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抗藥性細菌和黴菌治療之新進展

Update of Treatment: Multi-Drug Resistant Organism and Fungus

時　　間：114 年 6 月 28 日(星期六) 13:30~17:00
地　　點：臺北榮民總醫院 致德樓第五會議室
合辦單位：臺北榮民總醫院感染科
國立陽明交通大學急重症醫學研究所

13:30-13:40	***Opening Remarks***	林邑璁教授 Yi-Tsung Lin
	座長：馮長風 教授 (Chang-Phone Fung) **陳昕白 醫師 (Hsin-Pai Chen)**	
13:40-14:20	三代頭孢黴素抗藥性腸內菌的治療新知 Update of treatment of third-generation cephalosporin-resistant Enterobacterales	林邑璁教授 Yi-Tsung Lin
14:20-15:00	對碳青黴烯具抗藥性的革蘭氏陰性菌治療的新知 Update of treatment of carbapenem-resistant Gram-negative bacilli	莊茜醫師 Chien Chuang
15:00-15:30	***Coffee Break***	
	座長：許瀚水 教授 (Han-Shui Hsu) **王復德 教授 (Fu-Der Wang)**	
15:30-16:00	結核病診斷與治療的新進展 Cracking the code of tuberculosis: Breakthroughs in diagnosis and treatment	馮嘉毅教授 Jia-Yih Feng
16:00-16:30	金黃色葡萄球以及腸球菌的治療新知 Update of treatment of *Staphylococcus aureus* and Enterococcus spp	莊佑中教授 Yu-Chung Chuang
16:30-17:00	侵入性黴菌感染治療新知 Update of treatment of invasive fungal infection	陳抱宇醫師 Pao-Yu Chen
17:00-17:10	***Closing Remarks***	鄭玫枝教授 Mei-Jy Jeng

Update of treatment of third-generation cephalosporin-resistant Enterobacterales

三代頭孢黴素抗藥性腸內菌的治療新知

Yi-Tsung Lin

林邑璁

Division of Infectious Diseases, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan ,ROC

Institute of Emergency and Critical Care Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC

臺北榮民總醫院 內科部 感染科 及 國立陽明交通大學 急重症醫學研究所

The incidence of extended-spectrum β-lactamases-producing Enterobacterales (ESBL-E) infections increased rapidly worldwide, in large part due to a greater number of community-acquired infections. Routine ESBL testing is not performed by most clinical microbiology laboratories and non-susceptibility to ceftriaxone is often used as a proxy for ESBL production. ESBL are most prevalent in *Escherichia coli*, *Klebsiella pneumoniae*, *Klebsiella oxytoca*, and *Proteus mirabilis*. CTX-M enzymes, particularly CTX-M-15, are the most common ESBLs worldwide. ESBLs other than CTX-M with unique hydrolyzing abilities are variants of narrow-spectrum TEM and SHV β-lactamases with amino acid substitutions, but they have undergone less clinical investigation than CTX-M enzymes. AmpC β-lactamases are β-lactamase enzymes that are produced at basal levels by many Enterobacterales and increased AmpC enzyme production due to inducible *ampC* expression can increase MICs to certain antibiotics, most notably ceftriaxone, cefotaxime, and ceftazidime. *Enterobacter cloacae* complex, *Klebsiella aerogenes*, and *Citrobacter freundii* are the most common Enterobacterales at moderate to high risk for clinically significant AmpC production. Carbapenems are recommended as the preferred regimen for infections caused by third-generation cephalosporin-resistant Enterobacterales (3GCephRE), but the carbapenem-sparing strategy is also suggested. Recently, IDSA guidance updated the treatment for ESBL-E and Enterobacterales with moderate to high risk for clinically significant AmpC production due to an inducible *ampC* gene. ESCMID guidance addressed the treatment for 3GCephRE. In this presentation, I will review the updated updated treatment information for 3GCephRE.

