Preface

WHO's revised drug strategy, as adopted in resolution WHA39.27 of the Thirty-ninth World Health Assembly in 1986, calls for the preparation of model prescribing information which is being developed to complement WHO's Model List of Essential Drugs.[1] The objective is to provide up-to-date source material for adaptation by national authorities, particularly in developing countries, that wish to develop national drug formularies, drug compendia and similar material.[2]

The information is to be regarded as illustrative rather than normative. It is appreciated that it is not possible to develop an information sheet on a specific drug that is appropriate to circumstances prevailing in each of WHO's Member States and that some countries have already formally adopted texts of their own that have a statutory connotation.

This volume has been reviewed by internationally accredited experts and by certain nongovernmental organizations in official relations with WHO, including the International Federation of Pharmaceutical Manufacturers Associations, the International League of Infectious Diseases and the International Society of Chemotherapy.

[1] *The use of essential drugs. Ninth report of the WHO Expert Committee (including the revised Model List of Essential Drugs)*. Geneva, World Health Organization, 2000 (WHO Technical Report Series, No. 895).

[2] For details of volumes already published, see inside back cover.

Drug dosage

Most drug doses are given per kilogram of body weight or as fixed doses calculated for adults of 60 kg.

Storage conditions

Readers are referred to *The International Pharmacopoeia*, 3rd edition, Vol. 4 (Geneva, World Health Organization, 1994) for definitions concerning containers for drugs.

Abbreviations used

i.m. intramuscularly
i.v. intravenously

Introduction

Although many communicable diseases have been effectively contained, bacterial infections remain a major cause of morbidity and mortality, particularly in developing countries. Moreover, in both developed and developing countries, the risk of some serious bacterial infections has increased because of treatments such as chemotherapy for cancer and the emergence of diseases such as human immunodeficiency virus (HIV) infection and the acquired immunodeficiency syndrome (AIDS), which impair the patient's defences against infection.

Antimicrobials have reduced the morbidity and improved the survival of patients with bacterial infections and remain essential for the treatment of many kinds of bacterial disease. However, the increasing prevalence of strains of common pathogenic bacteria resistant to widely available, affordable antimicrobials is, in many cases, dangerously eroding their effectiveness. It is hoped that by encouraging the appropriate use of antimicrobials, the emergence and spread of antimicrobial resistance may be delayed.

Resistance to antimicrobials

The prevalence of antimicrobial resistance among pathogenic bacteria is increasing both among hospital patients and in the community. The emergence of such resistance may in part depend on the acquisition of new mechanisms of interference with antimicrobial activity and on the spread of resistant isolates between patients.

Selection of resistant bacteria

Resistance may be due to the following mechanisms:

- *Transfer of genes containing DNA coding for antimicrobial resistance located either on plasmids or on transposons*. Enteric bacteria are a common source of such genes, which have appeared in many species, including *Neisseria gonorrhoeae* and *Haemophilus influenzae*.

- *Spontaneous mutation of bacteria.* Selection of resistant variants allows a pre-existing resistant strain to emerge following treatment with an antimicrobial agent acting against susceptible organisms. For example, patients with staphylococcal infections treated with rifampicin alone often develop resistant staphylococcal isolates within a few days. A minor proportion of enteric bacteria may be resistant strains capable of producing high-level β-lactamases which are readily selected by cefalosporins, broad-spectrum penicillins and monobactams. Some bacterial species are heterogeneously resistant to fluoroquinolones and can, consequently, be selected by the drugs.
- *Antimicrobial-induced effects on the normal microflora*. Treatment with antimicrobials results in susceptible species becoming less common and naturally resistant species more frequent. Genes responsible for such resistance among species of the normal flora can be transferred to pathogens causing infections. It is thought that penicillin-resistant *Streptococcus pneumoniae* and vancomycin-resistant enterococci arose by such a transformation.

The selection of resistant bacteria is minimized by adherence to a few basic principles:

— use antimicrobials that are most appropriate for the cause of infection and the prevalence of local resistance;
— use adequate doses;
— ensure that the treatment course is completed.

For most bacterial infections a single antimicrobial is all that is required. However, in some circumstances combination therapy with two or more agents with different mechanisms of activity may be needed to minimize the emergence of resistance among certain species — for example in the treatment of infections caused by *Mycobacterium tuberculosis.*

Spread of resistant bacteria

The spread of antimicrobial-resistant bacteria was once considered to be mainly a problem associated with poor hygiene in hospitals. Poor hygiene contributes to the spread of resistant strains of bacteria, as has been demonstrated by reports of hospital-acquired (nosocomial) infections over recent years.

The introduction of a number of hygienic measures, including improved facilities for hand-washing, isolation of patients with multiresistant bacteria and improved aseptic techniques for invasive procedures has reduced the spread of pathogenic bacteria in hospitals.

The spread of antimicrobial-resistant strains in the community has presented problems in the treatment of infections of the respiratory tract, gastrointestinal tract, urinary tract, skin and soft tissues as well as in the treatment of some sexually transmitted diseases and meningitis. In many communities it is difficult to maintain hygienic procedures. Childhood infections are common in the community because transfer of microorganisms occurs readily. Antimicrobial-resistant bacteria are also readily spread by and between children.

The breakdown of infrastructure that frequently occurs in situations of armed conflict, famine and economic crisis also leads to outbreaks of infection. Such outbreaks are increasingly caused by bacteria with acquired resistance to antimicrobials.

Although hygienic measures are the main method for controlling the spread of antimicrobial-resistant as well as antimicrobial-susceptible bacteria, inappropriate use of antimicrobials also needs to be addressed. Inappropriate uses include the administration of antimicrobials when their use is not indicated and use of antimicrobials to which the pathogens are already resistant. The use of inappropriate antimicrobials, suboptimal doses, the wrong duration of treatment and excessive use of one particular class of drugs will also increase the prevalence of resistance. Problems such as uncontrolled access to antimicrobials and varying quality of some products may also increase the prevalence of resistance.

Role of laboratories in antimicrobial susceptibility testing and reporting of surveillance data

The majority of bacterial infections are treated on the basis of a presumptive etiological diagnosis determined by the clinical history and physical findings. Empirical therapy should be

based on local epidemiological data on likely pathogens and their patterns of antimicrobial susceptibility. For this reason, capacity for testing the antimicrobial susceptibility of priority pathogens, including those causing infection in the community, should preferably be available in several laboratories in different geographical locations in all countries. As a minimum, testing must be carried out in a national reference laboratory. Data should be collected on *Staphylococcus aureus*, *Pseudomonas aeruginosa* and Enterobacteriaceae. Information about community-acquired infections is usually more difficult to obtain, but data should be collected on *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Escherichia coli* and *Salmonella* and *Shigella* spp. A limited range of antimicrobials is important for different organisms. For *Streptococcus pneumoniae*, for example, information on resistance to benzylpenicillin, cefalosporins, sulfamethoxazole + trimethoprim, erythromycin and chloramphenicol has the highest priority. Information on antimicrobial resistance in *Mycobacterium tuberculosis* and *Neisseria gonorrhoeae* is also important.

Laboratories should apply internationally recognized methods of antimicrobial susceptibility testing and should ensure that the results are analysed and communicated appropriately in order that empirical treatment guidelines can be updated. There should be a well-functioning system of quality control in place. WHO has a software package (WHONET)[1] available to laboratories on request for epidemiological analysis of antimicrobial susceptibility data and can assist in the provision of laboratory training.

Not all infections require specific antimicrobial treatment and careful clinical judgement is essential to determine whether symptomatic treatment is sufficient. Microbiological investigations should always be carried out before treatment where possible when the etiology is uncertain, in severe infections when patients fail to respond to empirical therapy or develop a new infection during the course of treatment, or for public health purposes. Appropriate specimens for Gram-staining, culture

[1] Available on request from Anti-infective Drug Resistance and Containment, Communicable Disease Surveillance and Response, World Health Organization, 1211 Geneva 27, Switzerland.

and susceptibility testing should be obtained before starting antimicrobial therapy. In many situations microbiological identification of the pathogen is vital to determine the appropriate antimicrobial treatment. In contrast, group A β-haemolytic streptococci are routinely susceptible to benzylpenicillin and phenoxymethylpenicillin, making mandatory susceptibility testing unnecessary.

General principles of antimicrobial prescribing

Spectrum of activity

Ideally, the antimicrobial susceptibility of an organism should be known and the most effective and safe agent targeted to the infection should be used. This reduces the likelihood of selection of resistant microorganisms and superinfection. However, in most cases the suspected organism is assumed to be susceptible to a particular antimicrobial because of its known characteristics from surveillance data.

Pharmacokinetics and pharmacodynamics

The pharmacokinetics and pharmacodynamics of an antimicrobial are determined by three factors: the serum half-life, its distribution in the body tissues and fluids (e.g. cerebrospinal fluid) and its accumulation in phagocytic cells. The dosage should be consistent with the drug's half-life (e.g. a single daily dose for drugs with a serum half-life of 10–20 hours). Drugs that achieve high intracellular levels are necessary for infections with intracellular pathogens such as *Chlamydia* and *Legionella* spp. and *Coxiella burnetti*. For most infections the concentration of drug in the infected site (e.g. interstitial fluid, urine) is a key pharmacokinetic parameter. Binding of a small fraction of the drug to serum proteins contributes to the achievement of high extravascular concentrations; conversely, serum protein binding levels above 80–85% have an impact on passage from the blood to extravascular compartments, but are not per se indicative of tissue concentrations below therapeutic levels. In patients with renal or hepatic impairment, reduction of the dose may be required.

Oral versus parenteral administration

Antimicrobials should be administered by the most appropriate route in an optimum dose, since inadequate plasma levels

may lead to the development of resistance. Some clinical circumstances (e.g. patients who are severely ill or who have collapsed, or those with impaired bowel function) may require the use of parenteral antimicrobials. The excellent absorption of many oral antimicrobials (including β-lactams, chloramphenicol, doxycycline and fluoroquinolones) and the associated cost-benefits make oral administration usually the most appropriate form of antimicrobial therapy.

Adherence and ease of administration

Oral formulations are more convenient, generally cheaper and associated with less adverse effects than parenteral ones. Parenteral formulations also require trained medical staff for their administration and can have specific adverse effects not seen with orally administered drugs. Oral drugs with fewer doses are preferred. The appropriateness of the choice of drug for individual patients also depends on factors such as the patient's age, the presence of underlying disease, renal or liver impairment or allergies, concurrent therapy and whether the patient is pregnant.

Impact on normal microbial flora

If two antimicrobial agents have similar probable cure rates, cost and tolerance in a particular case, the agent having the least deleterious impact on the normal human microbial flora should be chosen. This may reduce or prevent adverse effects such as antimicrobial-associated diarrhoea and vaginal superinfections with *Candida* spp.

Cost of treatment

The drug with the lowest cost is preferred if efficacy, adherence and tolerance are comparable. However, the cost of the total treatment, and not only the unit cost of the drug, must be considered.

Antimicrobial combinations

In certain clinical settings it may be necessary to use two or more antimicrobials to achieve the desired effect. The common indications for combination therapy are:

- to obtain antimicrobial synergy (i.e. an effect unobtainable with either drug alone);

- to delay the development of resistance;
- to broaden the spectrum of antimicrobial activity against an infection of unknown etiology or involving more than one species.

Effect of commercial promotion

Individuals responsible for prescribing drugs and drug committees are commonly subject to commercial promotion in making choices about antimicrobials. Objective data and evidence of clinical efficacy should provide the basis for decisions for including antimicrobials in drug formularies.

Drug formularies

The list of antimicrobials to be included in the drug formulary of an institution should be established by consensus among the users in the institution represented in the drug committee (e.g. physicians, pharmacists, clinical pharmacologists, microbiologists and nurses). For each particular antimicrobial, the clinical indication (therapeutic, prophylactic or empirical) and the dosage (for adults, children and, if appropriate, patients with hepatic or renal impairment) must be mentioned. Objective information should be distributed by the committee, based on data from the manufacturer and independent drug information. The committee should conduct periodic evaluations of the functioning of the formulary.

Choice of antimicrobial and options for treatment

In this book, the recommendations for initial empirical treatment of infection are based on current knowledge of the prevalence of antimicrobial resistance. Most infections are treated initially on the basis of clinical evidence, without full knowledge of the causative organism or its susceptibility. As the prevalence of resistance varies considerably from one community to another, the recommendations are presented as a series of options. The local choice of an option for treatment will be influenced by the prevalence of resistance (where known), the availability and tolerability of the antimicrobial, and the cost of a full course of treatment. The range of antimicrobials listed in this book conforms, in the main, to the WHO Model

List of Essential Drugs[1] and to other recent publications by WHO.[2–5]

Rational use of the many different classes of antimicrobials depends on the points discussed above. Because of the inconsistent availability of drugs and the variation in the needs of patients — in turn a result of differences in age, hypersensitivity and factors influencing metabolic fate in the body — options are given rather than a single "best choice". The range of antimicrobials is wide but most conditions can be managed using well-established drugs rather than the newest ones.

Some institutions restrict certain antimicrobials as "reserve" agents. A reserve antimicrobial is one that is useful for a wide range of infections but, because of the need to reduce the risk of development of resistance and because of its relatively high cost, it would be inappropriate to recommend its unrestricted use. The drug should be included in the drug formulary of the institution with the clinical indications clearly defined and be made available without delay when needed. It should have restricted availability and be prescribed only under the supervision of a senior medical officer. Within this context the β-lactam drugs, the fluoroquinolones and vancomycin are particularly important.

β-Lactam antimicrobials

Resistance to β-lactam antimicrobials is generally due to the production of β-lactamases in staphylococci, enterobacteria, *Haemophilus* spp., gonococci and *Pseudomonas* spp. In several of

---

[1] *The use of essential drugs. Ninth report of the WHO Expert Committee (including the revised Model List of Essential Drugs)*. Geneva, World Health Organization, 2000 (WHO Technical Report Series, No. 895).

[2] *WHO model prescribing information: drugs used in sexually transmitted diseases and HIV infection*. Geneva, World Health Organization, 1995.

[3] *WHO Expert Committee on Malaria. Twentieth report*. Geneva, World Health Organization, 2000 (WHO Technical Report Series, No. 892).

[4] Gilles HM. *Management of severe malaria: a practical handbook*, 2nd ed. Geneva, World Health Organization, 2000.

[5] *The use of artemisinin and its derivatives as antimalarial drugs: report of a Joint CTD/DMP/TDR Informal Consultation, Geneva, 10–12 June 1998*. Geneva, World Health Organization, 1998 (unpublished document WHO/MAL/98.1086; available from Communicable Disease Research and Development, World Health Organization, 1211 Geneva 27, Switzerland).

these species and in others such as *Streptococcus pneumoniae* and enterococci, non-enzymatic mechanisms also occur. Many new β-lactam antimicrobials are included in the WHO Model List of Essential Drugs as reserve antimicrobials. In order to preserve the activity of these antimicrobials it is recommended that these agents are used only where rates of resistance to all normally appropriate essential drugs are high or for specific indications, as listed below.

The β-lactamase inhibitor amoxicillin + clavulanic acid is resistant to degradation by many of the enzymes produced by enterobacteria and *Bacteroides* spp. A specific indication for its use is in polymicrobial infections related to surgical conditions of the intestinal tract and female genital tract. Amoxicillin remains active against many common bacteria such as β-haemolytic streptococci and a high proportion of strains of *Haemophilus influenzae* in many countries. The emergence of strains of *Streptococcus pneumoniae* with reduced susceptibility to penicillins does not at this time justify replacement of this group of antimicrobials for the treatment of respiratory tract infections.

Many parenteral cefalosporins active against Gram-negative and Gram-positive bacteria are now widely used for the treatment of infection. WHO's Model List of Essential Drugs includes ceftriaxone as a reserve agent for the treatment of meningitis due to *Streptococcus pneumoniae* in areas where the incidence of resistance to penicillins is high. It has been listed as an example of a therapeutic group because the results of clinical trials indicate that cefotaxime is equally effective and may be preferred in some hospitals or treatment centres. Ceftriaxone is specifically recommended for the treatment of gonorrhoea and chancroid where resistance to other antimicrobials is common. At its eighth meeting in 1997,[1] the WHO Expert Committee on the Use of Essential Drugs noted that several other cefalosporins such as cefuroxime are widely used for chemoprophylaxis in surgery and for the treatment of respiratory infections. These cefalosporins are not as effective as ceftriaxone or cefotaxime in the treatment of meningitis due to

[1] *The use of essential drugs. Eighth report of the WHO Expert Committee*. Geneva, World Health Organization, 1998 (WHO Technical Report Series, No. 882).

Streptococcus pneumoniae. However, they may be used as alternatives for chemoprophylaxis in surgery or for treatment of respiratory infections in areas of penicillin resistance.

Chemoprophylaxis in surgery should be limited to the minimum number of doses required to ensure efficacy, usually one or two. Ceftriaxone and cefotaxime should never be used for chemoprophylaxis.

Ceftazidime is included in WHO's Model List of Essential Drugs because it is active against *Pseudomonas aeruginosa*. It is recommended that it should be used when the prevalence of resistance to gentamicin is high or when resistance to gentamicin only has been documented in a particular patient.

Imipenem + cilastatin is a broad-spectrum β-lactam antimicrobial included as a reserve agent for the treatment of severe infections with *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Acinetobacter* spp. resistant to all normally appropriate antimicrobials. Such resistant organisms are usually only found in tertiary care hospitals and, in particular, in intensive care units where antimicrobial usage is high.

Fluoroquinolones

Ciprofloxacin is a member of the fluoroquinolone family of antimicrobials. Although it is now listed as an essential drug, the comparative costs of alternative broad-spectrum products will be an important determinant of selection. Ciprofloxacin and certain other fluoroquinolones may still be considered of value as reserve agents. Their use may need to be restricted to the following circumstances:

- For typhoid fever and other systemic salmonella infections where strains of *Salmonella* spp. exist that are resistant to chloramphenicol, amoxicillin and sulfamethoxazole + trimethoprim.
- For severe shigellosis where *Shigella* spp. strains exist that are resistant to ampicillin, chloramphenicol, sulfamethoxazole + trimethoprim, tetracyclines and nalidixic acid.
- For gonorrhoea and chancroid, as alternatives to cefalosporins, when oral administration is appropriate.

- For certain hospital-acquired infections due to Gram-negative bacilli, including *Escherichia coli*, *Klebsiella* spp. and *Pseudomonas aeruginosa*, that are resistant to essential drugs such as amoxicillin, chloramphenicol and gentamicin.

Vancomycin

Meticillin-resistant strains of *Staphylococcus aureus* are usually resistant to all β-lactam antimicrobials and also to structurally unrelated drugs such as erythromycin, clindamycin, chloramphenicol, the tetracyclines and the aminoglycosides. The only effective reserve drug for infections due to these multiresistant organisms is vancomycin, which is expensive and must be administered intravenously.

Alternative agents

Many drugs included in WHO's Model List of Essential Drugs are preceded by a square symbol (□) to indicate that they represent an example of a therapeutic group and that various drugs could serve as alternatives. It is imperative that this is understood when drugs are selected at a national level, since choice is then influenced by the comparative cost and availability of equivalent products. Examples of acceptable substitutions include:

□ciprofloxacin: ofloxacin.

□cloxacillin: flucloxacillin, nafcillin, oxacillin or dicloxacillin.

□ceftriaxone: cefotaxime.

□cefazolin: cefalotin.

□cefalexin: cefradine.

Although these drugs are comparable, the doses may vary.

Upper respiratory tract infections

Infections of the upper respiratory tract represent the most common cause of antimicrobial use. The vast majority of such infections are of viral origin and do not require treatment with antimicrobials. Because of the potential misuse of antimicrobials in these conditions, some agents are specifically not recommended.

Acute pharyngitis

Most cases of pharyngitis are caused by viruses and do not require treatment with antimicrobials. The most common bacterial causes of pharyngitis are *Streptococcus pyogenes* (which may be associated with acute rheumatic fever) and *Corynebacterium diphtheriae*.

It may be difficult to distinguish between streptococcal and viral pharyngitis on clinical grounds alone. Tender, enlarged cervical lymph nodes and a scarlet fever-like rash are considered specific for *S. pyogenes*, but uncommon. Presence of the three major signs (fever >38 °C, intense pharyngeal pain, and absence of rhinitis and cough) has a high positive-predictive value for streptococcal pharyngitis. When these three signs are not all present, streptococcal etiology is unlikely. A rapid antigen test and culture techniques are available for the diagnosis of *S. pyogenes* infection, allowing specific therapy, but may not be cost-effective in certain circumstances. Other streptococcal serogroups (e.g. serogroups B, C and G) have also been associated with infections, but they do not cause rheumatic fever. In some cases peritonsillar abscesses may develop and surgical drainage may be needed. Routine testing for allergy to penicillins is not considered necessary.

Treatment

Benzathine benzylpenicillin 1.2 million IU i.m. in a single dose for adults and children >30 kg (children ≤30 kg: 30 000 IU/kg (maximum 1.2 million IU) i.m. in a single dose)

or

phenoxymethylpenicillin 500 mg (children: 10–20 mg/kg; maximum 500 mg) orally every 6 hours for 10 days

or

amoxicillin 500 mg (children: 15 mg/kg; maximum 500 mg) orally every 8 hours for 10 days.

Patients allergic to penicillins

Erythromycin 500 mg (children: 10–15 mg/kg; maximum 500 mg) orally every 6 hours for 10 days

or

cefalexin 500 mg (children: 15 mg/kg; maximum 500 mg) orally every 6–8 hours for 10 days.

Comments

Fluoroquinolones, tetracyclines, sulfamethoxazole + trimethoprim and combinations with aminopenicillins and β-lactamase inhibitors are not recommended.

Nasopharyngitis, rhinitis and common cold

Nasopharyngitis is characterized by the presence of rhinitis and pharyngitis with fever. It is very common in young children. The cause is viral and no antimicrobials are required in most cases for either treatment or chemoprophylaxis. Antipyretics (not aspirin in children) can be given to control high fever.

Rhinitis of bacterial origin, including diphtheria in infants (see page 19), can occur. The common cold is caused by viruses and does not require treatment with antimicrobials.

Otitis media

Acute otitis media

Upper respiratory tract infections of viral origin are frequently associated with mild redness of the tympanic membrane, but antimicrobials are generally not necessary. Acute otitis media, however, is an infection of the middle ear that occurs mostly in infants and children under 2 years of age. The bacterial

pathogens most often implicated are *Streptococcus pneumoniae* and *Haemophilus influenzae*. Vaccination against the latter pathogen has significantly reduced the recurrence of *H. influenzae*. Bacterial infection is suggested by the presence of acute onset of pain in the ear, fever, and redness and decreased mobility of the tympanic membrane. Patients presenting with these signs require antimicrobials; meningitis can be a complication.

Treatment

Amoxicillin 500 mg (children: 15 mg/kg; maximum 500 mg) orally every 8 hours for 5 days

or

amoxicillin 500 mg + clavulanic acid (children: amoxicillin 7.5–15 mg/kg + clavulanic acid; maximum 500 mg) orally every 8 hours for 5 days

or

sulfamethoxazole 400 mg + trimethoprim 80 mg (children: 20 mg/kg + 4 mg/kg; maximum 400 mg + 80 mg) orally every 12 hours for 5 days.

Comments

Amoxicillin + clavulanic acid is preferred in regions where β-lactamase-producing strains of *H. influenzae* are common. In a few regions, the incidence of penicillin-resistant *S. pneumoniae* is increasing. For this reason, higher doses of amoxicillin and amoxicillin + clavulanic acid are the treatment of choice. However, these penicillin-resistant strains are frequently also resistant to sulfamethoxazole + trimethoprim. For patients who are allergic to penicillins, cefuroxime axetil (250–500 mg orally every 12 hours for 5 days) is another alternative.

Erythromycin, tetracyclines, fluoroquinolones and most oral cefalosporins are not recommended.

Chronic otitis media

Chronic otitis media is characterized by a history of chronic discharge from one or both ears. If the eardrum has been ruptured for more than 2 weeks, secondary infection with a variety of organisms is common. Antimicrobial therapy is generally not recommended. The ear should be thoroughly washed with

clean water once daily and then dried three times daily for several weeks (until it remains dry).

Acute mastoiditis

Acute mastoiditis is a bone infection characterized by painful swelling behind or above the ear. It may be complicated by meningitis. The patient should be admitted to hospital, antimicrobials commenced and surgery considered.

Treatment

Chloramphenicol 1 g (children: 25 mg/kg; maximum 750 mg) i.v. or i.m. every 6–8 hours for 10–14 days

or

ampicillin 2 g (children: 25–50 mg/kg; maximum 2 g) i.v. every 6 hours for 10–14 days

or

ceftriaxone 1 g (children: 50 mg/kg; maximum 1 g) i.v. or i.m. every 12 hours for 10 days.

Intravenous formulations of ceftriaxone should be administered over at least 2 minutes.

Acute sinusitis

Acute sinusitis usually occurs as a complication of viral infections of the upper respiratory tract, although a small proportion of cases are associated with dental infections. It may also occur in patients with allergic rhinitis. Persistent purulent nasal discharge, sinus tenderness, facial or periorbital swelling and persistent fever are characteristic symptoms. Cough may also be present.

In adults, the presence of persistent purulent nasal discharge alone (with or without cough) is not an indication for antimicrobial therapy. However, antimicrobials should be considered if sinus tenderness, facial or periorbital swelling, or persistent fever are also present. Therapy should be primarily directed against *S. pneumoniae* and *H. influenzae* and is therefore similar to that recommended for acute otitis media, except that it should be continued for 7–10 days. Fluoroquinolones and most cefalosporins are not recommended.

Croup (laryngotracheobronchitis)

Croup is a clinical syndrome characterized by inflammation of the larynx and trachea. It involves primarily children under 3 years of age and is commonly preceded by an upper respiratory tract infection. It has a more gradual onset than epiglottitis. In many developed countries, croup is caused by viruses such as parainfluenza or influenza virus. Secondary bacterial infection is rare and antimicrobials are rarely indicated. However, severe cases should be treated as for epiglottitis (see below).

Epiglottitis

Epiglottitis presents as an acute, severe infection of the epiglottis and aryepiglottic folds accompanied by fever, a cherry red epiglottis and drooling. Severe disease is characterized by stridor, chest indrawing, hoarseness and inability to swallow. The patient should be admitted to hospital. Airway obstruction is always severe and intubation or tracheostomy is often needed. Antimicrobial treatment should be directed against the most common pathogen, *H. influenzae* serotype b.

Treatment

Adults and children >2 months

Chloramphenicol 1 g (children >2 months: 25 mg/kg; maximum 1 g) i.v. or i.m. every 6 hours for 5 days

or

ceftriaxone 2 g (children >2 months: 100 mg/kg; maximum 2 g) i.v. or i.m. every 24 hours for 5 days.

Intravenous formulations of ceftriaxone should be administered over 2 minutes.

Neonates

Cefotaxime 50 mg/kg (maximum 2 g) i.v. or i.m. every 8 hours for 5 days.

Comments

Neither chloramphenicol nor cefotaxime eliminates carriage of *H. influenzae* serotype b and a course of rifampicin 600 mg (neonates <1 month: 10 mg/kg (maximum 300 mg); children

≥1 month: 20 mg/kg (maximum 600 mg)) orally every 24 hours for 4 days is therefore recommended if either of these agents is used. Rifampicin treatment is not necessary if ceftriaxone is used.

In young children, consideration should be given to vaccination against *H. influenzae* serotype b (Hib).

Diphtheria

Laryngeal diphtheria may present with symptoms that include local manifestations (pharyngeal, laryngeal, tracheobronchial or cutaneous) and distant manifestations, in particular neurological effects secondary to dissemination of the diphtheria toxin. Presumptive diagnosis is based on epidemiological data and several clinical signs, including mildly painful pharyngitis with extending greyish adherent membrane, adenopathy, cervical swelling, paralysis of the palate, a harsh cough and a hoarse voice. The patient should be admitted to hospital. Diphtheria antitoxin 20 000–100 000 IU should be given immediately. If airway obstruction is severe, intubation or tracheostomy may be needed.

Treatment

Diphtheria antitoxin 20 000–100 000 IU i.v. or i.m. immediately

followed by either

procaine benzylpenicillin 1.2 million IU (children: 50 000 IU/kg; maximum 1.2 million IU) i.m. every 24 hours for 7 days

or

benzathine benzylpenicillin 1.2 million IU for adults and children >30 kg (children ≤30 kg: 30 000 IU/kg; maximum 600 000 IU) i.m. in a single dose

or

erythromycin 500 mg (children: 10–15 mg/kg; maximum 500 mg) orally every 6 hours for 7 days.

Comments

Vaccination with diphtheria–pertussis–tetanus (DPT) should be offered during convalescence.

Lower respiratory tract infections

Bronchitis

Acute bronchitis

In persons with a normal respiratory tract, acute infections of the trachea and bronchi are almost always viral in origin, although occasionally they may be caused by *Mycoplasma pneumoniae*. Fever and cough without cyanosis, chest indrawing, wheezing and rapid breathing are the main symptoms. If wheezing is present it is often due to asthma or bronchiolitis, in which case treatment is the same as for a viral infection of the respiratory tract and does not include antimicrobials.

Treatment

Amoxicillin 500 mg (children: 15 mg/kg; maximum 500 mg) orally every 8 hours for 5 days

or

doxycycline 100 mg (children >8 years: 2 mg/kg; maximum 100 mg) orally every 12 hours for 5 days (contraindicated during pregnancy)

or

sulfamethoxazole 800 mg + trimethoprim 160 mg (children: 20 mg/kg + 4 mg/kg; maximum 800 mg + 160 mg) orally every 12 hours for 5 days.

Comments

Cefalosporins and fluoroquinolones are not recommended for bronchitis.

Acute exacerbations of chronic bronchitis

Acute exacerbations of chronic bronchitis are often due to viral infection and do not require treatment with antimicrobials. Antimicrobial treatment should, however, be considered in patients with increasing cough, dyspnoea and increased production and purulence of sputum. The most common causative organisms are *H. influenzae*, *Moraxella catarrhalis* and *S. pneumoniae*.

Doses refer to adults, as this condition is rarely found in children.

Treatment

Amoxicillin 500 mg orally every 8 hours for 5 days

or

amoxicillin 500 mg + clavulanic acid orally every 8 hours for 5 days

or

sulfamethoxazole 800 mg + trimethoprim 160 mg orally every 12–24 hours for 5 days.

Comments

Chronic purulent bronchial infection and chronic airway disease are predominantly diseases of adults. Chronic suppurative lung disease in children (e.g. bronchiectasis) may occasionally require treatment with amoxicillin (30 mg/kg (maximum 1 g) orally every 8 hours for 5 days) or chloramphenicol (25 mg/kg (maximum 1 g) i.v. or i.m. every 6 hours for 5 days). Cystic fibrosis infections require specialist clinical management and laboratory services.

Chronic recurrent cough

Chronic cough is a common condition in adults and children associated with causes such as pollution, allergy, and passive and active smoking. Antimicrobials are not required. The occurrence of a chronic cough with persistent fever and weight loss should raise clinical suspicion of tuberculosis or bronchial cancer.

Pneumonia

The major symptoms of pneumonia are rapid breathing with cough. The respiratory rates above which pneumonia should be suspected are shown in the table overleaf.

In severe cases indrawing of the chest and cyanosis may also occur. Other symptoms and signs of pneumonia include pleural pain, fever and crepitations. Extrapulmonary features such as confusion or disorientation may predominate, and may

Cut-off points for rapid breathing

Age group	Cut-off point for rapid breathing (no. of breaths/min)
0–2 months	60
2–12 months	50
12–60 months	40
Adults and children >5 years	30

be the only signs in the elderly, immunosuppressed patients and malnourished children. The etiology of pneumonia varies greatly with the age and geographical location of the patient.

Pneumonia in adults and children aged over 5 years

The most important pathogen in this age group is *Streptococcus pneumoniae*, followed by atypical bacteria such as *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *Legionella* spp. and *Coxiella burnetti*. Options for treatment of these infections have been considered by expert committees in many countries. The recommendations of these committees are based on the prevalence of resistance of *S. pneumoniae* to macrolides and to penicillins, and on the prevalence of resistance of atypical pathogens to β-lactam antimicrobials. Patients with severe pneumonia should be admitted to hospital.

Groups at particular risk include those with pre-existing lung or heart disease, renal failure, diabetes, malnutrition or HIV infection, those who are dependent on alcohol, and the elderly. Clinical presentation and Gram-staining of sputum may aid in the diagnosis of the etiological pathogen(s).

Treatment

Ambulatory patients

Amoxicillin 500 mg (children: 15 mg/kg; maximum 500 mg) orally every 8 hours for 5 days

or

erythromycin 500 mg (children: 10–15 mg/kg; maximum 500 mg) orally every 6 hours for 5 days (14 days in cases of atypical pneumonia)

or

doxycycline 100 mg (children >8 years: 2 mg/kg; maximum 100 mg) orally every 12 hours for 7–10 days (contraindicated during pregnancy)

or

sulfamethoxazole 800 mg + trimethoprim 160 mg (children: 20 mg/kg + 4 mg/kg; maximum 800 mg + 160 mg) orally every 12 hours for 5 days.

Hospitalized patients

Benzylpenicillin 2 million IU (children: 50 000–100 000 IU/kg; maximum 2 million IU) i.v. or i.m. every 4–6 hours for 5 days

or

chloramphenicol 1 g (children: 25 mg/kg; maximum 750 mg) i.v. every 6 hours for 7 days

or

cefuroxime 1.0–1.5 g (children: 50–60 mg/kg; maximum 1.5 g) i.v. every 6–8 hours for 7 days

or

ceftriaxone 1 g (children: 50 mg/kg; maximum 1 g) i.v. or i.m. every 12–24 hours for 7 days.

Alternative regimen. Benzylpenicillin 2 million IU (children: 50 000–100 000 IU/kg; maximum 2 million IU) i.v. or i.m. every 4–6 hours for 7 days

plus

gentamicin 5–7 mg/kg i.v. daily in divided doses (children: 7.5 mg/kg i.v. in 1–3 divided doses daily) for 7 days (contraindicated during pregnancy).

In cases of atypical pneumonia, treatment is as described above, with the addition of erythromycin 1 g (children: 10 mg/kg; maximum 1 g) i.v. every 6 hours for 14 days.

Pneumonia due to Staphylococcus aureus

Treatment is as described on pages 28–29.

Comments

Benzylpenicillin may be used alone when *Streptococcus pneumoniae* is the suspected pathogen.

In regions where the prevalence of resistance of *S. pneumoniae* to penicillins is high, consideration should be given to increasing the dose of amoxicillin. Erythromycin should be used only in regions where the prevalence of resistance of *S. pneumoniae* to the drug is low.

Gentamicin is not recommended for patients with significant renal failure (creatinine clearance <20 ml/min). If gentamicin is used, close monitoring of serum concentrations is mandatory.

Pneumonia in children aged from 2 months to 5 years

In developing countries pneumonia in children aged from 2 months to 5 years is usually due to *Streptococcus pneumoniae* or *Haemophilus influenzae* or occasionally *Staphylococcus aureus*. In developed countries the disease is more likely to be of viral origin (respiratory syncytial virus or parainfluenza virus). However, in most cases an etiological pathogen is not identified and as a result, empirical antimicrobial therapy for pneumonia is the commonly accepted practice worldwide.[1] Pneumonia due to *Staphylococcus aureus* should be suspected if there is clinical deterioration despite treatment with chloramphenicol or other normally appropriate antimicrobials, or in the presence of pneumatocoele or empyema.

Treatment

Very severe pneumonia

Procaine benzylpenicillin 50 000 IU/kg (maximum 900 000 IU) i.m. every 24 hours for at least 5 days

or

benzylpenicillin 50 000–100 000 IU/kg (maximum 2 million IU) i.v. or i.m. every 4–6 hours for at least 5 days

[1] For further information, see *Acute respiratory infections in children: case management in small hospitals in developing countries*. Geneva, World Health Organization, 1990 (unpublished document WHO/ARI/90.5; available on request from Child and Adolescent Health and Development, World Health Organization, 1211 Geneva 27, Switzerland).

or

chloramphenicol 25 mg/kg (maximum 750 mg) i.v. or i.m. every 6 hours for at least 10 days (once clinical improvement occurs, oral dosage forms may be substituted)

or

ceftriaxone 50 mg/kg (maximum 1 g) i.v. or i.m. every 24 hours for at least 5 days.

Severe pneumonia

Benzylpenicillin 50 000–100 000 IU/kg (maximum 2 million IU) i.v. or i.m. every 4–6 hours for at least 5 days.

Mild pneumonia

Amoxicillin 15–25 mg/kg (maximum 500 mg) orally every 8 hours for 5 days

or

sulfamethoxazole 20 mg/kg + trimethoprim 4 mg/kg (maximum 800 mg + 160 mg) orally every 12 hours for 5 days

or

procaine benzylpenicillin 50 000 IU/kg (maximum 900 000 IU) i.m. every 24 hours for at least 3 days (once clinical improvement occurs, amoxicillin 15–25 mg/kg (maximum 500 mg) orally every 8 hours may be used to complete the treatment course of at least 5 days).

Pneumonia due to Staphylococcus aureus

Treatment is as described on page 29.

Pneumonia in neonates (aged up to 2 months)

In neonates not all respiratory distress is due to infection. However, as pneumonia may be rapidly fatal in this age group, suspected cases should be treated promptly and referred to hospital for parenteral treatment with antimicrobials. The most likely pathogens are *Streptococcus pneumoniae*, group B streptococci, *Escherichia coli*, Enterobacteriaceae and *Chlamydia trachomatis*. Severe cases may be caused by *Staphylococcus aureus*.

Treatment

Neonates should be treated for at least 5 days with continuation of therapy for 3 days after the child is well. If meningitis is suspected, treatment should be given for at least 14 days. In premature babies, the doses recommended here may need to be reduced.

Amoxicillin 30 mg/kg i.v. every 12 hours for at least 5 days

plus

gentamicin 2.5 mg/kg i.v. every 8 hours (neonates <7 days: 2.5 mg/kg i.v. every 12 hours) for a total of at least 5 days.

Alternative regimens. Cefotaxime 50 mg/kg i.v. every 12 hours for at least 5 days

or

chloramphenicol 25 mg/kg (maximum 750 mg) i.v. every 12 hours for at least 5 days (contraindicated in premature infants or neonates <7 days).

Comments

Cefotaxime is preferred to ceftriaxone for this age group. It is often administered in combination with ampicillin (50 mg/kg i.v. every 8 hours for at least 5 days), because of problems of resistance in Gram-negative enteric bacteria and the possibility of *Listeria* spp. infections in neonates.

Chloramphenicol should only be used when no alternatives are available, as it may cause the grey baby syndrome.

Legionellosis

Legionellosis, caused by *Legionella pneumophila,* is a waterborne infection spread by aerosolization. It mainly occurs in elderly persons with chronic obstructive airway disease, but may also occur in young, otherwise healthy, patients. It usually presents as severe pneumonia, often associated with non-pulmonary symptoms such as mental confusion, diarrhoea and renal failure. The diagnosis may be suggested by the presence of purulent sputum without pathogens visible on Gram-staining, and/or failure to respond to treatment with β-lactam antimicrobials.

Treatment

Erythromycin 1 g (children: 10 mg/kg; maximum 500 mg) i.v. every 6 hours for 10 days (once clinical improvement occurs, erythromycin 500 mg (children: 7.5 mg/kg; maximum 500 mg) orally every 6 hours may be substituted)

or

ciprofloxacin 750 mg orally every 12 hours for 10 days (contraindicated during pregnancy; not approved for this indication in children).

Pneumonia associated with HIV infection

Pneumocystis carinii is the most frequent pathogen, although in some areas, tuberculosis is more common. Other potential pathogens include *Candida albicans, Aspergillus fumigatus* and cytomegalovirus.

Doses refer to adults, as this condition is rarely observed in children.

Treatment for pneumonia due to Pneumocystis carinii

Sulfamethoxazole 75 mg/kg + trimethoprim 15 mg/kg i.v. or orally every 6–8 hours for 21 days.

Alternative regimen. Clindamycin 600 mg i.v. or orally every 6 hours for 21 days

plus

primaquine 15 mg orally every 6 hours for 21 days.

Aspiration pneumonia and lung abscesses

Aspiration pneumonia and lung abscesses are most frequently caused by penicillin-sensitive anaerobic bacteria such as *Peptostreptococcus* spp., as well as aerobic bacteria such as *Streptococcus pyogenes* and viridans streptococci. Sometimes penicillin-resistant pathogens such as *Bacteroides fragilis, Escherichia coli* and *Klebsiella pneumoniae* may be involved. Predisposing factors include impaired consciousness, bronchial obstruction, alcohol dependence, cerebrovascular accidents and intestinal obstruction.

Treatment

Benzylpenicillin 1–2 million IU (children: 50 000–100 000 IU/kg; maximum 2 million IU) i.v. or i.m. every 4–6 hours for 10–14 days

plus

metronidazole 500 mg (children: 12.5 mg/kg; maximum 500 mg) i.v. every 8–12 hours for 10–14 days (once clinical improvement occurs, metronidazole 400 mg (children: 10 mg/kg; maximum 400 mg) orally every 12 hours may be substituted; contraindicated during pregnancy).

Alternative regimen. Amoxicillin 500 mg + clavulanic acid (children: 15 mg/kg; maximum 500 mg) orally every 8 hours for 14 days

or

clindamycin 600 mg i.v. every 8 hours (children: 10 mg/kg; maximum 450 mg i.v. or i.m. every 6 hours) for 14 days (once clinical improvement occurs, clindamycin 300–450 mg (children: 5–10 mg/kg; maximum 450 mg) orally every 6–8 hours may be substituted).

Pneumonia due to *Staphylococcus aureus*

This form of pneumonia is especially common following a recent influenza infection.

Treatment

Adults and children >5 years

Cloxacillin 1–2 g (children >5 years: 50 mg/kg; maximum 2 g) i.v. or i.m. every 6 hours for 10–14 days

or

cefazolin 1–2 g (children >5 years: 15–25 mg/kg; maximum 2 g) i.v. or i.m. every 8 hours for 10–14 days

or

clindamycin 600 mg i.v. every 8 hours (children >5 years: 10 mg/kg; maximum 450 mg i.v. or i.m. every 6 hours) for 10–14 days (once clinical improvement occurs, clindamycin 300–450 mg (children >5 years: 5–10 mg/kg; maximum 450 mg) orally every 6–8 hours may be substituted)

or

vancomycin 1 g (children >5 years: 20 mg/kg; maximum 1 g) i.v. every 12 hours for 10–14 days.

Children aged from 2 months to 5 years

Cloxacillin 25–50 mg/kg (maximum 2 g) orally every 6 hours for at least 3 weeks

plus

gentamicin 7.5 mg/kg i.v. in 1–3 divided doses daily for at least 3 weeks (contraindicated during pregnancy).

Comments

Vancomycin should only be used if the pathogen is proven to be meticillin-resistant *Staphylococcus aureus* (MRSA).

Empyema

Empyema may complicate some bacterial pneumonias and requires prompt needle aspiration for bacterial diagnosis and surgical drainage. Prolonged treatment based on the results of Gram-staining and culture is often required.

Nosocomial pneumonia

Nosocomial pneumonia is pneumonia that is acquired in hospital 48 hours or more after admission. The responsible pathogens vary, depending on the hospital and country. Local information on the identification and susceptibility of common pathogens is therefore essential in devising initial therapy for such episodes. Multiresistant bacteria such as staphylococci, enterococci, enterobacteria, *Pseudomonas aeruginosa* and other aerobic bacteria may be responsible for such infections. Hospital-acquired legionellosis has also been described. Common sources of nosocomial infections include:

- Infected intravenous devices: Gram-positive bacteria, especially staphylococci.
- Indwelling urinary catheters: Gram-negative bacteria.
- Tracheostomy and ventilators: mixed bacterial flora.
- Post-surgical wound infections: variable — depends on the operation site.

