These guidelines have been withdrawn

MOH clinical practice guidelines are considered withdrawn five years after publication unless otherwise specified in individual guidelines. Users should keep in mind that evidence-based guidelines are only as current as the evidence that supports them and new evidence can supersede recommendations made in the guidelines.
### Levels of evidence and grades of recommendation

#### Levels of evidence

<table>
<thead>
<tr>
<th>Level</th>
<th>Type of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ia</td>
<td>Evidence obtained from meta-analysis of randomised controlled trials.</td>
</tr>
<tr>
<td>Ib</td>
<td>Evidence obtained from at least one randomised controlled trial.</td>
</tr>
<tr>
<td>IIa</td>
<td>Evidence obtained from at least one well-designed controlled study without randomisation.</td>
</tr>
<tr>
<td>IIb</td>
<td>Evidence obtained from at least one other type of well-designed quasi-experimental study.</td>
</tr>
<tr>
<td>III</td>
<td>Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.</td>
</tr>
<tr>
<td>IV</td>
<td>Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.</td>
</tr>
</tbody>
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#### Grades of recommendation

<table>
<thead>
<tr>
<th>Grade</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Requires at least one randomised controlled trial, as part of the body of literature of overall good quality and consistency, addressing the specific recommendation.</td>
</tr>
<tr>
<td>(evidence levels Ia, Ib)</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>Requires availability of well conducted clinical studies, but no randomised clinical trials on the topic of recommendation.</td>
</tr>
<tr>
<td>(evidence levels IIa, IIb, III)</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>Requires evidence obtained from expert committee reports or opinions, and/or clinical experiences of respected authorities. Indicates absence of directly applicable clinical studies of good quality.</td>
</tr>
<tr>
<td>(evidence level IV)</td>
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</tr>
<tr>
<td>GPP</td>
<td>Recommended best practice based on the clinical experience of the guideline development group.</td>
</tr>
<tr>
<td>(good practice points)</td>
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Use of Antibiotics in Adults
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**Statement of Intent**

These guidelines are not intended to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge advances and patterns of care evolve.

The contents of this publication are guidelines to clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not ensure a successful outcome in every case. These guidelines should neither be construed as including all proper methods of care, nor exclude other acceptable methods of care. Each physician is ultimately responsible for the management of his/her unique patient, in the light of the clinical data presented by the patient and the diagnostic and treatment options available.
Foreword

The increasing emergence of antibiotic resistance not only increases morbidity and mortality, but also leads to increased health care costs. With the current availability of numerous classes of antibiotics, and different types within classes, guidance is needed to assist medical practitioners in deciding when to use antibiotics, and which antibiotic to use to ensure patient recovery and curb the development of antibiotic resistance.

This set of guidelines addresses the main areas in which antibiotics are most commonly used. At the same time, circumstances commonly encountered in primary care, e.g. common cold, in which there is no evidence that antibiotics are useful are also discussed. This edition of the guidelines has been updated to include the latest evidence from scientific literature, and has been expanded to include new topics like acute bacterial meningitis and diarrhoea in adults.

It is hoped that all medical practitioners will find this set of guidelines of use in their management of patients with infectious diseases.

PROFESSOR K SATKU
DIRECTOR OF MEDICAL SERVICES
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Executive summary of recommendations

Details of recommendations can be found in the main text at the pages indicated.

What’s new in the revised guidelines

New sections in this edition of the guidelines include:

i) use of antibiotics in acute bacterial meningitis
ii) use of antibiotics in infectious diarrhoea in adults

Other sections have been revised, based on the rapid advances in antibiotic therapy and in infectious disease treatment:

• The section on bronchitis has been expanded to include recommendations for risk stratification and antibiotic therapy in patients with acute exacerbation of chronic bronchitis.
• The section on acute upper respiratory tract infections has additional recommendations for non-specific respiratory infections. The use of the Centor criteria to predict Group A beta-haemolytic streptococcal pharyngitis was also discussed. Influenza, SARS and vaccination are also discussed in this section.
• The Fine Pneumonia Severity Index has been included in the risk stratification subsection of the section on community-acquired pneumonia.
• Recommendations for infections in long-term care institutions and infected pressure ulcers have been added to the section on antibiotic use in the elderly.
• An algorithm for the management of urinary tract infections in adults has been added.
• New sections on cost-effectiveness issues and clinical quality improvement in antibiotic use have been added.

Principles of Antibiotic Use

**GPP** Antibiotics should be used only for treatment of patients with confirmed or suspected bacterial infections. Antibiotics may be used for prophylaxis where consequences of infection would be severe (pg 29). **GPP**
Antibiotics should only be chosen after considering the following questions:

1. Is there an infection?
2. What is the site of infection and the most likely causative organism?
3. Will the antibiotic reach the site of infection?
4. What side effects or drug interactions might this antibiotic have?
5. What adjustments should be made for the individual patient, e.g. the young infant, the elderly, patients with renal failure?
6. What is the appropriate dose and duration of treatment for the site and type of infection?

(PG 30)

Patients or their caregivers should be clearly instructed on the dose and the necessity of finishing a course of treatment (PG 28).

Use of Antibiotics in Acute Upper Respiratory Tract Infections (URTI) in Adults

Antibiotic use in URTI

The use of antibiotics for a large portion of URTIs is not recommended because these are viral infections, for which antibiotics do not provide clinical benefit (PG 34).

Grade B, Level IIa

Non-specific respiratory infections

Antibiotic treatment of adults with non-specific upper respiratory tract infection is not recommended (PG 36).

Grade A, Level Ia

The use of antibiotics is not recommended when there is purulent secretion from the nares or throat, in patients with uncomplicated URTI (PG 36).

Grade A, Level Ia
Acute pharyngitis (sore throat)

B Patients identified with Group A beta-haemolytic streptococcal pharyngitis should be treated with antibiotics to prevent complications (pg 37).

Grade B, Level III

A Group A beta-haemolytic streptococcal-positive patients should be treated with penicillin V, for seven days (pg 38).

Grade A, Level Ib

A Throat cultures are not recommended for the routine primary evaluation of adults with pharyngitis (pg 38).

Grade A, Level Ib

C Administer appropriate analgesics, antipyretics, and supportive care to all patients with pharyngitis (pg 38).

Grade C, Level IV

Acute epiglottitis

B The antibiotic of choice to treat acute epiglottitis is ceftriaxone or chloramphenicol (pg 40).

Grade B, Level IIb

Acute rhinosinusitis

B Sinus radiography is not recommended for diagnosis in routine cases (pg 41).

Grade B, Level IIb

B Symptomatic treatment and reassurance is the preferred initial management strategy for patients with mild symptoms of acute rhinosinusitis (pg 42).

Grade B, Level IIb

B Antibiotic therapy should be reserved for:

• Patients with moderately severe symptoms who meet the criteria for the clinical diagnosis of acute bacterial rhinosinusitis (symptoms that last >7 days and include maxillary pain in the face or teeth and purulent nasal secretions); and
• Patients with severe rhinosinusitis symptoms, regardless of duration of illness.

Grade B, Level IIb
A For the initial treatment of acute bacterial maxillary rhinosinusitis, amoxicillin or penicillin for 7-14 days is recommended (pg 42).

   Grade A, Level Ia

B Isolated infection of a frontal or sphenoid sinus is a rare but potentially dangerous condition, usually caused by bacteria, and should be referred to hospital for treatment (pg 42).

   Grade B, Level IIb

**Acute laryngitis**

**GPP** If symptoms last for more than 3 weeks, the condition is classified as chronic laryngitis, for which an underlying cause must be further investigated. Underlying causes include laryngeal polyps, cancer, laryngeal tuberculosis, and gastro-esophageal reflux (pg 43).

   GPP

B Antibiotic treatment for acute laryngitis currently should be reserved for high-risk patients, patients with severe symptoms, or in the presence of an identifiable organism on Gram stain and culture (pg 43).

   Grade B, Level IIb

**Acute otitis media**

B Antibiotics are unnecessary in acute otitis media (pg 44).

   Grade B, Level IIb

B Avoid local treatment with antimicrobial eardrops in acute otitis media (pg 45)

   Grade B, Level III

**Common cold**

A Antibiotics should not be given for the common cold (pg 45).

   Grade A, Level Ia

B Antibiotics should not be given for the common cold which is accompanied by mucopurulent rhinitis (pg 45).

   Grade B, Level III
Influenza

A Neuraminidase inhibitors (NIs) are effective for the prevention and treatment of influenza (pg 47).

Grade A, Level Ia

B The adamantanes, rimantadine and amantadine, are not recommended for influenza A because of increasing drug resistance (pg 47).

Grade B, Level III

Acute Bronchitis and Exacerbation of Chronic Bronchitis

B In a patient with an acute cough illness lasting less than 3 weeks, pneumonia should be ruled out by history and clinical examination. Chest X-ray for pneumonia is not necessary in the absence of red flags (pg 50).

Grade B, Level III

A Routine antibiotic treatment of acute bronchitis is not recommended, regardless of the duration of cough (pg 51).

Grade A, Level Ia

B Antibiotic therapy in acute bronchitis should be considered if the patient is ≥ 60 years or ill at the outset (pg 51).

Grade B, Level III

C Once a diagnosis of acute bronchitis has been made, the physician should address symptomatic treatment and patient expectations of the visit (pg 51).

Grade C, Level IV

B All cases of acute bronchitis should be followed up and antibiotics considered if they are not recovering (pg 52).

Grade B, Level III

Acute exacerbations of chronic bronchitis (AECB)

A Patients with acute exacerbation of severity of Anthonisen Type I (having increased dyspnea, increased sputum production, and increased sputum purulence) and Anthonisen Type II (two of the three symptoms) should be given antibiotic therapy (pg 54).

Grade A, Level Ib
A Patients with one or more of the following risk factors should be given antibiotic therapy: more than 4 exacerbations within the past year; a co-morbid condition, such as diabetes, asthma, or a history of coronary artery disease, or marked airway obstruction (pg 55).

Grade A, Level Ib

B Patients with exacerbations without an increase in purulent sputum do not need antibiotic therapy unless there is a consolidation on a chest radiograph or clinical signs of pneumonia (pg 55).

Grade B, Level IIa

B Patients with purulent exacerbations but who have no risk factors for treatment failure or no enhanced association with more virulent or resistant bacterial pathogens can be treated with an advanced macrolide (azithromycin, clarithromycin), a cephalosporin (cefuroxime), or doxycycline (pg 56).

Grade B, Level IIa

A Patients with purulent exacerbations and who have risk factors that are associated with an increased likelihood of treatment failure or infection with more virulent or resistant organisms should be given antibiotics with enhanced antimicrobial coverage, namely the newer fluoroquinolones (moxifloxacin, gemifloxacin*, gatifloxacin, levofloxacin) or amoxillin-clavulanate (pg 59).

Grade A, Level Ib

GPP In a patient with AECB requiring repeat antibiotic therapy within 3 months, a new class of antibiotics should be used (pg 60).

GPP

Use of Antibiotics in Community Acquired Pneumonia

Risk Stratification

B Risk stratification is a key step in the management of community acquired pneumonia (pg 64).

Grade B, Level IIa

* currently not available in Singapore.
All patients with severe community acquired pneumonia (Category IV) in the ICU should be treated empirically for *Burkholderia pseudomallei* (pg 69).

**Grade B, Level III**

**Inpatient Investigations**

Microbiological, haematological, biochemical and serological tests (see list below) are recommended for patients in risk Categories III and IV upon presentation.

The following microbiological tests should be done before starting antibiotics in patients with moderate to severe CAP (Categories III and IV). Initial microbiological studies may have limited value in the management of patients with low risk CAP (Categories I & II):

- Sputum Gram stain and aerobic culture (mycobacterial smear and culture where appropriate).
- Blood aerobic culture.
- Pleural fluid Gram stain and culture.
- Urine for *Legionella* antigen.

The other investigations are:

- Blood count with differentials, and smear for toxic granulations.
- Biochemistry, including renal and liver function (Blood gas where necessary).
- Consider HIV testing and work-up for *Pneumocystis carinii*.
- Optional serological testing for atypical agents.

(pgl 69)

**Grade C, Level IV**

**Empirical Antibiotic Therapy**

The initial choice for empirical antibiotic therapy should be based on the risk category and relative prevalence of major pathogens (pg 69).

**Grade A, Level Ib**

The quinolones are not recommended for the outpatient treatment of community acquired pneumonia in categories I & II (pg 69).

**Grade C, Level IV**
A A switch from I.V. to oral antimicrobials and prompt hospital release is recommended for patients in low-intermediate risk categories who respond promptly or become clinically stable after receiving initial antimicrobial treatment (pg 73).

Grade A, Level Ia

B Criteria for discharge from hospital.

- Stable vital signs for 24 hours (i.e. temperature <37.8°C, respiratory rate <24/min, systolic BP ≥90mmHg, O₂ saturation ≥90% while breathing room air).
- Patient able to take diet.
- Patient able to take oral antibiotics.
- No other active clinical or psycho-social problems requiring hospital stay.

(pg 73)

Grade B, Level III

B In addition to the usual outcomes of mortality and hospital length of stay, the time to the first dose of antibiotics in elderly patients (>65 years) should be a key indicator of the evaluation of the quality of community acquired pneumonia management (pg 74).

Grade B, Level III

Use of Antibiotics in Hospital Acquired Pneumonia

Classification of hospital acquired pneumonia and antibiotic use

B It is recommended that the initial empirical therapy be based upon targeting a core group of pathogens according to severity of illness, duration of hospitalisation and risk factors for specific pathogens (pg 77).

Grade B, Level III

A Piperacillin-tazobactam is as safe and effective as ceftazidime in the empirical treatment of severe hospital acquired pneumonia, hospital acquired pneumonia in the ICU and ventilator associated pneumonia.

(pg 77)

Grade A, Level Ib
C Antibiotics for patients with no risk factors; hospital acquired pneumonia of mild to moderate severity, and of early onset (≤ 5 days):

<table>
<thead>
<tr>
<th>Core pathogens</th>
<th>Core antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enteric Gram-negative bacilli</td>
<td>3rd-generation cephalosporin</td>
</tr>
<tr>
<td>- Klebsiella species and Escherichia coli</td>
<td>e.g. intravenous ceftriaxone, or β-lactam/β-lactamase inhibitor</td>
</tr>
<tr>
<td></td>
<td>e.g. intravenous ampicillin-sulbactam or amoxicillin-clavulanic acid, or fiber</td>
</tr>
<tr>
<td></td>
<td>e.g. ciprofloxacin.</td>
</tr>
<tr>
<td>Also,</td>
<td>Consider adding cloxacillin or clindamycin.</td>
</tr>
<tr>
<td>- Staphylococcus aureus</td>
<td>Consider adding azithromycin or clarithromycin.</td>
</tr>
<tr>
<td>- Hemophilus influenzae and Streptococcus pneumoniae</td>
<td>Alternative to above: newer quinolone as monotherapy.</td>
</tr>
<tr>
<td>If MRSA isolated ≥ 50% in ICU</td>
<td>Consider adding vancomycin.</td>
</tr>
</tbody>
</table>

(pg 79) Grade C, Level IV

C Antibiotics for patients with no risk factors, but late onset (>5 days) hospital acquired pneumonia, or severe hospital acquired pneumonia onset at any time (definition of severe hospital acquired pneumonia as for severe community acquired pneumonia):

<table>
<thead>
<tr>
<th>Core pathogens</th>
<th>Core antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>Ciprofloxacin or amikacin</td>
</tr>
<tr>
<td></td>
<td>PLUS either</td>
</tr>
<tr>
<td></td>
<td>an anti-pseudomonal β-lactam/β-lactamase inhibitor (piperacillin/or tazobactam), or</td>
</tr>
<tr>
<td></td>
<td>ceftazidime or carbapenems (imipenem, meropenem)</td>
</tr>
<tr>
<td>Resistant Acinetobacter species</td>
<td>Anti-pseudomonal cephalosporin (ceftazidime), or imipenam/meropenam, or amikacin</td>
</tr>
<tr>
<td>MRSA</td>
<td>Add vancomycin</td>
</tr>
</tbody>
</table>

(pg 80) Grade C, Level IV
Risk factors for specific pathogens and antibiotics to be added:

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Risk factor</th>
<th>Antibiotic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaerobic</td>
<td>Observed aspiration</td>
<td>Clindamycin, metronidazole, or β-lactam/β-lactamase inhibitor</td>
</tr>
<tr>
<td></td>
<td>Abdominal surgery</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Putrid discharge</td>
<td></td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>Coma</td>
<td>Vancomycin</td>
</tr>
<tr>
<td></td>
<td>Head injury</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diabetes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Renal failure</td>
<td></td>
</tr>
<tr>
<td>MRSA</td>
<td>Outbreaks</td>
<td>Vancomycin</td>
</tr>
<tr>
<td><em>Legionella</em> species</td>
<td>Corticosteroid use</td>
<td>Erythromycin</td>
</tr>
<tr>
<td></td>
<td>Outbreaks</td>
<td></td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>Prolonged ICU stay</td>
<td>As in severe hospital acquired pneumonia (see Table 11)</td>
</tr>
<tr>
<td></td>
<td>Antibiotic exposure</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chronic lung disease</td>
<td></td>
</tr>
<tr>
<td></td>
<td>AIDS</td>
<td></td>
</tr>
</tbody>
</table>

Use of Antibiotics in Acute Infectious Diarrhoea in Adults

**GPP** In any patient with diarrhoea, obtain the following history:
- age
- evidence of an immuno-compromised state
- previous use of antibiotics
- history of travel
- scale of outbreak

**GPP** Perform a focused physical examination in a patient with diarrhoea:
1. Look for signs of dehydration: loss of skin turgor, postural hypotension, increased pulse rate.
2. Record the temperature.
3. Examine the abdomen for tenderness or distension.
4. Perform a per rectal examination to look for the presence of blood in the stool.
In a patient with diarrhoea, look for red flags:
- Profuse, watery diarrhoea with dehydration.
- Passage of small volume stool, containing blood and mucus.
- Temperature ≥38.5°C.
- Passage of ≥6 times unformed stool in 24 hours.
- Duration of illness >72 hours.
- Severe abdominal pain, in a patient over the age of 50 years.
- Diarrhoea in the elderly (≥70 years of age).
- Diarrhoea in the immuno-compromised.

The presence of one or more of the above symptoms/signs suggests the diarrhoea is severe enough to warrant further evaluation and treatment.

Investigations

The faecal leucocyte, faecal lactoferrin, or Hemoccult™ test may be useful screening tests in patients with moderate to severe acute infectious diarrhoea. The tests may be used to differentiate inflammatory and non-inflammatory diarrhoeal syndromes (pg 85).

Grade B, Level III

Stool culture (salmonella, shigella and campylobacter) should be performed only in patients who have prolonged diarrhoea, or in patients who have clinical or biochemical evidence of inflammatory diarrhoea.

Grade A, Level Ib

For patients with diarrhoea that develops after three days of hospitalisation, or have recently received antibiotics or anti-neoplastics, an effort should be made to look for *Clostridium difficile* infection.

Grade A, Level Ib

Exposure of a traveller or hiker to untreated water and illnesses that persist for more than seven days should prompt evaluations for protozoal pathogens, especially giardia and cryptosporidium (pg 86).

Grade C, Level IV

Endoscopy should be reserved for the investigation of patients with persistent or chronic diarrhoea (pg 87).
Management

A Fluid and electrolyte replacement plays a pivotal role in the management of all patients with acute diarrhoea. Oral rehydration is the treatment of choice (pg 87).

Grade A, Level Ia

GPP If an anti-motility agent is required, loperamide may be used.

(pg 88) GPP

B Anti-motility agents should not be given to patients who have febrile dysentery (pg 88).

Grade B, Level IIa

A Anti-motility agents should not be given to patients who have suspected *Escherichia coli* O157:H7 infection, Shiga toxin-producing *Escherichia coli* infection, or frank bloody diarrhoea (pg 88).

Grade A, Level Ib

A In patients with moderate to severe inflammatory diarrhoea, an empirical course of quinolones can be given for 3-5 days (pg 89).

Grade A, Level Ib

A In patients with moderate to severe traveller’s diarrhoea, an empirical course of quinolones can be given for 3-5 days (pg 89).

Grade A, Level Ib

GPP Elderly patients with moderate to severe diarrhoea may also be started on empirical antibiotic therapy (with quinolones) (pg 89).

GPP

B All patients with moderate to severe infection with shigellosis should be treated with antibiotics. Patients with mild infections in the setting of good public health and hygiene can be observed (pg 90).

Grade B, Level IIa

A Routine treatment with antimicrobials for patients with non-typhoid salmonellosis is not recommended (pg 90).

Grade A, Level Ib
C Certain patients with intestinal salmonellosis should be treated – those who have fever and systemic toxicity, those with dysentery, the elderly, and patients who are immunocompromised or immunosuppressed.

Grade C, Level IV

B Certain patients with proven *Campylobacter* infection should be treated with antibiotics – those who are immunocompromised, the elderly, and healthy patients with moderate to severe dysentery or with evidence suggestive of bacteraemia (pg 91).

Grade B, Level IIa

A Patients with enterotoxigenic *Escherichia coli* infections should be treated with antibiotics (pg 91).

Grade A, Level Ib

A Patients with suspected or proven *Enterohaemorrhagic Escherichia coli (EHEC)* infection, especially with *Escherichia coli* O157:H7, should not be given antibiotics (pg 92).

Grade A, Level Ib

A All patients with proven *Vibrio cholera* infection should be treated with antibiotics (pg 92).

Grade A, Level Ib

B Patients with mild *Clostridium difficile* infection can be treated symptomatically and with withdrawal of the offending antibiotic (pg 92).

Grade B, Level IIa

A Patients with moderate to severe *Clostridium* disease warrant prompt antibiotic treatment, with either metronidazole or vancomycin (pg 93).

Grade A, Level Ib

Use of Antibiotics in Urinary Tract Infection

B It is not necessary to perform urine cultures in the management of uncomplicated cystitis in women. However, for the remainder of patients, pre-treatment cultures should be performed (pg 101).

Grade B, Level IIb
Management of uncomplicated UTIs

A Antibiotic therapy is not recommended in the management of patients with asymptomatic bacteriuria, except in pregnant women (pg 102).

Grade A, Level Ib

A The recommended 1\textsuperscript{st} line therapy for uncomplicated cystitis in women is a 3-day course of trimethoprim-sulphamethoxazole (pg 102).

Grade A, Level Ib

A Alternative treatment options for uncomplicated cystitis in women include the use of:

- Nitrofurantoin
- Fluoroquinolones
- 1\textsuperscript{st} and 2\textsuperscript{nd}-generation cephalosporins
- Trimethoprim
- β-lactam-lactamase-inhibitor combinations

(pg 103) Grade A, Level Ib

A The recommended duration of treatment of uncomplicated cystitis for various agents in women is:

- For 3 days with fluoroquinolones;
  Or
- For 7 days, with nitrofurantoin, 1\textsuperscript{st} and 2\textsuperscript{nd}-generation cephalosporins, trimethoprim and β lactam-lactamase inhibitor combinations.

(pg 103) Grade A, Level Ia

A Single-dose regimens are not recommended for routine use in the treatment of cystitis in women, as these regimens are less effective than multi-day regimens (pg 103).

Grade A, Level Ia

A Women with recurrent UTI should be treated with low dose antibiotic prophylaxis, using nitrofurantoin, trimethoprim-sulphamethoxazole, trimethoprim or cephalosporins (pg 105).

Grade A, Level Ib
C Initial therapy with intravenous cephalosporin and aminoglycoside, as for severe pyelonephritis, is recommended for the treatment of severe acute prostatitis (pg 107).
Grade C, Level IV

C Following clinical improvement, severe acute prostatitis should be treated with antibiotics, based on sensitivities, for a total duration of 4 weeks (pg 107).
Grade C, Level IV

C For patients with acute prostatitis of mild to moderate severity, initial therapy with oral fluoroquinolones, trimethoprim-sulphamethoxazole or trimethoprim is recommended. Treatment with antibiotics based on sensitivities should be given for a total duration of 4 weeks (pg 107).
Grade C, Level IV

A The recommended treatment for chronic bacterial prostatitis is fluoroquinolones for 4 weeks (pg 108).
Grade A, Level Ib

B Trimethoprim-sulphamethoxazole for 12 weeks can also be used in the treatment for chronic bacterial prostatitis (pg 108).
Grade B, Level III

C For patients with recurrent chronic prostatitis, suppressive, low-dose therapy with trimethoprim-sulphamethoxazole, trimethoprim or nitrofurantoin can be administered for 6 months or longer (pg 109).
Grade C, Level IV

A Antibiotic therapy is not indicated in the treatment of chronic prostatitis/chronic pelvic pain syndrome (pg 110).
Grade A, Level Ib

GPP Patients with symptoms of chronic prostatitis, but with negative urine or prostatic fluid cultures should be referred to a Urologist for further management (pg 110).
GPP
Pyelonephritis

A Treatment options for severe acute pyelonephritis include: parenteral 3rd-generation cephalosporins, aminoglycosides, fluoroquinolones, β-lactams or β-lactam-β-lactamase-inhibitor combinations. Antibiotics should be modified when urine culture results become available. Oral antibiotic therapy can be started following clinical improvement, with a treatment course of 14 days (pg 111).

Grade A, Level Ib

GPP Initial treatment with intravenous aminoglycoside, together with a 1st or 2nd-generation cephalosporin, is recommended for hospitalized patients with acute pyelonephritis, because of the low sensitivity of hospital-acquired Escherichia coli to ceftriaxone and ciprofloxacin in the local context (pg 111).

UTI in pregnancy

A Asymptomatic bacteriuria in pregnancy should be treated with antibiotics, based on culture and sensitivity, to reduce the risk of pyelonephritis and other complications (pg 112).

Grade A, Level Ia

B For acute cystitis in pregnancy, empirical therapy with 1st or 2nd-generation cephalosporins, nitrofurantoin or trimethoprim-sulphamethoxazole (caution in 3rd trimester) is recommended. Treatment should be modified based on culture results and appropriate antibiotics should be administered for 7 days (pg 112).

Grade B, Level III

B For pyelonephritis in pregnancy, empirical therapy with a 3rd-generation cephalosporin is recommended. Treatment should be modified based on culture results and appropriate antibiotics should be administered for 14 days (pg 113).

Grade B, Level III
Management of Complicated UTIs

C Antibiotic treatment of complicated urinary tract infections should be based on cultures and sensitivity. When symptoms warrant initiation of empirical therapy, cultures must be obtained prior to antibiotic therapy and therapy modified based on results (pg 114).

Grade C, Level IV

C For ill, hospitalized patients with complicated urinary tract infections, empirical treatment with intravenous 3rd-generation cephalosporins, fluoroquinolones, β-lactams or β-lactam-β-lactamase-inhibitor combinations is recommended. An alternative regimen using intravenous ampicillin together with an aminoglycoside is also effective. (pg 114)

Grade C, Level IV

A For complicated urinary tract infections of mild to moderate severity, initial therapy with oral fluoroquinolones or trimethoprim-sulphamethoxazole is recommended (pg 114).

Grade A, Level Ib

C For complicated urinary tract infections of mild to moderate severity, alternative regimens for empirical treatment include 2nd-generation cephalosporins, β-lactams, or β-lactam-β-lactamase-inhibitor combinations (pg 114).

Grade C, Level IV

GPP After the initiation of empirical antibiotic therapy, culture-based appropriate therapy is administered for 14 days as a minimum (pg 116).

GPP Symptomatic UTIs occurring in patients with a short-term indwelling urinary catheter should be treated by removing the catheter, followed by a 7-day course of antibiotics. For patients with long-term indwelling urinary catheters, symptomatic UTIs can be treated with a 7-day course of antibiotics (pg 116).

GPP In patients with renal impairment, effective antibiotic therapy requires the use of antibiotics which achieve therapeutic concentrations in the urine and are appropriately dose-adjusted for the level of renal failure. (pg 116)
Use of Antibiotics in Acute Bacterial Meningitis in Immunocompetent Adults

Diagnosis of acute bacterial meningitis

C Initial physical examination should include evaluation for:
   - level of consciousness
   - cranial nerve palsies
   - focal deficits
   - meningismus
   - increased intracranial pressure
   - critical trauma
   (pg 122)  
   Grade C, Level IV

B A lumbar puncture is recommended in all adult patients with suspected meningitis except when a clear contraindication exists (pg 122).

   Grade B, Level III

Antibiotic therapy

C If bacterial meningitis is suspected, antibiotic treatment must be started immediately, regardless of any investigations undertaken (pg 124).

   Grade C, Level IV

B In the treatment of meningitis with a typical meningococcal rash, intravenous penicillin G, 20-24 million units daily, should be given.

   (pg 124)  
   Grade B, Level III

B For adults without a typical meningococcal rash, intravenous ceftriaxone, 2g 12 hourly, should be given (pg 124).

   Grade B, Level III

C If the patient comes from an area where penicillin-resistant Streptococcus pneumoniae are common (MIC ≥ 0.1ug/ml) then add intravenous vancomycin 1g 12 hourly (pg 124).

   Grade C, Level IV
C & GPP For adults over the age of 50 years, history of alcoholism, diabetes and pregnancy without a typical meningococcal rash, consider adding intravenous ampicillin, 2g 4 hourly, to ceftriaxone as above (pg 124).

Grade C, Level IV & GPP

C If there is a clear history of anaphylaxis to β-lactams, give intravenous chloramphenicol 25 mg/kg (maximum 1g) 6 hourly. Add vancomycin 1g 12 hourly, because of the possibility of penicillin-resistant Streptococcus pneumoniae and likely failure of chloramphenicol in this group (pg 124).

Grade C, Level IV

B If Gram-negative diplococci are visible on Gram stain of cerebrospinal fluid (CSF), or if Neisseria meningitidis is isolated from CSF or blood, continue with intravenous penicillin G, 24 million units daily (pg 125).

Grade B, Level III

C For patients who do not have adequate response to penicillin, the treatment should be changed to ceftriaxone (pg 125).

Grade C, Level IV

C If penicillin-sensitive Streptococcus pneumoniae is isolated from CSF or blood, intravenous penicillin G 24 million units is recommended. If cephalosporin-sensitive Streptococcus pneumoniae is isolated, intravenous ceftriaxone 2g 12 hourly should be given. Add on intravenous vancomycin, 1g 12 hourly, if penicillin-resistant and cephalosporin-resistant Streptococcus pneumoniae is isolated from blood or CSF. Continue intravenous therapy for 10-14 days (pg 125).

Grade C, Level IV

B For Haemophilus influenzae meningitis, intravenous ceftriaxone, 2g 12 hourly, is recommended (pg 125).

Grade B, Level IIb

C If Gram-positive coccobacilli suggestive of Listeria monocytogenes is visible on Gram stain of CSF, or if Listeria monocytogenes is isolated from blood or CSF, intravenous ampicillin, 2g 4 hourly, and gentamicin 5 mg/kg 24 hourly (single or divided 8 hourly doses) for more than 21 days is recommended (pg 125).

Grade C, Level IV
Recommended duration of therapy according to the type of pathogen causing meningitis (pg 126).

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Recommended duration of therapy</th>
<th>Grade and level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Haemophilus influenzae</em></td>
<td>7-10 days</td>
<td>Grade B, Level IIb</td>
</tr>
<tr>
<td><em>Neisseria meningitidis</em></td>
<td>7-10 days</td>
<td>Grade B, Level III</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>10-14 days</td>
<td>Grade C, Level IV</td>
</tr>
<tr>
<td><em>Listeria monocytogenes</em></td>
<td>≥ 21 days</td>
<td>Grade C, Level IV</td>
</tr>
<tr>
<td>Gram-negative bacilli, other than <em>Haemophilus influenzae</em></td>
<td>21 days</td>
<td>Grade C, Level IV</td>
</tr>
</tbody>
</table>

The duration of therapy should be tailored to the individual patient on the basis of the clinical and microbiological response (pg 126).

Grade C, Level IV

**Adjunctive dexamethasone therapy in bacterial meningitis**

A In adults with suspected or proven pneumococcal meningitis, dexamethasone 10 mg 6 hourly should be given for 4 days with the first dose administered 15-20 min before, or at least concomittant with, the first dose of antimicrobial therapy (pg 126).

Grade A, Level 1b

A Dexamethasone should only be continued if the CSF Gram stain reveals Gram-positive diplococci or if blood or CSF cultures are positive for *Streptococcus pneumoniae* (pg 126).

Grade A, Level 1b

A Adjunctive dexamethasone should not be given to adult patients who have already received antimicrobial therapy as in this circumstance, dexamethasone is unlikely to improve patient outcome (pg 126).

Grade A, Level 1b

**Prevention of meningococcal meningitis**

C Chemoprophylaxis should be offered to close contacts of cases, irrespective of vaccination status, in those who have:
- Prolonged close contact with the case in a household setting during the seven days before onset of illness.
- Contact at a day-care centre.
- Transient close contact with a case where there was exposure to the patient’s secretions (e.g. through mouth-to-mouth resuscitation, endotracheal intubation or endotracheal tube management) around the time of admission to hospital.

(Changes)

Close contacts of patients with meningococcal infection should receive one of the following regimens:

- Rifampicin:
  Adults: 600 mg, 12 hourly for 2 days (4 doses).
  Children (1-6 years): 10 mg/kg, 12 hourly for 2 days (4 doses).
  Children (3-11 months): 5 mg/kg 12 hourly for 2 days (4 doses).

- Ciprofloxacin:
  Adults: 500 mg as a single dose.
  Children: Use of ciprofloxacin is not recommended.

- Ceftriaxone:
  Adults: 250 mg as a single intramuscular dose.
  Children (< 15 years): 125 mg as a single intramuscular dose.

(Changes)

If other antibiotics have been used for treatment, the index patient should receive prophylactic antibiotics for eradication of nasopharyngeal carriage before being discharged from hospital.

Use of Antibiotics in the Elderly

Unique Aspects of Infections in Older People

An infectious aetiology should be sought when there is:

- A change in functional status and the oral temperature is ≥37.2°C, or
- An increase in temperature of ≥1.3°C over the baseline.
Infection should be considered in the differential diagnosis of older people who present, within a short period of time:
  - With only non-specific symptoms, including functional decline; or
  - With atypical complaints.

Doctors should be alert to a leucocytosis with left shift or left shift alone, as these have good predictive value for diagnosing bacterial infections in older people (pg 133).

Treatment recommendations

Empirical antibiotic therapy for specific infections is a valid and practical option in older persons, given the higher risk of adverse outcomes, diverse infectious causes and increased difficulty in obtaining diagnostic specimens. In general, this therapy should include a broad-spectrum beta-lactam antibiotic (pg 134).

When culture results are not available yet, the choice of antibiotic should be guided by knowledge of the likely pathogens encountered in older people in different settings (pg 134).

Aminoglycosides should be reserved for selected situations: septic shock without a specific aetiological diagnosis, confirmed or suspected *Pseudomonas aeruginosa* infections, or where the cultured organism is only susceptible to an aminoglycoside (pg 134).

The patient’s renal function should always be considered when prescribing antibiotics in older people, particularly if the antibiotics are excreted primarily by the kidneys (e.g. aminoglycosides, fluoroquinolones, and some cephalosporins such as ceftazidime). Estimated creatinine clearance should be used to guide appropriate dosing of such antibiotics (pg 135).
There should be monitoring for adverse effects of antibiotics during therapy. In addition to specific adverse effects, geriatric syndromes or functional decline should also be considered as possible adverse effects of antibiotics. (pg 135)

Grade C, Level IV

Additional Antibiotic Consideration in the Elderly

GPP Awareness of potential drug-drug interactions should guide the choice of antibiotics (pg 135).

Grade C, Level IV

Assistance from caregivers who can help administer medications should be sought where necessary. Keeping the antibiotic regimen as simple as possible is also useful in improving compliance (pg 136).

Grade C, Level IV

Special Situations in the Elderly

The choice of antibiotic is usually guided by the likely spectrum of bacterial flora that might be encountered. Broad-spectrum antibiotics that include Gram-negative cover are usually required. For pneumonia in the setting of long-term care institutions, antibiotic cover for anaerobes (e.g. amoxicillin-clavulanate) should be considered if aspiration is a concern (pg 136).

Grade C, Level IV

The following measures to prevent aspiration are recommended:

Reduce the risk of aspiration by:
- Avoiding sedative medication;
- Minimising the use of nasogastric tubes; and
- Elevating the head of bed during and after feeding.

(pg 137)

Grade C, Level IV

Timely assessment of swallowing, at the bedside or by a speech therapist, can be useful in guiding any modification of feeding (e.g. consistency of fluids) (pg 137).

Grade C, Level IV
There should be proper treatment of periodontal disease and gingivitis (pg 138).

In treating aspiration pneumonia, use antibiotics that include broad-spectrum ones with anaerobic cover (such as amoxicillin-clavulanate), or the combination of a fluoroquinolone with either metronidazole or clindamycin (pg 138).

Patients with asymptomatic bacteriuria while on intermittent catheterisation should not be treated with antibiotics. The exception is the presence of possible “atypical representation” of infection (pg 138).

Systemic antibiotics should be used with more serious pressure ulcer infections, including those with spreading cellulitis, osteomyelitis and bacteraemia (pg 138).

Empirical antibiotics that are effective against Gram-positive and Gram-negative organisms as well as anaerobic organisms are needed. Monotherapy with piperacillin-tazobactum or a carbapenem, or combination therapy employing ciprofloxacin with either metronidazole or clindamycin are useful options. As tissue perfusion is usually poor in infected ulcers, intravenous antibiotic therapy should be administered initially (pg 139).
1 Guideline development and objectives

1.1 Guideline development

This is the second edition of the "Use of antibiotics in adults" guidelines. The topics included in this edition were selected after a careful review of the previous edition by the workgroup members.

These guidelines on antibiotic use have been developed based on the best available evidence as well as expert opinion of the multidisciplinary workgroup in areas where studies are lacking. In addition to tailoring the evidence to suit the practice of medicine in Singapore, local microbiology patterns and resistance trends were also taken into consideration.

1.2 Objectives

The main objective of these guidelines is to promote the proper and appropriate use of antibiotics so as to slow the emergence of antimicrobial resistance, and at the same time, ensuring that patients receive the appropriate treatment.

1.3 Target group

These guidelines are developed to provide a practical approach to the use of antibiotics for all medical practitioners, in particular primary care physicians.

1.4 What's new in the revised guidelines

New sections in this edition of the guidelines include:

   iii) use of antibiotics in acute bacterial meningitis  
   iv) use of antibiotics in infectious diarrhoea in adults

Other sections have been revised, based on the rapid advances in antibiotic therapy and in infectious disease treatment:

- The section on bronchitis has been expanded to include recommendations for risk stratification and antibiotic therapy in patients with acute exacerbation of chronic bronchitis.
• The section on acute upper respiratory tract infections has additional recommendations for non-specific respiratory infections. The use of the Centor criteria to predict Group A beta-haemolytic streptococcal pharyngitis is also discussed. Influenza, SARS and vaccination are also discussed in this section.
• The Fine Pneumonia Severity Index has been included in the risk stratification subsection of the section on community-acquired pneumonia.
• Recommendations for infections in long-term care institutions and infected pressure ulcers have been added to the section on antibiotic use in the elderly.
• An algorithm for the management of urinary tract infections in adults has been added.
• New sections on cost-effectiveness issues and clinical quality improvement in antibiotic use have been added.

