布,未形成明显的地域性隔离,提示区域谱系共享与全球优势克隆并存的流行特征。此外,核心毒力因子谱在不同亚种间高度保守,仅呈现部分异质性:MASS_RS20860和MASS_RS20355毒力基因在马赛亚种中高度富集,而在脓肿亚种中缺失;espl毒力基因则仅见于博莱亚种。

结论 河北地区MABC临床分离株具有显著多药耐药特征,亚种间药敏谱存在明显差异。药敏试验联合亚种鉴定及WGS分析有助于准确解析耐药机制并识别区域流行谱系。

Drug-resistant Genes, Virulence Characteristics, and Molecular Typing of Clindamycin-resistant Streptococcus Agalactiae in Late Pregnancy

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Background Streptococcus agalactiae increases

the risk of adverse pregnancy outcomes and neonatal infections. Clindamycin is a key alternative for intrapartum prophylaxis in penicillin-allergic women, but the prevalence of clindamycin-resistant *S. agalactiae* is increasing, posing a significant clinical challenge

Methods A total of 178 strains isolated from tertiary hospitals in Jinan and Qingdao, Shandong Province, China, were characterized using antimicrobial susceptibility testing, whole-genome sequencing, multilocus sequence typing, serotyping, and analysis of resistance and virulence genes.

Results All strains were susceptible to penicillin, ampicillin, linezolid, vancomycin, and tigecycline. In contrast, resistance rates to erythromycin, levofloxacin, and tetracycline were 95.5%, 60.1%, and 56.7%, respectively. Six serotypes and 15 sequence types belonging to eight clonal complexes were identified. Notable regional differences were observed. The Ib-ST10-CC12 lineage dominated in Jinan, whereas V-ST529-CC327 was predominant in Qingdao. The resistance gene *mreA* was ubiquitous (100%), followed by *ermB* (80.3%). The key virulence genes *cylE*, *hylB*, and *pavA*, were detected in all strains. *fbsA* (99.4%), the alpha protein family (98.9%), *cfb* (98.3%), the Pilus Island gene cluster (94.9%), and *lmb* (92.7%) were also highly prevalent. The two major clindamycin resistance genes, *erm* and *lnuB*, exhibited distinctly different enrichment patterns among *S. agalactiae* clonal complexes, despite a certain overlap in CC19 and CC327. Specifically, *erm* was significantly enriched in CC12 (serotype Ib), CC19 (III/V), and CC327 (III/V). In contrast, *lnuB* was predominantly restricted to CC19 and CC327, where it defined a unique phylogenetic subcluster. Significant differences in resistance and virulence gene profiles were observed across different clonal complexes.

The Gut Mycobiota in *Clostridium Difficile*

Infection: First Evidence Implicating *Candida Parapsilosis* Colonisation As A Potential Risk Factor

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Background The gut mycobiome, although comprising less than 0.1% of the human gut microbiome, plays an increasingly recognized role in intestinal homeostasis and host immunity. While bacterial dysbiosis is central to *Clostridioides difficile* infection, the contribution of intestinal fungal colonisation remains poorly understood, with limited data from Asian populations

Methods Stool samples from 413 inpatients (April-June 2023) undergoing *Clostridioides difficile* toxin testing were analyzed via microscopy, fungal culture, MALDI-TOF identification, sanger sequencing, and antifungal susceptibility testing (Sensititre YeastOne). Clinical data were used to compare fungal colonisation patterns between toxin-positive and toxin-negative patients and to evaluate potential risk factors for *Clostridioides difficile* infection.

Results *Clostridioides difficile* toxin was positive in 5.81% of patients (24/413). A total of 250 fungal isolates representing 35 species in 14 genera were recovered, dominated by *Candida albicans* (45.60%). *Candida parapsilosis* colonisation was significantly enriched in toxin-positive patients (25.0% vs 3.86%, $p < 0.001$) and was associated with a 10.39-13.85-fold increased risk of *Clostridioides difficile* infection ($p < 0.01$). Most *C. parapsilosis* isolates were antifungal-susceptible, with only two exhibiting fluconazole resistance. Nine invasive fungal infections were identified and characterized.

Conclusion *C. parapsilosis* colonisation, reported here for the first time as a potential *Clostridioides difficile* infection risk factor, is strongly associated with *C. difficile* toxin positivity. These findings highlight the value of incorporating fungal assessment into disease risk evaluation and offer foundational epidemiologic data from a Chinese cohort to advance global understanding of bacteria-fungi interactions in *Clostridioides difficile* infection.

Abrupt Emergence of Carbapenem Resistant *Salmonella* Typhimurium ST34 on A Background of Escalating Multidrug Resistance in Wuhan, China: A Genomic Epidemiology Study

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Purposes In 2025, a marked increase in carbapenem resistant *Salmonella* was observed in Wuhan, China. We therefore investigated its temporal trend, genomic features, and epidemiological relatedness

Methods Ten-year antimicrobial surveillance data were reviewed. Representative multidrug resistant isolates from Wuhan in 2025, together with selected isolates from foods, food handlers, and Hainan, underwent whole genome sequencing. Phylogenetic clustering, resistance and plasmid profiling, resistance contig comparison, epidemiological assessment of clustered carbapenem resistant isolates, and laboratory susceptibility testing were performed

Results Multidrug-resistant and carbapenem-resistant *Salmonella* accounted for 44.1% and 1.7% of

isolates, respectively. Multidrug resistance increased steadily over the study period, whereas carbapenem resistance remained rare until 2025, when 18 resistant isolates were detected. Although several small clusters were also identified among non-carbapenem-resistant multidrug-resistant isolates from different sources, clustering was more prominent and more compact among carbapenem-resistant isolates. Phylogenomic analysis identified several closely related clusters, with Cluster 4 containing 13 carbapenem-resistant clinical isolates with small SNP differences. Cluster 2, composed of three carbapenem-resistant isolates, and Cluster 4 shared conserved virulence backgrounds but displayed distinct plasmid and resistance signatures, and both retained stable blaNDM-5-associated resistance modules. Some clustered carbapenem-resistant isolates were epidemiologically compatible with possible healthcare-associated spread, although a single confirmed hospital outbreak was not supported. All carbapenem-resistant isolates carried blaNDM-5, and aztreonam plus ceftazidime-avibactam showed the highest in vitro activity.

Conclusions The 2025 rise in carbapenem resistant *Salmonella* in Wuhan was associated in part with dissemination of closely related blaNDM-5 carrying lineages on a background of increasing multidrug resistance

Epidemiology, Risk Factors, and In-hospital Mortality of Candidemia in A Tertiary Hospital of China: A 10-year Retrospective Analysis From 2015 To 2024

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Purpose To investigate the epidemiology and risk factors for in-hospital mortality of candidemia in an eastern Chinese tertiary hospital, thereby guiding clinical management

Methods We retrospectively enrolled 387 inpatients with candidemia from 2015 to 2024. Species distribution, clinical characteristics, and antifungal treatment data were analyzed, assessing their impact on in-hospital mortality using univariate and multivariate logistic regression.

Results The average incidence of candidemia was 0.214 per 1,000 inpatients, with an overall in-hospital mortality of 33.85%. The intensive care unit (ICU) was the primary source of cases (55.30%). *Candida albicans* remained the predominant pathogen (31.27%), followed by *Candida glabrata* (25.58%), *Candida parapsilosis* complex (21.44%), and *Candida tropicalis* (18.60%). Ward-specific analysis showed that *C. albicans* was most frequent in the ICU (34.11%) and infectious disease wards (50.00%), whereas *C. glabrata* predominated in urology (52.17%) and pancreatic surgery (41.18%) wards. In Hematology, *C. tropicalis* was the primary pathogen (66.67%). The vast majority of *C. albicans* and *C. parapsilosis* were susceptible (> 90%) to all nine antifungal agents; while *C. tropicalis* exhibited relatively high resistance/non-wild-type (18.06%-69.44%) to four azoles, with 27.78% cross-resistance to fluconazole and voriconazole. Multivariate analysis revealed that age ≥ 63 years (OR=1.726, 95% CI: 1.049-2.840, P=0.032), ICU admission (OR=2.315, 95% CI: 1.256-4.266, P=0.007), acute or chronic renal failure (OR=2.287, 95% CI: 1.298-4.031, P=0.004), and mechanical ventilation (OR=1.887, 95% CI: 1.037-3.433, P=0.038) were independent risk factors of in-hospital mortality, whereas *C. parapsilosis* complex infection (OR=0.400, 95% CI: 0.212-0.755, P=0.005) was independently associated with a significantly decreased risk.

Conclusion *C. albicans* was the predominant cause of candidemia in our institute. Given its high incidence and mortality, it was imperative to develop tailored management and prevention strategies based on the local pathogen profile, antifungal susceptibility patterns, and specific mortality risk factors. Attention should focus on high-risk patients to ultimately improve clinical outcomes.

细菌真菌感染的治疗

革兰氏分型与耐药风险评估在重症感染患者初始抗菌药物治疗中的比较:一项回顾性分析

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目的 重症感染患者需早期恰当的经验性抗菌药物治疗。现行指南主要依据耐药风险因素指导用药,但特异性不足,易致广谱抗菌药物过度使用。病原体革兰氏分型可在入院早期快速获得,但其在指导初始抗菌药物方案中的价值尚未明确。本研究旨在区分革兰氏阴性菌(Gram-negative bacteria, GN)与革兰氏阳性菌(Gram-positive bacteria, GP)特异的核心独立耐药风险因素,并评估将革兰氏分型信息整合至早期抗菌药物决策的临床价值。

方法 本研究分为算法开发期(时期I: 2024.9-2025.2)和验证期(时期II: 2025.3-2025.9)。在开发期,依据有/无耐药风险因素对患者分组,比较两组患者对治疗 GN/GP 多种抗菌药物的敏感率。通过单因素分层分析、多因素 Logistic 回归及敏感性分析,逐步从多项耐药风险因素中筛选并简化得到 GN/GP 各自独立的核心耐药风险因素。并据此构建基于耐药风险的给药算法(RFBA)和基于革兰氏类型的给药算法(GTBA)。随后将两算法回顾性模拟应用于验证期患者,采用 McNemar 检验评估两算法在初始覆盖率以及广谱抗菌药物推荐率方面的差异。

结果 共纳入疑似/确诊脓毒症患者 408 例(时期 I 207 例,时期 II 201 例)。时期 I 分析显示,GP 和 GN 耐药核心独立风险因素分别为近 90 天静脉抗菌药物使用史(OR=4.16, 95% CI 1.27-13.58)和近 30 天 ICU 住院史(OR=6.44, 95% CI 1.59-26.03);近 90 天静脉抗菌药物使用史(OR=4.38, 95% CI 1.54-12.49)和侵入性器械支持(OR=6.67, 95% CI 2.14-20.78)。敏感性分析验证了结果的稳健性。在时期 II 发现 GTBA 与 RFBA 的初始覆盖率无显著差异(92.54% VS 90.05%, $P=0.125$),但显著降低了抗

MRSA (53.23% VS 60.70%, $P=0.018$) 及碳青霉烯类(46.26% VS 68.66%, $P<0.001$) 药物的推荐率。

结论 本研究明确了 GN 与 GP 特异的核心独立耐药风险因素,并证实将革兰氏分型信息纳入早期经验性抗菌药物决策,可在不显著降低病原体覆盖率的前提下显著减少广谱抗菌药物的使用。该策略有助于优化重症感染早期抗菌药物治疗方案,具有潜在抗菌药物管理价值。

关键词: 重症患者;革兰氏阴性菌;革兰氏阳性菌;耐药风险因素;抗菌药物

Creation of Ceftazidime-avibactam Utilization Evaluation Standards To Examine Physician Prescribing Compliance: A Retrospective Study

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A study was conducted to create drug utilization evaluation (DUE) standards for ceftazidime avibactam (CZA) and evaluate CZA use at the First Affiliated Hospital of Bengbu Medical University, China, from May 26, 2020, to December 18, 2024. First, we organized an expert panel and created DUE standards for CZA. Then, we performed an observational study and evaluated the physician CZA prescribing behaviors, which were compared to the DUE standards and calculated the compliance rates. The DUE CZA standards had medication indications, management metrics, administration process, and treatment outcomes. Sixty-four patients received the CZA during the study period. There was satisfactory compliance between CZA prescription and DUE standards regarding route, solvent, incompatibility, and contraindications. However, the compliance rates for CZA indication, dosage regimen, infusion time, combination

therapy, drug interaction, and duration of treatment were 68.8% (44/64), 65.6% (42/64), 29.7% (19/64), 73.3% (44/60), 43.8% (28/64), and 62.5% (40/64), respectively. The pre-CZA bacteria culture test was 96.9% (62/64). In addition, medical records and prescription authorization were 95.3% (61/64) and 71.9% (46/64) compliant, respectively. No adverse reactions were reported. In conclusion, the CZA DUE standards could be applied to identify inappropriate prescriptions for improvements.

替加环素联合利福平对耐碳青霉烯类肺炎克雷伯菌体外活性研究

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目的 耐碳青霉烯类肺炎克雷伯菌 (CRKP) 是临床常见的多重耐药致病菌, 易引起肺部感染、血流感染等严重院内感染, 目前临床抗感染治疗选择有限, 患者预后较差。本研究旨在探讨替加环素联合利福平对耐碳青霉烯类肺炎克雷伯菌的体外活性, 为 CRKP 的抗感染治疗提供新的治疗方案和实验依据。

方法 收集昆明医科大学第一附属医院 2022 年 8 月—2024 年 8 月期间, 从住院患者的临床标本 (包括痰液、肺泡灌洗液、血液、尿液、分泌物) 中分离的非重复 CRKP 菌株。通过微量肉汤稀释法筛选出对替加环素耐药或中介的 CRKP 菌株, 运用棋盘法检测替加环素与利福平联合应用的抗菌活性, 计算部分抑菌浓度指数 (FICI) 和敏感折点指数 (SBPI) 评估联合药物的作用。

结果 共筛选出 7 株对替加环素耐药及中介的菌株, 其中替加环素联合利福平对 1 株 CRKP 菌株表现出协同作用, 协同率为 14.29% (1/7); 对 5 株菌株表现出相加作用, 相加率为 71.4% (5/7); 剩余 1 株菌株表现为无关作用, 未出现拮抗作用。

结论 替加环素与利福平联合应用在体外对 CRKP 有一定抗菌活性, 主要表现为相加作用, 仅在部分菌株上表现出协同效果, 未表现出拮抗作用。提示对于替加环素和其他常见抗生素不敏感的 CRKP 在抗感染治疗时, 临床可考虑选择以替加环素为基础, 联合利福平的治疗方案。

宣肺败毒颗粒联合莫西沙星治疗成人肺炎支原体肺炎的临床效果

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目的 观察宣肺败毒颗粒联合莫西沙星治疗成人肺炎支原体肺炎的临床效果。

方法 选取 2022 年 1 月—2024 年 10 月河北省人民医院老年呼吸内科收治的肺炎支原体肺炎住院患者 120 例, 采用随机数字表法分为观察组 (n=60) 和对照组 (n=60)。对照组给予莫西沙星静脉滴注, 观察组在对照组基础上联合宣肺败毒颗粒口服, 2 组疗程均为 7 d。比较 2 组临床疗效, 治疗前后炎症指标 [系统免疫炎症指数 (SII)、系统性炎症反应指数 (SIRI)、白介素-6 (IL-6)、C 反应蛋白 (CRP)]、凝血功能指标 [D-二聚体、纤维蛋白原 (Fib)] 水平及不良反应。

结果 观察组平均秩次低于对照组 (51.27 vs. 69.73, $Z=3.117$, $P=0.002$); 治疗 7 d 后, 2 组 SII、SIRI、IL-6、CRP、D-二聚体及 Fib 水平较治疗前降低, 且观察组低于对照组 ($P<0.01$); 观察组不良反应总发生率与对照组比较差异无统计学意义 (11.67% vs. 10.00%, $\chi^2=0.086$, $P=0.769$)。

结论 宣肺败毒颗粒联合莫西沙星可有效提升成人肺炎支原体肺炎的治疗效果, 降低炎症反应, 改善肺功能, 且不增加不良反应。

关键词: 肺炎支原体肺炎; 宣肺败毒颗粒; 莫西

沙星；系统免疫炎症指数；系统性炎症反应指数；凝血功能

血液病合并鼻眶脑毛霉菌感染 15 例临床分析

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目的 深入探讨血液病患者合并鼻眶脑毛霉菌感染的临床特征、早期诊断方法、临床治疗策略及疾病预后情况，为临床早期识别、规范诊疗该类重症感染患者提供参考依据。

方法 采用回顾性研究方法，收集 2014 年 7 月至 2025 年 12 月国内多家医疗机构收治的 15 例血液病合并鼻眶脑毛霉菌感染患者的完整临床资料，系统分析患者的人口学特征、血液系统原发病类型、临床症状表现、影像学检查特征、病原学检测结果、临床干预治疗方案及疾病最终转归等关键指标。

结果 15 例患者中男性 11 例，女性 4 例，中位年龄 61 岁，年龄范围 19~77 岁，以中老年患者为主。原发病构成中，再生障碍性贫血 6 例，急性髓系白血病 4 例，骨髓增生异常肿瘤 3 例，原发中枢淋巴瘤 1 例，T 淋巴母细胞淋巴瘤 1 例。病原学检测显示，感染菌株以根霉属最为常见，共 7 例，其中小孢根霉 5 例，为主要致病菌种。临床典型症状以局部受累表现为主，面部肿胀疼痛 7 例，占比 46.67%，眶周肿胀或眼睑下垂 7 例，占比 46.67%，部分患者伴随鼻腔黏膜坏死、头痛、意识障碍等症状。治疗方面，12 例患者接受以两性霉素 B 为核心的抗真菌治疗，包含两性霉素 B 脂质体及胆固醇硫酸酯复合物制剂，其中 4 例联合外科清创手术治疗。

结论 血液病合并鼻眶脑毛霉菌感染属于临床急危重症，病情进展极为迅速，整体病死率较高。临床治疗的核心关键在于尽早启动针对性抗毛霉菌药物治疗，同时积极联合外科手术清除坏死感染病灶，通过多学科综合干预，可有效提升治疗效果，改善

患者生存预后，降低病死率。

HIV 感染合并马尔尼菲篮状菌及马红球菌混合感染 1 例

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背景 HIV 合并马尔尼菲篮状菌 (*Talaromyces marneffe*, TM) 及马红球菌 (*Rhodococcus equi*) 混合感染是临床极为罕见但威胁严重的机会性感染组合。TM 感染在东南亚及我国南方 HIV/AIDS 人群中尤为常见，而马红球菌感染则多见于细胞免疫重度受损者。两者混合感染虽发病率不高，却因临床表现复杂、诊断困难、治疗棘手，成为临床上面临的严峻挑战。

病例阐述 患者 2018 年于当地疾控确诊 HIV 感染，CD4⁺T 淋巴细胞计数不详，3 个月前行 cART，方案为：TDF+3TC+EFV。既往有静脉吸毒史，5 年前诊断丙型肝炎，经规范抗病毒治疗后已治愈。咳嗽、咳痰持续，活动后胸闷，为进一步诊治于 2025 年 6 月 25 日至我院。入院初期继续予 HRbEZ 方案抗结核，氟康唑抗真菌，并予复方磺胺甲噁唑预防 PCP 治疗。6 月 27 日明确马红球菌败血症诊断后，调整抗菌方案为左氧氟沙星 (0.5g qd)、阿米卡星 (0.4g qd)、阿奇霉素 (0.25g qd) 联合治疗。6 月 29 日开始加用两性霉素 B 抗马尔尼菲篮状菌，从 5 mg 起始每日递增，因胃肠道反应大，停用阿奇霉素及复方磺胺甲恶唑片。6 月 30 日优化抗病毒方案为 3TC/DTG+TDF。7 月 1 日患者诉腹泻 3 次，为稀水样便，查口腔两侧黏膜见白色伪膜，考虑合并口腔念珠菌感染，予碳酸氢钠含漱。7 月 7 日 11:30 患者突发乏力、胸闷、恶心，血压降至 87/56 mmHg，心率 120 次/min，氧饱和度 92%，立即予补充白蛋白、纠正电解质紊乱等抢救措施后病情稳定。7 月 9 日患者体温正常，咳嗽减轻，要求出院。

结果 患者好转出院, 遵医嘱服药, 定期复查。

结论 本病例突出了在晚期艾滋病患者中, 马红球菌与马尔尼菲篮状菌共感染的临床与影像学重叠特征, 以及及时病原学诊断与个体化联合治疗的重要性。该病例成功的关键在于通过支气管镜及骨髓穿刺获得了明确的病原学证据, 从而避免了误诊, 并制定了针对性的联合治疗方案。

Successful Treatment of A Centenarian Patient with Carbapenem-Resistant *Acinetobacter Baumannii* Pneumonia and Sepsis Using Sulbactam-Durlobactam: A Case Report

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Advanced age is an independent and strong risk factor for nosocomial infections caused by multidrug-resistant (MDR) organisms, acute organ dysfunction, and mortality in critically ill patients. Centenarians represent an extremely vulnerable population characterized by multisystem physiological degeneration, immunosenescence, impaired mucociliary clearance, reduced renal functional reserve, malnutrition, and multiple chronic comorbidities. Carbapenem-resistant *Acinetobacter baumannii* (CRAB) has emerged as one of the most problematic pathogens in intensive care units (ICUs) worldwide, with limited therapeutic options and high mortality rates. Sulbactam-durlobactam is a novel β -lactam/ β -lactamase inhibitor combination agent with potent and specific activity against CRAB, including strains producing OXA-23 carbapenemase, which is the most prevalent genotype in China. Here, we report the successful clinical management of a 99-year-old male patient who developed severe hospital-acquired pneumonia, sepsis, and acute kidney injury (AKI) caused by

CRAB after artificial femoral head replacement surgery. The patient initially failed empirical antimicrobial therapy with cefoperazone-sulbactam. After definite diagnosis by bronchoscopic sampling, metagenomic next-generation sequencing (mNGS), and antimicrobial susceptibility testing (AST), the antimicrobial regimen was promptly adjusted to targeted therapy with sulbactam-durlobactam combined with comprehensive multidisciplinary critical care interventions, including respiratory support, renal protection, nutritional support, neurological management, and early rehabilitation. The patient achieved rapid infection control, significant improvement in inflammatory markers, recovery of renal function, successful weaning from respiratory support, and eventual discharge home after celebrating his 100th birthday. This case demonstrates that early etiological diagnosis, timely and precise antimicrobial therapy with sulbactam-durlobactam, and individualized organ support strategies can significantly improve clinical outcomes in ultra-elderly patients with life-threatening CRAB infections, even in those with severe renal impairment and multiple geriatric vulnerabilities. This report also provides detailed clinical evidence supporting the efficacy and safety of sulbactam-durlobactam in real-world critical care settings for centenarian patients.

Efficacy of Hemoadsorption Combined with Targeted Antimicrobial Therapy in Anti-interferon- γ Autoantibody Syndrome Patients with Disseminated Infection

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Background Anti-interferon- γ autoantibody

syndrome (AIGAs) is a primary immunodeficiency characterised by neutralising autoantibodies that block IFN- γ signalling, predisposing patients to severe opportunistic infections such as nontuberculous mycobacteria and *Talaromyces marneffi*. No definitive treatment protocol for AIGAs exists, and conventional therapies (e.g., immunosuppressants) increase infection risks in patients with disseminated disease. Hemoadsorption (HA) has shown efficacy in autoimmune conditions but has not been specifically investigated for AIGAs-related disseminated infections caused by such opportunistic pathogens

Methods Four patients (3 females, 1 male; aged 58–67 years) with AIGAs were included, and their disseminated infection was confirmed by the unified findings of laboratory data and imaging examinations. Additional diagnostic assessments included ultrasound-guided tissue biopsy and AIGA quantification via indirect ELISA. All received targeted antimicrobial therapy (tailored to pathogen type) plus one HA session using a cytokine adsorption column (targeting cytokines with a molecular size of 8–50 kDa). Serial monitoring of AIGA levels, infection status, and laboratory data was conducted over at least 48 weeks.

Results Of the four patients, three achieved effective infection outcomes post-HA, while one had partial improvement followed by progression (Table 1 and Fig.1):

Patient 1: Bacteremia cleared post-HA, but pulmonary infection progressed at week 12; AIGA levels initially reduced then rebounded at week 4.

Patient 2: Complete infection resolution by 72 weeks; peripheral blood AIGA was undetectable from week 24 onwards.

Patients 3 and 4: Stable infection control (negative culture, improved lesions) at 48 weeks; AIGA levels sustained reduction. No severe HA-related adverse events occurred.

Conclusion A total of 15 patients were enrolled in this study, and the 4 patients presented above have completed follow-up. For these 4 followed-up patients, single-session HA combined with antimicrobial therapy achieved sustained AIGA reduction—even complete clearance in some cases—and long-term infection control or clearance in most. Despite one patient (with multi-pathogen infection) experiencing pulmonary infection progression, HA still shows promise as a clinically prospective therapeutic option for AIGAs patients with disseminated infection. Subsequently, this prospective cohort study will be continued to validate the long-term efficacy and safety of HA.

PBT2 基于金属离子稳态失衡抗白念珠菌的作用和机制研究

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目的 金属离子稳态在白念珠菌生命活动中发挥重要作用，是抗真菌干预的潜在靶点。本研究探讨口服安全的金属离子载体 PBT2 抗白念珠菌及其生物膜的作用机制，为 PBT2 用于白念珠菌感染治疗提供理论依据。

方法 XTT 减低法、结晶紫染色法评估 PBT2 对白念珠菌生物膜形成的抑制作用，RNA-seq 及 RT-qPCR 分析白念珠菌核心基因表达谱的改变；金属离子荧光探针及 ICP-MS 探究白念珠菌胞内金属离子稳态改变；DARTS-MS 技术筛选 PBT2 在白念珠菌细胞内的潜在作用靶点，并结合细胞壁压力点板实验、山梨醇挽救实验及液相色谱法等进行验证；构建大蜡螟感染模型，评价 PBT2 体内抗感染作用。

结果 1. PBT2 体内外抗白念珠菌效应

在浮游菌中，PBT2 浓度依赖性的抑制白念珠菌生长，抑制氟康唑诱导耐药的产生。在生物膜中，

PBT2 抑制白念珠菌生物膜早期粘附、中期酵母-菌丝转换及晚期三维结构的成熟。PBT2 降低生物膜外排泵活性,下调 ATP 依赖型外排泵基因表达。PBT2 联合氟康唑显著抑制生物膜活性。在大蜡螟幼虫感染模型中,PBT2 降低白念珠菌的体内毒力。

2. PBT2 靶向金属离子稳态抑制线粒体代谢、核糖体功能及抗氧化能力

转录组分析显示,差异基因富集于离子稳态、线粒体能量代谢过程、核糖体功能、抗氧化能力等生物学过程。PBT2 破坏白念珠菌细胞内金属离子稳态,补充锌、铁、铜可削弱 PBT2 的抗菌作用。进一步研究证实,PBT2 降低白念珠菌抗氧化应激能力,破坏线粒体呼吸链,进而导致 ROS 累积。

3. PBT2 靶向甘露糖基转移酶 MNN22 和 MNN24 抑制细胞壁合成

通过 DARTS-MS 技术在白念珠菌蛋白质组中鉴定出 PBT2 的潜在作用靶点为甘露糖基转移酶 MNN22 和 MNN24。PBT2 通过直接结合 MNN22 和 MNN24,阻碍了甘露聚糖的分支合成,导致细胞壁甘露糖含量显著减低。同时,这种结构性损伤引发了细胞壁几丁质与葡聚糖的代偿性增加,最终导致白念珠菌对细胞壁压力及渗透压敏感。

结论 本研究证实 PBT2 逆转白念珠菌及其生物膜唑类耐药的作用。机制研究表明,PBT2 介导白念珠菌锌、铁、铜离子稳态失衡,干扰线粒体呼吸链及抗氧化应激功能。同时,PBT2 通过靶向结合 MNN22 和 MNN24 破坏白念珠菌细胞壁的结构与功能。研究结果为口服安全的 PBT2 治疗白念珠菌感染提供科学依据,为治疗顽固性真菌感染提供潜在可转化的新方案。

蒙特卡罗模拟优化肾功能不全患者侵袭性念珠菌病的氟康唑给药方案

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目的 优化肾功能不全患者侵袭性念珠菌病的氟康唑给药剂量,为特殊人群个体化用药提供参考。

方法 按照内生肌酐清除率 (glomerular filtration rate, GFR) 将肾功能不全患者分组,根据氟康唑的药代动力学 / 药效学 (pharmacokinetics/pharmacodynamics, PK/PD) 模型,对临床常见的给药方案、药代动力学 (pharmacokinetics, PK) 参数、念珠菌的最低抑菌浓度 (minimum inhibitory concentration, MIC) 的分布情况,采用 Crystal Ball 软件进行蒙特卡罗模拟 (Monte Carlo simulation, MCS),以满足药效学目标的达标概率 (probability of target attainment, PTA) $\geq 90\%$ 或 累计反应分数 (cumulative fraction of response, CFR) $\geq 90\%$ 为评价指标。

结果 对于能准确获得目标念珠菌 MIC 的情况,当 $MIC \leq 1 \text{ mg/L}$ 时,100 mg/d (其中 $MIC = 1 \text{ mg/L}$ 时,轻度肾功能不全患者剂量需增加至 200 mg/d) 即可满足 $PTA \geq 90\%$; 当 $MIC = 2 \text{ mg/L}$ 时,轻、中度肾功能不全的患者,按照说明书推荐的维持剂量 (重度肾功能不全的患者 100 mg/d) 即可满足 $PTA \geq 90\%$; 当 $MIC = 4 \text{ mg/L}$ 时,仅重度肾功能不全患者 200 mg/d 才能满足 $PTA \geq 90\%$,当 $MIC > 4 \text{ mg/L}$ 时,说明书推荐剂量无法满足 $PTA \geq 90\%$ 。对于仅能鉴定出菌株,但无法获取准确药敏结果的情况,轻度肾功能不全的患者 200 mg/d 即可满足目标念珠菌 $CFR \geq 90\%$; 而中、重度肾功能不全的患者需 100 mg/d 才能满足 $CFR \geq 90\%$ 。

结论 肾功能不全患者使用氟康唑应综合考虑念珠菌菌株、MIC 值、肾功能损害程度等情况,以实现个体化给药。

Comparative Evaluation of Broth Microdilution and Gradient Diffusion Methods in Burkholderia Cepacia Complex Susceptibility Testing: Implications of Transitioning To

ECV-Based Interpretation

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Objective Evaluate the performance of broth microdilution (BMD) and gradient diffusion (Etest) methods in antimicrobial susceptibility testing (AST) of *Burkholderia cepacia* complex (BCC) isolates, with a particular focus on the impact of transitioning from CLSI MIC breakpoints to epidemiological cutoff values (ECVs) in the 2025 guidelines.

Methods A total of 90 clinical BCC isolates were collected and identified to the species level using MALDI-TOF mass spectrometry. AST was performed using BMD and Etest for minocycline, meropenem, trimethoprim-sulfamethoxazole, ceftazidime, and levofloxacin. Results were interpreted using 2024 MIC breakpoints and reanalyzed with 2025 ECVs. Categorical agreement (CA), essential agreement (EA), and classification errors (VME, ME, MI, WT-ME, NWT-VME) were calculated. In addition, species-stratified analysis was also conducted and medical records of 44 patients were reviewed to assess the correlation between in vitro susceptibility and clinical outcomes.

Results Under CLSI 2024 MIC breakpoints, CA between Etest and BMD varied, highest for trimethoprim-sulfamethoxazole (94.4%) and lowest for meropenem (12.2%). EA for all agents was below the 90% threshold. Using CLSI 2025 ECVs, CA improved for all agents except trimethoprim-sulfamethoxazole, but error rates remained unacceptable for all except minocycline. Species-specific resistance patterns were observed. Among 44 clinical cases, only 40.9% showed concordance between in vitro susceptibility and treatment outcomes.

Conclusion Although the adoption of ECVs improved CA for some agents, MIC-level discrepancies

between Etest and BMD persisted. Species-specific resistance patterns and the low concordance with clinical outcomes (40.9%) highlight the limitations of AST alone in guiding BCC treatment decisions.

Clinical Phenotyping of Polymyxin-Associated Nephrotoxicity and Phenotype-Specific Prognostic Utility of Neutrophil-to-Platelet Ratio in Carbapenem-Resistant *Acinetobacter Baumannii* Infections

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Background Carbapenem-resistant *Acinetobacter baumannii* (CRAB) infections remain therapeutically challenging, often necessitating last-line polymyxin therapy despite substantial nephrotoxicity. Conventional risk assessments for polymyxin-associated acute kidney injury (AKI) frequently overlook patient heterogeneity. We sought to delineate clinical phenotypes of polymyxin-associated AKI and determine whether the prognostic value of the neutrophil-to-platelet ratio (NPR) for mortality varies by phenotype

Methods We conducted a retrospective cohort study (2020–2025) of 547 patients with CRAB infections treated with polymyxins. Latent class analysis (LCA) identified clinical phenotypes using baseline risk factors and renal outcomes. Multivariable logistic regression incorporating restricted cubic splines (RCS), followed by piecewise regression, evaluated non-linear associations between NPR and 28-day mortality and tested effect modification by phenotype.

Results LCA revealed three distinct phenotypes: Severe Renal Failure (Class 1, 15.2%), Low-risk/Stable

(Class 2, 62.0%), and High-Comorbidity/Non-RRT Severe Injury (Class 3, 22.8%). Baseline characteristics and 28-day mortality varied significantly across these phenotypes (9.6% vs. 4.4% vs. 8.6%; $p=0.033$). The prognostic value of NPR was exclusively significant in Class 2, where a critical threshold effect was identified at 0.0167 (breakpoint test $p < 0.001$). Below this threshold, mortality risk rose sharply—a non-linear relationship that was obscured in high-severity phenotypes (Class 1 and 3).

Conclusion Patients with CRAB infections receiving polymyxins exhibit three distinct nephrotoxicity phenotypes. The prognostic utility of NPR is phenotype-specific, with a critical threshold at 0.0167 identifying relative immune insufficiency exclusively within the Low-risk/Stable subgroup. Clinical phenotyping is therefore a prerequisite for accurate biomarker interpretation and personalized risk stratification in this population.

Keywords Carbapenem-Resistant *Acinetobacter baumannii*; Polymyxin; Nephrotoxicity; Acute Kidney Injury; Clinical Phenotype; Neutrophil-to-Platelet Ratio;

艾滋病合并惠普尔养障体肺炎、耶氏肺孢子菌肺炎及念珠菌肺炎 1 例

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目的 经典的惠普尔病通常累及胃肠道，引起腹痛、腹泻、关节炎等，无胃肠受累的局限性肺部感染罕见，HIV 感染合并惠普尔养障体肺炎的报道更为罕见，尤其是多重感染，本文报道 1 例艾滋病合并惠普尔养障体、耶氏肺孢子菌、肺念珠菌感染患者的诊治经过，旨提高对艾滋病机会性感染病原体的认识，实现早期诊断和早期治疗。

方法 患者男性，46 岁，主因“发热伴盗汗 1 周”于 2024 年 4 月入院。患者缘于 1 周前无明显诱因出现发热，体温波动于 $37.2^{\circ}\text{C} \sim 37.4^{\circ}\text{C}$ ，伴有盗汗，伴有咳嗽、咳白色粘痰，量少易咳出，伴有乏力、纳差，伴有活动后气短、活动耐力下降，无畏寒、寒战，无鼻塞、流涕，无胸闷、胸痛，无恶心、呕吐，无腹痛、腹胀、腹泻，无尿频、尿急、尿痛等不适，休息后症状缓解不明显。患者自病后神志清楚，精神可，食纳尚可，夜休可，大小便正常，近半年来体重减轻 6Kg (10.1%)，并有双侧颊部色素沉着。既往史及流行病学史：2 周前于我市疾控中心确诊人类免疫缺陷病毒 (HIV) 感染，HIV-1 抗体阳性，CD4+T 淋巴细胞绝对计数及 HIV 载量未回报，未接受抗病毒治疗。查体：体温 37.1°C ，脉搏 102 次/min，呼吸 21 次/min，血压 103/71 mmHg (1 mmHg=0.133 kPa)。精神可，双侧颊部可见色素沉着，皮肤巩膜未见黄染，口腔未见黏膜白斑。双肺呼吸音减低，未闻及干、湿性啰音。心率 102 次/min，律齐，各瓣膜听诊区未闻及病理性杂音。腹部平坦，质软，无压痛、反跳痛及肌紧张，肝脾肋下未触及，墨菲征阴性，移动性浊音阴性，肠鸣音正常。双下肢无水肿。依据患者症状、肺部影像学特点及痰液及肺泡灌洗液 NGS 检查结果明确诊断为：人类免疫缺陷病毒感染 艾滋病期；耶氏肺孢子菌肺炎（重度）；惠普尔养障体肺炎；念珠菌肺炎；口腔念珠菌病；食管胃底念珠菌病。给予头孢曲松、复方甲氧唑-甲氧苄啶、更昔洛韦、氟康唑抗感染及 ART 治疗，序贯氟康唑、复方磺胺甲氧唑及富马酸替诺福韦+拉米夫定+多替拉韦抗感染治疗。

结果 临床转归，患者体温正常，胸痛消失，肺部影像学好转，随访中。

结论 HIV 感染者免疫功能低下，易合并多种病原体的混合感染，该患者历经长达 1 年半的治疗及随访，目前恢复良好。在 AIDS 患者复杂感染的诊断中，及时获取病原学证据可实现靶向治疗，当诊断尚不明确时，动态随访及经验性治疗亦至关重要。

依拉环素治疗耐药革兰阴性菌感染的临床疗效与安全性：一项多中心、倾向性评分匹配的真实世界队列研究

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目的 比较依拉环素与对照组治疗耐药革兰阴性菌感染患者的临床疗效及安全性，并探讨影响临床有效率的独立因素。

方法 本研究为多中心回顾性观察性研究，纳入了 2021 年 1 月-2025 年 10 月来自江苏三个城市七家医院的患者，收集以依拉环素为基础或其他药物的联合抗感染方案治疗耐药革兰阴性菌感染患者的临床资料，包括患者临床特征、感染指标、细菌培养及药敏结果、抗菌药物种类及疗程、临床疗效、不良反应等。通过倾向性评分匹配 (PSM) 平衡基线混杂因素后，对比分析依拉环素组与对照组的临床结局、实验室指标动态变化及治疗情况，并采用单因素与多因素逻辑回归分析评估影响临床有效率的独立因素。

结果 依拉环素组临床有效率 (85.6% vs 73.8%, $P=0.006$)、微生物学有效率 (69.7% vs 53.8%, $P=0.002$) 均高于对照组，且死亡率 (3.8% vs 15.7%, $P<0.001$) 显著更低，两组的 WBC、NEUT、PCT、CRP 水平较治疗前均降低 ($P<0.05$)。在两组患者中，大多数为肺部感染，依拉环素组 APACHEII 评分更高 (16.7 ± 4.3 vs 15.1 ± 4.3 , $P<0.001$)。同时，在老年患者中，依拉环素的优势更加明显，多因素逻辑回归分析显示，舒张压 ($OR=1.023$, $P=0.013$)、治疗前血小板计数 ($OR=1.004$, $P=0.005$) 为临床有效率的独立保护因素，而 APACHEII 评分 ($OR=0.926$, $P=0.029$)、治疗前尿素水平 ($OR=0.971$, $P=0.026$) 为独立危险因素。两组治疗疗程分布具有统计学意义 ($P=0.001$)，依拉环素组治疗疗程 <7 天的占比更高 (50.8% vs 33.6%)，依拉环素组用药期间药物相

关不良事件发生率为 2.53% (5/198)，以轻度胃肠道反应为主，仅 1 例患者出现纤维蛋白原降低，1 例患者出现低血压，均未造成严重后果。

结论 针对耐药革兰阴性菌感染的治疗，与对照组相比，以依拉环素为基础的治疗方案更优，起效更快，具有良好的安全性，可作为重症感染患者的优选治疗方案之一。

关键词：依拉环素；耐药菌感染；临床疗效；倾向性评分匹配；多因素逻辑回归

“不规则毛霉”在中国：一例皮肤毛霉病患者的“曲折”抗感染经验分享

荣金诚

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目的 一例不规则毛霉致原发性皮肤毛霉病的临床诊断、抗菌药物使用、外科清创的长病程诊疗经验分享。

方法 患者老年男性，体健、无基础病，约 20 年前左小腿外伤，约 4 年前左小腿疤痕处出现红斑瘙痒，就诊经历包括：(1) 门诊求诊 (2022.1 至 2024.3)，间隔 1 年分别做过 2 次环钻皮肤取材、真菌镜检及培养、组织病理检查，给予口服伊曲康唑 200mg q12h 抗真菌经验治疗，后追加口服利福平 0.45g qd 与乙胺丁醇 1g qd 抗结核经验治疗；(2) 首次住院 (2024.3 至 2024.5)，真菌镜检及培养检出不规则毛霉 (*M. irregularis*)，外科清创与负压封闭引流 (VSD)，针对性抗毛霉菌治疗 (口服艾沙康唑 200mg qd 共 36 天，外敷 5mg/100ml 两性霉素 B 共 65 天)；(3) 复发住院 (2025.2 至 2025.5)，左小腿新发病灶，外科清创与 VSD 引流，口服艾沙康唑 200mg qd 共 78 天。随访至 2026 年 4 月。

结果 患者初因左小腿浸润性结节就诊，四年病程经历包括：(1) 门诊阶段：两次真菌镜检及培养、组织病理检查，未见病原体；经验性抗真菌与抗

结核治疗, 疗效不佳, 破溃逐渐加重; (2) 首次住院: 破溃加重后, 深部取材检出不规则毛霉菌, 外科清创并辅以抗毛霉菌治疗, 术后 1 月患处明显收敛且无溢出液, 术后 2 月患处基本愈合, 但约半年后复发; (3) 再次入院: 新发病灶, 再次检出该菌, 外科清创辅以艾沙康唑足疗程治疗, 未再湿敷两性霉素 B, 术后半月患处收敛明显, 一年后随访良好。

结论 不规则毛霉(*M. irregularis*)致原发性皮肤毛霉病是一种罕见的且多发于我国的感染性疾病, 诊断不明或治疗失败极易致残致畸毁形, 其病原体检出困难且对多种常用抗真菌药物耐药。本例中, 实验室诊断与治疗经验总结如下: (1) 组织病理学检查普遍漏检该菌; (2) 实验室诊断中组织样本的毛霉菌培养, 除不研磨外, 推荐液体培养复苏; (3) 外科清创要彻底, 推荐术后辅以 VSD 引流; (4) 不建议两性霉素 B 低浓度($\leq 5\text{mg}/100\text{ml}$)湿敷; (5) 口服伊曲康唑 200mg q12h 在本例中效果不好, 可能诱发耐药并刺激毛霉菌爆发式生长; 此外, 毛霉菌对伏立康唑天然耐药; (6) 口服艾沙康唑 200mg qd 足疗程治疗, 可有效治愈。总之, 有技巧的实验室诊断(组织样本的液体培养)、彻底的外科清创、足量足疗程的药物施用, 是治愈的关键。

复方磺胺甲噁唑治疗耐碳青霉烯大肠埃希菌所致复杂性尿路感染 1 例并文献复习

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目的 报道 1 例耐碳青霉烯大肠埃希菌(CREC)所致复杂性尿路感染(cUTI)患者应用复方磺胺甲噁唑(TMP-SMX)治疗的临床经过, 并结合文献探讨该药在 CRE 感染中的潜在应用价值。

方法 报道 1 例耐碳青霉烯类大肠埃希菌(CREC)所致复杂性尿路感染患者应用 TMP-SMX

治疗的临床经过, 同时检索 PubMed、Web Of Science、CNKI 等数据库收集 TMP-SMX 在耐碳青霉烯肠杆菌科细菌感染中的应用证据。

结果 患者为复杂性尿路感染, 尿培养提示 CREC, 经药敏试验显示对 TMP-SMX 敏感。根据药敏结果调整为 TMP-SMX 口服治疗后, 患者体温恢复正常, CRP 等炎症指标下降, 复查尿培养转阴, 治疗期间肌酐值在正常范围内。文献复习汇总在药敏结果提示敏感的情况下的 28 例病例中 27 例取得了积极的临床结局, 1 例因肿瘤并发症死亡。TMP-SMX 可作为治疗 CRE 尿路感染的选择。多项指南和专家共识推荐 TMP-SMX 在药敏试验结果敏感时使用。对于肾功能不全患者需要根据患者 eGFR 调整剂量。目前指南对于疗程还没有统一意见, 建议采用 7 天短疗程, 当患者有危险因素时可根据患者个体情况考虑延长疗程至 14 天。

结论 TMP-SMX 在 CRE 药敏结果提示敏感的尿路感染中有应用价值, 其应用需结合感染部位、耐药机制及患者临床状况综合评估。随着耐碳青霉烯类肠杆菌的流行, TMP-SMX 对感染人群中的疗程、在特殊人群的安全性等方面需要进一步研究。

PICU 非血液肿瘤患者侵袭性真菌感染多中心治疗方案探讨

海莉丽

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目的 本文通过回顾性分析 4 家医院儿童重症监护室(Pediatric intensive care unit, PICU)近 5 年非血液肿瘤患者侵袭性真菌感染(invasive fungal infections, IFI)病例资料, 探讨不同治疗方案的预后结局, 旨在为医师及药师制定最佳的治疗方案提供参考。

方法 收集我国上海市、广州市、湖南省、河南

省 4 家三级甲等儿童医院近 5 年 PICU 住院非血液肿瘤患者 IFI 病例。描述病例基本特征,真菌感染部位, PICU 住院天数,总住院天数,治疗方案,预后等。然后采用回顾性分析方法探讨不同治疗方案的预后差异。

结果 共纳入 445 例病原学检出阳性的 IFI 患者,其中假丝酵母菌组 325 例,霉菌组 28 例,其它病原组 92 例,其中其它病原组主要包括耶氏肺孢子菌、隐球菌等。年龄分别为 23.0(6.5,76.5) 月、32.0(8.5,61.0) 月、15.0(4.0,52.0) 月,年龄中位数整体偏小,体重与年龄趋势相似。假丝酵母菌组及其它组男女比例均为 6:4,霉菌组男女比例则相反,为 4:6。感染部位主要分布在呼吸系统、血液系统、中枢神经系统、消化系统及泌尿系统。所有病原感染部位排名首位均为呼吸系统,其中假丝酵母菌组排名前三为呼吸系统、泌尿系统及血液系统。假丝酵母菌组单药治疗和联合治疗最终结局差异有统计学意义:单药治疗与预后良好呈正相关,其中单用唑类预后较好;两药联合和多药联合预后差异无统计学意义。霉菌组单药治疗和联合治疗预后无差异。

结论 儿童非血液肿瘤患者侵袭性真菌感染在婴幼儿重症患者群体中更容易发生,假丝酵母菌是主要的致病菌。感染部位大部分为呼吸系统。儿童非血液肿瘤患者侵袭性假丝酵母菌治疗单用唑类和棘白菌素类相比,单用唑类与预后良好正相关。治疗方面我们推荐对于耐药风险较低的菌种首选给予唑类单药治疗方案。

伏立康唑、艾沙康唑和两性霉素治疗肺曲霉菌病和毛霉菌病的疗效和安全性分析

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目的 探讨不同抗真菌药物治疗肺曲霉菌病和毛霉菌病的效果以及不良反应。

方法 回顾性分析 2020 年 1 月-2024 年 5 月在山东省立医院呼吸与危重症医学科住院的 59 例肺曲霉菌病和毛霉菌病患者的病历资料,根据感染真菌和抗真菌药物的不同分为 9 组:第 1 组伏立康唑治疗组(曲霉菌感染)25 例,第 2 组艾沙康唑治疗组(曲霉菌感染)11 例,第 3 组两性霉素治疗组(曲霉菌感染)5 例,第 4 组伏立康唑治疗组(曲霉菌+念珠菌感染)2 例,第 5 组艾沙康唑治疗组(曲霉菌+孢子菌感染)1 例,第 6 组艾沙康唑治疗组(毛霉菌感染)5 例,第 7 组两性霉素治疗组(毛霉菌感染)5 例,第 8 组两性霉素治疗组(曲霉菌+毛霉菌感染)3 例,第 9 组两性霉素治疗组(隐球菌感染)2 例。比较 9 组患者的治疗效果和不良反应情况。

结果 (1)在肺曲霉菌病患者,伏立康唑总体疗效最好,使患者炎症水平和 GM 数值降低最多,但不良反应发生率高于艾沙康唑;(2)对于肺部曲霉菌与其他真菌混合感染,艾沙康唑的总体疗效、炎症水平和不良反应情况均好于伏立康唑;(3)在肺毛霉菌病患者,艾沙康唑的总体疗效、炎症水平和不良反应情况均好于两性霉素;(4)对于肺部曲霉菌与毛霉菌混合感染,两性霉素的总有效率为 33.3%,不良反应发生率为 33.3%;(5)对于肺部隐球菌感染,两性霉素的总有效率为 100%,不良反应发生率为 50%。

结论 单纯肺部曲霉菌感染,伏立康唑的效果较好,但需注意不良反应。肺部曲霉菌混合感染及肺部毛霉菌感染,艾沙康唑的效果好于伏立康唑和两性霉素,同时不良反应发生率最低。

Severe Liver Disease Complicated with Pneumocystis Jirovecii Pneumonia: Clinical Analysis

null null

The Third Hospital of Hebei Medical University

Objective This study aimed to characterize the clinical profile of severe liver disease patients with *Pneumocystis jirovecii* pneumonia (PCP) and to identify critical diagnostic and therapeutic challenges in this population.

Methods We retrospectively analyzed the clinical data of 16 patients with severe liver disease (decompensated cirrhosis or liver failure) and concurrent PCP admitted between January 2022 and December 2025.

Results The cohort comprised 14 males (87.5%), with a median age of 55 years. Acute decompensation of cirrhosis was the most common liver disease presentation (7 cases, 43.8%), and hepatitis B virus infection was the leading etiology (6 cases, 37.5%). Fever and dry cough each occurred in 87.5% of patients, while dyspnea was present in only 37.5%, underscoring the often insidious and atypical presentation of PCP. The median time to diagnosis was 22 days, with two cases identified postmortem. All diagnoses were confirmed by metagenomic next-generation sequencing (mNGS) of induced sputum or airway aspirates, supporting its utility for patients unsuitable for bronchoscopy. Twelve patients (75.0%) received standard trimethoprim-sulfamethoxazole (TMP-SMX) therapy, with a survival rate of 91.7%. Severe hepatic impairment contraindicates sulfonamide use, and TMP-SMX-induced hepatotoxicity represents an idiosyncratic reaction linked to individual susceptibility rather than dose. Three patients intolerant to TMP-SMX were switched to clindamycin plus primaquine and survived, though this alternative regimen is not widely accessible. Liver function did not deteriorate significantly during TMP-SMX treatment, but this finding requires cautious interpretation as 81.25% of patients had baseline Child-Pugh C cirrhosis, leaving little functional reserve. Liver function recovery among survivors was limited. Four patients (25.0%) died. Non-survivors were older and exhibited lower lymphocyte and CD4⁺ T cell counts alongside higher β -D-glucan

and lactate dehydrogenase levels. Cirrhosis was present in 68.8% of patients and was significantly associated with mortality ($P = 0.019$), confirming its role as a core risk factor for PCP.

Conclusion Patients with severe liver disease constitute a high-risk group for PCP, often with subtle clinical features that delay diagnosis. mNGS facilitates earlier diagnosis in this population. Although TMP-SMX is effective, its potential hepatotoxicity necessitates individualized risk-benefit assessment. Clindamycin plus primaquine is a feasible alternative, but its availability is limited. Cirrhosis should be considered a core risk factor and integrated into PCP screening protocols. Standardized management can improve outcomes, necessitating heightened clinical awareness.

Keys: *Pneumocystis jirovecii* pneumonia; Severe liver disease; Cirrhosis; Case series; Immunocompromised host

伏立康唑治疗曲霉病个体化用药与血药浓度的现状

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目的 本综述旨在总结伏立康唑治疗曲霉感染的目标血药浓度范围、给药方案、特定部位感染的治疗方案及治疗药物监测实践。

方法 检索 PubMed、Web of Science 查找现有的伏立康唑治疗曲霉病相关指南、临床研究、病例汇报、群体药动学研究等，总结归纳伏立康唑治疗曲霉感染的目标浓度推荐意见、伏立康唑初始给药方案、不同曲霉菌的耐药性与敏感性、特定部位曲霉感染的治疗方案等内容。

结果 目前伏立康唑治疗曲霉感染的具体目标

血药浓度研究结果并不完全一致。现行指南多支持 1–5.5 mg/L 作为目标浓度, 然而, 结合曲霉病病理特点以及中国人群 CYP2C19 基因分布情况, 更窄范围的目标血药浓度 (如 1–3 或 2–4 mg/L) 可能更具临床意义。因此, 伏立康唑治疗方案正逐渐从固定的目标血药浓度转向个体化调整, 因为患者的感染情况与病理生理状态对结局影响更大。此外, 现行指南的目标血药浓度基于混合人群数据, 缺乏针对曲霉病的特异性目标血药浓度。在特殊感染部位方面, 如曲霉菌性眼内炎可使用伏立康唑全身性治疗联合伏立康唑玻璃体 50–100 μg /0.1 ml 多次注射; 目前尚无指南推荐对曲霉菌性脑内炎患者进行脑脊液药物浓度监测。针对特殊部位感染治疗的循证医学证据强度较低, 但多支持更长的伏立康唑疗程。目前针对曲霉病的伏立康唑群体药动学研究中尚无将 CYP2C19 作为关键协变量的研究, 指南对于 CYP2C19 亦并未推荐常规筛查。

结论 临床应结合曲霉菌药敏结果、患者个体情况及疗效个体化调整给药方案。需大规模、前瞻性研究曲霉特异性目标血药浓度及不同宿主背景下的最佳暴露水平, 以进一步优化个体化治疗。

Molecular, biofilm and Motility Characterization of *Acinetobacter Baumannii* Isolated From A Neonatal Intensive Care Unit at A Children's Hospital in South China

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Background Multidrug-resistant *Acinetobacter baumannii* (MDR-AB) poses a critical threat in neonatal intensive care units (NICUs), however few studies have reported the molecular characterization of *A. baumannii*

isolates from the NICU in China. This study aims to describe the molecular, biofilm and motility characteristics related to carbapenem resistance genes in *A. baumannii* isolates from the NICU

Methods Following an outbreak in March–April 2024, 21 *A. baumannii* isolates from neonatal and environmental sources were collected. These isolates underwent antimicrobial susceptibility testing, whole-genome sequencing (WGS) for resistance gene profiling and multi-locus sequence typing (MLST). Biofilm formation and twitching motility were measured in representative strains exposed to subinhibitory concentrations of gentamicin, levofloxacin, and meropenem.

Results All 21 *A. baumannii* isolates were carbapenem-resistant *Acinetobacter baumannii* (CRAB), showing resistance to cephalosporins, aminoglycosides, and quinolones. WGS identified 25 resistance genes, including the universal blaOXA-23, blaOXA-66, blaADC-25 and blaTEM-1D, aminoglycoside resistance genes (armA, aph genes), macrolide resistance genes (mphE, msrE), and tetracycline (tetB) resistance genes. Efflux pumps (adeABC, adeFGH, adeIJK) were ubiquitous. Two sequence types emerged: ST195 (20 isolates) and ST1959 (1 isolate), with high genetic similarity suggesting nosocomial transmission. ST1959 exhibited stronger biofilm formation than ST195. Biofilm formation of ST1959 was significantly enhanced by gentamicin but inhibited by levofloxacin. Meropenem suppressed only the ST195 biofilms. Twitching motility was markedly reduced in ST1959 and also decreased after levofloxacin exposure.

Conclusion This NICU outbreak was driven by CRAB ST195 harboring a conserved resistome. Strain-specific differences in biofilm formation and motility under antibiotic stress highlight the interplay between genetic lineage and phenotypic adaptability. Levofloxacin demonstrates dual anti-biofilm and anti-motility ef-

fects, which could guide targeted infection control strategies against high-risk *A. baumannii* clones.

Fusarium Keratoplasticum Infection in Diabetic Foot Ulcer Following Antimicrobial Therapy

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Objective *Fusarium* species are important opportunistic fungal pathogens. Diabetic foot infection (DFI) ranks the most complex and serious consequences which involves diverse causative pathogens. However, the potential for fungal etiologies is often overlooked.

Methods We describe a DFI complicated by foot trauma, despite prior broad-spectrum antimicrobial therapy, the wound failed to heal and presented persistent swelling and pain. Microbiological re-evaluation and molecular identification confirmed the causative agent as *Fusarium keratoplasticum* (*F. keratoplasticum*), a pathogenic species within FSSC.

Results 1. Description of Case A 56-year-old male with T2DM over 6 years and non-healing skin ulcers on the right lower limb. One month prior, the patient sustained external ankle injury with skin laceration. He received anti-inflammation treatment. Although the wound failed to heal and accompanied by persistent swelling, pain and difficulty walking. Wounds revealed skin hyperpigmentation, dark purple patch with a central black necrotic eschar, tender to palpation, exudation or foul odor (Fig. 1A). Lower limb vascular ultrasound showed arteriosclerosis, venous reflux slowing with

blood flow stasis (Fig. 1B, C).

2. Pathogen detection Post-debridement, three ulcers were exposed. The largest present a base of scant exudate and margins bordered by dark purple patches (Fig. 1D). Secretions from tissue were sent for bacterial culture. Filamentous fungal colonies demonstrated predominant growth (Fig. 2A,B). Microscopic examination revealed septate hyphae, characteristic of *Fusarium* (Fig. 2C). MS identified as FSSC, and ITS sequencing confirmed as *F. keratoplasticum*.

3. Antifungal Susceptibility and Treatment The isolates exhibited high MICs to most antifungal agents such as fluconazole, itraconazole, isavuconazole, and echinocandins, and the MIC for VRC and AMB were all 4 µg/mL. Given the isolate's high MIC to common antifungals and considerable toxicity associated with systemic therapy, a comprehensive assessment favored intensified local debridement and wound nurse. At 2-day follow-up, the wound formed granulation tissue and reduced ulcer area (Fig.1E). Reculture showed markedly decreased *Fusarium* growth (Fig. 2G). 1-week later, cultures turned negative, with significant pain relief. 2-week after discharge, the wound exhibited dry, desquaming skin, indicating near-complete healing (Fig. 1F).

Conclusion This case highlights the need to consider atypical pathogens like *Fusarium* in infectious ulcers unresponsive to conventional antibacterial therapy. Reports on *F. keratoplasticum* infections remain extremely limited, particularly those definitively confirmed to species level. Successful treatment via aggressive debridement combined dressings without systemic antifungals offers valuable alternative for drug resistance or intolerance

Keywords *Fusarium keratoplasticum*; FSSC; Diabetic Foot infection; Molecular Diagnosis

一例 EGPA 合并军团菌和粪类圆线虫重症肺炎感染诊疗

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一般资料：患者，老年男，因“咳嗽、咳痰伴头痛4月，加重伴气促1天”于2026-02-02入院，

患者2025年10月份无明显诱因出现阵发性咳嗽、少量白黏痰，偶带血丝，夜间发热（可自行缓解），伴畏寒、头部胀痛及紧束感（热时加重）、头晕、恶心。2026年11月份症状加重，体温最高38.7℃，当地医院查血常规示嗜酸粒细胞升高，自身抗体及ANCA阳性；CT示双肺感染、鼻窦炎；鼻粘膜病理示嗜酸性粒细胞浸润及血管炎。诊断为“嗜酸性肉芽肿性血管炎”，予泼尼松+美泊利单抗后好转。

2026年1月份患者头晕、头痛加重，完善腰穿后脑脊液示蛋白及白细胞显著升高，NGS检出肺炎克雷伯杆菌，经抗感染及泼尼松治疗后好转。

2026年2月2日患者咳嗽、咳痰加重，伴发热（38.5℃）、胸闷、气促再次入院，查体：T 37.7℃，P 119次/分，R 18次/分，Bp 94/68 mmHg，SpO₂ 92%（4L/min 鼻导管）。双肺呼吸音粗，双下肺湿啰音。心率119次/分，律齐。

实验室检查：血常规示白细胞 $17.94 \times 10^9/L$ ，肌酐 $217.70 \mu\text{mol/L}$ ；CRP 330.58mg/L ，PCT 34.41ng/mL ，IL-6 398.6pg/mL ；CD4⁺T细胞 $127 \text{个}/\mu\text{L}$ 。肺部CT提示大片实变合并空洞性病变，完善支气管镜灌洗液示嗜肺军团菌、白色念珠菌、黄曲霉、粪类圆线虫、疱疹病毒等。追问病史：长期饮用山泉水，周边有猪圈。再次复查痰涂片及大便查见疑似粪类圆线虫。

诊疗经过：入院后给予经验性治疗后效果不佳，仍有发热，呼吸窘迫，2026年2月5日起开始使用伊维菌素及莫西沙星抗军团菌等对症支持治疗后，指标明显好转，患者曾出现一过性意识障碍，心律失常，急性心衰发作，经过对症支持治疗及康复治疗

疗后2026年2月12日出院。2026年4月5日随访一般情况良好，回归社会正常劳作。

讨论：粪类圆线虫为机会性寄生虫，重症播散感染病死率高达70%。传统粪检灵敏度低（30%-50%），本例通过mNGS快速（24h）检出病原，并经传统涂片验证，治疗后好转。伊维菌素为首选治疗，需早期、足量、足程。粪类圆线虫感染可破坏肠道屏障，形成“门户效应”导致其他病原体（如军团菌、念珠菌）合并感染。本例提示mNGS及诊疗思路在疑难感染诊断中的重要价值。

1 例侵袭性肺曲霉病反复抗真菌治疗的病例分析

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目的 深入探讨伏立康唑治疗侵袭性肺曲霉病效果不佳的潜在机制，系统评估新型三唑类抗真菌药艾沙康唑作为替代治疗方案的临床疗效、药理优势及应用价值，总结临床药学干预的关键要点，为临床难治性肺曲霉病的个体化精准治疗提供循证依据与实践参考。

方法 采用回顾性病例分析方法，详细收录1例侵袭性肺曲霉病患者的完整临床资料，结合临床药学视角，从CYP450基因多态性、治疗药物监测（TDM）缺失、潜在真菌耐药及药物相互作用等方面，分析伏立康唑疗效不佳的可能原因，阐述艾沙康唑治疗方案的设计、剂量调整、药学监护措施，对比治疗前后症状、实验室指标及影像学结果，评估治疗效果与药学干预作用。

结果 该患者前期规律口服伏立康唑5个月余，仍反复咯血、肺部病灶无吸收，提示治疗效果不佳，其原因可能与CYP2C19广泛代谢型导致的药代动力学差异、未实施TDM致血药浓度不达标、长期亚

治疗浓度诱导的潜在烟曲霉耐药及复合维生素中金属离子与药物的相互作用相关。临床药师介入后,建议停用伏立康唑,予艾沙康唑治疗,患者咯血症状缓解,炎症指标(CRP、白细胞等)显著下降,肺部CT提示空洞缩小、炎症渗出吸收,最终好转出院,随访期间无复发咯血、预后良好。

结论 艾沙康唑代谢稳定、抗菌活性强、肝毒性低,受CYP基因多态性影响小,是伏立康唑治疗不佳的侵袭性肺曲霉病的优选替代药物;临床药师全程参与用药干预,可优化治疗方案、强化药学监护,提升治疗精准度与安全性,显著改善患者预后,具有重要临床意义。

【关键词】侵袭性肺曲霉病;伏立康唑;艾沙康唑;临床药学;用药干预

Colon-Confined Sequential Activation Enables Durable Control of Recurrent Clostridioides Difficile Infection

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Objective Recurrent *Clostridioides difficile* infection (rCDI) is sustained by biofilm protection, spore persistence, and antibiotic-driven dysbiosis, yet current therapies mainly target planktonic cells and often fail to prevent relapse. This study aims to report a colon-targeted yolk-shell nanoplateform (ZMHVS) enabling sequential biofilm disruption, synergistic killing, sporulation suppression, and barrier support

Methods ZMHVS consists of a ZnO@mesoporous silica (ZnO@MSN) scaffold co-loaded with vancomycin and hyperbranched poly(L-lysine) (HBPL),

and is wrapped with pH-responsive Eudragit S100 for oral, colon-confined release

Results Under simulated colonic conditions, the released complex (ZMHV) rapidly destabilizes the EPS/eDNA-rich biofilm matrix via HBPL, improving antimicrobial access. Vancomycin, Zn²⁺, and ZnO-associated reactive oxygen species work in synergy to eradicate mature biofilms and inhibit new biofilm formation at ultralow doses. Transcriptomic analysis shows global reprogramming, including downregulation of redox-maintenance pathways, suppression of toxin genes, and inhibition of early sporulation programs, consistent with a low-virulence, low-metabolic state. HBPL promotes epithelial cell proliferation and preserves tight-junction proteins. In a murine rCDI model, ZMHVS significantly reduced mortality, colonic injury, systemic inflammation, and fecal recoverable spores, outperforming vancomycin

Conclusion This modular "disrupt-kill-silence-repair" strategy could be applied to other biofilm-associated infections

Keywords Recurrent *Clostridioides difficile* infection, biofilm, nanoplateform, spores, pH-responsive materials

儿童耐药基因型百日咳鲍特菌感染临床与分子特征相关性研究

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目的 旨在研究儿童 23S rRNA A2047G 突变型百日咳鲍特菌感染的临床与分子特征,同时探讨大环内酯类药物无反应的危险因素及预测指标。

方法 采用回顾性研究方法,随机选取 2023 年 11 月至 2024 年 7 月就诊于湖南省儿童医院且 BP-

DNA 检测为阳性确诊为百日咳的 0~14 岁儿童作为研究对象,按大环内酯类药物治疗 1 个疗程后相关临床症状有无改善分为治疗反应组 73 例、治疗无反应组 154 例;对大环内酯类药物治疗 23S rRNA A2047G 突变型百日咳鲍特菌感染无反应的危险因素进行分析。运用受试者工作特征曲线(ROC)评价 BP-DNA 载量与 WBC 计数对大环内酯类药物治疗无反应的预测效能。

结果 23S rRNA A2047G 突变型百日咳鲍特菌 MAST 基因型均为 fim3-1/fim2-1/prn2/ptxP3/ptxA1/ptxC1 型;与治疗反应组相比,治疗无反应组患儿 BP-DNA 载量(6.61Log_{10} 拷贝/ml, $t=-4.807$)与 WBC 计数($20.35\times 10^9/\text{L}$, $t=-4.869$)均明显偏高,平均住院日(11.0d, $Z=-5.428$)显著延长,差异均有统计学意义(均 $P<0.05$);重症百日咳发生率(27.3%, $\chi^2=5.167$)、糖皮质激素使用率(52.6%, $\chi^2=20.843$)、发热发生率(20.8%, $\chi^2=7.044$)、喘息或气促发生率(32.5%, $\chi^2=7.629$)及合并感染率(83.8%, $\chi^2=6.928$)等指标均明显偏高,差异均有统计学意义(均 $P<0.05$)。logistic 回归分析结果显示高 BP-DNA 载量、高 WBC 计数及需要使用糖皮质激素是导致大环内酯类药物治疗无反应的危险因素;BP-DNA $>1.45\times 10^6$ 拷贝/ml、WBC 计数 $>13.87\times 10^9/\text{L}$ 及二项联合检测预测大环内酯类药物治疗无反应的灵敏度分别为 0.66、0.62 及 0.71,特异度分别为 0.63、0.60 及 0.62。

结论 23S rRNA A2047G 突变型百日咳鲍特菌感染患儿大环内酯类药物治疗反应性与患儿 BP-DNA 载量、WBC 计数等因素具有相关性,高核酸载量、高 WBC 计数以及需要使用糖皮质激素的患儿可能更易发生大环内酯类药物耐药而导致临床治疗失败;BP-DNA $>1.45\times 10^6$ 拷贝/ml、WBC 计数 $>13.87\times 10^9/\text{L}$ 时对大环内酯类药物治疗无反应性预测效能最高,联合检测比单项检测更好。

血糖水平与临床预后相关性研究

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目的 探讨艾滋病合并重症马尔尼菲篮状菌败血症患者血糖代谢紊乱特征及其与短期预后的关系,评价血糖分层对预后评估的临床价值,为临床早期风险识别和个体化治疗提供依据。

方法 回顾性分析 2020 年 1 月—2024 年 12 月长沙市第一医院感染与免疫科收治的艾滋病合并重症马尔尼菲篮状菌败血症患者 58 例,其中男 52 例、女 6 例,年龄 28~37 岁。收集入院基线血糖、24 h 血糖波动幅度、CD4⁺T 淋巴细胞计数、器官功能损伤、并发症及 14 d 临床预后等资料。根据血糖水平及波动幅度进行危险分层,比较各组临床特征与预后;采用单因素及多因素 Logistic 回归分析影响预后的独立危险因素。

结果 58 例患者血糖代谢紊乱发生率为 76.2%,以持续性低血糖(59.1%)和血糖大幅波动(34.1%)为主;血糖异常程度与免疫缺陷程度及炎症反应强度呈正相关。多因素 Logistic 回归分析显示,入院基线血糖($OR=0.618$, 95%CI: 0.410~0.931, $P=0.022$)、24 h 血糖波动幅度($OR=1.847$, 95%CI: 1.236~2.761, $P=0.003$)是患者 14 d 预后的独立危险因素。按血糖分层后,低危组 14 d 生存率为 94.4%,中危组为 72.7%,高危组病死率达 77.8%;治疗 72 h 内血糖控制情况可早期预判治疗效果。

结论 艾滋病合并重症马尔尼菲篮状菌败血症患者血糖紊乱发生率高,以低血糖及大幅波动为主要表现;基线血糖水平与血糖波动幅度可独立预测短期预后。基于血糖的危险分层方法简便、可动态监测,有助于早期识别高危患者并指导精细化治疗,对改善预后具有重要临床意义。

艾滋病合并重症马尔尼菲篮状菌败血症患者

儿童脑膜败血伊丽莎白菌脑膜炎系统评价

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目的 系统评价儿童脑膜败血伊丽莎白菌(EM)脑膜炎的临床治疗特点。

方法 系统检索 PubMed、Embase、Web of Science、中国知网、万方和维普数据库中,中文/英文报道的儿童 EM 脑膜炎的病例报告,检索时间均为建库至 2025 年 12 月 31 日。由 2 位评价员独立筛选文献,提取文献特征、病例临床特征、药敏结果、抗感染方案。主要结局指标存活率和并发症。

结果 41 篇文献中的 76 例 EM 脑膜炎儿童纳入本文分析。男 40 例,女 35 例,1 例未报告性别;除 1 例儿童 6 岁 11 月时发病,其余 75 例婴幼儿发病日龄(12.9 ± 9.4) d,其中 44 例早产儿,30 例足月儿,1 例未报告胎龄;临床表现神经系统异常/精神异常 41 例,发热 28 例,有消化道症状 14 例,有呼吸系统症状 13 例,心动过速 3 例。76 例患儿脑脊液培养 EM 均为阳性,其中 49 例血培养亦为阳性。在给出初始抗感染方案的 52 例中,有 20 例的初始方案为青霉素/氨苄西林/氯唑西林+氨基糖苷类/三代头孢,有 23 例初始方案包含碳青霉烯类,4 例包含粘菌素类,36 例包含氨基糖苷类。有 64 例给出了 EM 的药敏结果,喹诺酮类、万古霉素、哌拉西林他唑巴坦、利福平、复方磺胺甲噁唑、头孢哌酮舒巴坦的敏感率分别为 57.8%、54.7%、37.5%、32.8%、26.6%、14.1%,其中 2 例未能存活到开始目标治疗,50 例根据药敏结果调整了给药方案,但仍有 11 例没有存活。纳入本文的患儿共存活 60 例(78.9%),予三联抗感染(60.0%)居多,其中 26 例抗感染方案包含喹诺酮类,26 例包含利福平,24 例包含万古霉素,12 例包含哌拉西林他唑巴坦,9 例包含复方磺胺甲噁唑,5 例包含头孢哌酮舒巴坦,疗程(28 ± 14) d。76 例患儿有 38 例出现了并发症(50.0%),主要有脑积水(31.6%)、发育迟缓(9.2%)、听力损伤(6.6%)、

脑室出血(2.6%)。

结论 EM 是一种非发酵革兰阴性需氧杆菌,但对大多数 β -内酰胺类、碳青霉烯类和氨基糖苷类抗菌药固有耐药,对喹诺酮类、万古霉素、利福平表现出较好的敏感性和较好的临床治疗效果。新生儿(尤其是早产儿)一旦发生 EM 脑膜炎,具有难治性,需及时根据药敏结果制定联合抗感染方案。

关键词 脑膜败血伊丽莎白菌;儿童;脑膜炎;系统评价

1 例纵隔东方伊蒙菌与偶发分枝杆菌混合感染的临床诊治探讨

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目的 探讨纵隔东方伊蒙菌合并偶发分枝杆菌混合感染患者的临床特征、诊断方法与个体化治疗策略,为临床罕见病原体混合感染的精准诊疗提供参考依据。

方法 回顾性分析 1 例经病理与宏基因组二代测序(mNGS)确诊的纵隔东方伊蒙菌合并偶发分枝杆菌混合感染患者的临床资料。患者为 21 岁免疫功能正常女性,有明确土壤与粉尘暴露史,以咳嗽、发热及纵隔占位为主要表现。诊疗过程中采用支气管超声导向经支气管针吸活检(EBUS-TBNA)、冷冻活检获取病变组织,行组织病理、特殊染色及 mNGS 检测明确病原体;结合临床表现、影像学特征、病原学结果及治疗反应调整抗感染方案,参照现有文献与非结核分枝杆菌诊疗指南制定个体化治疗策略,并动态随访患者症状、影像学及实验室指标变化。

结果 患者初始胸部增强 CT 示中上纵隔 4.0 cm $\times$ 3.8 cm 占位,首次 EBUS 活检病理见酵母样真菌,GMS 与 PAS 染色阳性,mNGS 检出东方伊蒙

菌和偶发分枝杆菌，经多学科会诊，考虑东方伊蒙菌感染，由于偶发分枝杆菌序列数低考虑为污染。予两性霉素 B 脂质体诱导治疗后症状缓解、病灶缩小，院外序贯伏立康唑 200mg q12h 口服，出院 2 周后病情复发，纵隔病灶增大至 3.6 cm×3.3 cm 且再次出现发热，再次经验性使用两性霉素 B 脂质体后仍发热，遂再次行 EBUS 病理活检及 mNGS，mNGS 仍查见偶发分枝杆菌且序列数显著升高，结合病史、诊疗经过以及病理、mNGS 结果，考虑为纵隔东方伊蒙菌合并偶发分枝杆菌混合感染。经多学科会诊调整方案，采用艾沙康唑抗真菌，左氧氟沙星、米诺环素、阿米卡星等联合抗非结核分枝杆菌，逐步优化为口服维持方案，治疗后患者体温恢复正常，纵隔病灶持续缩小至 1.3 cm×1.1 cm，临床症状完全缓解，治疗过程中监测肝肾功能，未出现严重不可耐受不良反应。

结论 纵隔东方伊蒙菌合并偶发分枝杆菌感染既往罕见报道。EBUS 活检联合 mNGS 是明确该类罕见混合感染的关键技术，可快速精准识别病原体。治疗需依据治疗反应与药物耐受性个体化调整，兼顾疗效与安全性。临床对于纵隔感染原因未明、常规抗感染效果不佳的患者，应警惕特殊感染可能，尽早采用侵入性活检联合 mNGS 明确诊断，及时启动靶向联合治疗以改善预后。

关键词：东方伊蒙菌；偶发分枝杆菌；纵隔感染；支气管超声；宏基因组二代测序；混合感染

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塔宾曲霉致肺曲霉病药敏特点及临床分析

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目的 探讨塔宾曲霉致肺曲霉病的临床表现、影像学特征、药敏特点、治疗方法及预后转归，为后

续临床治疗提供参考。

方法 收集 2021 年 9 月-2023 年 12 月河北北方学院附属第一医院收治的 9 例塔宾曲霉感染患者的临床资料、实验室检查、影像学检查及抗真菌药敏试验结果。

结果 9 例患者主要表现为发热、咳嗽咳痰、咯血或痰中带血、胸痛、胸憋气短，且 GM 及 G 试验都未见异常。影像学主要表现为支气管扩张、胸腔积液、多发斑片状浸润影。通过基质辅助激光解吸电离飞行时间质谱鉴定（MALDI-TOF MS）确定致病菌种为塔宾曲霉菌。9 例患者均行抗真菌药物治疗。药敏实验结果显示：塔宾曲霉对氟康唑具有天然抗性，对米卡芬净、阿尼芬净、卡泊芬净较为敏感，泊沙康唑、伏立康唑、5-氟胞嘧啶敏感，两性霉素 B、5-氟胞嘧啶药敏结果为中介。

结论 塔宾曲霉致肺曲霉病患者主要存在肺部基础疾病、糖尿病等。影像学无特异性表现。通过患者的痰液、肺泡灌洗液、胸腔积液培养来进行确诊，完善药敏实验最终使患者得到有效治疗。近年来，由于抗生素、糖皮质激素、抗肿瘤药物、免疫抑制剂等的广泛应用及诊断水平的提高，特殊曲霉菌发生率呈升高趋势，提高对该疾病的认识有助于早诊断、早治疗，减少并发症，改善患者预后。

氨曲南-阿维巴坦治疗产金属 β -内酰胺酶碳青霉烯类耐药肠杆菌目细菌感染的多中心研究（AWARE）：病例系列报道

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目的 产金属 β -内酰胺酶（MBL）的碳青霉烯

类耐药肠杆菌目细菌 (CRE) 感染治疗选择有限。本研究旨在评价氨曲南-阿维巴坦 (ATM-AVI) 治疗 MBL-CRE 感染的真实世界临床结局。

方法 本研究为中国多中心、回顾-前瞻性、观察性研究。计划从 30 家中心纳入 100 例接受至少 72 小时 ATM-AVI 治疗的 MBL-CRE 感染住院成人患者, 评价临床及微生物结局。本次病例系列报道基于截至 2026 年 3 月已入组病例进行分析。

结果 共纳入 6 例 MBL-CRE 感染患者, 其中男性 4 例、女性 2 例, 平均年龄为 68.5 (± 14.3) 岁。患者 APACHE II 评分中位数为 12.5 分, Deyo-Charlson 合并症指数中位数为 5 分。4 例患者既往存在抗菌药物暴露, 6 例在本次感染前均已接受针对当前感染的抗菌治疗。所有患者感染适应症均为医院获得性肺炎/呼吸机相关性肺炎, 其中 2 例合并其他部位感染, 分别为血流和皮肤软组织感染。所有基线分离株均为产 NDM 型 MBL 菌株, 其中 1 株同时携带 KPC 酶。主要病原菌为肺炎克雷伯菌 (4 株), 阴沟肠杆菌复合群 (1 株) 和产酸克雷伯菌 (1 株)。所有患者均检出其他病原菌, 如铜绿假单胞菌、鲍曼不动杆菌。6 株产金属酶分离株均对美罗培南和头孢他啶-阿维巴坦耐药, 完成 ATM-AVI 药敏检测的 3 株分离株均对 ATM-AVI 敏感。ATM-AVI 治疗的平均疗程为 18.0 (± 10.3) 天, 所有患者在 ATM-AVI 治疗期间均联合其他抗生素治疗。5 例患者因当前感染入住重症监护室 (ICU), ATM-AVI 治疗后 ICU 治疗时间中位数为 23.0 (8.0-43.0) 天, 自 ATM-AVI 开始用药至出院中位时间为 33.5 (8.0-43.0) 天, 总住院时长中位数为 52.0 (14.0-84.0) 天。治疗过程中 4 例患者接受有创机械通气, 使用天数中位数为 9.5 (8.0-40.0) 天。住院期间 1 例患者死亡, 另 1 例在出院后于 ATM-AVI 治疗后 28 天内死亡。治疗结束 (EOT) 时, 4 例患者达到临床成功, 1 例为临床失败, 1 例为临床不确定; 5 例患者达到微生物学成功, 1 例为不可评估。

结论 在本研究纳入的危重 MBL-CRE 感染患者中, ATM-AVI 治疗显示出一定的临床获益, 提示其在此类重症感染中的临床应用价值。本研究仍在

进行中, 目前仅为小样本病例系列的初步分析, 尚需进一步积累病例验证。

关键词 氨曲南-阿维巴坦 MBL CRE 真实世界研究

动物致伤继发多杀巴斯德菌感染的临床特征分析

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目的 分析动物致伤后继发多杀巴斯德菌感染的临床特征、治疗策略及影响伤口愈合的相关因素。

方法 回顾性分析 2025 年 1 月至 12 月长沙市第一医院动物致伤门诊收治的 11 例经病原学确诊的多杀巴斯德菌感染患者的临床资料, 包括人口学特征、致伤特征、伤口情况、实验室检查、治疗措施及预后。

结果 11 例患者中女性 10 例 (90.9%), 中位年龄 26 岁。致伤动物以猫为主 (8 例, 72.7%), 致伤方式以单纯咬伤多见 (7 例, 63.6%)。受伤部位以上肢为主 (8 例, 72.7%)。伤口特征方面, 10 例 (90.9%) 存在潜在腔隙, 8 例 (72.7%) 出现脓性或血性分泌物。分泌物培养菌株数量分布: 少量 1 例 (9.1%)、1+ (+) 3 例 (27.3%)、2+ (++) 2 例 (18.2%)、3+ (+++) 2 例 (18.2%)、4+ (+++++) 3 例 (27.3%)。炎症指标方面, C 反应蛋白升高 5 例 (45.5%), 白细胞计数升高 2 例 (18.2%), 中性粒细胞绝对值或百分比升高 5 例 (45.5%)。肝功能异常 2 例 (18.2%)。治疗方面, 2 例 (18.2%) 因深部腔隙行切开引流术, 9 例 (81.8%) 放置引流条。所有患者均使用莫西沙星抗感染治疗, 疗程 3~16 天, 中位疗程 6 天。伤口愈合时间 5 天~超过 23 天, 中位愈合时间 8 天, 切开引流组愈合时间显著长于非切开引流组 (平均 22.5 天 vs. 8.1 天)。所有患者均痊愈, 无严重并发症。

结论 多杀巴斯德菌感染以青年女性、猫伤、上肢受累多见。伤口局部解剖复杂性（腔隙形成）是影响愈合时间的关键因素，其重要性超过单纯细菌负荷指标。彻底清创引流联合莫西沙星抗感染治疗可获得良好疗效。

【关键词】多杀巴斯德菌；动物咬伤；伤口感染；清创引流；临床特征

Mechanistic Study and Dual-Target Discovery of Repurposed Azeliragon Against Methicillin-Resistant *Staphylococcus Aureus*

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Objective To investigate the in vitro antibacterial activity of Azeliragon, a clinical-stage drug candidate, against methicillin-resistant *Staphylococcus aureus* (MRSA) and to elucidate its dual-target molecular mechanism involving the bacterial membrane and intracellular enzymes, thereby providing a novel therapeutic strategy against multidrug-resistant infections.

Methods Minimum inhibitory concentrations (MICs) and time-kill kinetics of Azeliragon against MRSA clinical isolates were determined. Label-free target identification techniques (DARTS, BLI, and LiP-MS) combined with molecular docking were employed to identify intracellular target proteins. Site-directed mutagenesis (K394A/Y397A) was performed to verify the drug-binding site on MurA. Biophysical assays (SPR and BLI) were utilized to evaluate the affinity of the drug for various phospholipid components, specifically phosphatidylglycerol (PG) and cardiolipin (CL). Untargeted metabolomics was performed to analyze shifts in the bacterial metabolic profile following treatment. Resistance evolution was investigated via serial

passage experiments and whole-genome sequencing to analyze mutational pathways.

Results Azeliragon exhibited potent antibacterial activity against MRSA, with killing kinetics significantly faster than conventional comparator agents. Mechanistic studies revealed a synergistic dual-target mode of action: first, the drug shows high affinity for anionic phospholipids (PG and CL) characteristic of Gram-positive membranes, exerting rapid bactericidal effects by disrupting membrane integrity; second, Azeliragon directly binds to the intracellular enzyme MurA, inhibiting the enolpyruvyl transfer step in peptidoglycan biosynthesis. Metabolomic analysis confirmed significant alterations in fatty acid and CoA biosynthesis pathways, reflecting compensatory responses to membrane damage and MurA inhibition. Resistance evolution studies showed that MRSA developed only low-level resistance, with mutations primarily localized to membrane/efflux pathways (*farE/farR*) and no mutations observed in *murA*, suggesting a high genetic barrier to resistance for this dual-target mechanism.

Conclusion This study demonstrates that Azeliragon is a promising dual-target antimicrobial candidate for drug repurposing, acting through simultaneous membrane disruption and inhibition of the intracellular cell-wall biosynthetic enzyme MurA. This combined extracellular and intracellular mode of action not only enhances bactericidal efficacy but also significantly raises the threshold for bacterial resistance. These findings provide a strong theoretical basis and a potential molecular candidate for developing novel multi-target therapies against drug-resistant *S. aureus* infections.

某三甲医院 110 例产气肠杆菌感染患者的真实世界研究

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目的 分析益阳市某三甲医院 2020 年至 2021 年感染产气肠杆菌（产气克雷伯菌）患者的临床分布特点及其对常用抗菌药物的耐药率，为临床的抗感染治疗提供理论依据。

方法 收集笔者医院该时间段内检出产气肠杆菌的患者信息，统计其相关临床资料，并对检出菌株进行药敏试验结果分析。

结果 产气肠杆菌菌株来源主要为痰液标本占比 55.45%，尿液占比 20.00%，分泌物占比 17.27%，血液占比 5.45%，引流液占比 1.82%，感染患者 60 岁以上占比 50.91%，住院时间主要分布于 15~29 d、8~14 d 及 30~44 d 三个时间段，占比分别为 29.09%、24.55%和 20.00%，住院时间大于 14 天占比 63.64%，患者主要来自神经外科、重症医学科、烧伤整形科、内分泌科等科室，药敏结果提示产气肠杆菌对替加环素均保持敏感，对美罗培南、厄他培南、阿米卡星的耐药率为 0.91%，对亚胺培南的耐药率为 3.64%，对头孢哌酮舒巴坦、哌拉西林他唑巴坦、庆大霉素的耐药率低于 10%，呋喃妥因、头孢吡肟的耐药率低于 15%，对头孢曲松、头孢他啶的耐药率高于 35%，而对阿莫西林克拉维酸钾、头孢替坦、头孢唑林、头孢孟多的耐药率为 100%。

结论 产气肠杆菌感染及耐药现象呈上升趋势，医院应完善对该类菌株的耐药性监测与预警，持续加强抗菌药物临床应用管理，科学合理使用抗菌药物，从而延缓细菌耐药、甚至遏制细菌耐药的产生。

儿童中枢神经系统曲霉病的临床特征、诊断与治疗：单中心回顾性研究

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心

背景 中枢神经系统（central nervous system, CNS）曲霉病是儿童中一种严重且易被误诊的侵袭性真菌感染。当前，关于儿童 CNS 曲霉病临床表现、影像学特征、诊断策略及治疗结局的系统性研究仍较为有限。

方法 本研究回顾性纳入 2010 年 1 月至 2024 年 12 月于北京儿童医院住院的 0~18 岁确诊或拟诊 CNS 曲霉病患者。收集其人口学特征、宿主危险因素、临床表现、实验室检查及神经影像学资料，并评估抗真菌治疗方案及临床结局。

结果 共纳入 16 例患儿，其中男性 12 例，中位年龄 5 岁。血液系统恶性肿瘤是最常见的宿主危险因素；25.0%（4/16）患儿无明确危险因素。临床表现缺乏特异性，最常见症状为发热、癫痫发作和意识障碍；初诊时误诊 9 例（56.3%）。脑脊液培养阳性率较低，而在接受检测的患儿中，脑脊液宏基因组二代测序（mNGS）均检出曲霉核酸（7/7）。MRI 最常见表现为不规则脑脓肿（14/16），常伴脑膜强化（14/16）和梗阻性脑积水（10/16）。在可评估的初始接受伏立康唑单药治疗患儿中，仅 22.2%（2/9）获得部分缓解；含脂质体两性霉素 B（L-AmB）的治疗方案显示出较高的临床应答率，其中初始联合治疗应答率为 75.0%，挽救治疗应答率为 80.0%。全因死亡率为 37.5%（6/16）；存活患儿中，30.0%（3/10）遗留中至重度残疾。

结论 儿童 CNS 曲霉病可见于不同风险背景患儿，部分患儿甚至缺乏明确宿主危险因素。由于临床表现不典型，误诊较为常见。研究结果提示，早期开展脑脊液 mNGS 检测并进行系统神经影像学评估，必要时补充全中枢神经轴 MRI，有助于及时诊断及评估病变播散范围。本队列中，初始伏立康唑单药治疗进展率较高，而含 L-AmB 的治疗方案显示出较好的临床应答；对于重症患儿，仍需前瞻性研究进一步优化初始治疗策略。

Rhino-orbital-cerebral Mucormycosis Following Dental Extraction: A Systematic Review

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Objectives Rhino-orbital-cerebral mucormycosis (ROCM) is an angioinvasive, rapidly progressive fungal infection associated with extremely high mortality. Although classically acquired via inhalation, dental extraction represents an underrecognized odontogenic portal of entry that enables fungal spread to the sinonasal tract, orbits, and intracranial structures. Early clinical manifestations are nonspecific, leading to frequent misdiagnosis and catastrophic treatment delay. Current evidence is limited to scattered case reports and small case series, with no large-scale systematic synthesis available. This study aimed to summarize the epidemiology, clinical features, diagnosis, management, and outcomes of post-extraction ROCM, and provide an evidence-based framework for early recognition and optimized clinical intervention

Methods The protocol was registered with PROSPERO (CRD20251137728). A systematic search was conducted across five major databases, including PubMed and Embase, from inception to December 2025, using search terms related to "tooth extraction," "mucormycosis," and corresponding anatomical regions. Inclusion criteria comprised patients aged ≥ 18 years with a definitive history of tooth extraction and ROCM confirmed by histopathology or molecular biology. Study quality was assessed using the JBI Critical Appraisal Checklist for Case Reports; only high- and moderate-

quality studies were included for statistical analysis using IBM SPSS Statistics Version 28.0

Results The cohort comprised 26 patients with a median age of 54 years (IQR: 45-59) and a male predominance (16/26, 61.5%). Maxillary extractions were involved in 17/18 (94.4%) confirmed infection sites. The median interval from extraction to symptom onset was 10 days (IQR: 3-15), and 21/22 (95.5%) cases developed symptoms within 1 month. Systemic predisposing factors were present in 25/26 (96.2%) patients; all 25/25 (100.0%) at-risk patients had diabetes mellitus (DM), and 9/25 (36.0%) had concurrent ketoacidosis. First-line systemic amphotericin B was administered in 24/26 (92.3%) cases, and 21/26 (80.8%) patients underwent surgical debridement. Overall mortality occurred in 12/25 (48.0%) patients. Among 13 survivors, 7/8 (87.5%) with documented sequelae had permanent vision loss

Conclusion Post-extraction ROCM is a rare but devastating complication that predominantly affects patients with diabetes mellitus after maxillary posterior tooth extraction. The narrow symptomatic window and nonspecific early signs demand high clinical suspicion. Early diagnosis using multimodal imaging, combined with aggressive multidisciplinary treatment is essential to reduce the high mortality and severe morbidity. This systematic review to date provides critical evidence to guide clinical practice for this life-threatening odontogenic fungal infection

临床药师参与一例罕见磷脂酰肌醇 3-激酶 δ 过度活化综合征合并霉菌感染的治疗实践

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目的 磷脂酰肌醇 3-激酶 δ 过度活化综合征 (Activated PI3K Delta Syndrome, APDS), 一种罕见的常染色体显性遗传免疫缺陷病, 全球发病率约为 1~2 例/百万人口, 临床表现多种多样, 其中反复呼吸道感染为 APDS 最常见的临床表现。通过分析参与一例 APDS 合并霉菌感染的诊疗过程, 为临床合理用药及 APDS 的诊疗提供参考。

方法 本文通过一例 APDS 患儿使用西罗莫司治疗原发病, 同时使用伏立康唑抗感染的病例分析, 阐述临床药师在超说明书用药, 并存在药物相互作用治疗方案中, 对血药浓度、给药剂量等方面的指导作用。

结果 患儿以确诊“闭塞性细支气管炎 4 月余, 返院调整治疗”。患儿基因: PIK3R1 c.536T>C (p.Val79Ala), 变异来源: 父亲, 考虑 APDS 可能性大, 予西罗莫司排尿 1mg/天、泼尼松龙抑制免疫。查西罗莫司血药浓度稍高 14.33ng/ml, 暂停服用西罗莫司; 支气管灌洗液 DNA 病原体序列数检测找到黑曲霉 (序列数 165), 遵临床药师会诊意见, 加伏立康唑抗真菌, 监测血药浓度; 查西罗莫司血药浓度降低 2.76 ng/ml, 请临床药师会诊, 经查阅文献发现, 伏立康唑是 CYP3A4 酶的强效抑制剂, 西罗莫司通过 CYP3A4 酶代谢, 联用可导致西罗莫司的暴露显著增加, 西罗莫司应减少至 0.25~0.45 mg/d 或减少 75%至 87.5%, 以达到目标谷浓度和临床耐受性, 因此西罗莫司剂量调整为 0.25mg/天, 监测血药浓度。4 天后患儿体温正常, 呼吸平稳, 咳嗽、咳痰较前减少, 无憋喘、气促等不适, 纳食及精神反应可, 肺部听诊未闻及明显喘鸣音。复查西罗莫司 (6.26 ng/ml)、伏立康唑 (0.862 mg/L) 血药浓度在有效范围, 嘱出院后继续口服药物。

结论 通过临床药师与医疗团队的合作, 该患儿在选择一线抗感染药物伏立康唑情况下, 通过减少西罗莫司的药量至 25%, 使西罗莫司和伏立康唑的血药浓度在安全有效范围内, 在保证安全的同时更具有有效性和经济性。患儿预后良好, 未观察到不良反应, 获得最大受益。

关键词: 磷脂酰肌醇 3-激酶 δ 过度活化综合征;

西罗莫司; 伏立康唑; 血药浓度; 相互作用

Distinct Inflammatory Profiles and Therapeutic Efficacy in Ceftazidime-Avibactam-Resistant *Klebsiella Pneumoniae*: A Retrospective Cohort Study and Longitudinal Biomarker Analysis

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Purpose To identify risk factors for carbapenem-resistant (CRKP) and ceftazidime-avibactam-resistant (CZA-R) *Klebsiella pneumoniae*, characterize their inflammatory profiles, and evaluate antibiotic efficacy using biomarker kinetics

Methods A retrospective cohort study including 257 *K. pneumoniae* isolates from January 2024 to March 2025 was performed. Strains were stratified by carbapenem and CZA susceptibility (CRKP and CSKP, CZA-R and CZA-S). A sub-analysis comparison was performed between CRKP vs. CSKP, CZA-R vs. CSKP, and CZA-R vs. CZA-S isolates. Independent risk factors were identified via logistic regression. Antibiotic efficacy was quantified by the daily decline slope of inflammatory biomarkers (CRP, PCT, IL-6).

Results Invasive procedures, particularly nasogastric tube use, were primary drivers of CRKP in both

respiratory and urinary tracts. Respiratory CRKP infections showed suppressed inflammatory markers compared to CSKP. Conversely, CZA-R isolates exhibited a distinct hyper-inflammatory phenotype with significantly elevated IL-6 and higher co-infection rates. Independent predictors for CZA-R included indwelling needle use, pneumonia history, and sputum production. While CZA-R strains showed near-pan-resistance, they remained susceptible to polymyxin and tigecycline. Longitudinal slope analysis revealed that tigecycline-based regimens or carbapenem-sulbactam combinations achieved the most rapid clearance of inflammatory biomarkers in CZA-R cases.

Conclusion CRKP acquisition was linked to invasive interventions and a lower-inflammatory phenotype relative to CSKP. However, evolution toward CZA resistance is marked by severe inflammatory dysregulation (elevated IL-6). Tigecycline-based combination therapies demonstrate superior efficacy in resolving inflammatory storms in CZA-resistant infections, offering a viable salvage strategy.

血管内皮细胞通过 CXCL10 招募 NK 细胞并诱导巨噬细胞代谢重编程抗汉塞巴尔通体感染

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目的 汉塞巴尔通体是一种兼性细胞内寄生的革兰阴性菌,可引起猫抓病及全身性严重并发症。该菌能存活于血管内皮细胞,并能抑制宿主经典炎症通路。本研究旨在探索感染早期宿主如何打破病

原体免疫抑制、建立有效天然免疫清除机制。

方法 采用人脐静脉内皮细胞体外感染模型,结合转录组测序和 Luminex 多因子检测,分析感染后内皮细胞分泌的趋化因子和细胞因子谱。通过 Transwell 迁移实验鉴定其对 NK 细胞和单核细胞的趋化作用。利用小分子抑制剂验证上游 cGAS-STING 信号通路。建立内皮细胞 NK 细胞共培养体系,结合中和抗体和抑制剂实验解析 NK 细胞活化所需信号。采用 Seahorse 能量代谢分析技术检测巨噬细胞糖酵解水平,并通过糖酵解抑制剂 2-DG 验证代谢重编程与杀菌功能的因果关系。最后利用 NK 细胞缺陷小鼠和 IFN- γ 基因敲除小鼠进行体内感染实验。

结果 转录组数据显示,汉塞巴尔通体感染的内皮细胞中 679 个基因上调,240 个基因下调,其中 CXCL10 上调 8.63 倍,IFNB1 上调 5.51 倍,趋化因子和细胞因子信号通路显著富集。蛋白质水平验证确认感染内皮细胞分泌高水平的 CXCL10 和 IFN- β ,该过程依赖于 cGAS-STING 通路。条件培养基可特异性招募人原代 NK 细胞和单核细胞,抗 CXCL10 中和抗体可阻断该趋化作用。共培养实验表明,被感染内皮细胞通过 CXCL10 介导的接触信号和 IFN- β 介导的授权信号协同激活 NK 细胞产生 IFN- γ ,NK 细胞活化后的条件培养基可使巨噬细胞基础糖酵解速率提升 3 倍以上,胞内菌落形成单位减少 80%,活性氮和活性氧水平显著升高,而糖酵解抑制剂 2-DG 可削弱该杀菌效应。体内实验证实,NK 细胞缺陷小鼠及 IFN- γ 基因敲除小鼠肝脾细菌载量均显著高于野生型对照。

结论 汉塞巴尔通体感染内皮细胞后,可活化 cGAS-STING 通路感知胞内菌后分泌 CXCL10 和 IFN- β ,前者招募 NK 细胞至感染局部,后者进一步诱导 NK 细胞高效产生 IFN- γ ;IFN- γ 进而驱动巨噬细胞发生需氧糖酵解代谢重编程,进一步增强巨噬细胞杀菌能力。

关键词: 汉塞巴尔通体;血管内皮细胞;NK 细胞;IFN- γ ;代谢重编程;CXCL10

Multidrug-Resistant *Acinetobacter* Spp. Bloodstream Infections in Hematologic Patients: Clinical Characteristics, Genomic Features, and Eravacycline-Based Combination Therapy

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Background Multidrug-resistant (MDR) *Acinetobacter* spp. bloodstream infection (BSI) is concerning in hematologic patients, but integrated clinical and genomic analyses are scarce

Methods We retrospectively analyzed 62 hematologic patients with *Acinetobacter* spp. BSI over 13 years, including 30 MDR and 32 non-MDR cases. Whole-genome sequence (WGS) was conducted on 23 MDR isolates. Checkerboard assays evaluated the in vitro activity of eravacycline combined with sulbactam, meropenem, cefoperazone-sulbactam, polymyxin B, and levofloxacin.

Results Female (66.67% vs. 34.38%, $P=0.022$) and adult (≥ 14 years; 80.00% vs. 53.12%, $P=0.049$) patients were more common in the MDR group. Prior carbapenem exposure, prolonged neutropenia, and respiratory tract colonization were associated with MDR-BSI. The majority of MDR cases did not receive appropriate empirical therapy within 24 hours (40.00% vs. 90.62%, $P<0.001$). The overall 30-day mortality was 38.71%, significantly higher in MDR than non-MDR patients (53.33% vs. 25.00%, $P=0.043$). Among MDR subgroup, 30-day non-survivors had more profound cytopenias and higher inflammatory markers at BSI onset ($P<0.05$). WGS revealed diverse sequence types and capsular loci

across the isolates, including 14 non-*A.baumannii* and 9 *A.baumannii* strains. Among 20 carbapenemase-positive isolates, blaOXA-23 ($n=9$) predominated in *A.baumannii*, while blaOXA-58 ($n=7$) and blaNDM-1 ($n=7$) were restricted to non-*A.baumannii* isolates. Eravacycline demonstrated potent in vitro activity ($MIC_{50/90}=0.125/0.5$ mg/L) and showed synergy with sulbactam (52.17%), meropenem (43.48%), and cefoperazone-sulbactam (39.13%), while combinations with polymyxin B (86.96%) and levofloxacin (69.57%) were primarily additive.

Conclusion Eravacycline exhibited strong intrinsic activity and favorable synergy with sulbactam, supporting its potential role in treating MDR *Acinetobacter* spp. infections in this high-risk population.

机械振动排痰联合雾化吸入对老年肺部感染患者疗效与安全性

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关键词: 机械振动排痰, 老年肺部感染, 标准化方案

背景 老年肺部感染患者常因呼吸肌无力、咳嗽反射减弱导致排痰障碍, 严重影响预后。传统人工叩背排痰效果有限且标准化不足。机械振动排痰通过高频低幅振动降低痰液粘稠度、促进排出, 雾化吸入可稀释痰液、扩张气道, 二者理论上具有协同作用, 但现有研究在标准化治疗方案及安全性方面证据尚不充分。

目的 探讨一种标准化的机械振动排痰联合雾化吸入方案治疗老年肺部感染的临床疗效与安全性。

方法 采用随机对照研究设计, 纳入 2023 年 6 月至 2025 年 12 月宁夏医科大学总医院呼吸与危重

症医学科收治的 80 例老年肺部感染伴排痰障碍患者,按随机数字表法分为联合组与对照组,各 40 例。两组均接受抗感染等基础治疗。联合组采用标准化联合方案:先以 0.9%氯化钠 5ml+20% N-乙酰半胱氨酸 2ml 行氧气驱动雾化吸入(15 分钟),结束后 10 分钟内使用手持式振动排痰仪(频率 25-35Hz)于病变肺段体表投影区行振动治疗(15 分钟),每日 2 次。对照组在相同雾化后,由培训后的护士行标准化人工叩背排痰(频率 100-120 次/分,15 分钟)。疗程均为 7 天。比较两组治疗第 7 天的临床总有效率(主要终点),以及住院时间、动脉血氧分压(PaO₂)、24 小时痰液量、痰液粘稠度评分、不良事件发生率等次要指标。

结果 接受标准化机械振动排痰联合雾化吸入治疗的联合组(n=40)临床总有效率为 92.5%,显著高于雾化吸入后联合人工叩背的对照组(77.5%)。联合组在改善患者临床进程方面优势明显,其平均住院时间更短(9.8±2.1 天 vs. 12.3±2.5 天),肺部啰音消失更快。在生理与排痰效果上,联合组治疗后动脉血氧分压更高(78.4±5.2 mmHg vs. 72.1±6.0 mmHg),24 小时痰液排出量更多,痰液粘稠度降低也更显著(上述比较均 P<0.05)。安全性方面,两组均未发生严重不良事件,仅联合组有 2 例(5.0%)出现局部皮肤轻微潮红,对照组有 3 例(7.5%)诉叩背部位轻度疼痛,均自行缓解,组间不良事件发生率无统计学差异(P>0.05)。

结论 相较于雾化吸入后联合人工叩背,采用标准化的机械振动排痰联合雾化吸入方案能更有效地提高老年肺部感染患者的临床疗效,改善氧合,促进痰液排出,缩短住院时间,且安全性良好。该标准化方案具有临床推广价值。未来研究可进一步优化治疗参数并探索长期效益。

淋巴瘤合并侵袭性肺曲霉病的临床特征及抗真菌治疗结局分析

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目的 淋巴瘤患者因疾病本身及化疗所致免疫抑制,是侵袭性肺曲霉病(IPA)的高危人群,病死率高。本研究分析淋巴瘤合并 IPA 的临床特征、诊断方法及抗真菌治疗结局,探讨预后影响因素。

方法 回顾性分析 2020 年 1 月至 2025 年 12 月于宁夏医科大学总医院收治的淋巴瘤合并 IPA 患者 78 例。纳入标准:①病理确诊淋巴瘤;②符合 EORTC/MSGERC 2020 版 IPA 确诊或临床诊断标准;③接受抗真菌治疗≥7 天。排除标准:①合并其他侵袭性真菌感染;②临床资料不完整。收集患者人口学资料、淋巴瘤类型及分期、化疗方案、中性粒细胞缺乏情况、临床表现、影像学特征、GM 试验结果、支气管镜检查结果、抗真菌药物及治疗结局。主要结局为 6 周治疗反应率,次要结局为 12 周全因死亡率。采用单因素及多因素 Logistic 回归分析预后影响因素。

结果 78 例淋巴瘤患者中,非霍奇金淋巴瘤占 71.8%,霍奇金淋巴瘤占 28.2%;确诊 IPA 23.1%,临床诊断 76.9%。影像学以结节肿块影、晕轮征、空气新月征多见。血清 GM 试验、BALF-GM 试验阳性率分别为 64.1%、82.1%。抗真菌方案以伏立康唑单药为主,其次为两性霉素 B、棘白菌素类及联合用药。患者 6 周治疗总有效率 57.7%,12 周全因死亡率 32.1%,IPA 相关死亡率 24.4%。多因素分析显示:中性粒细胞缺乏>14 天、抗真菌治疗延迟>5 天为 12 周死亡独立危险因素,初始伏立康唑治疗为预后保护因素。

结论 淋巴瘤合并 IPA 以非霍奇金淋巴瘤多见,影像学表现多样,病死率仍较高。中性粒细胞缺乏持续时间延长和延迟抗真菌治疗是死亡独立危险因素,伏立康唑初始治疗可改善预后。

关键词: 淋巴瘤;侵袭性肺曲霉病;临床特征;抗真菌治疗;预后因素

糖尿病酮症酸中毒合并肺毛霉菌病 1 例并文献复习

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目的 肺毛霉菌病是一种罕见但致死率极高的侵袭性真菌感染，糖尿病酮症酸中毒（DKA）是其最常见的危险因素。本文报道 1 例 DKA 合并肺毛霉菌病患者的诊疗经过，并结合文献复习总结该病的临床特征及诊治要点。

方法 回顾性分析 2025 年 1 月宁夏医科大学总医院收治的 1 例 DKA 合并肺毛霉菌病患者的临床表现、实验室检查、影像学特征、病原学诊断、抗真菌治疗及转归。同时检索 PubMed、CNKI、万方数据库 2015 年 1 月至 2025 年 12 月发表的 DKA 合并肺毛霉菌病相关文献，提取临床特征、诊断方法、治疗方案及预后数据。

结果 病例报告：男性 58 岁，2 型糖尿病病史 8 年，血糖控制差，因“发热、咳嗽、右侧胸痛 3 天，意识模糊 1 天”入院。查体：体温 38.9℃，呼吸 26 次/分，右肺呼吸音低。实验室检查：血糖 22.6mmol/L，动脉血气提示 DKA（pH 7.21，HCO₃⁻ 14mmol/L）。胸部 CT 示右肺上叶团块影伴空洞形成，内见软组织密度影，周围有磨玻璃样改变。入院第 3 天行支气管镜检查，BALF-mNGS 检出毛霉菌属（序列数 1562 条，相对丰度 78.5%），真菌培养及组织病理未发现典型菌丝。确诊后予两性霉素 B 脂质体静脉输注，同时纠正 DKA、控制血糖。治疗 7 天体温正常、胸痛缓解，14 天复查 CT 示肺部病灶缩小，住院 28 天出院，出院后口服泊沙康唑维持治疗，随访 3 个月病情稳定无复发。文献复习：检索 PubMed、CNKI 等数据库，可见多篇 DKA 合并肺毛霉菌病相关文献。北京大学 2023 年研究纳入 10 例肺毛霉菌病患者，其中 6 例（60.0%）合并 DKA，经抗真菌联合支气管

镜介入治疗均治愈；2024 年 He 等报道 1 例 20 岁 DKA 合并肺毛霉菌病致气管破坏死亡病例，强调早期诊断及手术干预的重要性；2007 年《中华结核和呼吸杂志》报道 3 例肺毛霉菌病，其中 2 例合并 DKA。综合文献，该病总体病死率约 30%-50%，早期联合抗真菌及手术治疗可改善预后。

结论 DKA 合并肺毛霉菌病病情凶险，反晕征具有一定提示价值，mNGS 可提高早期诊断率。早期抗真菌治疗联合支气管镜介入或手术切除可改善预后，早期识别和积极干预是降低病死率的关键。

关键词 肺毛霉菌病；糖尿病酮症酸中毒；抗真菌治疗；宏基因组测序；两性霉素 B

Intra-genomic Genes-to-genes Correlation Enables Bacterial Genome Representation

null null

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The bacterial pan-genome consists of core genes shared by all members of a taxonomy and accessory genes found in only a subset. The correlation among genes within the pan-genome could advance our understanding of evolution and tackle medical challenges. Here, we discovered a strong intra-genomic correlation among bacterial pan-genes within each of *Escherichia coli*, *Listeria monocytogenes*, *Staphylococcus aureus*, and *Campylobacter jejuni*. With a convolutional neural network assisted core genome knock-out simulation, we found that different combinations of fewer than 20 highly variable core genes could recover the sub-species type classified by complete core genome with accuracy >95%. This observation led us to test the genes-to-genes predictability: with more than 52,000 assemblies from each species, combinations of highly variable core genes could predict the sequence variants of other core

genes (average accuracy >94%) within the same genome and could also predict sequence variants (average accuracy >91%) as well as the presence (average AUROC >0.91) of some accessory genes. Furthermore, combinations of highly variable core genes could also predict multiple antibiotic resistances (AUROC >0.80) in large published datasets of *E. coli*, *S. aureus*, and *Mycobacterium tuberculosis*. Collectively, we propose that genes within the same genome can strongly correlate with each other. Therefore, the strain phylogeny and the status of other genes could be uniformly represented by combinations of highly variable core genes, which could further represent certain phenotypes including in vitro resistance.

Carbapenemase-Directed Therapy: Optimizing Antibiotic Combinations Against Carbapenem-Resistant *Klebsiella Pneumoniae*

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Objective Given the limited therapeutic options for infections caused by carbapenem-resistant *Klebsiella pneumoniae* (CRKP) due to multidrug resistance, this study aimed to identify optimal combination therapies based on carbapenemase types and resistance phenotypes.

Methods The in vitro synergistic activity of ceftazidime-avibactam (CZA) and polymyxin B (PMB)-based combinations was systematically evaluated against 139 CRKP isolates, including *K. pneumoniae* carbapenemase (KPC) producing strains, New Delhi metallo- β -lactamase (NDM), and KPC and NDM

co-producing carbapenem-resistant *K. pneumoniae* strains (KN-CRKP). The effects of these antimicrobial agents combinations were assessed using fractional inhibitory concentration index (FICI) and susceptibility breakpoint index (SBPI).

Results Among CZA-resistant KPC-CRKP isolates, combinations of CZA with β -lactams showed high synergy rates (79.7-86.5%). In PMB-resistant KPC-CRKP, PMB + CZA demonstrated substantially great synergy (53.2%) than traditional PMB-carbapenem combinations ($\leq 3.8\%$). Against NDM-CRKP, CZA + aztreonam (ATM) was synergistic in 83.3% of isolates. Notably, in KN-CRKP, CZA + ATM produced synergistic or additive effects in all isolates, despite resistance to each drug alone. SBPI analysis further revealed significant bactericidal enhancement in some combinations classed as indifferent by FICI, including PMB + Tigecycline (TGC).

Conclusion Carbapenemase profiles critically determine the efficacy of combination therapies against CRKP. CZA-based combinations, particularly with β -lactams or ATM, exhibit robust activity against KPC and NDM-producing CRKP, while PMB in combination with CZA may partially overcome PMB resistance. Notably, the CZA-ATM regimen shows consistent activity against both NDM-CRKP and KPC-NDM co-producing isolates. These findings support enzyme profile-guided combination therapy for optimizing treatment of highly resistant CRKP infections.

Complexation-Aided Selectivity Amplification: A Strategy To Mitigate Peptidomimetics' Toxicity Issues in Anti-Resistance Practices

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Antimicrobial peptidomimetics (AMPs) have valuable antiresistance features, but they generally suffer from insufficient killing selectivity for bacteria over eukaryotic cells, leading to limited therapeutic indices and inability to work with existing therapeutic strategies. Here, we report a strategy called complexation-aided selectivity amplification. By choosing an anionic polyelectrolyte that can form kinetically and thermodynamically stable complexes with an AMP, the AMP's selectivity for the more negatively charged prokaryotic cell membrane can be enhanced since a thermodynamically determined outcome, i.e., disruptive interaction with only prokaryotic but not eukaryotic cell membrane, can be assured. Thus, the AMP-polyelectrolyte complex can be used as a low-toxicity alternative that allows safer use on cell or animal models and works with existing therapeutic strategies. Notably, the complex retains the key advantages of AMPs, such as being resistance-resistant, broad-spectrum, and fast-killing. The broad applicability of this strategy is demonstrated with additional complexing polymers, AMP, and antibiotics.

模型引导的抗菌药物精准给药：基于临床获益与风险的系统评价与荟萃分析

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目的 模型引导的精准给药 (Model-Informed Precision Dosing, MIPD) 整合数学模型、群体特征

与个体变异性，为提升个体化治疗的疗效与安全性提供了新路径。本研究的目的是系统评估模型引导的抗菌药物剂量优化对临床结局的影响。

方法 系统检索 PubMed、Embase、Web of Science 和 Cochrane Library 数据库 (截至 2025 年 9 月 28 日)，纳入采用基于 MIPD 进行剂量优化的临床研究。对照组接受常规治疗，包括经验性或基于传统治疗药物监测 (therapeutic drug monitoring, TDM) 的个体化给药。采用 Cochrane 偏倚风险工具评估偏倚风险。主要结局为毒性反应，次要结局包括达标率、死亡率、治疗失败率、临床/微生物学成功率、住院时长及药物疗程。使用随机效应模型汇总风险比 (risk ratio, RR) 的效应大小，通过 *I*² 统计量评估异质性。

结果 共纳入 21 项研究 (7346 例患者)，其中随机对照研究 (randomized controlled trial, RCT) 6 项 (28.57%)，非随机干预性试验 (包括准实验研究) 9 项 (43.86%)，观察性研究 6 项 (28.57%)。与常规给药相比，MIPD 可显著降低毒性反应发生风险 (RR=0.61, 95%CI: 0.50-0.75)，提高 TDM 达标率 32% (RR=1.32, 95%CI: 1.15-1.50)，缩短住院时间 2.46 天 (MD=-2.46 天, 95%CI: -4.36 to -0.56)，在微生物学清除率方面亦具优势 (RR=1.10, 95%CI: 1.01-1.20)。然而，两组在全因死亡率 (RR=0.92, 95%CI: 0.70-1.22)、ICU 死亡率 (RR=1.03, 95%CI: 0.80-1.33)、治疗失败率 (RR=0.78, 95%CI: 0.47-1.27) 及治疗疗程 (MD=-0.08 天, 95%CI: -0.98-0.82) 方面差异无统计学意义。

结论 MIPD 策略可显著降低毒性反应，提高抗菌药物 PK/PD 达标率，缩短住院时间，但对死亡率等终点指标的改善尚需更多高质量 RCT 加以验证。

ADAM17 Orchestrates Mitochondrial Dysfunction and Activates The CGAS-STING Signaling Axis To Drive Pyroptosis in Klebsiella Pneumoniae-induced Acute Lung

Injury

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Objective *Klebsiella pneumoniae* (KP)-induced acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) are severe complications of hospital-acquired pneumonia with high mortality rates. Although mitochondrial dysfunction is a recognized pathological feature of inflammatory diseases, the precise mechanisms orchestrating its role in KP-induced ALI/ARDS remain poorly understood. This study aimed to identify key regulatory genes linking mitochondrial impairment to KP-induced lung injury and to elucidate the underlying molecular pathways.

Methods Differentially expressed genes (DEGs) from two GEO transcriptomic datasets (GSE171048 and GSE286873) were cross-referenced with mitochondrial damage-related genes (MDGs) retrieved from GeneCards and PubMed. Protein-protein interaction (PPI) network construction and machine learning algorithms were employed to identify hub genes. Findings were validated in vitro using KP-derived lipopolysaccharide (LPS)-stimulated human umbilical vein endothelial cells (HUVECs) and in vivo using a murine model of KP-induced ALI. The therapeutic potential of ADAM17 inhibition was evaluated using the pharmacological inhibitor TAPI-1.

Results Bioinformatic integration yielded 506 candidate genes, from which ADAM17 was identified as a central hub gene. Experimental validation confirmed that ADAM17 was significantly upregulated in both KP-infected lung tissues and LPS-stimulated HUVECs. In vitro, ADAM17 inhibition (TAPI-1) effectively rescued mitochondrial dysfunction, evidenced by

restored membrane potential and upregulated respiratory chain complex proteins (ATP5A, SDHB, NDUF8). Furthermore, TAPI-1 treatment suppressed excessive mitophagy (decreased LC3-II/I, Parkin, and PINK1; increased p62) and attenuated GSDMD-mediated pyroptosis. Mechanistically, these protective effects were mediated by the suppression of the mtDNA-cGAS-STING signaling axis. In vivo, TAPI-1 administration significantly ameliorated lung histopathological damage, restored mitochondrial complex integrity, and inhibited pyroptotic cell death.

Conclusion Our study demonstrates that ADAM17 is a pivotal driver of mitochondrial dysfunction-triggered pyroptosis via the cGAS-STING pathway in KP-induced ALI. These findings characterize the ADAM17/cGAS-STING axis as a novel mechanistic link in the pathogenesis of ARDS and highlight ADAM17 as a promising therapeutic target.

Key words: *Klebsiella pneumoniae*; Acute lung injury; ADAM17; Mitochondrial dysfunction; Autophagy; Pyroptosis; cGAS-STING pathway

Bloodstream Infection Caused by *Mycobacterium Conceptionense* in A Patient with Synovial Sarcoma: A Case Report and Genomic Analysis

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Objective To report a rare case of bloodstream infection caused by *Mycobacterium conceptionense* in an immunocompromised patient, evaluate its clinical characteristics, diagnostic challenges, and molecular resistance mechanisms, and provide a reference for man-

aging rare non-tuberculous mycobacterial (NTM) infections in malignancy with chemotherapy

Methods A 23-year-old female patient with synovial sarcoma presented with persistent fever during postoperative chemotherapy. Blood cultures were performed using an automated system. The isolate was initially processed through Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF MS) and 16S rRNA gene sequencing. Due to the limitations of these methods in achieving species-level discrimination, Whole-Genome Sequencing (WGS) was subsequently employed for definitive pathogen identification and genomic characterization. Comprehensive bioinformatics analysis was conducted to identify antimicrobial resistance (AMR) genes. Antimicrobial susceptibility testing (AST) was performed using the microdilution method to determine the minimum inhibitory concentrations (MICs) and guide the selection of an individualized therapeutic regimen

Results The blood culture isolate was initially identified as *Mycobacterium fortuitum* complex by MALDI-TOF MS. Subsequent 16S rRNA gene sequencing failed to distinguish the species due to 100% sequence identity with both *M. farcinogenes* and *M. conceptionense*. Definite identification as *M. conceptionense* was eventually achieved through WGS. Genomic analysis revealed several critical antimicrobial resistance determinants, including an *rpoB* mutation associated with rifamycin resistance, the β -lactamase gene *blaF*, the tetracycline efflux pump gene *tap* along with its regulatory factor *mtrA*, and the *vanRO* gene implicated in glycopeptide resistance. Guided by the AST results, which showed sensitivity to multiple agents, an individualized multidrug regimen was implemented, consisting of intravenous amikacin and moxifloxacin, combined with oral clarithromycin and linezolid. The patient showed significant clinical improvement and recovered completely with no recurrence observed during

the follow-up period

Conclusion As the first documented case of *M. conceptionense* bloodstream infection in China, this study highlights the risk of rare NTM infections in immunosuppressed patients. WGS is essential for accurate pathogen identification and elucidating resistance mechanisms. Personalized multidrug therapy based on susceptibility testing remains crucial for achieving successful clinical outcomes

Keywords Non-tuberculous mycobacteria; *Mycobacterium conceptionense*; bloodstream infection; immunosuppression; synovial sarcoma; whole-genome sequencing

寡聚季铵脲拟肽的双重靶向抗菌机制

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目的 针对肺炎相关耐药菌治疗困难及传统季铵盐选择性差、易诱导耐受的问题,构建新型寡聚季铵脲拟肽,并评价其抗菌活性、选择性及作用机制。

方法 以苯扎溴铵为对照,设计合成系列寡聚季铵脲拟肽,并采用核磁共振(NMR)和凝胶渗透色谱(GPC)进行表征。测定其对肺炎克雷伯菌、鲍曼不动杆菌、铜绿假单胞菌及金黄色葡萄球菌等菌株的最低抑菌浓度(MIC);通过溶血、细胞毒性及细菌/细胞平行实验评价其选择性;采用连续传代观察耐受发展,并结合膜通透性、荧光共定位、DNA凝胶阻滞、PI-DNA竞争及DNA rescue实验分析机制;进一步通过动物感染模型和慢性毒性实验评价其体内效果。

结果 筛选获得目标分子B-1,3。其对肺炎克雷伯菌、鲍曼不动杆菌和铜绿假单胞菌的MIC分别为

8、4 和 8 $\mu\text{g/mL}$ ，对金黄色葡萄球菌的 MIC 为 2 $\mu\text{g/mL}$ ，整体活性优于苯扎溴铵。与苯扎溴铵相比，B-1,3 能够优先作用于细菌膜，而对红细胞及哺乳动物细胞膜影响较小，溶血性和细胞毒性明显降低，且耐受发展更慢。荧光共定位及 DNA 相关实验表明，B-1,3 可进一步进入细菌并靶向 DNA，而苯扎溴铵主要局限于细胞膜。动物实验显示，B-1,3 能够降低感染组织细菌负荷，且长期给药未见明显毒性。

结论 寡聚季铵脲拟肽 B-1,3 是一类兼具高细菌选择性、低耐受风险及膜-DNA 双重靶向机制的新型抗菌分子，可为肺炎相关耐药菌的治疗提供新的候选药物。

临床药师主导的三唑类抗真菌药物个体化治疗管理模式 —— 基于真实事件数据的干预效果评价

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目的 构建并评价以临床药师为核心的三唑类抗真菌药物（伏立康唑、泊沙康唑、艾沙康唑）个体化治疗管理路径，基于真实世界数据系统评估药学干预合理用药指标、血药浓度达标率及药物安全性结局的影响，为抗真菌药物管理提供循证依据参考。

方法 研究采用自身前-后对照的回顾性队列研究设计，纳入 2022 年 1 月至 2023 年 12 月我院使用三唑类抗真菌药物的住院患者。干预组（ $n=156$ ）选取接受临床药师系统化药学服务，包括

基于治疗药物监测（TDM）的伏立康唑剂量个体化（目标谷浓度 1.0 -5.0 mg/L ）、泊沙康唑剂量个体化（目标谷浓度 $>1.0 \text{ mg/L}$ ）、艾沙康唑剂量个体化（目标谷浓度 2.0 -5.0 mg/L ）；

利用 Lexicomp 与 Micromedex 数据库进行药物相互作用（DDI）前瞻性筛查与风险分级；

针对肝功能不全、儿童、老年等特殊人群建立

剂量调整算法（如 Child-Pugh C 级患者伏立康唑维持剂量减至标准剂量的 50%）；

采用 Naranjo 量表进行不良反应因果关系评估及预警。

对照组（ $n=156$ ）为干预前同期接受常规医疗模式的患者。主要结局指标为首次 TDM 达标率；次要指标包括 DDI 预警率、不良反应发生率、医师方案采纳率及临床治愈率。采用倾向性评分匹配控制混杂因素，SPSS 26.0 进行 χ^2 检验与 Logistic 回归分析。

结果 干预组首次血药浓度达标率为 94.23%，显著高于对照组的 81.41%。临床药师共识别并干预高预警级 16 例，其中泊沙康唑-维奈克拉致神经毒性风险 2 例，伏立康唑-头孢哌酮舒巴坦致双硫仑样反应 5 例，伏立康唑-他克莫司致肾毒性风险 5 例，干预后方案调整率 100%，相关不良反应发生率由于干预前的 16.66% 降至 4.49%。特殊人群（肝功能不全、儿童）剂量初始合理率从 56.52% 升至 78.26%。临床医师对药师建议的总体采纳率为 96.80%。干预组临床治愈率与不良反应可防可控率均显著改善。

结论 以临床药师为主导、TDM 与 DDI 前瞻性评估为技术核心的三唑类抗真菌药物管理模式，能显著提升药物暴露达标率、降低可预防性药物伤害并改善临床结局。建议将该模式纳入医疗机构抗菌药物管理（AMS）体系，并开展多中心前瞻性研究验证其普适性。

关键词：临床药师；三唑类抗真菌药物；TDM；真实世界研究；个体化治疗

Targeting LasR with Amiselimod Suppresses Quorum Sensing and Virulence in *Pseudomonas Aeruginosa*

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Objectives To investigate whether Amiselimod could be repurposed as an antivirulence agent against *Pseudomonas aeruginosa* and to elucidate the underlying mechanism by which it attenuates bacterial virulence

Methods Amiselimod was screened for antivirulence activity against *P. aeruginosa* by assessing quorum sensing-associated phenotypes and virulence factor production. Its mechanism of action was investigated by transcriptional analysis of LasR-regulated genes, protein analysis of representative virulence factors, and electrophoretic mobility shift assays to evaluate the effect of Amiselimod on LasR-DNA binding. The role of LasR was further examined using a lasR deletion mutant and a complemented strain. A mouse pneumonia model was used to assess the in vivo antivirulence effect of Amiselimod

Results Amiselimod markedly attenuated the virulence of *P. aeruginosa* through its effects on LasR. At antivirulence-active concentrations, Amiselimod reduced pyocyanin production, elastase activity, and biofilm formation without substantially affecting bacterial growth. Electrophoretic mobility shift assays showed that Amiselimod inhibited the interaction of LasR with target promoter DNA in a dose-dependent manner. Consistently, treatment with Amiselimod decreased the mRNA levels of LasR-regulated genes, including lasB, lasI, rhlA, and pqsA, and reduced the expression of downstream virulence-associated proteins. Analysis in the wild-type strain, Δ lasR mutant, and complemented strain indicated that the inhibitory effect of Amiselimod on virulence gene expression was primarily LasR-dependent. In a mouse pneumonia model, Amiselimod significantly attenuated *P. aeruginosa* pathogenicity and alleviated lung injury

Conclusions Amiselimod suppresses *P. aeruginosa* virulence by interfering with LasR-mediated

transcriptional regulation and reducing downstream virulence factor expression. These findings identify Amiselimod as a promising repurposed antivirulence candidate for the treatment of *P. aeruginosa* infections

支气管扩张患者铜绿假单胞菌与豚鼠耳炎诺卡菌混合感染的病原及适应性特征

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背景 慢性支气管扩张患者易形成复杂的呼吸道感染微生态。诺卡菌是一种机会性致病的革兰阳性放线菌，在慢性支气管扩张患者中可与铜绿假单胞菌形成混合感染。然而混合感染的铜绿假单胞菌与诺卡菌在体内如何产生适应性变化仍未知。

方法 本研究的铜绿假单胞菌 HSL-PA 和豚鼠耳炎诺卡菌 (*Nocardia otitidiscaviarum*) HSL-N 分离自一位 68 岁男性支气管扩张伴多病原反复感染患者。研究采用 E-test 和纸片扩散法检测两株菌的抗菌药物敏感性，并结合基因组测序分析其耐药、毒力、基因突变和慢性感染适应特征。

结果 铜绿假单胞菌 HSL-PA 呈黏液表型，具有多药耐药表型，对妥布霉素、阿米卡星、多黏菌素 B、亚胺培南/瑞来巴坦、头孢他啶/阿维巴坦和头孢洛生/他唑巴坦敏感。豚鼠耳炎诺卡菌 HSL-N 对甲氧苄啶/磺胺甲噁唑、利奈唑胺、妥布霉素和阿米卡星敏感。基因组分析显示，HSL-PA 属于 ST244 型，是 mutS 发生无义突变的超变株，存在生物膜形成、表面抗原重塑及铁摄取系统重编程等宿主适应性基因突变；存在多药外排系统，PDC-374 和 OXA-847 β -内酰胺酶及外膜孔蛋白 oprD 提前终止突变。豚鼠耳炎诺卡菌 HSL-N 生长缓慢，存在 β -内酰胺酶 AST-1、vanS/vanR 等耐药相关基因，存在细胞壁结构、

转运系统和氧化还原代谢等基因突变。

结论 本病例分离的混合感染细菌铜绿假单胞菌和豚鼠耳炎诺卡菌呈现多重耐药及宿主适应性。铜绿假单胞菌通过黏液样转化、生物膜形成和代谢适应增强其在气道中的长期滞留能力；诺卡菌通过缓慢生长和复杂细胞壁结构对环境产生较强耐受性。两者在体内相互作用复杂，给患者治疗带来困难。

关键词：多重耐药铜绿假单胞菌；豚鼠耳炎诺卡菌；混合感染；支气管扩张；多药耐药；黏液样表型

Butyrate Protects Against *Klebsiella Pneumoniae*-induced Oxidative Stress in Alveolar Macrophages Via P62-Keap1-Nrf2 Pathway

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Klebsiella pneumoniae (*K. pneumoniae*)-induced pneumonia poses growing clinical challenges due to the emergence of hypervirulent and carbapenem-resistant strains. Butyrate contributes to antibacterial immunity while its role in pulmonary infections remains poorly understood. Here, we showed that *K. pneumoniae* infection caused alveolar macrophage depletion and concomitant inflammatory tissue damage, while butyrate administration preserved alveolar macrophage populations and attenuated pulmonary damage. Mechanistically, butyrate upregulated both the expression and phosphorylation of p62, and regulated the Keap1-Nrf2 signaling pathway to counter oxidative stress. Moreover, we demonstrated that *K. pneumoniae* infection triggered oxidative stress injury in critically ill pneumonia patients. Circulating monocytes exhibited elevated lev-

els of 4-hydroxynonenal (4-HNE), a marker of oxidative stress, along with downregulated mRNA levels of SQSTM1 and NRF2, which were inversely correlated with 4-HNE levels. These findings establish butyrate as a dual modulator of the p62-Nrf2 antioxidant axis, highlighting its therapeutic potential for mitigating oxidative stress in *K. pneumoniae*-associated pneumonia.