Treatment

The recommendations for initial therapy vary, depending on the epidemiology and susceptibility of local pathogens. Antimicrobials with activity against Gram-positive and Gram-negative bacterial pathogens should be used. Suitable combinations include, for example:

cloxacillin 1–2 g (children: 50 mg/kg; maximum 2 g) i.v. every 6 hours for 7 days

plus

gentamicin 5–7 mg/kg i.v. daily in divided doses (children: 7.5 mg/kg i.v. in 1–3 divided doses daily) for 7 days (contraindicated during pregnancy).

Alternative regimens. Ceftazidime 1 g (children: 25 mg/kg; maximum 1 g) i.v. every 8 hours for 7 days

plus either

gentamicin 5–7 mg/kg i.v. daily in divided doses (children: 7.5 mg/kg i.v. in 1–3 divided doses daily) for 7 days (contraindicated during pregnancy)

or

ciprofloxacin 500 mg (children: 10 mg/kg; maximum 300 mg) i.v. every 12 hours for 7 days (contraindicated during pregnancy).

Comments

In hospitals with a high prevalence of meticillin-resistant *Staphylococcus aureus* (MRSA), vancomycin 1 g (children: 20 mg/kg; maximum 1 g) i.v. every 12 hours for 10–14 days should be added to the above regimens.

Imipenem 1–2 g + cilastatin in 3–4 divided doses (children: 60 mg/kg (maximum 2 g) in 4 divided doses) daily by i.v. infusion until at least 2 days after resolution of signs and symptoms of infection should be reserved for the treatment of infections resistant to all other drugs on WHO's Model List of Essential Drugs.

Other respiratory tract infections

Pertussis (whooping cough)

Pertussis (whooping cough) is characterized by a paroxysmal cough which consists of a deep inspiration, followed by a series of short coughs which end in a whooping sound.

Administration of erythromycin 50 mg/kg (maximum 2 g) orally in 4 divided doses daily for 14 days, initiated early in the coryzal phase of the disease, may shorten the course of the illness, which otherwise may last for weeks or months. However, diagnosis at this early stage is often difficult. Once the paroxysmal phase of the disease is reached, antimicrobial treatment is of no benefit except to eradicate any secondary pulmonary infection. Treatment with erythromycin eradicates the causative pathogen *Bordetella pertussis* from the nasopharynx, making the patient non-infectious to others; however, this is usually the only benefit of therapy. An effective vaccine is available to prevent infection.

Ornithosis

The causative organism of ornithosis (psittacosis) is *Chlamydia psittaci*, which is shed by birds (especially psittacine birds) that carry the infectious agent. The disease is transmitted to humans through contact with infected birds.

Treatment

Adults and children > 8 years

Doxycycline 100 mg (children >8 years: 2 mg/kg; maximum 100 mg) orally every 12 hours for 7–10 days (contraindicated during pregnancy).

Children ≤ 8 years of age

Erythromycin 10–15 mg/kg (maximum 500 mg) orally every 6 hours for 7–10 days.

Melioidosis

Meliodosis, caused by a free-living soil bacillus *Burkholderia pseudomallei*, occurs in south-east Asia and northern Australia.

It presents most commonly as severe pneumonia and/or septicaemia and has a high mortality.

Treatment

Ceftazidime 2 g (children: 50 mg/kg; maximum 2 g) i.v. every 8 hours for at least 14 days

plus either

sulfamethoxazole 1600 mg + trimethoprim 320 mg (children: 40 mg/kg + 8 mg/kg; maximum 1600 mg + 320 mg) orally or i.v. every 12 hours for at least 14 days

or

doxycycline 100 mg (children >8 years: 2 mg/kg; maximum 100 mg) orally or i.v. every 12 hours for at least 14 days (contraindicated during pregnancy).

Comments

Prolonged i.v. therapy is necessary for deep-seated infections, osteomyelitis and septic arthritis. After the initial intensive therapy, eradication of any secondary infection is recommended with oral sulfamethoxazole + trimethoprim or doxycycline for at least 3 months.

Perioral and dental infections

Generally, the causative organisms of oral and dental infections are mixed anaerobic and aerobic oral flora.

Gingival infections and periodontitis

In the absence of systemic signs and symptoms, antimicrobial therapy is not usually indicated for gingival infections and periodontitis. Local dental care to control bacterial plaque is necessary. Antimicrobial therapy should be considered if infection is accompanied by systemic signs or symptoms.

Treatment

Procaine benzylpenicillin 1 million IU (children: 50 000 IU/kg; maximum 1 million IU) i.m. every 24 hours for 5 days

or

phenoxymethylpenicillin 500 mg (children: 10–20 mg/kg; maximum 500 mg) orally every 6 hours for 5 days

or

metronidazole 400–500 mg (children: 10–12.5 mg/kg; maximum 250 mg) orally every 12 hours for 5 days (contraindicated during pregnancy)

or

erythromycin 250 mg (children: 7.5 mg/kg; maximum 250 mg) orally every 6 hours for 5 days.

Tooth abscesses and suppurative odontogenic infections

In the absence of systemic signs or symptoms, antimicrobial therapy is not usually indicated for tooth abscesses and suppurative odontogenic infections. In pericoronitis warm mouth rinses with saline or chlorhexidine, 0.2% solution, and a topical paint (e.g. polyvidone–iodine) are of benefit. Dental abscesses may require extraction of the infected tooth. Antimicrobial therapy should be considered if infection is accompanied by systemic signs or symptoms.

Treatment

Procaine benzylpenicillin 1 million IU (children: 50 000 IU/kg; maximum 1 million IU) i.m. every 24 hours for 3 days

or

phenoxymethylpenicillin 500 mg (children: 10–20 mg/kg; maximum 500 mg) orally every 6 hours for 3 days

or

amoxicillin 250 mg (children: 25 mg/kg; maximum 250 mg) orally every 8 hours for 3 days.

Acute cervical adenitis

In young children (<5 years), acute adenitis may be due to a variety of both infectious and non-infectious causes. Acute bilateral cervical adenitis is most commonly caused by *Streptococcus pyogenes*. The recommended treatment is the same as for acute pharyngitis (see pages 14–15), although children who are severely ill may require treatment with procaine benzylpenicillin 50 000 IU (maximum 1 million IU) i.m. every 24 hours for at least 10 days.

Acute adenitis at other sites in young children usually involves *Staphylococcus aureus* as well as *Streptococcus pyogenes*. In older children and adults, a wide range of other pathogens may also cause cervical adenitis, such as *Corynebacterium diphtheriae, Mycobacterium tuberculosis, Brucella* spp. and atypical mycobacteria. Initial empirical therapy, however, should be with an agent that is bactericidal against both staphylococci and streptococci (e.g. cefalexin). Erythromycin may be used for the treatment of patients who are allergic to penicillins. The dosage and duration of treatment are the same as for acute pharyngitis (see pages 14–15).

Gastrointestinal tract infections

Diarrhoeal disease

Three clinical presentations of diarrhoeal disease may require treatment with antimicrobials: acute watery diarrhoea, invasive diarrhoea (dysentery) and persistent diarrhoea.

Acute watery diarrhoea

Most cases of acute watery diarrhoea are caused by rotavirus and do not require treatment with antimicrobials. Antimicrobial treatment is indicated, however, in cases due to infection with *Vibrio cholerae*. All cases of watery diarrhoea require measures for the prevention and treatment of dehydration. Adequate nutrition should be maintained.

Cholera

Cholera is caused by *Vibrio cholerae* and is characterized by severe acute watery diarrhoea. Several litres of fluid may be lost within a few hours, causing severe dehydration. Cholera occurs in endemic and epidemic situations. The antimicrobial susceptibility of the local strains must be determined and multiple isolates tested during the course of an outbreak to confirm susceptibility.

It is now recognized that as many as 90% of patients with cholera require no more treatment than prompt and adequate oral replacement of the water and electrolytes lost in the diarrhoeal stool and vomitus. Those who are severely dehydrated require intravenous fluids and antimicrobials.

Treatment

Doxycycline 300 mg (children >8 years: 2 mg/kg; maximum 100 mg) orally in a single dose (contraindicated during pregnancy)

or

ciprofloxacin 1 g (children: 20 mg/kg; maximum 1 g) orally in a single dose (contraindicated during pregnancy).

Invasive diarrhoea (dysentery)

In developing countries invasive diarrhoea or dysentery is often due to *Shigella* spp., with less severe diarrhoea caused by *Campylobacter* spp. In some countries enteroinvasive *Escherichia coli* is also common.

Shigellosis

The susceptibility of *Shigella* spp. varies between countries, with multiresistant strains encountered in many regions. Therapy should initially be based on data on the susceptibility of local strains and modified once the results of stool culture and susceptibility tests are known. Neonates with bloody diarrhoea should be referred to hospital for treatment.

Treatment

Nalidixic acid 1 g (children ≥3 months: 15 mg/kg; maximum 1 g) orally every 6 hours for 5 days (contraindicated during pregnancy)

or

ciprofloxacin 1 g (children: 20 mg/kg; maximum 1 g) orally in a single dose (contraindicated during pregnancy).

Comments

Patients with infection due to *Shigella dysenteriae* serotype 1 should receive ciprofloxacin 500 mg (children: 10 mg/kg; maximum 500 mg) orally every 12 hours for 5 days (contraindicated during pregnancy).

Ciprofloxacin is the preferred treatment option in all cases, but because of its lower cost, nalidixic acid is used in some countries. It should be noted, however, that the use of nalidixic acid may result in reduced susceptibility of *Shigella* spp. to ciprofloxacin.

Enteritis due to Campylobacter jejuni

Many patients with enteritis due to *Campylobacter jejuni* are asymptomatic by the time the diagnosis has been established and therefore do not require treatment with antimicrobials. Treatment should only be considered for patients with persistent symptoms.

Treatment

Erythromycin 500 mg (children: 10 mg/kg; maximum 500 mg) orally every 6 hours for 7–10 days

or

ciprofloxacin 500 mg orally every 12 hours for 7–10 days (contraindicated during pregnancy).

Comments

Ciprofloxacin is not licensed for use in children for enteritis due to *Campylobacter jejuni*, but is frequently used, particularly in patients with fever and/or bloody stools. Some ciprofloxacin-resistant strains have been noted.

Diarrhoea due to enteroinvasive Escherichia coli

Antimicrobials are generally not required for the treatment of diarrhoea due to enteroinvasive *Escherichia coli*. Furthermore, there is some evidence to suggest that such treatment may worsen the disease.

Persistent diarrhoea

In general, routine treatment of persistent diarrhoea with antimicrobials is not effective and is not recommended. However, children with persistent diarrhoea caused by shigellosis, amoebiasis or giardiasis, or with associated non-intestinal infections, such as pneumonia, sepsis, upper respiratory tract infections or otitis media may require antimicrobials. Such treatment should follow standard guidelines.[1]

Severely malnourished children should receive broad-spectrum antimicrobials for several days when admitted to hospital.[2]

Persistent diarrhoea may also be associated with HIV infection. In this situation, pathogens may include *Salmonella*, *Cryptosporidium* or *Microsporidium* spp.

---

[1] See *The treatment of diarrhoea: a manual for physicians and other senior health workers*, 3rd rev. Geneva, World Health Organization, 1995 (unpublished document WHO/CDR/95.3; available from Communicable Diseases: Control, Prevention and Eradication, World Health Organization, 1211 Geneva 27, Switzerland).

[2] See *Management of severe malnutrition — a manual for physicians and other senior health workers*. Geneva, World Health Organization, 1999.

Acute enteric infections

Typhoid and paratyphoid fever

Typhoid and paratyphoid fever are caused, respectively, by the pathogens *Salmonella typhi* and *S. paratyphi*, which are specific to humans. Transmission occurs via contaminated water and/or food. Following treatment with antimicrobials, about 10% of patients relapse and 1–3% become chronic carriers of infection.

Treatment

Chloramphenicol 1 g (children 25 mg/kg; maximum 750 mg) orally every 6 hours for 10–14 days

or

ciprofloxacin 500–750 mg (children 10–15 mg/kg; maximum 500 mg) orally every 12 hours for 5–14 days (contraindicated during pregnancy)

or

sulfamethoxazole 800 mg + trimethoprim 160 mg (children: 20 mg/kg + 4 mg/kg; maximum 800 mg + 160 mg) orally every 12 hours for 3 days.

Chronic carriers

Ciprofloxacin 500–750 mg orally every 12 hours for 4–6 weeks (contraindicated during pregnancy; children: ampicillin 10 mg/kg (maximum 250 mg) i.m. every 6 hours for 4–6 weeks).

Comments

In many developing countries chloramphenicol is preferred, due to its lower cost. However, the prevalence of resistance to the drug is increasing. Ciprofloxacin is not licensed for either of these indications in children, but is frequently used in short courses. Chloramphenicol and ampicillin appear to be less effective than ciprofloxacin in treating chronic carriers of infection. However, prolonged use of ciprofloxacin in children should be avoided.

Infectious enteritis due to *Salmonella* spp. other than *S. typhi*

In infectious enteritis due to *Salmonella enteritidis*, treatment is the same as that recommended for typhoid fever (see above). In other circumstances antimicrobial therapy is not

recommended. However, chronic bacteraemia, metastatic infections or enterocolitis in patients with sickle-cell disease, HIV infection or other predisposing conditions must be treated.

In developing countries multiresistant salmonella infections (including septicaemia) may be nosocomial in origin, especially among children. Recommendations for antimicrobial therapy should be based on data on the susceptibility of local strains.

Enteritis due to enterotoxigenic *Escherichia coli*

Chemoprophylaxis against so-called "traveller's diarrhoea" is not indicated. Mild cases require no treatment. However, antimicrobial therapy should be considered if diarrhoea persists or is severe (e.g. more than five bowel movements per day, bloody diarrhoea and/or fever).

Treatment

Sulfamethoxazole 800 mg + trimethoprim 160 mg (children: 20 mg/kg + 4 mg/kg; maximum 800 mg + 160 mg) orally every 12 hours for 3 days

or

ciprofloxacin 500 mg (children: 10 mg/kg; maximum 500 mg) orally every 12 hours for 3 days (contraindicated during pregnancy).

Comments

Tetracycline, doxycycline, chloramphenicol and cefalosporins are not recommended. Ciprofloxacin is not licensed for use in children for this indication, but may be used for short courses if there are no suitable alternatives.

Intestinal protozoal infections

Amoebiasis

Amoebiasis is an uncommon form of bloody diarrhoea due to the protozoan *Entamoeba histolytica*. The diagnosis should be considered if a patient has persistent bloody diarrhoea (dysentery) despite therapy for shigellosis. Only certain strains of *E. histolytica* are pathogenic and asymptomatic carriers are common in endemic areas. Patients with invasive disease require consecutive treatment with a systemically active amoebicide followed by a luminal amoebicide in order to eliminate any surviving organisms in the colon. Clearance of cysts in the

faeces should be mainly considered in patients living in non-endemic areas.

Treatment

Metronidazole 10 mg/kg (maximum 250 mg) orally every 8 hours for 8–10 days (adults and children; contraindicated during pregnancy)

followed by

diloxanide furoate 500 mg (children: 6–7 mg/kg; maximum 500 mg) orally every 8 hours for 10 days.

Giardiasis

Giardia lamblia is a flagellated protozoan which is transmitted from person to person mainly via faecal contamination of food or hands. It occurs worldwide, particularly where sanitation is poor, and is a common cause of both acute and persistent diarrhoea among children in developing countries.

Treatment

Metronidazole 2 g (children: 30 mg/kg; maximum 1.2 g) orally every 24 hours for 3 days (contraindicated during pregnancy)

or

tinidazole 2 g (children: 50 mg/kg; maximum 2 g) orally in a single dose (contraindicated during pregnancy).

Necrotizing enterocolitis due to *Clostridium difficile*

This is a form of pseudomembranous enterocolitis caused by toxigenic *Clostridium difficile*, following alteration of the intestinal microflora. Previous use of antimicrobials, especially ampicillin, cefalosporins and clindamycin, is often implicated. Treatment with any suspect antimicrobial should be ceased immediately. If toxigenic *C. difficile* is proven or suspected, treatment should be initiated promptly.

Treatment

Metronidazole 200 mg (children: 12.5 mg/kg; maximum 200 mg) orally every 8 hours for 7–14 days (contraindicated during pregnancy).

Comments

Patients who fail to respond to treatment with metronidazole should receive vancomycin 125 mg (children: 5 mg/kg; maximum 125 mg) orally every 6 hours for 7–14 days.

Non-diarrhoeal gastrointestinal infections

Acute gastritis and peptic ulcer disease

Acute gastritis and peptic ulcer disease are commonly associated with infection of the mucosa of the upper gastrointestinal tract with *Helicobacter pylori*. If possible, presence of the organism should be confirmed by biopsy (for bacterial culture) or by a positive breath test (for ketones). Various treatment regimens have been used, of which the following options are suggested based on their efficacy, simplicity and availability. Only adult doses are described, as the condition is not usually found in children. Both regimens are associated with a 80–85% clearance rate.

Treatment

Bismuth salicylate 107.7 mg (1 tablet) orally every 6 hours for 2 weeks

plus

metronidazole 200 mg orally every 8 hours and 400 mg orally at night for 2 weeks (contraindicated during pregnancy)

plus either

tetracycline 500 mg orally every 6 hours for 2 weeks (contraindicated during pregnancy)

or

amoxicillin 500 mg orally every 6 hours for 2 weeks.

Alternative regimen. Omeprazole 40 mg orally every 24 hours for 2 weeks

plus

metronidazole 400 mg orally every 8 hours for 2 weeks (contraindicated during pregnancy)

plus

amoxicillin 500 mg orally every 8 hours for 2 weeks.

Acute cholecystitis

Acute cholecystitis is often associated with obstruction by calculi. The infecting organisms are predominantly ascending bowel flora, especially *Escherichia coli* and *Klebsiella* spp. Sudden onset of pyrexia, often with rigors, and pain and

tenderness in the right upper quadrant are characteristic. Jaundice is often an accompanying sign. Immediate surgery is required for gangrenous cholecystitis, associated perforation and abscess formation.

Treatment

Ampicillin 1–2 g (children: 25–50 mg/kg; maximum 2 g) i.v. or i.m. every 6 hours for up to 7 days

plus

gentamicin 5–7 mg/kg i.v. daily in divided doses (children: 7.5 mg/kg i.v. in 1–3 divided doses daily) for up to 7 days (contraindicated during pregnancy).

Acute peritonitis

Intra-abdominal sepsis may develop either as a result of an external injury (e.g. a stab wound), a ruptured intra-abdominal organ (e.g. appendicitis) or postoperatively following abdominal or pelvic surgery. Typically, the involved pathogens are the patient's own bowel flora (aerobes and anaerobes). Severe pain, vomiting and pyrexia are common. Other signs include rigidity, rebound tenderness and absent bowel sounds.

Treatment

Ampicillin 2 g (children: 50 mg/kg; maximum 2 g) i.v. or i.m. every 6 hours for at least 7 days

plus

gentamicin 5–7 mg/kg i.v. daily in divided doses (children: 7.5 mg/kg i.v. in 1–3 divided doses daily) for at least 7 days (contraindicated during pregnancy)

plus

metronidazole 500 mg (children: 12.5 mg/kg; maximum 500 mg) i.v. every 8–12 hours for at least 7 days (contraindicated during pregnancy).

For patients who are allergic to penicillins, ampicillin should be deleted from the above regimen.

Urinary tract infections

Urinary tract infections in women

Uncomplicated infections

Acute cystitis is the most common clinical manifestation of an uncomplicated urinary tract infection, especially in young women. Most infections are caused by *Escherichia coli*, while *Staphylococcus saprophyticus* is a less common pathogen. In women who are not pregnant, diagnostic signs of an acute infection of the lower urinary tract include dysuria, urgency and frequency of micturition, pyuria and the presence of high numbers of bacteria in the urine ($>10^5$/ml).

Treatment

Trimethoprim 300 mg orally every 24 hours for 3 days

or

nitrofurantoin 100 mg orally every 12 hours for 3 days

or

cefalexin 500 mg orally every 8 hours for 5 days.

Comments

Treatment of urinary tract infections during pregnancy should be based on the results of urine culture and antimicrobial susceptibility testing; however, trimethoprim should be avoided. The majority of such patients should be considered for urinary tract investigation in the puerperium.

Fluoroquinolones (e.g. ciprofloxacin) and most cefalosporins should not be used to treat uncomplicated urinary tract infections.

Complicated infections

Complicated urinary tract infections are those associated with structural abnormalities of the urinary tract or calculi, recurrent infections, or infections in patients with underlying diseases such as diabetes. Culture and antimicrobial susceptibility data should be available to direct therapy because of the potentially

wide range of multiresistant pathogens. The range of antimicrobials suitable for therapy include those described above.

Urinary tract infections in men

Urinary tract infections occurring in men should not be regarded as uncomplicated. An underlying abnormality of the urinary tract is common and there is often associated infection of the posterior urethra, prostate or epididymis. All males with a urinary tract infection should be investigated to detect a possible underlying abnormality. The treatment is the same as that recommended for acute cystitis in women, except that it should be continued for at least 14 days. The presence of underlying prostatitis, in particular, may require prolonged therapy with antimicrobials (see pages 45–46).

Urinary tract infections in children

When cystitis is confirmed by a positive urine culture, investigation is required to exclude an underlying abnormality of the urinary tract in boys of all ages, girls under 5 years and premenarcheal girls with recurrent urinary tract infections.

Fluoroquinolones, trimethoprim and most cefalosporins should be avoided in children unless deemed necessary on microbiological grounds.

Treatment

Cefalexin 12.5 mg/kg (maximum 500 mg) orally every 6 hours for 5–10 days

or

amoxicillin 7.5 mg/kg + clavulanic acid (maximum 250 mg) orally every 8 hours for 5–10 days.

Comments

Prophylaxis with antimicrobials (e.g. nitrofurantoin 50 mg orally at night) should be considered after cessation of the treatment course, until such time as urinary tract investigation and imaging have been completed.

Acute pyelonephritis

Bacterial infections of the renal parenchyma are usually due to the ascent of organisms via the ureter into the kidney. Most infections are due to *Escherichia coli* and some may be due to *Proteus, Klebsiella* or *Enterococcus* spp. Sudden onset of pain in one or both kidneys together with high fever and symptoms of infection of the lower urinary tract are characteristic. Rigors and vomiting may occur and occasionally septicaemic shock supervenes.

Treatment

Ampicillin 1–2 g (children: 50 mg/kg; maximum 2 g) i.v. or i.m. every 6 hours for up to 14 days

plus either

gentamicin 5–7 mg/kg orally daily in divided doses (children: 7.5 mg/kg orally in 1–3 divided doses daily) for 7 days (contraindicated during pregnancy)

or

ceftriaxone 1 g (children: 50 mg/kg; maximum 1 g) i.v. or i.m. every 24 hours for 14 days.

Comments

Gentamicin should be avoided in patients with significant renal impairment. Some clinicians use ceftriaxone alone. Following an initial response (e.g. resolution of fever) and depending on the clinical circumstances, consideration of a change to an active oral agent (e.g. oral ciprofloxacin 750 mg every 12 hours; contraindicated during pregnancy) to complete the treatment course may be appropriate.

Prostatitis

Acute prostatitis is characterized by symptoms of infection of the lower urinary tract, together with fever, pain in the perineal area and tenderness of the prostate. A number of pathogens may be responsible, including *Escherichia coli* and *Staphylococcus aureus*. In many cases no organism is identified. Most patients recover after treatment, but chronic prostatitis may develop which can be difficult to cure.

Doses refer to adults, as this condition is not found in children.

Treatment

Trimethoprim 200 mg orally every 12 hours for 4–6 weeks

or

ciprofloxacin 500 mg orally every 12 hours for 4–6 weeks.

Comments

Cases that fail to respond to treatment may be due to *Chlamydia trachomatis* or *Ureaplasma urealyticum*, and can be treated empirically with erythromycin 500 mg orally every 6 hours for 14 days or doxycycline 100 mg orally every 12 hours for 14 days.

Skin and soft tissue infections

Localized purulent skin lesions

Localized purulent lesions of the skin such as furunculosis and folliculitis do not usually require therapy with systemic antimicrobials, except in patients who are immunosuppressed, such as those with HIV infection or diabetes. However, more extensive lesions with collections of pus require drainage and antimicrobial treatment. The most frequent pathogens are staphylococci. The lesions should be covered with clean dressings.

Treatment

Cloxacillin 250–500 mg (children: 12.5–25 mg/kg; maximum 500 mg) orally every 6 hours for 5–7 days

or

cefalexin 500 mg (children: 12.5–25 mg/kg; maximum 500 mg) orally every 6 hours for 5–7 days

or

sulfamethoxazole 800 mg + trimethoprim 160 mg (children: 20 mg/kg + 4 mg/kg; maximum 800 mg + 160 mg) orally every 12 hours for 5–7 days.

Impetigo

Impetigo is a highly contagious superficial purulent skin disease caused by staphylococci, streptococci, or a combination of both organisms. It is particularly common in infants and small children. Glomerulonephritis is a severe complication which may occur if the infecting pathogen is a nephritogenic strain of *Streptococcus pyogenes*. Antimicrobial therapy is necessary in these cases to try to prevent transmission of the infection.

Treatment

Cloxacillin 250–500 mg (children: 12.5–25 mg/kg; maximum 500 mg) orally every 6 hours for 5–7 days

or

cefalexin 500 mg (children: 12.5–25 mg/kg; maximum 500 mg) orally every 6 hours for 5–7 days

or

sulfamethoxazole 800 mg + trimethoprim 160 mg (children: 20 mg/kg + 4 mg/kg; maximum 800 mg + 160 mg) orally every 12 hours for 5–7 days.

Cellulitis and erysipelas

Cellulitis and erysipelas are streptococcal infections of the subcutaneous tissues, which usually result from contamination of minor wounds. Both conditions are characterized by acute localized inflammation and oedema. The lesions are more superficial in erysipelas than in cellulitis and have a well defined, raised margin. Potentially fatal systemic toxaemia may supervene in patients who remain untreated. Recurrent cellulitis or erysipelas can result in chronic lymphoedema which may, in turn, serve as a predisposing factor for recurrent episodes of infection.

In infants, facial lesions similar to those of cellulitis and erysipelas may be caused by *Haemophilus influenzae*; however, this condition is rare in countries where *H. influenzae* vaccination programmes have been instituted.

Treatment

Procaine benzylpenicillin 1.5 million IU (children: 50 000 IU/kg; maximum 1.5 million IU) i.m. every 24 hours for 7–10 days

or

benzylpenicillin 1–2 million IU (children: 50 000–100 000 IU/kg; maximum 2 million IU) i.v. or i.m. every 6 hours for 7–10 days (once clinical improvement occurs, amoxicillin 500 mg (children: 7.5–15 mg/kg; maximum 500 mg) orally every 8 hours may be substituted)

or

cefazolin 1–2 g (children: 15 mg/kg; maximum 2 g) i.v. or i.m. every 8 hours for 7–10 days (once clinical improvement occurs, cefalexin 500 mg (children: 12.5–25 mg/kg; maximum 500 mg) orally every 6 hours may be substituted).

Streptococcal necrotizing fasciitis

Streptococcal necrotizing fasciitis is characterized by a fulminant spreading subcutaneous necrosis that affects fascial tissue following minor trauma with infection due to group A β-haemolytic *Streptococcus pyogenes*. Diagnosis is by Gram-staining and culture of tissue fluid. Treatment consists primarily of surgical debridement of the necrotic tissue together with appropriate antimicrobial therapy.

Clinical differentiation between streptococcal fasciitis and so-called "synergistic gangrene" may be difficult; in such cases treatment should be the same as for gangrene (see below).

Treatment

Benzylpenicillin 4 million IU (children: 100 000 IU/kg; maximum 4 million IU) i.v. or i.m. every 4 hours for at least 7 days

plus

clindamycin 600 mg i.v. every 8 hours (children: 10 mg/kg; maximum 450 mg i.v. every 6 hours) for at least 7 days.

Gangrene

Clostridial gangrene, following traumatic injuries of the limbs or surgical procedures, is characterized by rapidly spreading deep necrosis with gas in the tissue. A similar condition is "synergistic gangrene", which arises in the perineal area, generally following relatively minor trauma, and is associated with gradual sloughing of the skin and subcutaneous necrosis. Both conditions are caused by *Clostridium* spp., especially *C. perfringens* and *C. novyi.* Large Gram-positive bacilli seen on Gram-staining of exudate are suggestive of clostridial sepsis, while a mixture of Gram-positive cocci and bacilli and Gram-negative bacilli is indicative of synergistic gangrene. In both conditions the basis of treatment is immediate surgical debridement and antimicrobial therapy.

Treatment

Benzylpenicillin 4 million IU (children: 100 000 IU/kg; maximum 4 million IU) i.v. or i.m. every 4 hours for at least 7 days

plus

gentamicin 5–7 mg/kg i.v. or i.m. daily in divided doses (children: 7.5 mg/kg i.v. or i.m. in 1–3 divided doses daily) for at least 7 days (contraindicated during pregnancy)

plus

metronidazole 500 mg (children: 12.5 mg/kg; maximum 500 mg) i.v. every 8 hours for at least 7 days (once clinical improvement occurs, rectal formulations may be substituted; contraindicated during pregnancy).

For patients who are allergic to penicillins, benzylpenicillin should be replaced by clindamycin 600 mg (children: 10 mg/kg; maximum 450 mg) orally or i.v. every 6–8 hours.

Pyomyositis

Pyomyositis is characterized by a deep-seated muscle abscess, most commonly due to *Staphylococcus aureus*. Although pyomyositis may follow trauma, there may often be no obvious portal of entry, with infection due to haematogenous spread. Treatment includes drainage, identification of the pathogen (Gram-staining is usually diagnostic) and antimicrobial therapy.

Treatment

Cloxacillin 2 g (children: 25–50 mg/kg; maximum 2 g) i.v. or i.m. every 6 hours for 5–10 days (once clinical improvement occurs, cloxacillin 500 mg (children: 12.5–25 mg/kg; maximum 500 mg) orally every 6 hours may be substituted)

or

cefazolin 1–2 g (children: 15 mg/kg; maximum 2 g) i.v. or i.m. every 8 hours for 5–10 days (once clinical improvement occurs, cefalexin 500 mg (children: 12.5–25 mg/kg; maximum 500 mg) orally every 6 hours may be substituted)

or

clindamycin 600 mg i.v. every 8 hours (children: 10 mg/kg; maximum 450 mg i.v. every 6 hours) for 5–10 days (once clinical improvement occurs, clindamycin 300–450 mg (children: 5–10 mg/kg; maximum 450 mg) orally every 4–6 hours may be substituted).

Contaminated soft tissue injuries

Infections of the soft tissues frequently occur following crush injuries, stab wounds and related injuries, such as gunshot wounds. Such infections are usually caused by *Staphylococcus aureus*, *Streptococcus pyogenes*, anaerobic bacteria (especially *Clostridium* spp.) or aerobic Gram-negative bacteria.

Treatment

Cloxacillin 2 g (children: 25–50 mg/kg; maximum 2 g) i.v. or i.m. every 6 hours for 5–10 days (once clinical improvement occurs, cloxacillin 500 mg (children: 12.5–25 mg/kg; maximum 500 mg) orally every 6 hours may be substituted)

plus

gentamicin 5–7 mg/kg i.v. or i.m. daily in divided doses (children: 7.5 mg/kg i.v. or i.m. in 1–3 divided doses daily) for 5–10 days (contraindicated during pregnancy)

plus

metronidazole 500 mg (children: 12.5 mg/kg; maximum 500 mg) i.v. every 8 hours for 5–10 days (once clinical improvement occurs, oral or rectal formulations of metronidazole may be substituted; contraindicated during pregnancy).

Human and animal bites and clenched-fist injuries

Human and animal bites and clenched-fist (punching) injuries often become infected. Causative pathogens in human bites include *Staphylococcus aureus*, *Streptococcus* spp., *Eikenella corrodens* and β-lactamase-producing anaerobic bacteria. In animal bites the most common causes are *Pasteurella multocida*, *Staphylococcus aureus*, *Capnocytophaga canimorsus*, *Streptococcus* spp. and anaerobic bacteria.

Treatment should include thorough cleaning, debridement and immobilization of the wound and prophylactic antimicrobials. If infection is suspected cultures should be taken. Wounds at a high risk of infection include:

— wounds with delayed presentation (i.e. at least 8 hours);
— puncture wounds unable to be adequately debrided;

— wounds on the hands, feet or face;
— wounds with underlying structures involved;
— wounds in immunocompromised patients.

For wounds that fall into these categories and those that are moderate or severe in nature, presumptive treatment with antimicrobials should be considered.

Treatment

Procaine benzylpenicillin 1.5 million IU (children: 50 000 IU/kg; maximum 1.5 million IU) i.m. every 24 hours for 5 days

followed by

amoxicillin 500 mg + clavulanic acid (children: 15 mg/kg; maximum 500 mg) orally every 8 hours for 5 days.

Patients allergic to penicillins

Metronidazole 400–500 mg (children: 10–12.5 mg/kg; maximum 250 mg) orally every 12 hours for 5–10 days (contraindicated during pregnancy)

plus either

doxycycline 100 mg (children >8 years: 2 mg/kg; maximum 100 mg) orally every 24 hours for 5–10 days (contraindicated during pregnancy)

or

sulfamethoxazole 800 mg + trimethoprim 160 mg (children: 20 mg/kg + 4 mg/kg; maximum 800 mg + 160 mg) orally every 12 hours for 5–10 days.

Comments

The choice of treatment will be determined by the organisms cultured from the infected wound. In all cases, consideration should be given to prophylaxis against tetanus. Animal bites may also require prophylaxis against rabies.

Bone and joint infections

Osteomyelitis

Acute osteomyelitis arising in children and adults is usually caused by *Staphylococcus aureus* and less commonly β-haemolytic streptococci. In sickle-cell disease, osteomyelitis may be caused by *Salmonella* spp. Blood cultures and/or bone aspiration will help to establish an etiological diagnosis. Acute osteomyelitis generally requires treatment for 4–6 weeks, with most, if not all, therapy administered parenterally.

Osteomyelitis in adults

Treatment

Osteomyelitis due to Staphylococcus aureus

Cloxacillin 2 g i.v. or i.m. every 6 hours for at least the initial 14 days, but preferably the entire treatment course of 4–6 weeks (if the duration of parenteral therapy is less than 4–6 weeks, the treatment course should be completed with cloxacillin 1 g orally every 6 hours)

or

cefazolin 1–2 g i.v. or i.m. every 8 hours for 4–6 weeks (if the duration of parenteral therapy is less than 4–6 weeks, the treatment course should be completed with cefalexin 1–2 g orally every 6 hours)

or

clindamycin 600 mg i.v. every 8 hours for 4–6 weeks (if the duration of parenteral therapy is less than 4–6 weeks, the treatment course should be completed with clindamycin 300–450 mg orally every 6 hours).

Osteomyelitis due to β-haemolytic streptococci

Benzylpenicillin 2 million IU (1.2 g) i.v. or i.m. every 4–6 hours for 2–4 weeks (if the duration of parenteral therapy is less than 2–4 weeks, the treatment course should be completed with amoxicillin 1 g orally every 6–8 hours).

Osteomyelitis due to Salmonella spp.

Ciprofloxacin 750 mg orally every 12 hours for 6 weeks (contraindicated during pregnancy).

Osteomyelitis in children aged over 5 years

Osteomyelitis in children aged over 5 years is generally caused by *Staphylococcus aureus*. Treatment may include cloxacillin, which is reasonably well absorbed from the gastrointestinal tract in children, allowing a greater proportion of the total treatment regimen to be given orally than in adults.

Treatment

Osteomyelitis due to Staphylococcus aureus

Cloxacillin 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 4–6 hours for 4–6 days (or until clinical improvement occurs), followed by cloxacillin 25 mg/kg (maximum 500 mg) orally every 6 hours to complete the treatment course of 3–4 weeks

or

ceftriaxone 50–75 mg/kg (maximum 1 g) i.v. or i.m. every 24 hours for 4–6 days (or until clinical improvement occurs), followed by cloxacillin 25 mg/kg (maximum 500 mg) or cefalexin 25 mg/kg (maximum 500 mg) orally every 6 hours to complete the treatment course of 3–4 weeks

or

cefazolin 15 mg/kg (maximum 1 g) i.v. or i.m. every 8 hours for 4–6 days (or until clinical improvement occurs), followed by cefalexin 25 mg/kg (maximum 500 mg) orally every 6 hours to complete the treatment course of 3–4 weeks

or

clindamycin 10 mg/kg (maximum 450 mg) i.v. every 6 hours for 4–6 days (or until clinical improvement occurs), followed by clindamycin 10 mg/kg (maximum 450 mg) orally every 6 hours to complete the treatment course of 3–4 weeks.

Osteomyelitis in children aged up to 5 years

Haemophilus influenzae is the most common cause of osteomyelitis among children aged up to 5 years, especially among those not immunized against *H. influenzae* type b (Hib). The total duration of treatment is generally at least 3–4 weeks.

Treatment

Osteomyelitis due to Haemophilus influenzae or unknown pathogen

Children aged from 2 months to 5 years. Cloxacillin 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 4–6 hours for 4–6 days (or until clinical improvement occurs)

plus

ceftriaxone 50–75 mg/kg (maximum 1 g) i.v. or i.m. every 24 hours for 4–6 days (or until clinical improvement occurs)

followed by

amoxicillin 15 mg/kg + clavulanic acid (maximum 500 mg) orally every 8 hours to complete the treatment course of 3–4 weeks.

Neonates. Cloxacillin 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 4–6 hours for 4–6 days (or until clinical improvement occurs)

plus

cefotaxime 50–75 mg/kg (maximum 2 g) i.v. every 8 hours for 4–6 days (or until clinical improvement occurs)

followed by

amoxicillin 15 mg/kg + clavulanic acid (maximum 500 mg) orally every 8 hours to complete the treatment course of 3–4 weeks.

Osteomyelitis due to Staphylococcus aureus

Children aged from 2 months to 5 years. Cloxacillin 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 4–6 hours for 4–6 days (or until clinical improvement occurs)

plus

ceftriaxone 50–75 mg/kg (maximum 1 g) i.v. or i.m. every 24 hours for 4–6 days (or until clinical improvement occurs)

followed by

cloxacillin 12.5 mg/kg (maximum 500 mg) orally every 6 hours to complete the treatment course of 3–4 weeks.

Neonates. Cloxacillin 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 4–6 hours for 4–6 days (or until clinical improvement occurs)

plus

cefotaxime 50–75 mg/kg (maximum 2 g) i.v. every 8 hours for 4–6 days (or until clinical improvement occurs)

followed by

cloxacillin 12.5 mg/kg (maximum 500 mg) orally every 6 hours to complete the treatment course of 3–4 weeks.

Osteomyelitis due to Salmonella spp.

Children aged from 2 months to 5 years. Treatment options will depend on the susceptibility of the pathogen, but include the following:

cloxacillin 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 4–6 hours for 4–6 days (or until clinical improvement occurs)

plus

ceftriaxone 50–75 mg/kg (maximum 1 g) i.v. or i.m. every 24 hours for 4–6 days (or until clinical improvement occurs)

followed by either

sulfamethoxazole 20 mg/kg + trimethoprim 4 mg/kg (maximum 800 mg + 160 mg) orally every 12 hours to complete the treatment course of 6 weeks

or

amoxicillin 7.5–15 mg/kg (maximum 1 g) orally every 8 hours to complete the treatment course of 6 weeks

or

ciprofloxacin 10–15 mg/kg (maximum 500 mg) orally every 12 hours to complete the treatment course of 6 weeks.

Neonates. Treatment options will depend on the susceptibility of the pathogen, but include the following:

cloxacillin 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 4–6 hours for 4–6 days (or until clinical improvement occurs)

plus

cefotaxime 50–75 mg/kg (maximum 2 g) i.v. every 8 hours for 4–6 days (or until clinical improvement occurs)

followed by either

sulfamethoxazole 20 mg/kg + trimethoprim 4 mg/kg (maximum 800 mg + 160 mg) orally every 12 hours to complete the treatment course of 6 weeks

or

amoxicillin 7.5–15 mg/kg (maximum 1 g) orally every 8 hours to complete the treatment course of 6 weeks

or

ciprofloxacin 10–15 mg/kg (maximum 500 mg) orally every 12 hours to complete the treatment course of 6 weeks.

Comments

If acute osteomyelitis is not cured, chronic osteomyelitis may develop. Treatment of the latter condition comprises surgical debridement of dead bone and necrotic tissue, accompanied by antimicrobial therapy directed against the infecting pathogen for 4–6 weeks. Where prosthetic materials (e.g. fixation screws or plates, or artificial joints) are associated with osteomyelitis, cure is extremely difficult without removal of the prosthetic device.

Septic arthritis

Staphylococcus aureus is the most common pathogen in all age groups and should be treated with antimicrobial regimens similar to those recommended for osteomyelitis, although generally a 2–3-week treatment regimen is sufficient. However, depending on the patient's age, other pathogens may need consideration:

- Among infants aged up to 3 months and some elderly patients, Enterobacteriaceae (e.g. *Escherichia coli*) and group B streptococci are common.
- Infections with *Haemophilus influenzae* and *Streptococcus pneumoniae* need to be considered in children aged from 3 months to 6 years.
- Among sexually active young adults and teenagers, septic arthritis due to *Neisseria gonorrhoeae* is common.

Treatment

Until the results of blood and synovial fluid culture are known, initial empirical therapy should be given.

Initial empirical therapy

Adults. Cloxacillin 2 g i.v. or i.m. every 6 hours

plus

ceftriaxone 1–2 g i.v. or i.m. every 24 hours.

Children ≥ 2 months. Cloxacillin 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 6 hours

plus

ceftriaxone 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 24 hours.

Neonates. Cloxacillin 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 6 hours

plus

cefotaxime 50–75 mg/kg (maximum 2 g) i.v. every 8 hours.

Once the pathogen has been identified, treatment should be adjusted appropriately.

Septic arthritis due to Staphylococcus aureus

Adults. Cloxacillin 2 g i.v. or i.m. every 6 hours for 2–3 weeks (if the duration of parenteral therapy is less than 2–3 weeks, the treatment course should be completed with cloxacillin 1 g orally every 6 hours)

or

cefazolin 1–2 g i.v. or i.m. every 8 hours for 2–3 weeks (if the duration of parenteral therapy is less than 2–3 weeks, the treatment course should be completed with cefalexin 1–2 g orally every 6 hours)

or

clindamycin 600 mg i.v. every 8 hours for 2–3 weeks (if the duration of parenteral therapy is less than 2–3 weeks, the treatment course should be completed with clindamycin 300–450 mg orally every 6 hours).

Children > 5 years. Cloxacillin 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 4–6 hours for 4–6 days (or until clinical improvement occurs), followed by cloxacillin 25 mg/kg (maximum 500 mg) orally every 6 hours to complete the treatment course of 2–3 weeks

or

ceftriaxone 50–75 mg/kg (maximum 1 g) i.v. or i.m. every 24 hours for 4–6 days (or until clinical improvement occurs), followed by cloxacillin 25 mg/kg (maximum 500 mg) or cefalexin 25 mg/kg (maximum 500 mg) orally every 6 hours to complete the treatment course of 2–3 weeks

or

cefazolin 15 mg/kg (maximum 1 g) i.v. or i.m. every 8 hours for 4–6 days (or until clinical improvement occurs), followed by cefalexin 25 mg/kg (maximum 500 mg) orally every 6 hours to complete the treatment course of 2–3 weeks

or

clindamycin 10 mg/kg (maximum 450 mg) i.v. every 6 hours for 4–6 days (or until clinical improvement occurs), followed by clindamycin 10 mg/kg (maximum 450 mg) orally every 6 hours to complete the treatment course of 2–3 weeks.

Children aged from 2 months to 5 years. Cloxacillin 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 4–6 hours for 4–6 days (or until clinical improvement occurs)

plus

ceftriaxone 50–75 mg/kg (maximum 1 g) i.v. or i.m. every 24 hours for 4–6 days (or until clinical improvement occurs)

followed by

cloxacillin 12.5 mg/kg (maximum 500 mg) orally every 6 hours to complete the treatment course of 2–3 weeks.

