SLMA GUIDELINES ON THE USE OF ANTIMICROBIAL AGENTS

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Foreword

I am pleased to write this foreword to the "Guidelines on the use of antimicrobial agents" published by the Sri Lanka Medical Association (SLMA). Publication of these guidelines for drugs effective in the treatment of infections is a long-felt need. The objective is to provide clear, practical, independent, evidence-based information for prescribing antimicrobials at all levels of health care. These guidelines will assist prescribers in ensuring that patients receive optimum treatment.

About 20% of the state sector drug budget is used for purchase of antimicrobial drugs, especially antibiotics. Availability of guidelines will promote appropriate cost-effective prescribing in the state and private sectors.

I hope that the information provided will be used as well for undergraduate and post- graduate medical training, paramedical training, in-service training and supervision. It would be essential to revise these guidelines periodically and the comments of users should be taken into account when updating the guidelines.

I congratulate the editors, authors of chapters and others who contributed to develop this publication. I am confident that the publication "Guidelines on the use of antimicrobial agents" by the SLMA will promote rational use of antimicrobial drugs, thereby preventing unnecessary use, thus reducing antibiotic resistance.

Dr Athula Kahandaliyanage
Director General of Health Services

Introduction

Until recently, there was a widespread belief that war against infections was nearly over. Far from having being conquered infections have resurged dramatically. The microbial agents that caused them have adapted to exploit opportunities for change and spread. There is no doubt that this situation has arisen due to inappropriate or irrational use, and even abuse of antimicrobial drugs.

Such inappropriate use is due to two misconceptions.

a. that bacterial infection is more common than it is, in fact.
b. that antibiotics are largely non-toxic and can be used with impunity.

Apart from this, it is known that the cost of treatment with antimicrobials is rising. Needless to say, this is more important in developing countries, where antimicrobials could be obtained over the counter (OTC).

The Sri Lanka Medical Association decided to publish these guidelines to promote appropriate cost-effective prescribing. We have obtained the assistance of experts in each speciality to write the different chapters. We expect that these guidelines would be useful to all grades of medical officers such as junior doctors, consultants, junior and senior academics.

Professor Gita Fernando
Dr S D Atukorale

ANNEX 1

Abbreviations

ABST – antibiotic sensitivity test
ADL – adenolymphangitis
AFB – acid fast bacilli
AIDS – acquired immunodeficiency syndrome
AMC – Anti Malaria Campaign
AOM – acute otitis media
ATT – anti-tuberculous therapy
AUC – area under the (serum concentration time) curve

b.d. – twice a day
BV – bacterial vaginosis

CAP – community acquired pneumonia
CSF – cerebrospinal fluid
Cmax – peak serum level
Cmin – trough serum level
CNE – culture negative endocarditis
CNS – central nervous system
CoNS – coagulase negative staphylococci
CRP – C- reactive protein
CSOM – chronic suppurative otitis media
CT scan – commuted tomography scan
CTG - cardiotopography

DEC – diethylcarbamazine
DGI – disseminated gonococcal infection
DIC – disseminated intravascular coagulation
DMSA- dimercaptosuccinic acid (labelled with technetium-99)
DNA – deoxy-ribonucleic acid
DOTS – directly observed treatment short course
DTPA – diethylenetriaminepentacetic acid (labelled with technetium-99)

E - ethambutol
EEG – electroencephalogram
EMBSA – epidemic methicillin resistant *Staphylococcus aureus*
ERCP- endoscopic retrograde cholangio-pancreatography

ESR – erythrocyte sedimentation rate

FBC – full blood count
FDC – fixed drug combinations

g – gram
GABS – beta haemolytic streptocci of Lancefield Group A
GBS – Group B streptococci
GNB – Gram negative bacteria
G6PD- glucose 6-phosphate dehydrogenase

H- isoniazid
HAP – hospital acquired pneumonia
HIV – human immunodeficiency virus
HLR – high level resistance
HSV – herpes simplex virus
ICP – intracranial pressure
ICU – intensive care unit
IgE – immunoglobin E
im – intramuscular
IUALTD – International Union Against Tuberculosis and Lung Diseases
IUCD- intrauterine contraceptive device
IUGR – intrauterine growth retardation
iv - intravenous

JE – Japanese encephalitis

kg - kilogram
KOH – potassium hydroxide

L – litre
LP – lumbar puncture

mcg – microgram/s
MCUG – micturating cystourethrogram
mf - microfilariae
mg – milligram

MB – multibacillary (leprosy)
MDR – multidrug resistant
MIC – minimum inhibitory concentration
MGRSA – methicillin and gentamicin resistant *Staphylococcus aureus*
MRSA – methicillin resistant *Staphylococcus aureus*
MRI scan – magnetic resonance imaging scan
MSSA – methicillin susceptible *Staphylococcus aureus*
MTB – *Mycobacterium tuberculosis*

NCE - new chemical entity
NGU - non-gonococcal urethritis
NICU – neurointensive care unit
NPTCCD – National Programme for Control of Tuberculosis and Chest Diseases
NVE- native valve endocarditis

OTC – over the counter

PAE – post-antibiotic effect
PB – paucibacillary (leprosy)
PCR – polymerase chain reaction
PD- pharmacodynamic
PID – pelvic inflammatory disease
PK – pharmacokinetic
PTB – pulmonary tuberculosis
PVE – prosthetic valve endocarditis

q.i.d. – four times a day

R - rifampicin
RAT – rapid antigen detection test
RH – rifampicin + izoniazid (4RH – RH for 4 months)
RHE – rifampicin + izoniazid + ethambutol
RHZE – rifampicin + izoniazid + pyrazinamide + ethambutol
(2RHZE – RHZE for 2 months)
RHZES – rifampicin + izoniazid + pyrazinamide + ethambutol + streptomycin
S - streptomycin
SBP – spontaneous bacterial peritonitis

SIRS – sepsis with systemic inflammatory response
SSSS – staphylococcal scalded skin syndrome
S+P – sulphadoxine + pyrimethamine
STD – sexually transmitted disease
STI – sexually transmitted infections

TB – tuberculosis
TBM – tuberculous meningitis
t.d.s. – three times a day
TPE – tropical pulmonary eosinophilia
TSS – toxic shock syndrome

URTI – upper respiratory tract infection
UTI – urinary tract infection

VISA – vancomycin insensitive *Staphylococcus aureus*
VRSA – vancomycin resistant *Staphylococcus aureus*
VVC – vulvovaginal candidiasis
VZV – varicella zoster virus

WBD/DC –white blood count/ differential count
WHO – World Health Organisation

Z - pyrazinamide

ANNEX 2

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Chapter 1

ANTIMICROBIALS IN PREGNANCY AND LACTATION

Antimicrobials can have harmful effects on the fetus at any stage of the pregnancy. The nature of the effect is dependent on the time of administration. During the first trimester antimicrobials may cause congenital malformations (teratogenesis). The period of greatest risk is from the **third to tenth week** of pregnancy. During the second and third trimesters, antimicrobials may affect growth and functional development of the fetus or cause toxic effects on fetal tissue. Antimicrobials given before delivery, during labour or after delivery may cause adverse effects on labour or on the neonate. ***Always exclude pregnancy when prescribing for a woman of childbearing age***

Principles for prescribing antimicrobials during pregnancy

- Prescribe antimicrobials only if benefit to the mother is greater than the risk to the fetus
- It is advisable to avoid antimicrobials during the first 12 weeks of pregnancy.

If antimicrobials are indicated during the first 12 weeks
use only those considered to be not harmful

- Prescribe antimicrobials which have been used extensively and are not known to be harmful.
- Do not use new chemical entities (NCE)
- Take into account the altered pharmacokinetics in pregnancy:
  (a) increase in total body water, plasma volume, cardiac output causing dispersion of drugs in a larger distribution volume
  (b) haemodilution with a fall in plasma albumin, leading to a reduction in the bound fraction; there is a relative increase in the free fraction of drugs

As a result of altered pharmacokinetics the therapeutic concentration appropriate for a non-pregnant woman may not be the same as that for a pregnant woman and the dose may have to be increased. Ideally therapeutic drug monitoring is recommended:

- for antimicrobials with a low therapeutic index, when there is poor clinical response

- if there are features of toxicity
- Safety of antimicrobials in pregnancy is known to change with time. An antimicrobial which was considered to be unsafe a few years ago may be considered safe later on, based on post-marketing surveillance data.

Before giving any antimicrobials prescribers should update their knowledge on the safety of the drugs

Breast-feeding

Most antimicrobials are excreted in minimal amounts in breast milk. Infants are exposed to low doses, which are well below the therapeutic dose level for infants. Drugs cross the placenta more efficiently than into breast milk. Breast-feeding should be continued unless there is adequate evidence to indicate that: the drug taken by the mother will harm the infant and no other therapeutic equivalent can be given

The table indicates safety of antimicrobials in pregnancy and breast-feeding.

Antimicrobial use in pregnancy and breast-feeding

Antimicrobial	**Pregnancy**	**Breast-feeding**
Penicillins	Not known to be harmful	Not known to be harmful
Cephalosporins *exception-cefpirome*	Not known to be harmful Avoid	Not known to be harmful Avoid
Aminoglycosides	Avoid, unless essential; risk of auditory or vestibular nerve damage; greatest risk with streptomycin; ideally monitor serum aminoglycoside concentration	Not known to be harmful
Quinolones (ciprofloxacin,norfloxacin ofloxacin, levofloxacin**)** *exception-nalidixic acid*	Aviod, arthropathy in animal studies Not known to be harmful	Caution, monitor infant for diarrhea Monitor infant for haemolysis
Macrolides Erythromycin Clarithromycin	 Not known to be harmful Avoid, unless benefit outweighs risk	 Not known to be harmful Caution, monitor infant for diarrhea

Azithromycin	Use only if alternatives not available	Not known to be harmful
Roxithromycin	Not known to be harmful	Not known to be harmful
Telithromycin	Avoid	Avoid
Chloramphenicol	Risk of neonatal grey baby syndrome if given in 3rd trimester	Avoid if infant is preterm or < 1 month
Sulfonamides & trimethoprim		
Sulfasalazine,sulfadoxine	Risk of neonatal haemolysis if given in third trimester Folic acid should be given	Not known to be harmful for older healthy full term infants
Co-trimoxazole	Risk of teratogenesis as trimethoprim is a folate antagonist	Not known to be harmful for older healthy full term infantsAvoid if infant is preterm or < 1 month (monitor for haemolysis, jaundice)
Azoles		
Metronidazole	Avoid high dose regimens	Not known to be harmful, avoid high doses, can give milk a bitter taste
Tinidazole	Not known to be harmful	Uncertain
Nitrofurantoin	Not known to be harmful	Not known to be harmful, may cause neonatal haemolysis in preterm infants
Tetracyclines		
Tetracycline oxytetracycline doxycycline	Avoid, effects on skeletal development in animals, 1st trimester; dental discoloration in 2nd and 3rd trimesters	Avoid
Imipenem	Avoid, unless benefit outweighs risk.	Avoid
Meropenem	Use only if essential	Caution, monitor infant for diarrhea
Aztreonam	Avoid, no information available	Avoid
Sodium fusidate	Not known to be harmful	Not known to be harmful
Vancomycin	Use only if essential, ideally monitor plasma concentration	Not known to be harmful
Teicoplanin	Use if benefit outweighs risk.	Avoid
Clindamycin	Not known to be harmful	Not known to be harmful, monitor infant for diarrhea

Colistin	Avoid, risk of fetal toxicity	Avoid
Antituberculous drugs		
Isoniazid	Not known to be harmful	Monitor infant for hepatitis
Rifampicin	Not known to be harmful	Monitor infant for hepatitis
Ethambutol	Not known to be harmful	Not known to be harmful
Pyrazinamide	Use as benefit outweighs risk	Not known to be harmful
Streptomycin	Avoid	Avoid
Antileprotic drugs		
Dapsone	Risk of neonatal haemolysis, methaemoglobinaemia, 3rd trimester; give folic acid 5mg	Monitor infant for haemolysis
Clofazimine	Use if benefit outweighs risk.	Uncertain
Antimalarial drugs	Use as benefit outweighs risk	Not known to be harmful
exception-primaquine	Avoid	Avoid
Anti fungal drugs		
Amphotericin	Avoid, unless benefit outweighs risk.	Caution
Fluconazole	Avoid, multiple congenital abnormalities	Avoid
Clotrimazole	Not known to be harmful	Not known to be harmful
Econazole	Not known to be harmful	Not known to be harmful
Miconazole	Avoid, unless essential	Caution
Griseofulvin	Avoid, teratogenic in animals	Avoid
Ketoconazole	Avoid, teratogenic in animals	Avoid
Itraconazole	Avoid, use only if essential	Avoid
Nystatin	Not known to be harmful	Not known to be harmful
Anti viral drugs		
Anti HIV drugs	Refer to venereologist	
Aciclovir	Use as benefit outweighs risk	Not known to be harmful
Valaciclovir	Use as benefit outweighs risk	Uncertain
Ganciclovir	Avoid risk of teratogenesis	Avoid
Foscarnet	Avoid	Avoid
Ribavarin	Avoid	Avoid

Anthelmintics		
Mebendazole	Avoid in 1st trimester	Not known to be harmful
Albendazole	Avoid	Not known to be harmful
Pyrantel	Not known to be harmful	Not known to be harmful
Diethylcarbamazine	Avoid in 1st trimester, use if essential during 2nd and 3rd trimesters	Not known to be harmful

Further Reading

1. Therapeutic Guidelines, Antibiotics, Therapeutic Guidelines Limited, Melbourne, Australia, 2006
2. British National Formulary, 51st Edition 2006. BMJ Publishing Group Ltd & RPS Publishing. London
3. Guide to Pathogens and Antibiotic Treatment, Adis International, Auckland, New Zealand, 2001
4. Bennet PN, Brown MJ eds. Clinical Pharmacology. 9th edition 2003 Churchill Livingstone.215-277
5. Prescribing in Pregnancy, Obstetrics Clinics of North America. 1997;**24(**3) 617-629

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Chapter 2

BONE AND JOINT INFECTIONS

Osteomyelitis

Patients suspected of osteomyelitis or septic arthritis should be admitted to a hospital as soon as the disease is suspected, for initial assessment and immediate treatment.

Osteomyelitis is an infection of bone leading to inflammatory destruction of bone, bone necrosis and new bone formation. Depending on the onset of the disease, there are 3 subtypes; acute, subacute, and chronic

Types of osteomyelitis based on pathogenic mechanisms of infection include:

- Osteomyelitis following haematogenous spread of infection from a distant source
  e.g. furuncle, dental sepsis, gastrointestinal infection.
- Osteomyelitis secondary to a contiguous focus of infection. e.g. trauma, surgery
- Osteomyelitis associated with vascular insufficiency. e.g. diabetes, peripheral vascular disease.

Normally bone is resistant to infection. Some conditions that predispose to osteomyelitis include; large inoculums of organisms, trauma leading to bone damage and infarction, presence of a foreign body, and compromised host defenses. Bones affected include, tibia-50%, femur-30%, fibula-12%, humerus-3%, ulna-3%, and radius-2%

The causative organisms include:
Staphylococcus aureus, *Streptococcus spp*, Gram- negative bacilli such as *Escherichia coli* and *Pseudomonas aeruginosa*, Coagulase negative staphylococci, *Haemophilus influenzae*, *Anaerobes: Bacteriodes, Streptococci spp, Propionobacterium acnes, Mycobacterium tuberculosis*

Acute osteomyelitis
Presentation depends on age.

- Neonates or infants: generalized febrile illness with few localizing signs.
- Children:
  (a) Abrupt fever, irritability, lethargy, reluctance to use the limb, local signs of inflammation over the bone. **A child who is unwell having bone pain and tenderness has osteomyelitis unless proved otherwise.**
  (b) Rapid onset cellulitis
  (c) Intramuscular abscess

- Adults: fever, chills, swelling, erythema over the involved bone.

Suspect acute osteomyelitis, take an appropriate history, carry out examination and basic investigations.

The investigations include: WBC/DC, ESR, C-reactive protein (CRP), blood culture, X-rays of affected area, aspiration of soft tissue mass, ultrasound scan, isotope bone scan, and MRI

Management

(1) General management: hydration, nutrition and pain relief

(2) Specific management

Once the diagnosis is made and appropriate basic investigations are done give antibiotics.

Parenteral antibiotics are given at the beginning on a best guess basis.

Causative agents

The causative agent depends on the age of the patient and mode of spread.

Haematogenous osteomyelitis is usually due to a single causative organism.

Neonates:

Group B Streptococci, Staphylococcus *aureus*

Gram-negative bacilli e.g. coliforms such as *Escherichia coli*

Infants and children:

Staphylococcus aureus, Group A Streptococci, Gram-negative bacilli, Group B Streptococci, *Haemophilus influenzae*

Adults

Staphylococcus aureus, Gram-negative bacilli

Contiguous focus osteomyelitis

This is usually a polymicrobial infection, causative organisms include:

Staphylococcus aureus, Coagulase negative staphylococci

Streptococcus pyogenes, Enterococcus species, Gram- negative bacilli, Anaerobes

Osteomyelitis due to vascular insufficiency

Causative organisms include:

Staphylococcus aureus, Coagulase negative Staphylococci
Enterococci, *Proteus mirabilis, Pseudomonas aeruginosa*
Anaerobes

Antibiotics

Every patient should be treated with cloxacillin or flucloxacillin together with one of the following:
Ampicillin/amoxicillin, gentamicin, co-amoxiclav, cefuroxime or cefotaxime. Once the specific organism is identified appropriate antibiotics are given .Intravenous antibiotics are usually given for 7-10 days, till systemic symptoms subside, followed by oral antibiotics for **at least six weeks.** If specific organisms are not identified, antibiotics covering all likely causative organisms are continued for six weeks. Treatment should be monitored with repeated: WBC/DC, ESR, CRP, X-rays, etc.

In specific clinical situations uncommon organisms should be considered, in addition to organisms mentioned above.

(1) Osteomyelitis in haemoglobinopathies such as thalassaemia and sickle cell disease, the usual causative organism is: *Salmonella enteritica* sub-type *typhi;*

Antibiotics recommended:
Chloramphenicol 500 mg iv 6 hourly
Co-amoxiclav 1.2 g iv 8 hourly or 625 mg orally b.d. or t.d.s.
Ciprofloxacin 200 mg iv b.d. or 500 mg orally b.d.

(2) Intravenous drug addicts, the causative organisms include:
Pseudomonas aeruginosa, Serratia marcescens

Antibiotics recommended:
Ceftazidime 1-2 g iv 8 hourly
Ticarcillin/clavulanic acid 3.2g iv 8 hourly
Ciprofloxacin 200- 400 mg iv b.d.

(3) In foot punctures, likely causative organism is
Pseudomonas aeruginosa.

Antibiotics recommended:
Ceftazidime -2 g iv 8 hourly
Ticarcillin + clavulanic acid 3.2g iv 8 hourly
Ciprofloxacin – 200- 400 mg iv b.d. or 500 mg orally b.d.

(4) Animal bites, causative organisms include :
Staphylococcus aureus, Streptococcus pyogenes, Streptococcus viridans, Bacteriodes, Pasteurella multocida
Antibiotics recommended:
Benzylpenicillin 600 mg - 1.2 g iv 6 hourly
Ampicillin 500 mg 1g iv 6 hourly
Co-amoxiclav 1.2 g iv 8 hourly plus metronidazole if there is necrotic tissue.

If methicillin resistant *Staphylococcus aureus* (MRSA) is isolated give teicoplanin 200 mg iv b.d. or vancomycin 1 g iv b.d.

Chronic osteomyelitis
Chronic osteomyelitis is relapsing bone infection. The hallmarks of chronic osteomyelitis are the presence of dead bone (sequestrum), involucrum (reactive new bone), local bone loss, persistent drainage and sinus tracts.
This is more a surgical problem.
Antibiotics are given according to culture and sensitivity.

Common organisms include:
Staphylococcus aureus, Escherichia coli, Streptococcus pyogenes, Proteus spp, Pseudomonas aeruginosa, Coagulase negative Staphylococci, Anaerobes

Septic arthritis
Septic arthritis is inflammation of the synovial membrane caused by an infective organism. **This is an orthopaedic emergency.** The joint can get infected by haematogenous route, direct inoculation, or secondary to osteomyelitis

Presentation
- Generalized febrile illness- neonates may present as a septicaemic illness.

- Acute painful swollen joint. (In infants the hip is commonly affected. In children and adults the knee is commonly affected.)
- Acute loss of spontaneous movement of a limb. (pseudoparalysis)

Any acutely painful single swollen joint should be considered as septic arthritis unless proved otherwise.
Predisposing factors include; rheumatoid arthritis, diabetes, long term steroid use, and intra- articular injections. There is an absence of all movements of the joints. Investigations to be done include: WBC/DC, ESR, CRP, blood culture, joint aspiration and synovial fluid analysis, X-rays, ultrasound scan, MRI, and bone scan.

Management
(1) General management includes splinting, hydration, nutrition, and pain relief
(2) Specific management includes administration of appropriate antibiotics.

The causative agent depends on age of the patient.
Neonates

Group B Streptococci, *Staphylococcus aureus*, Gram negative bacteria e.g *E. Coli, Haemophilus influenzae, Treponema pallidum*

Children under 3 years

Haemophilus influenzae, Staphylococcus aureus, Gram negative bacilli, *Streptococcus spp*

Children over 3 years

Staphylococcus aureus

Adult under 50 years

Staphylococcus aureus, Neisseria gonorrhoeae

Adult over 50 years

Staphylococcus aureus.
Gram-negative bacilli e.g. *Pseudomonas aeruginosa*

The antibiotics are administered on a best guess basis indicated below.Every patient should be given cloxacillin /flucloxacillin together with one of the following, ampicillin, gentamicin, co-amoxiclav, cefuroxime or cefotaxime.

Appropriate antibiotic therapy should be continued for at least six weeks.
Initial treatment is given intravenously until systemic symptoms subside in about 7-10 days, followed by oral antibiotics. Treatment should be monitored by repeated ESR and CRP

If the patient does not respond within 48 hours, surgery (arthrotomy) is mandatory while continuing with antibiotics.
Choice of antibiotics

(1) *Staphylococcus aureus*:
Cloxacillin /flucloxacillin 500 mg-1g iv 6 hourly
Erythromycin 500 mg iv or orally 6 hourly
Fusidic acid, usually in combination with one of the above, 500 mg iv t.d.s.

(2) Methicillin resistant *Staphylococcus aureus* (MRSA):
Vancomycin 1 g iv b.d.
Teicoplanin 200 mg iv b.d.
Linezolid 600 mg orally b.d. (presently only formulation available)

If allergic to penicillins:
Erythromycin
Clarithromycin 500 mg iv b.d.
Azithromycin 250 -500 mg orally b.d.