Update of treatment of carbapenem-resistant Gram-negative bacilli

對碳青黴烯具抗藥性的革蘭氏陰性菌治療的新知

Chien Chuang

莊茜

Division of Infectious Diseases, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 內科部 感染科

Carbapenems have traditionally served as the last-resort antibiotics for treating severe infections caused by multidrug-resistant Gram-negative bacilli. However, the use of carbapenem leads to the emergence and dissemination of carbapenem-resistant Gram-negative bacilli (CRGNB), often linked to the production of carbapenemases. As a result, alternative treatment strategies must be explored.

Managing CRGNB infections poses a major challenge for healthcare systems worldwide due to the limited therapeutic options and high mortality. In recent years, significant advancements have been made in the treatment of CRGNB, focusing on novel therapeutic approaches. This presentation will provide a comprehensive overview of the current strategies for managing CRGNB infections, highlighting recent developments and challenges in the field. These include the introduction of new β-lactam/β-lactamase inhibitor combinations, such as ceftazidime/avibactam, ceftolozane/tazobactam, imipenem-cilastatin-relebactam, and meropenem/vaborbactam, which have demonstrated promising clinical efficacy. Additionally, the repurposing of existing antibiotics, such as colistin, minocycline, and fosfomycin, has been investigated as potential treatment options.

Effectively managing CRGNB infections requires a multifaceted approach, encompassing the development of novel antibiotics and the reconsideration of existing therapeutic strategies. This presentation will explore these aspects in detail, providing clinicians with up-to-date information to support informed decision-making in CRGNB management.

Cracking the code of tuberculosis: Breakthroughs in diagnosis and treatment

結核病診斷與治療的新進展

Jia-Yih Feng

馮嘉毅

Division of Pulmonary Infection and Immunology, Department of Chest Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

臺北榮民總醫院 胸腔部 呼吸感染免疫科

The diagnosis and treatment of tuberculosis (TB) require a multifaceted approach integrating microbiological, molecular, and clinical assessments. Diagnostic methods include acid-fast bacilli (AFB) smear microscopy, culture using solid and liquid media, molecular assays such as TB PCR and GeneXpert, and serological markers like adenosine deaminase (ADA) for extrapulmonary TB. The World Health Organization (WHO) recommends targeted next-generation sequencing (NGS) for drug resistance detection, including assays like Deeplex® Myc-TB and AmPORE TB. Treatment strategies for drug-susceptible TB involve a six-month regimen consisting of isoniazid (INH), rifampicin (RIF), pyrazinamide (PZA), and ethambutol (EMB) (2HRZE/4HR). Shorter four-month regimens incorporating rifapentine and moxifloxacin have been explored in clinical trials. For multidrug-resistant TB (MDR-TB), WHO endorses all-oral regimens such as BPaLM (bedaquiline, pretomanid, linezolid, and moxifloxacin) for six to nine months. Special considerations in treatment include drug dose adjustments in renal and hepatic impairment, fluoroquinolone-based regimens for extensively drug-resistant TB (XDR-TB), and vaccine strategies like BCG and M72/AS01 for TB prevention. Treatment failure is assessed by month-two culture conversion rates, with persistent positivity necessitating second-line therapy. Advances in TB immunopathogenesis, including host-directed therapies targeting T-cell exhaustion, are emerging as potential adjuncts. Overall, TB management integrates precise diagnostics with evolving therapeutic regimens to enhance treatment efficacy and combat resistance.

Update of treatment of Staphylococcus aureus and Enterococcus spp.

金黃色葡萄球以及腸球菌的治療新知

Yu-Chung Chuang

莊祐中

Division of Infectious Diseases, Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan, ROC

臺大醫院 內科部 感染科

The increasing prevalence of multidrug-resistant organisms (MDROs) poses a significant challenge to modern healthcare, further exacerbated by the slow pace of novel antimicrobial development. Among these, ESCAPE pathogens—particularly methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant enterococci (VRE)—remain critical concerns due to their limited treatment options and associated morbidity and mortality.