Neonates. Cloxacillin 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 4–6 hours for 4–6 days (or until clinical improvement occurs)

plus

cefotaxime 50–75 mg/kg (maximum 2 g) i.v. every 8 hours for 4–6 days (or until clinical improvement occurs)

followed by

cloxacillin 12.5 mg/kg (maximum 500 mg) orally every 6 hours to complete the treatment course of 2–3 weeks.

Comments

In some cases, especially in adults with infection due to *Staphylococcus aureus*, repeated aspiration or surgical washout of the joint may be necessary in addition to appropriate antimicrobial therapy.

Sexually transmitted diseases

Gonorrhoea

Gonorrhoea results from infection with the Gram-negative coccus *Neisseria gonorrhoeae.* Gonococcal and chlamydial infections often coexist. In women, gonorrhoea causes cervicitis. Examination of cervical smears is not reliable and cultures should be prepared whenever possible. In men, gonorrhoea is confirmed by demonstrating Gram-negative intracellular diplococci in urethral smears. Ideally, blood samples should be taken for serological tests to exclude concurrent infection with syphilis.

Treatment

All patients with gonorrhoea should be treated concurrently for chlamydial infection unless microbiological facilities exist to exclude the latter diagnosis. Sexual partners should be treated simultaneously.

Gonococcal conjunctivitis threatens sight and progresses rapidly. Since it is highly contagious, every effort should be made to prevent transmission of infection. Antimicrobial therapy should be started immediately and the eyes should be irrigated frequently with saline solution.

Uncomplicated anogenital gonococcal infections in adults

Ceftriaxone 250 mg i.m. in a single dose

or

spectinomycin 2 g i.m. in a single dose

or

ciprofloxacin 500 mg orally in a single dose (contraindicated during pregnancy).

Disseminated gonococcal infections in adults

Ceftriaxone 1 g i.m. every 24 hours for 7 days

or

spectinomycin 2 g i.m. every 12 hours for 7 days.

If there is evidence of meningeal or endocardial involvement, treatment should be extended to 2 weeks and 4 weeks, respectively.

Gonococcal conjunctivitis

Adults. Ceftriaxone 250 mg i.m. in a single dose

or

spectinomycin 2 g i.m. in a single dose

or

ciprofloxacin 500 mg orally in a single dose (contraindicated during pregnancy).

Neonates. Ceftriaxone 50 mg/kg (maximum 125 mg) i.m. in a single dose

or

cefotaxime 50 mg/kg (maximum 2 g) i.v. in a single dose

or

spectinomycin 25 mg/kg (maximum 75 mg) i.m. in a single dose.

If systemic treatment is not available and infection is confirmed, tetracycline, 1% ointment, should be instilled into each eye every hour, pending referral of the infant for parenteral therapy.

All infants should receive topical antigonococcal therapy immediately after birth. Tetracycline, 1% ointment, should be applied after gently cleansing the eyelids. Erythromycin, 1% ointment, is as effective, but more expensive. Some authorities recommend that therapy should continue for 7 days.

Comments

Neonates who fail to respond to treatment should be treated for chlamydial ophthalmia (see page 63).

Lymphogranuloma venereum

Lymphogranuloma venereum is caused by *Chlamydia trachomatis* serotypes L_1, L_2 and L_3. The primary genital lesion,

which is rarely demonstrable in women, usually occurs in men as a purulent ulcer on the penis that heals within a few days. After a latent period of days or months, an acute fluctuant inguinal lymphadenopathy develops. In the late stages of the disease, chronic lymphatic obstruction may result in lymphoedema (elephantiasis) of the external genitalia.

Treatment

Doxycycline 100 mg (children >8 years: 2 mg/kg; maximum 100 mg) orally every 12 hours for 14 days (contraindicated during pregnancy)

or

erythromycin 500 mg (children: 12.5 mg/kg; maximum 500 mg) orally every 6 hours for 14 days.

Other chlamydial infections

Chlamydia trachomatis (serotypes D–K) causes non-gonococcal urethritis in men. It may also cause epididymitis and chronic prostatitis. In women, infection is associated with cervicitis, salpingitis and endometritis. Infants born to mothers with cervical infection may develop purulent conjunctivitis (chlamydial ophthalmia) or pneumonia.

All patients with chlamydial infections should be treated concurrently for gonorrhoea, unless microbiological facilities exist to exclude the latter diagnosis. In every instance, sexual partners should be treated simultaneously.

Treatment

Doxycycline 100 mg (children >8 years: 2 mg/kg; maximum 100 mg) orally every 12 hours for 7 days (contraindicated during pregnancy)

or

erythromycin 500 mg (children: 10–15 mg/kg; maximum 500 mg) orally every 6 hours for 7 days.

Comments

Infants with chlamydial ophthalmia should be treated with erythromycin syrup, 12.5 mg/kg (maximum 500 mg) orally every 6 hours for 14 days.

Vaginitis

Vaginal discharge may be caused by candidiasis (due to *Candida albicans*), trichomoniasis (due to *Trichomonas vaginalis*) or bacterial vaginosis (due to *Gardnerella vaginalis* and vaginal anaerobes).

Treatment

Candidiasis

Nystatin pessaries 200 000 IU inserted high into the vagina nightly for 2 weeks (in some geographical areas, nightly doses as high as 1 million IU may be required).

Administration should be continued for 48 hours after clinical cure. Higher doses and a longer period of treatment may be required in immunocompromised patients.

Trichomoniasis

Metronidazole 2 g orally in a single dose (sexual partners should be treated simultaneously; contraindicated during pregnancy).

Bacterial vaginosis

Metronidazole 400–500 mg orally every 12 hours for 7 days (contraindicated during pregnancy).

Pelvic inflammatory disease

Acute pelvic inflammatory disease is often a consequence of sexually transmitted disease. The pathogens most commonly involved are *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. However, bacteria present in the normal vaginal flora, including streptococci, *Escherichia coli*, *Haemophilus influenzae* and anaerobes such as *Bacteroides*, *Peptostreptococcus* and *Peptococcus* spp. also often contribute. Trauma to the endocervical canal from an intrauterine device (IUD) may facilitate the ascent of these organisms into the endometrial cavity.

Treatment

If an intrauterine device is in place, it should be removed.

Ambulatory patients

Ceftriaxone 250 mg i.m. in a single dose

followed by

doxycycline 100 mg orally every 12 hours for 10 days (contraindicated during pregnancy)

plus

metronidazole 400–500 mg orally every 8 hours for 10 days (contraindicated during pregnancy).

Hospitalized patients with very severe disease

Gentamicin 5–7 mg/kg i.v. or i.m. every 24 hours or 1.5–2.0 mg/kg i.v. or i.m. every 8 hours for at least 4 days (or for 48 hours after clinical improvement occurs; contraindicated during pregnancy)

plus

clindamycin 900 mg i.v. every 8 hours for at least 4 days (or for 48 hours after clinical improvement occurs)

followed by

doxycycline 100 mg orally every 12 hours for 10–14 days (contraindicated during pregnancy).

Hospitalized patients with moderate or severe disease

Ceftriaxone 250 mg i.m. every 12 hours for at least 4 days (or for 48 hours after clinical improvement occurs)

followed by

doxycycline 100 mg orally every 12 hours for 10–14 days (contraindicated during pregnancy).

Alternative regimen. Ciprofloxacin 500 mg orally every 12 hours for at least 4 days (or for 48 hours after clinical improvement occurs; contraindicated during pregnancy)

plus

metronidazole 400–500 mg orally every 8 hours for at least 4 days (or for 48 hours after clinical improvement occurs; contraindicated during pregnancy)

followed by

doxycycline 100 mg orally every 12 hours for 10–14 days (contraindicated during pregnancy).

Syphilis

Syphilis is caused by the spirochaete *Treponema pallidum.* Transmission results almost exclusively from sexual contact with infected persons, but infection can also be transmitted from mother to fetus during pregnancy and through blood transfusion.

Where facilities and resources are available, all patients and their contacts should be concurrently tested and treated, as appropriate, for chlamydial infection, gonorrhoea and HIV infection according to national policy. Patients with a history of primary or secondary syphilis should be tested for the presence of specific antitreponemal antibodies, which indicate latent syphilis.

Doses are for adults, except where otherwise specified.

Treatment

Early syphilis (< 2 years' duration)

Benzathine benzylpenicillin 2.4 million IU i.m. in a single dose

or

procaine benzylpenicillin 1 million IU i.m. every 24 hours for 10 days.

Late syphilis (other than neurosyphilis)

Benzathine benzylpenicillin 2.4 million IU i.m. weekly for 3 weeks

or

procaine benzylpenicillin 1 million IU i.m. every 24 hours for 3 weeks.

Neurosyphilis

Benzylpenicillin 4 million IU i.v. every 4 hours for 2 weeks.

Alternative regimen. Procaine benzylpenicillin 1 million IU i.m. every 24 hours for 2 weeks

plus

probenecid 500 mg orally every 6 hours for 2 weeks.

Congenital syphilis

Children >2 years. Benzylpenicillin 200 000–300 000 IU/kg (maximum 2.4 million IU) i.v. or i.m. weekly in divided doses for 2 weeks.

Children ≤2 years. Benzylpenicillin 25 000 IU/kg (maximum 1.5 million IU) i.v. or i.m. every 12 hours for 10 days

or

procaine benzylpenicillin 50 000 IU/kg (maximum 1.5 million IU) i.m. every 24 hours for 10 days.

Patients allergic to penicillins

Doxycycline 100 mg (children >8 years: 2 mg/kg; maximum 100 mg) orally every 12 hours for 30 days (contraindicated during pregnancy)

or

erythromycin 500 mg (children: 7.5–12.5 mg/kg; maximum 250 mg) orally every 6 hours for 15 days.

Chancroid

Chancroid, which results from infection with *Haemophilus ducreyi*, is the most common cause of genital ulceration in developing countries and its incidence has been rising with increasing rates of HIV infection. Clinically, the disease is readily confused with syphilis. When facilities for dark-field microscopy and serological diagnosis of syphilis are not available, benzathine benzylpenicillin should always be administered at the same time.

Doses are for adults.

Treatment

Erythromycin 500 mg orally every 6 hours for 7 days

or

ciprofloxacin 500 mg orally in a single dose (contraindicated during pregnancy)

or

ceftriaxone 250 mg i.m. in a single dose

or

spectinomycin 2 g i.m. in a single dose.

Longer treatment courses may be necessary in immunocompromised patients.

Granuloma inguinale

Granuloma inguinale (donovanosis) is a chronic granulomatous infection caused by the Gram-negative encapsulated bacterium *Calymmatobacterium granulomatis.*

Doses are for adults.

Treatment

Sulfamethoxazole 800 mg + trimethoprim 160 mg orally every 12 hours for 14 days (or until the lesion has completely healed)

or

doxycycline 100 mg orally every 12 hours for 14 days (or until the lesion has completely healed; contraindicated during pregnancy)

or

chloramphenicol 500 mg orally every 6 hours for 3 weeks (or until the lesion has completely healed).

Cardiovascular infections

Infective endocarditis

Infective endocarditis is a difficult disease to diagnose and treat. It is most commonly caused by α-haemolytic ("viridans") streptococci, enterococci and *Staphylococcus aureus*. α-Haemolytic streptococci and enterococci usually affect previously damaged valves, whereas *S. aureus* can affect normal valves. Most cases of fulminant endocarditis are caused by *S. aureus*.

Blood cultures are usually positive and all efforts should be made to identify the responsible pathogen and to obtain antimicrobial susceptibility data before commencing treatment. All three pathogens may be resistant to common antimicrobials: α-haemolytic streptococci to penicillins; enterococci to penicillins, gentamicin (high-level resistance) and occasionally vancomycin; and *S. aureus* to penicillins. It is therefore essential to obtain blood cultures (preferably three sets, each from a separate venepuncture) before starting antimicrobial treatment.

When gentamicin is used in combination with a β-lactam antimicrobial in the treatment of endocarditis it should be administered every 8 hours. Basal plasma levels of gentamicin should not exceed 1 mg/l. If vancomycin is used, peak plasma levels of 30–40 mg/l and basal plasma levels of 5–15 mg/l are recommended. These levels are specific for the management of endocarditis and do not apply to other circumstances.

Initial empirical therapy

Treatment

Benzylpenicillin 3 million IU (children: 50 000 IU/kg; maximum 3 million IU) i.v. every 4 hours

plus

cloxacillin 2 g (children: 50 mg/kg; maximum 2 g) i.v. every 4 hours

plus

gentamicin 2 mg/kg (children: 2.5 mg/kg; maximum 80 mg) i.v. every 8 hours (contraindicated during pregnancy).

Patients allergic to penicillins or with nosocomial infections

Vancomycin 1 g (children: 20 mg/kg; maximum 1 g) i.v. every 12 hours

plus

gentamicin 2 mg/kg (children: 2.5 mg/kg; maximum 80 mg) i.v. every 8 hours (contraindicated during pregnancy).

Comments

The maximum period of gentamicin therapy without monitoring plasma levels should be 72 hours. There are currently no data available regarding once-daily gentamicin administration for the treatment of endocarditis. Accordingly the drug should be administered in 2–4 divided doses daily to maintain constant plasma levels. Once a pathogen has been identified, treatment should be amended as necessary.

Endocarditis due to α-haemolytic streptococci

α-Haemolytic streptococci are usually highly susceptible to benzylpenicillin. The minimum inhibitory concentration (MIC) of benzylpenicillin for the infecting strain should be determined, as this influences the need for and duration of concomitant gentamicin therapy. Most strains of α-haemolytic streptococci have both MIC and minimum bactericidal concentrations (MBC) of <0.2 mg/l, but a few demonstrate antimicrobial resistance (i.e. have an MBC/MIC ratio ≥32). For infections involving a resistant strain, or where the MIC is unknown, treatment should be as for strains resistant to benzylpenicillin (MIC = 0.25–1.0 mg/l).

Treatment

Uncomplicated endocarditis

Benzylpenicillin 3 million IU (children: 100 000 IU/kg; maximum 3 million IU) i.v. every 4 hours for 2 weeks

plus

gentamicin 1 mg/kg (adults and children) i.v. every 8 hours for 2 weeks (contraindicated during pregnancy).

Alternative regimen. Benzylpenicillin 3 million IU (children: 100 000 IU/kg; maximum 3 million IU) i.v. every 4 hours for 4 weeks.

Strains highly susceptible to benzylpenicillin (MIC ≤ 0.12 mg/l)
Benzylpenicillin 3 million IU (children: 100 000 IU/kg; maximum 3 million IU) i.v. every 4 hours for 4 weeks

plus

gentamicin 1 mg/kg (adults and children) i.v. every 8 hours for 2 weeks (contraindicated during pregnancy).

Strains resistant to benzylpenicillin (MIC = 0.25–1.0 mg/l)
Gentamicin 1 mg/kg (adults and children) i.v. every 8 hours for 4–6 weeks (contraindicated during pregnancy)

plus either

benzylpenicillin 3–4 million IU (children: 100 000 IU/kg; 4 million IU) i.v. every 4 hours for 6 weeks

or

ampicillin 2 g (children: 50 mg/kg; maximum 2 g) i.v. every 4 hours for 6 weeks.

Comments

α-Haemolytic streptococci with high-level resistance to penicillins are encountered in the USA, but are less common elsewhere. Treatment of such strains is usually with intravenous vancomycin plus gentamicin, as for prosthetic valve endocarditis (see page 73).

Endocarditis due to enterococci

The causative organisms of enterococcal endocarditis, such as *Enterococcus faecalis*, usually have reduced susceptibility to penicillins (MIC = 0.5–2.0 mg/l) and always require the concomitant use of gentamicin for optimal bactericidal activity.

Treatment

Gentamicin 1 mg/kg (adults and children) i.v. every 8 hours for 4–6 weeks (contraindicated during pregnancy)

plus either

benzylpenicillin 3–4 million IU (children: 100 000 IU/kg; maximum 4 million IU) i.v. every 4 hours for 6 weeks

or

ampicillin 2 g (children: 50 mg/kg; maximum 2 g) i.v. every 4 hours for 6 weeks.

Comments

Enterococci with high-level resistance to penicillins are encountered in the USA, but are less common elsewhere. Treatment of such strains is usually with intravenous vancomycin plus gentamicin, as for prosthetic valve endocarditis (see page 73). Enterococci should be tested for high-level resistance to aminoglycosides; if this is present, combination therapy with gentamicin will not be effective. Treatment of such strains is difficult and consultation with a specialist is recommended.

Endocarditis due to *Staphylococcus aureus*

Because of the frequency with which valvular destruction may rapidly progress and require surgical intervention, patients with endocarditis due to *Staphylococcus aureus* should be referred for early consultation with a cardiac surgeon.

Treatment

Strains susceptible to meticillin

Cloxacillin 2 g (children: 50 mg/kg; maximum 2 g) i.v. every 4 hours for 6 weeks

plus

gentamicin 1 mg/kg (adults and children) i.v. every 8 hours for 7 days (contraindicated during pregnancy).

Strains resistant to meticillin

Vancomycin 1 g i.v. every 12 hours (children: 40 mg/kg (maximum 1 g) i.v. in 2–4 divided doses daily) for 6 weeks.

Culture-negative endocarditis

Culture-negative endocarditis may be due to previous treatment with antimicrobials or to unusual microorganisms, such as fastidious streptococci, *Legionella* spp., *Bartonella* spp., *Coxiella burnetii* (the cause of Q fever) or fungi, including *Candida albicans.* Unless Q fever or fungal infection is strongly suspected, patients with culture-negative endocarditis should be treated with benzylpenicillin plus gentamicin, as for endo-

carditis due to enterococci (see page 71), followed by monitoring and adjustment of therapy as indicated.

Prosthetic valve endocarditis

Prosthetic valve endocarditis may be caused by staphylococci (particularly coagulase-negative staphylococci), *Corynebacterium* spp., *Streptococcus* spp., enteric Gram-negative rods, *Pseudomonas aeruginosa* and fungi, including *Candida albicans*. Because of increasing resistance of coagulase-negative staphylococci to cloxacillin, initial empirical therapy should include vancomycin plus gentamicin. Early consultation with a cardiac surgeon is imperative.

Treatment

Vancomycin 1 g i.v. every 12 hours (children: 40 mg/kg (maximum 1 g) i.v. in 2–4 divided doses daily) for 6 weeks

plus

gentamicin 1 mg/kg (adults and children) i.v. every 8 hours for 6 weeks (contraindicated during pregnancy).

Comments

If infection due to a Gram-negative bacterial pathogen is suspected, the dose of gentamicin should be increased to 2 mg/kg i.v. every 8 hours. Monitoring of gentamicin and vancomycin levels is important (see page 69).

Pericarditis and myocarditis

Pericarditis and myocarditis are not common and may be due to non-infectious causes such as rheumatic fever, collagen diseases, uraemia and myocardial infarction. Infectious causes include viruses (e.g. coxsackie viruses A and B), bacteria (e.g. *Staphylococcus aureus* and *Mycobacterium tuberculosis*), fungi and parasites (e.g. *Toxoplasma gondii*). Bacterial pathogens are treated according to their known or suspected antimicrobial susceptibility.

Rheumatic fever

Rheumatic fever is relatively rare in developed countries, but remains a common problem in developing countries. It occurs as a delayed sequela of infection with *Streptococcus pyogenes*.

Pharyngeal infection with *S. pyogenes* may be mild or subclinical. The mainstay of treatment for symptomatic acute disease is salicylates or corticosteroids (in severe cases), but a 10-day course of oral phenoxymethylpenicillin should also be given to eradicate the organism from the pharynx. For details of chemoprophylaxis in patients with a history of rheumatic fever, see pages 89–91.

Central nervous system infections

Meningitis

Bacterial meningitis is most often caused by *Haemophilus influenzae* serotype b, *Neisseria meningitidis* and *Streptococcus pneumoniae*. Childhood vaccination against *H. influenzae* serotype b is strongly encouraged to prevent meningitis.

Bacterial meningitis is an acute disease characterized by rapid onset of fever, severe headache and stiffness of the neck, followed by confusion and ultimately coma. In meningitis due to *N. meningitidis* a haemorrhagic rash may also be present. Meningitis due to *H. influenzae* mainly affects young children, but meningitis due to *N. meningitidis* and *S. pneumoniae* may affect any age group. A lumbar puncture should be performed, white cells counted and their type determined (granulocytes, lymphocytes) and a cerebrospinal fluid sample sent for culture and susceptibility testing of bacterial isolates. In areas endemic for the disease where the organism is not known, therapy should encompass all three possible pathogens. Because of the potential severity of this disease, treatment should be started promptly and not delayed for the results of lumbar puncture.

Initial empirical therapy

Treatment

Ceftriaxone 2 g (children: 50–100 mg/kg; maximum 2 g) i.v. or i.m. daily in one or two divided doses for up to 14 days.

Alternative regimen

Benzylpenicillin 3–4 million IU (children: 100 000 IU/kg; maximum 4 million IU) i.v. or i.m. every 4 hours for up to 14 days

plus

chloramphenicol 1 g (children: 25 mg/kg; maximum 1 g) i.v. every 6 hours for up to 14 days (once clinical improvement occurs, chloramphenicol 500–750 mg (children: 25 mg/kg; maximum 750 mg) orally every 6 hours may be substituted).

Comments

In areas where 10% or more of cases of invasive meningitis due to *S. pneumoniae* are caused by strains with intermediate resistance to benzylpenicillin, initial empirical therapy should be with ceftriaxone or cefotaxime (for neonates; see page 79).

Meningitis due to *Neisseria meningitidis*

Treatment

Benzylpenicillin 3–4 million IU (children: 100 000 IU/kg; maximum 4 million IU) i.v. or i.m. every 4 hours for up to 14 days

plus

chloramphenicol oily suspension 100 mg/kg (maximum 3 g) (children: 25 mg/kg; maximum 500 mg) i.m. every 24 hours for up to 14 days (once clinical improvement occurs, chloramphenicol 500–750 mg (children: 25 mg/kg; maximum 750 mg) orally every 6 hours may be substituted).

Prophylaxis

Rifampicin 600 mg (neonates <1 month: 5 mg/kg (maximum 300 mg); children ≥1 month: 10 mg/kg (maximum 600 mg)) orally every 12 hours for 2 days

or

ciprofloxacin 500 mg (adults and children) orally in a single dose (contraindicated during pregnancy).

Comments

Prophylaxis should be considered for patients and their close contacts, especially children.

Meningitis due to *Streptococcus pneumoniae*

Treatment

Strains susceptible to benzylpenicillin (MIC ≤ 0.06 mg/l)

Benzylpenicillin 3–4 million IU (children: 100 000 IU/kg; maximum 4 million IU) i.v. or i.m. every 4 hours for 10–14 days

or

ceftriaxone 2 g (children: 50–100 mg/kg; maximum 2 g) i.v. or i.m. daily in one or two divided doses for 10–14 days.

Patients who are very ill may require treatment for up to 3 weeks.

Strains showing intermediate resistance to benzylpenicillin (MIC = 0.125–1.0 mg/l)

Ceftriaxone 2 g (children: 50–100 mg/kg; maximum 2 g) i.v. or i.m. daily in one or two divided doses for 10–14 days.

Strains resistant to benzylpenicillin (MIC >1.0 mg/l) or ceftriaxone/ cefotaxime (MIC ≥1.0 mg/l)

Vancomycin 1 g i.v. every 12 hours (children: 20 mg/kg (maximum 1 g) i.v. every 6 hours) for at least 14 days

plus

ceftriaxone 2 g (children: 50–100 mg/kg; maximum 2 g) i.v. or i.m. every 12 hours for at least 14 days

plus

rifampicin 600 mg (children: 20 mg/kg; maximum 600 mg) orally every 24 hours for at least 14 days.

Comments

Several strains have been described that are resistant to cefotaxime or ceftriaxone (MIC ≥1.0 mg/l). Susceptibility tests should therefore be conducted before starting treatment to check whether the isolate is susceptible to cefotaxime or ceftriaxone. If the patient fails to respond to cefotaxime or ceftriaxone and continues to have a positive cerebrospinal fluid culture, the addition of vancomycin should be considered. If resistance to cefotaxime or ceftriaxone is commonly encountered, empirical therapy should be as for strains resistant to benzylpenicillin (MIC >1.0 mg/l) or ceftriaxone/ cefotaxime (see above).

Patients with benzylpenicillin-resistant or ceftriaxone/ cefotaxime-resistant *S. pneumoniae* should be referred to a specialist.

Meningitis due to *Haemophilus influenzae*

Treatment

Ceftriaxone 2 g (children: 50 mg/kg; maximum 2 g) i.v. or i.m. every 12 hours for 7–10 days

or

ampicillin 2–3 g (children: 50 mg/kg; maximum 3 g) i.v. every 4–6 hours for 7–10 days

or

chloramphenicol 1 g (children: 25 mg/kg; maximum 1 g) i.v. every 6 hours for 7–10 days.

Prophylaxis

Rifampicin 600 mg (neonates <1 month: 5 mg/kg (maximum 300 mg); children ≥1 month: 20 mg/kg (maximum 600 mg)) orally every 24 hours for 4 days.

Comments

Ampicillin and chloramphenicol should only be used if the isolate is known to be susceptible.

Prophylaxis should be considered for patients and their close contacts, especially children under 5 years. Ceftriaxone clears carriage, thus patients treated with this drug will generally not require prophylaxis with rifampicin.

Meningitis due to *Listeria monocytogenes*

Listeria monocytogenes is a common cause of meningitis and/or septicaemia in newborn babies and immunosuppressed adults.

Treatment

Adults

Benzylpenicillin 3 million IU i.v. or i.m. every 4 hours for at least 3 weeks

or

ampicillin 3 g i.v. every 6 hours for at least 3 weeks

or

sulfamethoxazole 800 mg + trimethoprim 160 mg i.v. every 6 hours for at least 3 weeks.

Neonates

Ampicillin 50 mg/kg (maximum 2 g) i.v. every 8 hours (neonates <7 days: 50 mg/kg (maximum 2 g) i.v. every 12 hours) for a total of 3 weeks

plus

gentamicin 2.5 mg/kg i.v. every 12 hours for 3 weeks.

Comments

Benzylpenicillin and ampicillin appear to be equally effective. Therapy often needs to be prolonged; some patients may require treatment for up to 6 weeks.

Although gentamicin is recommended for this indication in neonates, it does not appear to be of value in adults.

Neonatal meningitis

The organisms that cause neonatal meningitis are similar to those that cause neonatal septicaemia and pneumonia — namely *Streptococcus pneumoniae*, group A and group B streptococci and *Escherichia coli*. In some regions *Listeria monocytogenes* or *Enterococcus faecalis* may also be responsible. Treatment options are similar to those recommended for neonatal pneumonia (see pages 25–26).

Treatment (where the pathogen is unknown)

Ampicillin 50 mg/kg (maximum 2 g) i.v. every 8 hours (neonates <7 days: 50 mg/kg (maximum 2 g) i.v. every 12 hours) for a total of 7–10 days

plus either

gentamicin 2.5 mg/kg i.v. every 12 hours for 7–10 days

or

cefotaxime 50 mg/kg (maximum 2 g) i.v. every 12 hours for 7–10 days.

Comments

Meningitis due to *Listeria monocytogenes* is especially common in the first week of life — thus ampicillin should be included in the regimen.

Meningitis due to group B streptococci

Group B streptococci often colonize the vagina and rectum of pregnant women. These organisms can be transmitted to newborn babies during labour and cause infection. Meningitis and septicaemia occurring during the first week after birth may be particularly severe.

Treatment

Benzylpenicillin 50 000–75 000 IU/kg (maximum 2 million IU) i.v. every 4–6 hours (neonates <7 days: benzylpenicillin 50 000 IU/kg (maximum 2 million IU) i.v. every 8 hours) for a total of 3 weeks

plus

gentamicin 2.5 mg/kg i.v. every 12 hours for 3 weeks.

Comments

Chemoprophylaxis against vaginal or rectal infections with group B streptococci during pregnancy remains controversial. Some clinicians recommend administration of a single dose of benzylpenicillin during labour to women who have risk factors for perinatal transmission of infection, such as premature rupture of membranes or prolonged labour.

Brain abscess

Most brain abscesses are polymicrobial, the most common pathogens being *Streptococcus anginosus (milleri)* and anaerobic bacteria. Other pathogens, such as *Nocardia* spp. and *Toxoplasma gondii* (especially in HIV-infected patients), may also be responsible. Aspiration or surgical drainage should be considered to guide antimicrobial therapy and to reduce the volume of the abscess. The duration of treatment depends on the clinical response and radiological evidence of resolution of the abscess.

Treatment

Benzylpenicillin 3–4 million IU (children: 100 000 IU/kg; maximum 3 million IU) i.v. or i.m. every 4–6 hours

plus either

metronidazole 500 mg (children: 12.5 mg/kg; maximum 500 mg) i.v. every 8–12 hours (contraindicated during pregnancy)

or

chloramphenicol 1 g (children: 25 mg/kg; maximum 750 mg) i.v. every 6 hours.

Miscellaneous infections

Lyme disease

Lyme disease is caused by the spirochaete *Borrelia burgdorferi*, which is transmitted by a number of tick species, including *Ixodes dammini*. The disease presents as skin lesions (erythema chronicum migrans), headache, fever, malaise and fatigue. Some patients develop recurrent arthritis and occasionally neurological and cardiac complications.

Early disease

Treatment

Doxycycline 100 mg (children >8 years: 2 mg/kg; maximum 100 mg) orally every 12 hours for 10–21 days (contraindicated during pregnancy)

or

amoxicillin 500 mg (children: 15 mg/kg; maximum 500 mg) orally every 8 hours for 10–21 days.

Late disease (chronic arthritis, cardiac and neurological manifestations)

Doses refer to adults, as this condition is not found in children.

Treatment

Benzylpenicillin 4 million IU i.v. every 4–6 hours for 14–21 days

or

ceftriaxone 2 g i.v. or i.m. every 24 hours for 14–21 days.

Patients with neurological involvement usually require treatment for 21 days.

Relapsing fever

Relapsing fever is a louse-borne disease caused by the spirochaete *Borrelia recurrentis*, which occurs mainly in tropical countries.

Treatment

Doxycycline 100 mg (children >8 years: 2 mg/kg; maximum 100 mg) orally in a single dose (contraindicated during pregnancy)

or

erythromycin 500 mg (children: 12.5 mg/kg; maximum 500 mg) orally in a single dose

or

chloramphenicol 500 mg (children: 25 mg/kg; maximum 750 mg) orally in a single dose.

Leptospirosis

Leptospirosis is caused by spirochaetes of the *Leptospira* genus. The severity of the disease ranges from subclinical infection to serious haemorrhagic conditions with high mortality.

Treatment

Benzylpenicillin 2 million IU (children: 50 000 IU/kg; maximum 2 million IU) i.v. every 6 hours for 5–7 days

or

doxycycline 100 mg (children >8 years: 2 mg/kg; maximum 100 mg) orally every 12 hours for 5–7 days (contraindicated during pregnancy).

Brucellosis

Brucellosis is acquired from livestock, and is an occupational disease of butchers, farmers and abattoir workers. Most cases are caused by two related bacteria, *Brucella abortus* and *B. melitensis*; infection by the latter species is more severe. The disease is characterized by a fluctuating fever ("undulant fever"), aches and pains, and occasionally arthritis or osteomyelitis.

Treatment

Adults and children > 8 years

Doxycycline 100 mg (children >8 years: 2 mg/kg; maximum 100 mg) orally every 12 hours for 6 weeks (contraindicated during pregnancy)

plus either

streptomycin 1 g (children: 15 mg/kg; maximum 1 g) i.m. every 24 hours for 2 weeks (contraindicated during pregnancy)

or

gentamicin 5–7 mg/kg i.v. every 24 hours (children: 7.5 mg/kg i.v. in 1–3 divided doses daily) for 2 weeks (contraindicated during pregnancy)

or

rifampicin 600 mg (children: 15 mg/kg; maximum 600 mg) orally every 24 hours for 6 weeks.

Children ≤ 8 years

Sulfamethoxazole 20 mg/kg + trimethoprim 4 mg/kg (maximum 800 mg + 160 mg) orally every 12 hours for 6 weeks

plus either

rifampicin 15 mg/kg (maximum 600 mg) orally every 24 hours for 6 weeks

or

gentamicin 7.5 mg/kg i.v. in 1–3 divided doses daily for 2 weeks.

Tularaemia

Tularaemia is caused by *Francisella tularensis* and transmitted to humans from rodents through the bite of the deer fly, *Chrysops discalis*, and other insects. It has a number of febrile clinical presentations, including ulceroglandular, glandular, oculoglandular, oropharyngeal, typhoidal or pulmonary (tularaemic pneumonia).

Treatment

Streptomycin 15 mg/kg (adults and children; maximum 1 g) i.m. every 24 hours for 7–14 days (contraindicated during pregnancy)

or

gentamicin 1.5 mg/kg (adults and children) i.v. or i.m. every 8 hours for 7 days (contraindicated during pregnancy).

Comments

Ciprofloxacin 500 mg (children: 15 mg/kg; maximum 500 mg) orally every 12 hours for 10–14 days (contraindicated during pregnancy) and chloramphenicol 1 g (children: 25 mg/kg; maximum 1 g) i.v. every 6 hours for 7 days are also used for this indication.

Anthrax

Anthrax is primarily a septicaemic infection of livestock caused by *Bacillus anthracis*. Human infection mainly results from cutaneous inoculation of organisms from infected animals,

with the development of a cutaneous lesion. In addition to antimicrobials, anti-anthrax serum may be used, although its efficacy is controversial.

Treatment

Benzylpenicillin 4 million IU (children: 100 000 IU/kg; maximum 4 million IU) i.v. or i.m. every 4–6 hours for 7–10 days

or

doxycycline 100 mg (children >8 years: 2 mg/kg; maximum 100 mg) orally every 12 hours for 7–10 days (contraindicated during pregnancy)

or

ciprofloxacin 750 mg (children: 10–15 mg/kg; maximum 750 mg) orally every 12 hours for 7–10 days (contraindicated during pregnancy).

Plague

Plague is an acute infectious disease with a high fatality rate, caused by the bacterium *Yersinia pestis*. It is primarily a disease of ground rodents in Africa, the Americas and central and south-east Asia and is transmitted to humans from infected rodents by fleas. It may occur in epidemics. Cutaneous infection from the flea bites causes acute suppurative lymphadenitis (bubonic plague) with high fever, septicaemia and sometimes haemorrhage. Pneumonic plague, which is caused by the inhalation of airborne bacilli, may be rapidly fatal.

Treatment

Doxycycline 100 mg (children >8 years: 2 mg/kg; maximum 100 mg) orally every 12 hours for 7 days (contraindicated during pregnancy)

or

chloramphenicol 500 mg (children: 25 mg/kg; maximum 750 mg) orally or i.v. every 6 hours for 7–10 days

or

gentamicin 1.7 mg/kg (adults and children) i.v. or i.m. every 8 hours for 7 days (contraindicated during pregnancy)

or

streptomycin 1 g (children: 15 mg/kg; maximum 1 g) i.m. every 12 hours for 7–10 days (contraindicated during pregnancy).

Rickettsial infections

These infections include typhus fever due to *Rickettsia prowazekii* (epidemic typhus or louse-borne typhus), typhus fever due to *R. typhii* (murine typhus fever), typhus fever due to *R. tsutsugamashi* (scrub typhus), rickettsialpox due to *R. akari* and spotted fever due to *R. rickettsii* (Rocky Mountain spotted fever).

Treatment

Doxycycline 100 mg (children >8 years: 2 mg/kg; maximum 100 mg) orally every 12 hours for 7–10 days (or for 48 hours after resolution of fever; contraindicated during pregnancy)

or

chloramphenicol 500 mg (children: 15 mg/kg; maximum 500 mg) orally or i.v. every 6 hours for 7–10 days (or for 48 hours after resolution of fever).

Q fever

Q fever is a febrile infectious disease, usually acute, caused by *Coxiella burnetti*. On rare occasions infection may become latent and reappear as chronic Q fever, usually complicated by chronic hepatitis, thrombocytopenia and endocarditis. If left untreated, chronic Q fever with endocarditis is invariably fatal.

Treatment

Adults and children > 8 years

Doxycycline 100 mg (children >8 years: 2 mg/kg; maximum 100 mg) orally every 12 hours for 7–10 days (contraindicated during pregnancy).

Children ≤ 8 years

Erythromycin 10–15 mg/kg (maximum 500 mg) orally every 6 hours for 7–10 days.

Septicaemia

Septicaemia is invasion of the bloodstream by bacteria, giving rise to fever and hypotension. It may be associated with infection in specific sites (e.g. the lungs, urinary tract, gastrointestinal tract) or there may be no clear originating focus. Septicaemia occurs more commonly in patients who are immunosuppressed, including those with HIV infection and diabetes. In previously healthy persons, *Staphylococcus aureus*, *Streptococcus pneumoniae* and *Escherichia coli* are the most frequent causes, while in immunosuppressed patients, Gram-negative bacteria, including *Pseudomonas aeruginosa*, may also be responsible. Other febrile illnesses such as typhoid fever and malaria may be difficult to differentiate clinically from infections caused by these pathogens.

Initial empirical therapy

Initial empirical therapy should be directed against the most likely pathogens and subsequently amended when the responsible pathogen is identified and its susceptibility to antimicrobials tested. Since the treatment options depend on the most likely infective source, clinicians should consult the most appropriate section in these guidelines (e.g. urinary tract infections) for specific recommendations. If a good clinical response is observed but bacterial isolates appear to be resistant in vitro, the possibility that the isolate is a contaminant should be considered unless it is isolated repeatedly. A change of therapy may not be mandatory if the clinical response is adequate.

The pathogens responsible for hospital-acquired (nosocomial) septicaemia depend on the type of patient, the underlying disease and recent medical and surgical treatment. The microbial flora of hospitals vary greatly in type and susceptibility. The choice of initial therapy therefore depends on factors such as the characteristics of the patient and the likely source of sepsis.

Treatment

Adults and children > 5 years

Gentamicin 5–7 mg/kg i.v. every 24 hours or 1.5 mg/kg i.v. or i.m. every 8 hours (contraindicated during pregnancy)

plus either

cloxacillin 2 g i.v. every 4–6 hours

or

cefazolin 1–2 g i.v. every 8 hours

or

clindamycin 600 mg i.v. every 8 hours

or

chloramphenicol 750 mg i.v. every 6 hours.

Children aged from 2 months to 5 years

Cloxacillin 50 mg/kg (maximum 2 g) i.v. every 4–6 hours

plus

ceftriaxone 50 mg/kg (maximum 2 g) i.v. or i.m. every 24 hours.

Neonates

Ampicillin 50 mg/kg (maximum 2 g) i.v. every 8 hours (neonates <7 days: 50 mg/kg (maximum 2 g) i.v. every 12 hours)

plus

gentamicin 2.5 mg/kg i.v. every 12 hours.

Alternative regimen. Cloxacillin 50 mg/kg (maximum 2 g) i.v. every 4–6 hours

plus

cefotaxime 50–75 mg/kg (maximum 2 g) i.v. every 8 hours.

Drugs (for details of contraindications, etc., see individual drug entries)

Amoxicillin

Capsule or tablet, 250 mg, 500 mg (anhydrous)
Powder for oral suspension, 125 mg (anhydrous)/5 ml

General information

Amoxicillin is an aminopenicillin which is active against many strains of Enterobacteriaceae. It is better absorbed from the gastrointestinal tract than ampicillin. Thus, amoxicillin is used whenever oral administration is appropriate and ampicillin is used parenterally. Peak plasma concentrations are reached after 1–2 hours. It is largely excreted in the urine both as unchanged drug and as metabolites.

Clinical information

Uses

Treatment of:

- acute pharyngitis, acute cervical adenitis, acute otitis media, acute sinusitis and acute bronchitis
- pneumonia in adults and children >5 years
- mild pneumonia in children aged from 2 months to 5 years
- neonatal pneumonia, together with gentamicin
- acute exacerbations of chronic bronchitis in adults
- chronic suppurative lung disease in children
- tooth abscesses and suppurative odontogenic infections
- cellulitis and erysipelas, together with benzylpenicillin
- acute gastritis and peptic ulcer disease in adults, together with metronidazole and either bismuth salicylate or omeprazole
- osteomyelitis due to β-haemolytic streptococci in adults, together with benzylpenicillin
- osteomyelitis due to *Salmonella* spp. in children ≤5 years, together with cloxacillin and either ceftriaxone or cefotaxime
- Lyme disease (early stage).

Postsplenectomy prophylaxis.

Dosage and administration

Acute pharyngitis and acute cervical adenitis

Adults: 500 mg orally every 8 hours for 10 days.

Children: 15 mg/kg (maximum 500 mg) orally every 8 hours for 10 days.

Acute otitis media and acute bronchitis

Adults: 500 mg orally every 8 hours for 5 days.

Children: 15 mg/kg (maximum 500 mg) orally every 8 hours for 5 days.

Acute sinusitis

Adults: 500 mg orally every 8 hours for 7–10 days.

Children: 15 mg/kg (maximum 500 mg) orally every 8 hours for 7–10 days.

Acute exacerbations of chronic bronchitis in adults

500 mg orally every 8 hours for 5 days.

Chronic suppurative lung disease in children

30 mg/kg (maximum 1 g) orally every 8 hours for 5 days.

Pneumonia in adults and children >5 years

Ambulatory patients

Adults: 500 mg orally every 8 hours for 5 days.

Children >5 years: 15 mg/kg (maximum 500 mg) orally every 8 hours for 5 days.

Mild pneumonia in children aged from 2 months to 5 years

15–25 mg/kg (maximum 500 mg) orally every 8 hours for 5 days *or* 15–25 mg/kg (maximum 500 mg) orally every 8 hours to complete the treatment course of at least 5 days, following initial treatment with procaine benzylpenicillin 50 000 IU/kg (maximum 900 000 IU) i.m. every 24 hours for at least 3 days.

Neonatal pneumonia

30 mg/kg i.v. every 12 hours, together with gentamicin 2.5 mg/kg i.v. every 8 hours (neonates <7 days: gentamicin 2.5 mg/kg i.v. every 12 hours) for a total of at least 5 days.

Tooth abscesses and suppurative odontogenic infections

Adults: 250 mg orally every 8 hours for 3 days.

Children: 25 mg/kg (maximum 250 mg) orally every 8 hours for 3 days.

Cellulitis and erysipelas

Adults: 500 mg orally every 8 hours to complete the treatment course of 7–10 days, following initial treatment with benzylpenicillin 1–2 million IU i.v. or i.m. every 6 hours.

Children: 7.5–15 mg/kg (maximum 500 mg) orally every 8 hours to complete the treatment course of 7–10 days, following initial treatment with benzylpenicillin 50 000–100 000 IU/kg (maximum 2 million IU) i.v. or i.m. every 6 hours.

Acute gastritis and peptic ulcer disease in adults

500 mg orally every 6 hours for 2 weeks, supplemented by bismuth salicylate 107.7 mg (1 tablet) orally every 6 hours plus metronidazole 200 mg orally every 8 hours and 400 mg orally at night *or* 500 mg orally every 8 hours for 2 weeks, supplemented by metronidazole 400 mg orally every 8 hours and omeprazole 40 mg orally every 24 hours.

Osteomyelitis due to β-haemolytic streptococci in adults

1 g orally every 6–8 hours to complete the treatment course of 2–4 weeks, following initial therapy with benzylpenicillin 2 million IU i.v. or i.m. every 4–6 hours.

Osteomyelitis due to Salmonella spp. in children ≤5 years

Children aged from 2 months to 5 years: 7.5–15 mg/kg (maximum 1 g) orally every 8 hours to complete the treatment course of 6 weeks, following initial therapy with cloxacillin 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 4–6 hours and ceftriaxone 50–75 mg/kg (maximum 1 g) i.v. or i.m. every 24 hours for 4–6 days (or until clinical improvement occurs).