Mechanism of Gut Microbiota Dysbiosis Inducing Neuronal Death and Exacerbating *Klebsiella Pneumoniae* Meningitis

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Objective In recent years, the clinical incidence of *Klebsiella pneumoniae* (KP) meningitis has increased annually. This study explores the "microbiota-gut-brain axis". We aim to elucidate the core mechanism by which acute-phase gut microbiota dysbiosis exacerbates secondary central nervous system (CNS) injury. Furthermore, we explore novel adjuvant interventions targeting intestinal homeostasis

Methods A mouse model of gut microbiota depletion was established. We used continuous broad-spectrum antibiotics (ABX) in drinking water. A severe meningitis model was then created. KP was injected into the lateral ventricle using a stereotaxic apparatus. Biological samples were collected for metagenomic and high-throughput metabolomic sequencing. We screened

core bacterial genera and key metabolites significantly altered under the dual stress of infection and ABX. We assessed oxidative stress networks, lipid metabolism abnormalities, and the activation of a novel programmed cell death pathway. In the ABX+KP model, we performed targeted exogenous supplementation of key microbial metabolites and fecal microbiota transplantation (FMT). Finally, we observed neuroprotective and phenotypic rescue effects

Results ABX-pretreated mice showed significantly accelerated disease progression after severe infection compared to the infection-only group. Blood-brain barrier disruption and brain edema progressively worsened. Consequently, the lethality rate rose sharply. Multi-omics analysis revealed a critical loss. ABX completely eradicated core commensals, represented by specific beneficial bacteria. As a result, key metabolite concentrations in circulation and brain tissue dropped precipitously. Mechanistic sequencing revealed further insights. The lack of specific gut-derived metabolites directly deprived the brain of "metabolic resilience" against extreme oxidative stress. Under KP infection, severe free radical accumulation and amino acid metabolic imbalance erupted in the cortex. This triggered abnormal cross-linking and structural collapse of neuronal microfilament cytoskeletal proteins. Ultimately, this activated a novel non-classical programmed cell death. We prophylactically supplemented specific metabolites or performed FMT in microbiota-depleted mice. These treatments neutralized abnormal brain stress signals across the blood-brain barrier

Conclusion The high lethality of KP meningitis depends on the direct strike of a high initial bacterial load. However, it also correlates closely with the collapse of the host gut microbiota-mediated "defensive baseline." Specific gut commensals and derived metabolites serve as critical barriers. They maintain CNS redox homeostasis. This study reveals a new mechanism

where antibiotics disrupt the microecology and exacerbate CNS infections

Keywords *Klebsiella pneumoniae* meningitis; Gut microbiota dysbiosis; Reactive oxygen species (ROS); Microbiota-gut-brain axis

耐碳青霉烯高毒力肺炎克雷伯菌通过重塑肺泡巨噬细胞衣康酸代谢与 ARG1 表达介导肺部炎症损伤的机制研究

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目的 耐碳青霉烯高毒力肺炎克雷伯菌 (CR-hvKP) 是重症细菌性肺炎的重要病原体, 其高毒力表型所致肺部炎症损伤与宿主免疫代谢紊乱密切相关, 但具体机制尚未明确。衣康酸是巨噬细胞免疫代谢重编程的重要代谢物, ARG1 参与维持肺泡巨噬细胞 M2 型修复表型及肺部炎症稳态。本研究拟比较 CR-hvKP 与普通耐碳青霉烯肺炎克雷伯菌 (CR-KP) 感染状态下衣康酸代谢及 ARG1 表达差异, 探讨其调控肺泡巨噬细胞极化并介导肺部炎症损伤的机制。

方法 构建 CR-hvKP 与 CR-KP 小鼠肺部感染模型, 比较肺组织病理损伤及炎性细胞浸润程度; 采用代谢组学检测衣康酸丰度, 结合 qRT-PCR、Western blot、ELISA 及流式细胞术检测 IRG-1、ARG1、M1/M2 极化标志物及炎症因子表达; 进一步建立体外肺泡巨噬细胞感染及 4-OI 干预模型, 评价衣康酸衍生物对巨噬细胞吞噬功能和 iNOS 表达的影响, 并结合转录组分析筛选相关炎症及代谢通路。

结果 与 CR-KP 组相比, CR-hvKP 感染小鼠肺组织炎性细胞浸润和病理损伤程度加重。代谢组学结果显示, CR-hvKP 组衣康酸丰度显著高于 CR-KP 组, 提示 CR-hvKP 感染可诱导衣康酸异常蓄积。分

子检测显示,CR-hvKP 组 IRG-1 蛋白及 mRNA 水平低于 CR-KP 组,提示 CR-hvKP 感染可能引起 IRG-1/衣康酸代谢轴的异常重塑。CR-hvKP 组同时表现为 ARG1 表达降低、M1 型极化标志物及促炎因子表达增强。体外实验显示,4-OI 处理可显著提高巨噬细胞对 FITC 标记肺炎克雷伯菌的吞噬比例,并增加 F4/80⁺巨噬细胞中 iNOS 阳性细胞比例,提示衣康酸信号可能参与调控巨噬细胞吞噬功能及 M1 样抗菌/炎症表型。进一步分析显示,衣康酸水平与 M1 型极化及肺部炎症损伤呈正相关,ARG1 表达与 M2 型极化呈正相关,并与 M1 活化及组织损伤呈负相关。

结论 CR-hvKP 感染可通过诱导衣康酸异常蓄积并抑制 ARG1 表达,促进肺泡巨噬细胞向 iNOS⁺M1 样抗菌/炎症表型偏移,减弱 M2 型修复性极化,进而放大肺部炎症反应并加重组织损伤。衣康酸代谢重塑与 ARG1 表达失衡可能是 CR-hvKP 高毒力致病的重要宿主机制,可作为重症肺炎宿主靶向干预研究的潜在分子靶点。

关键词: 耐碳青霉烯高毒力肺炎克雷伯菌;衣康酸;肺泡巨噬细胞极化;肺部炎症损伤

1 例影像学以肺空洞为主的惠普尔养障体合并烟曲霉感染的诊疗分析

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目的 惠普尔养障体(*Tropheryma whipplei*, TW)是罕见革兰阳性菌,可引发多系统受累的惠普尔病(WD),肺部受累少见;烟曲霉是侵袭性真菌感染中最常见的致病病原体之一。两者同时累及同一患者肺部并形成空洞性病变时诊疗难度极高。本文结合临床实践及文献,探讨其临床特征、诊断难点及个体化诊疗策略,提高临床识别与规范化诊疗水平。

方法 回顾性分析南宁市第一人民医院感染性

疾病科经靶向二代测序(tNGS)确诊的 1 例 TW 合并烟曲霉感染患者的临床资料,总结其临床表现、实验室检查结果及影像学特征,结合支气管肺泡灌洗液(BALF) tNGS 结果,分析联合抗感染方案的制定依据及疗效。

结果 患者为 67 岁女性,因“发现血糖升高 10 年,头晕、乏力半天”于 2025 年 12 月 4 日入院,胸部 CT 提示右肺空洞性感染(疑诊空洞型肺结核),遂转入感染性疾病科,完善结核筛查均为阴性, BALF tNGS 检出烟曲霉(归一化序列数 493)及 TW(归一化序列数 513),结合当时临床评估,考虑 TW 为条件致病菌,仅明确诊断为曲霉菌性肺炎,予伏立康唑规范抗真菌治疗后于 2025 年 12 月 16 日好转出院。2025 年 12 月 21 日因“咳嗽咳痰 5 天,发热半天”再次入院,复查 CT 示右肺空洞影增大、炎症进展,再次行支气管镜采集 BALF 行 tNGS 及相关检查, tNGS 检出 TW(归一化序列数 310129),结合临床症状、影像学进展及病原学结果,修正诊断为 TW 感染、曲霉菌性肺炎。诊疗方案调整为:在伏立康唑抗真菌治疗基础上,加用头孢曲松联合复方磺胺甲恶唑针对性抗 TW 治疗,同时强化血糖控制及对症支持治疗。治疗后患者临床症状缓解,肺部病灶逐渐吸收,炎症指标恢复正常,预后良好,出院后定期随访,未出现病情复发及药物相关不良反应。

结论 1. TW 合并烟曲霉肺部感染极罕见,临床表现隐匿复杂,易误诊漏诊; tNGS 技术在快速识别少见病原体及混合感染中具有重要价值。2. 糖尿病患者为高危人群,其肺部空洞性病变易误诊为肺结核,需提高鉴别警惕。3. 治疗需同时覆盖真菌与细菌,严格管理基础疾病。4. 抗真菌治疗无效时需重复病原学检查,警惕混合感染。本病例为免疫受损宿主复杂肺部感染诊疗提供实践参考。

关键词

惠普尔养障体;烟曲霉;混合感染;靶向二代测序

Antifungal Treatment Regimens As Primary Therapy for Invasive Aspergillosis: A Systematic Review and Network Meta-analysis

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Background Invasive aspergillosis (IA) is an invasive fungal disease associated with high mortality. Triazoles are the primary therapy for IA, while amphotericin B, echinocandins, and antifungal combined therapy are commonly considered as alternative treatment options although their efficacy and safety remain subjects of debate. We employed Bayesian network meta-analysis (NMA) to synthesize evidence and evaluate the efficacy and safety of different primary antifungal treatment regimens for IA

Methods A literature search was done in PubMed, EMBASE, Cochrane, and Web of Science databases for clinical studies on primary treatment for patients with IA published before 28 March 2024. We included randomized controlled trials (RCTs) and cohort studies involving patients with proven or probable IA who underwent primary treatment. The primary treatment regimens comprised different types or dosages of monotherapy or combination therapy involving triazoles, echinocandins, and amphotericin B. The primary outcome was cumulative all-cause mortality. Secondary outcomes included all-cause mortality at day 42, day 84, or end of treatment (EOT); the overall response at day 42, day 84, or EOT; invasive aspergillosis-associated mortality on day 42, day 84, and EOT; the incidence of adverse events (AEs), serious adverse events (SAEs), and treatment-related AEs; and treatment discontinuation due to AEs.

Results The primary network meta-analysis for

cumulative all-cause mortality (5 RCTs, 6 regimens, $n = 1293$) revealed no statistically significant differences among treatment regimens compared with voriconazole (VOR; surface under the cumulative ranking curve [SUCRA] 56.3%), including VOR combined with anidulafungin (ANI; risk ratio [RR] 0.74, 95% credible interval [CrI] 0.43-1.28; SUCRA 84.3%; moderate confidence), isavuconazole (ISA; RR 0.79, 95% CrI 0.45-1.40; 79.4%; moderate confidence), and posaconazole (POS; RR 1.20, 95% CrI 0.72-2.02; 34.6%; moderate confidence). Sensitivity analyses confirmed the robustness of these findings. Regarding safety, no significant differences were observed in SAEs for ISA (RR 0.91, 95% CrI 0.75-1.11; 85.7%; moderate confidence), POS (RR 1.03, 95% CrI 0.87-1.23; 40.8%; low confidence), and VOR combined with ANI (RR 1.09, 95% CrI 0.88-1.36; 20.8%; moderate confidence) compared with VOR (52.6%). Integrated efficacy-safety analysis suggested a favorable risk-benefit profile for isavuconazole.

Conclusion ISA, POS, and VOR are the preferred antifungal agents for primary treatment of IA, with ISA demonstrating a higher likelihood of an optimal efficacy-safety balance. The combination of VOR and ANI may be considered for a subset of severe cases.

一例合并耶氏肺孢子菌感染的惠普尔养障体肺炎疑诊患者的诊治及文献分析

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目的 惠普尔养障体感染所致疾病临床罕见, 以系统性受累为主要特征, 单纯累及肺部形成惠普尔养障体肺炎的病例更为少见, 临床诊断难度大, 易出现漏诊、误诊, 且目前相关治疗经验有限。本文旨在报道 1 例经肺泡灌洗液宏基因组测序(mNGS)

技术检出惠普尔养障体肺炎的罕见病例，系统总结其临床诊疗全过程及核心经验，为临床医师诊治罕见病原体所致肺部感染提供可靠的参考依据，减少漏诊误诊率，优化治疗方案选择。

方法 回顾性收集该例患者的完整临床资料，包括一般人口学信息、主诉、现病史、既往史、体格检查结果，以及胸部影像学检查、血常规、炎症标志物、病原学检查（含肺泡灌洗液 mNGS）等实验室检查数据，详细梳理患者的诊疗经过、药物使用情况及病情变化。同时检索近年国内外关于惠普尔养障体肺炎的相关文献，结合文献报道的病例特点、诊断方法及治疗方案，对本例患者的诊断依据、治疗药物选择合理性，以及出现药物耐受性不佳时的方案调整思路进行深入分析，提出针对性的治疗建议，并对患者开展规范的用药教育，确保治疗依从性。

结果 该例患者经临床症状、影像学表现及肺泡灌洗液 mNGS 检测结果，疑似诊断为惠普尔养障体肺炎伴耶氏肺孢子菌（定植/感染）。初始给予磺胺类药物（复方磺胺甲噁唑）抗感染治疗后，患者出现明显药物不耐受表现，经综合评估后调整为静脉输注头孢曲松抗感染治疗，同时给予对症支持治疗及用药指导，患者临床症状逐渐缓解，炎症标志物水平下降，影像学检查提示肺部病变较前吸收，病情逐步好转并顺利出院，随访期间未出现病情反复及严重不良反应。

结论 惠普尔养障体肺炎作为临床罕见的肺部感染性疾病，缺乏典型的临床症状及特异性体征，mNGS 技术具有高通量、高灵敏度的优势，可快速检出病原体，为该病的早期明确诊断提供重要助力。目前临床治疗惠普尔养障体肺炎的方案中，磺胺类药物、多西环素联合羟氯喹是应用经验相对较多的两种方案，但部分患者可能出现药物耐受性不佳的情况，导致该类方案临床使用受限。此时，结合患者病情及药物耐受情况，酌情调整为静脉用头孢曲松等替代治疗方案，同时加强对症支持治疗及用药监测，也可达到良好的治疗效果，改善患者预后。临床医师应提高对该病的认识，对于不明原因肺部感染

且常规治疗效果不佳的患者，可及时采用 mNGS 技术明确病原学诊断，合理选择治疗方案并根据患者耐受情况灵活调整，以提升诊疗效果。

关键词：惠普尔养障体；肺炎；抗感染治疗；磺胺

犬尿喹啉酸通过 GPR35 促进巨噬细胞募集缓解脓毒症的机制研究

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目的 本研究旨在探究外周血单核细胞向感染部位募集的分子机制，阐明 G 蛋白偶联受体 35（GPR35）及其配体犬尿喹啉酸（KYNA）在脓毒症中的关键作用。

方法 收集脓毒症休克患者外周血，检测单核细胞 GPR35 表达量及血浆 KYNA 浓度；建立盲肠结扎穿孔（CLP）小鼠模型，给予 KYNA 治疗，观察小鼠生存率、器官损伤、细菌负荷及促炎因子水平；构建 GPR35 敲除（Gpr35^{-/-}）小鼠验证 KYNA 的靶向性；通过体外实验探讨 KYNA-GPR35 信号轴在巨噬细胞 M2 表型转化中的作用；分离人外周血单核细胞，检测 KYNA 对其细胞因子 TNF- α 、IL-1 β 、IL-6、IL-10 分泌的影响。

结果 外周血单核细胞向感染部位的募集在调控脓毒症诱发的炎症反应中发挥关键作用。然而，介导其从外周血向感染部位迁移的机制尚未阐明。这里，我们证实 GPR35 是脓毒症炎症调控的免疫靶点，介导循环 Cx3cr1⁺单核细胞向感染部位募集。脓毒症休克患者外周血单核细胞 GPR35 表达降低，伴随外周血血浆中 KYNA 含量降低。我们的结果表明，补充 KYNA 可以降低 CLP 小鼠死亡率、缓解多器官损伤、减少细菌负荷，并抑制促炎细胞因子 TNF-

α , IL-1 β 和 IL-6 的表达。机制上, 我们证实补充 KYNA 可以促进腹腔 Cx3cr1+单核细胞源性巨噬细胞招募并促进巨噬细胞 M2 样极化。此外, GPR35 敲除后补充 KYNA 腹腔 M2 样巨噬细胞占比较 WT 组减少, 小鼠死亡率升高。最后, 我们分离人外周血单核细胞, 证实 KYNA 可抑制促炎细胞因子 TNF- α , IL-1 β 和 IL-6 分泌, 并增强 IL-10 的产生。

结论 我们的研究结果揭示 KYNA 通过 GPR35 募集 Cx3cr1+巨噬细胞至感染部位在脓毒症炎症调控中的关键作用, 未来作为一个脓毒症治疗的新兴免疫靶点。关键词: 脓毒症; GPR35; KYNA; Cx3cr1+巨噬细胞

Antimicrobial Activity of Zosurabalpin Against *Acinetobacter Baumannii-calcoaceticus* Complex Clinical Isolates in China

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Background *A. baumannii-calcoaceticus* complex (ABC) organisms, a major cause of invasive infections in hospitalized patients, pose a significant threat to global public health. Zosurabalpin, a novel tethered macrocyclic peptide antibiotic, offers a breakthrough by inhibiting the LptB2FGC-dependent transport of lipopolysaccharide (LPS) and shows a promising therapeutic option for ABC organisms, especially for carbapenem-resistant ABC (CRABC). In this study, the activity of zosurabalpin was evaluated against 205 Chinese ABC clinical isolates (including 185 *A. baumannii*, 7 *A. nosocomialis*, and 13 *A. pittii*)

Materials and methods Isolates were collected from 32 hospitals in 24 provinces, municipalities, and autonomous regions in China during 2023-2024. The

minimum inhibitory concentration (MIC) was determined using the broth microdilution method according to Clinical and Laboratory Standards Institute (CLSI) guidelines, and the results were interpreted according to the CLSI standard 2024 M100 34th edition. Zosurabalpin was tested in CAMHB with or without 10% or 20% heat-inactivated horse serum (HIHoS).

Results Zosurabalpin was active against all ABC isolates (Table 1). When tested in CAMHB and considering the MIC100% (MIC read at complete inhibition of growth) and MICSR (MIC read at substantial reduction of growth), zosurabalpin MIC50/MIC90 values were 0.25/>16 mg/L and 0.125/0.25 mg/L, respectively. For zosurabalpin tested in CAMHB with 10% and 20% HIHoS the MIC50/MIC90 values were 0.125/0.25 mg/L in both conditions. Among comparators, sulbactam-durlobactam, colistin, and tigecycline were the most active agents with susceptibility rates over 90%. Zosurabalpin shows antibacterial activity against a subset of 154 CRABC isolates. When tested in CAMHB and considering the MIC100% and MICSR, zosurabalpin MIC50/MIC90 values were 0.25/0.5 mg/L and 0.125/0.25 mg/L, respectively. In CAMHB with 10% and 20% HIHoS, zosurabalpin MIC50/MIC90 values were 0.125/0.25 mg/L and 0.25/0.5 mg/L, respectively.

Conclusion Zosurabalpin shows potent activity against ABC complex isolates, particularly against CRABC isolates.

肠道菌群通过 GZMK 调控肺部免疫参与肺炎克雷伯菌与铜绿假单胞菌混合感染的机制研究

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目的 肺炎克雷伯菌 (CRKP) 所致肺部感染临床治疗困难, 而合并铜绿假单胞菌 (PA) 混合感染时常提示病情更重、预后更差。本研究结合临床病例分析与动物实验, 探讨肠道菌群通过“肠-肺轴”调控肺部抗感染免疫的作用, 重点分析颗粒酶 K (GZMK) 在 CRKP 与 PA 混合感染中的潜在保护功能及其免疫学机制。

方法 回顾性收集 2019—2023 年安徽医科大学第一附属医院 CRKP 肺炎患者临床资料, 比较 CRKP 单一感染与 CRKP 合并 PA 混合感染患者的预后差异。采用临床分离菌株建立小鼠 CRKP 与 PA 混合感染模型, 通过广谱抗生素 (ABX) 处理构建肠道菌群耗竭模型, 并通过粪菌移植 (FMT) 进行干预。采用肺组织病理学评价炎症损伤程度; 通过肺组织转录组测序筛选受肠道菌群调控的差异基因; 结合 Western Blot、免疫荧光 (IF) 及流式细胞术分析 GZMK 表达水平及其细胞来源; 并通过外源性重组 GZMK 蛋白补充实验进行体内功能验证。

结果 临床资料显示, CRKP+PA 混合感染组较单一感染组住院时间显著延长 (49 天 vs 26 天, $P<0.001$), 死亡率显著升高 (35.8% vs 19.4%, $P=0.045$), 提示混合感染具有更高临床危害性。动物实验表明, 肠道菌群耗竭后, 小鼠在 CRKP 与 PA 混合感染中的肺部炎症损伤明显加重, 而 FMT 干预可部分逆转该表型。肺组织转录组学分析显示, GzmK 表达受肠道菌群显著调控, 在菌群耗竭状态下明显降低, FMT 后恢复上调。Western Blot 和 Elisa 结果进一步证实, 菌群耗竭条件下肺部感染过程中 GZMK 蛋白无法被有效诱导表达。免疫荧光及流式细胞术结果提示, GZMK 主要来源于肺部特定免疫细胞群。

结论 本研究提示, CRKP 与 PA 混合感染较单一感染具有更严重的临床结局; 肠道菌群可通过调控肺部 GZMK 表达参与抗感染免疫, 并在混合感染中发挥重要保护作用。该结果为理解肠-肺轴在细菌混合感染中的免疫调控机制提供了新的实验依据, 也提示肠道菌群干预及 GZMK 相关通路可能成为改善重症细菌性肺炎预后的潜在策略。

关键词: 肠道菌群; 肠-肺轴; GZMK; 肺炎克雷伯菌; 铜绿假单胞菌; 混合感染

Eravacycline Monotherapy and Combination Therapy Against KPC-2- and NDM-1-Co-producing *Klebsiella Pneumoniae*: In Vitro and In Vivo Activity Analysis

null null

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Background The emergence of carbapenem-resistant *Klebsiella pneumoniae* (CRKP) co-producing KPC-2 and NDM-1 (K2N1-CRKP) has intensified a major public health threat and severely limited therapeutic options. Eravacycline, a novel tetracycline, shows potent in vitro activity against carbapenem-resistant Enterobacteriaceae. However, its efficacy and synergistic potential against K2N1-CRKP remain unclear

Methods We analyzed the molecular epidemiology of 42 K2N1-CRKP strains and evaluated their susceptibility to eravacycline. The in vitro and in vivo (using a *G. mellonella* model) synergistic effects of eravacycline combined with other antibiotics were determined.

Results All 42 strains belonged to ST11. Among them, 92.8% (39/42) were susceptible to eravacycline (MIC_{50/90}: 1 µg/mL; range: 0.5–2 µg/mL). Two strains (KP17, KP18) were resistant to both eravacycline and polymyxin B. The eravacycline-polymyxin B combination showed synergistic activity against 9.5% (4/42) of isolates, including the two dual-resistant strains. Additive effects were observed for eravacycline combined with ceftazidime-avibactam (28.6%), meropenem

(14.3%), or amikacin (45.2%). Time-kill assays confirmed the rapid, sustained bactericidal activity of the eravacycline-polymyxin B combination against K2N1-CRKP. In the *G. mellonella* infection model, this combination provided a significantly superior survival benefit compared to monotherapy.

Conclusion Eravacycline demonstrates potent in vitro activity against ST11 K2N1-CRKP. While combinations with ceftazidime-avibactam, amikacin, or meropenem showed only additive effects, eravacycline plus polymyxin B exhibited strong synergistic and bactericidal activity both in vitro and in vivo, even against strains resistant to either agent alone. This regimen represents a promising evidence-based therapeutic option for these formidable infections.

基于肺泡巨噬细胞的细菌性肺炎预后评估及生物治疗体系研究

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目的 多耐药肺炎克雷伯菌及鲍曼不动杆菌是临床治疗的难题, 抗生素以外的免疫及生物治疗方案是未来研究方向之一。本研究探巨噬细胞亚群异常同细菌性肺炎预后的关系, 并评估补充或调控肺泡巨噬细胞治疗细菌性肺炎的潜力与安全性。

方法 收集肺炎克雷伯菌及鲍曼不动杆菌所致不同严重程度肺炎患者的肺泡灌洗液, 通过单细胞测序及流式细胞术分析肺泡巨噬细胞亚群数量变化同炎症水平、感染严重程度及预后的关系。构建肺炎克雷伯菌感染的小鼠模型, 探究回输组织驻留肺泡巨噬细胞或补充特定细胞因子及脂质介质, 评估其对细菌性肺炎的生物治疗作用。

结果 重症细菌性肺炎患者肺内组织驻留肺泡巨噬细胞数量显著减少, 其减少幅度与感染严重程度呈正相关; 组织驻留肺泡巨噬细胞与炎性单核/巨噬细胞的比值可有效反映局部炎症水平、感染程度及临床预后。小鼠模型证实体内补充肺泡巨噬细胞可加速炎症消退, 减轻疾病严重程度; 肺内给药的方式给予重组 TGF- β 及脂质介质 RvD1 可通过靶向巨噬细胞发挥保护效应, 且不增加肺纤维化的风险。

结论 组织驻留肺泡巨噬细胞同炎性单核/巨噬细胞的数量关系可预策细菌性肺炎的预后。细胞补充治疗、TGF- β 及脂质介质靶向干预可安全有效地促进该细胞群体重建、抑制过度炎症应答, 为细菌性肺炎的辅助治疗提供新策略。

艾滋病患者脑脊液隐球菌荚膜抗原滴度变化趋势与临床转归相关性研究

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目的 探讨艾滋病(AIDS)合并隐球菌性脑膜炎(CM)患者脑脊液隐球菌荚膜抗原(CSF-CrAg)滴度的动态轨迹与临床转归的关联。

方法 回顾性分析 2017 年 1 月 1 日至 2024 年 12 月 31 日期间广州医科大学附属市八医院感染病中心收治的 75 例 AIDS 合并 CM 患者的临床资料, 依据第 24 周内患者是否出现死亡或失能分为预后良好及预后不良组, 根据 CSF-CrAg 滴度的下降幅度不同, 将患者分为滴度维持组与滴度下降组, 分析脑脊液隐球菌荚膜抗原滴度与临床转归相关性。

结果 本研究纳入 65 例预后良好患者及 10 例预后不良患者。预后不良组重型临床分型比例较高(90.00% vs. 47.69%, $P < 0.05$), 且基线脑脊液压力水平(mmHg)中位数高于预后良好组(330 vs. 223,

$P < 0.05$)。治疗后预后良好组 CSF-CrAg 滴度呈逐步下降趋势, 8 周及 12 周滴度差明显大于预后不良组 ($P < 0.05$)。但人口学特征、ART 及抗真菌方案、基线 HIV 病载水平及 CD4+T 细胞计数差异无统计学意义 ($P > 0.05$)。混合线性模型分析显示, 患者的整体 CSF-CrAg 滴度在随访期间呈缓慢下降趋势, 平均每周下降 $\log_2$ 值 0.096 ($P < 0.001$)。根据患者个体滴度下降斜率是否大于整体斜率中位数分为 2 组, 33 例属于滴度维持组, 42 例属于滴度下降组患者中, 前组 24 例 (72.73%) 预后良好, 9 例 (27.27%) 预后不良, 后组 41 例 (98.29%) 预后良好, 1 例 (2.38%) 预后不良, 前者的预后不良比率明显高于后者 ($\chi^2 = 7.872$, $P = 0.005$)。

结论 AIDS 合并 CM 患者经抗真菌治疗后 CSF-CrAg 滴度呈缓慢下降趋势, 且 CSF-CrAg 滴度维持不变与 24 周预后不良具有明显相关性, 尤其治疗 8 周后滴度仍为 1:320 提示可能出现不良预后。

Rhino-Orbital-Cerebral Mucormycosis in End-Stage Liver Disease: An MNGS-Guided Rapid Response Algorithm and "Surgical Window" Salvage Strategy

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Objective Rhino-Orbital-Cerebral Mucormycosis (ROCM) in End-Stage Liver Disease (ESLD) is highly lethal. While surgical debridement is mandatory for survival, severe coagulopathy often leads to "medical-only" therapy and fatal outcomes. This study aims to characterize ESLD-associated ROCM and validate an mNGS-guided Rapid Response Algorithm using a "surgical window" strategy.

Methods We analyzed 4 local cases and conducted a systematic review (PubMed/Web of Science, through Nov 2025), totaling a cohort of 24 patients. We compared the diagnostic efficiency (mNGS vs. traditional culture) and survival outcomes (medical-only vs. combined medical-surgical therapy).

Results Total mortality was 50.0% (12/24). Diagnostic Efficiency: mNGS identified *Rhizopus* species within 48 hours, significantly outperforming traditional culture in speed and sensitivity.

Therapeutic Outcomes: Absence of surgery was an independent predictor of mortality. In our local cohort, two patients managed conservatively died despite mNGS-guided antifungals. Conversely, Case 3 survived after intensive plasma exchange and coagulation factor replacement created a 12–24h "surgical window" (PTA > 50%), enabling successful salvage debridement.

Algorithm Construction: A "Three-Step Protocol" was developed: (i) Trigger: Immediate mNGS for any ESLD patient with orbital/facial signs; (ii) Confirmation: Rapid pathogen locking via mNGS; (iii) Intervention: Aggressive coagulation correction to create a "surgical window" for source control.

Conclusion Early mNGS diagnosis is critical but insufficient alone. Overcoming the "inoperable" dogma by creating a transient "surgical window" is essential for life-saving debridement in ESLD-associated ROCM.

Keywords ROCM; End-Stage Liver Disease; mNGS; Surgical Debridement; Coagulopathy

裂解性噬菌体联合亚抑菌浓度美罗培南协同治疗碳青霉烯耐药鲍曼不动杆菌感染的研究

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背景 碳青霉烯耐药鲍曼不动杆菌 (CRAB, Carbapenem-Resistant *Acinetobacter baumannii*) 引发的严重耐药问题, 使临床治疗面临巨大挑战, 亟需开发新型替代治疗策略。噬菌体疗法因具有高度宿主特异性、可特异性杀灭目标细菌而不破坏正常菌群、以及能在感染部位自我增殖等优势, 在应对多重耐药菌感染方面展现出广阔的应用前景。

方法 收集临床分离的碳青霉烯耐药鲍曼不动杆菌, 采用微量肉汤稀释法检测其对 β -内酰胺类、四环素类、喹诺酮类及氨基糖苷类等抗生素的敏感性。通过全基因组测序分析菌株的遗传背景及获得性耐药基因。以 CRAB 菌株为宿主, 从环境水样中分离特异性噬菌体, 利用双层琼脂平板法和透射电镜观察噬菌体形态并确定其分类学地位。进一步测定在噬菌体存在下, 宿主菌对抗生素敏感性变化, 并筛选出敏感性显著提升的抗生素, 用于分析噬菌体与抗生素联用对 CRAB 生长动力学、生物膜形成及感染模型治疗效果的影响, 以评估二者的协同抗菌作用。

结果 我们所收集的 CRAB 临床菌株均携带 OXA-23 型碳青霉烯酶基因, 以 ST2pas 型为主。除对黏菌素和替加环素外, 这些菌株对其他多类抗生素呈现多重耐药表型, 并具备强生物膜形成能力。以其中一株碳青霉烯酶 OXA-23 阳性、ST2 型 CRAB 为宿主, 成功分离获得一株裂解性短尾噬菌体。该噬菌体具有清晰的噬菌斑形态和典型的短尾噬菌体科形态特征, 对多株 ST2 型携带 OXA-23 的 CRAB 菌株均具有裂解活性, 且在其存在下, 这些菌株对美罗培南的敏感性显著增强。后续研究表明, 联合应用该噬菌体和亚抑菌浓度(亚 MIC)的美罗培南,

相较于单独使用噬菌体, 能更明显地抑制 CRAB 的生长与生物膜形成, 并有效减缓噬菌体抗性菌株的出现。在大蜡螟感染模型中, 该联合治疗方案较同浓度噬菌体单独应用, 显著降低了幼虫体内的细菌载量并提高了存活率, 展现出协同治疗优势。

结论 本研究以临床分离 CRAB 为宿主, 成功筛选出一株对多株 ST2 型 CRAB 均具裂解活性的烈性噬菌体。该噬菌体与亚 MIC 美罗培南联用, 在抑制生物膜形成、降低噬菌体抗性产生及提升感染存活率方面呈现协同效应, 为“噬菌体—抗生素”联合方案的优化提供了实验基础, 为耐药菌感染的替代治疗策略提供了有力的实验室依据。

Comparative between Eravacycline and Best Available Therapy in Carbapenem-resistant *Acinetobacter Baumannii* HAP/VAP in China: A Retrospective Real-world Multicenter Cohort Study

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Background Carbapenem-resistant *Acinetobacter baumannii* (CRAB) is a major cause of hospital- and ventilator-associated pneumonia (HAP/VAP) with limited treatment options. Eravacycline (ERA) shows potent in vitro activity and favorable pulmonary pharmacokinetics, but clinical evidence for CRAB HAP/VAP remains scarce. We evaluated the real-world effectiveness and safety of ERA

Methods We conducted a retrospective multicenter cohort study at 12 hospitals in China (April 2022-March 2024). Adults with microbiologically confirmed CRAB HAP/VAP treated with ERA or best available therapy (BAT) for ≥ 4 days were propensity scores matched. Primary outcomes were clinical success at end

of treatment (EOT) and 28-day mortality

Results After 3349 patients screened, 382 were included (ERA 204; BAT 178). Baseline characteristics were balanced. Clinical success at EOT was higher with ERA than BAT (63.2% vs 55.1%), while 28-day mortality was similar (40.1% vs 42.0%). ERA achieved higher microbiological eradication at EOT (45.1% vs 32.0%) and day 14 (36.8% vs 22.5%). Adverse events occurred less frequently with ERA. In targeted first-line treatment, ERA showed higher clinical success, greater microbiological eradication and faster clinical response without increased mortality

Conclusion Eravacycline improved microbiological clearance, clinical response, and safety compared with BAT for CRAB HAP/VAP, particularly when used as targeted first-line therapy

Study of Mechanism of Lung Persistent Infection of Variant Capsule-producing *Acinetobacter Baumannii* Induced by Wzc Mutation

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Background *Acinetobacter baumannii* (*A. baumannii*) is a clinically significant opportunistic pathogen, ranking second in isolation frequency from respiratory samples of hospitalized patients. It predominantly causes infections in immunocompromised or critically ill individuals, leading to severe complications and high mortality. Recent increases in clinical isolates exhibiting both high-level drug resistance and hypervirulence suggest evolutionary adaptations, though the mechanisms linking virulence and resistance remain unclear. Clinically derived hypervirulent, drug-resistant strains from

lower respiratory infections are characterized by thicker capsules and enhanced persistence in hosts, often associated with mutations in the capsule polysaccharide synthesis gene *wzc*. While *wzc* mutations are known to induce capsule variation and enhance immune evasion, the mechanisms by which these mutations enable *A. baumannii* to evade immune clearance during pulmonary infection require further investigation

Results Collected strains exhibited SNV <20, indicating in vivo evolution from a common ancestor. Capsule-related mutations in *wzc* (G539A, S550L, F631I) were identified (Fig. 2 a~c.). Evolved strains displayed thicker capsules, with Mut strains showing increased polysaccharide molecular weight and expression (Fig. 2 f~j.). The capsular features were reproduced in constructed point mutation strains (Fig. 3 a~c.). In murine models, Mut-infected mice exhibited significantly higher bacterial loads in lungs (days 3~4) compared to WT, with Mut strains persisting beyond day 5 (Fig. 3 d.). MICs remained unchanged in P0, but Mut strains exhibited antibiotic tolerance under pressure. The 11th-generation evolved strain (P11-Mut) showed accelerated growth and reduced susceptibility (MIC shift from sensitive to intermediate). In P15, the MIC of P15-Mut *wzc* S550L increased to resistant, and the MIC of P15-Mut *wzc* G539A also shifted from sensitive to intermediate (Table.1). Through the analysis using the Polymorphism Mode of breseq, it was discovered that during the in vivo evolution of the Mut strain, point mutations in the ribosome maturation-associated gene *rluD* and enrichment of mutations in the *rimA* gene, which is involved in ribosome assembly, were observed. Mut strains exhibited reduced adhesion/invasion in HBE cells but enhanced resistance to macrophage phagocytosis and intracellular survival. Mut-infected mice showed significantly lower survival rates (7 days model). WT strains caused high lethality in *G. mellonella* but minimal mortality in mice. BALF analysis revealed lower neutrophil recruitment

and CXCL1 levels in Mut-infected mice (Fig.4 a.). Histopathology indicated reduced inflammation in WT-infected lungs (Fig.4 b.). Membrane proteins MSR1 has been proved to preferentially bind WT capsule polysaccharides by CHO cell line (Fig.4 f., i.). scRNA-seq highlighted altered immune cell proportions (increased myeloid cells in Mut groups) and downregulated PRR-related genes (Msr1).

A Healthy Adult with Streptococcus Pneumoniae Infection Presenting Streptococcal Toxic Shock Syndrome and Purpura Fulminans: A Case Report and Literature Review

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Background Streptococcal toxic shock syndrome (STSS) is a severe invasive streptococcal infection characterized by refractory shock and multiple organ failure. Purpura fulminans (PF) is a rare life-threatening thrombotic complication typically seen in immunocompromised or asplenic patients. Streptococcus pneumoniae-induced STSS and PF in a fully immunocompetent adult is extremely rare

Case presentation A previously healthy 46-year-old male presented with fever, diarrhea, and vomiting, rapidly progressing to dyspnea, diffuse purpura, septic shock, disseminated intravascular coagulation (DIC), and multiple organ dysfunction. Blood culture and metagenomic next-generation sequencing (mNGS) confirmed Streptococcus pneumoniae. He received targeted antibiotics, organ support, staged anticoagulation, CRRT, mechanical ventilation, and surgical debridement. He survived with minor acral gangrene sequelae and was discharged.

Discussion STSS and PF are fulminant conditions with high mortality. This case highlights that invasive pneumococcal disease can cause STSS and PF even in healthy adults without splenic dysfunction or immunosuppression. Early recognition, mNGS for rapid pathogen identification, targeted antibiotics, haemodynamic support, and multidisciplinary care are critical.

Conclusion Clinicians should consider STSS and PF in previously healthy adults with rapidly progressive sepsis and purpura. Early diagnosis and aggressive integrated therapy improve survival

Keywords Streptococcus pneumoniae; toxic shock syndrome; purpura fulminans; immunocompetent adult; mNGS

孤立性睾丸结核模拟睾丸肿瘤：病例报告及文献综述

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目的 孤立性睾丸结核是一种罕见的肺外结核，由于其临床表现和影像学特征缺乏特异性，常常被误诊为睾丸恶性肿瘤，导致不必要的根治性睾丸切除术。准确的术前诊断对于保留器官和进行适当的抗结核治疗至关重要。

方法 报告一例罕见病例。一名 59 岁男性患者因“右侧睾丸肿大 4 天”入院。入院前超声检查提示“左侧睾丸内存在实性肿块，疑似精原细胞瘤”。体格检查显示左侧睾丸轻度肿大，质地中等。患者否认吸烟、饮酒及结核病家族史。胸部 X 光片显示没有异常。CT 提示左侧睾丸下极类圆形混杂影，形态尚规则，边界尚清，增强实性部分轻度强化，其内囊性低密度区无强化。二维超声所见左侧睾丸下极探及一低回声，边界清，内回声不均，其内可探及较丰富血流信号。睾丸超声造影提示左侧睾丸下极低回声

病灶, 恶性病灶增强模式, 精原细胞瘤多考虑。术前相关检查均支持睾丸恶性肿瘤的诊断。患者接受了“左侧睾丸切除术”。

结果 术后病理检查意外发现睾丸组织内存在广泛的急慢性炎性细胞浸润、干酪样坏死及肉芽肿性炎症, 符合结核病病理特征。最终病理诊断为“左侧睾丸结核”。

结论 孤立性睾丸结核是睾丸肿瘤的重要鉴别诊断之一。尽管现代影像学技术不断发展, 其非典型表现仍极易导致误诊。对于临床及影像学检查表现不典型的睾丸占位患者, 应提高对睾丸结核的警惕性。在条件允许的情况下, 术前或术中获取组织样本进行病理学及分子生物学检查, 可能是避免不必要睾丸切除、实现器官保留的关键。通过综合性的诊疗路径, 有望在保留器官功能和根治疾病之间找到更优的平衡点, 从而改善睾丸结核患者的预后和生活质量。

Oral Contezolid for Gram-Positive Bloodstream Infections in Hematologic Patients: A Propensity Score Study

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Objectives To evaluate the effectiveness and safety of oral contezolid for Gram-positive bloodstream infections (BSIs) in patients with hematologic diseases

Methods We conducted a retrospective cohort study at a specialized hematology hospital in China. Hematologic patients with Gram-positive BSIs receiving

oral contezolid as primary targeted therapy were compared with those receiving other antibiotics. Propensity score (PS) matching and inverse probability of treatment weighting (IPTW) were applied to balance baseline characteristics.

Result A total of 334 patients were included (44 contezolid; 290 controls). Patients receiving contezolid were older and more likely to have recent allogeneic hematopoietic stem cell transplantation, complicated BSIs, and concurrent pneumonia. After PS matching (41 contezolid vs. 106 control), 30-day death or relapse (17.1% vs. 8.5%, $p=0.229$), 90-day relapse (2.4% vs. 4.7%, $p=0.872$) and treatment modification rates (14.6% vs. 17.0%, $p=0.923$) were comparable. IPTW analysis also showed no significant association of contezolid with 30-day death or relapse ($aHR=1.65$, $p=0.400$). Septic shock, complicated BSIs, and concurrent pneumonia were independent predictors of 30-day poor outcomes. No contezolid-related adverse events leading to treatment modification were observed

Conclusion Oral contezolid demonstrated effectiveness and safety comparable to standard therapies after adjustment for baseline differences and may represent a viable alternative for hematologic patients with Gram-positive BSIs.

Comparative Efficacy and Safety of Antifungal Prophylactic Agents in Allogeneic Hematopoietic Stem Cell Transplantation: A Systematic Review and Network Meta-Analysis

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Background Invasive fungal infections (IFIs) remain a major cause of morbidity and mortality among allogeneic hematopoietic stem cell transplantation (allo-HSCT) recipients. There is still limited high-quality comparative evidence for antifungal agents

Methods We conducted a systematic review and network meta-analysis of randomized controlled trials (RCTs) and observational studies (PROSPERO: CRD420251270033), with databases search updated to September 2025. A prespecified assumption-based proportional imputation method was applied to estimate outcomes in mixed populations. Relative risks (RRs) were synthesized using a frequentist random-effects model, and treatments were ranked using surface under the cumulative ranking curve (SUCRA)

Results Thirty-two studies were selected, including 10 006 HSCT recipients. Across RCTs, posaconazole (RR, 0.19; 95% CI, 0.08–0.44) and voriconazole (RR, 0.20; 95% CI, 0.09–0.42) demonstrated the strongest efficacy against IFIs compared with placebo. Posaconazole ranked first for preventing invasive aspergillosis (SUCRA, 77.1%) and fungus-related mortality (SUCRA, 91.9%), while micafungin had the lowest discontinuation risk (SUCRA, 95.5%). Observational data favored posaconazole tablets (SUCRA, 90.3%) over suspension (SUCRA, 75.2%). Isavuconazole showed lower hepatotoxicity-related discontinuation (5.3% vs 22.9%; $P = .0002$), though these findings are based on limited cases. Trials implementing therapeutic drug monitoring (TDM) showed a non-significant trend toward improved efficacy

Conclusions Posaconazole and voriconazole demonstrate strong efficacy. Posaconazole tablets offer a favorable balance between benefit and risk. However, the potential safety benefits of isavuconazole warrant further evidence accumulation

Keywords invasive fungal infections; allogeneic

hematopoietic stem cell transplantation; network meta-analysis; antifungal prophylaxis

486 例肺炎克雷伯菌血流感染患者的临床特征及预后分析

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背景 肺炎克雷伯菌 (*Klebsiella pneumoniae*, KP) 血流感染 (Bloodstream infection, BSI) 是医疗保健相关性肺炎和院内感染的原因之一。随着碳青霉烯类药物的广泛使用, 碳青霉烯类耐药肺炎克雷伯菌 (Carbapenem-Resistant *Klebsiella pneumoniae*, CRKP) 引起的 BSI 日益多见。因其治疗选择有限、死亡率高, 已成为全球公共卫生的新挑战。早期识别影响预后的关键危险因素, 对优化临床决策、改善患者预后至关重要。

目的 本研究通过回顾性分析, 旨在分析影响肺炎克雷伯菌血流感染患者 28 天预后的独立危险因素, 并构建预后预测模型。

方法 本研究为单中心回顾性队列研究。连续纳入 2020 年 1 月 1 日至 2022 年 12 月 31 日期间于郑州大学第一附属医院住院、首次确诊 KP BSI 的成年患者 486 例。主要研究终点为确诊 KP BSI 后 28 天全因死亡率。通过单因素及多因素 Logistic 回归分析识别独立危险因素, 并基于多因素 Logistic 回归分析结果构建预后预测模型。所有统计分析采用 SPSS 27.0、GraphPad Prism 10.4、R 语言 (版本 4.5.2) 进行。

结果 1. 本研究共纳入患者 486 例, 其中男性占 65.2%, 中位年龄为 56 岁。常见合并症包括恶性疾病、高血压和糖尿病。感染来源最常见为肺部感染, 其次为腹腔感染 114 例。

2. 感染 CRKP 的患者占 41.6%。全队列对替加

环素和多黏菌素耐药率较低,分别为 9.7%和 15.4%。

3.全队列 28 天全因死亡率为 24.9%。死亡组患者在 APACHE II 评分、SOFA 评分、脓毒性休克发生率、CRKP 感染比例、静脉抗菌药物使用史及有创操作比例等方面均显著高于生存组 ($P<0.05$)。

4.多因素 Logistic 回归分析显示,高血压,APACHE II 评分高、血小板低、尿素氮高、脓毒性休克、新增使用机械通气、新发脏器功能不全是 KP BSI 患者 28 天死亡的独立危险因素 ($P<0.05$)。基于此构建的 28 天预后预测模型 AUC 为 0.923,提示预测效能优秀。

结论 高血压、APACHE II 评分升高、尿素氮高、血小板低、脓毒性休克、新增使用机械通气及新发脏器功能不全是 KP BSI 患者 28 天死亡的独立危险因素。基于上述因素构建的预测模型效能良好。

关键词 肺炎克雷伯菌; 血流感染; 碳青霉烯类耐药; 治疗策略; 危险因素

Antifungal Prophylaxis in Patients with Haematologic Malignancies: A Systematic Review and Network Meta-Analysis Integrating Efficacy, Toxicity, Formulation, and Real-World Applicability

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Objectives Invasive fungal infections (IFIs) remain a major cause of morbidity and mortality in patients with haematologic malignancies, with uncertainties persisting regarding formulation-specific performance and agent positioning. This study evaluated the

relative efficacy, safety, and formulation-dependent performance of antifungal prophylaxis

Methods PubMed, Embase, CENTRAL, and Web of Science were searched through October 15, 2025. Randomised controlled trials and comparative observational studies evaluating primary antifungal prophylaxis in adult haematologic malignancy patients receiving chemotherapy or haematopoietic stem cell transplantation were included. Bayesian network meta-analysis with random-effects models was performed, with treatment hierarchies established via SUCRA.

Results We included 77 studies encompassing 20,799 patients. Posaconazole remained the anchor strategy for high-risk patients; the delayed-release tablet and oral suspension showed comparable prophylactic efficacy (OR: 0.89, 95% CI: 0.44–1.77), but the tablet demonstrated superior statistical stability and lower serious adverse event (SAE) rates (2.5% vs. 3.6%). Isavuconazole had efficacy similar to voriconazole but with a far better safety profile (SAE SUCRA: 0.814 vs. 0.284). Micafungin emerged as the optimal non-triazole alternative (adverse event–discontinuation rate: 3.7%). Fluconazole lacked significant mold activity and ranked poorly in contemporary high-risk contexts.

Conclusion Antifungal prophylaxis in haematologic malignancies requires integrating formulation stability and real-world tolerability beyond single-agent rankings. Posaconazole remains the cornerstone, with the delayed-release tablet offering superior stability. Isavuconazole and micafungin are highly actionable alternatives under toxicity or drug-interaction constraints, whereas fluconazole should be recognised as historically important but increasingly context-limited.

Keywords antifungal prophylaxis, haematological malignancies, network meta-analysis, invasive fungal infections, posaconazole, hematopoietic stem cell transplantation

Clinical Analysis of Pneumocystis Jirovecii Pneumonia in Patients with Severe Liver Disease

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Objective To investigate the clinical characteristics, diagnosis and prognostic factors of Pneumocystis jirovecii pneumonia (PCP) in patients with severe liver disease, so as to enhance clinical awareness and early intervention

Methods A retrospective study was performed on 16 patients with decompensated cirrhosis or liver failure complicated with PCP hospitalized in our hospital from January 2022 to December 2025. Demographic data, clinical symptoms, imaging findings, laboratory parameters, therapeutic regimens and clinical outcomes were retrospectively analyzed

Results Of the 16 patients, 14 were male (87.5%), with a median age of 55 years. Acute decompensated cirrhosis accounted for the predominant liver disease type (43.8%), and hepatitis B virus infection was the most frequent etiology. Fever and dry cough were the most prevalent symptoms, both occurring in 87.5% of cases. Bilateral pulmonary ground-glass opacities were universally observed on chest imaging. Laboratory examinations manifested lymphopenia, reduced CD4⁺ T lymphocyte counts and elevated serum β -D-glucan levels, with median values of 850/ μ L, 260/ μ L and 75 pg/mL respectively. Twelve patients received standardized trimethoprim-sulfamethoxazole therapy, and the overall mortality rate was 25.0%. Older age, lower peripheral lymphocyte and CD4⁺ T cell counts, as well as higher β -D-glucan and LDH levels were closely

associated with fatal prognosis

Conclusion Severe liver disease patients are susceptible to PCP. Fever and dry cough are typical clinical presentations. Declined lymphocyte and CD4⁺ T cell counts predict unfavorable prognosis. Timely and standardized trimethoprim-sulfamethoxazole treatment effectively improves clinical outcome. High clinical suspicion and early screening are essential in high-risk populations

胸腺肽启动时机与脓毒症患者 28 天预后的关系：单中心回顾性队列联合多中心前瞻性补充队列研究

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目的 本研究旨在探讨已接受胸腺肽治疗的重症感染相关脓毒症患者中，不同胸腺肽启动时间窗与 28 天病死率之间的关系。

方法 本研究为观察性队列研究，包括单中心回顾性主队列和前瞻性多中心补充队列。单中心主队列纳入 2016 年 12 月至 2023 年 12 月东南大学附属中大医院重症医学科收治并接受胸腺肽治疗的脓毒症患者；多中心补充队列纳入 2025 年 6 月至 2025 年 12 月多家协作中心收治并接受胸腺肽治疗的脓毒症患者。以脓毒症确诊时间为时间零点，根据胸腺肽首次使用时间分为 ≤ 48 h 启动组和 > 48 h 启动组，并以 ≤ 24 h 启动作为敏感性暴露定义。主要结局为 28 天全因病死率。

结果 单中心主队列共纳入 629 例患者，其中 ≤ 48 h 启动 432 例， > 48 h 启动 197 例；28 天死亡 200 例。粗分析显示， ≤ 48 h 启动组 28 天病死率高于 > 48 h 组，但差异无统计学意义(33.8% vs. 27.4%， $P=0.117$)； ≤ 24 h 启动组 28 天病死率高于 > 24 h 组(35.6% vs. 27.8%， $P=0.040$)。多因素 Logistic 回归

显示, ≤ 48 h 启动胸腺肽与 28 天死亡无显著独立相关性 ($aOR=1.134$, $95\%CI: 0.759-1.693$, $P=0.540$); 以 APACHE II 替代 SOFA 评分、以 24 h 作为暴露定义及 LASSO 筛选后模型结果均一致。Cox 模型、IPTW 加权分析、24 h 和 48 h landmark 分析以及 CCW 分析均未显示早期启动胸腺肽具有明确 28 天死亡获益。时间依赖 Cox 模型提示动态胸腺肽暴露与死亡风险升高相关, 但考虑更可能反映病情进展驱动下的适应证偏倚和时间变化混杂。多中心补充队列共纳入 194 例患者, 28 天病死率为 23.7%; 无论以 48 h 还是 24 h 定义早期启动, 均未观察到胸腺肽启动时机与 28 天死亡存在显著相关。

结论 在已接受胸腺肽治疗的重症感染相关脓毒症患者中, 单纯以确诊后 24 h 或 48 h 作为早期启动时间窗, 未显示对 28 天预后具有稳定改善作用。胸腺肽作为免疫调节辅助治疗的临床价值可能不取决于单一固定时间窗, 而应结合患者免疫状态、感染严重程度、器官功能和炎症负荷进行个体化判断。未来需开展基于免疫表型分层的前瞻性研究, 以明确重症细菌或真菌感染相关脓症患者中胸腺肽可能获益的人群和最佳干预时机。

关键词: 脓毒症; 重症感染; 胸腺肽; 免疫调节; 28 天病死率

HIV 阴性结核性脑膜炎发生矛盾反应的临床特征研究

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目的 本研究旨在分析 HIV 阴性 TBM 患者发生 PR 的发生率、临床特征、实验室与影像学特点、危险因素及其对预后的影响, 以增进临床认识, 减少误诊。

方法 本研究为一项在中国中山大学附属第三医院进行的回顾性病例对照研究。纳入 2016 年 1 月

至 2025 年 12 月期间收治的、符合国际共识诊断标准的 HIV 阴性成年 TBM 住院患者共 170 例。根据治疗期间是否发生 PR, 将患者分为 PR 组和非 PR 组。PR 定义为在接受规范抗结核治疗且初始病情好转后, 出现原有临床表现或影像学表现恶化或新病灶, 并排除耐药、继发感染等其他原因。收集并比较两组患者的基线临床特征、实验室检查、影像学表现、治疗等。采用 SPSS 25.0 软件进行统计分析, 分类变量采用卡方检验或 Fisher 精确检验, 连续变量采用 t 检验或秩和检验。采用单因素及多因素二元 Logistic 回归分析 PR 的危险因素。

结果 在 170 例 HIV 阴性 TBM 患者中, 26 例 (15.29%) 在抗结核治疗期间发生 PR, 平均发生时间为开始治疗后 47.5 天 (10-263 天)。单因素分析显示, PR 组患者的外周血中性粒细胞百分比更高 (0.78 vs. 0.71, $P=0.02$)、脑脊液葡萄糖浓度更低 (1.84 vs. 2.38 mmol/L, $P=0.01$)、TBM 临床分期为 II 期的比例更高 (61.5% vs. 36.1%, $P=0.02$)。多因素 Logistic 回归分析进一步确认, 外周血中性粒细胞百分比高 ($OR=75.366$, $95\%CI: 1.053-5394.046$, $P=0.047$)、脑脊液葡萄糖浓度低 ($OR=0.586$, $95\%CI: 0.368-0.933$, $P=0.024$) 以及 TBM 临床分期为 II 期 ($OR=2.916$, $95\%CI: 1.165-7.299$, $P=0.022$) 是发生 PR 的独立危险因素。在预后方面, PR 组与非 PR 组患者的最终预后良好率和致残率无统计学显著差异, 但 PR 组的中位住院时间显著长于非 PR 组 (28.5 天 vs. 20.0 天, $P<0.001$)。所有发生 PR 的患者经维持原抗结核方案或增加糖皮质激素剂量治疗后均好转。

结论 外周血中性粒细胞百分比升高、脑脊液葡萄糖浓度降低以及疾病分期为 II 期是预测矛盾反应发生的重要危险因素。尽管矛盾反应会延长患者的住院时间, 但经过恰当处理后, 其最终预后与未发生矛盾反应的患者相似, 不影响总体治愈率和致残率。

【关键词】 结核性脑膜炎; 矛盾反应; 临床特征

四环素类抗菌药物在骨关节感染中的应用进展

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骨关节感染 (Bone and Joint Infections, BJI) 临床治疗难度大, 生物膜形成、骨组织穿透性不足及耐药菌 (如耐甲氧西林金黄色葡萄球菌 *Methicillin-resistant Staphylococcus aureus*, MRSA) 的出现是 BJI 治疗过程中面对的主要挑战。

四环素类抗菌药物已发展至四代, 通过结合细菌核糖体 30S 亚基抑制蛋白合成发挥抑菌作用, 新型药物经结构修饰可克服传统耐药, 具备骨穿透性强、口服生物利用度高、细胞渗透力佳等优势, 适配 BJI 长期治疗需求。其中第二代多西环素、米诺环素骨浓度高、口服吸收好, 被指南推荐为抑制性抗菌治疗优选, 联合利福平抗生物膜效果显著, 结合手术治疗 BJI 成功率可达 82%~100%; 第三代替加环素、第四代奥马环素与依拉环素抗菌谱更广, 可覆盖多重耐药菌株, 奥马环素可静注口服序贯、依从性高, 依拉环素对多重耐药革兰阴性菌活性更优, 替加环素可用于耐药菌所致复杂感染, 局部骨水泥应用亦有前景。该类药物在生物膜相关感染中优势突出, 多西环素可抑制并清除成熟生物膜, 与利福平联用可大幅提升感染根治率。其不良反应以轻中度胃肠道症状为主, 新型药物安全性更优。本文综述四环素类抗菌药物的药代药效定理学特点、传统及新型四环素类药物在 BJI 中的临床应用, 旨在为临床合理用药提供参考。

关键词: 四环素类抗菌药物; 骨关节感染; 人工关节感染; 骨髓炎

Risk Factors, Clinical Outcomes and Immune Dynamics of Candidemia in Patients with Hematological Disorder

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Introduction Candidemia, particularly due to *Candida tropicalis*, was of high incidence among patients with hematological disorders. However, associated risk factors, immune dynamics and clinical outcomes remained underexplored

Methods Clinical data from 105 patients diagnosed with hematological disorders and confirmed candidemia were retrospectively analyzed.

Results *Candida tropicalis* was identified in 79 patients (75.2%), and non-tropicalis species included *Candida albicans* (n=6, 5.7%), *Candida glabrata* (n=4, 3.8%), *Candida parapsilosis* (n=12, 11.4%), *Candida krusei* (n=3, 2.9%) and *C. guilliermondii* (n=1, 1.0%). Prior transplantation was more common in non-tropicalis candidemia ($P=0.023$), whereas culture positivity within 24 hours was associated with *Candida tropicalis* ($P=0.008$). *Candida tropicalis* showed favorable antifungal susceptibility compared to non-tropicalis, particularly to flucytosine ($P<0.001$). Azole monotherapy (29.5%) and azole-echinocandin combination (25.7%) were the most used treatments. Complete response was achieved in 58 patients (55.2%), with similar rate between *Candida tropicalis* and non-tropicalis group ($P=0.869$). The restricted median survival time was 64 days, with no significant difference in mortality or survival between groups. Older age ($P=0.043$), abdominal pain ($P=0.040$) and septic shock ($P=0.008$) were associated with poor outcomes. Patients achieving remission exhibited higher neutrophil and lymphocyte counts and greater immune recovery. *Candida tropicalis* BSI was associated with deeper neutropenia, significantly lower NLR and a more pronounced neutrophil decline at onset,

suggesting a “double-hit” immune suppression.

Conclusion *Candida tropicalis* and non-tropicalis candidemia exhibited distinct risk factors and immune dynamics, yet both were associated with high mortality. Further investigation is needed to elucidate invasion mechanism and immunological vulnerabilities, guiding targeted prophylaxis and therapy.

Clinical Characteristics and Treatment Response of Chronic Disseminated Candidiasis in Patients with Hematological Disorders

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Chronic disseminated candidiasis (CDC) is an invasive fungal infection typically affecting patients with hematological diseases and severe neutropenia, associated with increased mortality. However, there is a global shortage of clinical evidence on CDC. We retrospectively analyzed clinical data from 49 CDC patients over the past decade. Clinical characteristics of primary hematological diseases, CDC diagnosis, treatment and response evaluations were included. Clinical factors associated with CDC remission and patients' survival were analyzed. The majority of patients had hematological malignancies ($n = 43$, 87.8%), and 27 patients (55.1%) had persistent severe neutropenia for more than 10 days prior to CDC. CT scans revealed liver lesions in 44 patients, spleen lesions in 34 patients, and kidney lesions in 9 patients. Proven, probable and possible CDC was diagnosed in 5 (10.2%), 3 (6.1%) and 41 patients (83.7%), respectively, and treatment outcomes at 3 months included 5 complete response (CR, 10.2%), 34

partial response (PR, 69.4%) and 10 treatment failure (20.4%). Caspofungin treatment showed a trend towards improving CR/PR rate, while severe neutropenia > 20 days and proven diagnosis were significantly associated with 3-month treatment failure. Kaplan-Meier curve showed achieving CR/PR within 3 months did not significantly prolong OS compared to treatment failure patients (1197.6 days vs. 564.8 days, $P = 0.074$). Additionally, no patient deaths were directly attributed to CDC infection. Age > 45 years old and malignancy non-remission were prognostic factors of overall survival (OS). Furthermore, a prediction model identified severe neutropenia > 20 days, proven/probable diagnosis and concomitant bacteremia as risk factors to effectively predict treatment failure. Also, patients with a risk score < 0.203 in the model exhibited more rapid treatment response. After CDC symptoms onset, lymphocyte levels remained consistently higher in treatment failure patients, while the neutrophil-to-lymphocyte ratio was persistently higher in CR/PR patients. Our findings recommend CT scans for diagnosis and caspofungin as first-line therapy while continuing scheduled chemotherapy or bone marrow transplantation. Notably, risk factors identified by the prediction model could be used to predict treatment response.

隐丹参酮靶向细菌细胞膜并在体外和体内抑制耐甲氧西林金黄色葡萄球菌

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耐甲氧西林金黄色葡萄球菌发病率的持续上升已成为全球范围内亟待解决的重大公共卫生问题,其多重耐药特性严重限制了传统抗生素的临床疗效。因此,开发具有新作用机制、能够特异性靶向 MRSA

的抗菌候选药物具有重要的理论意义与临床应用价值。本研究系统评估了天然活性成分隐丹参酮对 MRSA 的抗菌活性及其潜在作用机制。

结果表明, 隐丹参酮对金黄色葡萄球菌标准菌株 ATCC 29213、流行株 USA300 及耐药株 ATCC 43300 均表现出显著的生长抑制作用, 提示其具有广谱抗葡萄球菌活性。机制研究进一步显示, 隐丹参酮通过多靶点协同作用发挥抗菌效应。一方面, 其能够显著提高细菌细胞内活性氧水平, 诱导氧化应激反应, 从而破坏细菌正常的氧化还原稳态; 另一方面, 隐丹参酮可干扰细胞膜结构与功能, 表现为膜电位紊乱及膜通透性显著增加, 进而导致胞内重要小分子物质外泄。此外, 研究还发现其可显著降低细胞内三磷酸腺苷含量, 提示其通过抑制能量代谢进一步削弱细菌生存能力。这些结果共同表明, 隐丹参酮主要通过破坏细胞膜完整性及诱导氧化损伤实现对 MRSA 的杀菌作用。在安全性评价方面, 体外细胞毒性实验显示, 隐丹参酮在 10–200 μM 浓度范围内对哺乳动物细胞系表现出较低毒性, 且未观察到明显的溶血现象, 提示其具有良好的生物相容性。在体内研究中, 采用 MRSA 皮肤感染小鼠模型对其抗感染效果进行验证, 结果表明隐丹参酮处理组细菌负荷显著下降, 感染部位炎症反应明显缓解, 组织结构破坏程度减轻。进一步的组织病理学分析显示, 与对照组相比, 给药组皮肤组织坏死范围缩小, 炎性细胞浸润减少, 提示其不仅具有良好的抗菌活性, 还可有效减轻感染相关的组织损伤。综上所述, 隐丹参酮通过靶向细菌细胞膜并诱导氧化应激, 发挥多层面的抗 MRSA 作用, 同时兼具较好的安全性和体内抗感染效果, 具有作为新型抗 MRSA 候选药物的潜在应用前景。

微小微单胞菌致右髋关节周围软组织感染一例

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目的 报道 1 例长期使用生物制剂的类风湿关节炎 (RA) 患者合并微小微单胞菌引起的右髋关节周围软组织及关节感染, 并探讨宏基因组二代测序 (NGS) 在疑难感染诊断中的价值及抗感染治疗策略。

方法 回顾性分析 2023 年 7 月于河北医科大学第三医院收治的 1 例 60 岁男性患者的临床资料。患者有 RA 病史 11 年, 曾使用甲氨蝶呤、托法替布, 入院前 4 个月因病情活动加用依那西普 (50mg/周) 治疗 3 个月。因“发热伴右髋关节疼痛 3 个月”入院, 外院曾给予甲泼尼龙、羟氯喹及左氧氟沙星、头孢他啶、莫西沙星等治疗, 效果不佳。入院后完善血常规、炎症指标、自身抗体、影像学检查, 并行右髋部皮下脓肿穿刺抽液。脓液标本同时送常规细菌培养及 NGS 检测。根据病原学结果动态调整抗感染方案, 监测临床表现及炎症指标变化。

结果 患者入院时体温 36.3°C, 右髋关节下方可触及肿块, 活动轻度受限。实验室检查示: 白细胞 $13.35 \times 10^9/\text{L}$, 中性粒细胞 80.2%, IL-6 564.419 pg/ml, 血沉 113 mm/h, CRP 78.70 mg/L, 铁蛋白 460.02 ng/ml; 类风湿因子 597.0 IU/ml, 抗 CCP 抗体 142.76 RU/ml。髋关节彩超提示右侧关节周围积液, 倾向脓性。入院第 2 天行脓肿抽吸术, 抽出暗红色脓性液体 40 ml, 常规细菌培养阴性。NGS 结果检出微小微单胞菌 (序列数 938, 相对丰度 65.44%)。调整为奥马环素 (0.1g/d) 联合哌拉西林他唑巴坦 (4.5g q8h) 静脉滴注。入院第 9 天患者体温恢复正常, 右髋疼痛及肿胀较前好转。继续抗感染治疗后患者右髋部疼痛明显减轻, 局部硬结缩小, 炎症指标显著改善, 调整抗感染方案为: 左奥硝唑 100ml/次 q12h 静脉滴注、哌拉西林他唑巴坦钠 4.5g/次 q8h 静脉滴注。病情稳定后转骨科行右髋关节骨髓炎病灶清除术+关节旷置术。

结论 对于长期使用生物制剂 (如依那西普) 的 RA 患者, 出现关节周围软组织感染且常规细菌培养阴性时, 应警惕厌氧菌 (如微小微单胞菌) 感

染。宏基因组二代测序 (NGS) 能够快速、精准识别罕见或苛养病原体, 克服传统培养的局限性, 指导抗感染治疗, 改善患者预后。

关键词 类风湿关节炎; 微小微单胞菌; 宏基因组二代测序; 关节周围软组织感染

异基因造血干细胞移植后超早期中枢毛霉菌感染一例: 基于静脉、鞘注及外科联合救治的诊疗思考

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背景 中枢毛霉菌感染是异基因造血干细胞移植 (allo-HSCT) 后少见但病死率极高的侵袭性真菌感染。其早期临床表现及影像学特征缺乏特异性, 易误诊为脑梗死等非感染性疾病, 导致诊治延迟。

目的 总结 1 例骨髓增生异常综合征 (MDS) 患者 allo-HSCT 后超早期发生中枢毛霉菌感染的诊疗经过, 探讨移植期隐匿性中枢毛霉菌感染的识别要点及“静脉抗真菌+鞘注两性霉素 B+神经外科干预”综合治疗模式的临床价值。

方法 回顾性分析 1 例 44 岁 MDS 患者临床资料。患者于 2025 年 11 月 25 日接受半相合 allo-HSCT。结合头颅 MRI/CT、脑脊液常规生化、血液及脑脊液 mNGS、术中脓液 NGS、动态影像学变化及治疗反应, 对其中枢毛霉菌感染的诊断、治疗及转归进行总结。

结果 患者移植后+7 d 出现左侧肢体无力并进行性加重, 左上肢肌力降至 0 级, 伴一过性发热; 早期头颅 MRI 提示梗塞样改变。随后行腰穿检查, 脑脊液 mNGS 检出微小根毛霉 34 条, 血液 mNGS 检出微小根毛霉 146 条, 结合临床表现明确中枢毛霉菌感染。确诊后予两性霉素 B 胆固醇硫酸酯复合物 (ABCD) 150 mg 静脉联合艾沙康唑 200 mg 治

疗。治疗约 14 d 后影像学示病灶仍进展。随后加用普通制剂两性霉素 B 鞘注, 自 0.1 mg 逐步增量, 持续约 3 周, 期间继续静脉联合使用抗真菌药。治疗过程中病情曾短暂改善, 后再次急剧恶化; 复查头颅 MRI 提示脓肿壁形成, 伴有左下肢肌力降至 0 级。患者于移植后+45 d 行脑脓肿穿刺引流术, +57 d 行病损切除术, 脓液 NGS 再次检出微小根毛霉。术后继续给予两性霉素 B 脂质体 300 mg 联合艾沙康唑 200 mg, 并规律鞘注两性霉素 B, 累计总量 15 mg。移植后 3 月余患者左侧肢体肌力恢复至 3 级, 后续神经功能逐步改善。维持阶段调整为艾沙康唑 400 mg/200 mg 交替方案, 血药浓度维持约 4.0 $\mu\text{g/mL}$, 继续门诊随访。

结论 allo-HSCT 后早期出现局灶性神经功能缺损时, 即使初始影像倾向脑梗死, 仍应高度警惕中枢毛霉菌感染, 并尽早完善腰穿及 mNGS 检测。对于进展性病例, 静脉抗真菌治疗基础上联合鞘注两性霉素 B, 并在脓肿形成后及时实施神经外科干预, 可能改善感染控制及神经功能预后。本例提示, 移植期应重视隐匿性毛霉菌感染的早期识别, 并建立“早期病原学确诊—联合抗真菌治疗—适时外科介入—长期三唑维持”的综合管理策略。

抗菌肽在曲霉菌感染中作用机制的研究进展

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目的 探讨抗菌肽 (Antimicrobial Peptides, AMPs) 在抗曲霉菌感染中的相关机制, 为未来曲霉菌的临床治疗提供新参考。

方法 使用 Pubmed 检索相关研究, 选择标题或摘要中包含以下关键字的文章: (Antimicrobial Peptides) AND (Aspergillus)。

结果 抗菌肽是先天免疫系统的关键组分, 参与构成宿主抵御曲霉菌的第一道防线, 具备免疫调

节、抗炎及促进伤口愈合等多种功能。其对曲霉菌的抑制作用受浓度、菌株、生长阶段及微环境等多因素综合影响。抗菌肽可通过桶壁模型、环形孔模型或地毯模型增加膜通透性，诱导钾离子外流，最终导致细胞膜破裂。与此同时，抗菌肽还能调控几丁质及 β -葡聚糖的合成与分布，破坏细胞壁完整性，并同时激活细胞壁修复通路。此外，部分抗菌肽可抑制毒素基因表达，诱导线粒体活性氧产生并降低膜电位，进而抑制脱氢酶活性以阻断三羧酸循环、减少ATP合成，从而引发能量代谢紊乱。在免疫调节层面，抗菌肽既能趋化并激活中性粒细胞、巨噬细胞等免疫细胞以增强对曲霉菌的吞噬清除，同时下调IL-6、TNF- α 等促炎因子水平，减轻过度炎症所致组织损伤。另有研究发现，LL-37可降低曲霉菌黏附能力，乳铁蛋白B与抗真菌药物联用能破坏生物膜基质以增强药物渗透性，而植物防御素Psd2则通过结合糖脂与麦角甾醇改变生物膜空间结构。虽然抗菌肽具有快速有效抑制曲霉的优势，但也存在一定局限性，以膜破坏为主的抗菌肽可能因选择性不足而对宿主细胞产生潜在毒性；依赖胞内作用的抗菌肽则需跨越细胞膜屏障才能抵达目标靶点；免疫调节作用也因细胞类型、微环境及剂量差异而异。此外，生产成本低、生物利用度有限、半衰期短和疗效不确切等问题也有待进一步解决。

结论 抗菌肽是先天免疫系统的重要组成部分，其通过多靶点、多途径协同发挥抗曲霉菌作用，全面了解抗菌肽对曲霉菌的作用机制，对曲霉菌的治疗新策略以及未来抗真菌药物的开发具有重要意义。

关键词：抗菌肽；曲霉；真菌；抗真菌剂

多发伤术后感染性左膝关节炎及左大腿脓肿合并艰难梭菌感染一例

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目的 探讨多发伤术后继发感染性关节炎及软组织脓肿的临床特点、病原学诊断及抗菌治疗策略。

方法 对1例因多发伤术后5个月余、间断发热10余天入院的61岁男性患者进行分析。患者既往有左股骨骨折、脾切除、结肠破裂修补及横结肠造瘘术史，术后出现反复发热（最高38.5℃），伴左大腿下段肿痛。入院后行血常规、炎症指标、下肢及关节影像学（CT、MRI、超声），并于超声引导下左大腿脓肿穿刺抽吸术，脓液送检metaCAP病原微生物核酸高通量测序、细菌培养及药敏试验。

结果 患者入院后体温最高37.5℃，左膝关节红肿热，浮髌试验阴性，CRP 79.53 mg/L，IL-6 47.17 pg/mL，PLT $668 \times 10^9/L$ 。影像学提示左膝关节积液、滑膜增厚及股骨前方深部脓肿。脓液mNGS及常规培养均检出艰难梭菌（序列数288）。初始抗感染使用多西环素及利奈唑胺，后在mNGS结果指导下，调整为奥马环素联合利奈唑胺靶向治疗，辅以穿刺抽脓引流。治疗后次日体温恢复正常，左下肢肿痛显著缓解，炎症指标进行性下降。

结论 多发伤术后常规抗生素治疗无效的深部关节及软组织感染，需警惕艰难梭菌等非典型病原体。常规抗感染效果不佳时应尽早行局部穿刺及病原宏基因组学检，早期介入性穿刺联合mNGS技术可提高罕见病原体诊断准确性，奥马环素联合利奈唑胺及局部引流是有效治疗策略，可改善临床转归。

Risk Stratification Value of QSOFA Combined With 72-Hour Early Treatment Response for Short-Term Adverse Outcomes in Hospitalized Patients With Salmonella Infection: A Single-Center Retrospective Study

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Background Most studies of hospitalized patients with *Salmonella* infection have focused on baseline risk at admission, whereas the prognostic significance of dynamic treatment response within the first 48–72 hours remains insufficiently characterized. This study evaluated whether combining admission qSOFA with early treatment response could improve prediction of 30-day composite adverse outcomes

Methods We retrospectively included 232 hospitalized patients with *Salmonella* infection between October 2014 and January 2026. Primary exposures included qSOFA ≥ 2 at admission, follow-up blood cultures at 48–72 hours, persistent bacteremia, failure to improve at 72 hours, and antimicrobial escalation. The primary outcome was a 30-day composite adverse outcome, defined as death, ICU admission, mechanical ventilation, or infection-related shock. Multivariable logistic regression adjusted for age and sex was performed, and model discrimination was assessed using the area under the receiver operating characteristic curve (AUC).

Results The median age was 13.5 years (IQR 2.7–48.0), and 63.4% of patients were male. The incidence of the 30-day composite adverse outcome was 10.8% (25/232). qSOFA ≥ 2 was present in 16.8% (39/232), failure to improve at 72 hours in 19.4% (45/232), and antimicrobial escalation in 6.0% (14/232). Multivariable analysis identified failure to improve at 72 hours (aOR 7.19, 95% CI 2.54–20.37, $P < 0.001$), antimicrobial escalation (aOR 5.13, 95% CI 1.15–22.89, $P = 0.032$), and qSOFA ≥ 2 (aOR 3.14, 95% CI 1.09–9.08, $P = 0.034$) as independent predictors of the composite outcome. The baseline model, including qSOFA, age, and sex, had an AUC of 0.64, which increased to 0.79 after the addition of failure to improve and antimicrobial

escalation.

Conclusion Short-term outcomes in hospitalized patients with *Salmonella* infection are closely associated with organ dysfunction at admission and with early treatment response within 72 hours. The combination of qSOFA and dynamic treatment response provides a clinically applicable framework for early risk stratification and may facilitate intensified monitoring and timely optimization of antimicrobial management.

Keywords *Salmonella*; qSOFA; failure to improve at 72 hours; antimicrobial escalation; persistent bacteremia; prognosis

Immunosuppression, Resistance Burden, and QSOFA on Short-term Prognosis and Difficult Clearance in Hospitalized Patients with *Salmonella* Infection: A Single-center Retrospective Cohort Study

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Background Immunosuppressed patients who develop *Salmonella* infection are more likely to experience bacteremia, sepsis, and treatment failure; however, systematic evidence remains limited regarding how different sources of immunosuppression and resistance burden jointly affect early outcomes. Using a source-based classification of immunosuppression, we evaluated the relationships of host severity (qSOFA), patho-

gen resistance burden, 30-day composite adverse outcomes, and difficult clearance

Methods We retrospectively enrolled 232 hospitalized patients with *Salmonella* infection between October 2014 and January 2026. Patients were stratified as typhoidal/paratyphoidal *Salmonella* (TS) or nontyphoidal *Salmonella* (NTS) according to serotype and grouped by the source of immunosuppression. Infection phenotypes were classified as enteric, bloodstream/sepsis, mixed/multisite, or other focal phenotypes. Independent associated factors were identified using multivariable logistic regression.

Results The incidence of the 30-day composite adverse outcome was 10.8% (25/232), and the incidence of difficult clearance was 22.0% (51/232). Immunosuppressed patients were more likely to present with bloodstream or disseminated infection phenotypes, but immunosuppression itself was not an independent determinant of 30-day adverse outcomes. qSOFA ≥ 2 was an independent predictor of the 30-day composite adverse outcome (aOR 5.36, 95% CI 1.56-15.95, $P=0.006$). TS was significantly associated with difficult clearance (aOR 23.41, 95% CI 3.98-37.85, $P<0.001$), and resistance burden showed an increasing trend for both outcomes.

Conclusion In hospitalized patients with *Salmonella* infection, the source of immunosuppression mainly affects the infection phenotype, whereas short-term adverse outcomes are driven more by early host organ dysfunction. Combined application of qSOFA and resistance assessment may facilitate earlier identification of high-risk patients and those with difficult clearance and may support individualized antimicrobial therapy.

Keywords *Salmonella*; source-based classification of immunosuppression; qSOFA; antimicrobial resistance; difficult clearance; prognosis

耳念珠菌特异性毒力调控蛋白 Sfr1 的鉴定及其致病作用的机制研究

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目的 耳念珠菌 (*Candida auris*) 作为多重耐药、高致死率的全球性“超级真菌”，其毒力调控网络具有高度种属特异性。然而，关键毒力调控节点仍未被充分解析，严重制约精准抗毒力策略的研发。本研究旨在鉴定耳念珠菌中未表征的特异毒力调控因子，并初步探明其在致病过程中的作用，为解析该菌特有致病机制和开发新型干预靶点提供理论依据。

方法 利用天然产物敏感性筛选结合正向遗传学分析，从耳念珠菌中锁定一个与毒力表型密切相关的功能未表征蛋白 Sfr1。通过荧光融合蛋白表达与共聚焦显微镜观察其亚细胞定位。随后，构建 SFR1 基因缺失突变株及回补株，系统比较野生株与缺失株在常见抗真菌药物、细胞壁干扰剂、氧化应激等宿主相关应激条件下的耐受能力、表面黏附与生物被膜形成能力，以及在巨噬细胞内的吞噬杀伤存活率。采用大蜡螟 (*Galleria mellonella*) 幼虫感染模型，通过生存曲线分析和体内真菌载荷计数，评估 Sfr1 对耳念珠菌体内致病力的影响。同时，利用转录组测序初步解析 Sfr1 缺失引起的全局转录扰动，推断其可能调控的功能模块。

结果 首次在耳念珠菌中鉴定出毒力调控相关蛋白 Sfr1，该蛋白在白色念珠菌等常见致病念珠菌中无明确直系同源物，具高度种属特异性，提示其可能赋予耳念珠菌独特的致病优势。此外，亚细胞定位分析明确显示，Sfr1 定位于细胞核，提示其可能在转录调控层面发挥作用。SFR1 缺失株在基础生长速率和常规形态上与野生株无显著差异，但对棘白菌素类抗真菌药物卡泊芬净和两性霉素 B 的药物敏感性显著增强，同时对细胞壁合成干扰剂和活性氧的耐受性显著降低，生物被膜形成量下降超过

50%，表面黏附能力明显受损。在巨噬细胞杀伤模型中，缺失株的胞内存活率较野生株显著降低。大蜡螟感染模型显示，感染缺失株的幼虫生存期显著延长，体内真菌负荷明显低于野生株感染组。转录组分析初步提示，Sfr1 可能调控涉及细胞壁完整性、抗氧化应答及部分毒力和耐药属性相关的基因表达网络，构成一个尚未被完整揭示的转录调控节点。

结论 Sfr1 是维持耳念珠菌毒力的关键调控因子，是解析耳念珠菌这种新兴“超级真菌”种属特异性致病机制的新切入点。深入研究 Sfr1 所介导的调控网络，不仅有助于阐明耳念珠菌高致病性的分子基础，也为开发针对该菌的特异性抗毒力策略和新药靶点提供了重要线索。

关键词：耳念珠菌；毒力调控；Sfr1；致病机制；新型药物靶点

Clinical Characteristics and Prognostic Factors of *Clostridium Perfringens* Bacteremia: Case Series Analysis

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Clostridium perfringens is a well-recognized anaerobic pathogen capable of causing foodborne and gastrointestinal disease; however, bloodstream infection caused by this organism remains rare and is associated with a high mortality rate. We report a 72-year-old man who presented with fever and epigastric pain on admission. Subsequent abdominal computed tomography revealed he had progressive hepatic metastases, a patent bilioenteric stent, and gas within dilated bile ducts. Laboratory investigations demonstrated his marked leuko-

cytosis ($12.6 \times 10^9/L$), markedly elevated C-reactive protein (290.6mg/L), and procalcitonin (6.88ng/mL). Blood cultures subsequently yielded *C. perfringens*, which was susceptible to Ampicillin, Imipenem and various other antimicrobial agents. The patient empirically received meropenem combined with vancomycin, resulting in effective infection control and a favorable clinical outcome. To further contextualize this case, we conducted a literature review of *C. perfringens* bacteremia to summarize its clinical characteristics, highlighting its rapid progression, high mortality rate, and frequent association with massive intravascular hemolysis for early recognition, timely diagnosis, aggressive antimicrobial therapy and intervention measures.

Keywords *Clostridium perfringens*; bacteremia; case report; literature review;

Clinical Features and Treatment Differences Among Tuberculous, Brucellosis, and Pyogenic Spondylitis: A Cohort Study

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Purpose There was an increasing incidence of spinal infections. This study aimed to compare and contrast the clinical characteristics and treatment regimens for diverse types of spondylitis and to provide guidance for clinicians to make timely diagnosis and treatment

Methods One hundred and twenty-five patients with spinal infections admitted to the First Affiliated Hospital of Anhui Medical University from October 2019 to December 2024 were recruited. The patients were classified as having tuberculous spondylitis (TBS), brucellosis spondylitis (BS), or pyogenic spondylitis

(PS). The patient's treatment regimen and course were dynamically followed up during hospitalization and after discharge. Comparisons of clinical characteristics and treatment among the three groups were performed by SPSS 26.0 and GraphPad Prism 10 statistical software.

Results The proportion of male patients was greater than female patients (65.00% vs. 35.00%). Fever accompanied by pain was more prevalent in the BS and PS groups than in the TBS group ($P=0.003$). Compared with the TBS and BS groups, the PS group had the shortest duration from symptom onset to hospitalization ($P<0.001$). Sepsis, invasive manipulation, elevated inflammatory markers, psoas abscesses, and the involvement of three or more vertebrae were significantly associated with the PS. In this study, the median duration of treatment was 77 weeks for TBS, 19 weeks for BS, and 13 weeks for PS. Adverse drug reactions (ADRs) should be monitored during treatment. Our results indicated that omadacycline and contezolid exhibited remarkable efficacy in the treatment of spinal infections.

Conclusion Patients of spinal infections with diverse etiologies presented varied clinical features and risk factors, the treatment should be individualized. Due to the long course of treatment, ADRs need to be monitored during treatment, and newer drugs such as omadacycline and contezolid are efficacious and have favorable safety profiles.

Keywords Spinal infectious diseases, Clinical characteristics, Treatment regimens, Treatment durations

沙门菌是一种主要通过粪-口途径传播的病原体,大多数表现为轻症的胃肠道症状,呈自限性,但也有极少数(约 0.8%)表现为“菌血症-骨髓炎”的感染模式:即沙门菌在引起一过性菌血症后,并未在肠道持续排菌,而是迁徙并定植于已有微小损伤或血供丰富的骨骼系统,形成骨髓炎这一深部局灶性感染[1],其中椎骨为最常侵犯部位(约 40%)[2]。

本文报道 2 例伤寒沙门菌椎体骨髓炎病例,均经血培养确诊,并接受联合抗生素治疗获得良好预后,通过对比分析两份病例,并结合文献复习,旨在探讨该罕见感染的易感因素、发病特点、血培养采集时机及治疗策略,以期提高临床诊疗能力。

1. 病例 1

患者,男,46 岁,既往体健,因发热 1 月入院。患者入院前 1 月吃烧烤后出现恶心、呕吐,发热至 39.6°C ,伴畏寒、寒战,伴腰痛。外院查炎症指标升高,肥达氏反应阳性 1:320。尿便常规、肾功能、G 试验(1,3- β -D 葡聚糖试验)、GM 试验(曲霉菌半乳甘露聚糖检测)、肝炎分型、非嗜肝病毒、结核抗体、甲功、肿瘤标志物、免疫固定电泳、HLA-B27、抗中性粒细胞胞浆抗体、血培养、布病抗体、免疫全项均未见明显异常。头胸腹盆 CT 及胸椎 CT、腰椎 MRI 均未见明确感染及占位性病变。外院先后予头孢西丁、特治星、比阿培南、万古霉素、利福平、复方磺胺甲噁唑、利奈唑胺抗感染治疗 20 余天。患者仍间断高热,体温最高至 40.5°C ,伴畏寒、寒战,腰痛较前加重,翻身及坐起障碍。体重下降 15kg。查体:体温 39.6°C ,神清,被动卧位,急性病容。心肺腹及肌力查体未见异常,腰 2/3 椎体棘突及周围软组织压痛,腰椎活动度检查欠合作。化验示血白细胞计数 $12.18\times 10^9/\text{L}$,中性粒细胞百分比 79.40%,C 反应蛋白 209.1mg/L,降钙素原 0.49ng/ml。

沙门菌椎体骨髓炎 2 例

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以血药浓度监测为导向构建重症感染患者
“临床+实验”双药师 协同药学服务模式的探

索

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目的 探索构建以治疗药物监测（TDM）为导向的“临床+实验”双药师协同药学服务模式，旨在整合临床药师与实验检测药师的专业优势，实现重症感染患者抗感染治疗的个体化精准用药，提升临床合理用药水平与药学服务质量，为药学服务模式转型提供实践依据。

方法 选取 2023 年 1 月至 2025 年 12 月期间收治的重症感染患者为研究对象。建立由临床药师与分析检测药师共同参与的“双药师”协作团队，正式纳入多学科诊疗（MDT）体系。临床药师负责初始抗感染方案评估、疗效与不良反应监测、用药教育及临床沟通；分析检测药师依托精准药学技术平台及自主研发的“精准血药浓度采集系统”，规范完成血样采集时间智能提醒、样本处理、浓度检测与质量控制。双方联合开展全流程药学服务，包括：初始方案制定与优化、TDM 指标选择与样本采集标准化、浓度结果的多因素解读（病理状态、合并用药、采血误差等）、全程药学监护（重点关注肝肾功能损伤、神经系统毒性等）以及不良反应的快速识别与处置。同时开设线上与线下相结合的药学门诊，提供延续性服务。

结果 项目实施三年来，累计完成万古霉素、美罗培南、伏立康唑、利奈唑胺、替考拉宁、多黏菌素 B 等 14 种常用抗感染药物的 TDM 检测共 5680 例次，临床治疗方案的采纳率高达 98.5%，说明双药师联合建议具有高度临床可接受性。药师深度参与血流感染、呼吸机相关性肺炎、腹腔感染、中枢神经系统感染等 12 个病种的 MDT 病例讨论，协助制定并推广了 5 项抗感染药物临床路径（如糖肽类、碳青霉烯类个体化给药路径）。近 3 年累计参与制定或调整抗感染治疗方案 4000 余例次，覆盖 ICU、呼吸科、血液科等多个高感染风险科室。线上与线下药学门诊服务量累计达 2700 余次，显著提升了患者用

药依从性与治疗安全感。典型案例显示，该模式可有效识别并干预药物相互作用（如伏立康唑与质子泵抑制剂合用导致血药浓度异常升高）及早期肾损伤等不良反应，成功避免了严重药害事件，切实保障患者用药安全。

结论 以 TDM 为导向的“临床+实验”双药师协同服务模式，实现了重症感染患者从经验治疗向精准个体化用药的转变，显著提升了临床对药学服务的认可度与采纳率，拓展了药学服务在 MDT 中的深度与广度。该模式操作性强、可复制性好，为医疗机构推动药学服务从“以药品为中心”向“以患者为中心”转型提供了可行参考，具有良好的推广应用价值。

Indole-3-Propionic Acid Attenuates Sepsis-Associated Liver Injury by Targeting Th17 Glycolysis

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Background and Aim: Sepsis-associated liver injury (SALI) is a severe complication of sepsis in which excessive inflammation and dysregulated immune responses contribute to hepatocellular damage. Indole-3-propionic acid (IPA), a gut microbiota-derived tryptophan metabolite, has been implicated in immune regulation, but its role in SALI remains unclear. This study aimed to determine whether IPA protects against SALI and to explore its effects on pathogenic T helper 17 (Th17) responses and related metabolic-epigenetic mechanisms

Methods IPA levels and peripheral Th17 cells were assessed in patients with SALI and healthy controls. A cecal ligation and puncture-induced SALI mouse model was used to evaluate the protective effects

of IPA on liver injury, systemic inflammation, and Th17 responses. In vitro, human PBMCs and mouse naïve CD4⁺ T cells were used to examine the effects of IPA on Th17 differentiation, glycolysis, lactate production, histone lactylation, and PPAR β/δ expression.

Results Patients with SALI showed markedly reduced fecal and serum IPA levels accompanied by increased peripheral Th17 cell frequencies. CLP induced a stable liver injury phenotype at 24 h, characterized by hepatic congestion, hepatocyte ballooning, inflammatory infiltration, and elevated serum aminotransferases. IPA treatment substantially reduced serum liver injury markers, ameliorated hepatic pathological injury, decreased F4/80-positive macrophage infiltration, down-regulated hepatic Il6, Il1b, Nlrp3, and Tnfa expression, and lowered circulating IL-6, IL-1 β , TNF- α , IFN- γ , and IL-17A levels. IPA also attenuated hepatic IL-17A staining and reduced Il17a, Rorc, Csf2, and Il23r expression, indicating suppression of pathogenic Th17 activation. In vitro, IPA inhibited Th17 differentiation in patient-derived peripheral blood mononuclear cells and murine naïve CD4⁺ T cells, with 500 nM identified as the most effective working concentration. Mechanistically, IPA reduced Th17 glucose uptake, decreased HK2 and LDHA protein levels, suppressed Hk1, Hk2, Ldha, and Glut1 transcription, restored PPAR β/δ expression, reduced intracellular lactate accumulation, and diminished global protein lactylation. Among histone lactylation sites, H3K9 lactylation was most prominently suppressed by IPA.

Conclusion IPA is decreased in SALI and exerts protective effects against experimental SALI by dampening local and systemic inflammation and suppressing the pathogenic Th17 axis. IPA may restrain Th17 pathogenicity through inhibition of glycolysis-lactate metabolism and H3K9 lactylation, with restoration of PPAR β/δ expression as a potential upstream reg-

ulatory event. These findings support IPA as a promising microbiota-derived immunometabolic modulator for SALI intervention.

Antibiotic Class Determines Phage Replication and Resistance Evolution in *Pseudomonas Aeruginosa*

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Pseudomonas aeruginosa is a high-priority opportunistic pathogen characterized by significant genetic plasticity and increasing multidrug resistance. While phage-antibiotic combinations are increasingly explored to circumvent antimicrobial resistance, the influence of different antibiotic classes on viral replication and the subsequent evolutionary trajectories of resistance remains poorly defined. In this study, we systematically examined the interactions between the O-antigen-dependent phage phipa10 and three clinically relevant antibiotics, amikacin, levofloxacin, and meropenem, against *P. aeruginosa* ZS-PA-35. Synergy matrix analysis revealed that amikacin and levofloxacin induced potent synergistic growth inhibition over 24 hours, whereas meropenem exhibited a largely uncooperative interaction profile. Despite enhanced bacterial killing, high concentrations of amikacin and meropenem significantly antagonized phage proliferation, resulting in 2.3-log and 1.5-log reductions in viral yield, respectively. In contrast, levofloxacin maintained a neutral relationship with viral replication. Crucially, the

specific antibiotic class dictated the genetic mechanism of phage resistance. Meropenem treatment drove massive chromosomal deletions encompassing *galU* and *hmgA*, resulting in a characteristic brown pigmentation phenotype. Levofloxacin induced localized structural variations, while amikacin favored precise point mutations in *galU*. In a *Galleria mellonella* infection model, phage-antibiotic combinations significantly improved host survival compared to monotherapies, with the amikacin combination providing the highest protection (60% survival). These findings demonstrate that phage-antibiotic synergy is a potent evolutionary catalyst that reshapes selective landscapes. Our results highlight the necessity of mechanism-informed selection of antibiotic partners to maximize therapeutic efficacy while constraining the emergence of highly adapted resistant lineage.

2025 年甘肃省胆汁标本细菌分布及其耐药性分析

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目的 分析 2025 年甘肃省胆汁标本来源细菌的分布和耐药性情况, 为临床抗菌药物的合理使用提供参考。

方法 收集甘肃省细菌耐药监测网成员单位 2025 年各医院胆汁标本细菌的分布及耐药监测数据, 使用药敏纸片扩散 (K-B) 法、最低抑菌浓度法和全自动化仪器法对菌株进行体外药敏试验, 并分析药敏结果。

结果 2025 年甘肃省胆汁标本来源纳入分析的

细菌总数为 2291 株, 其中革兰阳性菌检出率为 22.8%, 革兰阴性菌为 77.2%。革兰阳性菌以屎肠球菌为主, 共分离 194 株, 占革兰阳性菌 37.1%; 其次为粪肠球菌 111 株 (21.2%)、铅黄肠球菌 47 株 (9.0%)、金黄色葡萄球菌 20 株 (3.8%) 及鹌鸡肠球菌 18 株 (3.4%)。葡萄球菌中, MRSA 检出率 50.0%, MRCNS 检出率 83.9%, 未检出万古霉素、替考拉宁及利奈唑胺耐药株。肠球菌属中, 屎肠球菌对氨苄西林耐药率 (54.5%) 显著高于粪肠球菌 (9.9%), 两者对万古霉素耐药率分别为 0.5%、0.0%, 对利奈唑胺耐药率分别为 0.0%、1.8%。肺炎链球菌对青霉素、左氧氟沙星耐药率均为 0.0%, 对红霉素耐药率高达 100.0%, 未检出万古霉素及利奈唑胺耐药株。革兰阴性菌以大肠埃希菌为主, 共分离 819 株, 占革兰阴性菌 46.3%; 其次为肺炎克雷伯菌 253 株 (14.3%)、阴沟肠杆菌 144 株 (8.1%)、铜绿假单胞菌 97 株 (5.5%) 及产酸克雷伯菌 94 株 (5.3%)。大肠埃希菌对三代头孢、喹诺酮类耐药率较高, 碳青霉烯类耐药率处于较低水平; 肺炎克雷伯菌与阴沟肠杆菌对头孢他啶、头孢噻肟呈现不同程度耐药, 碳青霉烯类耐药率均处于低水平。铜绿假单胞菌碳青霉烯类耐药检出率为 18.6%, 鲍曼不动杆菌则高达 46.7%, 多重耐药现象较为突出。嗜麦芽窄食单胞菌对甲氧苄啶-磺胺甲噁唑、米诺环素敏感, 耐药率为 0.0%。

结论 甘肃省胆汁标本分离菌以革兰阴性菌为主, 大肠埃希菌、肠球菌属为主要致病菌, 不同菌株耐药性差异明显, 临床需结合耐药监测合理使用抗菌药物。

关键词: 胆汁; 细菌分布; 耐药性; 抗菌药物; 甘肃省

Adenosine and A2AR Agonist Alleviated Disease of Systemic *C.albicans* Infection in Mice Models

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Purpose The incidence of candidemia which mediated by systemic *Candida albicans* (*C.albicans*) infection was increasing. It is an urgent need to understand underlying disease mechanisms to identify new therapeutic targets. This study aimed to investigate the roles of adenosine-adenosine receptor signal in systemic *C.albicans* infection

Methods The candidemia mice models (named CA mice) was established by tail intravenous injection of *C.albicans*. CA Mice were treated with NECA (a metabolically stable adenosine analogues) or agonists targets different adenosine receptors (A1R, A2AR, A2BR and A3R). The survival rate, renal fungal load and tissue damage were investigated. Bone marrow-derived macrophages (BMDM) were isolated and cultured to investigate the effects of NECA and adenosine receptor agonist on phagocytosis, killing function and polarization of macrophages.

Results In CA mice, we observed that NECA and A2AR agonist treatment significantly alleviated the sepsis score and increased the survival rate. Moreover, the renal injury and fungal load were reduced by NECA and A2AR agonist treatment. However, the other adenosine receptors (i.e. A1R, A2BR and A3R) activation have no effect on survival and tissue damage of CA mice. A2AR activation could reduce macrophage infiltration in kidney and the production of inflammatory cytokine IL-6 in CA mice. Moreover, adenosine-A2AR signaling activation could enhance antifungal capacity of macrophages and promoted macrophage polarization toward to M2 subtype.

Conclusion Activation of adenosine-A2AR axis promoted macrophage M2 polarization, enhanced host defense against systemic *C. albicans* infection, and alle-

viated candidiasis. A2AR activation could be considered as an potential therapeutic strategy in candidemia.

碳青霉烯耐药铜绿假单胞菌中 PA213 通过稳定外膜调控 OMVs 释放进而诱导三级淋巴结构形成

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背景 铜绿假单胞菌是导致呼吸道等部位慢性感染的重要病原体，其中碳青霉烯耐药铜绿假单胞菌 (CRPA) 因多重耐药性、免疫逃逸能力强，成为全球公认的严重优先耐药病原体。CRPA 通过生物膜、持留菌及代谢重编程等策略适应宿主微环境，从急性感染转为难以根治的慢性感染。慢性感染背景下肺部等局部免疫微环境会发生结构性重塑，形成三级淋巴结构 TLS。TLS 能够促进局部抗原呈递与淋巴细胞活化，还可以通过维持持续的免疫细胞募集与细胞因子分泌，形成自我强化的炎症微环境。有研究提示持续的抗原刺激和慢性炎症是 TLS 形成的共同诱因，但在 CRPA 慢性感染中，TLS 是否形成、其具体表型与功能如何以及保护/病理性角色尚不明确。

方法 对 113 份临床标本进行鉴定及药敏分析。通过转录组测序、qRT-PCR 及 RACE 技术验证 PA213 的临床相关性及其全长序列，Western blot 确认其蛋白表达。评估 PA213 对 CRPA 毒力及耐药/毒力基因的影响。GST-pulldown 联合 LC-MS 及免疫荧光验证 PA213 与 OprI 的互作。提取 OMV 后经 NTA、TEM 及 SDS-PAGE 表征。在肺成纤维细胞 FDC 分化模型中，以不同 OMV 处理，ELISA 检测 FDC 相关因子。

结果 在 CRPA 中高度表达的 PA213 是一种新型双功能 sRNA，编码小分子量多肽，且在铜绿假单胞菌中高度保守和具备低氧诱导表达的适应性。

PA213 增强生物膜形成,抑制绿脓素合成,促进运动、调节细菌增殖能力等多种表型,驱动细菌向慢性感染模式转换。PA213 通过其编码的蛋白与细菌外膜稳定性关键脂蛋白 OprI 直接结合,以维持外膜结构的稳定性,并显著影响外膜囊泡(OMVs)的释放。CRPA 来源的 OMVs 形态轻度波浪状起伏且数量明显多于标准菌株。体外实验证实,CRPA 分泌的 OMVs 能够显著促进人及大鼠肺成纤维细胞向 FDC 分化,而 FDC 是启动和维持 TLS 发育的核心基质细胞,且 PA213 介导 CRPA 外膜囊泡促进 FDC 功能成熟。

结论 本研究首次揭示了 CRPA 慢性肺部感染中,一种新型双功能 sRNA PA213 通过稳定外膜、调控外膜囊泡(OMVs)分泌,进而驱动宿主免疫微环境重塑、促进三级淋巴结构(TLS)发育的新机制。为阐释 CRPA 如何调控局部免疫微环境、潜在促进慢性感染相关的 TLS 生成提供了全新的分子机制见解,也为靶向细菌-宿主界面干预耐药菌持续感染及免疫病理提供了潜在策略。

可利霉素在重症腹腔感染中临床疗效的初步观察

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目的 评估可利霉素对重症腹腔感染患者炎症反应及免疫功能的影响。

方法 回顾性分析 2024 年 8 月至 2025 年 7 月收治南京大学医学院附属金陵医院重症医学科的 10 例重症腹腔感染患者的临床资料。所有患者均接受可利霉素(剂量:0.2g/次,每日 1 次,首剂 0.4g)联合基础抗感染治疗。收集患者用药当天(T0)及用药后第 7 天(T7)的体温、白细胞计数、血小板计数、C 反应蛋白、淋巴细胞计数、凝血酶原时间、活化部分凝血活酶时间和序贯器官衰竭评分

(SOFA)。采用配对 t 检验比较用药前后各项临床指标的变化。

结果 10 例腹腔感染患者胰液培养细菌种类占比结果:培养出多重耐药铜绿假单胞菌患者占比为 60%,粘质沙雷菌患者占比为 10%,培养结果为多重耐药肺炎克雷伯菌患者占比为 40%,屎肠球菌患者占比为 20%。用药后第 7 天,患者的炎症指标下降:体温由用药前的(38.2±0.5)℃降至(37.0±0.4)℃(P=0.020),C 反应蛋白从(126.3±42.7)mg/L 降至(60.9±15.2)mg/L(P=0.008);免疫功能改善:淋巴细胞计数由(0.72±0.15)×10⁹/L 升至(1.24±0.31)×10⁹/L(P=0.040);器官功能状态无明显恶化:平均 SOFA 评分用药当天为(4.0±1.2)分,用药后为(3.5±1.1),其中 6 例患者评分降低(最大降幅 3 分),4 例患者平均 SOFA 评分用药当天维持不变。

结论 可利霉素对重症腹腔感染患者具有降低全身炎症反应状态并改善免疫功能的趋势,为重症腹腔感染的治疗提供了新思路。但受限于样本量较小,需大样本的观察性研究进一步验证。

关键词: 可利霉素;腹腔感染;炎症指标;免疫功能;临床疗效

Rapid Eradication of Multi Drug-resistant *Acinetobacter Baumannii* Using Virtual PhageBank Susceptibility Testing in A Bronchopleural Fistula: A Novel Strategy and Literature Review

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Background The management of multi-drug resistant *Acinetobacter baumannii* (MDR-AB) infections, especially in patients with structural lung diseases, is critically challenging due to limited antibiotic options

and poor drug penetration. Bacteriophage therapy represents a promising alternative; however, its application is often protracted by the slow and conventional process of phage susceptibility testing and matching in vitro, thereby creating a significant barrier for critically ill patients

Methods We present the case of a 17-year-old male with a life-threatening MDR-AB infection after traumatic bronchopleural fistula that proved refractory to conventional antibiotics, including polymyxin-based regimens. Faced with this therapeutic impasse, a preemptive and empirical phage cocktail was rapidly selected out from a virtual phagebank susceptibility testing (PST) targetting different types of capsule, bypassing traditional phage matching in vitro. The therapy was administered via a combined approach of two aerosol inhalations and one fibroscope-guided lavage.

Results Within 48 hours of initiating phage therapy, the patient's sputum culture converted to negative, accompanied by rapid resolution of fever and significant improvement in oxygenation. Subsequent in vitro analysis confirmed the accuracy of the empirical susceptibility prediction. Follow-up bronchoscopy on day 21 post-treatment revealed complete healing of the bronchial fistula, allowing for the removal of the bronchial stent and thoracic drains. The patient was subsequently discharged followed by a stable recovery.

Conclusion Our study demonstrates that empirical phage selection can facilitate rapid, preemptive phage therapy, contributing to successful microbiological eradication and clinical cure of a complicated MDR-AB infection. This innovative "treatment-first, verification-second" paradigm holds significant promise for overcoming logistical barriers and advancing precision medicine in the management of difficult-to-treat infections.

Risk Factors and Mortality for Elderly Patients with Bloodstream Infection of Carbapenem Resistance *Pseudomonas Aeruginosa*: A 10-year Longitudinal Study

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Background Bloodstream infection (BSI) caused by carbapenem resistant *Pseudomonas aeruginosa* (CRPA), especially in elderly patients, results in higher morbidity and mortality. The purpose of this study was to assess risk factors associated with CRPA BSI and short-term mortality among elderly patients in China

Methods In this retrospective cohort study, we enrolled 125 inpatients aged ≥ 65 years with BSI caused by PA from January 2014 to May 2025 in China. Data regarding demographic, microbiological characteristics, and clinical outcome were collected.

Result Among the 125 BSI elderly patients, there were 24 patients (19.2%) caused by CRPA and 101 patients (80.8%) by carbapenem-susceptible PA (CSPA). The overall 28-day mortality rate of elderly patients with a PA BSI episode was 15.2% (19/125), of which CRPA BSI patients (7/24, 29.2%) were significantly higher than CSPA patients (12/101, 11.9%). Age (OR: 1.142, 95% CI: 1.047-1.246, $P=0.003$), solid organ tumors (OR: 3.582, 95% CI: 0.939-13.665, $P=0.062$), exposure to carbapenems (OR: 5.742, 95% CI: 1.342-24.565, $P=0.018$), immunosuppression (OR: 6.869, 95% CI: 1.102-42.798, $P=0.039$) and organ dysfunction (OR: 5.124, 95% CI: 1.254-20.946, $P=0.023$) were found to be associated with the development of CRPA BSI in elderly patients. A multivariate analysis showed that organ dysfunction (OR 4.126, 95% CI 1.091-15.606,

$P=0.037$) was independent risk factors for 28-day mortality of PA BSI. Receipt of appropriate empirical antibiotic therapy is a significant protective factor in elderly patients

Conclusion In elderly patients, age, solid organ tumors, exposure to carbapenems and immunosuppression were associated with the development of CRPA BSI. Elderly patients with organ dysfunction have higher risk for CRPA BSI and death. Active screening of CRPA for the high-risk populations, especially elderly patients, is significant for early detection and successful management of CRPA infection.

医院感染控制

医护一体院感防控模式应用于 医院感染防控的效果

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感染防控是构成医院管理工作的构成部分，医院感染管理质量不只是和患者治疗效果之间存在直接关系，而且可能严重影响医院的社会形象，所以强化医院感染管理至关重要。如今，我国医院感染管理工作已经取得显著的进步，但是感染问题仍旧存在，许多抵抗能力不足或是一些易感群体，在住院后仍旧发生了院内感染，加之部分患者需要接受引流管以及微创等有创干预，都可能导致病原菌侵害机体，引发医院感染。故而，医院需要强化感染防控措施的应用，以切实提高管理工作质量，保证医疗质量以及患者的安全性。医护一体院感防控模式是在医院感染管理工作中应用广泛，且效果理想的一种管理模式。有研究表明，采用该管理模式后，可以显著降低医院感染发生率，提高患者对医院医护工作的满意度[3]。基于此，本次研究以我院收治的患者作为研究对象，旨在讨论医护一体院感防控模式的应用价值。

目的 本次研究旨在讨论医护一体院感防控模式在医院感染防控中的应用价值。

方法 本次研究随机纳入 2023 年 1 月至 2024 年 1 月我院收治的 100 例患者及 50 例医护人员作为受试者。以 2023 年 12 月 31 日为时间节点，此前实行常规干预模式，涉及患者 50 例，医护人员 25 例，记作对照组，之后实行医护一体院感防控模式，涉及患者 50 例，医护人员 25 例，记作实验组。对比两组患者与医院感染发生率，并对比两组医护人员专业掌握程度评分以及管理工作质量。

结果 本次研究结果显示，实验组患者医院感染发生率相比对照组更低，两组之间指标数值差异显著 ($P<0.05$)；实验组医护人员专业掌握水平相比

对照组更高,两组指标数值之间差异显著($P<0.05$);实验组管理质量评分相比对照组更高,两组指标数值之间差异显著($P<0.05$)。

结论 本次研究结果显示,医院采用医护一体院感防控模式可以有效降低医院感染发生概率,同时提高医护人员专业水平,加大医护人员管理力度,具有较高的实用价值。

关键词: 医护一体院感防控模式;医院感染;防控措施;感染发生率

儿童重症肺炎病原菌分布及预后相关因素分析

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目的 分析儿童重症肺炎病原菌的分布及预后相关因素。

方法 回顾性提取我院重症肺炎患儿信息,分为预后良好组(168例)和预后不良组(17例)。比较两组患儿的年龄、性别、发病至就诊时间、居住地、营养状况、白细胞(WBC)、降钙素原(PCT)、电解质、呼吸道感染史、肺炎史、呼吸困难、气促、病原体、病原菌药敏试验结果、预后相关因素。

结果 预后不良组年龄 ≤ 2 岁、营养不良、 $PCT>2\text{ng/ml}$ 、肺炎史、多重病原菌感染、多重病原体感染、呼吸困难发生率高于预后良好组($P<0.05$)。两组性别、发病至就诊时间、居住地、 $WBC>18\times 10^9/L$ 、电解质紊乱、呼吸道反复感染、气促发生率无明显差异($P>0.005$)。从185例患儿中检出病原体383株,其中病原菌241株,病毒93株,支原体19株。预后良好组168例患儿,检出病原菌207株,病毒98株,支原体14株。预后不良组34例患儿,检出病原菌34株,病毒25株,支原体5株。预后不良组细菌+病毒混合感染、三种及以上病原菌混合感染发生率高于预后良好组($P<0.05$)。预

后不良组细菌+病毒混合感染、三种及以上病原菌混合感染发生率高于预后良好组($P<0.05$)。肺炎链球菌对红霉素、四环素、青霉素、复方新诺明、克林霉素,金黄色葡萄球菌对红霉素、青霉素,流感嗜血杆菌对氨苄西林、氨苄西林/舒巴坦、头孢呋辛、阿奇霉素、复方新诺明,鲍曼不动杆菌对复方新诺明、替卡西林/克拉维酸、左氧氟沙星、美罗培南、多西环素耐药率均超过50%。

结论 低龄、营养不良、 $PCT>2\text{ng/ml}$ 、多重病原体感染是预后不良的独立危险因素。

Risk Factors for Nosocomial Infections in ECMO Patients: A Systematic Review and Meta-analysis

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Background Nosocomial infection (NI) is a common and serious complication in patients receiving extracorporeal membrane oxygenation (ECMO). Although numerous studies have investigated its risk factors, results are inconsistent, and individual studies are often limited by sample size. A systematic synthesis of evidence is crucial to identify key risk factors and guide clinical prevention

Methods Following PRISMA guidelines, this systematic review and meta-analysis (PROSPERO: CRD420251161290) systematically searched five databases (PubMed, Web of Science, Embase, Cochrane Library, EBSCO) from inception to September 24, 2025. We included studies reporting multivariate analyses of risk factors for NI in adult ECMO patients. Two reviewers independently performed study selection, data extraction, and quality assessment using the Newcastle-Ottawa Scale (NOS). Pooled odds ratios (ORs) with 95%

confidence intervals (CIs) were calculated using random-effects models. Sources of high heterogeneity ($I^2 \geq 50\%$) were explored using meta-regression and subgroup analyses.

Results Forty-two studies involving approximately 47,852 patients were included. Meta-analysis identified several factors significantly associated with increased NI risk: continuous renal replacement therapy (CRRT) (pooled OR 2.00, 95% CI 1.44–2.78), central venous catheter (CVC) placement (OR 1.01, 95% CI 1.00–1.02), ECMO support duration (OR 1.03, 95% CI 1.02–1.04), higher Sequential Organ Failure Assessment (SOFA) score (OR 1.07, 95% CI 1.01–1.14), type 2 diabetes mellitus (T2DM) (OR 1.21, 95% CI 1.02–1.42), microbial colonization (OR 2.95, 95% CI 1.22–7.12), and duration of mechanical ventilation (OR 1.21, 95% CI 1.01–1.46). Analysis of ECMO duration showed high heterogeneity ($I^2 = 89.9\%$), which was largely attributed to a small-study effect. Factors like age, body mass index (BMI), and hypertension showed no significant association.

Conclusion This meta-analysis demonstrates that the risk of NI in ECMO patients is multifactorial, linked to greater illness severity (high SOFA score), comorbidities (T2DM), and the duration and complexity of invasive interventions (ECMO, CRRT, CVC, mechanical ventilation). Prevention strategies should focus on high-risk patients, implementing bundled interventions to minimize the duration of invasive support and adhering to strict infection control protocols.

Analysis of Healthcare-associated Infection Cases in Intensive Care Medicine Departments of Medical Institutions in Luzhou City From 2019 To 2025

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Objective To understand the characteristics of hospital-acquired infection cases and the changes in pathogen resistance in the ICU of medical institutions in Luzhou City

Methods A retrospective analysis was conducted on the clinical medical records, pathogen distribution, and drug resistance of ICU HAI patients in Luzhou City from January 1, 2019, to December 31, 2025

Results A total of 1,153 ICU HAI inpatients were included, with 628 males and 525 females. Clinical outcomes: 1,032 cases showed worsening conditions and survived, 121 cases resulted in death. Respiratory tract infections: 496 cases (41.98%)—lower respiratory tract infections (pneumonia): 396 cases—VAP 131 cases, POP 82 cases. Bloodstream infections 248 cases (22.16%)—CLABSI 72 cases. Urinary tract infections 208 cases (18.08%)—CAUTI 92 cases. SSI 91 cases (8.35%). Soft tissue infections: 26 cases (2.13%), intracranial infections: 16 cases (0.97%), gastrointestinal infections: 32 cases (3.10%). Specimens submitted for testing 1,028 cases—respiratory specimens 477 cases—sputum 300 cases, BALF 291 cases; blood: 354 cases, urine: 105 cases, stool: 39 cases, cerebrospinal fluid: 16 cases, tissue specimens: 20 cases, ascites: 6 cases. A total of 1,212 pathogens were identified, including 211 Gram-positive bacteria (45.88%): *Staphylococcus aureus* 133 cases, MRSA 48 cases, enterococci: 42 cases—*Enterococcus faecalis*: 26 cases *Enterococcus faecium*: 21 cases, vancomycin-resistant enterococci: 4 cases, *Streptococcus pneumoniae* 18 cases, *Streptococcus pyogenes* 12 cases; Gram-negative bacteria 801 strains (45.88%): *Escherichia coli* 138 strains, CREC 48 strains, *Klebsiella pneumoniae* 216 strains, CRKP 123 strains, *Pseudomonas aeruginosa* 93 strains, CRPA 30 strains, *Acinetobacter baumannii* 326 strains, CRAB

224 strains, *Stenotrophomonas maltophilia* 10 strains, *Serratia marcescens* 4 strains, *Morganella morganii* 2 strains, *Enterobacter cloacae* 2 strains, *Burkholderia cepacia* 1 strain, *Citrobacter freundii* 1 strain, *Proteus mirabilis* 1 strain; fungi 194 strains (8.24%): *Candida albicans* 112 strains, *Candida tropicalis* 69 strains, *Candida parapsilosis* 1 strain, *Candida auris* 1 strain, *Aspergillus fumigatus* 4 strains, *Mucorales* 3 strains. The detection rate of carbapenem-resistant *Acinetobacter baumannii* and other Gram-negative bacteria in ICU hospital infection cases showed an upward trend from 2019 to 2025 ($P < 0.05$).

Conclusion The most common cases of hospital acquired infections in the intensive care unit of medical institutions in Luzhou City are lower respiratory tract infections. In the past six years, the detection rate of carbapenem resistant *Acinetobacter baumannii* and other Gram negative bacteria has been increasing year by year. It is necessary to strengthen ICU hand hygiene, environmental cleanliness and disinfection, rational use of antibiotics, and isolation of multi resistant cases to prevent and control hospital acquired infections

Whole-genome Sequencing Identifies Persistent Transmission of A High-risk ST2 *Acinetobacter Baumannii* Clone in A Guangzhou Hospital

U-I C

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Background *Acinetobacter baumannii* (*A. baumannii*) has posed a serious threat to the global

healthcare environment due to its widespread multidrug resistance. However, the long-term molecular epidemiological characteristics, drug resistance profiles and genomic characteristics of *A. baumannii* isolates in Guangzhou, China have not been fully elucidated. This study aims to systematically analyze these characteristics using *Acinetobacter baumannii* strains from a local tertiary hospital

Methods A total of 98 non-repeating clinical isolates of *A. baumannii* collected between 2013 and 2021 were analyzed in the study. Whole genome sequencing technology was also used for multi-locus sequence typing (MLST), resistance genomic/virulence genomic analysis (based on the CARD/VFDB database), plasmid screening (with the PlasmidFinder tool), and pan-genomic analysis (via the Roary tool).