(3) Group A and B Streptococci
Benzylpenicillin followed by phenoxymethylpenicillin

(4) Coliforms- *Escherichia coli*, *Klebsiella spp*: Ampicillin – 500 mg-1g iv/orally 6 hourly
Co-amoxiclav – 1.2 g iv 8 hourly or 625 mg orally b.d. or t.d.s
Cefuroxime – 750 mg - 1.5 gm iv 8 hourly
Cefotaxime – 1-2 g iv 8 hourly
Ceftriaxone 1-2 g iv once daily

(5) *Pseudomonas aeruginosa*
Ticarcillin/clavulanic acid – 3.2 g iv 8 hourly
Ceftazidime -1-2 g iv 8 hourly
Aminoglycosides 5mg/kg/dose iv once daily
Fluroquinalones 200-400 mg iv b.d.
Imipenem – 500 mg 1g iv 8 hourly
Meropenem - 500 mg 1g iv 8 hourly

(6) *Haemophilus influenzae*
Ampicillin 500 mg 1 g iv 6 hourly
Co-amoxiclav 1.2 g iv 8 hourly or 625 mg orally b.d. or t.d.s.
Ampicillin/ salbactum 1.5 g iv 8 hourly or 375 mg orally b.d.
Cefotaxime 1-2 g iv 8 hourly

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Chapter 3

INFECTIVE ENDOCARDITIS

Antimicrobial prophylaxis
Conditions where prophylactic antimicrobials are indicated include the following

(a) Cardiac conditions

- Prosthetic heart valves (high risk group)
- Complex congenital cyanotic heart diseases (high risk group)
- Previous infective endocarditis (high risk group)
- Surgically constructed systemic or pulmonary conduits (high risk group)
- Acquired valvular heart diseases
- Mitral valve prolapse with valvular regurgitation or severe valve thickening
- Non-cyanotic congenital heart diseases (except for

secundum type atrial septal defect) including bicuspid aortic valve
- Hypertrophic obstructive cardiomyopathy

(b) Diagnostic and therapeutic interventions likely to produce bacteraemia
- Bronchoscopy (rigid instrument)
- Cystoscopy during urinary tract infection
- Biopsy of urinary tract/prostate
- Dental procedures with the risk of gingival/mucosal trauma
- Tonsillectomy and adenoidectomy
- Oesophageal dilatation/sclerotherapy
- Instrumentation of obstructed biliary tracts
- Transurethral resection of prostate
- Urethral instrumentation/dilatation
- Lithotripsy
- Gynaecological procedures in the presence of infection

Prophylactic antibiotic regimens

	Not allergic to penicillin	Allergic to penicillin
Dental, oral, respiratory, and oesophageal procedures	Amoxicillin 2.0 g 1 hour before or amoxicillin or ampicillin 2.0 g iv 1/2 to 1 hour before	Azithromycin/clarithromycin 500 mg or clindamycin 600 mg 1 hour before
Genitourinary and gastrointestinal procedures		
High risk group:	Ampicillin or amoxicillin 2.0 g iv plus gentamicin 1.5 mg/kg iv 1/2 to 1 hour before procedure; 6 hours later, ampicillin or amoxicillin 1.0 g orally	Vancomycin 1.0 g (children 20 mg/kg) over 1 to 2 hours before procedure plus gentamicin 1.5 mg/kg iv or im

Moderate risk group:	Ampicillin or amoxicillin 2.0 g iv ½ to 1 hour before procedure; or amoxicillin 2.0 g orally 1 hour before	Vancomycin without gentamicin

Decision making for antibiotic treatment of native (NVE) and prosthetic valve endocarditis (PVE) due to streptococci

Regimen A: NVE; full susceptibility to penicillin (minimal inhibitory concentration [MIC] ≤0.1 mg/L)	
Patients ≤65 years, normal serum creatinine levels	Benzylpenicillin 12–20 million units/ 2 4 hours iv, divided into 4-6 doses for 4 weeks plus gentamicin 3 mg/kg/24 hours iv (maximum 240 mg/day), divided into 2–3 doses for 2 weeks
Same conditions as above with uncomplicated course and rapid clinical response to therapy	Benzylpenicillin 12–20 million units/24 hours iv, divided into 4-6 doses for 2 or 4 weeks with ambulatory treatment after 7 days treatment in hospital
Patients ≥65 years and/or serum creatinine level elevated or allergy to penicillin	Benzylpenicillin adapted to renal function for 4 weeks or ceftriaxone 2 g/24 hours iv[a] as single dose for 4 weeks
Patients allergic to penicillin and cephalosporins	Vancomycin 30 mg/kg/24 hours iv divided into 2 doses for 4 weeks
Regimen B: Susceptibility to penicillin (MIC 0.1 mg/L–0.5 mg/L) or PVE	
	• Benzylpenicillin 20–24 million units/24 hours iv divided into 4–6 doses or[a] ceftriaxone 2 g/24 hours iv as single dose both for 4 weeks plus gentamicin 3 mg/kg/24 hours iv, divided into 2–3 doses for 2 weeks[b] followed by ceftriaxone 2 g/24 hours iv for additional 2 weeks • Vancomycin as single drug treatment for 4 weeks (dosage see above)

Regimen C: Resistance to penicillin; MIC >0.5 mg/L[c]	
	Treatment as for infective endocsrditis due to enterococci

Notes:

[a] Especially for patients allergic to penicillin

[b] 2–3 mg/kg netilmicin once daily may be an alternative (peak serum level <16 mg/L).

[c] High level resistance (HLR) to penicillin or ceftriaxone (MIC >8 mg/l) and HLR to gentamicin (MIC >500 mg/l) or resistance to vancomycin or teicoplanin (MIC ≥4 mg/L) are rare among strains of streptococci. In such situations, extended susceptibility testing and a close cooperation with the clinical microbiologist are mandatory.

Decision-making for antibiotic treatment of infective endocarditis due to enterococci and penicillin-resistant streptococci

Penicillin (MIC ≤8 mg/L) and gentamicin (MIC <500 mg/L)	Benzylpenicillin, 16–20 million units in 4–6 divided doses plus gentamicin 3 mg/kg, iv, divided in 2 doses for 4-6 weeks
Penicillin-allergic patients and penicillin/gentamicin susceptible enterococcal isolates	Vancomycin 30 mg/kg/day iv in two divided doses plus gentamicin (dosage as above) for 6 weeks
Penicillin-resistant strains (MIC >8 mg/L)[a]	Vancomycin plus gentamicin (dosage as above) for 6 weeks
Vancomycin-resistant strains including strains with intermediate resistance to vancomycin (MIC 4-16 mg/L) or highly resistant to gentamicin[a]	Assistance of an experienced microbiologist is mandatory. If antimicrobial therapy fails, valve replacement should be considered early

Note:

[a] For resistant enterococci, treatment with oxazolidinone e.g. linezolid may be an option but should be initiated only after advice from a microbiologist.

Benzylpenicillin 1 million units = 600 mg penicillin

If microbiological laboratory facilities are not available, review of antibiotics is necessary if there is no response to therapy in 3-5 days. Features of clinical response include: defervescence of fever dimunition of polymorphonuclear leucocytosis, ESR,C reactive protein or red cells in the urine and clinical well-being of the patient.

Decision making for antibiotic treatment of infective endocarditis due to staphylococci

Regimen A: Native valve endocarditis	
MSSA[a] no allergy to penicillin	Cloxacillin[b] 8–12 g/24 hours iv, divided into 4 doses for at least 4 weeks[c] plus gentamicin 3 mg/kg/24 hours iv (maximum 240 mg/day), divided into 2-3 doses for the first 3–5 days of treatment
MSSA[a] "allergy" to penicillin[d]	Vancomycin 30 mg/kg/24 hours iv divided into 2 doses[e] for 4–6 weeks[f], plus gentamicin 3 mg/kg/24 hours iv (maximum 240 mg/d) divided into 2-3 doses for the first 3–5 days of treatment
MRSA[g]	Vancomycin 30 mg/kg/24 hours iv divided into 2 doses[e] for 6 weeks
Regimen B: Endocarditis involving prosthetic material/cardiac valve prostheses	
MSSA[a]	Cloxacillin[b] 8–12 g/24 hours iv, divided into 3–4 doses plus rifampicin 900 mg/24 hours iv divided into 3 doses, both for 6–8 weeks, plus gentamicin 3 mg/kg/24 hours iv (maximum 240 mg/day) divided into 2–3 doses for the first 2 weeks of treatment
MRSA[g],CONS[h,i]	Vancomycin 30 mg/kg/24 hours iv divided into 2 doses[e] for 6 weeks, plus rifampicin 900 mg/24 hours iv divided into 3 doses, plus gentamicin[j] 3 mg/kg/24 hours iv (maximum 240 mg/d) divided into 2–3 doses, all for 6–8 weeks

Notes:

[a] Methicillin-susceptible *Staphylococcus aureus*

[b] Or its congeners

[c] Except for drug addicts for whom a two-week regimen may be sufficient

[d] For both immediate (immunoglobulin E [IgE]) type and hypersensitivity reaction during treatment

[e] Infusion over at least 60 min

[f] Total treatment duration for patients initially treated with oxacillin should be at least 4 weeks. These patients should not have a second course of gentamicin treatment.

[g] Methicillin-resistant *S. aureus*

[h] Coagulase-negative staphylococci (CoNS). In oxacillin-susceptible CoNS, vancomycin should be replaced by cloxacillin.

[i] For resistant staphylococci, treatment with oxazolidinone may be an option but should be initiated only after advice from a microbiologist centre has been taken.

[j] If gentamicin susceptibility has been shown in vitro, gentamicin is added in MRSA for the full course but for CoNS only for the first two weeks of treatment. If the organism is resistant to all aminoglycosides, gentamicin may be substituted by a fluoroquinolone.

Antimicrobial treatment in culture negative endocarditis (CNE) or if therapy is urgent and the causative organism unidentified

NVE		
Vancomycin	15 mg/kg iv every 12 hours[a, b]	4-6 weeks
+ Gentamicin	1.0 mg/kg iv every 8 hours	2 weeks
PVE		
Vancomycin	15 mg/kg iv every 12 hours	4-6 weeks
+ Rifampicin	300-450 mg orally. every 8 hours	4-6 weeks

+ Gentamicin	1.0 mg/kg iv every 8 hours	2 weeks

Notes:
[a] Maximum 2 g/day
[b] Aminopenicillin may be added.
Although above antibiotics are recommended in developed countries, an alternative in Sri Lanka would be: penicillin and gentamicin for 3 days. If there is no response, cefuroxime to replace penicillin. If there is still no response, ciprofloxacin* to replace gentamicin. .
*Ciprofloxacin 200-400 mg iv bd for adults. It is best avoided in children.

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Antibiotic doses in infective endocarditis in children

Benzylpenicillin
Given as slow iv or infusion
Preterm neonate and neonate under 7 days of age; 50 mg / kg 12 hourly.
7 to 28 days age; 50mg /kg 8 hourly,
1 month to 18 years ; 50 mg / kg 4 to 6 hourly (maximum 2 to 4 g 4 hourly)

Flucloxacillin
Given as slow iv or infusion
Under 7 days; 25 – 50 mg / kg 12 hourly, slow iv or infusion (higher doses in severe infections)
7 to 21 days; 25 – 50 mg / kg.8 hourly (higher doses in severe infections)
1 month to 18 years; 50 mg / kg 6 hourly (maximum of 2 g 6 hourly)

Ampicillin
Under 7 days; 50 -100 mg /kg 12 hourly (higher dose in severe infections)

7 to 21 days; 50 – 100 mg /kg 8 hourly (higher dose in severe infections)
21 to 28 days; 50 – 100 mg / kg 6 hourly (higher dose in severe infections)
1 month to 18 years ; 50 mg / kg 4 to 6 hourly (maximum of 2 g 4 hourly)

Amoxicillin
< 7 days; 50 - 100 mg / kg 12 hourly (higher dose in severe infections)
7 to 28 days; 50 - 100 mg / kg 8 hourly (higher dose in severe infections)
1 month to 12 years; 50 mg / kg 6 hourly (maximum of 2 g 6 hourly)

Vancomycin
<29 weeks gestation; 15 mg / kg 24 hourly
29 to35 weeks gestation; 15 mg / kg 12 hourly
> 35 weeks gestation; 15 mg / kg 8 hourly
1 month 18 years; 15 mg / kg 8 hourly (maximum daily dose 2 g)

Ceftriaxone
Given as iv infusion over 60 minutes
Neonate; 20 to 50 mg / kg once daily
1 month to 12 years < 50 kg body weight; 50 to 80 mg / kg once daily
> 50 kg body weight or 12 to 18 years; 1 g daily (severe infection – 2 to 4 g daily)

Gentamicin
< 29 weeks gestation; 2.5 mg / kg 24 hourly
29 to 35 weeks gestation; 2.5 mg / kg 18 hourly
> 35 weeks gestation; 2.5 mg / kg 12 hourly
1 month to 12 years; 2.5 mg / kg 8 hourly
12 to 18 years; 5 mg / kg per day once daily or twice daily

Amikacin
Given as slow iv over 3 to 5 minutes
Neonate; loading dose of 10mg/ kg then 7.5 mg/ kg 12 hourly
1 month to 18 years; 7.5mg/ kg 12 hourly.

Netilmicin
Given im or iv over 3 to 5 minutes or iv infusion
Neonate under 7 days; 3mg/ kg 12 hourly
7 to 21; days 2.5 to 3mg / kg 8 hourly
1 month to 1 year; 2.5 - 3 mg / kg 12 hourly
1 -18 years; 3 mg / kg 8 hourly

In infective endocarditis if an aminoglycoside is combined with a beta-lactam, give the total daily dose of aminoglycoside in two to three divided doses.

Ceftazidime
Given as iv infusion
< 7 days; 2.5 – 5 mg / kg 24 hourly (higher dose in severe infections)
7 to 21 days; 2.5 - 5 mg /kg 12 hourly (higher dose in severe infections)
21 to 28 days; 2.5 mg – 5 mg / kg 8 hourly (higher dose in severe infections)
1 month to 18 years; 2.mg / kg 8 hourly (maximum 6 g daily)

Aztreonam
Give iv over 3 to 5 minutes or as infusion
< 7 days; 30 mg / kg 12 hourly
7 to 28 days; 30 mg / kg 6 to 8 hourly
1 month to 2 years; 30 mg / kg 6 to 8 hourly
2 years to 18 years; 30- 50 mg/ kg 6 to 8 hourly (higher dose in severe infections)
12 to 18 years; 1 g 8 hourly or 2 g 12 hourly

Imipenem or **meropenem**
Give by iv infusion (*use with caution in neonates*)
< 7days; 20 mg / kg 12 hourly
7 to 21 days; 20 mg / kg 8 hourly
3 weeks to 3 months; 20mg / kg 6 hourly
3 months to 18 years < 40 kg; 5 mg / kg 6 hourly
> 40 kg; 1 - 2 g per day in 3 to 4 divided doses

Co-amoxiclav
Give iv over 3 to 4 minutes or iv infusion
Preterm infants or neonates < 7 days; 30mg /kg 12 hourly
1 week to 3 months; 30 mg / kg 8 hourly
3 months to 12 years; 30 mg / kg 8 hourly, increased to 6 hourly in severe infections
12 to 18 years; 1.2 g 8 hourly, increased to 6 hourly in severe infections

Piperacillin/tazobactam
Give slow iv or infusion
Neonate - 90 mg/ kg 8 hourly
1 month to 12 months - 90mg / kg 6 to 8 hourly. Maximum 4 to 5 g 6 hourly
12 to 18 years - 2.25 to 4.5 g 6 to 8 hourly

Ticarcillin/clavulanic acid iv infusion
Neonate <7 days; 80 mg / kg 12 hourly
7 to 28 days; 80 mg / kg 8 hourly
1 month to 18 years; 80 mg/ kg 6 to 8 hourly. Maximum single dose 3.2 g

Cefotaxime im or iv
<7 days - 25 – 50 mg / kg 12 hourly. (higher dose in severe infections)
1 to 4 weeks - 25- 50 mg / kg 6 to 8 hourly.(higher dose in severe infections)
1 month to 18 years -50mg / kg 3 to 4 times a day. Maximum of 12 g per day

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Chapter 4

CENTRAL NERVOUS SYSTEM INFECTIONS IN ADULTS

Central nervous system (CNS) infections are associated with significant morbidity and mortality. The commoner and more important of these are meningitis, encephalitis, cerebral abscess, neuro-tuberculosis and cerebral malaria.

This chapter deals with the antimicrobial therapy of meningitis (bacterial, viral, and fungal), encephalitis, cerebral abscess and neuro-tuberculosis in adults. Management of cerebral malaria, and CNS infections in children are discussed elsewhere.

Meningitis

Background

Meningitis is the inflammation of the leptomeninges surrounding the brain. It can result from infections caused by bacteria, viruses (including HIV), *Mycobacterium tuberculosis* and fungi. It may also occur due to non-infective causes (e.g. malignancy, chemotherapy, radiation, drugs, chemicals), but these are rare.

Acute meningitis is an emergency. Treatment cannot wait for microbiological results, and should be started immediately on clinical suspicion, on empiric 'best guess' grounds. The acute presentation can be similar, irrespective of aetiology. Tuberculous and fungal meningitis usually present as subacute or chronic illnesses, but can mimic the more acute bacterial meningitis.

Common organisms (in adults)

Bacterial - *Streptococcus pneumoniae, Haemophilus influenzae Neisseria meningitides, Staphylococcus aureus Coagulase negative staphylococci* (head injury, neurosurgical procedures), *Listeria monocytogenes* (elderly, infancy, pregnancy, immunocomprised states) G*ram-negative bacill(*neurosurgical procedures, immunocomprised states)

Viral - Enteroviruses – *Echo, Coxsackie*
Mumps, *Herpes simplex virus* – type II (commoner), type I, *Lymphocytic choriomeningits virus*

Mycobacterium tuberculosis (TB)

Fungal - *Cryptococcus neoformans, Candida*, in immunocompromised states

Bacterial meningitis

Establishing the diagnosis:

Initial diagnosis is clinical (fever, headache, vomiting, photophobia, altered consciousness, signs of meningism, seizures, focal signs, signs of raised intracranial pressure).

Blood cultures must be taken at least from 2-3 different sites, as soon as possible (ideally within 30 minutes of admission), before antibiotic treatment is commenced. Cerebrospinal fluid (CSF) analysis from lumbar puncture (LP) is the mainstay of diagnosis, and should be done before antibiotic treatment (ideally within 30 minutes of admission).

A CT scan of brain should be done before LP in patients with papilloedema, other features suggestive of raised intracranial pressure, coma, or focal neurological signs. If there is a delay in obtaining culture samples, lumbar puncture or in CT scanning, empiric antibiotic therapy must be started without delay.

Antibiotic treatment

Empiric treatment:

- All patients with suspected acute meningitis should be treated as acute **bacterial** meningitis with empiric intravenous antibiotic therapy, until CSF and blood culture results are available.
- Cerebrospinal fluid (CSF) protein, glucose, cellular and Gram stain findings may be misleading, especially if antibiotics were previously given. CSF culture results take time, and may be falsely negative if there has been antibiotic treatment.
- Empiric treatment aims to provide broad antibacterial cover against the common microorganisms, mainly *S. pneumoniae*, *H. influenzae*, and *N. meningitidis*.

Recommended empiric treatment

1. Third generation cephalosporins
   - cefotaxime 2-3 g iv 6 hourly *or*
   - ceftriaxone 2g iv 12 hourly

   with or without vancomycin 0.5-1g iv 6-12 hourly

   Or
2. Benzylpenicillin (2.4 g 4 hourly), plus chloramphenicol (500-1000 mg 6 hourly)
   - The first regimen is generally recommended in most countries, due to penicillin resistance in pneumococci, and chloramphenicol resistance in *H. influenzae.*
   - Data regarding the relative prevalence of causative microorganisms and antibiotic sensitivity in Sri Lanka are limited. The available data and clinical experience suggests that the penicillin and chloramphenicol combination is still effective. This, and cost constraints, may compel us to use the second regimen as empiric treatment.
   - Vancomycin is added to cover cephalosporin resistant strains of *S. pneumoniae*.
   - Ampicillin iv (2g 4 hourly) is added to the empiric treatment regimen to cover possible *Listeria monocytogenes* infection in old age (over 60 years) and in states of immune deficiency (e.g. alcoholism, steroid therapy).

Specific treatment for organisms

- The antibiotic treatment may be changed to the most effective antibiotic for the identified pathogen, after culture and antibiotic sensitivity results are available.
- However, if there has been a good clinical response, consider continuing the empiric treatment regimen.

Streptococus pneumoniae

- penicillin-sensitive strains, benzylpenicillin remains the recommended drug.
- penicillin-resistant strains, give third-generation cephalosporins (cefotaxime or ceftriaxone) with or without vancomycin, depending on the resistance pattern.

Neisseria meningitidis

- benzylpenicillin
- alternative, ampicillin 2 g iv 4 hourly
- for penicillin-resistant strains, third-generation cephalosporins (cefotaxime or ceftriaxone)

Haemophilus influenzae

- third generation cephalosporins (cefotaxime or ceftriaxone)
- alternatives - chloramphenicol and ampicillin, but resistance may be common

Listeria monocytogenes

- ampicillin or benzylpenicillin

Aerobic gram-negative bacilli

- third generation cephalosporins + an aminoglycoside (eg; gentamicin 1-2 mg/kg iv 8 hourly)
- *Pseudomonas aeruginosa* meningitis, the recommended drug is ceftazidime
  (2 g iv 8 hourly). Ceftriaxone and cefotaxime are not effective

Staphylococcus aureus

- recommended drugs are nafcillin or oxacillin, which are not available in Sri Lanka at present; alternative is cloxacillin 1-2 g iv 4 hourly
- for penicillin-allergy, vancomycin (0.5-1g iv 6-12 hourly, adjusted to serum levels)
- methicillin-resistant *S. aureus* (MRSA) strains, vancomycin

Coagulase-negative Staphylococci,

- vancomycin

Anaerobes

- metronidazole (500 mg iv 8 hourly)

Duration of treatment:

- The optimal duration of antibiotic therapy is uncertain. The general recommendation is 10-14 days, but this needs to be

adjusted taking into consideration the clinical response, age and co-morbidity.

Duration for specific organisms – a rough guide

	days
S. pneumoniae	10-14
N. meningitidis	7
H. influenzae	7
Other Gram-negative bacilli	21

Ancillary treatment:
Steroids

- Bacteriolysis resulting from antibiotic treatment triggers an inflammatory cascade of events with release of cytokines and other inflammatory mediators, which are neurotoxic. These effects are most pronounced in the initial stages of treatment. This inflammatory process contributes to the early mortality and late neurological sequelae after bacterial meningitis.
- Steroid therapy at initiation of antibiotic treatment is believed to modulate this inflammatory response and improve early and late outcomes.

Intravenous dexamethasone is recommended as adjunctive treatment, starting before or with the first antibiotic dose.

Dose recommended, 0.15 mg/kg iv 6 hourly for 4 days (usual dose 8-10 mg iv 6 hourly)

Managing raised intracranial pressure - elevation of head end to 30°, give mannitol iv 1 mg/kg, consider hyperventilation

Treat other complications such as seizures, septicaemia, shock.

Viral meningitis

Viral meningitis (CSF – lymphocytic pleocytosis, negative Gram stain, normal glucose, negative culture; blood culture negative) is usually self-limiting, and requires no specific treatment. Treatment is usually supportive.

Specific antiviral treatment is only indicated in the setting of immunocompromised states such as HIV infection.

Fungal meningitis

Fungal meningitis usually occurs in immunocompromised states, such as HIV infection, organ transplant recipients, prolonged steroid treatment. Cryptococcal meningitis can sometimes occur in patients without any obvious immune-compromised state.

Fungal meningitis usually requires prolonged treatment with intravenous antifungal agents. The following is an outline for treatment in patients without HIV infection. Specialist advice from a microbiologist is recommended.

Cryptococcal meningitis

- iv amphotericin B (0.7 mg/kg/day) plus flucytosine (100 mg/kg/day) for 2 weeks.
- Repeat lumbar puncture after 2 weeks to assess clearing of organisms from CSF. Continue treatment if the infection has not cleared.
- Follow up treatment with intravenous fluconazole (400 mg/day) for a minimum of 10 weeks.

Candida species

- iv amphotericin B (0.7 mg/kg/day) plus flucytosine (100 mg/kg/day)

Viral encephalitis

Common organisms

- Arboviral – commonly Japanese encephalitis (JE)
- Herpes simplex virus (HSV)
- Varicella zoster virus (VZV)
- Mumps

Treatment is usually supportive. Specific antiviral therapy is available only for HSV and VZV encephalitides.

Specific treatment

HSV encephalitis

Diagnosis is usually established with detection of HSV-DNA using a PCR assay, which is not routinely available in Sri Lanka. HSV encephalitis may be suspected in patients with focal EEG changes in temporal lobes, and presence of red cells in CSF (in a non-traumatic LP).

Treatment, give aciclovir 10 mg/kg iv 8 hourly for 10-14 days
There is no available data regarding the relative prevalence of HSV encephalitis in Sri Lanka, and hence the value of routine empiric therapy with intravenous aciclovir in patients with encephalitis is not clear.

Varicella zoster encephalitis
Follows varicella infection.
Treatment, give aciclovir iv 10 mg/kg 8 hourly for 10-14 days

Supportive treatment

- Managing raised intracranial pressure – elevation of head end to 30°, mannitol iv 1 mg/kg.
- The place of intravenous dexamethasone is controversial.
- Treatment of seizures

Brain abscess and subdural empyema
Usually results from

- local spread from a contiguous focus of infection – middle ear, mastoids, paranasal sinuses
- haematogenous spread from a distant focus of infection
- direct infection following head trauma, neurosurgical procedures

Common organisms

Staphylococci – *S. aureus, S. epidermidis*
Streptococci – *S. milleri, S. pneumoniae*
Anaerobes - *Streptococci, Bacteroides*
Pseudomonas aeruginosa

Polymicrobial infection is common, especially in subdural empyema.