1.5 Review of guidelines

Evidence-based clinical practice guidelines are only as current as the evidence that supports them. Users must keep in mind that new evidence could supersede recommendations in these guidelines. The workgroup advises that these guidelines be scheduled for review three years after publication, or if new evidence appears that requires substantive changes to the recommendations.
2.1 **Introduction**

Appropriate selection and use of antibiotics is based on:

1. Characteristics of the aetiologic agent
   - Pattern of its susceptibility to antibiotics
2. Characteristics of the host
   - Immune status
   - The site of the infection
   - Function of body systems responsible for absorption and elimination of the drug
   - History of drug allergies
3. Characteristics of the drug
   - Pharmacokinetics (absorption, distribution into body tissues and elimination)
   - Pharmacodynamics (mechanism of action, the cidal or static nature of the antimicrobial effect and the rate at which it occurs)

Before definitive identification of the aetiological agent is made, initial choice of an empirical antibiotic regimen depends primarily on knowledge of the spectrum of organisms likely to cause infection at the infected site.

2.2 **Development of antibiotic resistance**

Antibiotic resistance poses a significant challenge to the treatment of bacterial infection. Resistance rates are continually increasing, largely as a function of misuse, widespread overuse of broad-spectrum antibiotics and societal pressures to prescribe antibiotics liberally. Once resistance develops, it can be transferred to other species via plasmids or other factors.

2.3 **Measures to combat the spread of antibiotic resistance**

1. The emergence of multi-resistant pathogens should be prevented by prudent use of antibiotics.
2. Carriers of multi-resistant strains should be isolated.
3. Use of antibiotics as growth promoters in animal husbandry should be restricted or eliminated to avoid unnecessary exposure to resistant pathogens in the food chain.

4. Improvement in the monitoring and reporting of antibiotic resistance is important. This is essential for providing a sound, long-term view of the emergence and development of antibiotic resistance.

Epidemiological and Historical Trends

The first clinical cases of methicillin-resistant *Staphylococcus aureus* (MRSA) were identified in 1961, only 2 years after methicillin became available for clinical use. Since then, the problem has increased dramatically, with the prevalence of MRSA reaching endemic proportions in some hospitals. On July 11, 1997, the first case of *Staphylococcus aureus* with intermediate sensitivity to vancomycin (VISA) was reported by the Centers for Disease Control & Prevention (CDC), Atlanta, USA. A fully vancomycin-resistant *Staphylococcus aureus* (VRSA) was reported in 2002, in a chronically ill patient who received multiple courses of antibiotics.

By the mid sixties, the first isolates of *Streptococcus pneumoniae* with reduced susceptibility to penicillin were described. Today, penicillin-resistant *Streptococcus pneumoniae* (PRSP) is widespread throughout the world.

The production of β-lactamases or extended-spectrum β-lactamases (ESBLs) by Gram-negative bacteria in hospitals is now well recognised. Reports of plasmid-mediated ESBLs were first described in Germany in 1983, where *Klebsiella pneumoniae* demonstrated the ability to transfer resistance to cephalosporins to *Escherichia coli*. ESBL-producing clinical strains have been isolated with varying frequency from many parts of the world. Increasing isolation of multi-resistant *Acinetobacter baumannii* has also been reported worldwide and it is now one of the most difficult nosocomially acquired Gram-negative pathogens to control and treat.

28
2.4 Cost of antibiotic resistance

Treating infections caused by resistant organisms often requires:
- the use of multiple antibiotics
- the use of expensive second or third line antibiotics
- prolonged hospital or intensive care unit (ICU) stay, with increased morbidity and mortality

To preserve the potency of existing antibiotics, clinicians must avoid careless use of antibiotics, limit their use only for bacterial infections, and prescribe them in the proper dose and for the correct duration.

2.5 Rational antibiotic use

Antibiotics are used in the following situations:

1. **Therapy for specific pathogens.** When cultures and sensitivities are known, the antibiotics may have to be changed accordingly in the case of continued infection. Factors to also consider include allergy, drug interactions and presence of liver or renal impairment.

2. **Empirical therapy,** when there is suspected or definite infection but the causative organism is not known. This will require some knowledge of the most likely organism and treatment should be adjusted when culture results are available or when there is no response.

3. **Prophylaxis,** where consequences of infection would be severe, e.g. endocarditis in patients with rheumatic heart disease, insertion of a prosthetic heart valve or prosthetic joint. For maximum efficacy, the timing of administration is important (30 minutes before skin incision and no longer than 24 hours after the operation). An antibiotic appropriate for the site of the procedure should be chosen.

GPP Antibiotics should be used only for treatment of patients with confirmed or suspected bacterial infections. Antibiotics may be used for prophylaxis where consequences of infection would be severe.

GPP
Antibiotics should only be chosen after considering the following questions:

1. Is there an infection?
2. What is the site of infection and the most likely causative organism?
3. Will the antibiotic reach the site of infection?
4. What side effects or drug interactions might this antibiotic have?
5. What adjustments should be made for the individual patient, e.g. the young infant, the elderly, patients with renal failure?
6. What is the appropriate dose and duration of treatment for the site and type of infection?

Patient compliance with antibiotics is important to achieve cure, as well as to prevent the development of resistance.

Patients or their caregivers should be clearly instructed on the dose and the necessity of finishing a course of treatment.

2.6 Cost-effectiveness issues in antibiotic use

Decision on when or whether to start antibiotic treatment should be based on the cost-effectiveness of the different treatment strategies. An example is illustrated in the section on recommendations for the treatment of acute rhinosinusitis. A study comparing treatment strategies for uncomplicated acute bacterial rhinosinusitis reported the cost per symptom-free day as US$3.09 for the clinical criteria-based treatment, US$3.95 for symptomatic treatment* and US$184.56 for empirical treatment†. Radiographic-guided treatment was found to be more expensive and less effective than the other 3 strategies. Clinical criteria-guided treatment was shown to be the most cost-effective strategy, and treatment based on radiographic findings was shown to be more expensive and less effective.¹

* In which no patients were initially treated with antibiotics
† In which all patients were initially treated with amoxicillin
Appropriate antibiotic choice takes into consideration effectiveness (including the impact of antibiotic resistance and local antibiotic resistance patterns), costs and adverse effects. In cases where a range of antibiotic treatments exists, and a choice of the best antibiotic has to be made, an important consideration is cost-effectiveness. An example is in the choice of antibiotics for the treatment of acute exacerbation of chronic obstructive pulmonary disease (COPD) and chronic bronchitis. It was reported that the use of azithromycin, amoxicillin clavulanate, ciprofloxacin, cefuroxime, cefaclor, cephradine or cefprozil was the dominant strategy, being more effective as well as cheaper, compared to agents such as amoxycillin and erythromycin.²

On the other hand, inappropriate or unnecessary antibiotic prescribing can be harmful to patients as well as to the community. It can cause the emergence and spread of resistant organisms, which would not only lead to clinical consequences, but also increased costs of heath care. It was reported that antibiotic-resistant bacteria generated US$4 billion to US$5 billion in costs to the US society and individuals yearly.³

There are many elements of the economic impact of antibiotic resistance. Apart from increased length of hospital stay, morbidity and mortality, there are also direct costs (e.g. diagnostic investigations, costs of administration of newer or more costly drugs), as well as indirect costs (e.g. loss of productivity of patients, costs to the drug industry resulting from diminishing marketability of their drugs).⁴
3 Use of Antibiotics in Acute Upper Respiratory Tract Infections in Adults

3.1 Introduction

3.1.1 Definition/aetiology

Acute upper respiratory tract infection (URTI) is a symptom complex of different syndromes that include:

- The common cold;
- Acute pharyngitis;
- Acute epiglottitis;
- Acute laryngitis;
- Acute otitis media; and
- Acute rhinosinusitis.

While most URTIs are viral in origin, a small minority are caused by bacteria, and it is not always easy to distinguish one from the other.

3.1.2 Bacterial resistance to antibiotics

There is widespread use of antibiotics to treat acute URTIs, in the hope of benefiting a small minority with a bacterial aetiology. This results in inappropriately treating a large number of viral infections with antibiotics. There is good evidence that this contributes significantly to the development of bacterial resistance to antibiotics in the community, at least in some countries.

Penicillin resistance in Streptococcus pneumoniae has increased in an epidemic manner in the past 10 years. Special attention to antibiotic-resistance profiles of Streptococcus pneumoniae is warranted, since it is the leading cause of community-acquired bacterial pneumonia, bacterial meningitis, bacterial sinusitis, and otitis media. Resistance to macrolides, doxycycline, trimethoprim-sulphamethoxazole, and second-generation and third-generation cephalosporins has also increased.
3.1.3 Curbing unnecessary use of antibiotics

Curbing the use of antibiotics in the community can result in reversal of antibiotic resistance by bacteria in the community.\textsuperscript{10-12} Intervention strategies to reduce community use of antibiotics must address the management of acute URTIs. This is because URTIs are the most frequent reasons for seeking medical attention, and are associated with up to 75\% of total antibiotic prescriptions each year. Transmission of \textit{Streptococcus pneumoniae} is enhanced during viral acute URTIs through increased respiratory and nasal secretions. As a result, antibiotic treatment of viral acute URTIs is particularly problematic, since it may selectively promote the acquisition and spread of antibiotic-resistant bacteria by patients.\textsuperscript{13}

The unnecessary use of antibiotics must be reduced in the following acute URTIs in adults:
- Uncomplicated acute bronchitis (not including acute exacerbations of chronic bronchitis);
- Acute rhinosinusitis;
- Pharyngitis; and
- Non-specific URTIs, including the common cold.

The diagnosis of these conditions is usually made in the presence of a clinical syndrome with a predominant clinical feature. Thus:
- A prominent acute cough is taken to signify acute bronchitis;
- Prominent nasal and sinus symptoms to signify rhinosinusitis;
- Prominent acute sore throat to signify pharyngitis;
- Acute respiratory symptoms in the absence of a predominant symptom to signify an ‘Upper respiratory tract infection’.

Each of these syndromes can be caused by a multitude of viruses, and occasionally bacteria. The degree of excess antibiotic use varies for each syndrome. Antibiotic treatment of colds, URTIs, or acute bronchitis is almost always inappropriate, because the vast majority of these syndromes have a viral cause. Antibiotic treatment of sinusitis and pharyngitis is sometimes justified but should be limited to appropriate subsets of patients.\textsuperscript{14}
3.1.4 Factors affecting antibiotic prescription

The decision to prescribe antibiotics for acute URTIs when they are unlikely to have any benefit is the result of a complex interaction between the patient, physician, and system factors.

1. **Patient expectations and demands for antibiotics have a strong association with excess antibiotic use.**\textsuperscript{9,15-19} Patient beliefs also play a role. For example, patients may believe erroneously that antibiotics are needed for green or yellow nasal discharge.\textsuperscript{20}

2. **Clinicians may believe that antibiotics will benefit, or prevent a bad outcome of, a condition.** While antibiotics benefit some patient sub-groups (such as the immuno-compromised, the frail and elderly, those with co-morbidity), there is no equal benefit among the general healthy population.\textsuperscript{21}

3. **System factors are also important.** Antibiotic prescription for URTIs is increased in busy practices, where there may be limited time to discuss non-antibiotic treatment alternatives. The way physicians are remunerated may also encourage the prescription of antibiotics.\textsuperscript{18,22}

Effective strategies to improve antibiotic prescribing behaviour in acute URTIs will need to address each of these factors.\textsuperscript{22}

3.1.5 Antibiotic use in URTI

\textbf{B} The use of antibiotics for a large portion of URTIs is not recommended because these are viral infections, for which antibiotics do not provide clinical benefit.\textsuperscript{9,14,23}

\textit{Grade B, Level IIa}

Patients and clinicians need to be persuaded that antibiotic use can be safely decreased in an otherwise-healthy patient based on the following pieces of evidence:

1. A large proportion of the antibiotics prescribed for acute respiratory tract infections are unlikely to provide clinical benefit to patients because these are viral infections.
Community-acquired pneumonia, acute bacterial rhinosinusitis, and selected cases of acute exacerbations of chronic bronchitis warrant antimicrobial therapy, whereas otitis media with effusion, acute bronchitis, most rhinosinusitis, and non-specific upper respiratory tract infections (including the common cold) are viral infections and do not require antibiotics.⁹,¹⁴,²³

2. Antibiotic treatment does not affect resolution of illness or loss of work time in URTIs.²⁴

3. The reduction of the routine use of antibiotics in management of acute URTIs in the otherwise-healthy adult does not result in adverse outcome.²²

4. Previous recent antibiotic use is an important risk factor for carriage of, and infection with, antibiotic-resistant *Streptococcus pneumoniae*, the risk of carriage being 2-9 times.⁹ Decreasing inappropriate use of antibiotics in ambulatory practice can reverse this trend of antibiotic resistance.¹⁰

3.2 Non-specific respiratory infections

3.2.1 Definition/aetiology

The non-specific respiratory infection is a common symptom-complex presentation of an upper respiratory tract infection in the adult. The non-specific respiratory infection, or acute rhinopharyngitis, is characterized by an acute infection where sinus, pharyngeal, and lower airway symptoms, although frequently present, are not prominent. With rare exceptions, this symptom complex has a viral cause.

When symptoms are severe, and particularly, when there is muscle ache and fatigue, the most common agent is influenza or parainfluenza. When symptoms are mild, rhinoviruses predominate. Other important agents include adenovirus and respiratory syncytial virus.²³
3.2.2 Antibiotic use in non-specific respiratory infections

Antibiotic treatment of adults with non-specific upper respiratory tract infection is not recommended.\textsuperscript{24} 

Grade A, Level Ia

Antibiotic use in URTIs does not enhance illness resolution. There is not enough evidence of important benefits from the treatment of URTIs with antibiotics to warrant their routine use in children or adults. There is a significant increase in adverse effects associated with antibiotic use in adult patients.\textsuperscript{24}

3.2.3 Purulent secretions and antibiotics

The use of antibiotics is not recommended when there is purulent secretion from the nares or throat, in patients with uncomplicated URTI.\textsuperscript{25-28}

Grade A, Level Ia

One study\textsuperscript{29} found that antibiotic prescription for adults with URTI is most common when purulent manifestations are present. However, purulent secretion from the nares or throat (commonly seen in patients with uncomplicated URTI) does not predict either bacterial infection or benefit from antibiotic treatment. These purulent manifestations have limited value in predicting antibiotic-responsive disease.\textsuperscript{25-28}

3.3 Acute pharyngitis (sore throat)

3.3.1 Antibiotic use in pharyngitis – pros and cons

1. The vast majority of immuno-competent adults with sore throat have acute infectious pharyngitis. Antibiotics confer relative benefits in the treatment of sore throat. However, the absolute benefits are modest.\textsuperscript{30}

Antibiotics shorten the duration of symptoms, but by a mean of only one day about halfway through the illness (the time of maximal effect), and only about sixteen hours overall. In addition, antibiotics also have side-effects.\textsuperscript{30}
2. There is a favourable outcome in the majority of cases of sore throat even when antibiotics are withheld.\(^1\)

However, antibiotic use should be considered in the following circumstances:\(^1\):
- When there are other explanations for the sore throat;
- In very ill patients;
- Suspected or previous rheumatic fever;
- Multiple episodes of tonsillitis;
- Quinsy; and
- Pregnancy.

### 3.3.2 Antibiotic use in Group A beta-haemolytic streptococcal (GABHS) pharyngitis

Patients identified with Group A beta-haemolytic streptococcal pharyngitis should be treated with antibiotics to prevent complications.\(^2\)

**Grade B, Level III**

Group A beta-haemolytic streptococcal pharyngitis is rare in adults >30 years old. In the vast majority of cases, acute pharyngitis in an otherwise-healthy adult is self-limiting, and rarely produces significant sequelae.

However, there is a case to be made for treating Group A beta-haemolytic streptococcal pharyngitis with antibiotics - to prevent the complications of acute glomerulonephritis, rheumatic fever and rheumatic carditis, even though these complications may account for only 5-15% in adult pharyngitis.\(^2\)

The most reliable clinical predictors of GABHS pharyngitis are three or four Centor criteria:
- Fever;
- Tonsillar exudates;
- Absence of cough;
- Tender anterior cervical lymphadenopathy (lymphadenitis).

Antibiotic therapy is limited to patients with three or four criteria. Patients with none or fewer than three criteria should not be treated with antibiotics, as they are unlikely to have GABHS infections. The
exception will be in immuno-compromised patients who will be prone to superinfections.

The presence of three or four criteria has a positive predictive value of 40-60%. The absence of three or four criteria has a negative predictive value of about 80%. Compared with throat culture, the sensitivity and specificity of three or four clinical criteria for identifying GABHS pharyngitis are 75% each.\textsuperscript{33-35}

**A** Group A beta-haemolytic streptococcal-positive patients should be treated with penicillin V, for seven days.\textsuperscript{36,37}

\textit{Grade A, Level Ib}

In one randomised trial,\textsuperscript{36} involving patients with sore throat, only GABHS-positive patients benefit from penicillin V in their clinical cure in the first few days, although this it is not always so. In another randomised trial,\textsuperscript{37} in patients with sore throat for less than 7 days and who had at least three Centor criteria, symptoms resolved 1.9 and 1.7 days earlier in patients taking penicillin for 7 days than in those taking penicillin for 3 days or placebo, respectively.\textsuperscript{37}

### 3.3.3 Throat swabs in pharyngitis

**A** Throat cultures are not recommended for the routine primary evaluation of adults with pharyngitis.\textsuperscript{34-36}

\textit{Grade A, Level Ib}

However, throat cultures may be indicated as part of the investigations of an outbreak of GABHS disease, for monitoring the development and spread of antibiotic resistance, or when pathogens such as gonococcus are being considered.

### 3.3.4 Symptomatic relief in pharyngitis

**C** Administer appropriate analgesics, antipyretics, and supportive care to all patients with pharyngitis.\textsuperscript{38}

\textit{Grade C, Level IV}

Paracetamol is the drug of choice for analgesia in sore throat.
Non-steroidal anti-inflammatory drugs are associated with gastrointestinal bleeding, nausea, vomiting, abdominal pain and diarrhoea. As such, the use of NSAIDs for symptom relief must be carefully weighed, as the symptoms of acute pharyngitis and tonsillitis tend to diminish quickly during the first 48-72 hours.\textsuperscript{38}

3.4 Acute epiglottitis

3.4.1 Definition/aetiology

Epiglottitis is an acute inflammation involving the epiglottis, valleculae, aryepiglottic folds, and arytenoids. The onset and progression of symptoms are rapid.

Viruses are the most common cause. However, infection by \textit{Haemophilus influenzae} type b (\textit{Hib}) is clinically important because it is the most deadly. In communities where childhood immunization against \textit{Hib} is widespread, epiglottitis is mainly a disease of adults.\textsuperscript{39}

3.4.2 Clinical features

Adults tend to present with pharyngeal symptoms of sore throat and odynophagia (pain on swallowing), cervical lymphadenopathy, and ear pain. Children most often have respiratory symptoms (stridor, dyspnoea, and chest retractions) and laryngeal symptoms.\textsuperscript{39}

3.4.3 Early diagnosis

Epiglottitis is an emergency that needs to be diagnosed early and referred immediately to hospital for further management. It can lead to life-threatening upper airway obstruction. Intubation is usually required, and tracheotomy may be needed.

The key characteristics in the history are\textsuperscript{40}:

- Sore throat (95%)
- Dysphagia (95%)
- Muffled voice (54%) and
- Usually no prodromal upper respiratory infection or cough

Clinically, one or more of the following may be present\textsuperscript{40}:

- Muffled voice (54%)
• Respiratory distress
• Drooling
• Stridor
• Cervical lymphadenopathy
• Hypoxia
• Severe pain on gentle palpation over the larynx
• Fever
• A tripod position may be observed – sitting up leaning forwards on outstretched arms with tongue out and head forward to ease the upper airway obstruction

3.4.4 Antibiotic treatment of acute epiglottitis

The antibiotic of choice to treat acute epiglottitis is ceftriaxone or chloramphenicol.\textsuperscript{41}

Empiric coverage for group A \textit{Streptococcus pneumoniae}, \textit{Staphylococcus pyogenes}, and \textit{Haemophilus influenzae} should be provided with ceftriaxone or chloramphenicol. Chloramphenicol should be used as a second-line drug because of its toxicity. In the past, ampicillin was the drug of choice, but with the increasing incidence of beta-lactamase-producing \textit{Hib}, second-generation and third-generation cephalosporins (e.g. cefotaxime sodium, ceftriaxone sodium, ceftazidime) are now first-line agents.\textsuperscript{41}

3.5 Acute rhinosinusitis

3.5.1 Definition

\textit{Sinusitis} refers to inflammation of the mucosa of the paranasal sinuses, regardless of cause. Because sinusitis is invariably accompanied by inflammation of the contiguous nasal mucosa, \textit{rhinosinusitis} is the preferred term. Most cases of rhinosinusitis involve more than one of the paranasal sinuses, most commonly the maxillary and ethmoid sinuses.\textsuperscript{42}

For purposes of diagnosis and treatment, rhinosinusitis is classified as:
• Acute (symptom duration <4 weeks);
• Subacute (symptom duration 4-12 weeks); and
• Chronic (symptom duration >12 weeks).
Patients may have recurrent acute attacks or acute exacerbations of chronic rhinosinusitis. Acute rhinosinusitis, however, makes up most cases in ambulatory care. Chronic and subacute bacterial sinus infections may require surgical consultation and management.

3.5.2 Aetiology/diagnosis

Most cases of acute rhinosinusitis diagnosed in ambulatory care are due to uncomplicated viral URTIs. Some cases are due to allergy and local irritants.

Cases due to allergy and irritants can usually be distinguished from infection on the basis of a careful history. Symptoms due to allergy and environmental irritants are:
- Usually more chronic or recurrent;
- Infrequently associated with purulent nasal discharge;
- Frequently include itching and sneezing; and
- Often associated with specific exposures.

Bacterial and viral rhinosinusitis are difficult to differentiate on clinical grounds. Epidemiologic estimates suggest that clinicians frequently misclassify viral upper respiratory tract infections as acute bacterial rhinosinusitis.\textsuperscript{22,43-46}

The clinical diagnosis of acute bacterial rhinosinusitis should be reserved for patients:
- With rhinosinusitis symptoms lasting 7 days or more;
- Who have maxillary pain or tenderness in the face or maxillary teeth (especially when unilateral); and
- Purulent nasal secretions.

Patients with rhinosinusitis symptoms that last fewer than 7 days are unlikely to have bacterial infection. Rarely, some patients with acute bacterial rhinosinusitis present with dramatic symptoms of severe unilateral maxillary pain, swelling, and fever.\textsuperscript{47-49}

\textbf{B} Sinus radiography is not recommended for diagnosis in routine cases.

\textbf{Grade B, Level IIb}
It has limited value in routine diagnosis of acute bacterial rhinosinusitis given the known high prevalence of abnormal radiological findings in patients with acute viral rhinosinusitis.\textsuperscript{50-52}

### 3.5.3 Treatment

**B** Symptomatic treatment and reassurance are the preferred initial management strategy for patients with mild symptoms of acute rhinosinusitis.\textsuperscript{47-49}

Grade B, Level IIb

**B** Antibiotic therapy should be reserved for:
- Patients with moderately severe symptoms who meet the criteria for the clinical diagnosis of acute bacterial rhinosinusitis (symptoms that last $>7$ days and include maxillary pain in the face or teeth and purulent nasal secretions); and
- Patients with severe rhinosinusitis symptoms, regardless of duration of illness.\textsuperscript{47-49}

Grade B, Level IIb

**A** For the initial treatment of acute bacterial maxillary rhinosinusitis, amoxicillin or penicillin for 7-14 days is recommended.\textsuperscript{53,54}

Grade A, Level Ia

*Streptococcus pneumoniae* and *Haemophilus influenzae* are the bacteria most commonly isolated from infected maxillary sinuses. *Streptococcus pyogenes, Branhamella (Moraxella) catarrhalis*, and anaerobic bacteria each account for a small percentage of bacterial sinus infections. For initial treatment, the most narrow-spectrum agent that is active against the likely pathogens (*Streptococcus pneumoniae* and *Haemophilus Influenzae*) should be used. Amoxicillin is commonly recommended, although higher-than-customary doses may be required in some cases.\textsuperscript{53} For acute maxillary sinusitis, current evidence is limited, but supports penicillin or amoxicillin for 7-14 days.\textsuperscript{54}

### 3.5.4 Isolated infection of the frontal or sphenoid sinus

**B** Isolated infection of a frontal or sphenoid sinus is a rare but potentially dangerous condition, usually caused by bacteria, and should be referred to hospital for treatment.\textsuperscript{42}

Grade B, Level IIb
Patients with this type of infection are usually seriously ill and may show signs of cavernous sinus thrombosis or meningitis, and should be referred.\textsuperscript{42}

3.6 Acute laryngitis

3.6.1 Definition

Laryngitis is an inflammation or infection of the larynx and vocal cords, causing hoarseness or loss of voice. Like a cough, laryngitis may persist long after the acute infection is over.

\textcolor{red}{GPP} If symptoms last for more than 3 weeks, the condition is classified as chronic laryngitis, for which an underlying cause must be further investigated. Underlying causes include laryngeal polyps, cancer, laryngeal tuberculosis, and gastro-esophageal reflux. \textcolor{red}{GPP}

3.6.2 Aetiology

Acute laryngitis is most often caused by the same viruses and bacteria which cause colds, sore throats, coughs, sinusitis and bronchitis.

The most common aetiology for acute laryngitis is an infectious source, usually a viral URTI. At the time of the acute laryngitic episode, many patients are carriers of bacteria, \textit{Branhamella (Moraxella) catarrhalis} and \textit{Haemophilus influenzae} being the most common organisms identified. In patients with these organisms in the nasopharynx, the dysphonia during their acute laryngitis is more severe than in patients with negative cultures.\textsuperscript{55}

Less common causes of acute laryngitis are allergies, shouting or straining the voice, continual coughing in order to bring up phlegm, gastro-esophageal reflux disease (GERD), heavy smoking or drinking, inhaling toxic fumes, and mouth-breathing.

3.6.3 Treatment

\textcolor{red}{B} Antibiotic treatment for acute laryngitis currently should be reserved for high-risk patients, patients with severe symptoms, or in the presence of an identifiable organism on Gram stain and culture.\textsuperscript{56,57} \textcolor{red}{Grade B, Level IIb}
Use a narrow-spectrum antibiotic, e.g. erythromycin. The treatment for GERD-related laryngitic conditions is the treatment of GERD itself.\textsuperscript{56,57}

3.7 Acute otitis media

3.7.1 Definition/aetiology

Acute otitis media is inflammation of the middle ear, and is nearly always preceded by an URTI. It is largely a childhood disease and is relatively uncommon in adults.\textsuperscript{58}

In adults, the most common organisms include viruses, \textit{Haemophilus influenzae} and \textit{Streptococcus pneumoniae}. In childhood, \textit{Haemophilus influenzae} is less prevalent.\textsuperscript{58-60}

3.7.2 Treatment

B Antibiotics are unnecessary in acute otitis media.\textsuperscript{61-63} \textit{Grade B, Level IIb}

About 80% of acute otitis media will resolve within 3 days without antibiotic treatment. There is some evidence that treatment with antibiotics improves short-term symptoms, although evidence is lacking for any gain in medium-term to long-term outcome.\textsuperscript{61} There is also concern that over-prescribing of antibiotics contributes to increased bacterial resistance. The Standing Medical Advisory Committee (Department of Health, UK) concluded that: “antibiotics are probably unnecessary in acute otitis media. Reassurance, time and adequate pain relief are required”.\textsuperscript{61-63}

In adults, amoxicillin is effective against the common bacteria and can be used for the treatment for otitis media in adults, if treatment with an antibiotic is preferred. In people with penicillin allergy, clarithromycin or azithromycin are effective against most common pathogens including \textit{Haemophilus influenzae}. Erythromycin may be useful, but has low activity against \textit{Haemophilus influenzae}.\textsuperscript{64-66} Amoxicillin-clavulanate is the drug of choice for second-line therapy.\textsuperscript{66,67} It has good activity against beta-lactamase-producing bacteria, e.g. \textit{Moraxella}. Other beta-lactamase stable antibiotics (e.g. second-generation and third-generation cephalosporins) offer no clear advantages over amoxicillin-clavulanate.\textsuperscript{66,67} In some areas,
trimethoprim may be effective, but this will depend on local resistance patterns and the infecting organism.

Avoid local treatment with antimicrobial eardrops in acute otitis media.\textsuperscript{63,66}  
\textbf{Grade B, Level III}

Local treatment with antimicrobial eardrops should generally be avoided as there is a possibility of ototoxic adverse effects.\textsuperscript{63,66} They also contribute to the development of antibiotic resistance.

3.8 Common cold

\textbf{A} Antibiotics should not be given for the common cold.\textsuperscript{68}  
\textbf{Grade A, Level Ib}

Controlled trials of antibiotic treatment of the common cold have consistently failed to show that treatment changes the course of outcome.\textsuperscript{68}

\textbf{B} Antibiotics should not be given for the common cold which is accompanied by mucopurulent rhinitis.\textsuperscript{50}  
\textbf{Grade B, Level III}

The presence of mucopurulent discharge without facial pain or toothache indicates mucopurulent rhinitis rather than bacterial sinusitis. In a prospective study of patients with symptoms of the common cold,\textsuperscript{50} 75-95\% had purulent rhinitis, and 80\% had viral infections.

3.9 Influenza

In the last century, numerous pandemics and epidemics of influenza have caused a very high mortality and morbidity global burden, making it the most important viral human disease.

3.9.1 Diagnosis

It is not easy to distinguish influenza from the common cold and other flu-like illnesses caused by respiratory viruses or bacteria. Up to 70\% of patients with influenza-like illness may not be infected with an influenza virus.\textsuperscript{69} However, influenza is more likely to have an abrupt
onset of fever, cough, severe myalgia, sore throat, headache and malaise.

Influenza is routinely diagnosed clinically. Laboratory cultures are currently impractical for making influenza treatment decisions, taking up to 2 weeks for results, although office diagnostic kits may be used. However, these office tests have an up to 30% false negative result compared to culture, and there may also be false positives.69

The features in Table 1 help in differentiating influenza from the common cold. The predictive value increases during an epidemic. Clusters of more severe or common features (marked with an asterisk) are more predictive of influenza.

Table 1  Comparison of influenza and the common cold69

<table>
<thead>
<tr>
<th>Features</th>
<th>Influenza</th>
<th>Common cold</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset*</td>
<td>Abrupt</td>
<td>More gradual</td>
</tr>
<tr>
<td>Fever*</td>
<td>Common: 37.7-40.0°C</td>
<td>Uncommon, or only 0.5°C increase</td>
</tr>
<tr>
<td>Cough (dry)*</td>
<td>Common, severe</td>
<td>Mild to moderate</td>
</tr>
<tr>
<td>Myalgia*</td>
<td>Severe, common</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>Severe, common</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Anorexia</td>
<td>Common</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Headache</td>
<td>Severe, common</td>
<td>Mild, uncommon</td>
</tr>
<tr>
<td>Malaise</td>
<td>Severe</td>
<td>Mild</td>
</tr>
<tr>
<td>Fatigue, weakness</td>
<td>More common than in common cold. Lasts 2-3 weeks</td>
<td>Very mild, short lasting</td>
</tr>
<tr>
<td>Chest discomfort</td>
<td>Common, severe</td>
<td>Mild to moderate</td>
</tr>
<tr>
<td>Stuffy nose</td>
<td>Occasional</td>
<td>Common</td>
</tr>
<tr>
<td>Sneezing</td>
<td>Occasional</td>
<td>Common</td>
</tr>
<tr>
<td>Sore throat</td>
<td>Occasional</td>
<td>Common</td>
</tr>
</tbody>
</table>

* Clusters of more severe or common features are more predictive of influenza.

(Modified from Montalto NJ et al, 2003)
Severe Acute Respiratory Syndrome (SARS)

It is appropriate to briefly mention SARS at this juncture. The outbreak of the severe acute respiratory syndrome (SARS), a new viral infection caused by a coronavirus, throws in a completely new dimension in our approach to acute URTIs. This disease is indistinguishable from acute URTIs at onset. It is characterized by rapid progression to breathlessness and is a highly infectious disease with a mortality rate of more than 10%. A high index of suspicion during an outbreak is the only way in which we can diagnose SARS early, take steps to isolate cases and contain further spread. A patient presenting with a fever and URTI symptoms needs to be asked for a history of recent travel within the previous 14 days from onset of symptoms, and possible contact with known SARS patients. If the history is positive for any of these, the patient must be immediately quarantined in hospital until a definitive diagnosis is clear. In SARS, the fever may temporarily improve but eventually recur, and by around day 6 of the illness, the fever may become persistently high (38°C or higher). By this time, the patient will be acutely ill. A complete resolution of symptoms by day 6 is therefore a good confirmation that the patient’s illness is not SARS.

3.9.2 Neuraminidase inhibitors

A Neuraminidase inhibitors (NIs) are effective for the prevention and treatment of influenza.⁷⁰

Grade A, Level Ia

B The adamantanes, rimantadine and amantadine, are not recommended for influenza A because of increasing drug resistance.⁷¹

Grade B, Level III

Treatment must be instituted within 48 hours of the onset of illness to be effective. Chemoprophylaxis with NIs is possible but they are not generally accepted as a substitute for influenza vaccination. Currently, the NI in common use is oseltamivir. Zanamivir needs to be given by inhalation. Oseltamivir is given orally, 75mg bd for 5 days for adults.

Antiviral prophylaxis with NI may be continued for 2 weeks after appropriated vaccination of people at high risk. This does not interfere with antibody response to the vaccine.
The adamantanes, rimantadine and amantadine are not recommended for influenza A because of increasing drug resistance. A study in the United States of 209 influenza A (H3N2) viruses isolated from 26 states showed a change in the M2 gene known to confer resistance to both amantadine and rimantadine. Two of 8 influenza A (H1N1) viruses contained the same mutation. The adamantanes are ineffective against influenza B.

3.9.3 Vaccination

Vaccination (immunoprophylaxis) is the preferred choice of prophylaxis. The vaccines available in Singapore are all either inactivated split virion (Fluarix, Fluvax, Vaxigrip, Vaxigrip Paediatric use) or subunit vaccines (Agrippal) containing influenza H and N antigens. FluAd is a sub-unit vaccine additionally adjuvanted with MF59C.1, a patented adjuvant.

There are limited data which suggest that adjuvanted vaccines confer greater immunogenicity in the elderly population.  

Current influenza vaccines are not recommended for children under 6 months of age. Influenza vaccine should not be given to people who have had an allergic reaction to a previous dose or with known allergic reaction to eggs manifested as urticaria, angioedema or anaphylaxis. Persons with acute febrile illness usually should not be vaccinated until their symptoms have abated. However, minor illnesses with or without fever do not contraindicate the use of influenza vaccine, particularly among children with mild upper respiratory tract infection or allergic rhinitis.

Persons 9 years of age and older require only a single dose. Children aged between 6 months and 8 years who have previously never been vaccinated require 2 doses, given at least 4 weeks apart. For children 6 months to 8 years who have been previously vaccinated, 1 dose should be sufficient.

In general, protection acquired from influenza vaccination lasts 4-6 months.
4 Acute Bronchitis and Exacerbation of Chronic Bronchitis

4.1 Acute bronchitis

4.1.1 Definition

Acute bronchitis may be defined as an acute respiratory tract infection (RTI) in which cough, with or without phlegm, is a predominant feature. As a case definition, the duration of the cough should be less than 3 weeks.\(^{73}\)

Most cases of acute bronchitis occur in otherwise healthy adults, in whom this acute cough illness can be called “uncomplicated acute bronchitis”.\(^{74}\) Some clinicians diagnose acute bronchitis only when productive cough is present; others insist on the presence of purulent sputum.\(^{75}\) For the standardization of diagnosis, the working definition of cough “with or without phlegm” should be used. Acute bronchitis in patients with underlying chronic obstructive pulmonary disease (See section 4.2), congestive heart failure, or immunosuppressed patients is outside the scope of this section.

Cough lasting longer than 3 weeks exceeds the case definition for acute bronchitis; such patients should be considered to have persistent cough or chronic cough illness. Irwin et al (1998) have developed a well-defined approach to the adult with persistent cough.\(^{76}\)

4.1.2 Infective aetiology

The vast majority of cases (more than 90%) of uncomplicated acute bronchitis have a non-bacterial cause. The bacterial pathogens that have been established as causes of acute bronchitis are *Bordetella pertussis*, *Mycoplasma pneumoniae*, and *Chlamydia pneumoniae* (TWAR – Taiwan Acute Respiratory Disease – strain).\(^{74}\)

Gonzales et al (2001)\(^{74}\) in a review of the MEDLINE database (1966 to October 1999) concluded that only *Bordetella pertussis*, *Mycoplasma pneumoniae*, and *Chlamydia pneumoniae* (TWAR) have been established as non-viral causes of uncomplicated acute bronchitis in adults. As a group, these agents are associated with 5% to 10% of all
cases of acute bronchitis in adults. Since Gram stain and culture of sputum do not reliably detect *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, or *Bordetella pertussis*, these tests are not recommended in the evaluation of patients with uncomplicated acute bronchitis.

Although *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis* have been found in adults with acute bronchitis, these studies generally failed to exclude patients who have underlying lung disease, failed to distinguish between colonization and infection, or did not differentiate adequately patients who had pneumonia\textsuperscript{77} from those who had acute bronchitis when determining causative agents.\textsuperscript{74,78}

The specific viruses most frequently associated with acute bronchitis, in order of frequency of occurrence, are influenza, parainfluenza, respiratory syncytial virus (RSV), coronavirus, adenovirus, and rhinoviruses.\textsuperscript{78}

Recent studies have demonstrated the importance of RSV as the etiology of acute respiratory infections in adults.\textsuperscript{78-80} Most young and middle aged adults develop asymptomatic or mildly symptomatic disease, often closely resembling influenza\textsuperscript{81} but some can have more severe clinical disease, even in otherwise healthy adults.

### 4.1.3 Ruling out pneumonia in acute cough illness

\textcolor{red}{\textbf{B}} In a patient with an acute cough illness lasting less than 3 weeks, pneumonia should be ruled out by history and clinical examination. Chest X-ray for pneumonia is not necessary in the absence of red flags.\textsuperscript{74,78,82-86}

\textbf{Grade B, Level III}

In the patient with an acute cough illness, note that acute upper RTIs account for 70\% of primary diagnoses in adults. Asthma and pneumonia, which are lower respiratory tract disorders, account for 6\% and 5\% of all acute cough illness respectively.\textsuperscript{74} The diagnosis of asthma is difficult to establish because of the transient bronchial hyper-responsiveness (and abnormal results on spirometry), which many patients with uncomplicated acute bronchitis will also have.\textsuperscript{74}

Cohort studies\textsuperscript{82-85} have identified the following decision rules for determining patients who do not have pneumonia and in the absence of these red flags, a chest X-ray to exclude pneumonia is not necessary\textsuperscript{86}:
- Absence of abnormalities in vital signs (heart rate ≥100/min, respiratory rate ≥24/min, oral temperature ≥38°C);
- Absence of focal consolidation on chest examination (e.g. rales, aegophony, and fremitus).

