These guidelines have been withdrawn

MOH clinical practice guidelines are considered withdrawn five years after publication unless otherwise specified in individual guidelines.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.

CLINICAL PRACTICE GUIDELINES

Use of Antibiotics in Paediatric Care

Ministry of Health

NMRC
National Medical Research Council

Chapter of Paediatricians
Academy of Medicine
Singapore

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MOH Clinical Practice Guidelines 3/2002

Levels of evidence and grades of recommendation

Levels of evidence

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

Grades of recommendation

Grade	Recommendation
A (evidence levels Ia, Ib)	Requires at least one randomised controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation.
B (evidence levels IIa, IIb, III)	Requires availability of well conducted clinical studies but no randomised clinical trials on the topic of recommendation.
C (evidence level IV)	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.
GPP (good practice points)	Recommended best practice based on the clinical experience of the guideline development group.

CLINICAL PRACTICE GUIDELINES

Use of Antibiotics in Paediatric Care

MOH Clinical Practice Guidelines 3/2002

Available on the MOH website: http://www.gov.sg/moh/pub/cpg/cpg.htm

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, nor should they be construed as including all proper methods of care or excluding 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

Antibiotics have played a critical role in the war against bacterial infections since the discovery of penicillin by Sir Alexander Fleming in 1928. The effectiveness of these drugs has resulted in their widespread use by doctors and has benefitted a countless number of patients. On the other hand, the indiscriminate or inappropriate use of antibiotics can accelerate the development of anti-microbial resistant bacterial strains. This has become an increasing source of concern for public health and infectious disease specialists as multi-drug resistance may be the Achilles heel in our war against bacteria. The judicious use of antibiotics is therefore an important way to reduce the problem of anti-microbial resistance.

Since the previously published clinical practice guidelines on the Use of Antibiotics in Adults in April 2000, the need for separate guidelines on the use of antibiotics in children was recognised. The Ministry therefore approached the Chapter of Paediatricians of the Academy of Medicine to undertake this important task. The workgroup appointed by the Ministry has developed these guidelines to aid doctors when they prescribe antibiotics for childhood infections. The guidelines include advice on the appropriate indications, selection and recommended dosages of antibiotics. I hope that doctors, particularly primary care physicians will find these guidelines useful when treating paediatric infections, and by doing so, also assist in our efforts to reduce the problem of antibiotic resistance.

Finally, I would like to record the Ministry's gratitude to the workgroup for their hard work and commitment in producing this set of guidelines.

PROFESSOR TAN CHORH CHUAN
DIRECTOR OF MEDICAL SERVICES

Contents

Executive summary of recommendations

RESPIRATORY TRACT INFECTIONS

UPPER RESPIRATORY TRACT INFECTIONS

A Upper respiratory tract infections are usually viral in origin and often do not require antibiotics.

Grade A, Level Ia

Acute Rhinitis

A Antibiotics are not indicated for acute rhinitis since the majority are viral in origin.

Grade A, Level Ia

Pharyngitis and tonsillitis

The following antibiotics should only be given to an older child with possible *Streptococcus group A* infection who looks unwell, has prolonged fever, sore throat, exudates over the tonsils and enlarged, tender cervical lymph nodes:

A Penicillin V (50mg/kg/day divided 6hrly for 10 days)

Grade A, Level Ia

A Amoxycillin (50mg/kg/day divided 8hrly for 6days) or

Grade A, Level Ia

A Erythromycin (50mg/kg/day divided 6-8hrly for 10 days for patient with penicillin allergy)

Grade A, Level Ib

Acute sinusitis

A Acute sinusitis is commonly bacterial in origin and requires amoxycillin or cotrimoxazole* [Trimethoprim (TMP) 8mg/kg/day plus Sulfamethoxazole (SMX) 40mg/kg/day divided 12hrly] for 7-10 days if there is a history of penicillin allergy.

Grade A, Level Ia

C If there is no response after 72 hours, it is advisable to switch to amoxycillin/clavulanate (amoxycillin 50mg/kg/day + clavulanate 7mg/kg/day divided 12hrly) or ampicillin/sulbactam (25-50mg/kg/day divided 12hrly).

Grade C, Level IV

GPP Referral to an ENT specialist is recommended in the presence of complications or when symptoms persist beyond three weeks.

Acute otitis externa

C Acute otitis externa is commonly caused by *Staphylococcus aureus.* Topical antimicrobial eardrops (e.g. polymyxin, framycetin) are sufficient for mild infections. Severe infections can be treated with oral cloxacillin for 7 days or erythromycin (if the patient is allergic to penicillin).

Grade C, Level IV

Acute otitis media

A Acute otitis media can be treated with amoxycillin for 7 days.

Grade A, Level Ia

Contra-indicated in children with G6PD deficiency

If there is no response after treatment for 72 hours, high dosages of the following are recommended:

- **A** amoxycillin/clavulanate

Grade A, Level Ia

- **A** cefuroxime (15-30mg/kg/day divided 12hrly)

Grade A, Level Ib

A In the presence of penicillin allergy, treat with erythromycin or cotrimoxazole*.

Grade A, Level Ia

Recurrent otitis media and otitis media with effusion

A A child with recurrent otitis media and otitis media with effusion should be referred to an ENT surgeon.

Grade A, Level Ia

LOWER RESPIRATORY TRACT INFECTIONS

Acute bronchiolitis

A Acute bronchiolitis is caused by respiratory viruses (mainly Respiratory Syncytial Virus) and antibiotics are not indicated. Antibiotics can be considered in the presence of bacterial superinfection.

Grade A, Level Ib

Acute laryngotracheobronchitis

C Respiratory viruses, mainly parainfluenza virus, are responsible for acute laryngotracheobronchitis. Antibiotics are not indicated.

Grade C, Level IV

Contra-indicated in children with G6PD deficiency

Acute bronchitis

A Acute bronchitis is mainly viral in origin and antibiotics are not routinely recommended.

Grade A, Level Ia

B A macrolide is recommended in an older child when mycoplasma infection is suspected.

Grade B, Level III

Pneumonia

C Referral to hospital is recommended for newborns with pneumonia.

Grade C, Level IV

C In children less than 2 years old, the majority of pneumonias are viral in aetiology and antibiotic therapy is not warranted. Bacterial infection is suggested by toxic appearance, prolonged fever, cough and breathlessness persisting for more than 1 week, crepitations or decreased breath sounds on auscultation, leukocytosis and lobar consolidation. Amoxycillin or erythromycin is the drug of choice. If drug resistant *Streptococcus pneumoniae* is suspected, high dose amoxycillin is indicated. Second line drugs include amoxycillin/clavulanate or ampicillin/sulbactum.

Grade C, Level IV

C For children older than 2 years old, amoxycillin (high dose if resistant *Streptococcus* p*neumoniae* is suspected) is recommended. Second line drugs include amoxycillin/clavulanate or ampicillin/sulbactum. A macrolide is recommended if mycoplasma infection is suspected or penicillin allergy is present.

Grade C, Level IV

GASTROINTESTINAL DISEASES

GPP The mainstay of management of gastroenteritis is the prevention and correction of dehydration and electrolyte imbalance.

Viral diarrhoea

GPP Viral diarrhoea should not be treated with antibiotics.

Nontyphoidal salmonella infection

A Nontyphoidal salmonella infection should not be treated routinely with antibiotics.

Grade A, Level Ia

C Antibiotics are required for patients with evidence of extra-intestinal spread such as septicaemia, in the very young (< 3 month old) and in the immunocompromised child.

Grade C, Level IV

C Cotrimoxazole* (TMP, 10mg/kg/day plus SMX, 50mg/kg/day divided 12hrly), ampicillin (200mg/kg/day divided 6hrly) or a third generation cephalosporin (e.g ceftriaxone 75-100mg/kg/day 24hrly) can be given for up to 14 days.

Grade C, Level IV

Escherichia coli diarrhoea

C When the disease is severe, antibiotics such as cotrimoxazole* or ampicillin for 5 to 7 days may be required.

Grade C, Level IV

Contra-indicated in children with G6PD deficiency

Shigellosis

B Shigellosis responds to antibiotics. Cotrimoxazole*, ampicillin or a third generation cephalosporin can be given for up to 5 days.

Grade B, Level IIa

Cholera

C Antibiotics decrease the duration of diarrhoea, excretion of organisms in the stool and total amount of fluid loss. Doxycycline (6mg/kg as a single dose) is the drug of choice for children above 8 years old.

Grade C, Level IV

Campylobacter gastroenteritis

C Erythromycin (50mg/kg/day divided 6hrly) for 7 to 10 days can be used for patients with severe ongoing illness or if risk factors are present.

Grade C, Level IV

Yersinia enterocolitis

C Diarrhoea is self-limiting except for the immunocompromised child who may respond to a third generation cephalosporin in combination with gentamicin (5mg/kg/day in divided doses).

Grade C, Level IV

Amoebiasis

C Antibiotics are employed in the eradication of the amoeba. Treatment consists of metronidazole (35-50mg/kg/day divided 8hrly orally for 10 days) or tinidazole (50-60mg/kg/day as a single dose daily for 3 days) followed by paromomycin (25-35mg/kg/day divided 8hrly for 7 days).

Grade C, Level IV

Contra-indicated in children with G6PD deficiency

Giardiasis

A Metronidazole (22.5mg/kg/day divided 8hrly orally for 7 days) is effective.

Grade A, Level Ia

Cryptosporidium

C Diarrhoeal illness is self-limiting except for the immunocompromised child. Those who are seriously ill may respond to paromomycin in combination with azithromycin.

Grade C, Level IV

Helicobacter pylori

B Eradication of *Helicobacter pylori* is important in the prevention of recurrence of *Helicobacter pylori*-associated peptic ulcer disease. Treatment consists of omeprazole, clarithromycin and metronidazole for 1 to 2 weeks

Grade B, Level III

ACUTE BACTERIAL MENINGITIS

GPP Blood culture, CSF microscopy and culture should be carried out when a clinical diagnosis of meningitis is made. Empirical antibiotics should be started with necessary alteration when the culture and sensitivities become available

B For infants below 1 month of age, the likely organisms are Group B Streptococcus, *E. coli* or *Listeria monocytogenes.* Ampicillin** (200-300mg/kg/day divided 4-8hrly) + gentamicin or ampicillin + cefotaxime** (100-200mg/kg/day divided 6-12hrly) / ceftriaxone** (50-75mg/kg/day 12-24hrly) are the drugs of choice.

Grade B, Level III

*****Please refer to main text***

B For infants between 1 and 3 months of age, the likely organisms include Group B *Streptococcus, Escherichia coli, Listeria monocytogenes, Streptococcus pneumoniae, Neisseria meningitidis* and *Haemophilus influenzae* type b. Ampicillin plus ceftriaxone/ cefotaxime are the drugs of choice.

Grade B, Level III

A For infants above 3 months of age, the likely organisms include *Streptococcus pneumoniae, Neisseria meningitidis* and *Haemophilus influenzae* type b. The drug of choice is ceftriaxone or cefotaxime.

Grade A, Level Ib

C Vancomycin** (60mg/kg/day divided 6hrly) is added when antibiotic resistant *Streptococcus pneumoniae* is suspected.

Grade C, Level IV

A Chemoprophylaxis** should be considered in contacts of patients with *Haemophilus influenzae* type b or meningococcal meningitis.

Grade A, Level Ib

B If antibiotics other than ceftriaxone or cefotaxime were used to treat *Haemophilus influenzae* type b or meningococcal meningitis, rifampicin** is given at the end of therapy to clear nasopharyngeal carriage

Grade B, Level IIb

URINARY TRACT INFECTIONS

GPP Paediatric patient with a clinical diagnosis of urinary tract infection should have a urine sample obtained for culture and sensitivity before commencement of antibiotics.

*****Please refer to main text***

LOWER URINARY TRACT INFECTION/ACUTE CYSTITIS

B Patients with dysuria, urinary frequency, suprapubic pain, pyuria or balanitis can be managed on an outpatient basis.

Grade B, Level III

All neonates, young infants and febrile children are excluded from this diagnosis. Antibiotics in order of preference are:

A Cotrimoxazole*****: TMP 8mg plus SMX 40mg/kg/day divided 12hrly

Grade A, Level Ib

A Nitrofurantoin*****: 5-7mg/kg/day divided 6hrly

Grade A, Level Ib

A Cephalosporins such as cephalexin, 50mg/kg/day divided 8hrly, especially in patients with G6PD deficiency

Grade A, Level Ib

B Trimethoprim, especially in patients with G6PD deficiency: 6-8mg/kg/day divided 12hrly

Grade B, Level IIa

Duration of treatment:

A < 7 years old : 7 – 10 days

Grade A, Level Ia

A > 12 years old : 3 days of TMZ+SMX can be considered

Grade A, Level Ia

C 7 – 12 years old: 7 – 10 days

Grade C, Level IV

****Contra-indicated in children with G6PD deficiency***

UPPER URINARY TRACT INFECTION/
ACUTE PYELONEPHRITIS

Antibiotics in order of preference:

C For a baby younger than 28 days old: Ampicillin plus gentamicin

Grade C, Level IV

C For an infant older than 28 days old: Gentamicin

Grade C, Level IV

B Ceftriaxone or cefotaxime:
For neonate with hyperbilirubinaemia, cefotaxime is preferred.

Grade B, Level III

Duration of therapy:

GPP Antibiotic regimes should be given for a total of 10 to 14 days.

GPP Neonate <28 days old: intravenous therapy until no fever for 48–72 hours then convert to appropriate oral therapy based on culture/ sensitivity.

GPP Infant >28 days old: parenteral antibiotic therapy until clinical response has been demonstrated for 24 hours, then convert to appropriate oral therapy.

BACTERIAL SKIN INFECTIONS

Impetigo

B The majority of impetigo cases are caused by *Staphylococcus aureus*, some by a combination of both *Staphylococcus aureus* and *Streptococcus pyogenes* and few by *Streptococcus pyogenes.* The drug of choice is oral cloxacillin (30-50mg/kg/day divided 6hrly) or oral cephalexin (30-50mg/kg/day divided 8hrly). For children with

penicillin allergy, alternatives include erythromycin (30–50mg/kg/day divided 6hrly) or cotrimoxazole* (TMP 8mg + SMX 40mg/kg/day divided 12hrly). Duration of treatment ranges from 5 to 10 days:

Grade B, Level III

Ecthyma

B Ecthyma is caused by *Streptococcus pyogenes, Staphylococcus aureus* or a combination of the two organisms. Treatment consists of oral cloxacillin, cephalexin or erythromycin for 1 to 2 weeks.

Grade B, Level III

GPP Local cleansing with chlorhexidine twice daily is helpful.

Blistering dactylitis

B Blistering dactylitis is usually caused by *Streptococcus pyogenes*. Treatment involves incision and drainage of large blisters, and a 7 to 10 day course of penicillin V (25-50 mg/kg/day divided 6hrly), amoxycillin (20-50mg/kg/day divided 8hrly) or erythromycin.

Grade B, Level III

Folliculitis

B Folliculitis is commonly caused by *Staphylococcus aureus.* Treatment consists of chlorhexidine wash and oral cloxacillin, cephalexin or erythromycin for 7 to 10 days.

Grade B, Level III

Furunculosis and carbuncles

B Furunculosis and carbuncles are infection of hair follicles by *Staphylococcus aureus*. Larger lesions should be incised and drained if fluctuant. Appropriate antibiotics include cloxacillin, cephalexin or erythromycin for 7 to 10 days or until inflammation has subsided.

Grade B, Level III

Contra-indicated in children with G6PD deficiency

B Other measures include eliminating predisposing factors, using chlorhexidine cleanser, iron supplementation for refractory furunculosis with low serum iron and eliminating nasal carriage with chlorhexidine, bacitracin, tetracycline or 2% mupirocin ointment. However, long term and unrestricted use of mupirocin has been associated with the development of mupirocin resistance. Therefore judicious use is advocated and only in MRSA carriers.

Grade B, Level IIa

Cellulitis and erysipelas

B Cellulitis and erysipelas can be treated with a combination of amoxycillin plus cloxacillin, cephalexin, erythromycin, or a combination of intravenous cystalline penicillin G (100,000 - 250,000 units/kg/day divided 6hrly) and cloxacillin.

Grade B, Level III

For facial/periorbital cellulitis in young children, admission to hospital is warranted and the following antibiotics are recommended:

B Intravenous ampicillin/sulbactam (150mg/kg/day divided 8hrly)

Grade B, Level III

Or

C Ceftriaxone (50-100 mg/kg/day intravenously divided 12-24hrly)

Grade C, Level IV

Perianal streptoccal dermatitis

C The recommended therapy for perianal streptococcal dermatitis is oral penicillin V, amoxycillin or erythromycin for 10 to 14 days.

Grade C, Level IV

Necrotising fasciitis

C Necrotising fasciitis is a medical emergency. Prompt surgical debridement is the most important aspect of therapy. High dose intravenous penicillin G (250,000 – 450,000 units/kg/day divided 4-6hrly) is used to treat Group A streptococcal infection. Additional antibiotics will depend on clinical assessment and culture results.

Grade C, Level IV

Staphylococcal scalded skin syndrome

C Treatment includes hospitalisation, supportive measures and cloxacillin.

Grade C, Level IV

Toxic shock syndrome

C Besides hospitalisation, intravenous fluid support, cloxacillin ± clindamycin (25-40mg/kg/day divided 8hrly) is used in staphylococcal TSS and penicillin G and clindamycin in streptococcal TSS.

Grade C, Level IV

Methicillin-resistant *Staphylococcus aureus* infection

A For nasal colonisation, topical mupirocin or topical fusidic acid plus oral cotrimoxazole can be used

Grade A, Level Ib

C For mild to moderate infections, guided by culture sensitivity results, a combination of at least 2 oral antibiotics - fusidic acid (20-50mg/kg/day every 8hrly), clindamycin (10 - 40mg/kg/day divided 8hrly), co-trimoxazole*, or minocycline‡ (1-2mg/kg/day divided 12hrly) are recommended.

Grade C, Level IV

Contra-indicated in children with G6PD deficiency
‡Not recommended for children younger than 8 years old

C For moderate to severe infection, vancomycin (40-60mg/kg/day divided 8-12hrly) is the antibiotic of choice.