Diagnosis
Diagnosis depends on neuroimaging (CT or MRI scanning). Lumbar puncture is not recommended. Aspirate from the abscess is used for microbiological diagnosis. Blood culture may provide useful information. Investigations should also focus on the detection of a focus of primary infection.

Empiric therapy

Cerebral abscess

Similar to empiric treatment in bacterial meningitis.

Two main antibiotic regimens effective.

1. third generation cephalosporins (cefotaxime or ceftriaxone) and metronidazole

Or

2. Benzylpenicillin and chloramphenicol
   - The addition of an anti-staphylococcal penicillin is recommended if infection with *S. aureus* is suspected. Nafcillin is the recommended drug. Cloxacillin is an alternative.
   - for penicillin allergy, give vancomycin and metronidazole

Subdural empyema

Anti-staphylococcal penicillin **and** third generation cephalosporin (cefotaxime or ceftriaxone) **and** metronidazole

- nafcillin is recommended as anti-staphylococcal penicillin, cloxacillin is an alternative
- use vancomycin for penicillin allergy

Specific therapy

Will be guided by culture and antibiotic sensitivity.

- vancomycin – in MRSA infection and in penicillin/ cephalosporin resistance
- nafcillin is recommended for *Staphylococcus aureus*, cloxacillin is an alternative

Antibiotic treatment should be continued for 4-8 weeks, and the duration should be decided on the clinical response.

Drug dosage is similar to that in treatment of bacterial meningitis.

Ancillary treatment

- Refer for urgent neurosurgical evaluation, as surgical aspiration or evacuation is an important component of treatment.
- Dexamethasone 4-8 mg iv 6 hourly for cerebral abscess
- Treat focus of infection
- Supportive treatment includes management of raised intracranial pressure, treatment of seizures

Spinal epidural abscess

Usually results from

- haematogenous spread from a distant focus of infection
- local spread from vertebral osteomyelitis

Common organisms :

Staphylococci – *S. aureus (commonest), S. epidermidis*
Gram negative bacilli, *Pseudomonas aeruginosa*
Mycobacterium tuberculosis

Diagnosis

Diagnosis depends on spinal imaging, ideally MRI scanning. Lumbar puncture is not recommended. Blood culture may provide useful information. Investigations should also focus on the detection of a focus of primary infection.

Empiric therapy

Anti-staphylococcal penicillin **and** third generation cephalosporin (cefotaxime or ceftriaxone) **and** metronidazole

- nafcillin is recommended as anti-staphylococcal penicillin, cloxacillin is an alternative
- use vancomycin for penicillin allergy

Specific therapy

Will be guided by culture and antibiotic sensitivity.

- Vancomycin, in MRSA infection and in penicillin/cephalosporin resistance
- Nafcillin is recommended for *Staphylococcus aureus.* cloxacillin is an alternative

Antibiotic treatment should be continued for 4-6 weeks, and the duration should be decided on the clinical response.

Ancillary treatment

- Refer for urgent neurosurgical evaluation, as surgical aspiration or evacuation is an important component of treatment.
- Intravenous dexamethasone – 4-8 mg 6 hourly
- Treat focus of infection

Tuberculosis of the central nervous system

Neuro-tuberculosis (tuberculosis of the CNS) includes diverse clinical presentations. These include:

Intracranial - Tuberculous meningitis (TBM)
tuberculoma, tuberculous arteritis – leading to infarcts or haemorrhages

Spinal - Tuberculosis of the spine – with spinal cord or root compression tuberculous arachnoiditis

Tuberculous meningitis

Establishing the diagnosis

A high index of suspicion is necessary as the classic symptoms and signs of meningitis may be absent in TBM. A prodrome of non-specific symptoms (anorexia, malaise, lethargy, fatigue, vomiting) and low grade fever may provide a clue to diagnosis. Evidence of TB elsewhere is seen in only a minority (10-30%) of patients.

Diagnosis depends on LP and CSF examination (high protein, low sugar, lymphocytic or mixed cellular pleocytosis). Definitive diagnosis requires demonstration of TB bacilli in CSF by smear examination (acid- and alcohol- fast bacilli on Ziehl-Nielsen staining), positive culture for *M. tuberculosis*, or detection of *M. tuberculosis* DNA by PCR techniques. A positive tuberculin (Mantoux) test can aid diagnosis, but in Sri Lanka may not always indicate active disease. The value of serological tests in diagnosis is unclear.

Treatment *(See Chapter 18 on TB for drug doses, treatment in drug resistant TB, and other relevant information on drugs).*

1. **Anti-tuberculous treatment (ATT)**
   The ideal duration of ATT is unclear. The WHO recommends 6 months of treatment, similar to pulmonary TB (category 1 treatment). However, other authorities advise continuation of ATT for 12 months.
   2 months initial phase – rifampicin, isoniazid and pyrazinamide, and ethambutol or streptomycin as fourth drug 10 months maintenance phase - rifampicin and isoniazid

2. Steroids

Concurrent steroid therapy improves survival, and possibly neurological outcome in TB meningitis, but the exact mechanism of benefit is unclear.

Dexamethasone is now recommended as adjunctive therapy, starting at the time of initiation of ATT.

For moderately ill to severely ill patients (altered consciousness or focal signs):

Dexamethasone 0.4mg/kg/day iv for 1 week, tapered by 0.1 mg/kg/day each week for 4 weeks, followed by oral dexamethasone, 4 mg/day for 1 week, tapered by 1 mg/day each week, for 4 weeks

For patients without altered consciousness or focal signs:

Dexamethasone, 0.3 mg/kg/day in week 1, 0.2 mg/kg/day in week 2, followed by oral dexamethasone 0.1 mg/kg/day for 1 week, 3 mg/day for 1 week tapered by 1 mg/day each week, for 4 weeks

3. Surgery

Surgical treatment may be needed to relieve hydrocephalus due to blockage of CSF pathways by basal exudates.

Intracranial tuberculoma

Tuberculomata are well defined granulomata which may produce focal symptoms and signs related to their location, seizures, and features related to raised intracranial pressure (headache, vomiting, papilloedema). They may co-exist with TBM.

Diagnosis is based on neuroimaging studies (CT, MRI).

Treatment

- Anti-tuberculous treatment
- Steroid therapy
- Surgery may be needed for tuberculomas that do not respond to ATT, produce focal deficits or cause raised ICP.

Tuberculomas may paradoxically enlarge at the initiation of ATT, but these usually regress with time during treatment.

TB of the spine

Spinal cord compression in tuberculous spondylitis occurs due to paraspinal abscess formation or vertebral collapse. Progressive paraparesis is the usual presentation. Localised pain, tenderness and bony deformity over the spine may be noted.

Plain X-rays of the spine may show vertebral collapse and paraspinal shadows, but MRI scanning is the investigation of choice.

Treatment includes – ATT for 12 months, iv dexamethasone, and surgical decompression.

Tuberculous arachnoiditis

TB arachnoiditis produces neurological symptoms by compression or ischaemia of the spinal cord or the spinal nerve roots. Diagnosis depends on myelography or MRI.

Treatment recommended: ATT for 12 months, surgery if there is failure to respond to medical therapy.

Further Reading

1. Quagliarello VJ, Scheld WM. Treatment of bacterial meningitis. *New England Journal of Medicine*1997: **336**; 708-16
2. Solomon T, Daung NM, Kneen R, Gainsborough M, Vaughn DW, Khanh VT. Japanese encephalitis. *Journal of Neurology, Neurosurgery and Psychiatry* 2000: **68;** 405-415
3. Garg RK. Tuberculosis of the central nervous system. Postgraduate Medical Journal 1999; **75**: 133-40
4. Thwaites G, Chau TTH, Mai NTH, Droboniewski F, McAdam K, Farrar J. Tuberculous meningitis. *Journal of Neurology Neurosurgery and Psychiatry* 2000;**68**:289-99

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Chapter 5

CENTRAL NERVOUS SYSTEM INFECTIONS IN CHILDREN

Infections

- Acute bacterial meningitis
- Tuberculous meningitis
- Brain abscess

Acute bacterial meningitis

Acute bacterial meningitis during the neonatal period

The aetiology of acute bacterial meningitis and its treatment during the neonatal period (0-28 days) are generally different from those in older infants and children. However, there is considerable overlap of the organisms causing acute bacterial meningitis in the neonatal and post-neonatal periods, especially during the second month of life. Therefore, the period from **birth to two months** needs to be considered as the neonatal period for the purpose of management of acute bacterial meningitis in children.

Source: 1. Maternal vaginal flora
2. Environment to which the neonate is exposed

The age at presentation will suggest both the probable organism and the likely mode of acquisition. Presentation in the first week of life (early onset), particularly the first 2 days of life, reflects vertical transmission, while later onset infection suggests hospital associated or community acquired. The corresponding organisms are different; early onset meningitis is more likely to be caused by Group B streptococci (GBS), *Escherichia coli* and *Listeria monocytogenes*, while other Gram-negative organisms as well as staphylococcal species are more likely in late onset meningitis.

Aetiology

1. Enteric Gram-negative bacilli – Coliforms, *Escherichia coli*, *Klebsiella, Enterobacter, Citrobacter, Salmonella, Proteus, Pseudomonas and Serratia*
2. Group B streptococci (GBS)
3. *Listeria monocytogenes*

** Bacteria that typically account for meningitis in older age groups such as *Haemophilus influenzae type b*, *Neisseria meningitidis*, and *Streptococcus pneumoniae* are infrequent causes of meningitis in the neonatal period

** Preterm (<32 weeks), very low birth weight (< 1.5kg) babies on prolonged neonatal intensive care (NICU) stay are liable to infection by commensal flora, especially coagulase negative staphylococci (CoNS), Enterococci and Candida albicans. These organisms tend to show multiple antibiotic resistance.

As with other medical problems in neonates, signs and symptoms of bacterial infection of the central nervous system (CNS) are generally few in number and nonspecific in nature. Manifestations that can suggest meningitis, as well as other serious illness, include temperature instability, lethargy, respiratory distress, poor feeding, vomiting, and diarrhoea. Signs suggestive of meningeal irritation, including neck stiffness, bulging fontanelle, convulsions and opisthotonus, occur only in a minority of neonates with bacterial meningitis and cannot be relied on.

Antibiotic treatment
Appropriate antibiotic treatment is a critical aspect of management. Antibiotic choice is empirical, based on age of onset, likely pathogens, and antibiotic susceptibility patterns. Empirical choice in a particular neonatal unit must consider data regarding pathogens and their susceptibility within the unit. Antibiotics are subsequently modified according to culture and ABST results.

Treatment summary
- Performing a lumbar puncture and a blood culture are recommended if there are signs of sepsis in a neonate (as part of septic screen)
- Treatment should be by the intravenous route
- Recommended empirical antibiotic therapy for meningitis in the **first week** of life: ampicillin + gentamicin and/or cefotaxime
- Empirical antibiotic therapy for meningitis **after the first week** of life: ampicillin + cefotaxime + an aminoglycoside other than

gentamicin such as amikacin or netilmicin (if gentamicin resistance is high).

- Cefotaxime is preferable to ceftriaxone and ceftazidime in neonates; ceftriaxone may aggravate neonatal hyperbilirubunaemia and ceftazidime has a relatively narrow spectrum.

Ampicillin (300mg/kg/day)

< 7 days - 8 hourly

> 7 days - 4-6 hourly

Cefotaxime (50mg/kg/dose)

< 7 days – 12 hourly

7 – 21 days – 8 hourly

> 21 days – 6-8 hourly

Gentamicin

Newborn infant less than 7 days of age

Gestational age	Dose	Dose frequency
< 28 weeks	4mg/kg	36 hourly
28-32 weeks	4mg/kg	24 hourly
32-38 weeks	4mg/kg	18 hourly
> 38 weeks	3.5mg/kg	12 hourly

Newborn infant more than 7 days of age

Gestational age	Dose	Dose frequency
< 28 weeks	4mg/kg (loading dose) followed 24 hours later by daily dose of 3mg/kg	24 hourly
28-32 weeks	4mg/kg (loading dose) followed 18 hours later by 4mg/kg/dose	18 hourly
32-38 weeks	3.5mg/kg	12 hourly
> 38 weeks	3mg/kg	8 hourly

Whenever possible therapy with gentamicin should be guided by assay of blood gentamicin level. Babies with impaired renal function need meticulous monitoring of drug levels and delay in dosage frequency to 36-48 hours if indicated.

In the acute inflammatory stage gentamicin crosses the blood-brain barrier adequately but with the reduction of the inflammatory reaction less may pass through. Therefore the dose should not be reduced.

Other aminoglycosides

Amikacin

Gestational age	Postnatal age	Dose	Dose frequency
< 35 weeks	< 14 days	10mg/kg	24 hourly
	> 14 days 10mg/kg	10mg/kg (loading dose) then 7.5mg/kg	12 hourly
< 35 weeks	< 14 days	10mg/kg (loading dose) then 7.5mg/kg	12 hourly
	> 14 days	7.5mg/kg	12 hourly
Any	> 1 month	7.5mg/kg	12 hourly

Netilmicin

Gestational age	Postnatal age	Dose	Dose frequency
< 32 weeks	< 7 days	3mg/kg	18 hourly
	> 7 days	3mg/kg	12 hourly
> 32 weeks	< 7 days	3mg/kg	12 hourly
	> 7 days	3mg/kg	8 hourly
Any	1 month to 2 years	2.5mg/kg	8 hourly

Subsequent management in a patient with an initial positive CSF culture

- Repeat lumbar puncture at 24 – 48 hours after initiating antibiotic therapy
- If CSF culture is still positive after 48-72 hours and / or there is suspicion of neurological complications perform cerebral ultrasound or CT scan
- Reassess therapy based on culture and antibiotic susceptibility results; therapy should be narrowed to cover the specific pathogen isolated

Treatment of neonatal meningitis caused by specific pathogens

Group B streptococci (GBS)

High dose benzylpenicillin (270mg/kg/day)

< 7 days - 8 hourly
> 7 days - 6 hourly
Combine penicillin with gentamicin until the baby is clinically stable. The rationale for this choice is that in vitro and animal studies suggest improved outcome with the combination over penicillin given alone. Discontinue aminoglycoside when clinically stable and CSF sterilized (usual duration 5-7 days).

Gram-negative enteric pathogens
If a Gram-negative enteric pathogen is isolated, use cefotaxime and an amnioglycoside. Discontinue amninoglycoside 2 weeks after CSF sterilization and complete course with the cefotaxime (3 to 4 weeks).

** If *Pseudomonas aeruginosa* is isolated use ceftazidime or cefixime instead of cefotaxime.
** Infants with obstructive ventriculitis complicating Gram-negative meningitis may require intraventricular administration of aminoglycoside to assist in sterilization of CSF. However, this route is not recommended routinely.

Listeria monocytogenes
Ampicillin + gentamicin initially; discontinue gentamicin once the CSF has been sterilized and the patient improved clinically.

Coagulase negative staphylococci (CoNS)
CoNS rarely invade CSF except as a complication of CoNS bacteraemia accompanying intraventricular haemorrhage, in the presence of a foreign body (a ventriculoperitoneal shunt), or after contamination following neurosurgery. Most CoNS are resistant to multiple antibiotics. The recommended drug for proven CoNS meningitis is vancomycin (20mg/kg/dose 18 hourly for babies < 30 weeks; 12 hourly for babies 30-37 weeks; 8 hourly for babies >37 week gestation).

Duration of therapy:
There are no controlled clinical trials to guide the recommended duration of antibiotic therapy for neonatal meningits. However, historically, therapy has been continued for 2-3 weeks after CSF sterilization. This equates to a minimum of 14 days of iv antibiotics for

GBS and Listeria meningitis and 21 days for Gram negative organisms, after CSF sterilization.

- Consider longer duration therapy if focal neurological signs persist at two weeks, if > 72 hours is required to sterilize CSF, or if obstructive ventriculitis, infarcts, enchephalomalacia, or brain abscess are found by neuroimaging studies. A repeat LP may guide duration of therapy in these cases. Neurosurgical opinion should be sought.
- All patients with neonatal meningitis should have serial assessments of the head size, hearing and development. First audiologic evaluation should take place 4-6 weeks after resolution of meningitis.

** If cefotaxime is not available chloramphenicol may be used with caution; if blood levels are kept between 15-25mg/l toxicity is extremely rare. However, it should be used with extreme caution in preterm babies

** Meropenem has not been sufficiently studied for safety and efficacy in neonates, and is not recommended unless an extended spectrum beta lactamase producing organism is identified. In this situation meropenem in combination with an aminoglycoside should be administered for the entire course of therapy.

** Herpes simplex is a rare but important cause of meningoencephalitis, and aciclovir therapy (20mg / kg / dose, 8 hourly) must be started promptly if the outcome is to be favourable. This pathogen should be considered in all cases of meningitis where the initial Gram stain is negative for bacteria. If proven treatment course is for 21 days.

Acute bacterial meningitis in infants and children over two months (2 months – 12 years)

Common organisms
Haemophilus influenzae type b, Streptococcus pneumoniae, Neisseria meningitidis

The organisms causing acute bacterial meningitis in infants and children beyond the neonatal period resemble those in adults, but

vaccination status plays a major role in deciding the relative contribution of these organisms. Prompt and early treatment of bacterial meningitis reduces the mortality and morbidity of the disease. Since CSF microscopy and culture are vital in directing antibiotic therapy lumbar puncture should be performed as soon as possible.

Initial empirical therapy
cefotaxime 50mg/kg/dose (up to 2g), iv 6 hourly
or
ceftriaxone 100mg/kg/24hours (up to 4g), iv in 1 or 2 divided doses

** If a third generation cephalosporins is not available a combination of benzylpenicillin (210 mg/kg/24 hours in divided doses 4-6 hourly) and
Chloramphenicol (100mg/kg/24hours; 6 hourly) could be used as empirical therapy

Specific therapy and duration
Once the organism and the antibiotic sensitivity are known therapy may need to be changed; Patients who receive antibiotics before LP or who do not have an identifiable pathogen but with evidence of CSF infection should continue the empirical regimen for 7-10 days.

S. pneumoniae
Benzylpenicillin (for susceptible strains) or cefotaxime for 10-14 days

** Vancomycin may be needed together with cefotaxime or ceftriaxone for penicillin resistant strains (MIC of > 0.125mg/L). Seek microbiologists advice in such situations.

N meningitides
Benzylpenicillin for 5-7 days

***Haemophilus influenzae* type b**
Cefotaxime or ceftriaxone for 7-10 days. If these are not available, chloramphenicol may be given.

Gram-negative bacteria (*E.coli, Klebsiella, Pseudomonas* etc)
Cefotaxime, ceftriaxone or cetazidime (for pseudomonas) for 3 weeks or 2 weeks after CSF sterilization (negative CSF)

Place for repeat lumbar puncture
Routine repeat LP is not indicated in uncomplicated *S pneumoniae*, *H ifluenzae* and *N meningitidis* meningitis.

In Gram-negative meningitis, and *S pneumoniae* resistant to beta lactams, a repeat LP 24-48 hours after treatment is indicated.
If focal signs are present or the child does not respond to treatment, a parameningeal focus may be present and a CT or MRI scan should be performed.

Place of corticosteroids
Dexamethasone should be given prior to starting antibiotics, in a dose of 150 mcg/kg, 6 hourly for 4 days by slow iv injection.
Giving an initial dose of dexamethasone, before commencing antibiotics has been shown to reduce complications in the children with Hib meningitis

Prophylaxis of children (household and other close contacts)
Hib meningitis
Rifampicin (neonate 10 mg/kg; child 20mg/kg up to 600mg orally, once a day for 4 days)

Meningococcal meningitis
Rifampicin (neonate 5mg/kg; child 10mg/kg up to 600mg orally, 12 hourly for 2 days

Or

Ceftriaxone 125mg i.m.

Tuberculous meningitis
Tuberculosis of the CNS results in generalized inflammation of the brain and the spinal cord, and delay in treatment will result in permanent neurological disability or death. Hence, early diagnosis and immediate treatment is essential. Tuberculous meningitis is commonest in children under 5 years of age, often occurring within 6 months and usually 2 years after primary infection. The optimal chemotherapy is the use of a combination of drugs with good CSF penetration and low toxicity to the patient. Recommended duration of treatment is 9-12 months

First 2 months - isoniazid (10mg /kg) + rifampicin (15-20mg /kg) + pyrazinamide 35mg/kg followed by isoniazid and rifampicin for the rest of the course.
In a very sick child unable to retain oral drugs initial treatment should be given intravenously or via nasogatric tube, changing over to the oral route when the child improves. Intrathecal therapy is not indicated.
Steroids may be of value in reducing the inflammatory exudates and the development of adhesions which are responsible for hydrocephalus and basilar arachnoiditis. Recommended regime is dexamethasone 0.6mg/kg/day iv 6 hourly for 5-7 days followed by prednisolone 2mg/kg/day for 2-4 weeks and gradually tailed off.
A CT scan should be performed whenever possible to detect cerebral oedema and hydrocephalus.
A tuberculoma is treated similarly to tuberculous meningitis. Large lesions may require surgical excision.

Brain abscess or subdural empyema
Infecting organism depends on the underlying predisposing factor, but most brain abscesses are polymicrobial.

Organisms isolated:
Streptococci (*S.viridans, S. milleri, S. pneumoniae and microaerophillic*), Anerobes (*Bacteroides spp, Fusobacterium spp, Prevotela spp* etc), *Nocardia spp*, Enteric gram-negative bacilli (when likely origin is the ear), *Staph aureus* (after trauma or surgery)

Aspiration of the abscess or empyema is essential to guide antimicrobial therapy.

Initial therapy
Benzylpenicillin (60mg/kg up to 1.8g 4 hourly)
+
Cefotaxime (50mg/kg up to 2g 6 hourly or ceftriaxone 50mg/kg up to 2 g iv 12 hourly
+
Metronidazole 12.5mg/kg up to 500mg; iv 8 hourly

Secondary to penetrating wound/neurosurgery
Vancomycin 15mg / kg up to 500mg iv 6 hourly
+
Cefotaxime or ceftriaxone

In a child with cyanotic heart disease
Benzylpenicillin and metronidazole

Duration
Depends on the organism and response to treatment but usually is 4-6 weeks. Refer for neurosurgical advice.

Epidural abscess
Frequently associated with adjacent osteomyelitis or disc infection; therefore likely to be caused by a single organism, usually *Staph. aureus*. Urgent surgery is indicated.

Initial therapy
Cloxacillin 50mg/kg up to 2g iv 6 hourly
+
Gentamicin (child <10 years 7.5mg/kg; >10years 6mg/kg); iv daily
Subsequent management is as for osteomyelitis.

Further reading

1. American Academy of Paediatrics. Group B streptococcal infections. In: Pickering LK, Baker CJ, Long SS, McMillan JA, eds. Red Book 2006; Report of the Committee on Infectious Diseases. 27th Edition. Elk Grove Village IL; *American Academy of Paediatric*s 2006: 620-7
2. Medicines for children. Royal College of Paediatrics and Child Health 1999
3. Therapeutic Guidelines: Antibiotics. Therapeutic Guidelines Limited, Melbourne Australia 2006

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Chapter 6

EAR NOSE AND THROAT INFECTIONS

In ENT disease antibiotics are delivered to the site in the following manner.

- Topical
- Oral
- Parenteral

Ear infections

1. **Acute otitis media (AOM)**: antibiotics are indicated in acute otitis media early to prevent complications such as perforation leading to chronic forms of otitis media. AOM begins as a viral infection; hence some may recommend not using antibiotics in most cases without tympanometric evidence of AOM. But in Sri Lanka where middle ear investigations are not freely accessible it is better to start antibiotics and use it for a full course of at least 7 – 10 days if clinically AOM is suspected. As the common flora are *S. pneumoniae, Moraxella catarrhalis* and *H. influenzae* the following are recommended by the oral route: co-amoxiclav/ clarithromycin/ cefuroxime/ azithromycin

   As an alternative a single dose of i.v. ceftriaxone is recommended for AOM

   Amoxicillin would cover a large percentage of *S. pneumoniae* and *H.influenzae*

A course of intravenous antibiotics is rarely used in AOM unless a complication such as acute mastoiditis or meningitis is suspected; In this situation the iv forms of co-amoxiclav / cefuroxime / ceftriaxone / cefotaxime can be used. A course of 2 to 3 weeks will be needed depending on the condition. There is no place for topical antibiotics in AOM.

