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**ANTIMICROBIAL THERAPY**

**Table 3** - Therapy of Native Valve Endocarditis Caused by Highly Penicillin-Susceptible Viridans Group Streptococci and *Streptococcus bovis*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Regimen | Dosage\* and Route | Duration, wk | Strength of Recommendation | Comments |
| Aqueous crystalline penicillin G sodium | 12–18 million U/24 h IV either continuously or in 4 or 6 equally divided doses | 4 | IA | Preferred in most patients >65 y or patients with impairment of 8th cranial nerve function or renal function |
| **or** |  |  |  |  |
| Ceftriaxone sodium | 2 g/24 h IV/IM in 1 dose | 4 | IA |  |
|  | Pediatric dose†: penicillin 200 000 U/kg per 24 h IV in 4–6 equally divided doses; ceftriaxone 100 mg/kg per 24 h IV/IM in 1 dose |  |  |  |
| Aqueous crystalline penicillin G sodium | 12–18 million U/24 h IV either continuously or in 6 equally divided doses | 2 | IB |  |
| **or** |  |  |  |  |
| Ceftriaxone sodium | 2 g/24 h IV/IM in 1 dose | 2 | IB |  |
| **PLUS** |  |  |  |  |
| Gentamicin sulfate‡ | 3 mg/kg per 24 h IV/IM in 1 dose | 2 |  |  |
|  | Pediatric dose: penicillin 200 000 U/kg per 24 h IV in 4–6 equally divided doses; ceftriaxone 100 mg/kg per 24 h IV/IM in 1 dose; gentamicin 3 mg/kg per 24 h IV/IM in 1 dose or 3 equally divided doses∥ |  |  |  |
| Vancomycin hydrochloride¶ | 30 mg/kg per 24 h IV in 2 equally divided doses not to exceed 2 g/24 h unless concentrations in serum are inappropriately low | 4 | IB | Vancomycin therapy recommended only for patients unable to tolerate penicillin or ceftriaxone; vancomycin dosage should be adjusted to obtain peak (1 h after infusion completed) serum concentration of 30–45 μg/mL and a trough concentration range of 10–15 μg/mL |
|  | Pediatric dose: 40 mg/kg per 24 h IV in 2–3 equally divided doses |  |  |

Minimum inhibitory concentration ≤0.12 μg/mL

\*Dosages recommended are for patients with normal renal function.

**Table 4** – Therapy of Native Valve Endocarditis Caused by Strains of Viridans Group Streptococci and *Streptococcus bovis* Relatively Resistant to Penicillin

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Regimen | Dosage\* and Route | Duration, wk | Strength of Recommendation | Comments |
| Aqueous crystalline penicillin G sodium | 24 million U/24 h IV either continuously or in 4–6 equally divided doses | 4 | IB | Patients with endocarditis caused by penicillin-resistant (MIC >0.5 μg/mL) strains should be treated with regimen recommended for enterococcal endocarditis (see Table 8) |
| **or** |  |  |  |
| Ceftriaxone sodium | 2 g/24 h IV/IM in 1 dose | 4 | IB |
| **PLUS** |  |  |  |
| Gentamicin sulfate† | 3 mg/kg per 24 h IV/IM in 1 dose | 2 |  |
|  | Pediatric dose‡: penicillin 300 000 U/24 h IV in 4–6 equally divided doses; ceftriaxone 100 mg/kg per 24 h IV/IM in 1 dose; gentamicin 3 mg/kg per 24 h IV/IM in 1 dose or 3 equally divided doses |  |  |
| **or** |  |  |  |  |
| Vancomycin hydrochloride‡ | 30 mg/kg per 24 h IV in 2 equally divided doses not to exceed 2 g/24 h, unless serum concentrations are inappropriately low | 4 | IB | Vancomycin§ therapy recommended only for patients unable to tolerate penicillin or ceftriaxone therapy |
|  | Pediatric dose: 40 mg/kg 24 h in 2 or 3 equally divided doses |  |  |