Grade C, Level IV

1 Introduction

1.1 Aim and scope of guidelines

Emergence of antibiotic-resistant bacteria has become a worrisome subject. Judicious use of antibiotics is an important means to delay the problem of antibiotic resistance. These guidelines on the Use of Antibiotics in Paediatric Care are intended to provide guidance for practitioners to use antibiotics in a rational manner when dealing with childhood infections. The scope of these guidelines includes the choice of antibiotics for use with the appropriate indications, correct dosages and the adequate duration needed to achieve optimal results. These guidelines serve as an aid to clinical practice and are not meant to be comprehensive, nor do they address all available antibiotics. High-risk patients such as those who are immunocompromised, have chronic debilitating disease or serious cardiopulmonary conditions are not covered in these guidelines.

As disease states evolve, patient evaluation is important and the individual medical practitioner has to tailor the management to obtain the best outcome. The physician in charge should decide carefully the appropriate choice when antibiotics are indicated. It should be noted that the correct choice of an antibiotic would depend on the clinical picture of the patient as well as the bacterial culture and sensitivity. It must be recognised that disease states may evolve along different paths and therefore, periodic patient evaluation is very important.

1.2 Guidelines development

The Ministry of Health approached the Chapter of Paediaticians, Academy of Medicine to develop these guidelines. Together with the Singapore Paediatric Society, the Chapter appointed chairpersons of five subcommittees to look into antibiotic management of five groups of paediatric infections. The drafts were distributed to the following institutions/organisations for vetting and feedback: Chapter of Paediatricians; Singapore Paediatric Society; College of Family Physicians; Departments of Paediatrics and Neonatology at KK Women's and Children's Hospital and National University Hospital; Department of Neonatology, Singapore General Hospital;

National Skin Centre; Family Health Service, Ministry of Health; East Shore Hospital; Gleneagles Medical Centre Ltd; Mount Alvernia Hospital; Mount Elizabeth Hospital Ltd; Thomson Medical Centre; Raffles Medical Group Ltd; Singapore Baby and Child Clinic; Deputy Director (Clinical Services), National Neuroscience Institute; and Head, Department of Pharmacology, National University of Singapore. A panel discussion was convened to discuss the drafts and the feedback received from the various groups of doctors. Amendments were made and finally editing was carried out.

1.3 Target Group

These guidelines on the rational use of antibiotics in paediatric infections were developed for all doctors who take care of children.

2 Use of antibiotics in paediatric respiratory infections

2.1 Introduction

Upper respiratory tract infections (URTI) account for a high proportion of clinic visits to the family physician. Children younger than 5 years of age experience 3 to 8 episodes of URTI per year.[1-3] Most URTI are minor, of short duration and self-limiting. The majority, approximately 90%, are caused by viruses for which antibiotics are not necessary. [4] The high incidence of URTI in contrast with the low incidence of lower respiratory tract infections (LRTI) suggests a low rate of development of viral or bacterial LRTI after URTI. Despite the viral etiology of URTI, antibiotics are frequently administered in the hope of preventing LRTI. However, a meta-analysis of randomised clinical trials has shown that antibiotics do not prevent LRTI.[5]

Unnecessary antibiotic use has led to selection of resistant strains of bacteria in the respiratory tract. Antibiotic resistance is an increasing problem in developing countries,[6-7] including Singapore.

Streptococcus pneumoniae is the commonest bacteria causing community-acquired pneumonia with isolation rates as high as 76%.[8] In a local study of hospitalised children admitted for lower respiratory tract infections, penicillin-resistant *Streptococcus pneumoniae* was not present in 1988 but was as high as 17% by 1995.[9] Most recently in 1997, 55% of *Streptococcus pneumoniae* isolated were penicillin resistant, of which 86% of these isolates were also multidrug resistant.[10] In another study done in children attending childcare in Singapore, 24.3% were colonised by *Streptococcus pneumoniae* of which 29% were penicillin resistant. The incidence in the general population is likely to be even lower but the onus is on the primary care physician to stem this alarming trend by the judicious use of antibiotics.

Risk factors for acquiring drug resistant *Streptococcus pneumoniae* include extremes of age (especially young children), recent or prophylactic use of antibiotics, coexisting illness or underlying disease, immunodeficiency syndromes, day care centre attendances, recent hospitalisations and institutionalised patients.[11-19]

Antibiotic resistance is not confined to *Streptococcus pneumoniae* alone. *Haemophilus influenzae* resistant to ampicillin is reported to be 40% in Singapore.[20] Despite this, amoxycillin still remains the drug of choice for treating *Streptococcus pneumoniae* infection , but a higher dose should be used in those at risk of acquiring penicillin-resistant infection.

2.2 Upper respiratory tract infections

Upper respiratory tract infections include rhinitis, pharyngitis and tonsillitis.

A Upper respiratory tract infections are usually viral in origin and often do not require antibiotic treatment.

Grade A, Level Ia

2.2.1 Acute rhinitis

Acute infective rhinitis or the common cold is common in children. The usual presentation is that of nasal obstruction and discharge. This must be differentiated from conditions such as allergic rhinitis and vasomotor rhinitis that are more chronic in nature. In very young children, a nasal foreign body also has to be excluded. Symptomatic relief of the nasal congestion and secretions is sufficient. Mucopurulent nasal discharge is a common feature of uncomplicated viral rhinitis and is not an indication for antibiotics.[23]

A Acute rhinitis is usually viral in etiology and hence antibiotics are not indicated.[5, 21-22]

Grade A, Level Ia

Table 2.1 Acute Rhinitis

Diagnostic Features	Aetiological Agents	Indications for Antibiotics	Grade/ Level
• Nasal congestion • Rhinorrhoea • Cough } need not always • Fever } be present[1]	• Mainly viral[5] (>90%) • Bacterial agents include *S. pneumoniae* *H. influenzae* *M. catarrhalis*[21]	**Antibiotics not indicated** Treat with appropriate antibiotic if bacterial infection present Mucopurulent rhinitis is not an indication for antibiotics[23]	**A / Ia**

2.2.2 Pharyngitis and tonsillitis

Antibiotics should not be given for pharyngitis or tonsillitis especially when associated with symptoms of rhinorrhoea, cough, conjunctivitis and diarrhoea as the majority of these are caused by viruses. Antibiotics should only be given for treatment of Streptococcal pharyngitis or tonsillitis to avoid the risk of developing rheumatic fever.[24] This usually occurs in an older child who looks unwell with prolonged fever, exudates over the tonsils and enlarged, tender lymph nodes. The recommended antibiotic is penicillin V for 10 days[25-26] or amoxycillin for 6 days.[27-29]

Table 2.2 Pharyngitis/Tonsilitis

Diagnostic Features	Aetiological Agents	Indications for Antibiotics	Choice of Antibiotics	Grade/ Level
• Fever • Sorethroat • Pain on swallowing • Tender cervical lymph nodes **Symptoms suggestive of viral etiology:** • running nose • sneezing • conjunctivitis • cough • diarrhoea • anterior stomatitis • discrete ulcers	• Majority are viral (especially age <4yrs). • Commonest bacterial agent is *Streptococcus group A*	**Majority do not require antibiotics** Antibiotics indicated for:- • Age > 4 years with appropriate features without viral symptoms • <u>OR</u> positive throat culture* or rapid antigen test When bacterial infection is suspected, a throat culture or rapid antigen test can be useful[25-26] Antibiotics can be delayed for up to 9 days pending culture results[39]	Oral: Penicillin V(50mg/kg/day divided 6-8hrly) x 10 days[25-26] Amoxycillin x 6 days[27-29] Penicillin-allergy: Erythromycin(50mg/kg/day divided 6-8hrly) x 10 days[25-26] Parenteral: IM Benzathine Pen G[25-26] 0.6 million units < 27 kg 1.2 million units > 27 kg	**A / Ia** **A / Ib** **A / Ia** **A / Ia**

**When obtaining a throat culture, vigorously swab both tonsillar surfaces and posterior pharynx*

2.2.3 Acute sinusitis

Acute sinusitis presents with fever, mucopurulent rhinorrhoea, cough and facial pain. A definitive diagnosis is made only after 7 days of symptoms[30-32] as prior to this, the presentation is very similar to acute rhinitis. The majority of acute sinusitis is caused by bacteria and require treatment with antibiotics. An adequate course of therapy is necessary, as there is a risk of intracranial sepsis.

GPP **If pre-septal cellulitis occurs when symptoms persist after 3 weeks despite adequate antibiotic treatment, referral to an ENT specialist is recommended**

Adjunctive therapy such as nasal decongestants and antihistamines are useful[33].

Table 2. 3 Acute Sinusitis

Diagnostic Features	Aetiological Agents	Indications for Antibiotics	Choice of Antibiotics	Level of Evidence
• Fever • Purulent nasal discharge or post-nasal drip • Cough • Periorbital swelling • Facial pain/tenderness • Headache • Foul smelling breath	• *Streptococcus pneumoniae* • *Haemophilus influenzae* • *Moraxella catarrhalis*[36-37] Other organisms include • *α-haemolytic Streptococcus* • Viruses	Antibiotics indicated as majority are bacterial[33,38] In the presence of symptoms for more than 3 weeks or presence of complications e.g pre-septal cellulitis, intracranial sepsis, referral to ENT specialist is necessary	Amoxycillin (50mg/kg/day divided 8hrly) x 7-10 days[33] Penicillin allergy: Cotrimoxazole* (TMP 8mg/kg/day +SMX 40mg/kg/day divided 12hrly) x 7-10 days 2nd line drugs: If no response after 72 hrs Amoxycillin/ Clavulanate (amoxycillin 50mg/kg/day + clavulanate 7mg/kg/day divided 12hrly) **or** Ampicillin/ Sulbactam (25-50mg/kg/day divided 12hrly) If still symptomatic after 10 days, continue for another 7 days[38]	**A/Ia** **C/IV**

**Contra-indicated in children with G6PD deficiency*

2.2.4 Acute otitis externa

C Acute otitis externa is commonly caused by *Staphylococcus aureus.* Topical antimicrobial eardrops (e.g. polymyxin, framycetin) are sufficient for mild infections. Severe infections can be treated with oral cloxacillin for 7 days or erythromycin (if the patient is allergic to penicillin).

Grade C, Level IV

Table 2..4 Acute Diffuse (Bacterial) Otitis Externa

Diagnostic Features	Aetiological Agents	Indications for Antibiotics	Choice of Antibiotics	Grade /Level
• Fever • Pain • Erythema and edema of the external auditory canal • Enlarged cervical lymph nodes • Itching	*S. aureus*	• For mild infection: topical drops alone	Topical antimicrobial eardrops[40-41]	**C / IV**
		• For severe infection: add oral antibiotics	Oral antibiotics: Cloxacillin[40, 42] (50mg/kg/day divided 6hrly) x 7 days Penicillin allergy: Erythromycin	**C / IV**

2.2.5 Acute otitis media

Evidence from randomised controlled trials comparing antibiotic therapy for acute otitis media (AOM) with no therapy demonstrated a small but significant treatment benefit with 15% of children showing improvement and resolution of symptoms (approximately 80% of untreated children have clinical resolution by 7 to 14 days compared with 95% of those treated with antibiotics)[34]. *Streptococcus pneumoniae* is the most important cause of AOM.

The Therapeutic Working Group convened by the Centers for Disease Control and Prevention (CDC), Atlanta, has issued consensus guidelines for the management of AOM. Oral amoxycillin should remain the first line antimicrobial agent for treating AOM. In view of the increasing prevalence of drug-resistant *Streptococcus pneumoniae* (DRSP), higher dosages of amoxycillin are recommended in appropriate situations. [35]

Table 2.5 Acute Otitis Media

Condition	Diagnostic Features	Aetiological Agents	Indications for antibiotics	Choice of Antibiotics	Grade/ Level
Acute otitis media (AOM)	Otalgia (must be present) Bulging red tympanic membrane with or without a fluid level Otorrhea Fever Nonspecific signs include: • Rhinorrhea • Cough • Irritability • Headache	*Streptococcus pneumoniae* Nontypable *Haemophilus influenzae* *Moraxella catarrhalis* *Group A Streptococcus* *Staphylococcus aureus* Viruses	For AOM	Amoxycillin x 7 days[34-35, 43] If less than 2 yrs old, attends childcare and had antibiotics in the past 3 months – consider higher dose[35] (80-90mg/kg/day) Penicillin allergy: Erythromycin[34] Cotrimoxazole* (check G6PD status) [34] 2nd line drugs: If no response after 72h of treatment High dose Amoxycillin/ Clavulanate,[35, 44] Cefuroxime[35, 43] (15-30mg/kg/day divided 12hrly) NB. For < 2 yrs old, a longer course of up to 10 days may be indicated[45-46]	**A/Ia** **C/IV** **A/Ia** **A/Ia** **A/Ib** **A/Ia**
Recurrent AOM	More than 3 episodes of AOM in 6 months or more than 4 episodes in 1 year		Refer to ENT specialist		

**Contra-indicated in children with G6PD deficiency*

Condition	Diagnostic Features	Aetiological Agents	Indications for antibiotics	Choice of Antibiotics	Grade/ Level
Otitis media with effusion (OME)	Fluid in the middle ear in the absence of signs and symptoms of acute infection		Antibiotics not indicated [46-47](If effusion persists for greater than 3 weeks, child should be referred to ENT specialist)		**A/Ia**

2.3 Lower respiratory tract infections

Lower respiratory tract infections such as bronchiolitis, acute laryngotracheobronchitis, bronchitis and pneumonia are major causes of morbidity in infants and children accounting for 15% of all hospital admissions.

2.3.1 Acute bronchiolitis

Acute bronchiolitis occurs in young children below the age of 2 years. The main etiological agent is the Respiratory Syncytial Virus. Children present with upper respiratory tract symptoms progressing on to tachypnoea, crepitations and wheeze.

A Antibiotics are not indicated unless bacterial co-infection is suspected[48-49]

Grade A, Level Ib

Table 2.6 Acute Bronchiolitis

Diagnostic Features	Aetiological Agents	Indications for Antibiotics	Grade/ Level
• Age: < 2 years • Fever • Cough • Rhinitis • Tachypnoea • Crepitations • Rhonchi	Respiratory viruses, mainly Respiratory Syncytial Virus Risk of bacterial superinfection is 1.2%[58]	**Antibiotics are not indicated for acute bronchiolitis**[48-49] Consider antibiotics if bacterial superinfection suspected. Signs suggesting bacterial superinfection include: • Fever > 1 week • Prolonged symptoms > 1 week • High white cell count • CXR showing definite consolidation • Bacterial pathogen isolated	**A / Ib**

2.3.2 Acute laryngotracheobronchitis

Acute laryngotracheobronchitis occurs in young children who are less than 6 yrs old. There are symptoms of an upper respiratory tract infection associated with a gradual onset of stridor. The child usually does not appear toxic.

C The commonest etiological agent in acute laryngotracheobronchitis is the Parainfluenza virus and antibiotics are not indicated. [50-51]

Grade C, Level IV

Differential diagnoses of stridor in children include acute epiglottitis, bacterial tracheitis and retropharyngeal abscess. These conditions require an urgent referral to the hospital. In young children with a sudden onset of stridor, foreign body aspiration must be excluded.

Table 2.7 Acute Laryngotracheobronchitis (ALTB) or Croup

Diagnostic Features	Aetiological Agents	Indications for Antibiotics	Grade/ Level
• Usually aged 6 month to 6 years (peak 1 – 2 years) • Antecedent mild URTI • Stridor • Hoarseness of voice • Barking cough • Respiratory distress • Not toxic looking	Respiratory viruses mainly Parainfluenza virus	Antibiotics are not indicated[50-51]	**C/ IV**

2.3.3 Acute bronchitis

A Acute bronchitis is an inflammatory condition involving the airways. It is usually precipitated by a viral infection and is self-limiting. Antibiotics are not routinely recommended.

Grade A, Level Ia

Occasionally *Mycoplasma pneumoniae*[52] can be a causative agent. Children present with symptoms of an upper respiratory tract infection associated with tachypnoea, crepitations and rhonchi. The appearance of the sputum is not predictive of a bacterial infection.[53] They occur in older children as opposed to viral bronchiolitis which occurs in younger children.

B A macrolide is recommended in an older child when mycoplasma infection is suspected.

Grade B, Level III

Table 2.8 Acute Bronchitis

Diagnostic Features	Aetiological Agents	Indications for Antibiotics	Grade/ Level
• Cough (< 3 weeks duration) • Coarse crepitations ± rhonchi • Fever	Mainly viral agents[59] Bacterial agents include: • *Mycoplasma pneumoniae*[59] • *Streptococcal pneumoniae* • *Haemophilus influenzae* • *Staphylococcus aureus* [4]	**Antibiotics not routinely recommended**[60-61] Consider antibiotics if bacterial superinfection suspected. Signs suggesting bacterial superinfection include: • Fever > 1 week • Prolonged symptoms > 1 week • High white cell count • CXR showing definite consolidation • Bacterial pathogen isolated	**A / Ia**

2.3.4 Pneumonia

Community-acquired pneumonia remains a serious cause of morbidity and mortality in children.

Although the majority of pneumonias are viral in etiology and do not warrant antibiotic treatment, therapy should be administered if a bacterial etiology is suspected. The choice of antibiotic is based on the frequency of the pathogens in the various age groups, local antibiotic resistance patterns, clinical presentation and host factors.[54] Clinical, laboratory and radiographic findings are not specific in differentiating bacterial and viral etiologies.[55]

The main bacterial etiological agent causing severe pneumonia is *Streptococcus pneumoniae*. Risk factors for acquiring drug resistant *Streptococcus pneumoniae* include extremes of age (especially young children), recent or prophylactic use of antibiotics, coexisting illness or underlying disease, immunodeficiency syndromes, day care centre attendances, recent hospitalisations and institutionalised patients.[11-19]

If pneumonia develops in this high-risk group, higher doses of amoxycillin should be used for treatment. Several studies have shown that the clinical presentation and outcome of therapy did not differ between patients with penicillin-susceptible versus those with nonsusceptible isolates of *Streptococcus pneumoniae*.[56-57] Thus the recommendation is to use high dose amoxycillin or β-lactam agents.