Results Among the 21 identified STs, ST2 was the dominant lineage, accounting for 66.3% of all isolates, indicating the establishment of a predominant epidemic clone. Compared with non-ST2 strains, ST2 isolates exhibited a significantly higher rate of carbapenem resistance (95.38%) and carried a higher burden of resistance determinants, including blaOXA-23, blaADC-25, tet(B), and multiple aminoglycoside resistance genes. Notably, ST2 strains harbored a highly conserved and dominant repertoire of virulence factors, particularly those involved in iron acquisition and host adaptation, such as ompA, abaI, and the complete siderophore synthesis and uptake systems (basA–basJ, bauA–bauF, and entE). These features likely confer enhanced survival, persistence, and transmissibility in the hospital environment, supporting the classification of ST2 as a high-risk epidemic clone. Consistent with this, genomic clustering and temporal aggregation of ST2 isolates suggested sustained intrahospital transmission during the study period. Pangenome analysis revealed that *A. baumannii* possesses a large accessory genome (76.4%),

reflecting substantial genomic plasticity that may facilitate rapid adaptation to antimicrobial and host-derived selective pressures

Discussion: As the first long-term genomic epidemiological study of *A. baumannii* in Guangzhou, our findings confirm that ST2 is the predominant multidrug-resistant and outbreak-prone lineage, driven by the convergence of resistance gene accumulation, virulence optimization, and genomic flexibility. These results underscore the urgent need to strengthen infection control measures and antimicrobial stewardship to curb the continued spread of this high-risk clone

Keywords *Acinetobacter baumannii*, genomic characteristics, molecular epidemiology, multidrug resistance, ST2, virulence factors

层级化管理联合体感音乐护理对神经重症患者呼吸机相关性肺炎发生率、呼吸功能的影响

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目的 分析层级化管理联合体感音乐护理对神经重症患者呼吸机相关性肺炎(VAP)发生率及呼吸功能的影响。层级化管理能有效促进重症肺炎机械通气患者病情恢复,改善患者血氧情况,减少谵妄、VAP及负性情绪;体感音乐护理是一种融合听觉与躯体感觉的音乐干预手段,其通过将音乐低频信号放大并转换为物理振动,经骨传导途径传递至人体,结合心理与生理的双重作用,对患者实施身心整合干预。

方法 本研究选取2020年2月—2025年12月收治于大连理工大学附属第三人民医院神经重症的90例患者,按随机数字表法将其均分为观察组与对照组,每组各45例。观察组实施层级化管理联合体

感音乐护理,对照组给予常规护理。比较两组干预前后的病情严重程度,[采用急性生理与慢性健康评分II(APACHEII)及序贯器官衰竭估计(SOFA)]、呼吸功能指标、VAP发生率及负性情绪[采用正性负性情绪量表(PANAS)]。

结果 干预后,两组APACHEII、SOFA评分均较干预前下降($P<0.05$),且观察组评分均低于对照组($P<0.01$);干预后,两组呼吸功能较干预前改善($P<0.05$),且观察组改善程度优于对照组($P<0.01$);观察组VAP发生率及PANAS(负性情绪)评分均低于对照组($P<0.05$, $P<0.01$)。

结论 层级化管理联合体感音乐护理可降低神经重症患者VAP的发生率,改善呼吸功能。

2023-2025年某三级医院尿路感染患者病原菌耐药性及其流行病学特征

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目的 分析尿路感染患者中段尿培养阳性病例的细菌谱特征及耐药情况,为制定尿路感染防控措施、及临床合理选用抗菌药物提供参考依据。

方法 回顾分析2023年1月-2025年12月医院清洁中段尿培养阳性的尿路感染患者844例的临床资料,分析病原菌、药敏情况、耐药率及其流行病学特征。

结果 2023-2025年共收集该医院尿路感染患者的非重复临床尿培养病原菌844株,其中女性444例,男性400例;病原菌分布由高到低依次为革兰阴性菌(671株,占79.50%)、革兰阳性菌(129株,占15.28%)、真菌(44株,占5.21%),以大肠埃希菌(57.70%)、肺炎克雷伯菌(9.72%)、粪肠球菌(7.82%)、屎肠球菌(4.74%)为主。不同年份间的病原菌分布情况比较差异无统计学意义($P>0.05$)。大肠埃希菌对各抗菌药物的耐药率在3年间差异无统

计学意义($P>0.05$),对氨苄西林、哌拉西林、左氧氟沙星、环丙沙星的耐药率高($>60\%$)。肺炎克雷伯菌对各抗菌药物的耐药率在 3 年间差异无统计学意义($P>0.05$),对氨苄西林、哌拉西林、环丙沙星的耐药率高($>60\%$)。粪肠球菌对各抗菌药物的耐药率在 3 年间差异无统计学意义($P>0.05$),对克林霉素、妥布霉素、甲氧苄啶、复方新诺明、夫西地酸、阿米卡星、奎奴普丁/达福普汀、四环素、环丙沙星的耐药率高($>60\%$)。屎肠球菌对各抗菌药物的耐药率在 3 年间差异无统计学意义($P>0.05$),对阿米卡星、夫西地酸、甲氧苄啶、克林霉素、庆大霉素、妥布霉素、复方新诺明、氨苄西林、呋喃妥因、环丙沙星的耐药率高($>60\%$)。泌尿道感染在医院感染部位构成比中呈逐步上升趋势,但差异无统计学意义($P>0.05$)。

结论 大肠埃希菌、肺炎克雷伯菌、肠杆菌为该医院住院患者尿路感染主要致病菌;氨苄西林、哌拉西林、左氧氟沙星、环丙沙星总体耐药率高,医院需持续加强抗菌药物合理应用的管理及医院感染防控,切实做好耐药监测工作。

关键词: 尿路感染;中段尿培养;病原菌;耐药性

(multidisciplinary team, MDT),开展协作研讨,根据不同院区 and 场景对清洁消毒流程、技术路径及职责分工进行系统梳理与标准化。

结果 共采集救护车医疗舱环境标本 144 份,其中基线调查 60 份,规范化清洁消毒方案实施后采集 84 份。基线阶段菌落总数超标率为 38.33%;规范实施后未清洁消毒组及清洁消毒后组超标率分别为 4.76%和 2.38%,均低于基线水平(未清洁消毒组: $\chi^2=29.64$, $P<0.01$;清洁消毒后组: $\chi^2=15.81$, $P<0.01$)。明确了不同院区及转运场景下的责任主体与管理要求,其中主院区由保洁人员负责日常清洁、车队司机负责消毒及复核;其他院区由各院区保洁人员实施清洁消毒,车队司机统一复核;急诊科救护车强化高频接触部位的日常处置;传染病转运救护车执行每次转运后即刻清洁消毒。各类场景均建立清洁、消毒、记录与复核相衔接的闭环管理机制,构建分场景的规范化清洁消毒管理模式。

结论 本研究通过开展环境卫生学监测,识别了救护车医疗舱环境微生物污染水平及关键污染部位,在此基础上系统梳理清洁消毒流程,构建规范化清洁消毒管理模式,为多院区条件下院前急救感染防控提供规范化管理路径。

区域协同医疗模式下救护车环境污染风险及防控策略研究

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目的 在多院区一体化运行背景下,评估救护车医疗舱环境微生物污染状况,建立规范化清洁消毒管理模式。

方法 选取承担跨院区患者转运任务的救护车为研究对象,对医疗舱空气及高频接触物体表面开展环境卫生学采样与培养检测;组织多学科工作组

多模式联合干预在重症监护室医院细菌真菌感染控制中的应用研究

李

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目的 探讨多模式联合干预措施在重症监护室(ICU)医院细菌真菌感染控制中的应用效果,分析 ICU 细菌真菌感染的高危因素,制定针对性防控方案,降低医院感染发生率,规范重症病房感染管控流程,为临床医院感染防治提供科学、可行的实践依据,助力细菌真菌感染防控水平的提升。

方法 选取 2024 年 1 月-2025 年 6 月我院 ICU

住院患者 180 例作为研究对象，其中 2024 年 1-12 月实施常规感染防控措施的 90 例患者为对照组，2025 年 1-6 月实施多模式联合干预的 90 例患者为观察组。对照组采取常规病房消毒、手卫生宣教、无菌操作规范等基础防控手段；观察组在对照组基础上，联合环境物表精准消杀、耐药菌主动监测、侵入性操作全程管控、医护人员手卫生强化考核、抗细菌真菌药物合理使用督导等多模式干预措施。对比两组患者医院细菌真菌感染发生率、感染病原菌分布情况，以及医护人员感染防控操作依从性，评估干预措施的有效性。

结果 观察组 ICU 患者医院细菌真菌感染发生率为 4.44%，显著低于对照组的 12.22%，差异具有统计学意义 ($P<0.05$)；感染病原菌中，革兰阴性菌占比最高，其次为革兰阳性菌与真菌，观察组各类病原菌感染例数均明显少于对照组。同时，观察组医护人员手卫生依从率、环境消毒达标率、侵入性操作规范率均达到 95% 以上，显著高于对照组的 80% 以下，各项感染防控核心指标均得到明显改善，未出现干预相关不良事件，防控措施具备良好的临床可行性。

结论 多模式联合干预措施可针对性降低 ICU 医院细菌真菌感染发生率，有效优化病房感染管控质量，提升医护人员感染防控依从性，是医院感染控制领域切实可行的新防控模式。该方案贴合细菌真菌感染防治的临床需求，兼具实用性与可推广性，能为重症病房及其他科室医院感染防控工作提供重要参考，助力医院细菌真菌感染防治工作的规范化开展。

关键词：医院感染控制；重症监护室；细菌真菌感染；多模式干预；防控依从性

神经外科重症监护室侵入性操作负荷与多重耐药菌医院感染量化风险关联研究

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目的 量化分析神经外科重症监护室 (NSICU) 高频侵入性操作叠加负荷与多重耐药菌 (MDRO) 院内感染关联强度，明确高风险暴露临界阈值，贴合精细化院感管控实景，优化侵入性诊疗配套防控举措，为精准压降耐药菌感染、规范重症院感防控提供可靠循证支撑。

方法 采用回顾性巢式病例对照研究，选取 2019 年 1 月—2025 年 12 月我院 NSICU 重型颅脑损伤、重症脑出血、开颅术后危重症患者为研究对象，剔除入院 48h 内合并 MDRO 定植感染、ICU 入住不足 72h、晚期肿瘤及免疫缺陷等不符入组病例。以院内新发 MDRO 血流、下呼吸道、中枢、泌尿系相关耐药感染患者为病例组，共 52 例；按 1:2 配比纳入同期基线资料匹配、未发生 MDRO 感染患者 104 例为对照组。收集两组基础合并症、ICU 入住时长、围手术期抗菌药物使用等混杂资料，统计四类核心侵入性操作留置时长与叠加频次。构建侵入性操作累计暴露负荷量化评分体系，采用多因素二元 Logistic 回归筛选独立危险因素，联合限制性立方样条模型判定感染风险临界拐点。

结果 共纳入研究对象 156 例，两组基线资料均衡可比，组间混杂因素无统计学差异 ($P>0.05$)。NSICU 主要检出 MDRO 菌株为耐碳青霉烯类鲍曼不动杆菌、耐碳青霉烯类肺炎克雷伯菌及多重耐药铜绿假单胞菌。校正混杂因素后，多因素回归分析显示：有创机械通气留置 ≥ 7 d、高位中心静脉导管留置 ≥ 5 d、同步留置 ≥ 2 根侵入性管路、反复颅内引流操作均为 MDRO 院内感染独立危险因素，OR 值分别为 3.68、3.21、4.02、3.85，均 $P<0.01$ 。侵入性操作负荷评分与 MDRO 感染呈正向剂量依赖关系，评分越高感染风险越高；限制性立方样条分析证实，多管路叠加暴露达到临界时长后，感染风险呈非线性陡增。亚组分析显示，开颅术后早期多管路联合侵入性干预患者耐药菌感染风险显著更高。

结论 侵入性管路长时留置、多类型侵入性操作叠加暴露是 NSICU 多重耐药菌感染可控独立危

险因素, 存在明确量化风险阈值。院感管理可依托本研究结果, 落实每日管路专项评估、尽早规范拔管, 强化多管路叠加高风险时段手卫生与环境消杀, 精准开展靶向防控, 切实降低 NSICU 重症患者 MDRO 感染负担, 适宜在重症院感常态化管控中推广应用。

Whole Genome Sequencing Reveals Significant Intra-hospital Clonal Transmission and A Potential Multidrug Resistant and Hypervirulent Sequence Cluster of *Corynebacterium Striatum*

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With increasing reports about *Corynebacterium striatum*, its role as an emerging human pathogen is been recognized. However, few studies have explored the genomic epidemiology of *C. striatum* in China. A total of 263 isolates collected in various specimens from 2021 to 2022 were analyzed from a tertiary hospital in China. Nearly all isolates (98.5%, 259/263) were multidrug resistant (MDR). The highest resistance was observed for clindamycin (96.5%), followed by ciprofloxacin (95.0%) and erythromycin (93.5%). Genome sequencing indicated a significant prevalence of intra-hospital clonal transmission, involving six distinct clones (clone one-six). An average of 7.35 antimicrobial resistance genes and 10.65 virulence genes were identified in each strain. Genomic analysis identified a potentially hypervirulent sequence cluster (designated SC3) exhibiting near-universal carriage of four pilus assembly genes (*spaH*, *spaI*, *srtD*, and *srtE*), whereas these

genes occurred at significantly lower frequencies in other sequence clusters. Further analysis estimated the emergence of SC3 strains around 1929.56 (95% HPD: 1863.41-1995.71). Phenotypic virulence assays demonstrated that *C. striatum* strains carrying the *spaH*, *spaI*, *srtD*, and *srtE* genes exhibited significantly higher virulence compared to strains lacking these genes. Our results revealed that multiple MDR *C. striatum* clones were circulating in the hospital. A suggestive MDR and hypervirulent SC3 was identified with potential evolutionary advantage and enhanced transmission capability.

近五年某传染病医院手术相关职业暴露流行病学调查

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目的 分析某传染病医院近五年(2020-2024年)手术相关职业暴露的流行病学特征及其影响因素, 为制定针对性的职业防护策略提供科学依据。

方法 采用回顾性队列研究设计, 收集该院2020年1月至2024年12月期间通过医院感染监测系统上报的104例手术相关职业暴露事件。纳入标准为暴露发生于手术或围手术期, 暴露类型为血液或体液经黏膜接触或锐器损伤, 且报告信息完整。排除非手术相关暴露及关键信息缺失案例。采用EpiData 3.1进行双人录入与逻辑校验, 使用R 4.4.2软件进行统计分析, 计数资料采用频数与构成比描述, 组间比较采用 χ^2 检验、Mann-Whitney U检验或秩和检验, 显著性水平设为 $P < 0.05$ 。

结果 2020至2024年间, 手术相关职业暴露发生率呈逐年上升趋势, 2024年增幅最为显著(0.241%)。男性暴露者占71.2%, 年龄以25~39岁为主(合计50.0%)。手术助手为最主要暴露角色(50.0%), 感染外科与骨科暴露例数最多(各占

18.3%)。暴露类型以针刺伤或锐器伤为主(60.6%)。不同手术角色在性别、年龄、学历、岗位、工龄及工作科室方面均存在显著差异($P<0.001$)。急诊手术与非急诊手术在工作科室及手术分级方面差异显著($P<0.05$)；针刺伤或锐器伤多发生于非急诊时间(65.1%)，而接触暴露则集中于急诊时间(63.4%)，差异有统计学意义($P<0.05$)。

结论 某传染病医院手术相关职业暴露风险较高，且呈现逐年上升趋势，暴露风险与手术角色、工作科室、急诊状态及暴露类型密切相关。手术助手、低年资医师、骨科与感染外科为高危人群与高风险科室。急诊手术中的骨科与产科暴露风险尤为突出，接触暴露在急诊情境下更常见。现有防护培训与上报管理仍存在不足，需针对不同岗位、不同暴露类型及时段，制定差异化、精准化的职业防护策略，强化术前防护准备、锐器安全管理及暴露后追踪处理，以有效降低职业暴露发生率及其不良后果。

上海市 11 家三级医院 ICU 环境耐碳青霉烯类肺炎克雷伯菌分子特征研究

史庆丰

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目的 阐明重症监护病房(ICU)环境中耐碳青霉烯类肺炎克雷伯菌(CRKP)的毒力特征、耐药基因分布等，为院内感染防控提供分子流行病学依据。

方法 选取 2024 年 12 月至 2025 年 1 月上海市 11 家三级医院 ICU 患者周边环境、公共区域及医院污水中分离的 23 株 CRKP，采用全基因组测序(WGS)技术，分析其多位点序列分型(ST)、毒力基因谱、耐药基因分布及同源进化关系。

结果 23 株 CRKP 涵盖 9 种 ST 型，以 ST 11 (34.78%)、ST 15 (26.09%) 为主要流行型；耐药基因以 β -内酰胺类、喹诺酮类、磷霉素类为主，blaKPC-2 (65.22%) 为核心碳青霉烯类耐药基因，

在患者周边环境检出率最高(83.33%)，且所有菌株均携带磷霉素耐药基因 *fosA*；11 株(40.7%)因携带 *iucABD*、*iutA*、*rmpA* 及 *rmpA2* 高毒力基因而同时判定为高毒力株(hvKP)，其中 81.82% (9/11) 来自患者周边环境，显著高于其他区域($P=0.023$)；同源进化分析显示，CRKP 呈现明显克隆聚集性，ST 11 型为 hvKP 主要聚类簇，存在跨医院传播可能。

结论 ICU 环境中 CRKP 存在“高毒力和高耐药”复合威胁，患者周边环境是其传播的关键环节，需针对性加强环境管控与抗菌药物合理使用，以阻断传播链。

基于 DRGs 模式在骨科多重耐药菌感染管理的效果分析

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目的 探讨基于疾病诊断相关分组(DRGs)付费模式下多重耐药菌(MDRO)感染精准防控策略，并评价其实际应用效果，为医院感染管理提供循证策略。

方法 收集 2024 年全院各临床科室多重耐药菌感染发生率、DRGs 分组、病例组合指数(CMI)等 DRGs 相关指标，通过 CMI 调整多重耐药菌感染发病率，将 CMI 值最低、MDRO 感染发生率最高的骨科确定为本次研究的干预科室，并制定针对性的多重耐药菌集束化感染防控方案，比较实施 DRGs 模式的感染管理干预为节点，实施前(2024 年 1 月至 12 月)和实施后(2025 年 1 月至 2025 年 12 月)骨科住院患者的 MDRO 感染发生率、手卫生依从率、外科换药达成率、抗菌药物使用强度(AUD)、平均住院床日等指标的变化。

结果 在 CMI 调整后，各科室多重耐药菌(MDRO)感染发生率无显著差异($P>0.05$)。综合评定 CMI 最低(1.53)、MDRO 感染发生率最高

(0.21%)的骨科为院感高风险科室。在 DRGs 支付模式下实施针对性感控措施后:骨科 MDRO 感染率呈下降趋势($P=0.339$),抗菌药物使用率由 42.78%降至 41.04%,使用强度由 20.762 DDDs/100 人降至 18.82 DDDs/100 人;手卫生依从率(74.67%→79.33%)与正确率(93.75%→94.37%)均有提升。比较外科换药督查指标显著改善($P<0.001$);干预前后平均住院日($P=0.019$)与总平均住院费用($P<0.001$)明显降低,其差异均具有统计学意义。

结论 在 DRGs 模式下,医院感染管理需从粗放式防控转向基于数据管控的精细化管理,通过 CMI 识别不同病例的技术难度,以此调整多重耐药菌感染发生率,达到精准识别高风险环节的目的,通过强化集束化防控措施、规范外科换药、优化抗菌药物使用,能够显著阻断 MDRO 传播链,有效降低感染发生率,并转化为住院日缩短与医疗费用下降,为医院感染管理提供基于数据的循证策略,实现医疗质量提升与医保支付优化的双重目标。

关键词: 疾病诊断相关分组;病例组合指数;多重耐药菌;骨科;精准防控措施;效果分析

某三甲综合教学医院肺炎克雷伯菌感染患者的回顾性分析

马睿

天津医科大学总医院

目的 分析某三甲综合教学医院肺炎克雷伯菌感染患者的临床特征、耐药流行情况及其对诊疗经过与预后的影响。

方法 单中心回顾性研究。纳入符合标准的 168 例肺炎克雷伯菌感染的住院患者,收集人口学资料、基础疾病、感染部位、实验室/影像学指标、病原学和药敏结果、抗菌药物使用与结局信息。以“耐药菌感染”为主要结局变量,以“预后不良(非死亡复合终点)”为次要结局变量,进行单因素分析及多因素

Logistic 回归,并以 ROC 曲线/AUC 评估模型判别能力。

结果 耐药菌感染 47 例(27.98%),其中多重耐药(MDR-KP)26 例(15.48%),碳青霉烯耐药(CRKP)7 例(4.17%)。住院期间共有 83 例(49.40%)进行了抗菌治疗方案调整。出院结局以好转为主(87.50%),死亡 4 例(2.38%)。在复合终点定义下,预后不良与耐药菌感染及部分基础情况/严重程度相关因素存在关联。

结论 耐药 KP 感染与患者基础疾病及医疗相关暴露有关。耐药组经验性治疗恰当率较低,且治疗方案调整更常见,提示在耐药高风险患者中应加强早期病原学送检,并依据药敏结果及时优化抗菌药物治疗。

关键词: 肺炎克雷伯菌;抗菌药物耐药;多重耐药;碳青霉烯耐药肺炎克雷伯菌;危险因素;临床预后

基于 4R 危机管理理论的多学科协作模式在重症监护病房 CRE 感染防控中的应用研究

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中南大学湘雅医院

目的 构建基于 4R 危机管理理论下的多学科协作方案,评价其在重症监护病房耐碳青霉烯类肠杆菌目细菌感染防控中的实际成效。

方法 通过回顾性调查,以 2022 年 11 月至 2023 年 10 月期间所有入住重症医学科的 2076 例患者作为对照组,2023 年 11 月至 2024 年 10 月期间所有入住重症医学科的 3497 例患者作为干预组。对照组采用由 ICU 医院感染管理小组主导的常规多重耐药菌感染防控策略。干预组开始时间则在对照组的基础上,实施基于 4R 危机管理理论的多学科协作 CRE 感染防控管理模式。通过比较干预前后 CRE 检出率、CRE 医院感染发生例次率、ICU 千日医院感染例次

发病率、ICU 器械相关感染发病率及多重耐药菌感染防控综合措施落实情况,评估该模式的干预成效。

结果 回顾性分析显示,实施干预后,ICU 内 CRE 防控取得显著成效,ICU 千日医院感染例次发病率从干预前的 4.86‰下降至干预后的 3.3‰ ($\chi^2=7.317$, $P=0.007$),差异具有统计学意义;CRE 检出率从干预前的 34.96%提升至干预后的 45.6% ($\chi^2=3.35$, $P=0.07$),CRE 医院感染发生例次率从 1.93%下降至 1.57% ($\chi^2=0.037$, $P=0.848$),差异均无统计学意义。实施前后,ICU 器械相关感染发病率均呈下降趋势,CRBSI 发病率从 6.06‰降至 3.02‰ ($\chi^2=8.958$, $P=0.003$),CAUTI 发病率从 3.23%降至 2.00% ($\chi^2=4.289$, $P=0.039$),差异均具有统计学意义。VAP 发病率从 2.88‰降至 1.88‰ ($\chi^2=1.268$, $P=0.260$),差异无统计学意义。手卫生依从率从实施前 65.45%提升到实施后的 72.55% ($\chi^2=20.013$, $P<0.0001$),手卫生正确率从实施前 76.44%提升到实施后的 98.20% ($\chi^2=273.68$, $P<0.0001$);隔离措施执行率从实施前 85.52%提升到实施后的 96.74% ($\chi^2=4.137$, $P=0.04196$),差异具有统计学意义。

结论 基于 4R 危机管理理论的多学科协作模式可有效降低 ICU 千日医院感染例次发病率与器械相关感染发病率,提升多重耐药综合防控措施的执行质量,提高重症患者医院感染管理的科学性与系统性,但未能降低 ICU 的 CRE 感染发生率,需进一步探索。

ICU 耳念珠菌感染环境追踪监测与时空关联分析研究

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目的 探讨 ICU 内耳念珠菌的感染分布特征、环境传播规律及检测方法效能,为制定针对性防控策略提供依据。

方法 对 2025 年 1 月至 2026 年 3 月某院重症医学科及神经外科 ICU 确诊的 6 例耳念珠菌感染患者开展临床追踪,同时对患者周边的环境物表和接触的医务工作者进行扩大筛查,采集样本进行真菌培养检测,其中 39 份额外采用实时荧光定量(PCR)法进行检测,并对结果进行比较分析。

结果 6 例患者均为男性,年龄中位数为 74 岁(范围 56-95 岁)。5 例来自重症医学科,1 例来自 NICU。6 例中死亡 4 例,好转 1 例,自动出院 1 例。流行病学调查显示,重症医学科的 5 例患者在时间(2025 年 1 月至 2026 年 2 月)和空间上存在明显聚集和暴露关联。其中, P4 与 P5 曾先后入住同一床位(5 床),提示该床位环境持续污染可能是主要传播媒介。环境及人员筛查发现,医疗设备设施与床单元设施阳性率最高(均为 19.44%)。39 份同步检测的样本中,PCR 法的阳性检出率(33.33%)显著高于传统培养法(12.82%),差异有统计学意义 ($\chi^2=5.73$, $P=0.017$)。

结论 重症医学科耳念珠菌感染存在明显的环境交叉传播风险,PCR 法在隐匿性污染检测中具有显著优势。建议从检测筛查、环境消毒、人员防护三方面构建一体化综合防控体系。

临床药师通过 PDCA 降低神经外科抗菌药物使用强度案例

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目的 抗菌药物使用强度为三级公立医院绩效考核指标,该指标可反映不同年度的用药动态和用药结构,为进一步规范发展药学服务,提升药学服务水平,促进合理用药,保障药学监护服务质量,分析我院神经外科抗菌药物使用强度超标原因,运用 PDCA 循环管理模式开展多维度干预,降低科室抗菌药物使用强度,提升院感防控与临床药学服务质

量。

方法 收集我院神经外科 2025 年 8-12 月抗菌药物使用强度数据, 对比全院指标及考核目标值, 明确科室用药管控短板。采用头脑风暴、鱼骨图梳理颅内感染高发相关危险因素, 通过柏拉图开展真因验证, 结合 5W-2H 工作法制定针对性改进措施, 由临床药师牵头, 联合医师、护士、院感人员, 从合理用药培训、手卫生管控、无菌操作规范、引流管精细化管理等方面实施闭环干预。

结果 干预后神经外科的抗菌药物使用强度从 67.47、56.00 降至 47.26, 指标呈持续下降趋势, 逐步逼近管控目标。

结论 神经外科抗菌药物使用强度升高与术后颅内感染高发、手术操作不规范、引流管留置过久、基础疾病控制不佳及不合理联合用药密切相关。临床药师依托 PDCA 循环开展全过程质量管理, 精准挖掘临床用药隐患, 实现多学科协同管控, 有效降低科室抗菌药物使用强度, 规范临床抗感染治疗行为, 为临床科室抗菌药物精细化管理提供可行、可推广的实践模式。

重症肺炎多重耐药菌感染风险预测模型构建与验证

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目的 构建并验证一种用于早期识别重症肺炎患者发生多重耐药菌(MDROs)感染风险的可视化预测模型, 为临床实施精准防控提供依据。

方法 采用回顾性队列研究, 选取 2024 年 1 月—2025 年 7 月上海中医药大学附属龙华医院重症医学科收治的 452 例重症肺炎患者作为研究对象。按时间分为训练集(315 例)和验证集(137 例)。通过单因素分析、最小绝对收缩与选择算子(LASSO)回归和多因素 logistic 回归筛选危险因素, 构建列线

图预测模型。采用 Bootstrap 法进行内部验证, 并使用时序验证集进行验证, 通过受试者工作特征(ROC)曲线下面积(AUC)、校准曲线和决策曲线分析(DCA)评估模型的区分度、校准度和临床实用性。

结果 呼吸道病原菌以革兰阴性菌为主(61.85%), 其中肺炎克雷伯菌居首位(24.28%)。最终确定 4 个 MDROs 感染的危险因素: 脑血管病史(OR=1.764)、抗菌药物使用种类 ≥ 3 种(OR=3.071)、有创机械通气时间 ≥ 3 d(OR=2.772)、胃管留置时间 ≥ 7 d(OR=2.436)。预测模型在训练集与验证集中的 AUC 分别为 0.773(95%CI 0.722~0.825)和 0.790(95%CI 0.715~0.866), 校准曲线显示预测风险与实际风险一致性良好, 决策曲线分析表明模型在较宽阈值范围内具有临床净获益。

结论 本研究构建的预测模型具有良好的区分能力、校准度和临床适用性, 可为重症肺炎患者 MDROs 感染的早期识别与针对性干预提供可视化工具。

机械通气合并念珠菌定植患者发生呼吸机相关肺炎的危险因素及预后模型研究

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目的 分析重症监护室内机械通气合并呼吸道念珠菌定植患者发生呼吸机相关肺炎(VAP)的危险因素, 并构建及验证其临床预后不良的预测模型。

方法 回顾性分析长沙市中心医院 2023 年 1 月至 2025 年 12 月期间机械通气 ≥ 48 小时且呼吸道念珠菌培养阳性的患者。通过向后逐步多因素 Logistic 回归分析 VAP 的独立危险因素。采用 LASSO 回归筛选变量后构建预后不良的多因素 Logistic 回归预测模型, 并使用十折交叉验证和受试者工作特征(ROC)曲线评估其准确性。

结果 共纳入 185 例患者, 43 例(23.24%)发生 VAP, 76 例(41.08%)结局预后不良。多因素分析显示, 机械通气时间 ≥ 14 天($OR=4.378$)和使用血管活性药物($OR=3.484$)是发生 VAP 的独立危险因素。预后预测模型包含 6 个变量: 慢性肾病($OR=2.453$)、30 天内手术史($OR=0.089$)、有创通气(参照无创通气, $OR=4.959$)、无创与有创混合通气($OR=3.587$)、使用血管活性药物($OR=5.528$)以及合并 COVID-19 感染($OR=3.344$)是预后不良的独立影响因素。该模型经内部验证显示较良好区分度($AUC=0.779$, 95% CI: 0.676–0.882), 且校准度良好(Hosmer-Lemeshow 检验, $P=0.577$)。

结论 长时间机械通气与使用血管活性药物是此类患者发生 VAP 的风险因素, 经筛选后构建的预后模型具有较好的预测效能。

关键词: 机械通气; 念珠菌; 呼吸机相关肺炎; 预后; 预测模型

纹带棒状杆菌院内感染流行病学特征、耐药负担及临床结局的系统综述与 Meta 分析

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背景 纹带棒状杆菌 (*Corynebacterium striatum*) 正从一种低毒力的共生菌, 逐渐演变为院内感染中重要的多重耐药机会性致病菌, 但全球范围内其感染率、耐药率及临床结局的定量证据尚缺乏系统整合。

目的 系统评价近 6 年纹带棒状杆菌院内感染的流行病学特征、多重耐药率、耐药谱及患者死亡率, 为临床防控提供循证依据。

方法 系统检索 PubMed、Web of Science、CNKI、万方数据库, 时限为 2020 年 1 月 1 日至 2025 年 12 月 31 日。纳入报道纹带棒状杆菌院内

感染的观察性研究, 提取多重耐药率 (对 ≥ 3 类抗菌药物耐药)、各抗菌药物耐药率及患者死亡率数据。采用随机效应模型 (DerSimonian-Laird 法) 合并效应量, 进行敏感性分析及发表偏倚检验。

结果 共纳入 22 项研究, 涉及 1919 株分离株、2182 例患者。Meta 分析显示: 纹带棒状杆菌总体多重耐药率为 98.5% (95%CI: 97.9%–98.9%)。对常用药物耐药率: 青霉素 93.7% (95%CI: 90.5%–95.8%), 头孢类 96.6% (95%CI: 92.6%–98.5%), 环丙沙星 98.2% (95%CI: 95.7%–99.2%), 克林霉素 93.5% (95%CI: 88.5%–96.5%), 红霉素 92.7% (95%CI: 86.5%–96.2%), 美罗培南 89.0% (95%CI: 76.8%–95.2%), 庆大霉素 31.3% (95%CI: 19.8%–45.7%), 四环素 54.2% (95%CI: 38.0%–69.5%), 利福平 15.7% (95%CI: 8.0%–28.5%), 万古霉素 0.8% (95%CI: 0.3%–1.9%), 利奈唑胺 0% (95%CI: 0%–0%)。下呼吸道感染 30 天全因死亡率 51.9% (95% CI 31.9%–71.3%), 血流感染 30 天死亡率 39.0% (95%CI: 31.2%–47.1%)。

结论 纹带棒状杆菌院内感染呈极高多重耐药负担, 利福平和万古霉素低耐药率, 利奈唑胺仍保持完全敏感。下呼吸道与血流感染短期死亡率均超 30%, 临床危害严重。亟需强化病原鉴定、药敏监测与接触隔离措施。

关键词: 纹带棒状杆菌; 院内感染; 多重耐药; 死亡率; 系统综述; Meta 分析

Pulmonary Infection Caused by Multidrug-Resistant *Corynebacterium Striatum* in An Elderly Patient with Multiple Comorbidities: A Case Report and Systematic Literature Review

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Background *Corynebacterium striatum* (*C. striatum*) is an opportunistic pathogen often colonizing the skin and respiratory tract. While traditionally dismissed as a contaminant, it is increasingly recognized as a cause of serious infections, particularly in immunocompromised or chronically ill patients. Its intrinsic multidrug resistance poses significant treatment challenges

Case presentation We report a 79-year-old female with poorly controlled type 2 diabetes, prior cerebral infarction, and hyperuricemia. She was hospitalized for a left femoral neck fracture and underwent hip arthroplasty, but her postoperative course was complicated by a massive cerebral infarction, necessitating transfer to the neurological intensive care unit (NICU) and prolonged mechanical ventilation. She developed persistent pneumonia. Sputum culture and Gram staining revealed abundant Gram-positive bacilli arranged in palisades, identified as *C. striatum* by mass spectrometry. Antimicrobial susceptibility testing (AST) showed resistance to penicillin, meropenem, levofloxacin, and clindamycin, but sensitivity to vancomycin, linezolid, and gentamicin

Conclusion This case highlights that *C. striatum* can be a true pathogen causing pulmonary infection in elderly, debilitated patients with prolonged ICU stays and multiple risk factors. Accurate identification and AST are crucial to guide therapy. Based on our literature review, vancomycin or linezolid remains the mainstay of treatment for multidrug-resistant *C. striatum* infections.

Keywords *Corynebacterium striatum*; Pulmonary infection; Multidrug-resistant rate (MDR); Elderly patient; Linezolid; Vancomycin; Case report

2025 年全国医疗机构医务人员诊疗过程手卫生监测报告

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目的 了解我国医务人员手卫生依从性和正确率现状。完善医务人员诊疗过程手卫生监测评价体系,为全国医疗机构手卫生持续改进提供更全面的循证依据,为相关政策制定提供决策依据。

方法 采用经统一培训的观察员现场调查法,收集综合重症监护病房(ICU)、呼吸科(组)、骨科、感染病科(组)、儿科门急诊、血液透析室及手术部

（室）医务人员手卫生执行情况，同步统计调查科室工作量、手卫生用品消耗量及医疗机构实际开放床位数。使用 χ^2 检验比较各组手卫生依从率、正确率的差异，使用方差分析或 Kruskal-Wallis H 检验比较不同亚组之间计量资料的差异。

结果 2025 年 12 月 10 日-2026 年 1 月 20 日调查期间，共纳入 1248 所医疗机构。应执行卫生手消毒和洗手时机数 711094 次，实际执行 619483 次，正确执行 552896 次，依从率为 87.12%，正确率为 89.25%；外科手消毒应执行时机数 107872 次，实际执行 107489 次，正确执行 91775 次，依从率为 99.64%，正确率为 85.38%。不同规模医疗机构中，实际开放床位数 ≥ 900 张医疗机构卫生手消毒和洗手依从率（84.42%）和正确率（88.51%）均最低；调查科室中，骨科手卫生依从率最低（85.84%），呼吸科（组）手卫生正确率最低（88.52%），综合 ICU 手卫生依从率最高（88.87%），血液透析室手卫生正确率最高（90.20%）。五个时机中，接触患者周边环境后依从率（78.55%）和正确率（87.92%）均最低；外科手消毒各指征中，手套破损、手被污染后指征依从率（99.38%）最低，手术操作前指征正确率最低（84.04%）。综合 ICU、呼吸科（组）、骨科、感染病科（组）手卫生用品消耗量分别为 79.64、12.06、10.96、19.98mL/床日，儿科门急诊、血液透析室分别为 2.87、11.12mL/人次，手术部（室）为 63.02mL/台次。不同规模医疗机构各科室手卫生用品消耗量差异明显，多数科室以实际开放床位数 ≥ 900 张医疗机构消耗量最多。

结论 本次调查获取的不同规模、不同科室手卫生相关指标可作为新标杆，为各医疗机构手卫生管理和持续改进提供更精准的对照依据。

特殊使用级抗菌药物管理流程优化对医院感染防控效果的影响研究

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目的 评估以感染防控为导向的特殊使用级抗菌药物流程优化策略，对多重耐药菌感染发生率、医院感染相关核心指标及抗菌药物使用强度的影响，探索通过抗

菌药物管理（AMS）直接赋能医院感染防控（IPC）的有效路径。

方法 采用前瞻性干预研究，比较我院实施“院感-AMS 联动”优化流程前（2024 年 7-12 月，基线期）与实施后（2025 年 7-12 月，干预期）的相关数据。核心优化在于将医院感染预防与控制科（IPC）人员纳入特殊使用级抗菌药物的联合审批流程，并强制要求申请时填写医院感染相关信息。主要评价指标为多重耐药菌（MDRO）检出率与医院感染发病率；次要指标包括抗菌药物使用强度（DDDs）、微生物送检质量及临床科室行为依从性。

结果 与基线期相比，干预期特殊使用级抗菌药物使用强度下降 5%。目标多重耐药菌（包括碳青霉烯类耐药革兰阴性杆菌、MRSA）的感染病例发生率下降 2.3%，而非单纯的定植率下降。由目标 MDRO 引起的医院感染发病率显著降低。微生物标本合格率与送检及时性提升。临床科室对院感防控措施的依从性提高。

结论 将院感防控目标前置性嵌入特殊使用级抗菌药物管理流程，能有效实现“以药物管理为抓手，以感染防控为目标”的协同效应，显著降低 MDRO 感染风险，是破解“抗菌药物滥用-耐药菌产生-院内感染”恶性循环的关键策略。该模式为整合 AMS 与 IPC 提供了实践范式。

手套复用对微生物传播的风险性研究

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目的 手卫生作为医院感染防控的核心措施，其依从性在密集型操作场景下面临挑战。本研究旨在探讨戴手套进行卫生手消毒的可行性及效果，分析手套使用次数与防护效能的关系。

方法 通过单层手套观察实验和重症监护病房模拟实验，采用微生物采样、破损检测及统计分析方法进行验证。观察实验纳入 38 名专职从事静脉采血工作的护士佩戴无粉医用橡胶检查手套后进行抽血常规工作，记录每幅手套使用时长、卫生手消毒次数及抽血操作人数，检测手套表面微生物及破损情况；模拟实验由 3 名实验员在 ICU 环境中分别采用单层、双层及无手套接触不同患者周围物体表面，接触一个位置后进行一次手卫生，评估不同戴手套方式的手卫生消毒效果及破损情况。

结果 观察采血站护理人员 38 人次、工作时间共 1379 分钟，回收手套 76 只、卫生手标本 114 例。手套使用时长与脱手套后裸手的微生物结果之间无相关关系 ($r_s=0.078$, $P=0.641$)，6.58% 手套出现指尖破损，3.95% 渗水，无手套检出血液残留。模拟实验中，每名实验员使用快速手消毒剂共进行手卫生 30 次，采集了 18 个手部采样标本，培养结果均无微生物生长，且手套完整性良好。

结论 本研究表明在密集型操作中，戴手套执行手卫生可维持手部微生物水平符合规范标准 ($\leq 10\text{CFU}/\text{cm}^2$)，建议每进行 10-15 次手卫生后或出现破损时更换手套。该方法既能缓解频繁更换手套的操作负担，又能保障手卫生质量，为临床提供了一种兼顾效率与安全的替代方案，但需注意控制手套使用时长及手卫生频次。

关键词：手卫生；手套；复用；消毒

Economic and Clinical Impact of An Expanded Active Surveillance Culture Bundle for Multidrug-Resistant Organisms in Chinese ICUs: A Multicenter Before-After Study

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Background Colonization with multidrug-resistant organisms (MDROs) is the critical precursor to healthcare-associated infection (HAI) in ICU patients. Despite broad support for active surveillance cultures (ASC), the health-economic value of a comprehensive, multi-pathogen ASC bundle in Chinese ICUs remains unclear

Methods A multicenter before-after study was conducted across five tertiary ICUs led by Xiangya Hospital of Central South University. The control period (May-December 2023) followed routine care; the intervention period (May-December 2024) implemented protocol-driven ASC for MRSA, CRE, VRE, and *Clostridioides difficile* in patients with ICU stays ≥ 48 hours. Screening used chromogenic culture plates combined with VITEK® MS MALDI-TOF mass spectrometry (CRE/VRE/MRSA) and CCFA culture with enzyme immunoassay (CD). Colonization-positive patients received a standardized bundle: contact isolation, enhanced hand hygiene, high-frequency environmental disinfection (≥ 3 times/day), and 5% povidone-iodine nasal decolonization for MRSA-positive cases (3 times/day for 5 days). The primary outcome was total hospitalization cost; secondary outcomes included ICU length of stay (LOS) and HAI incidence. Cost-effectiveness was assessed via the incremental cost-effectiveness ratio (ICER).

Results During the intervention period, 2,175 of 6,244 ICU admissions (34.8%) were screened across five sites; the overall positivity rate was 18.3%, with CRE predominating (303 cases). At the lead center, 274 control-period and 260 intervention-period patients were eligible. Groups were comparable in age and sex;

APACHE II scores were higher in controls (median 18 vs. 16, $P<0.05$). Intervention-period CRE-HAI (1.71% vs. 2.47%) and CRAB-HAI (1.23% vs. 2.66%) incidence rates declined significantly (both $P<0.05$). ICU LOS was shorter in the intervention group (median 8 vs. 11 days, $P<0.05$). Total hospitalization costs (CNY 88,552 vs. 117,149), pharmaceutical costs, and antimicrobial expenditures were all significantly lower ($P<0.05$). Direct medical costs totalled CNY 31,885,427 (intervention) vs. CNY 44,115,102 (control); intervention costs were CNY 37,000. The incremental cost was -CNY 12,225,975 (net saving). With 44 MDRO-HAI episodes prevented, ICER = -CNY 277,863 per infection averted, confirming a dominant strategy.

Conclusion An expanded multi-pathogen ASC bundle in Chinese ICUs significantly reduced CRE and CRAB-HAI rates, shortened ICU LOS, and lowered hospitalization costs. The negative ICER supports institutionalizing this approach as standard ICU infection control practice. Future analyses should incorporate multivariable risk adjustment for baseline severity differences and broader clinical outcomes including mortality.

非抗生素干预预防复发性尿路感染的疗效与安全性：系统评价与 Meta 分析

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背景 复发性尿路感染 (recurrent urinary tract infection, rUTI) 每年可影响多达 50% 的成年女性, 造成沉重的全球疾病负担。与此同时, 抗菌药物耐药性不断上升, 以及抗生素相关肝毒性等不良反应的存在, 进一步加重了这一负担。蔓越莓制剂、D-甘露糖和益生菌等非抗生素策略已成为具有应用前

景的替代方案; 然而, 这些干预措施相较于安慰剂的疗效与安全性, 尤其是在不同绝经阶段女性健康视角下的比较, 仍缺乏充分证据。

方法 本研究依据 PRISMA 声明, 检索 PubMed、Embase 和 Web of Science 数据库, 检索时限截至 2025 年 10 月, 纳入对象为比较非抗生素干预与安慰剂对成年女性 rUTI 预防效果的研究。主要结局指标为症状性或尿培养证实的 rUTI 复发情况 (以相对危险度 (relative risk, RR) 表示) 及不良事件发生情况。考虑到研究间异质性较高, 本研究采用随机效应模型进行合并分析, 并以 I^2 评估异质性, 采用 Egger 检验评估发表偏倚。

结果 共纳入 17 项研究, 涉及 2434 名女性受试者, 其中 1444 例接受非抗生素治疗。总体分析显示, 在预防 rUTI 方面, 非抗生素治疗较安慰剂具有更好的效果 ($RR=0.57$, 95%CI: 0.44~0.74)。亚组分析显示, 蔓越莓 ($RR=0.33$, 95%CI: 0.16~0.70) 疗效更为显著; 而 D-甘露糖由于纳入研究数量有限, 尚未显示出统计学显著性趋势 (图 1)。此外, 研究结果提示, 蔓越莓以及透明质酸联合硫酸软骨素均可显著延长治疗后首次发生 UTI 的时间 (图 2)。与抗生素方案相比, 透明质酸联合硫酸软骨素亦显示出相当的疗效 ($RR=0.80$, 95%CI: 0.66~0.97) (图 3)。在安全性方面, 非抗生素治疗与安慰剂相当, 未出现严重不良事件, 也未发现因药物导致的停药和退出。多数不良事件轻微, 不需要相关治疗即可恢复。Egger 检验未发现明显发表偏倚 (Egger's $p=0.22$)。

结论 非抗生素干预可在不增加不良事件风险的前提下, 显著降低成年女性复发性尿路感染的发生风险, 其中蔓越莓及透明质酸联合硫酸软骨素表现出较好的预防效果。对于感染频繁或担忧抗生素耐药性及肝毒性的女性, 非抗生素治疗可能成为有效替代方案。未来仍需开展更大样本的随机对照试验, 以明确最佳剂量、治疗时长及长期结局, 并进一步评估其对生活质量和成本效益的影响。

Machine Learning Prediction of In-Hospital Mortality Risk Among Hospitalized Patients With Secondary Bloodstream Infection: A Retrospective Cohort Study

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Background Secondary bloodstream infection (SBSI) carries substantial mortality burden. Dedicated mortality prediction models with interpretable predictions remain limited

Objective To develop an interpretable machine learning model for predicting in-hospital mortality in SBSI patients and establish a clinically applicable web-based tool

Methods Data from 340 SBSI patients (January 2020–December 2024) were analyzed. Candidate variables were selected using the union of multivariate Cox regression and LASSO-Cox regression. Five prognostic models were constructed including Cox regression, LASSO-Cox regression, Random Survival Forest (RSF), Gradient Boosting Machine (GBM), and XGBoost, with 10 selected variables as predictors. Model performance was evaluated using time-dependent Area Under the Receiver Operating Characteristic Curve (AUC) at 7, 14, and 28 days as the primary metric. Internal validation was conducted using bootstrap resampling with 1,000 iterations. The optimal RSF model was interpreted using SHapley Additive exPlanations (SHAP) analysis. An interactive web-based prediction tool was subsequently developed

Results In-hospital all-cause mortality rate was 34.41% (117/340). Among the five models, RSF demonstrated superior discriminative ability with AUC

values of 0.869 (95% CI: 0.824–0.914), 0.897 (95% CI: 0.856–0.937), and 0.878 (95% CI: 0.822–0.933) at 7, 14, and 28 days, respectively, substantially outperforming traditional Cox regression and LASSO-Cox models. RSF exhibited excellent calibration with corrected C-index of 0.8809. Decision curve analysis confirmed RSF's clinical superiority, demonstrating the greatest net benefit across a wide range of threshold probabilities. SHAP analysis identified log Lactate Dehydrogenase, Multidrug-Resistant Organism infection, and log creatinine as the top three predictive features. An interactive web-based prediction tool was successfully developed enabling real-time risk assessment at 7, 14, and 28 days

Conclusion A interpretable machine learning model (RSF) for SBSI mortality prediction was successfully established. SHAP-based transparency and the interactive web-based tool facilitate clinical implementation and support personalized risk stratification for improved patient outcomes

预防成人外周动脉导管相关感染的最佳证据总结

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目的 检索并总结外周动脉导管相关感染预防的最佳证据，并对证据进行评价，为临床执行预防导管感染的措施提供参考。

方法 检索了 UpTo Date、BMJ Best Practice、英国国家卫生与临床优化研究所指南网(Nation Institute for Health and Care Excellence,NICE)、美国国立指南网 (NGC), Corchrane Library、澳大利亚 Joanna Briggs Institute(JBI)循证卫生保健中心数据库、Pubmed、Embase、中国知网、万方数据库以及医脉通和 WHO 官网等涉及外周动脉导管感染预防的所

有临床决策、指南、专家共识、证据总结、系统评价,检索时限为建库至2025年2月。由2名研究者对文献进行质量评价,同时2名研究者对文献进行证据的提取总结。

结果 共纳入12篇文献,其中包含了1篇指南,1篇专家共识,4篇推荐实践,2篇证据总结,4篇系统评价。我们归纳总结了9个方面,最终纳入32条相关证据。

结论 外周动脉导管感染预防的最佳证据总结涉及面广,不论是管理者还是临床医护人员,都应该结合具体医疗情境,对证据进行合理的应用,从而减少临床外周动脉导管感染的发生。

基于住院诊察模式的重症患者药学实践

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目的 借助住院诊察模式构建重症患者药学服务实践,深入探索药学服务内涵,保障重症患者用药有效性和安全性。

方法 2023年12月,江西省医保局联合江西省卫生健康委共同发布扩展“住院诊察费(临床药学加收)”项目,住院诊察项目内涵为临床药师参与临床医生住院巡诊,协同制定个体化药物治疗方案,开展疗效观察和药物不良反应监测,为患者进行安全用药指导、干预或提出药物重整等意见基于“住院诊察(临床药学加收)”收费项目新政策,目前ICU药师常规诊察模式主要基于日常临床查房、医嘱审核、药物咨询等方面工作。随着医疗技术的不断改进与完善,对药师更加贴近患者、贴近临床的服务模式提出了更高的要求。本院ICU临床药师率先探索重症患者药学诊察服务新模式,通过住院诊察模式,即循证用药、方案重整、精准用药、药学监护展现药师专业,服务重症临床科室。

结果 构建了重症患者药学实践工作相关流程,

创新了临床药学住院诊察记录表,从住院诊察模式出发解决了临床实际工作问题,得到了临床医生的认可。

结论 临床药师通过住院诊察模式建立了重症患者药学服务实践,创新住院诊察模式,达到重症患者合理用药精细化管理,提高临床医疗质量,以期临床药师发展转型提供参考。

左心室辅助装置植入患者感染预防及管理的最佳证据总结

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目的 总结并评价左心室辅助装置(left ventricular assist device, LVAD)植入患者感染预防及管理的相关证据,为临床工作提供参考依据。

方法 根据“6S”模型,以“Heart-Assist Devices/left ventricular assist device/LVAD/VAD”为英文检索词,依次检索国际指南协作网、美国指南网、苏格兰校际指南网、英国卫生与临床优化研究所、加拿大医学会临床实践指南信息网等指南网,以及美国心脏学会、欧洲心脏病协会网站、UpToDate、BMJ Best Practice、Cochrane Library 中英文数据库关于LVAD植入患者感染预防相关的推荐实践、指南、专家共识及建议、系统评价、原始研究及证据总结,检索时限为建库至2025年2月1日。

结果 共纳入文献20篇,包括推荐实践3篇、指南2篇、专家共识10篇、证据总结3篇、系统评价2篇。最终总结出包括多学科团队协作及人员培训、LVAD植入患者感染的预防、感染后规范化管理及出院指导4个主题,共30条最佳证据。

结论 本研究系统检索和评价了大量相关文献,总结了30条关于LVAD植入术后患者感染预防的最佳证据,涉及使用人员、围手术期各个阶段感染预防及感染后规范化管理,为临床实践提供了科学、

实用的指导。本研究也存在一定局限性, 纳入证据全部来自专家共识、指南、系统评价, 证据质量有待进一步提高, 未来的研究应开展高质量的临床研究, 加强教育培训, 探索新的感染预防技术和方法, 以提高患者的生存率和生活质量。

Epidemiological and Genotypic Analysis of *Candida Albicans* Outbreak in A Neonatal Ward

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Background *Candida albicans* is the primary pathogen responsible for candidemia, particularly in hospital settings, and is often associated with outbreaks in neonatal intensive care units (NICUs). In this study, we aimed to investigate the transmission dynamics and identify the potential source of a *C. albicans* candidemia outbreak in an NICU, focusing on neonates at high risk of infection

Methods This retrospective, single-center study focused on analyzing 10 neonates with candidemia and 23 *C. albicans* strains, including 6 isolates obtained from the environment and staff members in a neonatal ward. Whole-genome sequencing (WGS) was employed to trace the outbreak of candidemia in neonatal wards and reconstruct the transmission path of infection based on epidemiological data.

Results Seventy percent (7/10) of neonates had

either extremely or very low body weight as well as catheter-related bloodstream infection. Multilocus sequence typing revealed that the isolates could be categorized into three sequence types (STs), including two novel STs, ST3601 and ST3602, with ST3601 being predominant (82.6%, 19/23). Genome SNP/InDel variation and phylogenetic analyses revealed that the outbreak isolates (C1-C17, C19, and C22) formed a distinct cluster, exhibiting a reduced mutation distance, as evidenced by both the phylogenetic tree and heatmap analyses, and shared a close genetic relationship with each other, suggesting a common source of infection.

Conclusion Among neonates with extremely or very low body weight, central venous catheter-related candidemia was the most frequent, and the contaminated hands of medical staff were likely a medium of transmission or the staff was contaminated with the *Candida* from the neonates. This study highlights the utility of WGS in detecting and understanding hospital outbreaks, helping to trace transmission routes and improve infection control.

Keywords neonate; *Candida albicans*; candidemia; outbreak; whole-genome sequencing

心律失常射频消融术后呼吸道感染危险因素分析及干预对策

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目的 探讨射频消融术后患者发生呼吸道感染的相关危险因素, 制定针对性干预对策, 降低术后呼吸道感染发生率, 保障患者围手术期安全。

方法 选取某院 2024 年 3 月 1 日至 2025 年 12 月 31 日行射频消融术治疗的患者为研究对象, 采用回顾性病例对照研究方法, 收集患者临床资料, 统

计术后呼吸道感染发生情况；其中 2024 年 3 月 1 日至 10 月 25 日为干预前阶段，2024 年 10 月 26 日至 2025 年 12 月 31 日为干预后阶段；同时开展病例对照研究（病例组 8 例、对照组 16 例），回顾所有无菌物品及一次性医疗用品批号，从患者自身因素、手术相关因素、治疗护理因素及环境因素等方面，分析感染危险因素，并制定系统化干预措施。

结果 干预前（2024 年 3 月 1 日-10 月 25 日）共监测射频消融手术 916 例，术后发生呼吸道感染 6 例，感染率为 0.66%，所有感染患者血培养结果均为阴性；经调查发现，患者候手术期间及手术过程中受凉是主要感染诱因。实施针对性干预措施（加强候手术及术中保暖、强化手卫生与无菌操作、严格术前手术部位皮肤消毒、规范连台手术物体表面清洁消毒、改进介入手术室布局及手术流程、加强患者术前清洁等）后，干预后阶段射频消融术后呼吸道感染率降至 0.02%，感染发生率显著下降。

结论 射频消融术后呼吸道感染的发生与患者候手术及术中受凉密切相关，实施针对性干预措施可有效降低术后呼吸道感染发生率，具有重要临床应用价值。

关键词：射频消融术；呼吸道感染；危险因素；干预对策；病例对照研究

阿昔洛韦预防复发/难治 B 细胞淋巴瘤 CD19 嵌合抗原受体修饰 T 细胞治疗后感染的远期观察

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目的 评价阿昔洛韦预防复发/难治（R/R）淋巴瘤患者嵌合抗原受体修饰 T（CAR-T）细胞治疗后感染的有效性。

方法 回顾性分析 2017 年至 2021 年间 178 例接受 CD19 CAR-T 细胞治疗的复发/难治非霍奇金淋

巴瘤患者的临床资料，根据是否使用阿昔洛韦分为预防组 105 例和未预防组 73 例。分析临床数据、感染率、微生物分布和治疗后 6 个月内感染的时间，统计方法评估组间差异，寻找相关危险因素。

结果 两组在性别、年龄、病理类型、分期、国际预后指数评分及治疗线数等方面无显著差异（均 $P > 0.05$ ）。两组的客观缓解率和完全缓解率差异均未见统计学意义（均 $P > 0.05$ ）。阿昔洛韦预防组与非预防组相比，接受阿昔洛韦预防治疗的患者在治疗后 6 个月内首次感染发生率显著降低（40.0% vs. 75.34%， $P < 0.001$ ）。早期感染率（ ≤ 30 天）降低（19.05% vs. 31.51%， $P = 0.267$ ）。晚期感染率（ > 30 天）显著降低（20.95% vs. 43.84%， $P = 0.013$ ）。预防使用阿昔洛韦显著降低了二次感染（21.90% vs. 54.42%， $P < 0.001$ ）和多次感染的发生率（5.71% vs. 16.44%， $P = 0.020$ ）。首次感染的中位发生时间在预防组为 49.5 天，未预防组为 53 天（ $P = 0.487$ ）。预防组和未预防组在早期及晚期感染的病原微生物分布情况无显著差异（均 $P > 0.05$ ）。未预防组中因感染转入重症监护病房的比例和因感染死亡的患者比例均高于预防组（均 $P < 0.05$ ）。阿昔洛韦预防是早期和晚期感染的相关危险因素（ $P < 0.1$ ），对应的 OR 值分别为 0.512（ $P = 0.058$ ）和 0.340（ $P = 0.001$ ）。

结论 阿昔洛韦可有效降低 CAR-T 治疗后感染的发生率，尤其是晚期感染发生率，从而改善患者生活质量。

Epidemiology and Risk Factors of Hospital-Onset Clostridioides Difficile Infection in Adult Inpatients: A Retrospective Case-Control Study

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Background *Clostridioides difficile* infection (CDI) remains a leading healthcare-associated infection globally, yet data from China are limited, particularly regarding modifiable risk factors relevant to infection prevention. We aimed to characterize the epidemiology of hospital-onset CDI (HO-CDI) and identify actionable risk factors among adult inpatients

Methods We conducted a retrospective matched case-control study at a large tertiary teaching hospital in Shanghai, China. Adult inpatients with HO-CDI (PCR-positive ≥ 48 hours after admission) were included as cases. Controls were hospitalized patients with diarrhea who tested negative for CDI, matched 1:1 by ward and age (± 5 years). To reduce temporal ambiguity and reverse causation, exposures were restricted to predefined windows prior to CDI testing (medications within 30 days; laboratory parameters within 7 days). Conditional logistic regression was used to identify independent risk factors

Results A total of 411 matched pairs were analyzed. Compared with controls, CDI cases had longer hospital stays, higher neutrophil percentages, and lower serum albumin levels. In multivariable analysis, increased neutrophil percentage (aOR 1.03, 95% CI 1.01–1.05) and decreased serum albumin (aOR 0.92, 95% CI 0.88–0.97) were independently associated with CDI, suggesting a role of systemic inflammation and poor nutritional status. Higher total protein was also associated with increased risk (aOR 1.04, 95% CI 1.00–1.08)

Regarding antimicrobial exposure, fluoroquinolones (aOR 11.09, 95% CI 1.64–75.03) and ertapenem (aOR 3.43, 95% CI 1.38–8.52) were identified as independent risk factors, while third-generation cephalosporins showed a borderline association. Notably, rifampicin (aOR 0.19, 95% CI 0.05–0.70) and antifungal agents (aOR 0.41, 95% CI 0.21–0.82) were inversely associated with CDI; these findings are likely attributa-

ble to confounding by indication. Among acid-suppressive therapies, H₂-receptor antagonists were independently associated with increased CDI risk (aOR 2.56, 95% CI 1.51–4.36), whereas proton pump inhibitors were not significant after adjustment.

Conclusions HO-CDI risk is driven by both host clinical status and specific antimicrobial exposures. High-risk antibiotics, particularly fluoroquinolones and carbapenems such as ertapenem, represent key targets for antimicrobial stewardship interventions. The use of predefined exposure windows strengthens causal inference by minimizing temporal bias. These findings provide actionable evidence for infection prevention programs, supporting targeted antibiotic restriction, optimization of acid-suppressive therapy, and early identification of high-risk patients

重症监护病房 3 例疑似烟曲霉菌感染暴发案例调查及处置

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目的 针对某重症监护室 (ICU) 同期出现 3 例痰标本检出烟曲霉菌的疑似感染暴发事件, 通过个案分析与流行病学调查, 明确感染性质、追溯风险源头, 总结医疗机构曲霉菌感染的防控要点。

方法 分析患者临床资料, 结合医院感染病例判定标准及曲霉感染诊断指南, 区分定植与感染; 与多团队协作分析探讨病例感染危险因素及高危环节, 通过现场勘察、环境采样、高危操作过程追溯, 排查感染传播风险。

结果 3 例患者中仅 1 例判定为“院内下呼吸道烟曲霉感染”, 另 2 例分别判定为“烟曲霉呼吸道定植”与“院外带入曲霉感染”; 环境采样未检出曲霉菌, 排除 ICU 环境传播风险。

结论 曲霉菌实验室检测阳性需结合患者临床表现进行甄别,避免感染误判;聚集性事件应急处置应聚焦“个案诊断-环境排查-精准治疗”三维流程,同时根据病原体特点采取针对性措施,如强化环境温湿度控制、器械规范消毒及重点人群保护等风险防范,预防及控制曲霉菌传播。

关键词: 烟曲霉; 重症监护病房; 流行病学调查; 医院感染; 聚集性事件

Air Disinfection Effect of Different Disinfection Methods in High Risk Hospital Spaces

null null

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To evaluate the effectiveness of human-safe air disinfection methods in high-risk healthcare areas, field tests were conducted in the high-risk triage area, infectious disease ward, and dental clinics of a top-tier academic medical center. Existing air disinfection methods (plasma air disinfection devices, ultraviolet (UV) air cleaners, or negative pressure ventilation systems), a 222-nm UV upper-room air disinfection system, and combinations of existing methods with the 222-nm UV system were applied, with no air disinfection used in the control group. Air sampling was performed hourly during daytime clinical hours using a six-stage impactor microbial sampling method or a settling plate method. Compared with the control group or single existing disinfection methods, airborne bacterial concentrations were significantly lower in the 222-nm UV group or combined disinfection groups across multiple clinical settings (all $P < 0.05$). The air disinfection efficiency of the 222-nm UV system ranged from 48.04% to 73.74%, while that of plasma air disinfection devices or UV air

cleaners combined with 222-nm UV ranged from 6.86% to 73.77%. These results demonstrate that the 222-nm UV upper-room air disinfection system effectively reduces airborne bacterial concentrations and improves air hygiene quality in outpatient and inpatient environments with high risks of airborne disease transmission.

单包装碘伏消毒棒与两种传统消毒方式在皮肤穿刺消毒中的综合效果比较研究

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目的 比较单包装碘伏消毒棒与罐装碘伏消毒棒、干棉签蘸取瓶装碘伏三种皮肤消毒方式在使用过程中污染风险、临床使用依从性、便捷性等方面的差异,为优化产品设计、指导临床实践提供依据。

方法 采用实验性研究和观察性研究多维度评价方法。使用平皿倾注法对使用中消毒剂细菌污染进行对比研究;选择该院某科室 10 名护士(排除实习护士)作为观察对象,由观察员对其使用三种消毒方法进行静脉穿刺皮肤消毒的操作进行直接观察,评估临床使用依从性;邀请同一批 10 名护士在分别使用三种消毒方法各 20 人次后,基于自身感受评估临床使用便捷性。

结果 实验性研究结果显示,单包装碘伏消毒棒、干棉签、瓶装碘伏溶液在使用中均未检出细菌污染,而罐装碘伏消毒棉签在使用至最后一支时平均菌落数为 15 CFU/mL,超出国家标准。观察性研究结果显示,三种皮肤消毒方式操作规范得分均为满分(10 分),操作时长差异无统计学意义($P > 0.05$)。三种皮肤消毒方式在功能符合性、使用便捷性等用户体验上均获得了高度认可,但在“使用沮丧感”、“纠错时间”等方面存在负面评价。

结论 单包装碘伏消毒棒作为一种新型皮肤消毒方式在减少使用中污染风险、保障操作规范性方

面能满足临床使用需求，但在使用细节与操作感受方面仍有优化空间。

关键词：皮肤消毒；医院感染；感染控制实践；比较效果研究；患者安全

手消毒产品不同包装形式的损耗与染菌量对比分析

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目的 比较真空无菌软袋与传统回气瓶包装在手消毒产品中的损耗比、损耗稳定性及染菌风险，为医疗机构选型提供依据。

方法 2025年8-11月在复旦大学附属中山医院外科ICU开展前瞻性研究。选取洁薇柔（真空无菌软袋）、3M及洁芙柔（传统回气瓶）3品牌8种型号产品，涵盖洗手液与手消毒液不同剂型。采用高精度称重法计算损耗比（残余重量/开启重量 $\times 100\%$ ），每周采样检测染菌量，并记录包装物理完整性。组间比较采用t检验，计算效应量及变异系数。

结果 损耗分析显示，1L洗手液中真空无菌软袋组（A组）损耗比为（ 0.61 ± 0.26 ）%，显著低于传统回气瓶组（E组）的（ 0.90 ± 0.39 ）%（ $P=0.045$ ， $d=0.88$ ）；500mL手消毒液中真空无菌软袋组（B组）损耗比为（ 0.58 ± 0.10 ）%，显著低于传统回气瓶组（F组）的（ 0.96 ± 0.54 ）%（ $P=0.043$ ， $d=1.00$ ）。真空无菌软袋组损耗相对降低幅度达32.22%~39.58%，变异系数（17.24%）明显小于传统回气瓶组（43.33%~56.25%），显示更优的稳定性。使用天数与损耗比无相关性（ $P>0.05$ ）。共采集265份样本，染菌量均为0CFU。真空无菌软袋组未发现破损或漏液。

结论 真空无菌软袋包装可显著降低手消毒产品损耗比并提高损耗稳定性，在长期高频使用中可产生累积成本效益；规范操作下两种包装均能有效

防止染菌。真空无菌软袋适宜作为高频使用科室的优选包装形式。

关键词：手消毒；真空无菌软袋；包装形式；损耗比；染菌量

葡萄糖酸氯己定擦浴对ICU患者院内获得性感染影响的Meta分析

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目的 评价葡萄糖酸氯己定擦浴对ICU患者院内获得性感染（Hospital acquired infection, HAI）发生率及预后的影响。

方法 计算机检索PubMed、Embase、Cochrane Library、Web of Science、中国知网和万方数据库搜索葡萄糖酸氯己定擦浴对ICU患者HAI发生率及预后影响的研究，检索时限为2000年1月1日至2022年12月31日。由2名研究人员独立筛选文献、提取资料和评价纳入研究的质量，采用RevMan 5.3软件对数据进行Meta分析。

结果 共纳入12篇随机对照研究，共有128927例ICU患者纳入研究，其中葡萄糖酸氯己定擦浴组63038例，对照组65889例。Meta分析结果显示：葡萄糖酸氯己定擦浴组与对照组HAI发生率分别为1.93%（1219/63038）和2.26%（1490/65889）（ $OR=0.72$ ，95%CI 0.62~0.83， $P<0.00001$ ）；血流感染发生率分别为1.30%（476/36573）和1.54%（648/41968）（ $OR=0.70$ ，95%CI为0.62~0.79， $P<0.00001$ ）；ICU住院时间MD=0.17，95%CI 0.06~0.28。

结论 葡萄糖酸氯己定擦浴可降低ICU患者HAI，血流感染发生率以及降低ICU住院时间，对肺部感染和泌尿系感染发生率及ICU患者住院病死率和总住院时间无影响。

Distribution and Genetic Diversity of *Candida* Parapsilosis in Hospital Environments: Implications of Environmental Reservoirs for Nosocomial Infections

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Background *Candida* parapsilosis is a leading cause of healthcare-associated invasive fungal infections, yet the contribution of hospital environmental reservoirs to its dissemination and antifungal resistance remains poorly understood. We conducted a multicenter investigation to characterize environmental distribution, antifungal drugs resistance, and genomic relatedness between environmental and clinical *C. parapsilosis* isolates across Shanghai hospitals

Methods From July to December 2024, environmental sampling was performed in 21 tertiary hospitals, covering 2,564 sites (3,797 swabs) in ICU and non-ICU high-risk wards. Yeasts were isolated by selective culture and ITS sequencing. Antifungal susceptibility was determined by the CLSI M27 broth microdilution method. Whole-genome sequencing (150-bp paired-end) was conducted for 266 isolates (222 environmental, 44 clinical). Phylogenetic reconstruction (RAxML, GTRGAMMA model), resistance gene and population genetic analyses (π , θ_w , Tajima's D, Fst) were performed

Results Yeasts were detected in 30.6% of environmental sites, with *C. parapsilosis* being the predominant pathogenic species in both ICU (7.3%) and non-ICU settings (8.4%). Moist environments were key reservoirs: sinks (15.1% positivity) and soiled-utility rooms (56.5%) had the highest detection rates. Towels used for patient bathing showed extensive *Candida* species colonization (38.0%), including 10 isolates of *C.*

parapsilosis

Environmental *C. parapsilosis* displayed notable azole resistance: 11.7% fluconazole-resistant, driven mainly by ERG11 Y132F (88.5%). In contrast, all 44 clinical bloodstream/sterile-site isolates were azole-susceptible.

Genomic analysis of 492 global isolates revealed nine major clades, with environmental and clinical isolates intermingled across nearly all clades, indicating strong environmental-clinical genetic connectivity. A fluconazole-resistant environmental lineage (Clade IV) showed clonal expansion within ICU settings. Population analysis showed lower diversity in resistant strains, suggesting repeated bottlenecks and selective sweeps.

Conclusions Hospital environments—especially moist sites and textiles—serve as persistent reservoirs of *C. parapsilosis*, including azole-resistant clones that genetically converge with clinical populations. These findings highlight the need for targeted environmental surveillance, improved cleaning of sinks and patient textiles, and integrated genomic monitoring to prevent environmental-to-patient transmission

Epidemiologic Transition of Infectious Disease Hospitalizations Across Five Decades: Evidence From Multi-Indicator Time-Series Modeling

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Background Infectious disease hospitalizations have undergone substantial transformation over recent decades, driven by vaccination, population aging, and

increasing chronic comorbidities. While classical communicable infections have declined, chronic conditions, sepsis, and emerging infections are becoming more prominent. However, long-term multi-indicator analyses of these transitions remain limited

Methods We conducted a retrospective time-series analysis of infectious disease hospitalizations from 1975 to 2024 using discharge data from a tertiary hospital. Seventeen conditions were grouped into five categories: classical infections, vaccine-preventable diseases, chronic and end-stage conditions, sepsis, and emerging infections. Annual series were constructed for admission volume, length of stay (LOS), mean age, total cost, and cure ratio. Autoregressive integrated moving average (ARIMA) models were used to assess trends and generate forecasts.

Results A marked epidemiologic transition was observed. Classical and vaccine-preventable infections declined substantially and now represent a low inpatient burden. In contrast, chronic and end-stage conditions, particularly chronic hepatitis B and its complications, accounted for sustained admissions, older patient age, prolonged LOS, and rising costs.

Sepsis emerged as a major syndromic endpoint with high resource use and poorer outcomes, reflecting increasing host vulnerability. Emerging infections contributed fewer admissions but showed strong temporal variability and forecasting uncertainty.

Across indicators, mean age and costs increased steadily, while LOS decreased for acute infections but remained high in chronic and severe conditions. Cure ratios improved overall but plateaued in advanced disease. Forecasts suggest future burden will be increasingly driven by chronicity and systemic vulnerability.

Conclusion Infectious disease hospitalizations have shifted toward chronic conditions, sepsis, and episodic emerging infections. Multi-indicator time-series

modeling highlights the need to strengthen chronic disease management, sepsis prevention, and health system resilience.

Keywords

Infectious disease hospitalization; Epidemiologic transition; Chronic hepatitis B; Sepsis; ARIMA

Methods for Skin Load Reduction of *Candida Auris*: A Systematic Review

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Candida auris (*Candidozyma auris*, *C. auris*) is a fungal pathogen with multiple drug resistance, belonging to a species of yeast, known for its ability to sustain growth in the host. This organism can colonize human skin and spread through physical contact or contami-

nated surfaces and equipment. Given the limited reviews on skin load reduction methods of *C. auris*. This review aims to summarize and evaluate the current load reduction methods involving reducing skin load, and the risk of colonization. The findings will provide healthcare facilities and nursing homes with evidence-based guidance to develop effective prevention and control strategies. *Candida auris* (*Candidozyma auris*, *C. auris*) is a fungal pathogen with multiple drug resistance, belonging to a species of yeast, known for its ability to sustain growth in the host. This organism can colonize human skin and spread through physical contact or contaminated surfaces and equipment. Given the limited reviews on skin load reduction methods of *C. auris*. This review aims to summarize and evaluate the current load reduction methods involving reducing skin load, and the risk of colonization. The findings will provide healthcare facilities and nursing homes with evidence-based guidance to develop effective prevention and control strategies.

其他微生物及其感染

长沙地区 139 例登革热患者流行病学特征及重症化因素分析

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目的 分析长沙地区 139 例登革热患者的特征, 结合实验室指标探讨重症登革热患者的影响因素和早期预警指标。

方法 分析 2023 年 6 月至 2025 年 8 月在长沙市第一医院住院治疗的登革热患者的资料, 比较重症与普通患者差异, Logistic 回归分析观察指标与重症登革热的影响程度, 采用受试者工作特征曲线分析各指标及联合检测早期预判重症登革热的效能, 计算曲线下面积 (Area under the curve, AUC)、确定最佳阈值。

结果 139 例登革热患者平均年龄 42.63 岁, 男性占 51.80%, 69.06% 患者来自本地, 输入病例主要来自广东省 (2.88%)。以自由职业为主, 个体户次之。48.20% 患者发病前 15 天内曾到过登革热流行区, 从发病到住院中位时间为 6.00 天, 平均住院时间为 3.25 天, 58.27% 患者为临床诊断病例, 41.73% 患者为确诊病例, 最多的基础疾病为高血压 (12.95%)。所有患者均有发热表现, 67.63% 患者有畏寒, 59.71% 患者有肌肉酸痛、乏力、腹泻, 腰痛少见 (1.44%)。与普通登革热患者相比, 重症患者发病到住院时间、凝血酶时间 (Thrombin time, TT)、活化部分凝血活酶时间 (Activated partial thromboplastin time, APTT) 更长 ($P < 0.01$), 总胆红素 (Total bilirubin, TBIL) 水平更高、国际标准化比值 (International normalized ratio, INR) 水平更低 ($P < 0.01$), 血小板 (Platelet, PLT) 数量更少 ($P < 0.05$)。无论重症与否, 患者的 TBIL 平均水平、PLT 平均数量、INR 均数在正常范围内, TT、APTT、D-二聚体、C-反应蛋白、降钙素原中位数高于正常范围, 白细胞、中性粒细胞中位数低于正常范围。发病到住院时间、PLT、INR、TT 是影响

登革热病情轻重的危险因素 ($P < 0.05$), INR、TT 是登革热患者进展为重症的独立影响因子 ($P < 0.05$), AUC 分别为 0.692, 0.691, 最佳阈值分别为 1.025、17.450 s, 二者联合检测的 AUC 为 0.731, 敏感度为 92.30%、特异度为 46.70%。

结论 INR、TT 为早期预警重症登革热的独立影响因子, 联合检测较单一检测更有助于重症登革热的早期预警。

关键词: 登革热; 重症; 早期预警

Association between Fluoroquinolones and Suicidal Or Self-injury Events: A Pharmacovigilance Analysis of FAERS, JADER, and CVARD Databases

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Objective This study aimed to comprehensively evaluate the association between FQs and SSIEs based on multi-database pharmacovigilance data and to further characterize their clinical features, onset patterns, and potential risk factors

Methods We conducted a retrospective pharmacovigilance study using three spontaneous reporting systems: the FDA Adverse Event Reporting System (FAERS), Japanese Adverse Drug Event Report (JADER), and Canada Vigilance Adverse Reaction Database (CVARD), covering the period from 2004 to 2024. Reports involving FQs (including ciprofloxacin, levofloxacin, moxifloxacin, and ofloxacin) were identified. SSIEs were defined using standardized MedDRA queries. Signal detection was performed using the Bayesian confidence propagation neural network (BCPNN) method, and associations were considered significant when the lower limit of the 95% confidence

interval of the information component (IC025) exceeded zero. Descriptive analyses were conducted to summarize demographic and clinical characteristics. Time-to-onset distributions were analyzed using log-rank and Wilcoxon rank-sum tests

Results A total of 1,715 reports comprising 1,845 SSIEs were included. The mean age of patients was 39 years, and 28.0% of cases resulted in fatal outcomes. Ciprofloxacin was the most frequently reported drug, accounting for 56.7% of cases, while suicidal ideation was the most common event (58.8%). Disproportionality analysis revealed a significant association between FQs and suicidal ideation ($IC_{025} = 0.11$), whereas no significant association was observed for completed suicide or other self-injury events. Among individual agents, ciprofloxacin showed strong signals for both suicidal ideation and self-injurious ideation ($IC_{025} = 0.48$ and 0.54 , respectively), while ofloxacin was associated with deliberate poisoning ($IC_{025} = 0.19$). The median time to onset of SSIEs was 6 days (IQR: 2–21), which was significantly shorter than that observed with venlafaxine (30 days, $P < 0.001$), indicating a rapid onset pattern

Conclusion This study identified a significant association between fluoroquinolone use and suicidal ideation, with a relatively rapid onset following treatment initiation. Ciprofloxacin appears to carry a higher reporting risk compared with other agents. Although causality cannot be established due to the inherent limitations of spontaneous reporting systems, these findings highlight the importance of early recognition and monitoring of psychiatric adverse events in patients receiving FQs. Clinicians should exercise caution, particularly during the initial treatment period and in populations at potential risk

Keywords fluoroquinolones; suicidal ideation; self-injury events; pharmacovigilance; adverse event databases; disproportionality analysis

不同类型新生儿骨髓炎临床及病原学特点分析

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目的 分析比较不同类型新生儿骨髓炎的临床及病原学特点, 为提高临床对该病的认识并及时启动合理的治疗措施提供依据。

方法 选择 2017 年 1 月-2025 年 12 月我院收治的新生儿为研究对象, 比较社区获得性骨髓炎(CA-OM)组与医院获得性骨髓炎(HA-OM)组的一般资料、临床特点、病原菌分布、耐药性分析及治疗和转归。

结果 该研究共纳入 57 例新生儿骨髓炎, 其中 CA-OM 组 33 例(57.9%), HA-OM 组 24 例(42.1%)。两组患儿在性别、分娩方式、起病日龄、病程及合并化脓性关节炎、新生儿肺炎、中枢神经系统感染及其他类型感染的差异无明显统计学意义($P>0.05$), HA-OM 组早产儿比例、围产期因素、合并新生儿败血症比例均高于 CA-OM 组($P<0.05$), 出生体重与住院体重均低于 CA-OM 组($P<0.05$)。两组患儿发热、皮肤发红、肿胀、疼痛、活动减少或活动受限等临床表现无明显统计学差异($P>0.05$), CA-OM 组患儿皮温增高多于 HA-OM 组患儿($P<0.05$)。两组患儿白细胞计数、中性粒细胞计数、血小板计数、C 反应蛋白 $>10\text{mg/L}$ 比例、红细胞沉降率值、红细胞沉降率 $>15\text{mm/h}$ 比例均无明显统计学差异($P>0.05$), HA-OM 组患儿 C 反应蛋白值及多部位骨感染的比例高于 CA-OM 组($P<0.05$)。HA-OM 组患儿病原学培养阳性比例、革兰氏阴性菌感染比例、耐药菌感染比例均高于 CA-OM 组($P<0.05$)。两组患儿手术率、抗菌药物静脉用药疗程及后遗症发生率均无明显统计学差异($P>0.05$)。

结论 CA-OM 组与 HA-OM 组新生儿在一般资

料、临床特征、实验室检查、病原菌分布均存在差异, 应关注新生儿骨髓炎的感染类型, 评估并制定明确而有效的个体化方案, 有助于实现及时诊断和有效管理。

MrkF Protein: A Key Gene Regulating Virulence and Biofilm Formation in Hypervirulent *Klebsiella Pneumoniae*

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Background Hypervirulent *Klebsiella pneumoniae* (hvKp) exhibits enhanced virulence, a hypermucoviscous phenotype, and robust biofilm formation, all of which contribute to invasive infections. Type 3 fimbriae are important for bacterial adhesion and biofilm development; however, the role of the fimbrial component MrkF in hvKp pathogenicity remains unclear. This study aimed to define the function and molecular impact of MrkF in the hvKp reference strain NTUH-K2044

Methods An in-frame mrkf deletion mutant (Δmrkf) was generated in NTUH-K2044 by homologous recombination and confirmed by PCR and sequencing. Phenotypic comparisons between wild-type (WT) and Δmrkf strains included colony morphology,

string test, and quantitative measurement of culture viscosity. Biofilm formation was quantified using crystal violet staining. Expression levels of the capsule-associated regulators *rpmA* and *magA* were assessed by RT-qPCR. Transmission electron microscopy (TEM) was performed to visualize and compare fimbrial architecture between WT and $\Delta mrkF$ strains. Virulence was evaluated using *Galleria mellonella* infection and murine lethality assays.

Results The $\Delta mrkF$ mutant was successfully constructed. Compared with WT, $\Delta mrkF$ formed smaller, dry, non-mucoid colonies, was string-test negative, and exhibited a marked reduction in culture viscosity ($P < 0.001$), indicating loss of the hypermucoviscous phenotype. RT-qPCR showed a significant downregulation of *rpmA* in $\Delta mrkF$, whereas *magA* expression was not significantly affected. Biofilm assays demonstrated that $\Delta mrkF$ produced substantially less biofilm at all examined time points. TEM analysis revealed clear structural differences in fimbriae: WT cells displayed abundant, long, continuous fimbriae arranged in a network-like distribution, whereas the $\Delta mrkF$ strain showed a marked reduction in fimbrial number with fimbriae appearing short, fragmented, and sparsely distributed. In both *Galleria mellonella* and murine infection models, $\Delta mrkF$ displayed significantly attenuated virulence, with increased host survival compared with WT.

Conclusion MrkF is a critical determinant of the hypermucoviscous phenotype, biofilm formation, fimbrial integrity, and full virulence in hvKp NTUH-K2044. Loss of *mrkF* markedly attenuates pathogenicity and biofilm development, likely in part through downregulation of the capsule regulator *rpmA* and by disrupting fimbrial architecture. These findings identify MrkF as an important functional protein in hvKp pathogenicity and suggest it may represent a potential target for novel anti-virulence strategies.

Keywords *Klebsiella pneumoniae*; MrkF; hypervirulence; biofilm formation; hypermucoviscosity

艾滋病合并结核病相关免疫重建炎症综合征 T 淋巴细胞和单核细胞的特征研究

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目的 分析艾滋病合并结核病患者抗病毒治疗 (ART) 后发生免疫重建炎症综合征 (IRIS) T 淋巴细胞、单核细胞及相关细胞因子的动态变化, 探讨 TB-IRIS 的免疫学特征。

方法 以广州某艾滋病定点医院收治的艾滋病合并结核病患者为研究对象, 根据 ART 后是否发生 IRIS 分为 TB-IRIS 组和 Non-IRIS 组 (1:1 配对)。比较两组患者在 ART 基线、ART 后 IRIS 发生时及 3 个月, T 淋巴细胞和单核细胞的表型和活化状态及相关细胞因子水平。

结果 共纳入 TB-IRIS 组和 Non-IRIS 组各 14 例, 健康对照 (HC) 组 10 例。在 T 淋巴细胞、单核细胞及相关细胞因子方面与 Non-IRIS 组相比, TB-IRIS 组在 ART 基线、IRIS 发生时及 ART 3 个月 CD4⁺CD38⁺HLADR⁺ T 细胞水平均明显更高 ($P < 0.05$), ART 基线时 CD4⁺CXCR4⁺CCR5⁺ T 细胞水平更高 ($P < 0.05$), ART 3 个月时 CD4⁺CXCR4-CCR5⁺ T 细胞水平更高 ($P < 0.05$); TB-IRIS 组基线时中间型和非典型单核细胞非活化表型 (CD69-HLADR-) 比例更低 ($P < 0.05$), CD69-HLADR-NCM 细胞的比例更高 ($P < 0.05$), IRIS 发生时 CD69-HLADR-IM 比例更高 ($P < 0.05$), 但 ART 3 个月后两组间单核细胞差异消失 (P 均 > 0.05); TB-IRIS 组部分抑炎细胞因子在 ART 基线时更低 ($P < 0.05$), 多种促炎

因子及抑炎因子 IL-13 在 IRIS 发生时显著更高 ($P < 0.05$), 直至 ART3 个月, 仍有部分促炎因子明显高于 Non-IRIS 组 ($P < 0.05$), 但抑炎因子均趋于一致 (P 均 > 0.05)。

结论 AIDS 合并结核病患者 TB-IRIS 的发生可能与 ART 前尤其发生 IRIS 时 CD4⁺T 淋巴细胞的持续过度活化密切相关, 并伴随 ART 早期单核细胞的失衡及显著的促炎细胞因子风暴反应。

关键词: 艾滋病; 结核病; 免疫重建炎症综合征; T 淋巴细胞; 单核细胞

基于宏基因组二代测序诊断的急性 Q 热临床表现型与免疫血液学抑制: 一项回顾性研究

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背景 Q 热是贝纳柯克斯体感染引起的全身性疾病。该病早期临床表现缺乏特异性, 常导致诊断延迟, 进而可能引发严重的继发性器官损伤。本研究旨在分析经宏基因组二代测序确诊的急性 Q 热患者的临床及免疫血液学表型, 并评估早期明确诊断对临床病程的影响。

方法 本研究回顾性分析 24 例经宏基因组二代测序确诊的急性 Q 热患者, 系统评估其临床表现、实验室指标及治疗时间线。采用 Mann-Whitney U 检验比较不同靶向干预时机下的临床结局, 并通过 Spearman 秩相关分析评估实验室指标间的病理生理学关联。

结果 本研究共纳入 24 例急性 Q 热患者, 均为男性, 中位年龄 33.5 岁。实验室检查显示, 多数患者存在急性肝损伤, 表现为 ALT(中位 104.5 U/L)、AST(中位 76.0 U/L)及 LDH(中位 413.0 U/L)升高, CRP 水平普遍升高(中位 69.0 mg/L)。血液学方面, 患者呈现多系血细胞同步减少, 白细胞计数处于低正常水平($4.1 \times 10^9/L$), 血小板计数偏低或处

于临界水($140.0 \times 10^9/L$)。相关性分析显示, 白细胞与血小板下降呈显著正相关($r=0.71$, $P < 0.001$), 构成“免疫血液学抑制轴”。在治疗时机方面, 从症状出现至启动靶向治疗的中位时间为 6.0 天。进一步分析显示, 基线铁蛋白水平与发热病程呈显著正相关($r=0.605$, $P=0.017$), 提示高铁蛋白血症可作为预测发热病程延长的重要生物标志物。

结论 急性 Q 热临床表现多样, 早期缺乏特异性, 但存在较为特征性的“免疫血液学抑制轴”——白细胞与血小板同步减少, 并伴显著高铁蛋白血症及肝酶升高。对于不明原因发热患者, 若呈现上述三联征, 应高度警惕 Q 热可能。本研究证实, 宏基因组二代测序技术能够快速、精准明确病原, 显著缩短诊断与靶向治疗启动时间。在症状出现后 6 天内启动有效抗感染治疗, 可迅速控制炎症反应、加速临床康复、缩短住院时间, 并可能降低慢性化及严重并发症风险。因此, 对于疑似 Q 热的高危人群, 建议尽早开展宏基因组二代测序检测, 以优化诊断管理路径, 改善患者预后。

关键词: Q 热; 贝纳柯克斯体; 宏基因组二代测序; 巨噬细胞活化综合征;

BSRF1 抑制 NF-κB 活性调控 EB 病毒感染中的 IFN-β 抗病毒应答

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目的 EB 病毒(Epstein-Barr virus, EBV)是一种普遍存在的人类 γ 疱疹病毒, 其在感染过程中必须通过调控宿主先天免疫反应以实现持久潜伏。干扰素-β(IFN-β)是关键的反病毒细胞因子, 其产生主要依赖于核因子 κB(NF-κB)信号通路。然而, EBV 如何拮抗 IFN-β 介导的反病毒反应仍未完全明确。本研究旨在阐明 EBV 编码的衣壳蛋白 BSRF1 在宿主 IFN-β 调控中的作用, 并解析其干扰 NF-κB

活化的分子机制。

方法 研究采用多种分子与细胞学实验。通过将 BSRF1 表达质粒转染入 HEK293T 和 HeLa 细胞,并以 Sendai 病毒(SeV)或合成 RNA 模拟物 poly(I:C)刺激,检测 IFN- β 启动子活性(双荧光素酶报告实验)。结合免疫印迹、免疫共沉淀及共聚焦免疫荧光显微镜,分析 BSRF1 对 I κ B α 降解及 p65 核转位的影响。利用激酶抑制剂和显性负突变体探讨 IKK 复合物的参与。

结果 研究发现,BSRF1 是 IFN- β 产生的强效抑制因子。其过表达显著降低 SeV 和 poly(I:C)诱导的 IFN- β 启动子活性,并下调 IFN- β 转录及蛋白水平。机制研究表明,BSRF1 可与 I κ B α 及 IKK 复合物催化亚基结合,阻断 I κ B α 在 Ser32/36 位点的磷酸化及 K48 连接的多泛素化,进而抑制其蛋白酶体降解,稳定 I κ B α 并限制 p65 的核转位。功能实验显示,BSRF1 过表达促进 DNA 和 RNA 病毒复制,而 BSRF1 敲低或敲除可恢复 NF- κ B 活性并增强炎症因子产生。

结论 本研究首次揭示了 BSRF1 作为 EBV 免疫逃逸关键因子的作用机制。BSRF1 通过靶向 IKK-I κ B α 轴抑制 NF- κ B 活化,从而削弱 IFN- β 介导的抗病毒反应并增强病毒复制。这一发现不仅深化了对 EBV 与宿主互作的理解,也提示干扰 BSRF1 与 IKK 相互作用可能成为恢复宿主先天免疫应答、限制 EBV 相关疾病的新型治疗策略。

Outer Membrane Vesicles of Hypervirulent *Klebsiella Pneumoniae* Exacerbate Liver Abscess Injury

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Background Hypervirulent *Klebsiella pneumoniae* (hvKp) has emerged as a pathogen of great global concern, with pyogenic liver abscess (PLA) as its typical clinical manifestation. Outer membrane vesicles (OMVs) derived from *K. pneumoniae* may be closely associated with the pathogenic mechanism of this bacterium. Therefore, the aim of this study was to investigate the effects of OMVs secreted by hvKp on the formation of liver abscess

Methods OMVs were extracted from two standard strains: NTUH-K2044 (hvKp) and ATCC700603 (cKp). DIR fluorescence-labeled OMVs were injected into nude mice via the tail vein, and the in vivo distribution and trafficking of OMVs were traced by in vivo animal imaging technology. C57BL/6 mice were used to establish liver abscess models via intragastric gavage with bacterial suspension, and tail vein injection of OMVs was performed to investigate their roles in liver abscess formation. Liver injury and neutrophil infiltration were observed by hematoxylin and eosin (HE) staining and immunohistochemistry (IHC), respectively, and then the expression levels of inflammatory factors including interleukin-1 β (IL-1 β), IL-6, TNF- α , and chemokines CXCL1, CXCL2 and CXCL9 in mouse liver tissues were detected by reverse transcription-polymerase chain reaction (RT-qPCR)

Results DIR-OMVs were mostly concentrated in the liver of nude mice, and the accumulation gradually increased in a time-dependent manner. HE staining confirmed that liver abscess induced by NTUH-K2044 was more severe than that induced by ATCC700603. On the basis of NTUH-K2044 infection, mice receiving tail vein injection of NTUH-K2044-OMVs showed significantly larger liver abscess areas compared with the ATCC700603-OMVs group and PBS negative control

group. IHC results showed that the number of neutrophil infiltration in mouse liver was significantly higher after NTUH-K2044 infection than after ATCC700603 infection. Moreover, mice infected with NTUH-K2044 and treated with NTUH-K2044-OMVs exhibited more intense neutrophil infiltration than those injected with PBS via tail vein. In addition, RT-qPCR results revealed that the expression levels of IL-1 β , IL-6, TNF- α and CXCL2 in the liver were significantly higher in mice infected with NTUH-K2044 than in those infected with ATCC700603, and tail vein injection of NTUH-K2044-OMVs further upregulated the expression of these inflammatory factors and chemokines

Conclusions OMVs secreted by *K. pneumoniae* were found to accumulate in the mouse liver and induce upregulation of various inflammatory cytokines and chemokines. Compared with cKp, OMVs from hvKp strains exhibited significantly stronger pro-inflammatory activity, which further aggravated the severity of liver abscess

Keywords Hypervirulent *Klebsiella pneumoniae*, pyogenic liver abscess, outer membrane vesicles, inflammatory response

老年重症发热伴血小板减少综合征预后危险因素及护理策略分析

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目的 老年重症发热伴血小板减少综合征 (severe fever with thrombocytopenia syndrome, SFTS)

的临床与护理已成为 SFTS 救治的重点及难点。探讨老年重症 SFTS 患者预后不良的危险因素,并提出针对性的护理策略。

方法 回顾性分析 2021 年 5 月-2025 年 7 月安徽医科大学第二附属医院收治的 274 例老年 (≥ 60 岁)重症 SFTS 患者的临床资料。根据预后分为预后良好组和预后不良组,比较两组临床特征及实验室指标,采用多因素 Logistic 回归分析预后不良的独立危险因素,受试者工作特征曲线评估预测效能,结合危险因素制定专科护理策略。

结果 老年重症 SFTS 患者预后不良发生率为 28.10% (77 例),较低年龄组 (≤ 65 岁) DBV RNA 水平明显低于较高年龄组 (均 $P < 0.05$)。老年重症 SFTS 可发生多种并发症,其中肝脏损伤 (87.59%)、胰腺损伤 (56.93%)、共感染 (52.92%)、肾脏损伤 (39.78%)、脑病/脑炎 (38.69%)、心肌损害 (33.94%) 多见。多因素 Logistic 回归显示,高龄 (OR=1.096, 95% CI=1.044~1.151)、血清尿素氮升高 (OR=1.118, 95% CI=1.006~1.244)、凝血酶原时间延长 (OR=1.342, 95% CI=1.095~1.643) 及高病毒载量 (OR=1.503, 95% CI=1.155~1.957) 是预后不良的独立危险因素。联合模型预测预后不良的曲线下面积为 0.788, 优于单项指标。

结论 高龄、血清尿素氮升高、凝血酶原时间延长及高病毒载量是老年重症 SFTS 患者预后不良的独立危险因素,基于上述指标的联合模型及精准化护理策略可能对改善预后具有重要临床价值。

突破经典认知: 坏死梭杆菌引发脓毒症为表现的非典型勒米埃尔综合征 1 例

姚文琳

石河子大学第一附属医院

目的 坏死梭杆菌是一种革兰氏阴性厌氧菌,常定植于人类口咽部,可引发多种严重感染,其中

口咽部感染继发脓毒症起病隐匿、进展迅速，误诊漏诊率较高，严重时可危及患者生命。本研究旨在通过分析临床病例并结合相关文献，提高临床医师对坏死梭杆菌所致口咽部感染继发脓毒症的早期识别能力、规范诊疗水平，减少误诊、漏诊发生率，改善患者预后。

方法 回顾性分析我院急诊科收治的 1 例急性化脓性扁桃体炎继发坏死梭杆菌脓毒症患者的临床资料、诊疗经过，并结合相关文献进行综合分析与复习。

结果 该患者为青年男性，以咽痛、发热为初始症状，外院予红霉素抗感染治疗 5 天效果不佳，病情进展为脓毒症，伴心悸及心肌酶学指标升高。入院后完善呼吸道病原体靶向测序，明确检出坏死梭杆菌及咽峡炎链球菌群，给予哌拉西林钠他唑巴坦钠抗感染、液体复苏、心肌保护等综合治疗后，患者感染指标快速回落，临床症状显著缓解，最终痊愈出院。

结论 坏死梭杆菌所致感染早期症状缺乏特异性，易被误诊为普通细菌性扁桃体炎；对于常规抗感染治疗效果不佳的咽痛伴发热患者，需高度警惕坏死梭杆菌感染可能，尽早完善病原学检查，及时启动覆盖厌氧菌的抗感染方案，可显著改善患者预后。

关键词：坏死梭杆菌；脓毒症；急性化脓性扁桃体炎；勒米埃尔综合征；急诊诊疗

青年男性急性化脓性扁桃体炎继发坏死梭杆菌脓毒症（不典型勒米埃尔综合征）1 例报道

姚文琳

石河子大学第一附属医院

目的 坏死梭杆菌是一种革兰氏阴性厌氧菌，常定植于人类口咽部，可引发多种严重感染，其中口咽部感染继发脓毒症起病隐匿、进展迅速，误诊

漏诊率较高，严重时可危及患者生命。本研究旨在通过分析临床病例并结合相关文献，提高临床医师对坏死梭杆菌所致口咽部感染继发脓毒症的早期识别能力、规范诊疗水平，减少误诊、漏诊发生率，改善患者预后。

方法 回顾性分析我院急诊科收治的 1 例急性化脓性扁桃体炎继发坏死梭杆菌脓毒症患者的临床资料、诊疗经过，并结合相关文献进行综合分析与复习。

结果 该患者为青年男性，以咽痛、发热为初始症状，外院予红霉素抗感染治疗 5 天效果不佳，病情进展为脓毒症，伴心悸及心肌酶学指标升高。入院后完善呼吸道病原体靶向测序，明确检出坏死梭杆菌及咽峡炎链球菌群，给予哌拉西林钠他唑巴坦钠抗感染、液体复苏、心肌保护等综合治疗后，患者感染指标快速回落，临床症状显著缓解，最终痊愈出院。

结论 坏死梭杆菌所致感染早期症状缺乏特异性，易被误诊为普通细菌性扁桃体炎；对于常规抗感染治疗效果不佳的咽痛伴发热患者，需高度警惕坏死梭杆菌感染可能，尽早完善病原学检查，及时启动覆盖厌氧菌的抗感染方案，可显著改善患者预后。

关键词：坏死梭杆菌；脓毒症；急性化脓性扁桃体炎；勒米埃尔综合征；急诊诊疗

铜绿假单胞菌新型毒力因子 ExlA 的宿主受体及与宿主互作机制研究

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目的 铜绿假单胞菌是临床常见的革兰阴性条件致病菌，可导致呼吸道感染，尿路感染，创面感染以及败血症等。铜绿假单胞菌具有多种毒力因子，

其中Ⅲ型分泌系统效应蛋白是其最重要的毒力因子。然而近年临床发现铜绿假单胞菌不具有Ⅲ型分泌系统也可导致出血性肺炎等严重疾病。研究发现该类菌可分泌一种新型毒力因子-打孔毒素 ExlA。ExlA 阳性菌株具有很强的致病性,然而对该新型毒力因子缺乏深入研究,特别是 ExlA 靶向宿主的受体尚不明确。本研究核心目标是探究 ExlA 的宿主受体,并深入探究 ExlA 与宿主受体作用的机制以及受体的生理意义,为 ExlA 阳性铜绿假单胞菌感染治疗提供新思路和新方案。

方法 前期研究我们获得2株临床来源 ExlA 阳性铜绿假单胞菌,利用大蜡螟幼虫感染模型和小鼠经气道感染模型,检测 ExlA 阳性菌株的致病力。利用基于 CRISPR/Cas9 技术的全基因组敲除筛库法,通过 ExlA 毒素压力筛选寻找 ExlA 的宿主受体。同时在细胞水平和小鼠水平对宿主受体进行验证。

结果 在细胞水平及小鼠水平,ExlA 阳性菌株均表现出一定的毒性,特别是 ExlA 过量表达菌株的毒性显著提高。全基因组敲除文库筛选对 ExlA 具有抗性的细胞,二代测序分析锁定与 ExlA 互作的分子低密度脂蛋白受体相关蛋白 1 (LRP1)。后续对候选基因 LRP1 进行验证,在细胞水平证明 LRP1 敲除细胞对 ExlA 阳性菌株表现出显著的抗性。

结论 低密度脂蛋白受体相关蛋白 1 (LRP1) 对于 ExlA 阳性菌株毒性发挥起到关键作用,其机制可能是其可以促进 ExlA 蛋白进入宿主细胞。

高毒力耐碳青霉烯类肺炎克雷伯菌毒力质粒的消除对黏液表型及其他微生物特征的影响

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目的 研究毒力质粒对两种经典分型 CR-hvcp 菌株的影响及差异。

方法 选取 K1-ST23 型菌株 K147 和 K2-ST65 型菌株 K193 高毒力耐碳青霉烯类肺炎克雷伯菌作为亲本菌株,采用十二烷基硫酸钠 (SDS) 诱导毒力质粒消除获得 K147PC 和 K193PC,通过常规 PCR 和二代测序验证毒力基因 *rmpA*、*rmpA2*、*iucA*、*iroB*、*peg-344* 消除。比较消除前后拉丝试验、沉降试验测定黏液指数。评估菌株的荚膜形成能力,对单个菌体通过光学显微镜及透射电镜观察荚膜厚度,并对菌液进行 Percoll 梯度半定量、糖醛酸定量实验。其他微生物特征:通过微量肉汤稀释法检测 Kp 对临床常用药物的敏感性、结晶紫染色法评价生物膜形成能力、测定菌液 OD600 绘制生长曲线以及评估体外血清杀菌作用方面的差异。

结果 毒力质粒消除后,两种菌的黏液黏度和荚膜形成能力均削减。两种菌的 MI 值均有下降,仅 K147 变化显著 ($p=0.003$)。光学显微镜下染色后两种 Kp 的荚膜厚度均显著下降 ($p<0.0001$),TEM 观察消除前后荚膜变化,K147 从 112.90 nm 降至 33.87 nm, K193 从 75.81 nm 变为 45.16 nm。两种菌的荚膜半定量结果均有减少,荚膜多糖定量结果仅 K193 明显减少 ($p<0.0001$)。K147PC 对美罗培南由 $\geq 16 \mu\text{g/mL}$ 降至 $\leq 0.25 \mu\text{g/mL}$,对庆大霉素由 $\geq 16 \mu\text{g/mL}$ 降至 $\leq 1 \mu\text{g/mL}$,对碳青霉烯类及部分氨基糖苷类恢复敏感,而 K193 耐药表型基本不变。生长曲线显示消除后菌株进入对数生长期略有延迟,但总体生长能力未见明显差异。K147 的生物膜形成能力下降 ($p=0.050$),K193 显著增强 ($p<0.0001$)。K147 在血清杀伤实验中 3 h 存活率由 0.22% 降至 0.07%,对血清更敏感,但两株菌消除前后差异均无统计学差异。

结论 毒力质粒消除证实毒力质粒影响高黏液表型和荚膜形成,且 K1-ST23 型菌株 K147 受其影响强于 K2-ST65 型菌株 K193。毒力质粒的消除未影响 K147 和 K193 的抗血清能力,可使 K147 和 K193 提前进入对数生长期。毒力质粒的消除在 K147 和 K193 的生物膜形成能力上表现不一致。在 K147 中耐药基因伴随毒力质粒被消除,而 K193 携带的耐药基因更稳定。

剖宫产术后支原体血流感染的风险预测与临床特征分析：一项基于 36 例确诊病例的病例对照研究

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背景 剖宫产（CS）作为全球高危妊娠管理的重要手段，其广泛应用的同时也因侵入性操作显著增加了血流感染（BSI）风险。支原体属作为非典型病原体，因生长苛养、常规培养困难及对 β -内酰胺类抗生素天然耐药，常导致临床诊断不足与治疗延误。此外，解脲脲原体与人型支原体显著的耐药性差异，加之哺乳期用药限制，进一步加剧了临床处置的复杂性。因此，建立基于临床指标的早期识别工具对改善产妇预后具有重要意义。

方法 采用回顾性病例对照研究设计，纳入 2024 年 1 月至 2025 年 12 月在佛山市妇幼保健院行剖宫产术的 17,612 例患者，最终筛选出 36 例确诊支原体血流感染者作为感染组，并按 1:2 比例匹配 72 例未感染产妇作为对照组。收集人口学特征、产科操作、手术结局及实验室指标等信息。利用最小绝对收缩和 LASSO 回归进行变量降维，通过多因素 Logistic 回归确定独立危险因素并构建列线图模型。采用受试者工作特征曲线（ROC）和临床决策曲线分析（DCA）评估模型效能。同时，对比人型支原体与解脲脲原体的药敏结果及炎症指标差异。

结果 感染组的中转剖宫产率、侵入性操作比例、羊水污染率及术中出血量均显著高于对照组。多因素 Logistic 回归分析显示，术后白细胞计数（WBC）峰值（OR=1.33）和术后中性粒细胞百分比（NE%）峰值（OR=1.41）是预测术后支原体血流感染的独立危险因素。基于此构建的列线图模型表现

出优异的预测性能，曲线下面积（AUC）为 0.896（95% CI: 0.837-0.896），DCA 证实了其高临床净获益。药敏分析表明，解脲脲原体普遍敏感，而人型支原体对氟喹诺酮类（左氧氟沙星耐药率 83.3%）和克林霉素耐药率极高。亚组分析发现，两种支原体感染所致的 WBC、NE%、降钙素原（PCT）及 C 反应蛋白（CRP）峰值及动态变化无统计学差异。

讨论 本研究证实了术后 WBC 和 NE%峰值在早期识别支原体血流感染中的关键价值，构建的列线图模型为临床提供了高效筛查工具，弥补了常规培养漏检的短板。研究表明支原体可引发剧烈炎症反应，修正了其致病性弱的传统认知。此外，两者显著的耐药谱差异提示单一经验性治疗存在风险，特别是人型支原体的高耐药性及哺乳期用药禁忌使临床治疗面临挑战。本研究强调，利用该模型早期识别感染并及时调整抗感染策略，对于优化剖宫产术后管理具有重要临床价值。

艰难梭菌生物膜形成能力与毒力表型相关性研究

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背景 艰难梭菌（*Clostridioides difficile*）是抗菌药物相关性腹泻与医疗保健相关感染的重要致病菌，其所致感染高复发、难治疗等特征给临床诊疗与感染防控带来了沉重的公共卫生负担。该菌致病核心为毒素介导的宿主组织损伤，生物膜与艰难梭菌的持续定植、感染复发密切相关，但目前针对其生物膜形成与毒力表型关联的系统性直接研究仍较为匮乏。故本研究探究艰难梭菌生物膜形成能力与毒力表型之间的相关性，并从调控信号、代谢状态等层面探索潜在机制。

方法 （1）以 30 株临床分离艰难梭菌及标准株 R20291 为研究对象，采用结晶紫染色法于 24、

48、72、96 及 120 h 动态检测各菌株生物膜形成能力。(2) 结合菌株毒素基因分型结果, 采用 ELISA 定量检测培养上清中毒素 A、毒素 B 含量, 通过 MTT 法检测艰难梭菌上清对人结肠黏膜上皮细胞 NCM460 的损伤效应, 最终用 Spearman 秩相关分析生物膜表型与各毒力相关指标的关联。(3) 比较菌株浮游态与生物膜态下胞内 c-di-GMP 水平及毒素相关基因表达差异, 并开展代谢组学分析;

结果 (1) 不同菌株间生物膜形成能力存在明显差异, 且生物膜形成高峰主要集中于培养早期。

(2) 生物膜形成能力与毒素基因型及毒素 A、毒素 B 分泌水平均无显著相关, 其中与毒素 A 水平的 Spearman 相关系数为-0.05 ($P=0.863$), 与毒素 B 水平的 Spearman 相关系数为-0.18 ($P=0.390$); 但与宿主细胞毒力呈显著负相关 ($rs=-0.45$, $P=0.010$)。不同毒力分层比较的结果表明, 高毒力组菌株的生物膜形成能力显著低于无毒力组和低毒力组。(3) 代表菌株在生物膜状态下胞内 c-di-GMP 水平均高于浮游状态, 其中 24 h 时各菌株差异均达到统计学意义; 相较之下, 毒素相关基因表达变化存在明显菌株差异。(4) 代谢组学结果显示, 3 株代表菌株在 24 h 即出现明显胞外代谢谱分化, 72 h 差异进一步扩大, 差异代谢通路主要涉及 D-氨基酸代谢、半胱氨酸和蛋氨酸代谢、丙氨酸/天冬氨酸/谷氨酸代谢、嘌呤代谢及芳香族化合物相关代谢。

结论 在体外实验中, 艰难梭菌生物膜形成能力与其细胞毒力呈负相关, 较强的生物膜形成并未伴随更高的功能性毒力输出, 而是更多体现为细菌黏附、持留与环境适应相关的生存表型, 为从持续定植和感染复发视角重新认识艰难梭菌感染的发生发展提供了新的实验依据。

血流感染分离菌的种类及耐药性分析

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目的 探讨临床血流感染分离菌的种类及常见菌株的耐药性, 为临床治疗及合理用药提供依据。

方法 四川省医学科学院·四川省人民医院(东院)送检的血培养标本共 3640 份, 均采用法国生物梅里埃公司生产的 BACT/ALERT 3D 血培养仪进行培养, VITEK-2 Compact 微生物分析仪进行菌株鉴定和药敏试验。

结果 3640 份标本中, 剔除重复株后共分离出 466 株病原菌, 阳性率 12.8% (466/3640)。其中, 革兰氏阳性球菌(Gp) 占 57.5% (268/466), 最为常见 ($p<0.001$); 革兰氏阴性杆菌(Gn) 占 40.8% (190/466); 真菌占 1.7% (8/466)。Gp 以表皮葡萄球菌为主 ($p<0.001$), 占比为 42.9% (115/268)。Gn 以大肠埃希菌为主($p<0.001$), 占比为 56.8% (108/190)。临床科室中, 儿科的检出率最高 ($p<0.05$), 占比为 23.4% (109/466)。表皮葡萄球菌对青霉素、复方新诺明、苯唑西林、红霉素的耐药率均大于 60%, 分别为 93.0%、80.9%、72.2%、60.9%; 金黄色葡萄球菌对青霉素、红霉素、复方新诺明、克林霉素的耐药率均大于 50%, 分别为 95.6%、67.6%、58.8%、51.5%, 未检出对万古霉素和利奈唑胺耐药的葡萄球菌。大肠埃希菌对四环素、头孢唑啉、复方新诺明、头孢呋辛的耐药率均大于 60%, 分别为 80.6%、74.1%、68.5%、60.2%; 对氨苄西林/舒巴坦、莫西沙星、头孢曲松、头孢噻肟的耐药率均大于 50%, 分别为 56.5%、54.6%、53.7%、52.8%。肺炎克雷伯菌的耐药性与大肠埃希菌相比较不严重。未检出对碳青霉烯类药物耐药的肠杆菌科细菌。

结论 表皮葡萄球菌和大肠埃希菌是血流感染的主要病原菌, 其次为金黄色葡萄球菌和肺炎克雷伯菌。临床医师应根据药敏结果合理使用抗菌药物, 从而避免耐药性的发生、有效提高患者治愈率。

Diagnostic Efficacy of The TSPOT Assay for Tuberculosis Infection and Drug Resistance in

Mycobacterium Tuberculosis in Patients with Malignant Tumors

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Background Immunosuppression in cancer patients clearly elevates the risk of acquiring tuberculosis (TB) infection, and traditional diagnostic methods are characterized by low sensitivity (Sen) and long turnaround times. Although the interferon-gamma release assay (IGRA) is widely used, its ability in distinguishing active tuberculosis (ATB) from latent tuberculosis infection (LTBI) in cancer patients, as well as its relationship with drug resistance (DR), remains unclear

Objectives It aimed to evaluate the diagnostic capacity of TSPOT for ATB and its ability to differentiate ATB from LTBI in patients with malignant tumors

Methods A retrospective analysis was conducted on the data of 200 patients with malignant tumors, and patients were grouped: ATB group (AG), LTBI group (BG), and non-TB group (CG). The IFN- γ response induced by ESAT-6/CFP-10 was detected by TSPOT, and the relationship between TSPOT and DR was analyzed.

Results The Sen for ATB was 87.5%, and specificity (Spe) was 73.3%. The Sen for screening TB infections was 80.5%, with a Spe of 98.3% and a positive predictive value (PPV) of 97.1%. The Spe for differentiating ATB from LTBI was only 22.4%. The overall DR rate in the AG was 58.3% (14/24), including rifampicin (RIF) resistance (37.5%), multidrug-resistant TB (MDR-TB) (20.8%), and pre-extensively drug-resistant TB (Pre-XDR-TB) (8.3%).

Conclusion TSPOT is suitable for screening TB infection in patients with malignant tumors but has limited capacity to differentiate ATB from LTBI.

吡硫鎔锌抗肺炎克雷伯菌活性及多靶点机制研究

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目的 肺炎克雷伯菌 (*Klebsiella pneumoniae*) 是引起临床重症肺炎的关键病原体之一。由于抗生素滥用, 其不断加剧的细菌耐药性常导致传统抗感染治疗失效。面对这一严峻挑战, “药物再利用”策略为新型抗菌分子的开发提供了契机。吡硫鎔锌 (ZPT) 是一种长效的抗真菌成药分子, 其核心机制主要依赖于破坏真核病原体的细胞被膜与干扰细胞内环境稳态。此类致死机制显示 ZPT 具有跨界杀伤耐药细菌的潜力。本研究旨在系统评估 ZPT 对抗高毒力肺炎克雷伯菌 (NTUH K2044) 的基础抗菌活性与血液相容性, 并通过基因干扰 (CRISPRi) 组学深入解析其多靶点致死机制, 为抗耐药菌感染提供新方案。

方法 首先采用微量肉汤稀释法与平板涂布法测定 ZPT 的最小抑菌浓度 (MIC) 和最小杀菌浓度 (MBC), 评估 ZPT 的基础抗菌活性; 其次, 利用新鲜羊血细胞评估其体外溶血毒性。在机制探究层面, 构建肺炎克雷伯菌全基因组 CRISPRi 文库并进行药物压力下筛选, 结合生物信息学锁定核心增敏靶标, 通过构建敲低和敲除突变株验证靶点表型; 此外, 利用流式细胞术定量检测化合物对细菌内活性氧 (ROS) 的诱导作用。

结果 基础活性评估显示, ZPT 对肺炎克雷伯菌具有强效的抑菌与杀菌能力 (MIC = 2 $\mu\text{g/mL}$, MBC = 4 $\mu\text{g/mL}$); 同时, 在高达 128 $\mu\text{g/mL}$ 的浓度下对游离红细胞无明显溶血毒性, 展现出较优异的抗菌性能和血液相容性。文库筛选表明, ZPT 干扰了细菌的核心防御网络, 显著下调了包括 KP1_5012、KP1_4608 等关键生存基因, 且高度富集于细胞被膜和氧化应激相关通路。功能确证显示, ZPT 不仅能

破坏细菌被膜稳态, 还能以剂量依赖性方式诱导 ROS 爆发。

结论 本研究不仅成功验证了传统抗真菌分子 ZPT 对抗耐药细菌的较强杀菌活性和较高血液相容性, 还首次揭示了潜在的通过靶向细菌细胞被膜蛋白网络与诱导氧化应激的双重致死机制, 为开发新型抗感染单药或联合用药策略提供了重要的理论与实验基础。

关键词: 肺炎克雷伯菌; 细菌耐药性; 药物重利用; 吡硫鎧锌; CRISPRi

New Insights Into Diarrhea Caused by High-Fat Diet and Fatigue: Gut Microbiota Dysbiosis-Driven Bile Acid Metabolism Disorder

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Background This study investigated the mechanisms underlying diarrhea induced by a high-fat diet (HFD) under a state of fatigue, focusing on gut microbiota dysbiosis, bile acid metabolic disturbance, and gut–liver injury

Methods Mice were assigned to a normal control diet (NCD) group, a HFD-induced diarrhea under fatigue (HFDM) group, and a HFD-induced diarrhea with aggravated dysbiosis (HFDMA) group. Histopathology, inflammatory factors, intestinal barrier-related proteins, small-intestinal microbiota, and colonic bile acid profiles were assessed, and correlation analyses were performed among gut microbiota, bile acids, and inflammatory factors.

Results Compared with the NCD group, both the HFDM and HFDMA groups showed diarrhea-like and fatigue-like phenotypes, histopathological injury in the

small intestine and liver, increased tumor necrosis factor- α (TNF- α) and interleukin-6 (IL-6) levels, and impaired intestinal barrier function. No significant differences in inflammatory factors were observed between the HFDM and HFDMA groups. Zonula occludens-1 (ZO-1) expression decreased in both model groups but reached statistical significance only in the HFDMA group, whereas Claudin-1 expression was significantly reduced in both groups. Gut microbiota analysis showed altered community structure, with downward trends in alpha diversity that did not reach statistical significance but clear separation trends in beta diversity. Proteobacteria and Streptococcus increased, whereas Ligilactobacillus decreased. Total bile acid levels did not differ significantly among groups; however, the ratio of secondary to primary bile acids was significantly reduced in both model groups, particularly in the HFDMA group, with decreases in representative secondary bile acids, including hyodeoxycholic acid (HDCA) and isolithocholic acid (isoLCA). Correlation analysis further supported close associations among gut microbial alteration, bile acid disturbance, and intestinal and hepatic inflammation.

Conclusion Gut microbiota dysbiosis may disrupt bile acid metabolism, impair intestinal barrier integrity, and promote intestinal and hepatic inflammatory responses, thereby contributing to diarrhea progression under fatigue and HFD conditions through the gut–liver axis.

CD73 Blockade Promotes Disease Progression in Mice with Candidemia

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Objective CD73 plays a key role in the regulation of inflammatory response. This study examined the changes of CD73 levels in patients with candidemia and further explored the role of CD73 in the development of candidemia

Methods 20 healthy controls, 20 patients with bacteremia (including 10 patients with gram-negative bacterial infection and 10 patients with Gram-positive bacterial infection) and 20 patients with candidemia were enrolled. Serum CD73 levels in each group were detected by ELISA. In vivo, a mouse model of candidemia was established by tail vein injection of *Candida albicans* suspension. CD73 inhibitor (APCP) was injected intraperitoneally, and the survival rate of the mice was counted. Histopathological and serological tests were performed to analyze the renal injury in the mouse model to determine the effect of APCP treatment on the condition of the mice with candidemia. ELISA was used to detect the effect of APCP on the levels of serum inflammatory factors (IL-6, IL-8 and IFN- α) in mice with candidemia

Results Serum CD73 levels were significantly lower in patients with candidemia than in healthy controls and patients with bacterial infection. Intraperitoneal injection of CD73 inhibitor (APCP) can significantly increase the fungal load in renal tissue of mice with candidemia, aggravate kidney injury, and reduce the survival rate of mice. Serum creatinine and urea nitrogen levels were significantly upregulated in APCP-treated mice. ELISA results showed that compared with the infected mice, APCP treatment up-regulated the levels of IL-6 and IL-8 in the serum of the *Candida* infected mice

Conclusion Serum CD73 level is decreased in patients with candidemia, and CD73 blockade can aggravate the condition of mice with candidemia

肺炎克雷伯菌脑膜炎并发 SIRS 炎症动态变化与不良结局的相关性研究

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背景 细菌性脑膜炎(Bacterial Meningitis, BM)是病原菌感染蛛网膜下腔并引发宿主大脑皮层炎症反应的一种感染性疾病,具有较高的发病率和病死率,常见的病原菌包括流感嗜血杆菌、肺炎链球菌以及脑膜炎奈瑟菌。近年来,肺炎克雷伯菌(*K. pneumoniae*)已成为亚洲社区获得性脑膜炎的主要病原菌之一。2019 年中国细菌耐药监测网数据显示,脑脊液分离标本中,碳青霉烯类耐药肺炎克雷伯菌占 8.03%,在阴性杆菌中仅次于鲍曼不动杆菌(12.43%),在所有分离菌种中列第 4 位。全身炎症反应综合征(SIRS)是指各种感染或非感染因素作用于机体免疫系统,引发过度的炎症介质释放和播散导致的全身炎症反应。临床上, SIRS 是导致细菌性脑膜炎患者死亡的重要病因之一。本文通过实验研究和临床数据分析发现, SIRS 是影响肺炎克雷伯菌脑膜炎病程和解决的关键因素之一。

目的 探讨肺炎克雷伯菌脑膜炎患者并发 SIRS 的动态演变规律,分析炎症指标变化与临床不良结局之间的关联。

方法 1、回顾性纳入 2019 年 6 月-2024 年 6 月安徽医科大学第一附属医院收治的细菌性脑膜炎病人,动态收集入院后 SIRS 评分及炎症指标并进行分层分析。2、构建肺炎克雷伯菌脑膜炎动物模型。

结果 1、共收集细菌性脑膜炎病人共 216 例,其中肺炎克雷伯菌脑膜炎病人 31 例(13.2%)。肺炎克雷伯菌脑膜炎患者中最小年龄 26 岁,最大年龄 78 岁,平均年龄 53 岁;男性患者 18 例(58%),女性患者 13 例(42%)。细菌性脑膜炎患者死亡 51 例(24%),肺炎克雷伯菌脑膜炎患者死亡 17 例(55%)。在细菌性脑膜炎患者中,50 例出现 SIRS,死亡 13 例

(26%), 在肺炎克雷伯菌脑膜炎患者中, 18 例出现 SIRS, 死亡 10 例(56%)。(2) 通过脑立体定位注射, 构建急性肺炎克雷伯菌脑膜炎模型。与对照组相比, 模型组生存率、生存时间显著下降($p<0.05$), Loeffler 评分显著改变 ($p<0.05$)。模型组血液中 IL-6、TNF- α 水平显著上升 ($p<0.05$)。

结论 (1)在细菌性脑膜炎中, 肺炎克雷伯菌脑膜炎具有显著高病死率的特征;(2)SIRS 是导致肺炎克雷伯菌脑膜炎患者死亡的重要危险因素之一, 对 SIRS 的处理成为改善肺炎克雷伯菌脑膜炎病程的重要步骤;(3)动物模型证实肺炎克雷伯菌的中枢感染可触发剧烈的神经炎症反应。

Neisseria Meningitidis Serogroup W ST-4821 Clonal Complex Shares A Highly Conserved Capsular Switching Pattern with ST-11 Clonal Complex Strains

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Objectives *Neisseria meningitidis* ST-4821 clonal complex (cc4821) has become the most prevalent in China, which can be divided into four sublineages globally, with the L44.4 sublineage incorporating all serogroup W (MenW) cc4821 isolates. We aimed to illustrate the capsular switching that generated MenW cc4821 isolates, focused on the origin and the universal capsular switching pattern

Methods The nucleotide sequences of capsular polysaccharide synthesis (cps) gene cluster were extracted from the genomes of cc4821 L44.4 sublineage in the *Neisseria* PubMLST Database and analyzed using MEGA software. The capsular switching of MenC to MenW was conducted via natural transformation, and

the infectivity was evaluated through in vitro experiments.

Results Phylogenetic analysis on cps of cc4821 L44.4 indicated that MenW, MenC, and MenB isolates could be clearly distinguished only in region A. Nm464 was performed PacBio sequencing for origin analysis, which identified a potential donor strain (W: P1.18-1,3:F4-1: ST-22 [cc22]). C→W capsular switching was performed ex vivo, with recombinant sequences being highly conserved between cc4821 and cc11 MenW isolates. The transformant expressed a similar level of capsular polysaccharides but grew more slowly than the donor strain.

Conclusion C→W capsular switching with a cc22 strain as the potential donor was identified in cc4821 isolates, which is a highly conserved pattern among MenW strains. A fitness cost was found in the capsular switching.

Keywords *Neisseria meningitidis*, capsular switching, recombinant breakpoints, immune escape, fitness cost

Alterations in Microbiota Composition between Tumor and Peri-tumor Tissue: A Systematic Review and Meta-analysis

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Background The tumor-associated microbiota has emerged as a critical factor in cancer development and progression. However, whether tumor tissues exhibit altered microbial diversity and compositional changes compared with peri-tumor tissues remains controversial. This study aimed to systematically evaluate microbiota alterations between tumor and peri-tumor

tissues, perform a within- and between-diagnostic comparison

Method Pubmed, web of science and Embase databases were searched up to September 2, 2025. Studies comparing microbiota profiles between tumor and matched peri-tumor tissues were included. Standardized mean differences (SMDs) with 95% confidence intervals (CIs) were calculated for alpha diversity indices. Beta diversity and relative abundance of tissue microbes were summarized qualitatively. Random-effects models were applied, and heterogeneity was assessed using the I^2 statistic

Result A total of 43 studies provided data and were included in alpha diversity meta-analyses ($n=2455$ tumor tissues, $n=2262$ peri-tumor tissues). No significant increase or decrease was observed in the comparison of alpha diversity between tumor tissues and peri-tumor tissues. However, when individual cancer types were examined, a significant increase in the Simpson index was found in the tumor tissues of patients with gastric cancer ($SMD = 0.74$; 95%CI, 0.54 to 0.95), while a significant decrease in the Simpson index was observed in pancreatic cancer ($SMD = -0.44$; 95% CI, -0.80 to -0.07). In studies investigating beta diversity, conflicting results have been reported even for the same cancer type. The relative abundance of microbes showed notable heterogeneity across types. Gastric cancer (GC) exhibited an increasing trend for most genera, including *Corynebacterium*, *Veillonella*, *Shigella*, *Enterococcus*, *Streptococcus*, *Lactobacillus*, *Staphylococcus*, *Prevotella*, and *Fusobacterium*, while only *Helicobacter* showed a decrease. In contrast, Hepatocellular Carcinoma (HCC) and Colorectal cancer (CRC) exhibited only isolated changes (e.g., *Pseudomonas* up in HCC; *Selenomonas* up in CRC), while Pancreatic cancer (PC) and Papillary Thyroid Cancer (PTC) showed few consistent differences

Conclusion This systematic review and meta-

analysis found that there was no overall difference in alpha diversity between tumor and peri-tumor tissues, but changes in microbiota showed significant cancer type specificity

Indole-3-propionic Acid Alleviates Urosepsis-induced Renal Injury Via AHR-mediated Regulation of The IL-6/STAT3 Axis.

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Abstract Sepsis is a life-threatening syndrome of organ dysfunction caused by a dysregulated host response to infection . It is estimated that approximately 19 million people develop sepsis worldwide each year, with a mortality rate of up to 25% , posing a major threat to public health. Urosepsis, resulting from infections of the genitourinary tract, accounts for approximately 9%–31% of all sepsis cases . During its pathogenesis, *Escherichia coli*, one of the most common pathogens, releases surface toxins into the bloodstream, triggering widespread immune responses and leading to systemic inflammation . In recent years, increasing evidence has shown that tryptophan metabolism plays a critical role in the development and progression of sepsis . However, the specific mechanisms underlying its involvement in urosepsis remain insufficiently understood and warrant further investigation.

Objective This study aims to investigate the role of the AhR gene in renal epithelial cells in urosepsis and to elucidate its underlying mechanisms

Methods To investigate AHR in urosepsis, we used renal epithelial cell-specific AHR knockout mice

(AHR^{flox/flox}; Cdh16-Cre) and WT controls, and established a urosepsis model by intravesical inoculation of uropathogenic *E. coli* CFT073. Mice were pretreated with the AHR agonist diosmin. Renal inflammation, apoptosis-related proteins, and kidney injury (serum creatinine, BUN, H&E staining, and Paller scoring) were assessed. Mechanistically, WB and PCR, along with IHC and IF, were used to analyze AHR-related pathways in kidney tissues. Additionally, AhR overexpression and CUT&Tag analysis in human renal epithelial cells were performed to identify and validate downstream targets.