Neonates: 7.5–15 mg/kg (maximum 1 g) orally every 8 hours to complete the treatment course of 6 weeks, following initial therapy with cloxacillin 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 4–6 hours and cefotaxime 50–75 mg/kg (maximum 2 g) i.v. every 8 hours for 4–6 days (or until clinical improvement occurs).

Lyme disease (early stage)

Adults: 500 mg orally every 8 hours for 10–21 days.

Children: 15 mg/kg (maximum 500 mg) orally every 8 hours for 10–21 days.

Postsplenectomy prophylaxis

Adults: 250 mg orally every 24 hours.

Amoxicillin (continued)

Children >2 years: 20 mg / kg (maximum 250 mg) orally every 24 hours.

Contraindications
Known hypersensitivity to penicillins.

Precautions
Facilities should be available for treating anaphylaxis whenever penicillins are used. Patients should be questioned carefully about previous allergic reactions before the first dose is administered. If a skin rash develops during treatment or no improvement occurs within 2 days, the patient should be transferred to a different class of antimicrobial.

Use in pregnancy
There is no evidence that amoxicillin is teratogenic. It may be used during pregnancy.

Adverse effects
Hypersensitivity reactions range in severity from skin rashes to immediate anaphylaxis. Erythematous maculopapular rashes are common and usually occur within 3–14 days after the start of treatment, initially appearing on the trunk and thereafter spreading peripherally to involve most of the body. In most instances the rash is mild and subsides after 6–14 days despite continuation of therapy.

Diarrhoea can occur. Interstitial nephritis, neutropenia and thrombocytopenia have been reported.

Overdosage
Overdosage can cause convulsions, paralysis and even death.

Excessive blood concentrations can be lowered by haemodialysis.

Storage
Preparations should be stored in tightly closed containers, protected from light.

Amoxicillin + clavulanic acid

Tablet, 500 mg of amoxicillin + 125 mg of clavulanic acid

General information

The two components of this combination product operate synergistically because clavulanic acid binds to β-lactamases and thereby competitively protects the amoxicillin against resistant β-lactamase-producing strains. Both components are well absorbed after oral administration and are distributed into the lungs, pleural fluid and peritoneal fluid. They are largely excreted unchanged in the urine.

Clinical information

Uses
Treatment of:

- infections caused by susceptible β-lactamase-producing strains of *Escherichia coli*, *Haemophilus influenzae*, *Klebsiella* spp. and *Staphylococcus aureus* (where amoxicillin alone is not appropriate)
- acute otitis media and acute sinusitis
- acute exacerbations of chronic bronchitis in adults

- aspiration pneumonia and lung abscesses
- human and animal bites and clenched-fist injuries, together with procaine benzylpenicillin
- urinary tract infections in children
- osteomyelitis due to *Haemophilus influenzae* or unknown pathogen in children ≤5 years, together with cloxacillin and either ceftriaxone or cefotaxime.

Prophylaxis in contaminated surgery.

Dosage and administration

The dosage for amoxicillin + clavulanic acid is expressed in terms of the amoxicillin component.

Acute otitis media

Adults: amoxicillin 500 mg + clavulanic acid orally every 8 hours for 5 days.

Children: amoxicillin 7.5–15 mg/kg + clavulanic acid (maximum 500 mg) orally every 8 hours for 5 days.

Acute sinusitis

Adults: amoxicillin 500 mg + clavulanic acid orally every 8 hours for 7–10 days.

Children: amoxicillin 7.5–15 mg/kg + clavulanic acid (maximum 500 mg) orally every 8 hours for 7–10 days.

Acute exacerbations of chronic bronchitis in adults

Amoxicillin 500 mg + clavulanic acid orally every 8 hours for 5 days.

Aspiration pneumonia and lung abscesses

Adults: amoxicillin 500 mg + clavulanic acid orally every 8 hours for 14 days.

Children: amoxicillin 15 mg/kg + clavulanic acid (maximum 500 mg) orally every 8 hours for 14 days.

Human and animal bites and clenched-fist injuries

Adults: amoxicillin 500 mg + clavulanic acid orally every 8 hours for 5 days, following initial therapy with procaine benzylpenicillin 1.5 million IU i.m. every 24 hours for 5 days.

Children: amoxicillin 15 mg/kg + clavulanic acid (maximum 500 mg) orally every 8 hours for 5 days, following initial therapy with procaine benzylpenicillin 50 000 IU/kg (maximum 1.5 million IU) i.m. every 24 hours for 5 days.

Urinary tract infections in children

Amoxicillin 7.5 mg/kg + clavulanic acid (maximum 250 mg) orally every 8 hours for 5–10 days.

Osteomyelitis due to Haemophilus influenzae or unknown pathogen in children ≤5 years

Children aged from 2 months to 5 years: amoxicillin 15 mg/kg + clavulanic acid (maximum 500 mg) orally every 8 hours to complete the treatment course of 3–4 weeks, following initial therapy with cloxacillin 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 4–6 hours and ceftriaxone 50–75 mg/kg (maximum 1 g) i.v. or i.m. every 24 hours for 4–6 days (or until clinical improvement occurs).

Neonates: amoxicillin 15 mg/kg + clavulanic acid (maximum 500 mg) orally every 8 hours to complete the treatment course of 3–4 weeks, following initial therapy with cloxacillin 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 4–6 hours and cefotaxime 50–75 mg/kg (maximum 2 g) i.v. every 8 hours for 4–6 days (or until clinical improvement occurs).

Prophylaxis in contaminated surgery

Adults: amoxicillin 500 mg + clavulanic acid i.v. at induction of anaesthesia.

Children: amoxicillin 125 mg + clavulanic acid i.v. at induction of anaesthesia.

Amoxicillin + clavulanic acid (continued)

Contraindications
Known hypersensitivity to penicillins.

Precautions
Facilities should be available for treating anaphylaxis whenever penicillins are used. Patients should be questioned carefully about previous allergic reactions before the first dose is administered. If a skin rash develops during treatment or no improvement occurs within 2 days, the patient should be transferred to a different class of antimicrobial.

Use in pregnancy
There is no evidence that amoxicillin + clavulanic acid is teratogenic. It may be used during pregnancy.

Adverse effects
Hypersensitivity reactions range in severity from skin rashes to immediate anaphylaxis. Erythematous maculopapular rashes are common and usually occur within 3–14 days after the start of treatment, initially appearing on the trunk and thereafter spreading peripherally to involve most of the body. In most instances the rash is mild and subsides after 6–14 days despite continuation of therapy.

Hepatotoxicity is more frequent than with amoxicillin.

Diarrhoea can occur. Interstitial nephritis, neutropenia and thrombocytopenia have been reported.

Overdosage
Overdosage can cause convulsions, paralysis and even death.

Excessive blood concentrations can be lowered by haemodialysis.

Storage
Preparations should be stored in tightly closed containers, protected from light.

Ampicillin

Tablet, 250 mg (as sodium salt)
Powder for injection, 500 mg (as sodium salt) in vial

General information

Ampicillin is a semisynthetic penicillin which is active against many strains of Enterobacteriaceae, including shigellae. It is moderately absorbed from the gastrointestinal tract. Peak plasma levels are attained after approximately 2 hours. The drug is concentrated in the bile, undergoes enterohepatic circulation and is excreted in appreciable amounts in the faeces.

Clinical information

Uses
Treatment of:

- acute mastoiditis
- typhoid and paratyphoid fever in children who are chronic carriers
- acute cholecystitis, endocarditis due to α-haemolytic streptococci resistant to benzylpenicillin and endocarditis due to enterococci, together with gentamicin

- acute peritonitis, together with gentamicin and metronidazole
- acute pyelonephritis, together with gentamicin or ceftriaxone
- meningitis due to *Haemophilus influenzae*
- meningitis due to *Listeria monocytogenes* in adults
- neonatal meningitis due to *Listeria monocytogenes* and neonatal septicaemia (initial empirical therapy), together with gentamicin.
- neonatal meningitis due to unknown pathogen, together with gentamicin or cefotaxime.

Dosage and administration

Intravenous formulations of ampicillin should be administered over 2 minutes.

Acute mastoiditis

Adults: 2 g i.v. every 6 hours for 10–14 days.

Children: 25–50 mg / kg (maximum 2 g) i.v. every 6 hours for 10–14 days.

Typhoid and paratyphoid fever in children who are chronic carriers

250 mg i.m. every 6 hours for 4–6 weeks.

Acute cholecystitis

Adults: 1–2 g i.v. or i.m. every 6 hours, together with gentamicin 5–7 mg / kg i.v. daily in divided doses for up to 7 days.

Children: 25–50 mg / kg (maximum 2 g) i.v. or i.m. every 6 hours, together with gentamicin 7.5 mg / kg i.v. in 1–3 divided doses daily for up to 7 days.

Acute peritonitis

Adults: 2 g i.v. or i.m. every 6 hours, together with gentamicin 5–7 mg / kg i.v. daily in divided doses and metronidazole 500 mg i.v. every 8–12 hours for at least 7 days.

Children: 50 mg / kg (maximum 2 g) i.v. or i.m. every 6 hours, together with gentamicin 7.5 mg / kg i.v. in 1–3 divided doses daily and metronidazole 12.5 mg / kg (maximum 500 mg) i.v. every 8–12 hours for at least 7 days.

Acute pyelonephritis

Adults: 1–2 g i.v. or i.m. every 6 hours for up to 14 days, supplemented for the first 7 days by gentamicin 5–7 mg / kg orally daily in divided doses *or* for 14 days by ceftriaxone 1 g i.v. or i.m. every 24 hours.

Children: 50 mg / kg (maximum 2 g) i.v. or i.m. every 6 hours for up to 14 days, supplemented for the first 7 days by gentamicin 7.5 mg / kg orally in 1–3 divided doses daily *or* for 14 days by ceftriaxone 50 mg / kg (maximum 1 g) i.v. or i.m. every 24 hours.

Endocarditis due to α-haemolytic streptococci resistant to benzylpenicillin (MIC = 0.25–1.0 mg/l) and endocarditis due to enterococci

Adults: 2 g i.v. every 4 hours for 6 weeks, supplemented for 4–6 weeks by gentamicin 1 mg / kg i.v. every 8 hours.

Children: 50 mg / kg (maximum 2 g) i.v. every 4 hours for 6 weeks, supplemented for 4–6 weeks by gentamicin 1 mg / kg i.v. every 8 hours.

Meningitis due to Haemophilus influenzae

Adults: 2–3 g i.v. every 4–6 hours for 7–10 days.

Children: 50 mg / kg (maximum 3 g) i.v. every 4–6 hours for 7–10 days.

Ampicillin should only be used if the isolate is known to be susceptible.

Prophylaxis with rifampicin 600 mg (neonates < 1 month: 5 mg / kg (maximum 300 mg); children ≥ 1 month: 20 mg / kg (maximum 600 mg)) orally every 24 hours for 4 days should be considered

Ampicillin (continued)

for patients and their close contacts, especially children under 5 years.

Meningitis due to Listeria monocytogenes

Adults: 3 g i.v. every 6 hours for at least 3 weeks.

Neonates: 50 mg/kg i.v. every 8 hours (neonates <7 days: 50 mg/kg i.v. every 12 hours) for a total of 3 weeks, supplemented by gentamicin 2.5 mg/kg i.v. every 12 hours.

Treatment must be continued for at least 48–72 hours after the patient becomes asymptomatic.

Therapy often needs to be prolonged in adults; some patients may require treatment for up to 6 weeks.

Neonatal meningitis due to unknown pathogen

50 mg/kg (maximum 2 g) i.v. every 8 hours (neonates <7 days: 50 mg/kg (maximum 2 g) i.v. every 12 hours) for a total of 7–10 days, supplemented by *either* gentamicin 2.5 mg/kg i.v. every 12 hours *or* cefotaxime 50 mg/kg (maximum 2 g) i.v. every 12 hours.

Initial empirical therapy for neonatal septicaemia

50 mg/kg (maximum 2 g) i.v. every 8 hours (neonates <7 days: 50 mg/kg (maximum 2 g) i.v. every 12 hours), supplemented by gentamicin 2.5 mg/kg i.v. every 12 hours.

Contraindications

Known hypersensitivity to penicillins.

Precautions

Facilities should be available for treating anaphylaxis whenever penicillins are used. Patients should be questioned carefully about previous allergic reactions before the first dose is administered. If a skin rash develops during treatment or no improvement occurs within 2 days, the patient should be transferred to a different class of antimicrobial.

Use in pregnancy

There is no evidence that ampicillin is teratogenic. It may be used during pregnancy.

Adverse effects

Hypersensitivity reactions range in severity from skin rashes to immediate anaphylaxis. Erythematous maculopapular rashes are common and usually occur within 3–14 days after the start of treatment, initially appearing on the trunk and thereafter spreading peripherally to involve most of the body. In most instances the rash is mild and subsides after 6–14 days despite continuation of therapy.

Diarrhoea is more frequent than with amoxicillin.

Interstitial nephritis, neutropenia and thrombocytopenia have been reported.

Overdosage

Overdosage from large intravenous doses can cause convulsions, paralysis and even death.

Excessive blood concentrations can be lowered by haemodialysis.

Storage

Preparations should be stored in tightly closed containers, protected from light.

Benzylpenicillin

Powder for injection, 600 mg (= 1 million IU), 3 g (= 5 million IU) (sodium or potassium salt) in vial

General information

Benzylpenicillin is a β-lactam antibiotic produced by *Penicillium notatum*. It is bactericidal against streptococci, *Haemophilus* spp., neisseriae, many anaerobes and spirochaetes.

After intramuscular injection, peak plasma concentrations are reached within 15–30 minutes. It is widely distributed throughout the body. It does not readily enter the cerebrospinal fluid, except when the meninges are inflamed. It has a plasma half-life of 30–45 minutes and is excreted mainly in the urine.

Clinical information

Uses

Benzylpenicillin is used when high concentrations of a narrow-spectrum penicillin are required.

Treatment of:

- pneumonia in adults and children >5 years, together with gentamicin
- atypical pneumonia in adults and children >5 years, together with gentamicin and erythromycin
- very severe and severe pneumonia in children aged from 2 months to 5 years
- aspiration pneumonia and lung abscesses, together with metronidazole
- cellulitis and erysipelas and osteomyelitis due to β-haemolytic streptococci in adults, together with amoxicillin
- streptococcal necrotizing fasciitis, together with clindamycin
- gangrene, together with gentamicin and metronidazole
- neurosyphilis in adults and congenital syphilis
- infective endocarditis (initial empirical therapy), together with cloxacillin and gentamicin
- endocarditis due to α-haemolytic streptococci, endocarditis due to enterococci and culture-negative endocarditis, together with gentamicin
- meningitis (initial empirical therapy) and meningitis due to *Neisseria meningitidis*, together with chloramphenicol
- meningitis due to *Listeria monocytogenes* in adults and meningitis due to benzylpenicillin-susceptible *Streptococcus pneumoniae*
- neonatal meningitis due to group B streptococci, together with gentamicin
- brain abscess, together with metronidazole or chloramphenicol
- Lyme disease (late stage) in adults, leptospirosis and anthrax.

Dosage and administration

Benzylpenicillin is destroyed by gastric acid and must be administered parenterally. The powder for injection should be diluted in "water for injection" in accordance with the manufacturer's instructions.

Pneumonia in adults and children >5 years

Hospitalized patients

Adults: 2 million IU i.v. or i.m. every 4–6 hours for 5 days *or* 2 million IU i.v. or i.m. every 4–6 hours, together with gentamicin 5–7 mg/kg i.v. daily in divided doses for 7 days.

Children >5 years: 50 000–100 000 IU/kg (maximum 2 million IU) i.v. or i.m. every 4–6 hours for 5 days *or* 50 000–100 000 IU/kg (maximum 2 million IU) i.v. or

Benzylpenicillin (continued)

i.m. every 4–6 hours, together with gentamicin 7.5 mg/kg i.v. in 1–3 divided doses daily for 7 days.

Patients with atypical pneumonia should also receive erythromycin 1 g (children: 10 mg/kg; maximum 1 g) i.v. every 6 hours for 14 days.

Benzylpenicillin may be used alone when *Streptococcus pneumoniae* is the suspected pathogen.

Very severe and severe pneumonia in children aged from 2 months to 5 years

50 000–100 000 IU/kg (maximum 2 million IU) i.v. or i.m. every 4–6 hours for at least 5 days.

Aspiration pneumonia and lung abscesses

Adults: 1–2 million IU i.v. or i.m. every 4–6 hours for 10–14 days, together with metronidazole 500 mg i.v. every 8–12 hours (once clinical improvement occurs, metronidazole 400 mg orally every 12 hours may be substituted).

Children: 50 000–100 000 IU/kg (maximum 2 million IU) i.v. or i.m. every 4–6 hours for 10–14 days, together with metronidazole 12.5 mg/kg (maximum 500 mg) i.v. every 8–12 hours (once clinical improvement occurs, metronidazole 10 mg/kg (maximum 400 mg) orally every 12 hours may be substituted).

Cellulitis and erysipelas

Adults: 1–2 million IU i.v. or i.m. every 6 hours for 7–10 days (once clinical improvement occurs, amoxicillin 500 mg orally every 8 hours may be substituted).

Children: 50 000–100 000 IU/kg (maximum 2 million IU) i.v. or i.m. every 6 hours for 7–10 days (once clinical improvement occurs, amoxicillin 7.5–15 mg/kg (maximum 500 mg) orally every 8 hours may be substituted).

Streptococcal necrotizing fasciitis

Adults: 4 million IU i.v. or i.m. every 4 hours, together with clindamycin 600 mg i.v. every 8 hours for at least 7 days.

Children: 100 000 IU/kg (maximum 4 million IU) i.v. or i.m. every 4 hours, together with clindamycin 10 mg/kg (maximum 450 mg) i.v. every 6 hours for at least 7 days.

Gangrene

Adults: 4 million IU i.v. or i.m. every 4 hours for at least 7 days, together with gentamicin 5–7 mg/kg i.v. or i.m. daily in divided doses and metronidazole 500 mg i.v. every 8 hours (once clinical improvement occurs, rectal formulations of metronidazole may be substituted).

Children: 100 000 IU/kg (maximum 4 million IU) i.v. or i.m. every 4 hours for at least 7 days, together with gentamicin 7.5 mg/kg i.v. or i.m. in 1–3 divided doses daily and metronidazole 12.5 mg/kg (maximum 500 mg) i.v. every 8 hours (once clinical improvement occurs, rectal formulations of metronidazole may be substituted).

Osteomyelitis due to β-haemolytic streptococci in adults

2 million IU i.v. or i.m. every 4–6 hours for 2–4 weeks (if the duration of parenteral therapy is less than 2–4 weeks, the treatment course should be completed with amoxicillin 1 g orally every 6–8 hours).

Neurosyphilis in adults

4 million IU (2.4 g) i.v. every 4 hours for 2 weeks.

Congenital syphilis

Children >2 years: 200 000–300 000 IU/kg (maximum 2.4 million IU) i.v. or i.m. in divided doses weekly for 2 weeks.

Children ≤2 years: 25000IU/kg (maximum 1.5 million IU) i.v. or i.m. every 12 hours for 10 days.

Initial empirical therapy for infective endocarditis

Adults: 3 million IU i.v. every 4 hours, together with cloxacillin 2g i.v. every 4 hours and gentamicin 2mg/kg i.v. every 8 hours.

Children: 50000IU/kg (maximum 3 million IU) i.v. every 4 hours, together with cloxacillin 50mg/kg (maximum 2g) i.v. every 4 hours and gentamicin 2.5mg/kg (maximum 80mg) i.v. every 8 hours.

Endocarditis due to α-haemolytic streptococci

Uncomplicated endocarditis

Adults: 3 million IU i.v. every 4 hours, together with gentamicin 1mg/kg i.v. every 8 hours for 2 weeks *or* 3 million IU i.v. every 4 hours for 4 weeks.

Children: 100000IU/kg (maximum 3 million IU) i.v. every 4 hours, together with gentamicin 1mg/kg i.v. every 8 hours for 2 weeks *or* 100000IU/kg (maximum 3 million IU) i.v. every 4 hours for 4 weeks.

Strains highly susceptible to benzylpenicillin (MIC ≤ 0.12mg/l)

Adults: 3 million IU i.v. every 4 hours for 4 weeks, supplemented for the first 2 weeks by gentamicin 1mg/kg i.v. every 8 hours.

Children: 100000IU/kg (maximum 3 million IU) i.v. every 4 hours for 4 weeks, supplemented for the first 2 weeks by gentamicin 1mg/kg i.v. every 8 hours.

Strains resistant to benzylpenicillin (MIC = 0.25–1.0mg/l)

Adults: 3–4 million IU i.v. every 4 hours for 6 weeks, supplemented for 4–6 weeks by gentamicin 1mg/kg i.v. every 8 hours.

Children: 100000IU/kg (maximum 4 million IU) i.v. every 4 hours for 6 weeks, supplemented for 4–6 weeks by gentamicin 1mg/kg i.v. every 8 hours.

Endocarditis due to enterococci and culture-negative endocarditis

Adults: 3–4 million IU i.v. every 4 hours for 6 weeks, supplemented for 4–6 weeks by gentamicin 1mg/kg i.v. every 8 hours.

Children: 100000IU/kg (maximum 4 million IU) i.v. every 4 hours for 6 weeks, supplemented for 4–6 weeks by gentamicin 1mg/kg i.v. every 8 hours.

Initial empirical therapy for meningitis

Adults: 3–4 million IU i.v. or i.m. every 4 hours for up to 14 days, supplemented by chloramphenicol 1g i.v. every 6 hours (once clinical improvement occurs, chloramphenicol 500–750mg orally every 6 hours may be substituted).

Children: 100000IU/kg (maximum 4 million IU) i.v. or i.m. every 4 hours for up to 14 days, supplemented by chloramphenicol 25mg/kg (maximum 1g) i.v. every 6 hours (once clinical improvement occurs, chloramphenicol 25mg/kg (maximum 750mg) orally every 6 hours may be substituted).

Meningitis due to Neisseria meningitidis

Adults: 3–4 million IU i.v. or i.m. every 4 hours for up to 14 days, supplemented by chloramphenicol oily suspension 100mg/kg (maximum 3g) i.m. every 24 hours (once clinical improvement occurs, chloramphenicol 500–750mg orally every 6 hours may be substituted).

Children: 100000IU/kg (maximum 4 million IU) i.v. or i.m. every 4 hours for up to 14 days, supplemented by chloramphenicol oily suspension 25mg/kg (maximum 500mg) i.m. every 24 hours (once clinical improvement occurs,

Benzylpenicillin (continued)

chloramphenicol 25 mg / kg (maximum 750 mg) orally every 6 hours may be substituted).

Meningitis due to Streptococcus pneumoniae (strains susceptible to benzylpenicillin (MIC ≤ 0.06 mg/l))

Adults: 3–4 million IU i.v. or i.m. every 4 hours for 10–14 days.

Children: 100 000 IU / kg (maximum 4 million IU) i.v. or i.m. every 4 hours for 10–14 days.

Patients who are very ill may require treatment for up to 3 weeks.

Meningitis due to Listeria monocytogenes in adults

3 million IU i.v. or i.m. every 4 hours for at least 3 weeks.

Therapy often needs to be prolonged in adults; some patients may require treatment for up to 6 weeks.

Neonatal meningitis due to group B streptococci

50 000–75 000 IU / kg (maximum 2 million IU) i.v. every 4–6 hours (neonates <7 days: 50 000 IU / kg (maximum 2 million IU) i.v. every 8 hours) for a total of 3 weeks, supplemented by gentamicin 2.5 mg / kg i.v. every 12 hours.

Brain abscess

Adults: 3–4 million IU i.v. or i.m. every 4–6 hours, together with *either* metronidazole 500 mg i.v. every 8–12 hours *or* chloramphenicol 1 g i.v. every 6 hours.

Children: 100 000 IU / kg (maximum 3 million IU) i.v. or i.m. every 4–6 hours, together with *either* metronidazole 12.5 mg / kg (maximum 500 mg) i.v. every 8–12 hours *or* chloramphenicol 25 mg / kg (maximum 750 mg) i.v. every 6 hours.

The duration of treatment depends on the clinical response and radiological evidence of resolution of the abscess.

Lyme disease (late stage) in adults

4 million IU i.v. every 4–6 hours for 14–21 days.

Patients with neurological involvement usually require treatment for 21 days.

Leptospirosis

Adults: 2 million IU i.v. every 6 hours for 5–7 days.

Children: 50 000 IU / kg (maximum 2 million IU) i.v. every 6 hours for 5–7 days.

Anthrax

Adults: 4 million IU i.v. or i.m. every 4–6 hours for 7–10 days.

Children: 100 000 IU / kg (maximum 4 million IU) i.v. or i.m. every 4–6 hours for 7–10 days.

Contraindications

Known hypersensitivity to penicillins or cefalosporins.

Precautions

Facilities should be available for treating anaphylaxis whenever penicillins are used. Patients should be questioned carefully about previous allergic reactions before the first dose is administered. If a skin rash develops during treatment, the patient should be transferred to a different class of antimicrobial.

Rapid intravenous administration of large doses of sodium benzylpenicillin may cause hyperkalaemia, dysrhythmias and cardiac arrest, particularly in patients with impaired renal function.

Use in pregnancy

There is no evidence that benzylpenicillin is teratogenic. It may be used during pregnancy.

Adverse effects

Hypersensitivity reactions are most common, ranging in severity from skin rashes to immediate anaphylaxis.

Pain and sterile inflammation can occur at the site of intramuscular injection; phlebitis or thrombophlebitis sometimes follows intravenous administration. Accidental injection into a peripheral nerve causes severe pain and dysfunction.

Unduly high concentrations of benzylpenicillin in the brain can result in confusion, convulsions, coma and fatal encephalopathy.

Interstitial nephritis has been reported. Neutropenia and thrombocytopenia are rare.

Overdosage

Overdosage with large intravenous doses can cause convulsions, paralysis and even death.

Excessive blood concentrations can be lowered by haemodialysis.

Storage

Powder for injection should be stored in vials at 2–8 °C.

Benzathine benzylpenicillin

Powder for injection, 1.44 g of benzylpenicillin (= 2.4 million IU) in 5-ml vial

General information

Benzathine benzylpenicillin is a repository preparation of benzylpenicillin which is available for parenteral use. It is designed to provide a tissue depot from which the drug is slowly absorbed over a period of 12 hours to several days. It takes 13–24 hours to reach its peak plasma concentration, which is maintained over a period of about 14 days. It is detectable in the urine for 3–4 weeks.

Clinical information

Uses

Treatment of:

- acute pharyngitis, acute cervical adenitis and diphtheria
- early and late syphilis (other than neurosyphilis) in adults.

Prevention of recurrence of rheumatic fever due to group A β-haemolytic streptococci.

Dosage and administration

Acute pharyngitis and acute cervical adenitis

Adults and children >30 kg: 1.2 million IU i.m. in a single dose.

Children ≤30 kg: 30 000 IU/kg (maximum 1.2 million IU) i.m. in a single dose.

Diphtheria

Adults and children >30 kg: 1.2 million IU i.m. in a single dose, following initial therapy with diphtheria antitoxin 20 000–100 000 IU i.v. or i.m.

Children ≤30 kg: 30 000 IU/kg (maximum 600 000 IU) i.m. in a single dose, following initial therapy with diphtheria antitoxin 20 000–100 000 IU i.v. or i.m.

Vaccination with diphtheria–pertussis–tetanus (DPT) should be offered during convalescence.

Early syphilis in adults

2.4 million IU i.m. in a single dose.

Benzathine benzylpenicillin (continued)

Late syphilis (other than neurosyphilis) in adults
2.4 million IU i.m. weekly for 3 weeks.

Prevention of recurrence of rheumatic fever due to group A β-haemolytic streptococci
Adults and children >30 kg: 1.2 million IU i.m. every 3–4 weeks.

Children ≤30 kg: 600 000 IU i.m. every 3–4 weeks.

Contraindications
Known hypersensitivity to penicillins or cefalosporins.

Precautions
Facilities should be available for treating anaphylaxis whenever penicillins are used. Patients should be questioned carefully about previous allergic reactions before the first dose is administered. If a skin rash develops during treatment, the patient should be transferred to a different class of antimicrobial.

Use in pregnancy
There is no evidence that benzathine benzylpenicillin is teratogenic. It may be used during pregnancy.

Adverse effects
Hypersensitivity reactions are most common, ranging in severity from skin rashes to immediate anaphylaxis.

Pain and sterile inflammation can occur at the site of intramuscular injection. Accidental injection into a peripheral nerve causes severe pain and dysfunction.

Interstitial nephritis has been reported.

Neutropenia and thrombocytopenia are rare.

Storage
Powder for injection should be stored in vials at 2–8 °C.

Procaine benzylpenicillin

Powder for injection, 1 g of benzylpenicillin (= 1 million IU), 3 g of benzylpenicillin (= 3 million IU) in vial

General information

Procaine benzylpenicillin is a repository preparation of benzylpenicillin which is available for parenteral use. It is designed to provide a tissue depot from which the drug is slowly absorbed over a period of 12 hours to several days. It produces a peak plasma concentration within 1–3 hours and is excreted over a period of several days.

Clinical information

Uses
Treatment of:

- diphtheria
- very severe pneumonia in children aged from 2 months to 5 years
- mild pneumonia in children aged from 2 months to 5 years, together with amoxicillin

- gingival infections, periodontitis, tooth abscesses and suppurative odontogenic infections
- severe acute cervical adenitis in children <5 years
- cellulitis and erysipelas
- human and animal bites and clenched-fist injuries, together with amoxicillin + clavulanic acid
- early and late syphilis in adults, and congenital syphilis in children ≤2 years
- neurosyphilis in adults, together with probenecid.

Dosage and administration

Diphtheria

Adults: 1.2 million IU i.m. every 24 hours for 7 days, following initial therapy with diphtheria antitoxin 20 000–100 000 IU i.v. or i.m.

Children: 50 000 IU/kg (maximum 1.2 million IU) i.m. every 24 hours for 7 days, following initial therapy with diphtheria antitoxin 20 000–100 000 IU i.v. or i.m.

Vaccination with diphtheria–pertussis–tetanus (DPT) should be offered during convalescence.

Very severe pneumonia in children aged from 2 months to 5 years

50 000 IU/kg (maximum 900 000 IU) i.m. every 24 hours for at least 5 days.

Mild pneumonia in children aged from 2 months to 5 years

50 000 IU/kg (maximum 900 000 IU) i.m. every 24 hours for at least 3 days (once clinical improvement occurs, amoxicillin 15–25 mg/kg (maximum 500 mg) orally every 8 hours may be used to complete the treatment course of at least 5 days).

Gingival infections and periodontitis

Adults: 1 million IU i.m. every 24 hours for 5 days.

Children: 50 000 IU/kg (maximum 1 million IU) i.m. every 24 hours for 5 days.

Tooth abscesses and suppurative odontogenic infections

Adults: 1 million IU i.m. every 24 hours for 3 days.

Children: 50 000 IU/kg (maximum 1 million IU) i.m. every 24 hours for 3 days.

Severe acute cervical adenitis in children < 5 years

50 000 IU/kg (maximum 1 million IU) i.m. every 24 hours for at least 10 days.

Cellulitis and erysipelas

Adults: 1.5 million IU i.m. every 24 hours for 7–10 days.

Children: 50 000 IU/kg (maximum 1.5 million IU) i.m. every 24 hours for 7–10 days.

Human and animal bites and clenched-fist injuries

Adults: 1.5 million IU i.m. every 24 hours for 5 days, followed by amoxicillin 500 mg + clavulanic acid orally every 8 hours for 5 days.

Children: 50 000 IU/kg (maximum 1.5 million IU) i.m. every 24 hours for 5 days, followed by amoxicillin 15 mg/kg + clavulanic acid (maximum 500 mg) orally every 8 hours for 5 days.

Early syphilis in adults

1 million IU i.m. every 24 hours for 10 days.

Late syphilis (other than neurosyphilis) in adults

1 million IU i.m. every 24 hours for 3 weeks.

Neurosyphilis in adults

1 million IU i.m. every 24 hours, together with probenecid 500 mg orally every 6 hours for 2 weeks.

Procaine benzylpenicillin (continued)

Congenital syphilis in children ≤ 2 years
50 000 IU / kg (maximum 1.5 million IU) i.m. every 24 hours for 10 days.

Contraindications
Known hypersensitivity to penicillins or cefalosporins.

Precautions
Facilities should be available for treating anaphylaxis whenever penicillins are used. Patients should be questioned carefully about previous allergic reactions before the first dose is administered. If a skin rash develops during treatment, the patient should be transferred to a different class of antimicrobial.

Use in pregnancy
There is no evidence that procaine benzylpenicillin is teratogenic. It may be used during pregnancy.

Adverse effects
Hypersensitivity reactions are common, ranging in severity from skin rashes to immediate anaphylaxis.

Pain and sterile inflammation can occur at the site of intramuscular injection. Accidental injection into a peripheral nerve causes severe pain and dysfunction.

Interstitial nephritis has been reported.

Neutropenia and thrombocytopenia are rare.

Storage
Powder for injection should be stored in vials at 2–8 °C.

Cefalexin

Capsule, 250 mg, 500 mg

General information

Cefalexin is a first-generation cefalosporin that is active against many Gram-positive aerobic cocci but has limited activity against Gram-negative bacteria. It is rapidly and completely absorbed from the gastrointestinal tract. Its plasma half-life is 0.5–1.2 hours. It is excreted in the urine as unchanged drug.

Clinical information

Uses
Treatment of:

- acute pharyngitis and acute cervical adenitis in patients allergic to penicillins
- urinary tract infections
- pyomyositis, cellulitis and erysipelas, together with cefazolin
- localized purulent skin lesions and impetigo
- osteomyelitis and septic arthritis due to *Staphylococcus aureus* in adults, together with cefazolin
- osteomyelitis and septic arthritis due to *Staphylococcus aureus* in children > 5 years, together with ceftriaxone or cefazolin.

Dosage and administration
Acute pharyngitis and acute cervical adenitis in patients allergic to penicillins
Adults: 500 mg orally every 6–8 hours for 10 days.

Children: 15 mg / kg (maximum 500 mg) orally every 6–8 hours for 10 days.

Urinary tract infections
Women: 500 mg orally every 8 hours for 5 days (for uncomplicated infections).

Men: 500 mg orally every 8 hours for at least 14 days.

Children: 12.5 mg / kg (maximum 500 mg) orally every 6 hours for 5–10 days.

Localized purulent skin lesions and impetigo
Adults: 500 mg orally every 6 hours for 5–7 days.

Children: 12.5–25 mg / kg (maximum 500 mg) orally every 6 hours for 5–7 days.

Cellulitis and erysipelas
Adults: 500 mg orally every 6 hours to complete the treatment course of 7–10 days, following initial therapy with cefazolin 1–2 g i.v. or i.m. every 8 hours.

Children: 12.5–25 mg / kg (maximum 500 mg) orally every 6 hours to complete the treatment course of 7–10 days, following initial therapy with cefazolin 15 mg / kg (maximum 2 g) i.v. or i.m. every 8 hours.

Pyomyositis
Adults: 500 mg orally every 6 hours to complete the treatment course of 5–10 days, following initial therapy with cefazolin 1–2 g i.v. or i.m. every 8 hours.

Children: 12.5–25 mg / kg (maximum 500 mg) orally every 6 hours to complete the treatment course of 5–10 days, following initial therapy with cefazolin 15 mg / kg (maximum 2 g) i.v. or i.m. every 8 hours.

Osteomyelitis due to Staphylococcus aureus in adults and children >5 years
Adults: 1–2 g orally every 6 hours to complete the treatment course of 4–6 weeks, following initial therapy with cefazolin 1–2 g i.v. or i.m. every 8 hours.

Children >5 years: 25 mg / kg (maximum 500 mg) orally every 6 hours to complete the treatment course of 3–4 weeks, following initial therapy with *either* ceftriaxone 50–75 mg / kg (maximum 1 g) i.v. or i.m. every 24 hours *or* cefazolin 15 mg / kg (maximum 1 g) i.v. or i.m. every 8 hours for 4–6 days (or until clinical improvement occurs).

Septic arthritis due to Staphylococcus aureus in adults and children >5 years
Adults: 1–2 g orally every 6 hours to complete the treatment course of 2–3 weeks, following initial therapy with cefazolin 1–2 g i.v. or i.m. every 8 hours.

Children >5 years: 25 mg / kg (maximum 500 mg) orally every 6 hours to complete the treatment course of 2–3 weeks, following initial therapy with *either* ceftriaxone 50–75 mg / kg (maximum 1 g) i.v. or i.m. every 24 hours *or* cefazolin 15 mg / kg (maximum 1 g) i.v. or i.m. every 8 hours for 4–6 days (or until clinical improvement occurs).

In some cases, especially in adults, repeated aspiration or surgical washout of the joint may be necessary.

Contraindications
Known hypersensitivity to other β-lactamase antimicrobials.

Precautions
Transient increases in liver enzymes may occur.

Use in pregnancy
There is no evidence that cefalexin is teratogenic. It may be used during pregnancy.

Cefalexin (continued)

Adverse effects

Hypersensitivity reactions are the most common adverse effects. Skin rashes are relatively frequent, while urticaria, bronchospasm and anaphylaxis are uncommon. Nausea, vomiting and diarrhoea have been reported.

Rarely, antimicrobial-associated pseudomembranous colitis due to *Clostridium difficile* occurs. When this is suspected, treatment should be immediately discontinued.

Reversible cholestatic jaundice has been reported.

Storage

Capsules should be stored in tightly closed containers.

Cefazolin

Powder for injection, 500 mg in vial

General information

Cefazolin is a first-generation cefalosporin that is active against many Gram-positive aerobic cocci but has limited activity against Gram-negative bacteria. It is poorly absorbed from the gastrointestinal tract and must be administered parenterally. Its plasma half-life is 1.2–2.2 hours. It is excreted as unchanged drug in the urine.

Clinical information

Uses

Treatment of:

- pneumonia due to *Staphylococcus aureus* in adults and children >5 years
- cellulitis, erysipelas and pyomyositis, together with cefalexin
- osteomyelitis and septic arthritis due to *Staphylococcus aureus* in adults and children >5 years, together with cefalexin
- septicaemia (initial empirical therapy) in adults and children >5 years, together with gentamicin.

Prophylaxis in clean surgery.

Prophylaxis in contaminated surgery, together with metronidazole.

Dosage and administration

Pneumonia due to Staphylococcus aureus in adults and children >5 years

Adults: 1–2 g i.v. or i.m. every 8 hours for 10–14 days.

Children >5 years: 15–25 mg/kg (maximum 2 g) i.v. or i.m. every 8 hours for 10–14 days.

Cellulitis and erysipelas

Adults: 1–2 g i.v. or i.m. every 8 hours for 7–10 days (once clinical improvement occurs, cefalexin 500 mg orally every 6 hours may be substituted).

Children: 15 mg/kg (maximum 2 g) i.v. or i.m. every 8 hours for 7–10 days (once clinical improvement occurs, cefalexin 12.5–25 mg/kg (maximum 500 mg) orally every 6 hours may be substituted).

Pyomyositis

Adults: 1–2 g i.v. or i.m. every 8 hours for 5–10 days (once clinical improvement

occurs, cefalexin 500 mg orally every 6 hours may be substituted).

Children: 15 mg / kg (maximum 2 g) i.v. or i.m. every 8 hours for 5–10 days (once clinical improvement occurs, cefalexin 12.5–25 mg / kg (maximum 500 mg) orally every 6 hours may be substituted).

Osteomyelitis due to Staphylococcus aureus in adults and children > 5 years

Adults: 1–2 g i.v. or i.m. every 8 hours for 4–6 weeks (if the duration of parenteral therapy is less than 4–6 weeks, the treatment course should be completed with cefalexin 1–2 g orally every 6 hours).

Children > 5 years: 15 mg / kg (maximum 1 g) i.v. or i.m. every 8 hours for 4–6 days (or until clinical improvement occurs), followed by cefalexin 25 mg / kg (maximum 500 mg) orally every 6 hours to complete the treatment course of 3–4 weeks.

Septic arthritis due to Staphylococcus aureus in adults and children > 5 years

Adults: 1–2 g i.v. or i.m. every 8 hours for 2–3 weeks (if the duration of parenteral therapy is less than 2–3 weeks, the treatment course should be completed with cefalexin 1–2 g orally every 6 hours).

Children > 5 years: 15 mg / kg (maximum 1 g) i.v. or i.m. every 8 hours for 4–6 days (or until clinical improvement occurs), followed by cefalexin 25 mg / kg (maximum 500 mg) orally every 6 hours to complete the treatment course of 2–3 weeks.

In some cases, especially in adults, repeated aspiration or surgical washout of the joint may be necessary.

Initial empirical therapy for septicaemia in adults and children > 5 years

1–2 g i.v. every 8 hours, together with *either* gentamicin 5–7 mg / kg i.v. every 24 hours *or* gentamicin 1.5 mg / kg i.v. or i.m. every 8 hours.

Prophylaxis in clean surgery

Adults and children: 1 g i.v. at induction of anaesthesia (if the operation is prolonged beyond 3–4 hours a further 1-g dose should be administered).

Prophylaxis in contaminated surgery

Adults and children: 1 g i.v., together with metronidazole 500 mg i.v. at induction of anaesthesia (if the operation is prolonged beyond 3–4 hours, a further 1-g dose of cefazolin should be administered).

Contraindications

Known hypersensitivity to other β-lactamase antimicrobials.

Precautions

Transient increases in liver enzymes may occur.

Use in pregnancy

There is no evidence that cefazolin is teratogenic. It may be used during pregnancy.

Adverse effects

Hypersensitivity reactions are the most common adverse effects. Skin rashes are relatively frequent, while urticaria, bronchospasm and anaphylaxis are uncommon. Nausea, vomiting and diarrhoea have been reported. Rarely, antimicrobial-associated pseudomembranous colitis due to *Clostridium difficile* occurs. When this is suspected, treatment should be immediately discontinued.

Reversible cholestatic jaundice has been reported.

Storage

Powder for injection should be stored in tightly closed containers.

Cefotaxime

Powder for injection, 500 mg in vial

General information

Cefotaxime is a semisynthetic third-generation cefalosporin. It is bactericidal against Gram-negative organisms, including *Pseudomonas aeruginosa*, and certain Gram-positive bacteria. After intramuscular administration, it is widely distributed throughout the body and is excreted primarily unchanged in the urine.

Clinical information

Uses

Treatment of:

- severe croup (laryngotracheobronchitis) in neonates
- epiglottitis in neonates, together with rifampicin
- neonatal pneumonia
- osteomyelitis due to *Haemophilus influenzae* or unknown pathogen in neonates, together with cloxacillin and amoxicillin + clavulanic acid
- osteomyelitis due to *Salmonella* spp. in neonates, together with cloxacillin and either sulfamethoxazole + trimethoprim or amoxicillin or ciprofloxacin
- septic arthritis (initial empirical therapy) and osteomyelitis and septic arthritis due to *Staphylococcus aureus* in neonates, together with cloxacillin
- neonatal gonococcal conjunctivitis
- neonatal meningitis due to unknown pathogen, together with ampicillin
- septicaemia (initial empirical therapy) in neonates, together with cloxacillin.

Dosage and administration

Severe croup (laryngotracheobronchitis) in neonates

50 mg / kg i.v. or i.m. every 8 hours for 5 days.

Epiglottitis in neonates

Neonates aged 1–2 months: 50 mg / kg i.v. or i.m. every 8 hours for 5 days, supplemented for the first 4 days by rifampicin 20 mg / kg (maximum 600 mg) orally every 24 hours.

Neonates < 1 month: 50 mg / kg i.v. or i.m. every 8 hours for 5 days, supplemented for the first 4 days by rifampicin 10 mg / kg (maximum 300 mg) orally every 24 hours.

Neonatal pneumonia

50 mg / kg i.v. every 12 hours for at least 5 days.

Cefotaxime is often administered in combination with ampicillin (50 mg / kg i.v. every 8 hours for at least 5 days), because of problems of resistance in Gram-negative enteric bacteria and the possibility of *Listeria* spp. infections in neonates.