Minimum inhibitory concentration (MIC) >0.12 μg/mL–≤0.5 μg/mL

Dosages recommended are for patients with normal renal function

**Table 5** – Therapy for Endocarditis of Prosthetic Valves or Other Prosthetic Material Caused by Viridans Group Streptococci and *Streptococcus bovis*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Regimen | Dosage\* and Route | Duration, wk | Strength of Recommendation | Comments |
| **Penicillin-susceptible strain (minimum inhibitory concentration ≤0.12 μg/mL)** | | | | |
| penicillin G sodium Aqueous crystalline | 24 million U/24 h IV either continuously or in 4–6 equally divided doses | 6 | IB | Penicillin or ceftriaxone together with gentamicin has not demonstrated superior cure rates compared with monotherapy with penicillin or ceftriaxone for patients with highly susceptible strain; gentamicin therapy should not be administered to patients with creatinine clearance of <30 mL/min |
| **or** |  |  |  |
| Ceftriaxone | 2 g/24 h IV/IM in 1 dose | 6 | IB |
| **WITH or WITHOUT** |  |  |  |
| Gentamicin sulfate† | 3 mg/kg per 24 h IV/IM in 1 dose | 2 |  |
|  | Pediatric dose‡: penicillin 300 000 U/kg per 24 h IV in 4–6 equally divided doses; ceftriaxone 100 mg/kg IV/IM once daily; gentamicin 3 mg/kg per 24 h IV/IM, in 1 dose or 3 equally divided doses |  |  |
| **or** |  |  |  |  |
| Vancomycin hydrochloride§ | 30 mg/kg per 24 h IV in 2 equally divided doses | 6 | IB |  |
|  | Pediatric dose: 40 mg/kg per 24 h IV or in 2 or 3 equally divided doses |  |  |
|  | | | | |
| **Penicillin relatively or fully resistant strain (minimum inhibitory concentration >0.12 μg/mL)** | | | | |
| penicillin sodium Aqueous crystalline | 24 million U/24 h IV either continuously or in 4–6 equally divided doses | 6 | IB |  |
| **or** |  |  |  |  |
| Ceftriaxone | 2 g/24 h IV/IM in 1 dose | 6 | IB |  |
| **PLUS** |  |  |  |  |
| Gentamicin sulfate | 3 mg/kg per 24 h IV/IM in 1 dose | 6 |  |  |
|  | Pediatric dose: penicillin 300 000 U/kg per 24 h IV in 4–6 equally divided doses |  |  |  |
| Vancomycin hydrochloride | 30 mg/kg per 24 h IV in 2 equally divided doses | 6 | IB | Vancomycin therapy is recommended only for patients unable to tolerate penicillin or ceftriaxone |
|  | Pediatric dose: 40 mg/kg per 24 h IV in 2 or 3 equally divided doses |  |  |

Dosages recommended are for patients with normal renal function.

**Table 6** – Therapy for Endocarditis Caused by Staphylococci in the Absence of Prosthetic Materials

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Regimen | Dosage\* and Route | Duration | Strength of Recommendation | Comments |
| **Oxacillin-susceptible strains** | | | | |
| Nafcillin or oxacillin† | 12 g/24 h IV in 4–6 equally divided doses | 6 wk | IA | For complicated right-sided IE and for left-sided IE; for uncomplicated right-sided IE, 2 wk (see full text) |
| **WITH** |  |  |  |  |
| Optional addition of gentamicin sulfate‡ | 3 mg/kg per 24 h IV/IM in 2 or 3 equally divided doses | 3–5 d |  |  |
|  | Pediatric dose§: Nafcillin or oxacillin 200 mg/kg per 24 h IV in 4–6 equally divided doses; gentamicin 3 mg/kg per 24 h IV/IM in 3 equally divided doses |  |  | Clinical benefit of aminoglycosides has not been established |
|  |  |  |  |  |
|  |  |  |  |  |
| *For penicillin-allergic (nonanaphylactoid type) patients:* | | Consider skin testing for oxacillin-susceptible staphylococci and questionable history of immediate-type hypersensitivity to penicillin | | |
| Cefazolin | 6 g/24 h IV in 3 equally divided doses | 6 wk | IB | Cephalosporins should be avoided in patients with anaphylactoid-type hypersensitivity to β-lactams; vancomycin should be used in these cases§ |
| **WITH** |  |  |  |  |
| Optional addition of gentamicin sulfate | 3 mg/kg per 24 h IV/IM in 2 or 3 equally divided doses | 3–5 d |  | Clinical benefit of aminoglycosides has not been established |
|  | Pediatric dose: cefazolin 100 mg/kg per 24 h IV in 3 equally divided doses; gentamicin 3 mg/kg per 24 h IV/IM in 3 equally divided doses |  |  |  |
|  | | | | |
| **Oxacillin resistant strains** | | | | |
| Vancomycin∥ | 30 mg/kg per 24 h IV in 2 equally divided doses | 6 wk | IB | Adjust vancomycin dosage to achieve 1-h serum concentration of 30–45 μg/mL and trough concentration of 10–15 μg/mL (see full text for vancomycin alternatives) |
|  | Pediatric dose: 40 mg/kg per 24 h IV in 2 or 3 equally divided doses |  |  |  |