2. **Chronic suppurative otitis media (CSOM**): CSOM without cholesteatoma should be treated with antibiotics. The organisms causing CSOM are usually mixed with *Pseudomonas aeruginosa* taking a prominent place among other species such as *Proteus*, *Staphylococcus* and *Bacteroides*. (It is important to address the primary foci of infection in the middle ear in the overall

management of this condition, which is beyond the scope of this essay) A culture of the ear discharge should be taken when the facilities are available to review the effectiveness of the antibiotics started empirically.

a. **Topical antibiotics:** during the past several years the use of topical eardrops has been accepted as a method of treating a discharging ear. This has been due to the introduction of the fluoroquinolone group of topical ear drops. Twice a day instillation of fluoroquinolone drops has been shown to be effective in controlling CSOM. The duration is usually 10-14 days and should be combined with aural toilet whenever necessary. The following drops can be used: ciprofloxacin / norfloxacin / ofloxacin

   Chloramphenicol ear drops are not used now as it has been shown to have an irritant effect on the external ear canal.

b. **Oral antibiotics:** during an acute exacerbation of CSOM oral antibiotics could be used to supplement topical treatment. Here too the fluoroquinolones play a major role. The following are commonly used, guided by the culture reports: ciprofloxacin / ofloxacin. These are best combined with metronidazole to cover the anaerobes. Fluoroquinlones are best avoided in children.

c. **Intravenous antibiotics:** the place of iv antibiotics is more in CSOM than in AOM. CSOM not responding to oral antibiotics is treated with culture guided iv antibiotics. CSOM with complications such as meningitis will need iv antibiotics usually in combination. The duration will depend on the severity of the condition, and the presence of complications such as meningitis or brain abscess. Commonly used antibiotics are: ciprofloxacin; ceftriaxone / ceftazidime / co-amoxiclav / imipenem. These could be combined with metronidazole. Co-amoxiclav is not active against *Pseudomonas aeruginosa.*

   MRSA infections may occur in CSOM and should be treated as described elsewhere in this book.

3. **Acute otitis externa:** this could be due to bacterial infection following minor trauma such as scratching the ear, or due to a

fungal infection. It could also be due to a furuncle in the ear canal. The infection often causes oedema of the ear canal resulting in pain and deafness. Often a topical steroid should be added to the treatment. Treatment is as follows.

a. **Ear drops:** these are given as a combination with a steroid, instilled into the ear canal 3 times a day. It is best to insert a sterile ear wick after aural toilet is done, and to soak it with the solution to keep the medication in contact with the skin. A 7 – 14 day course may be needed. Commonly used preparations for bacterial otitis externa are: neomycin and hydrocortisone / neomycin, polymyxin and hydrocortisone / neomycin and betamethasone.
b. **Oral antibiotics:** in mild cases of acute otitis externa oral antibiotics are not indicated. However if there is any evidence of a spreading infection it is best to start on oral antibiotics such as co-amoxiclav / azithromycin / cefuroxime

c. **Intravenous antibiotics:** iv antibiotics must be used whenever a cartilage infection (perichondritis) is suspected at least for a week to ten days or even longer in severe cases. A swab should be taken from the exudates over the raw surface in perichondritis following burns or trauma as these cases will require long periods of antibiotics. The commonly used drugs are: co-amoxiclav / ciprofloxacin / azithromycin / ceftazidime / cefotaxime / imipenem

4. **Otomycosis:** it is important to recognize fungal infections clinically, to instil the appropriate ear drops. If combined antibiotic steroid drops are used the condition could get rapidly worse. The fungi usually involved are *Aspergillus fumigatus* and *niger*, *Candida albicans* and *tropicalis*. Aural toilet is vital in this condition with medication instilled at least for 10 days. The medications that can be used are clotrimazole ear drops / econozole lotion

5. **Malignant otitis externa:** in diabetics and immunocompromised individuals a severe form of otitis externa due to *P.aeruginosa* may be seen. Severe pain with granulation tissue in the ear canal in a non-resolving otitis externa should alert one to this diagnosis. Once culture is positive intensive

treatment should be started with intravenous anti-pseudomonal antibiotics according to culture for at least 6 weeks. This should be guided with CT scan assessments of the behaviour of the infection. Recommended antibiotics for this condition are: ceftazidime / ciprofloxacin / ticarcillin-clavulanic acid / gentamicin or a reserve aminoglycoside such as amikacin or netilmicin, or a carbapenem like imipenem or meropenem

Nasal and sinus infections

1. **Vestibulitis:** nasal vestibular infections are commonly due to furuncles, usually due to staphylococcal infections. Oral antibiotics are recommended with or without topical applications depending on clinical judgement. It is important to advise the patient to keep the affected area undisturbed and to continue the medication for the recommended course, as cavernous sinus thrombosis is a rare complication. In well localized furuncles topical application with the following antibiotics will suffice.
   fusidic acid cream / sodium fusidate ointment
   Effective oral antibiotics include: cloxacillin / co-amoxiclav / erythromycin / azithromycin
2. **Acute sinusitis:** usually follows a viral URTI when the sinuses becomes secondarily infected with *Strep..pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis*. It results in prolongation of headache, nasal block, and a general feeling of being unwell. The duration of antibiotic treatment should be at least for 7 - 10 days. Oral antibiotics usually suffice. The recommended antibiotics are: Front-line: erythromycin / doxycyline / co-amoxiclav / cefuroxime / clarithromycin / azithromycin / levofloxacin
   In resistant cases where Gram-negative rods and anaerobes are implicated: ofloxacin / ciprofloxacin with or without metronidazole

3. **Chronic sinusitis:** chronic sinusitis is a prolonged sinus infection usually due to a mixed bacterial flora, with the possibility of fungal infections. Unresolving sinusitis with X ray or CT scan changes indicates chronic sinusitis. Management of chronic sinusitis involves surgery as well. Chronic sinusitis should be investigated using endoscopic and imaging techniques before

treatment regimens are started.. The antibiotic treatment would depend on the culture results and will have to be decided on a case-by-case basis, keeping anaerobic organisms also in mind. Associated foci of infection such as dental causes should be addressed.

Throat infections

1. **Acute pharyngitis and tonsillitis: t**he aetiology of acute pharyngitis is mostly viral and rarely bacterial. The presence of rhinorrohea, cough or conjunctivitis favours a viral aetiology. Infectious mononucleosis produces a exudative tonsillitis with posterior cervical lymphadenopathy.

   Infection by Group A beta haemolytic streptococci (GABHS) is significant due to the complications it can produce. The presence of tonsillar or pharyngeal exudates, tonsillar enlargement and tender anterior cervical nodes suggest this diagnosis. The treatment should be based on guidelines. Usually non-GABHS infections do not require antibiotic treatment. In acute bacterial pharyngitis the streptococcal score can be used to differentiate non GABHS from GABHS infections. The score is arrived at according to the following chart.

   Fever – 1, absence of cough – 1, tender anterior cervical adenopathy -1, tonsillar swelling or exudates - 1, younger than 15 years – 1, age 15 – 45 years – 0, older than forty five -1.

   Analysing the result; 0 to 1 points: streptococcal infection ruled out

   1 to 3 points: order Rapid Antigen Detection Test (RAT) and treat accordingly

   4 to 5 points: probable streptococcal infection, consider empiric antibiotics.

   However in the absence of facilities for RAT tests, a clinical diagnosis based on the above features is recommended. A throat culture should be taken from from the tonsillar area or the posterior pharyngeal wall. For a confirmed or suspected case of GABHS infection the recommended treatment is phenoxymethylpenicillin.

   The dose of oral penicillin is as follows:

   Acute attack of GABHS infection: 500 mg 6 hourly in adults and 250 mg 6 hourly in children for 10 days. For prevention of

GABHS tonsillitis in children with rheumatic fever give same dose twice a day.

2. **Peritonsillitis and peritonsillar abscess:** in these conditions a mixed flora is commonly seen and requires a wider cover of antibiotics. For an abscess surgical drainage is also indicated. The following antibiotics are used iv: co-amoxiclav / cefotaxime / ceftriaxone with or without metronidazole

3. **Acute epiglotitis and supraglottic infection:** seen mainly in children of around 3-7 years. It is diagnosed from the history of an upper respiratory infection which leads to fever and rapidly progressing dysphagia and throat pain. The child will be very ill and toxic. Contrary to the common belief stridor is not seen until very late in the disease and drooling and dysphagia should be the pointers to the disease. **The throat should not be examined with a tongue depressor as it may lead to respiratory arrest.** An X ray of the neck will demonstrate the enlarged epiglottis. Management is primarily in an intensive care unit (ICU) with intubation together with appropriate antibiotics against *H.influenzae* type b. These should be combined with steroids to reduce the swelling of the epiglottis.

   In adults a similar condition is seen where the supraglottic larynx is inflamed and oedematous. The treatment is as above but the need for ICU care does not usually arise.
   The recommended antibiotics are: cefotaxime / cefuroxime / ceftriaxone / chloramphenicol

4. **Acute laryngitis:** acute laryngitis is often viral in origin and does not require antibiotic treatment.

Further reading

1. McIsaac WJ, Goel V, To T, Low DE. The validity of a sore throat score in family practice. *CMAJ 2000*; **163**:811-5

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Chapter 7

EYE INFECTIONS

Conjunctivitis

Conjunctivitis is inflammation of the conjunctiva, usually caused by an infective organism.

Types of conjunctivitis based on the pathogenic organism

- Viral
- Bacterial (including chlamydial)

Organisms responsible include:

Viral

Adenovirus, Herpes simplex virus, *Molluscum contagiosum*
Enterovirus, Coxsackie virus

Bacterial

Staphylococcus aureus, Streptococcus pneumoniae, Haemophilus influenzae especially in children, *Moraxella lacunata, Neisseria gonorrhoeae,* Coliform bacteria, *Chlamydia trachomatis*

It is important to differentiate each of these clinically as management depends on diagnosis.

Diagnosis of viral conjunctivitis

- Often a history of exposure to an infected person (incubation period is about 8 days)
- Infection may be unilateral or bilateral
- Ocular discomfort, rather than pain
- Diffuse redness of the conjunctiva
- Watery discharge
- Tender pre auricular lymph node present
- Systemic symptoms may be associated, commonly upper respiratory tract symptoms

Diagnosis of bacterial conjunctivitis

- Diffuse redness of conjunctiva
- Purulent discharge
- Lid oedema,
- Oedema of the conjunctiva

Gonococcal conjunctivitis

Suspect gonococcal conjunctivitis in a neonate if it occurs around the third day after birth. There is severe purulent discharge, with thick yellow pus, marked conjunctival redness, eyelid oedema and conjunctival oedema (hyperacute conjunctivitis)

Diagnosis of chlamydial conjunctivitis

- Symptoms are less severe than bacterial conjunctivitis.
- Suspect in young adults if symptoms of mild conjunctivitis go on for weeks to months.
- Suspect if associated with urethritis or cervicitis
- Suspect in a neonate if conjunctivitis occur around the second week. May be associated with pneumonia in neonates and infants
- Suspect if associated with casual sexual contact

Diagnosis is confirmed by doing conjunctival scraping and finding typical elementary bodies on direct fluorescent antibody test. Viral and bacterial conjunctivitis have to be differentiated from allergic conjunctivitis

Diagnosis of allergic conjunctivitis

- Always bilateral
- Diffuse redness of the conjunctiva
- Prominent itching
- Oedematous conjunctiva
- Stringy mucoid discharge

Management of a patient presenting with suspected conjunctivitis

The patient should be referred to an ophthalmologist.

Urgent

- When diagnosis in doubt; when a red eye cannot be differentiated from other causes of red eye such as iritis and angle closure glaucoma, Refer all patients if red eye is associated with reduced vision, unequal pupils, pain or vomiting.
- Neonates suspected of having gonococcal conjunctivitis
- Patients who have had intraocular surgery (especially trabeculectomy)
- Patients who wear contact lenses

Indications for non-urgent referral

- No response after one week of treatment
- Worsening of symptoms, and reduction of vision in spite of appropriate treatment
- Recurrent conjunctivitis in the same eye in an infant. This may be associated with delayed canalization of the nasolacrimal duct, and may need surgery.
- If gonococcal, herpetic or chlamydial conjunctivitis is suspected

Management

General

This is directed at preventing transmission of the disease, by personal hygienic measures such as

- Avoiding touching eyes
- Not sharing towels with others
- Washing hands frequently
- Avoiding work places, schools, social gatherings
- Washing and keeping the eye clean

Non-specific

- Cool compresses
- Artificial tears
- For the management of severe cases of gonococcal conjunctivitis, frequent (every 30 -60 minutes) irrigation of the conjunctival sac with normal saline. Such lavages will help to remove inflammatory cells, proteases, and debris that may be toxic to the ocular surface and contribute to corneal ulceration and perforation

Specific

Viral

- No specific treatment is necessary for viral conjunctivitis
- No antibiotics, topical or systemic is necessary
- Prescription of steroids should be restricted to the ophthalmologist; refer to ophthalmologist
- if the symptoms are not improving after about one week
- if the vision is blurred
- if there is photophobia
- if there are conjunctival membranes formed, which need removal

Bacterial

Initial treatment is empiric and cultures are indicated in;

- neonates and immunocompromised patients
- very severe purulent conjunctivitis to exclude gonococcus
- if unresponsive to initial therapy

The following antibiotic drops or ointments commonly used.
Chloramphenicol, gentamicin, ciprofloxacin, ofloxacin, fusidic acid (*effective against S.aureus*), tobramycin, framycetin
The dosing schedule is 4 times daily for approximately 5 to 7 days unless otherwise indicated. Antibiotics drops are used during the day and ointments at night

Gonococcal conjunctivitis in the neonate

Is treated with ceftriaxone 25 to 50 mg im or iv as a single dose. Topical applicati ons include penicillin, ciprofloxacin drops, erythromycin, bacitarcin ointment, Investigate and treat parents for genital infection.

Gonococcal conjunctivitis in adults;

Treatwith ceftriaxone 1g im as a single dose. Those with corneal ulceration should be admitted to hospital and treated with iv ceftriaxone. Ceftriaxone im preparation should not be given iv

Chlamydial conjunctivitis

Adults:

A single dose of azithromycin 1g orally is effective in early active inflammatory stages.

One of the following antibiotics is recommended.

Oral tetracycline 250 mg q.i.d. for 3 weeks, doxycycline 100mg b.d. for 3 weeks, erythromycin 500mgs q.i.d. for 3 weeks.

Neonates:

Systemic erythromycin 2.5 mg/kg oral q.i d for 14 days is recommended; investigate and treat parents for genital infection.

Blepharitis

Blepharitis is an inflammation of the lids that has two forms

(1) Anterior- often caused by *S. aureus* infection of the skin, cilia, follicles, or accessory glands of the eyelids

(2) Posterior- infection or inflammation of the Meibomian sebaceous glands.

The eyelid inflammation produces a red eye by secondarily involving the conjunctiva or cornea. Individuals who have rosacea or seborrheic dermatitis of the scalp and face are especially vulnerable to the posterior form of chronic blepharitis.

Anterior blepharitis

Management:

Lid hygiene- scrub lid margins with diluted baby shampoo (one or two drops of baby shampoo in a 5 ml of warm water) using a cotton cap applicator or a cloth two to three times daily.

Antibiotics such as fusidic acid ointment must be rubbed onto the anterior lid margin with a clean finger after all crusts have been removed. Systemic antibiotics may be needed in long-standing severe infections

Posterior blepharitis

Doxycycline 100 mg b.d. for a week and then once daily for 2-3 weeks, but may need to be continued longer.

Or

Tetracycline 250 mg q.i.d. for a week and then twice daily for 2-3 weeks. Refer if the symptoms and signs do not respond after several weeks

Chalazion
A painless nodule of the lid caused by chronic lipogranulomatous inflammation of the Meibomian glands (lipid secreting glands of the lids)

Treatment
- Small chalazia disappear spontaneously.
- Apply warm compresses to the affected eye twice daily
- If associated with chronic blepharitis treat.
- If painful and infected, and there is accompanying celluliti of the lids systemic antibiotics can be given. Usually infection is caused by *S. aureus* and is treated with cloxacillin.
- Refer if mass fails to disappear after 2 months, surgical excision may be necessary.
- Recurrent chalazia should be biopsied to rule out Meibomian gland carcinoma

Stye
Stye or external hordeolum is an inflammation of the ciliary or accessory glands of the anterior lid margin. It presents as a painful tender local swelling in the lid often with pustule formation. It is caused by *S. aureus*. Styes are common in a setting of chronic blepharitis.

Treatment
- Apply warm compresses to the affected eye twice daily
- Removal of the affected eyelash
- If chronic blepharitis is the underlying condition treat it
- Topically applied antibiotics are generally not effective and not indicated, unless an accompanying blepharoconjunctivitis is present, when fusidic acid ointment is recommended. Systemic cloxacillin is given if there is preseptal cellulitis.
- Refer if the mass fail to disappear because surgical excision may be necessary.

Acute dacrocystitis
Dacryocystitis or inflammation of the lachrymal sac is caused by bacterial infection in the setting of an obstructed nasolacrimal passage in adults. It is seen in infants whose nasolacrimal passages remain closed and presents with excessive tearing and /or mucopurulent discharge. Discharge from the punctum sometimes can be elicited by pressing at the lower lid mass (overlying the lachrymal sac)

Causative organisms
S. aureus or *S. pyogenes*

Recommended antibiotics
Before starting treatment culture and antibiotic sensitivity should be done of the discharge. In the elderly, diabetics and the immunocopromised, Gram-negative infection may occur. Systemic antibiotics commonly used are: cloxacillin, amoxicillin, ciprofloxacin, tetracycline. Referral to an ophthalmologist is needed as external drainage or surgery to open a passage for tears into the nose (dacryocystorhinostomy) may be necessary

Refer infants early, preferably before 9 months of age as probing of the nasolacrimal passages may be necessary.

Microbial keratitis (corneal ulcer)
This has to be referred to an ophthalmologist.

Endophthalmitis
Infection of the intraocular layers of the eye. This usually follows a penetrating injury of the globe or intraocular surgery.

Diagnosis of endophthalmitis
- History of penetrating injury or surgery
- Severe pain in the eye
- Marked reduction in vision
- Redness

This needs emergency referral to an ophthalmologist.

Antibiotic administration into eye
- Most preparations can be used for one month after opening.
- Head should be tilted backwards.

- Drug should be instilled into the lower conjunctival sac.
- When two different preparations are used, leave an interval of few minutes before using the second.
- Tip of the bottle or tube should not touch the lashes or conjunctiva.

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Chapter 8

GASTROINTESTINAL TRACT INFECTIONS

a) Candida oesophagitis

Is a relatively common condition in patients on steroids, and those who are immuno-compromised. Patients may present with either difficulty or pain during swallowing. There may be visible thrush in the throat. Diagnosis is by endoscopy and biopsy. The predisposing cause should be treated.

Treatment:

Fluconazole 50mg (child: 3mg/kg) orally for 14 days

Or

Ketoconazole (child: 5mg/kg up to) 200mg orally with food, daily for 14 days. If response is poor, specialist opinion should be sought.

b) Diverticulitis

Diverticulitis results from inflammation of one or more diverticula of the colon. Patients are usually over the age of 40 years, and present with lower abdominal pain, in the left iliac fossa. The lower abdomen is tender on palpation and there may be guarding and rigidity. In the acute phase, confirmation can be done by computerized tomography (CT). Complications include: abscess formation, peritonitis and fistulation (colo-vesical, colo-vaginal etc.)

Treatment:

- For mild infection, localized to the bowel wall give co-amoxiclav 625mg, 12 hourly for 5 to 10 days or, metronidazole 400mg

orally, 8 hourly plus cephalexin 500mg orally, 6 hourly for 5 to 10 days

- For severe infection, with or without bowel perforation: patient should be kept "nil by mouth", give iv fluids, analgesia and broad-spectrum antibiotics. Give ampicillin 2g iv, 6 hourly plus gentamicin 5mg/kg iv once daily (space out dose frequency if there is renal impairment) plus metronidazole 500mg iv, 8 hourly. If gentamicin is contraindicated, as a single preparation, give ticarcillin-clavulanate 3.2g iv, 8 hourly
- For patients allergic to penicillin, give metronidazole 500mg iv, 8 hourly plus cefotaxime 1g iv, 8 hourly

Pericolic abscesses, peritonitis, strictures and fistulae require surgical management.

c) Gastro-duodenal ulcers (associated with *Helicobacter pylori*)

Gastric and duodenal ulcers caused by *Helicobacter pylori*, ideally need to be confirmed by upper gastro-intestinal endoscopy and other laboratory investigations.

Eradication therapy

Omeprazole 20mg orally, twice daily for 7 days, plus clarithromycin 500mg orally, twice daily for 7 days, plus amoxicillin 1 g orally, twice daily for 7 days

For patients allergic to penicillins, substitute amoxicillin with metronidazole (400mg orally thrice daily). In patients with treatment failure the same combination of drugs can be given for 14 days.

d) Ano-rectal abscess

There are four main varieties: perianal (60%), ischio-rectal (30%), sub-mucous and pelvi-rectal. Perianal abscess usually occurs following an infection of the anal glands. Patients present with pain and constitutional symptoms which are not as severe as in ischio-rectal abscesses. Surgical drainage is mandatory and antibiotics are only an adjunct to surgery. Pus should be sent for culture and ABST.

- *For mild infections*
  Co-amoxiclav 625mg orally, 12 hourly plus metronidazole 400mg orally, 8 hourly, for 5 to 10 days

  Or

  Cephalexin 500mg orally, 6 hourly plus metronidazole 400mg orally, 8 hourly, for 5 to 10 days

- *For severe infection*
  Ampicillin 2g iv, 6 hourly plus gentamicin 5mg/kg iv once daily (space out dose frequency if there is renal impairment) plus metronidazole 500mg iv, 8 hourly
  If gentamicin is contraindicated, give Ticarcillin-clavulanate 3.2g iv, 6 hourly plus metronidazole 500mg iv, 8 hourly. For patients allergic to penicillin, give metronidazole 500mg iv, 8 hourly plus cefotaxime 1g iv, 8 hourly or ceftriaxone 1g iv, daily

e) Acute cholecystitis

This is usually associated with calculi in the gallbladder and commonly affects middle-aged women. They present with pain in the right hypochondrium associated with fever. A positive Murphy's sign is helpful in the clinical diagnosis. Ultrasound scan findings of peri-cholecystic fluid collections and an oedematous gallbladder wall are confirmatory. Most patients (90%) can be managed conservatively: "nil orally", iv fluids, analgesics and antibiotics. Stepdown oral therapy may be started after about 48 hours, if the patient responds to iv therapy. This is continued for another 5 to 7 days. Patients who deteriorate may be developing an empyema of the gallbladder, and may need surgical intervention.

- *Initial treatment*
  Ampicillin 1g iv, 6 hourly plus gentamicin 5mg/kg iv, once daily (adjust dose for renal function)
- For patients allergic to penicillins or when gentamicin is contraindicated, as a single drug give cefotaxime 1g iv, 8 hourly (ceftriaxone should be **avoided** as it is known to cause biliary sludge)

  Or

  Ciprofloxacin 200-400mg iv, twice daily

- If biliary obstruction is present, add metronidazole (500 mg iv, 8hourly) to cover anaerobes.

  For step-down oral therapy, give co-amoxiclav 625mg orally, 12 hourly with or without metronidazole 400mg orally 8 hourly

g) Ascending cholangitis

Patients typically have pain in the right hypochondrium, jaundice and fever with chills (Charcot's triad). The most common cause is the presence of stones in the common bile duct. A blood culture should be done before commencing antibiotic therapy.