Note that the presence or absence of purulent sputum is not in the decision rules above because purulence (by itself) is a poor indicator of bacterial infections.\(^{87}\)

Note also that the decision rules given above have limited application in the elderly because they may present with atypical manifestations of pneumonia (and without vital sign or examination abnormalities).\(^{88}\)

### 4.1.4 Antibiotic use in acute bronchitis

**A** Routine antibiotic treatment of acute bronchitis is not recommended, regardless of the duration of cough.\(^{74,89}\)

*Grade A, Level Ia*

Four meta-analyses so far have been conducted. They show that patients taking antibiotics for acute bronchitis reduced the duration of productive cough by only half a day.\(^{74,89}\) Against this is the risk of side effects of nausea, vomiting and headache as well as the societal cost of increasing antibiotic resistance.

**B** Antibiotic therapy in acute bronchitis should be considered if the patient is ≥ 60 years or ill at the outset.\(^{90}\)

*Grade B, Level III*

A prospective study\(^{90}\) of adult patients with lower RTIs in the community found that pneumococcal infection was common (40%) in:
- people who were 60 years or older,
- those who had underlying chronic disease,
- people with both features.

### 4.1.5 Approach to patient with acute bronchitis

**C** Once a diagnosis of acute bronchitis has been made, the physician should address symptomatic treatment and patient expectations of the visit.\(^{78}\)

*Grade C, Level IV*
Symptomatic treatment of acute bronchitis with cough mixtures, bronchodilators and paracetamol is important to relieve the acute symptoms. The physician should assess the severity of the patient’s illness because it has affected the patient’s activities enough to seek care and acute bronchitis significantly decreases quality of life. Treatment discussions should focus on alleviating symptoms and provide realistic expectations for the duration of symptoms. For those with prolonged or severe cough or bronchial hyperresponsiveness, bronchodilator treatment and antitussives can be considered.

Patients should be informed that they should expect their cough to last 10 to 14 days after the office visit if it is due to acute bronchitis. The physician should also inform the patient the symptoms that should prompt a return to the clinic, such as deterioration of general condition, increasing fever, or rusty sputum.

For patients who request antibiotics for clear viral infections, providers can discuss the lack of benefit and the risks of inappropriate antibiotic use, such as the development of antibiotic-resistant infections, and the side effects that antibiotics may cause.78

All cases of acute bronchitis should be followed up and antibiotics considered if they are not recovering.90

Grade B, Level III

In a study on clinical lower respiratory tract infections,90 it was observed that even in previously well and younger adults:
- bacterial infection was present in nearly a quarter of cases;
- recovery was not rapid in all cases.91

Hence, all cases presenting initially should be followed up and antibiotics considered if they are not recovering. If antibiotics are deemed necessary in such cases, the choice of antibiotics can be selected as appropriate from the same antibiotic choice for Category I or II Community Acquired Pneumonia (CAP) (see page 68).

4.2 Acute exacerbations of chronic bronchitis (AECB)

In the literature, the terms “acute exacerbation of chronic bronchitis” (AECB) and “acute exacerbation of chronic obstructive pulmonary disease” (AECOPD) are used interchangeably. Current interest in this subject is high because ACEB results in accelerated decline in lung
function and imposes a considerable burden of morbidity, mortality, and health care costs as a result of healthcare visits and hospitalisations.

4.2.1 Definition

An acute exacerbation of chronic bronchitis (AECB) may be defined as a sustained worsening of the patient's symptoms from the stable state and beyond the normal day-to-day variations, is acute in onset, and may necessitate additional treatment. Commonly reported symptoms are one or more of the following: increased sputum production, increased sputum purulence, and increased dyspnea.\textsuperscript{92}

The above definition is based on that described by Burge & Wedzicha, 2003.\textsuperscript{92} Two clinical aspects are emphasized in the above definition, namely, the sustained worsening of symptoms beyond the day-to-day variations which is the signal of the onset of an exacerbation, and the patient's reported symptoms which were first used as the criteria for assessing the severity of an exacerbation by Anthonisen et al.\textsuperscript{93}

The sustained worsening of symptoms is a feature noted in the recent definitions of AECB UK in the National Institute of Clinical Excellence guidelines, 2004\textsuperscript{94} and the Canadian Thoracic Society's guidelines, 2004.\textsuperscript{95}

Seemungal et al\textsuperscript{96} have also in the 1990s proposed a definition made up of major and minor criteria: an AECB was defined by presence of 2 major criteria or 1 major and 1 minor criteria. The cardinal symptoms of Antonisen et al were used as the major criteria. The minor criteria were: increased nasal discharge/nasal congestion, wheeze, sore throat, and cough. Using these criteria, Seemungal et al concluded from their studies that every patient has 2-3 exacerbations per year.\textsuperscript{96,97}

4.2.2 Infective aetiology

Eighty percent of the exacerbations of chronic bronchitis are due to infection, with half due to aerobic bacteria, and one-third due to viruses. Environmental triggers and failure of compliance to therapy make up the remainder.\textsuperscript{98,99}
Reviews by Sethi\textsuperscript{98,99} of the results of bronchoscopic studies of the distal airways\textsuperscript{98-101} showed that consistently, similar pathogenetic bacteria were present in approximately 50% of patients during exacerbations. These were: \textit{Streptococcus pneumoniae}, \textit{Haemophilus influenzae}, \textit{Moraxella catarrhalis}, \textit{Pseudomonas aeruginosa}, other Gram-negative and other Gram-positive bacteria. That these were causal organisms rather than epiphenomenon were indicated by the presence of inflammatory markers and also increased bacterial load of the same organisms in the sputum during exacerbations. Mono et al\textsuperscript{101} also found that in stable chronic bronchitis, 25% of patients had colonization of bacterial pathogens in the distal airways. This colonization is not benign and results in continuing inflammation of the airways.

\textbf{As the stage of disease severity changes from stage I to stage II to stage III, the predominant bacterial pathogens change respectively from \textit{Streptococcus pneumoniae} and Gram-positive cocci to non-typeable \textit{Haemophilus influenzae} and \textit{Moraxella catarrhalis}, and to enteric Gram-negative bacilli and \textit{Pseudomonas}, respectively.}\textsuperscript{104}

Eller et al, \textsuperscript{104} in a paper in 1998, reporting the relationship between bacteriological etiology and lung function in 112 patients with a chronic bronchitis exacerbation, found that as the chronic bronchitis disease state worsened from stage I (FEV-1 greater than 50% predicted) to II (FEV-1 between 35% and 50%) to III (FEV-1 less than 35%), the flora of the pathogens changed. In those with mild disease (stage I), \textit{Streptococcus pneumoniae} and Gram-positive cocci were the most frequently isolated pathogens. In the moderately severe patients (stage II), non-typeable \textit{Haemophilus influenzae} and \textit{Moraxella catarrhalis} were the most prevalent. In patients with severe disease (stage III), enteric Gram-negative bacilli and \textit{Pseudomonas} were prevalent.

\section*{4.2.3 Indications for antibiotic therapy}

\textbf{A} Patients with acute exacerbation of severity of Anthonisen Type I (having increased dyspnea, increased sputum production, and increased sputum purulence) and Anthonisen Type II (two of the three symptoms) should be given antibiotic therapy.\textsuperscript{93} 

\textbf{Grade A, Level Ib}
In the first large, prospective, placebo-controlled study of antibiotic use in patients with AECB reported in 1987 (also known as the Winnipeg study), Anthonisen et al\textsuperscript{93} stratified their patients by severity of the acute exacerbation into type I (increased sputum production, increased sputum purulence, and increased dyspnea), type II with two of the three symptoms, and type III with one of the three symptoms plus increased nasal discharge/nasal congestion, wheeze, sorethroat, and cough.

During a 3.5-year period, 173 patients who experienced a total of 362 exacerbations were treated with either placebo or antibiotic (amoxicillin, TMP-SMX, or doxycycline). Type I exacerbations benefited the most with resolution of symptoms in 63% of the antibiotic treated exacerbations and 43% of the placebo group. Type II exacerbations also benefited. Patients with type III exacerbation (only 1 symptom) did not show any benefit.

\textbf{A} Patients with one or more of the following risk factors should be given antibiotic therapy: more than 4 exacerbations within the past year; a co-morbid condition, such as diabetes, asthma, or a history of coronary artery disease, or marked airway obstruction.\textsuperscript{105} 

\textit{Grade A, Level Ib}

Grossman et al (1998)\textsuperscript{105} conducted a one year community-based study of antibiotic treatment in patients with acute exacerbation. The study results showed that antibiotic use was associated with clinical and economic benefits in patients with risk factors and the greatest benefit were to patients with the most risk factors. Those without risk factors are referred to as “simple chronic bronchitis” as opposed to “complicated chronic bronchitis” in those with one or more risk factors.

\textbf{B} Patients with exacerbations without an increase in purulent sputum do not need antibiotic therapy unless there is a consolidation on a chest radiograph or clinical signs of pneumonia.\textsuperscript{106} 

\textit{Grade B, Level IIa}

Stockley et al (2000),\textsuperscript{106} in a study of 121 COPD patients with acute exacerbations presenting to primary care physicians in the United Kingdom, stratified into those with green purulent sputum and those with white or clear sputum, showed the presence of green purulent sputum was 94.4% sensitive and 77.0% specific for the yield of high bacterial load and indicates a clear subset of patient episodes identified
at presentation likely to benefit most from antibiotic therapy. All patients who produced white (mucoid) sputum during an acute exacerbation improved without antibiotic therapy.

4.2.4 Patient stratification and antibiotic therapy

Patients with purulent exacerbations but who have no risk factors for treatment failure or no enhanced association with more virulent or resistant bacterial pathogens can be treated with an advanced macrolide (azithromycin, clarithromycin), a cephalosporin (cefuroxime), or doxycycline.\textsuperscript{99,107-110}

Grade B, Level IIa

Table 2 (page 57) and Figure 1 (page 61) shows the stratification of patients for antibiotic therapy.\textsuperscript{99,107-110} Patients with simple AECB have no risk factors for treatment failure and antibiotic therapy should be targeted against the most likely pathogens (\textit{Haemophilus influenza}, \textit{Moraxella catarrhalis}, and \textit{Streptococcus pneumoniae}). A 10-day course of a second generation macrolide (azithromycin, clarithromycin), third generation cephalosporin (cefuroxime, cefpodoxime*, cefdinir*) or doxycycline will suffice. Sethi & Murphy (2004)\textsuperscript{99} pointed out that amoxicillin is not an appropriate choice in this group of patients because of the considerable incidence of beta-lactamase production among \textit{Haemophilus influenzae} and \textit{Moraxella catarrhalis}, two of the major pathogens of exacerbation. Clarithromycin has been formulated into a 5-day course of 500 mg extended release tablets compared to the 250 mg immediate release tablets bd for 7 days; this has resulted in better efficacy and compliance.\textsuperscript{111} Telithromycin*, the first ketolide in the market has also made its appearance with a dose of 800 mg daily for 5 days and this is an effective and well-tolerated alternative to a standard 10-day course of amoxicillin-clavulanate 500 mg/125 mg tds for AECB.\textsuperscript{112}

\* currently not available in Singapore.
<table>
<thead>
<tr>
<th>Stage of disease</th>
<th>Baseline clinical status</th>
<th>Symptoms and risk factors</th>
<th>Probable pathogens</th>
<th>Treatment and alternatives for treatment failure</th>
</tr>
</thead>
</table>
| I                | Chronic bronchitis without risk factors (Simple COPD) | Exacerbation in established chronic bronchitis patient  
- Increased dyspnea  
- Increased sputum  
- Increased sputum purulence | *Haemophilus influenzae*  
*Moraxella catarrhalis*  
*Streptococcus pneumoniae*  
*Haemophilus parainfluenzae* | Antibiotics of first choice  
- 2nd generation macrolide (azithromycin, clarithromycin)  
- 3rd generation cephalosporin (cefuroxime, cefpodoxime*, cefdinir*)  
- Doxycycline  

Alternatives for treatment failure  
(Do a chest radiograph to rule out PTB first)  
- Fluoroquinolone (moxifloxacin), gemifloxacin*, gatifloxacin, levofloxacin) or  
- β-lactam/β-lactamase inhibitor (amoxicillin clavulanate)  
- Ketolide (Telithromycin*) |

* currently not available in Singapore.
<table>
<thead>
<tr>
<th>Stage of disease</th>
<th>Baseline clinical status</th>
<th>Symptoms and risk factors</th>
<th>Probable pathogens</th>
<th>Treatment and alternatives for treatment failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>II</td>
<td>Chronic bronchitis with risk factors (complicated COPD)</td>
<td>As above plus 1 or more of the following:  - FEV₁ less than 50% predicted  - More than 4 exacerbations/yr  - Cardiac disease  - Use of home oxygen  - Chronic oral steroid used  - Antibiotic use in the past 3 months</td>
<td>As above plus:  - <em>Klebsiella</em> spp +  - Other Gram-negative pathogens  - Increased probability of β-lactam resistance</td>
<td>Antibiotics of first choice  - Fluoroquinolone (moxifloxacin, gemifloxacin*, gatifloxacin, levofloxacin) or  - β-lactam/β-lactamase inhibitor (amoxicillin clavulanate) Alternatives for treatment failure  - May require parenteral therapy  - Consider referral to a specialist or hospital</td>
</tr>
<tr>
<td>III</td>
<td>Chronic suppurative bronchitis</td>
<td>As above plus  - continuous year-round production of purulent sputum  - Some have bronchiectasis  - FEV₁ less than 35% predicted  - History of chronic bronchitis more than 10 years</td>
<td>As above plus:  - <em>Pseudomonas aeruginosa</em>  - Multiresistant Enterobacteriaceae</td>
<td>Antibiotics of first choice  - Ambulatory patients: Tailor treatment to airway pathogen: <em>Pseudomonas aeruginosa</em> – common (ciprofloxacin)  - Hospitalised patients: parenteral therapy – fluoroquinolone or IV anti-pseudomonal agent (Amikacin)</td>
</tr>
</tbody>
</table>

(Sources: Sethi & Murphy, 2004; Adams & Anzueto, 2000; Martinez & Anzueto, 2005; Akalin, 2001)

* currently not available in Singapore.
Patients with purulent exacerbations and who have risk factors that are associated with an increased likelihood of treatment failure or infection with more virulent or resistant organisms should be given antibiotics with enhanced antimicrobial coverage, namely the newer fluoroquinolones (moxifloxacin, gemifloxacin*, gatifloxacin, levofloxacin)\textsuperscript{113-118} or amoxicillin-clavulanate.\textsuperscript{119}

Grade A, Level Ib

The newer fluoroquinolones\textsuperscript{113-118} are effective against the key pathogens found in AECB namely \textit{Streptococcus pneumoniae}, \textit{Haemophilus influenzae}, \textit{Moraxella catarrhalis} and the atypical respiratory pathogens. Overall, these drugs achieve clinical cure rates of around 90\% of patients. The concern is their overuse and misuse which will render this class of drugs ineffective. Hence, we need to emphasise that we limit the use of these drugs in primary care. Also, since the use of quinolones results in delayed diagnosis and treatment of pulmonary tuberculosis (PTB), the use of these drugs for chest infections should never be done without a chest radiograph to rule out active PTB first.

Agents such as moxifloxacin and gemifloxacin with high AUC24/MPC or C(max)/MPC ratios against \textit{Streptococcus pneumoniae} are preferred, and agents such as ciprofloxacin with low ratios should be avoided. For agents such as levofloxacin and gatifloxacin, with intermediate ratios against \textit{Streptococcus pneumoniae}, it may be worthwhile considering alternative dose administration strategies such as higher dosages, to eradicate low-level resistant variants. This must of course be balanced against the potential of toxicity. The higher dosage allows for a shorter course. Thus, in a prospective clinical trial in which patients with AECB were stratified by underlying factors into uncomplicated AECB and complicated AECBs, it was found that for complicated AECB, 5 days of levofloxacin 750 mg once daily was comparable to 10 days of amoxicillin-clavulanate 875/125 mg bd. For uncomplicated AECB, 3 days of levofloxacin 750 mg once daily was comparable to 5 days of azithromycin with 500 mg on day 1 and 250 mg daily from day 2-5.\textsuperscript{118}

A shorter, 5-day course of amoxicillin-clavulanate at 2,000/125 mg has been formulated. This was shown to be as effective clinically as the longer, 7-day course of amoxicillin-clavulanate at 875/125 mg, with high bacteriological efficacy and no difference in tolerability.\textsuperscript{119}

* currently not available in Singapore.
In a patient with AECB requiring repeat antibiotic therapy within 3 months, a new class of antibiotics should be used.

Patient treated with antibiotics appear to have an increased risk of developing resistance to the same class of antibiotics within a finite time interval. Hence, if there is a need to repeat antibiotic therapy, a new class of antibiotics should be used.
Figure 1  Algorithm outlining a risk-stratification approach to antibacterial therapy of acute exacerbations of chronic bronchitis.\textsuperscript{99,107}

No Risk factors
- Age $<$65 and
- FEV\textsubscript{1} normal and
- $<$4 AECB in 12 mth and
- No comorbidities

**1 cardinal symptom**

Suspected AECB
- Increased DYSPNEA?
- Increased SPUTUM VOLUME
- Increased SPUTUM PURULENCE?

No
- Further workup

Yes

Risk factors (one or more)
- Age $<$65 or
- FEV\textsubscript{1} $<$50\% predicted or
- $>$4 AECB in last 12 months or
- Cardiac disease or
- Others: home oxygen, chronic oral steroid use, antibiotic use in past 3 months

No

**Simple COPD**
- Advanced macrolide (azithromycin, clarithromycin)
- Ketolide (telithromycin)
- Cephalosporin (cefuroxime, cefpodoxime\textsuperscript{*}, cefdinir\textsuperscript{*})
- Doxycycline

Yes

**Complicated COPD**
- Fluoroquinolone (moxifloxacin, gemifloxacin, gatifloxacin, levofloxacin)
- Amoxicillin-clavulanate

Chronic suppurative bronchitis
(at risk of pseudomonas infection)
- Consider ciprofloxacin and obtain sputum culture

Worsening clinical status or inadequate response in 72 hours

Re-evaluate
- Consider sputum culture

\textsuperscript{*} currently not available in Singapore

Sources: Sethi & Murphy, 2004; Brunton et al, 2004 (adapted)
5 Use of Antibiotics in Community Acquired Pneumonia

5.1 Introduction

Pneumonia is the most common cause of death from infectious disease in Singapore.\textsuperscript{120} In the last decade, there has been an increase in the incidence of deaths due to pneumonia. More people have died from pneumonia than from acute myocardial infarction per year since 1993.\textsuperscript{120}

Clinical practice guidelines have been published by many influential groups.\textsuperscript{121-124} The guidelines recommend the practice of stratifying patients into various severity and mortality risk groups (see Table 3 on page 65). Stratification has been validated by large prospective studies. It is the basis for recommendations regarding the appropriate location of patients for initial treatment.\textsuperscript{120,125} In addition, most of the guidelines also recommend an empirical approach for the initial choice of antibiotic, based on the relative incidence of aetiological agents.\textsuperscript{120,125} Quantitative risk stratification of patients with community-acquired pneumonia (CAP) is the basis for clinical decision on the location of treatment, intensity of diagnostic evaluation and initial antibiotic treatment. The safety (mortality and morbidity) and efficacy (frequency, duration of hospitalization and costs) in Singapore of this new empirical approach, which tends to de-emphasize the identification and treatment of specific pathogens, is uncertain.

The hospital management of CAP is much more expensive than outpatient care. Low-intermediate risk patients experience very good outcomes and may be safely managed on oral antibiotics with proper follow-up and monitoring.\textsuperscript{125,126} These low-intermediate risk patients constitute up to 75\% of all patients with CAP, and 25\% of patients hospitalized with pneumonia.\textsuperscript{127,128} The correct identification and appropriate outpatient treatment of low-intermediate risk cases is therefore a key aspect of the cost-effective management of CAP.

The prevalence of pathogens causing CAP in Singapore and their antibiotic susceptibility patterns differ considerably from that reported in the West.\textsuperscript{129-131} Therefore, this guideline contains specific recommendations more appropriate for adults with CAP in Singapore.
In March 2003, the emergence of the Severe Acute Respiratory Syndrome (SARS), a respiratory infection due to a novel coronavirus, caused widespread concern in Singapore and globally, because it can be actively transmitted in the community and healthcare workers. Thus, doctors need to be aware of the current case definition and appropriate action steps for SARS (see Figure 2 on page 75). Similarly, Avian influenza is a new and rapidly evolving respiratory infection with potential for rapid spread in the community.

5.2 Microbiology and epidemiology

5.2.1 Microbiology

Even with extensive diagnostic studies, about 50% of patients with CAP will have no likely aetiological diagnosis. This is due to:

- Prior treatment with antibiotics.
- The unreliability of sputum examination.
- The difficulty in isolating some pathogens with current techniques.

*Streptococcus pneumoniae* is the most commonly identified pathogen (65%). Next in frequency are *Haemophilus influenzae* (about 10%) and the atypical agents *Mycoplasma pneumoniae* and *Legionella* species (about 10%). *Staphylococcus aureus* (2%) and the Gram-negative bacilli (1%) are rare pathogens in CAP. It is not possible to distinguish the aetiological agent with certainty on clinical and radiological grounds. Furthermore, 5-10% of pneumonia may be due to multiple infections.\textsuperscript{120-124}

5.2.2 Local epidemiology

There has been a dramatic increase in the incidence of penicillin (currently about 40% in some hospitals) and multiple drug-resistant *Streptococcus pneumoniae* in Singapore in recent years.\textsuperscript{129} This must be taken into consideration in the empirical treatment of patients with severe CAP.

The incidence and virulence of Gram-negative bacillary CAP is much higher in Singapore than the West. In particular, *Burkholderia pseudomallei* and *Klebsiella pneumoniae* account for about 25% of severe CAP in Singapore, and they are associated with greater than 50% mortality.\textsuperscript{130,131} Thus, we recommend that empirical treatment for
these pathogens should be started for all patients with CAP admitted to the intensive care unit.

*Mycobacterium tuberculosis* is a major pathogen and accounts for 15-20% of CAP in Singapore.\textsuperscript{132} The majority of patients (greater than 70%) with pulmonary tuberculosis (PTB) is diagnosed and treated promptly based on radiological and sputum smear results.\textsuperscript{132} Owing to its high prevalence, the possibility of PTB should be considered in all patients (especially the elderly) presenting with CAP.

There is a rising incidence of immunocompromised patients with Human Immunodeficiency Virus (HIV) infection who present with CAP. In Singapore, respiratory infections in Acquired Immune Deficiency Syndrome (AIDS) usually present either as *Pneumocystis carinii* pneumonia (disproportionate hypoxaemia with mild chest radiograph abnormalities) or PTB (extensive nodal disease and/or wide dissemination). Thus, consider the possibility of PTB, HIV infection and SARS in all patients presenting with CAP in Singapore (see Figure 2 on page 75).

5.3 **Definition of pneumonia and of risk stratification**

5.3.1 **Definition and diagnosis of pneumonia**

Pneumonia is defined as the presence of fever greater than 38°C, cough with purulent sputum, and a new infiltrate on the chest radiograph.

Pneumonia cannot be diagnosed reliably by the physical examination alone (sensitivity 47-69%, specificity 58-75%); pneumonia can only be diagnosed reliably with a chest radiograph.\textsuperscript{133} An abnormality on the chest film consistent with infection is mandatory for diagnosis. Patients with fever and cough but with normal chest films have either acute sinusitis or bronchitis, and they may not need antibiotic treatment (see Chapter 4).

5.3.2 **Risk stratification**

Risk stratification is a key step in the management of community acquired pneumonia.\textsuperscript{121-126}

*Grade B, Level IIa*
The need for hospital/emergency department referral and intensive care is based on the risk categories in Table 3-7.

Risk stratification has been developed and evaluated in Western countries to manage CAP cost-effectively, by avoiding or minimizing hospital stay.\textsuperscript{125,134} It remains to be seen if this strategy is applicable to CAP in Singapore. Risk stratification should therefore not supersede clinical judgment in deciding on the need to refer and hospitalize patients.

\textbf{Table 3} \hspace{1cm} \textbf{Risk stratification}\textsuperscript{119}

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Risk</th>
<th>Mode of Management</th>
</tr>
</thead>
</table>
| I             | Low      | • Out-patient treatment (follow-up in 48 hours).  
               |           | • <65 years and no co-morbidity, + no physical or radiological signs of severity (see Table 4).  
               |           | • No modifying risk factors (Table 5). |
| II            | Low      | • Consider out-patient treatment (follow-up in 48 hours).  
               |           | • ≥65 years without co-morbidity, or <60 years with co-morbidity, + no physical, radiological or laboratory (in borderline cases) signs of severity (see Tables 4 and 6).  
               |           | • or with modifying risk factors for choice of antibiotic (Table 5) |
| III           | Intermediate | • ≥65 years with morbidity or any signs of severe disease (see Tables 4 and 6).  
               |           | • Evaluate mortality risk using Fine Pneumonia Severity Index (PSI)\textsuperscript{134}  
               |           | • PSI ≤ 90 consider home treatment  
               |           | • PSI >90 consider in-patient treatment (general ward).  
               |           | • With or without modifying risk factors (see Table 5). |
| IV            | High     | • Intensive care treatment (see Table 7).  
               |           | • With or without risk of \textit{Pseudomonas aeruginosa} (Table 5). |

(Modified from American Thoracic Society, Guidelines for the management of adults with community acquired pneumonia: diagnosis, assessment of severity, antimicrobial therapy, and prevention, 2001)
Table 4  Co-morbidity, physical and radiological signs of clinical severe community acquired pneumonia\textsuperscript{121}

<table>
<thead>
<tr>
<th>Co-morbid condition</th>
<th>• Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Heart failure</td>
</tr>
<tr>
<td></td>
<td>• Cerebrovascular disease</td>
</tr>
<tr>
<td></td>
<td>• Diabetes mellitus</td>
</tr>
<tr>
<td></td>
<td>• Renal disease</td>
</tr>
<tr>
<td></td>
<td>• Liver disease (including alcohol abuse)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Abnormalities on physical examination</th>
<th>• Altered mental status</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Pulse ≥ 125/min</td>
</tr>
<tr>
<td></td>
<td>• Respiratory rate ≥ 30/min</td>
</tr>
<tr>
<td></td>
<td>• Systolic BP &lt; 90 mmHg</td>
</tr>
<tr>
<td></td>
<td>• Temperature ≥ 40°C or &lt; 35°C</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Abnormalities on chest radiograph</th>
<th>• Multi-lobar infiltrates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Cavitation</td>
</tr>
<tr>
<td></td>
<td>• Pleural effusion</td>
</tr>
</tbody>
</table>

(Modified from American Thoracic Society, Guidelines for the management of adults with community acquired pneumonia: diagnosis, assessment of severity, antimicrobial therapy, and prevention, 2001)

Table 5  Modifying risk factors for specific pathogens\textsuperscript{121}

<table>
<thead>
<tr>
<th>Penicillin and multi-drug resistant pneumococci</th>
<th>• Age &gt; 65 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• β-lactam therapy within the past 3 months</td>
</tr>
<tr>
<td></td>
<td>• Alcoholism</td>
</tr>
<tr>
<td></td>
<td>• Immune suppressive illness</td>
</tr>
<tr>
<td></td>
<td>• Exposure to a child in day care center</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Enteric Gram-negatives</th>
<th>• Residence in a nursing home</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Underlying cardiopulmonary disease</td>
</tr>
<tr>
<td></td>
<td>• Multiple co-morbidities</td>
</tr>
<tr>
<td></td>
<td>• Recent antibiotic therapy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>\textit{Pseudomonas aeruginosa}</th>
<th>• Bronchiectasis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Corticosteroid therapy</td>
</tr>
<tr>
<td></td>
<td>• Broad spectrum antibiotic therapy</td>
</tr>
<tr>
<td></td>
<td>• Malnutrition</td>
</tr>
</tbody>
</table>

Table 6  Fine pneumonia severity index\textsuperscript{125}

<table>
<thead>
<tr>
<th>CHARACTERISTIC</th>
<th>POINTS ASSIGNED*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic factor</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>Age (yr)</td>
</tr>
<tr>
<td>Women</td>
<td>Age (yr) - 10</td>
</tr>
<tr>
<td>Nursing home resident</td>
<td></td>
</tr>
<tr>
<td>Coexisting illnesses\textsuperscript{†}</td>
<td></td>
</tr>
<tr>
<td>Neoplastic disease</td>
<td>+30</td>
</tr>
<tr>
<td>Liver disease</td>
<td>+20</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>+10</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>+10</td>
</tr>
<tr>
<td>Renal disease</td>
<td>+10</td>
</tr>
<tr>
<td>Physical-examination findings</td>
<td></td>
</tr>
<tr>
<td>Altered mental status\textsuperscript{‡}</td>
<td>+20</td>
</tr>
<tr>
<td>Respiratory rate ≥30/min</td>
<td>+20</td>
</tr>
<tr>
<td>Systolic blood pressure &lt;90 mmHg</td>
<td>+20</td>
</tr>
<tr>
<td>Temperature &lt;35°C or ≥40°C</td>
<td>+15</td>
</tr>
<tr>
<td>Pulse ≥125/min</td>
<td>+10</td>
</tr>
<tr>
<td>Laboratory and radiographic findings</td>
<td></td>
</tr>
<tr>
<td>Arterial pH &lt;7.35</td>
<td>+30</td>
</tr>
<tr>
<td>Blood urea nitrogen ≥30 mg/dl</td>
<td>+20</td>
</tr>
<tr>
<td>(11 mmol/liter)</td>
<td></td>
</tr>
<tr>
<td>Sodium &lt;130 mmol/liter</td>
<td>+20</td>
</tr>
<tr>
<td>Glucose ≥250 mg/dl (14 mmol/liter)</td>
<td>+10</td>
</tr>
<tr>
<td>Hematocrit &lt;30%</td>
<td>+10</td>
</tr>
<tr>
<td>Partial pressure of arterial oxygen</td>
<td>+10</td>
</tr>
<tr>
<td>&lt;60 mmHg\textsuperscript{§}</td>
<td></td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>+10</td>
</tr>
</tbody>
</table>

* A total point score for a given patient is obtained by summing the patient’s age in years (age minus 10 for women) and the points for each applicable characteristic.

\textsuperscript{†} Neoplastic disease is defined as any cancer, except basal- or squamous-cell cancer of the skin, that was active at the time of presentation or diagnosed within one year of presentation. Liver disease is defined as a clinical or histologic diagnosis of cirrhosis or another form of chronic liver disease, such as chronic active hepatitis. Congestive heart failure is defined as systolic or diastolic ventricular dysfunction documented by history, physical examination, and chest radiograph, echocardiogram, multiple gated acquisition scan, or left ventriculogram. Cerebrovascular disease is defined as a clinical diagnosis of stroke or transient ischemic attack or stroke documented by magnetic resonance imaging or computed tomography. Renal disease is defined as a history of chronic renal disease or abnormal blood urea nitrogen and creatinine concentrations documented in the medical record.

\textsuperscript{‡} Altered mental status is defined as disorientation with respect to person, place, or time that is not known to be chronic, stupor, or coma.

(Source: Fine MJ et al, 1997)
Table 7  High risk features

- Respiratory failure needing mechanical ventilation.
- Shock needing vasopressors >4 hours.
- \( \text{PaO}_2/\text{FiO}_2 < 250 \).
- Oliguria <80 ml urine output over 4 hours.
- Renal failure needing dialysis.
- Progression of radiological disease.

(Modified from American Thoracic Society, Guidelines for the management of adults with community acquired pneumonia: diagnosis, assessment of severity, antimicrobial therapy, and prevention, 2001)

5.3.3  Risk categories

Category I (Low risk: outpatient treatment)
Patients with clinically mild disease, and with no co-morbidity nor risk factors (see Table 4) fall in the low-risk category. They may be safely treated initially with oral antibiotics and monitored at home. They should be reviewed in the clinic within 24-48 hours to ensure that they have improved with initial treatment.

Category II (Low risk: consider outpatient treatment)
Outpatient treatment may also be considered for patients with co-morbidity or risk factors but are clinically stable. The choice of empiric antibiotics should cover the suspected pathogens such as multi-drug resistant pneumococci, Gram-negative Enterobacteriaceae or Pseudomonas aeruginosa (see Tables 5-8).

Category III (Intermediate risk: outpatient vs hospital ward treatment)
Selected clinically stable patients in this category with Fine PSI ≤90 may be safely managed as outpatients. Hospital admission is usually considered for elderly patients with PSI >90 and all patients who show physical and radiological signs of clinical severity (Table 7). The pathogens are similar to patients in category II but the recommended treatment should be intravenous antibiotics for most patients unless they do not show modifying risk factors. (see Tables 5-8).

Category IV (High risk: intensive care treatment)
The most practical way to define severe CAP is a case that requires admission to the intensive care unit. All patients in Singapore should receive empiric treatment for Burkholderia pseudomallei, and those
with specific risk factors should also be covered for *Pseudomonas aeruginosa* (see Tables 5-8).

**B** All patients with severe community acquired pneumonia (Category IV) in the ICU should be treated empirically for *Burkholderia pseudomallei*.¹³⁰,¹³¹

Grade B, Level III

### 5.4 Inpatient investigations

**C** Microbiological, haematological, biochemical and serological tests (see list below) are recommended for patients in risk Categories III and IV upon presentation.¹²¹-¹²⁵,¹³⁵-¹³⁷

The following microbiological tests should be done before starting antibiotics in patients with moderate to severe CAP (Categories III and IV). Initial microbiological studies may have limited value in the management of patients with low risk CAP (Categories I & II)¹³⁵-¹³⁷.

- Sputum Gram stain and aerobic culture (mycobacterial smear and culture where appropriate).
- Blood aerobic culture.
- Pleural fluid Gram stain and culture.
- Urine for *Legionella* antigen.

The other investigations are:
- Blood count with differentials, and smear for toxic granulations.
- Biochemistry, including renal and liver function (blood gas where necessary).
- Consider HIV testing and work-up for *Pneumocystis carinii*.
- Optional serological testing for atypical agents.

Grade C, Level IV

### 5.5 Empirical antibiotic therapy

**A** The initial choice for empirical antibiotic therapy should be based on the risk category and relative prevalence of major pathogens.¹²⁵,¹²⁶,¹³⁸-¹⁴²

Grade A, Level Ib

**C** Quinolones are not recommended for the outpatient treatment of community acquired pneumonia in risk categories I & II.¹⁴¹,¹⁴³

Grade C, Level IV
The initial choice of empirical antibiotic treatment is summarised in Table 8. It is based upon the risk category and relative prevalence of major pathogens in Singapore. Alternative regimens are listed but not necessarily in the preferred order. There is no evidence to suggest that any single regimen is superior to the others.\textsuperscript{138-143} Where possible, the least expensive effective treatment should be administered.

Table 8  Empirical antibiotic for initial treatment of community acquired pneumonia\textsuperscript{121-124}

<table>
<thead>
<tr>
<th>CLASS</th>
<th>ANTIBIOTIC</th>
<th>DOSAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>OUTPATIENT (ORAL)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Category I</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Macrolide:</td>
<td>Erythromycin</td>
<td>500 mg, 6H, x 7-10 days</td>
</tr>
<tr>
<td></td>
<td>Erythromycin ES</td>
<td>800 mg, bd, x 7-10 days</td>
</tr>
<tr>
<td></td>
<td>Clarithromycin</td>
<td>500 mg, bd, x 7-10 days</td>
</tr>
<tr>
<td></td>
<td>Azithromycin</td>
<td>500 mg, x 5 days</td>
</tr>
<tr>
<td>OR</td>
<td>Tetracycline</td>
<td>Doxycycline</td>
</tr>
<tr>
<td>Category II</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2nd generation cephalosporin</td>
<td>Cefuroxime</td>
<td>500 mg, bd, x 7-10 days</td>
</tr>
<tr>
<td>OR</td>
<td>Penicillin+(\beta)-lactamase inhibitor</td>
<td>Amoxicillin-clavulanic acid</td>
</tr>
<tr>
<td>PLUS</td>
<td>Ampicillin-sulbactam</td>
<td>PLUS</td>
</tr>
<tr>
<td>Macrolide</td>
<td>Macrolide (as above) or doxycycline</td>
<td></td>
</tr>
<tr>
<td><strong>Outpatients or INPATIENT (ORAL or INTRAVENOUS +ORAL)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Category III - No cardio-pulmonary disease or modifying factor</td>
<td>(\geq 10) million U per day ((\pm) oral macrolide)</td>
<td>2 MU 4H, intravenous</td>
</tr>
<tr>
<td>Penicillin (high dose)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>New macrolide</td>
<td>Clarithromycin</td>
<td>500 mg bd</td>
</tr>
<tr>
<td>OR</td>
<td>Azithromycin</td>
<td>500 mg om</td>
</tr>
<tr>
<td>New quinolone</td>
<td>Levo/Moxi-floxacin</td>
<td>500-750 mg (Levo) or 400 mg (Moxi) om, intravenous or oral</td>
</tr>
<tr>
<td>CLASS</td>
<td>ANTIBIOTIC</td>
<td>DOSAGE</td>
</tr>
<tr>
<td>-------</td>
<td>------------</td>
<td>--------</td>
</tr>
<tr>
<td>Category III – with cardio-pulmonary disease or modifying risk factor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-pneumococcal quinolone</td>
<td>Levo/Moxi-floxacin</td>
<td>500-750mg (Levo) or 400 mg (Moxi) om, intravenous or oral</td>
</tr>
<tr>
<td>OR</td>
<td>Ceftriazone (± oral macrolide)</td>
<td>2 g, om, intravenous</td>
</tr>
<tr>
<td>3rd generation cephalosporin OR</td>
<td>Amoxicillin-clavulanic acid</td>
<td>1.2 g, 8H intravenous</td>
</tr>
<tr>
<td>Penicillin+β-lactamase inhibitor</td>
<td>Ampicillin-sulbactam (Augmentin or Unasyn), and both groups (± oral erythromycin)</td>
<td>1.5 g, 8H intravenous</td>
</tr>
<tr>
<td>Category IV (Intensive care)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No risk for Pseudomonas aeruginosa</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Macrolide</td>
<td>Erythromycin PLUS EITHER</td>
<td>500-1000 mg 6H intravenous</td>
</tr>
<tr>
<td>PLUS EITHER</td>
<td>Ceftazidime, or</td>
<td>1-2 g, 8H intravenous</td>
</tr>
<tr>
<td>3rd generation cephalosporin or β-lactam, or lincomamide, or glycopeptide)</td>
<td>Cloxacillin</td>
<td>1 g 6H intravenous</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>Clindamycin</td>
<td>400-600 mg, 6-8H, intravenous</td>
</tr>
<tr>
<td>OR New quinolone PLUS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3rd generation cephalosporin</td>
<td>Levo/Moxi-floxacin PLUS</td>
<td>1 g 12H intravenous (to monitor levels)</td>
</tr>
<tr>
<td>Risk for pseudomonas aeruginosa</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti pseudomonal quinolone PLUS</td>
<td>Ciprofloxacin PLUS</td>
<td>750 mg om (Levo) or</td>
</tr>
<tr>
<td>Carbapenem</td>
<td></td>
<td>400 mg (Moxi) om intravenous</td>
</tr>
<tr>
<td>OR</td>
<td>Imipenem/Meropenem</td>
<td>1-2 g, 8H, intravenous</td>
</tr>
<tr>
<td>Anti pseudomonal β-lactam PLUS Aminoglycoside PLUS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Either macrolide or respiratory quinolone</td>
<td>Imipenem/Piperacillin-tazobactam PLUS</td>
<td>4.5 g, 8H</td>
</tr>
<tr>
<td>Amikacin PLUS</td>
<td>Either Azithromycin (I.V.)</td>
<td>750 mg - 1g, om</td>
</tr>
<tr>
<td>OR</td>
<td>or Levo/Moxi-floxacin</td>
<td>500 mg, om</td>
</tr>
<tr>
<td></td>
<td></td>
<td>750 mg, om (Levo) or 400 mg om (Moxi) intravenous</td>
</tr>
</tbody>
</table>

(Sources: Niederman MS et al, 2001; BTS Guidelines 2001; Mandell and Niderman M, 1993; Bartlett JG et al, 1998.)
Outpatient treatment (Categories I-III & Fine PSI ≤ 90) should cover *Streptococcus pneumoniae* and *Mycoplasma pneumoniae*. Either macrolides or tetracyclines fulfil this dual role.

