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PRACTICE GUIDELINES

Guidelines for the treatment of methicillin-resistant *Staphylococcus aureus* infections in Taiwan

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Methicillin-resistant *Staphylococcus aureus* (MRSA) continues to be one of most important causes of health care-associated infections. Its ubiquity and increasing vancomycin nonsusceptibility have contributed to the complexity of treatment of infections caused by this pathogen.

Guidelines on the therapeutic monitoring of vancomycin and treatment of MRSA infections were recently issued by the Infectious Disease Society of America. In the advent of the issuance of these guidelines, a symposium on the "Treatment of MRSA Infections in Taiwan" was held in early 2012 to address the management of these infections in the local settings. Experts on infectious diseases in Taiwan convened and issued a guideline for the treatment of MRSA infections involving the skin and soft tissue, musculoskeletal, respiratory, cardiovascular, and central nervous systems.

Other important issues addressed in the symposium were the reporting of minimum inhibitory concentrations (MICs), the dosage, and therapeutic drug monitoring of vancomycin. Determination of vancomycin MIC was recommended in patients with complicated MRSA infections or treatment failure. Vancomycin dosages of 30—60 mg/kg of actual body weight per day given at an interval of 6—12 hours were recommended for patients with normal renal function. For seriously ill patients, including patients with bacteremia, sepsis, meningitis, osteomyelitis, pneumonia, and severe skin and soft tissue infections, a loading dose of 25—30 mg/kg (based on actual body weight) may be considered. Serum trough levels should be obtained just before the fourth or fifth dose and vancomycin dosage should be adjusted to attain trough serum vancomycin concentrations of 15—20 μg/mL when the vancomycin MIC is $\leq$1 μg/mL (Table 1).

The guidelines were established based on the local epidemiology, susceptibility patterns of MRSA, and expert consensus. The guidelines were approved by the board members of the Infectious Disease Society of Taiwan (IDST). Free access to these guidelines is provided in the *Journal of Immunology, Microbiology and Infection* (www.ejmii.com and www.e-jmii.com) and the web site of IDST (http://www.idsroc.org.tw/) to increase the access for medical practitioners in Taiwan.

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Table 1 Recommendations for the treatment of methicillin-resistant *Staphylococcus aureus* infections in Taiwan

Diagnosis	Adults		Pediatric dosage	Duration	Comments
	Antibiotic of choice	Alternatives			
Skin and soft-tissue infection (SSTI)					
Simple abscess or boils	Incision and drainage	—	—	—	—
Outpatient SSTI	TMP–SMX (160–320/800–1600 mg PO q12h)	Linezolid 600 mg PO q12h	TMP–SMX (4–6 mg/kg/dose based on TMP) PO q12h	5–10 d	Clindamycin could be used when susceptibility results are available. Rifampin could be added to any of the suggested treatment regimens.
	Doxycycline 100 mg PO q12h	—	Doxycycline: ≤45 kg, 2 mg/kg/dose PO q12h; >45 kg, adult dose[1]	5–10 d	
	Minocycline 200 mg st, then 100 mg PO q12h	—	Minocycline 4 mg/kg PO × 1, then 2 mg/kg/dose PO q12h	5–10 d	
	Fusidic acid 500 mg PO q8–12h or 750 mg q12h	—	Fusidic acid PO[2]	5–10 d	
	—	—	Linezolid 10 mg/kg/dose PO/IV q8h, not to exceed 600 mg/dose[3]	—	—
Inpatient SSTI (complicated SSTI)	Vancomycin 30–60 mg/kg/day IV in two to four divided doses[a]	Linezolid 600 mg IV/PO q12h	Vancomycin 15 mg/kg/dose IV q6h	7–14 d	—
	Teicoplanin 6–12 mg/kg/dose IV q12h × three doses, then QD	Daptomycin 4 mg/kg/dose IV QD	Teicoplanin 10 mg/kg IV q12h × three doses, then 6–10 mg/kg QD	7–14 d	—
	—	Tigecycline 100 mg st, then 50 mg IV q12h	Linezolid 10 mg/kg/dose PO/IV q8h, not to exceed 600 mg/dose[3]	7–14 d	—
Bacteremia					
Uncomplicated bacteremia[b]	Vancomycin 30–60 mg/kg/day IV in two to four divided doses[a]	Daptomycin 6 mg/kg/dose IV QD	Vancomycin 15 mg/kg/dose IV q6h	≥2 wk	Addition of gentamicin or rifampin to vancomycin is not recommended.
	Teicoplanin 6–12 mg/kg/dose IV q12h × three doses, then QD	—	Teicoplanin 10 mg/kg IV q12h × three doses, then 6–10 mg/kg QD	≥2 wk	
Complicated bacteremia	Vancomycin 30–60 mg/kg/day IV in two to four divided doses[a]	Daptomycin 6–10 mg/kg/dose IV QD	Vancomycin 15 mg/kg/dose IV q6h	4–6 wk	Defined as bacteremia not meeting the criteria of uncomplicated bacteremia. Addition of gentamicin or rifampin to vancomycin is not recommended. Transition from parenteral to oral agents should be done cautiously and is not recommended in those with complicated bacteremia.
	Teicoplanin 6–12 mg/kg/dose IV q12h × three to six doses, then 6–12 mg/kg/dose QD	—	Teicoplanin 10 mg/kg IV q12h × three doses, then 6–10 mg/kg QD	4–6 wk	
	—	—	Daptomycin 6–10 mg/kg/dose IV QD	—	
Infective endocarditis	—	—	—	—	—
Native valve endocarditis	Vancomycin 30–60 mg/kg/day IV in two to four divided doses[a]	—	Vancomycin 15 mg/kg/dose IV q6h	4–6 wk	Addition of gentamicin or rifampin to vancomycin is