Initial treatment

Ampicillin 2g iv(child:50mg/kg), 6 hourly plus gentamicin 5mg/kg (Child<10years:7.5mg/kg; ≥10 years: 6mg/kg) iv, daily for up to 3 days, then change therapy, see below (adjust dose frequency for impaired renal function)

- In patients with a history of previous biliary tract surgery, endoscopic retrograde cholangio-pancreatography (ERCP) or known biliary obstruction, add metronidazole (child: 12.5mg/kg) 1g iv, 8 hourly to the above regimen.
- Alternatively, for patients allergic to penicillin or when gentamicin is contraindicated (e.g. renal impairment), use cefotaxime 1g(child: 50mg/kg) iv, 12 hourly
  When afebrile change to co-amoxiclav 625mg (child: 25mg/kg) orally, 12 hourly for a total treatment duration of 7 days
- In patients unresponsive to initial therapy or requiring iv therapy beyond 3 days, blood culture results may provide a guide to appropriate therapy. In the absence of this information, use piperacillin/tazobactam 4.5g (child: 112.5mg/kg) iv 8 hourly

  Or

  Ticarcillin-clavulanate 3.2g (child: 51.7mg/kg) iv, 6 hourly

h) Acute peritonitis due to a perforated viscus

Surgical intervention is usually required. Antibiotics should be commenced with the diagnosis, and should be continued peri- and post-operatively

Ampicillin (child: 50mg/kg) 2g iv, 6 hourly plus gentamicin 5mg/kg (Child<10years:7.5mg/kg; ≥10 years: 6mg/kg) iv, daily

(adjust dose for impaired renal function) plus metronidazole 1g (child: 12.5mg/kg) iv, 8 hourly

- Alternatively if gentamicin is contraindicated (e.g. renal impairment) give piperacillin/tazobactam 4.5g(child: 112.5mg/kg) iv, 8 hourly or ticarcillin/clavulanate 3.2g(child: 51.7mg/kg) iv, 6 hourly
  plus metronidazole 500mg iv, 8 hourly
- For patients allergic to penicillin, give metronidazole 1g(child:12.5mg/kg) iv, 8 hourly plus cefotaxime 1g(child: 50mg/kg) iv, 8 hourly.
- For patients with immediate hypersensitivity to penicillin, replace ampicillin with vancomycin 1g iv 8 hourly

i) Acute peritonitis – spontaneous bacterial peritonitis (SBP)

This commonly affects patients with chronic renal and liver disease. The largest group includes patients with cirrhosis. Up to 25% of cirrhotics could develop SBP. About 30% of patients with SBP are asymptomatic. In others the disease develops insidiously and localizing signs of peritonitis are present but often minimal. The most common manifestations include abdominal pain, fever, rebound tenderness and absent bowel sounds. Once suspected, peritoneal fluid should be aspirated for culture and Gram staining. Blood culture is positive in about 70% of patients.

Treatment

Cefotaxime 1g (child: 50mg/kg) iv, 8 hourly or ceftriaxone (child: 50mg/kg up to) 1g iv, daily or 12 hourly. Change the antibiotic in the wake of culture sensitivity results. Therapy should be continued until clinical signs of infection have resolved (usually for 5 to 10 days)

j) Acute pancreatitis

The two main causes are biliary calculi (50-70%) and consumption of alcohol (25%). Pain is acute in onset, severe and is initially in the epigastrium. It is typically relieved by sitting or leaning forwards. There is usually guarding in the upper abdomen. A serum amylase four times above normal is indicative of the disease. Important differential diagnoses to consider include perforated peptic ulcer, acute cholecystitis and inferior myocardial infarction.

- Initial management is conservative and include "nil orally", iv fluids, analgesics. Antibiotic prophylaxis is recommended for patients who have severe acute necrotizing pancreatitis (ideally after confirmation by abdominal CT).

  Give ampicillin 2g iv, 6 hourly plus gentamicin 5mg/kg iv once daily (space out dose frequency if there is renal impairment) plus metronidazole 500mg iv, 8 hourly

  Or

  Metronidazole 500mg iv, 8 hourly for 7 days plus cefotaxime 1 to 2 g iv, 8 hourly for 7 days OR Ceftriaxone 1 to 2 g iv, daily for 7 days.

  Or

  Imipenem 500mg 1g iv, 8 hourly for 7 days

  Or

  Meropenem 500mg iv, 8 hourly for 7 days

  Or

  Piperacillin-tazobactam 4.5g iv, 8 hourly for 7 days.

Further reading

1. Therapeutic Guidelines. Antibiotics. Therapeutic Guidelines Limited, Melbourne, Australia 2006
2. British National Formulary, BMJ Publishing Group Limited,& Royal Pharmaceutical Society of Great Britain, 51st Edition 2006
3. Russel RCJ, Williams NS, Bulstrode CAK eds. Bailey & Love's Short Practice of Surgery,. 24th Edition. 2004. Hodder and Arnold. London

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Chapter 9

ANTIBIOTICS IN GYNAECOLOGY

Introduction

Antibiotics used in gynaecology are discussed under the following.

- Pelvic inflammatory disease (PID)
- Post-abortal infections
- Post-surgical infections
- Prophylactic antibiotics before gynecological surgery

Pelvic inflammatory disease (PID)

This is a topic covered under sexually transmitted disease and gynaecology. The diagnosis is mostly on clinical grounds and on non-specific evidence such as fever, vaginal discharge and abdominal pain The signs such as lower abdominal tenderness or vaginal discharge are also non-specific and inconclusive.

It is important to recognize that PID is a chronic condition which may lead to sub- fertility. Labeling a patient as having PID results in medical practitioners repeatedly prescribing different antibiotics often in an irrational manner and sometimes missing significant pathology. The role the gynaecologist is to accurately identifying patient with chronic PID by performing a laparoscopy, thereby excluding other more sinister aetiology.

Although laparoscopy may not reveal intratubal infections it is an important diagnostic tool. The use of antibiotics in PID is discussed in detail in Chapter 17.

Post-abortal infections

Abortions are categorized into spontaneous and induced. When there is coexisting infection the abortion is a septic abortion. Spontaneous abortion being a process initiated as a natural event is only rarely associated with infection. However, infection may occur in second trimester abortions and secondary to subsequent surgical intervention. Infection is not common in first trimester spontaneous abortions.

Induced and illegally performed abortions are often associated with infection. The circumstances under which they are performed and some of the resultant injuries may make them more vulnerable to severe sepsis.

This has made the term septic abortion more or less synonymous with criminal abortion.
In septic abortions the patient:

- presents late
- may have secondary complications such as septicemia, renal failure, disseminated intravascular coagulopathy or multi-organ failure
- may have a good outcome if treated aggressively with appropriate antibiotics
- is preferably managed in a specialist unit because often ICU care or surgical intervention may be needed.

Microbiological samples should be taken before starting antibiotics. However, antibiotics should be started empirically before results are available.
The common causative organisms include:
Coliforms such as *E. coli, S. aureus,* Streptococci haemolytic and non-haemolytic, *P. aeruginosa*

In the presence of severe sepsis or secondary complications of infection

- High dose benzylpenicillin by slow infusion 2.4- 4.8 g for 24 hours or cefotaxime iv 2-8 g daily in divided doses with metronidazole iv infusion 500 mg over 30 minutes 8 hourly.
- A single dose of gentamicin 5mg/kg daily iv with ampicillin 1g iv 6 hourly and metronidazole iv infusion 500 mg over 30 minutes 8 hourly.
- Newer penicillins such as ticarcillin-clavulanate 3.2 g iv 8 hourly or piperacillin-tazobactam 4.5 g iv 8 hourly could be used with or without metronidazole .as an alternative.

In the presence of infection but no evidence of septicaemia

- Cefuroxime 750mg-1.5g iv 6-8 hourly with metronidazole 500 mg iv infusion over 30 minutes, 8 hourly
- Gentamicin 5mg/kg iv daily with ampicillin 500 mg iv 6 hourly and metronidazole combination
- Co-amoxiclav 1.2 g iv 8 hourly with metronidazole.

In the prescence of mild sepsis with minimal evidence, or when there is a history of interference with no evidence of sepsis

- Oral amoxicillin 500mg 8 hourly with oral metronidazole 400mg 8 hourly
- Oral co- amoxiclav 625 mg b.d or 8 hourly with oral metronidazole

Early surgery is indicated when there is

- Evidence of peritonitis
- Suspicion of bowel injury
- No response to antibiotics after 48 hours

Infection following pelvic surgery

After minor surgical procedures

This may follow minor procedures such as hysterosalpingography or dilatation and curettage. The causative organism is often *E. coli* but the possibility of other organisms such as *S.s aureus* or MRSA has to be considered. Prophylactic antibiotics are not recommended for minor procedures except in special circumstances such as valvular heart disease.

In the presence of severe infection:

- Gentamicin 5mg/kg iv daily with ampicillin 1g iv 6 hourly and metronidazole 500mg iv over 30 minutes 12 hourly
- Cefuroxime 750mg-1.5g iv 6-8 hourly with metronidazole iv 500mg over 30 minutes twice daily.

After major surgical procedures

Vaginal hysterectomy is well known to carry a higher risk of infection and subsequent complications. The proximity to the perineal area, makes coliforms and anaerobes the common causative organisms. Rarely other organisms such as *P. aeruginosa* or MRSA may be responsible.

Early and aggressive therapy is mandatory as some of the complications such as secondary hemorrhage could be disastrous unless the infection is controlled early

- Gentamicin 5mg/kg iv daily with ampicillin iv 1g 6 hourly and metronidazole 500mg iv over 30 minutes 8 hourly.

- Cefuroxime 750mg-1.5g iv 6-8 hourly with metronidazole 500mg over 30 minutes twice daily
- Newer penicillins such as ticarcillin-clavulanate 3.2g iv 8 hourly or piperacillin-tazobactam 4.5 g iv 8 hourly could be used with or without metronidazole as an alternative.

Lack of response to antibiotics or the identification of an ultrasonically detected mass should alert one to a pelvic collection of pus which may need drainage.

Deep seated infections following abdominal gynecological surgery are rather uncommon unless they are associated with bowel injury, foreign body or other predisposing factors such as diabetes or endometriosis.

Prophylactic perioperative antibiotics

Perioperative prophylactic antibiotic use is recommend for vaginal hysterectomy. They may be used for abdominal hysterectomy under special situations

Commonly used prophylactic antibiotics which are given at the time of induction of anaesthesia are given below.

- Cefuroxime 750mg -1.5 g iv
- Co-amoxiclav 1.2 g iv over 5 minutes
- Ampicillin 500m iv and metronidazole infusion 500mg combination

They are given as a single dose and repeated only if the procedure takes more than two hours.

Further reading

1. Mears A, Bingham JS. *Tutorials in Obstetrics and Gynecology. Royal College of Obstetricians and Gynecologists of the UK.*2004; **l6(3)**:138-144 File://F.\Extenza-Pelvic inflammatory disease.htm
2. Atukorala S D. Rational Use of Antibiotics. 1998 Ministry of Health, Sri Lanka p11

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Chapter 10

HELMINTHIASIS

Gastrointestinal nematodes

Diseases

- Roundworm infection (Ascariasis)
- Hookworm infection (*Necator americanus* infection)
- Whipworm infection (Trichuriasis)
- *Enterobius vermicularis* infection (Enterobiasis)
- *Strongyloides stercoralis* infection (Strongyloidiasis)
- Larva migrans

Diagnosis: Microscopic examination of saline or iodine smears of stools is used in diagnosis. Roundworm, hookworm and whipworm ova have characteristic appearances. Perianal swabs should be used to confirm the diagnosis of *Enterobius* infection. Detection of *Strongyloides* larvae in stools needs special techniques. Although stool microscopy is the recommended method for confirmation of diagnosis it has limitations. Two or three samples may need to be examined. There is the possibility that a thorough examination of the stool may not be performed. Because of these and the ready availability of effective, safe and cheap anthelmintics patients are treated on suspicion. If the adult worms, larvae or their eggs or ova are detected it is considered as an indication for treatment even if symptom are not present.

Treatment

Roundworm infection

Give mebendazole 100mg twice daily for 3 days or 500mg as a single dose *or* albendazole 400mg as a single dose, *or* pyrantel 10mg/kg as a single dose. For mebendazole and albendazole the adult and paediatric doses are the same. If the infection is heavy pyrantel is recommended.

Hookworm infection

Give mebendazole 100mg twice daily for 3 days. The 3 day course of mebendazole is recommended rather than the 500mg single dose

therapy for better results. Alternatives include albendazole (400mg), or pyrantel (10mg/kg for 3 days). A 3 day course of albendazole is recommended for heavy infections.

Whipworm infection
Give mebendazole 100mg twice daily for 3 days or 500mg as a single dose, *or* albendazole 400mg as a single dose. Pyrantel is considered to be ineffective against this worm.

Enterobiasis
A single dose of mebendazole 100mg *or* albendazole 400mg *or* pyrantel 10mg/kg is given. This has to be followed by a second dose after 2 weeks. To eradicate this infection treatment of the entire household and detailed attention to their personal hygiene is required.

Strongyloidiasis
Give albendazole 400mg for 3 days

Mebendazole is effective against four of the worms stated above. Apart from killing the adult worms, mebendazole affects the eggs of roundworm, whipworm and hookworm so that they fail to develop to the larval stage. Side-effects are mild and include transient diarrhoea, abdominal pain and dizziness. Migration of roundworms is rare and is seen with heavy worm loads.
Albendazole has an anthelmintic spectrum similar to mebendazole. It is preferred to mebendazole in the treatment of strongyloidiasis. Albendazole is known to produce elevation of liver enzymes and transient leucopenia.

Pyrantel acts as a cholinergic agonist causing depolarization and contracture of the muscle cells of the worms. It is well tolerated and the side-effects include abdominal pain, cramps, nausea, vomiting, headache, dizziness and drowsiness.

Mass treatment
As part of routine antenatal care all mothers are given a course of anthelmintic therapy (mebendazole 100mg twice daily for 3 days) during the second trimester. As we have most experience with mebendazole, it is recommended during the second and third

trimesters. It is not recommended during the first trimester. Most of the patients having helminths (especially children) have multiple problems such as anaemia, vitamin deficiency and malnutrition. These need appropriate treatment and follow up.

Larva migrans

Skin penetrating larvae of dog and cat hookworms migrate in the superficial layers of the skin producing cutaneous larva migrans. The diagnosis is based on inspection of the lesion.

Treatment

Tiabendazole 25mg/kg twice daily for 2 days, or freezing (cryotherapy) of the lesion using liquid nitrogen, or albendazole 400mg for 3 days; children 10mg/kg/day) in 2 divided doses for 3 days. Tiabendazole is not available in Sri Lanka. Rare cases of visceral larva migrans are treated with albendazole (400mg for 5 days).

Gastrointestinal cestodes

Tapeworms

Sporadic cases of beef and pork tapeworm infection are reported and there is a perception that more cases are seen now compared to two decades ago.

Treatment

For *adults* give niclosamide, 2g as single dose, for those with <10 kg body weight, 0.5g, 10-35 kg body weight, 1g , or praziquantal, 5-10mg / kg as single dose. However, both drugs are not routinely available in Sri Lanka. Rare cases of hymenolepis infections need treatment with niclosamide. For *adults* give 2g on day one followed by 1g daily for 6 days, or praziquanta, 15-25mg/ kg as single dose.

Tissue nematodes

In Sri Lanka the tissue nematode causing disease is the filarial worm *Wuchereria bancrofti.*

Disease manifestations include:

- acute lymphatic filariasis (acute adenolymphangitis)
- chronic lymphatic filariasis (lymphoedema and elephantiasis)
- tropical pulmonary eosinophilia (TPE)

Some patients are asymptomatic.

Treatment

Acute lymphatic filariasis (acute adenolymphangitis):

Mild attacks: advise rest and give paracetamol; local precipitating factors need treatment with local antibiotics or antifungals.

Moderate to severe attacks: in addition to rest and paracetamol, oral or parenteral antibiotics (phenoxymethylpenicillin, benzylpenicillin, amoxicillin or erythromycin) are given. Diethyl carbamazine (DEC) is not recommended during the acute attack.

Once the acute attack has subsided, if the patient continues to have microfilariae (mf) in the blood, or is antigen positive (or if these tests are not available or cannot be performed) the patient is given a single dose of DEC 6mg/kg. This dose could be repeated 6 monthly or annually. The duration of treatment has to be determined by the test results or appearance of acute attacks. Recent studies have shown that a single dose of DEC is equally effective, and that a 12 day course is not needed.

Proper care of the affected limb is extremely important in preventing recurrences of acute adenolymphangitis (ADL) and the following are recommended:

(a) washing the affected limb thoroughly with soap and water twice daily.
(b) keeping the nails clipped and clean
(c) preventing local injury and infection
(d) prompt treatment of minor bacterial and fungal infections
(e) regular use of well-fitting footwear
(f) raising the affected limb at night

A small subset of patients getting repeated attacks of ADL my be given prophylactic penicillin (phenoxymethylpenicillin twice daily or monthly im benzathine penicillin).

Chronic manifestations (lymphoedema and elephantiasis):

DEC is not the definitive treatment at this stage. However, if there is evidence of acute infection (detection of mf or filarial antigen) a single dose of DEC (6mg/kg) is given. This may be repeated six monthly or annually as long as the patient is getting acute exacerbations. Recent studies have shown that treatment with DEC is not needed during acute attacks of ADL occurring in a background of lymphoedema.

Foot care is important to prevent attacks of ADL. Once lymphoedema is established achieving a cure is often not possible.

Tropical pulmonary eosinophilia (TPE): give DEC 6mg/kg for 21 to 28 days. Repeat treatment may be necessary depending on the symptoms.

Asymptomatic subjects:
Asymptomatic but mf- positive, and mf-negative but filarial antigen positive people are detected at night blood filming and by serology. DEC is given as a single dose 6mg/ kg; The criteria for follow up, re-treatment and duration of follow up are not established but treatment at every 6 to 12 monthly intervals seems appropriate. Advise them to take drugs as recommended by Filariasis Elimination Program.

Mass treatment: the National Plan for Elimination of Lymphatic Filariasis for Sri Lanka is uses the mass treatment strategy to control filariasis. Such a strategy brings down the microfilraemia in the community to low levels and when this is maintained for about 6 years transmission of the disease is significantly reduced. Annual single doses of albendazole 400mg plus DEC 6mg/kg are given to all residents in the endemic provinces of Sri Lanka.

Adverse effects of DEC include fever, headache, dizziness, anorexia, vomiting, malaise and urticaria and these are more prominent in people having high mf counts. Peripheral blood may show eosinophilia. Most of the side-effects improve in a few days. Sometimes nodules (due to dead adult worms) may appear in the groin area. Exacerbation of the lymphoedema and lymphangitis may occur.

In some countries ivermectin is used in the management of filariasis. This drug is not available for human use in Sri Lanka.

Further reading:
1. Anitha K, Shenoy RK. Treatment of lymphatic filariasis: Current trends. Indian Journal of Dermatology, Venereology and Leprology 2001; **67**:60-65
2. Liyanage TS. National Programme to eliminate lymphatic filariasis in Sri Lanka. Proceedings of a WHO regional workshop for programme managers. Kuala Lumpur, Malaysia, 2002

3. Weerasuriya MV, Samarawickrama WA. Advances in the epidemiology and diagnosis of lymphatic filariasis in Sri Lanka: some highlights from the Matara Research Project. In. Filariasis in Asia and Western Pacific Islands. Asian Parasitology Series Monograph vol 3, ed. Yano A., Chiba, Japan, 2004, p233-245
4. WHO Model Prescribing Information – Drugs used in Parasitic Diseases Ed 2, WHO Geneva, 1995 pp 91-122

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Chapter 11

MALARIA

Malaria is one of the most widespread parasitic diseases in the world and continues to be a major cause of morbidity and mortality globally. In Sri Lanka, the incidence of malaria has declined considerably, from 687,259 in 1987 (epidemic year) to 1640 in 2005.

Mortality from malaria in Sri Lanka has been low (53 reported deaths 0.79 / 1000 patients in 2001). There have been no deaths in 2004, 2005 and 2006. *Plasmodium vivax* accounted for 92% and *Plasmodium falciparum* 8% cases in 2005. Our principal vector is *Anopheles culicifacies.*
Plasmodium vivax infection usually runs a benign course. Severe, life-threatening malaria is nearly always caused by *P. falciparum*. Death from *P. falciparum* infections results from delayed diagnosis and treatment.

Ideally the diagnosis of malaria should be confirmed by a positive blood film. However, a negative blood film does not exclude a diagnosis of malaria, especially in *P.falciparum* where the parasite could be sequestered in the spleen, bone marrow or deep in the cerebral vasculature. Hence a patient who is febrile and gives a

history of travel to an endemic area with highly suggestive clinical features should be treated as a case of malaria even though the blood film is negative. With the decline in the incidence of malaria in Sri Lanka, it is now pertinent to ask for a history of foreign travel especially to India and Africa (including Madagascar).

Chemotherapy of uncomplicated malaria

(Adapted from Guidelines for use of chemotherapy for treatment of malaria in Sri Lanka issued by the Anti Malaria Campaign (AMC), Department of Health in Sri Lanka, 2004.)

Treatment for *P. vivax* malaria (microscopically confirmed)

Daily dosage here is indicated in the number of tablets.

Age (years)	Drug	D 1	D 2	D 3	D 4	D 5
< 1	Chloroquine Primaquine	½	½	¼		
1 – 5	Chloroquine Primaquine	1 ½	1 ½	½ ½	½	½
6 – 10	Chloroquine Primaquine	2 1	2 1	1 1	1	1
11 – 15	Chloroquine Primaquine	3 1 ½	3 1 ½	1 ½ 1 ½	1 ½	1 ½
> 15	Chloroquine Primaquine	4 2	4 2	2 2	2	2

Primaquine therapy should be continued in the same daily dosage for 14 days.

Treatment of *P. falciparum* malaria (microscopically confirmed)

Age (years)	Drug	D 1	D 2	D 3
< 1	Chloroquine Primaquine	½	½	¼
1 – 5	Chloroquine Primaquine	1 1 ½	1	½
6 – 10	Chloroquine Primaquine	2 3	2	1
11 – 15	Chloroquine Primaquine	3 4 ½	3	1 ½
> 15	Chloroquine Primaquine	4 6	4	2

Treatment of mixed infections or clinically suspected malaria patients: (with no microscopical confirmation) -same as for infections caused by *P. vivax*.

Children

1. *P. vivax* infection:
   Chloroquine 10 mg / kg / day for the 1st and 2nd day.
   5 mg / kg / day on 3rd day.
   Primaquine 0.25 mg / kg per day

2. *P. falciparum* infection
   Chloroquine 10 mg / kg / day for the 1st and 2nd day.
   5 mg / kg / day on 3rd day.
   Primaquine one stat dose of 0.75 mg / kg

Primaquine should not be given to pregnant women, children below one year, and for those suspected or known to be suffering from glucose-6- phosphate- dehydrogenase enzyme deficiency.

Guidelines for the detection and treatment of chloroquine resistant *P. falciparum* patients

1. Detection
   The following categories of patients may be considered to be chloroquine resistant.
   a. Patients who have completely followed the 3 day chloroquine regimen, but who still have *P. falciparum* asexual parasites (ring forms) in peripheral blood smears after 7 days of commencement of the treatment.
   b. Patients who have completely followed the 3 day chloroquine regimen, but who return with fever within a period of 28 days of commencement of treatment, and having *P. falciparum* asexual parasites (ring forms) in peripheral blood smear.
   c. Any person contracting a *P. falciparum* infection while taking weekly chemo prophylactic treatment (using chloroquine)

2. Treatment
   Such patients should be treated with the drug combination sulfadoxine + pyrimethamine (S+P). One such tablet (Fansidar) contains sulfadoxine 500 mg and pyrimethamine 25 mg and is available from the AMC on request.

Treatment schedule with (S+P)

(daily dosage indicates the number of tablets)

Age	Drug	Stat dose
0 – 2 months	Not given	
3 – 12 months	(S + P)	¼ to ½
1 – 5 years	(S + P) Primaquine	¾ 1 ½
6 – 10 years	(S + P) Primaquine	1 ½ 3
11 – 15 years	(S + P) Primaquine	2 ¼ 4 ½
> 15 years	(S + P) Primaquine	3 6

Note: The single dose of primaquine should be given only if primaquine has not been administered within the preceding seven days. (S + P) is not recommended during the 1st two months of infancy, during the last trimester of pregnancy, and for persons known to be allergic to sulpha drugs. Such *P. falciparum* patients who are resistant to chloroquine may be treated with quinine (oral or parenteral as described later.)