The new quinolones are also effective but should be reserved for more severe CAP (Category III and above only).\(^{134}\) However, we do not recommend the use of the new “respiratory” quinolones for the empirical outpatient treatment of pneumonia in very low risk patients (categories I & II) for the following reasons:

(a) There is no conclusive evidence from randomized controlled studies that these drugs are superior to others for CAP management in the outpatient setting;\(^ {143,144}\)

(b) Resistance to this class of drugs is rising in the community;

(c) There will be inappropriate use of these drugs in a “trickle-down” effect for less severe respiratory infections such as upper respiratory infections and bronchitis;

(d) Since these drugs have anti-mycobacterial activity, the empirical use of quinolones has been associated with delays (21 days versus 5 days) in the diagnosis and treatment of pulmonary tuberculosis.\(^ {145}\)

Hospitalized patients with moderate illness (Category III and Fine PSI > 90) should be treated initially with an intravenous antibiotic against virulent and possibly drug-resistant *Streptococcus pneumoniae* (DRSP). High-dose penicillin or ceftriaxone is effective against DRSP causing CAP. These antibiotics will not, however, be effective against DRSP causing bacterial meningitis. The importance of adding a macrolide to cover atypical pathogens in this category (category III) of patients is questionable. Prospective studies suggest that patients with mild to moderate CAP caused by atypical pathogens have very good outcomes despite inappropriate treatment. Alternatively, either the new macrolides such as azithromycin (or clarithromycin) or newer quinolone antibiotics (Levo-/moxi-floxacin) may be offered as oral mono-therapy in this group of patients.

Severely-ill patients should be treated with intravenous antibiotics which cover *Streptococcus pneumoniae, Burkholderia pseudomallei, Klebsiella pneumoniae, Staphylococcus aureus*, and atypical pathogens. No single antibiotic is adequate here. The treatment for severe *Burkholderia pseudomallei* infection must include either ceftazidime (I.V. 2g every 8H) or imipenem (I.V. 500 mg every 6H).\(^ {146}\) The efficacy of new quinolones in severe CAP is uncertain.
All treatments should be reviewed 48-72 hours after the first dose of antibiotic, with regard to new microbiological information, clinical response and adverse effects.

5.6 Step-down or switch therapy in low or intermediate risk categories

A A switch from I.V. to oral antimicrobials and prompt hospital release is recommended for patients in low or intermediate risk categories who respond promptly or become clinically stable after receiving initial antimicrobial treatment.\textsuperscript{147-152}

Grade A, Level Ia

Patients who were initially in the low or intermediate risk categories (fine PSI \( \leq 90 \)) and who responded promptly to empirical antibiotics constitute up to 70\% of hospitalized CAP.\textsuperscript{126} A rapid step-down or switch therapy from I.V. to oral antibiotics and prompt discharge from hospital have been found to be a safe and cost-effective strategy (relapse rate about 1\% with no mortality).\textsuperscript{147-152} The switch to oral medication is usually instituted on day 3 when resolution of fever occurs or clinical stability is achieved. Patients may go home on that very same day. Recent observational studies suggest that there may be no need to keep patients for another day in hospital after a switch to oral therapy.\textsuperscript{147-152} With conventional management these patients remain in hospital for about 6-7 days. However, patients who do not fulfil criteria for clinical stability (see Table 9) at discharge are at risk of death or re-admission.\textsuperscript{153} With this early release policy it may be prudent to review patients within 48 hours and/or give written instructions about the risk of relapse.

Table 9 B Criteria for discharge from hospital\textsuperscript{147-152}

- Stable vital signs for 24 hours (i.e. temperature <37.8°C, respiratory rate <24/min, systolic BP ≥90 mmHg, \( O_2 \) saturation ≥90\% while breathing room air).
- Patient able to take diet.
- Patient able to take oral antibiotics.
- No other active clinical or psycho-social problems requiring hospital stay.

Grade B, Level III
5.7 Recommendations for evaluation

A recent prospective study showed that the key outcomes (length of hospitalization and mortality) in adult patients with CAP in Singapore are comparable to those from large studies in developed countries.\textsuperscript{128} The average length of stay was 8.4 days and mortality rate was 13%. There is little evidence that longer stays are associated with better outcomes.\textsuperscript{154} In a large audit of US Medicare patients 65 years old and above with CAP, administering antibiotics within 4 hours of hospital arrival was associated with improved survival.\textsuperscript{155}

In addition to the usual outcomes of mortality and hospital length of stay, the time to the first dose of antibiotics in elderly patients (>65 years) should be a key indicator of the evaluation of the quality of CAP management.

Grade B, Level III
Figure 2  Management of community acquired pneumonia

Severe Acute Respiratory Syndrome
* Case definitions
http://www.who.int/csr/sars/casedefinition/en/
† MOH guidelines

Consider Severe Acute Respiratory Syndrome & consult the latest WHO case definition* and MOH guidelines† on action steps.

Confirm pneumonia with chest radiograph

Consider PTB or HIV

Risk stratify

Low
Outpatient treatment
Oral macrolide

Intermediate
Calculate Fine PSI$^{125}$
PSI $\leq 90^{134}$
Outpatient treatment
Oral respiratory quinolone
PSI $> 90$
General ward treatment
New macrolide/respiratory quinolone
KIV step down & home on day

High
KIV ICU treatment
IV combination: antibiotics
6 Use of Antibiotics in Hospital Acquired Pneumonia

6.1 Introduction

Among nosocomial infections, hospital acquired pneumonia (HAP) is associated with the highest mortality. Patients develop HAP following aspiration (either frank or “micro-aspiration”) of upper airway secretions contaminated by bacteria acquired from the hospital environment.

Upper airway colonization, and thus the risk of HAP, is related to the:
- Severity of the underlying illness,
- Duration of hospitalization,
- Duration of intubation (if any), and
- Intensity of antibiotic exposure.

The most widely discussed guideline on the management of HAP is the official statement published by the American Thoracic Society and the Infectious Diseases Society of America in 2005.\textsuperscript{156} The efficacy of this guideline has not been validated in large prospective studies. Most of the recommendations are based on expert opinion, rather than evidence from randomized controlled studies.

6.2 Epidemiology of HAP in Singapore

The main pathogens of HAP in Singapore are similar to those reported in the West. The predominant bacteria are Gram-negative bacilli (\textit{Pseudomonas aeruginosa} and Enterobacteriaceae) and \textit{Staphylococcus aureus} (especially methicillin-resistant \textit{Staphylococcus aureus} or MRSA).\textsuperscript{157} Among the Gram-negative bacilli, \textit{Klebsiella} and \textit{Acinetobacter} species are notably “difficult” pathogens in Singapore.\textsuperscript{157} Infection with MRSA, which accounts for greater than 50\% of \textit{Staphylococcus aureus} isolates, has been an endemic and widespread problem in many local hospitals for some years.\textsuperscript{157}

The increasing resistance of Gram-negative pathogens to both β-lactam antibiotics (including 3\textsuperscript{rd}-generation cephalosporins and β-lactam-β-lactamase inhibitors) and aminoglycosides over the past decade is a cause for alarm.\textsuperscript{157} The \textit{in vitro} resistance levels to both classes of
antibiotics is currently around 20%. Polymicrobial infections are also more common in HAP than in community acquired pneumonia (CAP), and this complicates empirical antibiotic choice.

6.3 Definition, diagnosis and classification

6.3.1 Definition and diagnosis

HAP is defined as pneumonia presenting 48 hours or more after hospital admission. HAP in elderly patients with multiple medical problems may present with non-specific symptoms and signs. Therefore, it may be difficult to distinguish HAP from other complications such as pulmonary congestion, atelectasis, drug reactions, non-pulmonary sepsis, acute respiratory distress syndrome and pulmonary embolism.

The diagnosis of ventilator-associated pneumonia (VAP) is especially difficult. The usual clinical signs of fever, purulent tracheal aspirate and new radiographic chest infiltrates have a sensitivity of less than 50%\(^\text{158-161}\). Techniques which obtain uncontaminated lower respiratory secretions, combined with quantitative bacteriological cultures, are a little better than bedside judgement. But these techniques are invasive, much more expensive and not widely available\(^\text{159-161}\). These invasive techniques have been compared with non-invasive methods in 4 randomized controlled trials with inconclusive results\(^\text{159-161}\).

6.3.2 Classification of HAP and antibiotic use

B It is recommended that the initial empirical therapy be based upon targeting a core group of pathogens according to severity of illness, duration of hospitalisation and risk factors for specific pathogens\(^\text{156,160-164}\).

Grade B, Level III

A Piperacillin-tazobactam is as safe and effective as ceftazidime in the empirical treatment of severe hospital acquired pneumonia, hospital acquired pneumonia in the ICU and ventilator-associated pneumonia\(^\text{165-167}\).

Grade A, Level Ib
The purpose of classifying HAP is to guide initial antibiotic choice. The recommendation for initial antibiotic choice is based upon targeting a group of core pathogens according to:

1) Severity of illness
2) Duration of hospitalization, and
3) Risk factors for specific pathogens (to also avoid antibiotics which patients were recently exposed to).

There are 3 groups of patients with HAP, each with their core pathogens and antibiotic regimens identified. The following is an adaptation of the classification scheme proposed by the American Thoracic Society:

1) HAP of early onset (≤ 5th hospital day), of mild-to-moderate severity, and the absence of special risk factors:

Patients in this group should be treated for Gram-negative bacillary sepsis, with a consideration to cover for MRSA (see Table 10). A newer broad-spectrum quinolone may be an alternative as monotherapy in this group of patients. Another choice could be a 3rd-generation cephalosporin, plus an aminoglycoside.

2) HAP onset after 5 days, and/or clinically severe disease (severe HAP may be defined in the same way as severe/high risk CAP - see Chapter 5, Table 7), and the absence of special risk factors:

This group of patients should be treated empirically for *Pseudomonas aeruginosa* and MRSA with a combination of antibiotics (see Table 11). Ciprofloxacin, imipenem and meropenem are the most active antibiotics against serious hospital-acquired Gram-negative infections in Singapore. Ceftazidime and amikacin remain active against about 80% of serious hospital-acquired *Pseudomonas aeruginosa* infections. However, the other cephalosporins and aminoglycosides perform poorly against other Gram-negative bacilli. Thus, their role in the initial empirical treatment of serious HAP is diminishing. The newer quinolones do not show better activity than ciprofloxacin against *Pseudomonas aeruginosa*. Three randomized controlled studies have concluded that in the treatment of severe HAP or HAP in the critical care unit or VAP, piperacillin-tazobactam is at least as safe and effective as ceftazidime (both drugs used in combination with an aminoglycoside).
3) HAP in patients with special risk factors:

The relevant antibiotic should be added in HAP when there is a risk for specific pathogens, in addition to the antibiotic cover for the core pathogens (see Table 12 on page 80). The role of newer classes of antibiotics such as 4\textsuperscript{th}-generation cephalosporins (cefepime or cefpirome) in the treatment of HAP is uncertain.

**Table 10** Antibiotics for patients with no risk factors; hospital acquired pneumonia of mild to moderate severity, and of early onset (≤ 5 days)\textsuperscript{156}

<table>
<thead>
<tr>
<th>Core pathogens</th>
<th>Core antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enteric Gram-negative bacilli - <em>Klebsiella</em> species and <em>Escherichia coli</em></td>
<td>3\textsuperscript{rd}-generation cephalosporin e.g. intravenous ceftriaxone, or β-lactam / β-lactamase inhibitor e.g. intravenous ampicillin-sulbactam or amoxicillin-clavulanic acid, or quinolone e.g. ciprofloxacin.</td>
</tr>
<tr>
<td>Also, - <em>Staphylococcus aureus</em></td>
<td>Consider adding cloxacillin or clindamycin.</td>
</tr>
<tr>
<td>- <em>Hemophilus influenzae and Streptococcus pneumoniae</em></td>
<td>Consider adding azithromycin or clarithromycin.</td>
</tr>
<tr>
<td>If MRSA isolated ≥ 50% in ICU</td>
<td>Alternative to above: newer quinolone as monotherapy.</td>
</tr>
<tr>
<td></td>
<td>Consider adding vancomycin.</td>
</tr>
</tbody>
</table>

Table 11  
Antibiotics for patients with no risk factors, but late onset (>5 days) hospital acquired pneumonia, or severe hospital acquired pneumonia onset at any time (definition of severe hospital acquired pneumonia as for severe community acquired pneumonia)\(^{156}\)

<table>
<thead>
<tr>
<th>Core pathogens</th>
<th>Core antibiotics</th>
</tr>
</thead>
</table>
| *Pseudomonas aeruginosa*  | Ciprofloxacin or amikacin  
PLUS either  
an anti-pseudomonal $\beta$-lactam/$\beta$-lactamase inhibitor  
(piperacillin/tazobactam), or  
ceftazidime or carbapenems (imipenem, meropenem) |
| Resistant *Acinetobacter* species | Anti-pseudomonal cephalosporin (ceftazidime), or  
imipenam/meropenam, or amikacin        |
| MRSA                      | Add vancomycin                                                                  |

Grade C, Level IV


Table 12  
Risk factors for specific pathogens and antibiotics to be added\(^{156}\)

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Risk factor</th>
<th>Antibiotic</th>
</tr>
</thead>
</table>
| Anaerobic           | Observed aspiration  
Abdominal surgery  
Putrid discharge | Clindamycin, metronidazole, or $\beta$-lactam/$\beta$-lactamase inhibitor |
| *Staphylococcus aureus* | Coma  
Head injury  
Diabetes  
Renal failure | Vancomycin                                                                  |
| MRSA                | Outbreaks                    | Vancomycin                                                                  |
| *Legionella* species | Corticosteroid use  
Outbreaks | Erythromycin                                                                |
| *Pseudomonas aeruginosa* | Prolonged ICU stay  
Antibiotic exposure  
Chronic lung disease  
AIDS | As in severe hospital acquired pneumonia  
(see Table 11 above) |

Grade C, Level IV

6.4 Comments

These recommendations for initial empirical therapy are based upon the American Thoracic Society consensus statement and published data on HAP in Singapore over the past decade. The prior microbiological information, clinical progress, epidemiological background and antibiotic exposure of the patients should be taken into consideration. The clinician must also be aware of the local (ward, unit, hospital) prevalence and antibiotic profiles of the core nosocomial pathogens.

Carefully designed antibiotic rotation or restriction strategies appropriate to local microbial flora may result in decline in antibiotic resistance.\textsuperscript{168,169} There is no clear evidence, however, that these steps will improve patient outcomes. Successful application of non-invasive ventilation will avoid the need for tracheal intubation and reduce the risk of HAP and VAP.\textsuperscript{168,170}

Following initial treatment, patients must be evaluated for a clinical response and microbiological results taken into account. Both may be expected within 72 hours. In this regard, definitive identification of a nosocomial pathogen - such as from positive blood cultures or positive isolates from lower respiratory secretions using protected specimen techniques - would be most relevant. There is uncertainty, however, about the cost-effectiveness of using invasive techniques in the routine diagnosis of HAP. Failure to respond or further deterioration will also necessitate consideration of non-infectious illness rather than inappropriate antibiotic cover.
7 Use of Antibiotics in Acute Infectious Diarrhoea in Adults

7.1 Introduction

Most cases of acute diarrhoea only require supportive treatment. Certain diarrhoeas need more to be done. A careful evaluation of a patient, with a good history and physical examination is essential for making correct decisions about the need for admission, further investigation and treatment. This also leads to savings from unnecessary investigations (like routine stool cultures), and unnecessary use of antibiotics.

This chapter deals with acute infectious diarrhoea in the community and hospital populations, but does not include the management in immuno-compromised patients. Persistent diarrhoea and chronic diarrhoea need a detailed workup and are outside the focus of this chapter.

7.2 Definitions

“Diarrhoea” is defined as an alteration of normal bowel movements characterized by an increase in water content, volume or frequency of stool. Acute diarrhoea runs its course in less than 14 days. Diarrhoea lasting longer than 14 days and up to 30 days is persistent diarrhoea. Chronic diarrhoea is diarrhoea that has lasted more than 30 days. An increase in frequency of bowel movements to 3 or more stools per day is generally used as a definition of diarrhoea for epidemiological investigations.\textsuperscript{171,172}

For the purpose of management:
- Mild diarrhoea is said to occur when there are six or less stool movements a day;
- Moderate diarrhoea when there are more than six stool movements a day; and
- Severe diarrhoea when the frequency is associated with severe abdominal pain and high fever.
7.3 Diarrhoeal syndromes

From a diagnostic and management point of view, it is useful to divide acute diarrhoeas into 2 distinct clinical syndromes: non-inflammatory and inflammatory (See Table 13 for common causative organisms). There is some overlap between the two syndromes, and diarrhoea which is watery initially can evolve into an inflammatory type of diarrhoea. Figure 3 (page 97) shows the algorithm for managing acute diarrhoeas.

### Table 13 Organisms in acute diarrhoeas

<table>
<thead>
<tr>
<th>Diarrhoeal syndromes</th>
<th>Organisms commonly implicated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-inflammatory</td>
<td>Viruses: Norwalk -like agents, Rotavirus, Bacteria: <em>Clostridium perfringens</em>, <em>Staphylococcus aureus</em>, <em>Vibrio cholerae</em> Parasites: <em>Giardia lamblia</em>, <em>Entamoeba histolytica</em></td>
</tr>
<tr>
<td>Inflammatory</td>
<td><em>Shigella</em>, <em>Salmonella</em>, entero-haemorrhagic <em>Escherichia coli (EHEC)</em>, enteroinvasive <em>Escherichia coli (EIEC)</em>, <em>Campylobacter</em>, <em>Clostridium difficile</em>.</td>
</tr>
</tbody>
</table>

1. **Watery, non-inflammatory diarrhoea syndrome**

This is typified by watery stool of large volume. The stool does not contain pus or blood. The patient can have nausea, vomiting, abdominal colic and low-grade fever. The syndrome includes the so-called “toxin-induced food poisoning”. In most cases, this diarrhoea is self-limiting and benign. Antibiotics are usually not required. Investigations are generally unnecessary unless cholera is suspected.

2. **Inflammatory diarrhoea syndrome**

This is characterized by frequent, small volume stools, which may be bloody. It is often accompanied by fever, tenesmus and severe abdominal pain. Stool microscopy shows either blood or pus cells. This syndrome implies invasions or mucosal damage by the
organism/bacteria or cytotoxins. Where the illness is moderate to severe, further investigations are needed.

7.4 Evaluation of the patient

The aim of evaluation is to distinguish patients with mild, self-limiting diarrhoea from those requiring further investigations admission or empirical antibiotic therapy.

**GPP** In any patient with diarrhoea, obtain the following history:
- age
- evidence of an immunocompromised state
- previous use of antibiotics
- history of travel
- scale of outbreak

**History**

1. **Age.** The very-young and the elderly are more prone to the complications of dehydration and sepsis. The majority of mortality occurs in these two extremes of age.

2. **Evidence of an immunocompromised state.** This group includes: patients with liver cirrhosis, those on long-term steroids or immunosuppressive agents, and HIV-infected patients. Like the elderly, this group is more prone to sepsis and infection by atypical organisms.

3. **Previous use of antibiotics, or recent or current hospitalisation.** Patients in this group have to be investigated for nosocomial infections, particularly *Clostridium difficile* infections.

4. **History of travel.** Diarrhoea occurring when travelling falls into the category of traveller’s diarrhoea. The expected causative organisms are those which occur in the visited country. These patients are often infected by toxigenic strains of *Escherichia coli*, and they respond very well to empirical antibiotic therapy.

5. **Scale of outbreak.** This is important from a public health point of view. It may lead to identification of a common source of infection, and prevent further spread of the organism.
Perform a focussed physical examination in a patient with diarrhoea:
1. Look for signs of dehydration: loss of skin turgor, postural hypotension, increased pulse rate.
2. Record the temperature.
3. Examine the abdomen for tenderness or distension.
4. Perform a per rectal examination to look for the presence of blood in the stool.

In a patient with diarrhoea, look for red flags:
- Profuse, watery diarrhoea with dehydration.
- Passage of small volume stool, containing blood and mucus.
- Temperature ≥38.5°C.
- Passage of ≥6 times unformed stool in 24 hours.
- Duration of illness >72 hours.
- Severe abdominal pain, in a patient over the age of 50 years.
- Diarrhoea in the elderly (≥70 years of age).
- Diarrhoea in the immuno-compromised.

The presence of one or more of the above symptoms/signs suggests the diarrhoea is severe enough to warrant further evaluation and treatment.

7.5 Investigations

In acute diarrhoea, investigations are indicated only when the diarrhoea is moderate or severe or there is a suspicion that this is an inflammatory diarrhoea.

Screening tests

The faecal leucocyte, faecal lactoferrin, or Hemoccult™ test may be useful screening tests in patients with moderate to severe acute infectious diarrhoea. These tests may be used to differentiate inflammatory and non-inflammatory diarrhoeal syndromes.171,173-175

Grade B, Level III

The above three tests have a sensitivity of about 70% and specificity of about 50%. A positive test supports a diagnosis of bacterial diarrhoea with inflammation. Commonly implicated pathogens include
Salmonellae, Shigellae, Campylobacter, Yersinia, non-cholera Vibrios and Clostridium difficile. A positive result in a patient with moderate to severe infectious diarrhoea would be an indication to start empirical antibiotics.

Stool culture

A Stool cultures (for salmonella, shigella and campylobacter) should be performed only in patients who have prolonged diarrhoea, or in patients who have clinical or biochemical evidence of inflammatory diarrhoea.171,176-178

Grade A, Level Ib

Routine stool culture for every patient with acute infective diarrhoea gives a positive yield of only between 2 and 3%. Stool culture should be reserved for the sicker patients who require further evaluation (These are usually patients with prolonged diarrhoea or those with evidence of inflammatory diarrhoea) or when there is a suspected outbreak, as this is important from a public health point of view.

While routine stool cultures detect the usual enteric bacteria, a more specific culture is needed when certain organisms are suspected, e.g. Escherichia coli O157:H7, Yersinia, Clostridium difficile. The correct culture medium should be used, and the laboratory should be alerted of the suspicion.

A For patients with diarrhoea that develops after three days of hospitalisation, or have recently received antibiotics or anti-neoplastics, an effort should be made to look for Clostridium difficile infection.172,177,179,180

Grade A, Level Ib

In such patients, stool cultures for standard bacterial pathogens (Salmonella, Shigella, Campylobacter, etc.) have been proven to be unproductive. These patients should have cultures for Clostridium difficile in addition to assays for Clostridium toxins.

C Exposure of a traveller or hiker to untreated water and illnesses that persist for more than seven days should prompt evaluations for protozoal pathogens, especially giardia and cryptosporidium.181

Grade C, Level IV
Protozoal parasites are uncommon causes of traveller’s diarrhoea, but increase in importance when it lasts beyond a week when viral and bacterial causes have run their course or bacterial causes have been treated. The testing of one or two specimens by means of enzyme immunoassay has a sensitivity of more than 95% and is considerably better than older methods based on microscopical examination.

**Endoscopy**

**GPP** Endoscopy should be reserved for the investigation of patients with persistent or chronic diarrhoea.

Sigmoidoscopy is useful:
- If there is the possibility of inflammatory bowel disease or ischaemic colitis;
- In diagnosing pseudomembranous colitis, which has a characteristic endoscopic appearance.

### 7.6 General management

**Initial rehydration**

**A** Fluid and electrolyte replacement plays a pivotal role in the management of all patients with acute diarrhoea. Oral rehydration is the treatment of choice.

[172,182-186]

**Grade A, Level Ia**

Rehydration is often all that is needed in patients with diarrhoea. In patients who are mildly dehydrated, fruit juices or isotonic drinks often suffice. In more severely dehydrated patients, intravenous hydration might be required.

If a patient can take orally, rehydrating solutions like Pedialyte™ or Rehydrolyte™ are useful. Oral rehydrating solutions are cheaper and superior to intravenous solutions if the patient can take orally, and are not associated with the pain of intravenous solutions. An added advantage of oral rehydrating solutions is there is no possibility of fluid overload, as the thirst resolves with rehydration.
Rehydration is important in the elderly, who are more prone to ischaemic episodes involving the heart, intestines or cerebrovascular system when they become dehydrated.

**Anti-motility agents**

If an anti-motility agent is required, loperamide may be used.\(^{187,188}\)

Anti-motility agents should not be given to patients who have febrile dysentery.\(^{188}\)

Anti-motility agents should not be given to patients who have suspected *Escherichia coli* O157:H7 infection, Shiga toxin-producing *Escherichia coli* infection, or frank bloody diarrhoea.\(^{180,188,189}\)

Anti-motility agents are useful primary or adjunct drugs in the treatment of acute diarrhoea. They provide symptomatic relief and in mild diarrhoea, can be the only treatment needed. However, in certain conditions, as follows, they should not be used.

Anti-motility agents should not be given to:
- Patients with febrile dysentery, as it may prolong the disease.
- Patients with suspected *Escherichia coli* O157:H7 infection, as it might precipitate the haemolytic uraemic syndrome.
- Patients under 2 years of age.

### 7.7 Antimicrobial therapy

Most patients with acute diarrhoea need not be treated with antimicrobial drugs. The vast majority of diarrhoeal cases are effectively resolved by the host defence mechanisms.

#### 7.7.1 Indications

Antimicrobial therapy is indicated when:
- There is evidence of intestinal mucosal invasion or sepsis.
- The condition is potentially life-threatening.
- There is a need to decrease faecal excretion of organisms and prevent spread, e.g. in Shigellosis.
- There is moderate to severe traveller’s diarrhoea as antimicrobial therapy shortens the course and alleviates the symptoms by up to a day.

### 7.7.2 Empirical antibiotic therapy

**A** In patients with moderate to severe inflammatory diarrhoea, an empirical course of quinolones can be given for 3-5 days.\(^{190-193}\)

*Grade A, Level Ib*

Severe inflammatory diarrhoea implies the presence of invasion of the intestinal mucosa. Invasion can lead to frank bacterial enterocolitis, bacteraemia with septic complications, toxic megacolon and intestinal perforation. Prompt antibiotic treatment has been found to shorten the clinical course, improve the outcome, and shorten the carriage of any enteric pathogens.

**A** In patients with moderate to severe traveller’s diarrhoea, an empirical course of quinolones can be given for 3-5 days.\(^{194,195}\)

*Grade A, Level Ib*

Traveller’s diarrhoea is diarrhoea acquired while travelling overseas. The aetiology varies from region to region. The most common organisms implicated are the enterotoxigenic *Escherichia coli* (ETEC), *Salmonellae, Shigellae* and, less commonly, viruses. Parasites like *Giardia lamblia* or *Entamoeba histolytica* should also be considered if travel has been to countries endemic for these parasites. Campylobacter is a leading cause of traveller’s diarrhoea in Thailand and also is common in Nepal.\(^{196}\) There is no need for any antimicrobial therapy in mild traveller’s diarrhoea. However, prompt treatment of moderate to severe diarrhoea results in a more rapid resolution of symptoms and course of disease. There is no need for laboratory tests unless the diarrhoea persists.

**GPP** Elderly patients with moderate to severe diarrhoea may also be started on empirical antibiotic therapy (with quinolones).
Elderly patients with diarrhoea have a higher mortality rate. This is because they tend to suffer from the more severe complications of dehydration - myocardial infarction, ischaemic colitis and renal failure. These patients should be rehydrated aggressively. Elderly patients are also more prone to bacteraemia, and the septic complications of invasive diarrhoea. They should be treated empirically with antibiotics when the diarrhoea is anything more than mild.

### 7.7.3 Specific antibiotic therapy

Specific antimicrobial therapy is given when a treatable pathogen is identified in stool samples submitted to the laboratory. Not all positive cultures need to be treated. Certain bacterial infection must be treated, e.g. *Shigella*, ETEC, *Vibrio cholerae*. Other bacterial infection (e.g. *Salmonella*, *Campylobacter*, *Yersinia*, *Aeromonas*) need to be treated only under certain circumstances\(^\text{197}\) (see Table 14 on page 94 for pathogens and antimicrobial therapy).

### Shigellosis

All patients with moderate to severe infection with shigellosis should be treated with antibiotics. Patients with mild infections in the setting of good public health and hygiene can be observed.\(^\text{198,199}\)

**Grade B, Level IIa**

Shigellosis is a highly infectious organism and studies have shown that even a small inoculum can cause person-to-person spread. It has public health importance especially in enclosed communities as it can lead to widespread outbreaks. Patients with mild infection in the presence of good hygiene conditions can be observed as the risk of spread will be less.

### Salmonellosis

Routine treatment with antimicrobials for patients with non-typhoid salmonellosis is not recommended.\(^\text{172,182,183}\)

**Grade A, Level Ib**
Certain patients with intestinal salmonellosis should be treated – those who have fever and systemic toxicity, those with dysentery, the elderly, and patients who are immunocompromised or immunosuppressed.182

**Grade C, Level IV**

Intestinal salmonellosis is a common cause of diarrhoea disease. In healthy patients, it is usually benign and runs its course. Treatment with antibiotics in these patients, while shortening the clinical course of disease, can lead to delayed clearance of the organisms. Random use of quinolones has led to increasing antibiotic resistance. However, the organism can lead to bacteraemia in certain patients (at the extremes of age, HIV/AIDS, liver cirrhosis, uraemia, malignancy, long-term steroid use). These patients should be treated with antibiotics.

**Campylobacter infection**

Certain patients with proven *Campylobacter* infection should be treated with antibiotics – those who are immunocompromised, the elderly, and healthy patients with moderate to severe dysentery or with evidence suggestive of bacteraemia.172,182,183

**Grade B, Level IIa**

*Campylobacter* infection is a condition with a clinical syndrome similar to *Salmonellae* and *Shigellae* infections. Antibiotics are seldom indicated in confirmed *Campylobacter* infection as it is often self-limiting, is rarely chronic, and person-to-person transmission is uncommon. This makes *Campylobacter* infection less of a public health hazard.

**Enterotoxigenic Escherichia coli (ETEC) infection**

Patients with enterotoxigenic *Escherichia coli* infections should be treated with antibiotics.182,185,194,195

**Grade A, Level Ib**

ETEC infection is very common among patients with traveller’s diarrhoea and responds promptly to antibiotics. To date, no significant quinolone resistance has been reported.
Entero-haemorrhagic Escherichia coli (EHEC) infection

A Patients with suspected or proven EHEC infection, especially with Escherichia coli O157:H7, should not be given antibiotics.\textsuperscript{189,200} 

Grade A, Level Ib

Escherichia coli O157:H7 infection can cause severe haemorrhagic colitis, with the haemolytic uraemic syndrome (HUS). Retrospective studies have found that antibiotics prolong bloody diarrhoea and increase fatality. Recent studies have shown an increased risk of HUS. Anti-motility agents have also been found to increase the risk of HUS. Treatment in these patients should be good supportive care.

Cholera

A All patients with proven Vibrio cholera infection should be treated with antibiotics.\textsuperscript{201,202} 

Grade A, Level Ib

Cholera is characterized by voluminous diarrhoea. It is a self-limiting non-invasive disease. The primary treatment is aggressive hydration, electrolyte replacement and correction of acidosis. Antibiotics have been found to reduce stool frequency, duration of illness and faecal shedding of bacteria.

The choice of antibiotic varies according to the pattern of resistant strains. The standard treatment is tetracycline 500 mg 4 times a day, or single dose doxycycline 300 mg. However, as resistant strains have been reported, a single dose of a quinolone (ciprofloxacin 1 g or norfloxacin 800 mg) is very effective.

Mild Clostridium infection

B Patients with mild Clostridium difficile infection can be treated symptomatically and with withdrawal of the offending antibiotic.\textsuperscript{203,204} 

Grade B, Level IIa

While Clostridium difficile is part of the normal human flora in about 5% of normal population, the carrier rate is increased among patients who have been hospitalised or have recently received antibiotics or anti-neoplastic agents. Antibiotics commonly implicated include:
ampicillin, amoxicillin-clavulanate, second and third generation cephalosporins and clindamycin. The spectrum of disease ranges from mild diarrhoea to life-threatening colitis.

The diagnosis is confirmed by the presence of *Clostridium difficile*-associated antigen, combined with a positive test for either exotoxin A or B. The Cytotoxin B tissue culture assay is, however, the most specific test for detection of toxigenic *Clostridium difficile*.

**Moderate to severe Clostridium infection**

A Patients with moderate to severe Clostridium disease warrant prompt antibiotic treatment, with either oral metronidazole or vancomycin.\(^{203-205}\)

Grade A, Level Ib

Metronidazole is a drug of choice as studies have shown equal efficacy with vancomycin. With the advent of vancomycin resistant enterococci, metronidazole is the preferred first choice of antibiotic.
<table>
<thead>
<tr>
<th>Organism</th>
<th>Suggested antibiotics</th>
<th>Alternative antibiotics</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-typhoidal species of Salmonella</td>
<td>Fluoroquinolone* 5-7d</td>
<td>TMP-SMZ, 160-800 mg b.i.d. 5-7d Ceftriaxone#, 1 g b.i.d. 7-14 d</td>
<td>Antibiotics are usually not required, except in certain situations.*</td>
</tr>
<tr>
<td>*Shigella species</td>
<td>Fluoroquinolone* 3d</td>
<td>TMP-SMZ, 160-800 mg b.i.d. 3 d Nalidixic acid, 1 g/day 5 d Ceftriaxone#, 1 g b.i.d. 5-7 d Azithromycin, 250 mg single dose</td>
<td>Presents as fever, bloody diarrhoea.</td>
</tr>
<tr>
<td>Campylobacter species</td>
<td>Erythromycin 500 mg b.i.d. 5d</td>
<td>Fluoroquinolone* 5d</td>
<td>Antibiotics are usually not required, except in certain situations.b Quinolone-resistant Campylobacter is prevalent in Thailand.196,206,207</td>
</tr>
<tr>
<td>Yersinia species</td>
<td>Fluoroquinolone* 3d</td>
<td>Combination of doxycycline and aminoglycoside, or TMP-SMZ, or fluoroquinolone.</td>
<td>Antibiotics are usually not required.c</td>
</tr>
</tbody>
</table>

*a* antibiotics may be required in severely ill patients, or age <6 months or >65 years old, or immunocompromised hosts, or septicemia prone conditions e.g. patients with prosthesis, valvular heart disease, or severe atherosclerosis, or malignancy, or uremia, or uncontrolled diabetes mellitus.

*b* antibiotics may be required in severely ill patients, traveller’s diarrhoea

*C* antibiotics may be required in severely ill patients, associated bacteremia, or when bacteremia is suspected, or immunocompromised hosts.

*fluoroquinolone, for example 300 mg ofloxacin, 400 mg norfloxacin, or 500 mg ciprofloxacin b.i.d.

# antibiotics for suspected septicemic cases.
<table>
<thead>
<tr>
<th>Organism</th>
<th>Suggested antibiotics</th>
<th>Alternative antibiotics</th>
<th>Remarks</th>
</tr>
</thead>
</table>
| Enterotoxigenic *Escherichia coli* | Fluoroquinolone * 3d   | TMP-SMZ, 160-800 mg b.i.d. 3d | Antibiotics are usually not required, but may be required in certain situations.  
   d antibiotics may be required in severely ill patients, traveller’s diarrhoea, or immunocompromised hosts, or septicemia prone conditions, or uncontrolled diabetes mellitus. |
| Enteropathogenic *Escherichia coli* |                          | TMP-SMZ, 160-800 mg b.i.d. 3d | Antibiotics have no established therapeutic value and are usually not required, except in (if susceptible) in certain situations.  
   d Antibiotics are needed (mostly in children). |
| Enterohaemorrhagic *Escherichia coli* (ETEC) | --                      | --                      | Presents as afebrile, bloody diarrhoea  
   d Role of antibiotics is unclear and administration should be avoided as they may be harmful (may predispose to hemolytic uremic syndrome). |
| *Aeromonas* species             | Fluoroquinolone * 3d   | TMP-SMZ, 160-800 mg b.i.d. 3d (if susceptible) | Associated with travel in Asia.  
   e Antibiotics are usually not required, except in certain situations.  
   e antibiotics may be required in septicemic prone conditions e.g. cirrhosis, or immunocompromised hosts. |
| *Vibrio cholera* O1            | Tetracycline, 500 mg q.i.d. 3d | Doxycycline, 300 mg single dose  
   d TMP-SMZ, 160-800 mg b.i.d. 3d  
   d Fluoroquinolone* 3d |  
   * fluoroquinolone, for example 300 mg ofloxacin, 400 mg norfloxacin, or 500 mg ciprofloxacin b.i.d. |
<table>
<thead>
<tr>
<th>Organism</th>
<th>Suggested antibiotics</th>
<th>Alternative antibiotics</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Vibrio</em> O139</td>
<td>Tetracycline, 500 mg q.i.d. 3d</td>
<td>Doxycycline, 300 mg single dose</td>
<td>Antibiotics are usually not required, except in certain situations.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TMP-SMZ, 160-800 mg b.i.d. 3d</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fluoroquinolone* 3d</td>
<td></td>
</tr>
<tr>
<td>Other non-O1 <em>Vibrio</em> spp.</td>
<td>Tetracycline, 500 mg q.i.d. 3d</td>
<td>Doxycycline, 300 mg single dose</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fluoroquinolone* 3d</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ceftazidime* 3d</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 g q 6 h 5-7d</td>
<td></td>
</tr>
<tr>
<td><em>Vibrio</em> parahemolyticus 47</td>
<td>Tetracycline, 500 mg q.i.d. 3d</td>
<td>Doxycycline, 300 mg single dose</td>
<td>Antibiotics are usually not required, except in certain situations.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fluoroquinolone* 3d</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gentamicin* 3d</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>80mg 5-7d</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cefotaxime* 3d</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 g q.i.d. 5-7d</td>
<td></td>
</tr>
<tr>
<td><em>Clostridium</em> difficile</td>
<td>Metronidazole, 250-500 mg q.i.d. 10-14d</td>
<td>Vancomycin, 125-250 mg q.i.d. 10-14d</td>
<td>Offending antibiotics should be withdrawn if possible.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Giardia lamblia</td>
<td>Metronidazole, 250-750 mg tds 7-10d</td>
<td>Tinidazole 500 mg x 4 tablets as stat dose.</td>
<td>Consider giardiasis for diarrhoea persisting for more than 7 days.</td>
</tr>
</tbody>
</table>

*fluoroquinolone, for example 300 mg ofloxacin, 400 mg norfloxacin, or 500 mg ciprofloxacin b.i.d.*

antibiotics for suspected septicemic cases.
Figure 3  Algorithm for the management of acute diarrhoea

- **Hospital-acquired**
  - Investigate (look for *Clostridium Difficile*)

- **Community-acquired***
  - Mild
  - Symptomatic treatment

- **Travel history**
  - Moderate/Severe***
  - Empirical antibiotics

- **Persistent diarrhoea***
  - More than 7 days
  - Consider giardiasis and other protozoa

- **Mild**
  - Optional: Stools for WBC, RBC, lactoferrin
  - Non-inflammatory
  - Symptomatic therapy

- **Moderate/Severe***
  - Inflammatory***

- **Symptomatic therapy**
  - Resolves
  - Diarrhoea persists*** (more than 72 hours)
    - Further investigations and evaluation: stools for culture/sensitivity, full blood count, electrolytes.
    - Other specific investigations: special culture media, endoscopy.