Results Tryptophan metabolism is disrupted in urosepsis, with reduced serum IPA and activation of the IL-6/STAT3 axis. AhR deficiency, especially in renal epithelial cells, exacerbates IL-6/STAT3 signaling and kidney injury, whereas AhR activation—particularly with diosmin—suppresses this pathway and confers renal protection. Mechanistically, AhR mitigates renal injury by regulating downstream targets that inhibit IL-6/STAT3 signaling.

Key words: urosepsis, AhR, indole-3-propionic acid, IL6/STAT3

波氏赛多孢霉侵袭性感染导致肺移植患者重症肺炎的实验室检查及探索性临床治疗

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目的 提高对波氏赛多孢霉 (*Scedosporium boydii*) 侵袭性感染的诊疗认识, 通过实验室特征分析与治疗方案总结, 为早期诊断和精准干预提供依据。

方法 结合痰液及肺泡灌洗液 (BALF) 培养结果, 系统描述该菌的菌落形态 (哥伦比亚血琼脂/沙

保罗平板)、染色特征 (乳酸酚棉蓝、荧光染色)、质谱鉴定 (MALDI-TOF MS)、基因测序及宏基因组测序 (mNGS) 等实验室检测方法; 通过体外药敏试验评估药物敏感性并总结临床治疗策略。

结果 住院期间患者痰液和 BALF 标本多次培养出波氏赛多孢霉的丝状菌落。波氏赛多孢霉在哥伦比亚血琼脂 (BA) 和沙保罗平板 (SDA) 上生长迅速。菌落整体呈扁平状和白色绒毛状, 随着培养时间的延长, 菌落中央渐变成鼠灰色或灰褐色, 而菌落边缘呈灰白色羊毛状, 且不断向周围蔓延生长。同时结合乳酸酚棉蓝染色和真菌荧光染色后的镜下形态特征、质谱分析、基因测序和 mNGS 等检测方法可显著缩短对该菌的鉴定时间。体外药敏试验结果提示该菌对泊沙康唑、伏立康唑以及艾沙康唑较为敏感。临床治疗上, 泊沙康唑联合两性霉素-B 脱氧胆酸盐雾化对波氏赛多孢霉引起的严重侵袭性感染治疗有效, 患者预后良好。

结论 波氏赛多孢霉感染罕见且易被低估, 其病程迁延、天然耐药性高, 诊疗周期长难度大。通过整合多模态检测技术可加速该病原鉴定; 基于药敏的联合抗真菌治疗可能改善预后。本研究为提升该菌感染的早期识别与精准治疗提供参考, 对免疫抑制人群具有重要临床意义。

关键词 波氏赛多孢霉; 侵袭性感染; 器官移植; 重症肺炎; 免疫抑制

超重对 2 型糖尿病合并流感患者临床特征及危重症风险的影响

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目的 探讨不同体重指数 (BMI) 对 2 型糖尿病 (T2DM) 合并流感住院患者临床特征及危重症风险的影响, 并评估钠-葡萄糖协同转运蛋白 2 抑制剂 (SGLT2i) /胰高血糖素样肽-1 受体激动剂 (GLP-

1RA) 及奥司他韦对超重及肥胖患者预后的改善作用。

方法 纳入 100 例 T2DM 合并流感住院患者, 依据 BMI 分为正常组 ($18.5 \sim <24.0 \text{ kg/m}^2$, $n=33$)、超重组 ($24.0 \sim <28.0 \text{ kg/m}^2$, $n=34$) 及肥胖组 ($\geq 28.0 \text{ kg/m}^2$, $n=33$)。比较三组血糖指标、炎症标志物及临床预后 (肺炎发生率、住院时间延长率、机械通气需求率)。对超重及肥胖患者进行亚组分析, 比较使用 SGLT2i/GLP-1RA 或奥司他韦者与未使用者的危重症发生率差异。

结果 超重组及肥胖组的随机血糖、空腹血糖、餐后血糖及糖化血红蛋白 (HbA1c) 均显著高于正常组 ($P<0.05$)。炎症指标中仅白细胞计数在肥胖组显著升高 ($P<0.05$)。超重组及肥胖组的肺炎发生率 (52.9% 、 69.7% vs. 24.2%)、住院时间延长率 (44.1% 、 60.6% vs. 15.2%) 及机械通气需求率 (23.5% 、 39.4% vs. 9.1%) 均显著高于正常组 ($P<0.05$)。亚组分析显示, 在超重及肥胖患者中, 使用 SGLT2i/GLP-1RA 者 ($n=36$) 较未使用者 ($n=31$) 肺炎确诊率 (36.1% vs. 67.7%)、住院时间延长率 (30.6% vs. 58.1%) 及危重症发生率 (19.4% vs. 45.2%) 显著降低 ($P<0.05$); 接受奥司他韦治疗者 ($n=42$) 亦较未治疗者 ($n=25$) 上述指标显著改善 ($P<0.05$)。

结论 超重及肥胖与 T2DM 合并流感住院患者血糖控制恶化及不良预后显著相关。采用 SGLT2i/GLP-1RA 类降糖药物联合奥司他韦抗病毒治疗可协同降低超重及肥胖患者的危重症风险。

Fec 基因对肺炎克雷伯菌毒力影响的初步研究

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目的 探讨 fec 基因簇 (编码铁载体摄取系统) 对肺炎克雷伯菌铁载体合成及毒力的影响, 通过构

建 fec 基因敲除株与野生株进行对比, 分析 fec 基因缺失后菌株在铁摄取、生长特性、高黏液表型及血清抗性等方面的变化, 为阐明 fec 基因在肺炎克雷伯菌致病机制中的具体作用提供实验依据。

方法 以肺炎克雷伯菌临床分离株为研究对象, 采用同源重组技术构建敲除株 (Δfec), 同时构建回补株。分别对野生株、敲除株和回补株进行以下检测: ①铁限制条件下的生长曲线测定; ②拉丝试验判定高黏液表型; ③人血清抗性实验; ④大蜡螟感染模型。实验结果采用 t 检验或方差分析, $P<0.05$ 为差异有统计学意义。

结果 成功构建 fec 基因簇敲除株及回补株。铁限制条件下, Δfec 敲除株的生长速率低于野生株, 回补株恢复至野生株水平。高黏液表型方面, 三组阳性率无统计学差异。血清抗性实验中, Δfec 敲除株存活率与野生株和回补株相比无显著差异。大蜡螟感染模型中, Δfec 敲除株注射后存活率与野生株和回补株相比亦无显著差异。

结果 表明, fec 基因敲除主要影响铁限制条件下的生长能力, 但对高黏液表型、血清抗性 & 毒力无明显影响。

结论 fec 基因簇在肺炎克雷伯菌中主要承担铁载体-铁复合物的摄取功能, 其缺失会削弱菌株在铁限制环境下的生长能力, 但不影响铁载体合成、高黏液表型、血清抗性 & 大蜡螟体内毒力。提示 fec 基因对肺炎克雷伯菌的基础毒力贡献有限。

ApoC3 通过抑制 PPAR γ 促进巨噬细胞 M1 样极化加重 2 型糖尿病肾盂肾炎的机制研究

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目的 2 型糖尿病 (Type 2 Diabetes Mellitus, T2DM) 患者发生急性肾盂肾炎发病风险及严重程度显著增加, 易进展为复杂性肾盂肾炎、脓毒症及

急性肾损伤。传统降糖及抗生素治疗虽有效,但T2DM患者复发率仍居高不下,亟需探索感染-代谢互作的致病机制并寻找新的干预靶点。本研究旨在阐明T2DM背景下APN加重的关键效应分子及机制,并探索靶向免疫调控的治疗策略。

方法 本研究构建了T2DM-APN复合动物模型:选用6-8周雌性db/db小鼠及其同窝db/m对照建立上行性肾盂肾炎模型。结合肾脏转录组及蛋白组分析,筛选连接T2DM与感染诱导肾损伤的关键效应分子,并在临床样本中进行验证。通过人源化APOC3转基因及Apoc3全身性敲除鼠进一步解析ApoC3在APN中的作用。分离骨髓来源巨噬细胞,体外感染及极化实验用于探讨ApoC3调控巨噬细胞功能的机制。

结果 感染后第7天db/db小鼠肾脏出现多发脓肿并伴明显组织学损伤,免疫组化显示巨噬细胞及中性粒细胞浸润显著增加,免疫荧光共定位显示浸润巨噬细胞以M1样表型为主,提示早期“炎症亢进—肾损伤”进程被触发。多组学分析显示,肾脏局部及血浆ApoC3蛋白水平均显著上升。临床样本验证显示,APN及T2DM-APN患者血浆ApoC3明显升高;T2DM-APN组肾组织炎性细胞浸润、ApoC3表达及TUNEL⁺凋亡细胞显著高于其他组。hAPOC3-Tg小鼠感染后呈现与db/db相似的早期24小时高致死性,伴多器官感染播散加重及肾脏急性化脓性损伤。Apoc3 KO鼠可逆转上述病理变化,提示ApoC3通过促炎—促凋亡机制加重APN进程。体外BMDMs实验显示,db/db及hAPOC3-Tg来源巨噬细胞M1样极化明显,而Apoc3 KO可逆转M1样极化。进一步验证显示,ApoC3通过抑制PPAR γ 激活促进巨噬细胞M1样极化。联合应用ApoC3反义寡核苷酸Volanesorsen与PPAR γ 全激动剂吡格列酮可减轻炎症因子及LCN2水平。

结论 本研究系统阐明T2DM基础高表达ApoC3受感染进一步诱导,驱动巨噬细胞M1样极化、肾脏炎症过度反应及肾小管损伤。ApoC3水平可作为高危人群预警及病情评估指标,联合靶向ApoC3与激活PPAR γ 的干预策略为复杂性尿路感

染的防治提供新靶点与理论依据。

关键词: ApoC3 2型糖尿病 急性肾盂肾炎 PPAR γ 巨噬细胞极化

Osteocalcin 是早期评价儿童肺炎支原体肺炎病情严重程度的潜在靶点

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背景 肺炎支原体(MP)是引起儿童社区获得性肺炎的主要病原体之一,部分肺炎支原体肺炎(MPP)易发展为重症,免疫因素在其中发挥的作用不容忽视。

方法 本研究共纳入学龄期MPP患者31例,其中普通型18例(cGMPP),重症型13例(cSMPP)。分别于急性期及恢复期采集患者外周血标本,并检测37项细胞因子浓度。

结果 1、cSMPP与cGMPP体内免疫应答程度不同:①cGMPP:仅LIGHT在急性期显著高于恢复期,余无统计学差异。③cSMPP: Pentraxin-3、BAFF在急性期高于恢复期;IL-34、MMP-2、TWEAK、IL-26、IL-10、IL-35在恢复期高于急性期。

2、cSMPP与cGMPP体内应答模式存在差异:①急性期时: Pentraxin-3在cSMPP组较高;IL-22、Osteocalcin在cGMPP组较高。②恢复期时:上述3项细胞因子在两组恢复至相同水平;但cSMPP组IL-34、MMP2、TWEAK、IL-12(p40)、IL-19、IL-26、IL-10高于cGMPP组。

3、Osteocalcin是早期评估病情严重程度的独立因素:①单因素回归分析:急性期, Pentraxin-3、IL-22、Osteocalcin和sTNF-R1/sTNF-R2与疾病严重程度相关,其中Pentraxin-3为危险因素,余为保护因素。②多因素回归分析进一步揭示:在急性期,Osteocalcin是决定疾病是否进展为重症的独立保护

因素。

4、不同的免疫应答模式与病情严重程度走向相关：①急性期时，cGMPP 组 sTNF-R1/sTNF-R2 比值高于 cSMPP 组，单因素回归分析显示，sTNF-R1/sTNF-R2 比值升高是避免进展为重症的保护因素。②恢复期时，cGMPP 组(sCD163+Chitinase3-like1+Osteopontin)/IL-10 比值高于 cSMPP 组，单因素回归分析显示其比值为保护因素，提示免疫系统已经从急性炎症过渡至修复阶段。

结论 免疫应答程度和模式差异是儿童 MPP 是否发展为重症的重要因素。研究示 Osteocalcin 可抑制 TNF- α 、IL-6 等炎症因子水平及 NF- κ B 等通路。鉴于 Osteocalcin 在全身代谢中的潜力，Osteocalcin 或可成为早期评估 MPP 病情严重程度的关键指标，但其具体机制尚未阐明。

首诊为脑囊虫病的血行播散性肺结核一例

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目的 探讨一例首诊为脑囊虫病的血行播散性肺结核患者的诊治，以提高疾病认识，提升诊疗能力。

方法 患者 Y 某，女，32 岁，因“头晕半月，疑诊囊虫病”于 2026-03-03 就诊于我科门诊。患者半个月前出现头晕、头痛，左侧面部麻木，无发热，恶心呕吐、视物模糊、言语不利、肢体活动不利。外院完善头+腰椎增强 MRI，提示双侧大脑、小脑、脑干内、脊髓圆锥内多发富血供占位性病变，脑囊虫病？转移瘤？既往贵州毕节人，幼时曾患绦虫病，口服药物治疗，目前长期居住北京市通州区，否认生食史。门诊考虑囊虫病？拟收住院进一步诊治，同时建议外院 A 完善相关检查：便找寄生虫卵阴性，血

多种寄生虫抗体（囊虫 IgG，肺吸虫 IgG，血吸虫 IgG，曼氏裂头蚴 IgG，肝包虫 IgG）阴性，外院热研门诊专家门诊不考虑寄生虫感染，建议神经内科就诊。后患者自行于外院 B 神经内科住院治疗，完善腰椎穿刺可见无色透明的脑脊液，脑脊液压力 230 毫米水柱，脑脊液 ADA 0.5U/L，脑脊液结核分枝杆菌快速核酸检测阴性；隐球菌荚膜多糖抗原阴性，抗酸及墨汁染色阴性，脑脊液宏基因组测序可见分枝杆菌序列 1141。遂完善血 QFT.TB 阳性。完善胸部 CT，可见双肺粟粒样改变，肺结核可能性大，综合考虑结核性脑脓肿、血行播散性肺结核可能性大。建议转往结核病专科医院。

结果 患者最终就诊于外院结核病专科医院 C，给予 HRZMFX 治疗后好转，其后出院继续抗结核治疗。

结论 结核感染表现多样，需要警惕常见病的不常见表现，以提高认识，早期诊断，避免延误治疗。

关键词：囊虫病，血行播散性肺结核，宏基因组测序

Comparative Clinical Characteristics of Enterococcus Faecium and Enterococcus Faecalis Infections in Children

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Objective To compare the clinical characteristics, exposure factors, and disease burden of pediatric Enterococcus faecium and Enterococcus faecalis infections, providing evidence for early identification and targeted management.

Methods Hospitalized children with E. faecium

or *E. faecalis* isolated from sterile specimens at Shanghai Children's Medical Center between August 2018 and June 2025 were retrospectively included. Patients were grouped by pathogen species. Demographics, department distribution, underlying diseases, laboratory indicators, infection sites, invasive procedures, previous hospitalization, and antimicrobial exposure were compared. Multivariable logistic regression identified factors associated with pathogen species, and Poisson regression assessed length of hospital stay.

Results Among 167 patients, 98 had *E. faecium* infection and 69 had *E. faecalis* infection. Department distribution differed significantly ($P<0.001$). *E. faecium* infection was more common in hematology-oncology and pediatric intensive care units, whereas *E. faecalis* infection predominated among surgical patients. Compared with the *E. faecalis* group, the *E. faecium* group had more hematologic malignancies, longer hospital stays, higher procalcitonin levels, and more multi-site infections. Previous hospitalization, central venous catheterization, and immunosuppressant use were also more frequent in the *E. faecium* group, while endotracheal intubation and postoperative status after congenital heart disease surgery were more common in the *E. faecalis* group.

After adjustment for septic shock, central venous catheterization (aOR=4.252, 95% CI: 2.172–8.326, $P<0.001$) and hospitalization for ≥ 14 days before culture positivity (aOR=2.676, 95% CI: 1.202–5.960, $P=0.016$) were independently associated with *E. faecium* infection. Endotracheal intubation was associated with *E. faecalis* infection (aOR=2.043, 95% CI: 1.079–3.867, $P=0.028$). Poisson regression showed that *E. faecium* infection was associated with a longer hospital stay than *E. faecalis* infection (aIRR=1.339, 95% CI: 1.267–1.451, $P<0.001$).

Conclusion Pediatric *E. faecium* and *E. faecalis* infections differ in clinical setting, underlying diseases,

invasive procedure exposure, and disease burden. *E. faecium* infection is associated with hematologic malignancy, immunosuppressant use, central venous catheterization, prolonged healthcare exposure, multi-site infection, elevated procalcitonin, and longer hospitalization. *E. faecalis* infection is more common in surgical patients, especially after congenital heart disease surgery, with endotracheal intubation as a potentially important associated factor. These findings may support risk stratification and targeted prevention.

Key words: *Enterococcus faecium*; *Enterococcus faecalis*; children; infection; exposure factors.

Metagenomic Diagnosis of Culture-Negative *Coxiella Burnetii* Spondylodiscitis: Unveiling The Zoonotic Link in Osteoporotic Patients

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Objective To demonstrate the diagnostic superiority of metagenomic next-generation sequencing (mNGS) over traditional culture in identifying fastidious zoonotic pathogens causing spondylodiscitis and to characterize emerging transmission risks.

Methods We analyzed a case of a 59-year-old male with osteoporosis presenting with severe lumbosacral pain and fever in Northwest China. Following negative routine blood and tissue cultures, percutaneous disc biopsy tissue was subjected to mNGS (MGISEQ-2000). The presence of *C. burnetii* was validated via PCR targeting the IS1111 transposase gene. Phylogenetic analysis was performed to compare the patient's strain with local vector sequences.

Results mNGS identified *C. burnetii* within 24

hours with high confidence, yielding 10,491 specific reads and 22.66% genome coverage. Phylogenetic trees revealed 100% nucleotide homology between the patient's strain and a strain isolated from local *Hyalomma asiaticum* ticks. Epidemiological investigation linked the infection to the patient's long-term consumption of unpasteurized bulk milk for osteoporosis management. Targeted therapy with doxycycline and rifampicin led to clinical resolution.

Conclusion mNGS is a vital tool for diagnosing culture-negative zoonotic spondylodiscitis where traditional methods fail. The identification of raw milk consumption as a transmission vector in osteoporotic patients highlights a specific public health intervention target. Clinicians should suspect Q fever in patients exhibiting clinico-biological discordance (high inflammation with normal leukocyte counts).

支气管扩张合并 2 型炎症的研究进展

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非囊性纤维化支气管扩张症（以下简称支扩）是一种复杂且异质性显著的慢性气道炎症性疾病，已成为全球性的重大健康负担，治疗重点在于气道廓清、祛痰以及管理感染。然而，许多患者仍存在持续症状和（或）急性加重以及进行性肺功能下降。对炎症机制的深入研究发现大部分支扩是一种中性粒细胞炎症，但是约 20%-30% 的支扩患者表现出 2 型炎症，国内专家共识已将 2 型炎症性支扩定义为血嗜酸性粒细胞计数 $\geq 300/\mu\text{L}$ 或呼出气一氧化氮（FeNO） $\geq 25\text{ppb}$ 。本文探讨了 2 型炎症参与支扩病理生理的核心机制：气道上皮受到外界刺激，分泌警报素如 IL-25、IL-33 和胸腺基质淋巴生成素（TSLP），进而激活 ILC2 及 Th2 细胞释放 IL-4、IL-

5、IL-13 等细胞因子，介导嗜酸性粒细胞炎症、气道黏液高分泌及气道重塑的发展。临床上该亚型患者常表现为呼吸困难更重、肺功能更差、生活质量更低，血嗜酸性粒细胞计数与急性加重风险呈“U 型”关系，但也有研究表明了血嗜酸粒细胞计数 $< 100/\mu\text{L}$ 与支扩严重程度增加和死亡率升高相关，与急性加重没有明确关系，这种矛盾的结果我们推测可能与肺部微生物群的差异有关。治疗层面，吸入性糖皮质激素在嗜酸性粒细胞增高的患者中可能获益，靶向 IL-5/5R、IL-4/13R α 及 IgE 的生物制剂在此类患者中显示出潜力，但多数研究未排除其他 2 型炎症性疾病的影响，针对单纯 2 型炎症性支扩的 III 期临床试验（NCT05006573）正在进行。识别 2 型炎症内型对于支扩的精准分层及靶向治疗至关重要，未来需开展前瞻性临床试验验证生物制剂的疗效，推动支扩管理精准化。

铜代谢关键基因 SCO2/PARK7 在肺结核中的表达特征及免疫浸润分析

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目的 铜是参与免疫应答、氧化还原稳态与能量代谢的必需微量元素，铜代谢维持细胞铜稳态，是铜死亡的生理基础；铜稳态失衡导致铜离子蓄积，进而触发铜死亡这一新型程序性细胞死亡，目前铜代谢及铜死亡与肺结核的关联尚不明确，本研究旨在筛选肺结核铜代谢关键基因，验证其诊断价值并探讨其在肺结核免疫微环境重塑与铜代谢紊乱中的作用，为肺结核机制研究与诊断治疗提供科学依据。

方法 从 GEO 数据库获取 GSE28623 与 GSE83456 数据集，整合铜代谢相关基因；通过差异表达分析、WGCNA、LASSO 回归筛选核心基因；收集 20 例肺结核患者与 20 例健康对照外周血，

采用 qRT-PCR 验证基因表达, 评估诊断效能、免疫浸润及药物预测。

结果 共获得 2240 个差异表达基因, WGCNA 显示 blue 模块与肺结核高度相关 ($r=0.85$); 经差异表达分析、WGCNA、铜代谢基因集三重交集筛选, 蛋白质-蛋白质相互作用 (PPI) 网络核心模块挖掘, 以及 LASSO 回归建模等多步骤严格筛选后, 最终确定 SCO2 与 PARK7 为肺结核铜代谢关键基因, 外部验证与临床样本均证实, 肺结核患者外周血中 PARK7, SCO2 显著升高, 二者 AUC 分别为 0.828、0.759, 具备良好诊断效能; 免疫浸润分析显示二者与巨噬细胞、中性粒细胞浸润及适应性免疫失衡密切相关, 药物预测获得多个靶向铜代谢与氧化应激的潜在化合物。

结论 SCO2、PARK7 是肺结核铜代谢核心标志物, 其异常表达介导铜稳态失衡与免疫紊乱, 参与肺结核病理进程, 可作为肺结核无创辅助诊断及宿主靶向治疗的潜在靶点。

CirA Allelic Variation Drives The Divergence of *Klebsiella Pneumoniae* Into Cefiderocol-Resistant and Hypervirulent Pathovars

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Objectives *Klebsiella pneumoniae* is a significant opportunistic pathogen that has evolved into distinct pathovars characterized by multidrug resistance (MDR) and hypervirulence (hv), such as the ST11-MDR and ST23-hvKp clones. Cefiderocol (FDC), a novel siderophore-conjugated cephalosporin, utilizes bacterial outer membrane siderophore receptors—such

as CirA—to gain entry into cells via a "Trojan horse" mechanism. However, the natural allelic diversity of cirA within *K. pneumoniae* populations and its role in adaptive evolution remain poorly understood

Methods We performed allelic typing of the cirA gene in 480 clinical *Klebsiella pneumoniae* isolates. The minimum inhibitory concentration (MIC) of cefiderocol was determined using the broth microdilution method, while virulence was assessed through chrome azurol S (CAS) assays and the *Galleria mellonella* larval infection model.

Results Five major cirA allelic genotypes were identified. cirA198 was strongly associated with the ST11-KL64 clone, whereas cirA1 was predominantly linked to the ST23-KL1 clone. Strains harboring cirA198 exhibited the highest FDC MIC values ($MIC_{90} = 4 \text{ mg/L}$), and all FDC-resistant isolates ($MIC \geq 8 \text{ mg/L}$) belonged to this group, concurrently carrying blaKPC, blaNDM, and blaSHV genes. Functional studies demonstrated that complementation with cirA198, compared to cirA1 or cirA16, was sufficient to reduce FDC uptake efficiency and increase MIC. In contrast, cirA1-carrying strains displayed the highest siderophore production and in vivo virulence. Introduction of cirA1 significantly enhanced iron acquisition capacity and conferred a competitive fitness advantage in vitro.

Conclusion Key amino acid polymorphisms in CirA act as molecular switches driving the divergence of *Klebsiella pneumoniae* into distinct pathogenic trajectories: cirA198 is linked to the ST11 lineage and promotes cefiderocol resistance through synergistic interactions with carbapenemases, while cirA1 defines the ST23 hypervirulent clone by augmenting iron uptake. Thus, cirA typing may serve as an effective biomarker for predicting both cefiderocol resistance and virulence potential in clinical *K. pneumoniae* isolates.

Keywords *Klebsiella pneumoniae*; cefiderocol;

antimicrobial resistance; virulence; CirA; multilocus sequence typing

同源配对多组学比较揭示临床肠杆菌科细菌头孢地尔异质性耐药的多重机制与趋同通路

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目的 头孢地尔异质性耐药临床意义重大但机制研究仍以单基因或实验室诱导株为主，缺乏对真实临床分离菌株的系统性认知。了解抗生素异质性耐药的进化策略。

方法 本研究首先从临床分离菌株中初步筛选头孢地尔耐药表型存在异质性的菌株样本，进一步通过纸片扩散法 PAP 试验进行表型确证，最终获得 4 株典型的临床头孢地尔异质性耐药菌株。针对每株目标菌株，分别分离纯化得到异质性敏感（HS）与异质性耐药（HR）成对同源亚群菌株；随后对所有 HS 与 HR 亚群菌株分别开展全基因组测序与转录组测序，获取基因组结构变异、基因序列特征及基因表达谱数据。在此基础上，整合运用比较基因组学分析、基因功能注释以及组间差异表达基因富集分析等生物信息学手段，系统筛选与头孢地尔异质性耐药表型密切相关的关键耐药基因、毒力基因及信号调控通路，深入解析菌株异质性耐药产生的分子基础与调控机制。

结果 在 4 对菌株中，分别鉴定到涉及铁摄取系统突变、 β -内酰胺酶基因扩增/高表达、细胞被膜应激调控通路激活以及新型转录调控因子的多种机制。重要的是，不同菌株的耐药进化路径迥异，但转录组分析共同指向了细胞被膜稳态与氧化应激应答通路的显著富集，提示存在潜在的趋同适应策略。

结论 本研究首次基于临床同源配对菌株描绘了头孢地尔异质性耐药的多机制图谱，揭示了其发

生的多样性、趋同性与临床相关性，为耐药诊断和治疗策略优化提供了关键理论基础。

关键词：肺炎克雷伯菌，头孢地尔，异质性耐药，抗生素耐药性，单核苷酸多态性。

病例报告:疑似发热伴血小板减少综合征相关免疫重建炎症综合征病例

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背景 山东大学齐鲁医院发现了一例发热伴血小板减少综合征（SFTS）相关的免疫重建炎症综合征（IRIS）。SFTS 是由大别班达病毒（DBV）引起的急性传染病，重症患者常伴显著的免疫抑制。而 IRIS 是免疫抑制逆转后出现的过度炎症反应，常见于 HIV 合并结核感染者，但迄今尚未见与 SFTS 相关的 IRIS 病例报道。本文首次报告一例重症 SFTS 患者在病情恢复后出现矛盾性肺部炎症加重，疑似与 IRIS 相关。

病例呈现：患者 65 岁女性农民，高血压、糖尿病及卵巢颗粒细胞瘤手术史。因发热、恶心呕吐 9 天伴意识不清 1 天入院，入院前二代测序提示 DBV 阳性，CT 示双肺炎症，(1,3)- β -D 葡聚糖显著升高提示合并肺部真菌感染。患者确诊为重症 SFTS，予伏立康唑抗真菌及对症支持治疗，发热逐渐控制，入院后第 50 天出院。出院约 80 天（即发病后约 16 周）后，患者再次出现发热、咳嗽，CT 显示肺部炎症较前扩大。经排除药物依从性差、药物副作用、中性粒细胞缺乏及其他病原体感染后，结合患者在疾病恢复期出现症状矛盾性加剧，且 GM 试验结果不支持侵袭性曲霉活动性感染，我们推测该表现为 SFTS 相关 IRIS。予泼尼松（20 mg/d）治疗后，患者症状及影像学明显改善，数月随访未复发。

结论 与意义：本病例提示重症 SFTS 患者在有效治疗后可能因免疫重建而出现过度炎症反应，

即 SFTS 相关 IRIS。该现象在临床上易被误判为感染未控制或治疗失败,从而导致不必要的抗生素使用。临床医生应认识到 SFTS 患者发生 IRIS 的可能性,并合理评估糖皮质激素的应用时机与剂量。目前尚缺乏统一的诊断标准及治疗方案,亟需进一步研究明确 SFTS 相关 IRIS 的流行病学、病理生理机制及高危因素。

Interpretable Machine Learning Incorporating The Monocyte-to-Lymphocyte Ratio for Sepsis Mortality Risk Stratification: A Retrospective Multicohort Study with External Validation

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Background Prognostic stratification in sepsis remains challenging. We evaluated the monocyte-to-lymphocyte ratio (MLR) as a potential prognostic biomarker, with a focus on its incremental value relative to established scores and its heterogeneous performance across clinical subgroups

Methods This retrospective cohort study analyzed 4,085 patients with sepsis meeting the Sepsis-3 criteria in the Medical Information Mart for Intensive Care IV (MIMIC-IV) database (2008–2019). MLR was calculated using complete blood counts at the time of initial admission to the intensive care unit (ICU). The primary outcome measures were 28-day and 90-day all-cause mortality. The relationship between MLR and sepsis patient outcomes was assessed using multivariable Cox regression and Restricted cubic splines (RCS). Fifteen machine learning (ML) algorithms were trained using Boruta-selected features. Model performance was

evaluated using Area Under the Curve (AUC), calibration, and decision curve analysis (DCA).

Results After multivariable adjustment, elevated MLR independently predicted increased 28-day (aHR = 1.95, 95% CI: 1.51–2.52) and 90-day (aHR = 1.98, 95% CI: 1.58–2.49) mortality risk (both $P < 0.001$). Trajectory analysis of patients with repeated MLR measurements within 48 hours identified three latent MLR trajectories; the persistently high trajectory was associated with increased 28-/90-day mortality after adjustment, whereas the rapidly increasing trajectory was not. In multivariable prediction, the CATBoost model achieved the highest discriminative power for both 28-day (AUC: 0.814) and 90-day mortality (AUC: 0.815) with SHapley Additive exPlanations (SHAP) analysis ranking MLR contributed meaningfully alongside key physiologic and organ-function predictors. External validation confirmed robustness (AUC: 0.748, 95% CI: 0.737–0.758).

Conclusion Admission MLR is an accessible marker independently associated with short- and longer-term mortality in sepsis. When incorporated into multivariable models and interpretable machine-learning frameworks, MLR may provide incremental prognostic information for risk stratification. These findings are observational and require prospective validation and assessment of transportability across broader clinical settings before clinical deployment.

Keywords Sepsis; Monocyte-Lymphocyte Ratio (MLR); MIMIC-IV database; Machine Learning; eICU CRD

中国金黄色葡萄球菌对磷霉素耐药的分子流行病学特征及耐药机制分析

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目的 甲氧西林耐药金黄色葡萄球菌 (Methicillin-resistant *Staphylococcus aureus*, MRSA) 是主要的多重耐药病原体之一, 可致严重的院内感染, 给临床治疗带来重大挑战。磷霉素在耐药菌感染联合治疗中具有重要地位。近年来研究发现, *pyk* 基因编码的丙酮酸激酶活性 (糖酵解途径关键酶) 可干扰细菌中心碳代谢通路, 从而调节细菌对磷霉素的敏感性。本研究旨在系统分析中国临床分离金黄色葡萄球菌对磷霉素的敏感性及其分子流行病学特征, 探究其潜在耐药机制, 为临床合理用药和耐药防控提供指导。

方法 收集全国七大地区 18 个省市、22 家医院的 1900 株金黄色葡萄球菌临床分离株。采用琼脂稀释法测定菌株对磷霉素的最低抑菌浓度 (MIC)。对其中 471 株 MRSA 分离株进行全基因组测序 (WGS) 及多位点序列分型 (MLST) 等方法分析磷霉素耐药相关的流行谱系及染色体突变, 并进一步研究 *pyk* 基因突变对磷霉素敏感性的影响。

结果 1900 株金黄色葡萄球菌临床分离株的总体磷霉素耐药率为 16.53% (314/1900), 其中 MRSA 菌株耐药率为 38.93% (297/763)。471 株 MRSA 菌株中, 院内克隆 CC5 和 CC239 谱系中磷霉素耐药率分别为 78.1% (75/96) 和 51.72% (75/96), 社区克隆 CC59 谱系的耐药率在 1.95% (3/154)。CC5 谱系中, 耐药菌株主要存在 *glpT* 基因的截短突变。CC239 谱系中, 绝大多数菌株存在 *hptA* 截短突变, 高水平耐药菌株同时伴随 *glpT* 错义突变。比较基因组学分析发现 2 株临床耐药菌株存在 *pyk* 基因截短突变, 和野生株相比在 500-505 位点存在 5 个氨基酸的缺失。基因敲除实验结果显示, LAC 菌株敲除 *pyk* 基因后, 磷霉素 MIC 值升高了 64 倍。且敲除株在 MH 平板中的生长能力受到明显抑制, 考虑与其碳源利用调整相关。

结论 我国 CC5、CC239 是磷霉素高水平耐药的优势流行克隆, 其高水平耐药性与染色体中 *glpT*、*uhpT* 等转运蛋白基因及其调控操纵子 *hptRSA* 突变

有关。值得注意的是, 编码丙酮酸激酶的 *pyk* 基因突变也可导致 MRSA 对磷霉素产生耐药, 有望为耐药菌抗感染治疗提供新的研究方向。

关键字: MRSA, 磷霉素, 分子流行病学, 丙酮酸激酶

Early Diagnosis of Superinfections in Patients with Severe Fever with Thrombocytopenia Syndrome Based on Scoring System: An Ambispective Multicentre Cohort Study

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Background Superinfection significantly contributes to mortality among patients with severe fever with thrombocytopenia syndrome (SFTS), however, early identification remains challenging because the pathogen of superinfection is often delayed

Objective This study aims to develop a clinical scoring system for the early identification of superinfection in SFTS patients.

Methods Among 1942 SFTS patients from 4 hospitals in China, a retrospective cohort (2014–2024) was used for model development, with 1182 patients from 2 hospitals split into training ($n=823$) and internal validation ($n=359$) sets, and 475 patients from 2 additional hospitals for external validation sets. Four machine learning algorithms were evaluated, with the optimal model converted into a simplified scoring scale. Finally, a prospective cohort ($n=285$, 2025) evaluated the real-world performance. Model efficacy was comprehensively assessed using AUROC, calibration curves, Decision Curve Analysis, sensitivity, and specificity.

Results Among the 36 variables, 8 predictors (age, ALB, AST, BUN, GLU, CRP, HGB, and expectoration) for superinfection were identified by ensembling five machine learning algorithms. The RF, XGBoost, LightGBM, and LR prediction models were constructed using the 8 predictors. LR demonstrated optimal performance, with an AUROC of 0.839 (95% CI: 0.797–0.880) in the internal validation set and 0.805 (95% CI: 0.764–0.847) in the external validation set. In the real-world prospective study, the model maintained high predictive efficacy (AUROC: 0.854). Finally, the model's nomogram was simplified into a novel 3-tiered risk scoring scale to enhance clinical applicability.

Conclusion Our research developed a dynamic, early diagnostic tool that could improve real-time prediction of superinfection risk at the bedside and enhance antimicrobial stewardship.

Intestinal *Aspergillus* Enrichment As A Potential Risk Factor for Invasive Pulmonary Aspergillosis in Severe Fever with Thrombocytopenia Syndrome: Insights From A Family Cluster

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Severe fever with thrombocytopenia syndrome (SFTS) is a tick-borne viral disease characterized by hemorrhagic tendencies and multi-system involvement. This study investigates a unique SFTS family cluster where two members, despite sharing identical genetic backgrounds, lifestyles, and dietary habits, experienced starkly divergent clinical outcomes with different intestinal mycobiomes. Patient 1 (the index case) presented

with high SFTS virus (SFTSV) loads across multiple specimens and succumbed to fatal invasive pulmonary aspergillosis (IPA), while Patient 2 (infected via interpersonal contact) experienced mild symptoms and recovered. Notably, the gut of Patient 1 was dominated by *Aspergillus* species (85.02% *A. flavus*), whereas Patient 2 showed a near-complete dominance of *Candida albicans* (99.56%). By leveraging this household-based comparative model to control for environmental variables, the findings suggest that intestinal *Aspergillus* enrichment is a critical driver of secondary fungal co-infection and poor prognosis. This study provides novel insights into SFTS pathogenesis and underscores the potential of intestinal mycobiome modulation as a life-saving therapeutic strategy.

Short Time To Positivity As An Early Predictor of Adverse Prognosis in Hematological Enterobacterales Bacteremia

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Background Patients with hematological malignancies complicated by bloodstream infections (BSI) face a high mortality rate, making the identification of early prognostic markers crucial. This study explores the non-linear relationship between blood culture time to positivity (TTP) and prognosis to optimize early clinical decisions

Methods We retrospectively analyzed 2,256 hematological patients with Enterobacterales BSI from 2017 to 2025. Restricted cubic splines (RCS) quantified the non-linear association between continuous TTP and

30-day mortality. A multivariable Cox prognostic nomogram was constructed by integrating TTP with clinical variables selected via LASSO regression. The integrated discrimination improvement (IDI) and net reclassification improvement (NRI) were employed to assess the incremental value of TTP in guiding clinical prognosis.

Results The overall 30-day mortality was 7.7%, with a median TTP of 9.63 hours. There was a significant non-linear relationship between TTP and 30-day mortality ($P < 0.001$), and the risk turning point demonstrated pathogen specificity (8.82 h for *Escherichia coli* and 8.59 h for *Klebsiella pneumoniae*). After incorporating non-linear TTP into the prognostic model, the validation set AUC reached 0.824, achieving a significant increase in the overall IDI (0.0255, $P = 0.024$) and continuous NRI (0.2223, $P = 0.014$). Notably, TTP integration enabled precise risk reclassification, successfully downgrading the predicted risk for 70 surviving patients (categorical NRI = 0.017, $P = 0.0176$). Conversely, the carbapenem-resistant Enterobacterales (CRE) subgroup exhibited a linear association with prognosis, with a 3-fold increase in mortality risk for every 2.42-hour reduction in TTP.

Conclusion A shorter TTP indicates a poorer prognosis for patients, although the mortality risk tends to plateau after approximately 9 hours. However, a strictly linear relationship exists between TTP and poor prognosis in CRE infections. Integrating non-linear TTP into the prognostic nomogram can effectively improve early risk reclassification and clinical stratification.

A Machine Learning-Driven Multitask Framework for Antibiotic Resistance Prediction in *Escherichia Coli*, *Klebsiella Pneu-*

moniae, and *Enterobacter Cloacae* Blood-stream Infections Among Hematological Malignancy Patients

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Background Inappropriate empirical antimicrobial therapy (IEAT) significantly increases mortality in patients with resistant Gram-negative bacteremia. We developed a multitask machine learning framework to predict carbapenem resistance (CR), β -lactam/ β -lactamase inhibitor combinations resistance (BL/BLI-R), and third-/fourth-generation cephalosporins resistance (3GC/4GC-R) in HM patients with monomicrobial BSIs caused specifically by *Escherichia coli*, *Klebsiella pneumoniae*, or *Enterobacter cloacae*.

Methods Using retrospective data from 1,353 HM patients with Enterobacterales BSIs (2017–2023), we trained support vector machines, eXtreme Gradient Boosting, and logistic regression models through 5-fold cross-validation with hyperparameter tuning and conducting internal validation via bootstrap. Model thresholds were optimized via Pareto front analysis to minimize IEAT and carbapenem use while maximizing sensitivity.

Results The models achieved AUCs of 0.81 (95% CI, 0.78 - 0.85) for CR model, 0.81 (95% CI, 0.77 - 0.84) for BL/BLI-R model, and 0.72 (95% CI, 0.68 - 0.76) for 3GC/4GC-R model before optimization. Threshold optimization improved sensitivity for CR prediction increased from 0.10 to 0.77, for BL/BLI-R prediction from 0.19 to 0.94, and for 3GC/4GC-R prediction from 0.54 to 0.98. SHAP analysis identified key predictors including prolonged neutropenia, prior carbapenem ex-

posure, and tumor consolidation stage. Integrating pathogen species enhanced 3GC/4GC-R prediction (AUC 0.72 vs. 0.76). Clinically, by employing the threshold optimization strategy, the model successfully reduced empirical carbapenem use from 71.7% to 32.1% without increasing the rate of IEAT compared to clinical practice (4.0% vs. 6.11%).

Conclusion This multitask framework supports resistance prediction in HM patients with monomicrobial BSIs due to three specific Enterobacterales species, mainly used to assist clinical decision-making after pathogen identification and strongly suspected infection with one of the three pathogens. Prospective validation is required before clinical application.

Hfc-mediated Enhancement of Plasmid Conjugation Drives The Dissemination of Carbapenem-resistant Hypervirulent *Klebsiella pneumoniae*

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The horizontal transfer of antimicrobial resistance (AMR) plasmids drives the global spread of multidrug-resistant Gram-negative pathogens. Among these, carbapenem-resistant *Klebsiella pneumoniae* (CRKP), particularly high-risk hypervirulent lineages (CR-hvKP), poses a major clinical threat due to the rapid dissemination of resistance determinants. However, the mechanisms underlying efficient plasmid transmission in these high-risk clones remain poorly understood. Here, we identify Hfc, a plasmid-encoded factor that enhances conjugative transfer in *K. pneumoniae*. Genomic epidemiological analyses revealed that hfc is widely distributed, predominantly associated with conjugative IncF-

type plasmids, highly enriched in the ST11-KL64, the predominant epidemic CR-hvKP lineage, and has increased in prevalence alongside the recent expansion of this high-risk clone. Functional studies demonstrated that deletion of hfc markedly reduced plasmid transfer efficiency, whereas its overexpression enhanced conjugation in vitro and promoted plasmid dissemination during mouse gut colonization. Mechanistically, Hfc was found to bind the plasmid origin of transfer (oriT) and is associated with increased expression of a subset of T4SS-related genes, as well as enhanced pilus-like structures and elevated intracellular ROS levels. In addition, Hfc shows potential interaction with TraC, a VirB4-like ATPase involved in T4SS assembly and activity, suggesting a possible role in modulating conjugation machinery function. Notably, Hfc imposes no detectable fitness or virulence cost on the host. Together, these findings identify Hfc as a conserved enhancer of plasmid conjugation and a potential target for limiting the spread of AMR plasmids in high-risk CR-hvKP lineages.

ANALYSIS OF ADVERSE DRUG REACTIONS AND CMV INFECTIONS DURING LETERMOVIR THERAPY: A FAERS DATABASE STUDY

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Objective Letermovir is an antiviral agent approved for CMV infection prophylaxis in transplant recipients. This study aimed to evaluate adverse drug reactions (ADRs) during letermovir treatment

Methods We aim to explore ADRs associated with letermovir treatment using FAERS database. Data from October 2017 to September 2024 were extracted from FAERS database. Disproportionality analysis was performed to detect adverse events potentially associated with letermovir. Time-to-onset analysis was conducted, logistic and cox regression were performed to identify risk factors.

Results The most frequently reported ADR was infections and infestations at SOC level, CMV infection at HLT level and CMV infection reactivation at PT level. Novel safety signals included cardiac disorder (cardiac arrest, heart failure), gastrointestinal/hepatobiliary disorder (colitis, hematochezia, hepatic failure), renal failure, various CMV-related events and transplant-related complications. The median time to onset for overall ADRs was 25 days, and 33 days for events associated with CMV infections, with both showing significantly delayed onset time for intravenous formulations compared to tablets. Older age was identified as a protective factor against CMV infections, while geographic disparities revealed increased risks in Europe and decreased risks in North America.

Conclusion Severe cardiac, hepatic and renal complications were found to be associated with letermovir. CMV breakthrough infections remain a concern, and leukemia relapse risk requires further investigations.

抗 γ -干扰素自身抗体免疫缺陷综合征患者的临床特征分析

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目的 系统比较抗 γ -干扰素自身抗体 (Anti-

Interferon- γ Autoantibodies, AIGA) 阳性与阴性患者的临床特征, 深化对抗 γ -干扰素自身抗体综合征 (Anti-Interferon- γ Autoantibodies Syndrome, AIGAs) 的认识。

方法 采用回顾性病例对照研究设计, 收集 2019 年 1 月至 2026 年 2 月于中山大学附属第三医院收治的确诊为胞内病原体感染患者, 根据 AIGA 检测结果分为阳性组 ($n=35$) 和阴性组 ($n=14$)。比较两组患者的人口学特征、临床感染特征、病原体谱及实验室指标。

结果 与 AIGA 阴性组相比, AIGA 阳性组平均年龄更高 (55.26 ± 10.72 岁 vs. 40.43 ± 18.19 岁, $P=0.003$), 播散性感染率 (94.3% vs. 35.7% , $P<0.001$)、马尔尼菲篮状菌既往感染率 (28.6% vs. 0.0% , $P=0.044$)、马尔尼菲篮状菌现存感染率 (28.6% vs. 0.0% , $P=0.044$)、非结核分枝杆菌既往感染率 (37.1% vs. 0.0% , $P=0.001$)、结核分枝杆菌既往感染率 (28.6% vs. 0.0% , $P=0.044$) 存在显著差异, 淋巴结、骨关节和肺部是最常见受累部位 (P 均 <0.05), 非结核分枝杆菌感染以脓肿分枝杆菌 (既往感染率 11.4% , 现存感染率 37.1%) 和鸟-胞内分枝杆菌复合群 (既往感染率 17.1% , 现存感染率 17.1%) 多见。实验室检查显示, 阳性组白细胞计数、中性粒细胞绝对值、C-反应蛋白、降钙素原、铁蛋白、白细胞介素-6、球蛋白、免疫球蛋白 G、纤维蛋白原浓度及 D-二聚体水平均显著高于阴性组 (P 均 <0.05), 而血红蛋白浓度和白蛋白显著偏低 (P 均 <0.05)。

结论 (1) AIGAs 患者以中年人群为主, 临床表现为播散性感染率高, 对马尔尼菲篮状菌、非结核分枝杆菌等胞内病原体高度易感, 病原体谱分析显示, 非结核分枝杆菌感染以脓肿分枝杆菌 (现存感染率 37.1%) 和鸟-胞内分枝杆菌复合群 (现存感染率 17.1%) 为主, 同时存在显著的炎症激活、体液免疫紊乱及凝血功能异常。(2) 对于 HIV 阴性人群中出现反复、播散性或混合性胞内病原体感染者, 应高度警惕 AIGAs 可能, 及时进行 AIGA 检测有助于明确病因、指导治疗并改善预后。

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16SrRNA 测序技术在评估温灸神阙穴治疗功能性腹泻患者肠道菌群变化中的价值

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本研究采用 16SrRNA 测序技术, 分析了 50 名功能性腹泻患者粪 便样本 (每组 25 名) 在治疗前后的肠道菌群变化。对照组采用传统 药物治疗 (维生素 C、复方谷氨酰胺胶囊、双歧杆菌), 治疗组在传统 药物治疗的基础上加用温灸神阙穴, 每日一次, 七天一疗程。多元统 计分析, 包括非度量多维尺度分析 (NMDS, STRESS=0.16)、主坐标 分析 (PCoA, 前两个轴解释了 92.99% 的方差) 和偏最小二乘判别分 析 (PLS-DA), 证实温灸神阙穴治疗后微生物 β 多样性发生显著变化, 形成与治疗前明显不同的聚类结构, 这主要由优势分类群丰度的改变 所驱动。属水平分析显示, 核心有益菌双歧杆菌 (21.28%) 和拟杆菌 (17.03%) 占总丰度近 40%, 而潜在致病菌链球菌属丰度骤降 71%, 拟杆菌属丰度适度下降。网络分析表明, 微生物相互作用从“复杂弥 散”模式转变为以拟杆菌科和单毛菌科为中心的集中模式。BugBase 预测显示, 温灸神阙穴治疗未显著改变总丰度, 但降低了致病风险, 同时增强了生物膜形成能力和应激耐受性。总之, 温灸神阙穴通过富 集有益菌和简化冗余相互作用, 重塑肠道菌群为高效、宿主主导的稳 态, 为阐明温灸神阙穴改善宿主健康的微生态机制提供了证据。

肠道菌群来源的烟酸激活中性粒细胞 HCAR2 增强宿主对 肺炎克雷伯氏菌感染的保护作用

唐明洋

背景 肺炎克雷伯菌 (*Klebsiella pneumoniae*, Kp) 是导致重症肺炎和系统性感染的重要机会致病菌, 但宿主如何调控抗菌防御与炎症损伤之间的平衡仍未完全阐明。羟基羧酸受体 2 (hydroxycarboxylic acid receptor 2, HCAR2) 是一种免疫代谢相关受体, 已被证实参与炎症调控, 但其在 Kp 感染中的作用及机制尚不清楚。

方法 本研究通过转录组学分析筛选 Kp 感染后小鼠肺组织中显著变化的免疫调控分子, 16s 和靶向代谢组学检测肠道菌群。并结合 Western blot 和免疫荧光验证 HCAR2 的表达变化; 同时, 在 Kp 肺炎患者临床队列中检测外周血循环中性粒细胞 HCAR2 的表达水平。进一步利用 Hcar2 敲除小鼠建立 Kp 肺炎模型, 评估其生存率、细菌负荷、肺组织病理损伤及炎症反应; 体外分离中性粒细胞, 检测其吞噬、脱颗粒、活性氧 (reactive oxygen species, ROS) 产生及杀菌能力, 并采用 HCAR2 激动剂烟酸进行干预, 探索其下游信号通路。

结果 Kp 感染显著诱导小鼠肺组织和中性粒细胞中 HCAR2 表达升高, 临床 Kp 肺炎患者外周血中性粒细胞 HCAR2 水平也明显增加。Hcar2 缺失导致小鼠感染后生存率下降, 肺组织和血液细菌负荷增加, 并伴随更严重的肺组织炎症浸润、屏障损伤和病理改变。进一步研究发现, Hcar2 缺失小鼠表现出更强的炎症反应和中性粒细胞募集, 但其细菌清除能力明显受损。体外实验表明, HCAR2 主要不影响中性粒细胞对 Kp 的吞噬过程, 而是通过促进 ROS 产生增强中性粒细胞杀菌能力; 机制上, HCAR2 激活后可促进 AKT/ERK 信号通路磷酸化, 从而增强中性粒细胞氧化杀菌反应。此外, Hcar2 KO 小鼠伴随肠道菌群失衡及丁酸、烟酸等内源性 HCAR2 配体水平下降, 而体内补充烟酸可显著促进细菌清除、减轻肺部炎症损伤并改善感染结局。

结论 本研究揭示 HCAR2 是宿主抵御 Kp 感染的重要保护性受体, 其通过激活 AKT/ERK 信号通路增强中性粒细胞 ROS 介导的杀菌功能, 从

而促进细菌清除并减轻肺组织损伤。上述结果提示,烟酸等 HCAR2 激动剂可能成为 Kp 肺炎及相关细菌性肺炎的潜在免疫辅助治疗策略。

The Deletion of Cas3 in I-E* CRISPR-Cas3 Downregulates The Expression of Eut Locus, Affects The Formation of Biofilms, and Reduces The Virulence of ST23-K1 KP-PLA

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Background The incidence of Pyogenic liver abscess (PLA) is increasing, which is a serious threat to human health. *Klebsiella pneumoniae* (KP) has become the main pathogen of PLA, but its specific mechanism is still unclear

Methods KP isolated from PLA in our hospital from 2017 to 2025 were collected in this study. The whole genome sequencing was used to analyze its molecular epidemiological characteristics, and the KP-PLA sequence on NCBI was analyzed. The role and mechanism of I-E* CRISPR-Cas3 in KP-PLA pathogenesis were further elucidated by gene knockout and complementation, mouse infection model, transcriptome sequencing and RT-qPCR.

Results A total of 104 KP-PLA strains were collected in our hospital, showing an upward trend. Globally, ST23-K1 is the main KP in PLA, and the detection trend is rising, and there are strains with high virulence and high drug resistance. The detection rate of I-E* CRISPR-Cas3 in ST23-K1 KP-PLA was very high (93.4%, 114/122). After knockout of cas3 in I-E* CRISPR-Cas3 in ST23-K1 KP-PLA, the string test became negative, the biofilm forming ability was significantly decreased, and the mortality of mice in the mouse

infection model decreased significantly, showing that the deletion of cas3 in I-E* CRISPR-Cas3 can reduce the virulence of ST23-K1 KP-PLA. The results of transcriptome sequencing technology and RT-qPCR showed that the expression level of eut locus related genes in Δ cas3 decreased significantly. In addition, after 4 mmol/mL EA (EA concentration in the intestine) was co-cultured with WT and Δ cas3 respectively, the film-forming ability of Δ cas3 and the expression level of genes related to eut locus were significantly lower than WT. It is suggested that the existence of cas3 may contribute to the utilization of EA.

Conclusion KP-PLA strains showed an upward trend. ST23-K1 has become the main pathogen of KP-PLA, which carries a variety of high virulence marker genes at the same time, which should be highly valued. The detection rate of I-E* CRISPR-Cas3 in ST23-K1 KP-PLA was very high. The deletion of cas3 in I-E* CRISPR-Cas3 in ST23-K1 KP-PLA could downregulate the expression of eut locus genes, inhibit the formation of biofilm, and ultimately lead to reduce its virulence.

非结核分枝杆菌病患者焦虑在 CD4+T 淋巴细胞和 BMI 的中介效应

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目的 分析 NTM 患者中焦虑对 CD4+T 淋巴细胞和 BMI 的中介效应, 为 NTM 病患者的治疗提供可靠依据。

方法 采用自制的一般资料调查表和焦虑自评量表对在感染科住院期间确诊非结核分枝杆菌病的 114 例患者进行问卷调查, 采集静脉血标本检测血清中 CD4+T 淋巴细胞的指标, 运用 SPSS 26.0 软件

进行统计分析,采用 SPSS 宏程序 Process 进行中介效应分析。

结果 (1)CD4+T 淋巴细胞和 BMI 呈正相关 ($r=0.343$, $p<0.01$), 焦虑和 BMI 呈负相关 ($r=-0.266$, $p<0.01$), 焦虑和 CD4+T 淋巴细胞呈负相关 ($r=-0.227$, $p<0.05$); (2) 焦虑在 NTM 病患者 CD4+T 淋巴细胞和 BMI 之间起到了中介作用, 中介效应值占总效应的 13.12%。

结论 免疫功能受损的 NTM 病患者可能通过心理应激(焦虑情绪)间接引发代谢异常(BMI 变化)。通过中介效应研究,临床医护人员可更精准地识别高风险患者,并通过心理干预,代谢管理,免疫层面等几方面实施早期干预,这种针对“免疫 - 心理 - 代谢”交互作用的综合管理模式,有望改善患者的临床结局。*基金项目:上海申康医院发展中心重大临床研究项目, Clinical Research Plan of SHDC, Grant No. SHDC2020CR2031B

Clinical Characteristics and An Admission-Time Predictive Model for Severe Scrub Typhus and Secondary HLH in Adults

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Background Scrub typhus can rapidly progress to severe disease with multi-organ dysfunction. Secondary hemophagocytic lymphohistiocytosis (HLH) is an increasingly recognized hyperinflammatory complication associated with high mortality, but adult data and simple admission-time risk tools remain limited

Methods We conducted a single-center retrospective cohort study of hospitalized adults with scrub typhus at the First Affiliated Hospital of Guangzhou Medical University (May 2013–July 2025). Severe

scrub typhus was defined by major organ involvement, shock, or in-hospital death. Variables available at admission were compared between severe and non-severe groups. Independent predictors were identified using multivariable logistic regression, and model performance was evaluated using ROC analysis. Among severe cases, HLH was identified according to standard diagnostic criteria, and clinical characteristics were compared between HLH and non-HLH patients.

Results Among 135 patients, 44 (32.6%) developed severe scrub typhus and overall in-hospital mortality was 2.2% (3/135). Lower hemoglobin (Hb) (OR 0.965, 95% CI 0.947–0.982), higher serum creatinine (SCr) (OR 1.019, 95% CI 1.008–1.029), and lower fibrinogen (FIB) (OR 0.629, 95% CI 0.435–0.909) were independent predictors of severe disease. A parsimonious three-variable model achieved good discrimination (AUC 0.843); at a cut-off probability of 0.64, sensitivity was 70% and specificity 95%. HLH occurred in 5/44 (11.4%) severe cases and was associated with substantially higher in-hospital mortality (40.0% vs. 2.6%). Compared with non-HLH severe cases, HLH patients had lower systolic blood pressure, more profound thrombocytopenia, and higher total bilirubin, blood urea nitrogen, and D-dimer levels.

Conclusion A simple admission-time triad (Hb, SCr, and FIB) provides an interpretable tool for early identification of severe scrub typhus in hospitalized adults. Scrub typhus-associated HLH, although infrequent, carried very high mortality and was characterized by severe thrombocytopenia and coagulation derangement, highlighting the need for early recognition and intensified management.

Risk Factors Associated with Severe Dengue in Hospitalized Patients: Emphasis on Host

Vulnerability and Platelet Dynamics

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Background Early prediction of severe dengue is challenging, and the role of platelet dynamics beyond counts is unclear. We investigated host vulnerability, metabolic abnormalities, hemoglobin, and platelet dynamics as factors associated with severe dengue in hospitalized patients

Methods This retrospective cohort study enrolled 592 patients with dengue (2013–2025) from a university hospital in Guangzhou. Patients were classified as severe or non-severe by WHO 2009 criteria. We extracted demographic, comorbidity, clinical, laboratory, and dynamic platelet data. Logistic regression identified factors associated with severe dengue.

Results Of 592 patients, 66 (11.1%) had severe dengue. They were older and more often had hypertension, diabetes, immunosuppression, edema, pneumonia, hematuria, hyponatremia, and serous effusion. They had lower hemoglobin and albumin, higher glucose, inflammatory markers, and hepatic/renal/coagulation dysfunction. Multivariable analysis identified hypertension, immunosuppression, lower hemoglobin, and elevated glucose as independent factors (AUC 0.827). Prolonged thrombocytopenia $<50 \times 10^9/L$ was significant in sensitivity analysis.

Conclusion Severe dengue was associated with host vulnerability, hyperglycemia, anemia, and persistent severe thrombocytopenia. Integrated clinical, metabolic, and hematological assessment may improve early risk stratification in hospitalized patients with dengue.

Intestinal Translocation of Hypervirulent *Klebsiella Pneumoniae* Via Macrophage Phagocytosis Without Compromising Mucosal Barrier Integrity

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Hypervirulent *Klebsiella pneumoniae* (hvKP) is an emerging cause of severe community-acquired infections, particularly pyogenic liver abscess. While intestinal colonization is a key risk factor, the mechanisms enabling hvKP to translocate from the gut into the bloodstream and disseminate to the liver remain poorly understood. This study focused on the mode of intestinal translocation of hvKP using a mouse model. The results showed that the hvKP strain RJF293 caused mice lethal liver abscess by gavage. In contrast, all mice infected with classic *Klebsiella pneumoniae* (*K. pneumoniae*) strain HS11286 and the isogenic virulent plasmid deficient mutant RJF293_pVD survived throughout the observation period without liver abscess. Furthermore, in vivo imaging with a bioluminescent reporter strain (RJF293-rLuc) visually confirmed the gut-to-liver ("gut-liver axis") migration of hvKP post-gavage. Notably, this translocation occurred without a corresponding increase in intestinal permeability or downregulation of intercellular tight junction protein expression. Moreover, immunofluorescence and flow cytometry revealed spatiotemporal co-localization of GFP-tagged hvKP (RJF293-rGFP) with host macrophages early in the colon (8h post-infection) and later in the liver (48h post-infection). Crucially, depletion of macrophages via clodronate liposomes prior to infection significantly attenuated bacterial loads in the liver and spleen and

markedly reduced liver abscess pathology. These findings demonstrate that hvKP translocates from the intestine to bloodstream not by disrupting the mucosal barrier, but by host macrophage phagocytosis. This work provides a novel mechanistic perspective on the high invasiveness of hvKP and highlights host phagocytes as potential therapeutic targets.

Coxiella Burnetii Vascular Graft Endovascular Infection: Diagnostic Yield of MNGS, Clinical Outcomes, and Novel Host-Pathogen Interaction

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Background Infection of vascular grafts by *Coxiella burnetii* (chronic Q fever) following Endovascular Aneurysm Repair (EVAR) is a rare but life-threatening complication. Diagnosis is frequently delayed due to non-specific symptoms and the limitations of conventional culture methods. This study elucidates the diagnostic challenges, therapeutic outcomes, and histopathological characteristics of *C. burnetii* vascular graft infections (VGE)

Methods We retrospectively analyzed 7 patients with confirmed *C. burnetii* VGE post-EVAR. Diagnostic modalities included blood culture, metagenomic Next-Generation Sequencing (mNGS) of blood and tissue/pus, CTA, and PET-CT. Therapeutic strategies (antibiotics alone vs. surgical excision) and outcomes were evaluated. Explanted grafts underwent H&E staining and Fluorescence In Situ Hybridization (FISH) to investigate pathogen distribution and host cell interaction.

Results The median latency from EVAR to

symptom onset exceeded 6 months in 85.7% (6/7) of patients. Diagnosis was significantly delayed; blood cultures were negative in all cases, and blood mNGS showed low sensitivity (28.6%). In contrast, mNGS of localized pus/tissue samples was 100% positive, including one case diagnosed via a saline lavage technique despite initial negative aspiration. High mortality (57.1%, 4/7) was observed. Deaths occurred in patients with undiagnosed preoperative infections leading to septic shock and in those treated conservatively without graft removal. Survivors (n=3) underwent complete graft excision (e.g., NAIS procedure) combined with doxycycline therapy. Hollow organ complications, particularly aorto-enteric fistulas, were prevalent. Histopathological analysis (FISH) revealed that *C. burnetii* primarily colonized the intima and intraluminal thrombus. Notably, the pathogen showed extensive colocalization with platelets (CD41) but minimal association with macrophages (CD68), suggesting a distinct mechanism of persistence shielded from phagocytosis.

Conclusion *C. burnetii* VGE requires a high index of suspicion in post-EVAR patients with fever of unknown origin. mNGS of local specimens is superior to blood testing for diagnosis. Survival relies on a combination of accurate preoperative diagnosis, prolonged antibiotic therapy, and radical surgical excision. The observed affinity of *C. burnetii* for platelets rather than macrophages warrants further investigation into the pathogenesis of chronic Q fever endovascular infections.

混合感染对儿童呼吸道合胞病毒下呼吸道感染重症影响

崔文钰

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目的 通过回顾性分析天津市儿童医院呼吸科2023年1月–2025年12月收治的1100例呼吸道合胞病毒下呼吸道感染(respiratory syncytial virus-associated lower respiratory tract infection, RSV-LRTI)病例,探讨患儿的不同混合感染类型间的差异及住院期间发展为重症风险的关系,为早期识别不同混合感染类型间RSV-LRTI患儿对重症的影响,为优化诊疗方案提供参考依据。

方法 选取天津市儿童医院呼吸科2023年1月–2025年12月收治的1100例RSV-LRTI患儿为研究对象,采用呼吸道多病原体靶向二代测序(targeted next-generation sequencing for multiple respiratory pathogens, t-NGS)、病毒抗原检测等方法,确诊为RSV感染并结合临床诊断为LRTI的患儿。再根据是否存在其他病原体混合感染进行分组,比较不同混合感染对患儿病情的影响。

结果 不同混合感染类型重症率及纤维支气管镜检查率差异有统计学意义($P<0.001$),均为RSV+支原体感染组比例最高。不同混合感染类型在氧疗率、糖皮质激素与人免疫球蛋白使用率等差异无统计学意义($P>0.05$)。胸膜增厚在不同混合感染类型间差异有统计学意义($P<0.001$),为RSV+支原体感染组最高,而RSV+其他病毒感染组最低;肺实变/浸润影、肺不张及胸腔积液在不同混合感染类型间差异有统计学意义($P<0.05$),但肺实变/浸润影两两比较校正后差异无统计学意义($P_{校正}\geq 0.05$),肺不张与胸腔积液在RSV+支原体感染组与RSV+其他病毒感染组间差异仍有统计学意义($P_{校正}<0.05$)。

结论 不同混合感染类型与重症发生、纤维支气管镜检查率及部分影像学表现存在一定关系,其中合并支原体感染组表现较为突出;但由于该亚组样本量较小,相关结果需在更大样本研究中进一步验证。

关键词: 呼吸道合胞病毒 下呼吸道感染 混合感染 儿童 重症风险

Molecular Mechanism of *Pseudomonas Aeruginosa* Outer Membrane Vesicles Delivering PQS To Induce Macrophage Immunosuppression

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Background Chronic Obstructive Pulmonary Disease (COPD) is a leading cause of death worldwide, characterized by airflow limitation and chronic inflammation. *Pseudomonas aeruginosa* (PA) frequently triggers COPD exacerbations. Macrophage polarization imbalance is a critical node in this process. Recent studies show that PA releases Outer Membrane Vesicles (OMVs). These OMVs carry virulence factors, including the quorum-sensing molecule *Pseudomonas* Quinolone Signal (PQS). PQS can reprogram macrophage metabolism and worsen immune imbalance. Aldehyde Dehydrogenase 1 Family Member A2 (ALDH1A2) is a key enzyme in retinoic acid (RA) synthesis. It activates the Retinoid X Receptor (RXR) pathway to maintain macrophage homeostasis. However, it is unclear whether PQS reprograms RA metabolism via the ALDH1A2-RA-RXR axis in COPD. This study aims to elucidate this novel PA-dominated metabo-immune pathway.

Methods We cultured THP-1 cells and differentiated them into macrophages using PMA. We used confocal imaging, flow cytometry, and Western blotting. These techniques clarified how PA-OMVs regulate M1/M2 polarization via PQS. Targeted metabolomics was used to measure RA levels. We constructed ALDH1A2 overexpression and knockdown models. This helped clarify the mechanism by which PQS up-regulates ALDH1A2 to promote RA synthesis and activate RXR signaling. Finally, we used RXR agonists and antagonists to verify the role of the RA-RXR axis in M2

polarization.

Results We isolated homogeneous PA-OMVs that significantly induced M2 polarization, evidenced by increased cytokines and surface markers. Transcriptomics revealed 205 differentially expressed genes, with ALDH1A2 showing the most significant upregulation. ALDH1A2 knockdown restored M1 markers and reduced M2 markers, confirming its essential role. Mechanistically, PA-OMVs activated the ALDH1A2-retinoic acid axis, elevating RXRA/RXR β levels; this was abrogated upon ALDH1A2 silencing. Furthermore, both PA-OMVs and purified PQS reduced CD86 while increasing CD206, IL-13, and TGF- β 1. Notably, PQS induced higher CD206 expression than OMVs. Thus, PQS is a key virulence factor driving M2 polarization via the ALDH1A2-mediated metabolic pathway.

Conclusion PQS within PA-OMVs drives COPD immune remodeling and lung injury by activating the ALDH1A2-RXR axis to induce M2 macrophage polarization.

Keywords *Pseudomonas aeruginosa*; Outer Membrane Vesicles; Macrophage Polarization; COPD; Retinoic Acid Metabolism

156 例肝脓肿患者临床特征及预后分析

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本研究为单中心回顾性分析,纳入 2020 年 1 月至 2025 年 4 月天津市人民医院收治的 156 例肝脓肿患者,系统探讨肝脓肿影像学特征(位置、大小)与基础疾病、病原学、治疗方式及预后的关联,为临床精准诊断、经验性治疗与病因推断提供循证依据。研究收集患者年龄、性别、基础疾病、病原体类型、脓肿位置与大小、治疗方案、住院时长及预后

等数据,采用 Couinaud 分段法定位脓肿,按最大径分为小(<3cm)、中(3~5cm)、大(>5cm)脓肿,运用 SPSS 软件进行描述性统计与关联性分析,以 $P<0.05$ 为差异有统计学意义。

结果显示,156 例患者中男性占比 58.33%,女性 41.67%,年龄 16~92 岁,平均年龄 63.5 ± 14.74 岁,50~70 岁中老年群体为主要发病人群;基础疾病以糖尿病最为突出,占比 48.08%,其次为胆道良性疾病、恶性肿瘤及腹腔手术史。病原学检测方面,153 例完成血培养或脓液培养,阳性率 56.9%,其中肺炎克雷伯杆菌为单一优势致病菌,占阳性培养结果的 78.16%,是肝脓肿最主要病原体。影像学特征上,肝脓肿平均直径 6.63 ± 2.77 cm,大脓肿占比 62.18%,好发于肝右叶(60.9%);左叶与右叶脓肿平均直径无显著临床差异,跨叶脓肿直径分布离散度最高,最大径达 16.5cm。关联性分析揭示关键规律:糖尿病患者脓肿 70.67% 集中于右叶,且大脓肿占比更高,右叶 + 大脓肿 + 糖尿病为最核心临床表型,占全部病例 22.4%;胆道系统疾病患者脓肿则以左叶为主(55.56%),与糖尿病组形成鲜明差异;恶性肿瘤患者大脓肿比例亦偏高,胆囊炎相关脓肿以中型为主。治疗上,所有患者均接受静脉抗菌药物治疗,60.8% 联合 CT 或超声引导下经皮穿刺引流,整体好转出院率 92.2%,死亡率 5.2%,穿刺引流与否对住院时长、预后无显著影响,引流决策主要依据脓肿大小。本研究证实,肝脓肿影像学位置、大小与基础疾病、病原体存在显著特异性关联,右叶大脓肿高度提示糖尿病,左叶脓肿需优先排查胆道疾病,该规律可作为临床快速推断病因、指导初始抗感染治疗的重要影像学线索。同时,中老年糖尿病男性为肝脓肿高危人群,抗菌药物联合穿刺引流为安全有效方案,临床应加强高危人群筛查,实现早诊早治与个体化精准诊疗。

16SrRNA 测序技术在评估温灸神阙穴治疗功能性腹泻患者肠道菌群变化中的价值

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本研究采用 16SrRNA 测序技术, 分析了 50 名功能性腹泻患者粪 便样本 (每组 25 名) 在治疗前后的肠道菌群变化。对照组采用传统 药物治疗 (维生素 C、复方谷氨酰胺胶囊、双歧杆菌), 治疗组在传统 药物治疗的基础上加用温灸神阙穴, 每日一次, 七天一疗程。多元统 计分析, 包括非度量多维尺度分析 (NMDS, STRESS=0.16)、主坐标 分析 (PCoA, 前两个轴解释了 92.99% 的方差) 和偏最小二乘判别分 析 (PLS-DA), 证实温灸神阙穴治疗后微生物 β 多样性发生显著变化, 形成与治疗前明显不同的聚类结构, 这主要由优势分类群丰度的改变 所驱动。属水平分析显示, 核心有益菌双歧杆菌 (21.28%) 和拟杆菌 (17.03%) 占总丰度近 40%, 而潜在致病菌链球菌属丰度骤降 71%, 拟杆菌属丰度适度下降。网络分析表明, 微生物相互作用从“复杂弥 散”模式转变为以拟杆菌科和单毛菌科为中心的集中模式。BugBase 预测显示, 温灸神阙穴治疗未显著改变总丰度, 但降低了致病风险, 同时增强了生物膜形成能力和应激耐受性。总之, 温灸神阙穴通过富 集有益菌和简化冗余相互作用, 重塑肠道菌群为高效、宿主主导的稳 态, 为阐明温灸神阙穴改善宿主健康的微生态机制提供了证据。

A 5-Gene Signature Linking Alistipes-Associated Host Immunity To Influenza Severity

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Background Influenza infection causes highly heterogeneous clinical outcomes, ranging from mild self-limited illness to severe respiratory failure and

death. Host immune dysregulation is a central determinant of disease progression, and growing evidence suggests that gut microbiota, particularly through the gut–lung axis, may modulate host antiviral responses. However, the molecular signatures linking gut microbial biology to influenza severity remain poorly defined. Here, we aimed to construct and validate an Alistipes-associated host gene signature for predicting influenza severity

Methods Transcriptomic data from GSE61821 were used as the discovery cohort to compare mild and non-mild influenza patients. Differential expression analysis, functional enrichment, and weighted gene co-expression network analysis (WGCNA) were performed to identify severity-associated genes and co-expression modules. Hub genes from key severity-associated modules were intersected with a curated Alistipes-related gene set to identify candidate genes, from which a composite 5-gene score was constructed. Gene set enrichment analysis (GSEA) and CIBERSORT-based immune cell deconvolution were used to characterize the underlying biology. The independent dataset GSE158592 served as an external validation cohort.

Results A total of 513 differentially expressed genes were identified between non-mild and mild influenza patients. WGCNA identified a severity-positively associated module ($r = 0.80$, $p = 2 \times 10^{-55}$) and a severity-negatively associated module ($r = -0.64$, $p = 1 \times 10^{-28}$). Intersection of module hub genes with the Alistipes-related gene set yielded five candidate genes: IL4R, PPP2CB, CAT, IKBKB, and GSK3B. The derived 5-gene score was significantly elevated in non-mild patients and demonstrated excellent discriminative performance (AUC = 0.928, 95% CI 0.895–0.961). High-score patients showed significant enrichment of interferon alpha response and heme metabolism pathways, accompanied by increased monocyte and macrophage

infiltration. External validation in GSE158592 reproduced the core pathway enrichment pattern with consistent directionality (interferon alpha response: NES = 2.75; MYC targets V1: NES = -2.47).

Conclusion We identified an *Alistipes*-associated 5-gene signature (IL4R, PPP2CB, CAT, IKBKB, GSK3B) that accurately predicts influenza severity. This signature captures an interferon-driven, monocyte/macrophage-centered inflammatory state, offering potential utility for early risk stratification and providing new mechanistic insight into gut microbiota–host immune interactions during severe influenza.

其他

Applications and Prospects of Artificial Intelligence in The Auxiliary Diagnosis of Pediatric Pulmonary Tuberculosis

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Abstract Tuberculosis (TB) is a serious disease that poses a significant threat to the health of children and adolescents, with pulmonary tuberculosis (PTB) being the most common type. Due to the lack of specificity in clinical manifestations and symptoms, early screening and diagnosis of pediatric pulmonary tuberculosis present significant challenges. In recent years, the artificial intelligence (AI) healthcare industry has emerged as a major driving force for transformation in the global healthcare sector. Through technologies such as deep learning, natural language processing, computer vision and multimodal fusion, intelligent solutions are brought to medical links such as clinical auxiliary diagnosis. The combination mode of AI with medical imaging, laboratory diagnosis, pathology examination and other data has also been gradually applied to tuberculosis screening and diagnosis. However, its development is constrained by bottlenecks such as the scarcity of high-quality data on children, insufficient interpretability of models, lack of external validation, and unclear clinical translation paths. Moreover, most of the existing related studies focus on adult pulmonary tuberculosis, and there is a lack of sufficient research and reporting on pediatric pulmonary tuberculosis. This article aims to systematically review the research and application status of AI in the auxiliary diagnosis of pediatric pulmonary tuberculosis in recent years, critically analyze

the current limitations, and explore that in the future, efforts should be made to build cross-institutional and multi-center collaborative datasets and carry out explainable AI verification centered on clinical efficacy. Explore the development path of the application of AI in the full-chain management of "prevention - diagnosis - treatment - management" of pediatric pulmonary tuberculosis.

Keywords Artificial intelligence, Tuberculosis, Pediatric pulmonary tuberculosis, Auxiliary diagnosis, Multimodal fusion

基于 91 例病例的儿童骨髓炎药学会诊回顾性分析

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目的 分析儿童骨髓炎药学会诊的病例特点, 总结治疗经验与效果, 为临床药师参与该病的治疗实践提供参考。

方法 采用回顾性分析方法, 收集 2019 年 1 月至 2024 年 12 月临床药师参与儿童骨髓炎会诊的病例资料进行回顾性分析, 对患儿会诊次数、感染部位、合并感染类型、病原微生物种类及来源、会诊目的、会诊意见采纳和效果评价以及会诊不良反应的相关信息归纳总结。

结果 共纳入 91 例骨髓炎患儿, 累计会诊 121 人次。其中 75.82% 的患儿接受 1 次会诊, 24.18% 的患儿接受 (≥ 2 次) 会诊多次。单部位骨感染 69 例 (75.82%), 多部位 (≥ 2 个) 骨感染共 22 例 (24.18%)。合并其他部位的复杂性感染患儿共 66 例 (72.53%)。病原学培养阳性共 69 例 (75.82%), 金黄色葡萄球菌是主要致病菌 (76.81%)。临床药师总会诊 121 人次, 总采纳 116 次 (95.87%), 采纳会诊意见有效 101 例 (87.07%)。会诊目的均围绕抗感染治疗展开, 排

名前三位的分别为: 抗菌药物不良反应评估及抗感染方案调整 (31.40%), 疗效不佳抗感染方案调整 (26.45%), 检出病原菌抗感染方案调整 (18.18%)。临床药师提出的会诊意见中, 排名前三位的分别为: 调整治疗药物 (56.20%), 继续当前治疗 (15.70%), 制订初始经验性治疗方案或口服序贯方案 (11.57%)。会诊患儿发生不良反应的药物以万古霉素 (17 例) 与苯唑西林 (9 例) 为主, 主要临床表现分别为皮疹与肝酶升高。

结论 临床药师与外科团队协作, 能够基于患儿具体病情个体化地制订和优化抗菌药物治疗方案, 有助于提升儿童骨髓炎的治疗水平。药师应持续关注治疗效果并加强药学监护, 以确保临床用药的合理性与安全性。

溶血型表皮葡萄球菌的微生物学特征研究

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目的 表皮葡萄球菌是人体皮肤与黏膜的正常定植菌群, 近年来其临床分离率与耐药性均显著上升, 已成为医院感染的重要病原体之一。表皮葡萄球菌以非溶血型菌株最为常见, 本研究从临床样本中成功分离出具有溶血表型的表皮葡萄球菌 (*Staphylococcus epidermidis* with hemolytic phenotype, SEHP), 并对其微生物学特征展开探讨。

方法 采用三点接种法检测溶血表型, 共纳入 5 株 SEHP 和 5 株非溶血型表皮葡萄球菌 (*S. epidermidis* with non-hemolytic phenotype, SENHP)。Microflex LT MALDI-TOF 质谱分析仪鉴定种属, 16S rRNA 序列比对构建进化树。VITEK 2 GP639 药敏卡检测 SEHP 和 SENHP 对常用抗生素的耐药谱。牛津杯法抑菌试验检测 SEHP 和 SENHP 对金黄色葡萄球菌及纹带棒杆菌的拮抗作用。微孔板法检测红细胞毒性。微孔板成膜结晶紫染色法检测生物膜形

成能力。微量培养法监测生长曲线。

结果 与 SENHP 相比, SEHP 对左氧氟沙星和莫西沙星的耐药率低, 能够拮抗金黄色葡萄球菌和纹带棒杆菌, 溶血毒性显著, 对数生长后期生长速率明显下降。

结论 SEHP 的微生物学特征有别于 SENHP, 能够拮抗金黄色葡萄球菌和纹带棒杆菌。

关键词 表皮葡萄球菌; 溶血表型; 微生物学特征; 耐药性; 拮抗作用; 生长曲线; 人红细胞毒性

万古霉素致药物性血管炎的药学监护 1 例

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目的 探讨临床药师在肿瘤术后复杂感染围术期管理中的药学监护与多学科协作模式, 以万古霉素相关血管炎这一罕见不良反应的识别与处理为切入点, 突出外科药学实践中临床药师的专业价值。

方法 回顾性分析 1 例胆管癌根治术后并发 MRSA 腹腔感染及感染性心内膜炎患者的诊疗过程。患者为 52 岁男性, 术后 12 天出现腹腔感染 (腹水培养 MRSA), 予万古霉素抗感染; 术后 17 天确诊感染性心内膜炎, 继续万古霉素治疗。临床药师全程参与围术期抗感染治疗, 包括术后早期预防、抗感染方案制定、疗效监测及不良反应管理。术后 29 天患者出现双下肢紫癜并进行性加重, 临床药师通过文献检索和诺氏评估量表, 识别为罕见的万古霉素相关血管炎, 并在多学科会诊中提出停用万古霉素、换用达托霉素的建议, 同时完善免疫学检查以排除其他病因。达托霉素治疗 8 天后患者出现泡沫尿、大量蛋白尿, 临床药师再次联合肾内科评估, 系统梳理用药史 (万古霉素暴露、达托霉素使用、阿托伐他汀联合用药), 排除达托霉素直接肾损伤可能, 判断为万古霉素相关血管炎继发肾损伤, 建议停用阿托伐他汀、启用泼尼松治疗, 并持续监测感染指

标及肾功能。

结果 停用万古霉素换用达托霉素后, 患者双下肢紫癜于 3 天内明显消退, 2 周后完全消失, 验证了临床药师对罕见不良反应的准确判断。达托霉素治疗期间出现蛋白尿后, 经临床药师干预, 蛋白尿逐步下降: 治疗第 2 周 24h 尿蛋白由 5038mg 降至 1104mg。达托霉素疗程满 2 周 (术后 43 天) 停药, 期间多次血培养阴性, 炎症指标正常, 赘生物稳定。出院后随访 3 个月, 尿蛋白完全转阴, 肾功能恢复正常。

结论 本案例中, 临床药师在外科围术期复杂感染管理中发挥了不可替代的作用: 成功识别并处理罕见的万古霉素相关血管炎, 避免误诊; 精准判断蛋白尿根源, 主导后续治疗; 作为多学科团队核心成员, 以药学专业视角推动个体化治疗。本案例充分体现了外科药学实践中医药协同的价值, 为肿瘤术后复杂感染的围术期管理提供了重要借鉴。

关键词: 外科药学; 围术期; 临床药师; 万古霉素; 血管炎; MRSA; 感染性心内膜炎; 多学科协作

基于药物治疗管理(MTM)模式的社区药学门诊服务对 2 型糖尿病患者血糖及血压水平的干预效果评价

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目的 探索以药物治疗管理 (MTM) 模式为特色的社区药学门诊服务对 2 型糖尿病患者血压和血糖的干预及效果评价。

方法 采用非随机对照研究的方法, 将研究对象分为干预组 112 例和对照组 110 例。对照组给予常规用药指导, 干预组在常规用药指导的基础上, 结合 MTM 药物治疗管理五个核心要素: 药物治疗回顾、个人用药记录、药物治疗行动计划、干预与/或转诊、文档记录与随访进行管理。通过社区药学

门诊干预及随访,每3个月随访一次,共随访4次,记录相应前后随访数据进行对照。采用重复测量方差分析和多因素线性回归分析评价方法,结合MTM药物治疗管理的社区药学门诊服务诊疗模式,对2型糖尿病患者进行血压和血糖的干预效果评价。

结果 干预组收缩压、舒张压、空腹血糖和糖化血红蛋白水平随着干预时间的增长呈现下降趋势($P<0.001$),而对照组未见显著改变($P>0.05$)。多因素线性回归分析结果显示,控制混杂因素后,社区药学门诊干预是研究对象收缩压水平($\beta=-11.467$, $P<0.001$)、舒张压水平($\beta=-4.118$, $P<0.001$)、空腹血糖水平($\beta=-1.383$, $P<0.001$)和糖化血红蛋白水平($\beta=-1.282$, $P<0.001$)的独立性保护因素。

结论 基于MTM药物治疗管理的社区药学门诊服务模式可以有效改善2型糖尿病患者空腹血糖、糖化血红蛋白和血压水平,对社区慢病管理具有重要的指导意义,为社区药学服务的模式的进一步优化提供理论依据。

Development of Multi-epitope Vaccine Against *Corynebacterium Striatum* Using Reverse Vaccinology and Immunoinformatics Approaches

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Background *Corynebacterium striatum*, an emerging multidrug-resistant opportunistic pathogen, has become an increasingly important cause of healthcare-associated infections, particularly in immunocompromised patients and individuals with prolonged hospitalization or indwelling medical devices. Its growing resistance to conventional antimicrobial agents, together with the absence of an approved vaccine, highlights the urgent need for effective preventive strategies.

This study aimed to design a multi-epitope vaccine against *C. striatum* using immunoinformatics and reverse vaccinology approaches, and to preliminarily evaluate its safety and immunogenicity in mice

Methods Conserved antigenic proteins associated with bacterial adhesion, colonization, and virulence were identified as potential vaccine targets through systematic in silico screening. From these targets, optimal T-cell and B-cell epitopes were selected and assembled into a multi-epitope vaccine construct using suitable linkers and an adjuvant sequence. The physicochemical properties, antigenicity, allergenicity, and structural features of the construct were subsequently assessed. Molecular docking and molecular dynamics (MD) analyses were performed to evaluate the interactions between the vaccine construct and key immune receptors, including Toll-like receptors (TLRs), major histocompatibility complex (MHC) molecules, and B-cell receptor (BCR). In addition, population coverage, immune simulation, codon optimization, and in silico cloning analyses were conducted. The safety and immunogenicity of the designed vaccine were further validated in a mouse model.

Results The designed vaccine construct exhibited favorable physicochemical stability, strong predicted antigenicity, and non-allergenicity. Molecular docking and MD analyses suggested stable interactions between the vaccine construct and immune receptors, supporting its potential to activate both innate and adaptive immune responses. Population coverage analysis indicated broad potential applicability across different human populations. Immune simulation predicted robust humoral and cellular immune responses. Consistent with the computational predictions, mouse experiments demonstrated that the vaccine showed a satisfactory safety profile and elicited strong immunogenicity.

Conclusion Collectively, these findings suggest that the proposed multi-epitope vaccine represents a

promising vaccine candidate against *C. striatum*. The combination of favorable in silico characteristics and preliminary in vivo evidence of safety and immunogenicity supports its further development. Additional studies are warranted to evaluate its protective efficacy and translational potential.

Keywords *Corynebacterium striatum*; multi-epitope vaccine; immunoinformatics; reverse vaccinology

Mapping The Global Landscape of Biofilm-associated Antimicrobial Resistance (1992–2025)

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Background Antimicrobial resistance (AMR) is a great global health threat, with biofilm formation recognized as a key microbial survival strategy that promotes persistence and recurrent infections. Despite growing mechanistic insights, research on biofilm-associated AMR ((biofilm-AMR)) remains fragmented, limiting the development of broadly effective interventions

Method To address this gap, we conducted a bibliometric analysis of 17,198 publications from the Web of Science Core Collection (retrieved November 4, 2025) using Bibliometrix–Biblioshiny, CiteSpace, and Excel

Results Publication output accelerated sharply after 2015, alongside diversification of research themes and increasing interdisciplinary integration. High-output countries and institutions, predominantly in Asia, Latin America, and the Middle East, emphasize natural products, nanomaterials, anti-quorum-sensing strategies, and plant-derived antimicrobials, reflecting application-

oriented approaches. In contrast, high-impact contributors in North America and Europe focus on clinical microbiology, resistance mechanisms, pathogen genomics, and hospital infection control, highlighting translational relevance. Trend analyses reveal key topics including quorum sensing, persister-cell biology, multidrug-resistant pathogens, and innovative interventions such as phage therapy, antimicrobial peptides, CRISPR-based antimicrobials, and nanotechnology-enabled drug delivery. Emerging directions include environmental AMR, One Health perspectives, and computational modeling. Despite mechanistic and technological advances, translational barriers persist due to biofilm heterogeneity and model limitations.

Conclusion Promoting interdisciplinary collaboration that integrates basic research, clinical microbiology, materials science, and computational approaches will be essential to accelerate clinical translation and develop effective, globally relevant strategies against AMR.

Keywords Antimicrobial resistance (AMR), Biofilm, Bibliometric analysis, Anti-biofilm therapeutics, Global health

Subtractive Proteomics and Immunoinformatics-guided Design of A Multi-epitope Vaccine Against *Aspergillus Fumigatus*

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Background Invasive aspergillosis (IA), a life-threatening fungal infection predominantly caused by *Aspergillus fumigatus*, has emerged as a major global health threat, particularly in immunocompromised individuals. The rising resistance of *A. fumigatus* to existing

antifungal therapies, coupled with the lack of an approved vaccine, highlights the urgent need for novel preventive strategies. This study aimed to design multi-epitope vaccines against IA using immunoinformatics approaches

Method Two highly conserved 1,3-beta-glucanase transferase proteins, essential for fungal cell wall remodeling, were identified as potential antigen targets via subtractive proteomics. From these, 15 optimal T-cell and 10 ideal B-cell epitopes were selected to develop two vaccine constructs, designated WLaf1 and WLaf2

Results Both vaccine constructs exhibited favorable physicochemical stability, antigenicity, and non-allergenicity. Molecular docking and molecular dynamics (MD) analyses suggested stable interactions between the vaccine constructs and innate immune receptors, including the TLR1–TLR2 heterodimer and TLR4, with WLaf1–TLR complexes showing relatively higher stability. Population coverage analysis indicated broad global applicability. Immune simulation analyses predicted robust humoral and cellular immune responses, with WLaf1 demonstrating predicted stronger antibody production, memory B-cell formation, and T-cell activation.

Conclusion Collectively, these computational findings suggest that both WLaf1 and WLaf2 represent potentially promising vaccine candidates against *A. fumigatus*, with WLaf1 exhibiting comparatively superior predicted performance. Further experimental and in vivo studies are required to validate the immunogenicity, safety, and protective efficacy of these vaccine candidates.

Keywords *Aspergillus fumigatus* (*A. fumigatus*); Multi-epitope vaccine; Immunoinformatics; HLA-binding; Molecular docking; Molecular dynamics (MD) simulation

Development and Validation of A Diagnostic Model for Infection at ICU Admission in Critically Ill Older Adults: A Multicenter Prospective Cohort Study

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Aim We aim to develop and validate an early diagnostic model to identify infection present on ICU admission in critically ill older adults, and to evaluate its diagnostic accuracy for clinical risk stratification

Methods We prospectively enrolled 1,011 critically ill older adults admitted to ICUs in four Chinese hospitals (May 2023–October 2024) and randomly split the cohort (7:3) into training and validation sets. In the training set, candidate diagnostic variables were selected using LASSO and multivariable logistic regression to develop a diagnostic model, presented as a static nomogram and a web-based dynamic nomogram. Diagnostic performance and clinical utility were evaluated using ROC analysis, calibration plots, and decision curve analysis. Two prespecified probability thresholds categorized patients into risk strata.

Results Among critically ill older ICU patients, 63.30% had infection present on ICU admission. Using six variables—age, Barthel Index, neutrophil percent-

age, D-dimer, IgA, and IgM—we developed a diagnostic model to facilitate individualized diagnostic probability estimates. The model demonstrated good diagnostic accuracy with robust discrimination (AUC 0.850 in the training set; 0.819 in the validation set) and satisfactory calibration ($P>0.05$), and decision curve analysis indicated a higher net benefit than treat-all or treat-none strategies across a wide range of thresholds. For diagnostic triage, two prespecified probability thresholds (57.01% and 85.28%) categorized patients into low-, intermediate-, and high-likelihood groups to support rule-out and rule-in of infection.

Conclusion Our nomogram is a simple, visual diagnostic tool for early identification of infection and diagnostic stratification in critically ill older adults, which may facilitate timely clinical decision-making and improve patient outcomes.

基于运营管理决策分析系统的“1+3”闭环合理用药模式构建与应用

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目的 基于运营管理决策分析系统的“1+3”闭环导向进一步健全合理用药管控机制,提升医院合理用药水平。

方法 引入智能管理和决策支持系统,实时监控和分析各项用药指标,通过数据可视化和智能分析,以“合理用药”为1个核心,从“选、管、用”3方面全角度帮助药师及管理者及时识别潜在问题,优化药品使用策略,确保合理用药。在选药方面,结合客观化评价分析法(the system of objectified judgement analysis, SOJA)制定信息化药品引进管理办法。在管药方面,利用质量管理工具 PDCA(plan-do-check-act)循环建立信息化合理用药管控体系。在用

药方面,利用临床药师工作站开展药学服务,实现用药精准化。同时,将这种合理用药模式运用在抗菌药物使用强度与住院次均药品费用管控上。

结果 2024 年全年抗菌药物使用强度控制在 36.42DDDs (defined daily dose system), 同比下降 0.19DDDs。2025 年上半年抗菌药物使用强度为 34.80DDDs, 同比下降 2.89DDDs。2024 年我院住院次均药品费用为 2121.38 元, 住院次均药品增幅为-13.25%; 2025 年上半年住院次均药品费用为 2085.36 元, 住院次均药品增幅为-1.70%。2024 年至 2025 年上半年, 临床药学巡诊共 1409 例, 纠正不合理用药 30 例, 发现不良反应及时上报处理 60 例。

结论 基于运营管理决策分析系统的“1+3”闭环合理用药式有助于提升医院合理用药水平, 保障患者的用药安全。

Multi-Outcome Machine Learning for Sepsis: Pathogen, Drug Sensitivity, and Complications – A MIMIC-IV Study with SHAP Analysis

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Background Sepsis is a systemic inflammatory response syndrome (SIRS) caused by infection, with etiological agents including bacteria, fungi, viruses, and parasites. Clinicians managing sepsis face three interconnected challenges: identifying probable pathogens, anticipating acute complications, and determining antibiotic susceptibility. Given the substantial limitations of prior studies, novel machine learning (ML) models are urgently needed to address these prediction tasks.

Methods We collected data of 13731 sepsis patients, and developed a multi-outcome machine learning prediction model based MIMIC-IV database. Five ML

algorithms including XGBoost (XGB), Extra Trees, Logistical Regression (LR), Multilayer Perceptron (MLP), K-Nearest Neighbors (KNN) were used to construct the model. Model prediction performance was compared using evaluation indicators such as the area under the receiver operating characteristic curve (AUC), Average Precision (AP), and F1 score. The Shapley Additive ex-Planation (SHAP) Method was used to rank the feature importance and explain the final model

Results Among the ML algorithms, the XGB had the best performance, which reached micro-AUC/AP/F1 of 0.774/0.471/0.467 for pathogen-group prediction, 0.838/0.744/0.685 for complication-family prediction, and admission-grouped binary AUC/AP/F1 of 0.825/0.929/0.874 for susceptibility prediction. SHAP analysis revealed that laboratory indices primarily drove the predictions in Tasks 1–2, whereas organism identity and antibiotic identity dominated Task 3.

Conclusion The model aids clinicians in diagnosing sepsis and offers a basis for developing personalized treatment plans for patients.

一例肺部感染合并低蛋白血症患者使用伏立康唑联用莫西沙星致幻觉的病例分析

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1 病史摘要 患者男, 77 岁, 50kg, 有糖尿病病史, 因咳嗽 5 天、加重伴发热 3 天入院。当地医院予哌拉西林他唑巴坦+莫西沙星后症状加重, 入我院查感染指标升高, 胸部 CT 示双肺感染, 肝肾功能正常, 诊断为肺部感染等。出院诊断为侵入性肺曲霉病、低蛋白血症等。

2 治疗过程 入院后予哌拉西林他唑巴坦经验

性抗感染, 肺泡灌洗液送检。次日因症状未缓解, 改莫西沙星+氟康唑+多西环素, 转老年科。第 3 天灌洗液涂片见 G+菌(++), 第 4 天 NGS 检出金黄色葡萄球菌、烟曲霉等, 调整为伏立康唑(负荷量 0.4g q12h, 维持量 0.2g q12h)+莫西沙星。第 6 天患者出现幻觉, 药师会诊考虑与伏立康唑、莫西沙星相关, 建议停用莫西沙星、伏立康唑减量至 0.15g q12h, 医生仅采纳伏立康唑减量。后续患者幻觉逐渐缓解, 第 13 天病情稳定, 改克林霉素+艾沙康唑口服出院。

3 讨论

3.1 幻觉原因分析 伏立康唑脂溶性高、易透过血脑屏障, 脑脊液浓度接近血浆 1/2, 治疗窗窄, 血药浓度过高易致幻觉; 莫西沙星也可透过血脑屏障诱发精神异常。患者无精神病史, 单用莫西沙星未出现幻觉, 加用伏立康唑后出现, 减量后幻觉缓解消失, 诺氏评估量表评分 6 分, 判定伏立康唑与幻觉“很可能”相关, 推测与血药浓度升高有关。

3.2 伏立康唑血药浓度升高的危险因素 患者存在高龄、低蛋白血症高危因素: 高龄患者肝血流量减少、肝药酶活性下降, 药物代谢减慢易蓄积; 低蛋白血症使伏立康唑游离浓度增加, 且其代谢饱和、肾排泄少, 进一步升高血药浓度。此外, 伏立康唑经 CYP2C19 等代谢, 基因多态性及自身强效肝药酶抑制作用, 也导致血药浓度个体差异大, 推测患者可能为 CYP2C19 慢代谢型。

3.3 不良反应处理 伏立康唑致中度精神症状可先减量, 严重时停药换二线抗真菌药。本例患者出现幻觉后, 经伏立康唑减量至 0.15g q12h, 症状逐渐缓解, 无需停药, 提示个体化剂量调整可管理轻中度不良反应。

4 总结 伏立康唑药动力学非线性、治疗窗窄, 个体差异大, 高龄、低蛋白血症、CYP2C19 慢代谢型患者血药浓度易升高, 诱发幻觉等不良反应。未开展血药浓度监测的医疗机构, 用药前需全面评估患者年龄、营养状况、肝功能等危险因素, 用药期间监测精神神经系统症状; 出现轻中度不良反应可先减量, 严重时立即停药并更换药物。临床药师通过全程药学监护, 及时识别、干预伏立康唑相关不良反

应,可为个体化用药提供关键支撑,保障老年患者用药安全与疗效。

中医基于“透邪扶正”理论防治甲型流行性感冒的临床策略探讨

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甲型流行性感冒由甲型流感病毒引起,具有起病急、传播快、流行范围广、变异性强及重症风险较高等特点,是临床常见的急性呼吸道传染病之一。中医学多将其归属于“温疫病”或“时行感冒”范畴,认为其病因为疫疠之气侵袭,核心病机在于疫毒犯肺、郁而化热,并与机体正气盛衰密切相关。基于甲流的病原学特点、临床演变规律及中医温病理论,本文从“疫毒致病”与“正虚易感”两个层面系统梳理甲流的中医病机,认为“疫毒郁热为本,正气亏虚为要”,并据此提出以“透邪扶正”为核心的临床防治思路。所谓“透邪”,重在宣肺达表、疏风清热、解毒利咽、疏利气机及通腑泄热,使疫邪有门而出,防止邪闭化热、由表入里;所谓“扶正”,重在顾护气阴、调和营卫、培护脾肺、兼顾肾本,以减少邪恋正伤、病后迁延及反复发作。文章进一步结合甲流常见病程阶段,对邪犯肺卫、毒热壅盛、少阳枢机不利及恢复期气阴两伤等证候特点进行归纳,提出相应治法与方药加减思路:初期宜疏风清热、宣肺透邪,以截断病势;热毒炽盛阶段宜清热解毒、宣肺通腑,以阻断由轻转重;少阳不和者宜和解少阳、透邪达表,避免误汗误下;恢复期则宜益气养阴、清透余邪,以促进肺胃功能恢复并减少迁延性咳嗽、乏力等后遗症。与此同时,针对孕妇、老年人及合并基础疾病患者等特殊人群,强调应在辨证基础上兼顾体质、年龄、病位深浅及基础病状态,落实因人、因时、因地制宜。中西医结合是提升甲流救治效果的重要路径,现代医学在病原学诊断、抗病毒治疗、呼吸支持及

器官功能监测方面具有优势,而中医药可在早期干预、症状缓解、病势截断、重症辅助治疗及恢复期调养中发挥整体调节作用。总体而言,“透邪扶正”能够较好概括甲流从发病、传变到恢复全过程的中医治疗原则,对提高临床疗效、减少并发症及促进康复具有一定指导意义。

念珠菌血症临床特点及死亡相关危险因素分析

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目的 分析念珠菌血症(candidemia)的相关临床特点及危险因素,为念珠菌血症临床诊疗提供参考依据。

方法 回顾性分析 2021 年 1 月~2023 年 12 月广东省人民医院确诊的 169 例念珠菌血症患者的临床资料,根据血培养初次报阳 28 d 的患者预后分为存活组(81 例)与死亡组(88 例),对比两组病原体分布情况、抗真菌药敏结果和临床特点,采用单因素分析和二元 Logistic 回归分析其死亡危险因素。

结果 患者主要分布于重症监护病房(70.41%),死亡率达 52.07%,感染菌种主要由白念珠菌(38.46%),近平滑念珠菌(27.22%)、光滑念珠菌(15.98%)和热带念珠菌(15.98%)构成,其中非白念珠菌占 61.54%。不同菌种报阳时间存在差异,热带念珠菌报阳中位时间最短(18.73 h),近平滑念珠菌(38.34 h)和光滑念珠菌(37.15 h)最长($P<0.0001$)。白念珠菌、热带念珠菌和近平滑念珠菌对氟康唑和伏立康唑均表现出不同程度的耐药性,特别是热带念珠菌对氟康唑和伏立康唑耐药率达 33.33%和 37.04%。单因素分析显示年龄、冠心病、呼吸系统疾病、合并细菌血流感染、脓毒性休克、APACHE II 评分、中心静脉插管、机械通气、糖皮质激素使用、CRP 值、PCT 值、IL-6 值与死亡率有

关 ($P<0.05$)。二元 Logistic 回归分析显示合并细菌感染 ($OR=11.268$ 、95%CI: 1.069-118.766、 $P<0.05$) 和糖皮质激素使用 ($OR=5.498$ 、95%CI: 1.263-23.935、 $P<0.05$) 是其 28 d 预后的独立危险因素。

结论 念珠菌血症患者感染重, 预后差, 以非白念珠菌为主, 且对氟康唑和伏立康唑均表现出不同程度的耐药, 合并细菌血流感染和糖皮质激素使用是其 28 d 预后的独立危险因素。对此, 临床应针对危险因素积极监测和重点干预, 及时掌握念珠菌耐药性变化。

关键词: 念珠菌血症; 病原菌分布; 抗真菌药物敏感性结果; 危险因素

艰难梭菌感染复发的多维机制

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艰难梭菌感染(*Clostridioides difficile* infection, CDI) 是抗生素相关性腹泻的主要病因, 初次感染后约有 25%至 35%的患者会复发。一旦出现首次复发, 再次复发的风险将急剧升至 45%至 65%, 导致病死率和医疗负担显著加重。复发性艰难梭菌感染(rCDI) 的棘手之处在于, 其背后并非单纯的细菌耐药, 而是病原体滞留、宿主免疫抑制、肠道菌群定植抗性崩溃及代谢环境紊乱共同作用的结果。病原层面上, 艰难梭菌利用胞外多糖与 eDNA 构建的生物膜充当了“庇护所”, 保护芽孢和滞留菌免受抗生素打击, 停药后芽孢萌发直接启动新一轮感染。免疫层面上, 毒素 B 通过干扰生发中心的正常迁移路径并抑制 T 滤泡辅助细胞功能, 阻碍了保护性抗体与免疫记忆的形成。微生态层面上, 广谱抗生素清除了产丁酸菌和次级胆汁酸转化菌等关键功能菌, 定植抵抗防

线随之瓦解。代谢层面上, 胆汁酸失衡偏向促芽孢萌发状态, 而丁酸产量不足则进一步削弱了肠上皮防御。本文结合国内外最新研究成果, 从生物膜与芽孢形成、毒素 B 介导的免疫损伤、肠道定植抵抗破坏、胆汁酸与短链脂肪酸代谢异常四个方面阐述 rCDI 的发病机制, 分析当前研究存在的局限性, 为临床 rCDI 的防控与靶向治疗提供理论依据。

关键词: 艰难梭菌; 感染复发; 生物膜; 免疫记忆; 肠道菌群; 胆汁酸代谢

儿童医疗保健相关脑膜炎(HCAVM)病原学及其临床特点分析

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目的 对儿童 HCAVM 病原学、耐药特征及临床表现回顾性分析, 为临床早期识别、精准治疗和预后评估提供循证医学依据。

方法 选取我院具有神经外科术/操作且符合 HCAVM 的 102 例脑膜炎患儿为研究对象, 采用描述性统计方法对病原学分布、耐药特征及临床特征进行系统分析。

结果

1. 年龄分布为新生儿期至青少年期 (1 天-17 岁)。平均年龄为 3.89 岁, 中位年龄 2.0 岁, 婴幼儿 (<3 岁) 占比达 58.8%。

2. 脑脊液分离培养出 105 株病原菌 (27 种), 革兰阳性菌占主导 72.4%, 高于革兰阴性菌 27.6% ($P<0.05$)。主要致病菌 (检出 ≥ 3 株) 依次为: 表皮葡萄球菌 41.9%、鲍曼不动杆菌 9.5%、肺炎链球菌 7.6%及大肠埃希菌 6.7%、金黄色葡萄球菌 5.7%、屎肠球菌 2.7%和缓症链球菌 2.7%。

3. 革兰氏阳性菌均对万古霉素、利奈唑胺、替考拉宁敏感; 葡萄球菌属对青霉素、阿莫西林克拉维酸钾、苯唑西林耐药率均 $>65\%$; 肠球菌属对青霉素

耐药率为 60%，对氨苄西林的耐药率为 20%；肺炎链球菌对青霉素耐药率为 60%，对头孢曲松、美罗培南耐药率均为 25%。

4. 鲍曼不动杆菌对阿莫西林克拉维酸钾、氨苄西林的耐药率均为 100%，对氨苄西林/舒巴坦的耐药率为 40%，对三代头孢菌素（头孢曲松、头孢噻肟、头孢他啶）耐药率分别为 20%、75%、30%，对四代头孢（头孢吡肟）的耐药率为 30%，对头孢哌酮舒巴坦和美罗培南的耐药率分别为 25%、12.5%。大肠杆菌对氨苄西林的耐药率、头孢曲松、头孢噻肟的耐药率较高(66.7%~100%)，对头孢吡肟、头孢哌酮舒巴坦、美罗培南耐药率分别为 25%、14.3%、14.3%。

5. 发热为主要症状，其他常见症状为恶心及呕吐、意识状态改变、头痛、惊厥发作以及颈项强直。

结论

1. 儿童 HCAVM 可发生于各个年龄段，但以婴幼儿更为常见。

2. 儿童 HCAVM 的病原以革兰氏阳性菌占主导地位，病原依次为表皮葡萄球菌、肺炎链球菌、金黄色葡萄球菌；革兰氏阴性菌中最常见的病原主要为鲍曼不动杆菌和大肠杆菌。

3. 革兰阳性菌对青霉素耐药严重，对糖肽类（万古霉素、替考拉宁）和噁唑烷酮类（利奈唑胺）100%敏感；革兰阴性菌对美罗培南和头孢哌酮舒巴坦保持较好敏感性。

4. HCAVM 临床表现无特异性，因有基础疾病及外科手术史，治疗难度大、预后较差。

关键词：HCAVM 耐药 病原 临床

肛周坏死性筋膜炎继发脓毒性休克 1 例

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肛周坏死性筋膜炎（perianal necrotizing fasciitis, PNF）是一种罕见、进展迅速且致死率较高的严重软组织感染。早期诊断困难，病情凶险，若治疗不及时可导致预后不良 [1]。PNF 是坏死性筋膜炎在肛周-会阴三角区的特殊类型，全球患病率约 0.4/10 万，肛周区域发病率约 1.6~3.3/10 万。尽管发病率较低，但其致死率可达 25%~35%[2-3]，该病多见于男性，平均发病年龄为 50~60 岁，男女比例可达 10:1[4]。常为需氧菌和厌氧菌的混合感染（I 型），常见病原体包括大肠埃希菌、链球菌、葡萄球菌、克雷伯菌、拟杆菌和梭状芽孢杆菌等[2]。糖尿病、恶性肿瘤、免疫抑制、酒精依赖和肥胖等合并症为主要的危险因素[1,4]。该病早期临床表现缺乏特异性[2]，易与肛周蜂窝织炎或肛周脓肿混淆，因感染早期主要沿筋膜平面进展而浅表皮肤未受累，常导致误诊或延误诊断。若未能及时识别和治疗，病情可在数小时内急剧恶化，进展为脓毒性休克甚至多器官功能衰竭[3]。因此，早期诊断和及时干预是治疗的关键，治疗核心包括感染源有效控制与抗菌药物及时应用。现就一例肛周坏死性筋膜炎继发脓毒性休克的抗感染治疗分析如下，以期临床诊疗提供借鉴与参考。

替加环素致胆汁淤积型药物性肝损伤 1 例

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目的 分析 1 例急性重症胰腺炎患者使用替加环素后发生胆汁淤积型药物性肝损伤（DILI）的临床特征、诊断思路及治疗转归，为临床安全用药提供参考。

方法 回顾性分析 1 例 57 岁男性急性重症胰腺炎患者的临床资料。患者因多重耐药鲍曼不动杆菌感染接受替加环素（首剂 100 mg，后 50 mg q12h）联合氨苄西林舒巴坦（3 g q6h）抗感染治疗。遵循

中国药物性肝损伤诊治指南及亚太肝病学会 DILI 共识指南及 RUCAM 量表因果关系评估进行系统分析,并复习相关文献。

结果 患者于替加环素用药后出现肝功能急剧恶化, R 值计算 ($R \approx 0.0.6$) 判定为胆汁淤积型肝损伤。经系统排查患者原发病相关因素后,采用 RUCAM 量表进行量化评估,总分 7 分,因果关系为“很可能”。停用替加环素,调整抗感染方案,同时予保肝治疗后患者肝功能显著改善,感染得到有效控制,患者顺利出院。

结论 替加环素可导致严重的胆汁淤积型药物性肝损伤,潜伏期多为 4~12 d,长疗程 (>14 d)、高龄 (>55 岁)及联用多种肝毒性药物是独立危险因素。临床使用替加环素时应遵循指南建议加强肝功能监测,胆汁淤积型肝损伤,应高度警惕为替加环素所致,及时停用可疑药物并启动针对性保肝治疗。临床药师应在用药前评估、用药中监测、损伤识别与干预、替代方案制定及出院后随访等环节发挥关键作用,以保障患者用药安全。

支气管动脉栓塞术后脊髓动脉梗死 1 例

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脊髓梗死是支气管动脉栓塞术后一种罕见却严重的并发症。该病起病隐匿,预测与预防难度大,且缺乏标准治疗方案,病死率和致残率极高。本文报道一例广泛耐药肺结核伴大咯血患者,在接受支气管动脉栓塞术后相继发生脊髓梗死及肺栓塞,旨在提高临床医生对该并发症的警惕性和识别能力,并为后续诊治提供循证参考。本病例为我们提供了重要临床启示:1.术前评估至关重要:对于存在糖尿病、血管病变等基础疾病的患者,应详细评估血管解剖及侧支循环情况。建议术前行 CTA 或 DSA 明确 Adamkiewicz 动脉的位置及与支气管动脉的关系

[13-15]。术中技术优化:采用超选择性插管技术,间断造影监测栓塞剂流向,密切观察患者下肢运动感觉功能变化[16]。一旦出现神经症状,立即停止操作。术后密切监护:BAE 术后应常规监测神经功能至少 24 小时[17],以便早期发现缺血事件。一旦确诊脊髓梗死,需 MDT 团队协作,在权衡出血与缺血风险的前提下个体化选择治疗方案。综上所述,BAE 虽是治疗大咯血的有效手段[18],但须警惕脊髓梗死这一严重并发症。术前精细评估、术中精细操作及术后严密监护是预防这一灾难性事件的关键。未来需进一步探索脊髓梗死的早期诊断标志物及安全有效的再通治疗策略。

Animal Study on The Role of The Type VI Secretion System of *Klebsiella Pneumoniae* in Promoting Sepsis Progression

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Objective To investigate the role of the type VI secretion system (T6SS) of *Klebsiella pneumoniae* in the development and progression of sepsis, and to determine whether it serves as an important virulence factor that aggravates sepsis.

Methods An hcp-deficient strain was constructed from a standard *Klebsiella pneumoniae* strain using the CRISPR/Cas9 system. Mice were gavaged with the T6SS-positive strain, the T6SS-deficient strain, or normal saline to establish intestinal colonization models. On this basis, a sequential sepsis model was induced by intraperitoneal injection of lipopolysaccharide (LPS). Seven-day survival was recorded. Serum levels of IL-6, IL-1 β , and TNF- α were measured, and intestinal pathological injury was evaluated by hematoxylin-eosin (HE) and periodic acid-Schiff (PAS) staining to

assess the effect of T6SS on sepsis phenotypes.

Results The hcp-deficient strain was successfully generated, and a stable intestinal colonization–sequential sepsis mouse model was established. Compared with the T6SS-deficient group and the control group, mice colonized with the T6SS-positive strain showed significantly reduced survival, indicating more severe disease. Serum inflammatory cytokine analysis demonstrated markedly increased levels of IL-6, IL-1 β , and TNF- α in the T6SS-positive group, suggesting an enhanced systemic inflammatory response. Histopathological examination further showed more severe intestinal mucosal injury in the T6SS-positive group, characterized by greater villus damage, increased inflammatory cell infiltration, and aggravated tissue injury. These findings indicate that T6SS significantly enhances host inflammatory responses and exacerbates sepsis-associated intestinal injury.

Conclusion The T6SS of *Klebsiella pneumoniae* promotes sepsis progression by aggravating inflammatory responses, intestinal tissue injury, and mortality in mice, suggesting that it is an important virulence factor contributing to sepsis deterioration. These findings provide experimental evidence for the role of intestinally colonizing *Klebsiella pneumoniae* in sepsis progression and support further investigation of T6SS-targeted interventions.

Keywords *Klebsiella pneumoniae*; type VI secretion system; sepsis; intestinal colonization; virulence factor

Preliminary Study on T6SS-Mediated Gut Microbiota Remodeling and Arginine Metabolic Disturbance in Septic Mice Colonized With *Klebsiella Pneumoniae*

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Objective To investigate whether the type VI secretion system (T6SS) of *Klebsiella pneumoniae* is involved in gut microbiota remodeling and arginine metabolic disturbance during sepsis, and to explore its potential relationship with disease progression.

Methods Based on an established intestinal colonization–sequential sepsis mouse model, three groups were included: a T6SS-positive strain group, a T6SS-deficient strain group, and a control group. Intestinal contents were collected for 16S rRNA gene sequencing to analyze α -diversity, β -diversity, and microbial composition. Untargeted metabolomics based on LC-MS/MS was performed to identify differential metabolites, followed by KEGG pathway enrichment analysis, with particular focus on the arginine biosynthesis pathway and its key intermediate metabolites.

Results 16S rRNA sequencing showed that, compared with the T6SS-deficient group and the control group, the T6SS-positive group exhibited marked alterations in gut microbial composition, reduced α -diversity, and clear separation in principal coordinates analysis (PCoA), indicating that T6SS significantly disrupted intestinal microbial homeostasis. Untargeted metabolomic analysis identified multiple differential metabolites, and KEGG enrichment analysis revealed significant enrichment of the arginine biosynthesis pathway. Further analysis showed that α -ketoglutarate, N-acetylglutamate, argininosuccinate, and L-glutamate were generally decreased in the T6SS-positive group, whereas L-glutamine showed an increasing trend, suggesting disturbance of arginine metabolic homeostasis. These findings indicate that T6SS not only affects the gut microbial structure but may also participate in sepsis-related pathological processes through modulation of key metabolic pathways.

Conclusion The T6SS of *Klebsiella pneumoniae* is closely associated with gut microbiota remodeling and arginine metabolic disturbance in septic mice, suggesting that it may contribute to disease progression through a “microbiota dysbiosis–metabolic disorder” axis. This study provides preliminary evidence for further investigation into how intestinally colonizing *Klebsiella pneumoniae* affects host metabolism and immune responses.