Table 2.9 Pneumonia

Age	Diagnostic Features	Aetiological Agents	Indications for Antibiotics	Choice of Antibiotics	Grade/ Level
New born	Fever Poor feeding Tachypnoea	• *Group B Streptococcus* • *Escherichia coli* • Enteric gram-negative bacilli • *Listeria monocytogenes* • *Enterococcus*	Recommend immediate referral to hospital		**C/IV**

Table 2.9 Pneumonia (con't)

Age	Diagnostic Features	Aetiological Agents	Indications for Antibiotics & Referral to Hospital	Choice of Antibiotics	Grade/ Level
< 2 years	Fever Chills Wet cough Tachypnoea	Predominantly viral. Respiratory syncytial virus and other respiratory viruses Bacterial agents include: • *Streptococcus pneumoniae* • *Haemophilus influenzae* • *Moraxella catarrhalis*	Antibiotics not indicated if viral Bacterial infection suggested by any of the following: • Fever > 1 week • Prolonged symptoms > 1 week • Presence of tachypnea, crepitations, decreased breath sounds, respiratory distress • Toxic appearance or unwell • High white cell count • CXR showing definite consolidation • Bacterial pathogen isolated Indications for referral to hospital • Immuno-compromised host • Toxic appearance • Dehydration • Tachypnoea • Unresponsive to previous treatment	Amoxycillin* x 7–10 days[62-64] Erythromycin x 10 days[65-68] 2nd line drugs: Amoxycillin/ Clavulanate or Ampicillin/ Sulbactam[65-70]	**C/IV**
> 2 years	Fever Chest pain Signs of consolidation	• *Streptococcus pneumoniae* • *Mycoplasma pnuemoniae* (esp age>5 yrs) • *Haemophilus influenzae* *Moraxella catarhalis* • Respiratory viruses		Amoxicillin* x 7–10 days[62-64] 2nd line drugs: Amoxycillin/ Clavulanate or Ampicillin/ Sulbactam[65-70] Macrolides if mycoplasma suspected [64] or penicillin allergy present	**C/IV**

** Higher dosage if Drug Resistant Streptococcus pneumoniae suspected*

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3 Use of antibiotics in paediatric gastrointestinal disease

3.1 Introduction

Infective gastroenteritis is common among young children. Most of the cases are due to viral infections with rotavirus being the most commonly identified virus in childhood gastroenteritis.

GPP The mainstay of management of viral gastroenteritis is the prevention and correction of dehydration and electrolyte disturbances.

As the clinical course is self-limiting, treatment such as the use of anti-diarrhoeal agents is unnecessary.

GPP The use of antibiotics in viral diarrhoea is contraindicated.

In Singapore, bacterial gastroenteritis is less common compared to viral gastroenteritis. Currently, the most commonly isolated bacterial species in childhood gastroenteritis is *Salmonella. Campylobacter* is less commonly identified. *Shigella*, *Escherichia coli* and cholera are rarely identified. It should be noted that *Escherichia coli* is not routinely looked for. Parasitic infestations such as giardiasis and amoebiasis are also rare in Singapore.

3.2 General indications for use of antibiotics

Before prescribing antibiotics, it is good clinical practice to send fresh specimens of the patient's stool for culture and sensitivity. Blood culture is indicated when extraintestinal spread is suspected. In culture-proven bacterial gastroenteritis, appropriate antibiotics are indicated in the following circumstances:

a. *Evidence of extra-intestinal spread (e.g. septicaemia, osteomyelitis).* Patients will appear toxic and have high swinging temperatures.

b. *Young infants*. Appropriate antibiotics may be indicated if the affected patient is younger than three months of age. This is because of an increased risk of septicaemia at this age.

c. *Immunocompromised patient*. Appropriate antibiotics are indicated in patients who are immunocompromised. Such patients include those with immunodeficiency and those on high dose corticosteroid or other immunosuppressive therapy.

3.3 Specific Infections

3.3.1 Non-typhoidal salmonella infection

A The clinical course of uncomplicated non-typhoidal *Salmonella* gastroenteritis in healthy children is self-limiting in nature. Furthermore, many antibiotics prolong the period during which *Salmonella* is carried in the gastrointestinal tract, increase the risk of bacteriologic relapse, and are associated with adverse effects.[1]

Grade A, Level 1a

C Antibiotic therapy for Salmonella infections in children is generally restricted to children with septicaemia and those with increased risk of invasive disease. These include: (1) children younger than 3 months old, (2) immunocompromised children and (3) children with pre-existing chronic gastrointestinal tract disease.

Grade C, Level IV

The antibiotic therapy for Salmonella infections in children is shown in Table 3.1.

Table 3.1 Antimicrobial therapy for nontyphoidal *salmonella* infections in children

Clinical Manifestations	Antimicrobial Agent	Dose	Grade /Level
Carrier state	None		**C/ IV**
Acute gastroenteritis	None		
Bacteremia	Amipicillin	200 mg/kg/day (max 4 g) divided 6hrly IV for up to 14 days	
	Cotrimoxazole* (Trimethoprim-sulfamethoxazole)	TMP 10 mg/kg/day (max 320 mg) plus SMX 50 mg/kg/day (max 1600 mg) divided 12hrly orally for 14 days	
	Chloramphenicol	100 mg/kg/day (max 4 g) divided 6hrly IV for up to 14 days	
	Ceftriaxone	75-100 mg/kg/day (max 4g) once a day IV for up to 14 days	
	Cefotaxime	200 mg/kg/day (max 4 g) divided 6hrly IV for up to 14 days	
Dissemination with localised suppuration (osteomyelitis)	Same as above	Administer for 4-6 weeks	

3.3.2 *Escherichia coli*

C In general, antibiotic therapy is not indicated in *Escherichia coli* gastroenteritis. However, in severe cases, cotrimoxazole* (trimethoprim-sulfamethoxazole) and ampicillin may be used. The dosages are similar to those used for Salmonella gastroenteritis (Table 3.1). The duration of treatment is 5 - 7 days.

Grade C, Level IV

Contra-indicated in children with G6PD defiency

3.3.3 Shigella

B Diarrhoea due to Shigella infection is uncommon in Singapore. Antimicrobial therapy is effective.[2, 3]

Grade B, Level IIa

For cases in which susceptibility is unknown or in ampicillin-resistant strains, cotrimoxazole* is the drug of choice. For cotrimoxazole-resistant organisms, ceftriaxone or cefotaxime can be used. The antimicrobial therapy should be administered for 5 days. Other drugs that can be used include nalidixic acid and quinolones.

Table 3.2 Antimicrobial therapy for shigella infection

Antimicrobial Agent	Dose	Comment	Grade/ Level
Cotrimoxazole*	TMP 10mg/kg/day (max 320 mg) plus SMX 50mg/kg/day (max 1600 mg) divided 12hrly orally or IV for 5 days	Drug of choice Some strains are resistant	**B/IIa**
Ampicillin	100 mg/kg/day (max 2gm) divided 6hrly orally or IV for 5 days	Only for ampicillin-susceptible strains	
Ceftriaxone	50 mg/kg/day once a day IV or IM up to 5 days	For TMP-SMX and ampicillin-resistant strains	
Nalidixic acid*	50 mg/kg/day divided 6hrly orally for 5 days	For TMP-SMX and ampicillin-resistant strains	
Norfloxacin	800 mg divided 12hrly orally for 3-5 days	Resistant strains; approved for persons>17 years of age	
Ciprofloxacin	1g divided 12hrly orally for 3-5 days	Resistant strains; approved for persons>17 years of age	

Contra-indicated in children with G6PD defiency

3.3.4 Cholera

Although cholera is a disease rarely encountered in children in Singapore, it remains an important pathogen in diarrhoeal diseases.

Contra-indicated in children with G6PD defiency.

The mainstay of management is the prevention and management of dehydration and its complications.

C Antibiotics have been shown to cause a decrease in the duration of diarrhoea, the duration of excretion of the organisms in the stools, and the total amount of fluid loss. Oral tetracycline (50 mg/kg/day, max 2g, divided 6hrly) for 3 days or doxycycline (6 mg/kg, max 300 mg) as a single dose is the drug of choice for cholera.[4, 5]

Grade C, Level IV

The use of tetracycline is contraindicated in children younger than 8 years of age. However, in severe diarrhoea, the benefits may outweigh the risk of staining the developing teeth.

C If the strain is resistant to tetracycline, cotrimoxazole* (TMP 10mg/kg/day plus SMX 50mg/kg/day divided 12hrly orally) for 3 days may be used.

Grade C, Level IV

3.3.5 Campylobacter

Campylobacter gastroenteritis is generally a mild disease, with most children recovering in less than a week, and therefore does not require antibiotic therapy. However, 20% of the cases have a relapsing, prolonged or severe illness.

C Erythromycin[6] shortens the duration of excretion of *Campylobacter jejuni* from the faeces, but it does not shorten the duration of the diarrhoea, unless it is given early in the course of the illness i.e., less than 4 days[7]. The dose is 50mg/kg/day (max 2g) divided 6hrly for 7 to 10 days.[4]

Grade C, Level IV

For resistant strains, the choice of the antibiotic will depend on the sensitivity of the organism.

Contra-indicated in children with G6PD defiency

3.3.6 Yersinia enterocolitica

Yersinia infection in children is uncommon in Singapore.

C Diarrhoea is usually a self-limiting disease that does not require therapy, except in immunocompromised children and in those with extrainterstinal spread. The seriously ill patients may respond to treatment with a third generation cephalosporin in combination with an aminoglycoside[8] e.g. gentamicin (5 mg/kg/day in divided doses).

Grade C, Level 1V

3.3.7 Amoeba

Treatment is determined by the degree of tissue invasion.

C Patients who have symptomatic intestinal amoebiasis with dysentery should receive therapy with metronidazole (35-50 mg/kg/day divided 8hrly orally for 10 days). Tinidazole (50-60 mg/kg/day as a single dose for 3 days) may be used instead. If there is hepatic involvement, tinidazole treatment should be extended to 5 days. To eradicate the amoebae from the intestine, paromomycin (25-35mg/kg/day divided 8hrly for 7 days) or diloxanide furoate (20mg/kg/day divided 8hrly for 10 days) is used following metronidazole therapy.[9, 10]

Grade C, Level 1V

3.3.8 Giardia

The most common presentations are watery diarrhoea, weight loss, crampy abdominal pain, failure to thrive or a sprue-like illness.

A Metronidazole (22.5mg/kg/day divided 8hrly orally for 7 days or 30mg/kg/day once a day for 3 days) is effective.[9-12]

Grade A, Level Ia

3.3.9 Cryptosporidium

In immunocompetent patients, diarrhoeal illness due to cryptosporidium is self-limiting. No specific antimicrobial therapy is required.

C Macrolide antibiotics such as erythromycin, azithromycin, spiramycin[13] and clindamycin may reduce the number of parasites and transiently, the stool volume. For immunocompromised hosts, paromomycin[14] (25-35 mg/kg/day divided 8hrly for 14-28 days) in combination with azithromycin can be used.[15]

Grade C, Level 1V

Table 3.3 Antibiotic treatment for gastroentereritis

Organism	Remarks	Antibiotics and its dose	
Non-typhoidal Salmonella	**No antibiotics** EXCEPT for • Septicaemia • <3 months old • Immuno-compromised	Cotrimoxazole*	TMP 10 mg/kg/dose (max 320 mg) plus SMX 50 mg/kg/day (max 1600 mg) divided 12hrly orally for up to 14 days.
		Ampicillin	200 mg/kg/day (max 4 g) divided 6hrly IV for up to 14 days
		Ceftriaxone	75-100 mg/kg/day (max 4g) once a day IV for up to 14 days
		Cefotaxime	200 mg/kg/day (max 4 g) divided 6hrly IV for up to 14 days
Campylobacter	Antibiotics for patient with severe ongoing disease	Erythromycin	50 mg/kg/day (max 2g) divided 6hrly for 7 to 10 days
E coli	**No antibiotics** EXCEPT for Severe cases	Cotrimoxazole*	orally for 5 to 7 days
		Ampicillin	200 mg/kg/day (max 4 g) divided 6hrly for 5 to 7 days

**Contra-indicated in children with G6PD deficiency*

Organism	Remarks	Antibiotics and its dose	
Shigella		Cotrimoxazole*	Orally for 5 days
		Ampicillin	100 mg/kg/day (max 2 g) divided 6hrly orally or IV for 5 days
		Ceftriaxone	50mg/kg/day once a day IV or IM for up to 5 days
Cholera		Tetracycline**	50 mg/kg/dose (max 2g) divided 6hrly for 3 days
		Doxycycline**	6 mg/kg (max 300 mg) as a single dose
		Cotrimoxazole*	orally for 3 days
Yersinia entercolitica	Antibiotics only for : Immunopromised child Extraintestinal spread	Ceftriaxone or Cefotaxime And Gentamicin	
Amoeba		Metronidazole	35-50 mg/kg/day divided 8hrly orally for 10 days
		Or	
		Tinidazole	50-60 mg/kg/day as a single dose for 3 days
		Followed by	
		Paromomycin	25-35 mg/kg/day divided 8hrly for 7 days
Giardia		Metronidazole	22.5mg/kg/day divided 8hrly orally for 7 days
Cryptosporidium	Antibiotics for immunocompromised host	Paromomycin And Azithromycin	

**Contra-indicated in children with G6PD deficiency*

*** Contra-indicated in children younger than 8 years old*

3.4 *Helicobacter pylori*

Helicobacter pylori eradication is important in the prevention of recurrence of *Helicobacter pylori*-associated peptic ulcer disease. There is currently no conclusive evidence for the preemptive treatment of asymptomatic individuals or those with non-ulcer dyspepsia for fear of gastric cancer development.

Table 3.4 *Helicobacter pylori* and Clinical Situations

Clinical Situations	Treatment Indicated	Grade/Level
Helicobacter pylori + peptic ulcer disease	Yes	**B/II**[16, 17]
Helicobacter pylori + asymptomatic	No	**B/II**[16, 17]
Helicobacter pylori + refractory iron deficiency anaemia*, even in the absence of ulcer disease	Yes	**B/III**[17, 18]

* *Other causes of iron deficiency anaemia must be excluded*

3.4.1 Diagnosis

Ideally, endoscopy should be performed for all children suspected of suffering from *Helicobacter pylori* infection before eradication therapy is instituted. A mucosal biopsy should be taken and assessed for the presence of *Helicobacter pylori* by either rapid urease testing, histological assessment or bacterial culture.

Serologic testing or urea breath tests are useful screening tools to indicate which child may benefit from diagnostic endoscopy. Patients should be assessed for bacterial eradication following therapy. Indirect methods such as the urea breath test may be useful.

3.4.2 Therapeutic regimes

Studies have shown that successful eradication of *Helicobacter pylori* requires the use of at least 3 agents: an acid neutralising agent (eg. proton pump inhibitor) and two antimicrobials. For patients who are allergic to clarithromycin or metronidazole, or for organisms resistant

to either antibiotic, amoxycillin may be used to replace either of the antibiotics.

An ideal treatment in children has yet to be determined. Currently triple therapy for 1 to 2 weeks is recommended.

Table 3.5 Triple Therapy for Eradication of Helicobacter pylori

Duration	Medication		Eradication Rate	Grade /Level
1 week[19]	Omeprazole	10 mg om (<20 kg) 20 mg om (>20 kg)	87.5%	**B/III**
	Clarithromycin	15 mg/kg/day (max 500 mg) divided 12hrly		
	Metronidazole	22.5 mg/kg/day (max 1200 mg) divided 8hr;y		
2 week[20]	Omeprazole	20 mg om (<10 years) 20 mg bd (>10 years)	93%	**B/III**
	Clarithromycin	250 mg bd (<10 years) 500 mg bd (>10 years)		
	Metronidazole	250 mg bd (<10 years) 500 mg bd (>10 years)		
1 week[21]	Bismuth	480 mg/1.73m^2/day (max 480 mg) divided qds	94%	**B/III**
	Clarithromycin	15 mg/kg/day (max 500 mg) divided 12hrly		
	Metronidazole	22.5 mg/kg/day (max 200 mg) divided 8hrly		

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4 Use of antibiotics in paediatric acute bacterial meningitis

4.1 Introduction

Bacterial meningitis can affect children of all ages. It is important to recognise and treat this disease promptly, as failure to do so will have dire consequences resulting in death or serious neurological sequelae.

The organisms causing acute bacterial meningitis vary according to the age of the child.

GPP Once a clinical diagnosis of acute bacterial meningitis is made, blood cultures and cerebrospinal fluid microscopy and cultures should be sent. Thereafter antibiotics should be started empirically with necessary alternatives when the culture and sensitivities become available.

Prompt antibiotic administration is essential to prevent additional damage to the brain. Antibiotics chosen must be known to cross the blood-brain barrier well in the presence of inflamed meninges and to reach bactericidal concentrations. Animal studies have shown that the antibiotic concentration in the CSF must reach 10-20 times higher than the minimal bactericidal concentration (MBC).[1] The antibiotics recommended have been shown to consistently achieve these concentrations during therapy for bacterial meningitis.

The focus here is on community-acquired meningitis and not nosocomial meningitis.

The diagnosis and interpretation of the CSF picture of bacterial meningitis will not be discussed here, but will be left to the clinician to decide if the patient has bacterial meningitis.

4.2 Empiric antibiotics by age for presumed bacterial meningitis

4.2.1 Age less than 1 month

B For infants below 1 month of age, likely organisms are Group B *Streptococcus* (GBS), *Escherichia coli*, and *Listeria monocytogenes*. The drugs of choice are ampicillin and gentamicin; or ampicillin and cefriaxone/cefotaxime.

Grade B, Level III

High dose ampicillin is required for group B streptococcal meningitis. Ampicillin will also cover *Listeria monocytogenes* and some strains of *Escherichia coli*. Gentamicin has in-vitro synergy with ampicillin for Group B streptococcus and also covers for *Escherichia coli* meningitis. However, bactericidal activity in the CSF is often low.[2]

Cefotaxime is preferred to other third generation cephalosporins because it has been used more extensively and is not excreted in the bile, nor displaces bilirubin from albumin unlike ceftriaxone.[3, 4, 5] Ceftriaxone can be used after 7 days of life if neonatal hyperbilirubinemia is absent. Cephalosporins alone should not be used in this age group because of the possibility of *Listeria monocytogenes* meningitis, which is cephalosporin-resistant but ampicillin-sensitive.

4.2.2 Age between 1 and 3 months

B In infants between 1 and 3 months of age, likely organisms are Group B *Streptococcus, Escherichia coli, Listeria monocytogenes, Streptococcus pneumoniae, Neisseria meningitidis* and *Haemophilus influenzae* type b. The drugs of choice are Ampicillin plus cefriaxone/cefotaxime.

Grade B, Level III

As the causal organisms in this age group overlap with those in age groups below 1 month and above 3 months, it is essential to cover for all the possible pathogens in these age groups.

4.2.3 Age above 3 months

A For infants above 3 months of age, the likely organisms include *Streptococcus pneumoniae, Haemophilus influenzae* type b and *Neisseria meningitidis.* The drugs of choice are ceftriaxone or cefotaxime.

