Table 5.1 Guidelines for known-pathogen therapy

	Drug of choice	Alternatives	Remarks
Acinetobacter baumannii	I.V. ampicillin-sulbactam + an aminoglycoside	• I.V. cefoperazone-sulbactam + an aminoglycoside (mixed infection with *P. aeruginosa*) • Fluoroquinolone + an aminoglycoside (if allergic to penicillin)	• Sulbactam is highly active against *Acinetobacter* • Resistance rates in 2010: ampicillin-sulbactam (24%), cefoperazone-sulbactam (24%), imipenem (37%), gentamicin (32%), amikacin (25%), ciprofloxacin (50%) • For multidrug-resistant isolates: consult microbiologist or infectious disease physician
Clostridium difficile	P.O. metronidazole (404–405)	P.O. vancomycin (if metronidazole fails as documented microbiologically)	• Mild/moderate disease: clinical efficacy of metronidazole = vancomycin • Severe disease, ileus or toxic megacolon: I.V. metronidazole + P.O. vancomycin + consult surgeon • First recurrence: same as primary infection based on severity of disease • Multiple recurrence: consult microbiologist or infectious disease physician, options include vancomycin taper or faecal microbiota transplant (406)

	Drug of choice	Alternatives	Remarks
***Enterobacter cloacae* complex**	• P.O./I.V. levofloxacin/ ciprofloxacin for urinary tract infection • I.V. cefepime (± an aminoglycoside) for severe infection • I.V. piperacillin-tazobactam	• I.V. carbapenem (for severe infection and/or ESBL-producing strain)	• Cefepime is highly active in vitro against almost all *Enterobacter* isolates • Emergence of AmpC derepressed mutants emerge in 20–40% of infections treated with the second or third generation cephalosporins. Use of these agents for serious infections is not recommended • One study in HK found high prevalence of ESBL production among *E. hormaechei* (a member of the *E. cloacae* complex) (407) • Resistance rate in 2010: levofloxacin (8%), gentamicin (4%), amikacin (1%) • For multidrug-resistant isolates: consult microbiologist or infectious disease physician

	Drug of choice	Alternatives	Remarks
***E. coli* (ESBL-neg)**	• I.V./P.O. ampicillin-sulbactam or amoxicillin-clavulanate (add an aminoglycoside if rapid bactericidal action desirable on clinical grounds)	• I.V./P.O. cefuroxime (if resistant to amoxicillin-clavulanate), add I.V./P.O. metronidazole (if mixed infection with anaerobes likely) • I.V. piperacillin-tazobactam + an aminoglycoside (if *P. aeruginosa* or *Acinetobacter* are co-pathogens)	
Haemophilus influenzae	• P.O. amoxicillin or P.O./I.V. ampicillin-sulbactam or amoxicillin-clavulanate or cefotaxime or ceftriaxone	• Fluoroquinolones (if allergic to penicillin)	• Amoxicillin-clavulanate also provides good coverage for *M. catarrhalis* and *S. pneumoniae*

	Drug of choice	Alternatives	Remarks
***Klebsiella pneumoniae* (ESBL-neg)**	• I.V./P.O. ampicillin-sulbactam or amoxicillin-clavulanate (add an aminoglycoside if rapid bactericidal action desirable on clinical grounds)	• I.V./P.O. cefuroxime (if resistant to amoxicillin-clavulanate), add I.V./P.O. metronidazole (if mixed infection with anaerobes likely) • I.V. piperacillin-tazobactam + an aminoglycoside (if *P. aeruginosa* or *Acinetobacter* are co-pathogens)	• Ampicillin-sulbactam less satisfactory because of poor inhibitory activity of sulbactam for SHV-1 ß-lactamase
***E. coli / K. pneumoniae* (ESBL-pos)**	• P.O. nitrofurantoin or P.O. amoxicillin-clavulanate (uncomplicated urinary tract infection and other mild infections)	• Carbapenem or I.V. β-lactam/β-lactamase inhibitor for bacteraemia or other serious infection	• Carbapenem has been shown to be effective clinically and is currently the ß-lactam agent of choice for serious infection by ESBL-pos *E. coli*/*Klebsiella* spp.