**Table 7** – Therapy for Prosthetic Valve Endocarditis Caused by Staphylococci

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Regimen | Dosage\* and Route | Duration, Wk | Strength of Recommendation | Comments |
| **Oxacillin-susceptible strains** | | | | |
| Nafcillin or oxacillin | 12 g/24 h IV in 6 equally divided doses | ≥6 | IB | Penicillin G 24 million U/24 h IV in 4 to 6 equally divided doses may be used in place of nafcillin or oxacillin if strain is penicillin susceptible (minimum inhibitory concentration ≤0.1 μg/mL) and does not produce β-lactamase; vancomycin should be used in patients with immediate-type hypersensitivity reactions to β-lactam antibiotics (see Table 3 for dosing guidelines); cefazolin may be substituted for nafcillin or oxacillin in patients with non–immediate-type hypersensitivity reactions to penicillins |
| **PLUS** |  |  |  |
| Rifampin | 900 mg per 24 h IV/PO in 3 equally divided doses | ≥6 |  |
| **PLUS** |  |  |  |
| Gentamicin† | 3 mg/kg per 24 h IV/IM in 2 or 3 equally divided doses | 2 |  |
|  | Pediatric dose‡: nafcillin or oxacillin 200 mg/kg per 24 h IV in 4–6 equally divided doses; rifampin 20 mg/kg per 24 h IV/PO in 3 equally divided doses; gentamicin 3 mg/kg per 24 h IV/IM in 3 equally divided doses |  |  |
|  | | | | |
| **Oxacillin resistant strains** | | | | |
| Vancomycin | 30 mg/kg 24 h in 2 equally divided doses | ≥6 | IB | Adjust vancomycin to achieve 1-h serum concentration of 30–45 μg/mL and trough concentration of 10–15 μg/mL (see full text for gentamicin alternatives) |
| **PLUS** |  |  |  |
| Rifampin | 900 mg/24 h IV/PO in 3 equally divided doses | ≥6 |  |
| **PLUS** |  |  |  |
| Gentamicin | 3 mg/kg per 24 h IV/IM in 2 or 3 equally divided doses | 2 |  |
|  | Pediatric dose: vancomycin 40 mg/kg per 24 h IV in 2 or 3 equally divided doses; rifampin 20 mg/kg per 24 h IV/PO in 3 equally divided doses (up to adult dose); gentamicin 3 mg/kg per 24 h IV or IM in 3 equally divided doses |  |  |

**Table 8** – Therapy for Native Valve or Prosthetic Enterococcal Endocarditis Caused by Strains Susceptible to Penicillin, Gentamycin, and Vancomycin

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Regimen | Dosage\* and Route | Duration, wk | Strength of Recommendation | Comments |
| Ampicillin sodium | 12 g/24 h IV in 6 equally divided doses | 4–6 | IA | Native valve: 4-wk therapy recommended for patients with symptoms of illness ≤3 mo; 6-wk therapy recommended for patients with symptoms >3 mo |
| **or** |  |  |  |  |
| Aqueous crystalline penicillin G sodium | 18–30 million U/24 h IV either continuously or in 6 equally divided doses | 4–6 | IA |  |
| **PLUS** |  |  |  |  |
| Gentamicin sulfate† | 3 mg/kg per 24 h IV/IM in 3 equally divided doses | 4–6 |  |  |
|  | Pediatric dose‡: ampicillin 300 mg/kg per 24 h IV in 4–6 equally divided doses; penicillin 300 000 U/kg per 24 h IV in 4–6 equally divided doses; gentamicin 3 mg/kg per 24 h IV/IM in 3 equally divided doses |  |  |  |
| **Unable to tolerate penicillin or ampicillin** | | | | |
| Vancomycin hydrochloride§ | 30 mg/kg per 24 h IV in 2 equally divided doses | 6 | IB | Vancomycin therapy recommended only for patients unable to tolerate penicillin or ampicillin |
| **PLUS** |  |  |  |  |
| Gentamicin sulfate | 3 mg/kg per 24 h IV/IM in 3 equally divided doses | 6 |  | 6 wk of vancomycin therapy recommended because of decreased activity against enterococci |
|  | Pediatric dose: vancomycin 40 mg/kg per 24 h IV in 2 or 3 equally divided doses; gentamicin 3 mg/kg per 24 h IV/IM in 3 equally divided doses |  |  |