Grade A, Level Ib

C The addition of vancomycin to ceftriaxone or cefotaxime is strongly recommended for the empiric treatment of bacterial meningitis if:

- **the child is very sick**
- **the CSF strongly suggests a bacterial meningitis**
- **the CSF gram stain is positive for gram-positive cocci.**

Grade C, Level IV

Ceftriaxone or cefotaxime are very effective in *Haemophilus influenzae* type b or meningococcal (*Neiserria meningitidis*) meningitis.[6]

C Due to the increasing antibiotic resistance of *Streptococcus pneumoniae* especially to ampicillin/penicillin, the empiric use of vancomycin in combination with ceftriaxone/cefotaxime is recommended as the initial therapy for bacterial meningitis.[7-9]

Grade C, Level IV

The combination of vancomycin and ceftriaxone is more effective than either drug alone against beta-lactam-resistant pneumococcal meningitis in the animal model. This combination is continued until the aetiologic agent is identified and the susceptibility tests are available. If the organism is sensitive to ceftriaxone or penicillin, then vancomycin should be discontinued and therapy completed with penicillins or ceftriaxone. However, if there is resistance to penicillin and ceftriaxone, the combination of both vancomycin and ceftriaxone is recommended. Failure with vancomycin alone was reported in both penicillin-sensitive and penicillin-resistant pneumococcal meningitis.[10] This may be due to the variability of penetration of vancomycin.

C For penicillin-resistant and ceftriaxone-resistant pneumococci, the other option is to use a combination of rifampicin with vancomycin plus ceftriaxone.[11,12]

Grade C, Level IV

Rifampicin is active against most, but not all, penicillin-non-susceptible pneumococci. Rifampicin should never be used alone as resistance had developed during monotherapy and rifampicin is only slowly bacteridcidal against *Streptococcus pneumoniae* in-vitro. Addition of rifampicin to vancomycin (with a third generation cephalosporin) after 24-48 hours of therapy should be considered if the organism is susceptible to rifampicin and;

a. after 24-48 hours of therapy, despite vancomycin and ceftriaxone, the clinical condition has worsened;
b. the subsequent Gram-stained smear or cultures of CSF indicates the failure to eradicate or reduce substantially the number of organisms **or** the organism has an unusually high cefotaxime or ceftriaxone MIC (≥ 4 μg/ml).

Consultation with an infectious disease specialist is indicated.

Chloramphenicol is no longer recommended for the treatment of meningitis. This is due to the rising resistance of *Haemophilus influenzae* to chloramphenicol and its clinical inferiority compared to ampicillin, ceftriaxone or cefotaxime.[6]

A The last option for penicillin-resistant and ceftriaxone-resistant *Streptococcus pneumoniae* is to use meropenem, provided the organism is susceptible as determined through sensitivity testing.

Grade A, Level Ib

However, as the 2 randomised-controlled trials using meropenem have included only a very small number of patients with penicillin-resistant or cephalosporin - resistant pneumococcal strains, the Committee feels that meropenem should only be used as a last resort pending further studies. In most cases, meropenem will be active against isolates nonsusceptible to penicillin and the epileptogenic potential is much

less than that of imipenem. Meropenem alone or in combination may provide a satisfactory alternative for patients who cannot tolerate vancomycin.[13,14]

The duration of antibiotic therapy is given in Table 4.2.

C The duration of antibiotic treatment is extended if the meningitis is complicated by the presence of brain abscess, subdural empyema or delayed CSF sterilisation. In such cases, the duration of antibiotics is individualised.[15]

Grade C, Level IV

B Intramuscular ceftriaxone is an acceptable alternative for completion of the ceftriaxone course when the patient is convalescing and has good peripheral perfusion. The serum concentration time-curves after IM and IV ceftriaxone are bioequivalent.[16,17]

Grade B, Level IIb

Table 4.1 Aetiologic agents in acute bacterial meningtitis and recommended empiric antibiotics

Age	Common organisms	Uncommon organisms	Antibiotic	Alternative	Duration	Comments
<1 month	GBS, *E. coli*, *Listeria*	*Salmonella*, *S. aureus*, *P. aeruginosa*, CONS, Gram-negative bacilli	Ampicillin + Gentamicin	Ampicillin + Cefotaxime **or** Ceftriaxone*	GBS, Listeria: 14-21days Gram-negative bacilli: 21days	High dose crystalline pencillin/ampicillin is required for GBS. Gentamicin is synergistic with ampicillin for GBS
1-3 months	GBS, *E. coli*, *Listeria* *S. pneumoniae* Hib *N. meningitidis*	*Salmonella*, *S. aureus*	Ampicillin + Ceftriaxone	Ampicillin + Cefotaxime	*S. pneumoniae*: 10-14 days Hib:7-10 days *N. meningitis:* 5-7 days GBS, Listeria: 14-21 days Gram-negative bacilli:21 days	Due to overlap of organisms between <1 month and > 3 months age groups, it is essential to cover for these organisms
> 3 months	*S. pneumoniae*, Hib, *N. meningitidis*	GAS, Gram-negative bacilli	Ceftriaxone +/- Vancomycin§	Cefotaxime +/- Vancomycin§	*S. pneumoniae:* 10-14 days Hib:7-10 days *N. meningitis:* 5-7 days	Addition of vancomycin is strongly recommended if: • child is very sick • CSF is suggestive of bacterial meningitis or • CSF gram stain shows gram-positive cocci.

GBS = Group B Streptococcus, Hib = Haemophilus Influenzae type b, CONS = Coagulase negative Staphylococci,
GAS = Group A Streptococcus. Gram negative bacilli comprises Klebsiella, Escherichia coli, Citrobacter, Serratia
**Ceftriaxone can be used after 7 days of life and in the absence of neonatal jaundice*
§Rifampicin can be added to vancomycin with a third generation cephalosporin in selected cases of S. pneumoniae meningitis (see text)
The duration of antibiotic treatment is extended if the meningitis is complicated by the presence of brain abscess, subdural empyema & delayed CSF sterilisation. In such cases, the duration of antibiotic therapy is individualised.

Table 4.2 Specific antibiotic treatment and duration of treatment

Organism	Recommended	Alternative	Duration of therapy
Streptococcus pneumoniae[11]			
Penicillin senitive (MIC ≤ 0.06 ug/ml)	Penicillin G	Ampicillin or Ceftriaxone	10-14 days
Penicillin resistant-intermediate (MIC 0.1 – 1 ug/ml) or absolute (MIC ≥ 2 ug/ml) and ceftriaxone sensitive (MIC ≤ 0.25 ug/ml)	Ceftriaxone	Cefotaxime	10-14 days
Penicillin resistant – intermediate (MIC 0.1 – 1 ug/ml) or absolute (MIC ≥ 2 ug/ml) and ceftriaxone resistant – intermediate (MIC 0.5 –1 ug/ml) or absolute (MIC ≥ 2 ug/ml)§	Vancomycin + ceftriaxone	Rifampicin + ceftriaxone +vancomycin§	10-14 days
Neisseria meningitidis	Penicillin G	Ampicillin or ceftriaxone	5-7 days
Haemophilus influenzae type b	Ceftriaxone	Ampicillin (if sensitive)	7-10 days

The duration of antibiotic treatment is extended if the meningitis is complicated by the presence of: brain abscess, subdural empyema, delayed CSF sterilization. In such cases, the duration of antibiotics is individualised.[15]

§ Rifampicin can be added to vancomycin with a third generation cephalosoprin in selected cases of S pneumoniae meningitis (see text in Section 6.2.3).

Table 4.3 Other bacterial causes of meningitis

	Likely organisms	Uncommon organisms
Shunt	Coagulase-negative staphylococci, *Staphylococcus aureus*, *Propionibacterium acnes*, diptheroids	*Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae*, other Gram-negative bacilli, Enterococci
Post-head Trauma/ Neurosurgery	*Staphylococcus aureus*, *Streptococcus pneumoniae*, coagulase-negative staphylococci	Gram-negative bacilli (including *Pseudomonas aeruginosa)*
Immuno-Suppressed	*Streptococcus pneumoniae*, *Neisseria meningitidis*, Listeria, Gram-negative bacilli (including *Pseudomonas aeruginosa*)	Cryptococcus, Nocardia, Salmonella

Table 4.4 Drug doses for meningitis

Antibiotic	Body weight <2 kg Neonates < 7 days	Body weight <2 kg Neonates 7-28 days	Body weight >2 kg Neonates < 7 days	Body weight >2 kg Neonates 7-28 days	Children > 1 month
Penicillin G*	250,000-450,000 units/kg/day divided 8hrly	450,000 units/kg/day divided 6hrly	250,000-450,000 units/kg/day divided 8hrly	450,000 units/kg/day divided 6hrly	400,000 units/kg/day divided 4-6hrly
Ampicillin*	200-300 mg/kg/day divided 8hrly	300 mg/kg/day divided 4-6hrly	200-300 mg/kg/day divided 8hrly	300 mg/kg/day divided 4-6hrly	300-400 mg/kg/day divided 4-6hrly
Cefotaxime	100 mg/kg/day divided 12hrly	150 mg/kg/day divided 8hrly	150 mg/kg/day divided 8hrly	200 mg/kg/day divided 6hrly	225-300 mg/kg/day divided 6-8hrly
Ceftriaxone	50 mg/kg/day om	50 mg/kg/day om	50 mg/kg/day om	75 mg/kg/day om	100 mg/kg/day divided 12-24hrly
Vancomycin	30 mg/kg/day divided 12hrly	45 mg/kg/day divided 8hrly	30-45 mg/kg/day divided 8-12hrly	45-60 mg/kg/day divided 6-8hrly	60 mg/kg/day divided 6hrly
Gentamicin	2.5 mg/kg/dose every 12-18hrly	2.5 mg/kg/dose divided 8-12hrly	5 mg/kg/day divided 12hrly	75 mg/kg/day divided 8hrly	6 mg/kg/day divided 8hrly

**For group B streptococcal meningitis, a higher dose of penicillin or ampicillin is recommended. Gentamicin is added for synergistic effect with a penicillin antibiotic in the initial week of treatment.*[11]

4.3 Chemoprophylaxis

Chemoprophylactic agents against the various causative organisms is shown in Table 4.5

A Chemoprophylaxis protects susceptible persons from acquiring *Haemophilus influenzae* type b or meningococcal disease by eliminating colonisation in close contacts.

Grade A, Level Ib

B If an antibiotic other than ceftriaxone or cefotaxime was used for the patient with *Haemophilus influenzae* type b or meningococcal meningitis, rifampicin needs to be given at the end of therapy to clear nasopharyngeal carriage.

Grade B, Level IIb

B For the *Haemophilus influenzae* type b meningitis patient who is < 24 months old, vaccination against future *Haemophilus influenzae* type b invasive disease is indicated as they may have an impaired antibody response to the organism despite the development of meningitis.[18]

Grade B, Level IIb

Chemoprophylaxis against *Haemophilus influenzae* type b for contacts at child-care centres is complex and varies with the number of index patients, age of child-care centre contacts, previous *Haemophilus influenzae* type b vaccination of contacts and duration of time spent together at the child-care centre. For these reasons, chemoprophylaxis is decided on a case-by-case basis and should be in consultation with an Infectious Disease specialist

A Meningococcal vaccine is given only in outbreak settings and to children > 2 years old. This is because the quadrivalent (A, C, Y, W135) polysaccharide vaccine is poorly immunogenic except for meningococcus serogroup A in children < 2 years old.[19]

Grade A, Level Ib

Table 4.5 Chemoprophylaxis

Organism	Contacts	Drug and dose	Grade/ Level
Haemophilus influenzae type B	Household contacts if any child is < 4 years old	Rifampicin†	**A/Ib**
	Child-care attendees*	20 mg/kg om x 4 days (max 600 mg)	
	Index patient who has received antibiotics other than ceftriaxone for treatment	Adult : 600 mg om x 4 days	**B/IIb**
Neisseria meningitidis	Household contact especially young children	Rifampicin†	**A/Ib**
	Child care or nursery contact in previous 7 days	< 1 month : 10 mg/kg/day divided 12hrly x 2 days	
	Direct exposure to patient's secretions through kissing or sharing of toothbrushes or eating, mouth-mouth resuscitation, unprotected contact	> 1 month : 20 mg/kg/day divided 12hrly x 2 days	
	During endotracheal intubation in past 7 days before onset of illness	Adult : 600 mg bd x 2 days	**A/Ib**
		OR Ceftriaxone¶	
		≤ 12 yrs : IM 125 mg x 1 dose	
		> 12 yrs : 1M 250 mg x 1 dose	**A/Ib**
		OR Ciprofloxacin†	
		> 18 yrs : 500 mg x 1 dose	

**Check with Infectious Diseases specialist*
†Not for use in pregnant women
¶Recommended for pregnant women

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5 Use of antibiotics in paediatric urinary tract infection

5.1 Introduction

Urinary tract infection (UTI) is one of the most common bacterial infections seen in children. Although the majority of children with UTI have an excellent prognosis, there is a definite risk of renal damage following pyelonephritis especially in those with an underlying abnormality of the urinary tract, such as obstructive uropathy or vesicoureteric reflux[1-3]. Following infection, renal damage can occur as renal scarring and when scarring is extensive, this can lead to serious complications like hypertension and renal impairment[4-6]. Thus, early detection and appropriate treatment of urinary tract infections in the paediatric age group can minimize such serious complications.

Challenges in the management of urinary tract infection in children include the nonspecific clinical presentation of UTI in infancy, the difficulty in obtaining uncontaminated high quality urine samples for cultures, and the high recurrence rates of UTI [7]. For rational treatment of UTI, it is imperative that proper collection of urine for culture is obtained before institution of antibiotic therapy so that treament can be guided by the antibiotic sensitivity of the uropathogen. In a study of the treatment approach for acute pyelonephritis in children, general practitioners, paediatricians, and paediatric nephrologists were found to have significantly different treatment regimens. For instance, nephrologists favoured intravenous therapy, use of aminoglycosides or cephalosporins and hospitalization. In contrast, general practitioners and paediatricians preferred outpatient management, and treatment with oral beta-lactam antibiotics [8]. Thus, there is no clear consensus as to the treatment of acute pyelonephritis in young children. Indeed, the choice of antibiotic regimen in many centres is empirical and centre-specific.

This clinical guideline proposes an evidence-based approach to the treatment of urinary tract infections in children. These recommendations are limited by the small number of good clinical trials in children that address the various aspects of the treatment of urinary tract infection. Furthermore, the epidemiology and pathophysiology of urinary tract infections in the paediatric population

differ greatly from that of the adult population, thus making it difficult to extrapolate data from adults to children.

5.2 Clinical classification of urinary tract infection

Therapeutic regimen for UTI is based on whether the urinary tract infection is localized to the lower urinary tract or upper urinary tract involving the renal parenchyma. Table 5.1 outlined the clinical classification of childhood UTI. Ideally, recommendations should also be stratified according to specific paediatric age groups as the epidemiology and pathophysiology differ according to age. While young infants have invasive infection often involving pyelonephritis and even bacteremia, older children have more localized disease involving the lower urinary tract. Treatment therefore differs and is more aggressive when there is invasive disease or pyelonephritis, as in neonates and infants.

Table 5.1 Clinical classification of childhood UTI

Clinical Features	Upper Tract Infection	Lower Tract Infection
• Age	Generally < 2 years. Neonates and young infants are at high risk	Generally > 2 years.
• Sex	F = M in infancy F>> M past infancy	F > M
• Fever	+ (All febrile UIT have presumed pyelonephritis)	-
• Voiding problem - Dysuria - Frequency	-	+
• Suprapubic pain	-	+
• Loin pain	+	-
• Renal involvement	+	-

F = Female; M = Male

5.3 Aim of the guidelines

The objectives of the clinical guidelines are:

1. To delineate evidence based recommendations on the treatment of acute uncomplicated lower urinary tract infection/cystitis in the paediatric population.
2. To provide evidence based recommendations on the treatment of acute uncomplicated upper urinary tract infection/pyelonephritis in the paediatric population.

Management of complicated urinary tract infections (UTI) such as UTI in association with structural and functional renal tract abnormalities, subsequent antibiotic prophylaxis and radiographic investigations are not within the scope of these guidelines.

5.4 Bacteriology and antibiotic resistant pattern of uropathogens

In the adult population, E.coli remains the most common uropathogen, occurring in over three-quarters of all UTI. However other gram negative organisms as well as Enterococcus, are being more frequently encountered.[9] There was a significant increase in the proportions of uropathogens resistant to ampicillin and other beta-lactam antibiotics, with resistance seen in over 40% of organisms. Similarly, there is an increased resistance to co-trimoxazole, as well as to nitrofurantoin. Sensitivity to quinolones has remained unchanged. Studies based in the United States report ampicillin resistance in up to 70% of E.coli isolates,[10] and in a local study ampicillin resistance was found in 40% of E.coli isolates,[11] while E.coli sensitivities to cefazolin, cefotaxime, ceftriaxone, gentamicin and amikacin have remained high and close to 100%. In another study, it was also noted that susceptibility patterns depend on whether the infection is localized to the lower as opposed to the upper urinary tract.[12]

In the only published study that looked at the uropathogen sensitivities in childhood UTI,[13] it was found that over 95% of cases of UTI in the study population were caused by gram-negative organisms. Organism sensitivities to ciprofloxacin, gentamicin, cefotaxime, and cephalexin have remained over 95%.[13] Sensitivities to nitrofurantoin, co-trimoxazole, and trimethoprim alone have remained acceptable at

proportions above 85%. Resistance to ampicillin was at an unacceptable rate of greater than 50%.

Since the choice of empiric antibiotic therapy is ultimately based on the local epidemiology of uropathogens and their sensitivities, local bacteriologic sensitivities were reviewed. In the only local prospective study in young children with febrile urinary tract infection[1,14] the commonest uropathogen found was E.coli (81%) followed by Klebsiella (4.4%) Proteus mirabilis (4.4%). Local antibiotic sensitivity revealed gentamicin sensitivity for E. coli to be 96% and Klebsiella 88%, while Ceftriaxone sensitivity for E.coli was 99% and Klebsiella 86%. In a local study of community acquired urinary tract infections in adults, E.coli accounted for 68% of cases, Klebsiella 10%, Proteus 6% and gram-positive cocci in 10%.[9] Overall organism sensitivity to antibiotics in the study revealed a sensitivity of only 65% to co-trimoxazole, 78% to cephalexin, and 85% to nitrofurantoin. Specific E.coli sensitivities, however, were still acceptable at 93% for nitrofurantoin and 72% for cephalexin.

In summary, these data suggest that E.coli and other gram negative organisms remain as the predominant uropathogens. There is an increasing degree of resistance to ampicillin, first generation cephalosporins, and to a certain extent co-trimoxazole. Sensitivity remains high to third generation cephalosporins, aminoglycosides, quinolones and nitrofurantoin.