Osteomyelitis due to Haemophilus influenzae or unknown pathogen in neonates

50–75 mg / kg (maximum 2 g) i.v. every 8 hours, together with cloxacillin 25–50 mg / kg (maximum 2 g) i.v. or i.m. every 4–6 hours for 4–6 days (or until clinical improvement occurs), followed by amoxicillin 15 mg / kg + clavulanic acid (maximum 500 mg) orally every 8 hours to complete the treatment course of 3–4 weeks.

Osteomyelitis due to Staphylococcus aureus in neonates
50–75 mg / kg (maximum 2 g) i.v. every 8 hours, together with cloxacillin 25–50 mg / kg (maximum 2 g) i.v. or i.m. every 4–6 hours for 4–6 days (or until clinical improvement occurs), followed by cloxacillin 12.5 mg / kg (maximum 500 mg) orally every 6 hours to complete the treatment course of 3–4 weeks.

Osteomyelitis due to Salmonella spp. in neonates
50–75 mg / kg (maximum 2 g) i.v. every 8 hours, together with cloxacillin 25–50 mg / kg (maximum 2 g) i.v. or i.m. every 4–6 hours for 4–6 days (or until clinical improvement occurs), followed by *either* sulfamethoxazole 20 mg / kg + trimethoprim 4 mg / kg (maximum 800 mg + 160 mg) orally every 12 hours *or* amoxicillin 7.5–15 mg / kg (maximum 1 g) orally every 8 hours *or* ciprofloxacin 10–15 mg / kg (maximum 500 mg) orally every 12 hours to complete the treatment course of 6 weeks.

Initial empirical therapy for septic arthritis in neonates
50–75 mg / kg (maximum 2 g) i.v. every 8 hours, together with cloxacillin 25–50 mg / kg (maximum 2 g) i.v. or i.m. every 6 hours.

Septic arthritis due to Staphylococcus aureus in neonates
50–75 mg / kg (maximum 2 g) i.v. every 8 hours, together with cloxacillin 25–50 mg / kg (maximum 2 g) i.v. or i.m. every 4–6 hours for 4–6 days (or until clinical improvement occurs), followed by cloxacillin 12.5 mg / kg (maximum 500 mg) orally every 6 hours to complete the treatment course of 2–3 weeks.

Neonatal gonococcal conjunctivitis
50 mg / kg (maximum 2 g) i.v. in a single dose.

Neonatal meningitis due to unknown pathogen
50 mg / kg (maximum 2 g) i.v. every 12 hours, together with ampicillin 50 mg / kg (maximum 2 g) i.v. every 8 hours (neonates < 7 days: 50 mg / kg (maximum 2 g) i.v. every 12 hours) for a total of 7–10 days.

Initial empirical therapy for septicaemia in neonates
50–75 mg / kg (maximum 2 g) i.v. every 8 hours, together with cloxacillin 50 mg / kg (maximum 2 g) every 4–6 hours.

Contraindications
Known hypersensitivity to other β-lactam antibiotics.

Precautions
Blood concentrations of liver enzymes may rise transiently.

Use in pregnancy
There is no evidence that cefotaxime is teratogenic. It may be used during pregnancy.

Adverse effects
Hypersensitivity reactions are the most common adverse effects. Skin rashes are relatively frequent, while urticaria, bronchospasm and anaphylaxis are uncommon. Nausea, vomiting and diarrhoea have been reported. Rarely, antimicrobial-associated pseudomembranous colitis due to *Clostridium difficile* occurs. When this is suspected, treatment should be immediately discontinued.

Reversible cholestatic jaundice has been reported.

Storage
Powder for injection should be stored in tightly closed containers, protected from light.

Ceftazidime

Powder for injection, 250 mg (as pentahydrate) in vial

General information

Ceftazidime is a semisynthetic third-generation cefalosporin that is bactericidal against a wide range of Gram-negative bacteria, including *Pseudomonas aeruginosa*, and some Gram-positive bacteria. After intramuscular administration, the drug is widely distributed throughout the body and is excreted primarily unchanged in the urine.

Clinical information

Uses

Treatment of:

- nosocomial pneumonia, together with gentamicin or ciprofloxacin
- melioidosis, together with sulfamethoxazole + trimethoprim or doxycycline.

Dosage and administration

Nosocomial pneumonia

Adults: 1 g i.v. every 8 hours for 7 days, supplemented by *either* gentamicin 5–7 mg / kg i.v. daily in divided doses *or* ciprofloxacin 500 mg i.v. every 12 hours.

Children: 25 mg / kg (maximum 1 g) i.v. every 8 hours for 7 days, supplemented by *either* gentamicin 7.5 mg / kg daily in 1–3 divided doses *or* ciprofloxacin 10 mg / kg (maximum 300 mg) i.v. every 12 hours.

In hospitals with a high prevalence of meticillin-resistant *Staphylococcus aureus*, vancomycin 1 g (children: 20 mg / kg; maximum 1 g) i.v. should be added to the above regimens.

Melioidosis

Adults: 2 g i.v. every 8 hours for at least 14 days, supplemented by *either* sulfamethoxazole 1600 mg + trimethoprim 320 mg orally or i.v. every 12 hours *or* doxycycline 100 mg orally or i.v. every 12 hours.

Children >8 years: 50 mg / kg (maximum 2 g) i.v. every 8 hours for at least 14 days, supplemented by *either* sulfamethoxazole 40 mg / kg + trimethoprim 8 mg / kg (maximum 1600 mg + 320 mg) orally or i.v. every 12 hours *or* doxycycline 2 mg / kg (maximum 100 mg) orally or i.v. every 12 hours.

Children ≤8 years: 50 mg / kg (maximum 2 g) i.v. every 8 hours for at least 14 days, supplemented by sulfamethoxazole 40 mg / kg + trimethoprim 8 mg / kg (maximum 1600 mg + 320 mg) orally or i.v. every 12 hours.

After the initial intensive therapy, eradication of any secondary infection is recommended with oral sulfamethoxazole + trimethoprim or doxycycline for at least 3 months.

Contraindications

Known hypersensitivity to other β-lactamase antimicrobials.

Precautions

Blood concentrations of liver enzymes may rise transiently.

Use in pregnancy

There is no evidence that ceftazidime is teratogenic. It may be used during pregnancy.

Adverse effects

Hypersensitivity reactions are the most common adverse effects. Skin rashes are relatively frequent, while urticaria, bronchospasm and anaphylaxis are

uncommon. Nausea, vomiting and diarrhoea have been reported. Rarely, antimicrobial-associated pseudomembranous colitis due to *Clostridium difficile* occurs. When this is suspected, treatment should be immediately discontinued.

Reversible cholestatic jaundice has been reported.

Storage

Powder for injection should be stored in tightly closed containers, protected from light.

Ceftriaxone

Powder for injection, 250 mg (as sodium salt) in vial

General information

Ceftriaxone is a third-generation cefalosporin derived from *Cephalosporium acremonium*. It is highly active against Gram-negative cocci and bacilli. Like benzylpenicillin, it has a β-lactam ring.

After intramuscular administration, ceftriaxone is distributed widely throughout the body. It has a relatively long plasma half-life of about 8 hours and is excreted unchanged in both urine and bile.

Clinical information

Uses

Treatment of:

- acute mastoiditis
- epiglottitis in adults and children >2 months
- severe croup (laryngotracheobronchitis) in children >2 months
- pneumonia in adults and children >5 years and very severe pneumonia in children aged from 2 months to 5 years
- atypical pneumonia in adults and children >5 years, together with erythromycin
- acute pyelonephritis, together with ampicillin
- osteomyelitis due to *Staphylococcus aureus* in children, together with cloxacillin or cefalexin
- osteomyelitis due to *Haemophilus influenzae* or unknown pathogen in children aged from 2 months to 5 years, together with cloxacillin and amoxicillin + clavulanic acid
- osteomyelitis due to *Salmonella* spp. in children aged from 2 months to 5 years, together with cloxacillin and either sulfamethoxazole + trimethoprim or amoxicillin or ciprofloxacin
- septic arthritis (initial empirical therapy), together with cloxacillin
- septic arthritis due to *Staphylococcus aureus* in children, together with cloxacillin or cefalexin
- disseminated gonococcal infections, uncomplicated anogenital gonococcal infections and chancroid in adults
- gonococcal conjunctivitis in adults and neonates
- pelvic inflammatory disease in adults (ambulatory patients), together with doxycycline and metronidazole
- moderate and severe pelvic inflammatory disease in adults (hospitalized patients), together with doxycycline
- meningitis (initial empirical therapy), meningitis due to *Haemophilus influenzae* and meningitis due to benzylpenicillin-susceptible *Streptococcus pneumoniae*
- meningitis due to benzylpenicillin-resistant and ceftriaxone/cefotaxime-resistant *Streptococcus pneumoniae*, together with vancomycin and rifampicin
- Lyme disease (late stage) in adults

Ceftriaxone (continued)

- septicaemia (initial empirical therapy) in children aged from 2 months to 5 years, together with cloxacillin.

Dosage and administration

Ceftriaxone must be administered parenterally. Intravenous formulations of ceftriaxone should be administered over at least 2 minutes.

Acute mastoiditis

Adults: 1 g i.v. or i.m. every 12 hours for 10 days.

Children: 50 mg / kg (maximum 1 g) i.v. or i.m. every 12 hours for 10 days.

Severe croup (laryngotracheobronchitis) in children > 2 months

100 mg / kg (maximum 2 g) i.v. or i.m. every 24 hours for 5 days.

Epiglottitis in adults and children > 2 months

Adults: 2 g i.v. or i.m. every 24 hours for 5 days.

Children > 2 months: 100 mg / kg (maximum 2 g) i.v. or i.m. every 24 hours for 5 days.

In young children, consideration should be given to vaccination against *Haemophilus influenzae* type b.

Pneumonia in adults and children > 5 years

Hospitalized patients

Adults: 1 g i.v. or i.m. every 12–24 hours for 7 days.

Children > 5 years: 50 mg / kg (maximum 1 g) i.v. or i.m. every 12–24 hours for 7 days.

Patients with atypical pneumonia should also receive erythromycin 1 g (children: 10 mg / kg; maximum 1 g) i.v. every 6 hours for 14 days.

Very severe pneumonia in children aged from 2 months to 5 years

50 mg / kg (maximum 1 g) i.v. or i.m. every 24 hours for at least 5 days.

Acute pyelonephritis

Adults: 1 g i.v. or i.m. every 24 hours for 14 days, supplemented for up to 14 days by ampicillin 1–2 g i.v. or i.m. every 6 hours.

Children: 50 mg / kg (maximum 1 g) i.v. or i.m. every 24 hours for 14 days, supplemented for up to 14 days by ampicillin 50 mg / kg (maximum 2 g) i.v. or i.m. every 6 hours.

Osteomyelitis due to Staphylococcus aureus in children

Children > 5 years: 50–75 mg / kg (maximum 1 g) i.v. or i.m. every 24 hours for 4–6 days (or until clinical improvement occurs), followed by *either* cloxacillin 25 mg / kg (maximum 500 mg) *or* cefalexin 25 mg / kg (maximum 500 mg) orally every 6 hours to complete the treatment course of 3–4 weeks.

Children aged from 2 months to 5 years: 50–75 mg / kg (maximum 1 g) i.v. or i.m. every 24 hours, together with cloxacillin 25–50 mg / kg (maximum 2 g) i.v. or i.m. every 4–6 hours for 4–6 days (or until clinical improvement occurs), followed by cloxacillin 12.5 mg / kg (maximum 500 mg) orally every 6 hours to complete the treatment course of 3–4 weeks.

Osteomyelitis due to Haemophilus influenzae or unknown pathogen in children aged from 2 months to 5 years

50–75 mg / kg (maximum 1 g) i.v. or i.m. every 24 hours, together with cloxacillin 25–50 mg / kg (maximum 2 g) i.v. or i.m. every 4–6 hours for 4–6 days (or until clinical improvement occurs), followed by amoxicillin 15 mg / kg + clavulanic acid (maximum 500 mg) orally every 8 hours to complete the treatment course of 3–4 weeks.

Osteomyelitis due to Salmonella spp. in children aged from 2 months to 5 years

50–75 mg / kg (maximum 1 g) i.v. or i.m. every 24 hours, together with cloxacillin 25–50 mg / kg (maximum 2 g) i.v. or i.m. every 4–6 hours for 4–6 days (or until clinical improvement occurs), followed by *either* sulfamethoxazole 20 mg / kg + trimethoprim 4 mg / kg (maximum 800 mg + 160 mg) orally every 12 hours *or* amoxicillin 7.5–15 mg / kg (maximum 1 g) orally every 8 hours *or* ciprofloxacin 10–15 mg / kg (maximum 500 mg) orally every 12 hours to complete the treatment course of 6 weeks.

Initial empirical therapy for septic arthritis

Adults: 1–2 g i.v. or i.m. every 24 hours, together with cloxacillin 2 g i.v. or i.m. every 6 hours.

Children ≥2 months: 25–50 mg / kg (maximum 2 g) i.v. or i.m. every 24 hours, together with cloxacillin 25–50 mg / kg (maximum 2 g) i.v. or i.m. every 6 hours.

Septic arthritis due to Staphylococcus aureus in children

Children >5 years: 50–75 mg / kg (maximum 1 g) i.v. or i.m. every 24 hours for 4–6 days (or until clinical improvement occurs), followed by *either* cloxacillin 25 mg / kg (maximum 500 mg) *or* cefalexin 25 mg / kg (maximum 500 mg) orally every 6 hours to complete the treatment course of 2–3 weeks.

Children aged from 2 months to 5 years: 50–75 mg / kg (maximum 1 g) i.v. or i.m. every 24 hours, together with cloxacillin 25–50 mg / kg (maximum 2 g) i.v. or i.m. every 4–6 hours for 4–6 days (or until clinical improvement occurs), followed by cloxacillin 12.5 mg / kg (maximum 500 mg) orally every 6 hours to complete the treatment course of 2–3 weeks.

In some cases repeated aspiration or surgical washout of the joint may also be necessary.

Uncomplicated anogenital gonococcal infections and gonococcal conjunctivitis in adults

250 mg i.m. in a single dose.

All patients with gonorrhoea should be treated concurrently for chlamydial infection unless microbiological facilities exist to exclude the latter diagnosis. Sexual partners should be treated simultaneously.

Disseminated gonococcal infections in adults

1 g i.m. every 24 hours for 7 days.

If there is evidence of meningeal or endocardial involvement, treatment should be extended to 2 weeks and 4 weeks, respectively.

All patients with gonorrhoea should be treated concurrently for chlamydial infection unless microbiological facilities exist to exclude the latter diagnosis. Sexual partners should be treated simultaneously.

Neonatal gonococcal conjunctivitis

50 mg / kg (maximum 125 mg) i.m. in a single dose.

Chancroid in adults

250 mg i.m. in a single dose. (Longer treatment courses may be necessary in immunocompromised patients.)

Pelvic inflammatory disease in adults

Ambulatory patients

250 mg i.m. in a single dose, followed by doxycycline 100 mg orally every 12 hours and metronidazole 400–500 mg orally every 8 hours for 10 days.

Hospitalized patients with moderate or severe disease

250 mg i.m. every 12 hours for at least 4 days (or for 48 hours after clinical improvement), followed by doxycycline 100 mg orally every 12 hours for 10–14 days.

Initial empirical therapy for meningitis

Adults: 2 g i.v. or i.m. daily in one or two divided doses for up to 14 days.

Ceftriaxone (continued)

Children: 50–100 mg / kg (maximum 2 g) i.v. or i.m. daily in one or two divided doses for up to 14 days.

Meningitis due to Streptococcus pneumoniae

Strains susceptible to benzylpenicillin (MIC ≤ 0.06 mg/l)

Adults: 2 g i.v. or i.m. daily in one or two divided doses for 10–14 days.

Children: 50–100 mg / kg (maximum 2 g) i.v. or i.m. daily in one or two divided doses for 10–14 days.

Patients who are severely ill may require treatment for up to 3 weeks.

Strains showing intermediate resistance to benzylpenicillin (MIC = 0.125–1.0 mg/l)

Adults: 2 g i.v. or i.m. daily in one or two divided doses for 10–14 days.

Children: 50–100 mg / kg (maximum 2 g) i.v. or i.m. daily in one or two divided doses for 10–14 days.

Strains resistant to benzylpenicillin (MIC >1.0 mg/l) or ceftriaxone/cefotaxime (MIC ≥1.0 mg/l)

Adults: 2 g i.v. or i.m. every 12 hours for at least 14 days, supplemented by vancomycin 1 g i.v. every 12 hours and rifampicin 600 mg orally every 24 hours.

Children: 50–100 mg / kg (maximum 2 g) i.v. or i.m. every 12 hours for at least 14 days, supplemented by vancomycin 20 mg / kg (maximum 1 g) i.v. every 6 hours and rifampicin 20 mg / kg (maximum 600 mg) orally every 24 hours.

Patients should be referred to a specialist.

Meningitis due to Haemophilus influenzae

Adults: 2 g i.v. or i.m. every 12 hours for 7–10 days.

Children: 50 mg / kg (maximum 2 g) i.v. or i.m. every 12 hours for 7–10 days.

Lyme disease (late stage) in adults

2 g i.v. or i.m. every 24 hours for 14–21 days.

Patients with neurological involvement usually require treatment for 21 days.

Initial empirical therapy for septicaemia in children aged from 2 months to 5 years

50 mg / kg (maximum 2 g) i.v. or i.m. every 24 hours, together with cloxacillin 50 mg / kg (maximum 2 g) i.v. every 4–6 hours.

Contraindications

Known hypersensitivity to other β-lactam antimicrobials.

Precautions

Blood concentrations of liver enzymes may rise transiently.

Use in pregnancy

There is no evidence that ceftriaxone is teratogenic. It may be used during pregnancy.

Adverse effects

Hypersensitivity reactions are the most common adverse effects. Skin rashes are relatively frequent, while urticaria, bronchospasm and anaphylaxis are uncommon. Nausea, vomiting and diarrhoea have been reported. Rarely, antimicrobial-associated pseudomembranous colitis due to *Clostridium difficile* occurs. When this is suspected, treatment should be immediately discontinued.

Reversible cholestatic jaundice has been reported.

Storage

Powder for injection should be stored in tightly closed containers, protected from light.

Cefuroxime

Powder for injection, 250 mg

General information

Cefuroxime is a semisynthetic second-generation cefalosporin. It is bactericidal against certain Gram-negative bacteria. After intramuscular administration, it is widely distributed throughout the body and is excreted primarily unchanged in the urine.

Clinical information

Uses

Treatment of pneumonia in adults and children >5 years.

Dosage and administration

Adults: 1.0–1.5 g i.v. every 6–8 hours for 7 days.

Children >5 years: 50–60 mg/kg (maximum 1.5 g) i.v. every 6–8 hours for 7 days.

Contraindications

Known hypersensitivity to other β-lactamase antimicrobials.

Precautions

Blood concentrations of liver enzymes may rise transiently.

Use in pregnancy

There is no evidence that cefuroxime is teratogenic. It may be used during pregnancy.

Adverse effects

Hypersensitivity reactions are the most common adverse effects. Skin rashes are relatively frequent, while urticaria, bronchospasm and anaphylaxis are uncommon. Nausea, vomiting and diarrhoea have been reported. Rarely, antimicrobial-associated pseudomembranous colitis due to *Clostridium difficile* occurs. When this is suspected, treatment should be immediately discontinued.

Reversible cholestatic jaundice has been reported.

Storage

Powder for injection should be stored in tightly closed containers, protected from light.

Chloramphenicol

Capsule, 250 mg
Oral suspension, 150 mg (as palmitate)/5 ml
Powder for injection, 1 g (as sodium succinate) in vial
Oily suspension, 0.5 g (as sodium succinate)/ml in 2-ml ampoule

General information

Chloramphenicol is a synthetic broad-spectrum antimicrobial which is active against most Gram-negative and Gram-positive aerobic bacteria. It is also active against many anaerobic bacteria. It is primarily bacteriostatic and inhibits bacterial protein synthesis.

Chloramphenicol is rapidly absorbed from the gastrointestinal tract, is metabolized in the liver, and is readily

Chloramphenicol (continued)

distributed in most tissues and body fluids including the cerebrospinal fluid. The plasma half-life is 1.5–4.0 hours. It is excreted in the urine as metabolites.

Chloramphenicol crosses the placenta and is excreted in breast milk.

Clinical information

Uses

Treatment of:

- severe infections due to susceptible bacteria when other less toxic antimicrobials are ineffective or contraindicated
- acute mastoiditis
- epiglottitis in adults and children >2 months, together with rifampicin
- severe croup (laryngotracheobronchitis) in children >2 months
- chronic suppurative lung disease in children
- pneumonia in adults and children >5 years, very severe pneumonia in children aged from 2 months to 5 years and neonatal pneumonia
- atypical pneumonia in adults and children >5 years, together with erythromycin
- typhoid and paratyphoid fever and infectious enteritis due to *Salmonella enteritidis*
- granuloma inguinale in adults
- meningitis (initial empirical therapy), meningitis due to *Neisseria meningitidis*, and brain abscess, together with benzylpenicillin
- meningitis due to *Haemophilus influenzae*
- relapsing fever, tularaemia, plague and rickettsial infections
- septicaemia (initial empirical therapy) in adults and children >5 years, together with gentamicin.

The oily suspension has been found to be helpful in situations of catastrophic epidemics of meningococcal meningitis occurring mainly in sub-Saharan Africa, during which the medical services are overwhelmed by the epidemic. For this reason, the product should be reserved for use in epidemics of meningococcal meningitis when the overwhelming scale of the epidemic precludes any other form of antimicrobial therapy.

Dosage and administration

The dosage should be adjusted where plasma monitoring is feasible, to maintain plasma concentrations at 5–20 µg/ml.

The dosage should be reduced in patients with renal or hepatic impairment.

Acute mastoiditis

Adults: 1 g i.v. or i.m. every 6–8 hours for 10–14 days.

Children: 25 mg/kg (maximum 750 mg) i.v. or i.m. every 6–8 hours for 10–14 days.

Epiglottitis in adults and children >2 months

Adults: 1 g i.v. or i.m. every 6–8 hours for 5 days, supplemented by rifampicin 600 mg orally every 24 hours for the first 4 days.

Children >2 months: 25 mg/kg (maximum 1 g) i.v. or i.m. every 6 hours for 5 days, supplemented by rifampicin 20 mg/kg (maximum 600 mg) orally every 24 hours for the first 4 days.

In young children, consideration should be given to vaccination against *Haemophilus influenzae* serotype b.

Severe croup (laryngotracheobronchitis) in children >2 months

25 mg/kg (maximum 1 g) i.v. or i.m. every 6 hours for 5 days.

Chronic suppurative lung disease in children

25 mg/kg (maximum 1 g) i.v. or i.m. every 6 hours for 5 days.

Pneumonia in adults and children >5 years

Hospitalized patients

Adults: 1 g i.v. every 6 hours for 7 days.

Children: 25 mg/kg (maximum 750 mg) i.v. every 6 hours for 7 days.

Patients with atypical pneumonia should also receive erythromycin 1 g (children: 10 mg/kg; maximum 1 g) i.v. every 6 hours for 14 days.

Very severe pneumonia in children aged from 2 months to 5 years

25 mg/kg (maximum 750 mg) i.v. or i.m. every 6 hours for at least 10 days (once clinical improvement occurs, oral dosage forms may be substituted).

Pneumonia in neonates

25 mg/kg (maximum 750 mg) i.v. every 12 hours for at least 5 days (contraindicated in premature infants or neonates <7 days).

Chloramphenicol should be used for this indication only when no alternatives are available.

Typhoid and paratyphoid fever and infectious enteritis due to Salmonella enteritidis

Adults: 1 g orally every 6 hours for 10–14 days.

Children: 25 mg/kg (maximum 750 mg) orally every 6 hours for 10–14 days.

Granuloma inguinale in adults

500 mg orally every 6 hours for 3 weeks (or until the lesion has completely healed).

Initial empirical therapy for meningitis

Adults: 1 g i.v. every 6 hours for up to 14 days (once clinical improvement occurs, 500–750 mg orally every 6 hours may be substituted), supplemented by benzylpenicillin 3–4 million IU i.v. or i.m. every 4 hours.

Children: 25 mg/kg (maximum 1 g) i.v. every 6 hours for up to 14 days (once clinical improvement occurs, 25 mg/kg (maximum 750 mg) orally every 6 hours may be substituted), supplemented by benzylpenicillin 100 000 IU/kg (maximum 4 million IU) i.v. or i.m. every 4 hours.

Meningitis due to Neisseria meningitidis

Adults: oily suspension 100 mg/kg (maximum 3 g) i.m. every 24 hours for up to 14 days (once clinical improvement occurs, chloramphenicol 500–750 mg orally every 6 hours may be substituted), supplemented by benzylpenicillin 3–4 million IU i.v. or i.m. every 4 hours.

Children: oily suspension 25 mg/kg (maximum 500 mg) i.m. every 24 hours for up to 14 days (once clinical improvement occurs, chloramphenicol 25 mg/kg (maximum 750 mg) orally every 6 hours may be substituted), supplemented by benzylpenicillin 100 000 IU/kg (maximum 4 million IU) i.v. or i.m. every 4 hours.

Meningitis due to Haemophilus influenzae

Adults: 1 g i.v. every 6 hours for 7–10 days.

Children: 25 mg/kg (maximum 1 g) i.v. every 6 hours for 7–10 days.

Chloramphenicol should only be used if the isolate is known to be susceptible.

Prophylaxis with rifampicin 600 mg (neonates <1 month: 5 mg/kg (maximum 300 mg); children ≥1 month: 10 mg/kg (maximum 600 mg)) orally every 24 hours for 4 days should be considered for patients and their close contacts, especially children under 5 years.

Chloramphenicol (continued)

Brain abscess

Adults: 1 g i.v. every 6 hours, together with benzylpenicillin 3–4 million IU i.v. or i.m. every 4–6 hours.

Children: 25 mg / kg (maximum 750 mg) i.v. every 6 hours, together with benzylpenicillin 100 000 IU / kg (maximum 3 million IU) i.v. or i.m. every 4–6 hours.

The duration of treatment depends on the clinical response and radiological evidence of resolution of the abscess.

Relapsing fever

Adults: 500 mg orally in a single dose.

Children: 25 mg / kg (maximum 750 mg) orally in a single dose.

Tularaemia

Adults: 1 g i.v. every 6 hours for 7 days.

Children: 25 mg / kg (maximum 1 g) i.v. every 6 hours for 7 days.

Plague

Adults: 500 mg orally or i.v. every 6 hours for 7–10 days.

Children: 25 mg / kg (maximum 750 mg) orally or i.v. every 6 hours for 7–10 days.

Rickettsial infections

Adults: 500 mg orally or i.v. every 6 hours for 7–10 days (or for 48 hours after resolution of fever).

Children: 15 mg / kg (maximum 500 mg) orally or i.v. every 6 hours for 7–10 days (or for 48 hours after resolution of fever).

Initial empirical therapy for septicaemia in adults and children > 5 years

750 mg i.v. every 6 hours, together with *either* gentamicin 5–7 mg / kg i.v. every 24 hours *or* gentamicin 1.5 mg / kg i.v. or i.m. every 8 hours.

Contraindications

- Because of its unpredictable toxicity, chloramphenicol should never be used in diseases which are safely and effectively treated by other antimicrobials.
- Known hypersensitivity to chloramphenicol.
- Neonates <1 week and premature infants.
- Third trimester of pregnancy.

Precautions

When facilities are available, the blood count should be monitored. Because of the narrow margin between effective therapeutic and toxic dosages of chloramphenicol, the plasma concentrations should be monitored whenever possible.

Use in pregnancy

Safe use in early pregnancy has not been established. Chloramphenicol should be administered only when the need of the mother outweighs any potential risk to the fetus.

Adverse effects

The most serious adverse effect of chloramphenicol is bone-marrow depression. Irreversible aplastic anaemia, which is fatal in 50% of cases, can occur after a single dose. The risk of reversible aplastic anaemia increases with prolonged therapy.

Other haematological abnormalities including leukopenia, thrombocytopenia and impaired synthesis of haemoglobin are dose-related and usually reversible.

Grey baby syndrome characterized by vomiting, greenish diarrhoea, abdominal distension, hypothermia, flaccidity and respiratory and cardiovascular depression has been reported in premature and newborn infants. It has also been reported in infants born to mothers receiving chloramphenicol late in pregnancy.

Gastrointestinal symptoms, peripheral neuritis and optic neuritis are reported rarely.

Drug interactions

Chloramphenicol inhibits hepatic enzymes. It thus prolongs the half-life of drugs metabolized in the liver, including phenytoin, oral anticoagulants and steroids.

Concomitant administration of phenobarbital or rifampicin may decrease plasma concentrations of chloramphenicol.

Storage

Preparations should be stored in tightly closed containers protected from light. Following reconstitution, chloramphenicol injection is stable for 30 days. Cloudy solutions should be discarded.

Ciprofloxacin

Tablet, 250 mg (as hydrochloride)

General information

Ciprofloxacin is a synthetic fluoroquinolone that acts as a specific inhibitor of bacterial DNA gyrase. It has a broad spectrum of efficacy against both Gram-negative and Gram-positive aerobic bacteria. Transfer of genes containing DNA coding for antimicrobial resistance has been reported but as yet is of little clinical significance.

Ciprofloxacin is rapidly absorbed from the gastrointestinal tract. Peak plasma levels occur 0.5–1.5 hours after dosing. It is widely distributed in body tissues and concentrated in the bile. It has a plasma half-life of 3–5 hours and is excreted in the urine mainly as unchanged drug.

Clinical information

Uses

Treatment of:

- legionellosis in adults
- nosocomial pneumonia, together with ceftazidime
- cholera in patients who are severely dehydrated
- shigellosis, enteritis due to enterotoxigenic *Escherichia coli* and infectious enteritis due to *Salmonella enteritidis*
- enteritis due to *Campylobacter jejuni* in adults
- typhoid and paratyphoid fever
- uncomplicated anogenital infections, gonococcal conjunctivitis, chancroid and prostatitis in adults
- osteomyelitis due to *Salmonella* spp. in adults
- osteomyelitis due to *Salmonella* spp. in children ≤5 years, together with cloxacillin and either ceftriaxone or cefotaxime
- moderate and severe pelvic inflammatory disease in adults (hospitalized patients), together with metronidazole and doxycycline
- tularaemia and anthrax.

Prophylaxis against meningitis due to *Neisseria meningitidis*.

Dosage and administration

Legionellosis in adults

750 mg orally every 12 hours for 10 days.

Nosocomial pneumonia

Adults: 500 mg i.v. every 12 hours, together with ceftazidime 1 g i.v. every 8 hours for 7 days.

Ciprofloxacin (continued)

Children: 10 mg / kg (maximum 300 mg) i.v. every 12 hours, together with ceftazidime 25 mg / kg (maximum 1 g) every 8 hours for 7 days.

In hospitals with a high prevalence of meticillin-resistant *Staphylococcus aureus*, vancomycin 1 g (children: 20 mg / kg; maximum 1 g) i.v. every 12 hours for 10–14 days should be added to the above regimens.

Cholera in patients who are severely dehydrated and shigellosis

Adults: 1 g orally in a single dose.

Children: 20 mg / kg (maximum 1 g) orally in a single dose.

Patients with shigellosis due to *Shigella dysenteriae* serotype 1 should receive 500 mg (children: 10 mg / kg; maximum 500 mg) orally every 12 hours for 5 days.

Enteritis due to Campylobacter jejuni in adults

500 mg orally every 12 hours for 7–10 days.

Enteritis due to enterotoxigenic Escherichia coli

Adults: 500 mg orally every 12 hours for 3 days.

Children: 10 mg / kg (maximum 500 mg) orally every 12 hours for 3 days.

Ciprofloxacin is not licensed for use in children for this indication, but may be used for short courses if there are no suitable alternatives.

Typhoid and paratyphoid fever and infectious enteritis due to Salmonella enteritidis

Adults: 500–750 mg orally every 12 hours for 5–14 days.

Children: 10–15 mg / kg (maximum 500 mg) orally every 12 hours for 5–14 days.

Chronic carriers should receive 500–750 mg orally every 12 hours for 4–6 weeks (children: ampicillin 10 mg / kg (maximum 250 mg) i.m. every 6 hours for 4–6 weeks).

Prostatitis in adults

500 mg orally every 12 hours for 4–6 weeks.

Osteomyelitis due to Salmonella spp. in adults and children ≤ 5 years

Adults: 750 mg orally every 12 hours for 6 weeks.

Children aged from 2 months up to 5 years: 10–15 mg / kg (maximum 500 mg) orally every 12 hours to complete the treatment course of 6 weeks, following initial therapy with cloxacillin 25–50 mg / kg (maximum 2 g) i.v. or i.m. every 4–6 hours and ceftriaxone 50–75 mg / kg (maximum 1 g) i.v. or i.m. every 24 hours for 4–6 days (or until clinical improvement occurs).

Neonates: 10–15 mg / kg (maximum 500 mg) orally every 12 hours to complete the treatment course of 6 weeks, following initial therapy with cloxacillin 25–50 mg / kg (maximum 2 g) i.v. or i.m. every 4–6 hours and cefotaxime 50–75 mg / kg (maximum 2 g) i.v. every 8 hours for 4–6 days (or until clinical improvement occurs).

Uncomplicated anogenital gonococcal infections and gonococcal conjunctivitis in adults

500 mg orally in a single dose.

All patients with gonorrhoea should be treated concurrently for chlamydial infection unless microbiological facilities exist to exclude the latter diagnosis. Sexual partners should be treated simultaneously.

Chancroid in adults

500 mg orally in a single dose. (Longer treatment courses may be necessary in immunocompromised patients.)

Moderate or severe pelvic inflammatory disease in adults

Hospitalized patients

500 mg orally every 12 hours plus metronidazole 400–500 mg orally every 8 hours for at least 4 days (or for 48 hours after clinical improvement occurs), followed by doxycycline 100 mg orally every 12 hours for 10–14 days.

Tularaemia

Adults: 500 mg orally every 12 hours for 10–14 days.

Children: 10–15 mg/kg (maximum 500 mg) orally every 12 hours for 10–14 days.

Anthrax

Adults: 750 mg orally every 12 hours for 7–10 days.

Children: 10–15 mg/kg (maximum 750 mg) orally every 12 hours for 7–10 days.

Prophylaxis against meningitis due to Neisseria meningitidis

Adults and children: 500 mg orally in a single dose.

Contraindications

- Hypersensitivity to any quinolone.
- Pregnancy.

Precautions

Reduced dosage should be considered in patients with hepatic or renal impairment.

Ciprofloxacin should be administered cautiously to patients with epilepsy since seizures may be precipitated.

An adequate fluid intake must be ensured to prevent crystalluria.

Use in pregnancy and early childhood

Ciprofloxacin should not be used during pregnancy. Use in children is controversial, since quinolones have been shown to induce arthropathy in the weight-bearing joints of young animals. Although damage to growing cartilage has not been demonstrated in humans, use of quinolones is not generally recommended in children and adolescents. However, in severe infections the benefits are considered to outweigh the risk.

Adverse effects

Ciprofloxacin is generally well tolerated. The most frequently reported adverse effects are nausea, diarrhoea, vomiting, dyspepsia, abdominal pain, headache, restlessness, tremor, confusion, rash, dizziness and pruritus.

Myalgia, tendinitis, and hepatic and renal disturbances have also been reported.

Drug interactions

Plasma levels of theophylline may be increased. A prolonged bleeding time has been reported in patients receiving anticoagulants and ciprofloxacin concurrently.

The susceptibility of *Shigella* spp. to ciprofloxacin has been reported to be reduced in patients previously treated with nalidixic acid.

Overdosage

Gastric lavage is of value if performed promptly. Electrolyte balance must be maintained. Serum concentrations of ciprofloxacin may be lowered by dialysis.

Storage

Tablets should be stored in well-closed containers.

Clindamycin

Injection, 150 mg (as phosphate)/ml

General information

Clindamycin is a semisynthetic derivative of lincomycin belonging to the lincosamide group of antimicrobials. It is active against most aerobic Gram-positive cocci, including staphylococci and *Streptococcus pneumoniae*, as well as several anaerobic Gram-negative and Gram-positive organisms.

Following intramuscular or intravenous administration, clindamycin is rapidly hydrolysed and distributed into all tissues except the cerebrospinal fluid. The plasma half-life is 2–3 hours in adults and children with normal renal function but is prolonged in patients with renal disease. The drug is excreted in the urine.

Clindamycin readily crosses the placenta and is excreted in breast milk.

Clinical information

Uses

Treatment of:

- pneumonia due to *Pneumocystis carinii* in adults, together with primaquine
- pneumonia due to *Staphylococcus aureus* in adults and children > 5 years
- aspiration pneumonia and lung abscesses
- streptococcal necrotizing fasciitis, together with benzylpenicillin
- gangrene in patients allergic to penicillins, together with gentamicin and metronidazole
- pyomyositis
- osteomyelitis and septic arthritis due to *Staphylococcus aureus* in adults and children > 5 years
- very severe pelvic inflammatory disease in adults (hospitalized patients), together with gentamicin and doxycycline
- septicaemia (initial empirical therapy) in adults and children > 5 years, together with gentamicin.

Prophylaxis in contaminated surgery, together with gentamicin.

Dosage and administration

Pneumonia due to Pneumocystis carinii in adults

600 mg i.v. or orally every 6 hours, together with primaquine 15 mg orally every 6 hours for 21 days.

Aspiration pneumonia and lung abscesses

Adults: 600 mg i.v. every 8 hours for 14 days (once clinical improvement occurs, 300–450 mg orally every 6–8 hours may be substituted).

Children: 10 mg/kg (maximum 450 mg) i.v. or i.m. every 6 hours for 14 days (once clinical improvement occurs, 5–10 mg/kg (maximum 450 mg) orally every 6–8 hours may be substituted).

Pneumonia due to Staphylococcus aureus in adults and children > 5 years

Adults: 600 mg i.v. every 8 hours for 10–14 days (once clinical improvement occurs, 300–450 mg orally every 6–8 hours may be substituted).

Children > 5 years: 10 mg/kg (maximum 450 mg) i.v. or i.m. every 6 hours for 10–14 days (once clinical improvement occurs, 5–10 mg/kg (maximum 450 mg) orally every 6–8 hours may be substituted).

Streptococcal necrotizing fasciitis

Adults: 600 mg i.v. every 8 hours, together with benzylpenicillin 4 million IU i.v. or i.m. every 4 hours for at least 7 days.

Children: 10 mg / kg (maximum 450 mg) i.v. every 6 hours, together with benzylpenicillin 100 000 IU / kg (maximum 4 million IU) i.v. or i.m. every 4 hours for at least 7 days.

Gangrene in patients allergic to penicillins

Adults: 600 mg orally or i.v. every 6–8 hours, together with gentamicin 5–7 mg / kg i.v. or i.m. daily in divided doses and metronidazole 500 mg i.v. every 8 hours for at least 7 days (once clinical improvement occurs, rectal formulations of metronidazole may be substituted).

Children: 10 mg / kg (maximum 450 mg) orally or i.v. every 6–8 hours, together with gentamicin 7.5 mg / kg i.v. or i.m. in 1–3 divided doses daily and metronidazole 12.5 mg / kg (maximum 500 mg) i.v. every 8 hours for at least 7 days (once clinical improvement occurs, rectal formulations of metronidazole may be substituted).

Pyomyositis

Adults: 600 mg i.v. every 8 hours for 5–10 days (once clinical improvement occurs, 300–450 mg orally every 4–6 hours may be substituted).

Children: 10 mg / kg (maximum 450 mg) i.v. every 6 hours for 5–10 days (once clinical improvement occurs, 5–10 mg / kg (maximum 450 mg) orally every 4–6 hours may be substituted).

Osteomyelitis due to Staphylococcus aureus in adults and children > 5 years

Adults: 600 mg i.v. every 8 hours for 4–6 weeks (if the duration of parenteral therapy is less than 4–6 weeks, treatment should be completed with 300–450 mg orally every 6 hours).

Children > 5 years: 10 mg / kg (maximum 450 mg) i.v. every 6 hours for 4–6 days (or until clinical improvement occurs), followed by 10 mg / kg (maximum 450 mg) orally every 6 hours to complete the treatment course of 3–4 weeks.

Septic arthritis due to Staphylococcus aureus in adults and children > 5 years

Adults: 600 mg i.v. every 8 hours for 2–3 weeks (if the duration of parenteral therapy is less than 2–3 weeks, the treatment course should be completed with 300–450 mg orally every 6 hours).

Children > 5 years: 10 mg / kg (maximum 450 mg) i.v. every 6 hours for 4–6 days (or until clinical improvement occurs), followed by 10 mg / kg (maximum 450 mg) orally every 6 hours to complete the treatment course of 2–3 weeks.

In some cases, especially in adults, repeated aspiration or surgical washout of the joint may also be necessary.

Very severe pelvic inflammatory disease in adults

Hospitalized patients

900 mg i.v. every 8 hours, together with *either* gentamicin 5–7 mg / kg i.v. or i.m. every 24 hours *or* gentamicin 1.5–2.0 mg / kg i.v. or i.m. every 8 hours for at least 4 days (or for 48 hours after clinical improvement occurs), followed by doxycycline 100 mg orally every 12 hours for 10–14 days.

Initial empirical therapy for septicaemia in adults and children > 5 years

600 mg i.v. every 8 hours, together with *either* gentamicin 5–7 mg / kg i.v. every 24 hours *or* gentamicin 1.5 mg / kg i.v. or i.m. every 8 hours.

Clindamycin (continued)

Prophylaxis in contaminated surgery
Adults and children: 600 mg i.v., together with gentamicin 5 mg/kg i.v. at induction of anaesthesia.

Contraindications

- Hypersensitivity to lincosamides.
- Severe hepatic or renal impairment.
- A history of ulcerative colitis or antimicrobial-associated colitis.

Precautions

If clinically important or persistent diarrhoea occurs, treatment should be immediately discontinued.

Renal and hepatic function should be monitored when treatment is prolonged.

Use in pregnancy

Safe use in pregnancy has not been established. Clindamycin should be used only when the need of the mother outweighs the risk of harm to the fetus.

Adverse effects

Nausea, vomiting, diarrhoea and abdominal pain are the most common adverse effects. Rarely, antimicrobial-associated pseudomembranous colitis due to *Clostridium difficile* occurs. When this is suspected, treatment should be immediately discontinued.

Skin rashes and urticaria are frequent, while erythema multiforme and anaphylaxis are rare.

Drug interactions

Clindamycin may enhance the effect of neuromuscular-blocking agents.

Storage

Injections should be stored in tightly closed containers.

Cloxacillin[1]

Capsule, 500 mg (as sodium salt)
Powder for oral solution, 125 mg (as sodium salt)/5 ml
Powder for injection, 500 mg (as sodium salt) in vial

General information

Cloxacillin is a semisynthetic derivative of penicillin that is resistant to breakdown by the enzyme penicillinase. It has a broad spectrum of activity and is bactericidal against most strains of β-lactamase-producing *Staphylococcus aureus*.

Cloxacillin is absorbed from the gastrointestinal tract but food decreases its absorption. It is well distributed in the tissues, has a plasma half-life of about 30 minutes and is rapidly excreted in the urine mainly unchanged, but also as metabolites. It crosses the placenta and is excreted in breast milk.

Clinical information

Uses

Treatment of:

- pneumonia due to *Staphylococcus aureus* in adults and children >5 years

[1] Dicloxacillin, flucloxacillin, nafcillin or oxacillin may serve as alternatives.