	Teicoplanin 6–12 mg/kg/dose IV q12h × three to six doses, then 6–12 mg/kg/dose QD	—	Teicoplanin 10 mg/kg IV q12h × three doses, then 6–10 mg/kg QD	4–6 wk	not recommended.
	Daptomycin 6–10 mg/kg/dose IV QD	—	Daptomycin 6–10 mg/kg/dose IV QD	4–6 wk	
Prosthetic valve endocarditis	Vancomycin 30–60 mg/kg/day IV in two to four divided doses[a] + Rifampin 300 mg PO q8h ± Gentamicin 1 mg/kg/dose q8h	—	Vancomycin 15 mg/kg/dose IV q6h[4] + Gentamicin 1 mg/kg/dose IV q8h + Rifampin 5 mg/kg/dose PO/IV q8h	6 wk 6 wk 2 wk	—
Pneumonia	Vancomycin 30–60 mg/kg/day IV in two to four divided doses[a]	—	Vancomycin 15 mg/kg/dose IV q6h	7–21 d	—
	Linezolid 600 mg PO/IV q12h	—	Teicoplanin 10 mg/kg IV q12h × three doses, then 6–10 mg/kg QD	7–21 d	—
	Teicoplanin 6–12 mg/kg/dose IV q12h × three doses, then 6–12 mg/kg/dose QD	—	Linezolid 10 mg/kg/dose PO/IV q8h, not to exceed 600 mg/dose[3]	7–21 d	—
Central nervous system infection	—	—	—	—	—
Meningitis	Vancomycin 30–60 mg/kg/day IV in two to four divided doses[a] ± Rifampin 600 mg PO QD or 300–450 mg PO q12h[c]	TMP–SMX, TMP 5 mg/kg/dose IV q8–12h	Vancomycin 15 mg/kg/dose IV q6h	14 d	—
	Linezolid 600 mg IV/PO q12h	—	Linezolid 10 mg/kg/dose PO/IV q8h, not to exceed 600 mg/dose	14 d	—
Brain abscess, subdural empyema, spinal epidural abscess	Vancomycin 30–60 mg/kg/day IV in two to four divided doses[a] ± Rifampin 600 mg PO QD or 300–450 mg PO q12h[c]	TMP–SMX, TMP 5 mg/kg/dose IV q8–12h ± Rifampin 600 mg PO QD or 300–450 mg PO q12h[c]	Vancomycin 15 mg/kg/dose IV q6h	4–6 wk	—
	Linezolid 600 mg IV/PO q12h	—	Linezolid 10 mg/kg/dose PO/IV q8h, not to exceed 600 mg/dose[3]	4–6 wk	—
Osteomyelitis	Vancomycin 30–60 mg/kg/day IV in two to four divided doses[a]	Linezolid 600 mg PO/IV q12h	Vancomycin 15 mg/kg/dose IV q6h[5]	>6 wk	—
	Daptomycin 6 mg/kg/dose IV QD	—	Teicoplanin 10 mg/kg IV q12h × three doses, then 6–10 mg/kg QD	>6 wk	—
	TMP–SMX, TMP 4 mg/kg/dose PO/IVq8–12h + Rifampin 600 mg PO QD[c]	—	Linezolid 10 mg/kg/dose PO/IV q8h, not to exceed 600 mg/dose[3]	>6 wk	—
	Teicoplanin 6–12 mg/kg/dose IV q12h × three doses, then QD	—	Daptomycin 6–10 mg/kg/dose IV QD	>6 wk	—
	Fusidic acid 500 mg PO q8h or 750 mg q12h + Rifampin 600 mg PO QD or 300–450 mg PO q12h[c]	—	—	>6 wk	—