5.5 Treatment of lower urinary tract infection in children

B Lower urinary tract infection can be treated on an outpatient basis.

Grade B, Level III

Acute uncomplicated cystitis in children presents with classical symptoms of dysuria, suprapubic pain, cloudy urine, urinary frequency, pyuria and sometimes haematuria. These patients are older children, afebrile, with no renal involvement and can be treated on an outpatient basis. This category of patients **excludes all neonates and young infants** with UTI because of reported high incidence (6%[16] to 30%[17]) of concomitant bacteremia. Also **excluded are all children with febrile urinary tract infections** since at least 60% of patients with febrile UTI have radiographically demonstrable acute

pyelonephritis[3] and other studies have further suggested that permanent scarring occur in 36% of kidneys.[18]

5.4.1 Choice of antibiotics

Antibiotic regimens for treatment of lower urinary tract infection in children are multiple.

ANTIBIOTICS RECOMMENDED IN ORDER OF PREFERENCE ARE:

A Co-trimoxazole[19-21]
Prior to the use of this drug, a patient must not be G6PD deficient. Cure rate of more than 90% had been demonstrated.

Grade A, Level Ib

A Nitrofurantoin[22]
Prior to the use of this drug, a patient must not be G6PD deficient. Up to 100% short-term cure rate and a very low long-term recurrence rate of 8.7% had been achieved.

Grade A, Level Ib

B Trimethoprim[23]
Trimethoprim had successfully achieved a cure rate of 100%. This drug is especially useful in patients with G6PD deficiency where the use of sulfamethoxazole is contraindicated.

Grade B, Level IIb

B Cefadroxil[24]
This extends to other first generation cephalosporins, including cephalexin, as well as cefaclor. The use of cefadroxil in this study achieved a short-term cure rate of 80% and had a recurrence rate in up to 20% of cases.

Grade A, Level Ib

ANTIBIOTICS GENERALLY NOT RECOMMENDED:

B Fluoroquinolones[25-27]

Although fluoroquinolones had been widely used in the treatment of adult UTI, it is not recommended for routine use in children because of fear of potential emergence of antibiotic resistance and reported cases of toxicity especially arthropathy or cartilagenous injury in prepubertal children.

Grade B, Level III

B Amoxicillin

Amoxicillin had been used effectively for the treatment of UTI.[28] However due to recent reports of unacceptably high rates of organism resistance to amoxicillin,[9,10,15] it is not recommended as a form of monotherapy for the treatment of childhood UTI.

Grade B, Level IIb

5.4.2 Duration of treatment

A For children less than 7 years old treatment should be given for 7-10 days.

Grade A, Level Ia

At the present time, there is insufficient evidence to recommend short course therapy in the treatment of acute uncomplicated cystitis in children less than 7 years of age. [29]

A 3-day short course antibiotic therapy with co-trimoxazole is effective in children older than 12 years of age with acute uncomplicated cystitis.

Grade A, Level Ia

Two well-designed meta-analyses have shown that in the adult population with uncomplicated cystitis a 3-day course of co-trimoxazole is as effective as conventional treatment.[30,31] In the opinion of this working group these results can be extrapolated to children and adolescents aged 12 years or older.

C For children between the ages of 7-12 years, a 3-day short course therapy with co-trimoxazole can be considred and decided on case to case basis.

Grade C, Level IV

The decision for a short course of co-trimoxazole will depend on the level of confidence of the treating physician that the patient has a diagnosis of uncomplicated cystitis.

Antibiotics recommended for first line monotherapy and duration of treatment in paediatric patients with acute uncomplicated cystitis are summarized as in Table 5.2. Choice of antibiotics should be adjusted according to urinary culture results, once these are available.

Table 5.2 Antibiotic treatment of lower urinary tract infection

Choice of Antibiotics	Duration of treatment
1. Co-trimoxazole*: TMP 8mg + SMZ 40mg/kg/day divided 12 hourly 2. Nitrofuratoin*: 5-7 mg/kg/day divided 6 hourly 3. Cephalexin: 25-50mg/kg/day divided 8 hourly 4. Trimethoprim: 8mg/kg/day divided 12 hourly	< 7 years old: 7-10 days monotherapy >7 years old: 7-10 days monotherapy or 3 days TMP + SMZ (especially those >12 years old)

**Screen for G6PD deficiency*

5.5 Treatment of upper urinary tract infection/acute pyelonephritis in children

B Initial treatment of upper urinary tract infection in children requires intravenous antibiotics and hospitalisation.

Grade B, Level III

Although intravenous antibiotics are recommended for neonates less than 28 days of age[32], there is considerable controversy as to whether presumed pyelonephritis, as defined by febrile UTI, requires intravenous antibiotic therapy and in-hospital management in the older children. Because of the absence of well-designed clinical trials that compare the long-term outcome of paediatric patients with UTI treated with intravenous, as compared to, oral therapy[33], the working group recommends initial parenteral management for childhood acute pyelonephritis.

5.5.1 Choice of antibiotics

B Initial treatment for neonates (infants less than 28 days old) should be intravenous ampicillin and gentamicin.

Grade B, Level IIb

For infants less than 28 days of age, treatment of urinary tract infections should begin with intravenous ampicillin and gentamicin [17]. Based on the high likelihood of possible sepsis and menigitis in this population,[32] these infants should be hospitalized and undergo complete sepsis evaluation including blood and cerebrospinal fluid culture, in addition to a urine culture that is obtained either by catheterization or by suprapubic aspiration. Pending culture results and upon documentation of normal renal function, parenteral ampicillin and gentamicin are selected as initial antibiotic therapy in this age group (table 5.3), because the overwhelming majority of urinary tract infections in this age group are caused by E.coli and other gram-negative organisms.[9-16] Ampicillin is included in the regimen to cover the small percentage of infants with enterococcal urinary tract infections. Ceftriaxone and cefotaxime can be used as alternatives to gentamicin in infants with suspected meningitis, children with questionable renal function or those at risk of renal impairment. For neonates with hyperbilirubinaemia, cefotaxime is preferred because unlike ceftriaxone, it is not excreted in the bile nor does it displace bilirubin from albumin.

B Past neonatal age, treatment of upper urinary tract infection will depend on whether patient is ill-looking; with ill-looking patients requiring hospitalised treatment.

Grade B, Level IIb

Past neonatal age, children with febrile urinary tract infection who are ill-looking should be hospitalized for treatment. The term ill-looking or toxic-looking is based on clinical judgement but generally includes the following symptoms and signs: chills, rigors, lethargy, poor perfusion, marked hypoventilation or hyperventilation. Over 10% of young infants with such symptoms and signs had been found to have bacteriemia.[34]

GPP Past neonatal age, patients with a clinical diagnosis of acute pyelonephritis though not ill-looking should be treated initially with parenteral antibiotics.

For any infant greater than 28 days of age and children with a clinical diagnosis of pyelonephritis, who is not toxic-looking, despite a relatively low probability of bacteremia, the workgroup believes that under most circumstances, these patients should be treated initially with parenteral antibiotic until clinical response to antibiotics has been demonstrated. This recommendation is based on the increased risk of the development of renal scarring in patients with pyelonephritis.[1-3]

B Past neonatal age, children with upper urinary tract infection should be treated initially with intravenous aminoglycosides (gentamicin or amikacin) or alternatively intravenous cephalosporins (ceftriaxone or cefotaxime).

Grade B, Level III

Treatment may need adjustment once urine culture and sensitivities are known.

Aminoglycosides:

B **Gentamicin**[35]

Response to gentamicin reached over 91% on short-term assessment. Long term assessments wase not been carried out.

Grade B, Level III

B **Amikacin**[36]

Amikacin can be used as an alternative aminoglycoside.

Grade B, Level III

Note that the use of aminoglycosides longer than 3 days may require monitoring of aminoglycoside level due to risks of otoxicity and nephrotoxicity.

Cephalosporins:

B **Cefotaxime or Ceftriaxone**[37,38]

In a clinical trial of 173 patients with DMSA-documented pyelonephritis, short-term bacteriologic response rate achieved 100%, with a long-term bacteriologic recurrence rate of about 10%.

Grade B, Level IIa

Due to the widespread use of cephalosporins, there is an increasing prevalence of bacterial strains that have become resistant to third generation cephalosporins [10,38]. The workgroup recommends that cephalosporins should not be used as 1st line antibiotic therapy in childhood UTI despite high sensitivities of uropathogens to these cephalosporins, unless the patient is at risk of nephrotoxicity.

Ampicillin can be added to cover enterococcal infection when indicated.

5.5.2 Duration of treatment

C Treatment for upper urinary tract infection should be given for 10 to 14 days.

Grade C, Level IV

There is currently insufficient evidence to recommend short course therapy in paediaric patients with lower urinary tract infections.[21] This conclusion can be extended to paediatric patients with upper tract infection or pyelonephritis.

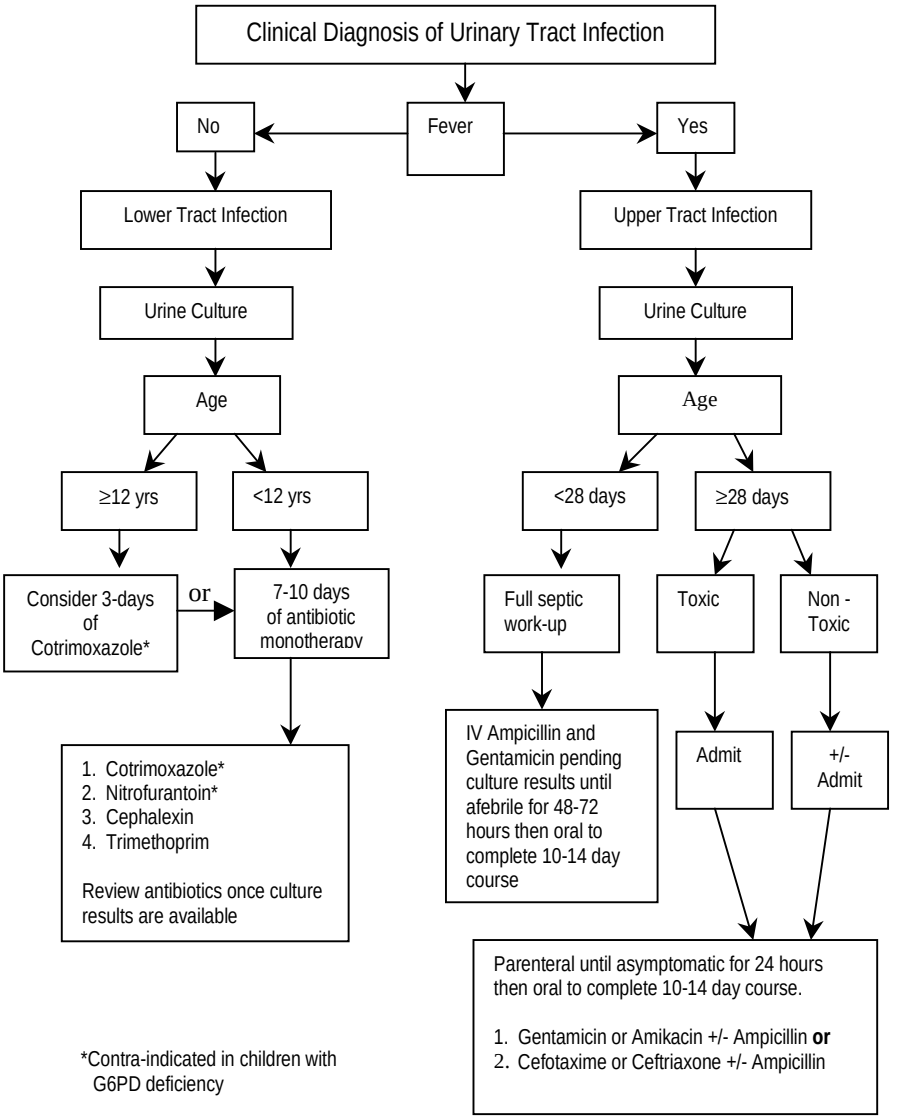
GPP In neonates, parenteral antibiotic therapy should continue until fever has settled for 48-72 hours before converting to oral antibiotics; In older infants and children, parenteral therapy should continue until fever has settled for at least 24 hours before converting to oral therapy.

Antibiotics recommended for initial treatment and duration of therapy for paediatric patients with upper urinary tract infection are summarized in Table 5.3

Table 5.3 Antibiotic treatment of upper urinary tract infection

Choice of Antibiotics	Duration of treatment
1. **Infant < 28 days** Ampicillin 50-100mg/kg/day divided 6hourly and Gentamicin 5-7.5mg/kg/day divided 12-8hourly **Infant > 28 days and child** Gentamcin 5-7.5mg/kg/day divided 8hourly 2. Ceftriaxone 50-100mg/kg/day divided 24hourly Or Cefotaxime 50-200mg/kg/day divided 6-8hourly	10-14 days **Infant < 28 days** IV therapy until no fever for 48-72 hrs before oral therapy **Infant > 28 days** Parenteral therapy until no fever for 24 hrs before oral therapy

Figure 5 Algorithm for the management of urinary tract infections in children



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6 Use of antibiotics in paediatric bacterial skin infections

6.1 Introduction

Bacterial skin infections are common in children. In a local study, it was the third most common condition seen in children after eczema and viral infections, accounting for 5% of the cases encountered.[1] This chapter will discuss some of the more common cutaneous bacterial infections seen in children including impetigo, ecthyma, folliculitis, furunculosis, erysipelas, cellulitis, staphylococcal scalded skin syndrome, blistering dactylitis and perianal streptococcal dermatitis.

6.2 Impetigo

6.2.1 Clinical presentation and bacteriology

This is a common skin infection in children, especially those younger than 6 years of age. In a local study, it accounted for 4.5% of the primary pyoderma cases seen.[2] Clinically, it starts as red papules that become vesicles and pustules which rupture easily to create thick, adherent, honey-coloured crusts surmounting an erythematous base. On the face, impetigo is commonly periorificial. It spreads rapidly and is highly infectious.

Impetigo may be a primary pyoderma affecting previously normal skin or it may complicate other dermatoses such as insect bites, scabies or atopic dermatitis. Most cases of impetigo are caused by *Staphylococcus aureus*, some to a combination of both *Staphylococcus aureus* and *Streptococcus pyogenes* and a few to *Streptococcus pyogenes* alone.[2,3] A local study showed that *Staphylococcus aureus* was the commonest organism isolated from the primary pyodermas, accounting for 67% of the organisms isolated, followed by streptococci, accounting for 15% of the organisms isolated.[2] *Staphylococcus aureus* is the predominant organism isolated in patients with impetiginised atopic dermatitis, being seen in 70% of the eczematous lesions. [4]

6.2.2 Management

This should cover for *Staphylococcus aureus*. Most *Staphylococcus aureus* strains are resistant to penicillin. Locally, 90% of the strains of *Staphylococcus aureus* are resistant to penicillin and ampicillin.[2]

B The treatment of choice for impetigo is oral cloxacillin (30 - 50 mg/kg/day divided 6hrly) or a cephalosporin such as oral cephalexin (30 - 50 mg/kg/day divided 8hrly).[5]

Grade B, Level III

B Oral erythromycin (30 - 50 mg/kg/day divided 6hrly) is a useful alternative in patients who are allergic to penicillin. [2, 6]

Grade B, Level III

Locally, 8% to 18% of the *Staphylococcus aureus* isolates are resistant to erythromycin.[2,4] Although antibiotic resistance does not immediately imply treatment failure, this increasing resistance of *Staphylococcus aureus* to erythromycin requires close monitoring.

B Cotrimoxazole (TMP 8 mg plus SMZ 40 mg/kg/day divided 12hrly) is a cheap and effective antibiotic in the treatment of impetigo.[2]

Grade B, Level III

93% to 100% of the strains of *Staphylococcus aureus* are sensitive to cotrimoxazole.[2,4] Cotrimoxazole is contraindicated in children with G6PD deficiency. The other disadvantage of cotrimoxazole is a higher incidence of adverse drug reactions compared to cloxacillin or erythromycin but is useful as an alternative drug in patients who are allergic to penicillin. The duration of treatment with the above antibiotics range from 5 to 10 days.[5]

Topical antibiotics that are commonly used include tetracycline, bacitracin ointment, gentamicin or chlorhexidine cream. No controlled trials exist for the use of these topical antibiotics in the treatment of impetigo.

6.2.3 Recurrent impetigo

Patients with recurrent impetigo should be evaluated for carriage of *Staphylococcus aureus*. The nares is the most common site of carriage, but the perineum, axillae and toewebs may also be colonised.[5] Nasal mupirocin 2% ointment applied to the nares four times daily for 5 days has been shown to eliminate nasal *Staphylococcus aureus* carriage.[7]

B Long term unrestricted use of mupirocin has been associated with the development of resistance.[8]

Grade B, Level IIa

Therefore judicious use is advocated and only in MRSA carriers.

6.3 Ecthyma

This is a pyogenic infection of the skin resembling impetigo but located deeper, producing ulceration that reaches the dermis and often covered by adherent crusts. Unlike impetigo, it heals with scarring. It is caused by *Streptococcus pyogenes*, *Staphylococcus aureus*, or a combination of the two[9]. The condition usually follows trauma to the skin for example insect bites, scabies and varicella. Poor hygiene and malnutrition are predisposing factors and the legs are often affected.

Most cases affect children ranging in age from 6 months to 18 years.[9] It begins with pustules and vesicles that become ulcerated and are covered with thick adherent crusts with surrounding erythema.

Improved hygiene and nutrition and treatment of scabies and any underlying condition are important.

B Treatment should be an oral antibiotic with activity against both *Staphylococcus aureus* and *Streptococcus pyogenes* such as cloxacillin, cephalexin or erythromycin.[10]

Grade B, Level III

The duration of treatment range from 1 to 2 weeks. Local cleansing with chlorhexidine twice daily is helpful.

6.4 Blistering dactylitis

6.4.1 Clinical presentation and bacteriology

This is an uncommon superficial skin infection usually caused by *Streptococcus pyogenes* (Group A beta-hemolytic streptococci), [11] and occasionally by *Staphylococcus aureus.*[12] It occurs most commonly on the fingers and occasionally the toes in children between 2 and 16 years of age.[11] Blisters on an erythematous base occur in the distal phalanges and may extend dorsally to involve the nail folds. Other sites of involvement include the proximal phalanges and the palm. The contents of the blister vary from thin and watery to purulent. In some cases, beta-hemolytic streptococci have been isolated from the tonsils, pharynx or nose suggesting that these sites are sources of the infection.