- pneumonia due to *Staphylococcus aureus* in children aged from 2 months to 5 years and nosocomial pneumonia, together with gentamicin
- localized purulent skin lesions, impetigo and pyomyositis
- contaminated soft tissue injuries, together with gentamicin and metronidazole
- septic arthritis (initial empirical therapy) in adults, together with ceftriaxone
- septic arthritis and osteomyelitis due to *Staphylococcus aureus* in adults
- septic arthritis (initial empirical therapy), septic arthritis and osteomyelitis due to *Staphylococcus aureus*, and septicaemia (initial empirical therapy) in children, together with ceftriaxone or cefotaxime
- osteomyelitis due to *Haemophilus influenzae* or unknown pathogen in children ≤5 years, together with amoxicillin + clavulanic acid and either ceftriaxone or cefotaxime
- osteomyelitis due to *Salmonella* spp. in children ≤5 years, together with either ceftriaxone or cefotaxime and either sulfamethoxazole + trimethoprim or amoxicillin or ciprofloxacin
- infective endocarditis (initial empirical therapy), together with benzylpenicillin and gentamicin
- endocarditis due to meticillin-susceptible *Staphylococcus aureus*, together with gentamicin
- septicaemia (initial empirical therapy) in adults, together with gentamicin.

Dosage and administration

Intravenous formulations of cloxacillin should be administered over 2 minutes.

Pneumonia due to Staphylococcus aureus

Adults: 1–2 g i.v. or i.m. every 6 hours for 10–14 days.

Children >5 years: 50 mg/kg (maximum 2 g) i.v. or i.m. every 6 hours for 10–14 days.

Children aged from 2 months to 5 years: 25–50 mg/kg (maximum 2 g) orally every 6 hours, together with gentamicin 7.5 mg/kg i.v. in 1–3 divided doses daily for at least 3 weeks.

Nosocomial pneumonia

Adults: 1–2 g i.v. every 6 hours, together with gentamicin 5–7 mg/kg i.v. daily in divided doses for 7 days.

Children: 50 mg/kg (maximum 2 g) i.v. every 6 hours, together with gentamicin 7.5 mg/kg in 1–3 divided doses daily for 7 days.

In hospitals with a high prevalence of meticillin-resistant *Staphylococcus aureus*, vancomycin 1 g (children: 20 mg/kg; maximum 1 g) i.v. every 12 hours for 10–14 days should also be added to the above regimens.

Localized purulent skin lesions and impetigo

Adults: 250–500 mg orally every 6 hours for 5–7 days.

Children: 12.5–25 mg/kg (maximum 500 mg) orally every 6 hours for 5–7 days.

Pyomyositis

Adults: 2 g i.v. or i.m. every 6 hours for 5–10 days (once clinical improvement occurs, 500 mg orally every 6 hours may be substituted).

Children: 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 6 hours for 5–10 days (once clinical improvement occurs, 12.5–25 mg/kg (maximum 500 mg) orally every 6 hours may be substituted).

Contaminated soft tissue injuries

Adults: 2 g i.v. or i.m. every 6 hours for 5–10 days (once clinical improvement occurs, 500 mg orally every 6 hours may

Cloxacillin (continued)

be substituted), supplemented by gentamicin 5–7 mg/kg i.v. or i.m. daily in divided doses and metronidazole 500 mg i.v. every 8 hours (once clinical improvement occurs, oral or rectal formulations of metronidazole may be substituted).

Children: 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 6 hours for 5–10 days (once clinical improvement occurs, 12.5–25 mg/kg (maximum 500 mg) orally every 6 hours may be substituted), supplemented by gentamicin 7.5 mg/kg i.v. or i.m. in 1–3 divided doses daily and metronidazole 12.5 mg/kg (maximum 500 mg) i.v. every 8 hours (once clinical improvement occurs, oral or rectal formulations of metronidazole may be substituted).

Osteomyelitis due to Staphylococcus aureus

Adults: 2 g i.v. or i.m. every 6 hours for at least the initial 14 days of therapy, but preferably the entire treatment course of 4–6 weeks (if the duration of parenteral therapy is less than 4–6 weeks, the treatment course should be completed with 1 g orally every 6 hours).

Children >5 years: 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 4–6 hours for 4–6 days (or until clinical improvement occurs), followed by 25 mg/kg (maximum 500 mg) orally every 6 hours to complete the treatment course of 3–4 weeks *or* 25 mg/kg (maximum 500 mg) orally every 6 hours to complete the treatment course of 3–4 weeks, following initial therapy with ceftriaxone 50–75 mg/kg (maximum 1 g) i.v. or i.m. every 24 hours for 4–6 days (or until clinical improvement occurs).

Children aged from 2 months to 5 years: 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 4–6 hours, together with ceftriaxone 50–75 mg/kg (maximum 1 g) i.v. or i.m. every 24 hours for 4–6 days (or until clinical improvement occurs), followed by 12.5 mg/kg (maximum 500 mg) orally every 6 hours to complete the treatment course of 3–4 weeks.

Neonates: 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 4–6 hours, together with cefotaxime 50–75 mg/kg (maximum 2 g) i.v. every 8 hours for 4–6 days (or until clinical improvement occurs), followed by 12.5 mg/kg (maximum 500 mg) orally every 6 hours to complete the treatment course of 3–4 weeks.

Osteomyelitis due to Haemophilus influenzae or unknown pathogen in children ≤ 5 years

Children aged from 2 months to 5 years: 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 4–6 hours, together with ceftriaxone 50–75 mg/kg (maximum 1 g) i.v. or i.m. every 24 hours for 4–6 days (or until clinical improvement occurs), followed by amoxicillin 15 mg/kg + clavulanic acid (maximum 500 mg) orally every 8 hours to complete the treatment course of 3–4 weeks.

Neonates: 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 4–6 hours, together with cefotaxime 50–75 mg/kg (maximum 2 g) i.v. every 8 hours for 4–6 days (or until clinical improvement occurs), followed by amoxicillin 15 mg/kg + clavulanic acid (maximum 500 mg) orally every 8 hours to complete the treatment course of 3–4 weeks.

Osteomyelitis due to Salmonella spp. in children ≤ 5 years

Children aged from 2 months to 5 years: 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 4–6 hours, together with ceftriaxone 50–75 mg/kg (maximum 1 g) i.v. or i.m. every 24 hours for 4–6 days (or until clinical improvement occurs), followed by *either* sulfamethoxazole 20 mg/kg + trimethoprim 4 mg/kg (maximum 800 mg + 160 mg) orally every 12 hours *or*

amoxicillin 7.5–15 mg/kg (maximum 1 g) orally every 8 hours *or* ciprofloxacin 10–15 mg/kg (maximum 500 mg) orally every 12 hours to complete the treatment course of 6 weeks.

Neonates: 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 4–6 hours, together with cefotaxime 50–75 mg/kg (maximum 2 g) i.v. every 8 hours for 4–6 days (or until clinical improvement occurs), followed by *either* sulfamethoxazole 20 mg/kg + trimethoprim 4 mg/kg (maximum 800 mg + 160 mg) orally every 12 hours *or* amoxicillin 7.5–15 mg/kg (maximum 1 g) orally every 8 hours *or* ciprofloxacin 10–15 mg/kg (maximum 500 mg) orally every 12 hours to complete the treatment course of 6 weeks.

Initial empirical therapy for septic arthritis

Adults: 2 g i.v. or i.m. every 6 hours, together with ceftriaxone 1–2 g i.v. or i.m. every 24 hours.

Children ≥2 months: 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 6 hours, together with ceftriaxone 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 24 hours.

Neonates: 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 6 hours, together with cefotaxime 50–75 mg/kg (maximum 2 g) i.v. every 8 hours.

Septic arthritis due to Staphylococcus aureus

Adults: 2 g i.v. or i.m. every 6 hours for 2–3 weeks (if the duration of parenteral therapy is less than 2–3 weeks, the treatment course should be completed with 1 g orally every 6 hours).

Children >5 years: 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 4–6 hours for 4–6 days (or until clinical improvement occurs), followed by 25 mg/kg (maximum 500 mg) orally every 6 hours to complete the treatment course of 2–3 weeks *or* 25 mg/kg (maximum 500 mg) orally every 6 hours to complete the treatment course of 2–3 weeks, following initial therapy with ceftriaxone 50–75 mg/kg (maximum 1 g) i.v. or i.m. every 24 hours for 4–6 days (or until clinical improvement occurs).

Children aged from 2 months to 5 years: 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 4–6 hours, together with ceftriaxone 50–75 mg/kg (maximum 1 g) i.v. or i.m. every 24 hours for 4–6 days (or until clinical improvement occurs), followed by 12.5 mg/kg (maximum 500 mg) orally every 6 hours to complete the treatment course of 2–3 weeks.

Neonates: 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 4–6 hours, together with cefotaxime 50–75 mg/kg (maximum 2 g) i.v. or i.m. every 8 hours for 4–6 days (or until clinical improvement occurs), followed by 12.5 mg/kg (maximum 500 mg) orally every 6 hours to complete the treatment course of 2–3 weeks.

In some cases, repeated aspiration or surgical washout of the joint may also be necessary.

Initial empirical therapy for infective endocarditis

Adults: 2 g i.v. every 4 hours, together with benzylpenicillin 3 million IU i.v. every 4 hours and gentamicin 2 mg/kg i.v. every 8 hours.

Children: 50 mg/kg (maximum 2 g) i.v. every 4 hours, together with benzylpenicillin 50 000 IU/kg (maximum 3 million IU) i.v. every 4 hours and gentamicin 2.5 mg/kg (maximum 80 mg) i.v. every 8 hours.

Endocarditis due to Staphylococcus aureus (strains susceptible to meticillin)

Adults: 2 g i.v. every 4 hours for 6 weeks, supplemented for the first 7 days by gentamicin 1 mg/kg i.v. every 8 hours.

Cloxacillin (continued)

Children: 50 mg / kg (maximum 2 g) i.v. every 4 hours for 6 weeks, supplemented for the first 7 days by gentamicin 1 mg / kg i.v. every 8 hours.

Initial empirical therapy for septicaemia

Adults and children >5 years: 2 g i.v. every 4–6 hours, together with *either* gentamicin 5–7 mg / kg i.v. every 24 hours *or* gentamicin 1.5 mg / kg i.v. or i.m. every 8 hours.

Children aged from 2 months to 5 years: 50 mg / kg (maximum 2 g) i.v. every 4–6 hours, together with ceftriaxone 50 mg / kg (maximum 2 g) i.v. or i.m. every 24 hours.

Neonates: 50 mg / kg (maximum 2 g) i.v. every 4–6 hours, together with cefotaxime 50–75 mg / kg (maximum 2 g) i.v. every 8 hours.

Contraindications

Known hypersensitivity to penicillins or cefalosporins.

Precautions

Facilities should be available for treating anaphylaxis whenever penicillins are used. Patients should be questioned carefully about previous allergic reactions before the first dose is administered. If a skin rash develops, the patient should be transferred to a different class of antimicrobial.

Rapid intravenous administration of large doses of cloxacillin may cause hyperkalaemia, dysrhythmias and cardiac arrest, particularly in patients with impaired renal function.

Use in pregnancy

There is no evidence that cloxacillin is teratogenic. It may be used during pregnancy.

Adverse effects

Hypersensitivity reactions are the most common adverse effects, ranging in severity from skin rashes to immediate anaphylaxis.

Phlebitis or thrombophlebitis sometimes follows intravenous administration.

Nausea, vomiting, flatulence, diarrhoea and epigastric pain can occur and may be severe enough to warrant discontinuation of the drug.

Interstitial nephritis has been reported. Neutropenia and thrombocytopenia are rare.

Overdosage

Overdosage can cause convulsions, paralysis and even death.

Excessive blood concentrations can be lowered by haemodialysis.

Storage

Preparations of cloxacillin should be stored in tightly closed containers. Solutions are stable for 3 days after reconstitution.

Doxycycline

Capsule or tablet, 100 mg (as hyclate)
Powder for injection, 100 mg (as hyclate) in ampoule

General information

Doxycycline is a broad-spectrum antibiotic derived from and closely related to oxytetracycline. It differs from the tetracyclines in being more extensively absorbed and more lipid-soluble, and possesses a longer serum half-life that is independent of the patient's renal status.

Clinical information

Uses

Treatment of:

- pneumonia and acute bronchitis in adults and children >8 years
- ornithosis and Q fever in adults and children >8 years
- melioidosis in adults and children >8 years, together with ceftazidime
- cholera in patients who are severely dehydrated
- prostatitis due to *Chlamydia trachomatis* or *Ureaplasma urealyticum* in adults
- human and animal bites and clenched-fist injuries in patients allergic to penicillins, together with metronidazole
- granuloma inguinale in adults
- lymphogranuloma venereum and other chlamydial infections in adults and children >8 years
- pelvic inflammatory disease in adults (ambulatory patients), together with metronidazole and ceftriaxone
- very severe pelvic inflammatory disease in adults (hospitalized patients), together with gentamicin and clindamycin
- moderate or severe pelvic inflammatory disease in adults (hospitalized patients), together with ceftriaxone or ciprofloxacin plus metronidazole
- syphilis in patients allergic to penicillins
- Lyme disease (early stage), anthrax, plague, relapsing fever, leptospirosis and rickettsial infections in adults and children >8 years
- brucellosis in adults and children >8 years, together with rifampicin or rifampicin plus either streptomycin or gentamicin.

Dosage and administration

Acute bronchitis in adults and children >8 years

Adults: 100 mg orally every 12 hours for 5 days.

Children >8 years: 2 mg/kg (maximum 100 mg) orally every 12 hours for 5 days.

Pneumonia in adults and children >8 years

Ambulatory patients

Adults: 100 mg orally every 12 hours for 7–10 days.

Children >8 years: 2 mg/kg (maximum 100 mg) orally every 12 hours for 7–10 days.

Ornithosis, Q fever and anthrax in adults and children >8 years

Adults: 100 mg orally every 12 hours for 7–10 days.

Children >8 years: 2 mg/kg (maximum 100 mg) orally every 12 hours for 7–10 days.

Melioidosis in adults and children >8 years

Adults: 100 mg orally or i.v. every 12 hours, together with ceftazidime 2 g i.v. every 8 hours for at least 14 days.

Doxycycline (continued)

Children >8 years: 2 mg/kg (maximum 100 mg) orally or i.v. every 12 hours, together with ceftazidime 50 mg/kg (maximum 2 g) i.v. every 8 hours for at least 14 days.

After the initial intensive therapy, eradication of any secondary infection is recommended with oral doxycycline for at least 3 months.

Cholera in patients who are severely dehydrated

Adults: 300 mg orally in a single dose.

Children >8 years: 2 mg/kg (maximum 100 mg) orally in a single dose.

Prostatitis due to Chlamydia trachomatis or Ureaplasma urealyticum in adults

100 mg orally every 12 hours for 14 days.

Human and animal bites and clenched-fist injuries in patients allergic to penicillins

Adults: 100 mg orally every 24 hours for 5–10 days, supplemented by metronidazole 400–500 mg orally every 12 hours.

Children >8 years: 2 mg/kg (maximum 100 mg) orally every 24 hours for 5–10 days, supplemented by metronidazole 10–12.5 mg/kg (maximum 250 mg) orally every 12 hours.

Lymphogranuloma venereum in adults and children >8 years

Adults: 100 mg orally every 12 hours for 14 days.

Children >8 years: 2 mg/kg (maximum 100 mg) orally every 12 hours for 14 days.

Granuloma inguinale in adults

100 mg orally every 12 hours for 14 days (or until the lesion has completely healed).

Other chlamydial infections and plague in adults and children >8 years

Adults: 100 mg orally every 12 hours for 7 days.

Children >8 years: 2 mg/kg (maximum 100 mg) orally every 12 hours for 7 days.

Pelvic inflammatory disease in adults

Ambulatory patients

100 mg orally every 12 hours, together with metronidazole 400–500 mg orally every 8 hours for 10 days, following initial therapy with ceftriaxone 250 mg i.m. in a single dose.

Hospitalized patients with very severe disease

100 mg orally every 12 hours for 10–14 days, following initial therapy with *either* gentamicin 5–7 mg/kg i.v. or i.m. every 24 hours *or* gentamicin 1.5–2.0 mg/kg i.v. or i.m. every 8 hours, together with clindamycin 900 mg i.v. every 8 hours for at least 4 days (or for 48 hours after clinical improvement occurs).

Hospitalized patients with moderate or severe disease

100 mg orally every 12 hours for 10–14 days, following initial therapy with *either* ceftriaxone 250 mg i.m. every 12 hours for at least 4 days (or for 48 hours after clinical improvement occurs) *or* ciprofloxacin 500 mg orally every 12 hours plus metronidazole 400–500 mg orally every 8 hours for at least 4 days (or for 48 hours after clinical improvement occurs).

Syphilis in patients allergic to penicillins

Adults: 100 mg orally every 12 hours for 30 days.

Children >8 years: 2 mg/kg (maximum 100 mg) orally every 12 hours for 30 days.

Lyme disease (early stage) in adults and children >8 years

Adults: 100 mg orally every 12 hours for 10–21 days.

Children >8 years: 2 mg/kg (maximum 100 mg) orally every 12 hours for 10–21 days.

Relapsing fever in adults and children >8 years

Adults: 100 mg orally in a single dose.

Children >8 years: 2 mg/kg (maximum 100 mg) orally in a single dose.

Leptospirosis in adults and children >8 years

Adults: 100 mg orally every 12 hours for 5–7 days.

Children >8 years: 2 mg/kg (maximum 100 mg) orally every 12 hours for 5–7 days.

Brucellosis in adults and children >8 years

Adults: 100 mg orally every 12 hours, together with rifampicin 600 mg orally every 24 hours for 6 weeks *or* 100 mg orally every 12 hours for 6 weeks, supplemented for the first 2 weeks by *either* streptomycin 1 g i.m. every 24 hours *or* gentamicin 5–7 mg/kg i.v. every 24 hours.

Children >8 years: 2 mg/kg (maximum 100 mg) orally every 12 hours, together with rifampicin 15 mg/kg (maximum 600 mg) orally every 24 hours for 6 weeks *or* 2 mg/kg (maximum 100 mg) orally every 12 hours for 6 weeks, supplemented for the first 2 weeks by *either* streptomycin 15 mg/kg (maximum 1 g) i.m. every 24 hours *or* gentamicin 7.5 mg/kg i.v. in 1–3 divided doses daily.

Rickettsial infections in adults and children >8 years

Adults: 100 mg orally every 12 hours for 7–10 days (or for 48 hours after resolution of fever).

Children >8 years: 2 mg/kg (maximum 100 mg) orally every 12 hours for 7–10 days (or for 48 hours after resolution of fever).

Contraindications

- Known hypersensitivity.
- Pregnancy.
- Age up to 8 years.

Precautions

Troublesome oesophagitis may be averted if the patient is propped up while swallowing capsules or tablets and washes them down immediately with a glass of water. Capsules and tablets should not be taken with milk or with magnesium or aluminium salts since these impair the absorption of doxycycline.

Use in pregnancy and early childhood

Doxycycline is generally contraindicated in pregnancy and during early childhood. However, it can be given to children aged up to 8 years in a single dose for the treatment of cholera and relapsing fever. Because it is deposited in developing teeth and bones and impairs skeletal calcification, it can result in abnormal osteogenesis and permanent staining of teeth, and occasionally causes hypoplasia of dental enamel.

Adverse effects

Gastrointestinal irritation is common and phototoxic reactions and increased vulnerability to sunburn have been reported.

Transient depression of bone growth is largely reversible, but discoloration of teeth and enamel hypoplasia are permanent.

Drug interactions

The action of oral anticoagulants may be potentiated. Severe renal failure has been

Doxycycline (continued)

reported in patients who have received a halogenated anaesthetic agent while taking doxycycline.

Storage

Doxycycline capsules, tablets and powder for injection should be kept in well-closed containers, protected from light.

Erythromycin

Capsule or tablet, 250 mg (as stearate or ethyl succinate)
Powder for oral suspension, 125 mg (as stearate or ethyl succinate)
Eye ointment, 1%

General information

Erythromycin is a macrolide antibiotic produced by *Streptomyces erythreus*. It has selective bacteriostatic activity against both streptococci and staphylococci and some Gram-positive bacilli.

Because erythromycin is inactivated by gastric juices, oral formulations are protected by an enteric coating. The drug diffuses rapidly into all tissues except the brain and cerebrospinal fluid, and readily crosses the placental barrier. The plasma half-life is approximately 90 minutes. Erythromycin is partially demethylated in the liver and excreted largely via the bile and faeces.

Clinical information

Uses

Treatment of:

- acute pharyngitis and acute cervical adenitis in patients allergic to penicillins
- diphtheria and legionellosis
- pneumonia in adults and children >5 years
- atypical pneumonia in adults and children >5 years, together with either chloramphenicol or cefuroxime or ceftriaxone or benzylpenicillin or benzylpenicillin plus gentamicin
- pertussis (whooping cough) in children
- ornithosis and Q fever in children ≤8 years
- gingival infections and periodontitis
- enteritis due to *Campylobacter jejuni*
- prostatitis due to *Chlamydia trachomatis* or *Ureaplasma urealyticum* and chancroid in adults
- lymphogranuloma venereum, chlamydial ophthalmia, other chlamydial infections, and syphilis in patients allergic to penicillins
- relapsing fever.

Prevention of neonatal gonococcal conjunctivitis and recurrence of rheumatic fever due to group A β-haemolytic streptococci in patients allergic to penicillins.

Postsplenectomy prophylaxis.

Dosage and administration

Erythromycin tablets should not be broken in half before administration.

Acute pharyngitis and acute cervical adenitis in patients allergic to penicillins

Adults: 500 mg orally every 6 hours for 10 days.

Children: 10–15 mg/kg (maximum 500 mg) orally every 6 hours for 10 days.

Diphtheria

Adults: 500 mg orally every 6 hours for 7 days, following initial therapy with diphtheria antitoxin 20 000–100 000 IU i.v. or i.m.

Children: 10–15 mg/kg (maximum 500 mg) orally every 6 hours for 7 days, following initial therapy with diphtheria antitoxin 20 000–100 000 IU i.v. or i.m.

Vaccination with diphtheria–pertussis–tetanus should be offered during convalescence.

Pneumonia in adults and children >5 years

Ambulatory patients

Adults: 500 mg orally every 6 hours for 5 days.

Children >5 years: 10–15 mg/kg (maximum 500 mg) orally every 6 hours for 5 days.

Patients with atypical pneumonia should receive treatment for 14 days.

Hospitalized patients with atypical pneumonia

Adults: 1 g i.v. every 6 hours for 14 days, supplemented for the first 5 days by benzylpenicillin 2 million IU i.v. or i.m. every 4–6 hours *or* for the first 7 days by *either* chloramphenicol 1 g i.v. every 6 hours *or* cefuroxime 1.0–1.5 g i.v. every 6–8 hours *or* ceftriaxone 1 g i.v. or i.m. every 12–24 hours *or* benzylpenicillin 2 million IU i.v. or i.m. every 4–6 hours plus gentamicin 5–7 mg/kg i.v. daily in divided doses.

Children: 10 mg/kg (maximum 1 g) i.v. every 6 hours for 14 days, supplemented for the first 5 days by benzylpenicillin 50 000–100 000 IU/kg (maximum 2 million IU) i.v. or i.m. every 4–6 hours *or* for the first 7 days by *either* chloramphenicol 25 mg/kg (maximum 750 mg) i.v. every 6 hours *or* cefuroxime 50–60 mg/kg (maximum 1.5 g) i.v. every 6–8 hours *or* ceftriaxone 50 mg/kg (maximum 1 g) i.v. or i.m. every 12–24 hours *or* benzylpenicillin 50 000–100 000 IU/kg (maximum 2 million IU) i.v. or i.m. every 4–6 hours plus gentamicin 7.5 mg/kg i.v. in 1–3 divided doses daily.

Legionellosis

Adults: 1 g i.v. every 6 hours for 10 days (once clinical improvement occurs, 500 mg orally every 6 hours may be substituted).

Children: 10 mg/kg (maximum 500 mg) i.v. every 6 hours for 10 days (once clinical improvement occurs, 7.5 mg/kg (maximum 500 mg) orally every 6 hours may be substituted).

Pertussis (whooping cough) in children

50 mg/kg (maximum 2 g) orally in 4 divided doses daily for 14 days.

Ornithosis and Q fever in children ≤8 years

10–15 mg/kg (maximum 500 mg) orally every 6 hours for 7–10 days.

Gingival infections and periodontitis

Adults: 250 mg orally every 6 hours for 5 days.

Children: 7.5 mg/kg (maximum 250 mg) orally every 6 hours for 5 days.

Enteritis due to Campylobacter jejuni

Adults: 500 mg orally every 6 hours for 7–10 days.

Children: 10 mg/kg (maximum 500 mg) orally every 6 hours for 7–10 days.

Prostatitis due to Chlamydia trachomatis or Ureaplasma urealyticum in adults

500 mg orally every 6 hours for 14 days.

Lymphogranuloma venereum

Adults: 500 mg orally every 6 hours for 14 days.

Children: 12.5 mg/kg (maximum 500 mg) orally every 6 hours for 14 days.

Chlamydial ophthalmia

12.5 mg/kg (as syrup; maximum 500 mg) orally every 6 hours for 14 days.

Erythromycin (continued)

Other chlamydial infections
Adults: 500 mg orally every 6 hours for 7 days.

Children: 10–15 mg/kg (maximum 500 mg) orally every 6 hours for 7 days.

Syphilis in patients allergic to penicillins
Adults: 500 mg orally every 6 hours for 15 days.

Children: 7.5–12.5 mg/kg (maximum 250 mg) orally every 6 hours for 30 days.

Chancroid in adults
500 mg orally every 6 hours for 7 days. (Longer treatment courses may be necessary in immunocompromised patients.)

Relapsing fever
Adults: 500 mg orally in a single dose.

Children: 12.5 mg/kg (maximum 500 mg) orally in a single dose.

Prevention of neonatal gonococcal conjunctivitis
A single application of eye ointment immediately after birth should be sufficient.

Prevention of recurrence of rheumatic fever due to group A β-haemolytic streptococci in patients allergic to penicillins
Adults and children: 250 mg orally every 12 hours.

Postsplenectomy prophylaxis
Adults: 250 mg orally every 24 hours.

Children: 7.5 mg/kg (maximum 250 mg) orally every 24 hours.

Contraindications
Known hypersensitivity to erythromycin or other macrolides.

Precautions
Hepatic function should be monitored in patients with a previous history of liver disease.

Use in pregnancy
Erythromycin has not been shown to be mutagenic, teratogenic or embryotoxic; it can be used during pregnancy.

Adverse effects
Nausea, vomiting and diarrhoea can occur.

Cholestatic hepatitis, which may present with symptoms suggestive of acute cholecystitis, occasionally complicates prolonged courses of treatment. Symptoms resolve rapidly when the drug is withdrawn.

Anaphylaxis and other hypersensitivity reactions are rare.

Drug interactions
Erythromycin, chloramphenicol and clindamycin have a similar bacteriostatic action and tend to be mutually antagonistic when administered together. Erythromycin decreases the rate of metabolism of carbamazepine and warfarin in the liver to a degree that can warrant readjustment of dosage.

Overdosage
Symptoms of overdosage include severe nausea, vomiting, diarrhoea and hearing loss. Induction of emesis or gastric lavage may be of value if undertaken within a few hours of ingestion.

Storage
Capsules and tablets should be stored in tightly closed containers. Suspension and eye ointment should be stored in well-closed containers protected from light.

Gentamicin

Injection, 10 mg, 40 mg (as sulfate)/ml in 2-ml vial

General information

Gentamicin is a broad-spectrum aminoglycoside produced by *Micromonospora purpurea*. It is bactericidal against many aerobic Gram-negative bacteria but has little activity against most Gram-positive organisms with the exception of staphylococci.

Gentamicin is poorly absorbed from the gastrointestinal tract. After parenteral administration, it is widely distributed in the body tissues and fluids. Its penetration into the cerebrospinal fluid is poor. Its plasma half-life is 2–4 hours and it is excreted unchanged in the urine. A small fraction is tightly bound intracellularly and accumulates in the body tissues. It readily crosses the placenta and is distributed in breast milk.

Clinical information

Uses

Treatment of:

- pneumonia in adults and children >5 years, together with benzylpenicillin
- atypical pneumonia in adults and children >5 years, together with benzylpenicillin and erythromycin
- nosocomial pneumonia, together with cloxacillin or ceftazidime
- pneumonia due to *Staphylococcus aureus* in children aged from 2 months to 5 years, together with cloxacillin
- neonatal pneumonia, together with amoxicillin
- acute cholecystitis and acute pyelonephritis, together with ampicillin
- acute peritonitis, together with ampicillin and metronidazole
- gangrene, together with metronidazole and either benzylpenicillin or clindamycin
- contaminated soft tissue injuries, together with metronidazole and cloxacillin
- very severe pelvic inflammatory disease in adults (hospitalized patients), together with clindamycin and doxycycline
- infective endocarditis (initial empirical therapy), together with benzylpenicillin and cloxacillin
- infective endocarditis (initial empirical therapy) in patients allergic to penicillins or with nosocomial infections, and prosthetic valve endocarditis, together with vancomycin
- endocarditis due to α-haemolytic streptococci, together with benzylpenicillin or ampicillin
- endocarditis due to enterococci, together with benzylpenicillin or ampicillin
- endocarditis due to meticillin-susceptible *Staphylococcus aureus*, together with cloxacillin
- culture-negative endocarditis, together with benzylpenicillin
- neonatal meningitis due to unknown pathogen and neonatal meningitis due to *Listeria monocytogenes*, together with ampicillin
- neonatal meningitis due to group B streptococci, together with benzylpenicillin
- brucellosis, together with doxycycline or sulfamethoxazole + trimethoprim
- tularaemia and plague
- septicaemia (initial empirical therapy) in adults and children >5 years, together with cloxacillin or cefazolin or clindamycin or chloramphenicol
- neonatal septicaemia (initial empirical therapy), together with ampicillin.

Gentamicin (continued)

Prophylaxis in contaminated surgery, together with clindamycin.

Dosage and administration

The dosages should be reduced in patients with renal impairment.

When gentamicin is used in combination with a β-lactam antimicrobial in the treatment of endocarditis, it should be administered every 8 hours. Basal plasma levels of gentamicin should not exceed 1 mg/l. The maximum period of gentamicin therapy without monitoring plasma levels should be 72 hours. If vancomycin is used, peak plasma levels of 30–40 mg/l and basal plasma levels of 5–15 mg/l are recommended. These levels are specific for the management of endocarditis and do not apply to other circumstances.

Pneumonia in adults and children >5 years

Hospitalized patients

Adults: 5–7 mg/kg i.v. daily in divided doses, together with benzylpenicillin 2 million IU i.v. or i.m. every 4–6 hours for 7 days.

Children >5 years: 7.5 mg/kg i.v. in 1–3 divided doses daily, together with benzylpenicillin 50 000–100 000 IU/kg (maximum 2 million IU) i.v. or i.m. every 4–6 hours for 7 days.

Patients with atypical pneumonia should also receive erythromycin 1 g (children: 10 mg/kg; maximum 1 g) i.v. every 6 hours for 14 days.

Pneumonia due to Staphylococcus aureus in children aged from 2 months to 5 years

7.5 mg/kg i.v. in 1–3 divided doses daily, together with cloxacillin 25–50 mg/kg (maximum 2 g) orally every 6 hours for at least 3 weeks.

Neonatal pneumonia

2.5 mg/kg i.v. every 8 hours (neonates <7 days: 2.5 mg/kg i.v. every 12 hours), together with amoxicillin 30 mg/kg i.v. every 12 hours for a total of at least 5 days.

Nosocomial pneumonia

Adults: 5–7 mg/kg i.v. daily in divided doses for 7 days, supplemented by *either* cloxacillin 1–2 g i.v. every 6 hours *or* ceftazidime 1 g i.v. every 8 hours.

Children: 7.5 mg/kg i.v. in 1–3 divided doses daily for 7 days, supplemented by *either* cloxacillin 50 mg/kg (maximum 2 g) i.v. every 6 hours *or* ceftazidime 25 mg/kg (maximum 1 g) i.v. every 8 hours.

In hospitals with a high prevalence of meticillin-resistant *Staphylococcus aureus*, vancomycin 1 g (children: 20 mg/kg; maximum 1 g) i.v. every 12 hours for 10–14 days should be added to the above regimens.

Acute cholecystitis

Adults: 5–7 mg/kg i.v. daily in divided doses, together with ampicillin 1–2 g i.v. or i.m. every 6 hours for up to 7 days.

Children: 7.5 mg/kg i.v. in 1–3 divided doses daily, together with ampicillin 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 6 hours for up to 7 days.

Acute peritonitis

Adults: 5–7 mg/kg i.v. daily in divided doses for at least 7 days, supplemented by ampicillin 2 g i.v. or i.m. every 6 hours and metronidazole 500 mg i.v. every 8–12 hours.

Children: 7.5 mg/kg i.v. in 1–3 divided doses daily for at least 7 days, supplemented by ampicillin 50 mg/kg (maximum 2 g) i.v. or i.m. every 6 hours and metronidazole 12.5 mg/kg (maximum 500 mg) i.v. every 8–12 hours.

For patients who are allergic to penicillins, ampicillin should be deleted from the above regimens.

Acute pyelonephritis

Adults: 5–7 mg/kg orally daily in divided doses for 7 days, supplemented for up to 14 days by ampicillin 1–2 g i.v. or i.m. every 6 hours.

Children: 7.5 mg/kg orally in 1–3 divided doses daily for 7 days, supplemented for up to 14 days by ampicillin 50 mg/kg (maximum 2 g) i.v. or i.m. every 6 hours.

Gangrene

Adults: 5–7 mg/kg i.v. or i.m. daily in divided doses for at least 7 days, supplemented by benzylpenicillin 4 million IU i.v. or i.m. every 4 hours and metronidazole 500 mg i.v. every 8 hours (once clinical improvement occurs, rectal formulations of metronidazole may be substituted).

Children: 7.5 mg/kg i.v. or i.m. in 1–3 divided doses daily for at least 7 days, supplemented by benzylpenicillin 100 000 IU/kg (maximum 4 million IU) i.v. or i.m. every 4 hours and metronidazole 12.5 mg/kg (maximum 500 mg) i.v. every 8 hours (once clinical improvement occurs, rectal formulations of metronidazole may be substituted).

For patients who are allergic to penicillins, benzylpenicillin should be replaced by clindamycin 600 mg (children: 10 mg/kg; maximum 450 mg) orally or i.v. every 6–8 hours.

Contaminated soft tissue injuries

Adults: 5–7 mg/kg i.v. or i.m. daily in divided doses for 5–10 days, supplemented by metronidazole 500 mg i.v. every 8 hours (once clinical improvement occurs, oral or rectal formulations of metronidazole may be substituted) and cloxacillin 2 g i.v. or i.m. every 6 hours (once clinical improvement occurs, cloxacillin 500 mg orally every 6 hours may be substituted).

Children: 7.5 mg/kg i.v. or i.m. in 1–3 divided doses daily for 5–10 days, supplemented by metronidazole 12.5 mg/kg (maximum 500 mg) i.v. every 8 hours (once clinical improvement occurs, oral or rectal formulations of metronidazole may be substituted) and cloxacillin 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 6 hours (once clinical improvement occurs, cloxacillin 12.5–25 mg/kg (maximum 500 mg) orally every 6 hours may be substituted).

Very severe pelvic inflammatory disease in adults

Hospitalized patients

5–7 mg/kg i.v. or i.m. every 24 hours or 1.5–2.0 mg/kg i.v. or i.m. every 8 hours, together with clindamycin 900 mg i.v. every 8 hours for at least 4 days (or for 48 hours after clinical improvement occurs), followed by doxycycline 100 mg orally every 12 hours for 10–14 days.

Initial empirical therapy for infective endocarditis

Adults: 2 mg/kg i.v. every 8 hours, together with benzylpenicillin 3 million IU i.v. every 4 hours and cloxacillin 2 g i.v. every 4 hours.

Children: 2.5 mg/kg (maximum 80 mg) i.v. every 8 hours, together with benzylpenicillin 50 000 IU/kg (maximum 3 million IU) i.v. every 4 hours and cloxacillin 50 mg/kg (maximum 2 g) i.v. every 4 hours.

Patients allergic to penicillins or with nosocomial infections

Adults: 2 mg/kg i.v. every 8 hours, together with vancomycin 1 g i.v. every 12 hours.

Children: 2.5 mg/kg (maximum 80 mg) i.v. every 8 hours, together with vancomycin 20 mg/kg (maximum 1 g) i.v. every 12 hours.

Endocarditis due to α-haemolytic streptococci

Uncomplicated endocarditis

Adults: 1 mg/kg i.v. every 8 hours, together with benzylpenicillin 3 million IU i.v. every 4 hours for 2 weeks.

Gentamicin (continued)

Children: 1 mg/kg i.v. every 8 hours, together with benzylpenicillin 100 000 IU/kg (maximum 3 million IU) i.v. every 4 hours for 2 weeks.

Strains highly susceptible to benzylpenicillin (MIC ≤ 0.12 mg/l)

Adults: 1 mg/kg i.v. every 8 hours for 2 weeks, together with benzylpenicillin 3 million IU i.v. every 4 hours for 4 weeks.

Children: 1 mg/kg i.v. every 8 hours for 2 weeks, together with benzylpenicillin 100 000 IU/kg (maximum 3 million IU) i.v. every 4 hours for 4 weeks.

Strains resistant to benzylpenicillin (MIC = 0.25–1.0 mg/l)

Adults: 1 mg/kg i.v. every 8 hours for 4–6 weeks, supplemented for 6 weeks by *either* benzylpenicillin 3–4 million IU i.v. every 4 hours *or* ampicillin 2 g i.v. every 4 hours.

Children: 1 mg/kg i.v. every 8 hours for 4–6 weeks, supplemented for 6 weeks by *either* benzylpenicillin 100 000 IU/kg (maximum 4 million IU) i.v. every 4 hours *or* ampicillin 50 mg/kg (maximum 2 g) i.v. every 4 hours.

Endocarditis due to enterococci

Adults: 1 mg/kg i.v. every 8 hours for 4–6 weeks, supplemented for 6 weeks by *either* benzylpenicillin 3–4 million IU i.v. every 4 hours *or* ampicillin 2 g i.v. every 4 hours.

Children: 1 mg/kg i.v. every 8 hours for 4–6 weeks, supplemented for 6 weeks by *either* benzylpenicillin 100 000 IU/kg (maximum 4 million IU) i.v. every 4 hours *or* ampicillin 50 mg/kg (maximum 2 g) i.v. every 4 hours.

Endocarditis due to meticillin-susceptible Staphylococcus aureus

Adults: 1 mg/kg i.v. every 8 hours for 7 days, together with cloxacillin 2 g i.v. every 4 hours for 6 weeks.

Children: 1 mg/kg i.v. every 8 hours for 7 days, together with cloxacillin 50 mg/kg (maximum 2 g) i.v. every 4 hours for 6 weeks.

Culture-negative endocarditis

Adults: 1 mg/kg i.v. every 8 hours for 4–6 weeks, supplemented for 6 weeks by benzylpenicillin 3–4 million IU i.v. every 4 hours.

Children: 1 mg/kg i.v. every 8 hours for 4–6 weeks, supplemented for 6 weeks by benzylpenicillin 100 000 IU/kg (maximum 4 million IU) i.v. every 4 hours.

Prosthetic valve endocarditis

Adults: 1 mg/kg i.v. every 8 hours, together with vancomycin 1 g i.v. every 12 hours for 6 weeks.

Children: 1 mg/kg i.v. every 8 hours, together with vancomycin 40 mg/kg (maximum 1 g) i.v. in 2–4 divided doses daily for 6 weeks.

If infection due to a Gram-negative bacterial pathogen is suspected, the dose of gentamicin should be increased to 2 mg/kg i.v. every 8 hours.

Neonatal meningitis

Meningitis due to unknown pathogen

2.5 mg/kg i.v. every 12 hours, together with ampicillin 50 mg/kg (maximum 2 g) i.v. every 8 hours (neonates <7 days: ampicillin 50 mg/kg (maximum 2 g) i.v. every 12 hours) for a total of 7–10 days.

Meningitis due to Listeria monocytogenes

2.5 mg/kg i.v. every 12 hours, together with ampicillin 50 mg/kg (maximum 2 g) i.v. every 8 hours (neonates <7 days: ampicillin 50 mg/kg (maximum 2 g) i.v. every 12 hours) for a total of 3 weeks.

Meningitis due to group B streptococci

2.5 mg/kg i.v. every 12 hours, together

with benzylpenicillin 50 000–75 000 IU / kg (maximum 2 million IU) i.v. every 4–6 hours (neonates <7 days: benzylpenicillin 50 000 IU / kg (maximum 2 million IU) i.v. every 8 hours) for a total of 3 weeks.

Brucellosis

Adults: 5–7 mg / kg i.v. every 24 hours for 2 weeks, together with doxycycline 100 mg orally every 12 hours for 6 weeks.

Children >8 years: 7.5 mg / kg i.v. in 1–3 divided doses daily for 2 weeks, together with doxycycline 2 mg / kg (maximum 100 mg) orally every 12 hours for 6 weeks.

Children ≤8 years: 7.5 mg / kg i.v. in 1–3 divided doses daily for 2 weeks, together with sulfamethoxazole 20 mg / kg + trimethoprim 4 mg / kg (maximum 800 mg + 160 mg) orally every 12 hours for 6 weeks.

Tularaemia

Adults and children: 1.5 mg / kg i.v. or i.m. every 8 hours for 7 days.

Plague

Adults and children: 1.7 mg / kg i.v. or i.m. every 8 hours for 7 days.

Initial empirical therapy for septicaemia

Adults and children >5 years: 5–7 mg / kg i.v. every 24 hours or 1.5 mg / kg i.v. or i.m. every 8 hours, supplemented by *either* cloxacillin 2 g i.v. every 4–6 hours *or* cefazolin 1–2 g i.v. every 8 hours *or* clindamycin 600 mg i.v. every 8 hours *or* chloramphenicol 750 mg i.v. every 6 hours.

Neonates: 2.5 mg / kg i.v. every 12 hours, together with ampicillin 50 mg / kg (maximum 2 g) i.v. every 8 hours (neonates <7 days: ampicillin 50 mg / kg (maximum 2 g) i.v. every 12 hours).

Prophylaxis in contaminated surgery

Adults and children: 5 mg / kg i.v., together with clindamycin 600 mg i.v. at induction of anaesthesia.

Contraindications

- Pregnancy.
- Myasthenia gravis.

Precautions

Gentamicin should be administered only by trained health personnel and care must be taken to ensure that the correct dose and duration of treatment is not exceeded. When possible, audiometry should be carried out. This is particularly important in neonates, elderly patients and patients with renal impairment or if the course of treatment is for more than 7 days. The patient should be monitored for renal toxicity or ototoxicity. Prolonged treatment should be avoided.

Adverse effects

Adverse effects are generally dose-related and where possible treatment courses should not be prolonged for more than 7 days. Vestibular and auditory damage and to a lesser extent, renal toxicity are the most serious adverse effects. Rarely, hypomagnesaemia occurs during prolonged therapy. Pseudomembranous colitis has also been reported.

Drug interactions

The risk of toxicity is increased when ethacrynic acid or furosemide is administered concomitantly.

The action of neuromuscular-blocking agents may be potentiated.

Storage

Preparations for injection should be stored in vials. Solutions are stable for up to 24 hours in most infusion fluids. Injections should not be mixed with other drugs in the same syringe.

Imipenem + cilastatin

Powder for injection, 250 mg (as monohydrate) + 250 mg (as sodium salt), 500 mg (as monohydrate) + 500 mg (as sodium salt) in vial

General information

Imipenem is a semisynthetic carbapenem antibiotic produced by *Streptomyces cattleya*, while cilastatin is a specific inhibitor of dihydropeptidase. Imipenem is inactivated by metabolism in the kidney and is potentially toxic to renal tubules; its combination with cilastatin prevents both renal inactivation and toxicity.

After intravenous infusion, imipenem + cilastatin is distributed widely throughout the body and is excreted in the urine both as unchanged drug and as metabolites.

Clinical information

Uses

Treatment of nosocomial pneumonia due to multiresistant *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Acinetobacter* spp.

Dosage and administration

The dosage is expressed in terms of the imipenem component.

Adults: 1–2 g daily in 3–4 divided doses by i.v. infusion.

Children: 60 mg / kg (maximum 2 g) daily in 4 divided doses by i.v. infusion.