- **Empirical therapy and/or,**
  - Specific therapy according to stool culture results

* Obtain faecal specimen for analysis if diarrhoea severe, bloody, inflammatory, or persistent or if outbreak suspected.
8 Use of Antibiotics in Urinary Tract Infection

8.1 Introduction

Urinary tract infections (UTIs) are among the most common bacterial infections encountered by medical practitioners and account for a large proportion of antibiotic usage in both hospital and general practice. The clinical presentation varies widely and antibiotic therapy is best guided by the clinical presentation.\textsuperscript{209-213} Though UTI can occur in both genders across all age groups, the majority of UTIs occur in sexually active women who are otherwise healthy.

8.2 Pathogenesis

There are 2 major routes for UTI:
1. \textit{Ascending route}. Following periurethral colonization, ascent of colonic bacteria via the urethra into the bladder leads to lower tract UTI. This is the more common mode of acquisition of UTI. Upper tract UTI or pyelonephritis occurs following upward migration of bacteria from the bladder to the kidneys via the ureters.
2. \textit{Haematogenous route}. Renal cortical abscesses that occur following \textit{Staphylococcus aureus} bacteraemia are an example of infection by this route.

8.3 Bacteriology

The common uropathogens are listed in Table 15.

<table>
<thead>
<tr>
<th>Table 15: Common Pathogens in Urinary tract infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>• \textit{Escherichia coli}</td>
</tr>
<tr>
<td>• \textit{Enterobacteriaceae}:</td>
</tr>
<tr>
<td>\textit{Klebsiella} species</td>
</tr>
<tr>
<td>\textit{Proteus} species</td>
</tr>
<tr>
<td>\textit{Enterobacter} species</td>
</tr>
<tr>
<td>• \textit{Pseudomonas} species</td>
</tr>
<tr>
<td>• \textit{Staphylococcus saprophyticus}</td>
</tr>
<tr>
<td>• \textit{Enterococcus} species</td>
</tr>
</tbody>
</table>
UTI in the community

In a recent survey of organisms leading to UTI in the community in Singapore, 91% were Gram-negative bacilli with *Escherichia coli* leading the group (67%) followed by *Klebsiella* (11%) and then *Proteus* (7%).\textsuperscript{214} Susceptibility of *Escherichia coli* to oral antibiotics is as shown below (Table 16).

**Table 16 Susceptibility of *Escherichia coli* to antibiotics\textsuperscript{214-215}**

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Isolates from the Community</th>
<th>Hospital Isolates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ciprofloxacin</td>
<td>98.5%</td>
<td>65.2%</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>98.5%</td>
<td>Not tested</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>97%</td>
<td>76%</td>
</tr>
<tr>
<td>Cephalexin</td>
<td>88.1%</td>
<td>42.7%</td>
</tr>
<tr>
<td>Amoxicillin-clavulanic acid</td>
<td>86.6%</td>
<td>54.7%</td>
</tr>
<tr>
<td>Trimethoprim-sulphamethoxazole</td>
<td>79%</td>
<td>52.8%</td>
</tr>
<tr>
<td>Amoxicillin/Ampicillin</td>
<td>59.7%</td>
<td>32.6%</td>
</tr>
</tbody>
</table>

(Sources: Ti TY et al, 2003; Urine cultures from SGH patients, 2002)

**UTI in hospitalised patients**

*Escherichia coli* was the most commonly isolated uropathogen from hospitalised patients at one Singapore hospital,\textsuperscript{213} but the sensitivity pattern to antibiotics was vastly different from that of community isolates. More than 80% were susceptible only to the following parenteral antibiotics, namely gentamicin, amikacin and imipenam; only 66% of the isolates were susceptible to ceftriaxone. Hospital isolates of *Escherichia coli* were less susceptible to oral antibiotics than community isolates (see Table 16).

The recommendations regarding antibiotic treatment in this chapter take into account the sensitivity patterns described above.
8.4 Diagnosis of UTI

A diagnosis of UTI is based on patient history, physical examination and laboratory findings.

8.4.1 History and physical examination

The typical symptoms of UTI are dysuria, urgency and/or frequency. Symptoms indicative of lower urinary tract involvement include new urinary incontinence, voiding of small volumes, suprapubic pain, nocturia and gross haematuria. A history of vaginal discharge and vaginal irritation significantly reduce the likelihood of UTI when present. Symptoms indicative of upper urinary tract involvement include flank pain and fever. A history of prior episodes of UTI and of the pattern of sexual activity, and the gender of the patient, are important in choosing the type and duration of antibiotic therapy.

The typical signs of UTI are fever and flank and/or suprapubic tenderness. As implied by the name, asymptomatic bacteriuria indicates the presence of bacteriuria in the absence of symptoms or signs of UTI.

Since patients with UTI can present with a wide range of symptoms, syndromes are defined below (see Table 17) by the level of renal involvement, i.e. upper versus lower tract; and the presence of complicating factors. (See Figure 4 on page 117).

Table 17 Urinary tract infection Syndromes

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower Tract UTI</td>
<td>Cystitis&lt;br&gt;Prostatitis</td>
</tr>
<tr>
<td>Upper Tract UTI</td>
<td>Acute pyelonephritis</td>
</tr>
<tr>
<td>Uncomplicated UTI</td>
<td>Absence of structural or functional abnormalities of the urinary tract</td>
</tr>
<tr>
<td>Complicated UTI</td>
<td>Presence of complicating factors: &lt;br&gt;- Urological structural or functional abnormalities&lt;br&gt;- Stones&lt;br&gt;- Obstruction&lt;br&gt;- Other renal conditions&lt;br&gt;- Diabetes mellitus&lt;br&gt;- Immunosuppression&lt;br&gt;- Genitourinary instrumentation, surgery&lt;br&gt;- Pregnancy</td>
</tr>
</tbody>
</table>
8.4.2 Urine analysis

Pyuria and bacteriuria are diagnostic of UTI. The sensitivity of tests for the detection of pyuria has been estimated as follows:\textsuperscript{213}:
- Detection by leukocyte esterase on dipstick - sensitivity of 75-96%;
- Detection by microscopic examination - sensitivity of 82-97%.

Vaginal discharge may contaminate urine specimens in women (epithelial cells seen on urine microscopy), and confound the detection of pyuria. Detection of bacteriuria by nitrite testing on dipstick is less sensitive as the test is only positive in the presence of nitrate-reductase-producing bacteria.

8.4.3 Urine culture

\textbf{B} It is not necessary to perform urine cultures in the management of uncomplicated cystitis in women. However, for the remainder of patients, pre-treatment cultures should be performed.\textsuperscript{212,213,216,217}

\textit{Grade B, Level IIb}

The detection of significant bacteriuria is a confirmatory test for the diagnosis of UTI. Though $\geq 10^5$ colony forming unit (cfu) per ml of urine is traditionally considered necessary to diagnose UTI, lower colony counts of $10^2-10^4$ cfu/ml can also cause symptomatic UTI.

In the management of the first episode of uncomplicated UTI in women, cultures are considered unnecessary, and detection of pyuria alone is adequate.\textsuperscript{212,213,216,217} However, urine cultures are essential, before and after treatment, for the following groups:
- Pregnant women
- Those with recurrent UTI
- Pyelonephritis
- All men with UTI
- All patients with complicated UTI

When cultures are indicated, mid-stream urine specimens should be dispatched before starting antibiotic therapy, and if the isolated organism is resistant, antibiotic therapy should be changed.
8.4.4  Investigation of the urinary tract

Women with recurrent UTI and all men with UTI should undergo renal imaging studies, such as intravenous urography, ultrasonography or voiding cystourethrogram. In men, a prostatic massage should be done and the secretion sent for culture.

8.5  Management of uncomplicated UTIs

Uncomplicated UTIs constitute the vast majority of UTIs in adults, and are generally diagnosed in otherwise healthy women. General management measures in all patients with UTI include drinking more water to increase urine output and the use of an analgesic or antipyretic for relief of pain or fever.

8.5.1  Asymptomatic bacteriuria in women

**A** Antibiotic therapy is not recommended in the management of patients with asymptomatic bacteriuria, except in pregnant women.\(^{218-220}\)

Grade A, Level Ib

Asymptomatic bacteriuria is diagnosed in the presence of \( \geq 10^5 \) cfu of bacteria/ml of urine in persons with no symptoms of UTI. Though any subgroup is at risk for asymptomatic bacteriuria, the elderly are at special risk.

Treatment of asymptomatic bacteriuria has not been shown to confer benefit in most subgroups, except in pregnant women.\(^{218-220}\) Even in the elderly and in diabetics, its treatment has not been shown to reduce risk of subsequent complications of infection or mortality.\(^{218,219}\) However, patients with complicating factors, such as renal transplant recipients, should have bacteriuria eradicated, while those undergoing invasive urologic procedures should receive appropriate prophylaxis.

8.5.2  Cystitis in women

**A** The recommended 1st line therapy for uncomplicated cystitis in women is a 3-day course of trimethoprim-sulphamethoxazole.\(^{221}\)

Grade A, Level Ib
Alternative treatment options for uncomplicated cystitis in women include the use of:

- Nitrofurantoin
- Fluoroquinolones
- 1<sup>st</sup> and 2<sup>nd</sup>-generation cephalosporins
- Trimethoprim
- β-lactam-lactamase-inhibitor combinations

Grade A, Level Ib

The recommended duration of treatment of uncomplicated cystitis for various agents in women is:

- For 3 days with fluoroquinolones;
- Or
- For 7 days, with nitrofurantoin, 1<sup>st</sup> and 2<sup>nd</sup>-generation cephalosporins, trimethoprim or β lactam-lactamase inhibitor combinations.

Grade A, Level Ia

Single-dose regimens are not recommended for routine use in the treatment of cystitis in women, as these regimens are less effective than multi-day regimens.

Grade A, Level Ia

Choice of antibiotic and duration of therapy

Cystitis is common in women and occurs in 20-40% of normal women during their lifetime. Several antibiotic regimens have been demonstrated to be effective in the treatment of acute cystitis in women. These regimens include the use of: trimethoprim-sulphamethoxazole (TMP-SMX), fluoroquinolones, nitrofurantoin, trimethoprim, 1<sup>st</sup> and 2<sup>nd</sup>-generation cephalosporins, β-lactam-lactamase-inhibitors and amoxicillin (See Table 18 on page 118).

The use of a particular antibiotic is based on:
- The patient's allergy history
- The susceptibilities of Escherichia coli in the community
- The likelihood of compliance with therapy
- The incidence of adverse effects

Based solely on uropathogen susceptibility to antibiotics in the community, the order of preference for empirical therapy in women with uncomplicated cystitis would be fluoroquinolones, 2<sup>nd</sup>-generation
cephalosporins, nitrofurantoin, 1st-generation cephalosporins, β-lactam-lactamase-inhibitors and TMP-SMX.

If based on likelihood of compliance with therapy, antibiotics that can be used for shorter courses would be advantageous. Longer duration of antibiotic therapy is also associated with increasing incidence of adverse effects. A meta-analysis222 has demonstrated the comparability of a 3-day course of either fluoroquinolones or TMP-SMX to successfully cure cystitis in otherwise-healthy women. The efficacy of 3-day course of the other antibiotics has not, however, been demonstrated. The reasons for failure of these drugs, studies suggest,221 is inability to reduce colonization of vaginal and rectal flora, and rapid excretion of these drugs from the urine.

Notwithstanding the preference for any 3-day antibiotic regimen over longer courses with other antibiotics, there is concern that using fluoroquinolones for empirical therapy in uncomplicated cystitis in women may reduce their utility in complicated UTI, due to the development of quinolone resistance in the community.211 In fact, the susceptibility patterns of hospital-acquired versus community-acquired Escherichia coli to fluoroquinolones is clear evidence of such a trend. A poor clinical outcome as a result of increasing resistance has prompted some expert committees to recommend that empirical antibiotic therapy should be restricted to settings where susceptibility is more than 80-90%.229

For the reasons listed above, a 3-day course of TMP-SMX has been recommended for 1st line therapy for uncomplicated cystitis in women. Indeed, a small study in Singapore documenting susceptibility of community-acquired Escherichia coli to TMP-SMX at 79% supports this treatment regimen for uncomplicated cystitis in women. Alternative regimens include the use of either fluoroquinolones for 3 days, or other antibiotics for 7 days. Single-dose regimens are less effective than multi-day regimens, and are not recommended for routine use.224,228,229,231

**Urine cultures**

Routine pre-treatment urine cultures are not necessary in the management of uncomplicated cystitis in women.
Patients with unresolved symptoms

Patients should be advised to return for follow-up if they have unresolved symptoms. These patients may have infections due to antibiotic-resistant bacteria, infection with *Staphylococcus saprophyticus*, or recurrent UTI (see below). These women should be reviewed and have urine cultures, and another antibiotic should be started while awaiting culture results. Treatment duration for a minimum of 7 days is preferred, and longer courses may be necessary if they have recurrent UTI.

In women with dysuria, but who have repeated negative urine cultures, the following infections should be considered and treated appropriately:
- Acute urethritis due to *Chlamydia trachomatis* and *Neisseria gonorrhoea*; or
- Vaginitis with *Candida* species and *Trichomonas vaginalis*.

8.5.3 Recurrent UTI

Women with recurrent UTI should be treated with low dose antibiotic prophylaxis, using nitrofurantoin, trimethoprim-sulphamethoxazole, trimethoprim or cephalosporins.\textsuperscript{232-239} Grade A, Level Ib

Re-infection versus relapse

Most cases of UTI recurrence are due to re-infection rather than relapse.\textsuperscript{232-233} A re-infection refers to an infection by a different organism, or an infection occurring more than 2 weeks after the index episode of UTI. On the other hand, a relapse refers to recurrence of an infection by the original pathogen, usually within 2 weeks after completion of antibiotic therapy. Re-infection in women can be treated as for uncomplicated cystitis. On the other hand, a relapse requires a prolonged course, for 2-6 weeks, of the appropriate antibiotic.

Management of frequent recurrences

After cure of the UTI, women with frequent recurrences (defined as >2 episodes in 6 months, or >3 episodes per year) can be managed by:
- Continuous low dose antibiotic prophylaxis for 3-12 months.
• Post-coital prophylaxis, in women who identify sexual intercourse as a precipitating factor.
• Intermittent self-treatment at onset of characteristic symptoms.

Choice of antibiotic and duration for prophylaxis

Nitrofurantoin, TMP-SMX, trimethoprim or 1st-generation cephalosporins (e.g. Cephalexin 250 mg), have all been demonstrated to be effective, administered nightly or post-coitally, in the prophylaxis of recurrent UTI in women.\textsuperscript{232-239} (See Table 18 on page 118).

The duration of prophylaxis can be tailored to the individual. Safety of these regimens for up to 12 months has been demonstrated. For patients who have recurrence after discontinuation of prophylaxis, antibiotics should be rotated. Though fluoroquinolones may also be useful for prophylaxis, their use should be minimized because of concerns regarding the promotion of antibiotic resistance.\textsuperscript{237,238}

General prophylactic measures

General measures in the prophylaxis of recurrent UTI in women include voiding after intercourse and avoidance of spermicides. Interestingly, cranberry juice (250 ml thrice daily) or cranberry tablets (twice daily) and estradiol-releasing vaginal rings (in postmenopausal women) have been demonstrated to be effective in the prophylaxis of recurrent UTI.\textsuperscript{240,241}

8.5.4 UTI in men

UTI in men is usually related to prostatic disease, urinary tract obstruction or instrumentation and thorough investigation is required to evaluate these causes. In their management, urine cultures are required before treatment to identify the organism and confirm sensitivity, and then after treatment to confirm cure.

Most UTIs in men are related to prostatitis and such patients should be ideally referred to a urologist for management. In the US, prostatitis is a condition recognised as an important health care issue with a 5-8% prevalence rate in the general population.

The US National Institute of Health Prostatitis Classification System includes:\textsuperscript{242}:
- Acute bacterial prostatitis
- Chronic bacterial prostatitis
- Chronic prostatitis/chronic pelvic pain syndrome
- Asymptomatic inflammatory prostatitis

Of these, antibiotics are indicated only in those with a bacterial aetiology (acute prostatitis and chronic bacterial prostatitis).

Urine cultures are invariably positive in those with acute prostatitis, whereas urine cultures are positive only during exacerbations in those with chronic bacterial prostatitis. Culture of prostatic secretions is necessary to confirm the diagnosis of chronic bacterial prostatitis (see below). These cultures of prostatic secretions are especially important as the majority of patients with prostatic symptoms have non-bacterial syndromes for which antibiotics are not indicated.

Despite the high prevalence of male UTI in the community, there are few controlled trials on their management and many of the guidelines suggested below are derived from opinions and/or clinical experiences of respected authorities.242-249

8.5.4.1 Acute prostatitis

C Initial therapy with intravenous cephalosporin and aminoglycoside, as for severe pyelonephritis, is recommended for the treatment of severe acute prostatitis.245

Grade C, Level IV

C Following clinical improvement, severe acute prostatitis should be treated with antibiotics, based on sensitivities, for a total duration of 4 weeks.245

Grade C, Level IV

C For patients with acute prostatitis of mild to moderate severity, initial therapy with oral fluoroquinolones, trimethoprim-sulphamethoxazole or trimethoprim is recommended. Treatment with antibiotics based on sensitivities should be given for a total duration of 4 weeks.245

Grade C, Level IV

In addition to the symptoms of prostatitis (low back pain, perineal, penile and sometimes rectal pain and obstructive voiding), acute
prostatitis is also associated with the symptoms of UTI (dysuria, frequency and urgency) and bacteraemia (fever, rigors and chills).

Physical findings include signs of UTI and bacteraemia. Patients may have an extremely tender, swollen and tense prostate gland.

Urine cultures are invariably positive and, frequently, blood cultures are also positive. In addition to the Gram-negative organisms usually reported in women with UTI, Staphylococcus aureus may also be the aetiological agent. Prostatic massage is contraindicated in acute prostatitis as it could precipitate bacteraemia.

General treatment measures include hydration and analgesia.

Empirical antibiotics should be initiated immediately; parenteral antibiotics are indicated in more ill patients. As the gland is inflamed, all antibiotics are able to penetrate the gland and patients can be treated with intravenous cephalosporin and gentamicin as for pyelonephritis in women. When clinically improved, patients should be treated with oral antibiotics based on bacterial susceptibilities for 4 weeks. TMP-SMX, fluoroquinolones or trimethoprim at twice daily dosage are preferred for oral therapy as they are able to penetrate the prostate gland (see Table 19 on page 119).

If patient is not systemically ill and oral antibiotics can be tolerated, fluoroquinolones, TMP-SMX or trimethoprim at twice daily dosage can be used. Treatment with antibiotics based on sensitivities should be given for a total duration of 4 weeks.

If there is no response to therapy, prostatic abscess should be excluded and appropriate treatment administered.\textsuperscript{245}

8.5.4.2 Chronic bacterial prostatitis

A The recommended treatment for chronic bacterial prostatitis is fluoroquinolones for 4 weeks.\textsuperscript{246} 

\textbf{Grade A, Level Ib}

B Trimethoprim-sulphamethoxazole for 12 weeks can also be used in the treatment for chronic bacterial prostatitis.\textsuperscript{244,248} 

\textbf{Grade B, Level III}
For patients with recurrent chronic prostatitis, suppressive, low-dose therapy with trimethoprim-sulphamethoxazole, trimethoprim or nitrofurantoin can be administered for 6 months or longer.\textsuperscript{248}

\textbf{Grade C, Level IV}

Men with chronic bacterial prostatitis may present with symptoms of UTI during exacerbations. Chronic bacterial prostatitis is a chronic inflammation of the prostate gland which presents with symptoms of genital pain including perineal, penile, testicular or lower abdominal pain usually for 3 months or more. There may be few clinical signs and prostatic tenderness may or may not be present.

Diagnosis is made by culture of the organism from prostatic secretions. Urine microscopy will show pyuria while urine cultures taken before starting antibiotics may be positive. Prostatic secretions (either, expressed prostatic secretion (EPS), ejaculate, or post-prostatic massage urine cultures) should also be sent for culture, to localise the bacteria to the prostate. A rise in bacteriuria by 1 log after prostatic massage also localises the infection to the prostate.

Thus, UTI in a male with symptoms/signs of chronic prostatitis should be treated as for chronic bacterial prostatitis with antibiotics that are lipid soluble and have the ability to penetrate the prostate gland, such as fluoroquinolones, TMP-SMX, trimethoprim or doxycycline at twice daily dosage (see Table 18 on page 118). Antibiotics should be changed according to sensitivity results. Studies indicate the superior efficacy of fluoroquinolones, (cure rate of 70% when given for 2 to 4 weeks) over TMP-SMX (cure rate of 40% when given for 12 weeks).\textsuperscript{246-248} Efficacy of antibiotic therapy should be evaluated after 4 weeks and the diagnosis reconsidered if prostatic cultures are repeatedly negative. Prolonged therapy for up to 12 weeks may be needed in some patients with persistent infection, while those with prostatic calculi or obstructive symptoms may need prostatic surgery.

When infection cannot be eradicated, long-term suppressive therapy with TMP-SMX, trimethoprim or nitrofurantoin can be administered for 6 months or longer, at doses used for prophylaxis of recurrent cystitis in women.\textsuperscript{248}
8.5.4.3 Chronic prostatitis/chronic pelvic pain syndrome

A Antibiotic therapy is not indicated in the treatment of chronic prostatitis/chronic pelvic pain syndrome.249

Grade A, Level Ib

GPP Patients with symptoms of chronic prostatitis, but with negative urine or prostatic fluid cultures, should be referred to a Urologist for further management.

GPP Most patients with symptoms of chronic prostatitis have abacterial prostatitis and are diagnosed to have chronic prostatitis/chronic pelvic pain syndrome (prostatodynia). Though white cells are found in expressed prostatic secretions, cultures of these secretions in these patients are repeatedly negative. Infection with Chlamydia, Ureaplasma or Mycoplasma has been suggested in the pathogenesis, but never proven. Nevertheless, due to the lag period between clinical presentation and availability of results from prostatic secretion cultures, most patients would have had a trial of antibiotics (usually 4 weeks of fluoroquinolone, TMP-SMX or doxycycline as for chronic bacterial prostatitis) (see Table 18 on page 118) by the time a diagnosis of chronic prostatitis/ pelvic pain syndrome is made. However, a recent randomised controlled trial demonstrated no benefit of either ciprofloxacin or tamsulosin, an alpha blocker, or both, versus placebo in reducing the symptoms of chronic prostatitis/chronic pelvic pain syndrome.249 These patients may need treatment with transurethral microwave thermotherapy, anti-inflammatory agents or alternative therapies. A urological referral is recommended for further management of this complex syndrome.

8.5.4.4 UTI with no prostatic symptoms or genitourinary abnormalities

A small proportion of men with UTI do not have any prostatic symptoms or genitourinary abnormalities. Uncircumcised males and those practicing anal-insertive sexual intercourse appear to be particularly prone to such infections. These patients can be successfully treated as for cystitis,250,251 with a 1-2 week course of antibiotic therapy (see Table 16 on page 99). Men with symptoms of UTI but repeatedly
negative cultures may have either gonococcal or non-gonococcal urethritis; these infections are generally sexually transmitted and both the patient and his sexual partner should be appropriately managed.

### 8.5.5 Pyelonephritis

**A** Treatment options for severe acute pyelonephritis include: parenteral 3rd-generation cephalosporins, aminoglycosides, fluoroquinolones, β-lactams or β-lactam-β-lactamase-inhibitor combinations. Antibiotics should be modified when urine culture results become available. Oral antibiotic therapy can be started following clinical improvement, with a treatment course of 14 days. 252-254

*Grade A, Level Ib*

**GPP** Initial treatment with intravenous aminoglycoside, together with a 1st or 2nd-generation cephalosporin, is recommended for hospitalized patients with acute pyelonephritis, because of the low sensitivity of hospital-acquired *Escherichia coli* to ceftriaxone and ciprofloxacin in the local context.

*GPP*

**A** Treatment options for mild acute pyelonephritis include: oral fluoroquinolones, trimethoprim-sulphamethoxazole, β-lactams or β-lactam-β-lactamase-inhibitor combinations. Antibiotics should be modified when results of urine culture become available. 252-255

*Grade A, Level Ib*

Acute pyelonephritis is an upper UTI associated with flank pain. In more severe illness, it is associated with fever, chills, nausea, vomiting, abdominal pain or signs of bacteraemia. The majority of patients are women. Patients with mild symptoms and those not vomiting may be treated as outpatients with oral antibiotics; those with more severe symptoms should be hospitalized for intravenous rehydration and parenteral antibiotics. 255

Several randomised controlled trials have demonstrated the efficacy of various antibiotics in successfully treating pyelonephritis. 252-254 In one trial in patients with pyelonephritis requiring initial parenteral therapy, 252 Ertapenem (a parenteral β-lactam) was comparable to ceftriaxone (a 3rd-generation cephalosporin), achieving cure in
approximately 85% in both arms. In this trial, initial 3-day parenteral therapy was followed by oral fluoroquinolone, for a total duration of therapy of 10-14 days (average 12 days). Another study demonstrated the efficacy of oral fluoroquinolones for 7-10 days in successfully treating mild acute pyelonephritis. However, increasing resistance of the most common pathogen (Escherichia coli) to commonly-used antibiotics, as well as differences in antibiotic resistance patterns in various communities, contribute to difficulties in guideline recommendations.

For hospitalised patients with acute pyelonephritis, due to the low sensitivity of hospital-acquired Escherichia coli to ceftriaxone and ciprofloxacin (66% and 65% respectively) a combination of an aminoglycoside with a cephalosporin is recommended for initial empirical therapy (see Table 19 on page 119). Urine cultures are recommended before starting antibiotics and therapy should be changed based on the culture and sensitivity results of the organism. Parenteral therapy is given until the patient is afebrile for 24 hours, and appropriate oral antibiotics given to complete a 14-day course of therapy.

Options for empirical oral antibiotic treatment for mild illness include fluoroquinolones or TMP-SMX. 1st and 2nd-generation cephalosporins or β-lactam-lactamase-inhibitors combinations can also be used. Antibiotics should be changed after culture results are available. While a 7-day course is adequate with fluoroquinolones (when the organism is sensitive), a longer course of 10-14 days is recommended for the other antibiotics.

8.5.6 UTI in pregnancy

A Asymptomatic bacteriuria in pregnancy should be treated with antibiotics, based on culture and sensitivity, to reduce the risk of pyelonephritis and other complications.

Grade A, Level Ia

B For acute cystitis in pregnancy, empirical therapy with 1st or 2nd-generation cephalosporins, nitrofurantoin or trimethoprim-sulphamethoxazole (caution in 3rd trimester) is recommended. Treatment should be modified based on culture results and appropriate antibiotics should be administered for 7 days.

Grade B, Level III
For pyelonephritis in pregnancy, empirical therapy with a 3<sup>rd</sup>-generation cephalosporin is recommended. Treatment should be modified based on culture results and appropriate antibiotics should be administered for 14 days.\textsuperscript{255}

Grade B, Level III

In pregnancy, dilatation of the urinary tract due to hormonal changes and relative obstruction of the pelvi-calyceal system due to the gravid uterus predispose to bacteriuria. This in turn is associated with the development of symptomatic UTI, pyelonephritis and premature labor.\textsuperscript{256}

Routine antenatal screening for asymptomatic bacteriuria, followed by treatment based on culture results, has been documented to reduce complications. Likewise, symptomatic UTI should be aggressively managed with antibiotics from the outset.\textsuperscript{220,256-258}

The choice of antibiotics is based on the severity of the illness, with a consideration of the safety of the antibiotic in question, during the particular stage of pregnancy. As a general rule, the penicillins, cephalosporins and nitrofurantoin are considered safe. Fluoroquinolones should be avoided, as should aminoglycosides (ototoxicity), and sulphonamides (associated with kernicterus in the neonate if administered late in pregnancy). The safety of β-lactam-lactamase-inhibitors combinations, imipenem and monobactams in pregnancy has not been documented, and these antibiotics should be administered with caution in pregnancy.

The treatment of asymptomatic bacteriuria should be guided by culture results. Treatment options include nitrofurantoin, amoxicillin, a cephalosporin, or TMP-SMX for 3 days. Urine cultures should be repeated after the course of antibiotics to ensure cure. If bacteriuria persists, a 7-day course of appropriate therapy is recommended.\textsuperscript{257-258}

With close follow-up of urine cultures, appropriate treatment or prophylaxis, cystitis and pyelonephritis in pregnancy can be avoided.

Acute cystitis can be treated with oral antibiotics (see Table 18 on page 118), using 1<sup>st</sup> or 2<sup>nd</sup>-generation cephalosporins, nitrofurantoin or TMP-SMX, while awaiting cultures. In general, pyelonephritis in pregnancy should be managed with intravenous antibiotics (see Table 19 on page 119), with a 3<sup>rd</sup>-generation cephalosporin being the safest choice.\textsuperscript{255}

Alternative regimens using amoxicillin or TMP-SMX together with
gentamicin have been utilized in pyelonephritis in pregnancy, but carry the danger of foetal ototoxicity due to gentamicin.255,257,258

Urine cultures are required before and after treatment to ensure cure. Once culture and sensitivity results are available, patients can be converted to appropriate therapy, for a total duration of 7 days in acute cystitis and for 14 days in pyelonephritis. Some patients with recurrent asymptomatic bacteriuria and/or symptomatic UTI may require prophylaxis with a suitable agent for the duration of the pregnancy.

8.6 Management of complicated UTIs

C Antibiotic treatment of complicated urinary tract infections should be based on cultures and sensitivity. When symptoms warrant initiation of empirical therapy, cultures must be obtained prior to antibiotic therapy and therapy modified based on results.239-262

Grade C, Level IV

C For ill, hospitalized patients with complicated urinary tract infections, empirical treatment with intravenous 3rd-generation cephalosporins, fluoroquinolones, β-lactams or β-lactam-β-lactamase-inhibitor combinations is recommended. An alternative regimen using intravenous ampicillin together with an aminoglycoside is also effective.209,261

Grade C, Level IV

A For complicated urinary tract infections of mild to moderate severity, initial therapy with oral fluoroquinolones or trimethoprim-sulphamethoxazole is recommended.263

Grade A, Level Ib

C For complicated urinary tract infections of mild to moderate severity, alternative regimens for empirical treatment include 2nd-generation cephalosporins, β-lactams, or β-lactam-β-lactamase-inhibitor combinations.209,261

Grade C, Level IV

Due to the wide spectrum of underlying conditions and aetiological agents involved in complicated UTI, therapeutic regimens for complicated UTI are based on sensitivity patterns of the organisms. Generally, antibiotics used for the treatment of complicated UTI are similar to those for treatment of uncomplicated UTI. However, as there
is a lower likelihood of eradication and higher likelihood of recurrence in complicated UTIs, the prolonged use of antibiotics can lead to antibiotic resistance. Thus, empirical therapy should be avoided and therapy should be given based on cultures and sensitivity of the uropathogen. When symptoms warrant the initiation of empirical therapy, urine cultures must be obtained prior to antibiotic therapy and therapy modified based on the results. The specific antibiotic used is based on renal function and severity of the illness.\textsuperscript{259-262}

For illnesses of mild to moderate severity, oral therapy with either fluoroquinolones or TMP-SMX has been demonstrated to be equally effective in randomised controlled trials\textsuperscript{263} (see Table 20 on page 120). Other antibiotics such as 2\textsuperscript{nd} and 3\textsuperscript{rd}-generation cephalosporins, \( \beta \)-lactam or \( \beta \)-lactam-lactamase-inhibitors combinations are also useful in clinical practice.

For hospitalized patients with complicated UTI and a more severe illness, empirical therapy with intravenous antibiotics is recommended (see Table 20 on page 120) and regimens using a 3\textsuperscript{rd}-generation cephalosporin, fluoroquinolones, \( \beta \)-lactams or \( \beta \)-lactam-lactamase-inhibitors combinations should be used.\textsuperscript{209} Alternative regimens using intravenous ampicillin together with an aminoglycoside are also effective, as \textit{Enterococcus} and \textit{Pseudomonas aeruginosa} are common pathogens in this setting.\textsuperscript{209,261} Monobactams and carbapenems are also useful in this setting, but should be reserved for patients who fail to respond to initial antibiotic therapy or for patients in whom the bacteria are known to be resistant to those antibiotics.

After starting empirical antibiotic therapy, the regimen should be modified based on culture results. The recommended duration of antibiotic therapy is generally 14 days unless the UTI is catheter-related (see below). In patients with lower tract symptoms, a 7-day course of antibiotics may be sufficient to eradicate the infection.\textsuperscript{261} Follow-up cultures are recommended after completing the course of appropriate antibiotic therapy. Prolonged therapy for up to 6 weeks may be indicated at times until the UTI is eradicated.

\subsection{8.6.1 Structural abnormality}

Patients with a structural abnormality (including stones, urinary stents and obstruction of the urinary tract) may have UTI with urease-producing organisms such as \textit{Proteus mirabilis}. 

115
After the initiation of empirical antibiotic therapy, culture-based appropriate therapy is administered for 14 days as a minimum.

Longer courses for 4 weeks may even be required in some patients while long-term suppressive therapy may be needed in others to prevent stone enlargement and progression of renal parenchymal damage.

8.6.2 Catheter-related UTI

The colonization of urinary catheters occurs at the rate of 5% per day. Thus antibiotics are not recommended for the treatment of asymptomatic UTIs.  

Symptomatic UTIs occurring in patients with a short-term indwelling urinary catheter should be treated by removing the catheter, followed by a 7-day course of antibiotics. For patients with long-term indwelling urinary catheters, symptomatic UTIs can be treated with a 7-day course of antibiotics.

Limiting the duration of catheterisation, and the use of closed bag systems have been demonstrated to reduce bacteriuria. While silver-coated urinary catheters have been suggested to reduce nosocomial UTI, more data is needed before widespread use can be recommended.

8.6.3 UTI in renal failure

In patients with renal impairment, effective antibiotic therapy requires the use of antibiotics which achieve therapeutic concentrations in the urine and are appropriately dose-adjusted for the level of renal failure.

Nitrofurantoin and aminoglycosides are ineffective in patients with renal failure as they fail to achieve adequate concentrations in the urine. Furthermore, as aminoglycosides are nephrotoxic, they require significant dose adjustment for renal dysfunction and their routine empirical use in these patients is best avoided. Generally, treatment is as for complicated UTI (see Table 20 on page 120).
Figure 4  Approach to management of urinary tract infections in adults

Symptoms of UTI in Adults

Female

Complicating factors?

No

Uncomplicated UTI

Lower tract symptoms only

Cystitis

3/7-day course

Upper tract symptoms

Pyelonephritis

14-day course

Yes

Complicated UTI

Lower tract symptoms only

7-day course

Upper tract symptoms

14-day course

Male

Acute symptoms?

No

Prostatitis symptoms?

Yes

Urine/Prostate secretions cultures +

No

Chronic pelvic pain syndrome

28-day course

Yes

Chronic prostatitis syndrome

7 to 14-day course

Persistence?