6.4.2 Diagnosis

Differential diagnoses include herpes simplex, epidermolysis bullosa, friction blisters and burns.[10] The diagnosis is suggested by gram stain of the contained fluid which demonstrates neutrophils and gram-positive cocci in chains. Cultures usually yield *Streptococcus pyogenes.*

6.4.3 Management

B Treatment involves incision and drainage of large blisters, application of potassium permanganate compresses and a 7 to 10 day course of oral penicillin V (25 - 50 mg/kg/day divided 6hrly) or oral amoxycillin (20-50 mg/kg/day divided 8hrly).[5,10] In penicillin-allergic patients, oral erythromycin is a satisfactory alternative.[5, 10]

Grade B, Level III

6.5 Folliculitis

6.5.1 Clinical presentation and bacteriology

This is the most common primary pyoderma seen locally.[2] *Staphylococcus aureus* is the most common cause of bacterial folliculitis in children, appearing usually on the scalp or extremities.[10] The use of topical steroids, especially the stronger ones is a predisposing factor. The lesions are crops of tiny dome-shaped purulent pustules, sometimes with a red areola surrounding the hairs.

6.5.2 Management

B Pre-disposing factors should be removed and treatment is with antibacterial washes containing chlorhexidine. Systemic penicillinase-resistant antibiotics such as cloxacillin, cephalexin or erythromycin should be given for 7 to 10 days.[5]

Grade B, Level III

Sites of *Staphylococcus aureus* carriage (anterior nares, perineum, axillae, toewebs, and external ear canals) should be sought in patients with recurrent folliculitis.

B For those who have failed chlorhexidine wash, topical mupirocin, four times daily for 5 days, can be considered.[5]

Grade B, Level III

B Long term unrestricted use of mupirocin has been associated with the development of resistance.[8]

Grade B, Level IIa

Therefore judicious use is advocated, and only in MRSA carriers.

6.5.3 Pseudomonal folliculitis

Pseudomonal folliculitis is most commonly acquired through the use of hot tubs, whirlpools, swimming pools and contaminated bath sponges.[13,14] It is caused by *Pseudomonas aeruginosa*, a gram-negative bacteria that flourishes in turbulent, warm, inadequately

chlorinated water. The rash appears 8 to 48 hours later and consists of pruritic erythematous follicular papules, vesicles and pustules. Lesions are usually concentrated in areas covered by the bathing suit, especially on the buttocks and this sign distinguish whirlpool folliculitis from other nonspecific folliculitis. The diagnosis is confirmed by culturing *Pseudomonas aeruginosa* from the skin and the infected water.

No treatment is needed for *Pseudomonas aeruginosa* folliculitis as the eruption clears spontaneously in 7 to 10 days in the absence of re-exposure.[14]

6.6 Furunculosis and carbuncles

6.6.1 Clinical presentation and bacteriology

When *Staphylococcus aureus* infect the hair follicle at a deeper level than in folliculitis, the inflammation extends to the dermis causing furuncles or carbuncles. Individual lesions are called furuncles or boils. When the infection involves several adjacent follicles, creating an inflammatory mass from which pus discharge through several follicular orifices, the lesion is called a carbuncle.

6.6.2 Predisposing factors

Local predisposing factors include maceration caused by friction and sweating and cutaneous injury such as abrasions and cuts. Patients with diabetes mellitus, anaemia, hypo-gamma-globulinemia, neutrophil function defects and general debility are particularly at risk.

6.6.3 Management

Management includes treating individual lesions, correcting predisposing factors and preventing recurrences.

B Larger lesions should be incised and drained if fluctuant.[15] Appropriate antibiotics include cloxacillin or cephalexin. [5,9]

Grade B, Level III

Erythromycin may be used in patients allergic to penicillin. Treatment should be continued for 7 to 10 days or until the inflammation has subsided. [5]

Steps to eliminate predisposing factors include

- Daily baths with antibacterial soaps or cleansers such as chlorhexidine
- Wearing loose-fitting clothes
- Frequent laundering of clothing, towels and bed linen
- Correction of systemic disorders[15]

Weijmer et al [16] found that 16 patients with recurrent furunculosis and without anaemia had significantly lower serum iron concentrations than controls. Symptoms resolved in 15 of 16 in 3 to 4 weeks of adding supplementary iron. Although the mechanism is unclear, there may be a relationship between low serum iron levels and an increased susceptibility to infection. The authors suggest studying the serum iron concentration in all patients with refractory recurrent furunculosis.

B If the serum iron level is low, iron supplementation should be added.

Grade B, Level III

Carriage of *Staphylococcus aureus* in the patient or in family members should be investigated in refractory recurrent disease. Intranasal use of 2% mupirocin ointment has been shown to eliminate nasal *Staphylococcus aureus* after a 5-day course in all patients treated, and 50% remained free of organisms after 5 months.[7]

B Long term unrestricted use of mupirocin has been associated with the development of resistance.[8]

Grade B, Level IIa

Therefore judicious use is advocated, and only in MRSA carriers.

6.7 Cellulitis and erysipelas

6.7.1 Cellulitis

Cellulitis is an acute inflammation of the dermis and subcutaneous tissue, often occurring in areas where the integrity of the skin is compromised. Tender, warm and erythematous induration of the skin with ill-defined margins is characteristic, usually associated with fever, regional lymphadenopathy and leukocytosis. Our local study showed that cellulitis accounted for 5% of all primary pyoderms seen in a skin referral centre.[2]

Common predisposing factors include trauma, ulcers, lymphatic stasis and tinea pedis.

Haemophilus influenzae infection is characterised by a dusky-coloured cellulitis on the cheeks or over the joints in children younger than 3 years of age. It is associated with fever, leukocytosis and toxemia.[17-20] In older children, other causative organisms include streptococci and staphylococci.

B In uncomplicated cellulitis, antibiotics against streptococci and staphylococci should be used, namely, a combination of amoxycillin and cloxacillin, cephalexin, erythromycin or a combination of intravenous crystalline penicillin G (100,000-250,000 units/kg/day divided 6hrly) and cloxacillin.

Grade B, Level III

A Intravenous ampicillin/sulbactam (150 mg/kg/day divided 8hrly) is a useful second-line alternative[21] especially in the presence of bone or joint infection.

Grade A, Level Ib

For facial/periorbital cellulitis in young children, admission to the hospital is warranted for both investigations and intravenous antibiotics.

B Cefoxitin (80 - 160 mg/kg/day divided 6hrly)[18],

Grade B, Level IIa

B Ampicillin/sulbactam[22] and

Grade B, Level III

C Ceftriaxone (50-100 mg/kg/day 24hrly) are effective.

Grade C, Level IV

Predisposing causes must be dealt with to prevent recurrences.

6.7 Erysipelas

Erysipelas differs from cellulitis in that it has well-defined margins. Otherwise it is often difficult to distinguish them, and can therefore be regarded as a form of superficial cellulitis. Moreover, they are both caused, in most cases, by streptococci, especially Group A *Streptococcus.*[23] Infection is believed to start at breaks in the skin, such as at ulcers, trauma sites, bites, excoriations and sites of superficial fungal infections. Venous and lymphatic insufficiency are important predisposing factors.

B Uncomplicated erysipelas can usually be treated on an outpatient basis. Oral amoxycillin plus cloxacillin, cephalexin, or erythromycin should be administered.[5]

Grade B, Level III

Predisposing causes must be dealt with to prevent recurrences.

6.8 Peri-anal streptococcal dermatitis/cellutitis

6.8.1 Clinical presentation and bacteriology

Peri-anal streptococcal dermatitis (peri-anal cellulitis) is often misdiagnosed because it appears more like a dermatitis rather than cellulitis around the anus. There is a male preponderance with a peak

incidence between the age of 3 to 4 years. Most commonly, it presents as a bright pink erythema extending a few centimeters from the anus. The second commonest form involves a painful and fissuring erythema with dried mucoid discharge. The third form presents as a beefy, red, thickened plaque with superficial crusting at the anal verge. Constipation and painful defecation are common accompanying features. Lesions may extend to involve the vulva and perineum. This disease is caused mainly by group A β-hemolytic streptococci. Possible routes of infection include digital contamination from the oropharynx or the skin.

6.8.2 Diagnosis

The differential diagnoses include candidiasis, pinworms, seborrhoeic dermatitis, psoriasis, inflammatory bowel disease and sexual abuse. Swab cultures from the perianal area for streptococci will establish the diagnosis.

6.8.3 Management

C Recommended therapy is oral penicillin V or amoxycillin for 10 to 14 days.[24]

Grade C, Level IV

Erythromycin can be used as a substitute in patients who are allergic to pencillin.

6.9 Necrotising fasciitis

6.9.1 Pathogenesis and clinical presentations

This is a medical emergency and admission to hospital is needed. Necrotising fasciitis can result from invasion by group A *Streptococci*, or other organisms, into the deep fascial compartments because of impaired host defenses in an immunocompromised child with aplastic anaemia, leukaemia or uncontrolled diabetes mellitus. Predisposing causes include skin abscesses, insect bites, chickenpox, intramuscular injections, omphalitis and surgical procedures.

The lesion begins as a tender erythematous plaque that promptly erupts with painful blisters on the surface. A purulent centre develops, followed by central necrosis and the formation of a black eschar. Frank gangrene sets in soon after. Patients are usually seriously ill, toxic and febrile. In doubtful cases, magnetic resonance imaging may help to distinguish it from cellulitis by demonstrating involvement of deep fasciae with fluid collections, thickening and enhancement after contrast administration.[25]

As many as 75% of cases may grow mixed flora on bacterial cultures.[26, 27] Some of these anaerobes and aerobes may be pathogenic and they include *Bacteroides fragilis, Clostridium perfringens, Peptostreptococcus* spp., *Escherichia coli, Pseudomonas aeruginosa*, coliforms and enterococci.

6.9.2 Management

Prompt surgical debridement is the most important aspect of therapy.

C For group A streptococcal infection, also known as streptococcal gangrene, and classically associated with chickenpox, high dose intravenous penicillin G (250,000-450,000 units/kg/day divided 4-6hrly) is the antibiotic of choice.[28, 29]

Grade C, Level IV

Addition of clindamycin (25-40mg/kg/day divided 6-8hrly) has also been recommended.[30] For the others, where anaerobes or gram-negative organisms may be involved, antibiotics used before obtaining bacteriologic cultures include ampicillin, gentamicin (5-7.5mg/kg/day divided 8-12hrly) + clindmycin; ampicillin, gentamicin + metronidazole (30mg/kg/day divided 6-8hrly); ampicillin-sulbactum + gentamicin; or imipenem (60-100mg/kg/day divided 6-8hly) + metronidazole.[31] Referral to an infectious disease specialist is useful. Mortality can be high despite aggressive treatment.

6.10 Staphylococcal scalded skin syndrome (SSSS)

6.10.1 Pathogenesis and clinical presentations

Presentation of this syndrome can range from localised bullae to generalised erythema and desquamation. A prior upper respiratory tract infection is common and an erythematous rash usually begins on the face, neck, axilla and groins. A distinctive fissuring may appear, especially around the eyes and mouth. The skin soon becomes tender and the epidermis comes off as sheets over 3 to 5 days, leaving behind huge areas of superficial erosions but without subsequent scarring. Complete recovery is expected in 10 to 12 days from onset. Staphylococcal exfoliative toxins (A and B) produced by phage group II *Staphylococcus aureus* account for the subgranular epidermolysis of the skin.[32]

6.10.2 Diagnosis

Important differential diagnoses to consider are toxic epidermal necrolysis (often from drug allergy), generalised exfoliative dermatitis, scarlet fever and sunburn. Cultures from the skin, nostrils and throat often grow coagulase positive *Staphylococcus aureus.*

6.10.3 Management

C Oral or intravenous cloxacillin is the treatment of choice.[33] Management of SSSS includes hospitalisation and supportive measures with non-stick dressings, bland emollients, burn cradle, intravenous fluids and close monitoring of hydration and electrolyte balance.

Grade C, Level IV

6.11 Toxic shock syndrome (TSS)

6.11.1 Clinical presentation

Toxic shock syndrome (TSS) typically involves a menstruating adolescent female who presents with a high fever, generalised rash, hypotension followed by desquamation of the palms and soles. The

following features must be present according to the diagnostic criteria for TSS:[34]

- Fever (temperature greater than 39.9°C)
- Rash (diffuse macular erythroderma)
- Desquamation 1 to 2 weeks after the onset of illness, particularly of the palms and soles.
- Hypotension (systolic pressure less than 90 mmHg for adults or below the fifth percentile for children, or orthostatic syncope)
- Involvement of 3 or more of the following organ systems:
  - Gastrointestinal (vomiting or diarrhoea at onset of illness)
  - Muscular (severe myalgia or creatine phosphokinase level greater than 2 times normal)
  - Mucous membranes (hyperaemia)
  - Hepatic (total bilirubin, liver enzymes more than 2 times normal)
  - Hematological (platelet less than 100 000/mm^3)
  - Renal (serum urea or creatinine greater than 2 times normal)
  - Central nervous system (disorientation or alterations in consciousness without focal neurological signs)
- Negative results for:
  - blood, throat and cerebrospinal fluid cultures
  - serologic tests for Rocky Mountain spotted fever, leptospirosis or measles

In non-menstruating TSS, CNS manifestations and anaemia are less frequent, whereas musculoskeletal involvements are more frequent than in menstruating TSS. Some common predisposing causes include postpartum infection, cutaneous abscesses, surgical wounds and burns. Fatality can be as high as 10%.[35] The disease is initiated by *Staphylococcus aureus* infection of the vagina (via prolonged tampon use), or of the upper respiratory tract and sinuses. The staphylococcal toxic shock syndrome toxin-1 (TSST-1) produced is responsible for the skin and systemic features.

6.11.2 Diagnostic criteria

Since the 1980s, there has been a marked increase in the recognition of highly invasive Group A streptococcal (GAS) infection associated with shock and organ failure, termed as streptococcal TSS. The diagnostic criteria are as shown:[29]

A. Isolation of Group A *Streptococcus*
   1. From a sterile site
   2. From a nonsterile body site

B. Clinical signs of severity
   1. Hypotension
   2. Clinical and laboratory abnormalities (requires two or more of the following):
      a. Renal impairment
      b. Coagulopathy
      c. Liver abnormalities
      d. Acute respiratory distress syndrome
      e. Extensive tissue necrosis, i.e. necrotising fasciitis
      f. Erythematous rash

Definite case is defined as A1 + B(1+2) and probable case as A2 + B(1+2). Most commonly, infection begins at a site of minor local trauma, which may not result in a break in the skin. The complications are severe; bacteremia associated with aggressive soft tissue infection, shock, adult respiratory distress syndrome and renal failure. 30% to 70% of patients die in spite of aggressive modern treatments.[36] Pyogenic toxins (A and B) and streptococcal superantigen (SSA) are involved in the pathogenesis of streptococcal TSS.

6.11.3 Management

Differential diagnoses of TSS include meningococcemia, leptospirosis, Kawasaki disease and the early stage of SSSS.

C The patient must be hospitalised for intravenous fluid correction and anti-staphylococcal antibiotics such as cloxacillin.[32]

Grade C, Level IV

C In streptococcal TSS, penicillin G should be administered.[37]

Grade C, Level IV

For both staphylococcal and streptococcal TSS, addition of clindamycin (25-40mg/kg/day divided 8 hrly) has shown added benefits.[38]

6.12 Methicillin-resistant staphylococcus aureus (MRSA)

6.12.1 Clinical presentation and diagnosis

MRSA infection of the skin and soft tissue deserves separate mention. There is a 10 to 25-fold increase in the prevalence of MRSA infection in the community over the past decade,[39,40] but it is still largely a nosocomial infection of a previous skin lesion and usually presents as an indolent, non-healing, raw ulcer. Patients at risk are those with burns, contaminated surgical wounds, chronic venous access sites and premature infants.

MRSA infection should be confirmed by a bacterial swab culture but it may be difficult to distinguish it from MRSA colonisation. Ideally, soft tissue and skin infections should be managed in specialised skin or infectious disease clinics. This will ensure adequate management and eradication of MRSA in the community.

6.12.2 Pathogenesis

The main mode of transmission in the hospital is via hands (especially from healthcare worker) which may become contaminated by contact with:

- colonised or infected patients
- colonised or infected body sites of the personnel themselves
- devices, items, or environmental surfaces contaminated with body fluids containing MRSA.

6.12.3 Management

Standard precautions, as described in the "Guideline for Isolation Precautions in Hospitals," are useful to control the spread of MRSA.[41] The standard precautions include:

- hand washing
- gloving
- masking
- gowning
- appropriate device handling
- appropriate handling of laundry

A For MRSA nasal colonisation, topical mupirocin or topical fusidic acid plus oral cotrimoxazole are equally effective.[42]

Grade A, Level Ib

B Topical mupirocin twice daily for one week has been shown to be effective in eradicating MRSA from nasal carriers.[43]

Grade B, Level III

B Topical mupirocin twice daily for 5 days has been used for treating mild cases of MRSA skin infection.[44]

Grade B, Level III

For mild to moderate soft tissue and skin infections, a combination of at least 2 oral antibiotics is advised in order to minimise development of multi-resistant strains of MRSA.

C The antibiotics selected would depend on culture sensitivity results. Some of the oral antibiotics used include: fusidic acid (20-50 mg/kg/day divided 8hrly), clindamycin (10-40 mg/kg/day divided 8hrly), cotrimoxazole (TMP 8mg plus SMZ 40mg/kg/day divided 12hrly), rifampicin[45] (10-20mg/kg/day divided 12-24hrly) and minocycline[‡] (1-2 mg/kg/day divided 12hrly).

Grade C, Level IV

C Intravenous vancomycin (40-60mg/kg/day divided 8-12hrly) is still the antibiotic of choice in moderate to severe MRSA infection.