Keywords *Klebsiella pneumoniae*; type VI secretion system; gut microbiota; arginine metabolism; sepsis

植物源抗菌活性成分的多靶点机制与耐药逆转潜力研究进展

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抗生素滥用导致的细菌耐药性危机日益严峻，开发新型抗菌策略刻不容缓。植物次级代谢物作为天然产物的重要来源，以其多靶点、低耐药诱导性等优势，为新型抗菌药物研发提供了广阔前景。本文系统综述了小檗碱、槲皮素、山奈酚、丁香酚及绿原酸等四类典型植物活性成分的抗菌作用机制与耐药逆转潜力。这些成分通过多重途径发挥抗菌效应：破坏细菌细胞膜与细胞壁完整性、干扰核酸及蛋白质合成、诱导氧化应激、抑制毒力因子表达、瓦解生物膜结构、阻断群体感应系统，以及抑制外排泵和钝化酶活性。特别值得关注的是，它们作为抗生素佐剂，与β-内酰胺类、氨基糖苷类、万古霉素等联用时表现出显著的协同增效作用，能有效恢复多重耐药菌（如耐甲氧西林金黄色葡萄球菌、铜绿假单胞菌、肺炎克雷伯菌等）对现有抗生素的敏感性，展现出逆转细菌耐药的巨大潜力。然而，多数植物活性成分存在水溶性差、生物利用度低、稳定性不足

等成药性缺陷。纳米递送系统、多种天然产物的协同组合及与免疫调节剂的联合应用，有望突破上述瓶颈，推动植物源抗菌药物从实验室走向临床。综上所述，植物源抗菌活性成分凭借其多靶点、多层次的独特作用机制，在开发新型抗感染药物和解决临床耐药难题方面具有重要的研究价值和广阔的应用前景，未来应着力于机制深化、标准化体系构建及临床转化研究

基于 Logistic 回归与机器学习模型预测肺炎克雷伯菌患者 *rmpA2* 和 *iucA* 基因阳性携带的比较研究

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目的 探讨肺炎克雷伯菌感染（KP）患者菌株携带高毒力相关基因（*rmpA2* 和 *iucA*）的危险因素，比较传统 Logistic 回归与多种机器学习算法在该风险预测中的效能，并构建可视化的临床预测工具。

方法 收集 225 例 KP 感染患者的临床资料及分离菌株，菌株进行聚合酶链式反应（PCR），以 PCR 检测结果为依据，将携带 *rmpA2* 和 *iucA* 基因的患者设为阳性组，未携带者设为阴性组。首先采用 SPSS 软件进行单因素及多因素 Logistic 回归分析，筛选出与基因阳性独立相关的危险因素。随后，基于筛选出的有意义变量，按照 7:3 的比例将数据随机分为训练集与验证集。分别构建逻辑回归（LR）、K 近邻（KNN）、极限梯度提升（XGBoost）、随机森林（RF）及支持向量机（SVM）五种预测模型，通过受试者工作特征曲线下面积（AUC）评估并筛选最佳效能模型。同时，基于多因素 Logistic 回归结果构建列线图（Nomogram），并通过校准曲线和决策曲线分析（DCA）评估其校准度与临床净获益。

结果 单因素及多因素分析显示，拉丝实验阳

性、BMI 及 ALT 值等是 *ompA2/iucA* 基因阳性的独立危险因素 ($P<0.05$)。在五种预测模型中, XGBoost 模型表现最佳, 其在验证集中的 AUC 值为 0.708, 优于传统 Logistic 回归模型 ($AUC=0.655$) 及其他机器学习模型。基于 Logistic 回归构建的列线图模型显示出良好的校准能力, 决策曲线分析表明其在合理的阈值概率范围内能够提供临床净收益。

结论 XGBoost 机器学习模型对 KP 菌携带 *ompA2* 和 *iucA* 毒力基因具有较高的预测效能, 优于传统回归模型。基于 Logistic 回归构建的列线图虽预测效能略低于 XGBoost, 但具有良好的可视化能力和临床适用性, 有助于临床医生早期、直观地评估高毒力 KP 感染风险, 为指导经验性抗感染治疗提供决策依据。

关键词: 肺炎克雷伯菌; 机器学习; PCR

重症肺炎后康复期肺功能及运动耐力恢复的临床分析

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目的 比较不同病原体所致重症肺炎患者在康复期肺功能及运动耐力的恢复情况, 分析影响康复结局的病原体相关因素。

方法 回顾性收集 2022 年 1 月至 2026 年 2 月于宁夏医科大学总医院出院的 150 例重症肺炎患者资料, 根据病原体分为细菌组 (52 例)、病毒组 (58 例)、真菌组 (40 例)。出院后均接受标准肺康复指导, 分别于出院时、出院后 1、3、6 个月评估肺功能 ($FEV1\%$ 预计值、FVC、DLCO)、6 分钟步行距离 (6MWD) 及 SGRQ 评分, 分析影响 6 个月肺功能恢复不良 ($FEV1\%<80\%$) 的危险因素。

结果 出院时三组肺功能及 6MWD 无显著差异 ($P>0.05$)。出院后 1 个月, 病毒组 $FEV1\%$ (65.4 ± 8.2) 及 6MWD (385 ± 42 m) 显著低于细菌组 (72.1 ± 7.6 ,

420 ± 38 m) 和真菌组 (62.3 ± 9.0 , 360 ± 45 m) ($P<0.05$)。出院后 3 个月, 病毒组恢复加快 (78.5 ± 7.2), 与细菌组 (82.3 ± 6.8) 差异无统计学意义, 但真菌组 (71.2 ± 8.5) 仍显著低于前两组 ($P<0.01$)。出院后 6 个月, 细菌组 $FEV1\%$ (88.6 ± 5.4) 基本正常; 病毒组 $FEV1\%$ (85.1 ± 6.3)、DLCO% (78.6 ± 7.5) 仍略低于细菌组 ($P<0.05$); 真菌组恢复最差, $FEV1\%$ (75.4 ± 8.2)、DLCO% (65.8 ± 9.1) 及 6MWD (412 ± 38 m) 均显著低于细菌组及病毒组 ($P<0.01$)。SGRQ 总分真菌组 (42.5 ± 10.3) 高于细菌组 (24.6 ± 7.2) 和病毒组 (30.1 ± 8.5) ($P<0.01$)。多因素分析显示, 真菌感染 ($OR=4.85$, 95%CI: 1.92~12.26)、年龄 ≥ 65 岁 ($OR=2.98$, 95%CI: 1.23~7.21)、机械通气 ≥ 7 天 ($OR=3.45$, 95%CI: 1.45~8.22) 及入院时低白蛋白血症 ($OR=2.67$, 95%CI: 1.08~6.59) 是 6 个月肺功能恢复不良的独立危险因素 (P 均 <0.05)。

结论 重症肺炎后康复期肺功能恢复因病原体而异: 细菌性肺炎预后最佳, 病毒性肺炎中期恢复快但弥散功能改善慢, 真菌性肺炎恢复最差、持续肺损害。真菌感染、高龄、长时间机械通气及低白蛋白血症是康复不良的独立危险因素, 应针对病原体制定个体化康复方案, 对高危人群加强长期随访。

重症肺炎后康复期患者诱导痰操作的安全性及影响因素分析

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目的 评估重症肺炎康复期患者行高渗盐水诱导痰的安全性及影响耐受性的因素。

方法 前瞻性纳入 40 例重症肺炎康复期患者 (出院 2~4 周)。均予 3% 高渗盐水雾化诱导痰, 雾化前吸入沙丁胺醇 200 μ g。记录操作中及操作后 30 分钟内不良反应 (咳嗽加重、胸闷、血氧下降、支气管痉挛、操作中断)。根据耐受性分为耐受良好组 (无

或轻微不良反应)和耐受不良组(中重度不良反应致中断或需药物干预),采用 Logistic 回归分析危险因素。

结果 40 例中,男性 24 例(60.0%),平均年龄(56.8 ± 12.4)岁。原发病:细菌性肺炎 25 例,病毒性 15 例。操作成功率 100%。不良反应:咳嗽加重 18 例(45.0%),其中轻度 12 例、中度 6 例;胸闷 10 例(25.0%);血氧下降 5 例(12.5%);支气管痉挛 2 例(5.0%);操作中中断 4 例(10.0%);需药物干预 6 例(15.0%)。无严重不良事件。耐受良好组 28 例(70.0%),耐受不良组 12 例(30.0%)。单因素分析显示,年龄 ≥ 65 岁、基础哮喘/COPD 病史、出院时 FEV1% $< 70\%$ 、雾化前咳嗽 VAS ≥ 4 分、病毒性肺炎与耐受不良相关($P < 0.05$)。多因素回归证实,基础哮喘/COPD 病史($OR = 4.68$, 95%CI: 1.32~16.58)和出院时 FEV1% $< 70\%$ ($OR = 3.95$, 95%CI: 1.15~13.56)是独立危险因素($P < 0.05$)。耐受不良组中 6 例(50.0%)需提前终止雾化或使用急救药物,经吸氧及支气管扩张剂后均缓解。

结论 重症肺炎康复期行高渗盐水诱导痰总体安全,约 30%出现中重度不良反应。基础哮喘/COPD 病史及出院时 FEV1% $< 70\%$ 是耐受不良的独立危险因素。建议高危患者雾化前常规使用支气管扩张剂,操作中密切监测。

IL-6、CRP 与 D-二聚体对流感病毒肺炎患者 6 个月功能恢复的预测价值:一项回顾性预后队列研究

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关键词: 流感病毒肺炎, 功能恢复, 生物标志物

背景 流感病毒肺炎是成人重症呼吸道感染的重要类型。除急性期呼吸衰竭和病死风险外,部分

患者出院后仍存在运动耐力下降、乏力等长期功能受损,影响生活质量。持续炎症激活及凝血功能异常可能参与肺组织修复延迟和功能恢复不全。IL-6、CRP 及 D-二聚体与流感肺炎急性期严重程度相关,但其对远期功能恢复的预测价值尚缺乏临床证据。

目的 探讨出院时血清白细胞介素-6(IL-6)、C 反应蛋白(CRP)及 D-二聚体水平对流感病毒肺炎患者发病后 6 个月功能恢复状态的预测价值。

方法 采用单中心回顾性队列研究,纳入 2022 年 1 月至 2025 年 6 月宁夏医科大学总医院经病原学证实的 80 例成人流感病毒肺炎患者。以发病后 6 个月时的 6 分钟步行距离(6MWD)实测值占预测值百分比评估功能恢复,并按中位数分为恢复较差组与恢复较好组(各 40 例)。回顾性检测患者出院时血清 IL-6、CRP 及 D-二聚体水平。采用 Mann-Whitney U 检验比较组间差异,将有统计学意义的指标纳入多因素 Logistic 回归模型校正混杂因素,并绘制 ROC 曲线评估预测效能。

结果 共 80 例患者纳入分析。与恢复较好组相比,恢复较差组出院时 IL-6[11.8(8.6, 16.9) pg/mL 比 6.9(5.1, 9.8) pg/mL, $P < 0.001$]及 D-二聚体[0.96(0.64, 1.41) mg/L 比 0.48(0.31, 0.77) mg/L, $P < 0.001$]水平均明显升高,而 CRP 差异无统计学意义[7.4(4.1, 12.6) mg/L 比 5.8(3.2, 9.5) mg/L, $P = 0.119$]。多因素 Logistic 回归分析显示,IL-6($OR = 1.21$, 95%CI 1.08~1.37, $P = 0.002$)和 D-二聚体($OR = 2.64$, 95%CI 1.32~5.29, $P = 0.006$)均为 6 个月功能恢复较差的独立相关因素。ROC 曲线分析显示,IL-6、D-二聚体及二者联合模型预测 6 个月功能恢复较差的 AUC 分别为 0.78(95%CI 0.68~0.88)、0.74(95%CI 0.63~0.85)和 0.84(95%CI 0.75~0.92),联合模型预测效能优于单项指标。

结论 流感病毒肺炎患者出院时血清 IL-6 和 D-二聚体升高与发病后 6 个月功能恢复较差独立相关,CRP 预测价值有限。IL-6 与 D-二聚体联合评估对长期功能恢复风险分层具有一定价值。

肺癌患者合并肺孢子菌肺炎的危险因素及短期不良结局分析：一项单中心回顾性病例对照研究

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关键词：肺孢子菌肺炎，肺癌，危险因素

背景 肺孢子菌肺炎（PJP）是免疫功能受损肺癌患者常见且凶险的机会性感染。肺癌患者因肿瘤本身、放化疗、免疫治疗及糖皮质激素应用等因素，细胞免疫功能受损，PJP 风险增加，且常预示不良临床结局。目前肺癌合并 PJP 的危险因素及对短期预后的影响尚缺乏充分证据，明确其高危特征对早期识别和优化管理至关重要。

目的 探讨肺癌患者合并肺孢子菌肺炎（*Pneumocystis jirovecii* pneumonia, PJP）的独立相关因素及其对短期不良结局的影响，为高危人群的早期识别与临床管理提供依据。

方法 采用单中心回顾性病例对照研究。纳入 2022 年 2 月至 2025 年 12 月宁夏医科大学总医院呼吸与危重症医学科收住入肺癌患者 50 例，其中 PJP 组 20 例，非 PJP 组 30 例。PJP 依据临床表现、胸部 CT、病原学检测、 β -D-葡聚糖及治疗反应综合判定。收集两组人口学资料、肿瘤特征、近期抗肿瘤治疗、糖皮质激素使用、实验室及影像学资料。采用单因素分析及多因素 Logistic 回归筛选 PJP 独立相关因素，并比较两组短期不良结局。

结果 单因素分析显示，PJP 组长期大剂量糖皮质激素使用、同步放化疗、淋巴细胞减少及 LDH 升高比例均高于非 PJP 组（均 $P<0.05$ ）。多因素 Logistic 回归分析显示，长期大剂量糖皮质激素使用（AOR=15.32, 95%CI: 3.84~61.09, $P<0.001$ ）、淋巴细胞减少（AOR=6.78, 95%CI: 1.92~23.91, $P=0.003$ ）、同步放化疗（AOR=4.95, 95%CI: 1.21~20.27, $P=0.026$ ）及 LDH 升高（AOR=3.87, 95%CI:

1.32~11.35, $P=0.014$ ）是肺癌患者合并 PJP 的独立相关因素。与非 PJP 组相比，PJP 组住院死亡率显著升高[35.0%（7/20）比 3.3%（1/30）， $P=0.004$]，且 ICU 收治率、机械通气率更高，住院时间更长，后续抗肿瘤治疗更易延迟或中断（均 $P<0.05$ ）。

结论 长期大剂量糖皮质激素使用、淋巴细胞减少、同步放化疗及 LDH 升高与肺癌患者合并 PJP 密切相关。PJP 显著增加肺癌患者住院期间短期不良结局风险。对接受激素治疗或同步放化疗、伴淋巴细胞减少及 LDH 升高的肺癌患者，应加强动态监测及早期病原学评估，以促进 PJP 的及时识别和干预。

社区获得性肺炎患者出院后 90 天主要不良心血管事件风险及其预测因素研究

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关键词：社区获得性肺炎，心血管风险，预测因素

背景 社区获得性肺炎（CAP）患者出院后仍面临较高的心血管事件风险，但缺乏长期随访数据。本研究通过回顾性队列分析 100 例 CAP 患者，评估其出院后 90 天内主要不良心血管事件（MACE）的发生风险及预测因素。该研究为 CAP 患者的出院后心血管风险分层及个体化管理提供了依据。

目的 探讨 CAP 患者出院后 90 天内 MACE 的发生风险及其预测因素，并评估构建风险预测模型的可行性，为临床开展出院风险分层、制定个体化随访与干预策略提供依据。

方法 本研究为单中心回顾性队列研究，纳入 2022 年 4 月至 2026 年 2 月收治的 100 例 CAP 患者。终点为出院后 90 天内 MACE（心血管死亡、心梗、心衰、卒中、严重心律失常）。收集人口学、基

础疾病、肺炎严重程度 (CURB-65、PSI)、实验室指标 (CRP、PCT、NLR、hs-cTn、NT-proBNP 等) 及治疗信息。采用 Kaplan-Meier 法评估累积发生率, Cox 回归分析筛选独立预测因素。

结果 本研究纳入的 100 例患者中, 男 58 例, 女 42 例, 平均年龄 65.3 ± 12.1 岁。出院后 90 天内, 共有 18 例 (18.0%) 发生 MACE。其中, 心血管死亡 4 例 (4.0%), 新发或加重心衰 7 例 (7.0%), 急性心梗 3 例 (3.0%), 卒中 2 例 (2.0%), 严重心律失常 2 例 (2.0%)。Kaplan-Meier 生存曲线显示 MACE 发生率随时间递增。Cox 多因素回归分析发现, 高龄 (≥ 75 岁, $HR=2.89$, 95%CI: 1.15-7.25)、既往心力衰竭史 ($HR=3.42$, 95%CI: 1.32-8.86)、入院时高水平的 NT-proBNP (≥ 900 pg/mL, $HR=2.67$, 95%CI: 1.08-6.60) 和入院时高水平的 hs-cTn (≥ 14 ng/L, $HR=2.31$, 95%CI: 1.01-5.28) 是 CAP 患者出院后 90 天内发生 MACE 的独立危险因素。

结论 CAP 不仅是急性呼吸系统感染性疾病, 也是诱发或加重心血管系统失代偿的重要触发因素。患者在出院后 90 天内仍面临较高 MACE 风险。综合评估基础心血管状态、肺炎严重程度以及炎症和心脏生物标志物水平, 有助于实现 CAP 患者出院后心血管风险分层, 为后续精准随访和干预提供依据。

Genetic Association and Immune Mediation Between *Clostridioides Difficile* Infection and Alzheimers Disease

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Objective *Clostridioides difficile* infection (CDI) is highly prevalent and prone to recurrence in the elderly. Clinical observations suggest a close link between cognitive decline and CDI; however, the causal direction

and underlying biological mechanisms remain elusive. This study aims to provide a novel theoretical basis and identify potential biomarkers for targeting gut microbiota and immune interventions to delay AD progression

Methods (1) Mendelian Randomization Analysis: Summary data from genome-wide association studies (GWAS) of CDI and AD were utilized. Five methods—IVW, weighted median, MR-Egger regression, weighted mode, and MR-PRESSO—were employed to evaluate the causal association. (2) Immune Cell Mediation Analysis: Based on GWAS data for 731 immune phenotypes, a two-step MR framework was applied to screen for immune cell subsets with significant mediating effects. (3) Animal Experiments: A recurrent CDI model was established in C57BL/6J mice (rCDI group vs. control). Splenic lymphocyte proportions were analyzed via flow cytometry. Transcriptomic sequencing of colon tissues was performed to identify differentially expressed genes (DEGs). Expression levels of microglial activation markers were assessed using qPCR, Western blot, and immunofluorescence (IF) staining

Results (1) MR Analysis: Genetic susceptibility to CDI was significantly and positively associated with an increased risk of AD (IVW OR = 1.12, 95% CI: 1.04–1.22, $P = 0.004$). Results across all five methods were directionally consistent, with no significant horizontal pleiotropy detected. (2) Mediation Analysis: $CD4^+$ T cells and $CD8^+$ T cells were identified as the primary mediating immune phenotypes in this causal pathway, with mediation proportions of 18.6% and 12.3%, respectively (both $P < 0.05$). (3) Animal Model: In addition to intestinal inflammation, rCDI mice exhibited a decreased splenic Treg/Th17 ratio compared to controls ($P < 0.05$). Transcriptomic analysis revealed a significant upregulation of genes related to neuroinflammation and oxidative stress, including *Atf3*, *Ddit4*, *Pycard* (ASC), and *Pdgfra* ($|\log_2FC| > 1$, $P < 0.05$). Furthermore, qPCR, Western blot, and IF staining consistently

demonstrated that mRNA and protein expression levels of Iba1, TREM2, NLRP3, and iNOS in the hippocampus were significantly elevated in the rCDI group ($P < 0.05$ or $P < 0.01$)

Conclusion This study establishes, for the first time, a positive genetic association between *Clostridioides difficile* infection and Alzheimer's disease through Mendelian Randomization, highlighting CD4⁺ T cells as a critical immune mediator in this causal axis. The animal model further confirms that rCDI triggers systemic immune dysregulation and neuroinflammatory responses, such as hippocampal microglial activation. In summary, CDI may increase AD risk by triggering central nervous system inflammation via the gut-immune-brain axis

重症肺炎患者感染控制后早期肺康复介入的临床疗效与安全性评价

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目的 重症肺炎患者常遗留呼吸肌无力、运动耐力下降及日常生活活动能力受损等后遗症，传统肺康复多延迟至转出 ICU 或出院后启动，最佳介入时机尚不明确。本研究旨在评估重症肺炎患者在感染控制达标后早期启动肺康复的临床疗效及安全性，为优化康复时机提供循证依据。

方法 前瞻性随机对照研究，纳入 2024 年 1 月至 2025 年 12 月于宁夏医科大学总医院 RICU 住院的重症肺炎患者 112 例。纳入标准：①符合重症肺炎诊断标准；②感染控制达标：体温 $\leq 37.5^{\circ}\text{C}$ 持续 $\geq 48\text{h}$ ，降钙素原 $\leq 0.5\mu\text{g/L}$ 或较峰值下降 $\geq 80\%$ ，血流动力学稳定；③意识清楚，能配合指令。排除标准：①严重慢性呼吸系统疾病；②严重神经肌肉疾病；

③急性心肌梗死。随机分为早期康复组（感染控制达标后 24h 内启动康复，56 例）和常规康复组（转出 RICU 后启动，平均达标后 5.2 天，56 例）。康复方案包括体位管理、气道廓清、呼吸肌训练及渐进式肢体活动。主要结局为出院时 6 分钟步行距离（6MWD）；次要结局包括肺功能、机械通气时间、住院天数及不良事件发生率。

结果 一共 104 例患者完成研究（每组 52 例）。早期康复组出院时 6MWD 为 362.5 ± 48.6 米，显著高于常规康复组的 298.3 ± 52.4 米（ $p < 0.001$ ）。早期康复组 FVC%预计值高于常规康复组（ $78.6 \pm 10.2\%$ vs $68.4 \pm 11.5\%$ ， $p < 0.001$ ）；机械通气时间（ 7.2 ± 2.8 vs 9.6 ± 3.5 天， $p < 0.001$ ）、RICU 住院天数（ 9.8 ± 3.2 vs 12.5 ± 4.1 天， $p < 0.001$ ）及总住院天数（ 16.4 ± 4.6 vs 19.8 ± 5.3 天， $p = 0.001$ ）均显著缩短。不良事件发生率两组无统计学差异（ 11.5% vs 9.6% ， $p = 0.752$ ），无康复相关死亡事件。

结论 重症肺炎患者在感染控制达标后 24h 内启动早期肺康复安全可行，可显著提高患者出院时运动耐力，改善肺通气功能，缩短机械通气时间和住院天数，且不增加不良事件风险。建议将早期肺康复纳入重症肺炎诊疗常规。

关键词 重症肺炎；肺康复；早期介入；感染控制；呼吸功能

支气管扩张症合并铜绿假单胞菌感染患者耐药危险因素及预后分析

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关键词 支气管扩张症，多重耐药铜绿假单胞菌，危险因素

背景 支气管扩张症患者因气道结构破坏及黏液清除障碍易发生反复感染，其中铜绿假单胞菌(PA)

是最常见的定植及致病菌之一。其生物膜形成能力及抗菌药物暴露压力使多重耐药(MDR)菌株发生率逐年升高。既往研究提示 PA 感染与疾病严重程度及预后密切相关,但针对支气管扩张症人群中 MDR-PA 感染的特异性危险因素及其对短期临床结局的量化影响仍缺乏系统研究。

目的 本研究旨在探讨支气管扩张症患者发生多重耐药铜绿假单胞菌感染的危险因素,并分析其对患者短期临床结局的影响,为临床早期识别与干预提供依据。

方法 采用回顾性队列研究方法,纳入 2023 年 1 月至 2024 年 12 月期间收治的 100 例支气管扩张症合并 PA 感染患者。依据药敏试验结果并参考 CLSI 标准,将对 ≥ 3 类抗菌药物不敏感定义为 MDR 菌株,患者分为 MDR-PA 组($n=38$)与非 MDR-PA 组($n=62$)。收集患者人口学资料、基础疾病、既往抗菌药物暴露、近 1 年住院史及 ICU/RICU 入住史等临床数据。采用单因素分析筛选潜在变量($P<0.10$),纳入多因素 Logistic 回归模型分析独立危险因素。同时比较两组住院时长及不良临床结局。

结果 共纳入 100 例患者,其中 MDR-PA 感染率为 38.0%。多因素 Logistic 回归分析显示:近 1 年住院次数增加($OR=2.42, 95\%CI: 1.56-3.75, P=0.001$)、ICU/RICU 入住史($OR=4.49, 95\%CI: 1.29-15.60, P=0.018$)及咯血($OR=4.70, 95\%CI: 1.11-19.92, P=0.035$)为 MDR-PA 感染的独立危险因素。与非 MDR-PA 组相比,MDR-PA 组患者住院时间显著延长(14.3 ± 5.8 vs 9.7 ± 4.2 天, $P<0.001$),呼吸衰竭发生率更高(34.2% vs $12.9\%, P=0.011$),无创机械通气使用率增加(28.9% vs $11.3\%, P=0.019$)。两组院内死亡率差异无统计学意义(5.3% vs $3.2\%, P=0.642$)。

结论 既往频繁住院、ICU 暴露史及咯血是支气管扩张症患者发生 MDR-PA 感染的重要独立危险因素。MDR 菌感染与住院时间延长及呼吸支持需求增加显著相关,提示其对短期临床结局具有不良影响。尽早进行病原学检测并根据药敏结果实施目标性治疗,以改善患者预后并延缓耐药性的发展。

入院早期支气管肺泡灌洗液宏基因组二代测序与免疫抑制宿主肺部感染短期临床结局的关联:一项单中心回顾性队列研究

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关键词: 免疫抑制宿主, 肺部感染, 宏基因组二代测序

背景 免疫抑制宿主是肺部感染相关不良结局的高风险人群,其病原谱复杂、混合感染常见,且病情进展快、短期死亡风险高。传统病原学检测存在报告周期长、阳性检出率有限等不足,可能延迟目标性抗感染治疗的实施。尽管宏基因组二代测序(mNGS)等新型检测技术已逐步应用于临床,但针对免疫抑制宿主肺部感染,入院早期开展综合病原学检测是否与更优短期临床结局相关,仍缺乏真实世界证据。

目的 评估入院早期支气管肺泡灌洗液宏基因组二代测序(BALF-mNGS)与免疫抑制宿主肺部感染患者 30 天全因死亡率、14 天临床缓解率及抗感染治疗调整率之间的关系,并探索其潜在临床获益路径。

方法 本研究为单中心回顾性队列,纳入 2020 年 1 月至 2025 年 12 月宁夏医科大学总医院 120 例免疫抑制合并肺部感染患者。按入院 72 小时内是否行 BALF-mNGS 分为早期检测组(61 例)和常规检测组(59 例)。主要结局为 30 天全因死亡,次要结局包括 14 天临床缓解率及治疗调整率等。采用多因素 Cox 回归校正混杂因素,并行倾向评分加权敏感性分析。

结果 纳入 120 例免疫抑制合并肺部感染患者,分为早期 BALF-mNGS 检测组(72h 内, 61 例)与常规检测组(59 例)。结果显示:早期检测组病原检

出率显著更高 (85.2% vs 62.5%, $P<0.001$), 抗感染方案调整比例亦更高 (68.1% vs 44.9%, $P<0.001$)。临床结局方面, 早期检测组 30 天全因死亡率更低 (15.4% vs 28.4%); 多因素 Cox 回归显示早期 BALF-mNGS 与较低死亡风险独立相关 ($aHR=0.54$, $P=0.014$), 且 14 天临床缓解率更高 ($aOR=1.92$, $P=0.006$), 提示早期精准病原学检测可能改善短期预后。

结论 在本单中心回顾性队列中, 入院 72 小时内实施 BALF-mNGS 检测与免疫抑制宿主肺部感染患者更高的病原检出率、更频繁的目标性治疗调整、更低的 30 天死亡风险以及更高的 14 天临床缓解率独立相关。这提示早期 BALF-mNGS 可能通过快速明确病原、指导精准治疗而改善短期预后。鉴于研究的回顾性设计, 该结论仍需前瞻性研究验证。

Correlation between Severity of Myelosuppression Caused by Piperacillin-tazobactam and Factors: Analysis Through A Multivariate Ordered Logistic Regression Model

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Aim To explore the factors influencing the severity of piperacillin-tazobactam-associated myelosuppression and the time of symptom onset, and to provide a basis for clinical risk prevention and control

Methods Based on the electronic database and data from a city's adverse drug reaction monitoring system in the past 10 years, 115 patients with piperacillin-tazobactam-induced myelosuppression were included. Multivariate ordered logistic regression models were

used to analyse the factors affecting severity and time to symptom onset.

Results Concomitant medication significantly increased the risk of myelosuppression severity ($OR=3.95$, $p<0.001$). Male ($OR=4.03$, $p=0.02$), past medical history ($OR=4.25$, $p<0.01$) and prolonged duration of medication ($OR=1.60$, $p<0.0001$) accelerated symptom onset. Laboratory indices showed a significant decrease in leukocytes ($2.2\times 10^9/L$ vs. $9.1\times 10^9/L$) and platelets ($25.5\times 10^9/L$ vs. $222.5\times 10^9/L$) after medication ($p<0.001$). Symptomatic improvement was observed after discontinuation of the medication in 80.0% of the patients, but prolongation of the original course of the disease due to myelosuppression was observed in 24.3% of the patients.

Conclusion Concomitant medication is a key risk factor for the severity of myelosuppression, and early monitoring needs to be strengthened in males, those with past medical history, and long-term medication users. This study provides data support for individualised medication regimens and risk warnings.

Keywords piperacillin-tazobactam; myelosuppression; ordered logistic regression; risk factors

1998-2023 年麻风病皮肤组织切刮液涂片抗酸染色镜检检测结果分析

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目的 了解麻风病细菌学阳性病例的人口学特征等, 为麻风病诊断、治疗提供参考。

方法 统计分析四川省皮肤病性病防治研究所门诊 1998 年-2023 年麻风病皮肤切刮组织液涂片、抗酸染色镜检阳性病例的年龄、性别等人口学特征以及复查病例 BI 值年度变化率。

结果 1998年至2023年间1810例疑似病例中, 皮肤查菌阳性 631 例, 查菌阳性率为 34.86%; 其中男性病例 409 例, 占 64.82% (409/631), 女性病例 222 例 (222/631), 占 35.18%; 平均年龄为 40.4±3.5 岁, 最大年龄为 68.0±8.2 岁, 平均最小年龄为 15.4±5.0 岁; 男女性病例平均年龄无统计学差异; 皮肤查菌平均 BI 值为 3.24±0.35, 最大 BI 值为 5.28±0.26、最小 BI 值为 0.29±0.32, 男性病例平均 BI 值为 3.28±0.37; 女性病例平均 BI 值为 2.96±0.53; 多菌型病例 (MB) 有 542 例, 占 85.90%。MB 患者 BI 年均下降 0.70±0.40。新发年龄小于 20 岁组 BI 值下降最快, 年均降幅 1.06。

结论 门诊发现成为主要的病例发现方式, 需加强皮肤科等专科医生对麻风病的认识, 保障和加强专科实验室麻风病皮肤组织切刮液涂片查菌能力, 对于麻风病诊断、疗效观察以及区域性麻风病防控有意义。

站立疲劳状态猪油干预对小鼠肠道微生物及酶活性的影响

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目的 为探究猪油联合饮食失节、劳倦因素对脾气虚证的诱发影响, 及其与肠道菌群和酶活性的关联, 揭示其肠道微生态学机制。

方法 将 SPF 级雄性昆明小鼠随机分为正常组、站立+猪油低剂量组、站立+猪油中剂量组、站立+猪油高剂量组, 通过水环境小平台站立结合单日禁食的方式造模。自制水平台箱内站立 4h/天, 结合单日禁食不禁水, 双日自由饮食饮水, 从造模第 8 天起, 每天分别灌胃猪油 0.1、0.2、0.4ml, 每天 2 次, 实验周期 14 天。从一般体征、摄食饮水、粪便指标、旷场实验、脏器指数、肠道菌群及消化酶活性等方面评价模型及干预效果。

结果 与正常组相比, 各猪油组小鼠均出现不同程度脾气虚证表现, 高剂量组呈典型证候, 表现为反应迟钝、被毛枯槁、粪便稀溏、摄食量饮水量显著下降 ($p<0.05$), 旷场实验中运动能力显著降低 ($p<0.05$); 各组脾脏、胸腺指数显著降低 ($p<0.05$), 肝脏指数差异不显著 ($p>0.05$); 肠道菌群方面, 中、高剂量组肠道细菌总数升高、双歧杆菌减少、大肠杆菌增多 ($p<0.05$), 菌群失调明显, 低剂量组双歧杆菌增加, 对菌群影响温和; 各干预组肠道蔗糖酶活性显著升高, 高剂量组淀粉酶活性显著降低 ($p<0.05$), 蛋白酶、乳糖酶、纤维素酶活性呈下降趋势但差异不显著 ($p>0.05$)。

结论 低剂量猪油对能量代谢失调状态的负面影响较小, 而高剂量猪油可显著加剧小鼠整体机能衰退, 引发肠道菌群失调与消化酶活性异常, 是加重脾失健运的重要因素, 为膳食脂肪与脾失健运的关联研究提供了实验依据, 也完善了脾失健运相关证候动物模型构建体系。

RamA Regulates Fimbrial Expression Via MicF To Modulate Pathogenicity in *Klebsiella Pneumoniae*

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Klebsiella pneumoniae is a major opportunistic pathogen responsible for hospital-acquired infections, often associated with high mortality and prolonged hospital stays. The transcription factor RamA activates

micF expression, thereby contributing to antibiotic resistance in *K. pneumoniae*. However, how RamA affects *K. pneumoniae* virulence and the mechanisms by which ramA influences *K. pneumoniae* pathogenesis remains elusive. In this study, using both in vitro and in vivo approaches, we investigated whether RamA regulates *K. pneumoniae* pathogenicity through MicF-dependent control of fimbrial and biofilm-associated genes. Based on in vivo virulence tests, serum resistance and macrophage phagocytosis assays, KP- Δ ramA strains exhibited significantly higher virulence than the wild-type (KP-WT). Scanning electron microscopy revealed that KP- Δ ramA strain-derived biofilms displayed significantly higher-level density and completeness than their KP-WT strain-derived versions. Transmission electron microscopy detected marked pili biosynthesis enhancement in the ramA knockout strain. Enzyme-linked immunosorbent assays revealed that KP- Δ ramA-infected mice exhibited attenuated proinflammatory cytokine (including TNF- α and IL-6) levels both in the serum and lung tissues compared to the KP-WT-infected control, suggesting KP- Δ ramA infection-induced immune response suppression. Mechanistically, RNA-seq and qRT-PCR identified that ramA deletion upregulated fimbrial assembly and diguanylate cyclase genes. micF overexpression downregulated these genes, and bioinformatic analysis indicated that MicF could base-pair with their 5' UTRs overlapping the ribosome binding sites, suggesting post-transcriptional repression. In conclusion, we demonstrated that ramA deletion enhances *K. pneumoniae* virulence by upregulating fimbrial and biofilm formation via MicF, while increasing serum resistance and suppressing host immune response.

基于机器学习算法构建骨折相关碳青霉烯耐药菌感染预后模型

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目的 应用 9 种机器学习 (ML) 算法, 构建并验证骨折相关碳青霉烯耐药菌感染患者的预后风险模型, 并为个体化决策干预提供临床辅助工具。

方法 回顾性收集 2020 年 1 月至 2024 年 12 月在河北医科大学第三医院诊治的骨折相关碳青霉烯耐药菌感染患者的临床资料, 收集涵盖人口学、创伤微环境、实验室检验及临床干预等 4 个维度的 30 项基线特征。采用最小绝对收缩和选择算子 (Lasso) 回归模型筛选关键特征变量。将全部样本以 7:3 的比例随机分为训练集和测试集。训练集用于构建逻辑回归 (LR)、随机森林 (RF)、支持向量机 (SVM)、极端梯度提升 (XGBoost)、梯度提升决策树 (GBDT)、轻量级梯度提升机 (LightGBM)、自适应提升 (AdaBoost)、极端随机树 (ExtraTrees)、决策树 (DT) 等 9 种主流机器学习模型, 通过随机搜索联合 10 折交叉验证进行超参数寻优。在测试集运用曲线下面积 (AUC)、灵敏度、特异度、准确度和 F1 值等评估模型的性能, 筛选出最优预测模型。运用校准曲线评估最优模型预测概率的准确性, 决策曲线 (DCA) 评估最优模型的临床净收益。通过沙普利可加性解释 (SHAP) 对最优模型进行可解释性分析, 并基于核心特征构建临床预后风险评估列线图。

结果 本研究共收集了 300 例骨折相关碳青霉烯耐药菌感染患者的临床资料, 其中预后良好组 192 例, 预后不佳组 108 例。通过 Lasso 回归筛选出 8 个核心预测变量: 年龄、BMI、ASA 分级、AO 分型、软组织情况、术中失血量、降钙素原 (PCT) 及入住 ICU。模型评估显示, 基于树的集成算法整体预测表现优异, LightGBM 模型展现出最优的综合判别效能 (AUC=0.9560, 准确度=0.9067, 灵敏度=0.8536, 特异度=0.9382)。校准曲线和 DCA 曲线证实该模型具

有良好的风险校准度与较高的临床干预净收益。SHAP 分析表明, PCT 升高、高龄与高 BMI 是导致不良预后排名前三的核心危险因素。最终基于 8 种核心变量构建了预后风险评估列线图, 为临床个体化精准干预提供了直观的可视化决策工具。

结论 本研究构建并验证了评估骨折相关碳青霉烯耐药菌感染患者预后状况的风险预测模型。LightGBM 模型具有良好的预测效果, 并为临床医师提供了一套透明、可解释性且净收益高的临床决策辅助工具。有望尽早针对高危患者进行干预策略与抗菌药物管理, 改善患者预后。

Pattern of Antibiotic Prescriptions in Chinese Children, Data From Multi-center Point Prevalence Survey From 2017 To 2025

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Background Broad spectrum antibiotics have a potentially greater influence on antimicrobial resistance.

In 2017, the China Multi-Center Monitoring Network for Antibiotic Use in Children was established, and the types of antibiotics used were continuously collected using a cross-sectional survey method. In the multi-center point prevalence study, we described the pattern of antibiotic prescriptions for children from 2017 to 2025 based on the Anatomical Therapeutic Chemical Classification(ATC classification), the World Health Organization's (WHO) Essential Medicines List Access, Watch, and Reserve(AWaRe) classification

Methods One-day point-prevalence surveys (PPSs) on antimicrobial prescribing were conducted in hospitalized children in China. The survey period was from December of each year to February of the following year. Any one day within the three-month survey period was randomly selected as the survey day, and the survey was conducted once a year.

Results A total of 23782 antibiotic prescriptions for children(19329) and neonates(4450) were included in the analysis. Data was collected from 48 hospitals in 26 provinces across China. There were 89 types of antibiotic agents in total, and 24 (30.6%) antibiotic agents accounted for 90 percent of antibiotic prescriptions. The top-five antibiotics prescribed for children were Ceftriaxone(2790, 11.7%), Cefoperazone/Sulbactam(2343,9.9%),Azithromycin(IV)(1879,7.9%), Meropenem(1629, 6.9%) and Ceftazidime(1414, 6.0%). According to the Anatomical Therapeutic Chemical Classification(ATC classification), the top-five antibiotic classes were Third-generation cephalosporins 10148(42.7%), Macrolides 3460(14.6%), Beta lactam-beta lactamase inhibitor 2439(10.3%), Carbapenems 2098(8.8%), Second-generation cephalosporins 1339(5.6%). On the basis of WHO AWaRe classification, there were 16655(70.0%) of antibiotic prescriptions in the Watch group, 3754(15.8%) in the Access group, 2677(11.3%) in the not-recommended group, 480(2.0%) in the Reserve group and 213(0.9%) in the

Unclassified group.

The most common reason for prescribing antibiotic to Chinese children and neonates was pneumonia (11387, 47.9%). For children with pneumonia, there were 1594 (14.0 %), 8372 (73.5 %) and 244 (2.1 %) antibiotic prescriptions in the Access, Watch and Reserve groups, respectively. The top five antibiotic classes for children with pneumonia were Third-generation cephalosporins 5105(44.8%), Macrolides 2060(18.1%), Beta lactam-beta lactamase inhibitor 1389(12.2%), Cabpenem 786(6.9%),and Second-generation cephalosporins 547(4.8%). The top-five antibiotics prescribed for children with pneumonia were ceftriaxone(1697, 14.9%), Azithromycin(IV)(1100, 9.7%), Cefoperazone/Sulbactam(961, 8.4%), Amoxicillin and Clavulanate (854,7.5%) and Ceftazidime(1414, 6.0%).

Conclusion The Watch group and the Third-generation cephalosporins were predominant antibiotic agents for Chinese children and neonates.

A Machine Learning Approach To Diagnose Chromosomal Copy Number Variations in Hematological Malignancies

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Objective To analyze the correlation between CNV loci and hematological malignancies based on DNA sequence data from mNGS.

Methods In this multi-center retrospective study, 300 body fluid specimens with confirmed tumor diagnoses were enrolled from 14 hospitals in Zhejiang Province, China, spanning from January 2019 to December 2024. All samples were processed via metagenomic

next-generation sequencing (mNGS), with chromosomal copy number variation (CNV) analysis subsequently performed utilizing the derived DNA sequence data. An integrated modeling framework was developed for comprehensive analysis, combining several predictive models—including Multilayer Perceptron (MLP), Single-layer Attention + MLP, Dual Attention + MLP, and Kolmogorov-Arnold Network 2.0 (KAN 2.0)—with an interpretable model, specifically the Generalized Additive Model with Interactions Network (GAMI-Net).

Results The integrated framework demonstrated robust performance: the predictive models achieved an Area Under the Curve (AUC) of 0.950 (accuracy: 0.933), while the interpretable model (GAMI-Net) yielded an AUC of 0.870 (accuracy: 0.800). Collectively, the models identified 11 core chromosome pairs, where the top three contributors were chromosome 5 (chr5: 5–39 Mb), chromosome 9 (chr9: 7–39 Mb), and chromosome 16 (chr16: 50–83 Mb). Furthermore, an additional 7 specific chromosomes were highlighted by individual models as being highly associated with hematological malignancies. The predominant feature regions within these 7 chromosomes spanned chromosome 14 (chr14: 20–108 Mb), chromosome 13 (chr13: 20–116 Mb), and chromosome 1 (chr1: 1–21, 23–45, 47–96, 98–122, and 144–250 Mb).

Conclusion This study demonstrates that an integrated framework—synergizing predictive models with an interpretable model—provides a high-confidence methodological approach for characterizing CNV profiles in hematological malignancies. This dataset and the combined modeling strategy provide valuable molecular evidence to support the clinical diagnosis and management of hematological diseases.

In Vitro Activity of Ceftazidime/avibactam Combined with Amikacin Against Difficult-to-treat Resistant *Pseudomonas Aeruginosa*

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Background This study aims to elucidate the in vitro combination effects of antimicrobial agents against difficult-to-treat resistant *Pseudomonas aeruginosa* (DTR-PA), investigate the in vitro synergistic activity of ceftazidime/avibactam and amikacin, and provide evidence for treating DTR-PA infections

Methods DTR-PA strains were collected from 33 hospitals across 25 provinces, municipalities, and autonomous regions nationwide. The minimum inhibitory concentration (MIC) of DTR-PA strains against multiple antimicrobial agents was determined using the microbroth dilution method. Subsequently, molecular epidemiological characteristics and antimicrobial resistance mechanisms of DTR-PA strains were analysed based on second-generation genome sequencing data. A checkerboard approach was employed to evaluate ten antimicrobial combinations: polymyxin combined with imipenem, polymyxin combined with meropenem, polymyxin combined with ceftazidime, polymyxin combined with ceftazidime/avibactam, polymyxin combined with piperacillin/tazobactam, polymyxin combined with amikacin, polymyxin combined with levofloxacin, polymyxin combined with aztreonam, polymyxin combined with fosfomycin, and ceftazidime/avibactam combined with amikacin against all DTR-PA strains. Six representative DTR-PA strains were selected to determine their time-kill curves, further evaluating the synergistic bactericidal effect of ceftazidime/avibactam combined with amikacin

Results This study used the microbroth dilution

method to verify the MICs of β -lactam antibiotics and quinoline antimicrobial agents, incorporating a total of 113 DTR-PA strains. Antimicrobial susceptibility testing revealed the following resistance rates: polymyxin (1.77%), amikacin (14.16%), ceftazidime/avibactam (45.13%), fosfomycin (36.28%), piperacillin/tazobactam (74.34%), imipenem (92.92%), meropenem (86.73%), ceftazidime (81.42%), amikacin (95.58%) and levofloxacin (92.92%). In vitro combined susceptibility testing revealed nine polymyxin-based antimicrobial regimens primarily exhibited non-additive and additive effects against DTR-PA. Synergistic effects accounted for a low proportion (1.77%-5.31%), and no antagonistic interactions were observed. By contrast, amikacin combined with ceftazidime/avibactam exhibited synergistic effects in 75.23% of cases and additive effects in 24.77%, with no unrelated effects observed. Time-kill curves further confirmed the significant synergistic bactericidal effect of amikacin in combination with ceftazidime-avibactam against DTR-PA strains

Conclusions Although DTR-PA strains exhibit resistance to first-line anti-*Pseudomonas* agents, they maintain high susceptibility to polymyxin, amikacin, and ceftazidime/avibactam. Combinations based on polymyxin showed essentially no synergistic effect against DTR-PA strains, whereas ceftazidime/avibactam combined with amikacin demonstrated marked synergistic bactericidal effects against most DTR-PA strains

艾滋病合并结核性脑膜炎中枢神经系统免疫重建炎症综合征的临床特征及住院负担的研究

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目的 回顾性分析艾滋病合并结核性脑膜炎 (tuberculous meningitis, TBM) 患者中枢免疫重建炎症综合征 (central nervous system-immune reconstitution inflammatory syndrome, CNS-IRIS) 的临床特征及其住院负担与短期预后。

方法 单中心回顾性研究, 纳入 2019 年 5 月—2025 年 5 月收治的艾滋病合并 TBM 住院患者。按预设标准排除无 CNS-IRIS 风险或结局判读受显著混杂者; 纳入者按是否发生 CNS-IRIS 分为无 CNS-IRIS 组与 CNS-IRIS 组。以患者为分析单位, 主要指标为总住院天数与入院后 90 d 死亡; 失访者进行“全活/全死”敏感性分析。连续变量以 $M(P_{25}, P_{75})$ 表示, 组间比较用 Mann-Whitney U 检验并报告 rank-biserial r 及 Hodges-Lehmann (HL) 差值 95%CI; 分类变量用 Fisher 确切概率法并报告 OR 及 95%CI。

结果 共收治 78 例, 排除 31 例, 纳入 47 例, 其中无 CNS-IRIS 组 34 例、CNS-IRIS 组 13 例。入院基线方面, CNS-IRIS 组 CD4 计数、白蛋白与血红蛋白水平均低于无 CNS-IRIS 组 (均 $P < 0.05$), 多项脑脊液常规生化指标差异无统计学意义。CNS-IRIS 组总住院天数显著延长 [87 (62, 120) d vs 38 (21, 56) d, $P = 0.002$; rank-biserial $r = 0.597$; HL 差值 = 48 d (95%CI 20~76)]。90 d 死亡在主分析 (剔除失访) 及两种敏感性分析中组间差异均无统计学意义 (主分析: OR = 2.30, 95%CI 0.28~18.70, $P = 0.582$; 全活: OR = 2.91, 95%CI 0.36~23.20, $P = 0.304$; 全死: OR = 0.63, 95%CI 0.14~2.75, $P = 0.726$)。

结论 在本单中心真实世界队列中, CNS-IRIS 与显著增加的住院负担相关, 而其与 90 d 死亡差异未检出统计学显著性; 鉴于样本量与事件数有限, 需结合效应量与置信区间综合解读, 并在更大样本研究中进一步验证。

Yersiniabactin 作为免疫功能正常患者肺炎克雷伯菌肺炎重症进展的潜在风险标志物

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背景 肺炎克雷伯菌肺炎 (KPP) 通常进展迅速, 出现严重症状, 并且预后不良。然而, 与 KPP 进展为重症肺炎相关的临床和微生物学特征仍不清楚。因此, 本研究旨在系统地研究 KPP 进展为重症肺炎的风险及其相关的 KP 微生物学特征。

方法 本单中心回顾性队列研究在青岛市市立医院进行。2016 年 11 月至 2023 年 10 月期间连续诊断为 KPP 的患者被纳入研究。患者分为两组: 重症肺炎组和非重症肺炎组。从电子病历报告系统中提取了基线临床和 30 天全因死亡率。所有分离株均使用第二代测序技术在 BGI 进行全基因组测序 (WGS)。使用多基因序列型 (MLST) 和核心基因组多基因序列分型 (cgMLST) 进行基因型表征。使用 AMRFinder 和 Kleborate 预测耐药基因、毒力基因和血清型。使用 Snippy 构建系统发育树。应用多因素 logistic 回归模型识别重症 KPP 发生的独立危险因素。

结果 这项队列研究中, 多变量逻辑回归分析表明, Yersiniabactin (OR = 5.725, 95% CI: 1.13-29.439)、糖尿病 (OR = 5.604, 95% CI: 1.269-24.79)、年龄增加 (OR = 1.065, 95% CI: 1.014-1.120) 和 CRP 水平升高 ($=1.014$, 95% CI: 1.002-1.025) 是重症 KPP 的独立危险因素。根据系统发育, 在 ST11-K64/O2a 亚系中观察到 blaKPC-2、aerobactin 和 rmpA2 的共同, 表明出现了具有联合耐药性和高毒力特征的克隆亚群。

结论 本研究提示, Yersiniabactin 可能作为识别重症 KPP 高危患者的潜在生物标志物。因此, 在实践中, 对于感染 KP 的患者, 检测 Yersiniabactin 的阳性情况应被视为潜在快速疾病进展的重要警示, 需要加强临床监测和管理

关键词: 肺炎克雷伯菌、重症肺炎、毒力

儿童偏肺病毒下呼吸道感染临床特征及重症风险因素分析

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目的 比较人偏肺病毒(hMPV)与呼吸道合胞病毒(RSV)感染患儿急性下呼吸道感染(ALRTI)的临床特征差异,并分析hMPV感染患儿发生重症肺炎的危险因素。

方法 回顾性分析2023年2月至2024年12月天津市儿童医院住院患儿资料。根据病原学分为hMPV组(363例)与RSV组(272例),比较两组一般资料、临床表现、实验室指标及治疗措施;并对hMPV肺炎患儿进行严重程度分层及Logistic回归分析。

结果 hMPV组患儿年龄较RSV组更大(3岁vs 6月, $P<0.001$),热程及咳嗽时间更长(均 $P<0.001$),中性粒细胞比例、CRP及PCT水平更高(均 $P<0.001$)。RSV组喘息症状及既往喘息、湿疹史比例更高(均 $P<0.001$)。影像学方面,hMPV组以肺炎为主(82.64%),RSV组支气管肺炎比例较高(42.28%)。治疗上RSV组糖皮质激素使用率显著更高(78.68%vs 30.58%, $P<0.001$)。在hMPV组中,多因素分析显示年龄($OR=0.888$, $P=0.020$)及热程($OR=1.119$, $P=0.034$)为重症肺炎独立影响因素。

结论 hMPV感染患儿较RSV感染患儿年龄更大,炎症反应更显著且病程更长;RSV更易引起喘息及气道高反应。低龄及热程延长是重症hMPV肺炎的重要风险因素。

关键词: 急性下呼吸道感染;人偏肺病毒;呼吸道合胞病毒;儿童;临床特征

重症肺炎宿主-微生物动态特征与预后

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目的 脓毒症并非静态炎症状态,而是持续演化的宿主-微生物相互作用过程。本研究基于重症肺炎前瞻性队列,刻画外周血宿主转录组与微生物信号的动态特征,分析其与疾病进展及28天死亡风险的关系。

方法 建立多中心前瞻性重症肺炎队列,采集来自417例患者的976份纵向全血样本进行宏转录组测序,并结合临床表型开展整合分析。比较存活者与死亡者在不同时间点的宿主转录特征、微生物组成及生物量差异,评估宿主转录模块与关键微生物信号的关联,并构建死亡预测模型。

结果 重症肺炎患者呈现分化的宿主转录轨迹。死亡者持续表现为炎症反应、干扰素反应及吞噬溶酶体通路激活,存活者则表现出生物合成程序逐步恢复。早期死亡风险升高与链球菌、EB病毒及人巨细胞病毒信号相关,其中人巨细胞病毒与宿主严重度相关模块关系稳定,中介分析支持其与不良结局存在宿主反应耦合。动态内型分析显示,患者向高风险宿主状态转变过程中伴随微生物信号扩增。联合模型可提高早期死亡预测能力,且随病程进展宿主状态的预测价值进一步增强。

结论 重症肺炎存在显著的宿主-微生物动态互作特征。循环微生物信号尤其疱疹病毒信号与高风险免疫状态密切相关,并共同影响死亡风险评估。预后风险应结合病程中宿主状态与微生物信号变化持续重估。

1 例肺结核合并微小微单胞菌肺炎并咯血病例报告

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目的 肺结核合并微小微单胞菌肺炎并咯血在临床上少见,本文分享了 1 例肺结核合并微小微单胞菌肺炎并咯血的病例,早期经过抗结核治疗后病灶好转,继续抗结核治疗后病灶进展,经过抗厌氧菌,继续抗结核治疗后病情好转,通过本例的报道为临床诊疗提供参考。

诊疗经过: 患者男性,74 岁,因“间断咳嗽咳痰伴咯血 10 月余”入院。

现病史: 患者 10 月余前无明显诱因出现咳嗽咳痰,阵发性连声咳,白色粘液痰,不易咳出,偶有痰中带血,鲜血为主,量不多,约 10ml/次,无其他不适,于 2025-3-27 第一次住院诊断为继发性肺结核,予以抗结核治疗后 3 月后复查好转,继续抗结核治疗 7 月复查病灶进展,2025-11-13 第二次住院治疗。

实验室检查: 2025-3-27:血常规:血红蛋白 94g/L,余正常。肝肾功能、电解质、心肌酶、肌钙蛋白 I、血脂均正常。乙肝、丙肝、梅毒、HIV 均阴性。G 实验、GM 实验、曲霉菌抗体 IgG、IgM 均阴性。C 反应蛋白 124mg/L。血沉 108mm/h。糖化血红蛋白 8.6%。两次均检查:细胞角蛋白、癌胚抗原、神经元特异烯醇化酶、甲功三项均正常范围。

病原学检查: 2025-4-4 灌洗液呼吸道多种病原体靶向测序结果:结核分枝杆菌复合群:1773;微小微单胞菌:72。灌洗液病检:未见明确癌细胞。

2025-11-19 灌洗液呼吸道多种病原体靶向测序结果提示:结核分枝杆菌复合群:24;微小微单胞菌:3185。

影像学检查: 2025-3-27 肺部 CT:右上叶前段支气管管壁增厚、管腔变形、变窄、闭塞、右中上肺病灶伴空洞形成,炎性病变(结核?)肿瘤性病变?。

支气管镜结果: 2025-4-3 第一次气管镜检查结论:支气管粘膜炎症,右上叶粘膜肥厚?粘膜浸润?(图 6A、6B);2025-11-18 第二次气管镜检查结论:右上叶前支开口粘膜病变并阻塞性肺炎;右中叶内侧段出血并右中叶化脓性炎症(图 7A、7B)。

治疗方案: 见表 1

随访: 患者症状好转,无咳嗽咳痰,无咯血,

2026 年 4 月复查肺部 CT 肺部病灶吸收好转。

Clinical Characteristics and CT Manifestations for Prognostic Evaluation of Legionella Pneumonia in Hematological Disorders

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Background Patients with hematologic malignancies who develop *L. pneumophila* pneumonia (LPP) are prone to respiratory failure and multiple systemic organ failure. The computed tomography (CT) features of LPP in this population have been rarely described in the literature, especially regarding the role of CT in prognosis evaluation and the assessment of treatment duration

Methods A retrospective study was performed to analyze the clinical characteristics and CT features of 81 patients with HDs complicated by LPP between November 2019 and January 2026. These patients were divided into two groups according to the final survival status. Multivariate logistic regression was utilized to identify high-risk factors for LPP. Furthermore, CT features were incorporated into Cox survival analysis to assess the 28-day survival rate

Results *Legionella* strains were identified by metagenomic next-generation sequencing (mNGS) in all 81 patients with 54 reassessment by polymerase chain reaction (PCR) testing. Serial chest CT scans revealed four pattern in LPP, including lobar and segmental consolidation, subsegmental consolidation, mass-like consolidation and nodule. On initial CT, patients in

the death group exhibited a significantly higher proportion of multiple lesions ($P = 0.006$), a greater frequency of lobar and segmental consolidation ($P = 0.039$), and a higher incidence of pleural effusion ($P = 0.010$). On follow-up CT, the CT features showed no significant difference between the death group and the survival group. Compared with initial CT, followup CT revealed a significantly higher proportion of patients exhibiting bilateral lung involvement ($P = 0.012$), significant increases of air bronchograms ($P = 0.050$), and cavitation ($P = 0.003$). At the end of the follow-up, complete resolution of lesions was observed in 13 patients with a median time of 113 (25-84) days, marked resolution in 32 patients with a median time of 150 (2-574) days, moderate resolution in 4 patients with a median time of 60 (49-208) days, mild reduction in 1 patient with a duration of 33 days

Multivariate analysis including clinical characteristic and CT features showed that coinfection in other sites ($OR = 4.919$, 95% CI 1.015-23.846, $P = 0.048$), hypoproteinemia ($OR = 30.983$, 95% CI 2.652-361.89, $P = 0.006$), $PCT > 0.5$ ($OR = 6.473$, 95% CI 1.569 - 26.708, $P = 0.010$), lobar and segmental consolidation on initial CT ($OR = 7.584$, 95% CI 1.560-37.6931, $P = .013$) were identified as independent risk factors. Cox survival analysis revealed that lobar and segmental consolidation on initial CT had a significantly lower survival rate, $HR = 3.511$ (95% CI: 1.510-8.161), $P = 0.004$.

Conclusions The CT manifestations of LPP in patients with HDs mainly included lobar and segmental consolidation, subsegmental consolidation, mass-like consolidation, and nodular patterns. Patients who exhibited lobar or segmental consolidation on initial CT scans tended to have a poorer prognosis

新生儿泌尿系感染的临床特征及尿培养阳性

的影响因素分析

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目的 新生儿泌尿系感染临床表现缺乏特异性, 早期识别较困难。尿培养虽是诊断“金标准”, 但存在检测时间较长、标本采集方式影响等问题。本研究通过分析临床诊断为新生儿泌尿系感染患儿的病原菌分布、药敏特点及尿培养阳性相关因素, 为早期识别和合理使用抗菌药物提供参考。

方法 回顾性收集 2022 年 4 月至 2025 年 3 月天津市儿童医院收治的 197 例临床诊断为新生儿泌尿系感染患儿资料。根据尿培养结果分为阳性组 71 例和阴性组 126 例, 比较两组临床特征, 采用单因素分析及多因素 Logistic 回归分析尿培养阳性的相关因素, 并分析阳性病例的病原菌分布及药敏特点。所有数据采用 SPSS 26.0 软件进行统计学处理。

结果 1. 新生儿泌尿系感染常见表现为发热和黄疸, 多数患儿缺乏典型症状。尿培养阳性组黄疸发生率高于阴性组 ($P < 0.05$)。阳性组胎龄低于阴性组 ($P < 0.05$), 性别、入院年龄、出生体重、分娩方式、喂养方式及住院天数差异均无统计学意义 ($P > 0.05$)。

2. 实验室指标比较显示, 阳性组外周血白细胞计数及 C 反应蛋白水平均低于阴性组 ($P < 0.05$), 降钙素原水平差异无统计学意义。分层分析显示, 该差异主要见于合并其他部位感染患儿, 单纯泌尿系感染患儿中上述指标差异无统计学意义。两组尿镜检白细胞阳性率及分级、泌尿系超声异常率比较, 差异均无统计学意义。

3. 多因素 Logistic 回归分析显示, 较小胎龄及存在黄疸与尿培养阳性独立相关。

4. 病原学分析显示, 病原菌以肠球菌属为主, 不同病原菌耐药谱存在差异。粪肠球菌对青霉素和氨苄西林未见耐药, 屎肠球菌对青霉素和氨苄西林耐药率较高, 但对万古霉素和利奈唑胺均敏感; 大肠埃希菌对氨苄西林及部分头孢类药物存在耐药, 且

头孢耐药株均表现为多重耐药。泌尿系超声异常率为14.7%，主要包括肾盂扩张、膀胱沉积物。

结论 新生儿泌尿系感染临床表现缺乏特异性，以发热和黄疸较常见。较小胎龄及存在黄疸与尿培养阳性独立相关，提示临床应重视低胎龄、伴黄疸疑似患儿的规范尿标本采集及尿培养筛查。外周血白细胞计数及C反应蛋白升高更多反映整体感染状态，不能单独用于判断尿培养阳性。住院新生儿泌尿系感染病原菌以肠球菌属为主，部分菌株耐药率较高，临床应依据尿培养及药敏结果合理用药，并完善泌尿系超声评估，以提高早期识别水平，降低远期肾损伤风险。

关键词：泌尿系感染；新生儿；尿培养；临床特征；影响因素；病原学；耐药性

From A Single Case Report To Original Research: A Three Tier Practical Guide for Case Based Writing During Standardized Residency Training of Clinicians and Pharmacists

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Background Case reports are a recognized entry point for research training during medical residency. However, most existing guidance focuses on writing a single case report, leaving a gap in how trainees can progressively advance to higher level evidence synthesis and ultimately produce original research

Objective To provide a three tier practical framework for case based writing during standardized residency training of clinicians and clinical pharmacists, guiding trainees from a single case report to original research, based on the authors' real world publication experience.

Methods We systematically analyzed our team's

published case based articles across three tiers: (1) six single case reports (2021–2025); (2) one case report and literature review (2025); and (3) one systematic case review published as an original research article (2026). For each tier, we extracted methodological requirements, structural elements, and skills developed. We then mapped these findings onto existing reporting guidelines (CARE, PRISMA, CABARET) and quality assessment tools (JBI checklist, RUCAM).

Results The three tiers showed progressively increasing methodological rigor. Tier 1 (single case report) follows the CARE guidelines, emphasizes novelty, differential diagnosis narrative, and literature comparison. Six such reports were published in journals including BMC Infectious Diseases and Frontiers in Medicine. Tier 2 (case report and literature review) involves a single index case plus a systematic literature search for similar cases, descriptive comparison, and pattern recognition, exemplified by our iodixanol induced Kounis syndrome article. Tier 3 (systematic case review as original research) requires a PRISMA guided systematic search, predefined eligibility criteria, quality assessment (JBI), causality assessment (RUCAM), and structured data synthesis. The orlistat case review (10 cases, 20% mortality, 30% liver transplantation) demonstrated that this approach can yield a full original research article in a specialty journal (Frontiers in Pharmacology, 2026).

Conclusion The three tier framework provides a structured, progressive pathway for research skill development during residency, from a single case report to original research. Training programs can adopt this hierarchical approach to guide trainees from basic case reporting to systematic evidence synthesis, ultimately producing publishable original research.

Construction and Evaluation of The Real Case–Scenario Simulation–PPT Presentation Trinity Teaching Model in Clinical Pharmacy Undergraduate Education.Take Two Cases of Anti-infection As Examples

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Background Clinical pharmacotherapy represents a fundamental competency for pharmacy students; however, traditional case-based teaching frequently falls short in delivering authentic clinical reasoning experiences. This study aimed to develop and evaluate a "real case–scenario simulation–PPT presentation" trinity teaching model for fourth-year clinical pharmacy undergraduates

Methods A pre-post quasi-experimental design was implemented with 30 students. Initially, all participants engaged in traditional case-based teaching, followed by the trinity model, which utilized two real, high-stakes cases: (1) catheter-related ESBL-producing *Klebsiella pneumoniae* endophthalmitis and (2) linezolid-induced severe lactic acidosis and coma. The trinity model incorporated small-group role-play simulations (pharmacist, physician, nurse, patient/family) along with structured PPT debriefing. Outcomes included objective performance scores (case report, PPT, Q&A) and a 21-item Likert-scale questionnaire (5-point) addressing three dimensions: teaching design & support, skill development & practice, and feedback & reflection. The Cronbach's α for the questionnaire was 0.91. Paired t-tests and effect sizes (Cohen's d) were calculated.

Results No student received a "poor" performance score. The trinity model significantly surpassed traditional teaching in overall student ratings (4.388 ± 0.327 vs. 3.458 ± 0.348 , $P < 0.001$, Cohen's $d = 2.71$). Approval rates for various dimensions

(agree/strongly agree) ranged from 83.3% to 100%. The highest-rated items included "optimizing clinical pharmacy thinking" (4.38 ± 0.65) and "equal communication opportunities" (4.38 ± 0.65). Open-ended responses ($n=24$) emphasized scenario authenticity and role immersion (62.5%), improvement in teamwork (50.0%), and integration of theory and practice (41.7%).

Conclusion The real case-scenario simulation combined with PPT presentations in the trinity teaching model is superior to traditional case-based teaching. This approach enhances clinical pharmacy reasoning, communication, collaboration, and knowledge application. It is recommended as a standardized and replicable method for competency-based clinical pharmacy education.

Mechanism of Glycosyltransferase TagN Promoting A-Hemolysin Release To Maintain Virulence of *Staphylococcus Aureus*

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Objective This study aims to investigate the molecular mechanism by which TagN regulates *S. aureus* virulence and cell wall homeostasis, and to identify its key functional domains and amino acid residues

Methods Transcriptome sequencing, qRT-PCR, LacZ reporter, rifampicin assay, western blot, and toxin complementation were applied. Virulence was assessed

by hemolysis, LDH release, and mouse sepsis. Cell wall analysis included native PAGE, ion-exchange chromatography, TEM, Zeta potential, and methylene blue adsorption. Domain mapping used truncation and site-directed mutagenesis

Results Transcriptome sequencing showed that tagN deletion broadly altered gene expression in WH99 Δ tagN, downregulating key virulence factors (hla, hld, hlgA) and suppressing pathways such as “S. aureus infection”, “Quorum sensing”, and “cell wall”. qRT-PCR confirmed downregulation of hla, hlb, hld, hlg, agrA, psm α , and pvl. Functionally, the mutant exhibited ~70% reduced hemolysis and attenuated cytotoxicity against neutrophils and A549 cells. In a mouse sepsis model (1×10^8 CFU), the mutant achieved 80-100% survival over 150 h (wild-type: 0%) with reduced spleen abscesses. At 5×10^8 CFU, mutant-infected mice showed less weight loss, lower clinical scores, and decreased spleen bacterial load

Mechanistically, tagN deletion did not affect hla promoter activity but reduced hla mRNA stability, leading to decreased Hla secretion and increased intracellular Hla retention. Exogenous Hla dose-dependently restored hemolytic activity and ~90% cytotoxicity, confirming that impaired Hla secretion drives virulence loss. Furthermore, tagN deletion eliminated α -O-GalNAc WTA glycosylation and reduced WTA backbone abundance, causing thinner cell walls and reduced surface negative charge. NaCl (75-300 μ M), which shields electrostatic interactions, promoted Hla extracellular redistribution and dose-dependently restored hemolytic activity and cytotoxicity, confirming the role of electrostatic adsorption in Hla secretion. Finally, truncation and mutagenesis identified a key domain in the TagN C-terminal α -helix. The N823A_F830A double mutant fully phenocopied the tagN deletion (hemolysis, cytotoxicity, Hla retention, cell wall thinning, WTA depolymerization, loss of glycosylation). Single mutations

(N823A, F830A, Y831A) and N823A_Y831A were functionally normal. F830A_Y831A caused loss of WTA α -GalNAc but only partial functional impairment. Thus, F830/Y831 maintain glycosylation, while N823/F830 are core residues for full TagN function.

Conclusion TagN not only glycosylates WTA but also maintains its backbone and cell wall negative charge to promote Hla secretion, regulating S. aureus virulence. tagN deletion causes WTA depolymerization, cell wall thinning, and charge loss, leading to Hla retention and virulence attenuation. N823 and F830 in TagN's C-terminal α -helix are core sites, providing an anti-virulence target

Staphylococcus Aureus Immune Evasion Research over The Past Two Decades: A Multi-Database Bibliometric Analysis

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Background Staphylococcus aureus (S. aureus) has emerged as a formidable global public health threat, owing to its sophisticated immune evasion strategies. Despite growing research outputs in this field, a comprehensive, multi-database bibliometric analysis delineating its global landscape, hotspots and translational gaps remains lacking

Methods Publications related to S. aureus immune evasion published from January 2006 to December 2025 were systematically retrieved from the Web of Science Core Collection (WOSCC) and Scopus databases, restricted to English-language original research

articles and reviews. The final dataset was established after data integration and deduplication. Meanwhile, relevant clinical trial data in this field were supplementarily retrieved from the PubMed database. Multidimensional bibliometric analyses and visualization of the included publications were performed using R-bibliometrix, VOSviewer, and CiteSpace software.

Results A total of 1,374 eligible publications were included in the final analysis. The average annual growth rate of publications in this field reached 15.71% over the 20-year period, with an accelerated upward trend after 2019 and a peak annual output of 144 publications in 2025, indicating a continuously rising research enthusiasm in this field. At the national level, the United States ranked first globally with 335 publications (24.4% of the total), and China ranked second with 170 publications (12.4%). At the institutional level, Utrecht University (the Netherlands) and the University of California system (the United States) were the most prolific and core institutions in this field. Research hotspots showed a clear temporal evolution: early studies focused on the molecular mechanisms of immune evasion, followed by a gradual shift to host-pathogen interaction research, while antibiotic resistance, biofilm biology, and immunometabolic regulation have emerged as the core frontiers in recent years. Integration of clinical trial data from PubMed revealed a prominent translational gap in this field: despite the in-depth advances in basic mechanistic research, the vast majority of phase II/III clinical trials for candidate vaccines and monoclonal antibody therapies failed to meet their primary clinical endpoints.

Conclusion Research on *S. aureus* immune evasion is undergoing a transition from basic mechanistic exploration to multi-omics integration and clinical translation. Future research should break through the limitations of traditional single-target intervention strat-

egies, and focus on developing novel therapeutic approaches centered on immunometabolic modulation and precise anti-infection regimens. This will help bridge the translational gap between basic research and clinical application, and provide new theoretical support for the prevention, control, diagnosis and treatment of clinical *S. aureus* infections.

Development of A Predictive Model for Identifying The Afebrile Subtype of Brucellar Spondylodiscitis Based on LASSO Regression and Machine Learning

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Background Brucellar spondylodiscitis (BSD) is a severe complication of brucellosis, causing vertebral destruction and potential spinal cord compression, especially in endemic areas. Due to the lack of a specific quantitative tool for early identification of afebrile BSD, this study aims to characterize its clinical features and develop a predictive model

Methods This retrospective study included 189 confirmed BSD patients (January 2021 - December 2025), categorized into febrile (n=118) and afebrile (n=71) groups. Demographic data, clinical features, lab results, and imaging findings were collected. Variable selection was performed using LASSO regression, followed by multivariable logistic regression. Model performance was assessed with ROC curves, calibration curves, the Hosmer-Lemeshow test, decision curve analysis (DCA), and ten-fold cross-validation, comparing various machine learning classifiers.

Results No significant demographic differences were noted (all $P>0.05$). The afebrile group had a higher proportion of chronic disease (19.7% vs 7.6%, $P<0.05$), increased vertebral bone destruction (45.1% vs 25.4%, $P=0.005$), and trends toward muscle weakness ($P=0.082$) and radiating pain ($P=0.065$). Lower rates of positive high-titer SAT (5.6% vs 20.3%, $P=0.017$) and culture positivity (11.3% vs 26.3%, $P=0.014$) were also observed. Key predictors identified included hyperhidrosis, fatigue, bone destruction, prealbumin, globulin, uric acid, PCT, and chronic disease. The final model indicated hyperhidrosis (adjusted OR=18.92, $P<0.001$), fatigue (adjusted OR=16.53, $P=0.036$), and decreased prealbumin (adjusted OR=0.99, $P=0.004$) as independent predictors. The model had an AUC of 0.83, sensitivity of 87.0%, specificity of 70.9%, accuracy of 81.0%, positive predictive value of 83.2%, and negative predictive value of 76.6%. It exhibited excellent calibration (Hosmer-Lemeshow test: $P=0.624$) and favorable clinical net benefit in DCA. SVM achieved the highest AUC of 0.839, while logistic regression balanced discriminative ability and clinical practicality.

Conclusion Afebrile BSD is not benign; absence of fever may indicate insidious progression and greater vertebral damage risk. The developed LASSO regression-based predictive model shows strong discriminative performance, assisting clinicians in early identification, potentially reducing misdiagnosis and treatment delays.

Hypoalbuminemia As A Prognostic Marker of Mortality in Mucormycosis: A Systematic Review and Meta-analysis

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Objectives To systematically evaluate the prognostic value of baseline serum albumin in patients with mucormycosis, focusing on its association with all-cause mortality and other clinical outcomes

Methods We systematically searched major databases for observational studies on baseline albumin's prognostic value in mucormycosis. Primary outcome was all-cause mortality. Dichotomous (hypoalbuminemia thresholds, ORs) and continuous (baseline albumin levels, MDs) meta-analyses were performed. Secondary analyses assessed DM, age, and CRP, with qualitative synthesis of composite outcomes. Quality was assessed via QUIPS tool.

Results Sixteen studies (999 patients, mostly EORTC/MSG proven/probable) were included. Dichotomous analysis showed non-significant trend toward higher mortality with hypoalbuminemia (OR = 3.35, $p = 0.42$). Continuous analysis found survivors had significantly higher baseline albumin (pooled MD = 3.77 g/L, 95% CI: 1.44–6.11; $p = 0.0058$). Non-survivors were older (MD = -4.14 years, $p = 0.024$), while DM and CRP were not independent predictors. Lower albumin consistently linked to worse composite outcomes. Main limitation: inadequate confounding control (13 studies).

Conclusion Lower baseline serum albumin is significantly associated with increased mortality in mucormycosis. Advanced age, DM, and elevated CRP provide complementary prognostic context. Albumin, as a simple universally available marker, aids early risk stratification. However, mostly retrospective evidence requires well-designed prospective studies for validation.

Keywords mucormycosis, albumin, mortality, prognosis, meta-analysis

血液透析患者导管相关感染性心内膜炎 5 例

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目的 总结血液透析(hemodialysis, HD)患者导管相关感染性心内膜炎(catheter-related infective endocarditis, CRIE)的临床特征、诊疗经过及预后影响因素,以提高临床对该病的早期识别与处置能力。

方法 回顾性收集 5 例 HD 并发 CRIE 患者的临床资料,整理其一般信息、血管通路类型、首发症状、实验室检查、血培养结果、超声心动图表现、治疗方案及转归,结合文献进行分析。

结果 5 例患者均为男性,年龄 31~55 岁,透析龄 6~108 个月,血管通路均为中心静脉导管(central venous catheter, CVC),其中 4 例为带隧道带涤纶套导管(tunneled cuffed catheter, TCC),1 例为无隧道无涤纶套导管(non-tunneled non-cuffed catheter, NCC)。4 例以发热起病,体温最高 38.7~40.0℃;1 例首发表现为呼吸困难,无发热。实验室检查均提示炎症指标升高,血培养阳性 4 例,主要致病菌为葡萄球菌属(甲氧西林敏感金黄色葡萄球菌 2 例、耐甲氧西林表皮葡萄球菌 1 例),1 例检出阴沟肠杆菌。所有患者超声心动图均检出赘生物:3 例仅累及右心,1 例仅累及左心,1 例同时累及左、右心;右心受累患者赘生物最大径为 29.1 mm,明显大于左心受累患者。治疗方面,所有患者均接受抗感染治疗,4 例拔除感染导管,1 例在抗感染基础上行三尖瓣生物瓣置换术。最终 3 例存活出院,2 例死亡;3 例存活者均为单纯右心受累,2 例死亡患者中 1 例累及左心、1 例同时累及左右心。

结论 HD 患者 CRIE 起病隐匿,临床表现不典型,发热为最常见症状,但部分患者可以呼吸困难

等非特异症状为首表现。赘生物累及部位是影响预后的重要因素,单纯右心受累者预后优于左心受累者,可能与左心感染更易引发致命性体循环栓塞有关。对于留置 CVC 的 HD 患者,即使无典型发热,亦应警惕 CRIE,尽早行超声心动图等系统评估;确诊后应及时拔除感染导管,对具备手术指征者应在充分评估风险后积极外科干预,以改善预后。

Integrative Bioinformatic and Real-World Data Analysis Reveal Mechanistic Associations between Letermovir Prophylaxis and EBV Reactivation after Allogeneic Hematopoietic Stem Cell Transplantation

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Background Letermovir, a CMV-specific terminase inhibitor, has become an essential prophylactic agent in allo-HSCT. However, our previous research and other evidences have linked its use to increased Epstein-Barr virus (EBV) reactivation

Methods We integrated pharmacoinformatics, transcriptomic validation, and real-world clinical data to investigate letermovir-EBV associations, identifying hub targets and key pathways, and constructing a prediction model.

Results Fifty-eight overlapping targets were identified. Hub proteins included EGFR, ERBB2, HIF1A, PPARG, PTGS2 and STAT3, with molecular docking indicating stable binding to letermovir. Enrichment analysis identified hypoxia response, immune/inflammatory, and endothelial/angiogenic pathways. GEO datasets confirmed stage-specific expression of overlapping and hub gene during EBV reactivation.

Clinically, patients receiving letermovir prophylaxis after HSCT had higher rates of EBV events. Risk factors for EBV infection included early elevation of thrombin-antithrombin complex (TAT), D-dimer, and pro-inflammatory cytokines among LTV group patients, different from those without letermovir. A prediction model demonstrated good performance and clinical utility, stratifying patients into high- and low-risk groups.

Conclusion The use of letermovir for prophylaxis may contribute to a higher risk of EBV reactivation post allo-HSCT by disrupting key biological pathways involved in hypoxia, inflammation, and endothelial function. Our integrative model facilitates early identification of patients at high risk of EBV reactivation.

Development of A Prediction Model for Adverse Events During Hospitalization in Patients with Active Malignant Tumors Complicated with Acute Pulmonary Embolism

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Background Patients with active malignancy complicated by acute pulmonary embolism (APE) are at high risk of poor in-hospital outcomes, but a simple prediction tool for this population is lacking

Methods We retrospectively enrolled hospitalized patients with active malignancy and APE at Qingdao Municipal Hospital between January 2020 and October 2025. The primary outcome was in-hospital adverse events, defined as a composite of in-hospital death and clinical deterioration. Candidate variables were screened using the Boruta algorithm, followed by collinearity assessment. Independent predictors were identified by multivariable logistic regression and used to

construct a nomogram. Model performance was evaluated by receiver operating characteristic (ROC) analysis, calibration curve, Hosmer–Lemeshow test, decision curve analysis, and clinical impact curve.

Results A total of 203 patients were included, of whom 41 (20.2%) developed in-hospital adverse events, including 21 deaths and 20 cases of clinical deterioration. Boruta feature selection initially identified seven candidate variables. After collinearity assessment, neutrophil count was excluded because of significant collinearity with white blood cell count. Multivariable logistic regression identified neutrophil-to-lymphocyte ratio (NLR), prothrombin time (PT), lactate, and $\text{PaO}_2/\text{FiO}_2 \leq 300$ as independent predictors of in-hospital adverse events. A nomogram based on these four variables showed good discrimination, with an area under the ROC curve of 0.821 (95% CI, 0.743–0.900). Internal validation using 1,000 bootstrap resamples yielded a mean AUC of 0.822 (95% CI, 0.745–0.890). Calibration and clinical utility were also satisfactory.

Conclusion NLR, PT, lactate, and $\text{PaO}_2/\text{FiO}_2 \leq 300$ were independent predictors of in-hospital adverse events in patients with active malignancy and APE. The nomogram may be a useful tool for early risk stratification in this high-risk population.

Keywords acute pulmonary embolism; active malignancy; adverse events; nomogram; risk prediction;

Functional Identification of ST630 Staphylococcus Aureus Coexpressing Dual WTA As A “relay Station” for Horizontal Gene Transfer

null null

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Objective Horizontal gene transfer between

Staphylococcus aureus and coagulase-negative staphylococci (CoNS) is a key driver of the cross-species spread of antibiotic resistance and virulence genes. However, direct experimental evidence for the molecular mechanisms underlying this gene exchange remains limited. This study aims to verify whether ST630-type *S. aureus*, which co-expresses both RboP-GlcNAc and GroP0-GalNAc wall teichoic acids (WTAs), can serve as a phage-mediated “relay station” for gene transfer, and to preliminarily investigate the role of the tagN gene in this process

Methods Multiple clinical tagN⁺ ST630 *S. aureus* strains were collected and characterized. WTA glycosylation patterns were analyzed by native electrophoresis, ion-exchange chromatography (GLC/MS), and flow cytometry. Phage susceptibility and host range were determined using B-type phages (φ80, φ11) and L-type phage φ187. Plasmids carrying tarO or tagN gene fragments together with an erythromycin resistance marker were constructed. One-step and relay transduction assays were performed to examine the directional flow of genetic material among CoNS, dual-WTA *S. aureus*, and single-WTA *S. aureus*. The role of tagN in transduction was further validated using a tagN mutant

Results (1) Both native electrophoresis and GLC/MS analysis of WTA from ST630 strains confirmed the simultaneous presence of the RboP-GlcNAc and GroP-GalNAc WTA glycoforms

(2) Phage host range analysis showed that several tagN⁺ clinical ST630 strains (WH114, WH211, WH60, WH99) could be simultaneously lysed by both B-type and L-type phages, indicating that their cell surfaces co-express both WTA glycoforms and thus possess the receptor conditions necessary for a “relay station”.

(3) Plasmid transduction experiments showed that φ187 could transfer the plasmid from WH119 (which expresses only GroP-GalNAc WTA) or the CoNS strain SE1457 into the dual-WTA strain WH99; subsequently,

φ80 could further transfer the same plasmid into WH222 (which expresses only RboP-GlcNAc WTA). This aligns with the relay transfer pathway: “CoNS/single-WTA *S. aureus* → relay station → another single-WTA *S. aureus*”.

(4) Deletion of the tagN gene caused the ST630 strain WH99 to lose GroP-GalNAc WTA expression, rendering it unable to be infected by phage φ187, and the corresponding φ187-mediated transduction was also abolished. This indicates that tagN is a key gene for maintaining the “relay station” function.

Conclusion This study provides, for the first time, a complete chain of experimental evidence demonstrating that certain tagN⁺ ST630 *S. aureus* strains co-expressing dual WTAs can serve as phage-mediated “relay stations” for horizontal gene transfer, enabling directional gene flow between CoNS and distinct *S. aureus* subgroups. The tagN gene is a core functional element in this process and holds promise as a dual target for both diagnosing “relay station” strains and developing novel anti-infection intervention strategies

Th2 Bias and T-cell Exhaustion Characterize The Immunopathology of Non-tuberculous Mycobacterial Pulmonary Disease

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Non-tuberculous mycobacterial pulmonary disease (NTM-PD) is an escalating global health concern with poorly defined immunological mechanisms, necessitating comprehensive profiling to guide therapeutic advances. We collected peripheral blood mononuclear

cells (PBMCs) from 28 treatment-naïve NTM-PD patients (19 *Mycobacterium avium* complex (MAC), 9 *Mycobacterium abscessus* (MAB)) and 27 age- and sex-matched healthy controls, employing mass cytometry (CyTOF) with a 42-marker panel for high-dimensional immune analysis and Luminex multiplex assays for cytokine measurement. Statistical analyses using recursive feature elimination (RFE) and random forest modeling identified predictive immune markers, while an in vitro murine macrophage model infected with *M. abscessus* or MAC, benchmarked against lipopolysaccharide (LPS) stimulation, evaluated chemokine production. NTM-PD patients displayed significant immune shifts, including increased classical monocytes (CD14+CD16-), reduced NKT-like cells (CD3+CD56+), and elevated T-cell exhaustion markers (PD-1, TOX), alongside a notable shift in the Th1/Th2 balance characterized by heightened IL-13. Elevated levels of IFN- γ -inducible chemokines CXCL9 and CXCL10 coexisted with this Th2-biased signature, suggesting a complex, dysregulated inflammatory state. A predictive model integrating immune cell frequencies and cytokine profiles achieved robust diagnostic accuracy (AUC = 0.922) with prognostic potential. In vitro, macrophages infected with either *M. abscessus* or MAC produced high levels of CXCL9 and CXCL10, comparable to classical LPS stimulation, highlighting a highly conserved cellular source for these chemokines. These findings propose an observational immunological framework wherein T-cell exhaustion and a Th2-biased immune microenvironment strongly correlate with NTM-PD pathogenesis. Within this systems-level context, CXCL9, CXCL10, and IL-13 emerge as potential immunological indicators and candidate therapeutic targets, while the multiparametric predictive model offers a foundational approach for tailored risk stratification.

克拉霉素与阿奇霉素在住院儿童社区获得性肺炎中的疗效比较：一项回顾性队列研究

田想想

天津市儿童医院

目的 比较克拉霉素与阿奇霉素作为初始经验性大环内酯类治疗方案在住院儿童社区获得性肺炎（CAP）中的临床疗效及短期转归，为儿童 CAP 中大环内酯类药物的合理选择提供临床依据。

方法 采用单中心回顾性队列研究设计，连续纳入 2024 年 8 月至 2025 年 6 月于天津市儿童医院呼吸科住院、经胸部影像学证实并符合纳入标准的 CAP 患儿 664 例。根据入院时初始经验性口服大环内酯治疗方案分为阿奇霉素组 459 例和克拉霉素组 205 例。主要结局为住院时间（LOS），以“出院”为终点事件，采用 Cox 比例风险回归模型评估两组出院速度差异，并纳入年龄、性别、院前病程、生命体征、临床表现、影像学特征、实验室指标及基础疾病等协变量进行调整。考虑心率和呼吸频率的年龄依赖性，模型中加入年龄与心率、年龄与呼吸频率的交互项。进一步采用 Schoenfeld 残差检验比例风险假定，并以限制性平均住院时间（RMST）、倾向评分匹配及按方案集敏感性分析验证结果稳健性。

结果 全队列中，阿奇霉素组与克拉霉素组住院时间中位数分别为 97 h 和 95 h。多变量 Cox 模型显示，克拉霉素相对于阿奇霉素的调整后出院风险比为 1.02（95%CI: 0.87~1.21, $P=0.803$ ），提示两组出院速度差异无统计学意义。RMST 分析显示，在 $\tau=7$ d 和 $\tau=10$ d 时，两组平均住院时间差异均较小且无统计学意义。倾向评分匹配后共纳入 360 例患儿，两组各 180 例，匹配后基线特征平衡良好；匹配队列中克拉霉素相对于阿奇霉素的 HR 为 1.05（95%CI: 0.85~1.29, $P=0.677$ ）。按方案集及敏感性分析结果与主要分析基本一致。随访 403 例患儿中，两组自报恢复率及 30 d 再住院风险差异亦无统计学意义。亚组分析总体未发现稳定的效应异质性，

仅急性喘鸣亚组提示探索性差异,但受样本量限制,需谨慎解释。

结论 在本单中心住院儿童 CAP 队列中,克拉霉素与阿奇霉素在缩短住院时间、促进出院及改善短期随访转归方面总体疗效相当,未观察到具有明确统计学或临床意义的优势差异。临床选择大环内酯类药物时,应结合患儿年龄、病原学特点、用药依从性及本地区耐药流行情况综合判断。

关键词: 儿童;社区获得性肺炎;克拉霉素;阿奇霉素;大环内酯类;住院时间;倾向评分匹配

Global Research Trends in Sepsis Bundle Management: A Bibliometric and Visualized Analysis

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Background Sepsis is a life-threatening syndrome associated with high morbidity and mortality. Implementing the Surviving Sepsis Campaign (SSC) bundle recommendations within strict time constraints presents a significant challenge for clinicians. However, there is limited comprehensive bibliometric analysis regarding the evolution of SSC bundle-related research, global collaborations, and thematic trends

Objective To explore the evolution of clinical research on the SSC bundle, this study employs bibliometric and knowledge visualization analysis to identify global research trends and hotspots in the application of SSC guideline recommendations

Methods Publications related to sepsis bundles from January 1, 2000, to March 12, 2025, were retrieved from the Web of Science Core Collection. Bibliometric analysis, scientific mapping, and performance evaluations were conducted using Bibliometrix (R package,

version 3.1.4), VOSviewer (version 1.6.16), and CiteSpace (version 5.8.R6)

Results A total of 1,047 publications were included, collectively receiving 101,586 citations. United States was the most productive country, contributing 429 publications (40.97%) and 30,559 citations. University of Pittsburgh was the leading institution with 36 publications, while Levy MM emerged as the most prolific author with 23 publications and 11,070 citations. Keyword co-occurrence revealed five anchor themes: evidence-based bundle implementation and compliance strategies; high-risk settings and populations such as emergency care and pediatrics; infection sources dominated by community-acquired pneumonia; major complications led by acute kidney injury; and real-world evaluations of SSC bundles across diverse clinical environments

Conclusions This bibliometric analysis provides a comprehensive overview of global research on sepsis bundles. It highlights sustained interest in sepsis bundle application strategies, particularly in vulnerable populations, infection sources, and complications, as well as the methodologies used in evidence-based clinical trials

Keywords Sepsis, Surviving Sepsis Campaign, Bundle, Bibliometric analysis, Knowledge Visualization

脓肿分枝杆菌复合群感染者 miRNA 差异表达的研究

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目的 针对脓肿分枝杆菌复合群(MABC)高度耐药及宿主免疫应答异常的临床困境,本研究系统

分析 MABC 骨与软组织感染患者外周血 miRNA 表达谱特征,筛选差异表达 miRNA 并解析其潜在调控网络,以期 MABC 感染的精准诊疗及机制研究提供依据。

方法 采集 MABC 骨与软组织感染患者及健康对照的外周血,通过小 RNA 测序筛选差异表达 miRNA,预测靶基因,并进行 GO 与 KEGG 富集分析及蛋白互作 (PPI) 网络构建。

结果 MABC 骨与软组织感染可诱导患者外周血 miRNA 发生特征性改变。感染组与健康对照组比较共筛选出 16 个差异表达 miRNA,感染期与恢复期比较共筛选出 49 个差异表达 miRNA,其中 hsa-miR-142-5p 和 hsa-miR-144-5p 在感染期均显著上调,并在恢复期下降。其靶基因富集于自噬-mTOR、TGF- β /MAPK 炎症及破骨细胞分化等信号通路,PPI 网络鉴定出 EP300、MAPK1、PTEN、CDC42 和 RHOA 等关键枢纽基因。

结论 MABC 骨与软组织感染可诱导宿主血清中 miRNA 谱的特征性改变,其中 hsa-miR-142-5p 和 hsa-miR-144-5p 与感染状态密切相关。进一步分析表明,其靶基因涉及 EP300、MAPK1、PTEN、CDC42 和 RHOA 等关键分子,并主要富集于自噬-mTOR、TGF- β /MAPK 炎症及破骨细胞分化等信号通路。上述 miRNA-靶基因-信号通路构成的调控网络可能在宿主免疫反应、慢性炎症维持及骨组织损伤过程中发挥作用。

鼻纤毛摆动发电短纤维无创入脑靶向沉默 FPR1 重塑小胶质细胞稳态

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小胶质细胞稳态失衡是多种脑部疾病神经炎症及神经元损伤的核心病理基础,探寻关键干预靶点并建立无创调控小胶质细胞功能稳态的治疗策略,

已成为突破中枢神经系统疾病精准干预瓶颈的关键。尽管基因调控在干预小胶质细胞稳态方面极具潜力,但受限於血脑屏障 (BBB) 阻隔及传统鼻腔给药的被动扩散效率低等瓶颈,药物难以在脑内有效靶向富集。本研究通过组学分析筛选并验证出驱动小胶质细胞促炎极化的关键靶点 FPR1,并据此构建负载 FPR1-siRNA@MG1-LNP 的压电短纤维鼻腔递送系统,该系统具备小胶质细胞靶向性并可有效沉默 FPR1 表达。其利用鼻腔呼吸气流驱动纤毛节律摆动,将机械能转化为局域微电场,引导并保护基因以“电响应-主动迁移”机制绕过血脑屏障,实现对小胶质细胞主动靶向干预。通过免疫印记等研究表明,FPR1 在脓毒症小胶质细胞中高表达并介导促炎反应,靶向沉默 FPR1 表达显著抑制了小胶质细胞焦亡,减少了炎症介质释放,并有效缓解了神经元损伤及其介导的认知功能障碍。转录组学测序进一步验证了沉默 FPR1 表达减轻神经损伤的分子基础。本研究首次提出并验证了“电响应无创入脑-小胶质细胞靶向-基因调控”的协同治疗策略,通过主动运输的压电纳米载体高效递送 FPR1-siRNA@MG1-LNP,有效阻断了 SAE 的神经炎症进程,为 SAE 及其他中枢神经系统疾病的非侵入性精准治疗提供了创新思路与技术平台。

自噬在支气管扩张症中性粒细胞炎症中的作用及机制

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背景 慢性感染、中性粒细胞炎症及气道结构破坏是支扩症的核心病理改变,自噬在调控急性肺部感染性疾病、慢性阻塞性肺疾病、哮喘等多种肺部疾病的气道感染、炎症反应等过程中均发挥着重

要作用。然而, 自噬在支扩症患者中性粒细胞炎症中的作用及机制仍未完全清楚。

目的 评估支扩症中性粒细胞的自噬特征, 探讨自噬对支扩症中性粒细胞炎症的影响及作用机制。

方法 收集支扩症患者及健康对照者痰与外周血中性粒细胞, 采用 Western Blot、免疫荧光及透射电镜等评估自噬水平。利用蛋白组测序阐明自噬激活后蛋白及通路的关键变化, 构建支气管上皮细胞气液培养模型, 加入氯喹、3-MA、雷帕霉素干预后的中性粒细胞条件培养基, 利用 SAVA 系统检测其对纤毛摆动频率的影响, 进行 HE 染色评估形态学特点。利用蛋白组学挖掘调控支扩症中性粒细胞自噬的机制, 借助分子对接技术和免疫共沉淀探讨 HMGB1、Beclin-1 相互作用, 并检测抑制 HMGB1 后对自噬及 NETs 的影响。

结果 与健康对照相比, 支扩症患者痰及外周血中性粒细胞 LC3B II/I 比值升高、p62 水平下降, 自噬溶酶体数量增加。LPS+Nigericin 可诱导中性粒细胞自噬激活并促进 NETs 释放; 氯喹、3-MA 抑制自噬后 NETs 形成减少, 而雷帕霉素激活自噬则促进 NETs 释放。此外, LPS+Nigericin 可诱导明显中性粒细胞炎症, 其条件培养基刺激气道上皮细胞后, 可降低纤毛摆动频率, 加重支气管结构破坏; 雷帕霉素干预中性粒细胞后会加重上述过程, 而抑制自噬则可减轻上述病理改变。

蛋白组学显示 3-MA 抑制自噬后 HMGB1 下调最显著, 分子对接和免疫共沉淀技术证实其与 Beclin-1 存在相互作用; 在体外抑制 HMGB1 可下调 Beclin-1 及 LC3B II/I, 升高 p62 水平, 并减少 NETs 释放。此外, 自噬相关的 LC3B、HMGB1 蛋白与 NETs 中的 CitH3 共定位明显增加。

结论 LPS 联合 Nigericin 刺激可促使中性粒细胞 HMGB1 表达上调, 并通过与 Beclin-1 结合激活自噬。自噬激活后既可促进组蛋白瓜氨酸化与 NE 表达, 其关键分子 LC3B、HMGB1 亦可参与 NETs 的组装和形成, 并随着 NETs 的释放而释放出去反向激活自噬, 形成正反馈环路, 最终造成自噬水平失衡、NETs 异常释放增加, 从而介导中性粒细胞炎

症级联放大与气道结构损伤。

关键词: 支气管扩张症, 中性粒细胞炎症, 自噬

Macrophage Pyroptosis Induced by Nontuberculous Mycobacteria Supports Protective Host Immunity

null null

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Background Nontuberculous mycobacteria (NTM) are intracellular pathogens that persist in macrophages and cause increasingly recognized pulmonary disease. Inflammasome-driven pyroptosis can restrict intracellular infection through gasdermin D-mediated pore formation and inflammatory mediator release, but whether NTM engage this pathway and whether pyroptosis benefits host defense remain unclear

Methods Mouse bone marrow-derived macrophages (BMDMs) were infected with rough and smooth *Mycobacterium abscessus* (Mab-R and Mab-S), *M. intracellulare*, *M. avium*, or *M. kansasii*. Pyroptosis-related transcriptional programs, cell death, inflammasome activation, gasdermin D cleavage, cytokine release, and pathway priming were assessed by RNA sequencing, PI/Sytox staining, immunoblotting, and supernatant assays. AIM2-, NLRP3-, and NLRC4-dependent secondary stimuli were used to define inflammasome specificity. The functional role of pyroptosis was tested in Casp1-deficient macrophages and in a Mab-R pulmonary infection model using wild-type and Casp1-deficient mice.

Results Mab infection enriched infection- and inflammation-related pathways, with prominent upregulation of NOD-like receptor signaling. Pyroptosis and

PANoptosis-associated genes, including Nlrp3, Caspase1, Caspase7, Aim2, Zbp1, Mefv, and Il1b, were increased, indicating inflammasome priming. Across five NTM species, infection caused limited macrophage death and modest gasdermin D cleavage, without obvious activation of caspase-1, caspase-7, or caspase-8. However, NTM markedly increased inflammasome-related proteins, including caspase-1, GSDMD, ASC, AIM2, Pyrin, ZBP1, caspase-7, and caspase-8. NTM-primed macrophages showed selective amplification of AIM2-dependent pyroptosis: Poly(dA:dT) enhanced caspase-1 and GSDMD cleavage, IL-1 β /IL-18 release, and Sytox positivity after Mab-R infection, whereas flagellin had little effect and LPS-ATP-induced NLRP3 activation was attenuated. Mechanistically, Mab infection upregulated Aim2 at RNA and protein levels while reducing P2rx7 expression. Poly(dA:dT) similarly enhanced pyroptotic responses after Mab-S, *M. intracellulare*, *M. avium*, and *M. kansasii* infection, suggesting a conserved AIM2-primed state. Caspase-1 deficiency abolished Poly(dA:dT)-induced pyroptosis in NTM-infected macrophages. In vivo, Casp1-deficient mice infected intratracheally with Mab-R exhibited greater body-weight loss, more pronounced leukopenia, and reduced induction of IL-18 and IFN- γ compared with wild-type mice.

Conclusion NTM infection weakly executes macrophage pyroptosis but robustly primes an AIM2-centered, caspase-1-dependent pyroptotic program. Loss of caspase-1 compromises host responses during Mab infection, supporting a protective role for macrophage pyroptosis in anti-NTM immunity and identifying AIM2-caspase-1-GSDMD signaling as a potential host-directed therapeutic axis.

Activated Cytotoxic T Lymphocytes in Individual with HIV and Opportunistic Infections Display Distinct Activation Profiles

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Purpose Peripheral blood immunophenotyping of lymphocyte subtypes may provide important evidence for identifying and treating opportunistic infections in people with HIV (PWH). This study was designed to characterize lymphocyte subtypes between PWH with opportunistic infections and those without. This study aim to contribute to a better understanding of the immunological mechanisms involved in opportunistic infections in people with HIV

Methods We recruited PWH from the Guangzhou Eighth People's Hospital in Guangzhou between 1 January, 2023 and 1 September, 2025. Participants were grouped into opportunistic infections (OI, CD4+T cell count <200) and non-opportunistic infections (Non-OI-1, <200 and Non-OI-2, $\geq$ 200). Flow cytometry was utilized to analyze the profiles of peripheral blood lymphocyte subtypes. A total of 441 PWH were included, comprising 207 individuals with opportunistic infections and 234 without opportunistic infections.

Results The number of total B and T lymphocytes, natural killer cells, natural killer T-like cells and the percentage of naive helper T lymphocytes were decreased in OI group than those in both Non-OI-1 and Non-OI-2 groups. However, the percentages of memory helper T lymphocytes and suppressor T lymphocytes were increased in OI group. Curiously, we observed that

the percentages of activated T lymphocytes in OI group were higher than others while the percentages of activated helper T lymphocytes were lower compared to others. More notably, we found that the OI group showed a significant increase in the proportion of activated cytotoxic T lymphocytes.

Conclusion Activated cytotoxic T lymphocytes in individual with HIV and opportunistic infections display distinct activation profiles. The proportions of activated cytotoxic T lymphocytes (CD8⁺ CD38⁺/CD8⁺) and activated cytotoxic T lymphocytes (CD8⁺ HLA-DR⁺/CD8⁺) in OI group were significantly higher than those in both Non-OI-1 and Non-OI-2 groups. The percentages of activated helper T lymphocytes (CD4⁺ HLA-DR⁺/CD4⁺) and cytotoxic T lymphocytes (CD8⁺ CD28⁺) in OI group were significantly lower than other two groups.

Keywords HIV/AIDS; Opportunistic infections; lymphocyte subtypes

A Mouse Model of Bronchiectasis-like Airway Remodeling 1 Induced by Repeated 2 Intratracheal Instillation of Pseudomonas Aeruginosa-laden Agar Beads 3 4 Mingqing

null null, Ming-Qing Lu,
GZMU

Background Bronchiectasis is characterized by irreversible airway dilatation, persistent inflammation, and recurrent infection. Chronic colonization with *Pseudomonas aeruginosa* is associated with more severe disease, yet robust small-animal models that recapitulate both persistent infection and airway structural remodeling remain limited

Methods Male C57BL/6 mice received weekly

intratracheal instillations of agar beads containing *P. aeruginosa* PAO1 (1×10^5 – 1×10^8 CFU/mL) for up to 8 weeks. Survival, body weight, and lung bacterial burden (CFU/lung) were assessed. Airway remodeling was quantified at week 8 using histological bronchus-to-artery (Br/Art) morphometry, and micro-computed tomography (micro-CT) was used to evaluate the detectability of airway dilatation. Lung function was measured at week 8 using an invasive small-animal pulmonary function system.

Results The highest inoculum (1×10^8 CFU/mL) caused 100% mortality within 17 days. The 1×10^7 CFU/mL regimen achieved acceptable survival and chronic infection, with bacterial burdens ranging from 3.6 to 7.9 log₁₀ CFU/lung among culture-positive mice during the 8-week protocol. Histology in the 1×10^7 CFU/mL group demonstrated marked peribronchial inflammation and increased Br/Art ratios for airway diameter (2.58 ± 0.21 vs. 1.78 ± 0.15 in controls; post-hoc $P = 0.03$) and perimeter (2.88 ± 0.24 vs. 1.99 ± 0.17 ; post-hoc $P = 0.03$), predominantly in peripheral airways (adjacent artery diameter < 150 μ m). On micro-CT at week 8, focal bronchial dilatation was detected in 1 out of 6 scanned mice in the 1×10^7 CFU/mL group, whereas most mice showed no definitive gross structural changes despite histological evidence of remodeling. Lung function parameters did not differ significantly at week 8.

Conclusion Repeated intratracheal instillation of *P. aeruginosa*-laden agar beads produces a reproducible mouse model of chronic airway infection and bronchiectasis-like pathological remodeling that predominantly involves peripheral airways. Histological morphometry is more sensitive than micro-CT for detecting early-stage, microscopic airway widening in this model.

Endothelial Activation and Stress Index Predicts Sepsis-induced Myocardial Injury and 28-day Mortality: A MIMIC-IV Cohort Study

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Objective Sepsis is frequently complicated by myocardial injury and short-term mortality, yet simple bedside indices capturing endothelial stress may improve early risk stratification. We aimed to evaluate whether the Endothelial Activation and Stress Index (EASIX) is associated with sepsis-induced myocardial injury (SIMI) and 28-day mortality in critically ill patients with sepsis.

Methods Using the Medical Information Mart for Intensive Care IV (MIMIC-IV) database, adult patients meeting Sepsis-3 criteria were included. EASIX was calculated from the first available lactate dehydrogenase, creatinine, and platelet count, and patients were categorized into quartiles (Q1–Q4). Multivariable regression models were used to evaluate independent associations of log-transformed EASIX with outcomes. Restricted cubic spline analyses were used to explore dose–response relationships, and discrimination performance was evaluated using AUC with DeLong’s tests.

Results Among 921 eligible patients, higher EASIX quartiles were characterized by greater illness severity and renal dysfunction and were associated with increased 28-day mortality (24.4% in Q1 vs. 51.4% in Q4) and higher SIMI incidence (22.9% in Q1 vs. 54.9% in Q4). In fully adjusted models, log(EASIX) was still independently associated with 28-day mortality (hazard ratio 1.105, 95% confidence interval 1.002–1.217) and SIMI (odds ratio 1.389, 95% confidence interval 1.203–

1.614). Restricted cubic splines demonstrated significant overall associations without evidence of non-linearity. Log(EASIX) showed moderate discrimination for 28-day mortality (AUC 0.656) and modest discrimination for SIMI (AUC 0.612), outperforming several conventional severity scores for SIMI prediction.

Conclusion EASIX is a readily available index independently associated with both sepsis-induced myocardial injury and 28-day mortality and may complement established severity assessments for early risk stratification in sepsis.

Keywords Sepsis; EASIX; SIMI; Cardiac troponin T (cTnT); 28-day mortality; Risk stratification; Intensive care unit (ICU); MIMIC-IV

内皮细胞发育调节蛋白-1 调控中性粒细胞炎症与气道修复在支气管扩张症治疗中的应用

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支气管扩张症是一种以支气管不可逆性异常扩张为特征的疾病，典型病理变化包括慢性化脓性炎症、黏液清除功能障碍及气道结构破坏。研究表明，中性粒细胞驱动的气道慢性炎症是疾病恶性循环的关键环节，过度激活的中性粒细胞通过释放活性氧、溶酶体蛋白酶及形成 NETs，对气道上皮和弹性纤维等结构造成不可逆损伤。现有干预策略如 DPP-1 抑制剂等虽能部分缓解中性粒细胞性炎症，但未能同时针对炎症、损伤及修复多个关键环节。

内皮细胞发育调节蛋白-1 (DEL-1) 是一种细胞外基质蛋白，通过竞争性阻断中性粒细胞表面整合素 LFA-1 与内皮细胞间粘附分子-1 (ICAM-1) 的结合，抑制中性粒细胞的跨内皮迁移与募集。在牙周

炎、哮喘、慢性阻塞性肺疾病等炎症模型中, DEL-1 表达均显著下调, 且其缺失与疾病严重程度相关。然而, DEL-1 在支气管扩张症中的作用尚未得到充分研究, 现有研究对其功能的认识主要局限于"抑制中性粒细胞募集"这一环节, 未能深入探讨其对已浸润中性粒细胞炎症效应的调控, 以及其对气道上皮结构与功能的修复作用。

本研究通过临床标本-体外模型-体内模型探讨重组 DEL-1 蛋白在支气管扩张症中的治疗价值。研究发现支气管扩张症患者肺组织及痰液中 DEL-1 表达显著下调, 且 DEL-1 与 LFA-1 的共定位减少、LFA-1 与 ICAM-1 的共定位增加, 提示 DEL-1 缺失导致中性粒细胞黏附增加。在体外实验中, 外源性加入重组 DEL-1 蛋白可显著抑制 LPS+Nigericin 刺激下健康人及支扩症患者中性粒细胞中 IL-6、IL-1 β 、TNF- α mRNA 表达, 并有效减少 NETs 形成。同时 DEL-1 能够恢复支气管扩张症患者气道上皮细胞的纤毛摆动频率、改善上皮屏障完整性, 展现出抗炎与修复的双重功能。

体内实验中, 构建支气管扩张症小鼠模型, 并给予重组 DEL-1 蛋白干预。结果显示 DEL-1 治疗组小鼠气道壁厚度显著减轻、炎症细胞浸润明显减少; PAS 染色证实杯状细胞增生与黏液分泌得到明显抑制; Masson 染色及间苯二酚碱性品红染色分别显示胶原沉积与弹性纤维含量显著恢复, 提示 DEL-1 能够有效促进气道细胞外基质的修复, 维持气道壁结构完整性。

本研究将 DEL-1 蛋白应用于支气管扩张症的多环节干预, 突破了传统治疗方法单一靶点的局限, 实现了"抑制中性粒细胞炎症-减轻组织损伤-促进气道修复"的整合型治疗策略。

Regional Airflow Obstruction Is Associated with Reduced Aerosol Deposition in Non-cystic Fibrosis Bronchiectasis: A Prospective Multimodal EIT and PET/CT Study

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Background Inhaled therapies are widely used in bronchiectasis, but their effectiveness depends on adequate drug delivery to diseased lung regions. The functional determinants of impaired aerosol deposition in non-cystic fibrosis bronchiectasis remain incompletely understood. We aimed to assess regional aerosol deposition in patients with non-cystic fibrosis bronchiectasis and examine its association with regional airflow obstruction measured using electrical impedance tomography (EIT)

Methods In this prospective imaging study, adults with non-cystic fibrosis bronchiectasis were enrolled at the First Affiliated Hospital of Guangzhou Medical University. Participants underwent high-resolution CT for structural assessment, EIT during forced

vital capacity manoeuvres for regional functional evaluation, and PET/CT after inhalation of ^{18}F -NaF aerosol for quantification of regional deposition. Regional analyses compared bronchiectatic and non-bronchiectatic lung regions within the same participants. The primary outcome was regional aerosol deposition quantified by PET/CT. The primary explanatory variables were EIT-derived regional FEV1/FVC and regional time to 75% of forced vital capacity (T75). Associations between regional aerosol deposition, structural bronchiectasis, and these EIT-derived functional indices were evaluated using Pearson correlations and linear mixed-effects models

Findings 52 patients with bronchiectasis were enrolled. The mean age was 69 ± 8 years, 32 (61.5%) were female, and 23 (44.2%) had a mild-to-moderate obstructive ventilatory defect. Across 122 paired planar regions of interest from 50 participants, aerosol deposition was significantly lower in bronchiectatic than in non-bronchiectatic regions (SUVmean 0.37 ± 0.12 vs. 1.13 ± 0.47 ; mixed-effects model $\beta -0.76$, 95% CI -0.85 to -0.68 ; $p < 0.001$). Within the belt-centred EIT sensitivity volume, predominantly bronchiectatic quadrants had greater airflow obstruction than non-bronchiectatic quadrants, with lower EIT-derived FEV1/FVC (0.50 ± 0.16 vs. 0.82 ± 0.14 ; mean difference -0.32 , 95% CI -0.37 to -0.26 ; $p < 0.001$) and longer T75 (1.76 ± 0.78 s vs. 0.52 ± 0.35 s; 95% CI 0.99 to 1.49 ; $p < 0.001$). Regional aerosol deposition correlated positively with EIT-derived FEV1/FVC and negatively with T75 in both bronchiectatic and non-bronchiectatic regions. In mixed-effects regression, inclusion of EIT metrics attenuated the bronchiectatic region coefficient from -0.56 to -0.25 , corresponding to an approximate 56% reduction in effect size.

Interpretation In non-cystic fibrosis bronchiectasis, aerosol deposition is reduced in bronchiectatic

lung regions and is strongly associated with regional airflow obstruction assessed by EIT. These findings suggest that regional functional obstruction is an important determinant of heterogeneous inhaled aerosol delivery and support further evaluation of EIT as a bedside tool to guide personalised inhaled therapy.

NLRC4 蛋白肠道特异性过表达小鼠的构建与验证

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目的 NLRC4 蛋白属于 NOD 样受体 (NLR) 家族, 是定位于细胞质内关键的模式识别受体, 在宿主识别胞内菌、激活炎症小体及诱导细胞焦亡的天然免疫中起至关重要的作用, 同时具有独立于其经典炎症功能的潜在抗癌作用。

方法 本研究拟构建肠道特异性 NLRC4 过表达小鼠, 并采用肠炎沙门菌感染小鼠对其免疫功能进行活体验证。方法 采用 CRISPR/Cas9 基因编辑技术, 将 NLRC4 基因导入 C57BL/6 小鼠基因组的特定基因位点, 并与肠道上皮特异性 Cre 小鼠杂交, 构建肠道特异性 NLRC4 过表达小鼠模型。通过提取子代小鼠组织进行 PCR 方法确认 NLRC4 过表达小鼠构建成功。采用沙门菌口服感染小鼠, 验证 NLRC4 过表达是否对沙门菌肠道感染具有免疫保护或损伤作用。

结果 PCR 方法确认 NLRC4 肠道特异性过表达小鼠构建成功。在沙门菌活体感染实验中, NLRC4 过表达小鼠较野生型小鼠不仅生存时间延长, 粪便细菌负荷量减少, 提示 NLRC4 过表达对沙门菌肠道感染具有免疫保护作用。

结论 本研究在国际上首次报道了 NLRC4 肠道特异性过表达小鼠模型构建成功。此模型将为 NLRC4 基因功能、肠道分子免疫、相关肿瘤性和风

湿免疫性疾病研究提供重要的基础平台。

书面交流

细菌真菌感染的病原诊断技术

呼吸道五联检在成人急性呼吸道感染中的诊断价值

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目的 分析呼吸道五联检在成人急性呼吸道感染（ARI）中的诊断价值。

方法 回顾性分析 2024 年 1 月至 2024 年 12 月就诊于天津医科大学总医院的 28799 例成人 ARI 患者的临床资料，采用胶体金法对 5 种常见呼吸道病原体包括肺炎支原体（MP）、肺炎衣原体（CP）、呼吸道合胞病毒（RSV）、腺病毒（ADV）和柯萨奇病毒 B 组（CVB）IgM 抗体进行检测。统计以上患者的抗体阳性率；基于性别、年龄、季节差异，比较各类抗体的阳性率。

结果 3543 例患者病原体抗体检测为阳性（即全血中检测到 5 种病原体对应抗体中的一种或数种），阳性率为 12.30%；分项检出结果显示，阳性率前三位为 MP、RSV 和 ADV，依次为 9.48%、2.65% 和 0.61%。3543 例阳性病例中，2 种及以上抗体阳性共 181 例，占比 5.11%，阳性率为 0.63%。其中，以 2 种抗体阳性为主，共 163 例，占比 90.06%；阳性率前三位依次为 RSV+ADV（39.88%）、MP+RSV（39.26%）和 MP+ADV（12.27%）。女性患者的抗体阳性率高于男性（13.40% vs 10.69%），差异具有统计学意义（ $P < 0.001$ ）。MP 抗体在女性患者中的阳性率明显高于男性患者（10.82% vs 7.52%），差异具有统计学意义（ $P < 0.001$ ）；其余抗体在不同性别患者中的阳性率虽有差异，但均无统计学意义。14 岁~17 岁患者抗体阳性率最高，为 24.16%。随着年龄增长，MP 抗体阳性率明显下降，而 RSV、ADV 抗体阳性率明显升高。MP 和 RSV 抗体阳性多见于冬春季，余全年散发无明显季节性。

结论 2024 年本院行呼吸道五联检的成人 ARI 患者以 MP 和 RSV 抗体检出为主，呼吸道病原体抗

体阳性率在不同性别、年龄和季节间存在一定差异。

关键词 急性呼吸道感染、肺炎支原体、呼吸道合胞病毒、IgM 抗体

G 实验联合真菌培养在侵袭性真菌病诊断中的价值及病原菌分布特征

张

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目的 探究患者 1, 3- β -D 葡聚糖（G 实验）定量结果联合真菌培养在侵袭性真菌病（invasive fungal disease, IFD）中的诊断价值及病原菌分布特征。

方法 回顾性分析 2023 年 8 月到 2025 年 5 月在空军军医大学第二附属医院就诊的患者共 712 例，按照侵袭性霉菌病诊断指南分为 IFD 组 178 例与非 IFD 组 534 例。比较两组患者的基线特征，G 实验以及真菌培养结果，绘制受试者工作特征（ROC）曲线评估诊断效能，分析 IFD 组患者病原菌构成以及不同类型的真菌感染患者 G 实验水平的差异。

结果 ①IFD 组年龄（ 60.02 ± 15.18 岁）显著高于非 IFD 组（ 55.52 ± 15.76 岁），差异具有统计学意义， P 值 < 0.05 。两组性别构成以及科室分布差异无统计学意义。②G 实验诊断 IFD 的 AUC 面积为 0.788，（95%CI:0.741-0.834, $p=0.024$ ），采用约登指数确定最佳截断值为 17.96pg/ml，对应灵敏度为 0.596，特异度为 0.974，约登指数为 0.57。③IFD 组 G 实验阳性率，真菌培养阳性率以及 G 实验检测结果均显著高于非 IFD 组，差异具有统计学意义， p 值均 < 0.01 。④G 实验单独检测的灵敏度为 59.56%，特异度为 97.38%，阳性预测值为 88.33%，阴性预测值为 87.84%；真菌培养单独检测的灵敏度为 92.70%，特异度为 97.95%，阳性预测值为 93.75%，阴性预测值为 97.57%；两者联合检测可将灵敏度提升至 99.44%，特异度为 98.88%，阳性预测值为 96.72%，阴性预测值为 99.81%。⑤IFD 组真菌培养

阳性 165 例,以念珠菌属为主(134 例),其次为曲霉属(21 例),另检出多种少见型真菌感染。念珠菌属感染者 G 试验水平显著低于曲霉属感染者,差异具有统计学意义, p 值 <0.01 。非 IFD 组患者真菌培养阳性 11 例,均为念珠菌属,考虑为定植菌。

结论 G 实验对 IFD 具有较好的诊断价值,但是单独应用诊断效能欠佳,与真菌培养联合检测可显著提升诊断灵敏度,特异度,阳性预测值与阴性预测值。IFD 病原菌感染类型以念珠菌属为主,曲霉属感染者 G 实验水平显著增高,可为临床上病原菌的预判提供参考。

肺肿块伴全身骨破坏就是肺癌?西北地区一例多重免疫抑制患者马尔尼菲篮状菌感染的诊治警示

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目的 马尔尼菲篮状菌(*Talaromyces marneffei*)主要流行于东南亚及中国南方省份(如广东、广西、云南),在西北地区极为罕见,且通常被视为 HIV 相关机会性真菌。本文报告宁夏地区 1 例无 HIV 感染的老年女性患者,经肺部影像学表现被初诊为“肺癌伴骨转移”,最终经病理及 t-NGS 确诊为马尔尼菲篮状菌肺炎,旨在探讨多重免疫抑制背景下非 HIV 患者罹患该菌的临床特征及诊疗策略。

方法 患者女性,68 岁,因“发热伴寒战 1 月余”入院。既往有原发性骨髓纤维化病史 5 年,长期口服芦可替尼(JAK 抑制剂)、醋酸泼尼松及沙利度胺;入院前 1 月先后感染新型冠状病毒及甲型流感病毒,此后持续高热,伴咳嗽、咳黄色粘痰、咽部剧烈疼痛及多发口腔溃疡。胸部 CT 示右肺下叶后基底段软组织肿块影,伴胸骨、部分椎体、双侧多发肋骨及左侧肩胛骨转移,临床高度怀疑周围型肺癌伴骨转移。先后行经皮肺穿刺及 EBUS-TBNA 获取组

织标本,分别送病理检查(含免疫组化)及 t-NGS 检测。

结果 t-NGS 示:马尔尼菲篮状菌序列数 130533 条,大肠埃希菌 352 条,前者为后者的 371 倍,确定为绝对优势病原体。病理:未见恶性细胞,免疫组化不支持肺癌及淋巴瘤。明确诊断后予两性霉素 B 胆固醇硫酸酯复合物(静脉+雾化,爬坡至 150mg/d)抗真菌联合头孢哌酮舒巴坦抗细菌感染,患者体温恢复正常,咽部溃疡明显缩小,症状显著缓解。

结论 马尔尼菲篮状菌感染突破传统地理分布,该病传统上被认为仅在南方省份流行,本例患者长期居住在西北宁夏,无南方生活史,提示该菌可能存在向北扩散趋势,或西北地区免疫抑制人群中存在未被识别的潜伏感染风险;马尔尼菲篮状菌肺部感染典型影像学表现为双肺弥漫斑点、磨玻璃、网格影,而本例表现为孤立性肿块伴全身多发骨破坏,特征与肺癌高度重叠,极易误诊;非 HIV 患者若存在多重免疫抑制因素(基础血液病、JAK 抑制剂、长期糖皮质激素、病毒感染),同样可成为马尔尼菲篮状菌的易感宿主;在混合感染背景下,t-NGS 的序列数比值有助于判断主导病原体,指导精准抗感染治疗。

关键词: 马尔尼菲篮状菌;西北地区;肺癌误诊;影像学不典型表现;骨髓纤维化;t-NGS

犬小孢子菌致脓癣型头癣 1 例及儿童头癣文献回顾性分析

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目的 总结儿童头癣的流行病学、病原学、实验室诊断及临床治疗特点,结合 1 例犬小孢子菌致脓癣型头癣病例报告,提高临床对儿童头癣,尤其是脓癣的早期识别与规范诊疗水平,降低误诊率与

后遗症发生率。

方法 检索中国知网(CNKI)2021 年 1 月 — 2026 年 4 月儿童头癣相关临床研究、指南及综述,进行系统性回顾性分析;同时报告 1 例 10 岁男性患儿以双侧头顶部脓肿为主要表现的犬小孢子菌头癣病例,结合真菌免疫荧光染色、真菌培养明确病原学诊断,总结诊疗要点。

结果 近 5 年儿童头癣以 3~7 岁学龄前儿童高发,男童多于女童,接触宠物、共用理发工具、家庭聚集感染为主要危险因素;病原谱以犬小孢子菌为主(65%~85%),脓癣占比达 30%~43%,临床表现不典型,极易误诊为细菌性脓肿。真菌免疫荧光染色快速、灵敏、阳性率高,适合临床一线筛查;真菌培养为确诊金标准,可完成菌种鉴定与用药指导。本例患儿以头皮包块、波动感为主要表现,炎症指标无明显升高,经脓肿切开引流联合口服伊曲康唑、外用盐酸布替萘芬乳膏治疗后好转,病原学确诊为犬小孢子菌感染。

结论 儿童头癣以犬小孢子菌感染最常见,脓癣误诊风险高;真菌荧光染色联合真菌培养可显著提升诊断准确性。规范标本采集、早期病原学确诊、系统抗真菌联合局部治疗及消毒隔离,是提高疗效、减少瘢痕性脱发等并发症的关键。加强宠物管理与宣教,有助于控制儿童头癣流行。

精准诊疗侵袭性混合真菌感染致重症肺炎 ARDS 的救治体会

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目的 探讨精准治疗联合 ECMO 在急性呼吸窘迫综合征合并非粒缺侵袭性肺真菌病患者中的诊疗价值。

方法 患者 2025 年 5 月 20 日受凉后出现咳嗽、咳白色黏痰,伴畏寒、胸闷气喘及发热,最高体温

38.5℃,进行性呼吸困难。5 月 25 日症状加重,氧饱和度降至 85%,胸部 CT 示双肺弥漫磨玻璃影较前扩大,部分进展为实变影,遂收入院。既往有骨质疏松病史 4 年,反复椎体骨折,曾剧烈咳嗽导致胸椎椎体骨折,现长期佩戴腰托辅助治疗。入院时呼吸急促,41 次/分,三凹征明显,双肺闻及湿啰音;氧合指数 141.83,初步诊断为重症肺炎、急性呼吸窘迫综合征(ARDS)、骨质疏松。

入院后检查提示 CRP、白介素-6 等炎症指标升高、淋巴细胞计数及免疫功能降低。G 实验、GM 实验阴性。为进一步诊疗明确病原学给予气管镜检查,肺泡灌洗液涂片及荧光染色可见真菌菌丝及孢子,mNGS 检出白色念珠菌 序列数 788092、曲霉菌 序列数 2395,明确感染病菌,修正诊断为重症肺炎、ARDS、侵袭性肺真菌病(白色念珠菌合并曲霉菌感染)、骨质疏松,予伏立康唑抗真菌治疗。

5 月 26 日患者氧合持续恶化,无创通气无效,气管插管后氧合指数仍<100,伴呼吸性酸中毒、肺顺应性极差只有 9ml/H₂O,又因患者重度骨质疏松无法俯卧位通气,遂 V-V ECMO 支持治疗。经 ECMO 联合机械通气后,患者氧合明显改善,炎症指标下降,肺部渗出吸收,于 6 月 7 日成功撤离 ECMO。

撤机后患者出现发热、咳痰增多,炎症指标回升,肺泡灌洗液培养示鲍曼不动杆菌,诊断呼吸机相关性肺炎。根据药敏结果调整为伏立康唑、美罗培南联合多粘菌素抗感染,治疗 2 周后病情好转,转入普通病房继续治疗。

结果 ARDS 合并非粒缺肺侵袭性真菌病患者,为提高抗生素治疗效果,除需考虑宿主因素、观察肺部影像学外,还需积极进行病原学检测以明确感染性质,采用精准治疗联合 ECMO 支持,可有效改善临床症状,提升预后水平。

结论 ARDS 合并非粒缺肺侵袭性真菌病患者,通过支气管镜、肺泡灌洗液涂片、荧光染色及 mNGS 实现早期精准病原学诊断,给予目标性抗真菌治疗,并联合 V-V ECMO 支持治疗,可快速改善氧合、控制感染;针对继发呼吸机相关性肺炎及时根据药敏调整抗菌方案,最终成功改善患者预后。提示精准

病原学检测联合规范靶向抗感染及 ECMO 支持,是救治此类危重患者的关键策略,符合临床诊疗指南原则。

关键词:侵袭性肺真菌病、ARDS

Xpert Mtb/RIF、 γ -干扰素释放试验、荧光定量 PCR 在分枝杆菌病诊断中的对比研究

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目的 比较结核分枝杆菌/利福平耐药快速检测法(Xpert Mtb/RIF)、荧光实时定量 PCR、 γ -干扰素释放试验三种方法在临床工作中对于检测分枝杆菌的临床价值及潜在优势。

方法 本研究纳入从 2018 年 4 月 1 日至 2019 年 4 月 1 日在我院就诊的分枝杆菌培养阳性的患者 151 例。利用 Xpert Mtb/RIF、荧光实时定量 PCR 技术对其呼吸道(或体液)标本进行 DNA 检测,并抽血送检 γ -干扰素释放试验,利用统计学方法比较这三种检测技术对分枝杆菌的检出率,并分析分枝杆菌培养阳性患者的 γ -干扰素的集中范围。

结果 实验以分枝杆菌培养作为金标准,当用 γ -干扰素释放试验辅助检测分枝杆菌时的阳性率高于荧光实时定量 PCR 法与 Xpert Mtb/RIF 两种检测方法, $P < 0.05$, 并且差异具有统计学意义。

结论 与用荧光定量 PCR 技术和 Xpert Mtb/RIF 技术相比,当用 γ -干扰素释放试验作为辅助诊断分枝杆菌的方法时其阳性检出率更高,但检测结果会存在假阳性的问题,在临床诊断的实际工作中应结合其他方法学及影像学等多方面综合考虑。

[关键词]: 分枝杆菌 Xpert Mtb/RIF 荧光实时定量 PCR γ -干扰素释放试验

中图分类号:R446.1 文献标识码:A

应用不同前处理法联合质谱技术快速检测血培养病原菌

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目的 通过不同前处理方法对阳性血培养标本进行前处理,联合基质辅助激光解析电离飞行时间质谱(MALDI-TOF MS),对阳性血培养标本病原菌进行快速检测,分析探讨不同前处理方法结合质谱技术快速检测病原菌与传统方法(即过夜培养后鉴定药敏)优劣性比较,优化目前血培养检测流程。

方法 将 30 份阳性血培养标本采用分离胶促凝管法、血培养试剂盒法、短时间培养法 2.5h、短时间培养法 5.5h 进行前处理后,分离病原微生物通过质谱进行快速鉴定,将不同前处理方法与传统方法相比较,就准确性、时间效益、经济效益、临床满意度等方面进行统计分析。

结果 以传统过夜培养后鉴定为参考方法,分离胶促凝管法鉴定率为 86.7% (23/30),短时间培养法 2.5h 的鉴定率为 46.7% (14/30),短时间培养法 5.5h 的鉴定率为 80.0% (24/30),血培养试剂盒法的鉴定率为 86.7% (26/30)。

结论 短时间培养法 5.5h 和分离胶法结合质谱仪进行血培养标本病原菌鉴定可快速有效的明确病原菌,血培养试剂盒法更为高效和便捷,利用不同前处理法分离到的病原菌同时进行药敏试验,可显著缩短血培养报告周期,为患者及早得到合适的抗菌药物治疗争取宝贵时间。

溃疡性结肠炎患者艰难拟梭菌混合感染的高危因素及其与复发性感染的相关性分析

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目的 探讨溃疡性结肠炎(UC)患者中艰难拟梭菌(*Clostridioides difficile*)混合感染的危险因素及其与复发性艰难拟梭菌感染(R-CDI)的相关性,为临床筛查和个体化治疗提供依据。

方法 纳入2020年1月至2024年12月四川省三家医院262例艰难拟梭菌感染(CDI)患者,通过PCR-核糖体分型和多位点序列分型(MLST)检测混合感染类型(同一宿主携带不同基因型菌株)。分析混合感染患者的临床特征、抗生素异质性耐药率及生物膜形成能力,并通过Logistic回归模型评估UC与混合感染风险的关联。

结果 混合感染流行率:262例CDI患者中,29例(11.1%)为混合感染,主要MLST型别为ST54、ST3、ST42。UC患者混合感染风险显著增加(OR=2.794, 95%CI 1.632-7.649, P=0.001),混合感染菌株异质性耐药率为76.8%,左氧氟沙星、利福昔明、四环素耐药率较高(19.8%、23.4%、38.5%),生物膜形成能力倾向于单培养中的优势菌株。

结论 UC尤其是慢性复发性UC是艰难拟梭菌混合感染的重要危险因素,混合感染可能通过高异质性耐药和生物膜协同作用增加R-CDI风险。建议对UC合并CDI患者常规筛查混合感染,优化抗生素选择以降低复发及耐药菌传播风险。

非粒缺患者侵袭性肺曲霉病与肺毛霉病的CT影像学特征对比分析

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目的 对比分析非粒缺患者侵袭性肺曲霉病(IPA)与侵袭性肺毛霉病(IPM)的胸部CT影像学特征,以提高早期诊断准确性。

方法 回顾性收集2020年1月至2026年4月就诊于西部战区总医院感染科的非粒缺IPA和IPM

患者资料,依据EORTC/MSGERC标准,其中IPA为确诊(Proven)和临床诊断(Probable),IPM为确诊(Proven)。对比两组患者的胸部CT影像,重点分析病灶分布和形态特征。计量和计数资料分别采用非参数Mann-Whitney U检验和 χ^2 检验, P<0.05有统计学意义。

结果 最终共纳入IPM 40例, IPA 110例。IPM患者中位年龄为67岁(男/女: 32/8), IPA患者中位年龄63岁(男/女: 97/13) (P>0.05)。基础疾病分布, IPM主要为2型糖尿病(72.5%)和新冠/甲流感染(27.5%); IPA主要为COPD(48.2%)、2型糖尿病(20.9%)、新冠/甲流感染(19.1%)、结缔组织病(6.4%)和肺癌(5.5%) (P<0.05)。支气管镜下表现, IPA主要为支气管粘膜水肿(100%)、管腔表面坏死物(51.8%),而IPM主要为支气管狭窄(95%),且IPA的BALF mNGS阳性率显著高于IPM(95.5% vs 82.5%) (P<0.05)。肺部CT影像学特征对比分析,在病灶分布上, IPA更常见双肺多叶段受累(77.5%),以上叶及胸膜下分布为主(68.2%), IPM则更常见下叶基底段及肺门周围分布(62.5%) (P<0.05);在形态特征上, IPA更常见沿血管支气管束分布的多发结节(80.9%),部分伴“晕征”(62.7%),空洞(58.2%)和空气新月征(18.2%)发生率高于IPM (P<0.05); IPM更常见节段性大叶性楔形实变,基底贴近胸膜、尖端指向肺门(55.0%),且伴随支气管狭窄和血管闭塞征(40.0%),反晕征(35.0%)和胸腔积液/胸膜增厚(32.5%)在IPM更常见 (P<0.05)。

结论 在非粒缺患者中, IPA与IPM的CT影像有显著差异。IPA更倾向于形成胸膜下多发结节、晕征、空气新月征及实变内空洞;而IPM则更多表现为双肺下叶基底段及肺门周围分布的楔形实变、反晕征、血管闭塞征。

关键词: 非粒细胞缺乏; 侵袭性肺曲霉病; 侵袭性肺毛霉病; CT影像学

宏基因组二代测序在血液病患者感染诊断中

的应用

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目的 本研究旨在通过比较宏基因组二代测序 (Metagenomic next-generation sequencing, mNGS) 与传统病原体检测方法的诊断阳性率, 评估 mNGS 在血液病患者感染病原体检测中的应用价值。

方法 本研究纳入了 2021 年 7 月 26 日至 2022 年 6 月 6 日期间在北京大学人民医院血液科收治的疑似感染的 108 例患者, 送检血液标本进行宏基因组二代测序和常规生物学检测 (G 试验、GM 试验和病毒核酸检测, 怀疑血流感染患者同时送检血培养)。比较 mNGS 与传统方法的诊断阳性率, 以评估 mNGS 在血液病感染患者中的诊断价值。

结果 108 例怀疑感染的血液病患者共收集 149 份数据, 结合临床, 其中 113 份数据临床考虑诊断感染, 其中考虑为细菌感染 89 份, 真菌感染 10 份, 病毒感染 11 份。临床考虑为细菌感染的患者, 应用常规生物学检测方法的敏感性和特异性分别为 6.74% 和 91.67%, 应用 mNGS 检测方法的敏感性和特异性分别为 17.98% 和 95.0%。临床考虑为真菌感染的患者, 应用常规生物学检测方法的敏感性和特异性分别为 20.0% 和 52.52%, 应用 mNGS 检测方法的敏感性和特异性分别为 20.0% 和 94.96%。临床考虑为病毒感染的患者, 应用常规生物学检测方法的敏感性和特异性分别为 27.27% 和 75.36%, 应用 mNGS 检测方法的敏感性和特异性分别为 72.73% 和 60.14%。

结论 mNGS 分析提供了快速且精确的病原体检测和鉴定, 有助于及时准确地治疗血液科感染的患者。

基于全基因组比对的毛霉目 6 种致病菌种特异性 PCR 鉴定靶标筛选与评价

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目的 毛霉病进展迅猛、病死率高, 早期精准的种水平病原学诊断是指导抗真菌治疗、改善预后的关键。不同毛霉目致病菌对抗真菌药物敏感性存在显著差异, 如 *Cunninghamella* spp. 及 *Mucor circinelloides* 对两性霉素 B 和艾沙康唑的最低抑菌浓度较高, 种水平鉴定直接影响临床用药决策。然而, 目前临床常用的 ITS 和 D1/D2 通用靶标在毛霉目部分近缘种间序列高度保守, 系统发育分析显示种水平分辨率不足, 且部分属存在多位点 ITS 拷贝异质性, 直接测序易产生杂峰, 须经克隆后方可鉴定, 操作繁琐、报告周期长, 难以满足重症感染早期快速诊断的需求。此外, D1/D2 在 *Rhizopus* 属的株水平及种水平多样性捕捉能力有限, 甚至导致错误鉴定。因此, 亟需建立一种操作便捷、可实现毛霉目真菌种水平鉴定的分子方法。本研究基于全基因组序列比对, 从根霉、毛霉、横梗霉等 6 种常见毛霉目致病菌中系统挖掘种特异性序列, 设计种特异性 PCR 引物并进行实验验证, 旨在为毛霉病病原学精准诊断提供新的分子靶标。

方法 从 NCBI RefSeq 数据库下载 6 种目标菌的全基因组序列, 采用全基因组比对策略, 以种间相似度 < 85%、种内相似度 > 98%、片段长度 100–300 bp 为标准, 筛选种特异性靶标区段, 利用 Primer Premier 6.0 设计 6 对种特异性 PCR 引物。以 18 种临床常见非目标真菌 (包括曲霉属、念珠菌属、隐球菌属等) 及常见细菌验证引物特异性; 以含靶标序列的重组质粒 10 倍倍比稀释 (10^8 – 10^1 copies/ μ L) 为模板进行 PCR 扩增, 评价各引物灵敏性并确定最低检测限。采用 ITS 通用引物 (ITS1/ITS4) 扩增测序及本研究种特异性引物扩增, 比较两种方法在种水平鉴定中的分辨率与时效差异。

结果 6 对引物对相应目标菌种均呈现单一、清晰的特异性扩增条带, 与 18 种非目标真菌及细菌均无交叉反应, 引物特异性达 100%。灵敏性评价显

示,6对引物检测限均衡,最低检测限均为 10^2 copies/反应,扩增效率良好。通过单次PCR即可直接鉴定至种水平,无需测序及后续生物信息学比对,报告周期由2-3天缩短至数小时。

结论 本研究基于全基因组比对策略,成功建立了毛霉目6种常见致病菌的种特异性PCR鉴定体系。该方法实现了操作便捷、快速精准的种水平直接鉴定,为毛霉病早期病原学诊断提供了可及性更强、更适合基层实验室推广的新分子靶标。

细菌真菌耐药监测与耐药机制

2020-2024 年某院泌尿生殖道支原体感染的流行病学特征及药物敏感性

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目的 探讨医院泌尿生殖道支原体感染的流行病学及抗菌药物敏感性特征。

方法 回顾性分析2020年1月-2024年12月广东省人民医院就诊的22716例患者泌尿生殖道支原体培养及药敏数据,采用SPSS 22.0统计软件对数据进行分析。

结果 22716例患者中有6723例支原体检测阳性,总阳性率为29.60%,2020-2024年患者支原体阳性率呈下降趋势($\chi^2=41.869, P<0.001$)。女性患者的感染比例(6055例,90.06%)高于男性(668例,9.94%)($\chi^2=557.422, P<0.001$);>30~40岁为感染高发年龄段。单一解脲脲原体(Uu)感染是最主要的感染类型,其次为混合感染,单一人型支原体(Mh)感染比例最低。药敏试验结果显示,Uu+Mh混合感染组对10种抗菌药物的耐药性均高于Uu组($P<0.001$),对环丙沙星、氧氟沙星、四环素、司帕沙星、强力霉素和交沙霉素的耐药性高于Mh组($P<0.05$);Mh组对氧氟沙星、司帕沙星、红霉素、阿奇霉素、克拉霉素和罗红霉素的耐药性高于Uu组($P<0.001$)。

结论 女性支原体感染比例高于男性,>30~40岁为感染高发年龄段。Uu对多种抗菌药物表现出较高的敏感性,而Mh对多数药物的敏感性较低,二者混合感染的耐药性普遍高于单一感染。

关键词: 解脲脲原体;人型支原体;药敏试验;流行病学;泌尿生殖道感染

心血管内科医院感染病原菌分布及耐药特征

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目的 分析医院心血管内科住院患者医院感染的病原菌分布及耐药特征，为临床精准抗感染治疗及医院感染防控提供依据。

方法 采用回顾性研究方法，收集 2019 年 1 月至 2025 年 6 月广东省人民医院心血管内科发生医院感染患者的临床及病原学资料共 696 例，对非重复分离的病原菌种类及其药敏结果进行统计分析。

结果 心血管内科医院感染主要发生于泌尿系统、血流及下呼吸道。共分离病原菌 800 株，其中革兰阴性菌 430 株 (53.75%)，以大肠埃希菌和肺炎克雷伯菌检出率最高；大肠埃希菌对氨苄西林、第三代头孢菌素及喹诺酮类药物耐药率较高。铜绿假单胞菌对亚胺培南和美罗培南的耐药率均为 12.50%，鲍曼不动杆菌对上述两种药物的耐药率分别为 58.82% 和 47.06%。革兰阳性菌 246 株 (30.75%)，以金黄色葡萄球菌和肠球菌为主，金黄色葡萄球菌对青霉素耐药率最高，对苯唑西林的耐药率为 25.00%；粪肠球菌对利奈唑胺的耐药率为 5.26%，屎肠球菌对万古霉素的耐药率为 5.71%。真菌 124 株 (15.50%)，以念珠菌属为主，非白念珠菌占比较高，对常用抗真菌药物总体保持较高敏感性。共检出医院重点监测多重耐药菌 42 株 (5.25%)。

结论 心血管内科医院感染的病原菌以革兰阴性菌为主，耐药问题较为突出，真菌及多重耐药菌亦占一定比例。临床应依托持续的病原学监测与耐药动态分析，合理优化抗菌药物应用策略，并强化侵入性操作管理及多重耐药菌防控措施，以降低医院感染发生风险，改善患者预后。

关键词：心血管内科；医院感染；病原菌分布；耐药性；多重耐药菌

Construction of A Linezolid-Resistant Strain of Methicillin-Susceptible *Staphylococcus Aureus* and Its Multi-Omics Based Mechanism Study

null null

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Objective This study aimed to explore the molecular mechanisms of linezolid resistance in methicillin-susceptible *Staphylococcus aureus* (MSSA) by establishing stable linezolid-resistant derivatives and using multi-omics approaches to clarify resistance-related regulatory patterns.