Treatment should be continued until at least 2 days after resolution of signs and symptoms of infection.

Contraindications

- Hypersensitivity to imipenem or cilastatin.
- Breastfeeding.

Precautions

The dosage should be reduced in patients with renal impairment or central nervous system disorders.

Use in pregnancy

Imipenem should not be withheld in life-threatening infections when the need of the mother outweighs any possible risk to the fetus.

Drug interactions

Increased toxicity with antivirals such as aciclovir has been reported.

Storage

Powder for injection should be stored in well-closed containers. After reconstitution, the solution is stable for up to 10 hours.

Metronidazole

Tablet, 200 mg, 250 mg, 400 mg, 500 mg
Oral suspension, 200 mg (as benzoate)/5 ml

General information

Metronidazole is a 5-nitroimidazole derivative with antimicrobial activity against anaerobic bacteria and some protozoa, including *Trichomonas vaginalis*.

Metronidazole is almost completely absorbed after oral administration. Its

plasma half-life is about 8 hours and it is excreted, largely in the urine, both unchanged and as metabolites.

Clinical information

Uses

Treatment of:

- aspiration pneumonia, lung abscesses and brain abscess, together with benzylpenicillin
- gingival infections and periodontitis
- amoebiasis, together with diloxanide furoate
- giardiasis and necrotizing enterocolitis due to *Clostridium difficile*
- acute gastritis and peptic ulcer disease in adults, together with bismuth salicylate plus either tetracycline or amoxicillin, or omeprazole plus amoxicillin
- acute peritonitis, together with ampicillin and gentamicin
- gangrene, together with gentamicin and either benzylpenicillin or clindamycin
- contaminated soft tissue injuries, together with cloxacillin and gentamicin
- human and animal bites and clenched-fist injuries in patients allergic to penicillins, together with doxycycline or sulfamethoxazole + trimethoprim
- trichomoniasis and bacterial vaginosis in adults
- pelvic inflammatory disease in adults (ambulatory patients), together with ceftriaxone and doxycycline
- moderate and severe pelvic inflammatory disease in adults (hospitalized patients), together with ciprofloxacin and doxycycline.

Prophylaxis in contaminated surgery, together with cefazolin.

Dosage and administration

Metronidazole should preferably be administered with or immediately after meals.

Aspiration pneumonia and lung abscesses

Adults: 500 mg i.v. every 8–12 hours for 10–14 days (once clinical improvement occurs, 400 mg orally every 12 hours may be substituted), supplemented by benzylpenicillin 1–2 million IU i.v. or i.m. every 4–6 hours.

Children: 12.5 mg / kg (maximum 500 mg) i.v. every 8–12 hours for 10–14 days (once clinical improvement occurs, 10 mg / kg (maximum 400 mg) orally every 12 hours may be substituted), supplemented by benzylpenicillin 50 000–100 000 IU / kg (maximum 2 million IU) i.v. or i.m. every 4–6 hours.

Gingival infections and periodontitis

Adults: 400–500 mg orally every 12 hours for 5 days.

Children: 10–12.5 mg / kg (maximum 250 mg) orally every 12 hours for 5 days.

Amoebiasis

Adults: 10 mg / kg (maximum 250 mg) orally every 8 hours for 8–10 days, followed by diloxanide furoate 500 mg orally every 8 hours for 10 days.

Children: 10 mg / kg (maximum 250 mg) orally every 8 hours for 8–10 days, followed by diloxanide furoate 6–7 mg / kg (maximum 500 mg) orally every 8 hours for 10 days.

Giardiasis

Adults: 2 g orally every 24 hours for 3 days.

Children: 30 mg / kg (maximum 1.2 g) orally every 24 hours for 3 days.

Necrotizing enterocolitis due to Clostridium difficile

Adults: 200 mg orally every 8 hours for 7–14 days.

Children: 12.5 mg / kg (maximum 200 mg) orally every 8 hours for 7–14 days.

Metronidazole (continued)

Acute gastritis and peptic ulcer disease in adults

200 mg orally every 8 hours plus 400 mg orally at night for 2 weeks, supplemented by bismuth salicylate 107.7 mg (1 tablet) orally every 6 hours plus *either* tetracycline 500 mg orally every 6 hours or amoxicillin 500 mg orally every 6 hours, *or* 400 mg orally every 8 hours for 2 weeks, supplemented by omeprazole 40 mg orally every 24 hours plus amoxicillin 500 mg orally every 8 hours.

Acute peritonitis

Adults: 500 mg i.v. every 8–12 hours for at least 7 days, supplemented by ampicillin 2 g i.v. or i.m. every 6 hours and gentamicin 5–7 mg/kg i.v. daily in divided doses.

Children: 12.5 mg/kg (maximum 500 mg) i.v. every 8–12 hours for at least 7 days, supplemented by ampicillin 50 mg/kg (maximum 2 g) i.v. or i.m. every 6 hours and gentamicin 7.5 mg/kg i.v. in 1–3 divided doses daily.

For patients who are allergic to penicillins, ampicillin should be deleted from the above regimens.

Gangrene

Adults: 500 mg i.v. every 8 hours for at least 7 days (once clinical improvement occurs, rectal formulations may be substituted), supplemented by benzylpenicillin 4 million IU i.v. or i.m. every 4 hours and gentamicin 5–7 mg/kg i.v. or i.m. daily in divided doses.

Children: 12.5 mg/kg (maximum 500 mg) i.v. every 8 hours for at least 7 days (once clinical improvement occurs, rectal formulations may be substituted), supplemented by benzylpenicillin 100 000 IU/kg (maximum 4 million IU) i.v. or i.m. every 4 hours and gentamicin 7.5 mg/kg i.v. or i.m. in 1–3 divided doses daily.

For patients who are allergic to penicillins, benzylpenicillin should be replaced by clindamycin 600 mg (children: 10 mg/kg; maximum 450 mg) orally or i.v. every 6–8 hours.

Contaminated soft tissue injuries

Adults: 500 mg i.v. every 8 hours for 5–10 days (once clinical improvement occurs, oral or rectal formulations may be substituted), supplemented by cloxacillin 2 g i.v. or i.m. every 6 hours (once clinical improvement occurs, cloxacillin 500 mg orally every 6 hours may be substituted) and gentamicin 5–7 mg/kg i.v. or i.m. daily in divided doses.

Children: 12.5 mg/kg (maximum 500 mg) i.v. every 8 hours for 5–10 days (once clinical improvement occurs, oral or rectal formulations may be substituted), supplemented by cloxacillin 25–50 mg/kg (maximum 2 g) i.v. or i.m. every 6 hours (once clinical improvement occurs, cloxacillin 12.5–25 mg/kg (maximum 500 mg) orally every 6 hours may be substituted) and gentamicin 7.5 mg/kg i.v. or i.m. in 1–3 divided doses daily.

Human and animal bites and clenched-fist injuries in patients allergic to penicillins

Adults: 400–500 mg orally every 12 hours for 5–10 days, supplemented by *either* doxycycline 100 mg orally every 24 hours *or* sulfamethoxazole 800 mg + trimethoprim 160 mg orally every 12 hours.

Children >8 years: 10–12.5 mg/kg (maximum 250 mg) orally every 12 hours for 5–10 days, supplemented by *either* doxycycline 2 mg/kg (maximum 100 mg) orally every 24 hours *or* sulfamethoxazole 20 mg/kg + trimethoprim 4 mg/kg (maximum 800 mg + 160 mg) orally every 12 hours.

Children ≤8 years: 10–12.5 mg/kg (maximum 250 mg) orally every 12 hours for 5–10 days, supplemented by sulfame-

thoxazole 20 mg/kg + trimethoprim 4 mg/kg (maximum 800 mg + 160 mg) orally every 12 hours.

Trichomoniasis in adults
2 g orally in a single dose.

Sexual partners should be treated simultaneously.

Bacterial vaginosis in adults
400–500 mg orally every 12 hours for 7 days.

Pelvic inflammatory disease in adults
Ambulatory patients
400–500 mg orally every 8 hours, together with doxycycline 100 mg orally every 12 hours for 10 days, following initial therapy with ceftriaxone 250 mg i.m. in a single dose.

Hospitalized patients with moderate or severe disease
400–500 mg orally every 8 hours, together with ciprofloxacin 500 mg orally every 12 hours for at least 4 days (or for 48 hours after clinical improvement occurs), followed by doxycycline 100 mg orally every 12 hours for 10–14 days.

Brain abscess
Adults: 500 mg i.v. every 8–12 hours, together with benzylpenicillin 3–4 million IU i.v. or i.m. every 4–6 hours.

Children: 12.5 mg/kg (maximum 500 mg) i.v. every 8–12 hours, together with benzylpenicillin 100 000 IU/kg (maximum 3 million IU) i.v. or i.m. every 4–6 hours.

The duration of treatment depends on the clinical response and radiological evidence of resolution of the abscess.

Prophylaxis in contaminated surgery
Adults and children: 500 mg i.v., together with cefazolin 1 g i.v. at induction of anaesthesia (if the operation is prolonged beyond 3–4 hours, a further 1-g dose of cefazolin should be administered).

Contraindications

- Known hypersensitivity to imidazoles.
- Pregnancy.
- Chronic alcohol dependence.

Precautions

Patients should be warned not to take any alcohol during treatment since disulfiram-like reactions can occur.

Adverse effects

In general, metronidazole is well tolerated, but mild symptoms of headache, gastrointestinal irritation and a persistent metallic taste are common. Less frequently, drowsiness, rashes and darkening of urine occur.

More serious reactions are rare and usually occur only during extended courses of treatment. They include stomatitis and candidiasis, reversible leukopenia, and sensory peripheral neuropathy, which is usually mild and rapidly reversible.

Ataxia and epileptiform seizures have been reported among patients receiving dosages considerably higher than those currently recommended.

Drug interactions

The action of oral anticoagulants is potentiated. Alcohol may induce abdominal pain, vomiting, flushing and headache.

Phenobarbital and corticosteroids lower plasma levels of metronidazole whereas cimetidine raises them.

Overdosage

No specific treatment exists. Emesis or gastric lavage may be of value within a few hours of ingestion.

Storage

Tablets and suspension should be kept in well-closed containers, protected from light.

Nalidixic acid

Tablet, 250 mg

General information

Nalidixic acid is a synthetic quinolone antimicrobial which acts as a specific inhibitor of bacterial DNA gyrase. It is bactericidal against Enterobacteriaceae, including many strains of *Shigella* spp.

It is rapidly and completely absorbed from the gastrointestinal tract. The plasma half-life is 1.5–8.0 hours and the drug is excreted in the urine, both unchanged and as metabolites.

Clinical information

Uses

Treatment of shigellosis in adults and children ≥3 months.

Dosage and administration

Adults: 1 g orally every 6 hours for 5 days.

Children ≥3 months: 15 mg/kg (maximum 1 g) orally every 6 hours for 5 days.

Contraindications

- Hypersensitivity to any quinolone.
- Age under 3 months.
- Pregnancy.

Precautions

Reduced dosage should be considered in patients with hepatic or renal impairment.

Nalidixic acid should be administered cautiously to patients with epilepsy since seizures may be precipitated.

An adequate fluid intake must be ensured to prevent crystalluria.

Nalidixic acid has been shown to induce arthropathy in the weight-bearing joints of young animals. It should only be used in children if other agents are ineffective.

Adverse effects

The most frequently reported adverse effects are nausea and vomiting. Visual disturbances, headache, rashes, pruritus, urticaria, eosinophilia and photosensitivity also occur occasionally.

Hepatic and renal disturbances have also been reported.

Drug interactions

A prolonged bleeding time has been reported in patients receiving anticoagulants and nalidixic acid concurrently.

Use of nalidixic acid may result in reduced susceptibility of *Shigella* spp. to ciprofloxacin.

Overdosage

Gastric lavage is of value if performed promptly. Electrolyte balance must be maintained. Anticonvulsants may be needed for the treatment of seizures.

Storage

Tablets should be stored in well-closed containers.

Nitrofurantoin

Tablet, 100 mg

General information

Nitrofurantoin is a nitrofuran-type antimicrobial with bacteriostatic activity against *Escherichia coli* and certain other Gram-negative bacteria.

Nitrofurantoin is readily absorbed from the gastrointestinal tract. Between 20 and 60% of the dose is bound to plasma proteins. It is partially metabolized in the liver and excreted in the urine. Therapeutic concentrations are reached within 30 minutes of dosing.

Clinical information

Uses

Treatment of urinary tract infections in adults.

Prophylaxis against urinary tract infections in children.

Dosage and administration

Urinary tract infections in adults

Women: 100 mg orally every 12 hours for 3 days (for uncomplicated infections).

Men: 100 mg orally every 12 hours for at least 14 days.

Prophylaxis against urinary tract infections in children

50 mg orally at night.

Contraindications

Patients with impaired renal function.

Adverse effects

Nitrofurantoin is generally well tolerated at the doses used. The most frequently reported adverse effect is nausea. If doses of 100 mg every 6 hours are used, gastrointestinal symptoms may be more severe.

Peripheral neuritis, pulmonary reactions, hepatotoxicity and haematological changes have been reported.

Storage

Tablets should be stored in well-closed containers.

Nystatin

Pessary, 100 000 IU

General information

Nystatin is an antifungal polyene antibiotic derived from *Streptomyces noursei*. It is effective against infections caused by a wide range of yeasts and yeast-like fungi.

Clinical information

Uses

Treatment of vaginal candidiasis.

Dosage and administration

Vaginal candidiasis

200 000 IU as pessaries inserted high into the vagina nightly for 2 weeks (in some

Nystatin (continued)

geographical areas, nightly doses as high as 1 million IU may be required).

Administration should be continued for 48 hours after clinical cure. Higher doses and a longer period of treatment may be necessary in immunocompromised patients.

Contraindications and precautions

Treatment should be discontinued if symptoms of irritation or desensitization occur.

Use in pregnancy

Safe use in pregnancy has not been established. The need for treatment must be determined by the condition of the mother.

Adverse effects

Irritation rarely occurs after topical application.

Storage

Pessaries should stored below 15 °C in well-closed containers, protected from light.

Phenoxymethylpenicillin

Tablet, 250 mg (as potassium salt)
Powder for oral suspension, 250 mg (as potassium salt)/5 ml

General information

Phenoxymethylpenicillin is a semisynthetic derivative of penicillin for oral use. It is active against most Gram-positive bacteria but β-lactamase-producing strains (mainly staphylococci) are resistant.

It is well absorbed from the gastrointestinal tract and distributed widely in tissues. It is eliminated in the urine. It crosses the placenta and is eliminated in breast milk.

Clinical information

Uses

- Treatment of acute pharyngitis, acute cervical adenitis, gingival infections, periodontitis, tooth abscesses and suppurative odontogenic infections.
- Prevention of recurrence of rheumatic fever due to group A β-haemolytic streptococci in adults and children > 2 years.
- Postsplenectomy prophylaxis in adults and children > 2 years.

Dosage and administration

Acute pharyngitis and acute cervical adenitis

Adults: 500 mg orally every 6 hours for 10 days.

Children: 10–20 mg / kg (maximum 500 mg) orally every 6 hours for 10 days.

Gingival infections and periodontitis

Adults: 500 mg orally every 6 hours for 5 days.

Children: 10–20 mg / kg (maximum 500 mg) orally every 6 hours for 5 days.

Tooth abscesses and suppurative odontogenic infections

Adults: 500 mg orally every 6 hours for 3 days.

Children: 10–20 mg/kg (maximum 500 mg) orally every 6 hours for 3 days.

Prevention of recurrence of rheumatic fever due to group A β-haemolytic streptococci and postsplenectomy prophylaxis in adults and children >2 years

Adults: 250 mg orally every 12 hours.

Children >2 years: 125 mg orally every 12 hours.

Contraindications

Known hypersensitivity to penicillins or cefalosporins.

Precautions

Facilities should be available for treating anaphylaxis whenever penicillins are used. Patients should be questioned carefully about previous allergic reactions before the first dose is administered. If a skin rash develops, the patient should be transferred to a different class of antimicrobial.

Use in pregnancy

There is no evidence that phenoxymethylpenicillin is teratogenic. It may be used during pregnancy.

Adverse reactions

Hypersensitivity reactions are most common, ranging in severity from skin rashes to immediate anaphylaxis. Mild diarrhoea can also occur.

Storage

Preparations should be stored in well-closed containers.

Rifampicin

Capsule or tablet, 150 mg, 300 mg

General information

Rifampicin is a semisynthetic derivative of rifamycin, a complex macrocytic antibiotic that inhibits ribonucleic acid synthesis in a broad range of microbial pathogens.

Rifampicin is lipid-soluble. Following oral administration, it is rapidly absorbed and distributed throughout the cellular tissues and body fluids; if the meninges are inflamed, significant amounts enter the cerebrospinal fluid. A single dose of 600 mg produces a peak serum concentration of about 10 µg/ml in 2–4 hours, which subsequently decays with a half-life of 2–3 hours. It is extensively recycled in the enterohepatic circulation, and metabolites formed by deacetylation in the liver are eventually excreted in the faeces.

Since resistance readily develops, rifampicin must always be administered in combination with other effective antimycobacterial agents.

Clinical information

Uses

Treatment of:

- epiglottitis, together with chloramphenicol or cefotaxime
- meningitis due to benzylpenicillin-resistant or ceftriaxone/cefotaxime-resistant *Streptococcus pneumoniae*, together with vancomycin and ceftriaxone
- brucellosis, together with doxycycline or sulfamethoxazole + trimethoprim.

Rifampicin (continued)

Prophylaxis against meningitis due to *Neisseria meningitidis* and *Haemophilus influenzae*.

Dosage and administration

Rifampicin should preferably be given at least 30 minutes before meals, since absorption is reduced when it is taken with food.

Epiglottitis

Adults: 600 mg orally every 24 hours for 4 days, together with chloramphenicol 1 g i.v. or i.m. every 6 hours for 5 days.

Children >2 months: 20 mg/kg (maximum 600 mg) orally every 24 hours for 4 days, together with chloramphenicol 25 mg/kg (maximum 1 g) i.v. or i.m. every 6 hours for 5 days.

Neonates aged 1–2 months: 20 mg/kg (maximum 600 mg) orally every 24 hours for 4 days, together with cefotaxime 50 mg/kg (maximum 2 g) i.v. or i.m. every 8 hours for 5 days.

Neonates <1 month: 10 mg/kg (maximum 300 mg) orally every 24 hours for 4 days, together with cefotaxime 50 mg/kg (maximum 2 g) i.v. or i.m. every 8 hours for 5 days.

In young children, consideration should be given to vaccination against *H. influenzae* serotype b.

Meningitis due to benzylpenicillin-resistant or ceftriaxone/cefotaxime-resistant Streptococcus pneumoniae

Adults: 600 mg orally every 24 hours for at least 14 days, together with vancomycin 1 g i.v. every 12 hours and ceftriaxone 2 g i.v. or i.m. every 12 hours.

Children: 20 mg/kg (maximum 600 mg) orally every 24 hours for at least 14 days, together with vancomycin 20 mg/kg (maximum 1 g) i.v. every 12 hours and ceftriaxone 50–100 mg/kg (maximum 2 g) i.v. or i.m. every 12 hours.

Patients should be referred to a specialist.

Brucellosis

Adults: 600 mg orally every 24 hours for 6 weeks, together with doxycycline 100 mg orally every 12 hours.

Chidren >8 years: 15 mg/kg (maximum 600 mg) orally every 24 hours for 6 weeks, together with doxycycline 2 mg/kg (maximum 100 mg) orally every 12 hours.

Children ≤8 years: 15 mg/kg (maximum 600 mg) orally every 24 hours for 6 weeks, together with sulfamethoxazole 20 mg/kg + trimethoprim 4 mg/kg (maximum 800 mg + 160 mg) orally every 12 hours.

Prophylaxis against meningitis due to Neisseria meningitidis

Adults: 600 mg orally every 12 hours for 2 days.

Children ≥1 month: 10 mg/kg (maximum 600 mg) orally every 12 hours for 2 days.

Neonates <1 month: 5 mg/kg (maximum 300 mg) orally every 12 hours for 2 days.

Prophylaxis should be considered for patients and their close contacts, especially children under 5 years.

Prophylaxis against meningitis due to Haemophilus influenzae

Adults: 600 mg orally every 24 hours for 4 days.

Children ≥1 month: 20 mg/kg (maximum 600 mg) orally every 24 hours for 4 days.

Neonates <1 month: 5 mg/kg (maximum 300 mg) orally every 24 hours for 4 days.

Prophylaxis should be considered for patients and their close contacts, especially children under 5 years.

Contraindications

- Known hypersensitivity to rifamycins.
- Hepatic dysfunction.

Precautions

Serious immunological reactions resulting in renal impairment, haemolysis or thrombocytopenia are on record in patients who resume taking rifampicin after a prolonged lapse of treatment. In this rare situation it should be immediately and definitively withdrawn.

Careful monitoring of liver function is required in the elderly and in patients who are alcohol-dependent or have hepatic disease.

Patients should be warned that treatment may produce reddish discoloration of urine, tears, saliva and sputum, and that contact lenses may be irreversibly stained.

Use in pregnancy

Treatment should not be interrupted or postponed during pregnancy.

Vitamin K should be administered to the infant at birth because of the risk of postpartum haemorrhage.

Adverse effects

Rifampicin is well tolerated by most patients at currently recommended doses, although gastrointestinal intolerance can be unacceptably severe. Other adverse effects (skin rashes, fever, influenza-like syndrome and thrombocytopenia) are more likely to occur with intermittent than with daily administration. Temporary oliguria, dyspnoea and haemolytic anaemia have also been reported. These reactions subside when daily dosage is instituted.

Moderate rises in serum concentrations of bilirubin and transaminases, which are common at the onset of treatment, are often transient and without clinical significance. However, dose-related hepatitis can occur, which is potentially fatal. It is consequently important not to exceed the maximum recommended daily dose of 10 mg / kg (600 mg).

Drug interactions

Rifampicin induces hepatic enzymes, and may increase the dosage requirements of drugs metabolized in the liver. These include corticosteroids, steroid contraceptives, oral hypoglycaemic agents, oral anticoagulants, phenytoin, cimetidine, quinidine, ciclosporin and digitalis glycosides.

Patients should consequently be advised to use a nonhormonal method of birth control throughout treatment and for at least 1 month subsequently.

Biliary excretion of radiocontrast media and sulfobromophthalein sodium may be reduced and microbiological assays for folic acid and vitamin B_{12} disturbed.

Overdosage

Gastric lavage may be of value if undertaken within a few hours of ingestion. Very large doses may depress central nervous function. There is no specific antidote and treatment is supportive.

Storage

Capsules and tablets should be kept in tightly closed containers, protected from light.

Spectinomycin

Powder for injection, 2 g (as hydrochloride) in vial

General information

Spectinomycin is produced from *Streptomyces spectabilis*. It is most effective against *Neisseria gonorrhoeae*, in which it selectively inhibits protein synthesis.

It is rapidly absorbed after intramuscular injection and peak plasma concentrations occur after 1 hour. It is not significantly bound to plasma proteins and is excreted unchanged in the urine.

Clinical information

Uses

Treatment of:

- uncomplicated anogenital and disseminated gonococcal infections in adults
- gonococcal conjunctivitis in adults and neonates
- chancroid in adults.

Dosage and administration

All patients with gonorrhoea should be treated concurrently for chlamydial infection unless microbiological facilities exist to exclude the latter diagnosis. Sexual partners should be treated simultaneously.

Uncomplicated anogenital gonococcal infections in adults

2 g i.m. in a single dose.

Disseminated gonococcal infections in adults

2 g i.m. every 12 hours for 7 days.

If there is evidence of meningeal or endocardial involvement, treatment should be extended to 2 weeks and 4 weeks, respectively.

Gonococcal conjunctivitis

Adults: 2 g i.m. in a single dose.

Neonates: 25 mg / kg (maximum 75 mg) in a single dose.

Chancroid in adults

2 g i.m. in a single dose. (Longer treatment courses may be necessary in immunocompromised patients.)

Contraindications

Known hypersensitivity.

Precautions

In patients with renal impairment, spectinomycin should be used only when alternative therapies are inappropriate.

Use in pregnancy

Since safety in pregnancy has not been established, spectinomycin should be used in pregnant women only if the need outweighs any possible risk to the fetus.

Adverse effects

Hypersensitivity reactions occur rarely.

Pain at the injection site, nausea, fever, dizziness and urticaria have been reported.

Storage

Powder for injection should be stored in vials.

Streptomycin

Powder for injection, 1 g base (as sulfate) in vial

General information

Streptomycin is an aminoglycoside antibiotic derived from *Streptomyces griseus* that is used in the treatment of tuberculosis and sensitive Gram-negative infections.

Streptomycin is not absorbed from the gastrointestinal tract but, after intramuscular administration, it diffuses readily into the extracellular component of most body tissues and it attains bactericidal concentrations, particularly in tuberculous cavities. Little normally enters the cerebrospinal fluid, although penetration increases when the meninges are inflamed. The plasma half-life, which is normally 2–3 hours, is considerably extended in the newborn, in the elderly and in patients with severe renal impairment. It is excreted unchanged in the urine.

Clinical information

Uses

Treatment of:

- brucellosis in adults and children >8 years, together with doxycycline
- tularaemia
- plague.

Dosage and administration

Streptomycin must be administered by deep intramuscular injection. Syringes and needles should be adequately sterilized, to exclude any risk of transmitting viral pathogens.

Brucellosis in adults and children >8 years

Adults: 1 g i.m. every 24 hours for 2 weeks, supplemented by doxycycline 100 mg orally every 12 hours for 6 weeks.

Children >8 years: 15 mg/kg (maximum 1 g) i.m. every 24 hours for 2 weeks, supplemented by doxycycline 2 mg/kg (maximum 100 mg) orally every 12 hours for 6 weeks.

Tularaemia

Adults and children: 15 mg/kg (maximum 1 g) i.m. every 24 hours for 7–14 days.

Plague

Adults: 1 g i.m. every 12 hours for 7–10 days.

Children: 15 mg/kg (maximum 1 g) every 12 hours for 7–10 days.

Contraindications

- Known hypersensitivity.
- Auditory nerve impairment.
- Myasthenia gravis.
- Pregnancy.

Precautions

Should hypersensitivity reactions occur, as is common during the first weeks of treatment, streptomycin should be withdrawn immediately. Once fever and skin rash have resolved, desensitization may be attempted.

Streptomycin should be avoided, when possible, in children because the injections are painful and irreversible auditory nerve damage may occur. Both the elderly and patients with renal impairment are also vulnerable to dose-related toxic effects resulting from accumulation. Serum levels should be

Streptomycin (continued)

monitored periodically and dosage adjusted appropriately to ensure that plasma concentrations, as measured when the next dose is due, do not rise above 4 μg / ml.

Protective gloves should be worn when streptomycin injections are administered, to avoid sensitization dermatitis.

Use in pregnancy

Streptomycin should not be used in pregnancy. It crosses the placenta and can cause auditory nerve impairment and nephrotoxicity in the fetus.

Adverse effects

Injections are painful and sterile abscesses can form at injection sites. Hypersensitivity reactions are common and can be severe.

Impairment of vestibular function is uncommon with currently recommended doses. Dosage should be reduced if headache, vomiting, vertigo and tinnitus occur.

Streptomycin is less nephrotoxic than other aminoglycoside antibiotics. None the less, close monitoring of renal function is necessary. Dosage must be reduced by half immediately if urinary output falls, if albuminuria occurs or if tubular casts are detected in the urine.

Haemolytic anaemia, aplastic anaemia, agranulocytosis, thromboctyopenia and lupoid reactions are rare adverse effects.

Drug interactions

Other ototoxic or nephrotoxic drugs should not be administered to patients receiving streptomycin. These include other aminoglycoside antibiotics, amphotericin B, cefalosporins, etacrynic acid, ciclosporin, cisplatin, furosemide and vancomycin.

Streptomycin may potentiate the effect of neuromuscular-blocking agents administered during anaesthesia.

Overdosage

Haemodialysis can be beneficial. There is no specific antidote and treatment is supportive.

Storage

Solutions retain their potency for 48 hours after reconstitution at room temperature and for up to 14 days when refrigerated. Powder for injection should be stored in tightly closed containers protected from light.

Sulfadiazine

Tablet, 500 mg
Injection, 250 mg (sodium salt) in 4-ml ampoule

General information

Sulfadiazine is an intermediate-acting sulfonamide with a broad spectrum of activity against a wide range of Gram-positive and Gram-negative organisms.

Sulfadiazine is readily absorbed from the gastrointestinal tract and widely distributed in the body. The serum half-life is 10–12 hours. After partial acetylation in the liver it is excreted in the urine.

Clinical information

Uses

Prevention of recurrence of rheumatic fever due to group A β-haemolytic

streptococci in patients allergic to penicillins.

Dosage and administration

Adults: 1 g orally or i.v. every 24 hours.

Children: 500 mg orally or i.v. every 24 hours.

Contraindications

- Hypersensitivity to sulfonamides.
- Severe renal or hepatic dysfunction.
- Porphyria.
- Pregnancy during the third trimester.

Precautions

The blood count should be monitored twice weekly throughout therapy to detect signs of bone-marrow depression. Administration should be discontinued immediately should presumptive signs of hypersensitivity occur, such as skin rashes, dark urine and purpura. Any patient suspected of being sensitive to sulfonamides should never receive them again.

Sulfadiazine is less soluble in urine than many other sulfonamides. A high output of alkaline urine must be maintained during treatment to avoid crystallization. Patients should be advised to drink 1.0–1.5 litres of alkaline water daily.

Concomitant administration of other drugs that interfere with folic acid metabolism (apart from pyrimethamine) should be avoided whenever possible.

Use in pregnancy

Administration of sulfonamides can induce severe hypersensitivity reactions in the mother. Their action in displacing bilirubin from protein-binding sites has given rise to concern, based on data derived from premature neonates, that they may promote kernicterus. Although sulfonamides readily cross the placental barrier there is no conclusive evidence that the fetus is at risk.

Adverse effects

Nausea, vomiting, diarrhoea and headache sometimes occur.

Sulfonamide-induced hypersensitivity reactions, although uncommon, can be severe. They include rare life-threatening cutaneous reactions such as erythema multiforme (Stevens–Johnson syndrome) and toxic epidermal necrolysis.

Crystalluria may result in dysuria, renal colic, haematuria and acute renal obstruction.

Other infrequent reactions include granulocytopenia, thrombocytopenic purpura, agranulocytosis, aplastic anaemia and toxic hepatitis. Haemolysis occasionally occurs in individuals deficient in glucose-6-phosphate dehydrogenase.

Overdosage

Continuous forced diuresis may be beneficial and an alkaline urine should be maintained. Treatment is otherwise symptomatic.

Storage

Preparations should be stored protected from light.

Sulfamethoxazole + trimethoprim

Tablet, 100 mg of sulfamethoxazole + 20 mg of trimethoprim, 400 mg of sulfamethoxazole + 80 mg of trimethoprim, 800 mg of sulfamethoxazole + 160 mg of trimethoprim
Injection, 80 mg of sulfamethoxazole + 16 mg of trimethoprim/ml in 5-ml ampoule, 80 mg of sulfamethoxazole + 16 mg of trimethoprim/ml in 10-ml ampoule
Oral suspension, 200 mg of sulfamethoxazole + 40 mg of trimethoprim in 5-ml vial

General information

The two components of this combination product have a similar antimicrobial spectrum. They operate synergistically because they independently inhibit different steps in the enzymic synthesis of tetrahydrofolic acid, an essential metabolic process in susceptible bacteria. The combination enhances the antibacterial efficacy of the individual constituents and impedes the emergence of resistance.

Trimethoprim is absorbed more rapidly, is more widely distributed in tissues and enters the cerebrospinal fluid more readily than sulfamethoxazole. Both compounds are moderately bound to plasma proteins and have a plasma half-life of about 12 hours. The principal route of excretion is in the urine; approximately 50% of the trimethoprim and between 15 and 30% of the sulfamethoxazole are recovered as unchanged drug.

Clinical information

Uses

Treatment of:

- acute otitis media, acute sinusitis and acute bronchitis
- acute exacerbations of chronic bronchitis and pneumonia due to *Pneumocystis carinii* in adults
- pneumonia in adults and children >5 years and mild pneumonia in children aged from 2 months to 5 years
- melioidosis, together with ceftazidime
- typhoid and paratyphoid fever, infectious enteritis due to *Salmonella enteritidis* and enteritis due to enterotoxigenic *Escherichia coli*
- localized purulent skin lesions and impetigo
- human and animal bites and clenched-fist injuries in patients allergic to penicillins, together with metronidazole
- osteomyelitis due to *Salmonella* spp. in children ≤5 years, together with cloxacillin and either ceftriaxone or cefotaxime
- granuloma inguinale and meningitis due to *Listeria monocytogenes* in adults
- brucellosis in children ≤8 years, together with rifampicin or gentamicin.

Dosage and administration

Sulfamethoxazole + trimethoprim is usually given orally, but in severe infections it can be administered intravenously. Intravenous infusions should be administered in a 5% glucose solution in water over 60 minutes. Oral dosage forms should be substituted as soon as they can be ingested.

Acute otitis media

Adults: sulfamethoxazole 400 mg + trimethoprim 80 mg orally every 12 hours for 5 days.

Children: sulfamethoxazole 20 mg/kg + trimethoprim 4 mg/kg (maximum 400 mg + 80 mg) orally every 12 hours for 5 days.

Acute sinusitis

Adults: sulfamethoxazole 400 mg + trimethoprim 80 mg orally every 12 hours for 7–10 days.

Children: sulfamethoxazole 20 mg/kg + trimethoprim 4 mg/kg (maximum 400 mg + 80 mg) orally every 12 hours for 7–10 days.

Acute bronchitis

Adults: sulfamethoxazole 800 mg + trimethoprim 160 mg orally every 12 hours for 5 days.

Children: sulfamethoxazole 20 mg/kg + trimethoprim 4 mg/kg (maximum 800 mg + 160 mg) orally every 12 hours for 5 days.

Acute exacerbations of chronic bronchitis in adults

Sulfamethoxazole 800 mg + trimethoprim 160 mg orally every 12–24 hours for 5 days.

Pneumonia in adults and children >5 years

Ambulatory patients

Adults: sulfamethoxazole 800 mg + trimethoprim 160 mg orally every 12 hours for 5 days.

Children >5 years: sulfamethoxazole 20 mg/kg + trimethoprim 4 mg/kg (maximum 800 mg + 160 mg) orally every 12 hours for 5 days.

Mild pneumonia in children aged from 2 months to 5 years

Sulfamethoxazole 20 mg/kg + trimethoprim 4 mg/kg (maximum 800 mg + 160 mg) orally every 12 hours for 5 days.

Pneumonia due to Pneumocystis carinii in adults

Sulfamethoxazole 75 mg/kg + trimethoprim 15 mg/kg i.v. or orally every 6–8 hours for 21 days.

Melioidosis

Adults: sulfamethoxazole 1600 mg + trimethoprim 320 mg orally or i.v. every 12 hours for at least 14 days, supplemented by ceftazidime 2 g i.v. every 8 hours.

Children: sulfamethoxazole 40 mg/kg + trimethoprim 8 mg/kg (maximum 1600 mg + 320 mg) orally or i.v. every 12 hours for at least 14 days, supplemented by ceftazidime 50 mg/kg (maximum 2 g) i.v. every 8 hours.

After the initial intensive therapy, eradication of any secondary infection is recommended with oral sulfamethoxazole + trimethoprim for at least 3 months.

Typhoid and paratyphoid fever, infectious enteritis due to Salmonella enteritidis and enteritis due to enterotoxigenic Escherichia coli

Adults: sulfamethoxazole 800 mg + trimethoprim 160 mg orally every 12 hours for 3 days.

Children: sulfamethoxazole 20 mg/kg + trimethoprim 4 mg/kg (maximum 800 mg + 160 mg) orally every 12 hours for 3 days.

Localized purulent skin lesions and impetigo

Adults: sulfamethoxazole 800 mg + trimethoprim 160 mg orally every 12 hours for 5–7 days.

Children: sulfamethoxazole 20 mg/kg + trimethoprim 4 mg/kg (maximum 800 mg + 160 mg) orally every 12 hours for 5–7 days.

Human and animal bites and clenched-fist injuries in patients allergic to penicillins

Adults: sulfamethoxazole 800 mg + trimethoprim 160 mg orally every 12 hours for 5–10 days, supplemented by metronidazole 400–500 mg orally every 12 hours.

Sulfamethoxazole + trimethoprim (continued)

Children: sulfamethoxazole 20 mg / kg + trimethoprim 4 mg / kg (maximum 800 mg + 160 mg) orally every 12 hours for 5–10 days, supplemented by metronidazole 10–12.5 mg / kg (maximum 250 mg) orally every 12 hours.

Osteomyelitis due to Salmonella spp. in children ≤ 5 years

Children aged from 2 months to 5 years: sulfamethoxazole 20 mg / kg + trimethoprim 4 mg / kg (maximum 800 mg + 160 mg) orally every 12 hours to complete the treatment course of 6 weeks, following initial therapy with cloxacillin 25–50 mg / kg (maximum 2 g) i.v. or i.m. every 4–6 hours and ceftriaxone 50–75 mg / kg (maximum 1 g) i.v. or i.m. every 24 hours for 4–6 days (or until clinical improvement occurs).

Neonates: sulfamethoxazole 20 mg / kg + trimethoprim 4 mg / kg (maximum 800 mg + 160 mg) orally every 12 hours to complete the treatment course of 6 weeks, following initial therapy with cloxacillin 25–50 mg / kg (maximum 2 g) i.v. or i.m. every 4–6 hours and cefotaxime 50–75 mg / kg (maximum 2 g) i.v. every 8 hours for 4–6 days (or until clinical improvement occurs).

Granuloma inguinale in adults

Sulfamethoxazole 800 mg + trimethoprim 160 mg orally every 12 hours for 14 days (or until the lesion has completely healed).

Meningitis due to Listeria monocytogenes in adults

Sulfamethoxazole 800 mg + trimethoprim 160 mg i.v. every 6 hours for at least 3 weeks.

Therapy often needs to be prolonged; some patients may require treatment for up to 6 weeks.

Brucellosis in children ≤ 8 years

Sulfamethoxazole 20 mg / kg + trimethoprim 4 mg / kg (maximum 800 mg + 160 mg) orally every 12 hours for 6 weeks, together with rifampicin 15 mg / kg (maximum 600 mg) orally every 24 hours, *or* supplemented for the first 2 weeks by gentamicin 7.5 mg / kg i.v. in 1–3 divided doses daily.

Contraindications

- Known hypersensitivity to either component.
- Severe hepatic or renal dysfunction.

Precautions

In HIV-infected patients with pneumonia due to *Pneumocystis carinii* whose arterial oxygen tension is less than 70 mm Hg (9.33 kPa), the risk of death during the first few days of treatment can be substantially reduced if a corticosteroid is administered as soon as therapy is started.

Treatment should be suspended immediately should a rash or any other manifestation of sulfonamide hypersensitivity occur.

The risk of sulfonamide crystalluria is decreased by maintaining a urinary output of at least 1.5 litres daily. Whenever possible, plasma sulfonamide concentrations should be determined periodically.

Patients must be advised to seek medical advice should they develop a sore throat or fever during treatment. This advice can be of greater value than routine monitoring of the white cell count.

Since elderly patients may be more susceptible to severe adverse reactions, especially blood dyscrasias, their treatment should not be unnecessarily prolonged.

Patients deficient in folate may require supplementary calcium folinate to prevent megaloblastic anaemia.

Use in pregnancy

Safe use in pregnancy has not been established. Sulfamethoxazole + trimethoprim may be used, however, when the potential benefit to the mother outweighs any possible harm to the fetus. It should not be withheld in life-threatening diseases.

Adverse effects

The most common adverse effects are nausea, vomiting and skin rashes which are mild and reversible. In patients with HIV infection receiving sulfamethoxazole + trimethoprim for *Pneumocystis carinii* pneumonia, recurrent fever, neutropenia, thrombocytopenia and increases in serum transaminase levels also occur frequently.

Sulfonamide-induced hypersensitivity reactions, although uncommon, can be severe. They include life-threatening cutaneous reactions such as erythema multiforme (Stevens–Johnson syndrome) and toxic epidermal necrolysis.

Other infrequent reactions include leukopenia, neutropenia and thrombocytopenia and less commonly, agranulocytosis, megaloblastic anaemia, purpura and toxic hepatitis. Haemolysis occasionally occurs in individuals deficient in glucose-6-phosphate dehydrogenase.

Drug interactions

Maintenance requirements for sulfonylureas and coumarin anticoagulants are often reduced as a result of their displacement from plasma proteins by sulfamethoxazole.

Concomitant use of other inhibitors of folate metabolism (such as pyrimethamine, methotrexate and certain anticonvulsants) increases the risk of megaloblastic anaemia.

Overdosage

Symptoms of acute overdosage include vomiting, dizziness and confusion, followed by visual disturbances, petechiae, purpura and jaundice. Crystalluria, haematuria and anuria may also occur.

Emesis or gastric lavage may be of value within a few hours of ingestion. Provided urinary output is satisfactory, a high fluid intake should be maintained. Haemodialysis may be of value in eliminating some of the drug. Otherwise, treatment is symptomatic and supportive.

Storage

Tablets, oral suspension and concentrate for infusion should be stored, protected from light, in well-closed containers.

Tetracycline

Capsule or tablet, 250 mg of tetracycline hydrochloride
Eye ointment, 1% tetracycline hydrochloride

General information

Tetracycline is a broad-spectrum antibiotic derived from a species of *Streptomyces*. It induces bacteriostasis by inhibiting protein synthesis, and is selectively concentrated in susceptible organisms.

Tetracycline (continued)

Absorption occurs mainly from the stomach and small intestine. Peak plasma concentrations occur within 4 hours and decay with a half-life of about 8 hours. Excretion is primarily effected by filtration into the urine. Enterohepatic circulation results in high concentrations of tetracycline accumulating in the liver and bile. Bacteriostatic concentrations are maintained for up to 6 hours after topical administration.

Tetracycline crosses the placenta and is excreted in breast milk.

Clinical information

Uses

- Treatment of acute gastritis and peptic ulcer disease in adults, together with bismuth salicylate and metronidazole.
- Prevention and (when systemic treatment is not available) treatment of gonococcal conjunctivitis of the newborn.

Dosage and administration

Acute gastritis and peptic ulcer disease in adults

500 mg orally every 6 hours for 2 weeks, supplemented by bismuth salicylate 107.7 mg (1 tablet) orally every 6 hours plus metronidazole 200 mg orally every 8 hours and 400 mg orally at night.

Gonococcal conjunctivitis in neonates

Prevention: a single application of the ointment immediately after birth should be sufficient.

Treatment: ointment should be instilled into each eye hourly pending referral of the infant.

Contraindications

- Known hypersensitivity.
- Severe renal impairment.
- Pregnancy and early childhood (except for topical use to prevent or treat gonococcal conjunctivitis in neonates).

Precautions

Troublesome oesophagitis may be averted if the patient is propped up while swallowing capsules or tablets and washes them down immediately with a glass of water. Capsules and tablets should not be taken with milk or with magnesium or aluminium salts since these impair the absorption of tetracycline.

Time-expired capsules and tablets should be discarded. Degraded tetracycline has been reported to induce renal dysfunction indistinguishable from the Fanconi syndrome and skin lesions similar to those of systemic lupus erythematosus.

Use in pregnancy and early childhood

Tetracycline is generally contraindicated in pregnancy and early childhood. Because it is deposited in developing teeth and bones and impairs skeletal calcification, it can result in abnormal osteogenesis and permanent staining of teeth, and occasionally causes hyperplasia of dental enamel.

Adverse effects

Gastrointestinal irritation is common, as is depletion of the normal bowel flora, permitting overgrowth of resistant organisms. Irritative diarrhoea should be differentiated from enteritis due to suprainfection, particularly with coagulase-positive staphylococci, and from pseudomembranous colitis due to *Clostridium difficile*.

Phototoxic reactions occasionally result in porphyria-like skin changes and pigmentation of the nails.