Grade C, Level IV

[‡]***Not recommended for children younger than 8 years old***

Table 6.1 Treatment of bacterial skin infections

Condition	Medications	Grade/Level
Impetigo	1st line - Cloxacillin 30-50 mg/kg/day divided 6hrly	**B/III**
	- Cephalexin 30-50 mg/kg/day divided 8hrly	**B/III**
	Alternatives - Erythromycin 30-50 mg/kg/day divided 6hrly	**B/III**
	- Cotrimoxazole TMP 8 mg + SMX 40mg/kg/day divided 12hrly	**B/III**
Ecthyma	Cloxacillin) Cephalexin) Erythromycin) As above	**B/III**
Blistering Dactylitis	Pencillin V - 25-50 mg/kg/day divided 6hrly	**B/III**
	Amoxycillin - 20-50 mg/kg/day divided 8hrly	**B/III**
	Erythromycin - 30-50 mg/kg/day divided 6hrly	**B/III**
Folliculitis	Cloxacillin) Cephalexin) Erythromycin) As above	**B/III** **B/III** **B/III**
Furunculosis /Carbuncles	Cloxacillin) Cephalexin) Erythromycin) As above	**B/III** **B/III** **B/III**
	Incision and drainage when fluctuant	**B/III**
	Iron supplementation	**B/III**

Table 8.1 Treatment of bacterial skin infections *(cont'd)*

Condition	Medications	Level of evidence
Cellulitis/ Erysipelas	Amoycillin - 20-50 mg/kg/day divided 6hrly and Cloxacillin- 25-50 mg/kg/day divided 6hrly Erythromycin - 30-50 mg/kg/day divided 6hrly Cephalexin - 30-50 mg/kg/day divided 8hrly Ampicillin/ Sulbactam - 150 mg/kg/day divided 12hrly intravenously Ceftriaxone - 50-100 mg/kg/day divided 12-24hrly intravenously	**B/III** **B/III** **B/III** **A/Ib** **C/IV**
Perianal Strepto -coccal Dermatitis	Pencillin V - 25-50 mg/kg/day divided 6hrly Amoycillin - 20-50 mg/kg/day divided 8hrly Erythromycin - 30-50 mg/kg/day divided 6hrly	**C/IV**
Necrotising Fasciitis	Urgent surgical debridement Intravenous pencillin G 250,000-450,000 units kg/day divided 4-6hrly for streptococcal infections. Administration of other antibiotics depend on clinical assessment and culture results	**C/IV**
SSSS	Cloxacillin - 30-50 mg/kg/day divided 6hrly	**C/IV**
TSS	Staphylococcal TSS : Cloxacillin 30-50 mg/kg/day divided 6hrly ± Clindamycin 25-40mg/kg/day divided 8hrly Streptococcal TSS : Penicillin G 250,000-450,000 units/kg/day divided 4-6hrly ± Clindamycin 25-40 mg/kg/day divided 8hrly	**C/IV**

Table 8.1 Treatment of bacterial skin infections *(cont'd)*

Condition	Medications	Level of evidence
MRSA infection	Mild cases : topical mupirocin and combination of at least 2 oral antibiotics: (guided by culture & sensitivity results) - Fusidic acid 20-50 mg/kg/day divided 8hrly - Clindamycin 10-40 mg/kg/day divided 8hrly - Cotrimoxazole TMP 8 mg + SMX 40 mg/kg/day divided 12hrly - Rifampicin 10-20 mg/kg/day divided 12-24hrly - Minocycline‡ 1-2 mg/kg/day divided 12hrly Intravenous Vancomycin 40-60 mg/kg/day divided 8-12hrly for moderate to severe MRSA infection	**B/III** **C/IV** **C/IV**

‡*Not for children younger than 8 years old*

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Annex A 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.

Choose the best answer

Antibiotic use in paediatric respiratory conditions

1. Antibiotics are not necessary in the majority of acute respiratory infections in children because

A. bacterial resistance is very high in Singapore
B. more than 90% are caused by viruses
C. reduction in healthcare cost is most important
D. antibiotics are dangerous

2. Antibiotic resistance

A. is confined to *Streptococcus pneumoniae* only
B. is confined to *Hemophilus influenzae* only
C. is related to widespread inappropriate use of antibiotics
D. None of the above

3. In acute rhinitis

A. yellow sputum is an indication for antibiotic use
B. is usually caused by bacteria
C. can be differentiated from allergic rhinitis which is more chronic
D. none of the above

4. In acute sinusitis
A. antibiotics are indicated as majority are bacterial
B. referral to a specialist is indicated if there is no clinical response in 3 weeks
C. Amoxycillin is the first line drug of choice
D. all of the above

5. Acute pharyngitis
A. is usually viral in etiology and does not require treatment with antibiotics
B. associated with tender cervical lymph nodes is usually indicative of bacterial etiology
C. with the presence of rhinitis, sneezing and conjunctivitis suggests a viral etiology
D. all of the above

6. Acute sinusitis
A. is usually bacterial in origin
B. can only be definitively diagnosed after 7 days of symptoms
C. presents with fever, mucopurulent rhinorrhea and cough
D. all of the above

7. Acute bronchiolitis
A. is caused by respiratory viruses
B. usually occurs in infancy
C. is not treated with antibiotics
D. all of the above

8. Acute bronchitis
A. presents with fever, tachypnoea, crepitations and wheeze
B. is usually caused by viruses and antibiotics are not indicated
C. may be treated with macrolides as Mycoplasma is the main non-viral etiological agent
D. all of the above

9. The following is TRUE in penicillin-resistant *Streptococcal* infection

A. Amoxycillin must never be used
B. The first line antibiotic of choice is a cephalosporin
C. Antibiotic-resistant organisms cause more severe disease
D. High dose amoxycillin is the drug of choice

10. Pneumonia in neonates

A. can be treated with oral antibiotics at home
B. is usually caused by *Haemophilus influenzae*
C. must be treated with antibiotics effective against both gram-negative and gram-positive organisms
D. is commonly caused by S*treptococcus pneumoniae*

Use of antibiotics in paediatric gastrointestinal disease

11. In childhood gastroenteritis, appropriate antibiotics should be used if

A. there is evidence of septicaemia
B. the stools are bloody
C. the patient is dehydrated
D. there is a history of traveling abroad

12. In acute gastroenteritis due to *Salmonella* infection, the use of antibiotics

A. is effective in shortening the duration of illness
B. should be restricted to children with increased risk of invasive disease
C. be prohibited if the patient is G6PD deficient
D. should be administered simultaneously with an anti-diarrhoeal agent

13. In *Shigella* gastroenteritis, antimicrobial therapy is
A. associated with increased risk of intussusception
B. usually given as a stat dose only
C. indicated if the stools are bloody
D. effective in shortening the duration of diarrhoea

14. In cholera, antibiotic therapy has been shown to
A. cause an increase incidence of severe dehydration
B. be associated with haemolytic uraemic syndrome
C. cause a decrease in duration of diarrhoea
D. responsible for prolonged carrier state

15. *Campylobacter* diarrhoea is
A. treated with intravenous ceftriaxone
B. usually associated with intussusception
C. not seen in Singapore children
D. treated with erythromycin early in the course of the disease

16. Treatment of *H. pylori* infection in children is indicated
A. for children with epigastric pain
B. if there is associated diarrhoea
C. even though the patient is asymptomatic
D. if duodenal ulcer is present

Use of antibiotics in acute bacterial meningitis in children

17. The diagnosis of bacterial meningitis is classically based on
A. clinical features
B. blood culture
C. CSF microscopy
D. CSF culture

18. In the management of bacterial meningitis, the age of the child is an important consideration for
A. the causative organism
B. the choice of antibiotics
C. the way the antibiotic is administered
D. all of the above

19. For infants below 1 month of age, the most likely organism as the cause of acute meningitis is
A. *Pneumococcus*
B. *Meningococcus*
C. Group B *Streptococcus*
D. *Haemophilus* type b

20. For infants below 1 month of age suspected of acute meningitis, the empirical antibiotics to be started is
A. Ceftriaxone
B. Cefotaxime
C. Vancomycin
D. Ampicillin with gentamicin

21. In a very sick 3 year old child strongly suspected of bacterial meningitis, the empiric antibiotic treatment is
A. Ceftriaxone with vancomycin
B. Cefotaxime
C. High dose ampicillin
D. High dose pencillin G

22. In children above the age of 3 months, the most likely gram-negative coccobacillus causing bacterial meningitis is
A. *E. coli*
B. *Haemophilus influenzae* type B
C. *Neisseria meningitidis*
D. *Pseudomonas aeruginosa*

23. Chemoprophylaxis against *Haemophilus influenzae* type b is achieved with

A. Vaccination of close contacts
B. Treatment with cetriaxone
C. Treatment with rifampicin
D. Treatment with chloramphenicol

24. In a child who had *Haemophilus influenzae* type b meningitis, vaccination against future *Haemophilus influenzae* invasive disease

A. Is not indicated at all
B. Is given if the child is < 24 months old
C. Is given if there is *Haemophilus influenzae* nasopharyngeal carriage among family members
D. Is given if the child attends a child-care center

25. For beta-lactam resistant infection with *Streptococcus pneumoniae*, the antibiotic of choice is

A. Rifampicin
B. Vancomycin
C. Ampicillin
D. Vancomycin with ceftriaxone

26. Besides *Haemophilus influenzae* type b, chemoprophylaxis should also be considered for contacts of

A. *Streptococcus* group B
B. *Streptococcus pneumoniae*
C. *Neiseria meningitides*
D. *E. coli*

Use of antibiotics in paediatric urinary tract infection (UTI)

27. Febrile urinary tract infections in infants should be treated aggressively because

A. infants have higher incidence of renal involvement or pyelonephritis
B. infants have higher incidence of concomitent bacteremia
C. infants have higher incidence of underlying renal tract abnormalities
D. all of the above

28. Gentamicin is the recommended 1st line antibiotic in febrile UTI because

A. it is cheap
B. it is a safe drug
C. most uropathogens are gram negative bacteria sensitive to gentamicin
D. local antibiogram shows that all uropathogens are sensitive to gentamicin

Answer "True" or "False"

Use of antibiotics in paediatric bacterial skin infections

29. *Streptococcal* skin infections

A. Beta-hemolytic S*treptococci* are responsible for blistering dactylitis
True☐ False☐

B. Are consistently associated with elevated levels of anti-streptolysin O titres (ASOT)
True☐ False☐

C. Cellulitis is effectively treated with tetracycline in a patient who is allergic to penicillin
True☐ False☐

D. Peri-anal S*treptococcal* dermatitis causes peri-anal pruritus and blood streaked stools
True☐ False☐

E. Are not complicated by post-infection glomerulonephritis, unlike cases of S*treptococcal* throat infections
True☐ False☐

30. For each of the following questions, decide whether each statement is **True** or **False**

A. Bullous impetigo is caused by group A *Streptococcus*
True☐ False☐

B. Ecthyma is caused by either *Staphylococcus aureus* or *Streptococcus pyogenes*
True☐ False☐

C. Erysipelas is caused mainly by *Streptococcus pyogenes*
True☐ False☐

D. Unlike impetigo, ecthyma commonly heals with scarring
True☐ False☐

E. Cloxacillin is the drug of choice for the treatment of folliculitis
True☐ False☐

31. Regarding necrotizing fasciitis

A. *Staphylococcus aureus* is a common cause
True☐ False☐

B. Antibiotic therapy without surgery is usually successful
True☐ False☐

C. Pus is usually present in the subcutaneous tissue
True☐ False☐

D. Gas formation may occur in affected tissue
True☐ False☐

E. Predisposing causes include skin abscesses and chicken-pox
True☐ False☐

32. For each of the following questions, decide whether each statement is True or False

A. In Staphylococcal scalded skin syndrome, the skin separation is at the dermoepidermal junction
True☐ False☐

B. In Staphylococcal scalded skin syndrome, fissuring around the eyes and mouth and skin tenderness is characteristic
True☐ False☐

C. Needle aspiration of the leading edge of cellulitis usually yields a pathogen on culture
True☐ False☐

D. Hot-tub folliculitis is caused by *Psuedomonas aeruginosa*
True☐ False☐

E. Penicillin is effective therapy for Staphylococcal toxic shock syndrome.
True☐ False☐

Answers to MCQs - Use of Antibiotics in Paediatric Care

No	Answer	No	Answer	No	Answer
1	B	17	D	29E	False
2	C	18	D	30A	False
3	D	19	C	30B	True
4	D	20	D	30C	True
5	D	21	A	30D	True
6	D	22	B	30E	True
7	D	23	C	31A	False
8	D	24	B	31B	False
9	D	25	D	31C	True
10	C	26	C	31D	True
11	A	27	D	31E	True
12	B	28	C	32A	False
13	D	29A	True	32B	True
14	C	29B	False	32C	False
15	D	29C	False	32D	True
16	D	29D	True	32E	False

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MOH CLINICAL PRACTICE GUIDELINES 3/2002

Antibiotics in Paediatric Care

Ministry of Health

NMRC National Medical Research Council

Chapter of Paediatricians
Academy of Medicine
Singapore

Management of Paediatric Respiratory Infection

Upper Respiratory Tract Infection

A Upper respiratory infections are usually viral in origin and do not require antibiotics.

Grade A, Level Ia

A Mucopurulent nasal discharge is a common feature of uncomplicated viral rhinitis and is not an indication for antibiotics.

Grade A, Level Ib

A Majority of pharyngitis and tonsillitis are viral in origin and do not require antibiotics.

Grade A, Level Ib

A Antibiotics are indicated in pharyngitis or tonsillitis when streptococcal infection is suspected. Antibiotics of choice are penicillin, amoxycillin or erythromycin for patients with penicillin allergy.

Grade A, Level Ib

Otitis externa/media

C Mild acute otitis externa can be treated with topical antimicrobial eardrops. Severe infections can be treated with oral cloxacillin or erythromycin.

Grade C, Level IV

A Acute otitis media can be treated with amoxycillin for 7 days.

Grade A, Level Ia

A Recurrent otits media or otitis media with effusion should be referred to the ENT surgeon.

Grade A, Level Ia

Acute sinusitis

A Acute sinusitis is commonly bacterial in origin and requires amoxycillin or cotrimoxazole.

Grade A, Level Ia

Acute bronchilitis

A Acute bronchiolitis is caused by respiratory viruses and antibiotics are not indicated.

Grade A, Level Ib

Acute laryngo-tracheobronchitis

C Acute laryngo-tracheobronchitis is caused by respiratory viruses and antibiotics are not indicated.

Grade C, Level IV

Acute bronchitis

B Acute bronchitis is mainly viral in origin and antibiotics are not routinely recommended. A macrolide is recommended in an older child when mycoplasma infection is suspected.

Grade B, Level II

Condition	Aetiological Agents	Indications for antibiotics	Grade /Level
Acute rhinitis	• Mainly viral (>90%)	Antibiotics not indicated	A/1a
Pharyngitis/ tonsillitis	• Majority are viral (esp <4 yrs old) • Commonest bacterial agent: *Streptococcus* grp A	Majority do not require antibiotics Pencillin V (50mg/kg/day divided q6 - 8H) x 10 days Amoxycillinx6 days	A/1a A/1b
Acute sinusitis	• *Streptococcus pneumoniae* • *Haemophilus influenzae* • *Moraxella catarrhalis*	Amoxycillin (50mg/kg/day divided 8H) x 7-10 days	A/1a
Acute otitis externa	• *Staphylococcus aureus*	Mild infection: Topical eardrops Severe infection: Cloxacillin (50mg/kg/day divided 6H) x 7 days	C/IV C/IV
Acute otitis media	• *Streptococcus pneumoniae* • *Haemophilus influenzae* • *Moraxella catarrhalis* • Group A *Staphylococcus* • *Staphylococcus aureus*	Amoxycillin x 7 days If <2 yrs old, attends childcare and had antibiotics in the past 3 months - consider higher dose (80-90mg/kg/day)	A/1a
Acute bronchiolitis	• Respiratory viruses mainly RSV	Antibiotics not indicated	A/1b
Acute laryngo-tracheobronchitis	• Respiratory viruses mainly Parainfluenza virus	Antibiotics not indicated	C/IV
Acute bronchitis	• Mainly viral	Antibiotics not routinely recommended	A/1a
	• Bacterial agents include *Mycoplasma pneumoniae* *Streptococcal pneumoniae* *Haemophilus influenzae* *Staphylococcal aureus*	Macrolide when Mycoplasma suspected	B/II
Pneumonia Newborn	• Gp B *Streptococus* • *E. Coli* • Enteric gram - negative bacilli • *Listeria monocytogenes* • *Enterococcus*	Recommended immediate referral to hospital	C/IV
<2 yrs	• Predominantly viral • *Streptococcus pneumoniae* • *Haemophilus influenzae* • *Moraxella catarrhalis*	Antibiotics not indicated	C/IV
>2 yrs	• *Streptococcus pneumoniae* • *Mycoplasma pneumonia* (esp age >5 years) • *Haemophilus influenzae* • *Moraxella catarrhalis*	Amoxycillin x 7-10 days Macrolides if mycoplasma suspected	C/IV

Management of gastrointestinal diseases

GPP The mainstay of management of gastroenteritis is the prevention and correction of dehydration and electrolyte imbalance.

Viral diarrhoea

GPP Viral diarrhoea should not be treated with antibiotics.

Non-typhoidal salmonella infection

A Non-typhoidal salmonella infection should not be treated routinely with antibiotics.

Grade A, Level Ia

C Antibiotics are required for patients with evidence of extra-intestinal spread such as septicaemia, in the very young (<3 month old) and in the immunocompromised child.

Class C, Level IV

C Cotrimoxazole* (TMP, 10mg/kg/day plus SMX, 50mg/kg/day divided 12 hrly), ampicillin (200mg/kg/day divided 6hrly) or a third generation cephalosporin (eg. ceftriaxone 75-100mg/kg/day 24 hrly) can be given for up to 14 days.

Class C, Level IV

Escherichia coli diarrhoea

C When the disease is severe, antibiotics such as cotrimoxazole* or ampicillin for 5 to 7 days may be required.

Grade C, Level IV

Contra-indicated in children with G6PD deficiency

Shigellosis

B Shigellosis responds to antibiotics. Cotrimoxazole*, ampicillin or a third generation cephalosporin for up to 5 days can be given.

Grade B, Level IIIa

Cholera

C Antibiotics decrease the duration of diarrhoea, excretion of organisms in the stool and total amount of fluid loss. Doxycycline (6mg/kg as a single dose) is the drug of choice for children above 8 years old.

Grade C, Level IV

Campylobacter gastroenteritis

C Erythromycin (50mg/kg/day divided 6hrly) for 7 to 10 days can be used for patients with severe ongoing illness or if risk factors are present.

Grade C, Level IV

Yersinia enterocolitis

C Diarrhoea is self-limiting except for the immunocompromised child who may respond to a third generation cephalosporin in combination with gentamicin (5mg/kg/day in divided doses).

Grade C, Level IV

Amoebiasis

C Metronidazole (35-50mg/kg/day divided 8hrly orally for 10 days) or tinidazole (50-60mg/kg/day as a single dose daily for 3 days) followed by paromomycin (25-35mg/kg/day divided 8hrly for 7 days) should be used in the evaluation of the amoeba.

Grade C, Level IV

Contra-indicated in children with G6PD deficiency

Giardiasis

A Metronidazole (22.5mg/kg/day divided 8hrly orally for 7 days) is effective.