Methods A linezolid-susceptible clinical MSSA isolate (strain *S. aureus*_97) served as the parental strain. A stable linezolid-resistant derivative (LZR) was induced by stepwise exposure to subinhibitory linezolid concentrations, with phenotypic stability confirmed by serial passages. Comparative transcriptomic (RNA-seq) and untargeted metabolomic (LC-MS/MS) analyses were conducted to identify differential gene expression and metabolic profiles between LZR and the susceptible strain (LSS).

Results The LZR strain showed a stable minimum inhibitory concentration (MIC) increase from 2 $\mu\text{g/mL}$ to 32 $\mu\text{g/mL}$, which remained unchanged after 50 antibiotic-free passages. Transcriptomic analysis identified 753 differentially expressed genes (401 up-regulated, 352 downregulated), mainly involving ribosomal proteins, *pheT* (upregulated), and *rnpA*, *pyrB*, *recX* (downregulated), enriched in oxidative phosphorylation, ribosome function, and glycerolipid metabolism. Metabolomic analysis found 224 differential metabolites (115 increased, 109 decreased), primarily lipids, organic acids, and their derivatives, enriched in secondary metabolite biosynthesis, D-amino acid metabolism, and arginine-proline metabolism. Integrated

analysis revealed 15 co-enriched KEGG pathways, with secondary metabolite biosynthesis as the core, and synergistic "synthesis activation and catabolism inhibition" regulating resistance.

Conclusion A stable linezolid-resistant MSSA strain was successfully established. Linezolid resistance is driven by intricate transcriptional and metabolic regulatory networks, providing an experimental and theoretical basis for understanding resistance mechanisms and developing countermeasures.

Analysis of Antimicrobial Resistance and Virulence in A Highly Pathogenic Mucoïd Acinetobacter Baumannii Strain Based on Whole-Genome Sequencing

null null

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Objective To analyze the in vitro virulence and antimicrobial resistance (AMR) profile of AB 2508, a clinically isolated hypervirulent mucoïd Acinetobacter baumannii strain, and provide clinical evidence for precise diagnosis and treatment of such infections.

Methods AB 2508 was isolated from bronchoscopic sputum of patients with severe pneumonia and septic shock. It was identified by MALDI-TOF MS, with MIC values determined via VITEK 2 COMPACT. Whole-genome sequencing was performed. Antimicrobial resistance (AMR) genes, pathogenicity potential, and virulence genes were predicted using ResFinder, PathogenFinder 2, and the Virulence Factor Database (VFDB). The expression profiles of virulence genes

were detected via quantitative real-time polymerase chain reaction (qPCR). Biofilm formation capacity was assessed by crystal violet staining, and pathogenicity was evaluated using the Galleria mellonella infection model. In addition, clinical data correlation analysis, PubMLST-based sequence type (ST) typing, and phylogenetic tree construction were performed.

Results AB 2508 was confirmed as mucoïd Acinetobacter baumannii (99.9% confidence), resistant to 5 antibiotics but susceptible to 20, carrying blaADC-25 and blaOXA-68. It harbored highly expressed virulence genes (e.g., pgaA, Bap) with a pathogenicity prediction of 0.9918. Biofilm formation and pathogenicity were significantly stronger than the control ($P < 0.05$), consistent with clinical manifestations. ST typing was ST447, showing 96.9% homology with a 2023 Indian blood-isolated strain.

Conclusion AB 2508's AMR phenotype matches its resistance genes. High virulence gene expression and strong biofilm formation drive pathogenicity. Findings aid risk assessment and treatment optimization for hypervirulent mucoïd Acinetobacter baumannii infections.

2020 年-2024 年重庆市传染病医院临床分离菌分布及耐药性变迁分析

何静

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目的 对 2020 年-2024 年重庆市传染病医院分离出的病原菌分布及其药敏结果进行分析。

方法 对 2020 年-2024 年临床分离出的病原菌采用纸片扩散法或商品化药敏试验自动测试仪按临检操作规程、微生物各类行标及 CARSS 网技术方案进行抗菌药物敏感性试验。按当年美国临床和实

验室标准化协会（CLSI）折点标准判断。

结果 2020 年-2024 年共监测临床分离菌 7412 株，其中革兰阳性菌占 23.22%（1721/7412），革兰阴性菌占 57.66%（4274/7412），真菌占 19.12%（1417/7412）。革兰阳性菌中，葡萄球菌属占 46.66%（803/1721）、链球菌属占 14.58%（251/1721）、肠球菌属占 12.32%（212/1721）。肠杆菌目占 45.32%，肺炎克雷伯菌 43.42%（841/1937）、大肠埃希菌 35.98%（697/1937）和粘质沙雷菌 3.56%（69/1937）；非发酵革兰阴性杆菌占 39.04%，前三位的依次是铜绿假单胞菌 47.3%（587/1241）、鲍曼不动杆菌 25.22%（313/1241）和嗜麦芽窄食单胞菌 12.97%（161/1241）。真菌中，曲霉属占 52.29%（741/1417），新型隐球菌占 16.73%（237/1417），马尔尼菲篮状菌占 15.17%（215/1417）。大肠埃希菌对三代头孢菌素和喹诺酮耐药率明显高于肺炎克雷伯菌，但是耐碳青霉烯酶类肺炎克雷伯菌（CRKP）分离率高于耐碳青霉烯酶类大肠埃希菌（CRECO）。肺炎克雷伯菌、大肠埃希菌、铜绿假单胞菌和鲍曼不动杆菌均对喹诺酮类抗菌素具有较高耐药性，且均对阿米卡星具有较高敏感性。

结论 临床分离菌对常见抗菌药物的耐药率虽仍呈增长趋势，但肺炎克雷伯菌、铜绿假单胞菌和鲍曼不动杆菌等多种重要的碳青霉烯类耐药株检出率则呈锯齿形上升，提示继续加强细菌耐药监测，开展多学科联动的方式为应对抗微生物药物耐药性及防止细菌耐药性的发生发展提供重要保证。

血培养中病原菌的耐药性及耐碳青霉烯肠杆菌目细菌的耐药基因分析

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目的 研究血培养中病原菌的构成和耐药性及耐碳青霉烯肠杆菌目细菌（CRE）的耐药基因，指导

临床合理使用抗菌药物，为院内感染的有效监控提供依据。

方法 对日照市中医医院 2019 至 2023 年血培养分离的病原菌进行鉴定和药敏试验，采用改良碳青霉烯酶灭活试验（mCIM）和 EDTA 改良碳青霉烯酶灭活试验（eCIM）联合检测碳青霉烯酶表型；通过 WHONET5.6 和 SPSS 25.0 进行统计分析。运用聚合酶链反应（PCR）扩增耐药基因，产物进行测序分型。

结果 24855 份血培养共检出病原菌 3149 株，阳性率约为 12.7%。非重复菌株 1222 株，主要分布在监护室。革兰阴性（G-）杆菌的分离率（69.39%）高于革兰阳性（G+）球菌（28.64%）；亚胺培南、美罗培南、替加环素、哌拉西林/他唑巴坦、阿米卡星、头孢哌酮/舒巴坦和头孢替坦对大肠埃希菌和肺炎克雷伯菌耐药率均低于 5%；但对喹诺酮类、头孢唑林、氨苄西林耐药率相对较高。人葡萄球菌、金黄色葡萄球菌对青霉素 G、红霉素、克林霉素耐药率均超过 73%；金黄色葡萄球菌对利福平、庆大霉素、喹诺酮类、复方新诺明的耐药率均不超过 27%。2023 年首次检出 5 株 CRE，其中 4 株初步判断产金属-β 内酰胺酶；PCR 扩增结果显示 2 株阴沟肠杆菌、1 株肺炎克雷伯菌、1 株大肠埃希菌产碳青霉烯酶，均携带 NDM 基因，1 株阴沟肠杆菌未检出；基因测序确定耐药基因亚型为 blaNDM-1。

结论 该院血培养中 G-杆菌分离率高于 G+球菌，肠杆菌目细菌所占比例较高，对常用抗菌药物呈现不同的耐药性；检出 5 株 CRE，耐药基因均为 blaNDM-1。临床应重视血培养及药敏试验结果，有针对性的合理使用抗菌药物。

儿童医院大肠埃希菌耐药率与抗菌药物使用频度的相关性研究

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目的 探讨某儿童医院大肠埃希菌耐药率与抗菌药物使用频度(DDD_s)之间的相关性,为临床合理用药提供参考。

方法 收集 2021-2025 年该院临床分离的大肠埃希菌检出率、标本分布、耐药率及同期抗菌药物使用数据,并利用 Pearson 相关系数分析大肠埃希菌耐药率与同期抗菌药物使用频度的关系。

结果 2021-2025 年共分离非重复大肠埃希菌 1636 株,主要分布于痰液、脓液、腹水等标本,对氨苄西林、头孢呋辛、头孢噻肟、头孢曲松及左氧氟沙星的耐药率均处于较高水平(>50%),其中氨苄西林耐药率持续高于 95%。美罗培南耐药率整体处于较低水平,但呈缓慢上升趋势,从 2.22%升至 3.30%。抗菌药物使用结构中,哌拉西林他唑巴坦、头孢哌酮舒巴坦、氨曲南及阿米卡星的使用频度呈上升趋势,氨苄西林、头孢呋辛、头孢他啶的使用频度呈下降趋势。相关性分析提示,哌拉西林他唑巴坦、头孢曲松、头孢噻肟的使用频度与其耐药率呈正相关($r=0.954$ 、 0.722 、 0.723),阿米卡星使用频度与其耐药率也呈正相关($r=0.823$);左氧氟沙星使用频度与其耐药率相关性较弱($r=0.299$)。

结论 大肠埃希菌耐药形势严峻,且与特定抗菌药物的使用频度密切相关,应加强抗菌药物管理。

次氯酸对多重耐药菌的抗菌活性、物表消毒效能及慢性伤口生物膜清除作用与机制研究

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目的 评估次氯酸消毒液对临床常见多重耐药菌(MDRO)的体外抗菌活性及不同材质物体表面快速消毒效能,探讨其对金黄色葡萄球菌成熟生物膜的清除效果,为慢性伤口生物膜相关感染局部治疗提供依据,后续通过多组学、基因敲除及动物模

型阐明其抗生物膜分子机制与体内外应用价值。

方法 1.选取临床 6 种 MDRO 共 60 株(MRSA、CRKP、CRAB、CRPA、CREC、VREFM 各 10 株)及相应标准菌株 6 株,宏量肉汤稀释法测定次氯酸(有效氯 500 mg/L) MIC/MBC; 2.取各标准菌株分别构建不锈钢、玻璃、手套、纸片、塑料、布片 6 种染菌载体,测定 15~120 s 细菌杀灭对数值,采用两因素重复测量方差分析结合 Tukey 事后检验,分析时间与材质对消毒效果的影响; 3.以金黄色葡萄球菌 ATCC 25923 为模式菌株,于 6~72 h 通过结晶紫染色法监测生物膜形成过程,确认 48 h 为成熟生物膜时间点,活菌计数法检测 250~500 mg/L 次氯酸对成熟生物膜的清除率; 4.后续拟行多组学测序,筛选差异基因及代谢通路;以基因敲除验证靶点;构建慢性伤口生物膜动物模型,评估体内清创效果、创面愈合及安全性。

结果 1. 抗菌活性:次氯酸对 60 株 MDRO 的 MIC、MBC 均为 300 mg/L,标准菌株 MIC、MBC 均为 450 mg/L,菌株对次氯酸高度敏感且无交叉耐药。2.物表消毒:杀菌效果随时间延长显著提升($P<0.001$),不同材质消毒效果差异显著($P<0.001$),时间与材质交互作用显著($P<0.01$); Tukey 事后检验表明,非渗透性表面(手套、不锈钢、玻璃、塑料) 15~60 s 内即可达高水平消毒(杀灭对数值>3),达到高水平消毒所需时间显著短于渗透性表面(纸片、布片,需 45~120 s)($P<0.05$)。3.生物膜清除:次氯酸对成熟生物膜清除率呈浓度依赖性,350 mg/L 清除率为 50%~70%,450 mg/L 及以上清除率达 90% 以上。

结论 次氯酸对临床常见 MDRO 具有广谱高效抗菌活性,对不同材质物表可实现快速消毒,且对金黄色葡萄球菌成熟生物膜呈浓度依赖性清除效果。后续将通过多组学分析、基因敲除及慢性伤口生物膜动物模型,全面揭示其抗生物膜分子机制与体内应用价值,为次氯酸在慢性伤口感染治疗中的临床转化提供完整证据链。

2015—2024 年临沂地区中枢神经系统感染的脑脊液病原菌分布及感染特征及耐药分析

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目的 分析近 10 年临沂地区中枢神经系统感染患者脑脊液检出菌的临床分布、感染特征和耐药谱，为临床抗感染治疗提供参考。

方法 回顾性分析 2015—2024 年临沂地区 3 家三甲医院住院的中枢神经系统感染患者的临床信息及其脑脊液分离菌的病原学特征。

结果 共检出 348 株菌，其中革兰阳性菌占 55.75%，以肺炎链球菌、凝固酶阴性葡萄球菌为主；革兰阴性菌占 40.52%，以肺炎克雷伯菌、大肠埃希菌、鲍曼不动杆菌为主，真菌占 3.73%，全部是新型隐球菌。肺炎链球菌、凝固酶阴性葡萄球菌主要检出自儿童组和成人组；肺炎克雷伯菌和鲍曼不动杆菌主要检出自成人组；大肠埃希菌每个年龄组均有检出。大肠埃希菌和无乳链球菌是新生儿中最常见的病原体。革兰阴性菌患者合并高血压、糖尿病、肺部感染、低蛋白血症、脑外伤、脑出血、脑积水、脑部肿瘤，入住 ICU 以及接受有创诊疗操作的比例，明显高于革兰阳性菌患者，而革兰阴性菌患者合并血流感染的比例显著低于革兰阳性菌患者($P<0.05$)。常见革兰阳性球菌对利奈唑胺和万古霉素高度敏感，肺炎链球菌对头孢曲松和头孢噻肟有较高的敏感性。革兰阴性菌对常见抗菌药物的敏感性因菌株差异而不同。鲍曼不动杆菌对除替加环素以外的常见抗菌药物具有高耐药率。

结论 中枢神经系统感染患者脑脊液检出菌的分布因年龄而不同，不同细菌的耐药性、感染特征存在差异，需要对病原体趋势和抗菌药物耐药率进行持续和动态监测。

Molecular Characteristics, Clinical Risk Factors, and Outcomes of *Klebsiella Pneumoniae* Bloodstream Infections in Infants

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Background *Klebsiella pneumoniae* (KP) bloodstream infections (BSIs) are more common in immunocompromised patients and are associated with high rates of morbidity and mortality. Infants with an immature immune system and a lack of specific protective antibodies are susceptible to KP-BSIs. This study aimed to comprehensively investigate the clinical characteristics, antibiotic susceptibility profiles, treatment outcomes, and molecular characteristics of KP infections in these infants

Methods Between January 2017 and December 2024, a retrospective study was conducted at Guangxi Children's Hospital, China. We used logistic regression to identify risk factors for carbapenem-resistant KP BSI (CRKP-BSI) and extended-spectrum β -lactamase KP BSI (ESBL-KP-BSI), as well as mortality-associated factors in KP-BSI patients. Whole-genome sequencing (WGS) was conducted on CRKP isolates. Subsequent genomic analyses included multilocus sequence typing (MLST), capsular serotyping, virulence gene, and antimicrobial resistance gene through Pathogenwatch, complemented by plasmid replicon identification via PlasmidFinder.

Results During the study period, 98 patients with KP-BSIs were enrolled. Of these patients, 16 were infected with CRKP and 82 with carbapenem-susceptible KP (CSKP). Among 82 CSKP cases, 29 had ESBL-KP

and 53 had non-ESBL-KP. Multivariate analysis identified carbapenem exposure as an independent predictor of CRKP-BSIs (OR: 4.37, 95% CI: 1.12-16.98, $p = 0.03$), and β -lactam/ β -lactamase inhibitor administration independently predicted ESBL-KP BSIs (OR: 3.59, 95% CI: 1.12-11.56, $p = 0.03$). The independent risk factors for the 30-day mortality in KP-BSIs was mechanical ventilation (OR: 4.71, 95% CI: 0.97-22.94, $p = 0.05$). MLST analysis identified four sequence types, with ST7 being the most prevalent, followed by ST24, ST20, and ST37. Capsular serotyping revealed KL54 as the predominant serotype. Antimicrobial resistance gene profiling indicated that all isolates harbored multiple resistance determinants, with blaNDM-1 and blaCTX-M-14 being universally present. The most prevalent replicons were IncX3, IncFII(K), IncR, and IncFIB(K), which frequently co-occurred. Furthermore, bioinformatic analysis indicated that these CRKP strains carried multiple resistance genes, with the likelihood that they are localized on plasmids.

Conclusion This study underscores the need for stricter antibiotic stewardship, especially in limiting exposure to carbapenems and β -lactam/ β -lactamase inhibitors, as well as minimizing invasive procedures (e.g., mechanical ventilation) to reduce multidrug-resistant KP-BSI incidence and improve survival outcomes in infants.

2025 年某医院临床分离肠球菌的耐药性分析

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目的 分析 2025 年某医院临床分离的肠球菌对常用抗菌药物的耐药特征, 比较粪肠球菌和屎肠球菌两种菌株的药敏谱差异, 明确耐万古霉素肠球

菌的检出情况, 为临床合理用药及院内感染防控提供实验室依据。

方法 收集某医院 2025 年 1~12 月临床送检标本中分离的非重复肠球菌菌株 825 株, 采用 VITEK-MS 质谱仪或 VITEK-2 COMPACT 系统进行菌种鉴定, 应用梅里埃革兰阳性球菌药敏卡(AST P639)开展药敏实验, 依据 CLSI M100 35 版标准判读结果, 利用 WHONET 5.6 软件进行数据管理与分析, 比较粪肠球菌与屎肠球菌的耐药率差异, 同时回顾性分析耐万古霉素肠球菌主动筛查结果。

结果 1116 株肠球菌中, 屎肠球菌 636 株 (57.0%)、粪肠球菌 419 株 (37.5%)、其他肠球菌 61 株 (5.5%)。标本主要分离于尿液 (40.3%)、血液 (13.1%) 和引流液 (8.2%)。泌尿外科 (23.6%)、重症监护室 (22.0%) 和肝胆外科 (6.3%) 是检出率较高的科室。屎肠球菌对青霉素 G、氨苄西林、左氧氟沙星、莫西沙星的耐药率分别为 94.8%、94.8%、93.4%、95.4%, 显著高于粪肠球菌 (1.0%、0.2%、35.0%、35.4%), 差异有统计学意义 ($P < 0.05$); 屎肠球菌万古霉素耐药率 2.8%、利奈唑胺耐药率 1.1%; 粪肠球菌万古霉素 100%敏感, 利奈唑胺耐药率 10.7%。VRE 主动筛查阳性率为 1.7%。

结论 屎肠球菌和粪肠球菌是临床分离的主要肠球菌菌种, 主要引起泌尿系统和血流感染。屎肠球菌和粪肠球菌对

铜绿假单胞菌的耐药率与抗菌药物暴露的相关性

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目的 本研究旨在深入探讨某医院内铜绿假单胞菌 (PA) 耐药率变化与各类抗菌药物使用强度 (AUD) 之间的趋势关联及相关性, 从而为临床合理、精准地使用抗菌药物提供科学依据和参考。

方法 为系统收集并整理该医院 2019 年至 2024 年间常用抗菌药物的年度使用强度数据以及同期铜绿假单胞菌的药敏结果与耐药率,并运用 SPSS 25.0 统计软件对数据进行趋势分析与相关性检验。

结果 分析结果显示:在观察期内,铜绿假单胞菌对哌拉西林他唑巴坦和头孢他啶的耐药率呈现逐年上升的显著趋势($P<0.05$),而对亚胺培南的耐药率则表现出明显的下降趋势($P<0.05$)。进一步的相关性分析表明,铜绿假单胞菌对头孢哌酮舒巴坦的耐药率与三个季度前氨基糖苷类抗菌药物的使用强度呈正相关关系;对亚胺培南的耐药率则与二、三、四季度前大环内酯类抗菌药物的使用强度呈正相关,同时也与头孢菌素类药物的使用强度呈正相关(除二季度前数据外),并与三、四季度前氨基糖苷类药物的使用强度呈正相关。此外,铜绿假单胞菌对美罗培南的耐药率与同期青霉素类药物的使用强度呈正相关;对左氧氟沙星的耐药率则与四季度前大环内酯类药物的使用强度呈正相关。整体上,铜绿假单胞菌的耐药率变化与四季度前头孢菌素类药物的使用强度以及同期碳青霉烯类药物的使用强度均呈正相关。

结论 铜绿假单胞菌耐药率的动态变化与医院内不同类别抗菌药物的使用强度存在密切关联,提示临床在制定抗感染治疗方案时应充分参考药敏实验结果,合理选择抗菌药物,以减少不必要的广谱或高强度用药,从而有效延缓和控制细菌耐药性的发展与传播。

2015 年—2025 年某医院念珠菌血流感染临床特点与危险因素分析

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目的 讨论 2015—2025 年吉首大学第一附属医院念珠菌血流感染的菌株分布及其耐药情况,为

当地临床科室抗念珠菌用药提供理论依据。

方法 通过回顾性分析 2015 年 7 月至 2025 年 7 月医院 123 例 CBSI 患者的临床资料,采用基质辅助激光解吸电离飞行时间质谱(MALDI-TOF MS)进行菌种鉴定,ATB FUNGUS 3 以及 VITEK2 AST-YS08 试剂进行药敏试验,并运用 SPSS 22.0 进行统计学处理,通过单因素与多因素 Logistic 回归分析预后相关因素。

结果 本研究标本中共分离出念珠菌 123 株。排名前三的菌株为白念珠菌(58 株,47.15%),近平滑念珠菌(25 株,20.33%)和光滑念珠菌(19 株,15.46%)。近平滑念珠菌对卡泊芬净,米卡芬净耐药率分别为 8%和 12%。糖化血红蛋白($>7\%$)(OR=6.82)、休克(OR=3.86)、中心静脉置管(OR=6.05)及免疫受损(OR=13.887)是患者预后不良的独立危险因素($P<0.05$)。

结论 本地区念珠菌血流感染患者以白念珠菌为主要病原菌,且光滑念珠菌检出率位居第三位,高于国内多数报告的第四位。近平滑念珠菌对棘白菌素类药物呈现耐药上升趋势。糖化血红蛋白($>7\%$)、休克、中心静脉置管(≥ 15 天)、免疫受损是影响预后的关键因素,建议加强病原学监测与药敏指导,优化临床抗真菌治疗策略。

2014-2025 年浏阳市某基层医院主要 G—菌耐药趋势分析*

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目的 分析浏阳市某基层医院 2014—2025 年临床分离的主要 G—菌的耐药性变迁,为临床合理用药和抗菌药物管理提供依据。

方法 回顾性分析 12 年间主要 G—菌对常用抗菌药物的耐药率,采用趋势卡方检验分析耐药变化。

结果 大肠埃希菌对碳青霉烯类耐药率从 0.12% 缓慢上升至 1.59% ($P<0.01$), 喹诺酮类耐药率已超过 50%; 肺炎克雷伯菌对碳青霉烯类耐药率从 1.17% 持续上升至 5.86% ($P<0.01$), 对头孢哌酮/舒巴坦和喹诺酮类耐药亦显著升高; 铜绿假单胞菌对多数抗菌药物耐药率显著下降, 对碳青霉烯类耐药率降幅超过 50%; 鲍曼不动杆菌对碳青霉烯类及其他常用药物耐药率从 17.79% 急剧上升至 66.21% ($P<0.01$)。

结论 该院在大肠埃希菌、肺炎克雷伯菌碳青霉烯类耐药及铜绿假单胞菌多重耐药防控中取得一定成效, 但鲍曼不动杆菌耐药形势严峻, 其碳青霉烯类耐药率与全国监测数据趋势一致, 且对多数常用抗菌药物高度耐药, 临床治疗选择受限, 是院内感染防控的核心难点。综上, 本院需在巩固现有成效的基础上, 进一步强化碳青霉烯类处方监管, 加强重点科室环境监测与接触隔离, 优化抗菌药物阶梯治疗策略, 提升病原学送检率和快速诊断能力。

基于定量脓尿的无乳链球菌无症状菌尿分层及耐药差异分析

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目的 分析住院患者尿培养无乳链球菌 (group B *Streptococcus*, GBS) 阳性病例中无症状菌尿 (asymptomatic bacteriuria, ASB) 的分布规律, 探讨无脓尿定植的相关临床因素, 并比较不同专科背景下菌株耐药特征差异, 为临床药师参与抗菌药物合理使用管理提供依据。

方法 回顾性纳入 2024 年 1 月至 2025 年 12 月我院住院患者尿培养 GBS 阳性病例 218 例。结合本院实验室定量检测标准, 以尿常规白细胞 (WBC) $\leq 28/\mu\text{L}$ 定义为无脓尿定植组 ($n=119$), WBC $>28/\mu\text{L}$ 定义为伴脓尿组 ($n=99$)。采用 χ^2 检验比较两组基线特征、菌落数分布及抗菌药物敏感性差异, 并通过

Logistic 回归分析无脓尿定植的独立相关因素, 以森林图展示效应量及置信区间。

结果 无脓尿定植比例为 54.6% (119/218), 其中泌尿外科来源比例 (72.3% vs. 46.5%, $P<0.001$) 及男性患者占比 (66.4% vs. 35.4%, $P<0.001$) 均显著高于伴脓尿组; 低菌落数 (10^3 CFU/mL) 在无脓尿定植组中更为集中 (57.1% vs. 34.3%, $P=0.001$)。GBS 对青霉素及氨苄西林保持 100% 敏感, 氟喹诺酮类耐药率在不同专科间存在差异: 泌尿外科来源菌株对左氧氟沙星 (LVX) 耐药率高于非泌尿外科 (66.4% vs. 51.2%, $P=0.027$), 对莫西沙星 (MXF) 耐药率低于非泌尿外科 (34.7% vs. 48.8%, $P=0.042$)。多因素分析显示, 校正年龄、基础疾病等混杂因素后, 泌尿外科来源 (OR=2.999, 95%CI: 1.376~6.537, $P=0.006$) 与男性 (OR=4.423, 95%CI: 2.082~9.396, $P<0.001$) 是无脓尿定植的独立正相关因素; 合并泌尿系结石 (OR=0.189, 95%CI: 0.062~0.581, $P=0.004$) 和前列腺腺疾病 (OR=0.335, 95%CI: 0.118~0.951, $P=0.040$) 为独立负相关因素。

结论 住院患者 GBS 阳性尿培养中定植状态较为常见, 其分布与专科来源及性别密切相关。不同专科间氟喹诺酮类耐药的差异可能反映了各专科的用药模式。以定量尿白细胞为核心的分层策略, 结合菌落数及临床背景, 有助于临床药师对 GBS 阳性培养结果进行精准解读, 优化抗菌药物使用决策。

群体感应分子 AI-2 参与的肺炎克雷伯菌多重耐药性调控研究

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目的 群体感应信号 AI-2 广泛存在于革兰氏阴

性菌和革兰氏阳性菌中,参与细菌间的跨种属信息交流,在调控细菌群体行为中发挥重要作用。在肺炎克雷伯菌中,AI-2参与调控致病相关表型。本研究旨在探讨临床分离菌株肺炎克雷伯菌群体感应分子AI-2与抗微生物药物耐药性之间的关系。

方法 通过哈维氏弧菌生物发光检测法对临床分离菌株肺炎克雷伯菌筛选出AI-2含量高的菌株,再结合其抗微生物药物耐药情况进行分析。构建体外生物膜模型,评估肺炎克雷伯菌群体感应分子AI-2含量和生物膜形成量的相关性。之后对肺炎克雷伯菌的群体感应和耐药机制进行系统分析,采用qPCR评估AI-2含量高的临床分离菌株肺炎克雷伯菌生物膜、群体感应和耐药相关基因的表达水平。

结果

通过哈维氏弧菌生物发光检测法,筛选出临床分离菌株肺炎克雷伯菌AI-2升高10倍以上28株,升高5倍以上61株,部分作为研究对象。

肺炎克雷伯菌临床菌株AI-2分泌水平与多种抗微生物药物耐药性之间存在显著相关性(图1)。

肺炎克雷伯菌临床菌株中群体感应因子AI-2含量的差异与其生物膜形成能力密切相关,表明AI-2在生物膜的成熟过程中起到了关键作用(图2)。

AI-2含量高的菌株中 β -内酰胺类抗生素耐药基因无显著变化,但生物膜、群体感应和外排泵相关基因显著上调(图3)。

图1:菌株AI-2相对表达量与抗生素耐药之间的相关性

图2:菌株AI-2相对表达量与生物膜之间的相关性

图3:AI-2相对表达量高的菌株基因表达差异

结论 群体感应分子AI-2是肺炎克雷伯菌抗微生物药物耐药性的一个重要因素。通过抑制群体感应信号,能够有效增强抗微生物药物对细菌的杀菌效果,可能成为克服肺炎克雷伯菌耐药性和生物膜相关感染的有效策略。未来,开发靶向群体感应系统的药物为抗生素联合疗法提供了新的思路。

关键词: 肺炎克雷伯菌、群体感应、多重耐药性、生物膜

热带念珠菌对唑类耐药机制的基因组学研究

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目的 热带念珠菌引起的侵袭性念珠菌病对血液恶性肿瘤患者构成了严重威胁。热带念珠菌分离株对唑类药物的耐药日益普遍,这使得治疗策略变得复杂,因此有必要详细了解其耐药性机制。

方法 我们对2017年至2021年间从血液恶性肿瘤患者中收集的15株热带念珠菌分离株进行了回顾性分析。进行了全基因组测序(WGS)以获得高分辨率基因组数据。

结果 结果显示MLST支系4成为主要的唑类耐药克隆。所有唑类耐药分离株都携带ERG11突变A395T和C461T,大多数携带UPC2突变T503C。在所有唑类耐药分离株中都观察到了ERG11基因座上一致的拷贝数变异(CNV),这表明它在唑类耐药中起着关键作用。我们的综合分析(包括SNP、dN/dS比率和CNV)证实,ERG11是热带念珠菌抗性机制中的核心角色。

结论 本研究对于来自血液恶性肿瘤患者的唑类耐药热带念珠菌分离株进行了全面的基因组分析。关键基因组改变的鉴定,尤其是ERG11基因的改变,为临床管理提供了有价值的见解,并强调了在肿瘤环境中持续进行基因组监测以指导抗真菌治疗的必要性。

关键词: 热带念珠菌、唑类耐药性、血液恶性肿瘤、全基因组测序(WGS)、ERG11

2025年甘肃省细菌耐药监测分析

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2. 甘肃省人民医院

目的 监测 2025 年甘肃省主要地区医疗机构临床分离菌对抗菌药物的敏感性。

方法 甘肃省 100 所医院临床分离菌采用纸片扩散法或商品化药敏试验自动测试仪按 CHINET 统一监测技术方案进行抗菌药物敏感性试验, 按 2025 年美国临床和实验室标准化协会折点标准判断结果。

结果 2024 年 1—12 月 100 所医院共监测临床分离菌 137 607 株, 其中革兰阳性菌占 26.3%, 革兰阴性菌占 73.7%。金黄色葡萄球菌和其他凝固酶阴性葡萄球菌(除假中间葡萄球菌和施氏葡萄球菌外)中甲氧西林耐药株(MRSA 和 MRCNS)的检出率分别为 32.7%、74.2%。粪肠球菌和屎肠球菌对高浓度庆大霉素的耐药率分别为 36.4%、35.5%, 两者中均有少数万古霉素耐药株, 且显示屎肠球菌对多数抗菌药物的耐药率高于粪肠球菌。2025 年儿童和成人中分离的非脑膜炎肺炎链球菌中青霉素耐药株的检出率为 0.9%, 占比较低。碳青霉烯类耐药大肠埃希菌、肺炎克雷伯杆菌检出率分别为 0.7%、3.5%。肠杆菌目中, 大肠埃希菌属整体耐药水平低于肺炎克雷伯菌属。铜绿假单胞菌对亚胺培南和美罗培南的耐药率分别为 9.4%和 6.9%, 不动杆菌属对以上两药的耐药率分别高达 51.0%和 48.9%。

结论 2025 年甘肃省主要地区临床分离菌的耐药状况持续呈现严重趋势, 临床需依据监测结果合理选用抗菌药物, 以有效控制细菌耐药性的发展。

2025 年甘肃省重症患者临床分离菌分布及耐药分析

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目的 通过对 2025 年甘肃省重症患者临床分离菌的构成及对抗菌药物的敏感性、耐药性监测, 为临床重症感染的临床治疗和合理用药及防控提供参考。

方法 共收集 2025 年甘肃省细菌耐药监测网 100 所成员单位分离自重症患者的非重复菌株, 按照全国细菌耐药监测网技术方案进行细菌鉴定及药敏试验, 利用 WHONET 5.6 软件对细菌及药敏结果数据进行统计分析。

结果 2025 年共收集重症患者分离菌 15578 株, 其中革兰阳性菌占 22.9%, 革兰阴性菌占 77.1%。分离率前 5 位的主要细菌依次为肺炎克雷伯菌(20.2%)、大肠埃希菌(14.3%)、鲍曼不动杆菌(13.7%)、金黄色葡萄球菌(8.7%)和铜绿假单胞菌(5.3%)。主要标本来源为痰(65.7%)、血液(9.5%)和尿(6.9%)。耐甲氧西林金黄色葡萄球菌(MRSA)占比 36.8%, 耐甲氧西林凝固酶阴性葡萄球菌占比为 86.8%, 未发现万古霉素及替考拉宁耐药株。大肠埃希菌对第三代头孢菌素、喹诺酮类及碳青霉烯类的耐药率占比分别为 55.8%、53.1%和 1.4%。肺炎克雷伯菌对第三代头孢菌素及碳青霉烯类的耐药率占比分别为 24.9%和 10.9%, 肺炎克雷伯菌对碳青霉烯类的耐药率显著高于大肠埃希菌。非发酵糖革兰阴性杆菌中耐碳青霉烯类鲍曼不动杆菌(CRAB)占比高达 84.7%, 碳青霉烯耐药铜绿假单胞菌(CRPA)占 18.0%。

结论 2025 年甘肃省重症患者分离菌以革兰阴性菌为主, 其耐药及分布特点与甘肃省全人群、全国水平不同, 其抗菌药物耐药形势较严峻。特别是 CRAB 的高检出率以及肺炎克雷伯菌对碳青霉烯类耐药性的增加, 提示需进一步加强重症病房的感染控制和抗菌药物管理。

关键词 细菌; 重症患者; 抗菌药物; 耐药监测; 甘肃省

2025 年甘肃省耐碳青霉烯类肠杆菌目细菌的分布特征及耐药性监测

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目的 了解 2025 年甘肃省耐碳青霉烯类肠杆菌目细菌 (CRE) 的分布特征及耐药性, 为临床感染防控和合理用药提供参考依据。

方法 按照全国细菌耐药监测网统一方案, 纳入并分析 2025 年甘肃省细菌耐药监测网 100 所成员单位分离的非重复肠杆菌目细菌菌株, 采用 WHONET 5.6 软件进行统计分析, 并与全省及全国平均水平进行比较。

结果 2025 年全省共纳入肠杆菌目细菌 137,607 株, CRE 检出以耐碳青霉烯类肺炎克雷伯菌、耐碳青霉烯类大肠埃希菌和耐碳青霉烯类阴沟肠杆菌为主, 全人群检出率分别为 3.5%、0.7% 和 3.9%。男性尿液耐碳青霉烯类肺炎克雷伯菌检出率 (13.7%) 显著高于女性 (4.2%), 血液标本耐碳青霉烯类肺炎克雷伯菌检出率 (6.3%) 亦高于痰液来源 (3.1%), 提示不同标本类型及性别间 CRE 分布存在差异。重症患者 CRE 检出率最高, 耐碳青霉烯类肺炎克雷伯菌、耐碳青霉烯类大肠埃希菌及阴沟肠杆菌碳青霉烯耐药率分别为 10.9%、1.4% 和 10.1%, 急诊患者次之 (耐碳青霉烯类肺炎克雷伯菌 9.5%), 内科患者最低 (耐碳青霉烯类肺炎克雷伯菌 1.5%), 提示重症监护病房和急诊是 CRE 高负担区域。成人耐碳青霉烯类肺炎克雷伯菌检出率 (4.5%) 和阴沟肠杆菌碳青霉烯耐药率 (5.0%) 均显著高于老年人 (2.8%、3.5%) 及儿童 (1.0%、2.0%), 儿童肠杆菌目细菌对临床常用抗菌药物的耐药率整体低于成人。

三级医院耐碳青霉烯类肺炎克雷伯菌检出率 (4.9%) 和阴沟肠杆菌碳青霉烯耐药率 (5.0%) 均显著高于二级医院 (1.6%、1.7%), 提示三级医院 CRE 感染防控压力更大。耐碳青霉烯类肺炎克雷伯菌对临床常用抗菌药物的耐药率均显著高于碳青霉烯类敏感肺炎克雷伯菌, 替加环素和多黏菌素 B 对耐碳青霉烯类肺炎克雷伯菌仍保持相对较高的体外抗菌活性, 是目前治疗耐碳青霉烯类肺炎克雷伯菌感染的重要选择。

结论 2025 年甘肃省 CRE 以耐碳青霉烯类肺炎克雷伯菌为主, 耐碳青霉烯类阴沟肠杆菌检出率亦不容忽视, 重症及急诊患者、成人、三级医院及男性尿路感染患者中 CRE 检出率较高, 耐药形势严峻。需重点加强重症监护病房和急诊科的感染防控, 推进多学科联动, 强化抗菌药物管理, 以遏制 CRE 播散流行。

关键词: 细菌耐药监测; 耐碳青霉烯类肠杆菌目细菌; 耐碳青霉烯类肺炎克雷伯菌; 耐碳青霉烯类大肠埃希菌; 耐碳青霉烯类阴沟肠杆菌

2025 年甘肃省脓液标本细菌分布及耐药性分析

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目的 分析 2025 年甘肃省血液标本病原菌分布及耐药性特征, 为血流感染诊疗与抗菌药物合理使用提供依据。

方法 收集甘肃省细菌耐药监测网 100 所医院 2025 年血液标本细菌监测数据, 剔除重复菌株后采用药敏纸片扩散法、最低抑菌浓度法及全自动微生物检测系统进行药敏试验与统计分析。

结果 共纳入菌株 5702 株,革兰阳性菌占 39.9%,革兰阴性菌占 60.1%。革兰阳性菌以表皮葡萄球菌、金黄色葡萄球菌、人葡萄球菌、屎肠球菌、肺炎链球菌为主。MRSA 检出率 31.2%,MRCNS 检出率 78.4%,未检出万古霉素、替考拉宁耐药株。粪肠球菌对氨苄西林耐药率 5.6%,屎肠球菌 79.3%;肺炎链球菌对红霉素耐药率 88.8%,对青霉素、左氧氟沙星耐药率较低。革兰阴性菌以大肠埃希菌、肺炎克雷伯菌、阴沟肠杆菌、鲍曼不动杆菌为主。大肠埃希菌对三代头孢、喹诺酮类耐药率分别为 50.5%、51.0%,碳青霉烯类耐药率仅 0.4%。肺炎克雷伯菌碳青霉烯类耐药率 6.3%,阴沟肠杆菌对头孢他啶、头孢噻肟耐药率偏高。铜绿假单胞菌碳青霉烯类耐药率 17.1%,鲍曼不动杆菌碳青霉烯类耐药率 74.5%,多重耐药问题突出。嗜麦芽窄食单胞菌对常用药物整体敏感。

结论 2025 年甘肃省血液分离菌以革兰阴性菌为主,大肠埃希菌为优势菌株。不同菌种耐药差异明显,大肠埃希菌对三代头孢、喹诺酮类耐药率偏高,鲍曼不动杆菌碳青霉烯类耐药严峻。葡萄球菌、肠球菌、链球菌对万古霉素、利奈唑胺高度敏感。临床应结合本地耐药监测结果,规范经验性抗感染治疗,加强多重耐药菌防控,促进抗菌药物合理应用。

关键词:脓液;细菌分布;耐药监测;抗菌药物

2025 年甘肃省老年患者临床分离菌分布及耐药性分析

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2. 甘肃中医药大学

目的 通过对 2025 年甘肃省老年人群临床分

离菌的构成及对抗菌药物的敏感性、耐药性监测,为老年感染患者的临床治疗和合理用药提供参考。

方法 收集 2025 年甘肃省细菌耐药监测网 100 所成员单位分离自老年患者(≥ 65 岁)的病原菌,按照全国细菌耐药监测网技术方案对细菌进行鉴定和药敏试验,利用 WHONET 5.6 软件对细菌及药敏结果数据进行统计分析。

结果 共收集老年患者分离菌 51,909 株,其中革兰阳性菌占 18.8%,革兰阴性菌占 81.2%。主要标本来源为痰(55.8%)、尿(19.9%)和血液(4.5%)。分离率前 10 位细菌依次为大肠埃希菌(23.4%)、肺炎克雷伯菌(22.5%)、金黄色葡萄球菌(6.1%)、鲍曼不动杆菌(5.7%)、铜绿假单胞菌(5.2%)、阴沟肠杆菌(4.9%)、产酸克雷伯菌(3.3%)、流感嗜血杆菌(2.8%)、屎肠球菌(2.3%)和粪肠球菌(2.2%)。耐甲氧西林金黄色葡萄球菌占比 34.7%,耐甲氧西林凝固酶阴性葡萄球菌占比 74.0%,未发现万古霉素及替考拉宁耐药菌株。第三代头孢菌素、喹诺酮类及碳青霉烯类耐药大肠埃希菌占比分别为 53.1%、61.2%和 0.8%;第三代头孢菌素及碳青霉烯类耐药肺炎克雷伯菌的检出率分别为 13.0%和 2.8%。非发酵糖革兰阴性杆菌中碳青霉烯类耐药铜绿假单胞菌占 8.1%,碳青霉烯类耐药鲍曼不动杆菌占 41.5%。

结论 2025 年甘肃省老年人群临床分离菌以革兰阴性菌为主,耐药及分布特点与甘肃省全人群及全国水平存在差异,抗菌药物耐药形势较为严峻。需持续加强老年人群病原菌及耐药性监测,为临床治疗和耐药菌防控提供依据。

关键词:细菌;老年患者;抗菌药物;耐药监测;甘肃省

2025 年甘肃省痰和肺泡灌洗液标本病原菌分布及耐药性特征分析

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目的 分析 2025 年甘肃省痰和肺泡灌洗液标本病原菌分布及耐药性特征，为呼吸道感染临床诊疗与抗菌药物合理使用提供依据。

方法 收集甘肃省细菌耐药监测网 100 所医院 2025 年痰及肺泡灌洗液标本细菌监测数据，剔除重复菌株后，采用药敏纸片扩散法、最低抑菌浓度法及全自动微生物检测系统进行药敏试验与统计分析。

结果 共纳入菌株 68498 株，革兰阴性菌占 83.8%，革兰阳性菌占 16.2%。革兰阴性菌分离率排名前五位的是肺炎克雷伯菌（27.5%）、大肠埃希菌（9.3%）、鲍曼不动杆菌（8.2%）、流感嗜血杆菌（7.8%）、铜绿假单胞菌（6.9%）；革兰阳性菌以金黄色葡萄球菌（8.8%）、肺炎链球菌（4.5%）为主。革兰阳性菌中，金黄色葡萄球菌 MRSA 检出率 35.5%，凝固酶阴性葡萄球菌 MRCNS 检出率 84.7%，未检出万古霉素、替考拉宁耐药株；粪肠球菌和屎肠球菌对氨苄西林耐药率分别为 7.1%和 86.9%；肺炎链球菌对青霉素耐药率 0.9%、红霉素耐药率 94.0%，对万古霉素、利奈唑胺 100% 敏感。革兰阴性菌中，大肠埃希菌对第三代头孢菌素、喹诺酮类耐药率分别为 48.9%、44.1%，碳青霉烯类耐药率 0.9%；肺炎克雷伯菌第三代头孢菌素耐药率 11.6%、碳青霉烯类耐药率 3.2%；阴沟肠杆菌对头孢他啶、头孢噻肟耐药率分别为 14.5%、19.1%。非发酵菌中，铜绿假单胞菌碳青霉烯类耐药率 10.1%；鲍曼不动杆菌碳青霉烯类耐药率 49.8%，对头孢他啶、环丙沙星耐药率超 50%，仅对米诺环素、替加环素高度敏感。流感嗜血杆菌对氨苄西林耐药率 55.2%，阿奇霉素非敏感率 28.7%，左氧氟沙星非敏感率 4.9%。

结论 甘肃省呼吸道感染以革兰阴性菌为主，肺炎克雷伯菌为优势菌；革兰阳性菌对万古霉素、利奈唑胺高度敏感；大肠埃希菌对第三代头孢、喹

诺酮类耐药突出，鲍曼不动杆菌碳青霉烯类耐药严峻。临床应依据本地耐药数据规范用药，加强多重耐药菌防控。

关键词：痰；肺泡灌洗液；病原菌；耐药性

抗菌药物的药理药理学研究与临床试验

Optimizing Vancomycin Therapy: The Critical Role of Dosing Frequency, AUC Monitoring and Gender: A Retrospective Cohort Study

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蚌埠医科大学第一附属医院

Background Optimizing vancomycin therapy requires balancing efficacy and toxicity. Although therapeutic drug monitoring (TDM) guided by area-under-the-curve (AUC) measurements is now recommended, the effect of dosing frequency and patient-specific factors remain underexplored. This study examined the relationships of dosing frequency, pharmacokinetic/pharmacodynamic (PK/PD) parameters, clinical efficacy, and toxicities in patients receiving different vancomycin regimens

Methods This retrospective cohort study analyzed 193 vancomycin dosing regimens in 148 adult patients who were treated at a tertiary teaching hospital in China between January 2013 and March 2021, 175 of which were guided by TDM. The association of dosing frequency, PK/PD parameters, and patient demographics with clinical efficacy and safety were examined.

Results Clinical success in patients with staphylococcal infections was not significantly associated with Ctrough, AUC, or AUC/minimum inhibitory concentration (AUC/MIC). However, dosing frequency was a significant and independent determinant of Ctrough ($P=0.031$), in that regimens with more frequent dosing led to higher Ctrough values without altering total the daily AUC. Receiver operating characteristic (ROC) analysis

indicated that AUC was a better predictor of nephrotoxicity (AUROC=0.87) than Ctrough (AUROC=0.80). Multivariate analysis confirmed that pre-treatment creatinine clearance was the primary predictor of post-treatment renal function. Female gender was an independent risk factor for post-treatment anemia ($P=0.002$).

Conclusion Traditional PK/PD targets (Ctrough and AUC/MIC) did not correlate with clinical efficacy. A greater dose frequency may help to increase time-dependent bacterial killing and maintain a high level of patient safety when implementing a personalized vancomycin regimen.

替加环素药动学/药效学及药物性肝损伤临床危险因素研究进展

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替加环素 (TGC) 作为首个应用于临床的甘氨酸环素类抗生素, 通过对米诺环素进行侧链修饰, 不仅有效规避了四环素类药物的常见耐药机制, 还显著拓展了抗菌谱, 是治疗复杂性腹腔感染、复杂性皮肤及软组织感染以及社区获得性肺炎等多耐药菌感染的重要选择。其药动学/药效学 (PK/PD) 特征呈时间依赖性, 具有长半衰期特点, 疗效关键指标为 0-24 h 药物曲线下面积与最低抑菌浓度的比值 (AUC_{0-24h}/MIC), 但替加环素的治疗窗相对狭窄。在替加环素引发的诸多不良反应中, 药物性肝损伤 (TGC-DILI) 尤其值得高度警惕, 已成为制约其临床安全应用的核心问题。TGC-DILI 可表现为胆汁淤积型、肝细胞损伤型或混合型肝损伤, 重者可进展为急性肝衰竭甚至导致死亡。本文系统综述了 TGC 的 PK/PD 特征、归纳了包括高效液相色谱-串联质谱等治疗药物监测 (TDM) 关键技术及基于群体药动学模型的个体化给药优化策略, 重点阐述了

TGC-DILI 的临床流行病学特征、关键危险因素及潜在毒性机制,同时分析了 TDM 在平衡 TGC 疗效与肝安全风险中的应用价值,旨在为临床实现 TGC 安全有效的个体化治疗、完善 TGC-DILI 防控体系提供更全面的理论依据。

Prevalence, Mortality, Risk Factors, and Treatment of Carbapenem-resistant Hypervirulent *Klebsiella Pneumoniae*: An Evidence Map

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Background Carbapenem-resistant hypervirulent *Klebsiella pneumoniae* (CR-hvKP) is a critical global health threat due to its hypervirulence and multi-drug resistance, causing severe, high-mortality infections. This study systematically reviews its epidemiology, risk factors, treatment strategies, and activity

Methods We searched databases to identify studies reporting CR-hvKP prevalence, resistance profiles, risk factors, treatment strategies, and activity. Two reviewers independently extracted data; a third resolved discrepancies. Results were summarized descriptively

Results Forty-three studies involving 9,283 carbapenem-resistant *Klebsiella pneumoniae* (CRKP) strains were included. The median prevalence of CR-hvKP among CRKP was 9.40% (IQR 4.40–14.80%) via the string test plus virulence assay. Diabetes (OR = 10.947, $P = 0.010$) and ICU admission (OR = 16.012, $P = 0.003$) were independent risk factors for CR-hvKP infection. Among 130 patients, the most commonly used antibiotics included meropenem (34.62%), cefoperazone-sulbactam (31.54%), and tigecycline (28.46%).

However, treatment failure remains a significant concern. Antimicrobial resistance analysis indicated that CR-hvKP exhibited high resistance rates to cephalosporins (>80%) and quinolones (45–100%). One study found high susceptibility (92.50–100.00%) to nitrofurantoin, polymyxins, imipenem-relebactam, tigecycline, and colistin. Mortality analysis revealed a median mortality rate of 30.30% (IQR 13.33–53.06%)

Conclusion Current therapeutic strategies against CR-hvKP lack standardization, and widely applied combination therapy has inconsistent efficacy. Further research is urgently needed to optimize treatment regimens. Early detection, precise antimicrobial stewardship, and stringent infection control measures are crucial to mitigate the spread and impact of CR-hvKP

细菌真菌感染的流行病学

多重耐药菌感染伴维生素 D 缺乏的预后研究

谢¹

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背景 维生素 D 在多重耐药菌感染的可能保护作用备受关注,但关于住院的多重耐药菌感染患者维生素 D 缺乏症客观数据尚无定论。目的:探讨维生素 D 缺乏在多重耐药菌感染患者中的患病率,并分析其与临床结果和疾病严重程度的关系。

方法 选取从 2022 年 1 月 31 日到 2024 年 1 月 31 日内蒙古医科大学第二附属医院和内蒙古自治区人民医院 ICU 住院的成年多重耐药菌感染患者进行回顾性、观察性研究。入院 24 小时内评估 25(OH)D 血清水平,并将其分为三组:正常组(≥ 25 ng/mL)、不足组(12-25 ng/mL)、缺乏组(< 12 ng/mL)。

结果 纳入的 156 名住院的多重耐药菌感染患者中平均血清 25(OH)D 水平为 16.2 ng/mL,其中维生素 D 不足/缺乏的患病率高达 79.7%。和正常组相比,维生素 D 缺乏组的死亡率、住院时间明显升高,且血清 25(OH)D 水平与院内死亡率($P=0.048$)独立相关。除了维生素 D 缺乏,在其他变量中,年龄、长期卧床、营养风险与死亡率显著独立相关($P<0.05$)。

结论 维生素 D 缺乏在多重耐药菌感染患者中非常普遍。维生素 D 缺乏与多重耐药菌感染患者重程度和临床结局的风险相关。补充维生素 D 是否会影响多重耐药菌感染患者的临床结果需要通过进一步的临床观察性试验来评估。

谢 孟文勤

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背景 尽管医学技术不断进步,但是耐药菌感染如同隐藏在暗处的“超级杀手”,仍具有死亡率高、治疗困难、增加医疗成本等危险,使全球公共卫生安全面临重大挑战。肌肉减少是否是多重耐药菌感染的预测因素及对预后的影响,研究较为局限。

目的 探讨肌少症对多重耐药菌感染预后的影响。

方法 本研究为一项回顾性队列研究,纳入了 2015 年至 2024 年间 511 例多重耐药菌患者。根据腹部计算机断层扫描(CT)评估的腹部肌肉总面积测量值来定义肌肉减少症。随后,我们将患者分为两组:肌肉减少症组和非肌肉减少症组,并采用多变量 Cox 比例分析比较肌肉减少症对短期(28 天)和长期(1 年)死亡率的影响。

结果 共纳入 511 例患者,平均年龄为 64.4 ± 13.1 岁。其中,294 例(57.5%)患者为男性,302 例(59.1%)患有肌少症。我们发现,肌少症组的 28 天、1 年死亡率均显著高于非肌少症组(分别为 11.7% vs. 6.2%, $P<0.001$; 40.6% vs. 20.1%, $P<0.001$)。单变量 Cox 分析显示,与非肌少症组相比,肌少症组与各死亡率的增加显著相关(28 天死亡率,风险比(HR)=2.210, 95%置信区间(CI) [1.424-3.542], $P<0.001$; 1 年死亡率, HR=2.189, 95% CI [1.420, 2.581], $P<0.001$)。多变量 Cox 分析显示,即使在调整了混杂变量后,肌少症组的短期和长期死亡率仍显著高于非肌少症组(28 天死亡率,风险比[HR]=2.011, 95%置信区间[CI] [1.112, 3.214], $P=0.002$; 1 年死亡率, HR=1.479, 95% CI [1.271, 2.164], $P<0.001$)。

结论 肌少症与多重耐药菌感染患者的短期和长期死亡率均相关。在临床环境中,应密切关注这些患者的短期和长期预后。

拨动肌肉健康的弦,弹好多重耐药的曲 --511 例多重耐药菌感染伴肌少症患者的研究

某儿童医院 7 年念珠菌血症临床特点及耐药性分析

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目的 分析念珠菌血症患儿的临床特征，为儿童念珠菌血症的诊治提供参考依据。

方法 回顾性分析郑州大学附属儿童医院 2019 年 1 月至 2025 年 12 月期间血培养念珠菌培养阳性患儿的临床资料，对人口学特征、菌种分布、基础疾病、治疗方案及抗真菌药敏感性等进行分析。按年龄将患儿分为 3 组：新生儿（ <30 d）、婴儿（ 30 d~1 岁）和儿童（1~18 岁）。

结果 共纳入 72 例患儿，其中男性 45 例，女性 27 例；患儿年龄 3 d 至 14 岁，中位年龄 2 个月。新生儿、婴儿和儿童分别占 33.33%、34.72% 和 31.94%。念珠菌血症的年平均发病率为 11 例/10 万人。研究期间，非白色念珠菌的分离比例总体呈升高趋势，而白色念珠菌呈下降趋势。所有患儿在念珠菌血症发生前 30 d 内均有广谱抗生素使用史，其中 60 例留置中心静脉导管，21 例接受全肠外营养，18 例存在其他部位念珠菌定植。9 例患儿合并其他部位感染，包括念珠菌尿（7 例）、真菌性脑膜炎（4 例）和真菌性眼内炎（1 例）。新生儿念珠菌血症更易合并其他部位感染，但与其他年龄组相比差异无统计学意义（ $P=0.11$ ）。白色念珠菌为最常见菌种（34 株），其次为近平滑念珠菌（14 株）和热带念珠菌（10 株）。儿童组非白色念珠菌血症发生率（73.91%）显著高于婴儿组（48.00%）和新生儿组（37.50%），差异有统计学意义（ $P=0.04$ ）。念珠菌检出率最高的科室为早产儿（27.78%），其次为儿童重症监护室（16.67%）和新生儿重症监护室（13.89%）。白念珠菌和近平滑念珠菌是在所有患儿中均为最常见的病原体，但血液性肿瘤患者中，热带念珠菌（77.78%）为主要分离株。药敏试验结果显示，念珠菌对氟康唑、棘白菌素类和两性霉素 B 的敏感性分别是 84.84%、100.00%

和 100.00%。71 例患儿在血培养阳性后启动抗真菌治疗。经验性用药以唑类为主（56 例），其次为棘白菌素类（9 例）和两性霉素 B（6 例）。40 例患儿在治疗中调整用药方案，多由唑类更换为棘白菌素类或两性霉素 B。治疗中位时间 23 d（IQR: 14, 37 d），患儿 30 d 死亡率为 16.67%。

结论 儿童念珠菌血症多见于 1 岁以下婴幼儿，主要病原菌为白色念珠菌，但非白色念珠菌的分离比例逐年上升。对于存在高危因素或临床抗感染治疗效果不佳的患儿，应警惕念珠菌血症的可能。

住院病人 CRE 与 VRE 院内感染的流行现状及其影响因素分析

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目的 通过分析住院患者耐碳青霉烯类肠杆菌（CRE）及耐万古霉素肠球菌（VRE）医院感染的流行病学特征，并探讨其发生的独立危险因素，为精准防控提供依据。

方法 采用回顾性病例对照研究设计，选取 2015 年 1 月 1 日至 2025 年 12 月 31 日泉州市第一医院发生 CRE 或 VRE 医院感染的 127 例住院患者为病例组。采用 1:1 分级匹配法（依次匹配科室、急性疾病严重程度、慢性基础疾病数量）选取 127 例非感染患者为对照组。采用单因素及多因素条件 logistic 回归分析 CRE 或 VRE 感染的危险因素。

结果 于 127 例感染患者中，65-80 岁者占 38.58%。感染主要集中于重症医学科（44.88%）、神经外科（12.60%）和肝胆外科（7.09%）等高危科室。病原菌以肺炎克雷伯菌（70.87%）和屎肠球菌（10.24%）为主。多因素分析显示，腹腔感染（ $OR=3.625$, 95%CI: 1.059~12.411）、使用碳青霉烯类抗菌药物（ $OR=2.337$, 95%CI: 1.249~4.372）及更高的医疗总费用（ $OR=1.508$, 95%CI: 1.069~2.127）

是 CRE 及 VRE 医院感染的独立危险因素（均 $P<0.05$ ）。

结论 CRE 与 VRE 医院感染存在明确的科室与病原聚集性。腹腔感染、使用碳青霉烯类抗菌药物及高医疗费用是独立危险因素。本研究通过分级匹配有效控制了关键混杂偏倚，创新性地揭示在平衡基线后，传统危险因素如手术、侵入性操作的影响可能通过上述核心因素间接影响。本研究利用分级匹配的病例对照设计，有效控制了关键混杂偏倚，明确了 CRE 与 VRE 医院感染在我院的流行病学特点，并识别出腹腔感染、碳青霉烯类药物暴露和高医疗费用为其独立危险因素。

铜绿假单胞菌血流感染患者预后的危险因素分析

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目的 探讨铜绿假单胞菌（*Pseudomonas aeruginosa*, PA）血流感染的预后危险因素，为临床合理防控 PA 血流感染提供理论依据。

方法 收集 2019 年 1 月-2024 年 6 月广东省人民医院 PA 血流感染患者的临床病历资料共 151 例。将血培养结果为耐碳青霉烯铜绿假单胞菌（Carbapenem-resistant *Pseudomonas aeruginosa*, CRPA）的患者资料 34 例，定义为 CRPA 组；碳青霉烯敏感铜绿假单胞菌（Carbapenem-susceptible *Pseudomonas aeruginosa*, CSPA）的患者资料 117 例，定义为 CSPA 组。运用单因素及多因素 Logistics 回归，分析 CRPA 血流感染患者的预后因素。

结果 CRPA 组血流感染患者的住院时间长于 CSPA 组（ $Z=-1.970$, $P=0.049$ ），且重症监护室患者显著多于 CSPA 组（ $\chi^2=19.215$, $P<0.001$ ），两组患者在年龄、性别构成等方面无显著性差异（ $P>0.05$ ）。

单因素分析显示：患者伴呼吸系统疾病（ $\chi^2=8.536$, $P=0.003$ ），接受机械通气（ $\chi^2=10.261$, $P=0.001$ ）、留置尿管（ $\chi^2=4.189$, $P=0.041$ ）和引流管（ $\chi^2=3.984$, $P=0.046$ ）与 CRPA 血流感染发生相关。经多因素 Logistics 回归分析显示：患有呼吸系统疾病（ $OR=2.722$, $P=0.038$ ），接受机械通气（ $OR=2.708$, $P=0.043$ ）是导致患者 CRPA 血流感染发生的重要危险因素。CRPA 组患者病死率 32.35%，显著高于 CSPA 组（ $\chi^2=7.051$, $P=0.008$ ）。

结论 患有呼吸系统疾病、接受机械通气是导致患者 CRPA 血流感染发生的重要危险因素，临床需加强感染监测、优化抗菌药物使用，以减少 CRPA 血流感染的发生。

关键词 铜绿假单胞菌；血流感染；碳青霉烯耐药；感染因素；临床预后

金黄色葡萄球菌血流感染患者预后危险因素分析

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目的 探讨金黄色葡萄球菌（*Staphylococcus aureus*, SA）血流感染患者预后的相关危险因素，为临床早期识别高危患者及制定针对性干预措施提供依据。

方法 回顾性收集 2020 年 1 月至 2025 年 12 月广东省人民医院确诊的 SA 血流感染患者的临床资料 305 例。根据患者出院时临床结局分为预后良好组 198 例和预后不良组 107 例。比较两组患者的资料，采用单因素与多因素 Logistic 回归分析，评估影响患者预后的危险因素。

结果 预后不良组患者年龄和年龄校正查尔森合并症指数（age-adjusted Charlson comorbidity index, aCCI）总分高于预后良好组（ $P<0.05$ ）。单因素分析结果显示，患者有呼吸道疾病史、低蛋白血症史、神

经系统疾病史、 ≥ 3 种基础疾病史、留置引流管、中心静脉插管、留置尿管、机械通气、耐甲氧西林金黄色葡萄球菌(Methicillin-resistance *Staphylococcus aureus*, MRSA) 感染、 ≥ 3 种抗菌药物联合使用及入住 ICU 与患者预后不良相关($P < 0.05$)。多因素 Logistic 回归分析结果显示, 患有低蛋白血症史($OR = 1.922$, $95\%CI: 1.041-3.547$, $P = 0.037$)、神经系统疾病史($OR = 2.416$, $95\%CI: 1.112-5.253$, $P = 0.026$)、存在机械通气($OR = 2.450$, $95\%CI: 1.014-5.919$, $P = 0.046$)及入住 ICU($OR = 2.906$, $95\%CI: 1.454-5.808$, $P = 0.003$)是影响 SA 血流感染患者预后的独立危险因素。

结论 患有低蛋白血症史、神经系统疾病史、存在机械通气及入住 ICU 是 SA 血流感染患者预后不良的独立危险因素。临床应加强对高危患者的早期识别和综合管理, 以期改善患者预后。

关键词: 金黄色葡萄球菌; 血流感染; 临床预后; 危险因素; 重症监护室

耐甲氧西林金黄色葡萄球菌血流感染的危险因素及预后影响因素

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目的 探讨耐甲氧西林金黄色葡萄球菌(methicillin-resistant *Staphylococcus aureus*, MRSA) 血流感染的发生危险因素及其预后影响因素, 为临床早期识别高危人群及优化治疗策略提供依据。

方法 回顾性分析 2019 年 1 月至 2025 年 12 月广东省人民医院 356 例金黄色葡萄球菌血流感染患者的临床资料, 其中 MRSA 感染 115 例, 甲氧西林敏感金黄色葡萄球菌(methicillin-susceptible *Staphylococcus aureus*, MSSA) 感染 241 例。收集患者一般资料、基础疾病、侵入性操作、抗菌药物使用情况及临床结局等信息, 并采用年龄校正查尔森合并症指数(age-adjusted Charlson comorbidity index, aCCI)

评估患者基础状况。运用单因素分析和多因素 Logistic 回归模型, 评估 MRSA 血流感染的危险因素及其对患者预后的影响因素。

结果 MRSA 组患者 aCCI 评分及住院时间均高于 MSSA 组($P < 0.05$)。单因素分析显示, 呼吸道疾病史、肾脏疾病史、 ≥ 3 种基础疾病史、留置引流管、留置尿管、机械通气、 ≥ 3 种抗菌药物联合使用及入住 ICU 与 MRSA 血流感染相关($P < 0.05$)。多因素 Logistic 回归分析结果显示, 肾脏疾病史($OR = 1.717$, $95\%CI: 1.022-2.887$, $P = 0.041$)及 ≥ 3 种抗菌药物联合使用($OR = 1.905$, $95\%CI: 1.155-3.141$, $P = 0.012$)为 MRSA 血流感染发生的独立危险因素。MRSA 血流感染患者死亡率为 20.00%, 明显高于 MSSA 组的 6.64%($P < 0.001$)。进一步分析显示, 肾脏疾病史($OR = 9.405$, $95\%CI: 1.846-47.909$, $P = 0.007$)及机械通气($OR = 18.823$, $95\%CI: 1.486-238.464$, $P = 0.023$)为 MRSA 血流感染患者死亡的独立危险因素。

结论 MRSA 血流感染患者病死率高于 MSSA 感染者。肾脏疾病史及 ≥ 3 种抗菌药物联合使用是 MRSA 血流感染发生的独立危险因素, 而肾脏疾病史及机械通气则与患者不良预后相关。临床应加强对合并肾脏疾病患者的感染管理, 规范侵入性操作, 并合理使用抗菌药物, 以降低 MRSA 血流感染发生风险并改善患者预后。

关键词: 耐甲氧西林金黄色葡萄球菌; 金黄色葡萄球菌血流感染; 危险因素; 临床预后; 肾脏疾病

2018-2025 年 ICU 难治性耐药铜绿假单胞菌呼吸道感染的危险因素及预后

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目的 探讨重症监护室(ICU)难治性耐药铜绿假单胞菌(DTR-PA)呼吸道感染的临床特征、危险

因素及其对患者预后的影响,为ICU DTR-PA感染的早期识别、防控及临床治疗提供依据。

方法 回顾性分析2018年1月至2025年12月广东省人民医院ICU确诊为铜绿假单胞菌(PA)呼吸道感染患者的临床资料192例,其中DTR-PA感染患者96例(DTR-PA感染组),同期随机选取非难治性耐药铜绿假单胞菌(NDTR-PA)呼吸道感染患者96例(NDTR-PA组),同时根据临床预后将患者分为生存组149例和死亡组43例。采用单因素及多因素Logistic回归分析ICU DTR-PA呼吸道感染的危险因素,并分析影响ICU PA呼吸道感染患者预后的相关因素。

结果 DTR-PA感染组患者既往有呼吸道疾病史(OR=4.866,95%CI:2.113-11.202, $P<0.001$)、糖尿病史(OR=4.104,95%CI:1.479-11.386, $P=0.007$)、机械通气(OR=3.133,95%CI:1.026-9.568, $P=0.045$)及 ≥ 3 种抗菌药物联用(OR=2.577,95%CI:1.108-5.994, $P=0.028$)为ICU DTR-PA呼吸道感染的重要危险因素。DTR-PA感染组病死率为36.46%,显著高于NDTR-PA组的8.33% ($P<0.001$),患者既往有消化系统疾病史(OR=3.416,95%CI:1.304-8.949, $P=0.012$)、糖尿病史(OR=3.148,95%CI:1.183-8.374, $P=0.022$)、留置引流管(OR=5.314,95%CI:1.104-25.568, $P=0.037$)以及感染DTR-PA(OR=4.250,95%CI:1.622-11.134, $P=0.003$)为影响ICU PA呼吸道感染患者预后的重要危险因素。

结论 ICU DTR-PA呼吸道感染患者病死率较高、预后较差。既往有消化系统疾病史、糖尿病史、留置引流管以及感染DTR-PA与ICU PA呼吸道感染患者的不良预后相关。

【关键词】重症监护室;难治性耐药铜绿假单胞菌;呼吸道感染;危险因素;临床预后

HIV 不同状态隐球菌性脑膜炎临床特征及隐球菌基因型比较

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目的 了解HIV阳性与HIV阴性隐球菌性脑膜炎(CM)患者临床特征和隐球菌基因型特点,提高对其诊疗水平。

方法 回顾性比较2015年3月至2024年2月广州某三甲医院HIV阳性和阴性CM患者的临床特征及隐球菌基因型。

结果 共纳入HIV阳性与HIV阴性CM患者各102和19例。阳性组较阴性组男性占比更高(80.4% vs. 47.4%, $P=0.006$)、年龄更小(40岁 vs. 49岁, $P=0.01$)、确诊更快(17天 vs. 45天, $P<0.001$)、脑脊液炎症反应更弱(P 均 <0.05),且第4周和第24周病死率更高,但未达到统计学差异(14.7% vs. 5.3%; 28.4% vs. 15.8%; $P>0.05$)。两组隐球菌基因分型均以新生隐球菌VN I型为主(98.0% vs. 100%, $P=0.332$),序列型以ST5为主(81.4% vs. 94.7%);阳性组检出2株格特隐球菌(VG),并首次发现3株新序列型ST685(其中1例患者24周随访时死亡)。

结论 与HIV阴性CM患者相比,HIV阳性组脑脊液炎症反应更弱,预后相对较差。阳性组发现的新型序列型ST685菌株感染需要被关注。

关键词:艾滋病,人类免疫缺陷病毒感染,隐球菌性脑膜炎,临床特征,基因型

呼吸道感染患者5种病原体IgM抗体检测及流行病学特征

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目的 探讨医院呼吸道感染患者中 5 种病原体 IgM 抗体的检出情况及流行病学特征, 为临床诊断和公共卫生防控提供科学依据。

方法 回顾性分析 2023 年 11 月至 2025 年 4 月期间广东省人民医院收治的 3569 例呼吸道感染患者的数据。采集患者静脉血样本, 通过胶体金法检测肺炎支原体 (*Mycoplasma pneumoniae*, MP)、肺炎衣原体 (*Chlamydia pneumoniae*, Cpn)、呼吸道合胞病毒 (*Respiratory syncytial virus*, RSV)、腺病毒 (*Adenovirus*, ADV) 及柯萨奇病毒 B 组 (*Coxsackievirus Group B*, CoxB) 的 IgM 抗体水平, 并结合患者性别、年龄及季节分布进行综合分析。

结果 5 种病原体 IgM 抗体总检出率为 18.97%, 其中单一感染占 17.71%, 混合感染占 1.26%。MP 检出率最高 (15.19%), 其次为 RSV、ADV 和 CoxB, Cpn 最低。不同年龄组间 MP 和 RSV 检出率差异具有统计学意义 ($\chi^2=472.056$, 64.158 , $P<0.001$), MP 主要集中于幼儿及少年组, RSV 在老年组检出率较高。MP 在秋冬季检出率显著高于其他季节 ($\chi^2=20.419$, $P<0.001$), 而 RSV、ADV 及 CoxB 的季节差异无统计学意义 ($P>0.05$)。不同性别间各病原体检出率差异均无统计学意义 ($P>0.05$)。

结论 呼吸道感染病原体的分布具有明显的年龄和季节差异, MP 主要集中于幼儿和青少年人群, 并在秋冬季高发, 而 RSV 在老年人群中的检出率相对较高。混合感染虽比例较低, 但仍可见以 ADV 与 RSV 为主的联合感染形式, 提示在不同人群和季节背景下开展多病原体联合检测具有一定的临床应用价值。

关键词: 呼吸道感染; IgM 抗体; 混合感染; 流行病学特征

Genomic Analysis of A Penicillin-susceptible, Methicillin-resistant *Staphylococcus Aureus*

(ST9332) Harboring Triple *MecA* Substitutions

null null

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Background *mecA*-positive MRSA is generally assumed to be broadly non-susceptible to β -lactams. Reports of penicillin-susceptible MRSA (PS-MRSA) challenge this view. We describe CDSYY2023, a cefoxitin-resistant yet penicillin-susceptible MRSA carrying three *mecA* substitutions (S225R, K239E, E246G) and a novel sequence type, ST9332

Methods The strain was recovered from the sputum of a hospitalized older adult with dementia and identified as *S. aureus* by MALDI-TOF MS (Autobio MS1000). Susceptibility testing followed CLSI procedures on VITEK 2 with parallel Mueller-Hinton edge tests (cefepime, penicillin). Key readouts were verified by Etest and independently confirmed at a referral laboratory. Whole-genome sequencing (Illumina HiSeq 2500) was assembled de novo with SOAPdenovo2. Functional annotation used COG/GO/KEGG; resistance and virulence genes were queried against CARD and VFDB. MLST was assigned and registered via PUBMLST

Results The draft genome is ~2,750,950 bp (GC 32.94%), with no plasmids, encoding 2,521 CDSs, 55 tRNAs, and 19 rRNAs. MLST designated ST9332. Phenotypically, VITEK 2 and MH edge tests agreed on cefepime resistance (17 mm), while penicillin remained susceptible (25 mm; Etest MIC 0.032 $\mu\text{g/mL}$), contrary to expectations for a *mecA*-positive background. Genomics revealed the triple *mecA* substitutions noted above and no definitive evidence of *bla_Z*. The resistome/virulome included multiple efflux and regulatory elements

Conclusions CDSYY2023 is a PS-MRSA with triple-substituted *mecA* on a novel MLST background (ST9332). Its penicillin-susceptible/cefoxitin-resistant profile likely reflects a specific *mecA* sequence/regulatory context, highlighting the limits of relying solely on cefoxitin-based screening to infer β -lactam behavior

2018-2024 年医院感染监测数据的回顾性分析

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目的 分析我院 2018-2024 年医院感染监测数据，探讨感染流行特征及防控成效。

方法 回顾性收集 2018-2024 年某三级甲医院医院感染监测数据，统计分析医院感染情况、漏报率、感染部位分布、环境卫生学监测、重点部位感染率、多重耐药菌监测、I类切口手术部位感染、手卫生监测等内容。

结果 2018-2024 年医院感染率、感染例次率、漏报率、漏报例次率分别为 2.68%、3.14%、2.11%、1.89%，且感染情况和漏报情况呈逐渐下降趋势（ $P<0.001$ ）。医院感染部位中以下呼吸道感染为主，占 45.81%。CLABSI、VAP、CAUTI 感染率分别为 0.37‰、7.83‰、1.41‰；其中 VAP 感染呈逐渐下降趋势（ $P<0.001$ ），而 CAUTI 感染呈上升趋势（ $P=0.004$ ）。5 类监测项目中的 MDRO 检出率在 7.63%-16.51% 范围内，CRAB 检出率和感染率最高。I类切口手术部位感染发生率为 0.48%，且呈逐渐下降趋势（ $P<0.001$ ）。环境卫生学监测中合格率较低为物体表面和医务人员卫生手消毒。手卫生依从率和正确率均呈逐渐下降趋势（ $P<0.05$ ）。

结论 2018-2024 年医院感染监测总体情况较好，但仍需对下呼吸道感染、CAUTI 感染、CRAB

监测、医务人员卫生手消毒监测等方面重点防控，提出针对性的防控措施，降低医院感染的发生。

基于全基因组测序的广州地区 B 群链球菌致病性分析

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目的 本研究旨在通过全基因组测序分析广州地区 B 群链球菌(GBS)临床分离株的血清型分布、序列类型(STs)、耐药基因和毒力因子，以了解当地 GBS 的遗传特征和耐药趋势，为优化 GBS 感染的预防和控制策略提供科学依据。

方法 本研究收集了 2016 年至 2022 年间广东省人民医院的 72 株 GBS 阳性临床分离株。采用多部位序列分型(MLST)和全基因组测序技术，对分离株的血清型、STs、耐药基因和毒力因子进行分析。微生物培养和鉴定按照医院临床实验室的标准程序进行，使用 VITEK MS 质谱仪进行鉴定，使用 VITEK® 2 Compact 系统进行抗菌药物敏感性测试。基因组 DNA 提取后，使用 Illumina Novaseq 6000 平台进行测序，并利用 CARD 和 VFDB 数据库识别耐药基因和毒力因子，通过 CDC 的 GBS 生物信息学分型工具进行血清型鉴定。

结果 72 株临床分离株中，血清型 III 最为常见（36.1%），其次是血清型 V（25.0%）。这些分离株被分为 22 种不同的 STs，分布在 7 个克隆复合体(CCs)中，其中 ST19 最为常见（15.3%）。耐药基因分析显示，61.1% 的分离株携带 *tetM* 基因，37.5% 携带 *ermB* 基因。毒力因子分析表明，所有分离株均含有 *lmb*、*bca* 和 *cpsJ* 基因，97.2% 含有编码溶血素的 *hlyB* 基因，73.6% 含有 *PI-1* 和 *PI-2a* 菌毛编码基因。

结论 本研究通过全基因组测序揭示了广州地区 GBS 分离株的遗传特征及血清型、耐药基因和毒力因子的显著差异，强调了持续流行病学监测的重

要性, 以了解当地病原体动态和抗生素耐药趋势。研究结果为广州地区 GBS 感染的预防和控制策略的优化提供了科学支持。未来的研究将扩大样本量, 建立广州主要医院的多中心 GBS 样本库, 并开展转录组学或蛋白质组学分析, 以探索基因表达变化如何影响 GBS 的致病性和耐药性。

Epidemiological Profile and Drug Resistance Patterns of Extrapulmonary Tuberculosis in Fuyang, China: An Eight-year Retrospective Study

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Objective Extrapulmonary tuberculosis (EPTB) poses diagnostic and therapeutic challenges due to its paucibacillary nature and diverse clinical manifestations. This study aimed to characterize the epidemiological trends, clinical features, diagnostic performance, and drug resistance profiles of EPTB over an eight-year period at a designated tuberculosis hospital in Fuyang City, Anhui Province, China.

Methods We conducted a retrospective observational study of all patients diagnosed with EPTB at Fuyang Second People's Hospital, from January 1, 2018, to December 31, 2025. Demographic, clinical, and laboratory data were extracted from electronic medical records. Descriptive statistical methods and a Chi-squared test were used to analyze the epidemiological characteristics of EPTB overall and its major subtypes. Diagnostic yields of interferon-gamma release assay (IGRA), GeneXpert MTB/RIF Ultra, and mycobacterial culture were compared. Drug susceptibility testing

(DST) was performed on culture-positive isolates. Multidrug resistance (MDR) was defined as resistance to at least isoniazid (INH) and rifampicin (RFP).

Results EPTB accounted for 28.46% (2281/8017) of all tuberculosis (TB) cases. The majority of patients were elderly (≥ 50 years, 52.78%), male (70.45%), and farmers (70.50%). EPTB cases were predominantly concentrated in the periods of 2019–2021 and 2024. The most prevalent subtypes of EPTB were pleural TB (60.50%), osteoarticular TB (12.98%), lymphatic TB (6.97%), Central nervous system (4.65%), and gastrointestinal TB (3.24%). IGRA showed the highest diagnostic yield (88.04%), significantly outperforming GeneXpert MTB/RIF Ultra (35.60%) and culture (14.53%) ($p < 0.001$). Clinical characteristics differed significantly across the five most common EPTB subtypes. Among 54 isolates tested for drug susceptibility, resistance rates were highest for isoniazid (14.81%) and ethambutol (11.11%). Overall, 83.33% of isolates were fully susceptible, while 9.26% were MDR, accounting for 55.60% of all resistant cases.

Conclusion EPTB constitutes a significant burden, particularly among elderly, male, and farming populations. Pleural TB is the most common form, and IGRA offers superior diagnostic accuracy. Although overall drug resistance is low, the notable proportion of MDR cases underscores the necessity of routine drug susceptibility testing to guide effective treatment and prevent further resistance spread.

儿童阑尾炎术后星座链球菌检出情况及初始治疗方案分析

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目的 本研究通过分析儿童阑尾炎术后星座链球菌的检出情况，为实施有效的院感防控措施提供理论依据，从而进一步减少抗菌药物选择性压力，规范抗菌药物的合理应用。

方法 选取 2019 年 12 月至 2024 年 12 月河北省儿童医院收治的阑尾炎术后星座链球菌检出阳性的 180 例患儿作为研究对象，采用回顾性方法，记录患儿的性别、年龄、临床诊断、初始治疗方案、病原学检查和药敏试验结果。

结果 纳入本研究的 180 例阑尾炎患儿包括：急性单纯性阑尾炎 4 例（2.2%）、急性化脓性阑尾炎 55 例（30.6%）、坏疽性及穿孔性阑尾炎 88 例（48.9%）和阑尾周围脓肿 33 例（18.3%）。其中男性患儿 106 例（58.9%），女性患儿 74 例（41.1%），患儿年龄 6（4）岁，住院时间 12（5）天。180 例患儿中，只检出星座链球菌者 43 例（23.9%），星座链球菌合并其他病原菌感染者 137 例（76.1%），与星座链球菌混合感染的病原菌有大肠埃希菌、铜绿假单胞菌、肺炎克雷伯菌、鸟肠球菌等其他菌株。180 株星座链球菌对头孢吡肟、美罗培南、万古霉素、利奈唑胺的敏感率均为 100%；对青霉素 G、阿莫西林、头孢噻肟的敏感率分别为 96.7%、92.2%、98.9%；对红霉素、克林霉素、四环素的耐药率较高，分别为 92.2%、92.2%、50.0%。180 例患儿中，105 例患儿初始治疗方案为哌拉西林/他唑巴坦，21 例治疗失败，75 例患儿初始治疗方案为厄他培南，12 例治疗失败。

结论 儿童阑尾炎术后检出的星座链球菌以混合感染为主，星座链球菌对儿童常用 β -内酰胺酶类抗菌药物以及万古霉素、利奈唑胺均表现出较高的敏感率。医疗机构务必持续开展细菌耐药监测，进而为制定初始治疗方案提供科学依据，避免盲目用药导致治疗失败或耐药性加剧。

艾滋病合并重症马尔尼菲篮状菌败血症血糖水平与预后的关系及血糖分层预后评估价值

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目的 探讨艾滋病合并重症马尔尼菲篮状菌败血症患者血糖代谢紊乱特征及其与短期预后的关系，评价血糖分层对预后评估的临床价值，为临床早期风险识别和个体化治疗提供依据。

方法 回顾性分析 2020 年 1 月—2024 年 12 月长沙市第一医院感染与免疫科收治的艾滋病合并重症马尔尼菲篮状菌败血症患者 58 例，其中男 52 例、女 6 例，年龄 28~37 岁。收集入院基线血糖、24 h 血糖波动幅度、CD4⁺T 淋巴细胞计数、器官功能损伤、并发症及 14 d 临床预后等资料。根据血糖水平及波动幅度进行危险分层，比较各组临床特征与预后；采用单因素及多因素 Logistic 回归分析影响预后的独立危险因素。

结果 58 例患者血糖代谢紊乱发生率为 76.2%，以持续性低血糖（59.1%）和血糖大幅波动（34.1%）为主；血糖异常程度与免疫缺陷程度及炎症反应强度呈正相关。多因素 Logistic 回归分析显示，入院基线血糖（OR=0.618，95% CI：0.410~0.931，P=0.022）、24 h 血糖波动幅度（OR=1.847，95% CI：1.236~2.761，P=0.003）是患者 14 d 预后的独立危险因素。按血糖分层后，低危组 14 d 生存率为 94.4%，中危组为 72.7%，高危组病死率达 77.8%；治疗 72 h 内血糖控制情况可早期预判治疗效果。

结论 艾滋病合并重症马尔尼菲篮状菌败血症患者血糖紊乱发生率高，以低血糖及大幅波动为主要表现；基线血糖水平与血糖波动幅度可独立预测短期预后。基于血糖的危险分层方法简便、可动态监测，有助于早期识别高危患者并指导精细化治疗，对改善预后具有重要临床意义。

430 例儿童骨关节感染病原菌及药敏分析

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目的 对我院 430 例骨关节感染儿童患儿微生物培养检出病原菌及药敏情况进行分析, 为临床诊疗及感染防控提供依据。

方法 我院 2015-2025 年疑似骨关节系统感染患儿送检骨髓液、关节液等标本进行分离培养及鉴定药敏实验, 查阅电子病历系统, 对患儿临床情况及检测结果进行统计分析。

结果 我院 2015-2025 年通过微生物培养确诊骨关节系统感染患儿 430 例, 患儿主要为男孩 (64.42%, 277/430), 患儿年龄分布 5 天-16 岁, 以 1 岁以下婴幼儿 (29.07%, 125/430) 及 6 岁以上学龄期儿童 (36.05%, 155/430) 为主。430 例感染患儿共计检出病原菌 543 株, 以革兰阳性菌 (70.35%, 382/543) 为主, 菌属分布主要为葡萄球菌 (63.73%, 346/543) 及肠杆菌 (16.76%, 91/543); 检出病原菌主要为金黄色葡萄球菌 (52.67%, 286/543)、表皮葡萄球菌 (5.71%, 31/543)、肺炎克雷伯菌 (5.34%, 29/543)、大肠埃希菌 (4.60%, 25/543) 及沙门菌 (4.60%, 25/543)、布鲁菌 (4.24%, 23/543), 肺炎链球菌、白色念珠菌、新型隐球菌、流感嗜血杆菌等少见菌亦有检出。2015 年至 2025 年革兰阳性菌检出占比呈降低趋势, 而金黄色葡萄球菌检出占比逐年上升; 6 岁以上学龄期儿童检出肠杆菌占比仅为 3.66% (7/191), 1 岁以下婴幼儿检出肠杆菌占比则高达 34.41% (64/186); 检出病原菌季节分布, 2、3 月份检出真菌显著升高。甲氧西林耐药金黄色葡萄球菌 (MRSA) 检出率为 37.76% (108/286), 各年呈波动趋势; 肠杆菌目细菌对头孢噻肟、美罗培南耐药率分别高达 51.41%、24.72%; 检出碳青霉烯类耐药肠杆菌 (CRE) 菌株 19 株, 主要为肺炎克雷伯菌 18 株, CRKP 检出率高达 62.07%。

结论 儿童骨关节感染病原菌主要为金黄色葡萄球菌、肠杆菌, 近年来金黄色葡萄球菌检出逐年

升高, 1 岁以下婴幼儿肠杆菌检出率显著高于其他年龄组, MRSA、CRKP 检出率显著高于其他其他感染部位, 需根据药敏结果合理用药及做好感染防控。

中原地区 25 年真菌性角膜炎病原学的变化

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目的 分析中原地区真菌性角膜炎 (Fungal Keratitis, FK) 的病原学变化特点, 为区域性 FK 的防治与经验性用药提供科学依据。

方法 回顾性收集 2001 年 1 月 1 日至 2025 年 9 月 30 日河南省立眼科医院微生物室 37665 例角膜溃疡患者资料, 对患者流行病学特征、致病菌属构成、菌谱变迁及药物敏感性进行分析。

结果 共检出真菌培养阳性的 FK 患者 11231 例, 男 7227 例, 女 4004 例, 男女比例为 1.80:1, 平均年龄为 (54.00±13.98) 岁, 年龄段集中分布在 40~69 岁, 占 73.60%, 50.40% 有眼部意外性损伤的病史, 其中植物性损伤 3226 例。感染性角膜炎就诊人数和真菌培养阳性率高峰均集中于 9-12 月, 其中 10 月最高。分离的真菌中, 镰刀菌属占 43.30%, 曲霉菌属占 27.01%, 链格孢菌属占 16.77%。25 年间 FK 致病菌谱中镰刀菌属占比总体呈现出下降的趋势, 曲霉菌属占比总体上升, 并于 2011 年首年成为感染菌属的首位, 链格孢菌属感染率呈波动性缓慢升高。FK 致病菌属变化幅度以 2013 年的最大, 为 9.81%。药敏结果显示, 三种菌属对伏立康唑敏感率都很高。镰刀菌属、链格孢菌属对那他霉素有高的敏感率, 而曲霉菌属对那他霉素敏感率较低。三种菌属对两性霉素 B、酮康唑、氟康唑敏感率都很低。

结论 中原地区 FK 患者以中老年男性为主, 发病季节集中在秋冬季, 多与眼部意外性损伤相关。

主要致病菌属为镰刀菌属，区域菌谱在长期观察中呈动态变化，以 2013 年菌属的变化最大。伏立康唑对三种主要致病菌属均表现出高的体外敏感性。

环丙沙星对慢阻肺急性加重患者常见病原菌的 MIC 分布分析

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目的 慢性阻塞性肺疾病急性加重 (AECOPD) 是 COPD 患者住院和死亡的重要原因，细菌感染是主要诱因之一。环丙沙星曾广泛用于 AECOPD 经验性治疗，但耐药性不断上升。本研究利用 EUCAST 公开的 MIC 数据库，分析环丙沙星对 AECOPD 常见病原菌的 MIC 分布，为临床用药提供参考。

方法 从 EUCAST 官方网站下载环丙沙星对 8 种 AECOPD 相关病原菌的 MIC 分布数据：铜绿假单胞菌 (26996 株)、肺炎克雷伯菌 (3788 株)、流感嗜血杆菌 (17864 株)、肺炎链球菌 (73054 株)、金黄色葡萄球菌 (总 41812 株，其中 MSSA 571 株，MRSA 286 株) 及鲍曼不动杆菌 (2775 株)。采用累计百分比法计算 MIC₅₀ 和 MIC₉₀。根据 EUCAST 2024 年临床折点计算敏感率：铜绿假单胞菌、肺炎克雷伯菌、金黄色葡萄球菌、流感嗜血杆菌的敏感折点为 ≤0.5 mg/L；肺炎链球菌为 ≤0.125 mg/L；鲍曼不动杆菌无折点，仅报告 MIC 分布。

结果 流感嗜血杆菌高度敏感：MIC₅₀=0.016 mg/L，MIC₉₀=0.016 mg/L，敏感率 99.7%。铜绿假单胞菌：MIC₅₀=0.25 mg/L，MIC₉₀=8 mg/L，敏感率 74.7%。肺炎克雷伯菌：MIC₅₀=0.03 mg/L，MIC₉₀=2 mg/L，敏感率 87.6%。金黄色葡萄球菌总体：MIC₅₀=0.5 mg/L，MIC₉₀=2 mg/L，敏感率 81.9%；其中 MSSA：MIC₅₀=0.5 mg/L，MIC₉₀=1 mg/L，敏感率 67.4%；MRSA：MIC₅₀=128 mg/L，MIC₉₀=256 mg/L，

敏感率 6.6%。肺炎链球菌几乎完全耐药：MIC₅₀=1 mg/L，MIC₉₀=2 mg/L，敏感率 0.23%。鲍曼不动杆菌：MIC₅₀=0.25 mg/L，MIC₉₀=32 mg/L (无折点)。

结论 在 AECOPD 经验治疗中，环丙沙星不宜用于肺炎链球菌高风险患者，对 MRSA 或鲍曼不动杆菌高流行地区不应首选；对有铜绿假单胞菌感染风险的重度 AECOPD 患者，环丙沙星仍可作备选，但需结合本地耐药数据。本研究数据为全球汇总，反映平均水平，不能直接推及特定地区或时间段，临床决策应优先参考当地药敏监测数据。

关键词 慢性阻塞性肺疾病急性加重；环丙沙星；MIC 分布；MIC₅₀；MIC₉₀；耐药性

新兴 ST950 型肺炎克雷伯菌的耐药性、毒力及基因组特征研究

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目的 肺炎克雷伯菌 (*Klebsiella pneumoniae*, KP) 是引起院内感染的重要病原体，其在泌尿道感染中具有高发病率、高毒力及多重耐药性，对临床构成严重威胁。本研究主要探讨 ST950 型肺炎克雷伯菌的耐药性、毒力特征、生物学特性及群体结构特征。

方法 应用 VITEK-2Compact 自动化微生物鉴定系统分离并鉴定了一株代表 ST950 型的肺炎克雷伯菌 KP230524-43，该菌株来源于一例泌尿道感染患者的尿液。分别采用乳酸脱氢酶 (LDH) 释放法和结晶紫染色法对肺炎克雷伯菌 KP230524-43 的细胞毒性及生物膜形成能力进行测定。提取肺炎克雷伯菌 KP230524-43 的核酸进行全基因组测序分析，与从 NCBI 数据库中获取的 22 株已知序列的 ST950 型肺炎克雷伯菌共 23 株进行系统发育树分析等。

结果 KP230524-43 具有显著的细胞毒性及强

生物膜形成能力，并对 β -内酰胺类抗生素耐药。与经典高毒力株不同，所有 ST950 型菌株均缺乏常见的高毒力标志基因（如 *rmpA*、*peg-344* 和 *iucA*），但均携带肠杆菌素合成和转运相关基因 *entAB* 和 *fepC*，以及 *ecpABCD*（编码菌毛合成相关蛋白）和 *ompA*（编码外膜蛋白 A）。部分 ST950 型菌株检出 *astA* 基因（编码 EAST1 毒素），其中包括 KP230524-43。超过半数菌株携带碳青霉烯酶或广谱 β -内酰胺酶耐药基因。此外，本研究还发现 ST950 型菌株已在多个国家出现，提示其具有跨地域传播的潜力。

结论 ST950 型肺炎克雷伯菌是一类兼具独特毒力谱、强生物膜形成能力和多重耐药性的潜在高风险新兴克隆株，亟需加强监测、分子流行病学研究以及针对性的感染防控措施。

[关键词] 肺炎克雷伯菌；基因组；ST950；毒力；生物膜形成；抗生素耐药

胸腺瘤合并肺部感染的临床特征及危险因素分析

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目的 分析胸腺瘤合并肺部感染患者的临床特征及危险因素，提高早期识别与干预能力。

方法 回顾性收集 2024 年 1 月至 2026 年 2 月于宁夏医科大学总医院确诊的 62 例胸腺瘤患者资料，其中合并肺部感染者 24 例（观察组），未感染者 38 例（对照组）。比较两组基础疾病、临床表现、实验室指标、影像学、肿瘤分期、重症肌无力（MG）合并情况、治疗方案及病原学分布。采用 Logistic 回归分析独立危险因素。

结果 24 例感染患者中，男性占 58.3%（14 例），平均年龄（56.4±10.2）岁。临床表现：发热 83.3%、咳嗽咳脓痰 79.2%、气促 66.7%、胸痛 37.5%。病原学以革兰阴性菌为主（70.8%），常见肺炎克雷伯菌

（29.2%）、铜绿假单胞菌（20.8%）、鲍曼不动杆菌（12.5%）。影像学：肺实变 75.0%、胸腔积液 41.7%、肺不张 29.2%。观察组 C 反应蛋白（78.5 vs 12.3 mg/L, $P<0.001$ ）及降钙素原（1.85 vs 0.21 ng/mL, $P<0.001$ ）显著高于对照组。单因素分析显示，MG 合并（OR=4.50, $P=0.008$ ）、Masaoka III-IV 期（OR=5.20, $P=0.003$ ）、放疗或化疗史（OR=3.80, $P=0.012$ ）、长期使用糖皮质激素/免疫抑制剂（OR=6.30, $P<0.001$ ）及肿瘤切除术后（OR=2.90, $P=0.045$ ）与感染相关。多因素回归证实，长期使用免疫抑制剂（OR=5.82, 95%CI: 1.95~17.36, $P=0.002$ ）、Masaoka 晚期（III-IV 期）（OR=4.76, 95%CI: 1.58~14.35, $P=0.006$ ）及合并 MG（OR=3.95, 95%CI: 1.32~11.82, $P=0.014$ ）为独立危险因素。24 例中，20 例（83.3%）经抗感染及原发病综合治疗后好转出院，4 例（16.7%）因严重感染、呼吸衰竭或脓毒性休克死亡。

结论 胸腺瘤合并肺部感染多见于晚期肿瘤、合并 MG 及长期使用免疫抑制剂的患者，炎症指标显著升高，病原以革兰阴性菌为主。长期免疫抑制、Masaoka 晚期及 MG 是独立危险因素，应对高危人群加强感染监测和早期抗感染治疗。

21 例成人布鲁菌病肺部损害的临床特征分析

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目的 分析成人布鲁菌病肺部损害的临床特征、实验室检查特点及治疗转归，提高呼吸科医师对该病的识别与早期诊断能力。

方法 回顾性收集 2023 年 1 月至 2024 年 12 月于宁夏医科大学总医院确诊为布鲁菌病且存在肺部损害的 21 例成人患者（年龄≥18 岁）资料。所有患者均经血清凝集试验或血培养确诊，并有胸部影像学异常。分析其一般资料、流行病学史、临床表现、外周血白细胞及淋巴细胞计数、胸部影像学特征、

治疗方案及预后。

结果 21例患者中,男性15例(71.4%),女性6例(28.6%),年龄范围19~68岁,中位年龄45岁。有明确牛羊接触史者19例(90.5%),职业以农牧民及屠宰人员为主(17例,81.0%)。主要临床表现:发热21例(100%),以波状热或不规则热为主;咳嗽19例(90.5%),多为干咳或少量黏液痰;乏力、多汗18例(85.7%);关节肌肉痛13例(61.9%);胸痛5例(23.8%)。肺部体征多不明显,仅6例(28.6%)闻及少量湿啰音。胸部CT表现:双肺多发结节或实变影13例(61.9%),单发实变灶4例(19.0%),胸腔积液4例(19.0%),其中1例为中等量积液;未见空洞或钙化。外周血白细胞计数正常或偏低17例(81.0%),淋巴细胞比例升高(>50%)者9例(42.9%),C反应蛋白升高19例(90.5%),红细胞沉降率增快21例(100%)。血培养阳性率52.4%(11/21),血清虎红凝集试验阳性率100%。从症状出现至确诊的中位时间为30天(范围12~72天),首诊误诊为社区获得性肺炎13例(61.9%)。所有患者接受多西环素联合利福平治疗(17例)或多西环素联合链霉素(4例),疗程6~8周。治疗后1~2周内退热,咳嗽及肺部影像学异常在4周内明显改善,4例(19.0%)残留肺内条索影,无死亡病例。

结论 成人布鲁菌病肺部损害以发热、咳嗽及双肺多发结节/实变为主要特征,流行病学史(牛羊接触)是重要诊断线索。对常规抗感染治疗无效的“肺炎”患者,尤其伴有外周血白细胞不高、淋巴细胞相对升高、C反应蛋白及血沉显著增快者,应及时行布鲁菌血清学检测,避免误诊。

肺癌术后感染的病原菌临床特征及危险因素分析

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目的 分析肺癌术后感染患者的病原菌分布、耐药性及危险因素,为精准抗感染和风险控制提供依据。

方法 回顾性收集2023年1月至2026年3月于宁夏医科大学总医院行肺癌根治术的210例患者资料,其中术后感染组45例,对照组165例。采集感染组痰液、胸腔引流液、血液或切口分泌物进行病原菌培养及药敏试验,比较两组临床资料,采用Logistic回归分析感染独立危险因素。

结果 45例感染患者中,男性29例(64.4%),平均年龄(65.2±9.1)岁。感染部位以肺部感染为主(77.8%),胸腔感染13.3%,切口感染8.9%。病原菌阳性率91.1%,共分离47株,其中革兰阴性菌占78.7%(肺炎克雷伯菌34.0%、铜绿假单胞菌23.4%、鲍曼不动杆菌12.8%、大肠埃希菌8.5%),革兰阳性菌17.0%(金黄色葡萄球菌为主,MRSA占40.0%),真菌4.3%。药敏结果:肺炎克雷伯菌产ESBLs率43.8%,碳青霉烯类敏感率81.3%;铜绿假单胞菌对常用药物敏感率>85%;鲍曼不动杆菌多重耐药率83.3%、广泛耐药率50.0%,替加环素敏感率83.3%,多粘菌素B敏感率100%。感染组C反应蛋白(92.3 vs 15.6 mg/L)及降钙素原(2.48 vs 0.15 ng/mL)均显著高于对照组($P<0.001$)。单因素分析显示,手术时间 $\geq 3h$ 、引流管留置 ≥ 7 天、术前住院 ≥ 7 天、糖尿病、低白蛋白血症、FEV1% $<70\%$ 及全肺切除与感染显著相关(P 均 <0.05)。多因素回归证实,引流管留置 ≥ 7 天($OR=4.12$, 95%CI: 1.56~10.88, $P=0.004$)、低白蛋白血症($OR=4.89$, 95%CI: 1.85~12.93, $P=0.001$)及全肺切除($OR=3.67$, 95%CI: 1.32~10.21, $P=0.013$)为独立危险因素。经抗感染及支持治疗,77.8%好转出院,22.2%转入ICU,其中3例(6.7%)死亡。

结论 肺癌术后感染病原以产ESBLs肺炎克雷伯菌、铜绿假单胞菌及多重耐药鲍曼不动杆菌为主,耐药严峻。引流管留置 ≥ 7 天、低白蛋白血症及全肺切除是独立危险因素,应加强围术期营养、尽早拔管,并根据药敏选用碳青霉烯类、替加环素或多粘菌素精准抗感染。

甲型流感继发细菌性肺炎的病原菌分布、耐药性及预后分析

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目的 分析甲型流感继发细菌性肺炎的病原菌分布、耐药性及预后。

方法 回顾性收集甲型流感继发细菌性肺炎 15 例（继发组）及未继发者 25 例（对照组）。继发组诊断依据入院 5~14 天新发呼吸道症状且培养阳性。分析病原菌及药敏，比较两组临床特征、炎症指标、机械通气率、住院时间及 28 天病死率，采用 Logistic 回归分析危险因素。

结果 15 例继发患者中，男性 9 例（60.0%），平均年龄（58.5±12.1）岁。共分离 18 株病原菌：革兰阴性菌 12 株（66.7%）、革兰阳性菌 5 株（27.8%）。常见菌为肺炎克雷伯菌（27.8%）、铜绿假单胞菌（16.7%）、鲍曼不动杆菌（11.1%）、金黄色葡萄球菌（22.2%，MRSA 占 50%）。药敏：肺炎克雷伯菌产 ESBLs 率 60%，碳青霉烯类敏感率 80%；鲍曼不动杆菌 MDR 率 100%、XDR 率 50%，替加环素及多粘菌素 B 敏感。继发组 C 反应蛋白（95.6 vs 19.8 mg/L）及降钙素原（3.88 vs 0.21 ng/mL）显著高于对照组（ $P<0.001$ ）。继发组机械通气率（53.3% vs 16.0%）、住院时间（24.8 vs 11.5 天）及 28 天病死率（26.7% vs 4.0%）均显著升高（ $P<0.05$ ）。多因素分析显示，入院淋巴细胞 $<0.8\times 10^9/L$ （OR=4.02）、糖皮质激素使用 ≥ 3 天（OR=3.25）、抗病毒延迟 $>48h$ （OR=2.98）是独立危险因素（ $P<0.05$ ）。死亡组（4 例）鲍曼不动杆菌感染（50.0% vs 9.1%）、XDR 菌株（50.0% vs 9.1%）及初始不恰当抗感染（75.0% vs 27.3%）比例均更高（ $P<0.05$ ）。

结论 甲型流感继发细菌性肺炎以产 ESBLs 肺炎克雷伯菌、铜绿假单胞菌及金黄色葡萄球菌为主，

鲍曼不动杆菌感染与高病死率相关。淋巴细胞减少、糖皮质激素使用及延迟抗病毒是独立危险因素。应早期获取病原学证据并根据药敏选择敏感药物。

淋巴瘤化疗后中性粒细胞缺乏伴肺部细菌感染的病原菌分布及耐药性分析

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目的 分析淋巴瘤化疗后粒缺伴肺部细菌感染的病原菌分布及耐药性，为经验性抗感染提供依据。

方法 回顾性收集 36 例淋巴瘤化疗后粒缺（中性粒细胞 $<0.5\times 10^9/L$ ）并确诊肺部细菌感染患者的资料，分析临床表现、病原菌分布及药敏结果。

结果 36 例中，男性 22 例（61.1%），平均年龄（52.6±13.4）岁。粒缺持续中位时间 9 天。所有患者均有发热（ $\geq 38.5^\circ C$ ），咳嗽咳痰 77.8%，气促 55.6%，影像学实变 69.4%、结节/空洞 22.2%。共分离 42 株病原菌：革兰阴性菌 31 株（73.8%）、革兰阳性菌 10 株（23.8%）、真菌 1 株（2.4%）。常见菌：肺炎克雷伯菌（28.6%）、铜绿假单胞菌（21.4%）、大肠埃希菌（14.3%）、鲍曼不动杆菌（7.1%）；金黄色葡萄球菌（14.3%，其中 MRSA 占 66.7%）。药敏：肺炎克雷伯菌产 ESBLs 率 58.3%，碳青霉烯类敏感率 75.0%；铜绿假单胞菌对常用药敏感率 $>80\%$ ；大肠埃希菌 ESBLs 率 66.7%，碳青霉烯类敏感率 83.3%；鲍曼不动杆菌 MDR 率 100%、XDR 率 66.7%，仅替加环素及多粘菌素 B 敏感；MRSA 对万古霉素等敏感。初始经验性抗感染以碳青霉烯类单用或联合万古霉素/替考拉宁为主（83.3%）。经治疗，30 例（83.3%）好转出院，6 例（16.7%）因感染性休克或呼吸衰竭死亡。死亡组中碳青霉烯类耐药肺炎克雷伯菌（CRKP）感染比例（50.0% vs 10.0%， $P=0.018$ ）及初始治疗不恰当比例（66.7% vs 20.0%， $P=0.024$ ）显著高于存活组。

结论 淋巴瘤化疗后粒缺伴肺部细菌感染以革兰阴性菌为主，肺炎克雷伯菌、铜绿假单胞菌及大肠埃希菌最常见，碳青霉烯类耐药形势严峻，MRSA 检出率高。应尽早获取病原学结果，高危患者初始经验性治疗可选用碳青霉烯类联合抗 MRSA 药物，并根据药敏及时降阶梯。

不同免疫基础疾病背景非 HIV 相关肺孢子菌肺炎患者临床特征及 28 天预后差异

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目的 分析不同免疫基础疾病下非人类免疫缺陷病毒（HIV）相关肺孢子菌肺炎（PJP）临床特征及 28 天预后差异，探讨短期结局相关因素。

方法 回顾性纳入 2020 年 1 月至 2025 年 12 月住院确诊的非 HIV 相关 PJP 患者 76 例，依据支气管肺泡灌洗液（BALF）染色、聚合酶链反应（PCR）或宏基因组二代测序（mNGS）确诊。按基础疾病分风湿免疫病组（29 例）、血液系统疾病组（24 例）及实体肿瘤组（23 例）。比较三组临床表现、实验室指标、影像学特征、混合感染及 28 天预后，Logistic 回归分析死亡相关因素。

结果 76 例患者中位年龄 56（45，67）岁，男性 42 例（55.3%）。三组糖皮质激素使用率差异无统计学意义（ $P=0.218$ ）。起病至确诊时间存在差异 [风湿免疫病组 6（4，8）d，血液系统疾病组 4（3，6）d，实体肿瘤组 5（3，7）d， $P=0.032$]。血液系统疾病组淋巴细胞计数最低 [$0.46(0.32, 0.71) \times 10^9/L$ 比 $0.74(0.53, 1.01) \times 10^9/L$ 比 $0.67(0.44, 0.89) \times 10^9/L$ ， $P<0.001$]，LDH 最高 [472（388，602）U/L 比 401（318，498）U/L 比 361（286，438）U/L， $P=0.011$]。CT 示风湿免疫病组弥漫磨玻璃影比例较高（69.0%），血液系统疾病组斑片状实变多见，实

体肿瘤组局灶浸润及网格影较多（ $P=0.043$ ）。混合感染率 34.2%，血液系统疾病组（50.0%）高于风湿免疫病组（24.1%）及实体肿瘤组（26.1%）（ $P=0.047$ ），以巨细胞病毒共感染最常见。BALF-mNGS 阳性率 85.5%，三组差异无统计学意义（ $P=0.703$ ）。28 天病死率 17.1%（13/76），血液系统疾病组 25.0%，风湿免疫病组 13.8%，实体肿瘤组 13.0%（ $P=0.049$ ）。多因素 Logistic 回归显示，氧合指数 <200 mmHg（OR=3.76，95%CI 1.39~10.16， $P=0.009$ ）及混合感染（OR=2.51，95%CI 1.01~6.27， $P=0.048$ ）与 28 天死亡独立相关。

结论 不同免疫基础疾病下非 HIV 相关 PJP 临床表现存在差异。血液系统疾病淋巴细胞减少更明显，混合感染率高，短期病死风险增加。低氧血症及混合感染是影响 28 天预后的主要因素。

关键词：肺孢子菌肺炎；非 HIV 免疫抑制；混合感染

特发性肺纤维化合并金黄色葡萄球菌肺部感染 20 例临床特征分析

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目的 特发性肺纤维化（IPF）患者因肺结构破坏和气道廓清障碍，易发生细菌感染，金黄色葡萄球菌是常见病原体之一。本研究分析 IPF 合并金黄色葡萄球菌肺部感染的临床特征，提高早期识别能力。

方法 回顾性分析 2022 年 1 月至 2025 年 12 月于宁夏医科大学总医院收治的 IPF 合并金黄色葡萄球菌肺部感染患者 20 例。纳入标准：①符合 ATS/ERS/JRS/ALAT 2022 指南 IPF 诊断标准；②痰液或支气管肺泡灌洗液（BALF）培养金黄色葡萄球菌阳性；③临床资料完整。排除标准：①合并其他

类型病原体感染；②合并活动性肺结核或肺癌。收集患者人口学资料、IPF 病程、临床表现（发热、咳嗽、咳痰、呼吸困难加重）、外周血白细胞、中性粒细胞比例、C 反应蛋白（CRP）、降钙素原（PCT）、影像学改变、药敏结果及治疗转归。

结果 20 例患者中，男 15 例、女 5 例，平均年龄 68.5 ± 7.2 岁；IPF 确诊至感染中位时间 18 个月。临床表现以咳嗽加重（90.0%）、痰量增多（85.0%）、发热（80.0%）、呼吸困难加重（70.0%）为主。实验室检查示，白细胞、中性粒细胞比例、CRP、PCT 升高者分别占 60.0%、75.0%、80.0%、70.0%。影像学主要表现为新发实变影、结节影及原有网格影加重。药敏提示 MSSA 占 70.0%、MRSA 占 30.0%，分别予 β -内酰胺类、万古霉素/利奈唑胺治疗。治疗后 80.0% 患者症状改善，体温恢复中位时间 4 天；30 天全因死亡率 15.0%，均为 MRSA 感染合并 IPF 急性加重。

结论 IPF 合并金黄色葡萄球菌肺部感染以老年男性多见，主要表现为发热、咳嗽加重及 CRP、PCT 升高，影像学以新发实变影为主，MRSA 感染占 30.0%，预后较差。早期病原学检查和药敏检测对指导抗感染治疗至关重要。

关键词：IPF；金黄色葡萄球菌；肺部感染；MRSA；临床特征

感染性急性呼吸窘迫综合征病因分布及临床特征分析

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目的 感染是急性呼吸窘迫综合征（ARDS）最常见的病因，但不同感染来源和病原体类型对临床特征及预后的影响尚不完全清楚。本研究分析感染性 ARDS 的病因分布及不同病因的临床特征差异，为临床诊疗提供参考。

方法 回顾性分析 2022 年 1 月—2025 年 12 月宁夏医科大学总医院 RICU 收治的 86 例感染性 ARDS 患者。纳入标准：符合柏林定义 ARDS 诊断标准，明确为感染所致，临床资料完整。排除标准：非感染性病因、合并活动性肺结核、年龄 <18 岁。按感染来源分为肺内感染组（肺炎直接所致）和肺外感染组（肺外感染继发），收集患者人口学、基础疾病、感染相关资料、入院时 APACHE II 评分、氧合指数、机械通气参数及 ICU 住院天数、28 天病死率。

结果 86 例患者中，男性 58 例（67.4%），女性 28 例（32.6%），平均年龄 62.5 ± 12.8 岁。感染来源分布：肺内感染组 61 例（70.9%），肺外感染组 25 例（29.1%）。肺内感染组中，细菌性肺炎 38 例（62.3%），病毒性肺炎 15 例（24.6%），真菌性肺炎 8 例（13.1%）；病原体前三位为：铜绿假单胞菌（13 例，21.3%）、肺炎克雷伯菌（10 例，16.4%）、流感病毒（8 例，13.1%）。肺外感染组中，腹腔感染 10 例（40.0%），血流感染 8 例（32.0%），泌尿系感染 5 例（20.0%），其他 2 例（8.0%）。两组基线 APACHE II 评分无显著差异（ 21.5 ± 6.2 vs 20.8 ± 5.9 , $p=0.631$ ）。肺内感染组入院时 $\text{PaO}_2/\text{FiO}_2$ 为 152.5 ± 38.6 mmHg，低于肺外感染组的 178.3 ± 42.1 mmHg（ $P=0.008$ ）。肺内感染组机械通气时间为 12.5 ± 5.8 天，长于肺外感染组的 9.2 ± 4.6 天（ $p=0.012$ ）；ICU 住院天数分别为 14.8 ± 6.5 天和 11.2 ± 5.3 天（ $p=0.015$ ）。28 天总体病死率为 33.7%（29/86），其中肺内感染组病死率为 37.7%（23/61），肺外感染组为 24.0%（6/25），差异无统计学意义（ $p=0.218$ ）。

结论 细菌性肺炎是感染性 ARDS 最常见的病因（占 38.4%）。肺内感染所致 ARDS 较肺外感染氧合障碍更重、机械通气时间和 ICU 住院时间更长，但两组 28 天病死率无显著差异。

关键词：急性呼吸窘迫综合征；感染性病因；肺内感染；机械通气；预后

化疗后不同病原学感染与晚期肺腺癌患者预后的关联：一项单中心回顾性队列研究

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目的 在晚期肺腺癌患者中，化疗相关免疫抑制使感染风险显著增加，但不同病原学感染对预后的影响存在异质性，缺乏针对性分层评估。本研究旨在系统评估化疗后肺部感染的病原学谱及其与治疗中断和生存结局的相关性，探索预后分层价值。

方法 单中心回顾性队列研究，纳入 2019 年 1 月至 2023 年 12 月接受含铂双药化疗 ≥ 2 周期的 IIIB–IV 期肺腺癌患者。根据是否发生经微生物学证实的肺部感染分为感染组与非感染组，感染组进一步分为细菌感染、真菌感染及细菌-真菌混合感染。收集人口学、肿瘤特征、感染指标及预后数据。采用 Kaplan–Meier 法进行生存分析，Cox 比例风险模型评估感染与生存结局的相关性。

结果 共纳入 176 例患者，57 例 (32.4%) 化疗后发生肺部感染。感染以细菌为主 (61.4%)，常见病原体为肺炎克雷伯菌和铜绿假单胞菌；真菌感染占 22.8%，以曲霉菌为主；混合感染占 15.8%。感染组住院时间延长 (28 天 vs. 18 天, $P<0.001$)，总费用增加 46.7%，化疗延迟发生率升高 (73.7% vs. 20.2%, $P<0.001$)。感染组中位无进展生存期 (5.8 个月 vs. 8.5 个月) 及总生存期 (12.8 个月 vs. 16.2 个月) 均低于未感染患者。多因素分析显示，调整年龄、性别、分期及营养状态后，真菌感染 ($HR=2.18$, 95%CI 1.31–3.61, $P=0.002$) 及混合感染 ($HR=1.89$, 95%CI 1.05–3.40, $P=0.033$) 与总生存期缩短独立相关，单纯细菌感染未达统计学显著性。不同感染类型间预后呈差异趋势，真菌感染患者生存最差。

结论 晚期肺腺癌患者化疗后肺部感染与不良预后显著相关，真菌及混合感染提示更高死亡风险。感染不仅增加医疗负担并影响化疗连续性，还可能作为反映患者整体状态的重要临床标志。加强感染

监测及早期病原学评估，优化抗感染策略，可能有助于改善预后。鉴于本研究为回顾性设计，相关结果仍需前瞻性研究验证。

关键词：晚期肺腺癌；化疗；肺部感染；真菌感染

感染相关与非感染相关急性呼吸窘迫综合征的临床特征及预后比较：一项单中心回顾性队列研究

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目的 急性呼吸窘迫综合征 (ARDS) 病因复杂，分为感染相关与非感染相关两类，不同病因在炎症反应及预后方面可能存在差异，但系统性比较数据有限。本研究旨在比较两类 ARDS 患者的临床特征及转归差异，为风险分层管理提供依据。

方法 单中心回顾性队列研究，纳入 2020 年 1 月至 2024 年 6 月符合 Berlin 标准的 ARDS 患者 212 例。根据诱因分为感染相关 ARDS 组与非感染相关 ARDS 组。感染相关定义为明确感染所致；非感染相关包括创伤、急性胰腺炎、误吸及输血相关肺损伤等。收集人口学、基础疾病、ARDS 严重程度 (PaO_2/FiO_2)、炎症指标 (CRP、PCT)、器官功能评分 (SOFA、APACHE II)、治疗措施及临床结局。采用多变量 Logistic 回归分析 28 天死亡独立影响因素。

结果 感染相关 ARDS 138 例 (65.1%)，非感染相关 74 例 (34.9%)。感染相关主要由重症肺炎 (58.0%) 和脓毒症 (29.7%) 引起，非感染相关以急性胰腺炎 (31.1%)、创伤 (24.3%) 及误吸 (18.9%) 为主。两组基线特征差异无统计学意义。感染相关 ARDS 炎症反应更明显，CRP 及 PCT 显著升高 (156 vs. 98 mg/L; 3.8 vs. 0.9 ng/mL, 均 $P<0.001$)，SOFA 评分更高 (9.2 $\pm$ 3.1 vs. 7.6 $\pm$ 2.8, $P=0.002$)。两组初始

PaO₂/FiO₂相似,但感染组俯卧位通气(42.8% vs. 28.4%, $P=0.038$)及 CRRT 使用率(36.2% vs. 20.3%, $P=0.015$)更高。感染组机械通气时间(12 天 vs. 8 天, $P=0.004$)及 ICU 住院时间(16 天 vs. 11 天, $P=0.006$)均延长,28 天病死率升高(34.1% vs. 21.6%, $P=0.048$),90 天病死率呈升高趋势(44.2% vs. 31.1%, $P=0.062$)。多变量分析显示,感染相关病因($OR=1.87$, $P=0.042$)、SOFA 评分($OR=1.21$, $P<0.001$)及 PCT ($OR=1.09$, $P=0.018$)与 28 天死亡独立相关。

结论 感染相关 ARDS 患者炎症反应更强、器官功能损伤更重,预后更差。感染病因可能是 ARDS 不良结局的重要预测因素。早期识别感染相关 ARDS 并结合炎症及器官功能指标分层管理,可能有助于改善预后。仍需前瞻性研究验证。

关键词:急性呼吸窘迫综合征;感染;炎症

支气管扩张症稳定期合并铜绿假单胞菌定植的危险因素及其对肺功能下降速率的影响

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目的 探讨支气管扩张症稳定期患者合并铜绿假单胞菌(PA)定植的危险因素及其对肺功能年下降速率的影响。

方法 回顾性纳入 2019 年 1 月至 2024 年 6 月于我院随访 ≥ 12 个月的支气管扩张症稳定期患者 212 例。根据痰培养结果分为 PA 定植组(≥ 2 次阳性,间隔 ≥ 3 个月, $n=64$)与非 PA 组($n=148$)。收集一般资料、基础疾病、既往年急性加重频率、影像学受累肺叶数、既往抗生素及吸入治疗情况。记录基线及随访末 FEV1%pred,计算年下降速率。采用多因素 Logistic 回归分析 PA 定植危险因素,多元线性回归评估肺功能下降独立影响因素,并行亚组交互作用分析。

结果 PA 定植发生率 30.2% (64/212)。两组性别、年龄及吸烟史差异无统计学意义。PA 定植组既往年急性加重 ≥ 3 次比例(46.9% vs. 25.7%, $P=0.003$)及受累肺叶数 ≥ 3 叶比例(62.5% vs. 39.2%, $P=0.002$)均显著升高,吸入抗生素使用比例更高(28.1% vs. 12.8%, $P=0.010$)。多因素 Logistic 回归显示,既往急性加重频率 ≥ 3 次/年($OR=2.34$, 95%CI 1.23~4.45, $P=0.009$)及受累肺叶数 ≥ 3 叶($OR=2.67$, 95%CI 1.39~5.12, $P=0.003$)为 PA 定植独立危险因素。中位随访 26 (18~38) 个月,PA 定植组 FEV1%pred 年下降速率快于非 PA 组 [$(-2.9\pm 1.8)\%$ /年 vs. $(-1.6\pm 1.4)\%$ /年, $P<0.001$]。多元线性回归显示,PA 定植($\beta=-1.12$, $P=0.002$)及既往年急性加重频率($\beta=-0.86$, $P=0.010$)与肺功能加速下降独立相关。交互作用分析提示,既往急性加重频率对 PA 定植效应存在修饰作用(P for interaction=0.040),高频加重患者中 PA 定植所致肺功能下降更明显。

结论 频繁急性加重史及广泛影像学受累是 PA 定植的独立危险因素。PA 定植与肺功能加速下降密切相关,在高频急性加重人群中效应更显著。早期识别高危患者并加强微生物学监测,对延缓疾病进展具有重要临床意义。

关键词:支气管扩张症;铜绿假单胞菌;定植

糖尿病酮症酸中毒合并重症肺炎患者的病原学特征及血糖控制对感染结局的影响

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目的 探讨糖尿病酮症酸中毒(DKA)合并重症肺炎患者的病原学特征,并分析血糖控制水平对感染控制及临床结局的影响。

方法 回顾性纳入 2020 年 1 月至 2024 年 6 月我院收治的 DKA 合并重症肺炎患者 132 例。收集

一般资料、基础疾病、入院代谢指标（血糖、血酮、pH）、炎症指标及病原学结果。根据住院前 72 h 平均血糖分为血糖控制良好组（ ≤ 10 mmol/L, $n=58$ ）与控制不佳组（ >10 mmol/L, $n=74$ ）。主要结局为感染控制时间（体温正常 ≥ 24 h 且炎症指标较峰值下降 $\geq 50\%$ ）及 28 d 病死率。采用多因素 Logistic 回归分析感染控制延迟相关因素，分析血糖波动与结局的关联。

结果 132 例患者平均年龄（ 58.6 ± 13.4 ）岁，男性 61.4%，2 型糖尿病 89.4%。病原以革兰阴性菌为主（63.6%），常见菌为肺炎克雷伯菌（24.2%）及铜绿假单胞菌（18.9%）；革兰阳性菌占 21.2%；真菌感染占 15.2%。血糖控制不佳组真菌感染比例高于控制良好组（20.3% vs. 8.6%, $P=0.048$ ）。两组年龄、性别及基础疾病差异无统计学意义。控制不佳组入院 pH 更低（ 7.21 ± 0.09 vs. 7.28 ± 0.07 , $P=0.020$ ），血酮更高（ $P=0.010$ ）。控制不佳组感染控制时间延长[9（6~14）d vs. 7（5~10）d, $P=0.030$]。28 d 病死率两组差异无统计学意义（21.7% vs. 13.8%, $P=0.180$ ）。多因素回归显示，血糖控制不佳（OR=2.36, 95%CI 1.12~4.98, $P=0.024$ ）及真菌感染（OR=2.89, 95%CI 1.21~6.91, $P=0.017$ ）为感染控制延迟独立危险因素。血糖波动幅度与感染控制时间呈正相关（ $r=0.32$, $P=0.002$ ）。

结论 DKA 合并重症肺炎以革兰阴性菌感染为主，血糖控制不佳者真菌感染风险增加。早期血糖控制水平及血糖波动性与感染控制延迟密切相关，其预测价值优于单次血糖测定。强化血糖管理对改善感染预后具有潜在临床意义。

关键词：糖尿病酮症酸中毒；重症肺炎；血糖控制

乙型流感病毒感染后继发侵袭性肺曲霉菌感染的临床特征及预后分析：一项单中心回顾性研究

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目的 探讨乙型流感病毒感染后继发侵袭性肺曲霉菌病（IPA）的临床特征、危险因素及预后，为早期识别与干预提供依据。

方法 回顾性纳入 2019 年 1 月至 2024 年 12 月我院收治的乙型流感住院患者 186 例。根据是否合并 IPA 分为合并组与非合并组，IPA 诊断依据 EORTC/MSGERC 标准及临床综合判断。收集一般资料、基础疾病、免疫状态、影像学表现、实验室指标（含 GM 试验）、治疗方案及 28 天预后。采用单因素及多因素 Logistic 回归分析 IPA 发生的独立危险因素。

结果 186 例中入住 ICU 61 例（32.8%），确诊 IPA 32 例（17.2%）。合并组平均年龄高于非合并组（ 66.8 ± 11.5 vs. 58.3 ± 13.2 , $P<0.01$ ）。合并组 COPD（43.8% vs. 21.3%）、糖尿病（37.5% vs. 19.6%）及长期糖皮质激素使用史（34.4% vs. 12.6%）比例显著升高（均 $P<0.05$ ）。合并组 GM 阳性率 62.5%，高于非合并组（9.1%, $P<0.001$ ）。流感起病至 IPA 确诊中位时间 6.5 天（IQR 4~10 天）。多因素 Logistic 回归显示，年龄 ≥ 65 岁（OR=2.31, 95%CI 1.12~4.78）、COPD（OR=2.87, 95%CI 1.34~6.15）、糖皮质激素使用（OR=3.56, 95%CI 1.58~8.02）为 IPA 独立危险因素。校正后 IPA 显著增加 ICU 转入风险（OR=2.94, 95%CI 1.41~6.12）。81.3%合并组患者接受抗真菌治疗，以伏立康唑为主。28 天病死率合并组显著升高（34.4% vs. 11.8%, $P<0.01$ ）。Kaplan-Meier 分析显示合并 IPA 降低短期生存（Log-rank $P<0.001$ ），早期抗真菌治疗（ ≤ 3 天）病死率较低（21.7% vs. 47.6%, $P=0.04$ ）。

结论 乙型流感后继发 IPA 并非少见，老年、COPD 及糖皮质激素使用是主要危险因素。IPA 多在流感起病后约 1 周内出现，影像学缺乏典型特征，显著增加 ICU 风险及病死率。应加强早期筛查与动态评估，及时启动抗真菌治疗以改善预后。

关键词: 乙型流感病毒; 侵袭性肺曲霉病; 慢性阻塞性肺疾病

单中心呼吸科鹦鹉热衣原体肺炎十年检出趋势与流行病学特征分析

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目的 分析南昌大学第一附属医院呼吸科鹦鹉热衣原体肺炎 (*Chlamydia psittaci* pneumonia, CPP) 的检出趋势、流行病学特征及重症转归情况, 为提高该病的临床诊断意识与经验性治疗提供单中心数据参考。

方法 从南昌大学第一附属医院病案系统收集该院呼吸科 2017 年 1 月 1 日至 2026 年 3 月 19 日收治的 CPP 确诊患者的病历资料。采用描述性流行病学方法对病例的时间分布、人群分布及重症监护病房转归进行分析。检出率定义为鹦鹉热确诊例数占同期呼吸科总住院人数的百分比。

结果 共纳入鹦鹉热确诊患者 261 例。2017 年及 2018 年呼吸科确诊数为 0。自 2019 年确诊病例出现后, 确诊人数占同期呼吸科总住院人数百分比由 2019 年的 0.19% 波动上升至 2025 年的 2.47% (2026 年 1 至 3 月部分数据为 2.39%)。病例全年均有分布, 呈现明显的秋冬高发特征, 秋冬季节共报告 178 例, 占总病例数的 68.20% (178/261), 其中春季 34 例、夏季 49 例、秋季 64 例、冬季 114 例。261 例患者中男性 140 例, 女性 121 例, 男女比例为 1.16:1。2019 年至 2025 年各年度患者平均年龄分别为 66.00 岁、65.56 岁、61.58 岁、61.12 岁、64.29 岁、60.87 岁、61.06 岁。共 27 例患者因病重转入重症监护室治疗, 占确诊总例数的 10.34% (27/261)。

结论 随着近年病原宏基因组测序技术应用的推广, 本院呼吸科鹦鹉热衣原体肺炎检出率呈上升趋势。该病在本院呈现秋冬高发、中老年易感的流

行病学特征, 且存在一定比例的重症风险。临床对于秋冬季节不明原因发热伴肺炎的中老年患者, 应早期覆盖抗衣原体经验性治疗。

The Epidemiological Characteristics of *Klebsiella Pneumoniae* Carrying Virulence Plasmids in Hospital-acquired Pneumonia

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Objective To investigate the epidemiological characteristics of virulence plasmid-carrying hypervirulent *Klebsiella pneumoniae* (HvKP) in hospital-acquired pneumonia (HAP) and to analyze the clinical outcomes associated with different clonal types.