No

Refer Urologist

3-month course

Refer Urologist

Yes

Refer Urologist

Refer Urologist

Treat current episode

Give prophylaxis

3-day course for fluoroquinolones and trimethoprim-sulfamethoxazole.
### Table 18  Antibiotic therapy for lower urinary tract infections

<table>
<thead>
<tr>
<th>Infection</th>
<th>First line</th>
<th>Alternative</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Acute cystitis in women            | * PO trimethoprim-sulphamethoxazole 160/800 mg bd | * PO fluoroquinolones e.g.                       | • 3-day course recommended only for trimethoprim-sulphamethoxazole or fluoroquinolones.  
  - ciprofloxacin 250 mg bd  
  - ofloxacin 200 mg bd  
  - norfloxacin 400 mg bd  
  or  
  - PO 1<sup>st</sup> and 2<sup>nd</sup> generation cephalosporins e.g.  
    - cephalexin 500 mg bd  
    - cefadroxil 500 mg bd  
    - cefuroxime 125 mg bd  
  or  
  - PO nitrofurantoin 50 mg qds  
  or  
  - PO trimethoprim 100 mg bd | Treat for 7 days with other antibiotics.  
| Prophylaxis of recurrent cystitis in women | * PO trimethoprim-sulphamethoxazole 40/200 mg on | * PO nitrofurantoin 50 mg on  
  or  
  * PO trimethoprim 100 mg on  
  or  
  * PO cephalexin 250 mg on | Treat acute cystitis for 7 days first, followed by prophylaxis for 3-12 months nightly or post-coitaly. |
| Asymptomatic bacteruria in pregnancy | * PO nitrofurantoin 50 mg qds  
  or  
  PO 1<sup>st</sup> and 2<sup>nd</sup> generation cephalosporins e.g.  
    - cephalexin 500 mg bd  
    - cefadroxil 500 mg bd  
    - cefuroxime 250 mg bd | * PO amoxicillin 250 mg tds  
  or  
  * PO trimethoprim-sulphamethoxazole 160/800 mg bd | Treat for 7 days based on cultures.  
  Review antibiotics based on sensitivity.  
  Avoid sulphonamides in third trimester.  
  Fluoroquinolones are best avoided. |
| Acute cystitis in pregnancy        | * PO 1<sup>st</sup> and 2<sup>nd</sup> generation cephalosporins e.g.  
    - cephalexin 500 mg bd  
    - cefadroxil 500 mg bd  
    - cefuroxime 125 mg bd | * PO nitrofurantoin 50 mg qds  
  or  
  * PO trimethoprim-sulphamethoxazole 160/800 mg bd | Treat for 7 days.  
  Avoid sulphonamides in third trimester.  
  Check cultures after treatment. |
| Acute prostatitis                  | * I.V. antibiotics as for acute pyelonephritis if ill & hospitalized then oral antibiotics  
  * PO fluoroquinolones e.g.  
    - ciprofloxacin 500 mg bd  
    - ofloxacin 200 mg bd  
    - norfloxacin 400 mg bd | * PO trimethoprim-sulphamethoxazole 160/800 mg bd  
  or  
  * PO trimethoprim 200 mg bd | Treat with I.V. antibiotics till clinical response, then PO antibiotics for 4 weeks.  
  Exclude chronic prostatitis if recurrent. |
| Chronic bacterial prostatitis      | * PO fluoroquinolones e.g.  
    - ciprofloxacin 500 mg bd  
    - ofloxacin 200 mg bd  
    - norfloxacin 400 mg bd | * PO trimethoprim-sulphamethoxazole 160/800 mg bd  
  or  
  * PO trimethoprim 200 mg bd  
  or  
  * PO doxycycline 100 mg bd | Treat with fluoroquinolones for 4 weeks, with trimethoprim-sulphamethoxazole for 12 weeks.  
  If refractory or recurrent, refer urologist to exclude prostatic stone. |
| Acute cystitis in adult men        | * PO trimethoprim-sulphamethoxazole 160/800 mg bd | * PO fluoroquinolones e.g.  
    - ciprofloxacin 500 mg bd  
    - ofloxacin 200 mg bd  
    - norfloxacin 400 mg bd | Exclude prostatitis and GU abnormalities.  
  Treat for 7-14 days. |
Table 19  Antibiotic therapy for upper urinary tract infections

<table>
<thead>
<tr>
<th>Infection</th>
<th>First line</th>
<th>Alternative</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial</td>
<td></td>
<td></td>
<td>I.V. agents are given until the patient is afebrile for 24 hours followed by oral antibiotics, (as for mild illness below), based on susceptibility of organism for total of 14 days.</td>
</tr>
<tr>
<td>Therapy of acute uncomplicated</td>
<td>I.V. 1st or 2nd generation cephalosporins e.g.</td>
<td>I.V. ceftriaxone 1 g om or</td>
<td>I.V. fluoroquinolones e.g.</td>
</tr>
<tr>
<td>pyelonephritis</td>
<td>- cephalazolin 500 mg to 1 g bd</td>
<td>or</td>
<td>- ciprofloxacin 200 mg 12 hourly</td>
</tr>
<tr>
<td>Moderate severity</td>
<td>- cefuroxime 750 mg to 8 hourly</td>
<td>or</td>
<td>- ofloxacin 400 mg 12 hourly</td>
</tr>
<tr>
<td>Hospitalized patient</td>
<td>Plus</td>
<td>or</td>
<td>PO β-lactam-β-lactamase inhibitor combinations e.g.</td>
</tr>
<tr>
<td></td>
<td>I.V. gentamicin 1 mg/kg 8 hourly</td>
<td>or</td>
<td>- IV amoxicillin-clavulanic acid 1.2 g 8 hourly</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute</td>
<td>PO fluoroquinolones e.g.</td>
<td>PO trimethoprim-sulphamethoxazole 160/800 mg bd or</td>
<td>Treat for 14 days. 7 days are adequate in women treated with fluoroquinolones.</td>
</tr>
<tr>
<td>uncomplicated</td>
<td>- ciprofloxacin 500 mg bd</td>
<td>or</td>
<td>PO 1st and 2nd generation cephalosporins e.g.</td>
</tr>
<tr>
<td>pyelonephritis</td>
<td>- ofloxacin 400 mg bd</td>
<td>or</td>
<td>- cephalaxin 500 mg to 1 g bd</td>
</tr>
<tr>
<td>Mild illness, outpatient</td>
<td>- norfloxacin 400 mg bd</td>
<td>or</td>
<td>- cefadroxil 500 mg bd</td>
</tr>
<tr>
<td></td>
<td></td>
<td>or</td>
<td>- cefuroxime 250 mg to 500 mg bd</td>
</tr>
<tr>
<td></td>
<td></td>
<td>or</td>
<td>PO β-lactam-β-lactamase inhibitor combinations e.g.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- PO amoxicillin-clavulanic acid 625 mg bd</td>
</tr>
<tr>
<td>Acute</td>
<td>I.V. ceftriaxone 1 g om</td>
<td>I.V. gentamicin with doses adjusted carefully to levels (in cephalosporin allergic patients)</td>
<td>Treat for 14 days.</td>
</tr>
<tr>
<td>pyelonephritis</td>
<td></td>
<td>+/- I.V. ampicillin 500 mg 6 hourly</td>
<td>Pregnant women with pyelonephritis should be hospitalized to receive parenteral therapy.</td>
</tr>
<tr>
<td>in pregnancy</td>
<td></td>
<td>+/- trimethoprim-sulphamethoxazole in penicillin/cephalosporin allergic patients</td>
<td>Avoid fluoroquinolones in pregnancy.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Avoid sulphonamides in third trimester.</td>
</tr>
</tbody>
</table>
Table 20  Antibiotic therapy for complicated urinary tract infections

<table>
<thead>
<tr>
<th>Infection</th>
<th>First line</th>
<th>Alternative</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complicated pyelonephritis Moderate severity, Hospitalized patient</td>
<td>• I.V. 3rd generation cephalosporins e.g. - ceftriaxone 1 g om</td>
<td>• I.V. fluoroquinolones e.g. - ciprofloxacin 200 mg 12 hourly - ofloxacin 400 mg 12 hourly or • I.V. β-lactam-β-lactamase inhibitor combinations e.g. - Amoxicillin-clavulanic acid 1.2 g 8 hourly - **Piperocillin-tazobactam 2.25 g to 4.5 g 6-8 hourly or • I.V. β-lactams e.g. - Imipenem 500 mg 8 hourly - Meropenem 1 g 8 hourly or • I.V. Monobactams - Aztreonam 1 g 12 hourly • *I.V. ampicillin 500 mg 6 hourly plus 1 V. gentamicin 1 mg/kg 8 hourly • **I.V. anti-pseudomonal cephalosporins e.g. - ceftazidime 1 g 12 hourly</td>
<td>• I.V. agents are given until the patient is afebrile for 24 hours followed by oral antibiotics, (as for mild illness below), based on susceptibility of organism for total of 14 days. • Gentamicin is best avoided in patients with underlying renal disease. If administered, monitor serum gentamicin peak and trough levels and adjust dose to levels. • *For enterococi. • **For pseudomonas.</td>
</tr>
<tr>
<td>Complicated pyelonephritis Mild to moderate illness, Outpatient</td>
<td>• PO fluoroquinolones e.g. - ciprofloxacin 230 mg bd - ofloxacin 400 mg bd - norfloxacin 400 mg bd</td>
<td>• PO trimethoprim-sulphamethoxazole 160/800 mg bd or • PO nitrofurantoin 50 mg qds or • PO 1st, 2nd or 3rd generation cephalosporins e.g. - cephalexin 500 mg to 1 g bd - cefadroxil 500 mg bd - cefuroxime 250 mg to 500 mg bd - cefotuban 400 mg om or • PO β-lactam β-lactamase inhibitor combinations e.g. - PO amoxicillin-clavulanic acid 625 mg to 1 g bd or • PO trimethoprim 100 mg bd or • PO amoxicillin 500 mg tds or • PO nalidixic acid 500 mg tds</td>
<td>• Treat based on culture and sensitivity. • Treat for 14 days (except catheter related UTI, treat for 7 days).</td>
</tr>
</tbody>
</table>
9 Use of Antibiotics in Acute Bacterial Meningitis in Immunocompetent Adults

9.1 Introduction

Bacterial meningitis in adults is an uncommon but serious condition. Although the introduction of antibiotics made it curable, morbidity and mortality from the disease remain unacceptably high. In a US CDC study of 493 episodes of bacterial meningitis, the overall case fatality rate was 25%.266

9.2 Epidemiology and microbiology

The CDC report in 1986266 was a multi-state surveillance study of bacterial meningitis. The majority of cases were due to Haemophilus influenzae (45%), Streptococcus pneumoniae (18%) and Neisseria meningitidis (14%). The incidence of specific pathogens were most influenced by age.

In adults, the leading pathogens causing community-acquired meningitis are: Streptococcus pneumoniae, Neisseria meningitidis, Listeria monocytogenes and Group B streptococci.267

In Singapore, the pathogens are similar to those reported in other studies.268

Antibiotic resistant strains of Streptococcus pneumoniae have become prevalent in Asia269,270 and have emerged as a major problem in the United States.271

9.3 Diagnosis of acute bacterial meningitis

A diagnosis of acute bacterial meningitis is based on patient history, physical examination and laboratory findings.

The classical triad includes fever, nuchal rigidity and change in mental status.
Initial physical examination should include evaluation for:
- level of consciousness
- cranial nerve palsies
- focal deficits
- meningismus
- increased intracranial pressure
- critical trauma

Grade C, Level IV

A petechial or purpuric rash, predominantly in the extremities, in a patient with meningeal signs indicates a high probability of a meningococcal infection. This patient will require immediate treatment because of the rapidity with which the kind of infection can advance. About 50% of patients with meningococcal meningitis have such skin lesions.

1) **Lumbar puncture and cerebrospinal fluid (CSF) analysis:**

A lumbar puncture is recommended in all adult patients with suspected meningitis except when a clear contraindication exists.

Grade B, Level III

Contraindications to lumbar puncture include presence of signs of raised intracranial pressure or focal neurological signs unless there is a normal brain computerised tomographic (CT) scan. Other contraindications include severe shock, severely depressed or fluctuating consciousness level or coagulation disorder.

Importantly, papilloedema may be a late sign of raised intracranial pressure and a normal brain CT scan does not exclude raised intracranial pressure.

Table 21 on page 121 summarises the CSF parameters in acute meningitis.
Table 21  Classical cerebrospinal fluid parameters in acute meningitis\textsuperscript{276,277}

<table>
<thead>
<tr>
<th>Agent</th>
<th>Cells</th>
<th>Gram stain for bacteria</th>
<th>Bacterial antigen detection</th>
<th>Protein g/L (normal 0.1-0.4)</th>
<th>Glucose mmol/L (normal 2.3-4.5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral</td>
<td>$10^1 - 10^3$ (lymphocytes)</td>
<td>Negative</td>
<td>Negative</td>
<td>Normal or slightly high</td>
<td>Usually normal</td>
</tr>
<tr>
<td>Bacterial</td>
<td>&gt; $10^3$ (predominantly polymorphs)</td>
<td>Positive</td>
<td>May be positive</td>
<td>High</td>
<td>&lt; 50% of blood glucose</td>
</tr>
<tr>
<td>Tuberculous</td>
<td>$10^1 - 10^3$ (predominantly lymphocytes)</td>
<td>Positive</td>
<td>Negative</td>
<td>High or very high</td>
<td>&lt; 50% of blood glucose</td>
</tr>
</tbody>
</table>


Note: In partially treated bacterial meningitis, lymphocytes may predominate but the protein is often high.

2) Blood cultures

Blood cultures are positive in only 50% of patients with meningococcal infection who have not received parenteral antibiotics. However, the positive cultures fall to 5% or less if antibiotics have been given more than 1 to 2 hours before collection.\textsuperscript{275} Neisseria meningitidis can be isolated from the nasopharynx of up to 50% of patients with meningococcal disease, regardless of whether a dose of benzylpenicillin has been given.\textsuperscript{278}

9.4 Antibiotic therapy

For optimal antibiotic treatment, the drug must have a bactericidal effect in the CSF.

There are three factors affecting the bactericidal activity of an antibiotic in CSF: its relative degree of penetration into the CSF, its concentration there, and its intrinsic activity in infected CSF.
The concentration of antibiotic in the CSF needed for maximal bactericidal activity is at least 8-10-fold higher than the mean bactericidal concentration for the infecting organism.279,280

It is important to start antibiotics promptly given the potential for neurological morbidity and mortality. One of the most important factors contributing to delayed diagnosis and therapy is the decision to perform cranial CT before lumbar puncture.

I Initial therapy before pathogens are identified:

C If bacterial meningitis is suspected, antibiotic treatment must be started immediately, regardless of any investigations undertaken.281,282

Grade C, Level IV

B In the treatment of meningitis with a typical meningococcal rash, intravenous penicillin G, 20-24 million units daily, should be given.283,284

Grade B, Level III

B For adults without a typical meningococcal rash, intravenous ceftriaxone, 2g 12 hourly, should be given.281

Grade B, Level III

C If the patient comes from an area where penicillin-resistant Streptococcus pneumoniae are common (MIC ≥ 0.1ug/ml) then add intravenous vancomycin 1g 12 hourly.281

Grade C, Level IV

C & GPP For adults over the age of 50 years with a history of alcoholism, diabetes or pregnancy without a typical meningococcal rash, consider adding intravenous ampicillin, 2g 4 hourly, to ceftriaxone as above.281

Grade C, Level IV & GPP

C If there is a clear history of anaphylaxis to β-lactams, give intravenous chloramphenicol 25 mg/kg (maximum 1g) 6 hourly. Add vancomycin, 1g 12 hourly, because of the possibility of penicillin-resistant Streptococcus pneumoniae and likely failure of chloramphenicol in this group.281

Grade C, Level IV
Treatment may be modified once specific pathogens have been identified:

**B** If Gram-negative diplococci are visible on Gram stain of CSF, or if *Neisseria meningitidis* is isolated from CSF or blood, continue with intravenous penicillin G, 24 million units daily.\(^{285,286}\)

*Grade B, Level III*

**C** For patients who do not have adequate response to penicillin, the treatment should be changed to ceftriaxone.\(^{287}\)

*Grade C, Level IV*

**C** If penicillin-sensitive *Streptococcus pneumoniae* is isolated from CSF or blood, intravenous penicillin G 24 million units is recommended. If cephalosporin-sensitive *Streptococcus pneumoniae* is isolated, intravenous ceftriaxone 2g 12 hourly should be given. Add on intravenous vancomycin, 1g 12 hourly, if penicillin-resistant and cephalosporin-resistant *Streptococcus pneumoniae* is isolated from blood or CSF. Continue intravenous therapy for 10-14 days.\(^{287,288}\)

*Grade C, Level IV*

**B** For *Haemophilus influenzae* meningitis, intravenous ceftriaxone, 2g 12 hourly, is recommended.\(^{283}\)

*Grade B, Level IIb*

**C** If Gram-positive coccobacilli suggestive of *Listeria monocytogenes* is visible on Gram stain of CSF, or if *Listeria monocytogenes* is isolated from blood or CSF, intravenous ampicillin, 2g 4 hourly, and gentamicin 5 mg/kg 24 hourly (single or divided 8 hourly doses) for more than 21 days is recommended.\(^{283,287}\)

*Grade C, Level IV*

The duration of therapy depends on whether a pathogen is identified.\(^{283,285,286,289}\)
Table 22  Recommended duration of therapy according to the type of pathogen causing meningitis

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Recommended duration of therapy</th>
<th>Grade and level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Haemophilus influenzae</em></td>
<td>7-10 days²⁸³,²⁸⁷</td>
<td>Grade B, Level IIb</td>
</tr>
<tr>
<td><em>Neisseria meningitidis</em></td>
<td>7-10 days²⁸⁵</td>
<td>Grade B, Level III</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>10-14 days²⁸⁹</td>
<td>Grade C, Level IV</td>
</tr>
<tr>
<td><em>Listeria monocytogenes</em></td>
<td>≥ 21 days²⁸⁹</td>
<td>Grade C, Level IV</td>
</tr>
<tr>
<td>Gram-negative bacilli, other than <em>Haemophilus influenzae</em></td>
<td>21 days²⁸⁹</td>
<td>Grade C, Level IV</td>
</tr>
</tbody>
</table>

The duration of therapy should be tailored to the individual patient on the basis of the clinical and microbiological response.²⁹⁰,²⁹¹

Grade C, Level IV

9.5  Adjunctive dexamethasone therapy in bacterial meningitis

Early adjunctive dexamethasone therapy improves the outcome in adults with acute pneumococcal meningitis.²⁹²

In adults with suspected or proven pneumococcal meningitis, dexamethasone 10 mg 6 hourly should be given for 4 days with the first dose administered 15-20 min before, or at least concomitant with, the first dose of antimicrobial therapy.²⁹²

Grade A, Level 1b

Dexamethasone should only be continued if the CSF Gram stain reveals Gram-positive diplococci or if blood or CSF cultures are positive for *Streptococcus pneumoniae*.²⁹²

Grade A, Level 1b

Adjunctive dexamethasone should not be given to adult patients who have already received antimicrobial therapy as in this circumstance, dexamethasone is unlikely to improve patient outcome.²⁹²

Grade A, Level 1b
9.6 Prevention of meningococcal meningitis

Ten per cent of the population may carry meningococci at any one time. Carrier rates are less than 2% in children aged under 5 years, and 20 to 25% or higher in older teenagers and young adults.

Carriers rarely develop invasive disease but carry meningococci for long periods (a mean of 9 months), during which time they remain a potential source of infection.

Since the risk of secondary disease among close contacts is highest during the first few days after onset of disease in the index patient, chemoprophylaxis for close contacts should be administered as soon as possible. If it is given more than 14 days after onset of disease in the index case, chemoprophylaxis for close contacts is probably of limited or no benefit.293,294

Oropharyngeal or nasopharyngeal cultures are not helpful in determining the need for chemoprophylaxis in carriers.

Chemoprophylaxis should be offered to close contacts of cases, irrespective of vaccination status, in those who have293,294:

- Prolonged close contact with the case in a household setting during the seven days before onset of illness.
- Contact at a child-care centre.
- Transient close contact with a case where there was exposure to the patient’s secretions (e.g. through kissing, mouth-to-mouth resuscitation, endotracheal intubation or endotracheal tube management) around the time of admission to hospital.

Grade C, Level IV

Close contacts of patients with meningococcal infection should receive one of the following regimens294-296:

- Rifampicin:
  Adults: 600 mg, 12 hourly for 2 days (4 doses).
  Children (1-6 years): 10 mg/kg, 12 hourly for 2 days (4 doses).
  Children (3-11 months): 5 mg/kg 12 hourly for 2 days (4 doses).

- Ciprofloxacin:
Adults: 500 mg as a single dose.
Children: Use of ciprofloxacin is not recommended.

- Ceftriaxone:
  Adults: 250 mg as a single intramuscular dose.
  Children (< 15 years): 125 mg as a single intramuscular dose.

  Grade C, Level IV

Systemic therapy of meningococcal disease with antibiotics other than ceftriaxone may not reliably eradicate nasopharyngeal carriage of *Neisseria meningitidis*.

If other antibiotics have been used for treatment, the index patient should receive prophylactic antibiotics for eradication of nasopharyngeal carriage before being discharged from hospital.²⁹⁷

Grade C, Level IV
Figure 5  Algorithm for the initial management of a patient with acute meningitis

Acute Bacterial Meningitis

Typical meningococcal rash (petechial, purpuric)

- Adult >50y, history of alcoholism, diabetes or pregnant female

No rash

Area where penicillin-resistant *Streptococcus pneumoniae* prevalent

I.V. ceftriaxone, 2g 12H

I.V. ampicillin, 2g 4H

I.V. ceftriaxone, 2g 12H

CSF or blood culture:
Penicillin-sensitive *Streptococcus pneumoniae*

Blood/CSF culture:
Penicillin-resistant *Streptococcus pneumoniae*

Continued I.V. ceftriaxone, 2g 12H or switch to I.V. Penicillin

I.V. penicillin G, 24 million units daily

- Gram stain CSF: Gram negative diplococcus OR Blood/CSF culture: *Neisseria meningitides*

No response

Response

Switch to I.V. ceftriaxone, 2g 12H

Continue I.V. penicillin G, 24 million units daily

Continue I.V. Ceftriaxone 2g 12H + vancomycin, 1g 12H

Discontinue ceftriaxone.
Continue ampicillin, 2g 4H.
Add I.V. Gentamicin, 5mg/kg 24H

* To continue initial antibiotics if culture is negative and patient is responding
While many aspects of infection in older people are similar to those of young and middle-aged people, there are some distinct differences that could influence clinical management. These differences tend to be magnified in disabled and frail older people.

Unfortunately, good evidence for treatment strategies in this subset of older people is sparse. Therefore, in the absence of directly applicable clinical studies of good quality, expert opinion from respected authorities is relied upon.

10.1 Unique aspects of infections in older people

10.1.1 Risk

Older people have greater susceptibility to infections than younger people, due to host factors and environment factors.297

1. Host factors include:
   a. *Physiological changes of ageing*. For example, diminished blood perfusion, decreased cough reflex, thinning of skin and altered gastric motility may predispose to infections.
   b. *Chronic diseases*. For example, cerebrovascular disease may cause immobility, poor personal hygiene, poor cough reflex, impaired swallowing, and cognitive decline. All these result in an increased risk of pneumonia, urinary tract infection and pressure ulcers.
   c. *Alteration of host defence mechanisms*. This is due to age-related immune dysfunction (particularly in cell-mediated immunity).

2. Environmental factors include:
   a. *Hospitalisation*. Older people are hospitalised more often and tend to have a longer length of stay. This confers a higher risk of acquiring nosocomial infections.
   b. *Institutionalisation*. The probability of staying in long-term care facilities (such as nursing homes) is increased in older people, and this is in turn associated with more frequent infections.
10.1.2 Types of infections

Older people are more prone to specific infections, like:
- Urinary tract infection
- Pneumonia
- Intra-abdominal infections (especially cholecystitis, diverticulitis)
- Skin and soft-tissue infections
- Infective endocarditis
- Bacterial meningitis
- Tuberculosis
- Herpes zoster

10.1.3 Pathogens

Different pathogens cause infections in the elderly. Additional pathogens not often encountered in younger people may be responsible.

For example, community-acquired pneumonia may be caused by *Streptococcus pneumoniae* as with younger patients. However, in older patients, there is a higher incidence of other organisms such as *Haemophilus influenzae*, Gram-negative bacilli and *Staphylococcus*.

10.1.4 Consequences of infection

The contributing factors for the increased probability of adverse outcomes include:
- Age-related reduced physiologic reserve capacity
- Decreased host resistance
- Chronic disease
- Delayed diagnosis and treatment
- Decreased tolerance to investigative and therapeutic procedures
- Sub-optimal response to anti-microbial therapy
- Increased susceptibility to nosocomial infections
- Increased risk of adverse drug effects

10.1.5 Altered clinical presentation

Knowledge of altered clinical presentation in older patients should guide the clinician in the decision:
• To initiate relevant investigation
• To start antibiotics
• Of the choice of antibiotics

Fever
• Fever may be blunted or absent (in up to 25%). A blunted fever response to infection is associated with a poorer prognosis.\textsuperscript{300}
• Lack of fever response in bacteraemia and pneumonia occurs 2-3 times more often in older patients compared with younger ones.\textsuperscript{301,302}
• The onset of pyrexia may be delayed several hours.\textsuperscript{303}
• In some frail older patients, the fever response may be adequate but the temperature spike may be less than 37.8°C because of a lower baseline temperature.\textsuperscript{304}
• An oral temperature greater than 38.3°C in older patients is more likely to be associated with serious bacterial or viral infections, unlike in the young whose fevers are usually associated with benign viral infections.\textsuperscript{305,306}

Atypical manifestations
Atypical manifestations are common and may be the primary clinical presentation of an infection,\textsuperscript{299,307} and include signs and symptoms such as:
• Change in functional status
• Geriatric syndromes (e.g. delirium, impaired mobility, falls, incontinence)
• Decline in self-care (e.g. difficulty with Activities of Daily Living)

Therefore, the following practice points are recommended:

\textbf{B} An infectious aetiology should be sought when there is\textsuperscript{302}:
• A change in functional status and the oral temperature is \( \geq 37.2^\circ \text{C} \), or
• An increase in temperature of \( \geq 1.3^\circ \text{C} \) over the baseline.

\textit{Grade B, Level III}
Infection should be considered in the differential diagnosis of older people who present, within a short period of time:\(^{299}\):

- With only non-specific symptoms, including functional decline; or
- With atypical complaints.

Grade C, Level IV

Doctors should be alert to a leucocytosis with left shift or left shift alone, as these have good predictive value for diagnosing bacterial infections in older people.\(^{305}\)

Grade C, Level IV

10.2 Diagnostic approach\(^{299}\)

10.2.1 Diagnostic approach when typical symptoms are absent

Where there are typical clinical symptoms and signs of a particular site of infection (e.g. fever, cough and purulent sputum in pneumonia), the diagnostic approach is usually straightforward.

However, it is more difficult when typical features are absent. In this instance, two approaches (not mutually exclusive) can be considered:

1) Underlying disease(s):
This can be a guide to the possible site of infection and responsible organism. For example, prostatic obstruction is often associated with urinary tract infection, while bronchiectasis is often associated with pneumonia.

2) Functional status or level of care:
A reasonably useful differential diagnosis of more common infectious diseases can be obtained on the basis on classification into 3 categories:

i. Independent and healthy community
   - Pneumonia and other respiratory tract infections
   - Urinary tract infection
   - Intra-abdominal infection (e.g. cholecystitis, diverticulitis)

ii. Hospitalised patient
   - Urinary tract infection
- Pneumonia
- Surgical wound infections

iii. *Nursing home resident*
- Pneumonia
- Urinary tract infection
- Pressure ulcers

### 10.2.2 Approach to diagnostic tests

Diagnostic tests should be selected judiciously as invasive procedures are associated with higher risks in older patients. Risk-benefit balance and likely impact on final management should be considered - particularly with more risky and costly investigations.

Obtaining body fluids or tissue for microbiological examination is generally more difficult in older patients and is frequently not feasible. This is particularly so with expectoration of sputum and collection of a mid-stream voided specimen of urine. Consequently, it is often more difficult to obtain a precise aetiological diagnosis in many older patients.²⁹⁹

### 10.3 Treatment recommendations

Rapid diagnosis and prompt institution of appropriate antibiotics are essential for improved survival in older persons.³⁰⁸

*C* Empirical antibiotic therapy for specific infections is a valid and practical option in older persons, given the higher risk of adverse outcomes, diverse infectious causes and increased difficulty in obtaining diagnostic specimens. In general, this therapy should include a broad-spectrum beta-lactam antibiotic.

*Grade C, Level IV*

*C* When culture results are not available yet, the choice of antibiotic should be guided by knowledge of the likely pathogens encountered in older people in different settings.

*Grade C, Level IV*

*C* Aminoglycosides should be reserved for selected situations: septic shock without a specific aetiological diagnosis, confirmed or
suspected *Pseudomonas aeruginosa* infections, or where the cultured organism is only susceptible to an aminoglycoside.

**Grade C, Level IV**

C The patient's renal function should always be considered when prescribing antibiotics in older people, particularly if the antibiotics are excreted primarily by the kidneys (e.g. aminoglycosides, fluoroquinolones, and some cephalosporins such as ceftazidime). Estimated creatinine clearance should be used to guide appropriate dosing of such antibiotics.\(^{309}\)

**Grade C, Level IV**

C There should be monitoring for adverse effects of antibiotics during therapy. In addition to specific adverse effects, geriatric syndromes or functional decline should also be considered as possible adverse effects of antibiotics.

**Grade C, Level IV**

### 10.4 Additional antibiotic consideration in the elderly

#### 10.4.1 Drug-drug interactions

The elderly often take a number of medications at the same time. These may include anticoagulants, antiarrythmics, diuretics and other cardiac drugs. When taken with antibiotics, drug-drug interactions may occur.\(^{310}\) Examples include aminoglycosides with radiographic contrast increasing risk of nephrotoxicity, and metronidazole with warfarin increasing the anticoagulant effect.

**GPP** Awareness of potential drug-drug interactions should guide the choice of antibiotics.

**GPP**

#### 10.4.2 Drug compliance

With the frequent occurrence of polypharmacy, compliance with medications remains a challenge. Inability to follow instructions, impaired vision and poor memory are some of the contributing factors for noncompliance with prescribed antibiotics.\(^{310}\)
10.5 Special situations in the elderly

The following special situations in the elderly are considered below:

- Infections in long-term care institutions
- Aspiration pneumonia
- Urinary tract infection and intermittent urethral catheterisation

10.5.1 Infections in long-term care institutions (LTCIs)

Infections, and resultant morbidity and mortality, are common in frail older residents of LTCIs. Diagnosis may often be delayed because of the inability of some residents to verbalise their symptoms, as well as the altered presentation of their illness. Infections remain one of the most common reasons for hospitalisation and death in nursing home residents.

The bacterial flora in LTCIs tend to be intermediate between the relatively antibiotic-resistant hospital flora and those typical of community-acquired infections. In the case of pneumonia, Gram-negative bacilli and anaerobes are encountered more frequently although *Streptococcus pneumoniae* is still the most commonly isolated pathogen.

Clinical features of infection in residents in LTCIs may be absent or subtle. A change in either physical or cognitive function may be the main manifestation. In the US, for example, infection was found to be present in 77% of episodes of ‘decline in function’ such as delirium, incontinence, falling, deteriorating mobility, or failure to co-operate with rehabilitation.

The choice of antibiotic is usually guided by the likely spectrum of bacterial flora that might be encountered. Broad-spectrum antibiotics that include Gram-negative cover are usually required. For pneumonia in the setting of long-term care institutions, antibiotic...
cover for anaerobes (e.g. amoxicillin-clavulanate) should be considered if aspiration is a concern.\textsuperscript{313}

\textbf{Grade C, Level IV}

\subsection*{10.5.2 Aspiration pneumonia}

This type of pneumonia classically occurs following clinically-unapparent aspiration of microorganisms harboured in the nasopharynx. Anaerobic bacteria and Gram-negative bacilli may be more common.\textsuperscript{314}

Aspiration pneumonia should be suspected when there is\textsuperscript{315}:

- A condition that predisposes to aspiration
- Radiographic evidence of involvement of a dependent pulmonary segment:
  - Lower lobes in the upright position
  - Superior segments of the lower lobes and posterior segments of the upper lobes in the recumbent position

Conditions which predispose to aspiration include\textsuperscript{316}:

- Oesophageal dysfunction
- Poor cough reflex
- Altered level of consciousness
- Obstructive oesophageal disease
- Nasogastric tubes in situ

\textbf{Prevention}

The following measures to prevent aspiration are recommended:

\textcolor{green}{C} Reduce the risk of aspiration by\textsuperscript{317,318}:

- Avoiding sedative medication
- Minimising the use of nasogastric tubes
- Elevating the head of bed during and after feeding

\textbf{Grade C, Level IV}

\textcolor{green}{C} Timely assessment of swallowing, at the bedside or by a speech therapist, can be useful in guiding any modification of feeding (e.g. consistency of fluids).\textsuperscript{317}

\textbf{Grade C, Level IV}
There should be proper treatment of periodontal disease and gingivitis.\textsuperscript{318}  

**Grade C, Level IV**

**Treatment**

In treating aspiration pneumonia, use antibiotics that include broad-spectrum ones with anaerobic cover (such as amoxicillin-clavulanate), or the combination of a fluoroquinolone with either metronidazole or clindamycin.\textsuperscript{315}  

**Grade C, Level IV**

### 10.5.3 Urinary tract infections and intermittent urethral catheterisation

Urinary tract infection associated with use of indwelling urinary catheters is discussed in chapter 8. An area that deserves separate attention is intermittent urethral catheterisation because of its use in older people.

Intermittent catheterisation is associated with a lower incidence of bacteriuria than in indwelling urethral catheterisation.\textsuperscript{264}

**Grade C, Level IV**

Patients with asymptomatic bacteriuria while on intermittent catheterisation should not be treated with antibiotics.\textsuperscript{319} The exception is the presence of possible "atypical presentation" of infection.

**Grade C, Level IV**

### 10.5.4 Infected pressure ulcers

Pressure ulcers are a frequent complication of immobility in elderly persons. When infected, they are often polymicrobial in causation. Surgical debridement is necessary to remove necrotic tissue and to drain abscesses.\textsuperscript{320}

Systemic antibiotics should be used with more serious pressure ulcer infections, including those with spreading cellulitis, osteomyelitis and bacteraemia.\textsuperscript{320}  

**Grade C, Level IV**
Empirical antibiotics that are effective against Gram-positive and Gram-negative organisms as well as anaerobic organisms are needed. Monotherapy with piperacillin-tazobactum or a carbapenem, or combination therapy employing ciprofloxacin with either metronidazole or clindamycin are useful options.\textsuperscript{310,320} As tissue perfusion is usually poor in infected ulcers, intravenous antibiotic therapy should be administered initially.\textsuperscript{320}

\textit{Grade C, Level IV}
The following indicators for community acquired pneumonia are proposed:

<table>
<thead>
<tr>
<th>Indicator</th>
<th>i) Antibiotic timing: percentage of pneumonia patients who received first dose of antibiotics within 4 hrs after hospital arrival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Numerator (n)</td>
<td>Community Acquired Pneumonia patients who received their first dose of antibiotics within 4 hrs after arrival at the hospital.</td>
</tr>
<tr>
<td>Denominator (D)</td>
<td>Patients with Community Acquired Pneumonia (principal diagnosis code of pneumonia or principal diagnosis code of septicaemia with secondary diagnosis code of pneumonia or principal diagnosis code of respiratory failure with secondary diagnosis code of pneumonia)</td>
</tr>
<tr>
<td>Exclusions</td>
<td>Received in transfer from another acute care or critical access hospital; no working diagnosis of pneumonia at the time of admission; receiving comfort measures only (palliative care); no antibiotics received during the hospitalization or within 36 hrs of hospital arrival; insufficient arrival or antibiotic timing data; &lt;29 days of age.</td>
</tr>
<tr>
<td>Measurement</td>
<td>n/D x 100</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Indicator</th>
<th>ii) Initial antibiotic consistent with current recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Numerator (n)</td>
<td>Community acquired pneumonia patients who received an initial antibiotic regimen consistent with current guidelines during the first 24 hrs of hospitalization.</td>
</tr>
<tr>
<td>Denominator (D)</td>
<td>Patients with Community Acquired Pneumonia (principal diagnosis code of pneumonia or principal diagnosis code of septicaemia with secondary diagnosis code of pneumonia or principal diagnosis code of respiratory failure with secondary diagnosis code of pneumonia.</td>
</tr>
<tr>
<td>Exclusions</td>
<td>Patients who had no working diagnosis of pneumonia at the time of admission; patients who received comfort measures only; patients who were transferred from another acute care of critical access hospital; patients who were immunocompromised (based on comorbidity); patients who potentially had nosocomial pneumonia (index admission within 14 days of a previous admission); patients &lt;18 yrs old; patients who did not receive antibiotics during the hospitalization or within 36 hrs of arrival at the hospital; patients for whom hospital arrival or antibiotic timing administration data are not available.</td>
</tr>
<tr>
<td>Measurement</td>
<td>n/D x 100</td>
</tr>
</tbody>
</table>

(Source: CMS 7th scope of Work/The Quality Initiative: A Joint Hospital Quality Public Reporting Initiative/NQF).
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Acute Bronchitis In Adults


**Acute Bronchitis and Exacerbation of Chronic Bronchitis**


Use of Antibiotics in Community Acquired Pneumonia


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Use of Antibiotics in Acute Bacterial Meningitis in Immunocompetent Adults


Use of Antibiotics in Elderly


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Self-assessment (MCQs)

After reading the Clinical Practice Guidelines, you can claim one CME point under Category III (Self-Study) of the SMC Online CME System. Before you login to claim the CME point, we encourage you to evaluate whether you have mastered the key points in the Guidelines by completing this set of MCQs. This is an extension of the learning process and is not intended to “judge” your knowledge and is not compulsory. The answers can be found at the end of the questionnaire.

Instruction: Choose the right answer(s). There may be more than one answer for some questions.

1. Antibiotics are indicated in acute rhinosinusitis:
   A) Only if there are changes on radiography of the sinuses.
   B) Whenever there is mucopurulent discharge.
   C) If symptoms last for 7 days or more, with maxillary pain or tenderness in the face or maxillary teeth.
   D) If symptoms of rhinosinusitis are severe, regardless of the duration of the symptoms.

2. Acute upper respiratory tract infections are the most frequent reasons for seeking medical attention.
   A) They are associated with up to 75% of total antibiotic prescriptions each year.
   B) Antibiotic treatment may selectively promote the acquisition and spread of antibiotic-resistant bacteria.
   C) Patient expectations and demands for antibiotics is strongly associated with the excess use of antibiotics in these conditions.
   D) Antibiotic treatment in these conditions enhances illness resolution.

3. Regarding acute bronchitis,
   A) Cough, with or without phlegm, is a predominant feature.
   B) In the young otherwise healthy adult, the underlying cause is invariably bacterial.
   C) Pneumonia is a differential diagnosis.
   D) Purulent sputum must be present for the diagnosis of acute bronchitis.
4. Regarding antibiotic use in acute bronchitis,
   A) An antibiotic is always indicated even if the patient has minimal symptoms.
   B) All cases of acute bronchitis should be followed up and antibiotics considered if they are not recovering.
   C) Erythromycin is usually effective in bacterial infection.
   D) Antibiotics should be considered if the patient is > 60 years old.

5. A 45-year old man who walks into your clinic with right lower lobe pneumonia
   A) May be treated at home
   B) Should be referred to hospital
   C) Needs to be isolated
   D) Needs intravenous antibiotics

6. The choice of antibiotic in the initial treatment of community acquired pneumonia is based upon
   A) The radiologic pattern
   B) The severity of the fever
   C) The Gram stain results
   D) The risk stratification category

7. Hospital acquired pneumonia
   A) Develops after 1 week in hospital
   B) May be prevented by tracheal intubation
   C) Are more often polymicrobial than community acquired ones
   D) Are treated on the basis of blood culture results

8. Which of the following risk factor and pathogen relations are correct?
   A) Anaerobic pathogens with head injury
   B) Corticosteroid use with Staphylococcus aureus
   C) Pseudomonas with broad spectrum antibiotic use
   D) Legionella with diabetes

9. Empirical antibiotic therapy can be given under the following circumstances
   A) Most patients with acute diarrhoea
   B) In patients with moderate to severe inflammatory diarrhoea
   C) In patients with moderate to severe traveler’s diarrhoea
   D) In patients where diarrhoea has lasted for more than 2 weeks
10. Stool culture and sensitivity should be done
   A) In all patients with acute diarrhoea
   B) In all hospitalised patients who develop diarrhoea
   C) In sick patients with prolonged diarrhoea or evidence of
      inflammatory diarrhoea
   D) When there is a suspected outbreak of diarrhoeal illness by a
      single organism

11. In treatment of uncomplicated cystitis in women, treatment of
    choice is
   A) PO trimethoprim-sulphamethoxazole for 7 days
   B) PO quinolones for 7 days
   C) PO trimethoprim-sulphamethoxazole for 3 days
   D) PO 1st or 2nd generation cephalosporin for 3 days

12. Treatment of choice for prostatitis is
   A) I.V. Amoxicillin and Gentamicin for 2 weeks
   B) PO fluoroquinolones for 3 months, regardless of bacterial or
      abacterial etiology
   C) PO fluoroquinolones for chronic bacterial prostatitis
   D) PO trimethoprim-sulphamethoxazole for 2 weeks

13. In meningococcal meningitis
   A) A petechial or purpuric rash, predominantly in the
      extremities, in a patient with meningeal signs indicates a high
      probability of a meningococcal infection.
   B) Meningococci can be isolated from the nasopharynx of up to
      50% of patients with meningococcal disease
   C) Intravenous penicillin G 20-24 million units daily is the
      treatment of choice
   D) Gram positive diplococci may be seen on Gram stain of the
      CSF

14. The 3 leading causes of community-acquired bacterial meningitis
    in adults include:
   A) Streptococcus pneumoniae
   B) Haemophilus influenzae
   C) Neissela meningitidis
   D) Listeria monocytogenes
15. In a patient with fever and nuchal rigidity without a rash; the following are important considerations:
A) The local prevalence of ceftriaxone-resistant Streptococcus pneumoniae.
B) History of alcoholism or age above 50 years.
C) Confirmation of the diagnosis by a lumbar puncture before initiating antibiotic therapy.
D) History of allergy to beta lactams.