Hypersensitivity reactions are rare. Morbilliform rashes, urticaria, fixed drug eruptions, exfoliative dermatitis, cheilosis, glossitis, pruritus and vaginitis have been reported, as have angioedema, anaphylaxis and pseudotumour cerebri.

Drug interactions
The action of oral anticoagulants may be potentiated. Severe renal failure has been reported in patients who have received a halogenated anaesthetic agent while taking tetracyclines.

Storage
Tetracycline capsules, tablets and ointment should be kept in well-closed containers, protected from light.

Tinidazole

Tablet, 500 mg

General information

Tinidazole is a 5-nitroimidazole derivative with antimicrobial activity against anaerobic bacteria and certain protozoa. It is almost completely absorbed after oral administration. It is excreted largely in the urine, both unchanged and as metabolites.

Clinical information

Uses
Treatment of giardiasis.

Dosage and administration
Adults: 2 g orally in a single dose.

Children: 50 mg/kg (maximum 2 g) orally in a single dose.

Contraindications
- Hypersensitivity to azole derivatives.
- Pregnancy.
- Chronic alcohol dependence.

Precautions
Patients should be warned not to take any alcohol during treatment since disulfiram-like reactions can occur.

Adverse effects
In general, tinidazole is well tolerated, but mild symptoms of headache, gastrointestinal irritation and a persistent metallic taste are common. Less frequently, drowsiness, rashes and darkening of urine occur.

More serious reactions are rare and usually occur only during extended courses of treatment. They include stomatitis and candidiasis, reversible leukopenia, and sensory peripheral neuropathy, which is usually mild and rapidly reversible.

Ataxia and epileptiform seizures have been reported among patients receiving dosages considerably higher than those currently recommended.

Drug interactions
The action of oral anticoagulants is potentiated. Alcohol may induce abdominal pain, vomiting, flushing and headache.

Overdosage
No specific treatment exists. Emesis or gastric lavage may be of value within a few hours of ingestion.

Storage
Tablets should be kept in well-closed containers, protected from light.

Trimethoprim

Tablet, 100 mg, 200 mg

General information

Trimethoprim is an inhibitor of folic acid metabolism that is active against many Gram-positive cocci and Gram-negative bacilli.

Trimethoprim is well absorbed from the gastrointestinal tract and widely distributed in the tissues. It has a plasma half-life of about 11 hours and is excreted in the urine. It crosses the placenta and is excreted in breast milk.

Clinical information

Uses

Treatment of urinary tract infections and prostatitis in adults.

Dosage and administration

Urinary tract infections in adults

Women: 300 mg orally every 24 hours for 3 days (for uncomplicated infections).

Men: 300 mg orally every 24 hours for at least 14 days.

Prostatitis in adults

200 mg orally every 12 hours for 4–6 weeks.

Contraindications

- Pregnancy during the first trimester.
- Renal impairment (creatinine clearance <15 ml / minute).
- Porphyria.

Precautions

Trimethoprim should be used with caution in patients with folate deficiency, since haematological changes can occur. Folinic acid should be administered to these patients.

Use in pregnancy

Safe use in pregnancy has not been established. Treatment should be deferred until after the first trimester of pregnancy.

Adverse effects

The most frequent adverse effects are skin rashes and urticaria.

Rarely, exfoliative dermatitis and toxic epidermal necrolysis have been observed. Gastrointestinal disturbances have also been reported. Haematological reactions may occur in patients with folate deficiency.

Drug interactions

Trimethoprim inhibits hepatic metabolism.

Overdosage

Treatment is supportive and symptomatic.

Storage

Tablets should be stored in tightly closed containers, protected from light.

Vancomycin

Powder for injection, 500 mg (as hydrochloride) in 10-ml vial, 250 mg (as hydrochloride) in 5-ml vial

General information

Vancomycin is a glycopeptide antibiotic derived from *Nocardia orientalis*. It is bactericidal against a wide range of Gram-positive organisms such as staphylococci, group A β-haemolytic streptococci, *Streptococcus pneumoniae*, enterococci, *Corynebacterium* spp. and *Clostridium* spp. including *C. difficile*. It is not active against Gram-negative organisms, fungi or yeasts.

After intravenous administration vancomycin is widely distributed in the body tissues and diffuses readily into the pericardial, pleural, ascitic and synovial fluids. It has a plasma half-life of 4–6 hours and is excreted mainly in the urine as unchanged drug.

Clinical information

Uses

Treatment of:

- pneumonia due to meticillin-resistant *Staphylococcus aureus* in adults and children >5 years
- nosocomial pneumonia due to meticillin-resistant *Staphylococcus aureus*, together with gentamicin plus either cloxacillin or ceftazidime, or ciprofloxacin plus ceftazidime
- endocarditis due to meticillin-resistant *Staphylococcus aureus* (MRSA)
- necrotizing enterocolitis due to metronidazole-resistant *Clostridium difficile*
- endocarditis due to benzylpenicillin-resistant α-haemolytic streptococci and enterococci, infective endocarditis (initial empirical therapy) in patients allergic to penicillins or with nosocomial infections, and prosthetic valve endocarditis, together with gentamicin
- meningitis due to benzylpenicillin-resistant or ceftriaxone/cefotaxime-resistant *Streptococcus pneumoniae*, together with ceftriaxone and rifampicin.

Dosage and administration

Each i.v. dose should be dissolved in 100–200 ml of dextrose and infused over 1 hour.

When vancomycin is used in the treatment of endocarditis, peak plasma levels of 30–40 mg/l and basal plasma levels of 5–15 mg/l are recommended. If gentamicin is used, basal plasma levels should not exceed 1 mg/l. These levels are specific for the management of endocarditis and do not apply to other circumstances.

Pneumonia due to meticillin-resistant Staphylococcus aureus in adults and children >5 years

Adults: 1 g i.v. every 12 hours for 10–14 days.

Children >5 years: 20 mg/kg (maximum 1 g) i.v. every 12 hours for 10–14 days.

Nosocomial pneumonia due to meticillin-resistant Staphylococcus aureus

Adults: 1g i.v. every 12 hours for 10–14 days, supplemented for the first 7 days by gentamicin 5–7 mg/kg i.v. daily in divided doses *plus either* cloxacillin 1–2 g i.v. every 6 hours *or* ceftazidime 1g i.v. every 8 hours, or by ciprofloxacin 500mg i.v. every 12 hours plus ceftazidime 1g i.v. every 8 hours.

Vancomycin (continued)

Children: 20 mg/kg (maximum 1 g) i.v. every 12 hours for 10–14 days, supplemented for the first 7 days by gentamicin 7.5 mg/kg i.v. in 1–3 divided doses daily *plus either* cloxacillin 50 mg/kg (maximum 2 g) i.v. every 6 hours *or* ceftazidime 25 mg/kg (maximum 1 g) i.v. every 8 hours, or by ciprofloxacin 10 mg/kg (maximum 300 mg) i.v. every 12 hours plus ceftazidime 25 mg/kg (maximum 1 g) i.v. every 8 hours.

Necrotizing enterocolitis due to metronidazole-resistant Clostridium difficile

Adults: 125 mg orally every 6 hours for 7–14 days.

Children: 5 mg/kg (maximum 125 mg) orally every 6 hours for 7–14 days.

Endocarditis due to benzylpenicillin-resistant α-haemolytic streptococci and enterococci and initial empirical therapy for infective endocarditis in patients allergic to penicillins or with nosocomial infections

Adults: 1 g i.v. every 12 hours, together with gentamicin 2 mg/kg i.v. every 8 hours.

Children: 20 mg/kg (maximum 1 g) i.v. every 12 hours, together with gentamicin 2.5 mg/kg (maximum 80 mg) i.v. every 8 hours.

Endocarditis due to meticillin-resistant Staphylococcus aureus

Adults: 1 g i.v. every 12 hours for 6 weeks.

Children: 40 mg/kg (maximum 1 g) i.v. in 2–4 divided doses daily for 6 weeks.

Prosthetic valve endocarditis

Adults: 1 g i.v. every 12 hours, together with gentamicin 1 mg/kg i.v. every 8 hours for 6 weeks.

Children: 40 mg/kg (maximum 1 g) i.v. in 2–4 divided doses daily, together with gentamicin 1 mg/kg i.v. every 8 hours for 6 weeks.

If infection due to a Gram-negative pathogen is suspected, the dose of gentamicin should be increased to 2 mg/kg i.v. every 8 hours.

Meningitis due to benzylpenicillin-resistant or ceftriaxone/cefotaxime-resistant Streptococcus pneumoniae

Adults: 1 g i.v. every 12 hours for at least 14 days, supplemented by ceftriaxone 2 g i.v. or i.m. every 12 hours and rifampicin 600 mg orally every 24 hours.

Children: 20 mg/kg (maximum 1 g) i.v. every 6 hours for at least 14 days, supplemented by ceftriaxone 50–100 mg/kg (maximum 2 g) i.v. or i.m. every 12 hours and rifampicin 20 mg/kg (maximum 600 mg) orally every 24 hours.

Patients should be referred to a specialist.

Contraindications

Known hypersensitivity to vancomycin.

Precautions

Vancomycin must be used only in a hospital setting where plasma concentrations can be measured.

Dosage should be adjusted in accordance with the creatinine clearance rate in patients with impaired renal function.

Use in pregnancy

Safe use in pregnancy has not been established. Treatment should not be withheld, however, in life-threatening situations.

Adverse effects

If the drug is administered too rapidly, an acute erythematous rash occurs.

Ototoxicity and nephrotoxicity may occur, particularly when treatment is prolonged.

Drug interactions

Ototoxicity and nephrotoxicity may be exacerbated by concurrent administration of aminoglycosides and other ototoxic agents.

Overdosage

Limited information is available on the acute toxicity of vancomycin. Treatment of overdosage is supportive.

Storage

Powder for injection should be stored in well-closed containers.

Index

Note: Page numbers in bold type indicate main discussions.

Abscesses
  brain **80**, 102, 120, 145
  lung **27–28**, 95, 100, 124, 143
  muscle (pyomyositis) **50**, 107, 108–109, 125, 127
  peritonsillar 14
  tooth **33–34**, 93, 105, 148–149
Acinetobacter spp., resistance 12
Adenitis
  acute cervical **34**, 103, 105
    amoxicillin 92
    cefalexin 106–107
    erythromycin 134
    phenoxymethylpenicillin 148
Administration, drugs **7–8**
Allergies, penicillins 16, 94, 96, 125, 132
Alternative drugs **13**
Amoebiasis 37, **39–40**, 143
Amoxicillin 11, **92–94**
  bronchitis 20–21, 92
  cellulitis/erysipelas 48, 93
  contraindications 94
  dosage and administration **92–93**
  gastritis/peptic ulcer 41, 92
  Lyme disease 81, 93
  osteomyelitis 53, 56, 57, 93
  otitis media 16, 92
  overdosage 94
  perioral/dental infections 34, 93
  pharyngitis 15, 92
  pneumonia 22, 24–26, 28, 93
  postsplenectomy prophylaxis 91, 93–94
  precautions 94
  surgical prophylaxis 88
Amoxicillin + clavulanic acid 11, **94–96**
  bronchitis 21, 95
  contraindications 96
  dosage and administration **95**
  osteomyelitis 55, 95
  otitis media 16, 95
  overdosage 96
  pneumonia 28, 95
  precautions 96
  soft tissue injuries 52, 95
  surgical prophylaxis 88, 89, 95
  urinary tract infections 44, 95
Ampicillin **96–98**
  adverse effects 98
  cholecystitis 42, 97
  contraindications 98
  dosage and administration **97–98**
  endocarditis 71–72, 97
  mastoiditis 17, 97
  meningitis 77–79, 97–98
  neonatal meningitis 78, **79–80**, 98
  neonatal pneumonia 26
  neonatal septicaemia 87, 98
  overdosage 98
  peritonitis 42, 97
  precautions 98
  pyelonephritis 45, 97
  typhoid/paratyphoid 38
Animal bites **51–52**, 95, 105
  doxycycline 132
  metronidazole 144–145
  sulfamethoxazole + trimethoprim 157–158
Anthrax **83–84**, 102, 131
Antitoxin, diphtheria 19
Arthritis, septic, *see* Septic arthritis
Aspergillus fumigatus, HIV-associated pneumonia 27
Aspiration pneumonia **27–28**, 95
  benzylpenicillin 100
  clindamycin 124
  metronidazole 143

Bacillus anthracis 83
Bacteroides fragilis, aspiration pneumonia 27
Benzathine benzylpenicillin **103–104**
  chancroid 67
  diphtheria 19
  pharyngitis 14
  rheumatic fever prophylaxis 89, 90
  syphilis 66

Benzylpenicillin 6, **99–103**
adverse effects 103
anthrax 84, 102
brain abscess 80, 102
cellulitis/erysipelas 48, 100
contraindications 102
dosage and administration **99–102**
endocarditis 69–72, 97, 101
gangrene 49, 50, 100
leptospirosis 82, 102
Lyme disease 81, 102
meningitis 75–79, 101–102
neonatal meningitis 80, 102
osteomyelitis 53, 100
overdosage 103
pneumonia 23–25, 28, 99–100
precautions 102
streptococcal necrotizing fasciitis 49, 100
syphilis 67, 100–101
Bismuth salicylate, gastritis/peptic ulcer 41
Bites
human/animal **51–52**, 95, 105
doxycycline 132
metronidazole 144–145
sulfamethoxazole + trimethoprim 157–158
Bone infections (*see also* Osteomyelitis; Septic arthritis) **53–60**
Bordetella pertussis 31
Borrelia burgdorferi, Lyme disease 81
Borrelia recurrentis, relapsing fever 81
Brain abscesses **80**, 145
benzylpenicillin 102
chloramphenicol 120
Bronchiectasis 21
Bronchitis **20–21**, 157
amoxicillin 92, 95
doxycycline 131
Brucella spp. 34, 82
Brucellosis **82–83**, 133
gentamicin 141
streptomycin 153
sulfamethoxazole + trimethoprim 158
Burkholderia pseudomallei, melioidosis 31

Calymmatobacterium granulomatis, granuloma inguinale 68
Campylobacter spp., invasive diarrhoea **36–37**, **122**, **135**
Candida albicans
endocarditis 72, 73
HIV-associated pneumonia 27
vaginitis 64, 147–148
Candidiasis **64**, 147–148
Capnocytophaga canimorsus, animal bites 51
Cardiovascular infections (*see also* Endocarditis; Rheumatic fever) **69–74**
Carriers, typhoid/paratyphoid 38, 97
Cefalexin **106–108**
adverse effects 108
cellulitis/erysipelas 48, 107
cervical adenitis 34, 106–107
contraindications 107
dosage and administration **106–107**
osteomyelitis 53, 54, 107
pharyngitis 15, 106–107
purulent skin lesions 47, 48, 107
pyomyositis 50, 107
septic arthritis 58, 59, 107
substitutes 13
urinary tract infections 43, 44, 107
Cefalosporins 6, **11–12**, **106–107**
Cefazolin **108–109**
adverse effects 109
cellulitis/erysipelas 48, 108
contraindications 109
osteomyelitis 53, 54, 109
pneumonia 28, 108
pyomyositis 50, 108–109
septicaemia 87, 109
septic arthritis 58, 59, 109
substitutes 13
surgical prophylaxis 88, 89, 109
Cefotaxime **110–111**
contraindications 111
croup 110
gonorrhoea 62
meningitis 11–12, 76–77
neonatal epiglottitis 18, 110
neonatal gonococcal conjunctivitis 111
neonatal meningitis 79, 111
neonatal pneumonia **26**, 110
osteomyelitis 55, 56, 110–111
septicaemia 87, 111
septic arthritis 58, 60, 111

Ceftazidime **112–113**
hospital-acquired pneumonia 30, 112
melioidosis 32, **112**
Pseudomonas aeruginosa 12
Ceftriaxone **113–116**
chancroid 67, 115
contraindications 116
croup 114
dosage and administration **114–116**
drug interactions 123
epiglottitis 18, 114
gonorrhoea 61, 62, 115
Lyme disease 81, 116
mastoiditis 17, 114
meningitis 11–12, 75–78, 115–116
osteomyelitis 54–56, 114–115
overdosage 123
pelvic inflammatory disease 64, 65, 115
pneumonia 23, 25, 114
pyelonephritis 45, 114
septicaemia 87, 116
septic arthritis 58, 59, 115
substitutes 13
Cefuroxime 11, 23, **117**
Cellulitis **48**, 93, 100
cefalexin 107
cefazolin 108
procaine benzylpenicillin 104
Central nervous system infections (*see also* Brain abscesses; Meningitis) **75–80**
Cervical adenitis **34**, 92, 105
benzathine benzylpenicillin 103
cefalexin 106–107
erythromycin 134
phenoxymethylpenicillin 148
Cervicitis 61, 63
Chancroid 11, 12, **67–68**
ceftriaxone 115
ciprofloxacin 122
erythromycin 136
spectinomycin 152
Chemoprophylaxis, *see* Prophylaxis
Children (*see also* Infants; Neonates)
brucellosis 158
cervical adenitis **34**, 105
chronic suppurative lung disease 21, 92, 119
ciprofloxacin 123
congenital syphilis 66, 100–101, 106
doxycycline 133
epiglottitis **18–19**, 150
impetigo **47–48**
osteomyelitis **54–57**, 93, 95, 158
pneumonia **22–26**
pneumonia drugs 93, 99–100, 105, 119, 135
septic arthritis 107, 115
typhoid/paratyphoid carriers **97**
urinary tract infections **44**, 95
Chlamydia pneumoniae, pneumonia 22
Chlamydia psittaci, ornithosis 31
Chlamydia trachomatis
neonatal pneumonia 25
prostatitis 46, 132, 135
sexually transmitted diseases **62–63**, 64
Chlamydial infections 61
doxycycline 132
erythromycin 135–136
ophthalmia 63, 135
Chloramphenicol 6, **117–121**
adverse effects 120
brain abscess 80, 120
childhood suppurative lung disease 21, 119
contraindications 120
dosage and administration **118–120**
drug interactions 121
epiglottitis 18, 118
granuloma inguinale 68, 119
mastoiditis 17, 118
meningitis 75–76, 78, 119
plague 84, 120
pneumonia 23–26, 119
relapsing fever 82, 120
rickettsial infections 85, 120
septicaemia 87, 120
severe croup 118
tularaemia 83, 120
typhoid/paratyphoid 38, 119
Cholecystitis **41–42**, 97, 138
Cholera **35**, 122, 132
Cilastatin + imipenem, *see* Imipenem + cilastatin
Ciprofloxacin 12–13, **121–123**
anthrax 84, 123
chancroid 67, 122
cholera 35, 122
contraindications 123

dosage and administration **121–123**
drug interactions 123
enteritis 37, 39, 122
gonorrhoea 61, 62, 122
hospital-acquired pneumonia 30, 121–122
legionellosis 27, 121
meningitis prophylaxis 76, 123
osteomyelitis 54, 56–57, 122
overdosage 123
pelvic inflammatory disease 65, 123
shigellosis **36**
substitutes 13
tularaemia 83, 123
typhoid/paratyphoid 38, 122
urinary tract infections 45, 46
Clavulanic acid + amoxicillin, *see* Amoxicillin + clavulanic acid
Clenched-fist injuries **51–52**, 95, 105
doxycycline 132
metronidazole 144–145
sulfamethoxazole + trimethoprim 157–158
Clindamycin **124–126**
contraindications 126
dosage and administration **124–126**
drug interactions 126
gangrene 50, 125
lung abscesses 124
osteomyelitis 53, 54, 125
pelvic inflammatory disease 65, 125
pneumonia 27, 28, 124
pyomyositis 50, 125
septicaemia 87, 125
septic arthritis 58–59, 125
streptococcal necrotizing fasciitis 49,125
surgical prophylaxis 89, 126
Clostridium difficile, necrotizing enterocolitis **40**, 143, 164
Clostridium spp.
gangrene 49
soft tissue injuries 51
Cloxacillin **126–130**
adverse effects 130
contraindications 130
dosage and administration **127–130**
endocarditis 69, 72, 129–130
osteomyelitis 53–56, **128–129**
overdosage 130
pneumonia 28–30, 127
prosthetic valve endocarditis 73
purulent skin lesions 47, 127
pyomyositis 50, 127
septicaemia 87, 130
septic arthritis 58, 59, 60, 129
soft tissue injuries 51, 127–128
substitutes 13
Colds, common **15**
Colitis, *see* Enterocolitis
Combination therapy 4, **8–9**
Common cold **15**
Computer software, WHONET 6
Congenital syphilis 67, 100–101, 106
Conjunctivitis
antibacterial drugs 111, 115, 135–136, 152, 160
chlamydial 63
gonococcal **61–62**
Corynebacterium diphtheriae
cervical adenitis 34
pharyngitis 14
Corynebacterium spp., prosthetic valve endocarditis 73
Cost, treatment 8
Cough
chronic recurrent **21**
whooping, *see* Pertussis
Coxiella burnetti 7
pneumonia 22
Q fever 85
Croup (laryngotracheobronchitis) **18**, 110, 114, 118
Cystic fibrosis 21
Cystitis **43**, 44
Cytomegalovirus, HIV-associated pneumonia 27

Data collection, drug resistance **6**
Debridement, surgical 49, 51, 57
Dental infections (*see also* Tooth abscesses) **33–34**
Diarrhoeal disease **35–40**
acute watery **35**
invasive (dysentery) **36–37**
persistent **37**
Diloxanide furoate, amoebiasis 40
Diphtheria **19**
benzathine benzylpenicillin 103

erythromycin 134–135
procaine benzylpenicillin 105
Donovanosis, *see* Granuloma inguinale
Dosage, principles **7**
Doxycycline **131–134**
anthrax 84, 131
bronchitis 20, 131
brucellosis 82, 133
cholera 35, 132
contraindications 133
dosage and administration **131–133**
drug interactions 133–134
leptospirosis 82, 133
Lyme disease 81, 133
melioidosis 32, 131–132
ornithosis 31, 131
pelvic inflammatory disease 64–65, 132
plague 84
pneumonia 23, 131
prostatitis 46, 132
Q fever 85, 131
relapsing fever 81, 133
rickettsial infections 85, 133
sexually transmitted diseases 63, 67–68, 132
soft tissue injuries 52, 132
Drug formularies **9**, 10
Dysentery **36–37**

Eikenella corrodens, human bites 51
Empyema **29**
Endocarditis **69–73**
ampicillin 71–72, 97
benzylpenicillin 101
cloxacillin 129
culture-negative **72**, 101
gentamicin 137–140
α-haemolytic streptococci 69, **70–71**, 97, 101, 139–140
infective **69–72**, 101
prosthetic valve **73**, 140, 164
vancomycin 164
Endometritis 63
Entamoeba histolytica, amoebiasis **39–40**
Enteric infections **38–40**
Enteritis **36–37**, **38–39**
ciprofloxacin 122
erythromycin 135
sulfamethoxazole + trimethoprim 157
Enterobacteriaceae
amoxicillin 92
ampicillin 96
data collection 6
pneumonia 25
resistance 10
septic arthritis 57
Enterococcus spp.
endocarditis 69, **71–72**, 97, 140
neonatal meningitis 79
pyelonephritis 45
Enterocolitis, necrotizing **40**, 143, 164
Epididymitis 63
Epiglottitis **18–19**, 114
chloramphenicol 118
neonates 110
Erysipelas **48**, 93, 100
cefalexin 107
cefazolin 108
procaine benzylpenicillin **105**
Erythromycin 6, **134–136**
cervical adenitis 34, 134
chlamydial ophthalmia 63, 135
contraindications 136
diphtheria 19, 134–135
dosage and administration **134–136**
drug interactions 136
enteritis 37, 135
gingival infections 33, 135
legionellosis 27, 135
neonatal gonococcal conjunctivitis 136
ointment 62
ornithosis 31, 135
overdosage 136
pertussis **31**, 135
pharyngitis 15, 134
pneumonia 22–24, 135
postsplenectomy prophylaxis 91, 136
prostatitis 46, 135
Q fever 85, 135
relapsing fever 82, 136
rheumatic fever prophylaxis 90–91, 136
sexually transmitted diseases 63, 67, 135–136
Escherichia coli
cholecystitis 41
data collection 6
diarrhoeal disease 36, **37**, **39**, 122
enteritis 157

neonatal meningitis 79
pneumonia 25, 27
septicaemia 86
urinary tract infections 43, 45
Essential Drugs, WHO Model List of 9–10, 11, 12, 13
Eye infections, *see* Chlamydial ophthalmia; Conjunctivitis

Fasciitis, streptococcal necrotizing **49**, 100, 125
Fluoroquinolones **12–13**, **121–123**
Folliculitis **47**
Formularies **9**, 10
Francisella tularensis, tularaemia 83
Fungal infection, endocarditis 72, 73
Furunculosis **47**

Gangrene **49–50**, 100
clindamycin 125
gentamicin 139
metronidazole 144
Gardnerella vaginalis, vaginitis 64
Gastritis **41**, 93, 144, 160
Gastrointestinal infections
diarrhoeal **35–40**
non-diarrhoeal **41–42**
Gene transfer, antimicrobial resistance 3
Gentamicin **137–141**
brucellosis 82–83, 141
cholecystitis 42, 138
contraindications 141
dosage and administration **137–141**
drug interactions 141
endocarditis 69–72, 137–140
gangrene 50, 139
meningitis 78–79
neonatal meningitis 78–80, 140–141
pelvic inflammatory disease 65, 139
peritonitis 42, 138
plague 84, 141
pneumonia 23, **24**, 26, 29–30, 138
precautions 141
prosthetic valve endocarditis 73
pyelonephritis 45, 139
resistance 12
septicaemia 87, 141
soft tissue injuries 51, 139
surgical prophylaxis 88, 89, 141
tularaemia 83, 141
Giardiasis 37, **40**, 143
Gingival infections (*see also* Perioral infections) **33**, 105, 135, 143, 148
Glomerulonephritis, impetigo 47
Gonorrhoea 11, 12, **61–62**, 63
ceftriaxone 115
ciprofloxacin 122
spectinomycin 152
Granuloma inguinale (donovanosis) **68**, 119, 132, 158

α-Haemolytic streptococci, endocarditis 69, **70–71**, 97, 101, 139–140
β-Haemolytic streptococci, osteomyelitis 53, 93, 100
Haemophilus ducreyi, chancroid 67
Haemophilus influenzae
amoxicillin 11
chronic bronchitis 20
epiglottitis 18–19
gene transfer 3
infant facial lesions 48
infant osteomyelitis **54–55**, 95, 100, 114
meningitis 75, **77–78**, 97, 116, 119
meningitis prophylaxis 97–98, 119, 150–151
osteomyelitis 128
otitis media 16
pneumonia 24
septic arthritis 57
sinusitis 17
Haemophilus spp., resistance 10
Helicobacter pylori, gastritis/peptic ulcer 41
HIV infection
brain abscess 80
chancroid 67, 68
gastrointestinal infections 37, 39
pneumonia **27**
sulfamethoxazole + trimethoprim precautions 158
Hospital-acquired infections 4–5, 13
pneumonia **29–30**, 112, 121–122, 127, 138, 163–164
septicaemia 86
sources **29**
Human bite injuries **51–52**, 95, 105
doxycycline 132

metronidazole 144–145
sulfamethoxazole + trimethoprim 157–158

Imipenem + cilastatin 12, 30, **142**
Impetigo **47–48**, 157
cefalexin 107
cloxacillin 127
Infants (*see also* Children; Neonates)
chlamydial ophthalmia 63
facial lesions 48
osteomyelitis **54–57**, 95, 100, 114, 158
pneumonia **24–26**, 100
Infective endocarditis, *see* Endocarditis
Injuries, *see* Bites; Clenched-fist injuries
Intestinal infections, *see* Gastrointestinal infections
Intrauterine devices (IUDs) 64
Invasive diarrhoea (dysentery) **36–37**
IUDs, *see* Intrauterine devices
Ixodes dammini, Lyme disease 81

Joint infections (*see also* Septic arthritis) **53–60**

Klebsiella spp.
aspiration pneumonia 27
cholecystitis 41
pyelonephritis 45

Laboratories, role of **5–7**
β-Lactam drugs **10–13**, 69
Laryngotracheobronchitis, *see* Croup
Legionella spp. 7, 22, 26
Legionellosis **26–27**, 121, 135
Leptospirosis **82**
benzylpenicillin 102
doxycycline 133
Lesions, localized purulent skin **47**, 107, 127, 157
Listeria monocytogenes
meningitis **78–79**
meningitis drugs 98, 102, 140–141, 158
Lung abscesses **27–28**, 95, 100
clindamycin 124
metronidazole 143
Lung disease, chronic suppurative 21, 92, 119
Lyme disease **81**, 93
benzylpenicillin 102
ceftriaxone 116
doxycycline 133
Lymphogranuloma venereum **62–63**, 132, 135

Mastoiditis **17**, 97, 114, 118
Melioidosis **31–32**, 131–132, 157
Men
chlamydial infections 63
urinary tract infections **44**
Meningitis 11–12, 26, **75–80**
ampicillin 77–79, 97–98
benzylpenicillin 75–80, 101–102
cefotaxime 11–12, 76–77, 79, 111
ceftriaxone 11–12, 75–78, 115–116
chloramphenicol 75–76, 78, 119
gentamicin 78–80, 140–141
neonatal **78–80**, 98, 102, 111, 140–141
neonatal pneumonia 26
otitis media/mastoiditis 16, 17
prophylaxis 76, 78, 97–98, 123, 150–151
rifampicin 76–78, 97–98, 150–151
sulfamethoxazole + trimethoprim 78, 158
vancomycin 77, 164
Meticillin-resistant *Staphylococcus aureus* (MRSA) 13, 30, 163–164
Metronidazole **142–145**
amoebiasis 143
aspiration pneumonia 28, 143
brain abscess 80, 145
contraindications 145
dosage and administration **143–145**
drug interactions 145
gangrene 50, 144
gastritis/peptic ulcer 41, 144
giardiasis 143
gingival infections 33, 143
lung abscesses 143
necrotizing enterocolitis 40, 143–144
overdosage 145
pelvic inflammatory disease 65, 145
peritonitis 42, 144
protozoal infections 40
soft tissue injuries 51, 52, 144–145
surgical prophylaxis 88, 89, 145
trichomoniasis 145
vaginitis 64, 145

Microflora, normal 4, 8
Model List of Essential Drugs (WHO) 9–10, 11, 12, 13
Moraxella catarrhalis, chronic bronchitis 20
MRSA, *see* Meticillin-resistant *Staphylococcus aureus*
Mutations, resistant bacteria **4**
Mycobacterium tuberculosis
  cervical adenitis 34
  pericarditis/myocarditis 73
  resistance 4, 6
Mycoplasma pneumoniae
  bronchitis 20
  pneumonia 22
Myocarditis **73**

Nalidixic acid 36, **146**
Nasopharyngitis **15**
National reference laboratories 6
Necrotizing enterocolitis **40**, 143, 164
Necrotizing fasciitis, streptococcal **49**, 100, 125
Neisseria gonorrhoeae
  gene transfer 3
  resistance 6
  septic arthritis 57
  sexually transmitted diseases 61–62, 64
  spectinomycin 152
Neisseria meningitidis
  meningitis 75, **76**, 101–102, 119
  prophylaxis 123, 150
Neonates (*see also* Infants)
  ampicillin 26, **78–79**, 87, 98
  cefotaxime 110–111
  chlamydial ophthalmia 63
  croup 110
  epiglottitis 18, 110, 150
  gonoccocal conjunctivitis **62**, 111, 115, 136, 152, 160
  meningitis **78–80**, 98, 102, 111, 140–141
  osteomyelitis **55–57**, 110–111, 158
  pneumonia **25–26**, 93, 110, 119, 138
  septicaemia 87, 98
  septic arthritis 111
Neurosyphilis 66, 100, 105
Nitrofurantoin 43, 44, **147**
Nocardia spp., brain abscess 80
Nosocomial infections, *see* Hospital-acquired infections
Nystatin 64, **147–148**

Odontogenic infections **33–34**, 105, 148–149
Omeprazole, gastritis/peptic ulcer 41
Ophthalmia, chlamydial 63, 135
Oral administration **7–8**
Oral infections, *see* Perioral infections
Ornithosis (psittacosis) **31**, 131, 135
Osteomyelitis **53–57**, 95, 158
  benzylpenicillin 100
  cefalexin 107
  cefazolin 109
  ceftriaxone 114–115
  ciprofloxacin 122
  clindamycin 124
  cloxacillin 128
  β-haemolytic streptococci 53, 93, 100
  neonates **55–57**, 110–111, 158
Otitis media
  acute **15–16**, 92, 95, 158
  chronic **16–17**

Paratyphoid fever **38**, 97
  chloramphenicol 119
  ciprofloxacin 122
  sulfamethoxazole + trimethoprim 157
Parenteral administration **7–8**, 11
Pasteurella multocida, animal bites 51
Pathogens, identification 6–7
Pelvic inflammatory disease **64–65**, 115
  ciprofloxacin 123
  clindamycin 125
  doxycycline 132
  gentamicin 139
  metronidazole 145
Penicillins
  allergies 16, 94, 96, 125, 132
  antimicrobial resistance 16, 24
Peptic ulcer disease **41**, 93, 144, 160
Peptostreptococcus spp., aspiration pneumonia 27
Pericarditis **73**
Periodontitis **33**, 105
  erythromycin 135
  metronidazole 143
  phenoxymethylpenicillin 148

Perioral infections **33–34**, 93, 105
Peritonitis **42**, 97, 138, 144
Pertussis (whooping cough) **31**, 135
Pharmacodynamics **7**
Pharmacokinetics **7**
Pharyngitis **14–15**, 103, 106–107
  amoxicillin 92
  erythromycin 134
  phenoxymethylpenicillin 148
Phenoxymethylpenicillin **148–149**
  cervical adenitis 148
  perioral/dental infections 33, 34
  pharyngitis 15
  postsplenectomy prophylaxis 91
  rheumatic fever prophylaxis 89, 90
Plague **84–85**, 120
  chloramphenicol 120
  doxycycline 132
  gentamicin 141
  streptomycin 153
Pneumocystis carinii, pneumonia 27, 124, 157
Pneumonia **21–30**
  amoxicillin 22–26, 28, 93, 95
  aspiration **27–28**, 95, 100, 124, 143
  atypical 23
  benzylpenicillin 23–25, 28, 99–100
  cefazolin 28, 108
  cefotaxime 26, 110
  ceftriaxone 23, 25, 114
  children **24–26**, 100
  chloramphenicol 23–26, 119
  clindamycin 27, 28, 124
  cloxacillin 28–30, 127
  doxycycline 23, 131
  erythromycin 22–24, 135
  gentamicin 23–24, 26, 29–30, 138
  HIV infection **27**
  hospital-acquired **29–30**, 112, 121–122, 127, 138, 163–164
  legionellosis **26–27**
  neonates **25–26**, 93, 110, 119, 138
  procaine benzylpenicillin 105
  sulfamethoxazole + trimethoprim 157
  vancomycin 163–164
Postsplenectomy prophylaxis **91**, 94, 136, 149
Pregnancy
  ciprofloxacin 123
  clindamycin 126
  doxycycline 133
  gentamicin 141
  rifampicin 151
  sulfadiazine **155**
  urinary tract infections 43
Prescribing, general principles **7–9**
Primaquine, HIV-associated pneumonia 27
Probenecid, syphilis 66
Procaine benzylpenicillin **104–106**
  cellulitis/erysipelas 48, 105
  cervical adenitis 34, 105
  contraindications 106
  diphtheria 19, 105
  dosage and administration **105–106**
  perioral/dental infections 33, 34, 105
  pneumonia 24, 25, 105
  precautions 106
  soft tissue injuries 52, 105
  syphilis 66, 67, 105–106
Prophylaxis
  meningitis 76, 78, 97–98, 123, 150–151
  neonatal gonococcal conjunctivitis 136
  non-surgical **89–91**
  postsplenectomy **91**, 94, 136, 149
  rheumatic fever **89–91**, 104, 136, 149
  surgical 11–12, **88–89**, 95, 109, 126, 141, 145
  urinary tract infections 44, 147
Prostatitis **45–46**, 63, 122
  doxycycline 132
  erythromycin 135
  trimethoprim 162
Prosthetic implants
  osteomyelitis 57
  surgical prophylaxis **88–89**
  valve endocarditis **73**, 140, 164
Proteus spp., pyelonephritis 45
Protozoal infections, intestinal **39–40**
Pseudomonas aeruginosa
  data collection 6
  prosthetic valve endocarditis 73
  resistance 12
  septicaemia 86
Psittacosis, *see* Ornithosis
Publications, WHO 10
Punching injuries **51–52**, 95, 105
  doxycycline 132
  metronidazole 144–145

sulfamethoxazole + trimethoprim 157–158
Purulent skin lesions **47**, 107, 127, 157
Pyelonephritis **45**, 97, 114, 139
Pyomyositis **50**, 107, 108–109
clindamycin 125
cloxacillin 127

Q fever 72, **85**, 131, 135
Quality control, susceptibility testing 6

Relapsing fever **81–82**, 120, 133, 136
Reporting, surveillance data **5–7**
Reserve antimicrobials **10–13**
Resistance (antimicrobial) **3–6**, 9, 12–13
to benzylpenicillin 97
endocarditis pathogens 69–73, 164
to β-lactam drugs **10–12**
meningitis pathogens 77, 150, 164
MRSA 13, 30, 163–164
to penicillins 16, 24
Streptococcus pneumoniae 22, 24
Respiratory rates, pneumonia 21–22
Respiratory tract infections 11–12
lower **20–30**
upper **14–19**
Rheumatic fever 14, **73–74**
secondary prophylaxis **89–90**, 104, 136, 149
Rhinitis **15**
Rickettsial infections **85**, 120, 133
Rifampicin **149–151**
brucellosis 83, 150
contraindications 151
dosage and administration **150–151**
drug interactions 151
epiglottitis 18–19, 150
meningitis 77, 150
meningitis prophylaxis 76, 78, 97–98, 150–151
overdosage 151
Rocky Mountain spotted fever **85**

Salmonella spp.
data collection 6
enteric infections **38–39**, 119, 122, 157
infant osteomyelitis 158
osteomyelitis 53, 54, **56–57**
osteomyelitis drugs 111, 115, 122, 128–129
resistance 12
Salpingitis 63
Selection mechanisms, resistant bacteria **3–4**
Septicaemia **86–87**
ampicillin 98
cefazolin 109
cefotaxime 111
ceftriaxone 116
chloramphenicol 120
clindamycin 125
cloxacillin 130
gentamicin 141
neonates 111
Septic arthritis **57–60**
cefalexin 107
cefazolin 109
ceftriaxone 115
children 107, 115
clindamycin 125
cloxacillin 129
neonates 111
Sexually transmitted diseases **61–68**
Shigella spp. 6, 36
Shigellosis 12, **36**, 37, 122
Sickle-cell disease 39, 53
Sinusitis, acute **17**, 92, 95, 158
Soft tissue infections **47–52**, 95, 107
cloxacillin 127–128
gentamicin 139
metronidazole 144–145
Software, WHONET 6
Sources, hospital-acquired infections **29**
Spectinomycin **152**
chancroid 68
gonorrhoea 61, 62
Splenectomy, post-, prophylaxis **91**, 94, 136, 149
Spontaneous mutation, resistant bacteria **4**
Spotted fever 85
Staphylococcus aureus
cardiovascular infections 69, **72**, 73, 129–130, 140
cervical adenitis 34
data collection 6
meticillin-resistant (MRSA) 13, 30, 163–164

neonatal osteomyelitis 111
neonatal septic arthritis 111
osteomyelitis **53–56**, 107, 109, 114, 125, 128
pneumonia 24–25, **28–29**, 108, 124, 127, 138
prostatitis 45
pyomyositis 50
resistance 12
septicaemia 86
septic arthritis 57, **58–60**, 107, 109, 115, 125
soft tissue injuries 51
surgery 88
Staphylococcus saprophyticus, urinary tract infections 43
Staphylococcus spp., prosthetic valve endocarditis 73
Streptococcal necrotizing fasciitis **49**, 100, 125
Streptococcus anginosus (milleri), brain abscess 80
Streptococcus pneumoniae
bronchitis 20–21
data collection 6
meningitis 75, **76–77**, 79, 102, 116
otitis media 16
pneumonia 22, 24, 25
resistance 11–12
septicaemia 86
septic arthritis 57
sinusitis 17
Streptococcus pyogenes
aspiration pneumonia 27
cervical adenitis 34
data collection 6
impetigo 47
necrotizing fasciitis **49**
pharyngitis **14**
rheumatic fever 73–74
soft tissue injuries 51
Streptococcus spp.
bite injuries 51
neonatal meningitis 79–80
prosthetic valve endocarditis 73
Streptomycin **153–154**
brucellosis 82, 153
contraindications 153
dosage and administration **153**
overdosage 154
plague 85, 153
tularaemia 83, 153
Sulfadiazine 91, **154–155**
Sulfamethoxazole + trimethoprim 6, **156–159**
bronchitis 20–21, 157
brucellosis 83, 158
contraindications 158
dosage and administration **156–158**
drug interactions 159
enteric infections 38, 39
granuloma inguinale 68, 158
HIV-associated pneumonia 27
infant osteomyelitis 56, 57
melioidosis 32, 157
meningitis 78, 158
osteomyelitis 158
otitis media 16, 156
overdosage 159
pneumonia 23, 25, 27, 157
precautions 158–159
purulent skin lesions 47, 48, 157
sinusitis 157
soft tissue injuries 52, 157–158
typhoid/paratyphoid 157
Surgery
amoxicillin + clavulanic acid 95
cefazolin 109
chemoprophylaxis 11–12, **88–89**, 126
gentamicin 141
metronidazole 145
Surveillance data, reporting **5–7**
Susceptibility testing **5–7**
Syphilis 61, **66–67**
benzathine benzylpenicillin 103–104
benzylpenicillin 100–101
doxycycline 132
erythromycin 136
procaine benzylpenicillin 105–106

Testing, antimicrobial susceptibility 6
Tetracycline **159–161**
contraindications 160
dosage and administration **160**
drug interactions 161
gastritis/peptic ulcer 41, 160
neonatal gonococcal conjunctivitis 160
ointment 62

Tinidazole 40, **161**
Tooth abscesses **33–34**, 93, 105, 148–149
Toxoplasma gondii, brain abscess 80
Treatments, options **9–13**
Treponema pallidum, syphilis 66
Trichomonas vaginalis, vaginitis 64
Trichomoniasis **64**, 145
Trimethoprim 43, 46, **162**
Trimethoprim + sulfamethoxazole, *see* Sulfamethoxazole + trimethoprim
Tularaemia **83**, 120, 141, 153
Typhoid fever 12, **38**, 97
  chloramphenicol 119
  ciprofloxacin 122
  sulfamethoxazole + trimethoprim 157
Typhus fever **85**

Upper respiratory tract infections **14–19**
Ureaplasma urealyticum, prostatitis 46, 132, 135
Urethritis 63
Urinary tract infections **43–46**, 95
  cefalexin 107
  nitrofurantoin 147
  trimethoprim 162

Vaccination
  epiglottitis 19
  postsplenectomy prophylaxis 91
Vaginitis **64**, 147–148
Vaginosis 145
Vancomycin **13, 163–165**
  contraindications 164
  dosage and administration **163–164**
  endocarditis 69–72, 164
  meningitis 77, 164
  MRSA 163–164
  necrotizing enterocolitis 40, 164
  overdosage 165
  pneumonia 29, 30, 163–164
  prosthetic valve endocarditis 73
Vascular surgery, prophylaxis **88–89**
Vibrio cholerae 35
Viridans streptococci, pneumonia 27

WHONET software 6
Whooping cough (pertussis) **31**, 135
Women
  chlamydial infections 63
  urinary tract infections **43–44**
World Health Organization (WHO)
  Model List of Essential Drugs 9–10, 11, 12, 13
  WHONET software 6
Wounds (*see also* Bites; Soft tissue infections)
  contaminated soft tissue 48, **51–52**

Yersinia pestis, plague 84