Chloroquine resistant *P. falciparum* is seen very infrequently and is not a significant problem in Sri Lanka. Only a handful of multiple drug resistant cases have been reported in Sri Lanka and all these infections were acquired abroad.

Multiple drug resistant *P. falciparum* malaria is rare in Sri Lanka. For patients with multiple drug resistant malaria, mefloquine and artemether derivatives can be obtained from the AMC.

Severe and complicated malaria

Severe and complicated malaria is seen particularly in non-immune people entering highly endemic areas and in pregnant women and pre-school children living in endemic areas. An area is considered to be endemic for malaria if there is evidence of a significant degree of local transmission over successive years.

The early recognition of clinical features of severe malaria is essential, as 80% of malaria related deaths occur in the first 24 hours.

Management of cerebral malaria
Any patient with severe and complicated malaria should be treated in an intensive care unit if one is available.

Quinine iv is the drug currently recommended for the treatment of severe and complicated malaria in Sri Lanka. There are no documented cases of quinine resistance acquired in Sri Lanka.

Quinine therapy in severe and complicated malaria
Day 0: (1st day of treatment)
An intravenous infusion of quinine loading dose of 20 mg of salt / kg in 500 ml of 5% dextrose over 8 hrs followed by 10 mg / kg in 500 ml 5% dextrose eight hourly thereafter.
A rise in parasitaemia in the first 24 hours is common and does not imply treatment failure.
Days 1 – 3 intravenous infusion of quinine 10 mg / kg infusion. Once the patient regains consciousness and parasitaemia decreases, intravenous quinine can be stopped and oral quinine commenced at 600 mg 8 hourly for 7 days. The total dose of intravenous and oral quinine is ten days.

During quinine therapy, daily blood films should be done and the degree of reduction of parasitaemia noted. Asexual parasitaemia should decrease after the first 24 hours and disappear by day 5. If the parasite count has not fallen by at least 75%, 48 hours after starting treatment, it should be rechecked and if confirmed, a different regime should be considered. Advice from the AMC should be sought regarding use of new anti malarial therapy. .
A single dose of primaquine 45 mg in adults (6 tablets) is given on recovery.

The following are known complications of severe malaria:
Hypoglycaemia, severe anaemia, pulmonary oedema or adult respiratory distress syndrome, circulatory shock, blackwater fever (intravascular haemolysis), disseminated intravascular coagulation (DIC), acute fulminant liver cell failure, and acute renal failure,
Appropriate measures should be taken ideally in an ICU

Chemoprophylaxis

Chemoprophylaxis recommended for

a) Non-immune visitors to malaria endemic areas.
b) Non-immune persons residing in malarial endemic areas.
c) Pregnant women especially primigravidae living in endemic areas.

For prophylaxis chloroquine should be given 5 mg / kg body weight. The adult dose 300 mg taken one week before travel to endemic areas and continued on the same day of the week throughout the stay and continued for one month after the leaving the malarial area.

Weekly prophylaxis in long term settlers is confined to about 3 months in the expectation that, during this period, a satisfactory level of immunity would have been developed in this population to prevent the manifestation of life-threatening symptoms of the disease. Such a measure would also the serve to reduce prolonged chloroquine pressure and thereby the early emergence of chloroquine resistance.

The importance of personal prophylaxis using anti-mosquito devices cannot be over emphasized. The use of permethrin impregnated mosquito nets, electronic anti mosquito devices, coils, wearing of protective clothing and avoiding night exposure is of paramount importance.

Chemoprophylaxis with choloroquine does not give complete protection after exposure.

In a person who has taken chemoprophylaxis falciparum malaria must always be strongly suspected if fever with or without other symptoms develop after one week to two months after exposure. Sulphadoxine + pyrimethamine is indicated if uncomplicated falciparum malaria is diagnosed in such individuals.

Visitors from overseas may come with chloroquine, chloroquine + proguanil or mefloquine which are recommended for prophylaxis

Malaria in pregnancy

Malaria has pronounced effects on the pregnant mother and the unborn baby.

Maternal complications

Anaemia due to lysis of red cells is the commonest complication affecting the mother. Recurrent infections of malaria combined with malnutrition and hookworm infection can produce severe anaemia in

the mother. Clinically there is pallor, jaundice, splenomegaly and tender hepatomegaly. All cases of anaemia in pregnancy in the endemic areas should be screened for the malarial parasite.

Complications tend to be more common and severe in pregnancy. These include hypoglycaemia, pulmonary oedema, acute renal failure, hyperpyrexia, haemorrhagic shock leading to multiple organ failure. It is important that fits in cerebral malaria are differentiated from eclampsia, encephalitis, meningitis, hypoglycaemia and epilepsy.

Fetal complications

Malaria in pregnancy can cause any one of the following: abortion, stillbirth, intrauterine growth retardation (IUGR) due to placental insufficiency and congenital malaria. Low birth weight is frequently seen when mothers have had malaria. This may be due to IUGR and prematurity. Prematurity can contribute to neonatal deaths.

Congenital abnormalities have been observed at a slightly higher rate than normal in babies born to malarial mothers. Congenital malaria can result from transplacental spread or materno-fetal transmission at parturition.

Fetal death can occur at the height of the fever in the mother. Death of the fetus could also occur due to massive parasitisation of the placenta affecting its nutrition or due to congenital malaria.

Fetal monitoring

The fetus should be monitored for growth restriction and possible intra-uterine death. Fetal movement charts, cardiotopography (CTG), ultra sound scans and Doppler studies should be included in the fetal surveillance. Steroids to enhance fetal lung maturity should be considered in threatened preterm labour.

A blood smear from the cord or a heel should be performed soon after delivery to confirm congenital malaria.

Management

The principles of management include appropriate supportive care, effective antimalarial treatment, monitoring and treatment of complications and surveillance of fetal well-being.

Drug treatment

Malaria has to be treated whatever the stage of pregnancy. Chloroquine and quinine can be given in pregnancy, even in the first trimester. Therapeutic doses of these drugs are not harmful to the mother and the baby.

The standard treatment of malaria involves taking 4 tablets (600mg) of chloroquine on the first day, 4 tablets (600mg) on the second day and 2 tablets (300mg) on the third day. Primaquine is best avoided in pregnancy but can be given in the puerperium and is considered safe during breast-feeding. Chloroquine is given intravenously to women who cannot tolerate the tablets. When there is resistance to chloroquine, quinine can be used.

Chloroquine prophylaxis of 2 tablets per week should be given to all mothers living in endemic areas. Chloroquine prophylaxis should be combined with adequate measures to protect themselves from mosquito bites.

Other antimalarial drugs which can be used in pregnancy are sulphadoxine + pyrimethamine (S + P), mefloquine and artemether derivatives with consultation of the AMC

Further reading

1. Warell DA, Bradley DJ. Malaria in Warrel DA, Cox TM, Firth JD, Benz Jr EJ eds. Oxford Text Book of Medicine 4th Edition. 2004. pp 721-748
2. Fernandopulle R, Amarasekera N, Severe and complicated malaria: Diagnosis and management 1; *The Sri Lanka Prescriber* 1999; **7**: 7-9.
3. Fernandopulle R, Amarasekera N, Management of uncomplicated malaria: *The Sri Lanka Prescriber*, 1998; **6**:1-3.
4. Gitau GM, Jeldred JM. Malaria in pregnancy. *The Obstetrician & Gynaecologist* 2005; **7(1**): 2005.

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Chapter 12

METHICILLIN RESISTANT *STAPHYLOCOCCUS AUREUS* (MRSA)

Staphylococcus aureus is a bacterium causes superficial and systemic infections including post-operative wound infections, infection of burns, infections in immunocompromised patients and in those with vascular and other devices. Staff and patients often carry this organism in the nose, perineum, axilla and groin. If became resistant to penicillin soon after penicillin was introduced into clinical practice. This led to the development of penicillinase stable penicillins such a s methicillin, cloxacillin and flucloxacillin. Although methicillin was the prototype of anti-staphylococcal penicillins, cloxacillin and more recently flucloxacillin were used in therapy because of its superior cidal activity. In the late 1960s there was development of resistance by staphylococci to anti-staphylococcal penicillins, and this was referred to as methicillin resistant *Staphylococcus aureus* (MRSA). These isolates of MRSA were also resistant to all other penicillins and cephalosporins. Many were resistant to gentamicin also (MGRSA) and to macrolides. Strains of MRSA also had ability to spread and were called epidemic MRSA or EMRSA. Measures were taken worldwide to restrict the spread of MRSA strains. These strains were universally sensitive to glycopeptide antibiotics such as vancomycin and teicoplanin, until insensitivity was described in Japan. These were referred to as vancomycin insensitive *Staphylococcus aureus* (VISA) strains. Few countries have now reported vancomycin resistant *Staphylococcus aureus* referred to as VRSA. This situation has led to the development of new groups of antibiotics against resistant Gram-positive organisms. They include oxazolidinones (e.g. linezolid), streptogrammins, lipopeptides and newer glycopeptides.

Recommendations to curtail spread of MRSA

- MRSA is not more virulent than sensitive strains
- Culture of MRSA reflects colonization and by itself does not need glycopeptide antibiotic therapy, unless there is evidence of infection such as fever, signs of inflammation at site of infection, discharge from wounds, polymorphonuclear leucocytosis.

- As MRSA is endemic in most hospitals the following guidelines are useful in curtailing its spread in hospitals.

Isolation
- If possible, separate room or 'cohort' isolation is recommended (containment isolation)
- Separate nurse for colonized or infected group.
- Restrict visitors to bare minimum.
- Wash hands before and after attending on patient
- Gloves and aprons to be worn by attending staff
- Dispose used gloves and aprons

Staff (if 3 or more patients with MRSA are detected in the unit)
- Check MRSA carriage status by swabbing nose (axilla, perineum also beneficial).
- Nasal carriage - mupirocin cream applied to anterior nares three times daily for five days. Povidone iodine cream and sodium fusidate cream are alternatives.
- Skin carriage - soap and water or antiseptic detergent bath should suffice.
- Povidone iodine cream or chlorhexidine could be used.
- Hand-washing with soap and running water or with an antiseptic rub before and after attending on a patient. Dry with disposable towel.

Ward
- Ward rounds to be restricted to attending doctors only and to be done after seeing other patients. Teaching should be away from MRSA patients.
- Endeavour to transfer patients from high dependency units to less risk areas.

Closure of wards
- It is not necessary to close a ward completely.
- Closure is required if spread of MRSA is uncontrolled.

Terminal cleaning (after discharge, transfer or death)
- Responsibility is with nursing staff to remove all linen and send for autoclaving.

- Examine pillows for splits or defective seams and have them attended.
- Clinical waste should be sealed and preferably incinerated.
- Equipment used on a patient should be decontaminated.

Treatment of clinical infection
Glycopeptides such as vancomycin, teicoplanin are used. An oxazolidinone oral linezolid is available in the country at present.

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Chapter 13

ORAL AND DENTAL INFECTIONS

Odontogenic infections are polymicrobial, containing a mixture of aerobic and anaerobic Gram-positive and Gram-negative organisms.

Dental caries is a process in which the enamel and later dentine is demineralized by acids produced by bacterial fermentation of carbohydrates. The bacteria that initiate this process are viridans streptococci such as *Streptococcus mutans*, and lactobacilli perpetuate it. Host factors such as quantity and quality of saliva, composition of enamel and dentine also contribute to caries. The disease can be arrested in its early stages because of remineralization by relatively simple measures. Treatment in early stages consists of meticulous plaque control, dietary modification, use of fluorides and salivary stimulation for dry mouth. A toothbrush and dental floss will help to control plaque by mechanical means, while chlorhexidine gel or varnishes help in chemical control. A low fermentable carbohydrate diet will control lactobacilli and streptococcal bioburden. Fluorides help in remineralization and also have antimicrobial activity.

If untreated, caries can progress to inflammation and infection of pulpal tissue and periapical periodontitis. The latter could lead to dento-alveolar infections and osteomyelitis of jaw bones.

Dento-alveolar infections

The following antimicrobial agents are usually used for dento-alveolar infections, if an antimicrobial is deemed necessary.

(a) Phenoxymethylpenicillin (Penicillin V)

Adult: 500 mg 6 hourly orally for 5 days Child: 6-12 years 250mg, 1-5 years 125mg 6 hourly orally for 5 days

(b) Amoxicillin

Adult: 250mg 8 hourly orally, doubled in severe infections, for 5 days

Child: up to 10 years 125mg 8 hourly orally doubled in severe infections.

If severe; iv or infusion - Adult: 500mg 8 hourly. Child: 50-100 mg/kg daily in divided doses.

Co-amoxiclav

Adult: 375 mg 8 orally hourly, 625 mg orally b.d. or 8 hourly in severe infections for 5 days or 1.2 g iv over 15-30 minutes 8 hourly

(c) Metronidazole

Adult: 200mg orally 8 hourly for 3-5 days

Child: 1-3 years 50 mg orally 8 hourly, 3-7 years 100 mg orally 8 hourly.

7-10 years 100mg orally 8 hourly

Adult: 500mg iv 8 hourly, Child: 7.5mg/kg iv 8 hourly

(d) Cephalexin

Adult: 250mg orally 6 hourly for 5 days

Child: 1-5 year 125mg orally 8 hourly, 6-12 years 250mg orally 8 hourly

(e) Cefuroxime

Adult 250mg orally b.d. for 5 days, iv or infusion 750mg 8 hourly.

Child:30-100mg/kg daily in 3-4 divided doses.

Osteomyelitis of jaw bones
In addition to the above mentioned antimicrobial agents cloxacillin, clindamycin and fusidic acid could also be used in the treatment of osteomyelitis of jaw bones.
The dose and duration of treatment will depend on severity of the condition. These patients should be managed in an Oral and Maxillo Facial Unit (O.M.F)

Periodontal diseases are a group of related inflammatory disorders, initiated by dental plaque (bacteria) and causing destruction of the supporting structures of the teeth, namely the cementum, alveolar bone, periodontal ligament and dentogingival tissues.
Mechanical removal of plaque from root surfaces combined with a high degree of daily plaque removal by the patient, is a very effective. The antibiotics most often used are metronidazole and tetracycline orally or locally. The topical preparations provide high antimicrobial doses at diseased sites with a more focused targeting of pathogenic organisms. This is achieved by administrating the drug locally through the pocket orifice in gel form or a carrier system which allows a slow but sustained delivery at the site of action.
The available topical preparations are 25% metronidazole gel and 25% tetracycline impregnated fibres
The mouth rinses such as 0.2% chlorhexidine gluconate could also be beneficial. All chemical agents should be used as adjuncts to routine oral hygiene procedures.

Acute necrotising ulcerative gingivitis (Vincent's gingivitis)
This is a specific disease causing acute destruction of the periodontal tissues. The disease is attributed to infection by fusiform bacteria and spirochetes. Treatment includes improvement of oral hygiene, metronidazole 200- 400 mg t..d..s. for 5 days and mouthwashes. Mouthwashes which are useful include 0.2% chlorhexidine, hydrogen peroxide and freshly prepared potassium permanganate.

Pericoronitis
This is inflammation of the soft tissue around the crown of any partially erupted tooth commonly the lower third molar. Oral metronidazole or penicillin or both should be given in severe cases.

Facial injuries
They include soft tissue, as well as hard tissue injuries. These patients should also be managed in OMF units. Amoxicillin, co-amoxiclav, metronidazole, cephalexin, cefuroxime and cloxacillin are the antibiotics of choice for treatment of facial injuries.

Fungal infections
Candida albicans may be found in the mouths of healthy adults in the absence of any evidence of infection. *Candida albicans* infection (thrush) is one of the most common early manifestations of HIV/AIDS. The main forms, which are distinct both clinically and histologicaly are acute oral candidosis – thrush; denture - associated candidosis; angular cheilitis (it has been shown, that angular cheilitis can be caused by other organisms such as staphylococci) and candidal leukoplakia
Most cases of oral candidosis can be successfully treated by local measures, e.g. improvement of oral hygiene, and topical antifungal agents such as nystatin lozenges and miconazole oral gel. 0.2% chlorhexidine mouthwashes also have an antifungal activity.

Nystatin
Adult and child - 100,000 units 4 times daily after food for 7 days (continued for 2 days after lesions have resolved).
Immunosuppressed adult and child over one month may require higher doses. e.g.500,000 units 4 times daily.

Miconazole
This is used for local application in the mouth, but it is absorbed to the extent that potential interactions with drugs such as warfarin sodium need to be considered,
Adult: 5-10 ml in the mouth after food and retain near the lesions for 5 minutes each time 4 times daily.
Child: under 2 years 2.5 ml twice daily, 2-6 years 5ml twice daily, over 6 years 5ml four times daily
It also has antibacterial activity against staphylococcal species, and is useful in the management of angular cheilitis.

Fluconazole
This is used for oral candidosis that do not respond to topical antifungal drugs.
Adult: 50mg daily given for 7-14 days by mouth.
Child:3mg/kg daily by mouth

Viral infections
Herpes simplex and herpes zoster infections resolve spontaneously in immunocompetent subjects.
Management includes soft diet, adequate fluid intake, analgesics when required and 0.2% chlorhexidine, or doxycyline or povidone-iodine mouthwashes.

Tetracycline mouthwashes
Powder from a 250 mg tetracycline capsule can be stirred into a small amount of water and rinsed around the mouth for 2-3 minutes 4 times daily for 3 days

0.2% chlorhexidine
Rinse mouth with 10ml for about one minute twice daily
Solutions diluted to 0.1% is also effective.

1% povidone – iodine mouth wash
Adults and children over 6 years, up to 10ml. diluted with an equal quantity of warm water for up to 30 seconds, 4 times daily for 7-14 days

In severe herpes infections oral aciclovir is required.

Herpes simplex
Aciclovir: Adult 200 mg 5 times orally daily for 5 days. Child under 2 years half adult dose

Herpes zoster
Aciclovir: 800 mg orally 5 times daily for 7 days

Aciclovir cream (5%) is used to treat labial herpes simplex infections. Apply to lesions 5 times daily for 5-10 days.

Further reading
1. British National Formulary, 51st Edition 2006. BMJ Publishing Group Ltd & RPS Publishing. London
2. Frezzini C, Leao JC, Cedro M, Porter S. Aspects of HIV disease relevant to dentistry in the 21st century. *Dental Update* June 2006; **33(5):** 276-85
3. Roberts A. Bacteria in the mouth. *Dental Update* April 2005; **32(3):** 134-42
2. Dawson MP, Smith AJ. Superbugs and the dentist. *Dental Update* May 2006; **33(4):** 198-207
3. Shafer, Hine, Levy. Section II Diseases of microbial origin. In Saunders, ed. A textbook of oral pathology 4th Edition 2003. An Imprint of Elsevier. 340-53

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Chapter 14

RESPIRATORY TRACT INFECTIONS

Acute bronchitis

Is often of viral origin. Antibiotics are indicated only if there is secondary bacterial infection.

Exacerbations of chronic bronchitis.

Many patients are colonized with *Haemophilus influenzae*, *Strep.pneumoniae*, or *Moraxella catarrhalis*. (90 -95 % are betalactamase producers). Hence a growth on sputum culture does not always mean infection.

However, antibiotics will reduce the volume and purulence of sputum.

Give amoxicillin 500mg orally 8 hourly for 5 days, or doxycycline 200mg orally initially and then 100 mg daily for 5 days or erythromycin 500 mg orally 6hourly

If resistant to above, co-amoxiclav 625 mg 8 hourly or cephalosporins may be considered.

Community acquired pneumonia (CAP)
Community acquired pneumonia is defined as pneumonia occurring in patients not in hospital or within 48 hours of admission with no institutionalization or immunocompromised state.
Initially empirical therapy is indicated.
S. pneumoniae and *H.influenzae* are the usual organisms. Penicillins are good enough for empirical therapy. Atypical organisms implicated include M*ycoplasma pneumoniae, Legionella sp*. and *Chlamydia pneumoniae*. They are uncommon and need not be covered for empirical treatment.

See Table 1 for choice of antibiotics.

Mild to moderate CAP
Children: amoxicillin 50mg/kg in 3 divided doses **Or** erythromycin 50mg/kg in divided doses orally 6hourly.

Adults and children over 12 years:
Amoxicillin 500 mg orally 8 hourly, or doxycycline 200mg orally initially and then 100mg orally daily, or azithromycin 250mg orally b.d. or 500 mg once a day, or clarithromycin 250 -500 mg orally12 hourly **Or** 500 mg once a day, or levofloxacin 500 mg orally 12 hourly

Severe CAP
Co-amoxiclav 1.2 g 6 to 8 hourly, or cefuroxime 750mg to 1.5 g iv 6 hourly, or cefotaxime 1 g iv 8 hourly, together with clarithromycin 500mg 12 hourly. **Or** levofloxacin 500 mg iv b.d. or once daily.

Aspiration pneumonia and lung abscess from aspiration.
Benzylpenicillin 1.2g iv 4-6 hourly (child 30-60mg/kg/day), plus metronidazole 500mg iv 12 hourly for 1-2 days (child 7.5mg/kg/dose). Alternatively, as single agent, co-amoxiclav 1.2-2.4 g 8 hourly, or cefotaxime 2 g iv 6 hourly, or ticarcillin-clavulanate 3.2 g iv 6 hourly (child 50mg/kg/dose).

Alternatively, and if there is penicillin allergy, as a single agent, clindamycin 600 mg iv 8hourly (child 10mg/kg/dose) and then 600mg orally 8 hourly (child 7.5mg/kg/dose)

If Gram-negative organisms are suspected as in alcoholics, gentamicin 4-6mg/kg iv once daily (child <10yrs 7.5mg/kg, >10yrs 6mg/kg), or ciprofloxacin 200-400 mg iv b.d.

Staphylococcal pneumonia
Cloxacillin 2g iv 6 hourly (child 50mg/kg/dose) plus gentamicin 4-6mg/kg iv daily (child 6mg/kg/day)

With severe penicillin allergy or suspected MRSA infection, vancomycin 1g iv 12 hourly (child 40mg/kg/day iv in 2 divided doses) or teicoplanin 200 mg iv b.d. (child: 10 mg/kg/day).

Hospital acquired pneumonia (nosocomial infection) (HAP)
Hospital acquired pneumonia is defined as a pneumonia developing in a patient hospitalised for more than 48 hours. Aerobic Gram-negative bacteria and hospital pathogens such as MRSA are the commonest forms of infection. Culture of secretions usually indicate colonization, but ABST should guide therapy. See Table 2

Mild to moderate HAP (no specific risk factors)
Co-amoxiclav 625 mg orally 12 hourly (child 22.5mg/kg/dose) plus gentamicin 4-6mg/kg iv daily (child <10yrs 7.5mg/kg, >10yrs 6mg/kg), or cefotaxime 1g iv 8-12 hourly (child 50mg/kg/dose) plus gentamicin

Mild to moderate HAP (specific risk factors)
In diabetes, coma, head injury or renal failure, where *S.aureus* is more common, cloxacillin 2 g iv 6hrly (child 50mg/kg/dose) plus gentamicin 4-6mg/kg iv daily (child 6mg/kg/day)

If MRSA is present, vancomycin 1 g iv 12hourly, (child 40mg/kg/day iv in 2-4 divided doses).

Severe HAP
Gentamicin with or without imipenem or meropenem 500 mg –1 g iv 8 hourly. If aminoglycosides are contraindicated, substitute gentamicin with ciprofloxacin 400mg iv 12 hourly or 750mg orally 12 hourly. If MRSA is present add vancomycin or teicoplanin

Legionella pneumonia
Erythromycin 0.5 – 1 g iv 6 hourly initially and then orally 250 to 500 mg 6 hourly for 14 to 21 days. Or clarithromycin 500 mg b.d.