(*continued on next page*)

Table 1 (*continued*)

Diagnosis	Adults		Pediatric dosage	Duration	Comments
	Antibiotic of choice	Alternatives			
Septic arthritis	Vancomycin 30—60 mg/kg/day IV in two to four divided doses[a]	Linezolid 600 mg PO/IV q12h	Vancomycin 15 mg/kg/dose IV q6h[5]	3—4 wk	—
	Daptomycin 6 mg/kg/dose IV QD	—	Teicoplanin 10 mg/kg IV q12h × three doses, then 6—10 mg/kg QD	3—4 wk	—
	TMP—SMX, TMP 4 mg/kg/dose PO/IVq8-12h + Rifampin 600 mg PO QD[c]	—	Linezolid 10 mg/kg/dose PO/IV q8h, not to exceed 600 mg/dose[3]	3—4 wk	—
	Teicoplanin 6—12 mg/kg/dose IV q12h × three doses, then QD	—	Daptomycin 6—10 mg/kg/dose IV QD	3—4 wk	—
	Fusidic acid 500 mg PO q8h or 750 mg q12h + Rifampin 600 mg QD or 300—450 mg PO q12h[c]	—	—	3—4 wk	—

d = days; IV = intravenous; PO = oral; q8h = every 8 hours; q12h = every 12 hours; QD = every day; st = stat; TMP = trimethoprim; TMP—SMX = trimethoprim-sulfamethoxazole; wk, weeks.

Pediatric notes

1. Doxycycline is not recommended for children younger than 8 years of age.
2. Fusidic acid dosage: <1 year of age, 50 mg/kg/day PO q8h; 1—5 years of age, 250 mg PO q8h; 6—12 years of age, 500 mg PO q8h.
3. Linezolid dosage is 600 mg PO q12h for children ≥12 years of age and 10 mg/kg/dose PO q8h for children <12 years of age.
4. The routine use of gentamicin or rifampin in children with bacteremia or infective endocarditis is not recommended and should be individualized.
5. The duration of treatment for osteoarticular infections should be individualized and a course of 3—4 weeks and 4—6 weeks, respectively, for arthritis and osteomyelitis is recommended for children.

[a] Vancomycin dosage is recommended to be given every 6 hours in immunocompromised patients

[b] Uncomplicated bacteremia is defined as catheter removal in catheter-related infection, follow-up blood cultures performed on specimens obtained 2—4 days after the initial set that do not grow methicillin-resistant *Staphylococcus aureus*, defervescence within 72 hours of effective therapy, no evidence of metastatic infection, exclusion of endocarditis, no evidence of central catheter-related thrombophlebitis, no prostheses in the joints or intravascular space

[c] Experts' consensus.

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