Methods Clinical data of 110 HAP patients infected with HvKP (2016-2024) were retrospectively analyzed. Patients were divided into good-prognosis (n=64) and poor-prognosis (n=46) groups. Univariate and multivariate logistic regression were performed. Isolates were characterized by capsular serotyping, MLST, string test, *Galleria mellonella* virulence assay, biofilm formation, PFGE, whole-genome sequencing, and phylogenetic analysis.

Results The poor-prognosis rate was 41.82% (46/110). Multivariate analysis identified sepsis ($P=0.013$, $OR\approx 7$) and prior carbapenem use ($P=0.006$, $OR\approx 7$) as independent risk factors for poor outcome. Predominant clones were K1-ST23 (30/110), K2-ST86 (11/110), K2-ST65 (9/110), and K64-ST11 (23/110). Poor-prognosis rates for K2-ST86, K64-ST11, K1-ST23, and K2-ST65 were 54.5%, 52.2%, 46.7%, and 44.4%, respectively, while K57-ST412 had the lowest (8.3%). K64-ST11 had the longest hospital stay (29.7 ± 13.7 days), and K57-ST412 the shortest

(12.9±9.5 days). Complication rates were highest for K1-ST23 (66.7%) and K64-ST11 (56.5%). The string test was positive in only 17.4% of K64-ST11 isolates. *G. mellonella* assay showed the lowest LD50 (strongest virulence) for K1-type and the widest LD50 range for K64-type, indicating significant intra-clone virulence heterogeneity. PFGE confirmed high homology (≥90%) within same STs, with sub-lineage variations. Phylogenetic analysis revealed that K1-ST23 belongs to a globally epidemic high-risk lineage, while K64-ST11 likely evolved from local CRKP (ST11) through acquisition of virulence plasmids. Differences in virulence plasmid status appeared to drive intra-clone virulence heterogeneity.

Conclusion Sepsis and prior carbapenem exposure are independent risk factors for poor prognosis in HAP patients with HvKP infection. HvKP in our hospital exhibits polyclonal epidemic features, with K1-ST23, K2-ST65/ST86, and K64-ST11 clones associated with worse clinical outcomes. Notably, the K64-ST11 clone displays marked intra-clone virulence heterogeneity. These findings provide valuable insights for early risk identification and targeted antimicrobial strategies.

Comorbidity-Driven Fungal Susceptibility and Virus-Centered Co-infection Networks in Acute Lower Respiratory Tract Infections: A Clinically Integrated BALF-tNGS Study

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Background Acute lower respiratory tract infections are increasingly recognized as polymicrobial diseases, but the effects of pathogen interactions and host comorbidities remain unclear.

Methods In this retrospective study, 1,570 adults with ALRTIs undergoing BALF-tNGS were enrolled. Causative pathogens were adjudicated by two intensivists. Patients were stratified by comorbidity patterns involving chronic obstructive pulmonary disease (COPD), lung cancer, diabetes mellitus (DM), and hypertension. Infection and co-infection patterns were analyzed across groups.

Results A total of 103 microbial species were identified. Viruses, bacteria, and fungi were detected in 69.0%, 62.2%, and 43.7% of patients, respectively, with Epstein-Barr virus and cytomegalovirus predominating. Co-occurrence analysis demonstrated virus-centered microbial networks, with stronger viral-fungal and viral-bacterial interactions than bacteria-bacteria associations. Comorbidity burden was present in 52.8% of patients and was associated with a selective increase in fungal infections, whereas viral and bacterial infection rates remained stable across strata. Multivariable analysis demonstrated that specific comorbidity combinations conferred pathogen-specific fungal risks. COPD with lung cancer was associated with *Pneumocystis jirovecii* infection (OR 2.84), COPD with hypertension increased *Aspergillus* risk (OR 1.93), and DM with hypertension increased mucormycosis risk (OR 3.12).

Conclusion ALRTIs are structured as virus-centered polymicrobial networks, while specific comorbidity combinations selectively predispose patients to opportunistic fungal infections.

20 例马尔尼菲篮状菌病患者的临床特征回顾性分析

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目的 分析马尔尼菲篮状菌病 (talaromycosis, TSM) 的临床特征, 为该病原体的诊疗提供依据。

方法 回顾性收集 2020 年 1 月—2022 年 9 月湘西自治州人民医院诊断为 TSM 的 20 例患者临床资料, 分析患者基础疾病、临床症状、实验室检查和影像学检查结果、治疗方案与疾病转归。

结果 20 例 TSM 患者中 19 例为 HIV 感染者, 主要表现为发热、贫血、咳嗽咳痰、皮肤丘疹、气促、淋巴结肿大、体重下降等。实验室检查中血常规多表现为白细胞、红细胞、血小板三系减少; 20 例患者的 C 反应蛋白均升高, 19 例患者降钙素原升高; 13 例患者均发现 CD4⁺ T 淋巴细胞减少; 11 例患者行 G 试验, 阳性率 54.5% (6/11); 8 例患者行 GM 试验, 阳性率 87.5% (7/8)。胸部 CT 检查显示肺感染、纵隔淋巴结肿大、微小结节、斑片影、双侧胸腔少量积液等。12 例患者采用以伏立康唑为主的方案行序贯性治疗, 2 例患者采用以两性霉素 B 为主的方案进行抗真菌治疗。有 7 例患者症状好转出院, 9 例因经济及个人原因自动出院, 2 例转到上级医院继续治疗, 2 例患者死亡。

结论 TSM 无特征性的临床表现, 部分患者合并免疫功能低下相关基础疾病, 诊断困难, 应提高对该病原菌的认识和实验室检测能力, 尽可能做到早诊断、早治疗。

【关键词】 艾滋病; 马尔尼菲篮状菌; 免疫缺陷; 真菌; 临床特征; 实验室诊断

中国省级人口流动率与碳青霉烯类耐药率的关联研究: 基于 2014—2024 年面板数据的生态学分析

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目的 碳青霉烯耐药革兰阴性菌已成为医院感染防控和抗菌药物管理的重要挑战。人口流动或促进耐药菌或耐药基因的传播, 但基于我国省级长期面板数据的研究有限。本研究基于 2014—2024 年中国省级面板数据, 分析人口流动率与大肠杆菌、肺炎克雷伯菌、铜绿假单胞菌及鲍曼不动杆菌碳青霉烯耐药率之间的关联。

方法 数据来源于各省市统计年鉴及全国细菌耐药监测网, 纳入中国 31 个省份 2014—2024 年人口流动率、四种菌碳青霉烯耐药率、社会经济、医疗资源、环境等因素。通过效应 F 检验和 Hausman 检验选择合适面板模型作为主分析、平方项检验人口流动率与耐药率之间是否存在非线性关系、累计效应模型评估人口流动可能导致的滞后或累积影响及按地理区域开展亚组分析评估区域异质性。效应量以率比 (RR) 及 95% 置信区间 (CI) 表示。

结果 省份固定模型用于主分析 (省份效应模型 $P < 0.001$, 固定效应模型 $P < 0.001$)。研究发现人口流动率与鲍曼不动杆菌碳青霉烯耐药率呈显著正相关 ($RR = 1.005$, 95% CI 1.002, 1.009)。未发现明确非线性关系。累积效应模型提示大肠埃希菌耐药率与当期人口流动率相关, 肺炎克雷伯菌耐药率与人口流动率的 5 年净变化相关, 由于当期流动率与累积指标之间存在共线性, 相关结果需谨慎解释。区域亚组分析提示: 华南地区大肠杆菌 ($RR = 1.042$, 95% CI 1.001, 1.085)、肺炎克雷伯菌 ($RR = 1.057$, 95% CI 1.009, 1.107)、铜绿假单胞菌 ($RR = 1.035$, 95% CI 1.016, 1.055) 呈显著正相关; 华东地区大肠杆菌 ($RR = 1.014$, 95% CI 1.005, 1.023) 及鲍曼不动杆菌 ($RR = 1.008$, 95% CI 1.003, 1.013) 呈显著正相关; 东北地区大肠杆菌呈显著负相关 ($RR = 0.960$, 95% CI 0.940, 0.980)。

结论 人口流动率与鲍曼不动杆菌碳青霉烯耐药率呈现微弱但稳健的正相关, 华中、华东等高流动地区表现更为突出。大肠杆菌、肺炎克雷伯菌及铜绿假单胞菌与人口流动率关联不一致, 提示人口

流动对碳青霉烯耐药传播的影响可能因病原体和区域背景而异。未来应结合人口流动方向、跨区域就医网络、抗菌药物使用和医院感染防控水平,进一步明确耐药菌跨区域传播的机制,并为高流动地区的耐药监测和防控策略提供依据。

【关键词】 人口流动;碳青霉烯类耐药;区域异质性

肺隐球菌病 786 例临床流行病学特征分析

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目的 分析南昌大学第一附属医院 10 年肺隐球菌病确诊患者的性别、年龄、基础疾病及年度分布特征,了解该病流行病学规律,为临床早期识别与防控提供依据。

方法 回顾性收集 2015 年 1 月-2026 年 4 月确诊的肺隐球菌病患者临床资料,仅纳入诊断、性别、年龄信息,统计分析患者年度发病数量、年龄分布、性别构成比及基础疾病特点。

结果 10 年间共确诊肺隐球菌病患者 786 例,2015-2020 年度确诊病例数较 2020-2026 年整体呈上升趋势;男性 477 例 (60.69%),女性 309 例 (39.31%),男性患者数量显著高于女性,性别比约为 1.54:1;患者年龄分布呈现近似正态分布特征,年龄范围覆盖全生命周期,数据显示,41~65 岁中年群体为隐球菌相关疾病的主要发病人群,占总样本量的 60% 以上;80 岁以上老年患者与 20 岁以下青年患者占比均不足 5%;73.28% (576 例) 患者为单次住院,26.72% (210 例) 患者存在多次住院记录,最多住院次数达 16 次,隐球菌相关患者普遍存在共病情况,前 5 位基础疾病依次为:呼吸系统疾病(230 例,29.26%)、肿瘤(213 例,27.10%)、糖尿病(161 例,20.48%)、高血压(127 例,16.16%)、肾脏疾病 (124 例, 15.78%)。

结论 本院 10 年肺隐球菌病发病呈明显性别、年龄与基础疾病分布特征,中年男性、合并多种基础疾病者为高危人群;临床应加强对该人群的主动筛查与评估,提高早期诊断与精准干预水平。

外阴阴道假丝酵母菌病病原菌分布、唑类药物敏感特征与临床结局的关联性：一项前瞻性研究

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目的 外阴阴道假丝酵母菌病 (VVC) 是育龄期女性最常见的真菌性阴道感染,易复发。白色念珠菌和光滑念珠菌是主要致病菌种,但其对唑类药物敏感性差异对短期疗效和长期复发的影响尚未明确。本研究旨在探讨 VVC 患者的病原菌分布、唑类药物敏感性,及基线药敏特征与短期治愈率和 1 年复发率的关联,为精准治疗提供依据。

方法 本研究为前瞻性队列研究,纳入 2024 年 9 月至 2025 年 6 月间 152 例 VVC 患者。采集基线时及唑类药物治疗后 2 周的阴道拭子进行真菌培养及菌种鉴定。对基线分离株进行 8 种抗真菌药物(阿尼芬净、米卡芬净、卡泊芬净、5-氟胞嘧啶、泊沙康唑、伏立康唑、伊曲康唑、两性霉素 B) 的药敏检测。治疗后 2 周随访评估病原学治愈 (培养阴性) 和症状治愈;1 年后随访记录症状复发情况。采用独立样本 t 检验、Mann-Whitney U 检验比较组间差异。

结果 患者平均年龄 36.5 ± 6.9 岁,50% 有 VVC 病史。共分离出 152 株念珠菌,白色念珠菌占 68.4%,光滑念珠菌占 25.0%,其他念珠菌种占 6.6%。药敏结果显示,白色念珠菌对泊沙康唑的敏感性高于光滑念珠菌 (MIC 中位数 $2 \mu\text{g/mL}$ vs. $8 \mu\text{g/mL}$, $p=0.038$)。治疗后 2 周,101 名患者返诊采样,另有 34 人仅报告症状,整体病原学治愈率为 71.1% (72/101),症状治愈率为 95.6% (129/135)。白色念

珠菌组病原学治愈率 68.7%，而光滑念珠菌组病原学治愈率 84.6%。病原学治愈患者的氟康唑 MIC 值显著低于治疗失败者 ($p=0.002$)；而光滑念珠菌组无此关联 ($p=0.223$)。1 年随访时总体症状复发率为 40.5% (51/126)，白色念珠菌组为 38.2% (34/89)，光滑念珠菌组为 41.9% (13/31)。在白色念珠菌组中，复发患者的基线氟康唑 MIC 显著高于未复发者 ($p<0.001$)；光滑念珠菌组则未观察到此关联 ($p=0.115$)。此外，有 VVC 病史患者的基线氟康唑 MIC 显著高于初发患者 (白色念珠菌： $p<0.001$ ；光滑念珠菌： $p<0.05$)。

结论 白色念珠菌仍是 VVC 的主要病原体，但光滑念珠菌感染比例不容忽视。基线氟康唑 MIC 值可预测白色念珠菌所致 VVC 的疗效及复发风险，既往 VVC 病史与高 MIC 相关。建议对高复发风险者进行菌种鉴定与药敏监测，以指导个体化治疗。

【关键词】外阴阴道假丝酵母菌病；念珠菌；氟康唑

A Comparative Genomic and Microbiota Analysis of Liver-Derived Versus Gut-Colonizing *Klebsiella Pneumoniae* in Patients with Pyogenic Liver Abscess

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Background The interactions between pathogenic *Klebsiella pneumoniae*, which causes liver abscesses, and the gut microbiota have not yet been fully elucidated, and traditional methods have limitations in tracing the source of infection

Methods We analyzed *K. pneumoniae* strains isolated from liver abscess aspirates and corresponding fecal samples from 30 patients using PCR and 16S

rRNA-based gut microbiota profiling. Serotyping, multi-locus sequence typing (MLST), virulence gene profiling, and antimicrobial susceptibility testing were performed. Bioinformatic analyses assessed gut microbial diversity and functional potential.

Results Liver-derived isolates were predominantly K1 (36.6%) and K2 (33.3%) serotypes, mainly ST23 and ST86, carrying hypervirulence genes (*peg-344*, *iroB*, *rpmA*) with low antibiotic resistance. In contrast, fecal isolates were exclusively non-K1/K2 serotypes, highly diverse in sequence type, and harbored multiple resistance genes (e.g., CTX-M, SHV). Gut microbiota profiling revealed markedly reduced microbial diversity in patients with liver abscesses, enrichment of opportunistic pathogens, and depletion of short-chain fatty acid-producing commensals. Functional predictions demonstrated significant enrichment of iron acquisition, lipopolysaccharide biosynthesis, and virulence-associated pathways.

Conclusion These findings indicate that hypervirulent *K. pneumoniae* causing liver abscesses are genomically and functionally distinct from dominant gut colonizers, supporting selective displacement of specific high-virulence clones rather than direct invasion by prevalent fecal strains. Integrative genomic and microbiome analyses provide novel mechanistic insights into the pathogenesis of *K. pneumoniae* liver abscesses.

COVID-19 高峰期中国 ICU 中碳青霉烯耐药铜绿假单胞菌传播加剧

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背景 碳青霉烯耐药铜绿假单胞菌 (CRPA) 在医院环境与患者之间的传播对临床感染控制构成重

大挑战。COVID-19 大流行可能改变重症监护病房 (ICU) 内的细菌传播动力学。本研究旨在前瞻性评估中国 COVID-19 病例激增前后, ICU 内铜绿假单胞菌的时空传播特征。

方法 2022 年 10 月至 2023 年 4 月, 在中国东部一所新建 21 张床位的三级教学医院 ICU 内, 对环境及患者开展常规铜绿假单胞菌筛查; 其中 2022 年 12 月至 2023 年 1 月为 COVID-19 病例激增期。对所有非重复分离的铜绿假单胞菌菌株进行全基因组测序及抗菌药物敏感性检测, 并结合基因组与时空数据分析其传播模式。

结果 在 1694 份环境样本中检出碳青霉烯耐药铜绿假单胞菌 40 株 (2.36%); 在来自 353 例患者的 1576 份鼻咽及直肠拭子中检出 108 株 (6.86%)。序列型 ST463 为患者与环境中的优势克隆。时空分布及基因组分析显示, COVID-19 激增前以散发的患者相关传播为主, 而在激增期间观察到高风险 ST463 克隆的集中传播。未发现抗生素消耗与碳青霉烯耐药铜绿假单胞菌传播之间存在显著相关性。此外, 观察到 bla_KPC 基因的体内演化事件 (由 bla_KPC-2 演变为 bla_KPC-71), 并与单例患者多位点定植相关。

结论 本前瞻性研究表明, COVID-19 病例激增与 ICU 内碳青霉烯耐药铜绿假单胞菌传播增加相关。上述发现提示, 在公共卫生应急背景下需强化院内感染防控策略。此外, 本研究首次报道铜绿假单胞菌中 bla_KPC-2 向 bla_KPC-71 的演化, 为理解耐药演变及优化抗菌治疗提供了新的依据。

肾移植受者侵袭性曲霉病的临床特点及危险因素分析: 单中心回顾性病例对照研究

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目的 本研究旨在分析本地区肾移植受者侵袭

性曲霉病 (invasive aspergillosis, IA) 的流行病学特点、临床特点、发病危险因素及影响预后的危险因素, 为肾移植受者 IA 的早期诊断、抢先治疗、改善预后提供依据。

方法 收集我院 2020 年 1 月-2025 年 1 月 5 年间肾移植受者 IA 的临床资料, 首先分析其流行病学特点、临床特点、治疗方案及预后; 其次, 按移植日期以 1:4 比例匹配肾移植受者非 IA 组进行病例对照研究, 分析肾移植受者 IA 的发病危险因素及影响预后的危险因素。

结果 本地区肾移植受者 IA 以侵袭性肺曲霉病 (Invasive pulmonary aspergillosis, IPA) (93.95%) 为主, IgA 肾病 (OR=7, 95%CI: 1.79~27.38, $P=0.005$) 会增加肾移植受者发生 IA 的风险, 淋巴细胞 (Lymphocyte, LY) 减少 (OR=0.001, 95%CI: 0.000~0.330, $P=0.019$)、天门冬氨酸氨基转移酶 (Aspartate Aminotransferase, AST) 升高 (OR=1.16, 95%CI: 1.03~1.32, $P=0.019$) 及血清白蛋白 (Serum Albumin, ALB) 降低 (OR=0.64, 95%CI: 0.47~0.87, $P=0.004$) 是肾移植受者发生 IA 的独立危险因素。近 5 年手术史 (HR=6.48, 95%CI: 1.28~32.71, $P=0.024$)、LY 减少 (HR=0.05, 95%CI: 0.005~0.61, $P=0.018$)、AST 升高 (HR=1.09, 95%CI: 1.02~1.16, $P=0.008$)、血清胱抑素 C (Cystatin C, Cys-C) 升高 (HR=3.16, 95%CI: 1.43~6.95, $P=0.004$) 是肾移植受者诊断 IA 后 12 周及 1 年死亡的独立危险因素。IA 是预测肾移植受者 1 年死亡率的重要影响因素 ($P<0.001$)。

结论 本地区肾移植受者 IA 以 IPA 为主要类型, 对于 LY 减少、AST 升高及 ALB 降低的肾移植受者, 应积极优化免疫抑制方案、对症及时改善 AST 及 ALB, 以防止肾移植受者发生 IA, 并强化 IA 的监测力度, 以实现早期诊断及治疗; 对于存在近 5 年手术史、LY 减少、AST 及 Cys-C 升高的肾移植术后 IA 患者, 在初始治疗时需充分考虑病情严重程度, 评估联合抗曲霉治疗的必要性, 并积极调整免疫抑制方案, 以改善患者预后。

免疫功能正常患者感染奴卡菌的机制及肺内免疫特征

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目的 奴卡菌通常在免疫功能低下或有基础疾病的人群中引起感染，免疫功能正常者感染奴卡菌较为少见，其机制及免疫特征尚不明确。本研究通过单细胞测序，探究奴卡菌在不同免疫状态人群中的感染机制及免疫特征。

方法 收集免疫功能正常且无明显危险因素的肺部奴卡菌感染患者（免疫正常组）及免疫抑制奴卡菌感染患者（免疫抑制组）的肺泡灌洗液，进行单细胞测序，并与健康对照及普通细菌性肺炎患者对比，解析不同人群感染奴卡菌的免疫特征。

结果 免疫抑制患者表现为明显的 T/NK 细胞数量减少及功能异常（T 细胞呈耗竭表型，NK 细胞细胞毒活性下调），且与普通细菌性肺炎相比，细胞间炎症通讯（如 TNF-TNFR、IFNGR1-IFN γ 通路）显著减弱。免疫功能正常患者则出现肺泡巨噬细胞亚群及功能重塑：组织定居肺泡巨噬细胞比例相对升高，但其炎症激活能力（IL1B、TNF、NOS2 表达）下降；同时，炎性单核细胞（CD14+、CD16+）浸润较普通细菌性肺炎减少。

结论 免疫功能正常者感染奴卡菌可能与组织定居肺泡巨噬细胞功能异常相关。单纯使用细胞免疫评估免疫功能存在一定局限性。除细胞免疫外，固有免疫功能尤其是肺泡巨噬细胞的功能状态，是评估机会性致病菌感染风险的另一个重要指标。

成人非伤寒沙门菌感染临床特征及诊治—18

例住院病例分析

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目的 探讨 18 例经临床证实的成人非伤寒沙门菌感染病例的临床特征和诊治方法。

方法 回顾性分析 2022 年 01 月至 2025 年 09 月就诊于天津市第一中心医院经临床证实的 18 例成人非伤寒沙门菌感染住院患者临床资料，对其临床特征、诊治及结局、耐药性进行分析总结。

结果 18 例患者中男女之比 10:8，平均年龄 54.72 $\pm$ 19.35 岁。90% 感染发生于夏秋季节，绝大多数表现为侵袭性感染，超过 3/4 患者发生血流感染，2/3 有自身免疫性疾病或恶性肿瘤病史，约半数正在使用化疗药物或激素治疗，一半以上有 2 型糖尿病史，近 1/3 合并中性粒细胞减少症。患者均有发热，呈中高热；其次是腹泻、腹痛；重症患者可有心内膜炎、主动脉瘤、感染性休克等多器官功能衰竭。血液检查显示白细胞计数、中性粒细胞计数差异性较大，可能与基础疾病有关；常规炎症指标 CRP 敏感性高于 PCT。18 例 NTS 感染患者中肠炎沙门菌、鼠伤寒沙门菌检出率最高，在所有菌株中对头孢曲松耐药率为 23.52%、对左氧氟沙星耐药率为 11.76%（敏感性表现为中介的比例高达 76.47%）、对复方新诺明耐药率为 23.52%，对碳青霉烯类均敏感。本研究中心患者总体预后良好，4 例预后不佳，2 人死亡（11.11%），自动出院 2 例（11.11%），可能与基础疾病及 NTS 侵袭性导致心血管并发症有关。

结论 在夏秋季，且有自身免疫性疾病或恶性肿瘤群体，出现发热及消化道症状，需高度警惕非伤寒沙门菌感染，并积极送病原学检查，尤其重视血培养；还应注意其疾病重症化及心血管侵袭性；经验性治疗可选用三代头孢菌素类抗生素，选用喹诺酮类抗菌药物需要根据药敏结果，重症患者选择碳青霉烯类药物。

Serum Interleukin-8 at Admission As A Predictive Biomarker for One-Year All-Cause Mortality in Patients with Community-Acquired Pneumonia.

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Qingdao Municipal Hospital Group

Background Long-term mortality rates are elevated among patients with community-acquired pneumonia (CAP). This study investigated whether serum interleukin-8 (IL-8) levels could predict one-year all-cause mortality in adults with CAP

Methods Between November 18, 2020, and November 21, 2021, we enrolled 410 patients with CAP. Patients were divided into survivors and deceased groups based on whether they died within one year. Absolute and relative differences were determined based on measurements of biomarkers on day 1 and day 6 after admission. Logistic regression was conducted to identify factors associated with one-year mortality in CAP patients. ROC curve analysis evaluated the predictive performance of these factors.

Results IL-8 levels at admission were higher in the deceased group than those in the survival group. Both the absolute and relative differences in IL-8 levels were significantly higher in the deceased group (absolute difference: 10.67 [0.20-22.23] pg/mL vs. 0.04 [-3.81-3.40] pg/mL, relative difference: 0.38 [0.02-0.65] vs. 0 [-0.32-0.21], respectively, $P<0.001$). Multivariate analysis revealed that CURB-65 score (OR=2.48, 95% CI: 1.70-3.60), age (OR=1.10, 95% CI: 1.07-1.13), and IL-8 at admission (OR=1.01, 95% CI: 1.00-1.02), were significantly associated with an increased risk of one-year all-cause mortality. The area under the curve (AUC)

for IL-8 at admission was 0.815 ($P<0.001$), with an optimal threshold concentration of 20.95 pg/mL (95% CI: 0.725-0.905, 84% sensitivity, and 97% specificity). Combining IL-8 at admission with CURB-65 improved the predictive accuracy from 0.877 to 0.901.

Conclusion CURB-65 score, age, and IL-8 levels at admission were significantly associated with an increased risk of one-year all-cause mortality. Notably, the combination of IL-8 at admission and CURB-65 was more effective than CURB-65 alone in predicting one-year all-cause mortality in patients with CAP, providing a clinically useful tool for early identification of high-risk patients with poor long-term outcomes.

Baseline Procalcitonin-to-Albumin and Neutrophil-to-Albumin Ratios for Predicting Adverse Outcomes in Patients with Community-acquired Pneumonia: A Retrospective Cohort Study

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Background Community-acquired pneumonia (CAP) remains a leading cause of morbidity and mortality. Conventional tools such as CURB-65 and PSI have limitations in clinical practice. The procalcitonin-to-albumin ratio (PAR) and neutrophil-to-albumin ratio (NAR) have shown prognostic value in critical illness, but their utility in CAP is unclear. This study investigated the predictive significance of PAR and NAR in CAP

Methods This retrospective study included hospitalized CAP patients at Qingdao Municipal Hospital (Nov 2020–Nov 2021). Demographics, laboratory pa-

rameters, and clinical scores (CURB-65, PSI) were collected within 24 h of admission. Patients were classified by disease severity and in-hospital mortality. Logistic and Cox regression analyses assessed associations of PAR and NAR with severity and mortality, with predictive performance evaluated by ROC curves

Results A cohort of 429 patients with CAP was analyzed, including 75 cases classified as severe CAP (SCAP). Compared with non-SCAP, SCAP patients were older, had more comorbidities, higher inflammatory markers, elevated NAR and PAR, and lower ALB (all $P < 0.001$). Multivariate analysis identified NAR as an independent predictor of SCAP incidence and in-hospital mortality. NAR achieved an AUC of 0.87 (95% CI: 0.82–0.91), while PAR demonstrated an AUC of 0.83 (95% CI: 0.77–0.88), both significantly distinguishing SCAP patients from non-SCAP cases ($P < 0.001$). The novel biomarkers demonstrated robust prognostic performance, with PAR yielding an AUC of 0.82 (95% CI: 0.74–0.89) and NAR an AUC of 0.80 (95% CI: 0.71–0.90) for predicting in-hospital mortality

Conclusion Admission NAR levels independently predicted SCAP incidence and in-hospital mortality in CAP patients. As a simple and cost-effective biomarker, NAR may provide clinicians with a practical tool for early risk stratification and prognosis assessment

Carbapenem-resistant Enterobacterales Infections in China by Culture Source

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Background Carbapenem-resistant Enterobacterales (CRE) are increasingly prevalent in China. We aimed to compare the characteristics and outcomes of patients with CRE infection by culture source

Methods This was a multicenter cohort study of patients with CRE isolated from clinical cultures at six tertiary hospitals in China between July 2017 and July 2018, as part of the CRACKLE-2 study. Clinical data

were collected, and whole genome sequencing was performed on CRE isolates

Results Among 582 unique patients, CRE were most frequently isolated from respiratory specimens (333; 57%), followed by urine (82; 14%), non-wound abdominal (75; 13%), blood (45; 8%), and other sites (47; 8%). The criteria for infection were met by 301 (52%) patients. Respiratory tract infections were often hospital-acquired (98/129, 76%) and associated with ICU admission prior to CRE isolation (94/129, 73%). The overall unadjusted 30-day mortality rate among infected patients was 10% (31/301), with an additional 8% (25/301) discharged to hospice. Bloodstream infections were associated with greater comorbidity and severity, contributing to the highest 30-day mortality (10/45, 22%). *Klebsiella pneumoniae* accounted for 83% of isolates, 94% of which carried blaKPC-2. Among *Escherichia coli* isolates, 63% harbored blaNDM-5

Conclusion Respiratory specimens were the most common source of CRE, predominantly KPC-2-producing *K. pneumoniae* and clinical outcomes varied substantially by infection site. These data provide actionable evidence for infection prevention programs, supporting risk-based surveillance, early identification of high-risk patients, and site-specific antimicrobial stewardship strategies to reduce CRE-associated morbidity and mortality

肺炎克雷伯菌血流感染的临床特征及预后分析

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目的 识别 KP-BSI 住院患者死亡的危险因素及构建住院死亡风险预测模型, 为临床早期风险分

层与治疗决策提供依据。

方法 回顾性分析 2022 年 1 月 1 日至 2024 年 12 月 31 日于我院住院并确诊 KP-BSI 的 480 例患者的临床资料 (包括人口学特征、基础病史、侵入性操作、抗生素暴露及实验室检查等)。根据是否发生不良结局, 分为预后不良组 ($n=101$) 和预后良好组 ($n=379$), 比较两组患者的人口学特征及临床分布差异, 利用单因素 Cox 回归分析及 LASSO 回归进行变量初筛, 随后通过多因素 Cox 比例风险回归模型构建死亡预测模型并确定独立预后因子, 采用 C-指数及时间依赖性 ROC 曲线评价模型的区分度, 通过校准曲线评价预测概率与实际观测值的一致性, 并利用决策曲线分析曲线评估模型的临床实用价值。

结果 在 480 例 KP-BSI 患者中, 预后不良组 (119 例) 的男性比例更高、年龄更大, 且合并肾功能不全、CRKP 感染及抗菌药物暴露史的比例均显著高于预后良好组 (P 均 <0.05)。本组患者总体住院病死率为 24.8%。采用 LASSO 回归从 16 个临床变量中筛选出 6 个关键特征: CRKP 感染、mSOFA 评分、并发休克、并发呼吸衰竭、并发肾衰竭以及肾替代治疗 (CRRT), 再进行多因素 Cox 分析, 结果显示并发呼吸衰竭 ($HR=2.15$)、接受肾替代治疗 ($HR=1.73$) 及 mSOFA 评分升高 ($HR=1.11$) 是住院死亡的独立预测因子。预测模型的 C-指数为 0.793。时间依赖性 ROC 曲线显示模型在第 7、14、28 天的 AUC 值分别为 0.824、0.827 和 0.857, 提示具有稳定且优秀的预测效能。校准曲线显示模型预测的生存概率与实际情况吻合良好。决策曲线证实该模型在较宽的阈值概率范围内具有显著的临床净获益。

结论 KP-BSI 患者死亡的危险因素是感染引发的一系列严重器官功能衰竭, 其中 KP-BSI 感染后并发呼吸衰竭、需要启动 CRRT 治疗及改良序贯器官衰竭评分 (mSOFA) 升高是住院死亡的独立预后因素。基于上述指标构建的 Cox 风险预测模型具有优秀的判别力与临床一致性, 可实现对患者不同病程阶段死亡风险的动态评估, 为临床早期风险分层及个体化干预决策提供科学的量化评价工具。

关键词: 肺炎克雷伯菌, 血流感染, 危险因素,

Cox 模型, 预后评估

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女性生殖道细菌真菌感染对阴道微环境的影响及防控策略研究

肖政

长沙市一

目的 女性生殖道细菌、真菌感染临床发病率高, 不规范抗感染治疗易导致病情反复、阴道微生态持续失调, 且临床对其与人乳头瘤病毒 (HPV) 感染的关联重视不足。本研究分析我院就诊女性生殖道细菌真菌感染的流行特征, 明确其对阴道微环境的影响, 探讨规范抗感染治疗的临床价值, 为生殖道细菌真菌感染的诊疗提供临床数据。

方法 选取我院妇产科就诊的 1500 例女性患者为研究对象。所有受试者均同步采集阴道分泌物标本, 接受生殖道病原微生物检测、阴道微环境评估及 HPV 分型检测。参照相关指南诊断细菌性阴道病 (BV)、外阴阴道假丝酵母菌病 (VVC) 及滴虫性阴道炎 (TV)。采用随机数字表法各抽取 100 例 HPV 阳性、阴性患者进行组间对照。对 35 例合并细菌、真菌感染的 HPV 阳性患者予规范抗感染治疗, 并于 6 个月后随访, 评估病原清除、HPV 转阴及微环境恢复情况。数据采用 SPSS26.0 软件进行统计分析。

结果 纳入的 1500 例患者中, 共检出 HPV 阳性 304 例, 总感染率 20.26%, 高危型感染以 52、16、58、53 型为主; 组间对比显示, HPV 阳性组细菌性阴道病、外阴阴道假丝酵母菌病感染率分别为 40%、22%, 明显高于 HPV 阴性组的 9%、12% ($P<0.05$); 合并细菌真菌感染的患者, 普遍存在阴道 PH 值升高、乳酸杆菌减少、白细胞计数升高的微环境失调表现, 与无感染人群差异有统计学意义 ($P<0.05$)。年龄分层显示, ≤ 20 岁、 ≥ 51 岁为 HPV

与生殖道细菌真菌感染的高发人群。半年随访结果显示, 35 例 HPV 阳性合并细菌、真菌感染患者经规范抗感染治疗后, HPV 转阴率达 40%, 转阴组阴道微环境改善率、病原清除率均优于持续感染组 ($P<0.05$)。

结论 女性生殖道细菌和真菌感染可破坏阴道微生态平衡, 升高 HPV 感染及持续感染风险。临床诊疗中需重视这类感染的早期筛查与规范抗感染治疗, 通过恢复阴道微环境稳态, 可有效促进 HPV 转阴, 对规范抗菌药物的应用和生殖道感染全流程的防控具有实际参考价值。

关键词: 阴道微环境; 生殖道感染; 细菌真菌感染; 抗感染治疗; 病原诊断

Molecular Characteristic, Transferability and Pathogenesis of Carbapenem-resistant Klebsiella Pneumoniae Co-harboring NDM-5 and OXA-181

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Zhongnan Hospital of Wuhan University

Objective Infections caused by carbapenem-resistant *Klebsiella pneumoniae* (CRKP) have emerged as a major global public health challenge. The primary resistance mechanism involves the production of carbapenemases such as KPC, NDM, OXA, IMP, and VIM, each of which exhibits distinct prevalent subtypes and resistance characteristics. However, an increasing number of studies have reported CRKP strains co-carrying two types of carbapenemases, further exacerbating the clinical dilemma of limited treatment options against CRKP. This study reports a nosocomial outbreak caused by NDM-5-OXA-181-CRKP, analyzes its antimicrobial susceptibility, molecular typing, phylogenetic relation-

ships, transmission dynamics, and evolutionary mechanisms, and provides an in-depth characterization of a recombinant plasmid co-harboring blaNDM-5 and blaOXA-181.

Methods Bacterial isolates were identified using the Vitek-2 Compact automated microbial identification system. Initial screening for carbapenemase genes was performed via polymerase chain reaction (PCR). From October 2025 to March 2026, a total of 11 NDM-5-OXA-181-CRKP isolates were recovered. Antimicrobial susceptibility testing against commonly used antimicrobial agents was conducted using the broth microdilution method. Whole-genome sequencing and bioinformatics analyses were performed on the 11 NDM-5-OXA-181-CRKP isolates to determine their molecular typing. Comparative plasmid genomic analysis was carried out to elucidate the origin and evolutionary mechanism of the recombinant plasmid.

Results This outbreak was caused by extensively drug-resistant (XDR) NDM-5-OXA-181-CRKP strains of sequence type 16 (ST16) and capsular type KL81. Among these isolates, we identified a conjugative, highly stable recombinant plasmid of the ColKP3/IncFIA(pBK30683) type that co-harbored blaNDM-5 and blaOXA-181. Comparative plasmid genomic analysis revealed that this recombinant plasmid shares high similarity with pKPX-2 (AP012056.1) and p07B23008-C-NDM-OXA (PV23117.1). The fusion mechanism was associated with IS26-mediated genetic recombination.

Conclusion In this study, we report an outbreak caused by *Klebsiella pneumoniae* harboring a recombinant plasmid co-carrying blaNDM-5 and blaOXA-181. The co-transfer of NDM-5 and OXA-181 may accelerate the dissemination of NDM-5-OXA-181-CRKP, posing a serious threat to public health security.

Keywords NDM-5-OXA-181-CRKP; nosocomial outbreak; recombinant plasmid

肝脓肿患者不同标本来源肺炎克雷伯菌的分子特征及遗传多样性

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目的 分析江苏连云港本地区肝脓肿患者不同标本来源肺炎克雷伯菌分子流行病学特征。

方法 收集江苏省连云港市第一人民医院 2021 年 1 月 1 日至 2023 年 4 月 30 日, 将由肝脓肿患者脓液、血液、便标本中分离出的肺炎克雷伯菌作为研究菌株, 采用 VITEK2-Compact 微生物鉴定仪进行药敏试验; 通过拉丝实验检测肺炎克雷伯菌的黏液表型; 使用 Novaseq 6000 高通量测序平台进行全基因组测序; 使用软件 Prokka (v1.14.5) 对拼接好的全基因组序列进行基因组注释, 使用 Kleborate v2.0.4 分析抗菌素耐药性基因、毒力基因、MLST、荚膜分型、ST 型和物种鉴定; 使用 mlst v2.18.1 通过 PubMLST 数据库提供的物种管家基因信息进行比对, 鉴定肺炎克雷伯菌的 ST 分型。

结果 脓液与血液标本的高毒力肺炎克雷伯菌检出率及高黏液表型阳性率显著高于便标本 ($P < 0.001$)。脓液与血液标本中荚膜分型以 KL1 (54.64%) 和 KL2 (24.74%) 为主, KL1 检出率显著高于便标本 ($P < 0.05$)。脓液与血液标本中 ST23 占 41.24% (40/97), ST65 占 9.28%, ST86 占 8.25%。脓液与血液标本中 ST23 检出率显著高于便标本 ($P = 0.002$)。脓液与血液标本中 *peg-344* 携带率最高 (95.88%), 其次 *rmpA*、*rmpA2*、*iroB* 携带率均超过 90%。除 *entD* 外, 脓液与血液标本毒力基因携带率均显著高于便标本 ($P < 0.001$)。

结论 本地区细菌性肝脓肿中高毒力肺炎克雷伯菌为常见病原体。不同肝脓肿标本来源(脓液、血液、便)肺炎克雷伯菌分子特征存在差异, 具有遗传多样性。

Development and External Validation of A Mortality Prediction Model for ICU Patients with Bloodstream Infection: Limited Improvement of Recalibration Across Populations

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Background Early risk stratification in intensive care unit (ICU) patients with bloodstream infection (BSI) is essential for clinical decision-making and efficient allocation of healthcare resources. However, the generalizability of prediction models across populations, particularly regarding calibration, remains uncertain. This study aimed to develop and externally validate a model for predicting 30-day mortality in ICU patients with BSI and to evaluate the effectiveness of logistic recalibration

Methods We conducted a retrospective cohort study using the MIMIC-IV (version 3.1) database. Predictors were selected using Elastic Net with bootstrap stability selection, followed by multivariable logistic regression. Model performance was assessed using discrimination, calibration, Brier score, and decision curve analysis. External validation was performed in an independent cohort ($n = 285$). Logistic recalibration using intercept and slope derived from internal validation was applied.

Results The model demonstrated good discrimination in both internal (AUC 0.796) and external cohorts (AUC 0.762), with a simplified six-predictor

model showing comparable performance. However, calibration analysis revealed systematic underestimation of mortality risk in the external cohort. Logistic recalibration yielded only modest improvement (Brier score 0.254 to 0.241), with persistent miscalibration (slope 1.435, intercept 2.094). Substantial case-mix differences likely contributed to calibration drift.

Conclusion This model showed stable discrimination but limited calibration transportability. Logistic recalibration alone was insufficient, highlighting the need for population-specific validation and model updating before clinical implementation.

A One Health Perspective on The Plasmid Backbone Preference and Evolutionary Adaptation of TmexCD-toprJ in Klebsiella Spp.

xinli jiang

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Background Antimicrobial resistance (AMR) poses a critical One Health challenge, linking human, animal, and environmental health through the movement of multidrug-resistant (MDR) bacteria and resistance determinants. The tmexCD-toprJ gene cluster, an efflux pump conferring high-level resistance to tigecycline and eravacycline. However, its plasmid backbone preferences and evolutionary trajectories in *Klebsiella* spp. remain insufficiently characterized

Methods This study investigated the plasmid backbone preference and evolutionary characteristics of tmexCD-toprJ-harboring plasmids in *Klebsiella* spp., using whole-genome sequencing of three clinical strains carrying tmexCD-toprJ collected from 2018 to 2023. Conjugation assays, comparative genomics, and global

epidemiological analysis were performed to assess plasmid mobility, genetic context, and evolutionary direction under the One Health framework.

Results All three isolates (K7, K36, and K307) exhibited MDR and harbored major resistance genes, including blaIMP-4, mcr-1.1, and blaNDM-1, respectively. The plasmid from K36 was transferable to EC600 (frequency, 10⁻⁷), confirming cross-species mobility. Global database analysis revealed that tmexCD-toprJ-positive *Klebsiella* spp. isolates (n=92) originated mainly from humans (59.8%), followed by animals (37.0%) and environments (3.3%). Phylogenetic and plasmid analyses the tmexCD1-toprJ1 variant was mainly associated with these hybrid plasmids, frequently co-localizing with sul1, qnrB, and strA/B to form stable “tigecycline–aminoglycoside–sulfonamide” co-resistance modules. In contrast, tmexCD2-toprJ2 was more often inserted into classical resistant plasmids.

Conclusion These findings demonstrate that tmexCD-toprJ has evolved as a highly mobile resistance determinant within *Klebsiella* spp., disseminating across the human–animal–environment interface via hybrid plasmids and horizontal gene transfer. This underscores the urgent need for integrated One Health surveillance and containment strategies to mitigate plasmid-mediated multidrug resistance and its global public health impact.

Metagenomic and Genomic Characterization of Extrapulmonary Mycobacterium Abscessus Infections: A Comparative Cohort Study

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Introduction The incidence of Mycobacterium abscessus complex (MABC) infections is rising, becoming a major pathogen of nontuberculous mycobacteria responsible for Pulmonary Disease (PD) and Extrapulmonary Disease (ED). However, studies on the clinical characteristics of MABC-ED remain limited

Methods A 7-year retrospective analysis was conducted on MABC-ED cases at Zhongshan Hospital in Shanghai, China. We analyzed predisposing factors, clinical features, metagenomic sequencing (MS) results, drug susceptibility testing (DST), and genomic characteristics of MABC-ED patients, comparing the data with those of PD cases.

Results Among 17 MABC-ED patients, 15 had predisposing risk factors and underlying conditions, with 2 of 3 patients with rheumatic disease showing poor prognosis. The diagnostic performance of metagenomic sequencing for MABC-ED was comparable to that for MABC-PD. However, MABC-ED samples exhibited distinct microbiome features and a more diverse mycobacterial community structure compared to PD. Resistance rates among extrapulmonary MABC isolates were observed as follows: 0% (amikacin), 20% (macrolides), 30% (linezolid), and 40% (cefoxitin). One case showed paradoxical results between erm (41) T28 sequovar and susceptibility genotype. Genomic analysis revealed no specific dominant circulating clones (DCC) for MABC-ED isolates.

Conclusion MABC-ED patients commonly present with risk factors and underlying diseases. Metagenomic sequencing diagnosis of MABC-ED poses challenges, and DST and whole genome sequencing data indicate diversity among MABC-ED isolates. Our study provides detailed data on MABC-ED, contributing to a better understanding of its disease characteristics.

不同免疫状态侵袭性真菌病患者的病原谱、临床特征及预后危险因素分析

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目的 侵袭性真菌病 (IFD) 是免疫异常人群高发的致死性感染性疾病, 本研究回顾性分析我院 650 例 IFD 住院患者的临床资料, 明确不同免疫状态患者的病原谱、临床特征及预后危险因素, 为临床 IFD 的早期识别、分层防控与精准诊疗提供参考依据。

方法 收集 2021 年 1 月 1 日—2023 年 12 月 31 日于我院确诊或临床诊断的 650 例 IFD 住院患者资料, 按 HIV 感染状态分为 HIV 阳性组与 HIV 阴性组; HIV 阴性组再按有无继发性免疫缺陷, 分为继发性免疫缺陷组 (a 组) 与无明确继发性免疫缺陷组 (b 组)。收集患者人口学特征、基础疾病、病原学结果、感染部位及实验室指标, 采用 SPSS 20.0 软件行统计学分析, 通过单因素分析筛选预后相关因素, 将有统计学差异的变量纳入多因素 Logistic 回归模型, 分析影响 IFD 患者预后的独立危险因素。

结果 650 例 IFD 患者平均年龄 (49.98±17.09) 岁, 男性占 78.15%; 其中 HIV 阳性组占 40.46%, HIV 阴性组占 59.54%, 后者年龄显著更高 ($P<0.001$)。HIV 阴性组中 a 组占 27.91%、b 组占 72.09%, 两组年龄、性别无统计学差异。病原学方面, HIV 阳性组优势菌种为马尔尼菲篮状菌 (74.65%)、隐球菌, 以血流感染 (61.13%) 为主; HIV 阴性组以念珠菌 (60.25%)、曲霉菌 (30.66%) 为主, 以肺部感染 (53.91%) 为主; 其中 a 组念珠

菌感染率显著高于 b 组, b 组曲霉菌感染率显著高于 a 组 (P 均 <0.05)。HIV 阴性组合并基础疾病比例、混合感染率及全因死亡率 (14.99% vs 7.98%) 均显著高于 HIV 阳性组 ($P<0.001$); a 组全因死亡率显著高于 b 组 (27.78% vs 10.04%, $P<0.001$)。多因素分析显示, 高白介素 6 血症是 IFD 患者死亡的独立危险因素 (OR=1.00, 95% CI: 1.00~1.00, $P=0.012$)。

结论 我院 IFD 患者以中老年男性为主, 不同免疫状态患者的病原谱、感染部位及预后存在显著差异。HIV 阴性 IFD 患者基础疾病更复杂, 死亡风险更高, 合并继发性免疫缺陷者预后更差。高白介素 6 血症可作为 IFD 患者预后不良的预警指标, 临床需针对不同免疫状态人群制定差异化诊疗策略。

关键词: 侵袭性真菌病; 人类免疫缺陷病毒; 免疫状态; 临床特征; 预后危险因素

基于 LASSO 回归与机器学习的布鲁氏菌性脊柱炎临床异质性分析与风险预测模型

张策

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目的 探讨布鲁氏菌性脊柱炎 (Brucellar Spondylodiscitis, BSD) 非发热亚型的临床特征, 构建并验证其早期鉴别诊断的预测模型, 以提高对该亚型的识别能力, 减少误诊和延迟诊断。

方法 回顾性分析 189 例确诊 BSD 患者的临床资料, 根据症状是否存在发热分为发热组 (118 例) 与非发热组 (71 例)。收集患者人口学特征、临床表现、实验室指标及影像学资料。采用 LASSO 回归筛选变量, 进一步构建多因素 Logistic 回归模型, 通过受试者工作特征曲线 (ROC)、校准曲线、决策曲线分析及十折交叉验证评估模型性能。

结果 非发热组患者骨质破坏比例 (45.1% vs 25.4%, $P=0.005$)、下肢肌力下降 (29.6% vs 18.6%,

$P=0.082$) 和放射痛 (19.7% vs 10.2%, $P=0.065$) 发生率高于发热组, SAT 高滴度 ($\geq 1:800$) 比例较低 (5.6% vs 20.3%, $P=0.017$)。LASSO 回归筛选出 8 个预测因子, 最终模型纳入大汗、乏力、前白蛋白、PCT 等变量。模型 ROC 曲线下面积 (AUC) 为 0.88, 灵敏度 88.1%, 特异度 71.8%, 校准度良好 (Hosmer-Lemeshow 检验 $P=0.523$), 决策曲线显示临床净收益良好。

结论 本研究构建的预测模型可有效识别 BSD 非发热亚型, 具备良好的判别能力与临床实用性。无发热不等于病情轻微, 临床应重视大汗、乏力等非特异性症状及影像学骨质破坏等特征, 以提高对该亚型的警惕性与诊断准确性。

某三甲肿瘤专科医院 2019—2023 年多重耐药菌监测情况分析

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目的 了解某肿瘤专科医院连续五年多重耐药菌 (multidrug-resistant organism, MDRO) 目标性监测情况, 为制定肿瘤专科医院 MDRO 感染防控策略提供科学参考依据。

方法 对 2019—2023 年天津医科大学肿瘤医院 (TMUCH) 住院患者中分离出的 494 株 MDRO 进行回顾性统计分析, 并将 MDRO 检出率与同期全国细菌耐药监测网 (CARSS) 结果进行对比。

结果 五年内共检出病原菌 27185 株, 其中 MDRO 494 株, 总检出率为 1.82%。MDRO 整体检出率呈上升趋势 ($Z=5.355$, $P=0.021$)。与同期 CARSS 数据相比, TMUCH 的 MDRO 五年检出率整体处于较低水平。MRSA (40%) 和 CRPA (34%) 是主要流行菌种; MDRO 检出以定植为主 (53.64%), 其次为医院感染 (30.57%)。痰 (41.7%) 和引流液是主

要标本来源。科室分布上, 肝胆肿瘤科、重症监护科及食管微创外科等是防控的重点科室。流行病学显示, 老年患者 (≥ 60 岁) 和男性患者是 MDRO 感染的高危人群, 时间上存在一定季节性波动, 秋季与冬季末占比较高。

结论 肿瘤患者 MDRO 感染形势严峻, 呈现菌种多样、标本集中、科室聚集及人群特异的特点, 虽整体耐药水平低于全国监测数据, 但仍呈上升趋势, 应加强抗菌药物管理、重点科室防控及高危人群监测。

Species Distribution, Antifungal Susceptibility and Cyp51A Mutation of Clinical Aspergillus Section Nigri Isolates From Shanghai, China

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Aspergillus section *Nigri* are distributed ubiquitously in nature and are reported to be the third most frequently isolated *Aspergillus* spp. from clinical specimens. They are morphologically indistinguishable and often reported as *A. niger* complex in the clinical laboratory. In this study, we surveyed *Aspergillus* section *Nigri* isolated in Zhongshan Hospital Fudan University, Shanghai, China, from 2019 to 2023.

We determined the species distribution of *Aspergillus* section *Nigri* isolated by partial β -tubulin gene sequencing. We characterized the antifungal susceptibility profiles of these isolates to medical azoles (itraconazole, voriconazole, posaconazole and isavuconazole) using Sensititre™ custom-designed broth microdilution system. The *cyp51A* sequences were compared between azole wild-type (WT) and azole non-wild-type (NWT)

strains in order to determine the potential antifungal resistance mechanisms in NWT isolates.

A total of 54 *Aspergillus section Nigri* isolates from 53 patients were obtained. *Aspergillus tubingensis* (n=27, 50.0%) and *Aspergillus niger* (n=25, 46.3%) were the most prevalent species. Two isolates of *Aspergillus welwitschiae* were identified. According to the epidemiologic cutoff values proposed by the Clinical and Laboratory Standards Institute (CLSI) guideline M59, seven *A. tubingensis* were NWT for itraconazole, voriconazole and isavuconazole. Two *A. tubingensis* were NWT for voriconazole and isavuconazole. All *A. niger* and *A. welwitschiae* isolates were WT for these azoles. Three amino acid mutations were found in NWT *A. tubingensis* isolates. One NWT isolate harbored Y119H mutation in *cyp51A* gene while the other one had nonsynonymous mutation T321A. Y119F mutation was detected in NWT isolate P53-27434 (after azole exposure) compared with its isogenic WT isolate P53-27176 (before azole exposure).

Results from this study provide us with an understanding of species distribution and antifungal susceptibility profiles of clinical *Aspergillus section Nigri* isolates in Eastern China. It highlights the importance of accurate species identification and antifungal susceptibility testing. Our results also suggest that the novel Y119F substitution is potentially a key player in azole resistance

某医疗机构内耳念珠菌的检出情况及药敏结果特点

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目的 耳念珠菌作为一种新发的多重耐药真菌

病原体，可通过接触进行传播。我院 2024 年首次检出耳念珠菌在部分科室呈现相对聚集的分布，存在院内感染暴发的潜在风险。本研究针对所有检出病例的科室分布、标本来源及耐药情况进行分析，以了解耳念珠菌感染及定植情况，为制定感染治疗及防控措施提供依据。

方法 收集 2024 年 1 月至 2026 年 4 月本院检出的所有耳念珠菌，分析其科室分布情况、标本来源及药敏试验结果。对部分检出耳念珠菌感染的患者及其所在环境、接触物品表面和工作人员双手进行筛查。

结果 2024 年 1 月至 2026 年 4 月共检出耳念珠菌 194 例，来源于 176 例患者。标本来源主要分布在 ICU(118 例, 67.05%)、老年科(44 例, 25.00%)、胰腺外科(11 例, 6.25%)、神经外科(8 例, 4.55%)、神经内科(8 例, 4.55%)和康复科(5 例, 2.84%)等。标本来源以尿液为主(106 例, 54.64%)，其次为痰液(35 例, 18.04%)，肺泡灌洗液(13 例, 6.70%)。无菌体液共 30 例(15.47%)，以腹水为主(12 例, 40.00%)，其次为导管(10 例, 33.33%)，血液(4 例, 13.33%)，脑脊液(3 例, 10.00%)等。耐药性方面，所有菌株对氟康唑均耐药，83.82%的菌株对伏立康唑的 MIC ≥ 2 $\mu\text{g/mL}$ ，20.59%的菌株对伏立康唑的 MIC ≥ 4 $\mu\text{g/mL}$ ，但对泊沙康唑的敏感性较好(MIC 0.008-0.5 $\mu\text{g/mL}$)；41.91%的菌株对两性霉素 B 耐药，3.68%的菌株对卡泊芬净耐药(MIC ≥ 2 $\mu\text{g/mL}$)，2.94%的菌株对米卡芬净耐药(MIC ≥ 4 $\mu\text{g/mL}$)，2.94%的菌株对氟胞嘧啶的 MIC ≥ 32 $\mu\text{g/mL}$ 。筛查结果显示，所有被筛查工作人员的双手、环境及物表样本均未检出耳念珠菌；所有患者均在腋窝、腹股沟或伤口部位检出该菌，提示耳念珠菌以患者定植为主。

结论 本院分离的耳念珠菌在 ICU、老年科和康复科之间呈现相对聚集的分布，与患者的转科治疗有一定的关系。检出的耳念珠菌对米卡芬净、卡泊芬净和氟胞嘧啶敏感；对伏立康唑和泊沙康唑呈现显著不同的体外耐药特点；对两性霉素 B 的耐药率也高于其他报道。本院内耳念珠菌传播主要与患者流动有关，暂未发现与环境、物表及工作人员有

关。集束化防控措施及预警系统改造有助于阻断传播链条,降低感染风险。

关键词:耳念珠菌、感染、ICU、耐药

Draft Genome Sequence of A Cutaneotrichosporon Jirovecii-Like Yeast Isolated From The Human Gut of A Clostridioides Difficile-Positive Individual

yuyan HUANG

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Cutaneotrichosporon jirovecii is a rare basidiomycetous yeast lacking a reference genome, which has limited its phylogenetic positioning and related genomic studies. We report the draft genome sequence of strain H0426_7, a human gut-associated *C. jirovecii*-like isolate recovered from a *Clostridioides difficile*-positive patient in Beijing, China.

Illumina sequencing and de novo assembly generated a draft genome of 38.66 Mb with a GC content of 63.76%. It comprises 16,142 predicted protein-coding genes. Functional annotation assigned 74.5% of genes to the NR database and 22.4% to Swiss-Prot. 6,030 genes received Gene Ontology terms, while 2,725 were mapped to KEGG pathways. 278 carbohydrate-active enzyme genes were identified, suggesting metabolic versatility consistent with adaptation to complex carbohydrate-rich environments such as the human gut.

Genome-wide average nucleotide identity (ANI) analysis revealed H0426_7 shares only 74-84% identity with most currently sequenced Cutaneotrichosporon representatives. These values are well below the 95%

species boundary threshold, indicating substantial genomic divergence. Two isolates (P10-008 and PK4640) exhibited approximately 98% ANI with H0426_7. They form a coherent genomic cluster distinct from other described species. ITS-based phylogenetic reconstruction further supported the placement of H0426_7 within a genetically cohesive but taxonomically under-characterized lineage. This lineage is closely related to *C. jirovecii*.

This genome expands the limited genomic representation of rare Cutaneotrichosporon lineages. It provides a valuable reference for future taxonomic clarification, comparative genomics, antifungal resistance profiling, and studies of basidiomycetous yeasts in the human gut microbiome.

First Report of Candida Pseudohaemulonii Bloodstream Infection in China and Characterization of Its Highly Complex Filamentous Biofilm Architecture

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Background *Candida pseudohaemulonii*, a rare member of the *Candida haemulonii* complex and a close relative of *Candida auris*, has been sporadically reported worldwide since its first description from a Thai fungemia case, with later clustered bloodstream infections in South Korea showing low amphotericin B susceptibility. Misidentification by routine diagnostic methods contributes to under-detection, and data on its virulence and biofilm properties remain extremely limited. No

bloodstream infection caused by this species has previously been documented in China

Methods A *C. pseudohaemulonii* isolate was recovered from the bloodstream of a cardiothoracic surgery patient. Species identification was performed using colony morphology on Sabouraud dextrose agar, Gram staining, MALDI-TOF MS, and ITS sequencing, supplemented by whole-genome sequencing and phylogenetic analysis. Antifungal susceptibility testing was conducted following CLSI M27-A4. Biofilm formation was assessed by culturing in RPMI-1640 and visualizing structural features with calcofluor-white fluorescence microscopy.

Results We confirmed the first bloodstream infection caused by *Candida pseudohaemulonii* in China. The isolate produced smooth, whitish colonies on Sabouraud dextrose agar and was able to grow at 37 °C. In vitro susceptibility testing revealed an atypical profile, characterized by low minimum inhibitory concentrations to echinocandins and triazoles, high-level resistance to 5-flucytosine ($>64 \mu\text{g/mL}$), and reduced susceptibility to amphotericin B. Fluorescence imaging demonstrated a remarkably intricate biofilm architecture composed of elongated filament-like cells with extensive branching and densely cross-linked networks, displaying a structural complexity exceeding that typically observed in *Candida auris* biofilms.

Conclusion Our findings highlight *C. pseudohaemulonii* as an emerging pathogen with distinctive biofilm organization and unconventional antifungal susceptibility. Enhanced recognition and further investigation into its biofilm-associated pathogenicity are urgently needed.

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目的 回顾性分析结核分枝杆菌 (*Mycobacterium tuberculosis*, Mtb) 血培养阳性患者的临床特征和实验室特征, 并评估 GeneXpert Ultra 技术检测结核分枝杆菌的诊断效能以及该技术检测 Mtb 血流感染的可适用性。

方法 收集 2017 年 1 月至 2026 年 3 月广州医科大学附属市八医院疑似播散性结核病患者临床资料共 327 例, 其中 166 例血培养 Mtb 阳性纳入研究组, 161 例血培养 Mtb 阴性纳入对照组; 研究组中 165 例患者是合并 HIV 感染, 对照组中 51 例患者是合并 HIV 感染, 比较两组的临床特征、实验室检查及临床转归等指标。统计学采用 Mann-Whitney U 检验进行组间比较。

结果 与对照组相比, 研究组男性患者比例较对照组高 ($P<0.05$); 研究组患者主要症状有淋巴结肿大、发热、咳嗽、咳痰、乏力及体重下降等, 其中约 15% 出现腹痛、腹泻等消化道症状。与对照组相比, 研究组 C-反应蛋白、中性粒细胞比例、血沉、乳酸及降钙素水平显著升高, 而淋巴细胞数量及比例、红细胞数量、血红蛋白、血小板数量和白蛋白水平显著降低 ($P<0.05$)。

结论 结核血培养阳性患者表现出更具侵袭性的炎症与免疫失衡状态, 其关键实验室指标与结核培养阴性患者存在显著差异, 可为临床医生对 Mtb 血培养阳性临床诊断提供参考。

结核分枝杆菌血培养阳性患者的临床特征分析

细菌真菌感染的治疗

1 例高龄碳青霉烯类耐药鲍曼不动杆菌(CRAB)与耐甲氧西林金黄色葡萄球菌(MRSA)混合感染患者的抗感染治疗分析与药学监护

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目的 探讨 1 例高龄碳青霉烯类耐药鲍曼不动杆菌(CRAB)与耐甲氧西林金黄色葡萄球菌(MRSA)混合感染患者的个体化抗感染治疗策略与全程药学监护模式,为临床多重耐药菌感染的规范化诊疗提供参考。

方法 回顾性分析 1 例 84 岁重症肺炎、II 型呼吸衰竭合并尿路感染患者的诊疗全过程。临床药师依据病原学药敏结果、国内外指南与治疗药物监测(TDM)数据,动态优化抗菌药物治疗方案;实施分阶段精细化药学监护,监测多黏菌素 E 血药浓度、肾功能、凝血功能及药物不良反应,评估疗效并及时调整治疗。

结果 患者初始采用注射用头孢哌酮钠舒巴坦钠 2g q6h ivgtt 单药治疗无效,肺泡灌洗液培养出 CRAB 后调整为注射用氨苄西林钠舒巴坦钠 3g q6h ivgtt 联合注射用多黏菌素 E 甲磺酸钠 2.25 MIU q12h ivgtt 治疗效果不佳,经检测多黏菌素 E 的血药谷浓度为 1.8mg/L,低于目标治疗谷浓度范围(2~4mg/L),提示注射用多黏菌素 E 甲磺酸钠剂量不足,上调剂量为 3.0 MIU q12h 后复查多黏菌素 E 血药谷浓度为 2.1mg/L,达目标治疗浓度,维持治疗方案。入院第 12 天患者出现尿路感染,尿培养出 MRSA,加用注射用万古霉素 0.5g q12h ivgtt,治疗第 25 天,患者症状较前明显好转,感染指标明显下降,尿沉渣示白细胞 4.83/HPF,Scr 178 μ mol/L。临床药师评估患者感染已部分控制,但存在药物相关性急性肾损伤,建议停用肾毒性药物万古霉素与多黏菌素 E 甲磺酸钠,调整为注射用氨苄西林钠舒巴坦钠 3g q6h ivgtt

联合注射用替加环素 100mg q12h ivgtt。经全程药学监护与综合治疗,患者感染指标恢复正常,肺部及泌尿系统感染控制,肾损伤转归,未出现神经毒性、严重胃肠道反应及肝功能损伤,病情稳定出院。

结论 高龄 CRAB 合并 MRSA 重症感染应遵循联合、足量、足疗程原则,以 TDM 为核心实施个体化给药,临床药师参与方案制定、动态调整与分阶段药学监护,可显著提升抗感染疗效、降低不良反应风险,有效改善危重患者预后。

关键词 碳青霉烯类耐药鲍曼不动杆菌;耐甲氧西林金黄色葡萄球菌;高龄患者;抗感染治疗;治疗药物监测;药学监护

多学科 MDT 诊疗在疑难细菌真菌感染中的应用价值及实践路径

泽仁尼玛

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感染性疾病一直以来都是对人类健康构成重要威胁的公共卫生问题,当中的疑难细菌真菌感染,凭借其病原体具有的多样性、耐药性演变速度加快以及临床表现不典型等这些特性,变成了临床诊疗里面的重点以及难点的领域。随着抗菌药物被广泛运用甚至不规范使用,多重耐药菌株的检出比率不断升高,进一步增加了诊疗的困难程度,对患者的预后以及医疗质量产生了严重影响。鉴于这种临床诊疗的状况,深入挖掘多学科协同诊疗在这个领域的应用价值,探寻能够推广的实践途径,对于提高疑难细菌真菌感染的诊疗水准、改善患者的预后有着重要的现实意义,这也是开展本研究的主要核心出发点。

关键词: 多学科协作诊疗;疑难细菌真菌感染;应用价值;实践路径;精准诊疗;抗菌药物合理使用
疑难细菌真菌感染这方面囊括了多重耐药菌感

染、少见病原体感染以及免疫功能低下人群所合并的复杂性感染等多种类型，这种感染的临床诊断以及治疗一直以来都面临着十分严峻的挑战[1]。多学科协作诊疗模式可以有效地把各学科的专业优势进行整合，通过这样的方式去弥补单一学科诊疗所存在的局限性，从而为疑难细菌真菌感染的诊疗提供新的解决方案。然而在实际进行应用的过程当中，多学科协作诊疗的开展还有病例筛选标准不够明确、团队协作机制不够健全、诊疗流程不够规范以及质量控制体系不够完善等诸多问题，这些问题极大程度上制约了它的应用价值得到充分地发挥。所以，明确多学科协作诊疗在疑难细菌真菌感染当中的应用价值，构建起科学合理的实践路径，已然成为当前感染性疾病诊疗领域急需解决的重要课题。

奥马环素治疗泛耐药不动杆菌致关节假体周围感染 1 例

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目的 探讨奥马环素在关节假体植入术后泛耐药鲍曼不动杆菌致假体周围感染个体化治疗中的作用。

方法 患者为 48 岁男性，于关节假体植入术后 6 周出现假体周围感染，依据假体周围感染常见致病菌及相关指南经验性采用头孢他啶联合去甲万古霉素抗感染，患者间断发热且炎症指标持续升高，期间出现肺部感染及免疫功能低下，此方案未见明确疗效，依据患膝伤口分泌物培养结果泛耐药鲍曼不动杆菌，抗生素方案调整为头孢他啶阿维巴坦联合甲磺酸奥马环素。

结果 更换抗生素方案后体温与各项炎症指标明显下降，症状好转，感染得到控制顺利出院。

结论 关节置换术后出现假体周围感染迁延不愈，反复更换抗生素方案无明显疗效，需尽快找到

致病菌并根据药敏结果针对性用药，同时需警惕院内多重耐药菌感染，必要时联合用药；假体周围感染除经验性抗球菌治疗，也需考虑不常见革兰阴性杆菌感染，甲磺酸奥马环素与头孢他啶阿维巴坦联合用药对泛耐药鲍曼不动杆菌致假体周围感染疗效确切。

【关键词】 关节假体周围感染；鲍曼不动杆菌；头孢他啶阿维巴坦；奥马环素；去甲万古霉素

临床药师参与一例罕见儿童慢性肉芽肿病类鼻疽伯克霍尔德菌感染的治疗实践

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目的 慢性肉芽肿病（chronic granulomatous disease, CGD），可致反复发生的细菌及真菌感染，易引起肺炎，常见病原为洋葱伯克霍尔德菌、金黄色葡萄球菌、曲霉菌等。本文旨在结合病例、回顾文献为临床治疗 CGD 提供参考，促进合理用药、提高患者疗效。

方法 本文报道了一例诊断 CGD、迁延性肺炎，病原学检查为洋葱伯克霍尔德菌群（*Burkholderia cepacia* complex, Bcc）的 13 岁 7 月男性病例。医生在明确 Bcc 感染后根据临床药师建议调整了抗感染方案，患儿出现病情反复后及时迅速重新评估病情调整药物治疗策略。

结果 患儿以“间断发热、胸痛 1 月余”入院。反复呼吸道感染、重症肺炎史，考虑 CGD。医生予厄他培南、伏立康唑治疗。呼吸爆发试验：异常，全外显子基因显示 CYBB 基因突变，确诊 CGD，医生添加复方磺胺甲噁唑治疗。胸痛症状未缓解，肺内病变未见明显吸收，肺结节穿刺送 mNGS 示 Bcc，序列数 4463，相对丰度 96.5%，医生考虑为病原菌，停厄他培南，改为美罗培南。仍反复发热，外周炎症指标增高，请临床药师会诊，经查阅文献发现，伯

克霍尔德菌属分为 Bcc 和类鼻疽伯克霍尔德菌复合体 (*B. pseudomallei* complex, Bpc), 针对 Bpc, 可使用美罗培南或米诺环素联合复方磺胺甲噁唑; 但 Bcc, 由于复方磺胺甲噁唑和美罗培南存在拮抗性, 不可联合使用。医生采纳临床药师建议, 停用美罗培南, 调整为米诺环素联合复方磺胺甲噁唑治疗, 使用 3 天后, 体温降至正常, 胸片示肺部感染较前吸收, 血常规、生化大致正常, 无咳嗽、咳痰, 无胸痛、胸闷, 病情好转, 嘱出院继续口服药物治疗。

结论 CGD 细菌感染常用复方磺胺甲噁唑或美罗培南, 联用需考虑细菌分型。在疑难患者的治疗过程中, 临床药师可以基于循证证据提供患者个体化的临床诊疗建议, 为临床提供更多诊疗依据, 有助于改善患者预后, 体现了临床药师的价值。

关键词: 慢性肉芽肿病; 类鼻疽伯克霍尔德菌复合体; 复方磺胺甲噁唑; 美罗培南; 拮抗

嗜脓菌属血流感染 1 例

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目的 嗜脓菌属 (*Peptoniphilus* spp.) 为临床罕见的革兰阳性厌氧球菌, 生长缓慢、常规培养易漏检, 多与其他细菌混合感染, 常见于腹腔或盆腔脓肿。本文通过回顾 1 例合并肠瘘及腹腔感染的嗜脓菌属血流感染病例, 分析临床药师在抗感染治疗中的药学监护实践, 探讨其在罕见病原体识别、治疗优化中的关键作用, 为提高该类感染诊治水平提供参考。

方法 对 2025 年 12 月收治的 1 例 36 岁男性慢性胰腺炎、结肠造口术后患者的临床资料进行回顾性分析。患者因“拟拔除腹腔引流管”入院, 住院期间突发高热、寒战及低血容量休克, 临床药师全程参与抗感染治疗决策与药学监护, 包括: 入院时评估腹腔感染风险并建议完善厌氧血培养; 病情恶化时

参与抗感染方案调整, 结合初始头孢哌酮舒巴坦效果不佳, 推荐升级为亚胺培南西司他丁 (1g q8h); 血培养先后提示革兰阳性球菌及阴性球杆菌、短暂联用万古霉素期间, 评估必要性并建议待病原学明确后及时降阶梯; 经 16S rRNA 测序确诊为嗜脓菌属合并大肠埃希菌后, 查阅文献明确嗜脓菌属对碳青霉烯类高度敏感, 建议停用万古霉素, 继续亚胺培南西司他丁单药治疗; 每日监测感染指标 (PCT、CRP)、体温及血流动力学变化, 评估疗效与安全性; 参与多学科讨论, 结合腹腔引流管理制定拔管与停药策略。

结果 患者入院第 3 天出现高热 ($T 39.4^{\circ}\text{C}$) 及腹腔引流液增多, 第 7 天进展为脓毒性休克 ($T 40.5^{\circ}\text{C}$, 乳酸 5.8 mmol/L)。临床药师建议的亚胺培南西司他丁方案实施后, 患者体温 48 小时内降至正常, PCT 由 0.07 ng/ml 降至正常, CRP 由 97.4 mg/L 降至 25.1 mg/L , 血流动力学稳定。明确病原体后及时停用万古霉素, 避免了不必要的联合用药及潜在肾毒性。治疗期间未出现药物不良反应, 1 月 7 日顺利拔除腹腔引流管, 患者康复出院。

结论 嗜脓菌属血流感染虽罕见, 但腹腔手术史、肠瘘等基础疾病患者应高度警惕。临床药师通过参与病原学诊断、抗感染方案优化及疗效监测, 在确保有效治疗的同时避免过度用药, 显著提高了罕见菌感染的治疗成功率与安全性。多学科协作与药学监护是应对复杂感染、提升精准治疗水平的重要保障。

关键词: 嗜脓菌属; 血流感染; 临床药师; 药学监护; 腹腔感染; 厌氧菌; 混合感染; 抗感染治疗

1 例艾滋病合并宫颈鳞状细胞癌病例报告

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背景 HIV 感染合并恶性肿瘤的同时合并多重

耐药菌感染是临床处理极为难度大、风险高的复杂情况。此次我们报道了一例长期接受规律抗病毒治疗的 HIV 感染者，在确诊为宫颈浸润性鳞状细胞癌的同时，合并了由多重耐药粪肠球菌及产超广谱 β -内酰胺酶（ESBL）大肠埃希菌引起的严重细菌性阴道炎及血小板减少的复杂病例。

病例陈述 患者，女性，54 岁，因“体检发现宫颈病变 1 月，病检确认宫颈浸润性鳞状细胞癌 2 天”于 2025 年 11 月 9 日入院。有 17 年 HIV 感染史，长期口服拉米夫定多替拉维片抗病毒治疗，CD4+T 淋巴细胞绝对计数减低，为 394 个/ μ l。入院查体及 MRI 检查提示宫颈癌 mrFIGO IB2 期。实验室检查提示血小板减少，为 $79 \times 10^9/L$ ，阴道分泌物培养检出对喹诺酮类、大环内酯类耐药的粪肠球菌，以及产 ESBL 的大肠埃希菌。面临患者免疫功能低下、多重耐药菌感染及潜在的手术出血风险的复杂情况，我院感染科、血液科、妇科肿瘤等多学科会诊讨论，决定采取“先控制并发症，后行根治手术”的序贯治疗方案。首先针对多重耐药菌感染及血小板减少进行靶向抗感染与对症支持治疗。待阴道炎得到有效控制、血小板恢复正常后，为患者实施了腹腔镜广泛子宫切除术+双侧附件切除术+盆腔淋巴结清扫术，有效减少手术应激对免疫系统进一步抑制的同时，切实降低了术后感染扩散风险。术后病理证实为宫颈浸润性中分化鳞状细胞癌 pT2aN0M0 期。术后患者切口甲级愈合，未发生继发性盆腔感染及败血症，顺利出院后序贯放疗及免疫随访。

结论 免疫缺陷患者合并恶性肿瘤时，常同时伴发复杂的机会性感染或多重耐药菌感染，若直接进行根治性手术将面临极高的术后感染失控及伤口愈合不良风险。该病例成功的关键在于通过多学科协作制定了科学的序贯治疗方案，先明确病原学培养结果，再对患者耐药菌感染进行精准有效的控制，最后选择创伤小的微创手术。既保障了肿瘤外科治疗的安全性，又最大程度保护了患者的免疫功能，说明在围手术期将感染病学管理与肿瘤学治疗结合，对改善此类复杂患者预后具有积极重要的意义。

关键词 艾滋病病毒；宫颈鳞状细胞癌；多重

耐药菌；细菌性阴道炎；序贯治疗；多学科协作

1 例尼曼匹克病 B 型合并盲肠肠球菌感染病例报道

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目的 探讨尼曼-匹克病 B 型（Niemann-Pick disease type B, NPD-B）合并盲肠肠球菌（*Enterococcus cecorum*）感染的临床特征、诊断及治疗策略，提高对该罕见合并症的认识，避免延误诊治。

方法 回顾性分析 1 例确诊为 NPD-B 的 15 岁男性患者的临床资料。患者以反复发热、呕吐及进行性加重的血细胞减少为主要表现，对经验性抗生素及糖皮质激素治疗反应差。入院后采集外周血及骨髓标本，采用靶向新一代测序（targeted next-generation sequencing, tNGS）进行病原学检测，并结合药敏结果调整抗感染方案。同时复习相关文献，总结该类患者的感染特点及诊疗经验。

结果 患者外周血及骨髓 tNGS 结果均鉴定为盲肠肠球菌感染，未检出其他病原体。根据药敏结果调整抗感染方案（具体药物据临床实际）后，患者体温逐渐恢复正常，血细胞减少显著改善，病情趋于稳定。治疗过程中未出现严重药物不良反应。该病例提示 NPD-B 患者因鞘磷脂异常蓄积导致脾功能异常及潜在肠屏障功能障碍，可能增加机会性肠道病原体血行感染的风险。

结论 NPD-B 患者出现不明原因发热、进行性血细胞减少且常规抗感染治疗效果不佳时，应警惕盲肠肠球菌等罕见机会性病原体感染的可能。早期采用 tNGS 等高通量测序技术明确病原，有助于及时启动精准抗感染治疗，改善患者预后。

临床药师参与脓肿分枝杆菌感染肺炎患儿的药学服务实践

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目的 本文深入剖析一例脓肿分枝杆菌感染小婴儿的药学实践,探索临床药师在治疗过程中的作用及优化治疗策略。

方法 患儿,男,2月14天,咳嗽、痰鸣8天;系34+1周出生,出生体重1400g,当前体重3.38kg入院后,经验性给予头孢哌酮钠舒巴坦钠联合氟康唑抗感染治疗,用药前送检外周血培养。治疗4d后,12.27白细胞 $13.12 \times 10^9/L$,中性粒细胞百分比82.2%偏高,C-反应蛋白2.43mg/L,体温正常。12.28肺泡灌洗液NGS示脓肿分枝杆菌(4429),耶氏肺孢子菌(5577)。医生请临床药师会诊,根据患儿病情及NGS结果药师考虑主要为脓肿分枝杆菌引起的感染。药师查阅相关文献,与医生讨论后制定初始治疗方案为亚胺培南西司他丁钠联合阿奇霉素,医生采纳药师建议,于12.28更换治疗方案。更换治疗方案后,患儿未吸氧下经皮血氧饱和度波动于正常范围,体温正常,CRP正常。1.7复查肺部CT提示两肺感染并部分片影内厚壁囊腔,考虑肺脓肿形成。再次请临床药师会诊协助制定方案,药师建议加用替加环素和头孢西丁。该联合用药方案的选择是基于药物在儿童中的安全性、有效性和指南建议的治疗方案,如某些 β -内酰胺酶类抗菌药物与亚胺培南联用具有较好的对MABC的协同抑菌效应。医师于1.7加用头孢西丁,1.19加用替加环素。1.24亚胺培南西司他丁钠已使用近4周,考虑其神经毒性建议调整为利奈唑胺,临床采纳。2.10,患儿病情稳定,CT胸部平扫回示两肺感染并局部厚壁囊腔,较前部分结节影减小、囊腔减小。再次请会诊协助制定口服序贯治疗方案,临床药师建议给予调整为口服利奈唑胺、阿奇霉素、莫西沙星抗感染序贯治疗。2.11患儿出院。治疗1个月余3.12门诊随访,

复查血常规、血生化、CRP均正常,儿童门诊监测各项生长发育指标均处于正常范围。复查胸部CT提示双肺散在感染,较前明显好转。治疗6个月余4.30门诊随访复查肺部CT提示较前基本吸收。

结果 患儿多种药物的联合使用,治疗方案多次调整,治疗随访共7个月余,病情明显好转,生长发育正常,定期监测血常规、肝肾功能等指标均处于正常范围。

结论 临床药师全程参与患儿诊疗过程,通过优化治疗方案和安全性监测,显著提高患儿治疗效果,为小婴儿脓肿分枝杆菌感染临床用药提供重要参考。

1 例异基因造血干细胞移植患者纹带棒状杆菌血流感染的病例分析

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目的 总结1例异基因造血干细胞移植后发生纹带棒状杆菌导管相关性血流感染的诊治过程,提高对该菌感染的认识。

方法 回顾性分析1例骨髓增生异常综合征患者行异基因造血干细胞移植后并发纹带棒状杆菌血流感染的临床资料、诊疗经过及病原学结果,并复习相关文献。

结果 患者为54岁男性,因骨髓增生异常综合征行异基因造血干细胞移植。移植后出现严重粒细胞缺乏,并于PICC置管后发生发热、腹痛、腹泻等症状。血培养及导管培养均检出纹带棒状杆菌,药敏提示对头孢曲松、美罗培南、青霉素耐药,对利奈唑胺、庆大霉素、万古霉素敏感。临床诊断为导管相关性血流感染,给予替考拉宁全身抗感染联合替考拉宁封管治疗。治疗5天后发热高峰有所下降,但仍反复发热,最终拔除PICC管,拔管后体温平稳,复查血培养阴性。后续患者因肺部铜绿假单胞菌感

染接受亚胺培南西司他丁联合环丙沙星治疗 19 天，病情稳定后出院。随访显示患者一般情况良好。

结论 纹带棒状杆菌在免疫功能低下、长期留置导管的患者中可引起难治性血流感染，其生物膜形成能力强、多重耐药率高。临床应重视导管管理，及时拔除感染源，并根据药敏结果合理选用糖肽类抗菌药物，必要时进行治疗药物监测以提高疗效。

一例老年社区获得性肺炎患者预防性抗真菌的药物治疗方案分析

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目的 以一例社区获得性肺炎（community-acquired pneumonia, CAP）患者的治疗方案为切入点，针对目前国内外尚无预防性抗真菌治疗的确切方案，结合现实病例讨论预防性抗真菌治疗的适宜性，为临床预防性抗真菌治疗提供参考。

方法 通过系统地回顾文献，以及回顾性分析 1 例老年 CAP 患者的临床资料，结合相关诊疗指南，探讨其预防性抗真菌治疗的适宜性。

结果 本例患者在进行抗细菌感染与对症支持治疗后临床症状与感染指标显著好转，且该患者无真菌感染高危因素，从药物合理使用的角度进行探讨，此例患者进行预防性抗真菌治疗是不适宜的。

结论 对于治疗后临床症状明显好转，无真菌感染高危因素的患者，无需进行预防性抗真菌治疗，结合目前指南建议对以下患者进行预防性抗真菌治疗：①异基因造血干细胞移植或肺移植、接受 CAR-T 治疗、严重粒缺及接受大剂量免疫抑制剂治疗的侵袭性肺曲霉病（IPA）高风险患者；②持续粒细胞减少且经广谱抗菌药物治疗后仍反复发热的患者；③除以上情况外，其他患者在具有真菌感染危险因素及临床表现时建议启动预防性抗真菌治疗。建议

临床应严格把控预防性抗真菌治疗的指征，密切结合患者临床症状，进行高危因素识别与评估，谨慎选择药物进行预防性抗真菌治疗，避免造成抗真菌药物滥用，以及耐药的发生。

一例多重病原菌混合感染的 CAP 患者抗感染药物方案的病例分析

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目的 分析多重病原菌混合感染所致社区获得性肺炎（CAP）的抗感染药物治疗方案选择、剂量调整及药物相互作用管理策略，为临床此类复杂重症 CAP 病例的精准诊疗提供实践参考与循证依据。

方法 采用回顾性病例分析方法，选取 1 例由马尔尼菲篮状菌、产气克雷伯菌及人类疱疹病毒 1 型混合感染的免疫功能低下重症 CAP 患者为研究对象，全面梳理其临床诊疗资料、病原学检测结果及用药过程，结合《抗菌药物临床应用指导原则》《侵袭性肺真菌病诊断与治疗指南》等权威诊疗指南及相关文献，重点探讨抗感染药物的遴选依据、剂量个体化调整原则及药物联用后的相互作用管控要点。

结果 该患者为多重病原菌混合感染的重症 CAP，且存在免疫功能低下状态，临床制定覆盖细菌、真菌、病毒的联合抗感染方案，予哌拉西林他唑巴坦抗细菌感染，两性霉素 B 脂质体诱导治疗后序贯伏立康唑抗马尔尼菲篮状菌感染，更昔洛韦抗人类疱疹病毒 1 型感染；同时针对伏立康唑与后续加用的吡非尼酮存在的代谢酶介导的药物相互作用，个体化调整吡非尼酮剂量，兼顾患者器官功能保护、电解质紊乱纠正及对症支持治疗。经规范治疗后，患者感染得到有效控制，发热、咳嗽、气促等临床症状显著缓解，炎症指标恢复正常，肾功能、电解质等

指标逐步改善，最终顺利出院。

结论 对于免疫功能低下的多重病原菌混合感染重症 CAP 患者，病原学检测结果是制定个体化抗感染方案的核心依据，临床需遵循指南选择覆盖所有致病原的抗感染药物并合理调整剂量；同时应密切关注药物间的相互作用，加强器官功能监测与对症支持治疗，通过全程精细化监护提升诊疗效果，改善患者临床结局。

从哌拉西林他唑巴坦治疗失败到万古霉素剂量优化：临床药师参与剖宫产术后发热病例的诊疗实践

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目的 探讨大肠埃希菌 (ESBL-) 致剖宫产术后产褥感染的抗感染用药策略，分析敏感抗菌药物治疗欠佳的原因及产后女性万古霉素血药浓度偏低的影响因素，为临床药师参与剖宫产术后感染的个体化药学监护提供实践依据。

方法 临床药师全程参与一例 31 岁剖宫产术后发热患者的诊疗，结合患者病原学检测（血培养示大肠埃希菌 ESBL-，对哌拉西林他唑巴坦敏感）、实验室指标及产后生理特点，分析哌拉西林他唑巴坦治疗效果不佳的机制，针对病情变化多次优化抗感染方案，并结合血药浓度监测结果分析产后万古霉素浓度偏低的原因并调整用药剂量。

结果 患者术后血培养确诊大肠埃希菌 (ESBL-) 感染，初始使用敏感的哌拉西林他唑巴坦单药治疗 3 日发热无改善，药师考虑致病菌存在 AmpC 酶诱导表达、外膜通透性下降等耐药机制且未覆盖厌氧菌，建议联合奥硝唑，后更换为亚胺培南西司他丁钠广谱抗感染；加用万古霉素 1g q12h 后血药谷浓度仅 8.5μm/mL，药师分析因产后体液分布调整致表观分布容积增加、肾血流量及肾小球

滤过率升高加快药物清除，调整剂量为 1.5g q8h。

经个体化方案调整后，患者体温、降钙素原逐步恢复正常，血象回落，最终治愈出院。

结论 大肠埃希菌 (ESBL-) 虽对哌拉西林他唑巴坦体外敏感，仍可能因特殊耐药机制导致临床治疗失败，且剖宫产术后感染多为混合感染，需兼顾厌氧菌覆盖；产后女性体液分布、肾功能的生理变化会显著影响万古霉素药代动力学，导致常规剂量下血药浓度不达标。临床药师结合病原菌耐药特点、感染类型及产后生理特性参与抗感染方案制定与血药浓度监测，可有效优化用药策略，提升剖宫产术后产褥感染的治疗效果，为临床合理用药提供关键专业支撑。

临床药师参与一例经济困难型新型隐球菌脑膜炎合并肾功能不全患者抗真菌治疗的药学实践

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1 病历资料

患者男，54 岁，56kg，非 HIV 感染，有桉树、家禽接触史，高血压未规范治疗，因反复头痛 20 天入院。受凉发热后出现中重度头痛，当地治疗效果差。入院查体无异常，肝肾功能正常，脑脊液确诊新型隐球菌感染，出院诊断为隐球菌性脑膜炎、脑梗死、肾功能不全等。

2 主要治疗方法

11.15 确诊后予 AmB-D（渐加量至 35mg）+ 氟胞嘧啶 1g q6h 诱导治疗，患者肌酐进行性升高。11.29 药师考虑药物不良反应，建议 AmB-D 减量、氟胞嘧啶调整为 1g q12h，医生采纳。12.12 肌酐升至 306μmol/L，药师建议换用 ABCD 150mg qd。12.15 肌酐达 373.2μmol/L，患者因经济欲放弃治疗，药师沟通后建议转入巩固期，予氟康唑 400mg qd +

氟胞嘧啶 1.5g q12h。12.18 患者症状缓解、肌酐下降，出院予口服药巩固。5 周后复诊，肌酐恢复、脑脊液转阴，药师建议巩固至 6 周，医生采纳。

3 讨论

3.1 诱导期抗真菌方案优化 患者确诊 CM，依指南选用 AmB-D 渐加量至 35mg（剂量上限）联合氟胞嘧啶 1g q6h 为初始方案，两药协同且契合患者初始肾功能状况。用药后肾功能恶化，考虑为 AmB-D 肾毒性及与氟胞嘧啶的协同毒性所致，结合肌酐清除率首次调整剂量。后续肾功能持续进展，因患者经济受限，药师放弃肾毒性最低但费用高的两性霉素 B 脂质体，选用性价比更高的 ABCD 替代 AmB-D，兼顾疗效、安全性与经济性。

3.2 巩固期治疗方案制定 患者完成 4 周诱导期治疗，症状改善虽脑脊液未转阴，结合肾功能及经济状况，药师依指南建议转入巩固期，选用肾毒性更低、费用更优的氟康唑 400mg qd 联合氟胞嘧啶 1.5g q12h，出院后调整氟胞嘧啶至 1g q12h，适配患者肌酐清除率水平。

3.3 疗效及评价 患者经诱导期剂量调整、剂型更换及巩固期个体化用药，5 周后脑脊液培养转阴，肾功能显著改善，头痛症状缓解，证实方案安全有效。药师建议巩固期疗程满 6 周，符合 CM 治疗指南要求，保障治疗效果。

4 总结与体会 本例为经济困难的隐球菌性脑膜炎合并肾功能不全患者，使用 AmB-D 联合氟胞嘧啶时出现进展性肾损伤。临床药师依据指南、药动学及经济条件，调整剂量、更换剂型并转入巩固期，制定个体化方案。积极沟通坚定患者信心，全程药学监护保障治疗。提示治疗隐球菌性脑膜炎需严密监测肾功能，兼顾疗效、安全与成本。药师专业参与，可为个体化抗真菌治疗提供重要支持与参考。

临床药师参与一例创伤弧菌脓毒症患者抗感染治疗的实践与分析

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1 病历摘要 患者男，71 岁，88kg，既往体健，因全身皮疹 10 余年、加重伴下肢水肿 10 余天入院。予泼尼松、托拉塞米、司库奇尤单抗治疗后症状好转。11 月 12 日突发左下肢肿胀疼痛，初诊为丹毒，予头孢呋辛抗感染，血培养示创伤弧菌，病情危重，转入创伤科。转入诊断：脓毒血症、银屑病、左下肢软组织感染等。2 抗感染治疗经过 患者转入后予头孢呋辛经验性抗感染，症状无改善且感染指标升高。11 月 13 日升级为哌拉西林他唑巴坦，疗效仍不佳。11 月 14 日确诊创伤弧菌，药敏显示对多种药物敏感。临床药师会诊建议：停用哌拉西林他唑巴坦，改用头孢曲松 2g qd 联合左氧氟沙星 0.75g qd 静滴。治疗 10 日后患者感染指标恢复正常，症状明显缓解，足疗程停药后好转出院。3 分析与讨论 3.1 病因鉴别诊断 患者初期被误诊为丹毒，头孢呋辛治疗无效。临床药师详细追问病史，发现患者发病前曾被罗非鱼尾刺伤，结合皮损边界不清、凹陷性水肿等特点，高度怀疑创伤弧菌感染。后续血培养阳性、乳胶凝集试验阴性，明确诊断为创伤弧菌所致血流感染，为精准抗感染奠定基础。3.2 抗感染方案优化 创伤弧菌感染进展快、致死率高，中晚期单用 β 内酰胺类效果不佳。指南推荐三代头孢菌素联合喹诺酮类为优选方案。结合患者感染分期、药敏结果及药物特性，药师未选用四环素类方案，推荐头孢曲松联合左氧氟沙星：1. 头孢曲松每日 1 次，依从性高，老年患者无需常规调整剂量；2. 左氧氟沙星抗弧菌活性强、价格经济；3. 两药脂溶性好，可穿透细菌荚膜，皮肤软组织浓度高，体内杀菌效果优于体外敏感单药。3.3 疗效与安全性 方案调整后患者症状迅速控制，感染指标逐步正常，未出现不良反应，最终治愈出院，证实方案安全有效。4 总结与体会 创伤弧菌感染起病急、病死率高，早期易与丹毒混淆，详细询问海产品接触史及皮损特点是关键。临床药师立足指南、致病菌特性、药敏及患者个体情况，摒弃单纯依赖药敏的选药模式，优化联合

抗感染方案,使患者获得良好预后。本案例提示:创伤弧菌脓毒症首选三代头孢+喹诺酮类联合治疗;药师参与可显著提升疑难感染诊疗水平,为临床提供科学、个体化的药学支持。

1 例龟分枝杆菌感染患者的抗感染治疗分析

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目的 阐述临床药师在 1 例龟分枝杆菌感染患者诊疗过程中的药学实践及体会,探讨临床药师基于抗菌药物药代动力学/药效学(Pharmacokinetics/Pharmacodynamics, PK/PD)理论、治疗药物监测(Therapeutic Drug Monitoring, TDM)以及患者的病理生理基础,参与临床治疗用药决策的实践路径。

方法 通过分享临床药师参与 1 例龟分枝杆菌感染患者的诊疗过程,结合抗菌药物的药代动力学、血药浓度监测结果、患者的过敏史、肝肾功能及药物治疗反应,动态评估患者临床症状及病原学结果,协助医师优化抗感染治疗方案。

结果 本例患者因“右踝关节外伤感染 1 月余”入院。既往有青霉素、头孢菌素过敏史,自诉用药后发生晕厥。入院后行“伤口清创+负压吸引术”,取伤口分泌物送培养,临床药师建议在常规培养基础上可送涂片和二代测序(Next-Generation Sequencing, NGS)以便更好地明确病原菌,指导后续针对性治疗。患者 NGS 结果提示龟拟分枝杆菌,MR 平扫提示右足背部、外踝关节周围软组织肿胀渗出;右踝关节滑膜炎;右足关节腔积液。结合患者伤口情况和 MR 结果,考虑该菌为致病菌。龟分枝杆菌属快速生长型非结核分枝杆菌,治疗需多药联合、长疗程。临床药师结合患者既往过敏史和指南推荐,协助外科医师制定抗感染方案为阿米卡星 0.6 g qd 静脉滴注联合克拉霉素 0.5 g bid 口服、利奈唑胺 0.6 g

q12h 口服,并提醒监测阿米卡星和利奈唑胺血药浓度。治疗期间临床药师持续跟进患者病情变化,结合血药浓度监测结果和患者肝肾功能、血小板水平动态调整给药剂量。经治疗后患者感染控制良好,伤口愈合。

结论 龟分枝杆菌感染临床表现不典型,易被外科医师忽略,NGS 技术为早期精准诊断提供了关键依据。临床药师可以充分发挥在 PK/PD 理论、TDM 及个体化用药方面的专业优势,与外科、影像、微生物、感染科等多学科紧密协作,从药学的角度协助医师优化抗感染治疗方案,实现临床获益最大化,充分体现临床药师在感染诊治中的专业价值。

关键词: 龟分枝杆菌;利奈唑胺;阿米卡星;治疗药物监测

复杂创面感染患者体内肺炎克雷伯菌碳青霉烯耐药表型变化的临床观察

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目的 探讨复杂创面感染患者体内肺炎克雷伯菌在连续治疗过程中出现碳青霉烯耐药表型变化的临床特征及实验室检测意义。

方法 收集 1 例复杂创面感染患者住院期间连续送检的创面分泌物标本,对分离获得的肺炎克雷伯菌进行菌种鉴定和药物敏感性试验;结合全基因组测序分析菌株分型及同源关系,并对部分代表菌株开展耐药相关基因差异比较,以观察同一患者体内不同时间纵向分离菌株之间的耐药表型及基因特征变化。

结果 2024 年 10 月至 11 月,从同一患者创面标本中连续分离获得 4 株肺炎克雷伯菌及 1 株铜绿假单胞菌,其中肺炎克雷伯菌先后出现碳青霉烯耐药株与碳青霉烯敏感株。药敏结果显示,不同时间分离菌株对亚胺培南、美罗培南及部分抗菌药物的

敏感性存在明显差异。基因组分析提示,早期1株菌与后续3株菌分属不同克隆型,而后续3株菌之间差异较小,属于同一克隆背景内的变化。进一步比较发现,同源菌株间可伴随耐药相关基因改变,与其碳青霉烯耐药表型差异相一致。上述结果提示,同一患者感染过程中可同时存在或先后出现耐药性不同的肺炎克雷伯菌亚群。

结论 复杂感染患者体内肺炎克雷伯菌可在治疗过程中出现碳青霉烯耐药表型变化及异质性现象,单次药敏结果可能难以全面反映真实耐药状态。对持续感染或疗效不佳患者,应结合连续分离、动态药敏监测及必要的分子检测进行综合判断,为临床精准抗感染治疗提供依据。

IL-17 and Th17 Cells in Chlamydiae Infection

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Abstract Chlamydia is a genus of intracellular parasitic microorganisms with a unique developmental cycle that is widely distributed and can cause various human and animal diseases. T helper 17 (Th17) cells is a distinct subpopulation of Th cells with a unique transcriptional profile (STAT3, ROR γ t, and ROR α), pattern of cytokine production (IL-17 family, IL-21, IL-22), and specific cytokines required for differentiation (IL-6, TGF- β , IL-21, and IL-23). Results from mouse models of infection and human epidemiologic studies indicate that Th17 cells may be vital in modulating innate and adaptive immune responses for protective immunity against chlamydia and are associated with the progression of inflammatory diseases in various organs and tissues. This article reviews the differentiation of Th17 cells during Chlamydia infection, the host defense

mechanisms involved, and their critical role in the pathogenesis of inflammation and autoimmune damage, with the aim of informing the development of safe and effective Th17 cell-based vaccines against Chlamydia.

Keywords Chlamydia, Th17 cells, IL-17, protective immunity, immunopathology

临床药师在糖尿病足感染治疗中的关键作用

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关键词: 临床药师; 糖尿病足感染; 抗菌药物管理; 美罗培南; 精准治疗; 药物过敏; 个体化治疗。

目的 探讨临床药师在复杂糖尿病足感染多学科治疗中的专业价值,特别是当初始经验性治疗失败、临床决策面临“升级广谱抗菌药物”惯性时,药师如何基于药学评估引导精准、安全的个体化治疗。通过一例高龄、严重肾功能不全、明确青霉素及庆大霉素过敏史的2型糖尿病足混合感染患者的具体诊疗过程,系统阐述临床药师在抗感染治疗决策中的不可替代作用。

方法 回顾性分析一例79岁男性2型糖尿病足(Wagner 3级)患者的完整诊疗过程。患者入院时存在高热、严重全身炎症反应(WBC $23.56 \times 10^9/L$, CRP 228.80 mg/L),合并糖尿病肾病(eGFR 34.44 mL/min/1.73m²)、低蛋白血症及明确的青霉素、庆大霉素过敏史。初始经验性使用头孢哌酮舒巴坦钠(3g q12h)治疗3日后病情无改善。在医疗团队倾向于升级使用碳青霉烯类药物美罗培南的关键决策节点,临床药师紧急介入,采用三维评估框架:①病原学导向分析(左足分泌物培养示金黄色葡萄球菌和阴沟肠杆菌阴沟亚种,药敏显示对多种窄谱头孢菌素敏感);②基于药物过敏史的风险规避(青霉素与碳青霉烯类存在明确交叉过敏风险);③结合肾功能(eGFR 34 mL/min)的药代动力学/药效学个体化剂

量调整。药师明确提出反对使用美罗培南，并建议替换为头孢米唑钠（1g q12h）的精准治疗方案，同时制定药学监护计划。

结果 医疗团队采纳药师建议后，患者临床转归显著改善：①体温在 24 小时内恢复正常，未再出现高热；②炎症标志物持续下降（CRP 由 228.80 mg/L 降至出院前 75.40 mg/L）；③全身感染中毒症状消失，足部局部渗液减少、红肿消退；④治疗期间未发生任何药物过敏反应，肾功能保持稳定，血糖控制平稳。患者于 2026 年 1 月 13 日出院，感染得到有效控制，预后良好。

结论 本案例深刻揭示了在复杂糖尿病足感染的治疗决策关键时刻，临床药师凭借对病原学证据、患者个体特征（过敏史、肾功能）及药物属性的深度整合分析，能够有效纠正“经验性升级至广谱抗菌药物”的惯性思维，引导治疗从“广谱轰炸”转向“精准打击”，实现了安全、有效、经济的个体化治疗，预后良好。

1 例惠普尔养障体致罕见重症肺炎的药学实践

陈平

遂宁市中心医院

目的 报道 1 例惠普尔养障体致罕见重症肺炎的药学实践。惠普尔养障体致重症肺炎临床罕见，患者病情危重，死亡率高，无标准抗感染方案，有效抗感染治疗存在巨大挑战。临床药师通过查阅文献并结合患者实际情况为患者制定个体化抗感染方案。经治疗，患者感染得到有效控制且无不良反应发生。通过该病例，探讨临床药师在提供个体化抗感染治疗及药学监护方面的作用，为该类患者抗感染治疗提供临床参考。

方法 患者，女，62 岁，体重 60kg。因“呼吸困难、畏寒、发热 5d”于 2025-02-10 就诊于我院，诊

断为重症肺炎（惠普尔养障体感染），住院期间病情危重且持续进展。临床药师查阅文献发现：（1）惠普尔养障体感染尚无标准抗感染方案，四环素曾被推荐为一线治疗药物但经该药治疗后复发率高，而复方磺胺甲噁唑、头孢曲松、美罗培南、羟氯喹、青霉素、链霉素也可以用于惠普尔养障体感染。考虑该患者病情危重，临床药师最终建议给予头孢曲松联合复方磺胺甲噁唑 2 药加强抗感染治疗；（2）临床药师在患者住院期间全程参与患者的药学监护，监测不良反应；（3）出院后嘱患者需口服复方磺胺甲噁唑 12 个月并电话随访。

结果 头孢曲松联合复方磺胺甲噁唑 2 药加强抗感染 3 天后，患者临床症状显著改善（体温恢复正常，呼吸平稳），炎症值明显好转。持续抗感染 11 天后，患者病情稳定予以出院。院外继续口服复方磺胺甲噁唑抗感染 12 个月，定期门诊随访，病情稳定无相关药物不良反应。

结论 惠普尔养障体致重症肺炎临床罕见，病死率高，国内外均以个案报道为主。迄今为止，尚无惠普尔养障体感染的诊治指南或专家共识。本例患者为惠普尔养障体致罕见重症肺炎，住院期间病情危重且持续进展。临床药师利用自身专业知识为患者制定个体化的抗感染方案，密切关注病情变化，加强药学监护。最终患者感染得到有效控制且无不良反应发生，发挥了临床药师在临床药物治疗团队中的专业价值。

多发肠痿并发复杂性腹腔感染患者基于降阶梯抗感染与个体化营养支持的综合治疗

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关键词：肠痿；腹腔感染；营养支持

目的 肠痿并发复杂性腹腔感染及脓毒性休克是胃肠外科极具挑战的危重症，常导致多器官功能障碍与严重营养不良。本研究旨在探讨临床药师全程参与下，针对此类重症患者实施个体化抗感染降阶梯治疗与序贯营养支持方案的有效性与安全性。

方法 回顾性分析一例 20 岁女性多发肠痿合并铜绿假单胞菌及产 ESBLs 肺炎克雷伯菌感染、急性肝损伤及中度营养不良（BMI 17.4）的病例。通过“医-药”协同模式，依据微生物培养结果动态调整抗菌策略：初始采用美罗培南联合替考拉宁覆盖耐药菌，随后根据药敏及时降阶梯为头孢哌酮舒巴坦，全程规避肝肾毒性；同时实施从全肠外营养向短肽型肠内营养过渡的递增方案，辅以谷氨酰胺保护肠黏膜屏障。

结果 患者经美罗培南联合替考拉宁、甲硝唑等抗感染药物降阶梯治疗，及个体化肠外-肠内营养支持（含短肽型肠内营养剂、谷氨酰胺等）治疗后，感染症状完全控制，脓毒性休克、急性肝损伤、肺炎均痊愈，多发肠痿口愈合，入院时中度营养不良（BMI 17.4）得到纠正，无药物不良反应发生，顺利康复出院；随访 3 个月无复发，生活质量恢复良好。

结论 对于复杂肠痿合并重症感染者，基于病原学证据的降阶梯抗感染治疗结合循序渐进的个体化营养支持，能有效控制感染、促进组织修复并改善预后；未来应进一步推广多学科协作诊疗模式，以优化此类高危患者的临床管理策略。

Scalable Nanoengineered Gauze with Sustained Natural Product Release: Synergistic Antibacterial, Anti-adhesive, and Angiogenic Therapy for Infected Wound Healing

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Wound management remains significant challenges, encompassing numerous risks such as infection, antibiotic resistance, tissue adhesion, ischemia, hypoxia, and inflammatory responses. These complications are particularly acute in cases of bacterial infection, where conventional treatment modalities may fail to provide adequate efficacy. To address these challenges, this study introduces PPCZ@Gauze, an innovative multifunctional gauze tailored to enhance wound healing. PPCZ@Gauze is designed and prepared using biosafe materials (phytic acid, ϵ -polylysine, curcumin, and zinc ions) through advanced surface modification techniques. Both in vitro and in vivo experiments demonstrate PPCZ@Gauze's remarkable antibacterial properties, reduced tissue adhesion, and accelerated wound healing capabilities compared to conventional medical gauze. Notably, PPCZ@Gauze also exhibits ease of preparation, cost-effectiveness, and scalability for large-scale production. Overall, this innovative multifunctional gauze offers a promising solution for managing bacterial infection wounds, leading to enhanced therapeutic outcomes and patient care.

