(22)

多重抗藥性細菌以及黴菌最新治療趨勢

Update of theTreatment of Multidrug Resistant Organism and Invasive Fungal Infection

時　　間：113 年 6 月 22 日(星期六) 13:30~16:50
地　　點：臺北榮民總醫院 中正 12 樓胃腸科會議室

13:30-13:40	***Opening Remarks***	林邑璁教授 Yi-Tsung Lin
	座長：林邑璁 教授 (Yi-Tsung Lin)	
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 Li
14:20-15:00	Carbapenem 抗藥性的革蘭氏陰性菌治療的新知 Update of Treatment of Carbapenem-Resistant Gram Negative Bacilli	阮志翰醫師 Chih-Han Juan
15:00-15:30	***Coffee Break***	
	座長：陳昕白 醫師 (Hsin-Pai Chen)	
15:30-16:10	金黃色葡萄球以及腸球菌的治療新知 Update of Treatment in MRSA and VRE	莊佑中教授 Yu-Chung Chuang
16:10-16:50	侵襲性黴菌的治療新知 Update of Treatment of Invasive Fungal Infection	胡婉妍醫師 Un-In Wu

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

臺北榮民總醫院 內科部 感染科

The incidence of extended-spectrum β-lactamases-producing Enterobacterales (ESBL-E) infections increased rapidly in Taiwan, in large part due to a greater number of community-acquired infections. Routine EBSL testing is not performed by most clinical microbiology laboratories and non-susceptibility to ceftriaxone is often used as a proxy for ESBL production, although strains with other mechanisms may be falsely presumed to be ESBL-producers. 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 resulting from 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. Several guidelines or guidance have been issued in recent years for the treatment of multi-drug resistant microorganism. IDSA guidance addressed 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 third-generation cephalosporin-resistant Enterobacterales (3GCephRE). In this presentation, I will review the updated information for the treatment for 3GCephRE.

Update of treatment of carbapenem-resistant Gram-negative bacilli

Carbapenem 抗藥性的革蘭氏陰性菌治療的新知

Chih-Han Juan

阮志翰

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 long been considered the mainstay of treatment for serious infections caused by Gram-negative bacilli. However, the emergence and spread of carbapenem-resistant Gram-negative bacilli (CRGNB), often associated with the production of carbapenemases, have severely limited the utility of these antibiotics. As a result, alternative treatment options must be considered.

Treatment of CRGNB presents a significant challenge in healthcare due to limited treatment options and increasing resistance rates worldwide. In recent years, there have been significant updates in the management of CRGNB infections, focusing on the development of new treatment strategies. This speech will provide a comprehensive overview of the current approaches to the treatment of CRGNB, highlighting the latest advancements and challenges in the field. These include the use of novel beta-lactam/beta-lactamase inhibitor combinations, such as ceftazidime/avibactam, ceftolozane/tazobactam, imipenem-cilastatin-relebactam, and meropenem/vaborbactam, which have shown promise in clinical trials. Furthermore, the repurposing of existing antibiotics, such as colistin and minocycline, has also been explored as potential treatment options for CRGNB infections.

Overall, the management of CRGNB infections requires a multifaceted approach that includes the development of new antibiotics, and the exploration of alternative treatment strategies. This speech will explore these various aspects of CRGNB treatment, providing clinicians with the latest information to guide their management decisions.

Update of treatment in MRSA and VRE

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) presents a significant challenge in healthcare, a situation exacerbated by the slow development of new antimicrobials. Among these, the ESCAPE pathogens, including Methicillin-resistant *Staphylococcus aureus* (MRSA) and Vancomycin-resistant Enterococci (VRE), are particularly concerning.

While vancomycin has traditionally been the standard treatment for MRSA, its efficacy and safety are now under scrutiny. The current consensus recommends targeting an AUC/MIC ratio of 400–600 mg*hour/L for the effective treatment of serious MRSA infections. Advancements in the field have introduced emerging antimicrobials such as ceftaroline and novel glycopeptide antibiotics, which have shown efficacy against these resistant gram-positive bacteria. Studies suggest daptomycin may be more effective than vancomycin in treating MRSA bacteremia. Research is also focused on enhancing the effectiveness of vancomycin and daptomycin, including their combination with beta-lactams, particularly ceftaroline, and fosfomycin.

Linezolid currently stands as the only antibiotic approved for VRE infections. However, daptomycin, though not officially approved for VRE, is frequently used off-label, with recent studies suggesting it may rival linezolid in effectiveness for VRE bacteremia. Higher doses of daptomycin, exceeding the standard 6 mg/kg, are being considered for these cases. The latest guidelines recommend a dosage range of 8-12 mg/kg for *Enterococcus faecium* bacteremia. There was a tendency towards higher doses, such as > 11 mg/kg, being linked to improved outcomes. Furthermore, achieving optimal pharmacodynamic targets, measured by the AUC/MIC ratio, is crucial. Additionally, the combination of beta-lactams and fosfomycin with daptomycin is showing a synergistic effect in the treatment of VRE bacteremia.

This presentation will delve into these developments, discussing their clinical implications and the evolving strategies for managing MRSA and VRE infections.

Update of treatment of invasive fungal infection

侵入性黴菌感染治療新知

Un-In Wu

胡婉妍

Department of Medicine, National Taiwan University Cancer Center, Taipei, Taiwan ,ROC

Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan ,ROC

Department of Medicine, National Taiwan University College of Medicine, Taipei, Taiwan ,ROC

國立臺灣大學醫學院附設醫院癌醫中心分院

Invasive fungal infections (IFIs) represent a significant clinical challenge, particularly in immunocompromised individuals, necessitating constant updates in treatment strategies. Recent guidelines, including those for invasive candidiasis, cryptococcosis, and rare molds, have provided crucial insights into optimal management approaches.

Despite existing antifungal agents, limitations such as poor pharmacokinetic traits, toxicity, drug-drug interactions, limited clinical efficacy, and emerging antifungal resistance persist. Consequently, there is an urgent need for new antifungal agents to address these challenges. These new agents belong to well-known drug families like azoles, polyenes, or beta-D-glucan synthase inhibitors, or to families with entirely novel mechanisms of action. Some drugs have demonstrated a head start in terms of potential clinical implementation, showcasing promising pharmacokinetic profiles and potent antifungal activity.

In addition to advancements in treatment, recent developments have focused on preventive strategies, particularly in high-risk populations such as patients undergoing allogeneic hematopoietic stem cell transplant (HSCT). Moreover, updated recommendations for primary prophylaxis of IFIs in hematological patients and those receiving novel targeted therapies such as chimeric antigen receptor T-cell (CAR-T) therapy in acute myeloid leukemia (AML) have emerged. These recommendations aim to optimize prophylactic strategies and mitigate the risk of opportunistic infections in vulnerable patient populations.

These advancements underscore the dynamic landscape of IFI management, emphasizing the critical role of ongoing research efforts in developing innovative therapies and preventive strategies. Continued collaboration and guideline development are essential to further refine approaches and improve outcomes in the challenging realm of invasive fungal infections.