**Table 9** – Therapy for Native or Prosthetic Valve Enterococcal Endocarditis Caused by Strains Susceptible to Penicillin, Streptomycin and Vancomycin and Resistant to Gentamycin

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Regimen | Dosage\* and Route | Duration, wk | Strength of Recommendation | Comments |
| Ampicillin sodium | 12 g/24 h IV in 6 equally divided doses | 4–6 | IA | Native valve: 4-wk therapy recommended for patients with symptoms of illness <3 mo; 6-wk therapy recommended for patients with symptoms >3 mo |
| **or** |  |  |  |  |
| Aqueous crystalline penicillin G sodium | 24 million U/24 h IV continuously or in 6 equally divided doses | 4–6 | IA |  |
| **PLUS** |  |  |  |  |
| Streptomycin sulfate† | 15 mg/kg per 24 h IV/IM in 2 equally divided doses | 4–6 |  | Prosthetic valve or other prosthetic cardiac material: minimum of 6 wk of therapy recommended |
|  | Pediatric dose‡: ampicillin 300 mg/kg per 24 h IV in 4–6 equally divided doses; penicillin 300 000 U/kg per 24 h IV in 4–6 equally divided doses; streptomycin 20–30 mg/kg per 24 h IV/IM in 2 equally divided doses |  |  |
| **Unable to tolerate penicillin or ampicillin** | | | | |
| Vancomycin hydrochloride§ | 30 mg/kg per 24 h IV in 2 equally divided doses | 6 |  | Vancomycin therapy recommended only for patients unable to tolerate penicillin or ampicillin |
| **PLUS** |  |  |  |
| Streptomycin sulfate | 15 mg/kg per 24 h IV/IM in 2 equally divided doses | 6 |  |
|  | Pediatric dose: vancomycin 40 mg/kg per 24 h IV in 2 or 3 equally divided doses; streptomycin 20–30 mg/kg per 24 h IV/IM in 2 equally divided doses |  |  |  |

**Table 10** – Therapy for Native or Prosthetic Valve Enterococcal Endocarditis Caused by Strains Resistant to Penicillin and Susceptible to Aminoglycoside and Vancomycin

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Regimen | Dosage\* and Route | Duration | Strength of Recommendation | Comments |
| **Beta-Lactamase-producing strains** | | | | |
| Ampicillin-sulbactam | 12 g/24 h IV in 4 equally divided doses | 6 | IIaC | Unlikely that the strain will be susceptible to gentamicin; if strain is gentamicin resistant, then >6 wk of ampicillin-sulbactam therapy will be needed |
| **PLUS** |  |  |  |
| Gentamicin sulfate† | 3 mg/kg per 24 h IV/IM in 3 equally divided doses | 6 |  |
|  | Pediatric dose‡: ampicillin-sulbactam 300 mg/kg per 24 h IV in 4 equally divided doses; gentamicin 3 mg/kg per 24 h IV/IM in 3 equally divided doses |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |
| **Unable to tolerate ampicillin-sulbactam** | |  | | |
| Vancomycin hydrochloride§ | 30 mg/kg per 24 h IV in 2 equally divided doses | 6 | IIaC | Vancomycin therapy recommended only for patients unable to tolerate ampicillin-sulbactam |
| **PLUS** |  |  |  |
| Gentamicin sulfate† | 3 mg/kg per 24 h IV/IM in 3 equally divided doses | 6 |  |
|  | Pediatric dose: vancomycin 40 mg/kg per 24 h in 2 or 3 equally divided doses; gentamicin 3 mg/kg per 24 h IV/IM in 3 equally divided doses |  |  |  |
|  | | | | |
| **Intrinsic Penicillin Resistance** | | | | |
| Vancomycin hydrochloride‡ | 30 mg/kg per 24 h IV in 2 equally divided doses | 6 | IIaC | Consultation with a specialist in infectious diseases recommended |
| **PLUS** |  |  |  |  |
| Gentamicin sulfate† | 3 mg/kg per 24 h IV/IM in 3 equally divided doses | 6 |  |  |
|  | Pediatric dose: vancomycin 40 mg/kg per 24 h IV in 2 or 3 equally divided doses; gentamicin 3 mg/kg per 24 h IV/IM in 3 equally divided doses |  |  |  |