Grade A, Level Ia

Cryptosporidium

C Diarrhoea illness is self-limiting except for the immunocompromised child. Those who are seriously ill may respond to paromomycin in combination with azithromycin.

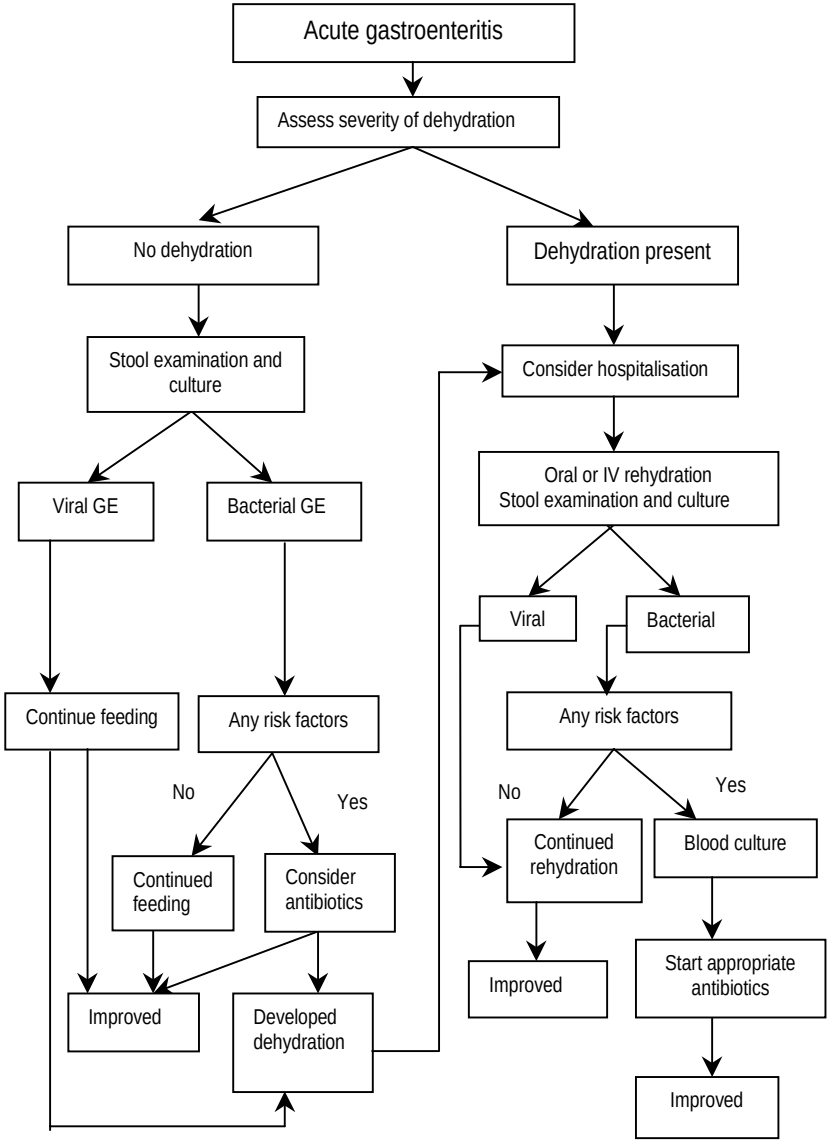
Grade C, Level IV

Helicobacter pylori

B Eradication of *Helicobacter pylori* is important in the prevention of recurrence of *Helicobacter pylori*-associated peptic ulcer disease. Treatment consists of omeprazole, clarithromycin and metronidazole for 1 to 2 weeks.

Grade B, Level III

Approach to acute gastroenteritis (GE)



Diagnosis and empiric antibiotic treatment of acute bacterial meningitis

GPP Blood culture, CSF microscopy and culture should be carried out when a clinical diagnosis of meningitis is made. Empirical antibiotics should be started with necessary alteration when the culture and sensitivities become available.

B For infants below 1 month of age, the likely organisms are Group B *Streptococcus*, *E. coli* or *Listeria monocytogenes*. Ampicillin** (200-300mg/kg/day divided 4-8 hrly) + gentamicin or ampicillin + cefotaxime** (100-200mg/kg/day divided 6-12 hrly)/ceftriaxone** (50-75mg/kg/day 12-24 hrly) are the drugs of choice

Class B, Level III

B For infants between 1 and 3 months of age, the likely organisms include Group B *Streptococcus*, *Escherichia coli*, *Listeria monocytogenes*, *Streptococcus pneumoniae*, *Neisseria meningitidis*, *Haemophilus influenzae* type b. Ampicillin plus ceftriaxone/cefotaxime are the drugs of choice.

Class B, Level III

A For infants above 3 months of age, the likely organisms include *Streptococcus pneumoniae, Neisseria meningitides, Haemophilus influenzae* type b. The drug of choice is ceftriaxone or cefotaxime.

Class A, Level Ib

C Vancomycin** (60mg/kg/day divided 6 hrly) is added when antibiotic resistant *Streptococcus pneumoniae* is suspected.

Class C, Level IV

***** Please refer to main text***

A Chemoprophylaxis** should be considered in contacts of Haemophilus influenzae type b or meningococcal meningitis.

Class A, Level Ib

B If antibiotics other than ceftriaxone or cefotaxime were used to treat *Haemophilus influenzae* type b or meningococcal meningitis, rifampicin** is given at the end of therapy to clear nasopharyngeal carriage.

Class A, Level Ib

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Specific antibiotic treatment and duration of treatment

Organism	Recommended	Alternative	Duration of therapy
Streptococcus pneumoniae[11]			
Penicillin senitive (MIC ≤ 0.06 ug/ml)	Penicillin G	Ampicillin or Ceftriaxone	10-14 days
	Ceftriaxone	Cefotaxime	10-14 days
Penicillin resistant intermediate (MIC 0.1 – 1 ug/ml) or absolute (MIC ≥ 2 ug/ml) and ceftriaxone resistant – intermediate (MIC 0.5 –1 ug/ml) or absolute (MIC ≥ 2 ug/ml)§	Vancomycin + ceftriaxone	Rifampicin + ceftriaxone +vancomycin§	10-14 days
Neisseria meningitidis	Penicillin G	Ampicillin or ceftriaxone	5-7 days
Haemophilus influenzae type b	Ceftriaxone	Ampicillin (if sensitive)	7-10 days

The duration of antibiotic treatment is extended if the meningitis is complicated by the presence of: brain abscess, subdural empyema, delayed CSF sterilization. In such cases, the duration of antibiotics is individualised.[15]

§ Rifampicin can be added to vancomycin with a third generation cephalosoprin in selected cases of S pneumoniae meningitis.

***** Please refer to main text pages 49-58***

Aetiologic agents in acute bacterial meningtitis and recommended empiric antibiotics

Age	Common organisms	Uncommon organisms	Antibiotic	Alternative	Duration (days)	Comments
<1 month	GBS, *E. coli*, *Listeria*	*Salmonella*, *S. aureus*, *P. aeruginosa*, CONS, Gram-negative bacilli	Ampicillin + Gentamicin	Ampicillin + Cefotaxime **or** Ceftriaxone*	GBS, *Listeria:* 14-21days Gram-negative bacilli: 21days	High dose crystalline pencillin/ampicillin is required for GBS. Gentamicin is synergistic with ampicillin for GBS
1-3 months	GBS, *E. coli*, *Listeria* *S. pneumoniae* Hib *N. meningitidis*	*Salmonella*, *S. aureus*	Ampicillin + Ceftriaxone	Ampicillin + Cefotaxime	*S. pneumoniae*: 10-14 days Hib:7-10 days *N. meningitis:* 5-7 days GBS, Listeria: 14-21 days Gram-negative bacilli:21 days	Due to overlap of organisms between <1 month and > 3 months age groups, it is essential to cover for these organisms
> 3 months	*S. pneumoniae*, Hib, *N. meningitidis*	GAS, Gram-negative bacilli	Ceftriaxone +/- Vancomycin§	Cefotaxime +/- Vancomycin§	*S. pneumoniae:* 10-14 days Hib:7-10 days *N. meningitis:* 5-7 days	Addition of vancomycin is strongly recommended if: • child is very sick • CSF is suggestive of bacterial meningitis or • CSF gram stain shows gram-positive cocci.

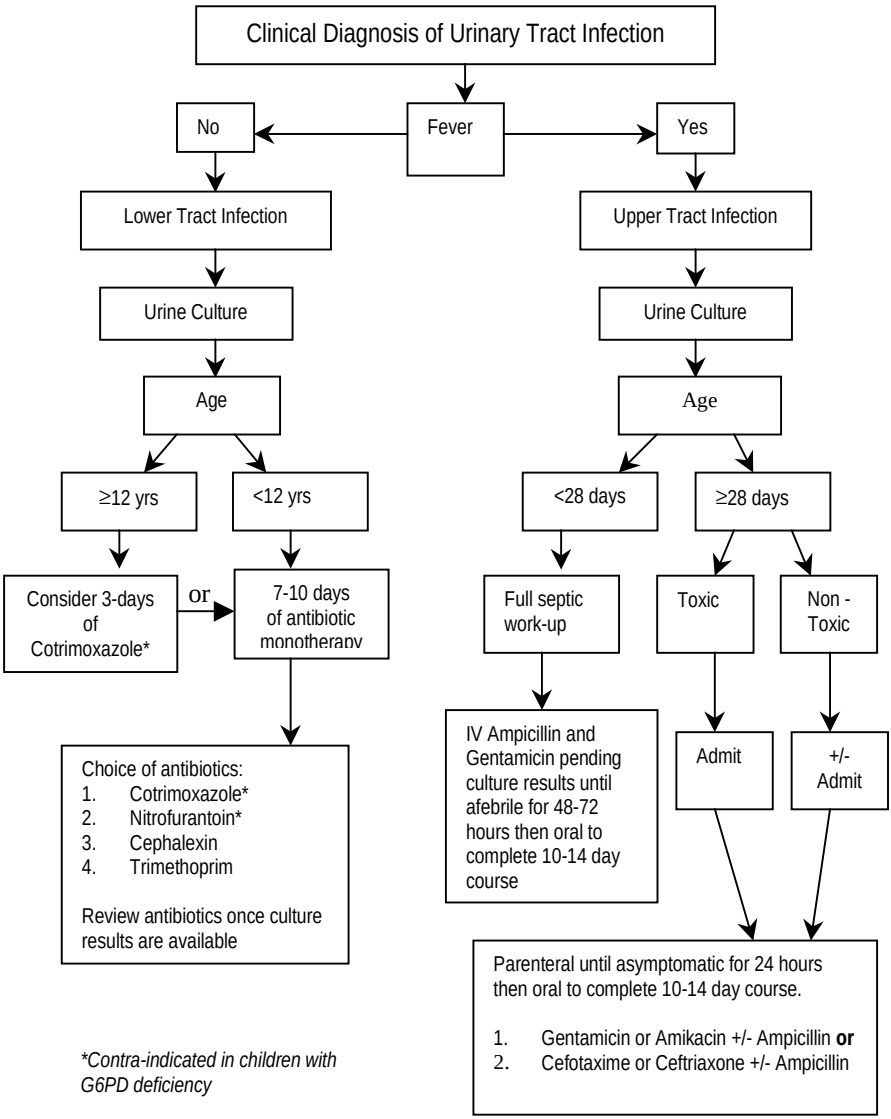
GBS = *Group B Streptococcus, Hib = Haemophilus Influenzae type b, CONS = Coagulase negative Staphylococci,*
GAS = *Group A Streptococcus. Gram negative bacilli comprises Klebsiella, Escherichia coli, Citrobacter, Serratia*
**Ceftriaxone can be used after 7 days of life and in the absence of neonatal jaundice*
§Rifampicin can be added to vancomycin with a third generation cephalosporin in selected cases of S. pneumoniae meningitis
The duration of antibiotic treatment is extended if the meningitis is complicated by the presence of brain abscess, subdural empyema & delayed CSF sterilisation. In such cases, the duration of antibiotic therapy is individualised.

Antibiotic drug doses for acute bacteria meningitis

Antibiotic	Body weight <2 kg Neonates <7 days	Body weight <2 kg Neonates 7-28 days	Body weight >2 kg Neonates <7 days	Body weight >2 kg Neonates 7-28 days	Children > 1 month
Penicillin G*	250,000-450,000 units/kg/day divided 8hrly	450,000 units/kg/day divided 6hrly	250,000-450,000 units/kg/day divided 8hrly	450,000 nits/kg/day divided 6hrly	450,000 units/kg/day divided 6hrly
Ampicillin*	200-300mg/kg/day divided 8hrly	300 mg/kg/day divided 4-6hrly	200-300mg/kg/day divided 8hrly	300 mg/kg/day divided 4-6hrly	300-400 mg/kg/day divided 4-6hrly
Cefotaxime	100 mg/kg/day divided 12hrly	150 mg/kg/day divided 8hrly	150 mg/kg/day divided 8hrly	200 mg/kg/day divided 6hrly	225-300 mg/kg/day divided 6-8hrly
Ceftriaxone	50 mg/kg/day om	50 mg/kg/day om	50 mg/kg/day om	75 mg/kg/day om	100 mg/kg/day divided 12-24hrly
Vancomycin	30 mg/kg/day divided 12hrly	45 mg/kg/day divided 8hrly	30-45 mg/kg/day divided 8-12hrly	45-60 mg/kg/day divided 6-8hrly	60 mg/kg/day divided 6hrly
Gentamicin	2.5 mg/kg/dose every 12-18hrly	2.5 mg/kg/dose divided 8-12hrly	5 mg/kg/day divided 12hrly	75 mg/kg/dose divided 8hrly	6 mg/kg/day divided 8hrly

**For group B streptococcal meningitis, a higher dose of penicillin or ampicillin is recommended. Gentamicin is added for synergy with a penicillin antibiotic in the initial week of treatment.*[11]

Algorithm for the management of urinary tract infections in children



**Contra-indicated in children with G6PD deficiency*

Management of bacterial skin infections

Impetigo

B The majority of impetigo cases are caused by *Staphylococcus aureus*, some by a combination of both *Staphylococcus aureus* and *Streptococcus pyogenes* and few by *Streptococcus pyogenes.* The drug of choice is oral cloxacillin (30-50mg/kg/day divided 6hrly) or oral cephalexin (30-50mg/kg/day divided 8hrly). For children with penicillin allergy, alternatives include erythromycin (30–50mg/kg/day divided 6hrly) or cotrimoxazole* (TMP 8mg + SMX 40mg/kg/day divided 12hrly). Duration of treatment ranges from 5 to 10 days.

Grade B, Level III

Ecthyma

B Ecthyma is caused by *Streptococcus pyogenes, Staphylococcus aureus* or a combination of the two organisms. Treatment consists of oral cloxacillin, cephalexin or erythromycin for 1 to 2 weeks.

Grade B, Level III

GPP Local cleansing with chlorhexidine twice daily is helpful.

Blistering dactylitis

B Blistering dactylitis is usually caused by *Streptococcus pyogenes*. Treatment involves incision and drainage of large blisters, and a 7 to 10 day course of penicillin V (25-50mg/kg/day divided 6hrly), amoxycillin (20-50mg/kg/day divided 8hrly) or erythromycin.

Grade B, Level III

Folliculitis

B Folliculitis is commonly caused by *Staphylococcus aureus.* Treatment consists of chlorhexidine wash and oral cloxacillin, cephalexin or erythromycin for 7 to 10 days.

Grade B, Level III

Contra-indicated in children with G6PD deficiency

Furunculosis and carbuncles

B Furunculosis and carbuncles are infection of hair follicles by *Staphylococcus aureus*. Larger lesions should be incised and drained if fluctuant. Appropriate antibiotics include cloxacillin, cephalexin or erythromycin for 7 to 10 days or until inflammation has subsided.

Grade B, Level III

B Other measures include eliminating predisposing factors, using chlorhexidine cleanser, iron supplementation for refractory furunculosis with low serum iron and eliminating nasal carriage with chlorhexidine, bacitracin, tetracycline or 2% mupirocin ointment. However, long term and unrestricted use of mupirocin has been associated with the development of mupirocin resistance. Therefore judicious use is advocated and only in MRSA carriers.

Grade B, Level III

Cellulitis and erysipelas

B Cellulitis and erysipelas can be treated with a combination of amoxycillin plus cloxacillin, cephalexin, erythromycin, or a combination of intravenous cystalline penicillin G (100,000-250,000 units/kg/day divided 6hrly) and cloxacillin.

Grade B, Level III

For facial/periorbital cellulitis in young children, admission to hospital is warranted and the following antibiotics are recommended:

B Intravenous ampicillin/sulbactam (150mg/kg/day divided 8hrly).

Grade B, Level III

C Ceftriaxone (50-100mg/kg/day intravenously divided 12-24hrly).

Grade C, Level IV

Peri-anal streptoccal dermatitis

C The recommended therapy for peri-anal streptococcal dermatitis is oral penicillin V, amoxycillin or erythromycin for 10 to 14 days.

Grade C, Level IV

Necrotising fascitis

C Necrotising fasciitis is a medical emergency. Prompt surgical debridement is the most important aspect of therapy. High dose intravenous penicillin G (250,000 – 450,000 units/kg/day divided 4-6hrly) is used to treat Group A streptococcal infection. Additional antibiotics will depend on clinical assessment and culture results.

Grade C, Level IV

Staphylococcal scalded skin syndrome

C Treatment includes hospitalisation, supportive measures and cloxacillin.

Grade C, Level IV

Toxic shock syndrome

C Besides hospitalisation, intravenous fluid support, cloxacillin ± clindamycin (25-40mg/kg/day divided 8hrly) is used in staphylococcal toxic shock syndrome (TSS) and penicillin G and clindamycin in streptococcal TSS.

Grade C, Level IV

Methicillin-resistant *Staphylococcus aureus* infection

A For nasal colonisation, topical mupirocin or topical fusidic acid plus oral co-trimoxazole can be used.

Grade A, Level Ib

C For mild to moderate infections, guided by culture sensitivity results, a combination of at least 2 oral antibiotics - fusidic acid (20-50mg/kg/day every 8hrly), clindamycin (10-40mg/kg/day divided 8hrly), co-trimoxazole*, or minocycline‡ (1-2mg/kg/day divided 12hrly) are recommended.

Grade C, Level IV

C For moderate to severe infection, vancomycin (40-60mg/kg/day divided 8-12hrly) is the antibiotic of choice.

Grade C, Level IV

Contra-indicated in children with G6PD deficiency
‡Not recommended for children younger than 8 years old