Vancomycin has long been the mainstay for MRSA infections; however, concerns regarding its efficacy and safety have prompted a shift in treatment strategies. Current guidelines emphasize the importance of achieving an area under the curve/minimum inhibitory concentration (AUC/MIC) ratio of 400–600 mg·h/L for optimal therapeutic outcomes in severe MRSA infections. Recent advancements have introduced novel agents such as ceftaroline and next-generation glycopeptides, which demonstrate potent activity against resistant Gram-positive bacteria. Furthermore, evidence suggests that daptomycin may offer superior efficacy compared to vancomycin in MRSA bacteremia. Ongoing research explores strategies to enhance the effectiveness of vancomycin and daptomycin, including combination therapies with β-lactams (e.g., ceftaroline) and fosfomycin, which have demonstrated promising synergistic effects.

For VRE infections, linezolid remains the only FDA-approved therapeutic agent. However, daptomycin, despite its off-label use, is increasingly considered an effective alternative, particularly in VRE bacteremia. Higher daptomycin dosing regimens—exceeding the conventional 6 mg/kg—are now recommended, with recent guidelines advocating for doses in the range of 8–12 mg/kg for Enterococcus faecium bacteremia. Emerging data suggest that even higher doses (>11 mg/kg) may be associated with improved clinical outcomes. Beyond dose optimization, achieving appropriate pharmacodynamic targets (AUC/MIC) and utilizing combination therapies—such as daptomycin with β-lactams or fosfomycin—are gaining attention for their potential synergistic effects in the treatment of VRE bacteremia. Additionally, early initiation of appropriate anti-VRE therapy has been correlated with improved patient outcomes.

This presentation will provide a comprehensive update on the evolving treatment landscape for MRSA and VRE, highlighting recent clinical evidence, and novel therapeutic strategies aimed at optimizing patient management in the era of increasing antimicrobial resistance.

Update of treatment of invasive fungal infection

侵入性黴菌感染治療新知

Pao-Yu Chen
陳抱宇
Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan, ROC
Department of Medicine, National Taiwan University College of Medicine, Taipei, Taiwan, ROC
臺灣大學附設醫院 內科部
臺灣大學 醫學院

Invasive fungal diseases (IFDs) have become a significant threat to human health over the past three decades, with rising incidence rates and expanding species of medical fungi. Advancements in hemato-oncological and immunologic therapeutics have contributed to antifungal resistance among various fungal species and at-risk patient populations. The COVID-19 pandemic has further exacerbated these threats, leading to a notable shift towards non-albicans Candida species and increased antifungal resistance, particularly among C. glabrata, C. parapsilosis, and C. auris. Additionally, the risks of pulmonary fungal infections following SARS-CoV-2 infections have risen, especially for Aspergillus, Mucorales, and potentially Cryptococcus.

Multidisciplinary experts have published global guidelines for the diagnosis and management of infections caused by several important medical fungi, including Candida, Cryptococcus, Mucorales, rare yeasts, and rare molds, as well as respiratory virus-associated pulmonary aspergillosis. These guidelines synthesize current evidence through comprehensive literature review and provide recommendations for each domain of IFD diagnosis and management. The Infectious Diseases Society of Taiwan (IDST) has endorsed these global guidelines, while the revised guidance by IDST complements the global guidelines due to specific local considerations, including variation of local epidemiology, availability of diagnostics, and issues about health economics. Given the high-quality evidence for antifungal use may be limited, in vitro data, case series and expert opinions, as well as local epidemiology, the heterogeneity of patient populations, and antifungal availability in Taiwan were incorporated in reviewing process of evidence.

This presentation aims to provide recommendations for IFD management, focusing on antifungal treatment options for both infectious disease specialists and first-line healthcare providers.