	Drug of choice	Alternatives	Remarks
Pseudomonas aeruginosa	I.V. piperacillin or ticarcillin-clavulanate or piperacillin-tazobactam + an aminoglycoside	• I.V. cefoperazone-sulbactam + an aminoglycoside (mixed infection with *Acinetobacter*) • I.V./P.O. levofloxacin/ ciprofloxacin + an aminoglycoside (if allergic to penicillin)	• Combination therapy recommended (for synergism) for all serious infection except for uncomplicated catheter-related bacteraemia • Piperacillin-tazobactam used instead of ceftazidime due to rapid rise in AmpC type and ESBL-producers in *Enterobacteriaceae* • For multidrug-resistant isolates: consult microbiologist or infectious disease physician
Methicillin-sensitive *S. aureus*	P.O./I.V. cloxacillin or amoxicillin-clavulanate or ampicillin-sulbactam or first generation cephalosporin	• I.V. cefazolin (if allergic to penicillin, but limited to those with minor allergy such as rash alone) • Clindamycin (if allergic to penicillin)	

	Drug of choice	Alternatives	Remarks
Methicillin-resistant *S. aureus*	I.V. vancomycin (bacteraemia or other invasive infections)	• I.V./P.O. linezolid or I.V. daptomycin if (1) vancomycin allergy - extensive rash, other than red-man syndrome develop after vancomycin, or (2) bacteraemia caused by MRSA with vancomycin ≥ 2 μg/mL	• Cotrimoxazole, fusidic acid or rifampicin are useful adjuncts for deep-seated infections (e.g. osteomyelitis) but these agents should not be administered as monotherapy • Most abscesses or uncomplicated skin and soft tissue infection caused by CA-MRSA could be treated with drainage and oral antibiotics with in vitro activities (e.g. clindamycin or cotrimoxazole) • Vancomycin intermediate *Staphylococcus aureus*/ vancomycin resistant *Staphylococcus aureus*: consult microbiologist or infectious disease physician
Mycoplasma pneumoniae	• P.O. doxycycline (or I.V. minocycline)	• P.O. azithromycin • I.V./P.O. levofloxacin or moxifloxacin	• Doxycycline preferred over azithromycin in view of increasing macrolide resistant *Mycoplasma pneumoniae* (379)

	Drug of choice	Alternatives	Remarks
Stenotrophomonas maltophilia	P.O./I.V. cotrimoxazole + I.V. ticarcillin-clavulanate	• I.V./P.O. cotrimoxazole + fluoroquinolone	• Cotrimoxazole + ticarcillin-clavulanate is synergistic in vitro. Cotrimoxazole is a key component in therapy • Combination therapy recommended for synergy and to prevent resistance • For cotrimoxazole-resistant strain, consult microbiologist or infectious disease physician
Streptococcus pneumoniae (for infection outside the central nervous system)	• Penicillin-sensitive: I.V. penicillin G (4–8 million unit/day, q6h) • Penicillin-intermediate: I.V. penicillin G (high dose, 12–18 million unit/day, q4h)[1] • Penicillin-resistant: I.V. cefotaxime or ceftriaxone	• ß-lactam/ß-lactamase inhibitor combination with the exception of cefoperazone-sulbactam (for mixed infections) • P.O./I.V. levofloxacin or P.O./I.V. moxifloxacin (if allergic to penicillin) for non-meningeal infections and penicillin-sensitive strains	• Most pneumococcal pneumonia can be treated with high dose amoxicillin or high dose amoxicillin-clavulanate • For pure pneumococcal infection, penicillin G instead of amoxicillin-clavulanate is preferred, switch therefore recommended • >70% resistant to erythromycin. Cross-resistance to clindamycin is very common • Resistance to erythromycin = resistance to other newer macrolides (clarithromycin, azithromycin)

	Drug of choice	Alternatives	Remarks
Streptococcus pneumoniae (for central nervous system infection)	• Penicillin-sensitive (MIC ≤ 0.06 µg/mL): I.V. penicillin G (18–24 million unit/day, q4h) or I.V. ampicillin 2 g q4h • Penicillin-resistant (MIC ≥ 0.12 µg/mL) and third-generation cephalosporin (MIC <1 µg/mL): I.V. cefotaxime 2 g q4h or I.V. ceftriaxone 2 g q12h • Penicillin-resistant (MIC ≥ 0.12 µg/mL) and third-generation cephalosporin (MIC ≥ 1 µg/mL): I.V. vancomycin plus I.V. cefotaxime 2 g q4h or ceftriaxone 2 g q12h		• MIC (meningitis) breakpoints for penicillin, ceftriaxone and cefotaxime to be used here • In *S. pneumoniae*, cross resistance between penicillin and ceftriaxone/cefotaxime is common (391,408). Local data indicates that approximately half of the penicillin-resistant (meningitis) isolates are intermediate/resistant (meningitis) to cefotaxime

Note:

[1] CLSI MIC (µg/mL) breakpoints for penicillin G: sensitive ≤ 0.06; intermediate 0.12–1; resistant ≥ 2. These breakpoints were decided mainly for the relevance on meningitis. For pneumococcal pneumonia, pharmacokinetic/dynamic data indicates that isolates with MIC of up to 1–2 µg/mL should be considered 'sensitive' to appropriate dose of penicillin, ampicillin and amoxicillin.