16. With regards to clinical presentation of infections in older patients:
A) Fever may be blunted or absent in up to 25%.
B) Onset of fever may be delayed (by several hours).
C) Atypical presentations such as functional decline and geriatric syndromes such as delirium, impaired mobility, falls and incontinence may be the primary manifestation of an infection.
D) Oral temperatures of > 38.3 degrees C are very likely to be caused by benign viral illness (as with the young).

17. In the treatment of infections in older people:
A) Empiric antibiotic therapy is a valid option.
B) The choice of antibiotic should be guided by knowledge of likely pathogens encountered in different settings when culture results are not available yet.
C) The most important factor to consider when prescribing antibiotics is the hepatic function.
D) Aminoglycosides should be reserved for selected situations such as suspected Pseudomonas aeruginosa infections.
Answer

1. C, D  (pgs 41, 42)
2. A, B, C  (pgs 33, 34)
3. A, C  (pgs 49, 50)
4. B, C, D  (pgs 51, 52)
5. A  (pg 68)
6. D  (pg 64)
7. C  (pg 77)
8. C  (pg 80)
9. B, C  (pg 89)
10. C, D  (pg 86)
11. C  (pg 102)
12. C  (pg 118)
14. A, C, D  (pg 121)
15. A, B, D  (pg 124)
16. A, B, C  (pg 132)
17. A, B, D  (pg 134)
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### Levels of evidence and grades of recommendation

#### Levels of evidence

<table>
<thead>
<tr>
<th>Level</th>
<th>Type of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ia</td>
<td>Evidence obtained from meta-analysis of randomised controlled trials.</td>
</tr>
<tr>
<td>Ib</td>
<td>Evidence obtained from at least one randomised controlled trial.</td>
</tr>
<tr>
<td>IIA</td>
<td>Evidence obtained from at least one well-designed controlled study without randomisation.</td>
</tr>
<tr>
<td>IIb</td>
<td>Evidence obtained from at least one other type of well-designed quasi-experimental study.</td>
</tr>
<tr>
<td>III</td>
<td>Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.</td>
</tr>
<tr>
<td>IV</td>
<td>Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.</td>
</tr>
</tbody>
</table>

#### Grades of recommendation

<table>
<thead>
<tr>
<th>Grade (evidence)</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (evidence levels Ia, Ib)</td>
<td>Requires at least one randomised controlled trial, as part of the body of literature of overall good quality and consistency, addressing the specific recommendation.</td>
</tr>
<tr>
<td>B (evidence levels IIA, IIb, III)</td>
<td>Requires availability of well conducted clinical studies, but no randomised clinical trials on the topic of recommendation.</td>
</tr>
<tr>
<td>C (evidence level IV)</td>
<td>Requires evidence obtained from expert committee reports or opinions, and/or clinical experiences of respected authorities. Indicates absence of directly applicable clinical studies of good quality.</td>
</tr>
<tr>
<td>GPP (good practice points)</td>
<td>Recommended best practice based on the clinical experience of the guideline development group.</td>
</tr>
</tbody>
</table>
Executive summary of recommendations

Details of recommendations can be found in the main text at the pages indicated.

What’s new in the revised guidelines

New sections in this edition of the guidelines include:

i) use of antibiotics in acute bacterial meningitis
ii) use of antibiotics in infectious diarrhoea in adults

Other sections have been revised, based on the rapid advances in antibiotic therapy and in infectious disease treatment:

- The section on bronchitis has been expanded to include recommendations for risk stratification and antibiotic therapy in patients with acute exacerbation of chronic bronchitis.
- The section on acute upper respiratory tract infections has additional recommendations for non-specific respiratory infections. The use of the Center criteria to predict Group A beta-haemolytic streptococcal pharyngitis was also discussed. Influenza, SARS and vaccination are also discussed in this section.
- The Fine Pneumonia Severity Index has been included in the risk stratification subsection of the section on community-acquired pneumonia.
- Recommendations for infections in long-term care institutions and infected pressure ulcers have been added to the section on antibiotic use in the elderly.
- An algorithm for the management of urinary tract infections in adults has been added.
- New sections on cost-effectiveness issues and clinical quality improvement in antibiotic use have been added.

Principles of Antibiotic Use

**GPP** Antibiotics should be used only for treatment of patients with confirmed or suspected bacterial infections. Antibiotics may be used for prophylaxis where consequences of infection would be severe (pg 29).

GPP
Antibiotics should only be chosen after considering the following questions:

1. Is there an infection?
2. What is the site of infection and the most likely causative organism?
3. Will the antibiotic reach the site of infection?
4. What side effects or drug interactions might this antibiotic have?
5. What adjustments should be made for the individual patient, e.g. the young infant, the elderly, patients with renal failure?
6. What is the appropriate dose and duration of treatment for the site and type of infection?(pg 30)

Patients or their caregivers should be clearly instructed on the dose and the necessity of finishing a course of treatment (pg 30).

Use of Antibiotics in Acute Upper Respiratory Tract Infections (URTI) in Adults

Antibiotic use in URTI

The use of antibiotics for a large portion of URTIs is not recommended because these are viral infections, for which antibiotics do not provide clinical benefit (pg 34).

Non-specific respiratory infections

Antibiotic treatment of adults with non-specific upper respiratory tract infection is not recommended (pg 36).

The use of antibiotics is not recommended when there is purulent secretion from the nares or throat, in patients with uncomplicated URTI(pg 36).

Acute pharyngitis (sore throat)

Patients identified with Group A beta-haemolytic streptococcal pharyngitis should be treated with antibiotics to prevent complications (pg 37).
The patient’s renal function should always be considered when prescribing antibiotics in older people, particularly if the antibiotics are excreted primarily by the kidneys (e.g. aminoglycosides, fluoroquinolones, and some cephalosporins such as ceftazidime). Estimated creatinine clearance should be used to guide appropriate dosing of such antibiotics (pg 135).

**Grade C, Level IV**

There should be monitoring for adverse effects of antibiotics during therapy. In addition to specific adverse effects, geriatric syndromes or functional decline should also be considered as possible adverse effects of antibiotics (pg 135).

**Grade C, Level IV**

**Additional Antibiotic Consideration in the Elderly**

**GPP** Awareness of potential drug-drug interactions should guide the choice of antibiotics (pg 135).

**GPP**

Assistance from caregivers who can help administer medications should be sought where necessary. Keeping the antibiotic regimen as simple as possible is also useful in improving compliance (pg 136).

**Grade C, Level IV**

**Special Situations in the Elderly**

The choice of antibiotic is usually guided by the likely spectrum of bacterial flora that might be encountered. Broad-spectrum antibiotics that include Gram-negative cover are usually required. For pneumonia in the setting of long-term care institutions, antibiotic cover for anaerobes (e.g. amoxicillin-clavulanate) should be considered if aspiration is a concern (pg 136).

**Grade C, Level IV**

The following measures to prevent aspiration are recommended:

- Avoiding sedative medication;
- Minimising the use of nasogastric tubes; and
- Elevating the head of bed during and after feeding.

**(pg 137)**

**Grade C, Level IV**

- Group A beta-haemolytic streptococcal-positive patients should be treated with penicillin V, for seven days (pg 38).
  **Grade A, Level Ib**

- Throat cultures are not recommended for the routine primary evaluation of adults with pharyngitis (pg 38).
  **Grade A, Level Ib**

- Administer appropriate analgesics, antipyretics, and supportive care to all patients with pharyngitis (pg 38).
  **Grade C, Level IV**

**Acute epiglottitis**

- The antibiotic of choice to treat acute epiglottitis is ceftriaxone or chloramphenicol (pg 40).
  **Grade B, Level IIb**

**Acute rhinosinusitis**

- Sinus radiography is not recommended for diagnosis in routine cases.
  **Grade B, Level IIb**

- Symptomatic treatment and reassurance is the preferred initial management strategy for patients with mild symptoms of acute rhinosinusitis (pg 42).
  **Grade B, Level IIb**

- Antibiotic therapy should be reserved for:
  - Patients with moderately severe symptoms who meet the criteria for the clinical diagnosis of acute bacterial rhinosinusitis (symptoms that last >7 days and include maxillary pain in the face or teeth and purulent nasal secretions); and
  - Patients with severe rhinosinusitis symptoms, regardless of duration of illness.
  **Grade B, Level IIb**

- For the initial treatment of acute bacterial maxillary rhinosinusitis, amoxicillin or penicillin for 7-14 days is recommended (pg 42).
  **Grade A, Level IIa**
Isolated infection of a frontal or sphenoid sinus is a rare but potentially dangerous condition, usually caused by bacteria, and should be referred to hospital for treatment (pg 42).

Acute laryngitis

If symptoms last for more than 3 weeks, the condition is classified as chronic laryngitis, for which an underlying cause must be further investigated. Underlying causes include laryngeal polyps, cancer, laryngeal tuberculosis, and gastro-esophageal reflux (pg 43).

Antibiotic treatment for acute laryngitis currently should be reserved for high-risk patients, patients with severe symptoms, or in the presence of an identifiable organism on Gram stain and culture (pg 44).

Acute otitis media

Antibiotics are unnecessary in acute otitis media (pg 45).

Avoid local treatment with antimicrobial eardrops in acute otitis media (pg 45).

Common cold

Antibiotics should not be given for the common cold (pg 45).

Antibiotics should not be given for the common cold which is accompanied by mucopurulent rhinitis (pg 47).

Influenza

Neuraminidase inhibitors (NIs) are effective for the prevention and treatment of influenza (pg 45).

Use of Antibiotics in the Elderly

Unique Aspects of Infections in Older People

An infectious aetiology should be sought when there is:
- A change in functional status and the oral temperature is ≥37.2°C, or
- An increase in temperature of ≥1.3°C over the baseline.

Infection should be considered in the differential diagnosis of older people who present, within a short period of time:
- With only non-specific symptoms, including functional decline; or
- With atypical complaints.

Doctors should be alert to a leucocytosis with left shift or left shift alone, as these have good predictive value for diagnosing bacterial infections in older people.

Treatment recommendations

Empirical antibiotic therapy for specific infections is a valid and practical option in older persons, given the higher risk of adverse outcomes, diverse infectious causes and increased difficulty in obtaining diagnostic specimens. In general, this therapy should include a broad-spectrum beta-lactam antibiotic.

When culture results are not available yet, the choice of antibiotic should be guided by knowledge of the likely pathogens encountered in older people in different settings.

Aminoglycosides should be reserved for selected situations: septic shock without a specific aetiological diagnosis, confirmed or suspected *Pseudomonas aeruginosa* infections, or where the cultured organism is only susceptible to an aminoglycoside.
Figure 5  
Algorithm for the initial management of a patient with acute meningitis

- **Acute Bacterial Meningitis**
- **Typical meningococcal rash (petechial, purpuric)**
  - Adult >50y, history of alcoholism, diabetes or pregnant female

- **No rash**
  - Area where penicillin-resistant Streptococcus pneumoniae prevalent
  - **I.V. ceftriaxone, 2g 12H**
  - **I.V. ampicillin, 2g 4H**

- **I.V. ceftriaxone, 2g 12H**
  - **I.V. vancomycin, 1g 12H**

- **CSF or blood culture:**
  - Penicillin-sensitive Streptococcus pneumoniae*
  - Blood/CSF culture:
    - Penicillin-resistant Streptococcus pneumoniae*

- **Continue I.V. ceftriaxone, 2g 12H or switch to I.V. Pencillin G**

- **Gram stain CSF:**
  - Gram negative: *Neisseria meningitides*
  - Blood/CSF culture:
    - Lactobacillus monocytogenes*

- **Discontinue ceftriaxone, Continue ampicillin, 2g 4H. Add I.V. Gentamicin, 5mg/kg 24H**

- **Switch to I.V. ceftriaxone, 2g 12H**

- **Response**
  - **Continue I.V. ceftriaxone 2g 12H + vancomycin, 1g 12H**

- **No response**
  - **Continue I.V. ceftriaxone, 2g 12H or switch to I.V. Pencillin G**

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**Acute Bronchitis and Exacerbation of Chronic Bronchitis**

- **B**  
  - The adamantanes, rimantadine and amantadine, are not recommended for influenza A because of increasing drug resistance (pg 47).  
  - **Grade B, Level III**

- **A**  
  - Routine antibiotic treatment of acute bronchitis is not recommended, regardless of the duration of cough (pg 51).  
  - **Grade A, Level Ia**

- **B**  
  - Antibiotic therapy in acute bronchitis should be considered if the patient is ≥ 60 years or ill at the outset (pg 51).  
  - **Grade B, Level III**

- **C**  
  - Once a diagnosis of acute bronchitis has been made, the physician should address symptomatic treatment and patient expectations of the visit (pg 51).  
  - **Grade C, Level IV**

- **B**  
  - All cases of acute bronchitis should be followed up and antibiotics considered if they are not recovering (pg 52).  
  - **Grade B, Level III**

**Acute exacerbations of chronic bronchitis (AECB)**

- **A**  
  - Patients with acute exacerbation of severity of Anthonisen Type I (having increased dyspnea, increased sputum production, and increased sputum purulence) and Anthonisen Type II (two of the three symptoms) should be given antibiotic therapy (pg 54).  
  - **Grade A, Level Ib**

- **A**  
  - Patients with one or more of the following risk factors should be given antibiotic therapy: more than 4 exacerbations within the past year; a co-morbid condition, such as diabetes, asthma, or a history of coronary artery disease, or marked airway obstruction (pg 55).  
  - **Grade A, Level Ib**

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*To continue initial antibiotics if culture is negative and patient is responding*
Patients with exacerbations without an increase in purulent sputum do not need antibiotic therapy unless there is a consolidation on a chest radiograph or clinical signs of pneumonia (pg 55).

Grade B, Level IIa

Patients with purulent exacerbations but who have no risk factors for treatment failure or no enhanced association with more virulent or resistant bacterial pathogens can be treated with an advanced macrolide (azithromycin, clarithromycin), a cephalosporin (cefuroxime), or doxycycline (pg 56).

Grade B, Level IIa

Patients with purulent exacerbations and who have risk factors that are associated with an increased likelihood of treatment failure or infection with more virulent or resistant organisms should be given antibiotics with enhanced antimicrobial coverage, namely the newer fluoroquinolones (moxifloxacin, gemifloxacin*, gatifloxacin, levofloxacin) or amoxicillin-clavulanate (pg 59).

Grade A, Level Ib

In a patient with AECB requiring repeat antibiotic therapy within 3 months, a new class of antibiotics should be used (pg 60).

GPP

- Contact at a day-care centre.
- Transient close contact with a case where there was exposure to the patient’s secretions (e.g. through mouth-to-mouth resuscitation, endotracheal intubation or endotracheal tube management) around the time of admission to hospital.

(pg 127) Grade C, Level IV

Close contacts of patients with meningococcal infection should receive one of the following regimens:

- Rifampicin:
  Adults: 600 mg, 12 hourly for 2 days (4 doses).
  Children (1-6 years): 10 mg/kg, 12 hourly for 2 days (4 doses).
  Children (3-11 months): 5 mg/kg 12 hourly for 2 days (4 doses).

- Ciprofloxacin:
  Adults: 500 mg as a single dose.
  Children: Use of ciprofloxacin is not recommended.

- Ceftriaxone:
  Adults: 250 mg as a single intramuscular dose.
  Children (< 15 years): 125 mg as a single intramuscular dose.

(pg 127) Grade C, Level IV

If other antibiotics have been used for treatment, the index patient should receive prophylactic antibiotics for eradication of nasopharyngeal carriage before being discharged from hospital (pg 128).

Grade C, Level IV

* currently not available in Singapore
Recommended duration of therapy according to the type of pathogen causing meningitis. (pg 126)

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Recommended duration of therapy</th>
<th>Grade and level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Haemophilus influenzae</em></td>
<td>7-10 days</td>
<td>Grade B, Level IIb</td>
</tr>
<tr>
<td><em>Neisseria meningitidis</em></td>
<td>7-10 days</td>
<td>Grade B, Level III</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>10-14 days</td>
<td>Grade C, Level IV</td>
</tr>
<tr>
<td><em>Listeria monocytogenes</em></td>
<td>≥ 21 days</td>
<td>Grade C, Level IV</td>
</tr>
<tr>
<td>Gram-negative bacilli, other than <em>Haemophilus influenzae</em></td>
<td>21 days</td>
<td>Grade C, Level IV</td>
</tr>
</tbody>
</table>

The duration of therapy should be tailored to the individual patient on the basis of the clinical and microbiological response (pg 126). Grade C, Level IV

**Adjunctive dexamethasone therapy in bacterial meningitis**

- In adults with suspected or proven pneumococcal meningitis, dexamethasone 10 mg 6 hourly should be given for 4 days with the first dose administered 15-20 min before, or at least concomittant with, the first dose of antimicrobial therapy (pg 126). Grade A, Level Ib

- Dexamethasone should only be continued if the CSF Gram stain reveals Gram-positive diplocci or if blood or CSF cultures are positive for *Streptococcus pneumoniae* (pg 126). Grade A, Level Ib

- Adjunctive dexamethasone should not be given to adult patients who have already received antimicrobial therapy as in this circumstance, dexamethasone is unlikely to improve patient outcome (pg 126). Grade A, Level Ib

**Prevention of meningococcal meningitis**

- Chemoprophylaxis should be offered to close contacts of cases, irrespective of vaccination status, in those who have:
  - Prolonged close contact with the case in a household setting during the seven days before onset of illness.

---

**Figure 1** Algorithm outlining a risk-stratification approach to antibacterial therapy of acute exacerbations of chronic bronchitis

- No Risk factors
  - Age <65
  - FEV1 normal
  - <4 AECB in 12 mth
  - No comorbidities

- Suspected AECB
  - Increased DYSPNEA?
  - Increased SPUTUM VOLUME
  - Increased SPUTUM PURULENCE?

- Risk factors (one or more)
  - Age ≥65 or
  - FEV1 <50% predicted or
  - ≥4 AECB in last 12 months or
  - Cardiac disease or
  - Others: home oxygen, chronic oral steroid use, antibiotic use in past 3 months

- Simple COPD
  - Advanced macrolide (azithromycin, clarithromycin)
  - Ketolide (telithromycin)
  - Cephalosporin (cefoxime, cefpodoxime*, cefdinir*)
  - Doxycycline

- Complicated COPD
  - Fluoroquinolone (moxifloxacin, gemifloxacin, gatifloxacin, levofloxacin)
  - Amoxicillin-clavulanate

- Chronic supplicative bronchitis
  - At risk of pseudomonas infection
    - Consider ciprofloxacin and obtain sputum culture

Worsening clinical status or inadequate response in 72 hours

Re-evaluate
- Consider sputum culture

* currently not available in Singapore
Use of Antibiotics in Community Acquired Pneumonia

Risk Stratification

Risk stratification is a key step in the management of community acquired pneumonia (pg 64).

Grade B, Level IIa

All patients with severe community acquired pneumonia (Category IV) in the ICU should be treated empirically for *Burkholderia pseudomallei*. (pg 69).

Grade B, Level III

Inpatient Investigations

Microbiological, haematological, biochemical and serological tests (see list below) are recommended for patients in risk Categories III and IV upon presentation.

The following microbiological tests should be done before starting antibiotics in patients with moderate to severe CAP (Categories III and IV). Initial microbiological studies may have limited value in the management of patients with low risk CAP (Categories I & II):

- Sputum Gram stain and aerobic culture (mycobacterial smear and culture where appropriate).
- Blood aerobic culture.
- Pleural fluid Gram stain and culture.
- Urine for *Legionella* antigen.

The other investigations are:

- Blood count with differentials, and smear for toxic granulations.
- Biochemistry, including renal and liver function (Blood gas where necessary).
- Consider HIV testing and work-up for *Pneumocystis carinii*.
- Optional serological testing for atypical agents.

(pg 69)

Grade C, Level IV

Empirical Antibiotic Therapy

The initial choice for empirical antibiotic therapy should be based on the risk category and relative prevalence of major pathogens (pg 69).

Grade A, Level Ib

For adults over the age of 50 years, history of alcoholism, diabetes and pregnancy without a typical meningococcal rash, consider adding intravenous ampicillin, 2g 4 hourly, to ceftriaxone as above.

Grade C, Level IV & GPP

If there is a clear history of anaphylaxis to β-lactams, give intravenous chloramphenicol 25 mg/kg (maximum 1g) 6 hourly. Add vancomycin 1g 12 hourly, because of the possibility of penicillin-resistant *Streptococcus pneumoniae* and likely failure of chloramphenicol in this group.

Grade C, Level IV

If Gram-negative diplococci are visible on Gram stain of cerebrospinal fluid (CSF), or if *Neisseria meningitidis* is isolated from CSF or blood, continue with intravenous penicillin G, 24 million units daily.

Grade B, Level III

For patients who do not have adequate response to penicillin, the treatment should be changed to ceftriaxone.

Grade C, Level IV

If penicillin-sensitive *Streptococcus pneumoniae* is isolated from CSF or blood, intravenous penicillin G 24 million units is recommended. If cephalosporin-sensitive *Streptococcus pneumoniae* is isolated, intravenous ceftriaxone 2g 12 hourly should be given. Add on intravenous vancomycin, 1g 12 hourly, if penicillin-resistant and cephalosporin-resistant *Streptococcus pneumoniae* is isolated from blood or CSF. Continue intravenous therapy for 10-14 days.

Grade C, Level IV

For *Haemophilus influenzae* meningitis, intravenous ceftriaxone, 2g 12 hourly, is recommended.

Grade B, Level IIb

If Gram-positive coccobacilli suggestive of *Listeria monocytogenes* is visible on Gram stain of CSF, or if *Listeria monocytogenes* is isolated from blood or CSF, intravenous ampicillin, 2g 4 hourly, and gentamicin 5 mg/kg 24 hourly (single or divided 8 hourly doses) for more than 21 days is recommended.

Grade C, Level IV
Use of Antibiotics in Acute Bacterial Meningitis in Immunocompetent Adults

Diagnosis of acute bacterial meningitis

- Initial physical examination should include evaluation for:
  - level of consciousness
  - cranial nerve palsies
  - focal deficits
  - meningismus
  - increased intracranial pressure
  - critical trauma
  (pg 122)  

Grade C, Level IV

A lumbar puncture is recommended in all adult patients with suspected meningitis except when a clear contraindication exists (pg 122).

Grade B, Level III

Antibiotic therapy

- If bacterial meningitis is suspected, antibiotic treatment must be started immediately, regardless of any investigations undertaken (pg 124).

Grade C, Level IV

- In the treatment of meningitis with a typical meningococcal rash, intravenous penicillin G, 20-24 million units daily, should be given (pg 124).

Grade B, Level III

- For adults without a typical meningococcal rash, intravenous ceftriaxone, 2g 12 hourly, should be given (pg 124).

Grade B, Level III

- If the patient comes from an area where penicillin-resistant Streptococcus pneumoniae are common (MIC ≥ 0.1μg/ml) then add intravenous vancomycin 1g 12 hourly (pg 124).

Grade C, Level IV

The quinolones are not recommended for the outpatient treatment of community acquired pneumonia in categories I & II (pg 69).

Grade C, Level IV

A switch from I.V. to oral antimicrobials and prompt hospital release is recommended for patients in low-intermediate risk categories who respond promptly or become clinically stable after receiving initial antimicrobial treatment (pg 73).

Grade A, Level Ia

Criteria for discharge from hospital.

- Stable vital signs for 24 hours (i.e. temperature <37.8°C, respiratory rate <24/min, systolic BP >90mmHg, O₂ saturation >90% while breathing room air).
- Patient able to take diet.
- Patient able to take oral antibiotics.
- No other active clinical or psycho-social problems requiring hospital stay.

(pg 73)

In addition to the usual outcomes of mortality and hospital length of stay, the time to the first dose of antibiotics in elderly patients (>65 years) should be a key indicator of the evaluation of the quality of community acquired pneumonia management (pg 74).

Grade B, Level III
Table 1  Fine pneumonia severity index

<table>
<thead>
<tr>
<th>CHARACTERISTIC</th>
<th>POINTS ASSIGNED*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic factor</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>Age (yr)</td>
</tr>
<tr>
<td>Women</td>
<td>Age (yr) - 10</td>
</tr>
<tr>
<td>Nursing home resident</td>
<td>+10</td>
</tr>
<tr>
<td>Coexisting illnesses</td>
<td></td>
</tr>
<tr>
<td>Neoplastic disease</td>
<td>+30</td>
</tr>
<tr>
<td>Liver disease</td>
<td>+20</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>+10</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>+10</td>
</tr>
<tr>
<td>Renal disease</td>
<td>+10</td>
</tr>
<tr>
<td>Physical-examination findings</td>
<td></td>
</tr>
<tr>
<td>Altered mental status</td>
<td>+20</td>
</tr>
<tr>
<td>Respiratory rate ≥30/min</td>
<td>+20</td>
</tr>
<tr>
<td>Systolic blood pressure &lt;90 mmHg</td>
<td>+20</td>
</tr>
<tr>
<td>Temperature &lt;35°C or &gt;40°C</td>
<td>+15</td>
</tr>
<tr>
<td>Pulse ≥125/min</td>
<td>+10</td>
</tr>
<tr>
<td>Laboratory and radiographic findings</td>
<td></td>
</tr>
<tr>
<td>Arterial pH &lt;7.35</td>
<td>+30</td>
</tr>
<tr>
<td>Blood urea nitrogen ≥30 mg/dl (11 mmol/liter)</td>
<td>+20</td>
</tr>
<tr>
<td>Sodium &lt;130 mmol/liter</td>
<td>+20</td>
</tr>
<tr>
<td>Glucose ≥250 mg/dl (14 mmol/liter)</td>
<td>+10</td>
</tr>
<tr>
<td>Hematocrit &lt;30%</td>
<td>+10</td>
</tr>
<tr>
<td>Partial pressure of arterial oxygen &lt;60 mmHg</td>
<td>+10</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>+10</td>
</tr>
</tbody>
</table>

* A total point score for a given patient is obtained by summing the patient’s age in years (age minus 10 for women) and the points for each applicable characteristic.

† Neoplastic disease is defined as any cancer, except basal- or squamous-cell cancer of the skin, that was active at the time of presentation or diagnosed within one year of presentation. Liver disease is defined as a clinical or histologic diagnosis of cirrhosis or another form of chronic liver disease, such as chronic active hepatitis. Congestive heart failure is defined as systolic or diastolic dysfunction documented by history, physical examination, and chest radiograph, echocardiogram, multiple gated acquisition scan, or left ventriculogram. Cerebrovascular disease is defined as a clinical diagnosis of stroke or transient ischemic attack or stroke documented by magnetic resonance imaging or computed tomography. Renal disease is defined as a history of chronic renal disease or abnormal blood urea nitrogen and creatinine concentrations documented in the medical record.

‡ Altered mental status is defined as disorientation with respect to person, place, or time that is not known to be chronic, stupor, or coma.
Management of Complicated UTIs

C Antibiotic treatment of complicated urinary tract infections should be based on cultures and sensitivity. When symptoms warrant initiation of empirical therapy, cultures must be obtained prior to antibiotic therapy and therapy modified based on results (pg 114).

Grade C, Level IV

C For ill, hospitalized patients with complicated urinary tract infections, empirical treatment with intravenous 3rd-generation cephalosporins, fluoroquinolones, β-lactams or β-lactam-β-lactamase-inhibitor combinations is recommended. An alternative regimen using intravenous ampicillin together with an aminoglycoside is also effective (pg 114).

Grade C, Level IV

A For complicated urinary tract infections of mild to moderate severity, initial therapy with oral fluoroquinolones or trimethoprim-sulphamethoxazole is recommended (pg 114).

Grade A, Level Ib

C For complicated urinary tract infections of mild to moderate severity, alternative regimens for empirical treatment include 2nd-generation cephalosporins, β-lactams, or β-lactam-β-lactamase-inhibitor combinations (pg 114).

Grade C, Level IV

GPP After the initiation of empirical antibiotic therapy, culture-based appropriate therapy is administered for 14 days as a minimum (pg 116).

GPP

GPP Symptomatic UTIs occurring in patients with a short-term indwelling urinary catheter should be treated by removing the catheter, followed by a 7-day course of antibiotics. For patients with long-term indwelling urinary catheters, symptomatic UTIs can be treated with a 7-day course of antibiotics (pg 116).

GPP

GPP In patients with renal impairment, effective antibiotic therapy requires the use of antibiotics which achieve therapeutic concentrations in the urine and are appropriately dose-adjusted for the level of renal failure (pg 116).

GPP
Use of Antibiotics in Hospital Acquired Pneumonia

Classification of hospital acquired pneumonia and antibiotic use

It is recommended that the initial empirical therapy be based upon targeting a core group of pathogens according to severity of illness, duration of hospitalisation and risk factors for specific pathogens (pg 77).

Grade B, Level III

Piperacillin-tazobactam is as safe and effective as ceftazidime in the empirical treatment of severe hospital acquired pneumonia, hospital acquired pneumonia in the ICU and ventilator associated pneumonia (pg 77).

Grade A, Level Ib

Antibiotics for patients with no risk factors; hospital acquired pneumonia of mild to moderate severity, and of early onset (≤ 5 days):

<table>
<thead>
<tr>
<th>Core pathogens</th>
<th>Core antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enteric Gram-negative bacilli</td>
<td>3rd-generation cephalosporin</td>
</tr>
<tr>
<td>- Klebsiella species and Escherichia coli</td>
<td>e.g. intravenous ceftriaxone</td>
</tr>
<tr>
<td></td>
<td>or β-lactam-β-lactamase inhibitor</td>
</tr>
<tr>
<td></td>
<td>e.g. intravenous ampicillin-sulbactam or amoxicillin-clavulanic acid, or quinolone</td>
</tr>
<tr>
<td></td>
<td>e.g. ciprofloxacin.</td>
</tr>
<tr>
<td>Also,</td>
<td>Consider adding cloxacillin or clindamycin.</td>
</tr>
<tr>
<td>- Staphylococcus aureus</td>
<td>Consider adding azithromycin or clarithromycin.</td>
</tr>
<tr>
<td>- Hemophilus influenzae and Streptococcus pneumoniae</td>
<td>Alternative to above: newer quinolone as monotherapy.</td>
</tr>
<tr>
<td>If MRSA isolated ≥ 50% in ICU</td>
<td>Consider adding vancomycin.</td>
</tr>
</tbody>
</table>

(pg 79) Grade C, Level IV

Pyelonephritis

Treatment options for severe acute pyelonephritis include: parenteral 3rd-generation cephalosporins, aminoglycosides, fluoroquinolones, β-lactams or β-lactam-β-lactamase-inhibitor combinations. Antibiotics should be modified when urine culture results become available. Oral antibiotic therapy can be started following clinical improvement, with a treatment course of 14 days (pg 111).

Grade A, Level Ib

Initial treatment with intravenous aminoglycoside, together with a 1st or 2nd-generation cephalosporin, is recommended for hospitalized patients with acute pyelonephritis, because of the low sensitivity of hospital-acquired Escherichia coli to ceftriaxone and ciprofloxacin in the local context (pg 111).

GPP

Treatment options for mild acute pyelonephritis include: oral fluoroquinolones, trimethoprim-sulphamethoxazole, β-lactams or β-lactam-β-lactamase-inhibitor combinations. Antibiotics should be modified when results of urine culture become available (pg 112).

Grade A, Level Ib

UTI in pregnancy

Asymptomatic bacteriuria in pregnancy should be treated with antibiotics, based on culture and sensitivity, to reduce the risk of pyelonephritis and other complications (pg 112).

Grade A, Level Ib

For acute cystitis in pregnancy, empirical therapy with 1st or 2nd-generation cephalosporins, nitrofurantoin or trimethoprim-sulphamethoxazole (caution in 3rd trimester) is recommended. Treatment should be modified based on culture results and appropriate antibiotics should be administered for 7 days (pg 112).

Grade B, Level III

For pyelonephritis in pregnancy, empirical therapy with a 3rd-generation cephalosporin is recommended. Treatment should be modified based on culture results and appropriate antibiotics should be administered for 14 days (pg 113).

Grade B, Level III
A Women with recurrent UTI should be treated with low dose antibiotic prophylaxis, using nitrofurantoin, trimethoprim-sulphamethoxazole, trimethoprim or cephalosporins (pg 105).

Grade A, Level Ib

C Initial therapy with intravenous cephalosporin and aminoglycoside, as for severe pyelonephritis, is recommended for the treatment of severe acute prostatitis (pg 107).

Grade C, Level IV

C Following clinical improvement, severe acute prostatitis should be treated with antibiotics, based on sensitivities, for a total duration of 4 weeks (pg 107).

Grade C, Level IV

C For patients with acute prostatitis of mild to moderate severity, initial therapy with oral fluoroquinolones, trimethoprim-sulphamethoxazole or trimethoprim is recommended. Treatment with antibiotics based on sensitivities should be given for a total duration of 4 weeks (pg 107).

Grade C, Level IV

A The recommended treatment for chronic bacterial prostatitis is fluoroquinolones for 4 weeks (pg 108).

Grade A, Level Ib

B Trimethoprim-sulphamethoxazole for 12 weeks can also be used in the treatment for chronic bacterial prostatitis (pg 108).

Grade B, Level III

C For patients with recurrent chronic prostatitis, suppressive, low-dose therapy with trimethoprim-sulphamethoxazole, trimethoprim or nitrofurantoin can be administered for 6 months or longer (pg 109).

Grade C, Level IV

A Antibiotic therapy is not indicated in the treatment of chronic prostatitis/chronic pelvic pain syndrome (pg 110).

Grade A, Level Ib

GPP Patients with symptoms of chronic prostatitis, but with negative urine or prostatic fluid cultures, should be referred to a Urologist for further management (pg 110).

GPP

C Antibiotics for patients with no risk factors, but late onset (>5 days) hospital acquired pneumonia, or severe hospital acquired pneumonia onset at any time (definition of severe hospital acquired pneumonia as for severe community acquired pneumonia):

<table>
<thead>
<tr>
<th>Core pathogens</th>
<th>Core antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>Ciprofloxacin or amikacin PLUS either</td>
</tr>
<tr>
<td></td>
<td>an anti-pseudomonal β-lactam/β-lactamase inhibitor</td>
</tr>
<tr>
<td></td>
<td>(pipercillin / tazobactam), or</td>
</tr>
<tr>
<td></td>
<td>ceftazidime or carbapenems (imipenem, meropenem)</td>
</tr>
<tr>
<td>Resistant Actinobacter species</td>
<td>Anti-pseudomonal cephalosporin (ceftazidime), or</td>
</tr>
<tr>
<td>MRSA</td>
<td>imipenem/meropenam, or amikacin</td>
</tr>
</tbody>
</table>

(pg 80) Grade C, Level IV

C Risk factors for specific pathogens and antibiotics to be added:

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Risk factor</th>
<th>Antibiotic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaerobic</td>
<td>Observed aspiration Abdominal surgery Putrid discharge</td>
<td>Clindamycin, metronidazole, or β-lactam/β-lactamase inhibitor</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>Coma Head injury Diabetes Renal failure</td>
<td>Vancomycin</td>
</tr>
<tr>
<td>MRSA</td>
<td>Outbreaks</td>
<td>Vancomycin</td>
</tr>
<tr>
<td>Legionella species</td>
<td>Corticosteroid use Outbreaks</td>
<td>Erythromycin</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>Prolonged ICU stay Antibiotic exposure Chronic lung disease AIDS</td>
<td>As in severe hospital acquired pneumonia (see Table 11)</td>
</tr>
</tbody>
</table>

(pg 80) Grade C, Level IV
Use of Antibiotics in Acute Infectious Diarrhoea in Adults

**GPP** In any patient with diarrhoea, obtain the following history:
- age
- evidence of an immuno-compromised state
- previous use of antibiotics
- history of travel
- scale of outbreak
  (pg 84)  

**GPP** Perform a focused physical examination in a patient with diarrhoea:
1. Look for signs of dehydration: loss of skin turgor, postural hypotension, increased pulse rate.
2. Record the temperature.
3. Examine the abdomen for tenderness or distension.
4. Perform a per rectal examination to look for the presence of blood in the stool.
  (pg 85)  

**GPP** In a patient with diarrhoea, look for red flags:
- Profuse, watery diarrhoea with dehydration.
- Passage of small volume stool, containing blood and mucus.
- Temperature ≥38.5°C.
- Passage of ≥6 times unformed stool in 24 hours.
- Duration of illness >72 hours.
- Severe abdominal pain, in a patient over the age of 50 years.
- Diarrhoea in the elderly (≥70 years of age).
- Diarrhoea in the immuno-compromised.

The presence of one or more of the above symptoms/signs suggests the diarrhoea is severe enough to warrant further evaluation and treatment.
  (pg 85)

---

Use of Antibiotics in Urinary Tract Infection

**B** It is not necessary to perform urine cultures in the management of uncomplicated cystitis in women. However, for the remainder of patients, pre-treatment cultures should be performed (pg 101).
  Grade B, Level IIb

Management of uncomplicated UTIs

**A** Antibiotic therapy is not recommended in the management of patients with asymptomatic bacteriuria, except in pregnant women (pg 102).
  Grade A, Level Ib

**A** The recommended 1st line therapy for uncomplicated cystitis in women is a 3-day course of trimethoprim-sulphamethoxazole (pg 102).
  Grade A, Level Ib

**A** Alternative treatment options for uncomplicated cystitis in women include the use of:
- Nitrofurantoin
- Fluoroquinolones
- 1st and 2nd-generation cephalosporins
- Trimethoprim
- β-lactam-lactamase-inhibitor combinations
  (pg 103)  

**A** The recommended duration of treatment of uncomplicated cystitis for various agents in women is:
- For 3 days with fluoroquinolones;
  Or
- For 7 days, with nitrofurantoin, 1st and 2nd-generation cephalosporins, trimethoprim and β lactam-lactamase inhibitor combinations.
  (pg 103)  

**A** Single-dose regimens are not recommended for routine use in the treatment of cystitis in women, as these regimens are less effective than multi-day regimens (pg 103).
  Grade A, Level Ia
Figure 3  Algorithm for the management of acute diarrhoea

- Acute diarrhoea
  - Hospital-acquired
  - Community-acquired
  - Travel history
  - Persistent diarrhoea
    - More than 7 days

Investigations

B  The faecal leucocyte, faecal lactoferrin, or Hemocult™ test may be useful screening tests in patients with moderate to severe acute infectious diarrhoea. The tests may be used to differentiate inflammatory and non-inflammatory diarrhoeal syndromes (pg 85).
  Grade B, Level III

A  Stool culture (salmonella, shigella and campylobacter) should be performed only in patients who have prolonged diarrhoea, or in patients who have clinical or biochemical evidence of inflammatory diarrhoea (pg 86).
  Grade A, Level Ib

A  For patients with diarrhoea that develops after three days of hospitalisation, or have recently received antibiotics or anti-neoplastics, an effort should be made to look for Clostridium difficile infection (pg 86).
  Grade A, Level Ib

C  Exposure of a traveller or hiker to untreated water and illnesses that persist for more than seven days should prompt evaluations for protozoal pathogens, especially giardia and cryptosporidium (pg 86).
  Grade C, Level IV

GPP  Endoscopy should be reserved for the investigation of patients with persistent or chronic diarrhoea (pg 87).
  GPP

Management

A  Fluid and electrolyte replacement plays a pivotal role in the management of all patients with acute diarrhoea. Oral rehydration is the treatment of choice (pg 87)
  Grade A, Level Ia

GPP  If an anti-motility agent is required, loperamide may be used (pg 88).
  GPP

B  Anti-motility agents should not be given to patients who have febrile dysentery (pg 88).
  Grade B, Level IIa
Anti-motility agents should not be given to patients who have suspected *Escherichia coli* O157:H7 infection, Shiga toxin-producing *Escherichia coli* infection, or frank bloody diarrhoea (pg 88).  