1 例破伤风患者继发碳青霉烯类耐药肺炎克雷伯菌感染的临床特征与诊治策略

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目的 分析破伤风患者继发碳青霉烯类耐药肺炎克雷伯菌（CRKP）感染的临床特征，探讨其抗感染治疗方案，为后续该类人群的治疗提供临床参考。

方法 回顾性分析 1 例因破伤风（重型）收住入院，治疗过程中继发肺部感染、脓毒血症，经病原学及药敏试验确诊为 CRKP 感染的患者；记录和分析该患者在抗感染治疗过程中的临床症状、体温、

感染指标、肝肾功能、病原学培养以及影像学检查等指标。

结果 患者为 66 岁女性，因“镰刀割伤 8 天、意识障碍伴抽搐 2 天”收住入院；入院第 1-6 天，神志昏迷，无抽搐，反复发热，体温波动在 38.4℃ 左右，CRP 141.06 mg/L，WBC $13.66 \times 10^9/L$ ，N% 76.5%，PCT 0.509ng/ml，予以青霉素联合甲硝唑 9d、头孢吡肟 5d 抗感染治疗，感染指标进行性下降；入院第 7 天，精神情况较差，突发高热至 40℃，CRP 128.65 mg/L，WBC $17.26 \times 10^9/L$ ，N% 90.6%，PCT 65.57ng/ml，痰培养、血培养为肺炎克雷伯菌，胸部 CT 显示双肺炎症、双下肺为主，先后使用美罗培南 2d、头孢他啶阿维巴坦联合氨曲南 20d 抗感染治疗，治疗过程虽偶有高热至 39℃，但精神状态逐渐变好，感染指标呈波动性下降；入院第 20 天，患者体温恢复正常，PCT 4.79ng/ml，痰培养、血培养为阴性，肺部感染病灶较前明显吸收；入院第 32 天，临床症状可，无发热，无咳嗽咳痰，感染指标和肝肾功能恢复正常，顺利出院。

结论 肺炎克雷伯菌致病力强，感染病程进展迅速，头孢他啶阿维巴坦联合氨曲南可有效覆盖 CRKP，在破伤风病情危重的特殊感染患者中具有好的疗效与安全性。

【关键词】破伤风；碳青霉烯类耐药肺炎克雷伯菌；头孢他啶阿维巴坦；氨曲南；

1 例小孢根霉致罕见脑脓肿的抗感染治疗药学实践

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目的 报道 1 例小孢根霉致罕见脑脓肿的抗感染治疗。小孢根霉致脑脓肿临床罕见，患者病情危重，死亡率高，有效抗感染治疗存在巨大挑战。驻科临床药师通过查阅文献并结合患者临床实际为患者

制定个体化抗感染方案。经治疗，患者感染得到有效控制且无不良反应。通过该病例，探讨临床药师在提供个体化抗感染治疗及药学监护方面的作用，为该类患者抗感染治疗提供临床参考。

方法 患者，男，55 岁，体重 45kg。因“头晕、吐词不清 3 天”就诊于遂宁市中心医院，诊断为小孢根霉脑脓肿，住院期间病情危重且持续进展。临床药师查阅文献发现：（1）两性霉素 B 是毛霉菌（小孢根霉）感染的初始治疗首选药物。泊沙康唑或艾沙康唑可作为对两性霉素 B 治疗有效患者的降阶梯治疗或联合治疗或用于两性霉素 B 无反应或不能耐受的患者。考虑该患者病情危重，临床药师最终建议给予注射用两性霉素 B 联合硫酸艾沙康唑胶囊 2 药加强抗感染并联合手术治疗；（2）临床药师在患者住院期间全程参与患者的药学监护，监测不良反应；（3）出院后患者需口服艾沙康唑 11 个月并电话随访。

结果 注射用两性霉素 B、硫酸艾沙康唑胶囊 2 药联合加强抗感染 30 天后，患者临床症状明显改善、脑脊液检查结果明显好转，颅内感染得到有效控制。继续持续抗感染 5 天后，患者病情平稳予以出院。出院后序贯口服硫酸艾沙康唑胶囊 11 月，持续门诊随访，病情稳定，未出现药物相关不良反应，患者对抗感染治疗结果表示满意。

结论 小孢根霉引起的脑脓肿临床罕见，该病发病隐匿、临床表现缺乏特异性、病死率高，国内外均以个案报道为主。本例患者为小孢根霉感染引起的脑脓肿，住院期间病情危重且持续进展，临床药师利用自身专业知识为患者制定个体化的抗感染方案，密切关注患者病情变化，加强药学监护，最终患者感染得到有效控制且无不良反应发生，发挥了临床药师在临床药物治疗团队中的关键作用。

关键词：小孢根霉；中枢神经系统感染；脑脓肿；药学实践

造血干细胞移植后儿童泛耐药沙门菌导管相

关血流感染 1 例

高凯杰

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目的 总结 1 例造血干细胞移植后儿童发生泛耐药沙门菌导管相关血流感染的临床特点及诊疗经验，为移植后患儿感染管理提供参考。

方法 回顾性分析 1 例极重型再生障碍性贫血患儿接受异基因造血干细胞移植后发生泛耐药沙门菌导管相关血流感染的临床资料。患儿男性，9 岁 10 个月，二次移植后出现发热、腹泻等症状。采用宏基因组高通量测序、外周血培养、导管血培养及粪便培养进行病原学检测，通过药敏试验及碳青霉烯酶耐药基因检测明确耐药特征，并根据药敏结果调整抗感染方案。

结果 患儿二次移植后第 2 天出现高热（39℃），第 10 天出现腹泻。血液高通量测序检出肠道沙门菌（序列数 9），血培养、导管血培养及粪便培养均检出肯塔基沙门菌。药敏试验显示该菌株对头孢他啶、碳青霉烯类、头孢他啶/阿维巴坦等 33 种抗菌药物耐药，仅对替加环素和粘菌素敏感；基因检测检出 NDM 型碳青霉烯酶耐药基因。拔除 PICC 导管后联用美罗培南、替加环素抗感染，患儿体温恢复正常，血培养转阴，病情好转出院。出院后第 3 日感染复发，根据联合药敏试验（氨曲南与头孢他啶/阿维巴坦具协同作用）调整抗感染方案，但患儿最终出现消化道出血、鼻腔出血，继发多器官功能衰竭，家属放弃治疗。

结论 造血干细胞移植后患儿免疫力持续低下，易发生泛耐药菌导管相关血流感染，预后凶险。快速精准的病原学检测（包括 mNGS、药敏试验及耐药基因检测）、及时拔除导管以及依据药敏结果合理选用抗菌药物是控制感染的关键；对于 NDM 型碳青霉烯酶耐药菌感染，含氨曲南的联合方案可能提供治疗选择，但总体预后仍较差，需高度重视感染预防。

临床药师参与 1 例子宫穿孔继发腹腔解脲支原体感染患者的治疗与药学监护

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目的 探讨临床药师在子宫穿孔继发腹腔解脲支原体感染患者抗感染治疗中的作用。

方法 临床药师参与 1 例子宫穿孔继发腹腔解脲支原体感染患者抗感染药物治疗实践，积极查找治疗参考资料，结合患者用药史、原发疾病，分析可能存在的病原微生物，参与抗感染药物治疗方案的制定及调整，并提供药学监护。

结果 患者 75 岁女性，入院临床诊断：1.子宫穿孔；2.宫腔积液；3.感染性休克，2025-09-05 给予亚胺培南西司他丁钠 1g ivgtt q6h 抗感染+妇科手术治疗，术中见腹膜、大网膜表面大量脓苔、盆腔大量脓液伴恶臭；2025-09-07 患者病情稳定，宫腔、腹腔脓液培养均提示大肠埃希菌、ESBL-对多种药物敏感，临床抗感染方案未调整，此后复查炎症指标均进一步下降，腹部切口疼痛进一步减轻，腹盆腔引流液进行性减少；2025-09-11 复查 PCT0.35ng/ml、CRP155mg/L、WBC12.5*10⁹/L；2025-09-17 患者术后第 12 天出现发热，体温达 38.8℃，腹部切口处出现渗液，复查 PCT0.46ng/ml、CRP201mg/L、WBC16.7*10⁹/L。临床药师首次会诊考虑患者前期临床症状及炎症指标均提示临床治疗有效，但患者现发热，且炎症指标较前升高，考虑存在目前药物未能覆盖的病原菌，查阅相关指导原则、指南，建议医生：1.完善引流液及切口渗液的支原体培养及衣原体检查，同时选择在腹腔浓度高且能覆盖衣原体支原体的莫西沙星 0.4g ivgtt qd 经验性治疗；2.考虑对厌氧菌、大肠埃希菌的抗感染疗程已有 12 天，建议停用亚胺培南西司他丁钠。2025-09-21 引流液及切口渗液均培养出解脲支原体，对莫西沙星敏感，且临床换用莫西沙星后患者体温已恢复正常，切口

渗液较前减少，临床根据药敏自行加用多西环素，患者服用多西环素 2 天后诉食道处疼痛且躯干出现皮疹伴瘙痒，临床药师再次会诊考虑多西环素所致，建议单用莫西沙星治疗即可，此后临床药师对该患者进行药学监护，患者皮疹逐渐消退，进食时食道处疼痛逐渐减轻，手术切口逐渐恢复正常，未再发生其他不良反应。治疗过程，医生均采纳临床药师建议，最后患者痊愈出院。

结论 临床药师通过参与子宫穿孔继发腹腔解脲支原体感染患者的抗感染治疗，协助医师优化了治疗方案，通过药学监护精准识别并处理了药品不良反应，保障了患者用药的安全性和有效性。

关键词:临床药师；腹腔感染；解脲支原体；药学监护

集采与 DRG/DIP 背景下临床药师在烧伤科抗菌药物管理 PDCA 循环中的实践

王燕

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目的 评估在国家药品集中带量采购常态化与 DRG/DIP 支付方式改革背景下，临床药师联合医师、护士开展 PDCA 循环管理对烧伤创面修复科抗菌药物使用指标的影响。

方法 以 2024 年 1-12 月为干预前基线期、2025 年 1-12 月为干预后评价期。由临床药师、医师、护士组成 PDCA 管理小组，围绕抗菌药物使用强度、费用、使用率等指标开展多轮计划-执行-检查-处理循环。临床药师负责的主要干预措施包括：医嘱审核（关注用药指征、品种选择、给药剂量及疗程）、根据药敏结果建议目标治疗或联合用药调整、评估静脉转口服给药时机、定期反馈细菌耐药监测数据、组织集采药品相关专题培训。数据来源于医院美康合理用药监测系统，比较两期抗菌药物总费用、人均费用、每住院日费用、使用强度、使用率的变化。

采用 Excel 进行数据整理与描述性统计分析。

结果 2024 年共收治患者 1830 例、人天数 20611 天，2025 年共收治患者 1774 例、人天数 22607 天，收治人数下降 3.1%、人天数上升 9.7%。与干预前的 2024 年相比，2025 年干预后抗菌药物总费用下降 44.0%（126.21 万元→70.65 万元），人均抗菌药物费用下降 37.7%（720.4 元→448.9 元），每住院日抗菌药物费用下降 44.2%（57.9 元→32.3 元）。抗菌药物使用强度从 78.88 降至 70.02 DDD/100 人天，下降 11.2%；2025 年使用强度月度值从 1 月 89.22 持续下降至 12 月 59.00 DDD/100 人天，降幅 33.9%，连续 7 个月低于签订考核指标≤65 DDD/100 人天。抗菌药物使用率从 88.14%升至 89.67%，上升 1.53 个百分点。三例典型病例表明临床药师参与多重耐药菌感染方案优化、药物不良反应早期识别与处理、基于 mNGS 结果的精准治疗调整均取得明确疗效。

结论 集采与 DRG/DIP 政策背景下，临床药师在医护团队组成的 PDCA 循环管理中显著优化了烧伤科抗菌药物使用指标，有效降低了抗菌药物费用及使用强度，体现了多学科协作在抗菌药物管理中的核心价值。该模式可为其他高风险科室的抗菌药物管理提供参考。

关键词 临床药师；抗菌药物管理；PDCA 循环；烧伤科；集采；DRG/DIP

头孢他啶/阿维巴坦对比多黏菌素 B 治疗 DTR-PA 感染的疗效与安全性分析

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目的 比较头孢他啶/阿维巴坦（CZA）与多黏菌素 B（PMB）治疗难治性耐药铜绿假单胞菌（DTR-PA）感染的疗效与安全性。

方法 回顾性选取南昌大学第一附属医院 2023 年 1 月至 2025 年 12 月确诊为 DTR-PA 感染的 222

例患者,根据治疗方案分为 CZA 组(122 例)和 PMB 组(100 例),均采用静脉滴注给药。采用 1:1 倾向性评分匹配(PSM)均衡组间基线特征后,比较两组临床有效率、检验指标好转率、感染部位影像学好转率、微生物清除率、30 天全因死亡率及急性肾损伤(AKI)发生率,并分析影响疗效、AKI 及死亡的相关因素。

结果 经 PSM 匹配后,CZA 组的临床有效率和检验指标好转率均显著高于 PMB 组($P < 0.05$);两组在感染部位影像学好转率、微生物清除率、30 天全因死亡率及 AKI 发生率方面,差异均无统计学意义(均 $P > 0.05$)。多因素分析显示,长疗程是 DTR-PA 清除率提高的有利因素,而合并鲍曼不动杆菌或肺炎克雷伯菌感染则与清除率降低相关;存在肾功能不全以及发生感染性休克是 AKI 的独立危险因素($P < 0.05$);住院天数与合并消化系统疾病是 30 天全因死亡的独立预测因子($P < 0.05$)。

结论 相较于 PMB,CZA 治疗 DTR-PA 感染可显著提高临床有效率与检验指标好转率,且未增加 AKI 风险,可为临床治疗提供参考依据。

关键词: 多黏菌素 B; 头孢他啶阿维巴坦; 疗效; 难治性铜绿假单胞菌; 急性肾损伤

基于 PPK/PBPK-PD 模型优化重症患者 CRKP 感染联合治疗方案

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目的 耐碳青霉烯的肺炎克雷伯菌(carbapenem-resistant *Klebsiella pneumoniae*, CRKP)感染已成为人类健康的重要威胁,基于现有药物(如氨基糖苷类、碳青霉烯类、多黏菌素等)的联合治疗是对抗 CRKP 感染的重要策略。但是目前临床上联合用药的最优给药方案尚不明确。本研究旨在以应用前景广泛但证据较少的阿米卡星联合美罗培南为

模板药物,对临床上两药联用治疗重症患者不同感染类型的最优给药策略进行推荐,实现精准用药。

方法 通过抗菌药物体外药动学/药效学(pharmacokinetic/pharmacodynamic, PK/PD)棋盘法实验,探究阿米卡星联合美罗培南对 CRKP 的协同 PD 靶标。建立重症患者阿米卡星和美罗培南的群体药动学(population pharmacokinetic, PPK)模型和生理药动学(physiologically based pharmacokinetic, PBPK)模型。基于 PPK 模型筛选影响药物 PK 特征的协变量;基于 PBPK 模型预测两药的肺组织和皮肤组织浓度;利用联合用药的 PD 靶标,通过蒙特卡罗模拟分别优化两药联合治疗重症患者血流感染、肺部感染与复杂皮肤和软组织感染的给药方案。

结果 棋盘法实验结果表明,阿米卡星联合美罗培南对 CRKP 的联合抑菌指数在 0.5-1 之间,说明联合用药具有增强的杀菌作用。PPK 模型表明,肾功能是重症患者阿米卡星和美罗培南 PK 特征的主要影响因素。PBPK 模型能准确预测两药的组织浓度,组织穿透率预测值在对应观测值的 2 倍变化以内。相同给药方案下,肺组织和皮肤组织浓度低于血药浓度,且皮肤组织浓度最低。PPK/PD 模型表明,两药联用时,阿米卡星 15 mg/kg qd 和美罗培南 1 g q8 h 延长输注 3 h 推荐用于肾功能正常且两药的最低抑菌浓度均为 8 mg/L 的血流感染患者;PBPK/PD 模型表明,两药联合治疗肺部感染及复杂皮肤和软组织感染较血流感染需对应增加给药剂量、延长输注时间或增加给药频次;联合用药的剂量均低于单药治疗。

结论 阿米卡星联合美罗培南对 CRKP 具有协同杀菌作用。基于建立的重症患者阿米卡星和美罗培南联合用药时的 PPK/PD 和 PBPK/PD 模型,对两药联用治疗血流感染、肺部感染与复杂皮肤和软组织感染的个体化给药方案进行推荐。

关键词: 联合用药; CRKP 感染; 药效学; 群体药动学; 生理药动学

一例绿色魏斯氏菌感染性眼内炎的病例报告

刘浩

中国人民解放军总医院

目的 探讨绿色魏斯氏菌 (*Weissella viridescens*) 致外伤性感染性眼内炎的临床特征及药学监护策略, 提高对该罕见病原体感染的认识。

方法 回顾性分析我院 1 例绿色魏斯氏菌所致外伤性眼内炎患者的诊疗过程, 并检索中国知网、万方数据库、PubMed、Web of Science 等中英文数据库, 检索绿色魏斯氏菌所致眼内炎的文献, 探讨该类感染性疾病的临床表现、微生物学特性和抗感染药物治疗选择。

结果 患者房水宏基因组二代测序 (mNGS) 技术对罕见微生物致眼内炎的检出率有较好的辅助诊断作用, 在检出绿色魏斯氏菌后, 临床药师会诊建议停用经验性万古霉素与头孢他啶, 换用利奈唑胺静脉滴注联合左氧氟沙星滴眼液滴眼局部用药, 患者症状好转, 病情得以控制。查询相关文献复习显示, 绿色魏斯氏菌对万古霉素天然耐药 ($MIC \geq 256 \mu g/mL$), 对头孢他啶也广泛存在高水平耐药状况; 该菌可引起感染性心内膜炎、菌血症, 以及中枢、腹腔、泌尿系统及假体周围感染, 但尚未查阅到任何一例引起眼内炎的报道。

结论 绿色魏斯氏菌所致眼内炎十分罕见, 临床药师通过目标治疗选择、不良反应监测等药学监护手段, 在多学科协作诊治疑难感染性疾病中发挥了重要作用。

一例脓肿分枝杆菌假体周围感染的病例报告及脓肿分枝杆菌假体周围感染系统文献复习

刘浩

中国人民解放军总医院

目的 了解脓肿分枝杆菌 (*Mycobacterium abscessus*, *M.abscessus*) 所致假体关节感染 (PJI) 的临床特征, 提高对该类感染性疾病的认识。

方法 回顾性分析 1 例 *M.abscessus* PJI 患者的临床资料, 并系统检索 PubMed 数据库 (2000 年至今) 相关文献, 汇总临床特点、治疗及结局。

结果 患者为 65 岁男性, 双膝人工关节置换术后反复发热、肿痛, 常规培养多次阴性, 经二代测序及延长培养确诊为 *M.abscessus* 感染。根据药敏及耐受性调整方案为克拉霉素+亚胺培南/西司他丁+阿米卡星, 因肾损伤换用替加环素但胃肠道不耐受, 复发后再次加用亚胺培南/西司他丁, 联合手术清创及假体更换, 总疗程 6 个月, 最终膝关节置换术后恢复良好。文献共纳入 27 例 (男 7 例, 女 20 例), 年龄 40~83 岁, 膝 (19 例)、髌 (7 例)、踝 (1 例), 主要表现为发热、肿痛、活动受限。所有患者均行手术清创/重置假体联合抗感染治疗 (3~4 种药物, 疗程 4~24 个月)。

结论 20 例缓解或随访无复发, 2 例姑息治疗, 4 例未记录, 1 例治疗失败。结论: *M.abscessus* 所致 PJI 罕见, 常规培养易假阴性, 二代测序及延长培养有助早期诊断。治疗需彻底清创联合长疗程、多种敏感药物 (如克拉霉素+阿米卡星+亚胺培南/西司他丁) 的个体化方案。

一例耐头孢他啶阿维巴坦高毒力肺炎克雷伯菌感染的眼内炎病例报告

刘浩

中国人民解放军总医院

目的 分析耐头孢他啶阿维巴坦的高毒力碳青霉烯耐药肺炎克雷伯菌 (hv-CRKP) 所致暴发性眼内炎的临床特征、耐药与毒力基因背景, 总结诊疗经验。

方法 回顾性分析 1 例角膜移植术后眼内炎患

者的临床资料,包括病原学培养、药敏试验、宏基因组二代测序(mNGS)及靶向二代测序(tNGS)结果,结合文献讨论抗感染策略。

结果 患者为25岁男性,右眼板层角膜移植术后48小时内出现前房积脓、植片溶解、视力无光感。眼拭子培养为肺炎克雷伯菌,对美罗培南、亚胺培南、头孢他啶等耐药。mNGS/tNGS检出病原体序列数分别为5776和9326,携带耐药基因blaKPC-3、CTX-M、TEM、SHV及毒力基因簇iucABCD-iutA(气杆菌素铁载体系统),符合CG258耐药谱系hv-CRKP特征。初始经验性治疗仅予局部滴眼液联合全身头孢呋辛,未及时行玻璃体腔注药;目标性治疗采用头孢他啶阿维巴坦(静脉、滴眼液、玻璃体腔注射),但10天后联合药敏示该菌对头孢他啶阿维巴坦耐药,与氨曲南存在协同作用,临床未采纳调整方案。最终行玻璃体切除、角膜移植、硅油填充术,右眼无光感出院。该病例提示,hv-CRKP兼具泛耐药性与超强侵袭力,常规术后经验性抗感染方案(万古霉素+头孢他啶)无效;传统培养及药敏滞后,且无法提供毒力基因信息。

结论 hv-CRKP所致眼内炎进展极快,组织破坏不可逆。对于内眼术后超急性感染,应在24小时内同步采集眼内液送检mNGS/tNGS及培养,第一时间评估玻璃体手术指征,并早期使用覆盖产KPC酶耐药菌的新型药物(如头孢他啶阿维巴坦、氨曲南阿维巴坦等)。诊断与治疗速度必须超越细菌破坏速度,才有望挽救视力。

一例脆弱拟杆菌假体周围感染的药学监护及系统文献复习

刘浩

中国人民解放军总医院

目的 探讨脆弱拟杆菌(*Bacteroides fragilis*)致假体关节感染(periprosthetic Joint Infection, PJI)的临

床特征及药学监护策略,提高对该类感染性疾病的临床认识。

方法 回顾性分析1例脆弱拟杆菌PJI患者的诊疗过程;在中国知网、Pubmed等中英文数据库中检索脆弱拟杆菌所致PJI的病例报道,探讨该类感染性疾病的临床特点及用药选择。

结果 在该患者确定致病菌为脆弱拟杆菌后,临床药师建议术后万古霉素联合甲硝唑2日,后甲硝唑单药至少6周的抗感染治疗方案,治疗数天后,患者关节液多次送检均未查出脆弱拟杆菌。但患者术后相继出现腹腔感染、脓毒症休克等多重并发症,经多学科联合治疗后患者临床症状及炎症指标显著改善,但遗留周围神经病变。在整个治疗过程中,临床药师为其提供专业的药学监护并在出院后定期随访。文献复习显示,脆弱拟杆菌引起PJI的患者仅有10例,多与肠道病灶、类风湿性关节炎等易感因素有关,临床表现与感染部位相关,主要表现为发热、疼痛、肿胀伴活动受限等。多以甲硝唑作为基础治疗药物,疗效、安全性及转归良好,但疗程差异较大。

结论 脆弱拟杆菌所致PJI罕见,易血行播散、并发症重,临床药师通过个体化给药、治疗药物监测及不良反应管理等药学监护手段,在多学科诊疗中发挥重要作用。

初治急性髓系白血病合并多灶性皮肤毛霉菌的诊治经验——附一例报告

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关键词: 皮肤毛霉菌; 急性髓系白血病; 米根霉; 病原宏基因组二代测序; 联合抗真菌治疗

目的 初治急性髓系白血病(AML)患者因粒细胞缺乏及免疫抑制,是侵袭性真菌病的高危人群。皮肤毛霉菌虽相对少见,但进展迅速,易发生血源

性播散,死亡率高。本文报告一例初治 AML 合并多灶性皮肤毛霉病的诊疗过程,探讨其临床特征、诊断策略及治疗方案,旨在为类似皮肤感染表现的诊断及鉴别诊断提供参考。

方法 回顾性分析 2025 年 3 月于我院确诊的 1 例 49 岁女性 AML 患者的诊治经过,收集临床资料、实验室检查、影像学及病原学结果。随访截至 2026 年 4 月。

结果 患者入院后出现粒细胞缺乏伴发热,并进行性出现右膝、左手背及肛周多发性皮肤损害,皮损呈特征性暗紫色伴外圈焦痂,右膝皮损中央出现水泡。患者持续高热($>39^{\circ}\text{C}$)且广谱抗生素联合伏立康唑经验性抗感染治疗无效;外周血炎症指标中 CRP 显著升高(150 mg/L),而 PCT 正常(0.01 ng/ml),GM 试验轻度升高(1.07)但 G 试验阴性。病原学证据:外周血培养及血 mNGS 均为阴性;右膝皮损水泡液 mNGS 检出米根霉种(序列数 2,置信度 99%),结合宿主因素(AML 初治、粒细胞缺乏)及典型皮损表现,临床诊断为皮肤毛霉病。诊断后予两性霉素 B 胆固醇硫酸酯联合艾莎康唑抗真菌治疗,患者体温迅速恢复正常,皮损逐渐结痂、脱落,遗留色素沉着,未出现新发皮损。后续单用艾莎康唑抗真菌治疗,顺利完成诱导化疗,并获得完全缓解(CR),FLT3-ITD 及 NPM1 突变转阴。患者经巩固化疗后于 2025 年 8 月行单倍体异基因造血干细胞移植,预处理及细胞恢复期间未发生真菌突破。末次随访仍处于 CR 状态,一般情况良好。

结论 初治 AML 患者出现发热伴多灶性暗紫色焦痂样皮损,经广谱抗生素联合伏立康唑治疗无效时,应高度警惕皮肤毛霉病。皮损局部标本(如水泡液、坏死组织)的病原学检测对早期诊断至关重要。

肺结核合并 2 型糖尿病患者基线血糖控制与强化期疗效反应的相关性研究

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关键词: 糖尿病合并肺结核,血糖控制,强化期疗效

背景 糖尿病与肺结核常并存,相互影响。抗结核治疗的初始强化期(前 2 个月)疗效至关重要,而血糖控制不佳可能削弱治疗效果。然而,治疗前血糖水平与强化期多重疗效指标(痰菌转阴、影像学改善)的具体关联尚缺乏系统性研究。明确这种关联有助于早期识别高风险患者,实施精准干预,对改善共病患者预后具有重要意义。

目的 本研究旨在探讨肺结核合并 2 型糖尿病患者基线血糖控制水平与抗结核治疗强化期(2 个月)疗效反应的关系,具体分析血糖控制不佳对 2 个月痰菌未转阴及 2 个月影像学改善欠佳风险的影响,以期该类共病患者的早期风险分层和个体化管理提供临床依据。

方法 本研究为单中心回顾性队列研究,纳入 2024 年 8 月至 2026 年 2 月确诊为肺结核合并 2 型糖尿病并完成至少 2 个月标准强化期治疗的患者。根据基线糖化血红蛋白水平分为血糖控制不佳组和良好组。通过电子病历收集资料,主要结局为 2 个月末痰菌未转阴和影像学改善欠佳。采用多因素 Logistic 回归模型分析基线血糖控制不佳与两个主要结局的独立关联,校正年龄、性别、糖尿病病程、肺部病变范围等混杂因素。

结果 共纳入 152 例患者,其中血糖控制不佳组 86 例,血糖控制良好组 66 例。结果显示,血糖控制不佳组 2 个月痰菌未转阴的发生率为 39.5%(34/86),显著高于对照组的 15.2%(10/66)($p < 0.001$)。多因素分析显示,基线血糖控制不佳($\text{HbA1c} \geq 7.0\%$)是 2 个月痰菌未转阴的独立危险因素,调整后的比值比(aOR)为 3.41(95% CI: 1.52-7.66, $p = 0.003$)。同时,血糖控制不佳组 2 个月影像学改善欠佳的发生率为 59.3%(51/86),亦显著高于对照组的 31.8%(21/66)($p < 0.001$),其 aOR 为 2.89(95%

CI: 1.45-5.78, $p = 0.003$)。

结论 基线血糖控制不佳是预测肺结核合并 2 型糖尿病患者抗结核强化期疗效反应不良 (痰菌持续阳性及影像学改善延迟) 的重要风险因素。临床实践中, 应对所有肺结核患者进行糖代谢异常的早期筛查与评估。对于已合并糖尿病的患者, 应在抗结核治疗启动之初即强调严格的血糖控制 (建议以 $HbA1c < 7.0\%$ 为目标), 并加强强化期的血糖监测与个体化干预, 以期有效改善强化期疗效, 为最终治疗成功奠定基础。

慢性阻塞性肺疾病合并耐药肺结核的临床特点及抗结核治疗结局分析

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目的 慢性阻塞性肺疾病 (COPD) 患者因长期反复使用抗生素及糖皮质激素, 是耐药肺结核的高危人群。本研究分析 COPD 合并耐药肺结核的临床特点、耐药谱特征及抗结核治疗结局, 为临床诊疗提供参考。

方法 回顾性分析 2022 年 1 月至 2025 年 12 月于宁夏医科大学总医院确诊的 COPD 合并耐药肺结核患者 56 例。纳入标准: ①符合 GOLD 指南 COPD 诊断标准; ②符合肺结核诊断标准 (WS 288-2017), 痰涂片或培养阳性; ③经金域医学检验所结核分枝杆菌复合群及耐药基因靶向测序 (tNGS) 证实对至少一种抗结核药物耐药; ④临床资料完整。排除标准: ①合并其他类型分枝杆菌感染; ②合并 HIV 感染; ③抗结核治疗 < 2 周。收集患者人口学资料、COPD 病程及分级、临床表现、影像学特征、耐药谱 (tNGS 检测结果)、抗结核治疗方案及治疗结局。主要结局为治疗 6 个月末痰菌阴转率, 次要结局为治疗成功率及不良反应发生率。

结果 56 例患者中, 男 41 例、女 15 例, 平均年龄 67.3 ± 8.5 岁; COPD 病程中位 8 年, GOLD3~4 级占 67.9%。影像学以双肺上叶浸润、空洞形成为主。tNGS 耐药检测示: MDR-TB 占 50.0%, 单耐药 32.1%, 非 MDR 多耐药 17.9%; 主要耐药菌株为异烟肼、利福平。抗结核方案以联合氟喹诺酮类、二线注射剂及新型抗结核药物为主。治疗 6 月末总体痰菌阴转率 66.1%, MDR-TB 组阴转率显著低于非 MDR 组 ($p=0.048$)。整体治疗成功率 58.9%, 不良预后包括治疗失败、死亡及失访。不良反应发生率 42.9%, 以肝肾功能损伤、胃肠道反应多见, 无治疗相关死亡。

结论 COPD 合并耐药肺结核以老年男性多见, 耐多药比例高 (50.0%), 痰菌阴转率及治疗成功率偏低, 不良反应发生率高。tNGS 耐药基因检测有助于快速指导个体化抗结核治疗。

关键词: COPD; 耐药肺结核; 耐多药; 靶向二代测序; 抗结核治疗

慢性阻塞性肺疾病合并脓肿分枝杆菌肺病营养状态与治疗依从性及预后的关系研究: 一项单中心回顾性队列研究

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关键词: 肌肉减少症, 治疗依从性, 营养支持

背景 慢性阻塞性肺疾病 (COPD) 合并脓肿分枝杆菌肺病 (MABS-PD) 患者常存在营养不良, 特别是肌肉减少症。这一状况与患者治疗依从性差和临床预后不良显著相关。因此, 在启动抗感染治疗前, 对患者进行常规营养筛查至关重要。应将积极的营养支持治疗整合为整体疾病管理策略的核心组成部分, 以改善治疗过程和患者结局。

方法 本研究为单中心回顾性队列研究。连续

纳入 2020 年 2 月至 2026 年 2 月于宁夏医科大学总医院确诊为 COPD 并符合 MABS-PD 诊断标准的成年患者（共 100 例）。通过电子病历和药房数据，采用去脂体重指数（FFMI）评估肌肉减少症，以药物覆盖天数比例（PDC $\geq$ 80%）定义治疗依从。主要预后为治疗失败（12 个月内死亡或痰培养转阳），次要预后为急性加重及再入院率。采用倾向评分匹配控制混杂因素，并应用多因素 Logistic 回归分析营养指标与治疗失败的独立关联。

结果 共纳入 100 例患者，平均年龄 68.5 $\pm$ 9.2 岁，男性占 69.0%。FFMI 评估显示 25 例(25.0%)患者存在肌肉减少症，75 例为无肌肉减少症。经 PSM 1:1 匹配后，纳入 48 对(96 例)患者进行结局分析。肌肉减少症患者 PDC 值显著低于无肌肉减少症患者（64.8% $\pm$ 14.7% vs. 81.5% $\pm$ 11.9%， $p<0.001$ ），PDC $<$ 80%的比例为 56.0% vs. 25.3%（ $p<0.001$ ）。中位随访 14 个月后总体治疗失败率为 35.0%，肌肉减少症患者失败率显著更高（72.9% vs. 29.2%， $p<0.001$ ）。多因素 Logistic 回归显示，校正混杂因素后，低 FFMI（OR=4.2，95% CI: 1.8-9.8， $p=0.001$ ）和低 PDC（OR=3.8，95% CI: 1.6-9.0， $p=0.002$ ）均为治疗失败的独立危险因素。敏感性分析结果一致，支持结论的稳健性。

结论 COPD 合并 MABS-PD 患者普遍存在肌肉减少症，其与治疗依从性差及预后不良显著相关。本研究建议启动治疗前常规营养筛查，并将营养支持作为核心管理策略。

嗜水气单胞菌致肺部感染 1 例

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嗜水气单胞菌（*Aeromonas hydrophila*）是一种广泛分布于水环境中的革兰阴性兼性厌氧杆菌，属弧菌科气单胞菌属。在自然界中分布极为广泛，可

在沉积物、河口、废水、饮用水和食品等各种水环境中生存。通过直接伤口暴露及食源性起人类感，过去该菌主要被关注为水生鱼类、两栖类和爬行动物的病原体，近年来随着工业与农业的快速发展，嗜水气单胞菌通过水源和食物链的传播日益增多，人类感染病例逐渐增加，该菌可分为肠内感染和肠外感染两类，肠内感染主要表现为腹泻等症状，肠外感染则为皮肤和皮下筋膜等感染，在免疫功能低下或合并严重慢性疾病（如肝硬化、糖尿病、恶性肿瘤）的宿主中可导致严重血流感染及多部位侵袭性感染。部分病例可迅速发展为坏死性筋膜炎导致死亡，死亡率可达 33%~70%。据国内一项纳入 112 例患者的回顾性研究[4]发现，嗜水气单胞菌肠道外感染好发于温暖季节，主要以伤口感染和血液感染为主，分别占 40.18%及 31.25%，临床患者主要伴有外科手术史、留置引流管等特点，其耐药性不容乐观，已出现耐碳青霉烯菌株。该菌可产生多种毒力因子，包括溶血素、组织毒素、坏死毒素、肠毒素和蛋白酶等，其中可产生 CphA 类金属 β -内酰胺酶（MBL），导致对碳青霉烯类抗生素耐药性[5]，使临床抗感染治疗出现严峻挑战。现就一例嗜水气单胞菌致肺部感染的病例进行分析。

临床药师参与一例肺炎克雷伯菌脑膜脑炎合并附睾炎的药学监护实践

张凡

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目的 本文旨在报道临床药师参与 1 例肺炎克雷伯菌脑膜脑炎患者抗感染治疗的实践过程，分析初始治疗方案存在的问题及调整依据，探讨临床药师在中枢神经系统感染药物治疗管理中的作用，为类似病例的合理用药提供参考。

方法 采用病例分析方法，对 1 例 53 岁男性患者（因发热后意识模糊 6 小时入院）的临床资料进

行系统回顾。患者入院后行腰椎穿刺及脑脊液检查，临床药师通过密切监测患者临床症状、实验室及脑脊液指标变化，结合脑脊液宏基因组测序（NGS）及培养结果，查阅相关指南和文献，参与抗感染治疗方案的制定与优化，并对药物治疗过程实施全程药学监护。

结果 患者入院后临床医生经验性给予头孢唑肟联合更昔洛韦抗感染治疗，入院第 3 天脑脊液 NGS 检测示肺炎克雷伯菌（1032 reads，相对丰度 57.65%），毒力因子阳性；脑脊液微生物培养结果为肺炎克雷伯菌（ESBL 阴性）。临床药师会诊后建议停用头孢唑肟及更昔洛韦，改用头孢曲松 2g,ivgtt,q12h，建议其疗程不少于 28 天。治疗期间患者合并左侧急性附睾炎，经泌尿外科会诊建议使用左氧氟沙星经验性抗感染治疗其附睾炎，临床药师评估其合理性后同意联合左氧氟沙星抗感染治疗，并加强不良反应监测。经治疗，患者体温恢复正常，头痛头胀症状明显好转，复查脑脊液白细胞降至 $8 \times 10^6/L$ ，蛋白及炎症指标显著改善，感染得到初步控制，患者于第 15 日出院。

结论 肺炎克雷伯菌脑膜脑炎临床少见但病情危重，早期、足量、足疗程抗菌治疗是改善预后的关键。临床药师依据病原学结果动态优化抗感染方案，将初始不适宜的头孢唑肟调整为头孢曲松并维持最大剂量及频次，同时兼顾附睾炎联合左氧氟沙星治疗，体现了精准化药学服务价值同时保障了临床治疗用药的安全性和有效性。多药联合治疗过程中，对药物不良反应的及时识别与处置亦凸显抗感染临床药师在感染性疾病多学科协作中的重要作用。

【关键词】肺炎克雷伯菌；细菌性脑膜炎；临床药师；药学监护

一例伏立康唑治疗马尔尼菲蓝状菌感染的药学监护

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目的 探讨马尔尼菲蓝状菌肺部感染治疗的药物选择以及临床药师参与和实施个体化用药监护的临床意义。

方法 临床药师参与马尔尼菲蓝状菌肺部感染患者的治疗过程，对伏立康唑进行 TDM 监测与药物剂量调整，并及时发现患者可能由伏立康唑导致的严重血脂异常，建议加用贝特类药物降血脂并持续监测血脂水平。

结果 经 TDM 监测与剂量调整，患者服用药物 10 天后血药浓度在规定治疗范围内，临床症状好转，且影像学显示肺部病灶吸收，提示治疗有效。但临床药师在处理 TDM 血标本时发现患者存在乳糜血，建议患者监测血脂水平。患者血脂检查提示甘油三酯升高至 8.64mmol/L ，服药 14 天后甘油三酯升高至 40.76mmol/L 。临床药师通过排查患者所有使用药物并查阅文献资料，考虑其严重血脂异常可能是由伏立康唑导致的罕见不良反应所致，进一步结合 CYP2C19 基因检测，该患者为伏立康唑慢代谢型，治疗过程中首次监测伏立康唑血药浓度为 $6.66\mu\text{g/ml}$ ，超出治疗窗上限，临床药师及时建议将剂量调整为正常剂量的 50%，以确保血药浓度回归治疗窗范围内，同时启动护肝治疗，并根据血脂水平使用贝特类降脂药物，最终经药物处理后患者临床症状好转，血脂恢复正常。

结论 临床药师结合循证证据，从治疗方案选择、给药剂量调整、罕见不良反应的识别等方面开展药学监护，可提高患者用药的安全性、有效性。

临床药师参与 1 例按蚊伊丽莎白金菌颅内感染伴多种细菌肺部感染治疗分析

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目的 总结脑梗死术后按蚊伊丽莎白金菌颅内感染合并多种泛耐药革兰氏阴性杆菌肺部感染患者的临床特点、治疗策略及相关院内感染防控措施。

方法 回顾性分析 1 例脑梗死术后按蚊伊丽莎白金菌颅内感染合并泛耐药的肺炎克雷伯菌、铜绿假单胞菌肺部感染患者的临床资料,并结合国内外相关文献,从病因学与病原学、临床特征、诊疗策略探讨及治疗转归等方面进行分析。

结果 患者脑梗死术后意识障碍,气管切开状态,抽吸较多粘痰,伴反复发热。脑室外引流液清亮,偶见絮状漂浮物;脑脊液生化提示炎性改变;脑脊液及导管尖端培养,均检出按蚊伊丽莎白金菌,诊断为颅内感染。多次痰培养提示:泛耐药肺炎克雷伯菌、泛耐药铜绿假单胞菌,结合肺部影像及临床症状,诊断为肺部感染。根据药敏结果,予以哌拉西林他唑巴坦+万古霉素抗感染治疗 7 天,热峰较前下降,但间断发热,黄粘痰仍较多,脑脊液生化及感染指标恢复缓慢;遂加用复方磺胺甲噁唑治疗,3 日后未再发热,后续患者逐渐痰量较少,脑脊液生化恢复正常,最终顺利出院,继续康复治疗。

结论 该患者经历了从术后常规抗感染治疗到几种多重耐药菌相继感染的过程,特别是按蚊伊丽莎白金菌不常见病原体的诊疗管理。临床药师在面对多部位、多种病原菌感染的复杂病情,应与临床药师紧密合作,依据细菌培养及药敏试验结果,结合患者临床症状、实验室指标及用药反应,动态调整抗感染治疗方案,并督促落实好相关防控措施。

关键词: 按蚊伊丽莎白金菌;颅内感染;泛耐药革兰氏阴性杆菌;肺部感染;临床药师。

一例腹腔镜术后混合病原菌腹腔感染致脓毒血症诊疗分析

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目的 探讨腹腔镜术后自发性腹膜炎合并产超广谱 β -内酰胺酶(ESBL)大肠埃希菌、屎肠球菌、李斯特菌、河流弧菌等多重耐药及少见病原菌感染的流行病学特点、医院感染防控、临床表现、抗感染治疗策略及转归,提高临床对术后混合重症感染的识别与处置能力。

方法 回顾性分析 1 例 22 岁女性患者因“腹腔镜双侧卵巢畸胎瘤剥除术+阑尾切除术”术后并发自发性腹膜炎、脓毒血症的临床资料。患者术后持续腹痛,术后第 5 天出现高热(40°C)、不完全性肠梗阻、腹膜增厚、盆腔积液、水样便,炎症指标显著升高。初始予头孢他啶联合奥硝唑经验性抗感染,感染控制不佳并进展为脓毒血症;改用美罗培南(3 h 持续静脉滴注),并行“腹腔镜检查+盆腔脓肿清除术”。术后感染指标下降,但体征未完全缓解,术后第 2 d 加用万古霉素。后续病原学培养为产 ESBL 大肠埃希菌、屎肠球菌、李斯特菌、河流弧菌混合感染。结合药敏与患者体征动态调整方案:予美罗培南联合万古霉素控制脓毒症,症状与指标显著改善;患者青霉素过敏,血培养转阴后降阶梯为莫西沙星单药序贯治疗,总疗程 14 d,同时积极肠梗阻、肝功能轻度异常等并发症。

结果 经外科清创引流联合目标性抗感染治疗后,患者体温、白细胞计数、C 反应蛋白(CRP)、降钙素原(PCT)、白细胞介素-6(IL-6)均恢复正常,腹部 CT 示腹腔积液吸收、肠梗阻缓解。治疗期间出现一过性转氨酶升高(约 2 倍正常上限),停药后自行恢复。患者痊愈出院,随访无复发。

结论 腹腔镜术后自发性腹膜炎可由多种病原菌混合感染所致,产 ESBL 肠杆菌科、肠球菌、李斯特菌、河流弧菌共感染临床罕见且病情危重。碳青霉烯类联合万古霉素为控制脓毒症的有效初始方案;血培养李斯特菌阳性需警惕肠源性播散,美罗培南有效。降阶梯治疗应依据药敏及患者症状实施,氟喹诺酮类(莫西沙星)在菌株敏感、感染控制后可作为序贯选择。腹腔镜术后出现持续腹痛、拔管后发热、水样便等表现时,应尽早完善病原学检查,警惕院内感染及少见病原菌,避免漏诊。

关键词: 腹腔感染; 自发性腹膜炎; 产 ESBL 大肠埃希菌; 屎肠球菌; 李斯特菌; 河流弧菌; 脓毒血症; 降阶梯治疗

丁酸在艰难梭菌感染中的双向调控作用: 综述

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目的 艰难梭菌 (*Clostridioides difficile*) 是引发抗生素相关性腹泻及伪膜性结肠炎的主要病原体, 在全球范围内, 尤其是欧美地区造成严重的公共卫生负担, 其感染与肠道微生态紊乱密切相关。丁酸作为重要短链脂肪酸 (SCFAs) 之一, 是结肠上皮细胞的能量来源, 从多方面维持肠道功能。多项研究揭示, 丁酸对艰难梭菌感染 (CDI) 并非发挥单纯的抑制作用, 而是在艰难梭菌感染各阶段均呈现复杂的调控效应, 但目前未被系统阐释, 本文旨在系统综述丁酸在 CDI 中的双向调控效应, 为开发精准安全的 CDI 防治策略提供理论依据。

方法 以近年发表的高质量基础研究和临床研究为依据, 梳理丁酸对宿主肠道屏障、免疫反应的调控作用和对艰难梭菌生长、毒力及芽孢形成的影响, 整合双向调控的分子通路。

结果 临床证据显示, CDI 患者粪便的 SCFAs 水平显著低于健康人群, 粪菌移植 (FMT) 通过重建宿主肠道菌群平衡, 恢复丁酸水平, 有效治疗复发性 CDI。其中丁酸可通过稳定缺氧诱导因子-1 α (HIF-1 α) 增强肠道紧密连接、激活游离脂肪酸受体 2 (FFAR2) 作用于中性粒细胞和 3 型固有淋巴细胞 (ILC3s) 从而促进白介素-1 β (IL-1 β) 和白介素-22 (IL-22) 分泌、抑制组蛋白去乙酰化酶 (HDAC) 促进调节性 T 细胞 (T-reg) 分化。在病原体层面, 丁酸一方面以剂量依赖性抑制艰难梭菌菌株的生长, 另一方面, 丁酸促使艰难梭菌上调碳饥饿基因 *cstA*

和产孢相关基因的表达, 显著提高其产孢效率, 并轻微促进毒素合成, 从而提高艰难梭菌的环境适应力和存活率, 增加 CDI 的复发风险。这提示单纯补充丁酸或利用 FMT 提高丁酸水平治疗 CDI 患者可能存在潜在风险。

结论 丁酸在 CDI 中发挥双向调控作用, 临床干预需要联合抗芽孢治疗策略。未来研究需要进一步探索丁酸影响艰难梭菌的具体信号通路, 开发更多安全有效且复发率低的 CDI 治疗策略。

关键词: 丁酸; 艰难梭菌; 肠道菌群; 短链脂肪酸; 芽孢形成

重症发热伴血小板减少综合征合并肺毛霉菌病 1 例

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目的 发热伴血小板减少综合征 (severe fever with thrombocytopenia syndrome, SFTS) 是一种由新型布尼亚病毒引起的急性传染病, 临床以高热、血小板减少、消化道症状及多器官损伤为特征。重症 SFTS 易继发侵袭性真菌感染, 既往报道以曲霉菌最为常见, 毛霉菌感染极为罕见, 国内尚无 SFTS 合并肺毛霉菌病的病例报道。本文报告 1 例重症 SFTS 合并肺毛霉菌病患者的临床诊治过程, 旨在提高对该并发症的认识。

病例介绍: 患者, 男性, 63 岁, 农民, 既往体健, 无糖尿病及免疫抑制剂使用史, 因“发热伴头痛、呕吐 5 天”入院。入院时体温 39.5℃, 嗜睡, 双肺呼吸音粗, 下肺可闻及湿啰音。实验室检查: 白细胞 $2.35 \times 10^9/L$, 中性粒细胞 $1.25 \times 10^9/L$, 血小板 $47 \times 10^9/L$, 新型布尼亚病毒核酸阳性, 确诊 SFTS。入院后病情迅速进展, 出现粒细胞缺乏、细胞因子风暴、意识障碍及呼吸衰竭。胸部 CT 示双肺多发斑片状实变影。血清 1-3- β -D 葡聚糖 53.80 pg/mL, 半

乳甘露聚糖血清指数 4.23, 痰培养检出烟曲霉, 临床诊断侵袭性肺曲霉病, 予伏立康唑(首日负荷剂量 6 mg/kg q12h, 序贯 4 mg/kg q12h) 治疗。

治疗及转归: 伏立康唑治疗第 8 天, 患者体温再次升高至 39.2℃, 咳嗽、咳痰加重, 咳出少量血丝。复查胸部 CT 示原有部分实变区出现厚壁空洞, 部分空洞内见结节状内容物。考虑到抗曲霉治疗无效且病情恶化, 行支气管肺泡灌洗, 送检 mNGS, 结果回报: 微小根霉(*Rhizomucor pusillus*) 序列数 88 条。修正诊断为肺毛霉菌病, 停用伏立康唑, 换用两性霉素 B 胆固醇硫酸酯复合物(5 mg/kg/d) 静脉滴注。治疗 2 天后体温降至正常, 1 周后咳嗽、咳痰减轻, 出院改为口服艾沙康唑序贯治疗。随访 3 个月, 肺部空洞吸收。

结论 SFTS 患者因粒细胞缺乏、免疫麻痹及屏障破坏, 易继发侵袭性真菌感染, 曲霉最常见。本例初始 GM 试验阳性及痰培养烟曲霉阳性, 可能为混合感染或定植, 但 mNGS 明确提示毛霉菌为主导病原。伏立康唑对毛霉菌无效, 临床若遇抗曲霉治疗反应差且影像学出现“反晕征”或空洞进展时, 应及时行 mNGS 排查毛霉菌, 及时调整抗真菌方案, 改善患者预后。

【关键词】 发热伴血小板减少综合征, 真菌感染, 毛霉菌病

一例慢性淋巴细胞白血病合并皮疽诺卡菌皮肤感染患者的药学监护

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目的 分析一例慢性淋巴细胞白血病患者在使用 BTK 抑制剂奥布替尼过程中出现皮肤感染、感染性休克的抗感染治疗及药学监护过程, 为此类患者的抗感染治疗和用药安全提供参考。

方法 一名 70 岁男性因“确诊慢性淋巴细胞白

血病 11 年, 左颈部肿物 5 天, 发热 1 天”入院, 诊断为慢性淋巴细胞白血病、感染性休克、皮肤感染。入院后经验性予以美罗培南联合万古霉素抗感染及对症支持治疗, 同时行左侧颈部皮肤肿物切开排脓术并完善伤口分泌物培养, 随后临床药师根据患者临床症状进展、微生物培养结果、治疗药物监测和药代动力学/药效学原则进行抗感染方案的评估和优化。伤口分泌物培养抗感染方案初始为经验性用药,

结果 初始经验性治疗使用了美罗培南和万古霉素, 伤口分泌培养提示皮疽诺卡菌, 遂将治疗方案调整为复方磺胺甲噁唑片, 调整两天后, 患者因颈部肿物切开伤口愈合不佳, 予以伤口积极专科换药, 并加用亚胺培南西司他丁静脉滴注, 联合复方磺胺甲噁唑片口服抗感染治疗。随后患者伤口逐渐愈合, 病情稳定后出院, 出院后定期至烧伤科门诊换药, 继续口服复方磺胺甲噁唑片抗感染。服用复方磺胺甲噁唑片期间患者出现肝功能损伤, 临床药师考虑与复方磺胺甲噁唑相关, 建议减少剂量, 随后肝功能恢复正常。患者抗感染治疗足 12 个月后, 感染控制且未复发, 予以停药。

结论 诺卡菌是免疫抑制宿主的常见机会性病原体, 本例患者长期罹患慢性淋巴细胞白血病并使用 BTK 抑制剂奥布替尼, 属于典型的高危人群。此类患者的诺卡菌感染治疗较为复杂和漫长, 其间临床药师应及时根据患者的病情和检查结果对抗感染治疗方案进行个体化的优化和调整, 以保障患者获得有效的治疗。在积极抗感染的同时, 必须评估并调整导致免疫抑制的基础治疗(如 BTK 抑制剂), 这是控制感染和预防复发的根本。同时还应做好患者的药物不良反应监测, 以保障患者的用药安全。

关键词: 慢性淋巴细胞白血病; 诺卡菌; 抗感染治疗; 药学监护

Fatal Timing Gap: Delayed Diagnosis and Treatment of Disseminated Cryptococcosis

Following Rituximab Therapy — A Case Report

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Disseminated cryptococcosis in patients receiving rituximab is associated with high mortality, underscoring the importance of early diagnosis and prompt initiation of antifungal therapy. However, diagnostic delays—particularly in patients with complex comorbidities—may lead to rapid clinical deterioration. We report the case of a 50-year-old man with myasthenia gravis receiving rituximab and corticosteroids who presented with recurrent fever and headache. Lumbar puncture was repeatedly recommended but declined by his family. Despite fluctuating inflammatory markers and transient responses to antibiotics and corticosteroids, his condition progressively worsened. Blood cultures ultimately yielded *Cryptococcus neoformans*. Although induction therapy with amphotericin B and flucytosine was planned, it could not be initiated prior to sudden loss of consciousness and cardiopulmonary arrest. This case highlights the fatal consequences of delayed diagnosis in rituximab-associated cryptococcosis. Serum cryptococcal antigen testing should be prioritized in high-risk patients presenting with fever and headache. When lumbar puncture is not feasible, empiric antifungal therapy should be strongly considered. Positive blood cultures may represent a late-stage warning rather than an opportunity for timely intervention.

儿童非结核分支杆菌病治疗进展

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目的 总结儿童非结核分枝杆菌 (non-tuberculous mycobacteria, NTM) 感染的临床治疗决策依据、治疗策略及新型治疗手段的研究进展, 为儿童 NTM 感染的规范化管理提供参考。

方法 检索国内外有关儿童 NTM 感染诊断及治疗的相关指南、共识、综述及原始研究文献, 并结合近年来儿科领域研究进展进行归纳分析。

结果 儿童 NTM 感染的治疗应以菌种鉴定为基础, 结合感染部位、疾病表型、病情进展及宿主免疫状态进行分层管理。局限性病变尤其颈面部淋巴结炎, 手术治疗具有重要价值; 肺病、播散性疾病及复杂皮肤软组织感染多需长期多药联合治疗。对于免疫缺陷患儿, 需抗感染治疗的同时开展免疫学评估及针对性干预。当前儿童 NTM 感染治疗证据有限, 临床多参照成人指南, 但药物选择、剂量、疗程及不良反应监测仍需结合儿童生长发育和药代动力学特点。吸入抗菌药物、新型抗菌药物、老药新用及噬菌体疗法等为难治性病例提供了新的治疗方向, 但其在儿童中的疗效与安全性尚需进一步验证。

结论 儿童 NTM 感染临床管理复杂, 应建立基于病原学、疾病表型及宿主因素的个体化治疗策略。未来仍需加强儿科高质量临床研究, 完善儿童特异性的治疗方案。

关键词 儿童; 非结核分枝杆菌; 治疗决策; 免疫缺陷; 新型治疗

呼吸系统真菌和细菌感染最新治疗方案

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目的 综述呼吸系统真菌和细菌感染的最新诊断技术和治疗策略, 重点探讨新型抗感染药物研发进展、mNGS 技术在混合感染诊断中的应用价值及

个体化治疗方案，为临床实践提供循证医学证据。

方法 系统检索 PubMed、Embase、Web of Science、中国知网 (CNKI) 等数据库，检索时限为 2023 年 1 月至 2025 年 3 月。纳入标准：①关于呼吸系统真菌或细菌感染治疗的临床研究和指南；②新型抗感染药物临床试验数据；③mNGS 等诊断技术临床应用研究。共纳入文献 18 篇，其中随机对照试验 8 篇、系统综述 3 篇、专家共识 5 篇、指南 2 篇。采用叙述性综述和网络 Meta 分析相结合的方法进行数据合成与分析。

结果 网络 Meta 分析显示，异伏立康唑治疗侵袭性曲霉病的有效反应率最高 (SUCRA 77.9%)，脂质体两性霉素 B 联合卡泊芬净在有效反应率和死亡率降低方面表现最佳 (SUCRA 分别为 84.1% 和 88.2%)。mNGS 在免疫功能低下患者疑似肺部感染中的诊断敏感性 (92.3%) 显著优于传统微生物检测方法 (65.7%)， $P < 0.05$ 。新型抗真菌药物 Rezafungin、Olorofim 和 Fosmanogepix 在临床试验中展现出良好的安全性和有效性，非唑类耐药菌株的治疗成功率达 73.5%。铜绿假单胞菌感染的联合治疗方案 (新型 β -内酰胺类/ β -内酰胺酶抑制剂+氨基糖苷类) 使临床治愈率提高至 68.4%。

结论 呼吸系统感染的治疗需结合先进诊断技术与个体化治疗方案，多学科协作是改善预后的关键。mNGS 技术在混合感染早期诊断中具有重要价值，新型抗感染药物为传统治疗失败患者提供了新的选择。未来研究方向应聚焦于精准医疗应用、免疫治疗探索及联合治疗优化。临床建议加强早期病原学检测、遵循指南选择一线药物、实施抗菌药物分级管理，并对难治性感染考虑联合治疗或新型药物应用。

【关键词】 呼吸系统感染；真菌感染；细菌感染；抗真菌药物；抗细菌药物；宏基因组二代测序；耐药性；治疗方案

菲氏军团菌肺炎 1 例并文献复习

刘丹 傅磊 张纯纯 葛书亚 沈磊 卞建军
蚌医二附院

目的 了解菲氏军团菌感染的临床特征，提高对菲氏军团菌感染的早期识别和诊治。

方法 报道本中心 1 例菲氏军团菌肺炎患者的诊疗经过，并以“菲氏军团菌”“军团菌”“*Legionella feeleii*”“*L. feeleii*”及“*Legionella*”为关键词，检索中国知网、维普、万方及 PubMed 数据库关于菲氏军团菌感染的文献病例报道，通过回顾性分析探讨其临床特征、诊断、治疗及预后。

结果 患者男性，68 岁，园艺工作者，因“确诊多发性骨髓瘤 4 年余，发热 4 天”入院，胸部 CT 示右下肺及左上肺炎症，外周血宏基因组二代测序 (mNGS) 检测出菲氏军团菌，确诊菲氏军团菌肺炎，同时继发噬血细胞综合征 (HPS)，给予莫西沙星、阿奇霉素抗感染，芦可替尼、地塞米松治疗 HPS，并人免疫球蛋白等支持治疗，患者病情好转。检索出符合条件的文献 11 篇，共 13 例病例，加上本病例，共纳入 14 例患者，其中男 8 例，女 6 例，中位年龄 62.5 (23~78) 岁；发病地区北美洲最常见为 6 例 (43%)，本病例为国内首次报道；近期使用激素、免疫抑制剂或接受化疗患者共 8 例 (57%)，其中血液系统恶性肿瘤患者共 6 例 (43%)，有 2 种及以上基础疾病或基础疾病合并外科手术或移植术患者有 7 例 (50%)；社区获得性感染来源 11 例 (79%)，感染来源未知 3 例 (21%)；最常见感染部位为肺部，共 11 例 (79%)；诊断方法有分离培养 9 例 (64%)，血清学检测 6 例 (42%)，基质辅助激光解吸电离-飞行时间质谱检测 (MALDI-TOF MS) 3 例 (21%)；分子学检测共 8 例 (57%)，其中 PCR 3 例 (21%)，16S rRNA 基因测序 2 例 (14%)，随机扩增多态性 DNA 标记 (RAPD) 2 例 (14%)，mNGS 1 例 (7%)。菲氏军团菌治疗以大环内酯类及喹诺酮类药物为主，单药治疗 8 例 (57%)，两药联合 3 例 (21.4%)；14 例患者中存活 10 例 (71%)，死亡 4 例 (29%)，存活患者的中位治疗疗程为 21 (11~43) 天。

结论 菲氏军团菌感染是一种罕见且病死率高的感染性疾病,在血液系统疾病及免疫功能低下患者中多发,病原学诊断十分重要,及时、足疗程抗感染治疗可提高生存率。

致肺部感染新型诺卡菌的鉴定、基因组分析及致病力研究

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目的 我们从一位患有慢性阻塞性肺病、糖尿病患者的胸水中获得 1 株未知的诺卡菌种,并对其进行系统的表型、生化特征鉴定,全基因组分析及致病力研究。

方法 采用形态学观察、染色及扫描电镜分析其细菌学特征;通过 API 20NE、API ZYM 及 API 50CH 系统及 Biolog 技术分析其生理生化特征;结合脂肪酸组成及呼吸醌类型进行化学分类学鉴定;利用全基因组测序构建系统发育树并开展比较基因组学分析;通过大蜡螟及小鼠感染模型评价其体内致病力。

结果 菌株 ZH-001T 呈革兰阳性、弱抗酸阳性,菌落表现为乳白至淡黄色、干燥粗糙、呈“咬琼脂”样特征。其具有较强环境适应能力和广泛碳源利用谱,酶学活性丰富。药敏显示其对多种药物不敏感,但对复方磺胺甲恶唑片和利奈唑胺敏感。脂肪酸以 C16:0、10-甲基 C18:0 及 C18:1 ω 9c 为主,呼吸醌以 MK-8(H4)为主型。基因组大小约 9.07 Mb, GC 含量为 68.3%。系统发育分析显示该菌株隶属于诺卡菌属,与 *Nocardia seriolae* 等近缘但形成独立分支。比较基因组学提示其具有大量特有基因区段及显著基因组重排。体内实验显示,与对照菌种相比, ZH-001T 在大蜡螟及小鼠模型中具有更高的死亡率,且可引起更严重肺部损伤,显示出更强的致病力。

结论 本研究鉴定出一株新的诺卡菌菌株 ZH-

001T,其在表型、生化特征及基因组水平上均具有独特性,并表现出较强致病潜能,提示其可能为临床重要的新型致病菌,为诺卡菌感染的诊断及治疗提供了新的依据。

一例截瘫患者脊柱截骨矫形术后暴发多部位多重耐药革兰阴混合感染的诊疗启示

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关键词: 截瘫患者;多重耐药革兰阴性杆菌感染;

目的 脊柱内固定术后感染是骨科手术中一种严重的并发症,尤其对于因外伤导致截瘫的患者,其风险显著增高。这类患者常因其神经源性膀胱、长期留置导尿管及免疫状态改变,成为医院获得性感染的高危群体,且临床表现常不典型,术后发生的感染严重影响疾病的预后与转归。本研究旨在探讨截瘫患者在接受复杂脊柱翻修术后暴发多部位、多重耐药革兰阴性杆菌感染的临床特点、诊疗挑战及管理策略。

方法 回顾性分析一例因胸椎骨折内固定术后二十余年、近八年内固定装置外露伴慢性感染的截瘫患者诊疗过程。在经历复杂的脊柱翻修手术后,爆发了多部位、多重耐药菌的严重感染。初始感染为手术部位的耐甲氧西林金黄色葡萄球菌(MRSA)感染,经治疗后一度稳定,但二次重大手术后迅速出现了泌尿系统的产超广谱 β -内酰胺酶肺炎克雷伯菌以及手术深部组织的多重耐药铜绿假单胞菌与产超广谱 β -内酰胺酶大肠埃希菌(MDR-GNB)的新发

感染。

结果 通过基于多部位（尿液、引流液、深部组织）微生物学证据的精准抗感染治疗，以及基于药敏结果将抗感染方案调整为美罗培南延长输注等多学科协作管理，并结合及时的外科清创，患者感染最终得到有效控制，脊柱后凸侧凸畸形明显矫正，无药物不良反应发生，最终治愈出院。

结论 本病例生动呈现了慢性感染、神经源性膀胱与重大手术应激共同作用下，截瘫患者发生内源性菌群易位及获得性多重耐药革兰阴性杆菌感染的极端风险。凸显了对于此类具有长期植入物、慢性感染史及神经源性膀胱的高危患者，在重大脊柱手术前后实施强化围手术期感染防控、主动多部位病原学监测以及精准目标治疗的重要性，为临床处理类似复杂感染提供了关键警示与治疗借鉴。

脂质体两性霉素 B 作为 CAR-T 后多发性骨髓瘤患者进展性侵袭性真菌感染的挽救治疗-个案报道

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背景 在 CAR-T 治疗后患者中管理真菌感染面临诸多复杂因素，包括严重的免疫抑制、有限的诊断工具、药物毒性以及持续存在或耐药的感染。尤其是在长期使用抗真菌药物后，进展性肺部疾病的治疗选择会进一步减少。

病例描述与结果

我们报告一例 50 岁男性患者，诊断为复发/难治性 IgG-κ 型多发性骨髓瘤，曾接受多线化疗、CAR-T 治疗及 PD-1 抑制剂维持治疗。在 CAR-T 治疗后，患者疑似合并真菌感染；检测到念珠菌属，并接受伏立康唑治疗。

出院后，患者继续口服伏立康唑治疗超过两个月。在此期间，患者反复出现发热和咳嗽，肺部病变

逐渐加重。再次入院后，胸部计算机断层扫描（CT）显示双肺多发结节、斑片状浸润影及实变区，尽管接受了长期唑类药物，影像学仍显示疾病进展。支气管肺泡灌洗液培养结果为阴性，血清半乳甘露聚糖和 β-D-葡聚糖检测也均为阴性，而痰涂片检查发现真菌孢子。患者最初继续使用伏立康唑，但出现了显著的神经精神毒性，因此治疗方案更换为静脉输注脂质体两性霉素 B 联合雾化吸入两性霉素 B。患者表现出快速的血流动力学稳定、咯血症状缓解、精神状态改善以及呼吸功能逐步恢复。血管活性药物支持治疗顺利停用。随访胸部 CT 显示双肺多发结节及浸润影明显消退。影像学改善情况见图 1。

结论 本病例突显了在 CAR-T 治疗后患者中抗真菌管理的复杂性，该患者同时合并脓毒症、真菌感染的诊断局限性以及长期伏立康唑暴露。伏立康唑相关的神经精神毒性进一步限制了这位危重患者的治疗选择。在这一具有挑战性的临床情境下，早期启用脂质体两性霉素 B 提供了有效的挽救治疗，带来了快速的临床稳定和影像学改善，突显了其在复杂和难治性真菌感染中的重要性。

临床药师参与一例肺诺卡菌病合并多种基础疾病患者的药学监护

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目的 通过对一例肺诺卡菌合并多种基础疾病患者的抗感染治疗经过进行分析，探讨临床药师在抗感染治疗及不良反应处理中个体化药学服务的作用，为临床合理用药提供参考。

方法 回顾性分析临床药师全程参与一例肺诺卡菌合并多种基础疾病患者的抗感染治疗过程，抗感染过程中患者先后出现肝功能、电解质异常，临床药师参与临床会诊，提出个体化用药建议，并监护患者的疗效和不良反应。

结果 患者女, 64 岁, 因“咳嗽 3 月余, 气促 2 月”入院, 胸部 CT 显示右肺中叶实变影, 经肺泡灌洗液 tNGS 检测确诊为肺诺卡菌感染, 结合循证资料, 临床初始经验性使用磺胺甲恶唑、亚胺培南西司他丁联合治疗, 复查肝功提示转氨酶等几项肝功能指标较前轻度升高。临床药师、消化内科会诊考虑药物性肝损伤可能, 根据药物不良反应关联性评价, 患者肝功能异常可能由磺胺甲恶唑、亚胺培南西司他丁引起, 综合患者情况, 建议将亚胺培南西司他丁改为阿米卡星, 后随访肝酶仍无明显改善, 并加用降酶类药物保肝治疗, 故予以磺胺甲恶唑减量, 肝酶稍好转, 但出现血钾值持续升高, 再次根据药物不良反应关联性评价, 患者血钾异常很可能由磺胺甲恶唑引起, 故停用磺胺甲恶唑, 患者呼吸道症状较前好转, 有出院意愿, 建议调整为米诺环素及阿莫西林克拉维酸钾联合治疗, 持续监测肝肾功、电解质水平。随访至今, 患者各项功能指标均较前明显好转。

结论 临床药师深度参与该患者抗感染治疗过程, 通过查阅指南和相关文献, 协助医生查找指标异常原因, 共同制定治疗方案并实施药学监护, 确保临床药物治疗效果, 保障患者用药安全, 为患者提供高质量的药学服务。

关键字: 磺胺甲恶唑; 亚胺培南西司他丁; 肺诺卡病; 不良反应; 药学监护

Tuberculosis Co-infection of Patients with Severe Fever with Thrombocytopenia Syndrome

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Background Severe fever with thrombocytopenia syndrome (SFTS) is an emerging infectious disease

characterized by fever, thrombocytopenia, gastrointestinal symptoms, and central nervous system manifestations. SFTS complicated by pulmonary infection can lead to further immunosuppression, increasing the risk of secondary *Mycobacterium tuberculosis* infection

Case Report: An 82-year-old female was admitted to the hospital with diarrhea and poor appetite. Laboratory tests revealed leukopenia and thrombocytopenia, and her nucleic acid test for the SFTS virus was positive, confirming a diagnosis of SFTS. The patient also presented with multi-organ damage (heart, liver, and kidneys) and pulmonary infection. *Mycobacterium tuberculosis* (Mtb) was detected by next-generation sequencing (mNGS) of bronchoalveolar lavage fluid. The patient was successfully recovered with antiviral and anti-infective therapies.

Conclusion The secondary Mtb infection should be considered in SFTS patients with pulmonary infection. Next-generation sequencing of pathogens facilitates early diagnosis and aids in formulating appropriate treatment strategies.

Catheter-Associated *Trichosporon Japonicum* Fungemia in A Patient with Diffuse Large B-Cell Lymphoma Following CAR-T Cell Therapy: A Case Report and Literature Review

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Background *Trichosporon japonicum* is a rare but highly lethal pathogen causing fungemia in im-mun-

ocompromised patients. With the expanding use of chimeric antigen receptor T (CAR-T) cell therapy, the spectrum of opportunistic fungal infections is changing, yet data on *T. japonicum* infections in this setting remain scarce

Case presentation: A 69-year-old man with diffuse large B-cell lymphoma developed catheter-associated fungemia after CAR-T cell reinfusion. He initially presented with neck pain and white oral mucosal patches, followed by fever four days later. *T. japonicum* was isolated from both peripheral blood and central venous catheter tip cultures, identified by microscopic examination, mass spectrometry, and molecular sequencing. Antifungal prophylaxis was initiated before fever onset based on close monitoring of white blood cell count, procalcitonin, interleukin-6, and C-reactive protein; treatment was subsequently adjusted according to species identification and antifungal susceptibility results. Infection was controlled within two weeks after catheter removal and immune recovery. The patient remained well at six-month follow-up

Conclusion This case adds to the limited literature on *T. japonicum* fungemia in patients receiving CAR-T therapy. Our experience, together with a review of the literature, underscores that successful management requires prompt catheter removal, immune restoration, and combination therapy with voriconazole and amphotericin B, as echinocandin monotherapy should be avoided. Awareness of this pathogen in immunocompromised patients is critical.

Key Words: *Trichosporon japonicum*, CAR-T cell therapy, catheter-related fungemia, voriconazole, amphotericin B

复杂尿路感染导致脓毒性休克合并对称性外周坏疽 1 例救治

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本文报道一例中年女性患者因大肠埃希菌感染引起多器官功能衰竭导致脓毒性休克(Septic Shock)、弥散性血管内凝血(Disseminated Intravascular Coagulation, DIC)及对称性外周坏疽(Symmetrical Peripheral Gangrene, SPG)的救治过程,并探讨 SPG 的病理机制。患者以腹痛发热起病,入院时存在严重内环境紊乱及多器官功能障碍,病原学检查证实为大肠埃希菌感染,影像学提示输尿管结石,入院行液体复苏与血管活性药物支持,急诊解除梗阻,联合抗感染;进展期出现血小板进行性下降及凝血功能紊乱,患者入院时存在四肢花斑,后发展为四肢末端紫绀、肿胀,最终形成湿性坏疽,此外患者存在急性肝、肾功能衰竭,经连续性肾脏替代治疗(Continuous Renal Replacement Therapy, CRRT)及双重血浆分子吸附系统(Double Plasma Molecular Adsorption System, DPMAS)支持;恢复期炎症指标逐步正常化,但遗留肢体缺血性损害,术后 1 年随访患者分次手术切除坏疽部分。面对同步发生的肝衰竭、肾衰竭及代谢性酸中毒,单一器官支持难以破局,团队联用 CRRT 与 DPMAS 实现肝、肾功能同步逆转,即使经历多器官衰竭与严重肢体坏死,通过感染源根除、个体化器官支持及创面管理,患者后期回访恢复较好,此类报道较少,微循环障碍、DIC 及血管活性药物等共同导致末梢灌注衰竭,提示液体复苏的关键,感染性休克患者需早期评估肢体灌注。

1 例胆肠吻合术后复发胆总管结石患者抗感染治疗引起药物热、白细胞减少的病例分析

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目的 分析 1 例胆肠吻合术后复发胆总管结石患者使用注射用哌拉西林钠他唑巴坦钠抗感染治疗后引起药物热、白细胞减少的病例,为临床胆肠吻合术后复发胆总管结石抗感染治疗提供参考。

方法 临床药师回顾性分析 1 例胆肠吻合术后复发胆总管结石患者抗感染,开腹左肝部分切除、胆总管切开取石、胆肠吻合口重建等的治疗方案。

结果 该患者因“20 天前无明显诱因右上腹疼痛,1 周前出现全身皮肤巩膜黄染”入院治疗,其既往有开腹胆管结石取石术、胆肠吻合术。入院检查显示:白细胞计数 $5.46 \times 10^9/L$,中性粒细胞百分比 84.8%,丙氨酸氨基转移酶 ALT 122U/L,总胆红素 $74.1 \mu\text{mol/L}$,直接胆红素 $63.5 \mu\text{mol/L}$,间接胆红素 $10.6 \mu\text{mol/L}$ 。入院即予给予注射用哌拉西林钠他唑巴坦钠 4.5g+0.9%NS 100ml 静滴 Q8H 抗感染治疗。入院第 12 天行“开腹左肝部分切除、胆总管切开取石、胆肠吻合口重建术”,手术历时 4 小时 55 分。期间腹部术区切口周围轻压痛,棉垫纱布敷料覆盖,少量渗血渗液。第 27 天,患者下午出现发热,体温 38.8°C ,脉搏 95 次/分。第 28 天下午体温 38.9°C ,脉搏 102 次/分。第 29 天患者白细胞计数 $2.90 \times 10^9/L$,停用注射用哌拉西林钠他唑巴坦钠。第 30 天患者无发热、畏寒情况出现。第 33 天复查血常规,白细胞计数 $5.88 \times 10^9/L$ 。

结论 胆肠吻合术后易诱发吻合口狭窄、胆管感染,在胆肠吻合术后复发胆总管结石选择抗菌药物治疗时,要考虑可覆盖的致病菌,避免不合理使用抗菌药物,例如品种选择不合理、用法用量不合理、盲目联用或盲目更换品种、疗程过长等应用,以减少药物不良反应的发生。

1 例肝肾功能不全患者机械瓣膜置换术后脓毒血症的抗感染治疗方案分析

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目的 分析 1 例肝肾功能不全患者机械瓣膜置换术后脓毒血症的抗感染治疗方案,为临床肝肾功能不全患者机械瓣膜置换术后脓毒血症的抗感染治疗提供参考。

方法 临床药师回顾性分析 1 例肝肾功能不全患者机械瓣膜置换术后脓毒血症的抗感染治疗方案。

结果 该患者因“体检发现心脏瓣膜异常 11 年,活动后心悸、胸闷 1+月”住院治疗。入院第 22 天行“胸腔镜下二尖瓣机械瓣膜置换+三尖瓣瓣环成形+左房折叠+股动静脉插管术”。第 23 天予“注射用头孢唑林钠 2g ivgtt q8h”预防感染,行“可视喉镜下行气管插管术”,抢救 1 次并成功。第 24 天,患者间断发热, T 38.9°C ,双肺呼吸音稍粗糙,右下肺呼吸音稍低,双下肺可闻及少量散在湿性啰音(WBC $12.99 \times 10^9/L$, N% 91.8%, CRP 266.33mg/L, e-PCT 0.55ng/ml, AST 82U/L, TBIL $26.6 \mu\text{mol/L}$, DBIL $8.6 \mu\text{mol/L}$, Cr $88 \mu\text{mol/L}$)予“注射用哌拉西林钠他唑巴坦钠 4.5g 泵入 q8h”抗感染,当日 22:58 患者心率增快达 178 次/分。第 25 天,患者仍发热, T 38.9°C ,抢救一次,更换为“注射用美罗培南 1g 泵入 q8h”抗感染。第 28 天,患者间断发热, T 39.4°C ,痰培养:产气肠杆菌,对美罗培南敏感。血培养革兰染色:革兰氏阴性杆菌。第 29 天,加用“注射用盐酸万古霉素 0.5g 泵入 q8h”抗感染。D33 病情改善,痰液减少,拔除气管插管。第 39 天,患者体温正常,炎症指标较前下降,停用万古霉素。第 45 天,患者一般情况可,予出院。

结论 患者抗感染治疗方案的调整依赖多种指标,药师应配合医师加强药学监护,促进临床合理用药。

关键词: 肝肾功能不全,脓毒血症,美罗培南,万古霉素,药学监护

1 例鹦鹉热衣原体肺部感染患者发生肝功能损害的治疗方案分析

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目的 分析 1 例鹦鹉热衣原体肺部感染患者发生肝功能损害的治疗方案，为临床鹦鹉热衣原体肺部感染患者发生肝功能损害的治疗提供参考。

方法 临床药师回顾性分析 1 例鹦鹉热衣原体肺部感染患者发生肝功能损害的治疗方案。

结果 该患者因反复发热 3 天入院，Tmax 39.4℃，伴畏寒、乏力。于外院予“阿莫西林克拉维酸钾、莫西沙星、布洛芬”等治疗后无好转，后转入我院继续治疗。入院后持续发热，确诊左上肺感染。在入院后辅查体温和炎症指标均升高（WBC 7.67×10⁹/L、N% 91.2%、LY% 5%、CRP 151.68mg/L、ESR 60mm/h、IL-6 64.1 pg/mL），肝、肾功能检查均正常（ALT 26U/L、AST 27U/L），给予莫西沙星氯化钠 0.5g ivgtt Qd 抗感染治疗。D4 患者仍发热 Tmax 39.4℃，伴咳嗽、咳白色粘痰，发热时仍感畏寒，遂更改抗感染治疗方案在莫西沙星基础上加用哌拉西林-他唑巴坦 4.5 g ivgtt q8h 联合治疗。D5 行支气管肺泡灌洗液（BALF）tNGS 回报：鹦鹉热衣原体（序列 31），追问患者病史确认家中饲养鸽子，在此期间复查肝功能出现 ALT 209U/L 升高，停用莫西沙星氯化钠注射液、哌拉西林他唑巴坦，换用盐酸多西环素肠溶胶囊 0.1g po Q12h 抗感染治疗。D6：加用谷胱甘肽 1.8g qd 联合双环醇片 25mg Po Tid 护肝对症治疗好转，D14 患者一般情况可，出院。出院后予多西环素肠溶胶囊序贯治疗，两周后复查炎症指标 CRP 2.56mg/L 恢复正常，一个月后复查肝功能 ALT 35U/L、AST 26U/L 恢复正常。

结论 对于不明原因引起的发热应详细询问禽类接触史，尽早行病原学检测，制定有效的方案，早期诊断和精准抗感染治疗是改善预后的关键。

关键词：鹦鹉热衣原体，肝功能损害，支气管肺泡灌洗，莫西沙星，多西环素

Infective Endocarditis Caused by *Phialemonopsis Curvata*: A Case Report

null null

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Phialemonium spp. are ubiquitous environmental opportunistic pathogenic fungi that cause invasive infections in both immunocompetent and immunocompromised hosts. To date, no cases of infective endocarditis caused by *Phialemonopsis curvata* have been reported.

We report the case of a 57-year-old man who underwent bilateral nephrectomy 18 years prior for end-stage renal disease and has since been on regular maintenance hemodialysis. Three months before presentation, he underwent transcatheter aortic valve implantation (TAVI) for severe aortic regurgitation. He presented with acute non-ST-segment elevation myocardial infarction complicated by third-degree atrioventricular block, for which he underwent percutaneous coronary intervention (PCI) and permanent pacemaker implantation. Postoperatively, two consecutive transthoracic echocardiography (TTE) examinations revealed suspicious vegetations on the prosthetic aortic valve, and abdominal computed tomography showed possible partial splenic infarction. Empirical antibacterial therapy yielded no significant clinical improvement and blood cultures grew only filamentous fungi, but matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) failed to identify the isolate to the species level. Two peripheral blood samples were then tested by probe capture-based targeted

next-generation sequencing, and both detected *Phialemoniopsis curvata*. Combination antifungal therapy with isavuconazole and amphotericin B liposome was initiated immediately, but the patient's condition deteriorated rapidly, and he died of multiple organ failure one week after treatment initiation.

This case demonstrates that in patients with prosthetic valve endocarditis who fail conventional antibacterial therapy, clinicians should maintain a high index of suspicion for fungal infections, especially those caused by rare pathogens. Early integration of multiple etiological diagnostic methods to identify the causative organism is essential to optimize treatment and improve patient outcomes.

鼻眶脑毛霉病 1 例病例报道

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鼻眶脑毛霉病(ROCM)是由毛霉目真菌引发的罕见侵袭性真菌感染,以血管侵袭和组织坏死为特征,致死率 50%-80%,全球发病率上升。糖尿病酮症酸中毒(DKA)是主要危险因素,该病临床表现缺乏特异性,早期诊断难,未及时治疗会导致死亡。本研究报道 1 例 60 岁 2 型糖尿病女性患者因 DKA 入院后并发 ROCM 的诊疗过程,以加深临床认知。患者有 10 余年 2 型糖尿病史,血糖控制不佳。20 天前因 DKA 住院确诊口腔真菌感染,本次因“呕吐伴全身乏力 1 天”入院,血糖高、尿酮体 3+、代谢性酸中毒,合并多种感染及电解质紊乱,头部 CT 有异常。入院后对症治疗病情仍进展,怀疑真菌感染,调整抗感染方案并完善检查,经脑脊液二代测序(NGS)确诊德氏根霉感染,明确为侵袭型真菌性鼻-眶-脑毛霉病。确诊后予两性霉素 B 脂质体治疗,建议联合泊沙康唑及手术清除坏死组织被

家属拒绝,患者病情恶化死亡。病例分析表明,ROCM 诊断需结合多方面,NGS 对毛霉菌感染有诊断优势。治疗上,控制基础疾病是前提,早期足量用两性霉素 B 脂质体是核心,外科清创改善预后重要。本病例提示,临床医生对 DKA 患者,尤其是有真菌感染史、感染加重及眼眶、颅内受累症状时,需警惕 ROCM。同时,医患沟通和患者依从性影响治疗实施,加强疾病科普不可忽视。

细菌抗噬菌体机制及对抗菌药物敏感性影响的研究进展:联合应用的前景与挑战

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多重耐药菌的全球传播与新型抗菌药物研发滞后的矛盾日益突出,亟需研发新型抗感染策略。噬菌体疗法因其独特的抗菌机制重新成为研究热点,但细菌对噬菌体抗性的产生限制了其临床应用。近年研究发现,细菌获得噬菌体抗性常伴随抗菌药物敏感性的改变,二者之间存在复杂的权衡效应与调控关联,为噬菌体-抗菌药物联合应用提供了关键理论基础。本文系统综述了细菌抗噬菌体防御机制的研究进展,包括吸附抑制、DNA 降解、细胞壁改变等先天防御系统,CRISPR-Cas、BREX、retron 等适应性免疫系统,以及群体感应、原噬菌体诱导等群体水平协同防御策略。在此基础上,重点分析了噬菌体抗性对抗菌药物敏感性的影响机制,主要表现为敏感性增强(如代谢负担权衡、细胞膜通透性改变、毒力-抗性权衡),同时也存在敏感性降低(如外排泵上调、生物膜增强、耐药基因水平转移)可能。进一步总结了噬菌体-抗菌药物联合应用的体外协同效应、临床个案治疗成功案例及初步临床试验进展。尽管联合应用策略展现出良好前景,但仍面临抗性进化复杂、制剂稳定性差、给药技术受限、法规体系不完善及高质量循证证据缺乏等挑战。未来通

过基因工程改造噬菌体、开发新型递送系统、推进多中心临床试验及建立统一法规框架,有望推动该联合策略成为应对多重耐药菌感染的常规防治手段,为遏制多重耐药菌的传播提供新的解决方案。

糖尿病血糖控制不佳患者肺部多重病原体感染病例报告

侯杰

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目的 探讨合并糖尿病等基础疾病患者多重病原体肺部感染的临床特点、诊断及治疗策略,为类似病例提供诊疗参考。

方法 分析名 74 岁合并 2 型糖尿病伴血糖控制不佳、冠状动脉粥样硬化性心脏病及既往慢性阻塞性肺部疾病的男性患者的临床资料及诊疗策略。

结果 患者主诉“咳嗽咳痰 20+天”,入院查体示桶状胸,右下肺呼吸音粗伴少许湿性啰音,无其它明显异常。胸部 CT 提示右肺中下叶见斑片影、磨玻璃影、片状实变影,右肺下叶病灶内见空洞形成,双肺散在小结节及少许慢性炎症。痰及肺泡灌洗液培养多次检出微孢根霉和白色念珠菌。常见 13 种呼吸道病原菌核酸、肺孢子菌核酸、结核杆菌核酸、结核感染 T 细胞 γ 干扰素释放试验、隐球菌抗原、血清 G 和 GM 试验均阴性,念珠菌 IgG 抗体阳性,肺泡灌洗液 GM 试验阳性。肺泡灌洗液 tNGS 检出粪肠球菌、流感嗜血杆菌、白色念珠菌、微孢根霉与烟曲霉等序列。该患者诊断为侵袭性肺曲霉病、肺毛霉病(微孢根霉)、念珠菌肺炎、细菌性肺炎(粪肠球菌、流感嗜血杆菌)及右肺脓肿。经美罗培南、哌拉西林钠他唑巴坦钠抗感染,氟康唑、艾沙康唑抗真菌,联合祛痰、降糖治疗后,患者症状明显改善,体征平稳,顺利出院。出院后予艾沙康唑继续抗真菌、规律降糖治疗及定期复查。

结论 糖尿病伴血糖控制不佳患者易发生真菌

与细菌混合多重肺部感染,结合影像学、痰培养和 tNGS 等病原学检测明确诊断,采用目标抗感染治疗,同时强化基础病管理,是改善患者预后的关键。

凉膈散对 LPS 诱导的急性肺损伤的保护作用及其机制

于鑫

武警特色医学中心

探讨凉膈散(LGS)对脂多糖(LPS)诱导的急性肺损伤(ALI)的保护作用,并阐明其作用机制。**方法:**将 40 只雄性的 C57BL/6 小鼠随机分为假手术组、模型组、低剂量 LGS 组和高剂量 LGS 组,每组 10 只。诱导建立 ALI 模型,造模 24 h 后取材。采用 HE 染色法观察各组小鼠肺组织病理形态表现并进行病理评分,流式细胞术检测各组小鼠肺组织中中性粒细胞和肺泡上皮细胞百分率,免疫组织化学染色法检测各组小鼠肺组织中髓过氧化物酶(MPO)水平,酶联免疫吸附试验(ELISA)法检测各组小鼠肺泡灌洗液中相关炎性介质白细胞介素 18(IL-18)、白细胞介素 1 β (IL-1 β)和白蛋白水平,Western blotting 法检测各组小鼠肺组织中高迁移率族蛋白 B 1(HMGB1)、NLR 家族 Pyrin 域蛋白 3(NLRP3)、含半胱氨酸的天冬氨酸蛋白水解酶 1(Caspase-1)和消皮素 D(GSDMD)蛋白表达水平。**结果:**HE 染色,与 SHMA 组比较,LPS 组小鼠肺组织病理损伤加重,病理评分明显升高($P<0.05$);与 LPS 组比较,LGSL 组和 LGSH 组小鼠肺组织病理学评分明显降低($P<0.05$)。流式细胞术,与 SHMA 组比较,LPS 组小鼠肺组织中中性粒细胞百分率明显升高($P<0.05$),肺泡上皮细胞百分率明显降低($P<0.05$);与 LPS 组比较,LGSL 组和 LGSH 组小鼠肺组织中中性粒细胞百分率明显降低($P<0.05$),肺泡上皮细胞百分率明显升高($P<0.05$)。**结论:**LGS 可通过降低中性粒细胞浸润和上皮

细胞焦亡以减轻 LPS 诱导的病理肺损伤和炎症反应，其机制可能与其通过 HMGB1 信号通路下调 NLRP3、Caspase-1 和 GSDMD 蛋白表达有关。

剂；16S rRNA 基因测序

肠源性耐碳青霉烯类大肠埃希菌致硬膜下脓肿病例报告

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背景 硬膜下脓肿是发生在硬脑膜与蛛网膜之间的化脓性感染，是一种罕见且危及生命的颅内感染。成人多继发于邻近化脓性病灶，通常由邻近鼻窦或中耳感染直接蔓延所致，也可由开放性颅脑损伤、颅脑术后感染、硬膜下血肿感染、面部感染、咽部感染、脑内脓肿破裂以及帽状腱膜下感染等引起，偶见于各种原因引起的血源性感染。致病菌以链球菌、葡萄球菌等多见，因耐碳青霉烯类大肠埃希菌通过肠道细菌易位而引发的硬膜下脓肿极为罕见，机制尚不明确。

病例介绍：本文报道一例 82 岁老年男性，胃癌根治术后长期接受免疫检查点抑制剂帕博利珠单抗治疗，发生免疫相关性肠炎，导致肠道屏障破坏及肠内菌群失调，进而继发耐碳青霉烯类大肠埃希菌菌血症及左侧额颞部硬膜下脓肿，血液及脓肿引流液培养为耐碳青霉烯类大肠埃希菌，患者接受两次颅脑钻孔引流术并联合针对性抗生素治疗后好转。免疫相关性肠炎通过破坏肠道屏障和诱发肠道菌群失调，可能促进耐药菌发生肠道易位，引发菌血症及颅内播散感染。临床应警惕免疫治疗患者的不典型硬膜下病变，早期进行综合抗感染及外科治疗，并关注肠道菌群恢复。

关键词：硬膜下脓肿；耐碳青霉烯类大肠埃希菌；新德里金属 β -内酰胺酶-1 型；免疫检查点抑制

其他微生物及其感染

被忽视的肺诺卡菌 2 例

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本文报道了 2 例肺诺卡菌病。2 例病例均有咳嗽、发热的临床表现，肺部 CT 呈现多形性病变(渗出、实变、空洞)，早期被误诊为肺结核。因支气管肺泡灌洗液培养和第二代宏基因测序，才明确诊断。通过抗诺卡菌治疗，患者病情已明显好转。本文旨在强调纵使典型临床表现和肺部影像学特征及抗酸染色阳性也不能确诊为肺结核，应重视病原学培养和菌种鉴定结果，避免误诊误治。诺卡菌病临床上没有特异性的诊断指标。咳嗽和发热是两个主要症状。诺卡菌病肺部影像学表现多样，以结节影、实变影及空洞多见，部分病例可合并胸腔积液或胸膜增厚，与肺结核、侵袭性真菌病甚至肺癌的影像学重叠率较高，误诊率高达 60%以上。本文报道 2 例患者肺部 CT 表现为双肺多形性病变（渗出、实变、空洞和结节影），尤其是第一例皮疽诺卡菌感染患者，其支气管肺泡灌洗液抗酸染色阳性，病初误诊为肺结核。诺卡菌最主要的特点是革兰染色形态及弱抗酸性，也是临床拟诊诺卡菌感染的重要依据。但部分菌种抗酸染色可呈现阳性。本文报道的皮疽诺卡菌感染病例，其抗酸染色和弱抗酸染色均为阳性，极易与结核或非结核分枝杆菌混淆。而蒴烯诺卡菌抗酸染色为阴性，弱抗酸染色为阳性。因此不能仅凭借肺部 CT 和抗酸染色的结果做出肺结核的诊断。总之，诺卡菌感染的诊治需综合临床表现、影像学及分子生物学技术，早期精准识别病原体并个体化调整抗菌方案是改善预后的关键。未来应加强耐药监测与新型治疗策略研究，以应对日益复杂的感染挑战。

1 例免疫缺陷合并皮肤结核患者诊疗过程分析

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目的 通过对一例经典案例的分析，讨论对于有免疫缺陷合并感染患者，在治疗过程中需要注意的几个关键因素：原发病控制情况、免疫制剂导致的免疫缺陷、药物相互作用，综合制定疾病的诊疗方案。

案例：患者 51 岁男性，基础“类风湿性关节炎、干燥综合征、周围神经病”史，规律服用泼尼松 5mg bid、托法替布治疗。入院前半月患者出现全身皮疹，初为红色团块结节样皮疹，后进展为脓疱、破溃流脓、溃疡，伴高热，完善皮损组织活检，示抗酸杆菌：检出 1+；MetaNGS：结核分枝杆菌复合群，诊断“皮肤结核”，予“异烟肼+利福平+乙胺丁醇+吡嗪酰胺”抗感染等治疗无改善，出现左侧肘部阵发性刀割样疼痛，吗啡镇痛无改善，出现双眼视力减退，为葡萄膜炎。后续调整方案为莫西沙星+利奈唑胺+利福平+乙胺丁醇+吡嗪酰胺抗结核，甲泼尼龙 40mg QD 抗炎。患者体温降至正常，无再发热，皮疹逐渐消退、结痂，左手肘疼痛改善，双眼充血及视力改善。

讨论：1、皮肤结核治疗方案：“皮肤结核（大疱-坏死溃疡型）”诊断明确，予异烟肼+利福平+乙胺丁醇+吡嗪酰胺抗结核治疗效果不佳，需考虑①耐药结核；②合并全身播散性结核、浆膜腔结核；③免疫重建炎症综合征；④合并 NTM 等其他病原菌感染。考虑患者为耐药结核，且合并周围神经病变，停用异烟肼，加用莫西沙星、利奈唑胺，联合利福平+乙胺丁醇+吡嗪酰胺抗结核治疗。2、托法替布与结核感染：患者 RD、SS 病史，使用托法替布（JAK 抑制剂）治疗，导致严重感染。使用托法替布的 RD 患者，可进行结核分枝杆菌潜伏感染筛查及结核病预防性治疗。3、糖皮质激素的使用：该患者为继发性肾上腺皮质功能减退、双眼葡萄膜炎及类风湿性

关节炎活动期，予甲泼尼龙 40mg qd 抗炎治疗。且利福平为 P450 强诱导剂，会加快糖皮质激素的代谢，降低其血药浓度。因此在该患者使用利福平抗结核治疗期间，糖皮质激素使用剂量及疗程需相应的增加。4、周围神经病变：该患者入院时有左侧肘部阵发性刀割样疼痛，肌电图提示上下肢周围神经损害（运动、感觉纤维均受累，轴索髓鞘均损害，轴索损害为主，双侧尺神经严重损害），提示周围神经病变所致尺神经炎，神经损伤程度重，考虑类风湿性血管炎所致周围神经病变，予甲泼尼龙 40mg qd 抗炎及营养神经治疗，患者左肘疼痛明显改善。

分层递进法在临床真菌学检验医师规范化培训中的应用

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传统的临床真菌学检验医师规范化培训模式以讲授为主，未能充分考虑住院医师知识水平和技能的差异，导致学习参与度和动力不足。分层递进教学法根据住院医师的能力、兴趣和需求，将其分为初级、中级和高级三个层次，并分别设定针对性的教学目标：初级层侧重基础知识与基本技能的掌握；中级层强调真菌培养、鉴别及药敏试验的独立操作；高级层聚焦复杂实验设计、科研能力与学术写作的提升。该教学法结合讲授、示范、案例教学和实验设计等多种教学手段，同时通过调整作业与考核形式，从基础实验记录到科研论文撰写，逐步实现能力评估的深度递进。为深入评估分层递进教学法的应用效果，对研究组采用分层递进教学法的培训效果与对照组进行系统性、多维度对比分析，重点比较两组在理论知识、实践能力、案例分析、创新思维、教学内容满意度及师生互动满意度等方面的表现。实践评估显示，研究组住院医师在理论测试、实验操作、案例分析及教学满意度等多个方面均显著优于

对照组。此外，通过引入教学反馈与改进机制，以及导师制度的实施，进一步增强了师生互动效果和个性化指导水平。分层递进教学法显著提升了住院医师的学习效果和综合能力，为临床真菌学领域的人才培养提供了有力支持，并为检验医学教学领域的改革和创新提供了参考。

关键词：分层递进教学法；临床真菌学；检验医师；规范化培训；师资建设

Mixed Infection with Multiple Bacteria and Microsporidia (*Enterocytozoon Bieneusi*) in A Post-Renal Transplant Patient: A Case Report

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Background Microsporidia are genetically diverse, obligate intracellular pathogens that are challenging to diagnose due to their resistance to conventional culture methods. *Enterocytozoon bieneusi* is a primary cause of microsporidiosis, particularly in immunocompromised individuals. This report details a complex case of mixed bacterial and microsporidial infection in a renal transplant recipient, highlighting the utility of advanced molecular diagnostics

Case presentation: A 37-year-old male with a 16-year history of renal transplantation presented with recurrent high fever, chills, and hematochezia. Initial workup revealed severe anemia, thrombocytopenia, and acute kidney injury. Blood cultures grew ESBL-producing *Escherichia coli* and *Klebsiella pneumoniae*. CT imaging suggested a duodenobiliary fistula. Due to persistent fever despite broad-spectrum antibiotics, metagenomic next-generation sequencing (mNGS) was performed, identifying *E. bieneusi* (185 reads) alongside multiple bacteria and viruses. Treatment was adjusted to

include meropenem, daptomycin, and albendazole, with careful modulation of immunosuppression. The patient subsequently tested positive for SARS-CoV-2 but showed significant clinical improvement with the adjusted regimen and was discharged after 24 days

Conclusion This case underscores the diagnostic value of mNGS in identifying rare, opportunistic pathogens in immunocompromised hosts. Successful management requires a multidisciplinary approach, combining targeted antimicrobial therapy, immunomodulation, and aggressive supportive care.

亚欧人群饮食差异与艰难梭菌感染风险的关联

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摘要：艰难梭菌感染（CDI）是医院获得性腹泻的主要病因之一，可导致严重感染性结肠炎甚至死亡，已成为全球公共卫生领域的重要挑战。除抗生素暴露外，饮食作为重要的可调控因素，近年来被认为在 CDI 的发生与转归中发挥关键作用。尤其是亚欧人群膳食模式的差异-以高脂、高蛋白、低膳食纤维为特征的“西方饮食”与富含膳食纤维的东方饮食，可能通过多层机制影响 CDI 风险。高脂低纤维饮食可通过改变胆汁酸代谢，增加促进艰难梭菌孢子萌发的初级胆汁酸，同时减少具有抑制作用的次级胆汁酸，从而增强其定植与生长能力。同时，该饮食模式还可降低肠道菌群多样性，削弱“定植抗性”，为艰难梭菌提供竞争优势。从菌体代谢角度看，艰难梭菌具有显著的营养适应能力，其通过 Stickland 反应利用脯氨酸、甘氨酸等氨基酸进行发酵以获取能量，高蛋白饮食可增加相关底物供给，从而促进菌体增殖及潜在毒力表达。相比之下，富含微生物群可及性碳水化合物的高纤维饮食可被肠道菌群发

酵生成短链脂肪酸。其中，丁酸在 CDI 中呈现双向调控作用：既可改善肠屏障功能并减轻炎症反应，又在特定条件下可促进孢子形成及毒素释放，提示其对艰难梭菌代谢与毒力调控具有复杂影响。此外，饮食相关微量营养素亦参与调节菌体行为，例如高锌摄入与疾病严重程度及复发风险增加相关，而钙、硒等元素可能影响孢子形成过程。某些可发酵碳源（如蔗糖或特定食品添加剂）还可通过改变肠道代谢环境或被特定菌株利用，从而增强其定植能力与代谢适应性。综上，亚欧饮食差异可通过影响胆汁酸谱、营养底物供给及肠道微生态结构，进一步调控艰难梭菌的代谢策略、毒力表达及环境适应能力，形成“饮食-代谢-毒力”调控轴，从而影响 CDI 的发生与结局。未来研究需结合多组学技术与临床干预研究，系统解析该调控网络，为 CDI 的精准预防与个体化治疗提供新的理论基础。

关键词：艰难梭菌感染；饮食差异；胆汁酸代谢；Stickland 反应；短链脂肪酸；肠道微生物

新冠病毒与细小病毒 B19 共感染致溶血危象及多脏器衰竭一例

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目的 新型冠状病毒（SARS-CoV-2）感染可诱发多种血液学异常，尤其在有慢性溶血性贫血基础病的患者中，易导致溶血危象。然而，当此类患者同时暴露于其他病原体时，溶血危象的病因可能呈现叠加性与复杂性，单一归因于新冠病毒易造成误诊和漏诊。本文报道一例有慢性溶血性贫血病史患者，在新冠病毒感染基础上共感染细小病毒 B19，最终表现为急性溶血危象继发多脏器功能衰竭的诊治，旨在提高临床医生对多重病原体共感染背景下溶血

危象的识别与综合诊治能力,避免单一病因思维定势,优化临床决策。

病例介绍:患者男,26岁,因“发热伴恶心、呕吐1天”就诊与我院感染科发热门诊。患者2026-1-19发热,Tmax 39℃,伴呕吐、腹泻,无咽痛、咳嗽、咳痰。就诊于外院血常规示WBC 14.39、HGB 93、PLT 312、CRP 24、TBil 75.8、DBil 13、IBil 62.1、肾功能可,予以补液、退热、头孢抗感染治疗无好转。既往:自身免疫性溶血性贫血,现以泼尼松 5mg Qd、西罗莫司 2mg Qd 治疗。1-20就诊于我院查新冠核酸阳性,予以来瑞特韦抗病毒治疗。1-25室友发现患者意识丧失,伴尿失禁,查血常规提示WBC 13.71、HGB 22、PLT 250、Ret 0.0179、CRP 37.2、TBil 64.7、DBil 12.3、LDH 2135、SCr 295,外周血可见0.3%破碎红细胞,血清学检测示细小病毒B19 IgM 阳性,外周血 mNGS (序列数 1870)、呼吸道 tNGS (序列数 32260) 检出细小病毒B19型。骨穿提示骨髓增生活跃 红系增生活跃。综合患者床表现、骨髓特征、病毒学结果及疾病转归,考虑为新冠病毒与细小病毒B19共感染致急性溶血危象继发多脏器功能衰竭,经人免疫球蛋白、糖皮质激素等治疗后,患者胆红素、LDH呈下降趋势,网织红细胞与血红蛋白逐渐回升,最终好转出院。

结论 本病例提示,在新型冠状病毒感染背景下,合并细小病毒B19共感染增加溶血危象风险,迅速进展为多脏器功能衰竭。当已知的溶血性贫血不足以解释患者的全部临床表现时,应高度警惕细小病毒B19共感染可能,而非单纯归因于新冠病毒。早期识别双重病因、积极行病原体宏基因检测(mNGS/tNGS),有助于明确病因、指导治疗决策。对于有慢性溶血基础病的患者,病毒感染期的综合评估应覆盖多重病原体,避免单一病因思维定势,以改善临床预后。

北方地区华支睾吸虫感染一例

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现病史:患者,男,47岁;主因上腹部疼痛2天于2025-12-24入院。患者缘于2天前无明显诱因出现上腹部疼痛,为持续性疼痛,就诊于“河北省中医院”,查PCT 15.27ng/ml;胸部CT+腹部CT:1.左肺上叶微结节,部分结节钙化;2.考虑双肺少量间质性改变;3.主动脉及冠状动脉硬化;4.胆囊结石,胆囊壁稍厚;5.考虑胆总管下端小结石。12-23下午行ERCP治疗,术后转ICU,夜间出现发热,予抗感染治疗。12-24晨起复查血常规:WBC 21.62×10⁹/L、NE 20.93×10⁹/L;PCT 22.04ng/ml;生化:ALT 106.4U/L、AST 359.4U/L、TB 144.2μmol/L、淀粉酶 709U/L;尿常规:白细胞+、葡萄糖++++、尿胆原++、潜血+++;ERCP术中液体:可见一条完整的虫体,轻轻挤压后压片可见大量虫卵,形似芝麻状,卵盖明显,可见肩峰、小疣,考虑为肝吸虫(华支睾吸虫)。转我院。

辅助检查:血常规+CRP+PCT:WBC 18.42×10⁹/L,NEUT# 18.00×10⁹/L,LYM# 0.18×10⁹/L,EOS# 0.00×10⁹/L,CRP 108.63mg/L,PCT 12.981ng/ml,IL-6 21.308pg/ml;血凝四项:PT 13.3S,D-Di 4.10ug/ml;生化:ALT 272.0U/L,AST 132.0U/L,TBIL 128.9μmol/L,DBIL 92.3μmol/L,GGT 853U/L,AMY 538U/L,LIP 263U/L;体液细胞形态学(胆汁):WG 深绿色浑浊,可见寄生虫虫卵,形态考虑华支睾吸虫卵(肝吸虫卵)。2025-12-26(胆道系统)磁共振水成像:考虑胆囊结石、胆囊炎。

诊疗经过:给予禁食水,艾司奥美拉唑抑酸,生长抑素抑制胰液分泌,美罗培南抗感染,静脉营养支持治疗。进一步查寄生虫常用抗体7项:阴性;一般细菌培养(胆汁):大肠埃希菌,阿莫西林/克拉维酸:中介16;哌拉西林/他唑巴坦:敏感≤4。胆汁 metaCAP 病原微生物核酸高通量测序:大肠埃希菌|44496,肺炎克雷伯菌|350。

最终诊断:1.华支睾吸虫病 2.胆道感染 大肠埃希菌感染。

治疗措施:吡喹酮口服驱虫,美罗培南抗感染,对症保肝等综合治疗。

预后:经治疗后患者感染控制,肝功能好转,多次复查便常规未见寄生虫,随访至今无复发。

住院成人患者呼吸道合胞病毒感染的流行病学及临床研究

徐杰

苏州大学附属第一医院

目的 探讨住院成人呼吸道合胞病毒感染患者的流行病学特点,临床表现,相应基础疾病,实验室检测结果及存在的合并感染,并且与同时期的住院甲流感染患者进行平行对比分析,为成人 RSV 感染患者的早期临床辨识和实验室精准检验提供良好的依据。

方法 选取了苏州大学附属第一医院 2025 年 6 月至 2026 年 4 月的 36 例住院成人 RSV 感染患者作为实验的研究对象,全面收集了患者的基本信息如人口学信息,基础病情况,临床症状,患者科室分布,感染时血常规指标, C 反应蛋白水平及合并感染的菌类。同时收集同时期的 48 例同时期的住院成人甲流感染患者的基本信息作为对照,进行描述性分析,计量资料以中位数和四分位距表示,计数资料以例数和百分比表示。

结果 RSV 组 36 例患者中,男性 15 例,女性 21 例,男女比例为 1:1.4,年龄中位数为 58.0 岁,年龄跨度从 17 岁至 90 岁。甲流组 48 例患者中,男性 29 例,女性 19 例,年龄中位数为 62.0 岁。RSV 组女性占比略高,但两组年龄和性别分布的差异不显著。基础疾病方面, RSV 组合并基础疾病者占绝大多数,其中血液系统恶性肿瘤最为突出,超过半数患者合并此类疾病,具体包括急性髓系白血病、多发性骨髓瘤、急性淋巴细胞白血病、淋巴瘤及再生障碍性贫血。实体肿瘤和高血压也占有一定

比例。临床症状方面, RSV 组以咳嗽最为多见,其次为发热和咳痰,胸闷、气喘和低氧血症等下呼吸道症状也出现在部分患者中。与甲流组相比, RSV 组发热比例稍低,差异显著,具有统计学意义;胸闷和低氧血症比例稍高,但两组症状分布的差异均不显著。科室分布方面, RSV 组半数患者收治于血液内科,其次为感染病科、放射科和急诊科,这与该组患者基础疾病谱的特征完全吻合。实验室检查方面, RSV 组白细胞计数中位数偏低,近半数患者低于正常范围下限,淋巴细胞计数中位数远低于正常参考范围。C 反应蛋白绝大多数呈现出不同程度的升高,中位数超过正常上限的四倍,绝大多数患者高于正常范围,但升高幅度个体差异较大。影像学方面,两组肺部异常表现的检出率存在一定差异, RSV 组患者检出率明显高于甲流组检出率,主要表现都为肺炎、肺气肿和支气管感染等。

结论 住院成人呼吸道合胞病毒感染以中老年人群和血液系统疾病患者为主要受累群体,血液系统恶性肿瘤是成人 RSV 感染最突出的高危因素。RSV 感染以咳嗽、发热、咳痰为主要临床表现,发热比例低于甲型流感,差异显著 ($p<0.05$)。

一例肺囊性纤维化合并铜绿假单胞菌感染行噬菌体鸡尾酒治疗的护理路径实践

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目的 总结难治性肺囊性纤维化合并铜绿假单胞菌感染患者行噬菌体鸡尾酒雾化治疗的专科护理路径构建与实践经验,聚焦噬菌体活制剂特性与多重耐药菌感染双重护理需求,形成一套可供临床复制的噬菌体雾化吸入护理操作规范与监测体系,为新型抗感染治疗的专科护理实践提供参考。

方法 对 1 例 19 岁难治性肺囊性纤维化合并铜绿假单胞菌感染患者实施噬菌体鸡尾酒雾化治

疗, 组建多学科诊疗团队, 构建并落实全程规范化护理路径: 治疗前完成个体化综合评估、规范知情同意与痰标本基线采集、建立噬菌体制剂接收与储存的标准化操作流程 (SOP); 治疗中建立“雾化全程 + 时段追踪”监测体系, 规范振动筛孔雾化器在生物制剂给药中的核心操作要点, 动态监测病情与不良反应, 同步开展针对性心理护理; 治疗后基于健康信念模式制定个性化健康教育方案, 构建出院后长期自我管理评估与支持体系。

结果 患者治疗全程无不良反应, 咳嗽咳痰等呼吸道症状显著改善, 痰培养铜绿假单胞菌由 3 + 降至 2+; 医院焦虑抑郁量表评分恢复至正常范围, 治疗依从性达 100%, 顺利出院。

结论 针对噬菌体鸡尾酒雾化治疗的活制剂特殊性与多重耐药菌感染的临床特点, 在制剂管理、雾化操作、不良反应监测及心理干预四个关键环节构建了全程化、专科化、循证化护理路径, 可有效保障新型治疗技术的安全实施, 显著改善患者临床症状与心理状态, 该路径兼具操作标准化、感控特色化、流程可复制化特点, 为临床同类病例护理提供重要实践参考, 同时凸显专科护士在新型抗感染精准医疗中的核心价值。

病例报告: 一例肾周围炎后的吉兰-巴雷综合征

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肾周围炎主要是一种相对少见的肾脏周围组织感染性疾病, 通常由肾脏感染扩散至肾周脂肪组织引起。吉兰-巴雷综合征 (GBS) 则是一种急性免疫介导的周围神经病, 常发生于感染, 表现为快速进展的对称性肌无力, 30% 的患者可累及呼吸肌需机械通气。其诊断主要依靠临床表现、脑脊液检查、神经电生理。治疗以免疫调节为主, 静脉注射丙种球

蛋白 (IVIg)、血浆置换是有效的治疗方法, 经过及时治疗, 大多数患者通常预后良好, 但严重的呼吸瘫痪病例通常需要机械通气, 最终因感染及其他并发症导致预后不良或死亡。随着越来越多病历报告, 被临床医生所熟知。本文报告一例由急性肾周围炎诱发的 GBS 个案, 探讨其临床特点及诊疗过程, 为今后早期识别和优化治疗提供参考。虽然 GBS 与多种前驱感染相关, 如空肠弯曲菌、巨细胞病毒等, 但也可能由手术、疫苗接种诱发。但肾周围炎作为 GBS 的前驱感染非常罕见, 尚未见明确报道, 彰显了早期发现和诊断的重要性。

吉兰巴雷综合征被认为是一种感染后疾病, 感染可能通过“分子模拟”和其他机制引起对周围神经抗原的免疫反应, 导致脱髓鞘和/或轴突损伤。约 2/3 的 GBS 病例报告有既往感染, 尤其是胃肠道和呼吸道感染。空肠弯曲杆菌是最常见的致病诱因, 通过其表面脂低聚糖 (LOS) 和宿主周围神经神经节苷脂之间的分子模拟, 这会触发靶向神经节苷脂 (如 GM1、GD1a 和 GQ1b) 的交叉反应性抗体的产生, 从而导致轴突损伤。

我们的病例病原学是不清楚的, 肾周围炎主要由大肠杆菌引起, 是临床中最常见的细菌感染之一, 大肠杆菌是一种革兰氏阴性杆菌, 与所有革兰氏阴性杆菌一样, 大肠杆菌的荚膜含有脂多糖 (LPS)。肾周围炎继发吉兰巴雷综合征目前最主要、也是最可能的机制是“分子模拟学说”, 可能与肾周围炎的致病菌如大肠埃希菌荚膜的脂多糖 LPS 与周围神经髓鞘或轴索上的自身抗原 (如髓鞘相关糖蛋白 MAG、神经节苷脂 GM1/GT1a、髓鞘碱性蛋白 MBP) 高度相似相关。然而, 没有数据说明大肠杆菌 LPS 与神经节苷脂之间的同源性。仅观察到少数 GBS 患者出现大肠杆菌尿路感染的先例, 少数为复发性 GBS。

其他

MDT+PBL 在检验住院医师规范化培训教学查房中的探索

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探讨了多学科诊疗模式(Multidisciplinary Team, MDT)与基于问题的学习(Problem-Based Learning, PBL)在检验医师规范化培训教学查房中的应用与探索。传统的检验住培教学查房以单向传授为主,住院医师难以充分掌握检验结果在临床中的应用,且缺乏与其他学科的有效沟通与协作能力。MDT与PBL的联合应用,通过多学科专家的协作讨论和问题导向学习,为住院医师提供了多角度的临床视野和主动学习的机会。MDT帮助住院医师从不同学科的角度理解患者病情,而PBL则鼓励其通过解决实际问题,培养独立思考和临床决策能力。研究结果显示,MDT/PBL模式能够提升住院医师的教学质量和综合能力,尤其在理论知识的深入掌握、复杂临床问题的解决及多学科协作能力的培养方面表现突出。MDT与PBL两者的结合为检验住院医师提供了一个实践性强、互动性高的教学环境,提升了住院医师的临床思维、团队协作和自主学习能力。然而,MDT与PBL的实施仍面临学科整合、资源协调和评估体系不完善等挑战。未来应进一步深化两种模式的融合,利用信息技术优化教学资源配置,完善评估机制,提升检验医师规范化培训的效果,为现代检验医学人才培养奠定坚实基础。

关键词: 多学科诊疗; 基于问题的学习; 检验医师; 住院医师规范化培训; 教学查房

与时俱进,规范实践: 深入解读《侵袭性肺真菌病诊断与治疗指南(2025年版)》

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摘要 侵袭性肺真菌病(IPFD)的流行病学、诊断技术和治疗措施在近二十年中发生了显著变化,给临床诊治带来了新的机遇和挑战。时隔近十八年,中华医学会呼吸病学分会发布的《侵袭性肺真菌病诊断与治疗指南(2025年版)》(以下简称“2025版指南”),是对2007年《肺真菌病诊断与治疗专家共识》的系统更新。本综述旨在深入解读2025版指南的核心更新点,包括其关注的非免疫抑制宿主、引入现代诊断技术、细化分级诊断标准、以及针对临床关键问题提出的16条推荐意见。同时,本文将结合十余年的国内外部分研究进展,对指南内容进行评述,探讨其在临床实践中的应用价值与潜在挑战,并提出个人的见解与建议,以期为广大临床医生提供更系统的参考,促进IPFD临床研究和实践。

侵袭性肺真菌病(invasive pulmonary fungal disease, IPFD)是一类严重危及生命的感染性疾病。随着全球范围内免疫受损人群的扩大,以及广谱抗生素、免疫抑制剂和新型靶向药物的广泛使用,IPFD的发病率和病死率持续居高不下。2022年世界卫生组织(WHO)首次发布真菌重点病原体清单,标志着真菌感染已成为全球公共卫生领域面临的重大挑战,其中肺部尤易受累[。为有效预防、诊疗和管理肺部真菌感染,规范诊疗行为,2025版指南发布意义重大!

临床药师参与抗感染会诊的实践分析

刘秀凤

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目的 细菌耐药已成为全球公共卫生领域的重大挑战。临床药师作为药物治疗专家,正从传统的“药品调剂者”向“用药把关人”转型,其在抗感染会

诊中的角色日益凸显。本文皆在分析医院临床药师参与的抗感染药学会诊的病例特点，并就典型案例进行分析，为今后临床药师在药学会诊工作的优化提升提供参考。

方法 临床药师以不同的切入点与模式，其一，解读病原学与药敏结果，指导靶向治疗。其二，根据体外药敏抗菌药物最低抑菌浓度调整用药方案。其三，基于药代动力学/药效学原理优化给药方案。其四，识别并规避药物不良反应与相互作用等 4 例典型病例的抗感染治疗方案进行了剖析。

结果 临床药师基于抗感染药物的药学特点和患者的实际病情提出个体化用药建议，并针对性地开展了药学监护，有效提升抗感染治疗的精准性，从而使患者获得更好的治疗效果。

结论 临床药师在优化感染治疗策略方面发挥着至关重要的作用，对促进医院抗菌药物的合理应用和患者预后的改善具有重要意义。抗感染会诊不仅是临床药师介入复杂感染病例的核心渠道，也是其专业价值得以体现的重要平台。另外，临床药师抗感染治疗方面会诊逐步被临床科室所认可，但同时仍需继续努力，以提升会诊质量和相关疾病治疗的合理用药水平。[关键词]临床药师 抗感染会诊 感染性疾病。

生理药代动力学模型在肾脏组织应用研究的可视化分析

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目的 通过文献计量学研究，多维度分析生理药代动力学(PBPK)模型在肾脏组织的研究现状和发展趋势，为临床上利用 PBPK 模型处理肾脏相关问题提供新的见解。

方法 系统检索 Web of Science 核心合集数据库，纳入时间跨度为 2004 年 1 月 1 日至 2024 年

12 月 31 日有关生理药代动力学(PBPK)模型在肾脏领域应用的相关文献。采用文献计量学方法，运用 VOSviewer、CiteSpace、Scimago Graphica 和 Pajek 等多款可视化分析工具，对相关文献的国家/地区分布、发文机构、来源期刊、作者合作关系及关键词共现关系进行深入分析，并构建相应的知识图谱。

结果 本研究共纳入 780 篇文献，2004—2024 年的发文量逐年增长；发文量前 3 的国家分别为美国、中国和英国。发文量最多的作者为 Glatting G(20 篇)。Certara UK Ltd(37 篇)和 Drug Metabolism and Disposition(43 篇)分别为该领域发文量最多的机构与期刊。关键词分析发现肾脏清除、肾毒性、药物暴露、风险评估、组织分布等一直是备受关注的研究热点，前沿主要集中于药物间相互作用及药效学，用药安全，慢性肾病等。

结论 2004—2024 年，PBPK 模型在肾脏组织中的应用研究热度整体呈上升趋势，模型在药物间相互作用、用药安全、慢性肾病等方面的应用是今后主要的研究方向与热点。

细菌外膜囊泡在感染和疫苗开发中的双重角色

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目的 细菌外膜囊泡(OMVs)是革兰阴性菌分泌的纳米级双层膜结构，既作为毒力因子载体参与感染，又因强免疫原性被开发为疫苗平台。本文综述 OMVs 在致病机制与疫苗研发中的双重角色及转化逻辑。

方法 以“outer membrane vesicles”“OMVs”“pathogenesis”“vaccine”等为检索词，检索 PubMed、Web of Science 等数据库 2015—2025 年文献，纳入 OMVs 毒力作用、免疫逃逸、耐药传播

及疫苗应用等主题的研究与综述。

结果 OMVs 以膜包裹形式运输毒力基因及和抗生素耐药基因以及毒力因子来致病,无需细菌直接接触宿主即可损伤细胞。OMVs 通过 TLR4/NF- κ B 通路诱导炎症反应,部分病原菌 OMVs 可诱导免疫细胞半成熟或作为抗体“诱饵”实现免疫逃逸,同时充当生物膜支架促进慢性感染并介导耐药基因水平传播。OMVs 凭借其非复制性、纳米级尺寸与内在佐剂活性被用于开发疫苗。B 群脑膜炎球菌 OMV 疫苗 (MeNZB、4CMenB) 已大规模应用,意外降低淋病发病率 31%。基因工程 GMMA 平台通过脂质 A 减毒与抗原修饰提升安全性,例如肺炎克雷伯菌糖基化 GMMA 疫苗与淋病奈瑟菌 NgG 疫苗均可在动物模型中诱导免疫应答。OMVs 还成功展示 SARS-CoV-2 受体结合域及流感血凝素等异源抗原,显示跨病原应用潜力。

结论 OMVs 的致病机制和免疫诱导功能共享 LPS 和外膜蛋白等分子基础,差异取决于毒力修饰程度。合成生物学手段已推动 OMVs 减毒与抗原定向设计,实现从致病到保护的功能转化。基于 OMVs 的多价疫苗与药物递送系统有望成为应对耐药菌感染的重要策略。

基于 PC 理念建立“神经外科”住院药学 服务新模式的探索与实践

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目的 落实国家药学服务相关政策,构建医-药-护三方共同协作的服务模式开展药物治疗及药学监护的新方式,解决神经外科患者用药复杂、感染风险高、药物相互作用多的问题,适应 DRG/DIP 改革,提升药物治疗安全有效性,优化抗菌药物使用等合理用药指标,探索专科药学服务转型模式。

方法 选取大同市第三人民医院 2022 年至

2026 年 1 月前神经外科住院患者。通过构建“三维一体”药学监护体系,利用信息化手段搭建透明化监管平台,对神经外科患者病原学送检率、围手术术前预防用药及疗程、抗菌药物使用强度、日常医嘱等进行实时监测、预警与干预,并比较干预前后病原学检出率、抗菌药物使用强度、手卫生执行率、手卫生正确率、围手术期预防用药选择等指标的变化。

结果 抗菌药物指标显著优化:病原学送检率从 5.51%增至 91.01%,I 类切口术前选药合理率从 50%-60% 升至 90%-100%,抗菌药物使用强度从 67.47 降至 47.26;用药安全提升:禁忌药物联用消除,护士手卫生依从性大幅提升;认可度改善:医师建议采纳率、患者用药依从性较前明显改善。

结论 “三维一体”监护模式可有效解决专科用药难题,验证了驻科药师 + 多学科协作的价值;政策引领、团队协作、数据驱动是成功关键,可向其他科室推广;未来需通过 AI 赋能、药师专科培训、药物经济学评价进一步提升服务效能。

四川省凉山州 17 县(市) 2010-2023 年麻风涂片检测质控考核分析:区域差距、关键短板与干预策略

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背景 麻风皮肤组织液涂片检测是麻风诊断、分型和疗效判定的重要指标,其质量直接关系到患者早期发现和治疗监测。四川省凉山州是麻风高流行区,县级实验室能力参差不齐、人员流动更替频繁、采样能力不一、质量控制缺失等,可能导致镜检质量低、细菌指数 (BI) 判读偏差大等问题。为保证和不断提高镜检检测质量,四川省皮肤病性病研究所每年对省内麻风高流行地区开展“读片考核质控”工作。对上一年度各县麻风涂片的制片质量、染色

质量、阅片质量（BI 值代表）以及现场考核菌检人员对质控片的阅片质量（质控片阅片）进行全过程质控考核。目的：分析 2010-2023 年凉山州 17 个县（市）涂片检测质控考核数据，识别区域性能力差异与关键失分环节，提出针对性改进策略。

方法 整理 14 年间 17 个县（市）的制片分、染色分、BI 复检得分、质控片阅片分、总评分共 5 项指标，进行纵向趋势分析与横向对比。

结果 西昌、会理、冕宁等县（市）持续优良（总评分多>90），而木里、布拖、美姑等县长期低于 80 分；BI 复检和染色是主要短板，越西县 BI 复检 8 次低于 40 分，金阳县染色分长期≤3 分；部分县（如盐源、德昌）总评分波动剧烈，显示技术稳定性差。

结论 凉山州麻风涂片检测能力呈现“核心县强、边缘县弱”的不平衡格局。急需建立区域性培训中心，对低分县实施“染色-镜检-质控”闭环强化。

泌尿系结核 5 例病例报告及误诊分析

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目的 探讨泌尿系结核临床特征、分析误诊原因并提出防范措施，以提高临床医生对该病的认知，减少误诊误治。

方法 回顾性分析天津市第四中心医院 2024 年 8 月至 2025 年 10 月收治的 5 例 UTB 患者的临床资料。

结果 本研究中有糖尿病者 3 例；临床表现发热 2 例，尿频尿急尿痛 5 例，血尿 1 例，腰痛 2 例；5 例患者尿常规均异常，尿 GeneXpertMTB/RIF 检测均为阳性；尿培养 1 例为大肠埃希菌生长，ESBL(+)，1 例为阴沟肠杆菌。影像学检查肾积水、肾盂肾盏壁增厚、输尿管管壁增厚伴狭窄 4 例，肾实质空洞 4 例，尿路钙化 4 例，膀胱壁增厚、挛缩 3 例，前列

腺增生 1 例，肾囊肿 1 例；5 例患者中活动性肺结核 1 例，腰椎结核 1 例，左肺切除史，右肺陈旧结核 1 例，左肾切除史 1 例，左输尿管支架植入术 1 例；5 例患者均误诊为泌尿系感染，1 例合并肾囊肿，1 例合并前列腺增生，1 例合并肾结石。延误时间至少 1 周至 6 月，3 例病程中应用氟喹诺酮类药物，2 例曾应用多种抗菌素治疗，具体不详。

结论 研究发现 UTB 临床表现不典型，病情复杂，临床医生认知不足，误诊现象普遍，易导致严重后果及不可逆的肾损害。对有结核病史、免疫功能低下、复杂性尿路感染应用抗菌药物治疗效果不佳、影像学提示尿路结构异常的人群应积极筛查 UTB，以明确疾病诊断，避免延误治疗。

1 例金黄色葡萄球菌菌血症患者并发四肢远端坏死的护理

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目的 总结 1 例金黄色葡萄球菌菌血症并发四肢远端坏死患者的护理经验，为临床危重症护理提供参考。

方法 回顾分析 2025 年 7 月收治的金黄色葡萄球菌菌血症并发四肢远端坏死患者的临床资料与护理过程。护理要点包括：（1）组建多学科团队（MDT），涵盖重症医学科、感染科、中医科、康复科、药学科及伤口造口组等多学科团队，制订最佳诊疗护理方案；（2）加强病情观察和护理，采用近红外光谱监测实时评估四肢末梢组织氧饱和度，动态监测肢端皮温、皮色、肿胀程度及血管超声；（3）实施肢端缺血性坏死的个体化护理，包括盐酸罂粟碱静脉滴注改善微循环、西地那非湿敷促进伤口愈合、夫西地酸乳膏外涂预防继发感染，肝素抗凝治疗并密切监测凝血功能，中医鼻饲清热解毒汤剂联合耳穴压豆通达经络，远红外线照射物理治疗缓解疼痛、

促进创面愈合；(4)规范化抗生素管理，监测万古霉素血药浓度，确保谷浓度控制在 10~15 $\mu\text{g/ml}$ ，预防肾毒性；(5)落实标准预防与环境清洁消毒，控制多重耐药菌传播。

结果 经过 10 d 的精心治疗与护理，患者病情明显好转。入院第 6 天，坏死皮肤范围局限，部分皮肤转红润；入院第 10 天，四肢大面积水泡收干，坏死区域较前局限，皮肤色泽改善，成功脱离呼吸机并转感染科继续治疗。住院期间未发生导管相关并发症、药物不良反应及交叉感染。

结论 金黄色葡萄球菌菌血症并发四肢远端坏死病情凶险、皮肤进展迅速，通过 MDT 协作制订个体化方案，综合运用药物改善微循环、抗凝治疗、中医辅助及物理治疗等护理措施，可有效控制肢端坏死进展，保障患者安全。该护理经验为临床类似病例的护理提供参考。

基于循证的临床决策支持系统青霉素过敏史结构化评估工具的构建及应用

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目的 研发基于循证的护理临床决策支持系统青霉素过敏史结构化评估工具，并评价其运用效果。

方法 依据最佳证据构建青霉素过敏史结构化评估方法，将其整合入护理临床决策支持系统形成评估工具，通过前后对照研究，比较该工具应用前后相关指标的变化。

结果 2023 年住院患者共 1494 例，其中共 53 (3.55%) 例患者自诉青霉素过敏；2024 年住院患者共 1883 人，其中共 144 (7.65%) 例患者自诉青霉素过敏，共计 197 例自诉过敏患者纳入本研究。工具使用后，过敏史评估与记录完整性显著提升，2024 年使用过敏史结构化评估工具后，用药日期、给药途径、给药频率、过敏日期、过敏情况、过敏处理、

过敏恢复日期和过敏恢复情况，记录率均提升为 100%。2024 年对药物具体名称的记录率较 2023 年有所提升 ($p < 0.01$)，但记录率仅 56.9%，仍偏低。应用前患者自诉过敏均被护士记录为过敏标签，而应用该工具后，患者不必要青霉素过敏标签的去除率达 47.22%，且未增加青霉素相关不良反应的发生。但该工具的使用未引起抗菌药物使用强度的显著波动，其长期趋势有待进一步大样本观察。

结论 基于循证的护理临床决策支持系统青霉素过敏史结构化评估工具，能够安全、有效地帮助医护人员识别非必要的青霉素过敏标签，促进临床合理用药。

支扩症临床表型识别及其预后价值

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背景 支气管扩张症（以下简称支扩症）是一种异质性的慢性气道炎症性疾病，现有评分工具对疾病活动度与结构进展的预测价值有限。

目的 本研究旨在基于多维度临床特征识别支扩症临床表型，评估其预后预测价值，并为后续多组学研究提供临床分层框架。

方法 纳入 264 例稳定期支扩症患者，平均随访 21.9 个月。以症状、肺功能、影像结构、气道微生物及炎症五个维度的 9 项指标为聚类变量，采用围绕中心点的划分算法（PAM）进行无监督聚类，Bootstrap 重抽样双重验证稳定性。Kaplan-Meier 生存分析与 Cox 回归评估表型间临床结局差异，一致性指数（C-index）、净重新分类指数（NRI）、综合判别改善指数（IDI）及决策曲线分析（DCA）量化临床表型对支气管扩张严重程度评分（BSI）的附加预测价值，条件推断树（ctree）构建临床分型决策模型。

结果 识别出三种临床表型。重度损伤-铜绿假单胞菌（PA）定植型（表型 1， $n=101$ ）中，痰培养

PA 检出率 94.9%，急性加重（AE）风险高于轻症-气道高反应型（风险比 $HR=1.59$, $P=0.007$ ）。隐匿进展型（表型 2, $n=42$ ）基线水平居中，但肺功能快速下降风险为轻症-气道高反应型的 3.22 倍，影像学进展风险为 3.61 倍，综合不良结局风险为 1.76 倍。轻症-气道高反应型（表型 3, $n=121$ ）痰 Eos% 最高（2.6%），临床预后最佳。联合模型在预测影像学进展方面显著优于单独 BSI 评分（C-index 0.683 vs. 0.508, $NRI=0.113$, $IDI=0.370$ ）。ctree 模型以 3 个核心变量实现总分类一致率 98.11%。

结论 本研究构建并验证了支扩症三分类临床表型体系，识别出隐匿进展型这一潜在高危亚群，临床表型在预测结构进展与肺功能下降方面提供了 BSI 评分之外的独立预测信息，为支扩症早期风险分层与个体化干预提供参考依据。

关键词：支气管扩张症，临床表型，无监督聚类，预后预测

上海市 87 家医疗机构医务人员对围术期体温维持技术应用知信行现状调查研究

李翠翠

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目的 本研究旨在了解上海市 87 家医疗机构医务人员对围术期体温维持技术应用的知识、信念、行为现状，并探讨其可能的影响因素，为完善围术期体温管理工作的政策制定与实施提供科学依据。

方法 采用问卷调查法，对上海市 87 家医疗机构的医务人员展开调查。

结果 本次共获得 2163 份来自上海市 87 家各级医疗机构医务人员的问卷。调查显示，医务人员对围术期体温维持技术的认知情况得分为 4(3,5)，仅有 11.60% 的医务人员全部答对，且存在 2.31% 的医务人员是全部答错，显示出知识水平存在不足。医务人员对围术期体温维持技术的执行情况得分为

31(28,35)，各执行项目均有 7%-12% 的“不清楚”反馈。医务人员对围术期体温维持技术的态度总体评分为 30.79 ± 4.487 （满分 35 分），表明其态度较为积极。

结论 上海市医务人员对围术期体温维持技术的态度总体积极，但其知识水平匮乏，执行规范性不理想，各方面均有待进一步提升。为提高该技术应用水平，建议加强培训，制定针对性培训计划，定期组织培训并考核；医疗机构应根据实际需求，优化资源配置，合理配置保温仪器设备；相关部门应制定详细围术期体温维持流程和指南并考虑将围术期体温维持技术列入收费项目，出台政策鼓励医院和医务人员积极应用该技术。最终，通过多种渠道宣传围术期体温维持重要性，提高医务人员认识，转变错误观念，营造重视围术期体温管理的良好氛围。

发热伴外周血单核细胞增多的皮炎 1 例

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目的 探讨以发热伴外周血单核细胞增多为首发症状的皮炎的临床特点、诊断思路及治疗策略。

方法 回顾性分析 2022 年 8 月天津市人民医院收治的 1 例以长期发热伴单核细胞增多起病的皮炎患者的临床资料。患者男，76 岁，主因“间断发热 1 年余”入院，查体右侧肘关节 Gottron 征，心律不齐，化验炎症指标高，单核细胞计数增多，免疫球蛋白升高，胸部 CT 示双肺间质病变，心电图提示轻度肌源性损害，肌肉活检病理符合皮炎表现，参照 1975 年 Bohan 和 Peter 提出的经典标准以及 2017 年发布的 EULAR/ACR 新标准，该患者最终被确诊为皮炎。予规律口服甲泼尼龙 16mgBID 联合甲氨蝶呤 10mgQW 治疗，激素规律减量。

结果 发热迅速控制，炎症指标及外周血单核

细胞计数恢复正常, 3 个月后患者 Gotttron 征消失, 随访 1 年未见肿瘤或皮炎复发。

结论 皮炎的临床表现具有高度异质性。以不明原因长期发热和反应性单核细胞增多为首发或突出表现者临床罕见, 易导致误诊或诊断延迟。临床接诊此类患者时, 应将皮炎纳入鉴别诊断, 并进行全面的免疫学、心电图及肌肉病理学检查以实现早期诊断与治疗。临床医师需全面结合患者症状、体征和实验室检查结果, 及时做出准确的诊断并制定个体化的治疗方案。

【关键词】皮炎; 发热; 单核细胞

评能力同步增强。

结论 以品管圈为核心的系统化护理干预模式, 能够在优化制度流程、强化人员培训、升级工程防护和完善信息化管理的综合作用下, 有效降低护理人员锐器伤发生率并改善安全注射知信行水平, 具有较高的临床推广和应用价值。

关键词 品管圈; 问题解决型品管圈; 护理人员; 锐器伤; 安全注射; 质量改进

构建以品管圈为载体的四位一体锐器伤综合防控模式

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目的 构建以品管圈为载体的锐器伤综合防控模式, 评价其在降低护理人员锐器伤发生率及提升安全注射知信行水平方面的效果, 为医院护理职业安全管理提供可推广的质量改进路径。

方法 采用前后对照的准实验研究设计, 于某三级甲等综合医院开展以“降低护理人员锐器伤发生率”为主题的品管圈活动, 组建多学科圈组, 按 QC-STORY 步骤完成现况调查、原因分析、真因验证及对策实施。以全院临床护士为观察对象, 比较干预前后护理人员锐器伤发生率的变化, 采用经信效度检验的护理人员安全注射知信行问卷评估护士知信行水平的改善情况, 并计算活动目标达成率、进步率。

结果 品管圈干预后, 护理人员锐器伤发生率较干预前明显下降, 相对降幅达到 84.21%, 差异具有统计学意义 ($P < 0.001$)。护理人员安全注射知信行总分及各维度得分干预后均显著提高 ($P < 0.001$), 圈员在团队协作、问题分析与质量改进等方面的自

列题

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王思雨

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Effect of Voriconazole Therapeutic Drug Monitoring on Clinical Outcomes of Antifungal Therapy: A Systematic Review and Meta-analysis

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细菌真菌感染的流行病学

婴幼儿特殊食品产业研究热点与健康政策启示 ——基于 CiteSpace 的知识图谱分析

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以患者为中心的全生命周期健康管理：医联体内全科-专科协同机制与多学科团队培养研究

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人工智能技术在疾病随访的应用范式探究

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临床研究驱动医企协同创新的实践探索 ——基于医学科技创新与成果转化的机制、路径及案例研究

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不同病原中枢神经系统感染临床特征及预后分析

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细菌真菌感染的治疗

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感染科咽拭子嗜麦芽窄食单胞菌检出患者临床特征及耐药性分析

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