**Table 11** – Therapy for Native or Prosthetic Valve Enterococcal Endocarditis Caused by Strains Resistant to Penicillin, Aminoglycoside, and Vancomycin

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Regimen | Dosage\* and Route | Duration | Strength of Recommendation | Comments |
| **E. Faecium** | | | | |
| Linezolid | 1200 mg/24 h IV/PO in 2 equally divided doses | ≥8 | IIaC | Patients with endocarditis caused by these strains should be treated in consultation with an infectious diseases specialist; cardiac valve replacement may be necessary for bacteriologic cure; cure with antimicrobial therapy alone may be <50%; severe, usually reversible thrombocytopenia may occur with use of linezolid, especially after 2 wk of therapy; quinupristin-dalfopristin only effective against E faecium and can cause severe myalgias, which may require discontinuation of therapy; only small no. of patients have reportedly been treated with imipenem/cilastatin-ampicillin or ceftriaxone + ampicillin |
| **or** |  |  |  |
| Quinupristin-dalfopristin | 22.5 mg/kg per 24 h IV in 3 equally divided doses | ≥8 |  |
|  | | | | |
| **E. Faecalis** | | | | |
| Imipenem/cilastatin | 2 g/24 h IV in 4 equally divided doses | ≥8 | IIbC |  |
| **PLUS** |  |  |  |  |
| Ampicillin sodium | 12 g/24 h IV in 6 equally divided doses | ≥8 |  |  |
| **or** |  |  |  |  |
| Ceftriaxone sodium | 2 g/24 h IV/IM in 1 dose | ≥8 | IIbC |  |
| **PLUS** |  |  |  |  |
| Ampicillin sodium | 12 g/24 h IV in 6 equally divided doses | ≥8 |  |  |
|  | Pediatric dose†: Linezolid 30 mg/kg per 24 h IV/PO in 3 equally divided doses; quinupristin-dalfopristin 22.5 mg/kg per 24 h IV in 3 equally divided doses; imipenem/cilastatin 60–100 mg/kg per 24 h IV in 4 equally divided doses; ampicillin 300 mg/kg per 24 h IV in 4–6 equally divided doses; ceftriaxone 100 mg/kg per 24 h IV/IM once daily |  |  |  |

**Table 12** – Therapy for Both Native and Prosthetic Valve Endocarditis Caused by HACEK Microorganisms

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Regimen | Dosage\* and Route | Duration, wk | Strength of Recommendation | Comments |
| Ceftriaxone† sodium | 2 g/24 h IV/IM in 1 dose | 4 | IB | Cefotaxime or another third- or fourth-generation cephalosporin may be substituted |
| **or** |  |  |  |  |
| Ampicillin- sulbactam‡ | 12 g/24 h IV in 4 equally divided doses | 4 | IIaB |  |
| **or** |  |  |  |  |
| Ciprofloxacin‡§ | 1000 mg/24 h PO or 800 mg/24 h IV in 2 equally divided doses | 4 | IIbC | Fluoroquinolone therapy recommended only for patients unable to tolerate cephalosporin and ampicillin therapy; levofloxacin, gatifloxacin, or moxifloxacin may be substituted; fluoroquinolones generally not recommended for patients <18 y old Prosthetic valve: patients with endocarditis involving prosthetic cardiac valve or other prosthetic cardiac material should be treated for 6 wk |
|  | Pediatric dose∥: Ceftriaxone 100 mg/kg per 24 h IV/IM once daily; ampicillin-sulbactam 300 mg/kg per 24 h IV divided into 4 or 6 equally divided doses; ciprofloxacin 20–30 mg/kg per 24 h IV/PO in 2 equally divided doses |  |  |