Mycoplasma pneumonia
Erythromycin 500mg 6 hourly orally (50mg/kg/day) for 14 days

Table 1. Specific therapy for pathogens causing pneumonia

Pathogen	First-line therapy	Second line therapy	Comments
	Benzylpenicillin or amoxicillin	Cefuroxime axetil or clarithromycin or co-amoxiclav	In the presence of decreased susceptibility to penicillin (MIC 0.1 to 1 mcg/ml):- benzylpenicillin or amoxicillin remain effective agents.In uncomplicated cases, continue therapy for 5 to 10 days
penicillin- resistant (MIC 2 to 4 mcg/ml)	Benzylpenicillin (high doses) or amoxicillin	Cefotaxime or ceftriaxome cefuroxime co-amoxiclav	Plasma concentrations achieved by parenteral administration are adequate to treat pneumococci with this degree of resistance. Vancomycin may be required MIC>4 mcg/ml
M. pneumoniae *C. pneumoniae*	Erythromycin Doxycycline	Newer macrolides or respiratory quinolines	duration of therapy should be 14 days
C.psittac i	Doxycyline	Newer macrolides	
Legionella spp (proven)	Ciprofloxacin or erythromycin with or without rifampicin or doxycycline	Newer macrolides	duration of therapy should be 21 days
H. influenzae	Ampicillin iv or amoxicillin	Co-amoxiclav or cefotaxime or ceftriaxone or cefuroxime axetil or doxycycline	If beta-lactamase producing, use second line agent Phenoxymethylpenicillin is inactive against *H. influenzae* Cefuroxime axetil 500mg orally, 12-hourly duration of therapy 7 to 10 days

Staph. aureus	Cloxacillin	Cephalothin or cephazolin	Duration of therapy should be 4 to 6 weeks. For MRSA, use vancomycin
Aerobic Gram-negative bacteria including *K. pneumoniae*	Gentamicin or ticarcillin/clavulanate or piperacillin/tazobactam ciprofloxacin or ceftriaxone	Imipenem or meropenem or ciprofloxacin or cefixime, duratrion of therapy 10 to 14 days	*For Enterobacter, Serratia* and *Acinetobacter spp*, use gentamicin and /or a second line agent or
P.aeruginosa	Gentamicin plus ticarcillin/clavulanate or ciprofloxacin iv	Gentamicin plus ceftazidime	2 active agents should be used Second-line agents detailed under aerobic GNB may also be given with gentamicin Duration of therapy 14 to 21 days

All fluroquinolines are best avoided as they should be reserved for multi -drug resistant TB (MDR)

Table 2. Antibiotics for hospital acquired pneumonia (HAP)

	First line therapy	**Second line therapy**	**Comment**
			Duration of treatment for all categories is 72 hrs after clinical response
Mild to moderate HAP			
No risk factors	Co amoxiclav or benzyl penicillin plus gentamicin	Cefotaxime or ceftriaxone	if allergic to penicillin or renal failure use second line therapy or fluroquinolines
With risk factors			
Witnessed aspiration or thoraco abdominal surgery	Benzylpenicillin plus gentamicin plus metronidazole or cefotaxime plus metronidazole	Ticarcillin /clavulanate	if allergic to penicillin use clindamycin or lincomycin

diabetes, coma, renal failure or head injury	cloxacillin plus gentamicin	vancomycin plus gentamicin	if proven MRSA, use vancomycin
Severe HAP	Gentamicin plus Ticarcillin/clavulanate	Imipenem or meropenem	if gentamicin contraindicated substitute ciprofloxacin vancomycin for MRSA
Regardless of severity, Previous antibiotics Structural lung disease Steroid therapy Over 5 days in ICU	Gentamicin plus beta lactamase inhibitor	Vancomycin for MRSA	should cover acenetobacter and pseudomonas

Further reading

1. Therapeutic Guidelines. Antibiotics. Therapeutic Guidelines Limited, Melbourne, Australia.2006
2 Current Medical Diagnosis and Treatment 2005.Lange Medical Books-McGraw Hill
3. British National Formulary 51st 7Edition 2006. BMJ Publishing Group Ltd & RPS Publishing. London

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Chapter 15

SEPSIS SYNDROME

Sepsis is a clinical situation in which there is evidence of infection plus a systemic inflammatory response (SIRS) as manifested by an altered temperature, tachycardia and increased respiratory rate.

Additionally, septic patients may have evidence of altered organ perfusion, disseminated intravascular coagulation and adult respiratory distress syndrome.

Cytokines are mainly responsible for the pathophysiological changes associated with systemic manifestations. Cytokines are produced when host cells such as monocytes and macrophages interact with microorganisms or their products. Thus sepsis syndrome is a constellation of signs and symptoms produced as a result of host response to infection, and most clinical manifestations are due to the effects of cytokines.

Microorganisms responsible for sepsis should be determined by **blood culture** as different organisms may cause sepsis. Depending on the focus of infection the aetiological agents of sepsis can be Gram positive and Gram-negative bacteria, fungi and parasites.

Antimicrobial therapy:
Although antimicrobial therapy is the mainstay of treatment, approaches aimed at correcting the predisposing factors have a critical bearing on the outcome of infection. e.g. removal of a catheter or a foreign body, draining of an abscess. Wherever possible microbiological opinion should be sought.

Empiric therapy
The principle of empiric therapy is to provide broad initial coverage. Suggested antibiotics in order of preference include the following.

1. ***Community acquired infection in the non-neutropenic patient (neutrophil count ≥ 1000/mm^3)***
    a. Suspected urinary tract source:
    co-amoxiclav, or a third generation cephalosporin (cefotaxime;ceftriaxone), or ciprofloxacin or ticarcillin-clavulanate ± an aminoglycoside
    b. Non-urinary tract source :
    A third generation cephalosporin + metronidazole or piperacillin-tazobactam or ticarcillin-clavulanate ± an aminoglycoside

2. ***Hospital acquired infection in a non-neutropenic patient***
   A third generation cephalosporin ± metronidazole, or piperacillin-tazobactam or ticarcillin-clavulanate + an aminoglycoside

3. ***Hospital acquired infection, neutropenic patient***
   piperacillin-tazobactam / ticarcillin-clavulanate + an aminoglycoside, or imipenem/meropenem ± an aminoglycoside, or cefipime ± an aminoglycoside, or ceftazidime or cefotaxime or ceftriaxone + an aminoglycoside

   If MRSA is suspected vancomycin or teicoplanin should be added.

4. ***Burns***
   ceftriaxone or ceftazidime + an aminoglycoside, or teicoplanin or vancomycin + piperacillin-tazobactam or ticarcillin-clavulanate + aminoglycoside if MRSA is suspected

* If gentamicin resistance is suspected use netilmicin or amikacin. However blood levels of aminoglycosides should be done out to determine effective and toxic levels in blood wherever possible.
** If infection is present in a long term indwelling vascular catheter add vancomycin or teicoplanin

Duration of therapy
Antibiotics should be given ***intravenously*** and the ***duration of therapy*** in normal hosts is a minimum of 7 days. Treatment of the neutropenic or immunocompromised patients will require longer duration of therapy. They should be afebrile for a minimum period of 5 days and the neutrophil count should be higher than 500/µl before antibiotics are stopped. If the response to therapy after 3 – 4 days is inadequate, review antibiotic therapy.

Dosage of antibiotics in sepsis syndrome
Ceftazidime
Adults :6g /day (2g 8 hourly). Each dose as an infusion over 30 minutes.
Children: 150mg/kg/day in 3 divided doses

Newborns: 50mg/kg/day in two divided doses as plasma half life is prolonged. After two weeks the dosage can be increased and after 4 weeks the dose recommended for children is appropriate

Ceftriaxone
Adults: 2g once every 24 hours but can be increased to 2g 12 hourly in severe infections in the immunocompromised. In patients with renal failure or those over 65 years the dose should not exceed 2g / day.
Children: 50 -100 mg / kg/ day in one or two divided doses
Newborns: 50 mg / kg / day in one or two divided doses

Cefotaxime
Adults: 8 – 12 g /day and administered in three to four divided doses. Each dose should be given as a 30 minute infusion diluted in iv fluid.
Children: 150 – 200 mg / kg/day
Newborns: 100 mg /kg / day

Piperacillin-tazobactam
Adults: 4.5g 8 hourly. If creatinine clearance is less than 40ml/min or serum creatinine is more than 200 µmol /litre (2.26 mg/dl) administer the drug 12 hourly.
Children: 112 mg / kg / 8 hourly

Ticarcillin-clavulanate
Adults: 3.2 g 6-8 hourly
Children: 80 mg / kg / 6 – 8 hrs

Imipenem
Each dose is best dissolved in 100 -200 ml of iv fluid and given over 30 min.
Dosage reduction required if creatinine clearance is less than 50 ml /min or serum creatinine is more than 300µmol /litre.(3.39 mg/dl)
Adults: 0.5g – 1g 6- 8hourly depending on the severity of infection
Children: 60 – 100 mg/kg/day in 3- 4 divided doses
Newborns: 40 mg /kg/ day in 2 divided doses
In central nervous system disorders best avoided due to the uncommon side effect of epilepsy.

Meropenem
Administration is same as for imipenem

Adults: 1g 8 hourly by 30 min infusion.
Children:10 -20 mg/kg / 8 hourly

Aminoglycosides : Serum level monitoring is recommended when aminoglycosides are administered. Toxicity is less with once daily therapy.

Gentamicin
Adults: 5.0 mg/kg/day. Once daily dose is adequate.
Children: < 5 years 7.5 mg /kg / day
> 5 years 6mg/kg/day
Newborns: 5mg/kg/day. From the second week onwards 7.5mg/kg/day can be given.

Amikacin
Adults: 15mg/kg/day or 1g/day
Children and newborns: 15mg/kg/day

Netilmicin
Adults: 6 mg /kg/day
Children: 6-7.5mg/kg/day
Newborns: 6 mg/kg/ day in two divided doses

Ciprofloxacin
Adults: 200 - 400mg 12 hourly over 30 to 60 minutes. Higher dose is recommended for Pseudomonas and Staph infections
Children: not recommended unless benefit outweighs risk. 5 – 10 mg /kg / day in two divided doses

Vancomycin
Adults: 500 mg every 6 hrs over 60 min or 1g every 12 hrs over 100 min
Children >1 month: 10 mg /kg every 6 hrs
Neonates >1 week: 15mg/kg initially and 10 mg /kg every 8 hrs
Neonate <1week: 10 mg /kg/every 12 hrs

Teicoplanin
Adults: 200 mg b.d.
Children: 10mg /kg/day as one dose or two divided doses

Metronidazole
Adults: 500mg in 100ml 8hourly infused over 30 min
Children: 7.5mg/kg/ 8 hourly

Specific therapy
This is based on the isolation of organisms from blood culture and antibiotic sensitivity test results.

Further Reading

1. Kucers A, Crowe SM, Grayson ML, Hoy JF, eds. The use of antibiotics. A clinical review of antibacterial, antifungal and antiviral drugs. 5th ed. 1997. Butterworth Heinemann UK
2. Mandell GL, Bennet JE, Dolin R, eds. Principles and practice of infectious diseases. 6th ed. 2004. Churchill Livingstone

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Chapter 16

SKIN AND SOFT TISSUE INFECTIONS

The permanent flora of the skin include *Staphylococcus epidermidis*, *Corynebacterium spp*, *Proprionobacterium acnes*, and *Pityrosporum ovale*. Transient bacterial flora, such as *Staphylococcus aureus* in the perinasal and perianal regions, *Enterobacteria* and *Pseudomonas* from the gut and soil, may remain alive on the skin for a few hours.The epidermal barrier is usually capable of preventing these from causing disease. Damage to this barrier and the reduction of the resident flora may lead to disease by the transient flora.

Common superficial skin infections
Impetigo: occurs more often in children and is caused by *Staphylococcus aureus* and *Streptococcus pyogenes*. In an otherwise healthy patient, if non-bullous and localized, use sodium fusidate or mupirocin cream or ointment b.d. If bullous or widespread, use oral cloxacillin with amoxicillin 500mg 6 hourly (25mg/kg per day in

divided doses for children). Alternatively, erythromycin 500mg 8 hourly (in children under 2 years 125mg every 6 hours, and 2-8 years 250mg every 6 hours), or cephalexin 500mg orally 8 hourly (25mg /kg daily in divided doses for children) or co-amoxiclav 625 mg b.d. (25mg/kg daily in divided doses for children) may be used. Good wound care is needed to prevent spread.

Ecthyma: appears as punched out shallow ulcers and are a result of poor hygiene and neglect of minor trauma, including insect bites and scabies. The initial treatment is oral antibiotics as in widespread impetigo. It is necessary to do a culture and antibiotic sensitivity from the deeper parts of the ulcer, since other organisms, such as *Psuedomanas aeruginosa* and *Esch.coli* may infect the ulcer.

Pyodermas: refer to streptococcal and staphylococcal skin infections that classically produce pus, and often result from an underlying cause, such as atopic dermatitis, eczema, insect bites, abrasions and cuts. Treatment is as for impetigo or ecthyma.

Folliculitis and furunculosis: *staphylococcus aureus* is the main pathogen. Topical antibacterials (mupirocin, or sodium fusidate) are usually adequate. When widespread, occurring around the nose and ear, large and recurrent, and with early surrounding cellulitis, oral antibiotics as for widespread impetigo are used. Fluctuant and large furuncles require incision and drainage. Perianal abscesses also need incision and drainage.

Other superficial bacterial skin infections

Erythrasma: is a superficial localized and mild skin infection caused by *Corynebacterium minutissimum*. The organism grows in moist warm flexural areas. Topical treatment is with erythomycin, clindamycin or miconazole. Oral erythromycin for 5 days is also very effective.

Pitted keratolysis: this is caused by micrococci and *Corynebacterium spp*, in patients with severe hyperhidrosis of the soles. Treatment consists of using drying agents, such as aluminium chloride in alcohol solution, and topical erythromycin, clindamycin, miconazole or clotrimazole

Paronychia: acute paronychia (whitlow) needs to be treated surgically. Chronic paronychia is caused by fungi, yeasts and bacteria and is a result of chronic nail-fold damage, such as constant scrubbing and ingrowing nails. The treatment of the underlying cause and keeping the nail-fold dry is vital. Treatment of the infection by alcoholic solutions of clotrimazole, econazole topically and bacterial infection by systemic antibiotics as for impetigo are also important.

Streptococcal perianal disease: is caused by *S.pyogenes* and presents as sharply demarcated erythema around the anal verge in children. Painful defecation, blood streaked stools, and perianal irritation are the common symptoms. A 10-14 day course of phenoxymethylpenicillin or erythromycin orally in a dose of 125 mg every 6 hours is curative.

Common infections of the dermis and subcutaneous tissue

Erysipelas and cellulites: cellulitis is a spreading infection of the skin extending to involve the subcutaneous tissue and is usually caused by *Streptococcus pyogenes* or *Staphylococcus aureus*. Erysipelas is a superficial cellulitis of the dermis with lymphatic involvement and is caused by a Streptococcal infection. In children with facial or peri orbital cellulitis *Haemophilus influenzae* may be pathogen.

If *Streptococcus* infection is suspected, benzylpenicillin by intramuscular or slow intravenous injection or infusion, 2.4 –4.8 g daily in four divided doses (children, up to 100mg/kg in 4 divided doses). The duration of treatment depends on the response, but should be about 10 days. Phenoxymethylpenicillin 500mg orally 6 hourly (children 10mg/kg) can be used for milder infections.

For infections where both streptococci and staphylococci are suspected benzylpenicillin, as stated above, and cloxacillin 500mg 6 hourly orally, co-amoxiclav, 1.2 g 8 hourly iv (children 25mg/kg 8 hourly) or orally 625 mg b.d. or 8 hourly. Alternatively, cefuroxime iv 750 mg 8 hourly in severe infections or cephalexin 500 mg orally 6 hourly in milder ones, could be used. It is necessary to look for and treat the possible site of entry of the bacterial infection, such as hidden tinea pedis. Surgical drainage and debridement may be required.

Necrotising fasciitis: is a serious condition requiring urgent surgical removal of devitalized tissue. The causative organisms are mixed

aerobes and anaerobes. A combination of benzylpenicillin, gentamicin and metronidazole intravenously must be started immediately and changed later on culture findings if indicated.

Leprosy

Leprosy is a disease caused by *Mycobacterium leprae*, with a long replication time, and hence a long incubation period. The disease is diagnosed by the presence of one or more hypopigmented well-defined patches, with significant loss of sensation over them. The patches may have an erythematous edge or entirely erythematous plaques. Superficial nerves may be thickened. In severe forms of the disease there may be numerous erythematous plaques, nodules and macules, some with no loss of sensation. In these patients there will be some peripheral loss of sensation or motor power.

Those with 5 or less patches are classified as paucibacillary (PB) and those with more than 5 patches are considered multibacillary (MB), for treatment purposes by the WHO. The treatment for PB leprosy is rifampicin 600mg once a month, and dapsone 100 mg daily for a period of 6 months. MB leprosy is treated with rifampicin 600mg once a month, clofazimine 300mg once a month and 50 mg daily, and dapsone 100mg daily for 12 months.

It is necessary to look for nerve tenderness, swelling of patches, increase of numbness or motor power and the onset of fever, arthralgia, muscle and joint pains and the appearance of new patches. These are **lepra reactions** that can occur before, during and after therapy. They need urgent treatment with oral steroids, in a starting dose of 40mg per day, in addition to the leprosy medication, and scrupulous care of the affected areas to prevent deformities. These cases are best managed in specialized units.

Severe and rare bacterial infections

Staphylococcal scalded skin syndrome: i a part of the spectrum of Staphylococcal toxin mediated infections, which includes bullous impetigo, SSSS, and toxic shock syndrome. SSS is a disease of children, with an onset of fever, malaise, irritability, erythema and skin tenderness. Flaccid blisters develop on large areas of the skin. The patients need to be hospitalized, rehydrated, and ß lactamase resistant

antibiotics, eg. cloxacillin, cephalexin must be given intravenously or orally.

Toxic shock syndrome: is a multisystem disease caused by the exotoxin produced by *Staphylococcus aureus*. The patient has a high fever, myalgia, vomiting, diarrhoea, and skin manifestations of diffuse erythema and oedema of the palms and soles, erythema of mucous membranes, a strawberry tongue, and hyperaemia of the conjunctiva. Treatment consists of supportive therapy for hypotension, removal of the cause of the staphylococcal infection and the use of an appropriate antibiotic systemically.

Streptococcal toxic shock syndrome: is caused by group A ß haemolytic streptocci, by the production of "superantigens". It is characterized by severe local pain and early organ failure. They require intense supportive therapy for the hypotension, and early surgical intervention. Clindamycin is essential for its treatment, particularly as it inhibits the production of bacterial toxins, the main cause of the shock.

Further reading

1. British National Formulary, 51st Edition 2006. BMJ Publishing Group Ltd & RPS Publishing. London. .
2. Therapeutic Guidelines. Antibiotics. ver13. Therapeutic Guidelines Limited, Melbourne, Australia.
3. Blume JE, Levine EG, Heymann WR. Bacterial diseases. In: Bolognia JL, Jorrizzo JL, Rapini RP eds. *Dermatology*. London: Mosby 2003:1117-1144.
4. Singh G, Kaur V, Singh S. Bacterial infections. In Valia RG ed. IADVL Textbook and atlas of dermatology, Bhalini Publishing House, Mumbai, India. 2003: 190-2005.

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Chapter 17

SEXUALLY TRANSMITTED INFECTIONS

The incidence of sexually transmitted infections (STI) is increasing in most parts of South-East Asia. Sri Lanka is no exception. The spectrum of has widened to include more than 20 bacterial, viral, fungal and protozoan infections. In Sri Lanka, genital herpes is the commonest form of STI reported during the past few years. A sudden upsurge in the incidence of gonorrhoea was observed in 2003 and 2004.

Most bacterial STI are curable if they are treated at an early stage. Viral STI could be controlled with proper management and counselling. These infections are responsible for serious complications and sequelae including infertility, fetal wastage, ectopic pregnancy, congenital abnormalities, cancer and even death. In addition STI facilitate the transmission of HIV. STI co-infection with HIV may require more careful management and follow up than in patients who are not HIV infected. Certain STI are transmitted during pregnancy from mother to the offspring.

STI case management comprises not only of antimicrobial therapy to obtain cure and reduce infectivity but also comprehensive care including partner management, counselling on sexual behaviour change, and promotion of safer sexual practices. Resistance of several sexually transmitted pathogens to antimicrobials is increasing, rendering some low-cost treatment regimens ineffective. As such guidelines for prescribing antibiotics should be country specific, based on recommendations of the National STD/AIDS Control Programme.

Gonorrhoea

Causative organism - *Neisseria gonorrhoeae*

Uncomplicated adult anogenital gonococcal infection (urethritis, endocervicitis, proctitise)

Recommended therapy:

Cefuroxime axetil 1g orally in a single dose + probenecid 1 g orally
or ceftriaxone 250 mg im single dose

Alternative therapy

Spectinomycin 2g im single dose

Gonococcal pharyngitis
Recommended therapy:
Ceftriaxone 250 mg im single dose

Adult gonococcal conjunctivitis
Recommended therapy
Ceftriaxone 1g im single dose
Since gonorrhoea and chlamydia co-infection is common, when treating gonococcal infection, concurrent anti- chlamydia treatment is recommended. Although chlamydial co-infection of the pharynx is unusual, co-infection at genital sites sometimes occurs. Therefore treatment for **both infections** is recommended. Sexual contacts should be offered epidemiological treatment (treating the sexual partners whether infected or not) for both gonococcal and chlamydia infections with the same treatment regimen given to the index patient

Neonatal gonococcal conjunctivitis
Untreated gonococcal and chlamydia endocervicitis in the mother could lead to neonatal conjunctivitis.
Recommended therapy:
Ceftriaxone 25-50mg / kg body weight (not exceeding 25 mg). im single dose Ceftriaxone should be administered cautiously to hyperbilirubinaemic infants, especially those born prematurely. The infant's eye should be carefully cleaned immediately after birth with isotonic saline till the discharge disappears. Alternative therapy (only when ceftriaxone is not available) spectinomycin 25 mg/kg (maximum 75 mg) im single dose. Because of the possibility of mixed infection concomitant treatment for *C. trachomatis* is recommended

Neonatal chlamydia conjunctivitis
Erythromycin syrup 50mg/kg per day orally 6 hourly for 14 days
Topical antibiotic therapy alone is inadequate, and unnecessary if systemic treatment is administered. **Both parents** should also be treated for gonococcal and chlamydia infections

Prevention of neonatal conjunctivitis
Recommended therapy:
1% tetracycline ophthalmic ointment in a single application for high risk infants at the time of delivery. The infant's eyes should be

carefully cleaned immediately after birth with isotonic saline till the discharge disappears
Gonococcal conjunctivitis can be prevented by using timely eye prophylaxis. However, ocular prophylaxis provides poor protection against chlamydia trachomatis infection.
The diagnosis and treatment of gonococcal and chlamydial infections in pregnant women is the best method for preventing neonatal gonococcal and chlamydial disease

Disseminated gonococcal infection (DGI)
DGI results from gonococcal bacteraemia. It manifests as petechial or pustular skin lesions, asymmetrical arthralgia, tenosynovitis or septic arthritis. The infection is complicated occasionally by perihepatitis and rarely by endocarditis or meningitis.
Recommended therapy:
Ceftriaxone 1g im or iv daily
Continue parenteral therapy for 24-48 hours after improvement begins, at which time treatment may be switched to oral therapy (cefuroxime 500mg oral b.d. together with probenecid 500mg oral 6 hourly) to complete at least 7 days of antimicrobial therapy

Gonococcal meningitis
Recommended therapy:
Ceftriaxone 1g iv b.d. for 10-14 days

Gonococcal endocarditis
Recommended therapy:
Ceftriaxone 1-2 g iv b.d. for at least 4 weeks
Patients treated for DGI, gonococcal meningitis and endocarditis should be treated presumptively for concurrent *C. trachomatis* infection unless appropriate testing excludes this infection.
Recommended therapy for C. trachomatis:
Doxycycline 100mg orally bd for 14 days
or tetracycline 500mg orally 6 hourly for 14 days
Alternative therapy:
Erythromycin 500mg orally 6 hourly for 14 days

Sexual contacts should be given epidemiological treatment for uncomplicated gonococcal and chlamydia infections

Non-gonococcal urethritis (NGU)
Causative organisms: *Chlamydia trachomatis* (the most frequent cause). *Mycoplasma genitalium, Ureaplasma urealyticum* have also been implicated *Trichomonas vaginalis infection and intra-meatal chancre, warts and herpetic lesions are rare causes.*

Mucopurulent cervicitis
Causative organisms: *Chlamydia trachomatis* and *Neisseria gonorrhoeae*

Chlamydia trachomatis infection
Causative organism: *Chlamydia trachomatis* (serovars type D to K)

Uncomplicated adult anogenital chlamydia infection (urethritis, endocervicitis, proctitis and pharyngitis)
Recommended therapy
Doxycycline 100 mg orally b.d. for 7 days or azithromycin 1g orally in a single dose. **Doxycycline and tetracycline are contraindicated in pregnancy and lactation**
Alternate therapy:
Erythromycin 500 mg orally 6 hourly for 7 days.