**Grade A, Level Ib**

In patients with moderate to severe inflammatory diarrhoea, an empirical course of quinolones can be given for 3-5 days (pg 89).

**Grade A, Level Ib**

In patients with moderate to severe traveller’s diarrhoea, an empirical course of quinolones can be given for 3-5 days (pg 89).

**Grade A, Level Ib**

**GPP** Elderly patients with moderate to severe diarrhoea may also be started on empirical antibiotic therapy (with quinolones) (pg 89).

**GPP**

All patients with moderate to severe infection with shigellosis should be treated with antibiotics. Patients with mild infections in the setting of good public health and hygiene can be observed (pg 90).

**Grade B, Level Iia**

Routine treatment with antimicrobials for patients with non-typhoid salmonellosis is not recommended (pg 90).

**Grade A, Level Ib**

Certain patients with intestinal salmonellosis should be treated – those who have fever and systemic toxicity, those with dysentery, the elderly, and patients who are immunocompromised or immunosuppressed (pg 91).

**Grade C, Level IV**

Certain patients with proven *Campylobacter* infection should be treated with antibiotics – those who are immunocompromised, the elderly, and healthy patients with moderate to severe dysentery or with evidence suggestive of bacteraemia (pg 91).

**Grade B, Level Iia**

Patients with enterotoxigenic *Escherichia coli* infections should be treated with antibiotics (pg 91).

**Grade A, Level Ib**

Patients with suspected or proven *Entero-haemorrhagic Escherichia coli* (*EHEC*) infection, especially with *Escherichia coli* O157:H7, should not be given antibiotics (pg 92).

**Grade A, Level Ib**

All patients with proven *Vibrio cholera* infection should be treated with antibiotics (pg 92).

**Grade A, Level Ib**

Patients with mild *Clostridium difficile* infection can be treated symptomatically and with withdrawal of the offending antibiotic (pg 92).

**Grade B, Level Iia**

Patients with moderate to severe *Clostridium* disease warrant prompt antibiotic treatment, with either metronidazole or vancomycin (pg 93).

**Grade A, Level Ib**
A Anti-motility agents should not be given to patients who have suspected *Escherichia coli* O157:H7 infection, Shiga toxin-producing *Escherichia coli* infection, or frank bloody diarrhoea (pg 88).

Grade A, Level Ib

A In patients with moderate to severe inflammatory diarrhoea, an empirical course of quinolones can be given for 3-5 days (pg 89).

Grade A, Level Ib

A In patients with moderate to severe traveller’s diarrhoea, an empirical course of quinolones can be given for 3-5 days (pg 89).

Grade A, Level Ib

GPP Elderly patients with moderate to severe diarrhoea may also be started on empirical antibiotic therapy (with quinolones) (pg 89).

GPP

B All patients with moderate to severe infection with shigellosis should be treated with antibiotics. Patients with mild infections in the setting of good public health and hygiene can be observed (pg 90).

Grade B, Level IIa

A Routine treatment with antimicrobials for patients with non-typhoid salmonellosis is not recommended (pg 90).

Grade A, Level Ib

C Certain patients with intestinal salmonellosis should be treated – those who have fever and systemic toxicity, those with dysentery, the elderly, and patients who are immunocompromised or immunosuppressed (pg 91).

Grade C, Level IV

F Certain patients with proven *Campylobacter* infection should be treated with antibiotics – those who are immunocompromised, the elderly, and healthy patients with moderate to severe dysentery or with evidence suggestive of bacteraemia (pg 91).

Grade B, Level IIa

A Patients with enterotoxigenic *Escherichia coli* infections should be treated with antibiotics (pg 91).

Grade A, Level Ib

A Patients with suspected or proven *Entero-haemorrhagic Escherichia coli* (EHEC) infection, especially with *Escherichia coli* O157:H7, should not be given antibiotics (pg 92).

Grade A, Level Ib

A All patients with proven *Vibrio cholera* infection should be treated with antibiotics (pg 92).

Grade A, Level Ib

B Patients with mild *Clostridium difficile* infection can be treated symptomatically and with withdrawal of the offending antibiotic (pg 92).

Grade B, Level IIa

A Patients with moderate to severe Clostridium disease warrant prompt antibiotic treatment, with either metronidazole or vancomycin (pg 93).

Grade A, Level Ib
Investigations

B The faecal leucocyte, faecal lactoferrin, or Hemocult™ test may be useful screening tests in patients with moderate to severe acute infectious diarrhoea. The tests may be used to differentiate inflammatory and non-inflammatory diarrhoeal syndromes (pg 85).

Grade B, Level III

A Stool culture ( salmonella, shigella and campylobacter) should be performed only in patients who have prolonged diarrhoea, or in patients who have clinical or biochemical evidence of inflammatory diarrhoea (pg 86).

Grade A, Level Ib

A For patients with diarrhoea that develops after three days of hospitalisation, or have recently received antibiotics or anti-neoplastics, an effort should be made to look for Clostridium difficile infection (pg 86).

Grade A, Level Ib

C Exposure of a traveller or hiker to untreated water and illnesses that persist for more than seven days should prompt evaluations for protozoal pathogens, especially giardia and cryptosporidium (pg 86).

Grade C, Level IV

GPP Endoscopy should be reserved for the investigation of patients with persistent or chronic diarrhoea (pg 87).

GPP

Management

A Fluid and electrolyte replacement plays a pivotal role in the management of all patients with acute diarrhoea. Oral rehydration is the treatment of choice (pg 87).

Grade A, Level Ia

GPP If an anti-motility agent is required, loperamide may be used (pg 88).

GPP

B Anti-motility agents should not be given to patients who have febrile dysentery (pg 88).

Grade B, Level IIa
Use of Antibiotics in Acute Infectious Diarrhoea in Adults

**GPP** In any patient with diarrhoea, obtain the following history:
- age
- evidence of an immuno-compromised state
- previous use of antibiotics
- history of travel
- scale of outbreak
  (pg 84)

**GPP** Perform a focused physical examination in a patient with diarrhoea:
1. Look for signs of dehydration: loss of skin turgor, postural hypotension, increased pulse rate.
2. Record the temperature.
3. Examine the abdomen for tenderness or distension.
4. Perform a per rectal examination to look for the presence of blood in the stool.
  (pg 85)

**GPP** In a patient with diarrhoea, look for red flags:
- Profuse, watery diarrhoea with dehydration.
- Passage of small volume stool, containing blood and mucus.
- Temperature ≥38.5°C.
- Passage of ≥6 times unformed stool in 24 hours.
- Duration of illness >72 hours.
- Severe abdominal pain, in a patient over the age of 50 years.
- Diarrhoea in the elderly (≥70 years of age).
- Diarrhoea in the immuno-compromised.

The presence of one or more of the above symptoms/signs suggests the diarrhoea is severe enough to warrant further evaluation and treatment.
  (pg 85)

---

Use of Antibiotics in Urinary Tract Infection

**R** It is not necessary to perform urine cultures in the management of uncomplicated cystitis in women. However, for the remainder of patients, pre-treatment cultures should be performed (pg 101).

  Grade B, Level IIb

Management of uncomplicated UTIs

**A** Antibiotic therapy is not recommended in the management of patients with asymptomatic bacteriuria, except in pregnant women (pg 102).

  Grade A, Level Ib

**A** The recommended 1st line therapy for uncomplicated cystitis in women is a 3-day course of trimethoprim-sulphamethoxazole (pg 102).

  Grade A, Level Ib

**A** Alternative treatment options for uncomplicated cystitis in women include the use of:
- Nitrofurantoin
- Fluoroquinolones
- 1st and 2nd-generation cephalosporins
- Trimethoprim
- β-lactam-lactamase-inhibitor combinations
  (pg 103)

  Grade A, Level Ib

**A** The recommended duration of treatment of uncomplicated cystitis for various agents in women is:
- For 3 days with fluoroquinolones;
  Or
- For 7 days, with nitrofurantoin, 1st and 2nd-generation cephalosporins, trimethoprim and β-lactam-lactamase inhibitor combinations.
  (pg 103)

  Grade A, Level Ia

**A** Single-dose regimens are not recommended for routine use in the treatment of cystitis in women, as these regimens are less effective than multi-day regimens (pg 103).

  Grade A, Level Ia
A Women with recurrent UTI should be treated with low dose antibiotic prophylaxis, using nitrofurantoin, trimethoprim-sulphamethoxazole, trimethoprim or cephalosporins (pg 105).

Grade A, Level Ib

C Initial therapy with intravenous cephalosporin and aminoglycoside, as for severe pyelonephritis, is recommended for the treatment of severe acute prostatitis (pg 107).

Grade C, Level IV

C Following clinical improvement, severe acute prostatitis should be treated with antibiotics, based on sensitivities, for a total duration of 4 weeks (pg 107).

Grade C, Level IV

C For patients with acute prostatitis of mild to moderate severity, initial therapy with oral fluoroquinolones, trimethoprim-sulphamethoxazole or trimethoprim is recommended. Treatment with antibiotics based on sensitivities should be given for a total duration of 4 weeks (pg 107).

Grade C, Level IV

A The recommended treatment for chronic bacterial prostatitis is fluoroquinolones for 4 weeks (pg 108).

Grade A, Level Ib

B Trimethoprim-sulphamethoxazole for 12 weeks can also be used in the treatment for chronic bacterial prostatitis (pg 108).

Grade B, Level III

C For patients with recurrent chronic prostatitis, suppressive, low-dose therapy with trimethoprim-sulphamethoxazole, trimethoprim or nitrofurantoin can be administered for 6 months or longer (pg 109).

Grade C, Level IV

A Antibiotic therapy is not indicated in the treatment of chronic prostatitis/chronic pelvic pain syndrome (pg 110).

Grade A, Level Ib

GPP Patients with symptoms of chronic prostatitis, but with negative urine or prostatic fluid cultures, should be referred to a Urologist for further management (pg 110).

GPP

C Antibiotics for patients with no risk factors, but late onset (>5 days) hospital acquired pneumonia, or severe hospital acquired pneumonia onset at any time (definition of severe hospital acquired pneumonia as for severe community acquired pneumonia):

<table>
<thead>
<tr>
<th>Core pathogens</th>
<th>Core antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>Ciprofloxacin or amikacin PLUS either an anti-pseudomonal β-lactam/β-lactamase inhibitor (pipercillin/tazobactam), or ceftazidime or carbapenems (imipenem, meropenem)</td>
</tr>
<tr>
<td>Resistant <em>Acinetobacter species</em></td>
<td>Anti-pseudomonal cephalosporin (ceftazidime), or imipenem/meropenem, or amikacin</td>
</tr>
<tr>
<td>MRSA</td>
<td>Add vancomycin</td>
</tr>
</tbody>
</table>

(pg 80) Grade C, Level IV

C Risk factors for specific pathogens and antibiotics to be added:

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Risk factor</th>
<th>Antibiotic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaerobic</td>
<td>Observed aspiration, Abdominal surgery, Putrid discharge</td>
<td>Clindamycin, metronidazole, or β-lactam/β-lactamase inhibitor</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>Coma, Head injury, Diabetes, Renal failure</td>
<td>Vancomycin</td>
</tr>
<tr>
<td>MRSA</td>
<td>Outbreaks</td>
<td>Vancomycin</td>
</tr>
<tr>
<td><em>Legionella species</em></td>
<td>Corticosteroid use, Outbreaks</td>
<td>Erythromycin</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>Prolonged ICU stay, Antibiotic exposure, Chronic lung disease, AIDS</td>
<td>As in severe hospital acquired pneumonia (see Table 11)</td>
</tr>
</tbody>
</table>

(pg 80) Grade C, Level IV
Use of Antibiotics in Hospital Acquired Pneumonia

Classification of hospital acquired pneumonia and antibiotic use

It is recommended that the initial empirical therapy be based upon targeting a core group of pathogens according to severity of illness, duration of hospitalisation and risk factors for specific pathogens (pg 77).

Grade B, Level III

Piperacillin-tazobactam is as safe and effective as ceftriaxone in the empirical treatment of severe hospital acquired pneumonia, hospital acquired pneumonia in the ICU and ventilator associated pneumonia (pg 77).

Grade A, Level Ib

Antibiotics for patients with no risk factors; hospital acquired pneumonia of mild to moderate severity, and of early onset (≤ 5 days):

<table>
<thead>
<tr>
<th>Core pathogens</th>
<th>Core antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enteric Gram-negative bacilli</td>
<td>3rd-generation cephalosporin e.g. intravenous ceftriaxone, or β-lactam/β-lactamase inhibitor e.g. intravenous ampicillin-sulbactam or amoxicillin-clavulanic acid, or quinolone e.g. ciprofloxacin.</td>
</tr>
<tr>
<td>Also, - Staphylococcus aureus</td>
<td>Consider adding cloxacillin or clindamycin.</td>
</tr>
<tr>
<td>- Hemophilus influenzae and Streptococcus pneumoniae</td>
<td>Consider adding azithromycin or clarithromycin. Alternative to above: newer quinolone as monotherapy.</td>
</tr>
<tr>
<td>If MRSA isolated ≥ 50% in ICU</td>
<td>Consider adding vancomycin.</td>
</tr>
</tbody>
</table>

(pg 79) Grade C, Level IV

Pyelonephritis

A Treatment options for severe acute pyelonephritis include: parenteral 3rd-generation cephalosporins, aminoglycosides, fluoroquinolones, β-lactams or β-lactam-β-lactamase-inhibitor combinations. Antibiotics should be modified when urine culture results become available. Oral antibiotic therapy can be started following clinical improvement, with a treatment course of 14 days (pg 111).

Grade A, Level Ib

GPP Initial treatment with intravenous aminoglycoside, together with a 1st or 2nd-generation cephalosporin, is recommended for hospitalized patients with acute pyelonephritis, because of the low sensitivity of hospital-acquired Escherichia coli to ceftriaxone and ciprofloxacin in the local context (pg 111).

GPP

A Treatment options for mild acute pyelonephritis include: oral fluoroquinolones, trimethoprim-sulphamethoxazole, β-lactams or β-lactam-β-lactamase-inhibitor combinations. Antibiotics should be modified when results of urine culture become available (pg 112).

Grade A, Level Ib

UTI in pregnancy

A Asymptomatic bacteriuria in pregnancy should be treated with antibiotics, based on culture and sensitivity, to reduce the risk of pyelonephritis and other complications (pg 112).

Grade A, Level Ia

B For acute cystitis in pregnancy, empirical therapy with 1st or 2nd-generation cephalosporins, nitrofurantoin or trimethoprim-sulphamethoxazole (caution in 3rd trimester) is recommended. Treatment should be modified based on culture results and appropriate antibiotics should be administered for 7 days (pg 112).

Grade B, Level III

B For pyelonephritis in pregnancy, empirical therapy with a 3rd-generation cephalosporin is recommended. Treatment should be modified based on culture results and appropriate antibiotics should be administered for 14 days (pg 113).

Grade B, Level III
Management of Complicated UTIs

Grade C, Level IV

Antibiotic treatment of complicated urinary tract infections should be based on cultures and sensitivity. When symptoms warrant initiation of empirical therapy, cultures must be obtained prior to antibiotic therapy and therapy modified based on results (pg 114).

Grade A, Level lb

For complicated urinary tract infections of mild to moderate severity, initial therapy with oral fluoroquinolones or trimethoprim-sulphamethoxazole is recommended (pg 114).

Grade C, Level IV

For complicated urinary tract infections of mild to moderate severity, alternative regimens for empirical treatment include 2nd-generation cephalosporins, β-lactams, or β-lactam-β-lactamase-inhibitor combinations (pg 114).

Grade A, Level lb

After the initiation of empirical antibiotic therapy, culture-based appropriate therapy is administered for 14 days as a minimum (pg 116).

Symptomatic UTIs occurring in patients with a short-term indwelling urinary catheter should be treated by removing the catheter, followed by a 7-day course of antibiotics. For patients with long-term indwelling urinary catheters, symptomatic UTIs can be treated with a 7-day course of antibiotics (pg 116).

In patients with renal impairment, effective antibiotic therapy requires the use of antibiotics which achieve therapeutic concentrations in the urine and are appropriately dose-adjusted for the level of renal failure (pg 116).
Table 1  Fine pneumonia severity index

<table>
<thead>
<tr>
<th>CHARACTERISTIC</th>
<th>POINTS ASSIGNED*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic factor</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>Age (yr)</td>
</tr>
<tr>
<td>Women</td>
<td>Age (yr) - 10</td>
</tr>
<tr>
<td>Nursing home resident</td>
<td>+10</td>
</tr>
<tr>
<td>Coexisting illnesses*</td>
<td></td>
</tr>
<tr>
<td>Neoplastic disease</td>
<td>+30</td>
</tr>
<tr>
<td>Liver disease</td>
<td>+20</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>+10</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>+10</td>
</tr>
<tr>
<td>Renal disease</td>
<td>+10</td>
</tr>
<tr>
<td>Physical-examination findings</td>
<td></td>
</tr>
<tr>
<td>Altered mental status†</td>
<td>+20</td>
</tr>
<tr>
<td>Respiratory rate ≥30/min</td>
<td>+20</td>
</tr>
<tr>
<td>Systolic blood pressure &lt;90 mmHg</td>
<td>+20</td>
</tr>
<tr>
<td>Temperature &lt;35°C or &gt;40°C</td>
<td>+15</td>
</tr>
<tr>
<td>Pulse ≥125/min</td>
<td>+10</td>
</tr>
<tr>
<td>Laboratory and radiographic findings</td>
<td></td>
</tr>
<tr>
<td>Arterial pH &lt;7.35</td>
<td>+30</td>
</tr>
<tr>
<td>Blood urea nitrogen ≥30 mg/dl (11 mmol/liter)</td>
<td>+20</td>
</tr>
<tr>
<td>Sodium &lt;130 mmol/liter</td>
<td>+20</td>
</tr>
<tr>
<td>Glucose ≥250 mg/dl (14 mmol/liter)</td>
<td>+10</td>
</tr>
<tr>
<td>Hematocrit &lt;30%</td>
<td>+10</td>
</tr>
<tr>
<td>Partial pressure of arterial oxygen &lt;60 mmHg†</td>
<td>+10</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>+10</td>
</tr>
</tbody>
</table>

* A total point score for a given patient is obtained by summing the patient’s age in years (age minus 10 for women) and the points for each applicable characteristic.

† Neoplastic disease is defined as any cancer, except basal- or squamous-cell cancer of the skin, that was active at the time of presentation or diagnosed within one year of presentation. Liver disease is defined as a clinical or histologic diagnosis of cirrhosis or another form of chronic liver disease, such as chronic active hepatitis. Congestive heart failure is defined as systolic or diastolic ventricular dysfunction documented by history, physical examination, and chest radiograph, echocardiogram, multiple gated acquisition scan, or left ventriculogram. Cerebrovascular disease is defined as a clinical diagnosis of stroke or transient ischemic attack or stroke documented by magnetic resonance imaging or computed tomography. Renal disease is defined as a history of chronic renal disease or abnormal blood urea nitrogen and creatinine concentrations documented in the medical record.

‡ Altered mental status is defined as disorientation with respect to person, place, or time that is not known to be chronic, stupor, or coma.

![Approach to management of urinary tract infections in adults](image_url)
Use of Antibiotics in Acute Bacterial Meningitis in Immunocompetent Adults

Diagnosis of acute bacterial meningitis

C Initial physical examination should include evaluation for:
  - level of consciousness
  - cranial nerve palsies
  - focal deficits
  - meningismus
  - increased intracranial pressure
  - critical trauma
  (pg 122)  

Grade C, Level IV

B A lumbar puncture is recommended in all adult patients with suspected meningitis except when a clear contraindication exists (pg 122).

Grade B, Level III

Antibiotic therapy

C If bacterial meningitis is suspected, antibiotic treatment must be started immediately, regardless of any investigations undertaken (pg 124).

Grade C, Level IV

B In the treatment of meningitis with a typical meningococcal rash, intravenous penicillin G, 20-24 million units daily, should be given (pg 124).

Grade B, Level III

B For adults without a typical meningococcal rash, intravenous ceftriaxone, 2g 12 hourly, should be given (pg 124).

Grade B, Level III

C If the patient comes from an area where penicillin-resistant Streptococcus pneumoniae are common (MIC ≥ 0.1ug/ml) then add intravenous vancomycin 1g 12 hourly (pg 124).

Grade C, Level IV

The quinolones are not recommended for the outpatient treatment of community acquired pneumonia in categories I & II (pg 69).

Grade C, Level IV

A A switch from I.V. to oral antimicrobials and prompt hospital release is recommended for patients in low-intermediate risk categories who respond promptly or become clinically stable after receiving initial antimicrobial treatment (pg 73).

Grade A, Level 1a

B Criteria for discharge from hospital.

- Stable vital signs for 24 hours (i.e. temperature <37.8°C, respiratory rate <24/min, systolic BP ≥90mmHg, O₂ saturation >90% while breathing room air).
- Patient able to take diet.
- Patient able to take oral antibiotics.
- No other active clinical or psycho-social problems requiring hospital stay.

(pg 73)  

Grade B, Level III

B In addition to the usual outcomes of mortality and hospital length of stay, the time to the first dose of antibiotics in elderly patients (>65 years) should be a key indicator of the evaluation of the quality of community acquired pneumonia management (pg 74).

Grade B, Level III
Use of Antibiotics in Community Acquired Pneumonia

Risk Stratification

Risk stratification is a key step in the management of community acquired pneumonia (pg 64).

Grade B, Level IIa

All patients with severe community acquired pneumonia (Category IV) in the ICU should be treated empirically for *Burkholderia pseudomallei*. (pg 69).

Grade B, Level III

Inpatient Investigations

Microbiological, haematological, biochemical and serological tests (see list below) are recommended for patients in risk Categories III and IV upon presentation.

The following microbiological tests should be done before starting antibiotics in patients with moderate to severe CAP (Categories III and IV). Initial microbiological studies may have limited value in the management of patients with low risk CAP (Categories I & II):

- Sputum Gram stain and aerobic culture (mycobacterial smear and culture where appropriate).
- Blood aerobic culture.
- Pleural fluid Gram stain and culture.
- Urine for *Legionella* antigen.

The other investigations are:

- Blood count with differentials, and smear for toxic granulations.
- Biochemistry, including renal and liver function (Blood gas where necessary).
- Consider HIV testing and work-up for *Pneumocystis carinii*.
- Optional serological testing for atypical agents.

(pg 69)

Grade C, Level IV

Empirical Antibiotic Therapy

The initial choice for empirical antibiotic therapy should be based on the risk category and relative prevalence of major pathogens (pg 69).

Grade A, Level Ib

For adults over the age of 50 years, history of alcoholism, diabetes and pregnancy without a typical meningococcal rash, consider adding intravenous ampicillin, 2g 4 hourly, to ceftriaxone as above.

Grade C, Level IV & GPP

If there is a clear history of anaphylaxis to β-lactams, give intravenous chloramphenicol 25 mg/kg (maximum 1g) 6 hourly. Add vancomycin 1g 12 hourly, because of the possibility of penicillin-resistant *Streptococcus pneumoniae* and likely failure of chloramphenicol in this group.

Grade C, Level IV

If Gram-negative diplococci are visible on Gram stain of cerebrospinal fluid (CSF), or if *Neisseria meningitidis* is isolated from CSF or blood, continue with intravenous penicillin G, 24 million units daily.

Grade B, Level III

For patients who do not have adequate response to penicillin, the treatment should be changed to ceftriaxone.

Grade C, Level IV

If penicillin-sensitive *Streptococcus pneumoniae* is isolated from CSF or blood, intravenous penicillin G 24 million units is recommended. If cephalosporin-sensitive *Streptococcus pneumoniae* is isolated, intravenous ceftriaxone 2g 12 hourly should be given. Add on intravenous vancomycin, 1g 12 hourly, if penicillin-resistant and cephalosporin-resistant *Streptococcus pneumoniae* is isolated from blood or CSF. Continue intravenous therapy for 10-14 days.

Grade C, Level IV

For *Haemophilus influenzae* meningitis, intravenous ceftriaxone, 2g 12 hourly, is recommended.

Grade B, Level IIb

If Gram-positive coccobacilli suggestive of *Listeria monocytogenes* is visible on Gram stain of CSF, or if *Listeria monocytogenes* is isolated from blood or CSF, intravenous ampicillin, 2g 4 hourly, and gentamicin 5 mg/kg 24 hourly (single or divided 8 hourly doses) for more than 21 days is recommended.

Grade C, Level IV
Recommended duration of therapy according to the type of pathogen causing meningitis. (pg 126)

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Recommended duration of therapy</th>
<th>Grade and level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemophilus influenzae</td>
<td>7-10 days</td>
<td>Grade B, Level IIb</td>
</tr>
<tr>
<td>Neisseria meningitidis</td>
<td>7-10 days</td>
<td>Grade B, Level III</td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
<td>10-14 days</td>
<td>Grade C, Level IV</td>
</tr>
<tr>
<td>Listeria monocytogenes</td>
<td>≥ 21 days</td>
<td>Grade C, Level IV</td>
</tr>
<tr>
<td>Gram-negative bacilli, other than Haemophilus influenzae</td>
<td>21 days</td>
<td>Grade C, Level IV</td>
</tr>
</tbody>
</table>

The duration of therapy should be tailored to the individual patient on the basis of the clinical and microbiological response (pg 126). Grade C, Level IV

**Adjunctive dexamethasone therapy in bacterial meningitis**

A In adults with suspected or proven pneumococcal meningitis, dexamethasone 10 mg 6 hourly should be given for 4 days with the first dose administered 15-20 min before, or at least concomittant with, the first dose of antimicrobial therapy (pg 126). Grade A, Level I b

A Dexamethasone should only be continued if the CSF Gram stain reveals Gram-positive diplococci or if blood or CSF cultures are positive for Streptococcus pneumoniae (pg 126). Grade A, Level I b

A Adjunctive dexamethasone should not be given to adult patients who have already received antimicrobial therapy as in this circumstance, dexamethasone is unlikely to improve patient outcome (pg 126). Grade A, Level I b

**Prevention of meningococcal meningitis**

C Chemoprophylaxis should be offered to close contacts of cases, irrespective of vaccination status, in those who have:

- Prolonged close contact with the case in a household setting during the seven days before onset of illness.

---

**Figure 1 Algorithm outlining a risk-stratification approach to antibacterial therapy of acute exacerbations of chronic bronchitis**

![Diagram of Algorithm](image)

- **No Risk factors**
  - Age <65
  - FEV1 normal
  - <4 AECB in 12 mth
  - No comorbidities

- **Suspected AECB**
  - Increased DYSPIA?
  - Increased SPUMT VOLUME
  - Increased SPUMT PURULENCE?

- **Risk factors (one or more)**
  - Age <65
  - FEV1 <50% predicted
  - ≥4 AECB in last 12 months
  - Cardiac disease
  - Others: home oxygen, chronic oral steroid use, antibiotic use in past 3 months

- **Simple COPD**
  - Advanced macrolide (azithromycin, clarithromycin)
  - Ketolide (telithromycin)
  - Cephalosporin (cefuroxime, cefpodoxime*, cefdinir*)
  - Doxycycline

- **Complicated COPD**
  - Fluoroquinolone (moxifloxacin, gemifloxacin, gatifloxacin, levofloxacin)
  - Amoxicillin-clavulanate

**Chronic suppurative bronchitis**

- (at risk of pseudomonas infection)
  - Consider ciprofloxacin and obtain sputum culture

- **Worsening clinical status or inadequate response in 72 hours**

- **Re-evaluate**
  - Consider sputum culture

* currently not available in Singapore
Patients with exacerbations without an increase in purulent sputum do not need antibiotic therapy unless there is a consolidation on a chest radiograph or clinical signs of pneumonia (pg 55).

Grade B, Level Ila

Patients with purulent exacerbations but who have no risk factors for treatment failure or no enhanced association with more virulent or resistant bacterial pathogens can be treated with an advanced macrolide (azithromycin, clarithromycin), a cephalosporin (cefuroxime), or doxycycline (pg 56).

Grade B, Level Ila

Patients with purulent exacerbations and who have risk factors that are associated with an increased likelihood of treatment failure or infection with more virulent or resistant organisms should be given antibiotics with enhanced antimicrobial coverage, namely the newer fluoroquinolones (moxifloxacin, gemifloxacin*, gatifloxacin, levofloxacin) or amoxicillin-clavulanate (pg 59).

Grade A, Level Ib

GPP In a patient with AECB requiring repeat antibiotic therapy within 3 months, a new class of antibiotics should be used (pg 60).

GPP

- Contact at a day-care centre.
- Transient close contact with a case where there was exposure to the patient’s secretions (e.g. through mouth-to-mouth resuscitation, endotracheal intubation or endotracheal tube management) around the time of admission to hospital.

Grade C, Level IV

Close contacts of patients with meningococcal infection should receive one of the following regimens:

- Rifampicin:
  - Adults: 600 mg, 12 hourly for 2 days (4 doses).
  - Children (1-6 years): 10 mg/kg, 12 hourly for 2 days (4 doses).
  - Children (3-11 months): 5 mg/kg 12 hourly for 2 days (4 doses).

- Ciprofloxacin:
  - Adults: 500 mg as a single dose.
  - Children: Use of ciprofloxacin is not recommended.

- Ceftriaxone:
  - Adults: 250 mg as a single intramuscular dose.
  - Children (< 15 years): 125 mg as a single intramuscular dose.

Grade C, Level IV

If other antibiotics have been used for treatment, the index patient should receive prophylactic antibiotics for eradication of nasopharyngeal carriage before being discharged from hospital (pg 128).

Grade C, Level IV

* currently not available in Singapore
Figure 5  Algorithm for the initial management of a patient with acute meningitis

- **Acute Bacterial Meningitis**
  - Typical meningococcal rash (petechial, purpuric)
  - I.V. ceftriaxone, 2g 12H
  - I.V. ampicillin, 2g 4H
  - I.V. penicillin G, 24 million units daily
  - CSF or blood culture: Penicillin-sensitive Streptococcus pneumoniae*
  - Blood/CSF culture: Penicillin-resistant Streptococcus pneumoniae*

- **No rash**
  - I.V. ceftriaxone, 2g 12H
  - I.V. vancomycin, 1g 12H
  - Area where penicillin-resistant Streptococcus pneumoniae prevalent

- **Switch to I.V. ceftriaxone, 2g 12H**
  - Continue I.V. ceftriaxone, 2g 12H or switch to I.V. Pencillin G
  - No response:
    - Gram stain CSF: Gram negative diplococci OR Blood/CSF culture: Neisseria meningitides*
  - Response:
    - Discontinue ceftriaxone, Continue ampicillin, 2g 4H.
      - Add I.V. Gentamicin, 5mg/kg 24H

- **Continue I.V. ceftriaxone 2g 12H + vancomycin, 1g 12H**

*To continue initial antibiotics if culture is negative and patient is responding*

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**Acute Bronchitis and Exacerbation of Chronic Bronchitis**

- **B** The adamantanes, rimantadine and amantadine, are not recommended for influenza A because of increasing drug resistance (pg 47).
  - Grade B, Level III

- **Acute exacerbations of chronic bronchitis (AECB)**
  - **A** Patients with acute exacerbation of severity of Anthonisen Type I (having increased dyspnea, increased sputum production, and increased sputum purulence) and Anthonisen Type II (two of the three symptoms) should be given antibiotic therapy (pg 54).
    - Grade A, Level Ib
  
  - **A** Patients with one or more of the following risk factors should be given antibiotic therapy: more than 4 exacerbations within the past year; a co-morbid condition, such as diabetes, asthma, or a history of coronary artery disease, or marked airway obstruction (pg 55).
    - Grade A, Level Ib

- **C** In a patient with an acute cough illness lasting less than 3 weeks, pneumonia should be ruled out by history and clinical examination. Chest X-ray for pneumonia is not necessary in the absence of red flags (pg 50).
  - Grade B, Level III

- **A** Routine antibiotic treatment of acute bronchitis is not recommended, regardless of the duration of cough (pg 51).
  - Grade A, Level Ia

- **B** Antibiotic therapy in acute bronchitis should be considered if the patient is ≥ 60 years or ill at the outset (pg 51).
  - Grade B, Level III

- **E** Once a diagnosis of acute bronchitis has been made, the physician should address symptomatic treatment and patient expectations of the visit (pg 51).
  - Grade C, Level IV

- **F** All cases of acute bronchitis should be followed up and antibiotics considered if they are not recovering (pg 52).
  - Grade B, Level III
Isolated infection of a frontal or sphenoid sinus is a rare but potentially dangerous condition, usually caused by bacteria, and should be referred to hospital for treatment (pg 42).

**Acute laryngitis**

**GPP** If symptoms last for more than 3 weeks, the condition is classified as chronic laryngitis, for which an underlying cause must be further investigated. Underlying causes include laryngeal polyps, cancer, laryngeal tuberculosis, and gastro-esophageal reflux (pg 43).

**Antibiotic treatment for acute laryngitis currently should be reserved for high-risk patients, patients with severe symptoms, or in the presence of an identifiable organism on Gram stain and culture (pg 44).**

**Acute otitis media**

**B** Antibiotics are unnecessary in acute otitis media (pg 45).

**Avoid local treatment with antimicrobial eardrops in acute otitis media (pg 45).**

**Common cold**

**A** Antibiotics should not be given for the common cold (pg 45).

**Antibiotics should not be given for the common cold which is accompanied by mucopurulent rhinitis (pg 47).**

**Influenza**

**A** Neuraminidase inhibitors (NIs) are effective for the prevention and treatment of influenza (pg 45).

**Use of Antibiotics in the Elderly**

**Unique Aspects of Infections in Older People**

**B** An infectious aetiology should be sought when there is:
- A change in functional status and the oral temperature is ≥37.2°C, or
- An increase in temperature of ≥1.3°C over the baseline.

**Infection should be considered in the differential diagnosis of older people who present, within a short period of time:**
- With only non-specific symptoms, including functional decline; or
- With atypical complaints.

**Doctors should be alert to a leucocytosis with left shift or left shift alone, as these have good predictive value for diagnosing bacterial infections in older people (pg 133).**

**Treatment recommendations**

**Empirical antibiotic therapy for specific infections is a valid and practical option in older persons, given the higher risk of adverse outcomes, diverse infectious causes and increased difficulty in obtaining diagnostic specimens. In general, this therapy should include a broad-spectrum beta-lactam antibiotic (pg 134).**

**When culture results are not available yet, the choice of antibiotic should be guided by knowledge of the likely pathogens encountered in older people in different settings (pg 134).**

**Aminoglycosides should be reserved for selected situations: septic shock without a specific aetiological diagnosis, confirmed or suspected *Pseudomonas aeruginosa* infections, or where the cultured organism is only susceptible to an aminoglycoside (pg 134).**
The patient’s renal function should always be considered when prescribing antibiotics in older people, particularly if the antibiotics are excreted primarily by the kidneys (e.g. aminoglycosides, fluoroquinolones, and some cephalosporins such as ceftazidime). Estimated creatinine clearance should be used to guide appropriate dosing of such antibiotics (pg 135).

Grade C, Level IV

There should be monitoring for adverse effects of antibiotics during therapy. In addition to specific adverse effects, geriatric syndromes or functional decline should also be considered as possible adverse effects of antibiotics (pg 135).

Grade C, Level IV

Additional Antibiotic Consideration in the Elderly

GPP Awareness of potential drug-drug interactions should guide the choice of antibiotics (pg 135).

GPP

Assistance from caregivers who can help administer medications should be sought where necessary. Keeping the antibiotic regimen as simple as possible is also useful in improving compliance (pg 136).

Grade C, Level IV

Special Situations in the Elderly

The choice of antibiotic is usually guided by the likely spectrum of bacterial flora that might be encountered. Broad-spectrum antibiotics that include Gram-negative cover are usually required. For pneumonia in the setting of long-term care institutions, antibiotic cover for anaerobes (e.g. amoxicillin-clavulanate) should be considered if aspiration is a concern (pg 136).

Grade C, Level IV

The following measures to prevent aspiration are recommended:

Reduce the risk of aspiration by:
- Avoiding sedative medication;
- Minimising the use of nasogastric tubes; and
- Elevating the head of bed during and after feeding.

(pag 137)

Grade C, Level IV

Group A beta-haemolytic streptococcal-positive patients should be treated with penicillin V, for seven days (pg 38).

Grade A, Level Ib

Throat cultures are not recommended for the routine primary evaluation of adults with pharyngitis (pg 38).

Grade A, Level Ib

Administer appropriate analgesics, antipyretics, and supportive care to all patients with pharyngitis (pg 38).

Grade C, Level IV

Acute epiglottitis

E The antibiotic of choice to treat acute epiglottitis is ceftriaxone or chloramphenicol (pg 40).

Grade B, Level IIb

Acute rhinosinusitis

E Sinus radiography is not recommended for diagnosis in routine cases.

(pag 41)

Grade B, Level IIb

Symptomatic treatment and reassurance is the preferred initial management strategy for patients with mild symptoms of acute rhinosinusitis (pg 42).

Grade B, Level IIb

Antibiotic therapy should be reserved for:
- Patients with moderately severe symptoms who meet the criteria for the clinical diagnosis of acute bacterial rhinosinusitis (symptoms that last >7 days and include maxillary pain in the face or teeth and purulent nasal secretions); and
- Patients with severe rhinosinusitis symptoms, regardless of duration of illness.

(pag 42)

Grade B, Level IIb

For the initial treatment of acute bacterial maxillary rhinosinusitis, amoxicillin or penicillin for 7-14 days is recommended (pg 42).

Grade A, Level Ia
Antibiotics should only be chosen after considering the following questions:
1. Is there an infection?
2. What is the site of infection and the most likely causative organism?
3. Will the antibiotic reach the site of infection?
4. What side effects or drug interactions might this antibiotic have?
5. What adjustments should be made for the individual patient, e.g. the young infant, the elderly, patients with renal failure?
6. What is the appropriate dose and duration of treatment for the site and type of infection? (pg 30)

Patients or their caregivers should be clearly instructed on the dose and the necessity of finishing a course of treatment (pg 30).

Use of Antibiotics in Acute Upper Respiratory Tract Infections (URTI) in Adults

Antibiotic use in URTI

The use of antibiotics for a large portion of URTIs is not recommended because these are viral infections, for which antibiotics do not provide clinical benefit (pg 34).

Non-specific respiratory infections

Antibiotic treatment of adults with non-specific upper respiratory tract infection is not recommended (pg 36).

The use of antibiotics is not recommended when there is purulent secretion from the nares or throat, in patients with uncomplicated URTI (pg 36).

Acute pharyngitis (sore throat)

Patients identified with Group A beta-haemolytic streptococcal pharyngitis should be treated with antibiotics to prevent complications (pg 37).