Chlamydia infection in pregnancy
Recommended therapy:
Erythromycin 500 mg orally 6 hourly for 7 days.
Alternative therapy:
Amoxicillin 500 mg orally t.d.s. for 7 days
Sexual contacts should be given epidemiological treatment for uncomplicated gonococcal and chlamydia infections

HIV infection
Patients with gonococcal or chlamydia infection also infected with HIV should receive the same treatment regimen as those who are HIV negative

Pelvic inflammatory disease
Causative sexually transmitted micro-organisms are *Neisseria gonorrhoeae and Chlamydia trachomatis.* Anaerobic bacteria (*Bacteroides spp* and *Peptostreptococcus*, *Peptococcus spp*),

facultative Gram-negative rods, and *Mycoplasma genitalium* have also been implicated.

PID is observed in association with post-abortion, post-partum and post–operative infections and following intra-uterine contraceptive device (IUCD) insertion. Such iatrogenic PID occurs when instrumentation facilitates the ascent of vaginal and cervical micro-organisms into the endometrial cavity.

Recommended therapy:-mild cases
Ceftriaxone 250 mg im single dose plus
doxycycline 100 mg orally b.d. for 14 days or tetracycline 500mg oral 6 hourly for 14 days. * plus metronidazole 400mg orally b.d. for 14 days
Severe cases
Parenteral regimen –A
Ceftriaxone 1g iv daily, plus doxycycline 100 mg iv b.d. plus metronidazole 500mg iv b.d. until there is clinical improvement. Then switch to oral therapy to complete 14 days of treatment

Or

Parenteral regimen –B
Clindamycin 900mg iv t.d.s plus gentamicin loading dose iv or im 2mg/kg followed by a maintenance dose 1.5mg/kg t.d.s.until there is clinical improvement. Then switch to oral therapy with doxycycline 100mg orally b.d. or clindamycin 450mg orally 6 hourly to complete a total of 14 days of treatment.
* If doxycycline or tetracycline is contraindicated use erythromycin 500 mg orally 6 hourly for 14 days.
If PID should occur with an IUCD in place, treat the PID using the recommended antibiotics. There is no evidence that removal of the IUCD provides any additional benefit.

Sexual partners of patients with PID due to STI should be given epidemiological treatment for gonococcal and chlamydia infections.

Epidymitis
The sexually transmitted form of epididymitis is commonly caused by *Neisseria gonorrhoeae* and *Chlamydia trachomatis.*

Recommended therapy:
Ceftriaxone 250 mg im single dose plus doxycycline 100 mg orally b.d. for 14 days or tetracycline 500mg orally 6 hourly for 14 days. If doxycycline or tetracycline is contraindicated use erythromycin 500 mg oral 6 hourly for 14 days. Sexual contacts should be given epidemiological treatment for uncomplicated gonococcal and chlamydia infections

Syphilis
Causative organism: *Treponema pallidum*

Early syphilis (primary chancre, secondary or latent syphilis of less than 2 years duration)
Recommended therapy:
Benzathine penicillin 2.4 million units (1.8g) im after sensitivity testing or procaine penicillin 1.2 million units im daily after sensitivity testing with probenecid 500mg 6 orally hourly for 10 consecutive days
For patients allergic to penicillin:
Doxycycline 100 mg orally b.d. for 15 days or tetracycline 500 mg orally 6 hourly for 15 days

Late latent syphilis (syphilis of more than 2 years duration) or latent syphilis of unknown duration
Recommended therapy
Benzathine penicillin 2.4 million units (1.8g) im weekly for 3 consecutive weeks or procaine penicillin 1.2 million units im once daily with probenecid 500mg orally 6hourly for 21 consecutive days

For patients allergic to penicillin:
Doxycycline 200 mg orally b.d. for 30 days or tetracycline 500 mg orally 6 hourly for 30 days

Epidemiological treatment should be offered to sexual partners only after evaluation according to their stage of syphilis

Syphilis in pregnancy
Penicillin should be given in the same dosage schedules as recommended for treatment of non-pregnant women according to the stage of syphilis.

Erythromycin should not be used because it does not reliably cure an infected fetus. Data are insufficient to recommend azithromycin or ceftriaxone for treatment of maternal infection and prevention of congenital syphilis. Pregnant women who have a history of penicillin allergy should be desensitized and treated with penicillin.
All babies born to mothers with genital ulcer disease suggestive of syphilis or mothers with diagnosed syphilis should be epidemiologically treated with a single dose of benzathinepenicillin 50,000 units /kg im in a single dose irrespective of maternal treatment during pregnancy with or without penicillin or referred to a STD clinic for evaluation. This is a public health requirement.

Neurosyphilis
Recommended therapy:
Benzylpenicillin G 4 million units iv every 4 hours for 10-14 days
Alternative therapy:
Procaine penicillin 2.4 million units imonce daily together with probenecid 500mg orally 6 hourly, both for 10-14 days

Cardiovascular syphilis
Recommended therapy:
Procaine penicillin 1.2 million units im once daily together with probenecid 500mg orally 4 times a day both for 21 days
If patient is allergic to penicillin:
Doxycycline 100mg orally b.d. for 30 days or erythromycin 500mg orally 6 hourly daily for 30 days

Before treating neuro and cardiovascular syphilis, give prednisolone 20mg orally twice a day for 2 days and continue for the first 48 hours of the course to reduce the risk of a Jarisch-Herxheimer reaction.

Syphilis and HIV infection
All stages of syphilis should be treated according to the recommendation for HIV negative patients

Early congenital syphilis (from birth up to 2 years of age)
Symptomatic infants
Recommended therapy:
Treat in consultation with a paediatrician.

Benzylpenicillin G 100,000-150,000 units/kg/day, administered as 50,000 units /kg /dose iv every 12 hours during the first 7 days and every 8 hours thereafter for a total of 10 days

Asymptomatic infants with serologic evidence of congenital syphilis
Benzathine penicillin 50,000 units /kg (1.8g) im single dose or benzylpenicillin G 50,000 units /kg /dose iv every 12 hours for a total of 10 days

Late congenital syphilis (Children >2 years old)
Benzathine penicillin 50,000 units /kg (up to 2.4 million) im weekly for 3 consecutive weeks
For patients allergic to penicillin
Erythromycin 7.5-12.5mg /kg orally 6 hourly for 30 days
Parents of the infant should be evaluated for syphilis and treated according to the stage of syphilis

Genital herpes
Causative micro-organism: *Herpes simplex virus* 2 or 1

Recommended therapy for first clinical episode of herpes simplex virus (HSV) infection
Aciclovir 200 mg orally 5 times a day for 7-10 days or aciclovir 400mg orally t.d.s. for 7-10 days or valaciclovir 1g orally b.d. for 7-10 days. Advice the patient to keep the ulcers clean by washing. There is no cure for herpes infection but the symptoms could be reduced by the use of systemic antiviral drugs.

Recommended therapy for recurrent episodes
Aciclovir 200 mg orally 5 times a day for 5 days or acilovir 800mg orally b.d. for 5 days or aciclovir 400mg orally t.d.s. for 5 days or valaciclovir 500mg orally b.d. for 3- 5 days. Most patients with a first episode of genital herpes will have recurrent episodes of genital lesions. Most of them do not need anti-viral treatment. Counselling and reassurance help to manage the lesions. Therapy may be necessary if symptoms are severe.
Suppressive therapy is recommended for patients who experience more than 6 episodes a year. This should be commenced after counselling. Therefore refer the patient to STD services. Partners should be counselled and evaluated

Genital herpes infection in pregnancy
Antiviral drugs are preferably avoided in the first trimester. The potential benefits for treatment should be balanced against the potential for adverse effects. Aciclovir is not known to be harmful and available data do not indicate an increased risk for major birth defects compared with the general population in women treated with aciclovir during the first trimester. The dose of aciclovir for pregnant women with first episode or severe recurrent herpes infection is the same as for non-pregnant women.

Neonatal herpes
Infants exposed to HSV during delivery as documented by virologic testing or observation of lesions should be followed up in consultation with a specialist. If lesions develop treat as given below.

Recommended therapy:
Aciclovir 20 mg /kg body weight iv 8 hourly for 21 days for disseminated CNS disease. If only skin or mucus membranes are affected 20 mg/kg iv 8 hourly for 14 days. If herpes conjunctivitis is present use 3% topical aciclovir ointment in addition to systemic therapy. Some recommend the use of aciclovir for infants born to women who acquire primary HSV infection near term because the risk for neonatal herpes is high for these infants

Genital herpes infection and HIV
Recommended therapy: Aciclovir 400 mg orally 3-5 times a day until lesions resolve. Most lesions of herpes in HIV infected persons will respond to treatment with aciclovir for longer than the standard recommended therapy.

Chancroid
Causative micro organism : *Haemophilus ducreyi*
Recommended therapy:
Ciprofloxacin 500 mg orally b.d for 3 days or ceftriaxone 250 mg im single dose or erythromycin 500mg orally 6 hourly for 7 days or azithromycin 1g orally single dose

Sexual partners of patients should be offered epidemiological treatment with the same treatment schedule

Trichomoniasis
Causative organism: *Trichomonas vaginalis.*
Recommended therapy:
Metronidazole 2g oral single dose or tinidazole 2 g oral single dose

Alternative therapy:
Metronidazole 400 mg given orally b.d. for 7 days
Warn patients to avoid alcohol while taking metronidazole and tinidazole
Sexual partners of patients should be offered epidemiological treatment with the recommended regimen

Trichomoniasis in pregnancy
Trichomoniasis has been associated with adverse pregnancy outcomes such as premature rupture of membranes, preterm delivery and low birth weight**.**
Although metronidazole is not recommended for use in the first trimester of pregnancy, treatment may be given where early treatment has the best chance of preventing adverse outcomes. A consistent association between metronidazole use during pregnancy and teratogenic or mutagenic effects in the newborn has not been demonstrated.
Some experts recommend alternative therapy with intra-vaginal clotrimazole 100mg pessaries for 6 days followed by systemic therapy later. Treatment as above in 2^{nd} and 3^{rd} trimesters

Neonatal trichomoniasis
Infections in the neonates usually resolves spontaneously within a few weeks. If symptoms or uro genital colonization persists past the 4^{th} week after birth treatmemt should be given.
Metronidazole 5mg/kg orally t.d.s. for 5 days

Trichomoniasis and HIV infection
Should receive the same treatment regimens as those who are HIV negative

Bacterial vaginosis (BV)
BV is an endogenous reproductive tract infection resulting from replacement of the normal lactobacillus sp in the vagina with

Gardnerella *vaginalis*, Mycoplasma *hominis* and anaerobes including *Mobilinicus*, *Bacteroides*, and *Peptostreptococcus* species.

If three out of four Amsel's criteria given below are met there is a 90% likelihood of BV. Milky, homogenous, adherent vaginal discharge, vaginal pH greater than 4.5, presence of clue cells, and fishy smell when 10% KOH is added to the discharge.
All women who have symptomatic disease need treatment.
Recommended therapy:
Metronidazole 400 mg orally b.d. for 7 days
Metronidazole gel 0.75% one full applicator (5g) intravaginally once a day for 5 –7 days
Alternative therapy
Clindamycin 300mg orally b.d. for 7 days

Recurrent BV is common and requires treatment with metronidazole or clindamycin for 10-14 days. Treatment of sexual partners with bacterial vaginosis has not been beneficial

Bacterial vaginosis in pregnancy
Adverse pregnancy outcomes such as premature rupture of membranes, chorioamnionitis, pre-term delivery and low birth weight have been associated with bacterial vaginosis.
Treatment as above with oral metronidazole or clindamycin
Metronidazole or clindamycin is not recommended for use in the first trimester of pregnancy.

Bacterial vaginosis and HIV infection
Should be treated with the same regimens as those who are HIV negative.

Vulvovaginal candidiasis (VVC)
VVC is often caused by C*andida albicans*, occasionally by other *Candida sp*. such as *Candida glabrata*
Recommended therapy for uncomplicated VVC
Intravaginal agents
Miconazole or clotrimazole 200 mg, inserted into the vagina once a day at night for three days, or clotrimazole 500 mg, inserted into the vagina as a single dose at night.

Oral agents
Fluconazole 150mg orally as a single dose or itraconazole 200mg b.d. for 1 day

Many women may prefer the simplicity of a single dose treatment.
If oral therapy is preferred for severe infection two sequential 150mg doses of fluconazole given 3 days apart is superior to a single 150mg dose

Alternative therapy
Nystatin 100,000 units (one pessary), inserted intravaginally once a day at night for 14 days, topical creams are recommended for mild cases.
Clotrimazole 1% cream apply twice a day for 7 days
Miconazole 2% cream apply twice a day for 7 days

Severe infections, women with uncontrolled diabetes mellitus, pregnancy may require treatment for 10-14 days.

Recurrent VVC
Recurrent VVC is defined as four or more episodes of symptomatic infections in one year. When it is certain that no reversible causes are present (antibiotic therapy, uncontrolled diabetes) after initial therapy has been completed maintenance therapy may be appropriate.

Initial therapy	Maintenance therapy
Clotrimazole 100mg vaginal tablet per day for 7 days	One 500mg vaginal tablet once a week
Fluconazole 150mg in a single dose or 150 mg in two sequential doses 3 days after initial dose	One 150mg tablet orally once per week

Although maintenance therapy should be continued for 6 months, 30-40% of women will have recurrences once therapy is discontinued. Since severe or recurrent VVC cause psycho-social problems it is best managed in consultation with a specialist.
Partner management
VVC is usually not acquired through sexual intercourse. Although treatment of sexual partners is not recommended topical applications may be considered for partners of women who have recurrent infection.

Candida in pregnancy
Asymptomatic colonisation with *Candida sp* is higher in pregnancy. Symptomatic candida is more prevalent throughout pregnancy. Only topical therapy is recommended. Longer courses may be necessary.

Vulvo-vaginal candida and HIV infection
Therapy for VVC should not defer from that for seronegative women.

It is not recommended for routine primary prophylaxis.

Lymphogranuloma venereum
Causative organism: *Chlamydia trachomatis* sero types L1, L2, L3

Recommended therapy:
Doxycycline 100 mg orally, b.d. for 21 days,
Alternative therapy:
Erythromycin 500 mg orally 6 hourly for 21 days.
(Only for those who cannot tolerate tetracycline)

Sexual partners of patients should be offered epidemiological treatment

Acute prostatitis
Urinary tract pathogens are usually involved although sexually transmitted pathogens may cause acute infection

Chronic prostatitis
Possible micro-organisms
*Chlamydia trachomatis, Ureaplasma urealyticum, Mycoplasma hominis***,** Gram negative rods-*Escherechia coli, Enterococci***.**
Recommended therapy:
Doxycycline 100 mg orally b.d. or tetracycline 500mg oral 6 hourly for 4-6weeks
Alternative therapy :
Erythromycin 500 mg orally 6 hourly for 4-6 weeks.
Ofloxacin 400mg orally b.d. for 4-6 weeks

Genital warts
Antibiotics are not required. Please refer patient for specialized treatment.

Antiretroviral therapy for HIV/AIDS
Patients should be referred to a specialist venereologist.

Further Reading

1. Center for Disease Control. Sexually Transmitted Diseases Treatment Guidelines 2006
2. British Association for Sexual Health.UK national guidelines on the management of sexually transmitted diseases 2003, www.bash.org.uk
3. World Health Organization. (2001) Guidelines for the management of Sexually transmitted infections WHO/HIV_AIDS/2001.01;WFO/RHR/01.10
4. National STD /AIDS Control Programme, Ministry of Health Sri Lanka.2002; Guide to Management of Sexually Transmitted Diseases.

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Chapter 18

TUBERCULOSIS

Introduction
Tuberculosis (TB) is caused by infection with *Mycobacterium tuberculosis* (MTB). Tuberculosis affects mostly the lungs (pulmonary tuberculosis) and less commonly extra pulmonary sites (extra-pulmonary tuberculosis).

E.g : Pleura – pleural effusion
Lymph nodes - lymphadenopathy
Meninges - meningitis
Spine - Pott's disease
Disseminated disease - miliary TB

Pulmonary disease which is the commonest form usually results in cavitatory disease (post primary pulmonary TB). About 65% of pulmonary TB patients are sputum positive for acid fast bacilli (AFB). Sputum positive pulmonary TB patient is defined as

a). Two or more initial sputum examinations are positive for AFB.

Or

b). One sputum smear examination (out of three) positive for AFB plus radiographic changes consistent with active pulmonary TB as determined by a clinician

Or

c). One sputum smear examination positive for AFB (out of three) plus sputum culture positive for MTB.

Essential anti-TB drugs and their role

Rifampicin (R)- bactericidal and active against extracellular dormant forms.

Isoniazid (H) – bactericidal.
Pyrazinamide (Z) – kills intracellular dormant forms.

Ethambutol (E)– bacteriostatic.

Streptomycin (S) – bactericidal

Principles of treatment of tuberculosis

a). Any treatment regimen should have three or more anti-TB drugs

In a MTB colony which has never been exposed to anti-TB drugs there can be few organisms which are resistant to a given anti TB drug not due to previous exposure to anti-TB drugs, but due to spontaneous genetic mutations. By combining drugs one can make sure that the organisms which are resistant to a given drug will be killed by another drug in the regimen.

b). Treatment duration is prolonged.

Mycobacteria metabolize and divide slowly. They exist in dormant forms too. Therefore to kill the entire population in a patient, drug treatment of long duration is needed.

Case definitions

New – a patient who has never had treatment for TB or who has taken anti-TB drugs for less than one month.

Relapse – a patient previously treated for TB who has been declared cured or treatment completed and is diagnosed to have active TB again.

Defaulter – a patient who has interrupted treatment for two months or more.

Treatment failure – a patient who is sputum smear positive at five months or later during treatment. .

Treatment regimens

National Programme for Control of Tuberculosis and Chest Diseases (NPTCCD) recommends adherence to two treatment regimens which are approved by the World Health Organization (WHO) and International Union Against Tuberculosis and Lung Diseases (IUATLD). They are called category 1 and Category 2 treatment.

Category 1 treatment consists of six months of rifampicin (R) and isoniazid (H) supplemented by pyrazinamide (Z) and ethambutol (E) during the first two months, ie. 2RHZE 4RH. This category of treatment is for all new patients. (for both pulmonary and extra-pulmonary).

Where ethambutol cannot be used, as in the case of small children who may not be able to tell about visual disturbances which may occur as an adverse effect to ethambutol, it can be replaced with streptomycin. Ethambutol should also be replaced with streptomycin in meningeal TB as the former does not cross the blood brain barrier. Some sources recommend 9 – 12 months treatment (continuation phase with R & H prolonged to 7 – 10 months) when there is neurological involvement, although WHO recommends that six months treatment is adequate.

Category 2 treatment consist of eight months of rifampicin, isoniazid and ethambutol supplemented by pyrazinamide during the first three months and streptomycin during the first two months, ie. 2RHZES, 1RHZE, 5RHE. This is for relapses, defaulters who come again with sputum smear positive disease and treatment failures.

Dosage
Rifampicin – 10mg/kg/day
Isoniazid – 5mg/kg/day
Pyrazinamide – 30mg/kg/day
Ethambutol – 15mg/kg/day
Streptomycin – 15mg/kg/day

Monitoring of treatment
Patients with pulmonary TB (sputum AFB positive and negative) should be assessed by sputum smear examination at intervals. Sputum examination should be done at the end of 2, 5 and 6 months on those patients on category 1 treatment and at the end of 3, 5 and 8 months on those patients on category 2 treatment. If the sputum is still positive after two months of category 1 or three months of category 2 treatment, initial or intensive phase of treatment should be prolonged by further one month.

When should one do pre-treatment sputum AFB culture?
In this era of drug resistant TB, ideally pre-treatment sputum AFB culture should be done on all pulmonary TB patients. However this is not possible due to inadequate facilities. Therefore culture should at least be done on pre category 2 treatment, pre category 1 treatment where the patient is at a higher risk of harbouring drug resistant strains (eg:- heath care workers, contacts of known drug resistant TB patients, HIV positives etc.), and on those who are going to be commenced on treatment as sputum negative PTB.

Why should treatment be supervised?
One of the biggest problems that the NPTCCD encounters is defaulting treatment which leads to relapses and drug resistant TB. Defaulter rate for the year 2002 in Sri Lanka is 14% which is even higher in some districts eg. Colombo and Gampaha. Supervised treatment which is one of the components of Directly Observed Treatment Short course (DOTS) strategy recommended by the WHO helps to minimise the problem of defaulting treatment. This means that a person who is responsible to the TB control programme and easily approachable by the patient supervises intake of anti TB drugs. Supervised treatment is recommended at least during the initial phase of treatment.

Fixed Dose Combinations (FDC) of essential oral anti-TB drugs in combinations of RHZE, RHE and RH are available in Chest Clinics. They improve compliance as the number of tablets to be taken daily is less and the chance of omitting some drugs from the combination is eliminated.

Formulations available:
One tablet of (RHZE) contains R 150mg, H 75mg, Z 400mg and E 275mg
One tablet of (RHE) contains R 150mg, H 75mg and E 275mg
One tablet of (RH) contains R 150mg and H 75mg,

Common adverse reactions to anti-TB drugs
Minor adverse reactions – treatment can be continued.

- Reddish discoloration of urine.
- Arthralgia.
- Mild itching without a rash.

Major adverse reactions – treatment should be stopped immediately and appropriate measures taken by a doctor trained in the management of TB.

- Deterioration of appetite, nausea, vomiting.
- Skin rash.
- Visual disturbances.

Patients should be advised not to eat red fish eg. balaya, kelawalla.

Conclusion
Treatment of tuberculosis is best done under the supervision of the NPTCCD. It is because chest clinics are prepared to deal with defaulter tracing, arranging community based supervised treatment, proper case recording to compile national data, arranging special leave/medical boards etc. Medical practitioners, to whom this document is intended, can play an active role in the control of tuberculosis by way of case finding and implementation of DOTS. MDR TB and HIV TB co infection should be referred to a specialist in the field.

Further reading
1). Treatment of tuberculosis. WHO/CDS/TB/2003.313 Geneva.
2). Chemotherapy and management of tuberculosis in the UK. *Thorax* 1998:**53**:536-548.
3). Administrative report of National Programme for Tuberculosis and Chest Diseases 2002.

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Chapter 19

URINARY TRACT INFECTIONS IN ADULTS

Urinary tract infection
A urinary tract infection occurs when there are 10^5 organisms / ml in culture. However, 10^3 organisms /ml on 3 consecutive days with symptoms may be considered for treatment

Recurrence of bacteriuria with the same organism within 7 days of completion of antibacterial treatment is a relapse. Implies a failure to eradicate infection.

Reinfection: bacteriuria is absent after treatment for at least 14 days, followed by recurrence of infection with usually different organisms.

Organisms include:

Esch. Coli, Klebsiella spp., Enterococci, Proteus mirabilis (indicates stagnant urine when a surgical reference is advised)
P. aeroginosa, Staphylococcus saprophyticus

Cystitis
Is usually uncomplicated in an adult non-pregnant female and is treated with:

Cotrimoxazole 960 mg b.d. for 3 days
Or cefalexin 600 mg b.d. for 5 days
Or co-amoxiclav 625 mg 12 hourly for 5 days

Or nitrofurantoin 50 mg 6 hourly for 5 days

Since amoxicillin resistance is high it should not be used unless susceptibility is known.

Fluroquinalones (e.g. ciprofloxacin, ofloxacin, norfloxacin) should not be used as frontline therapy. Single dose therapy is not recommended.

A 7 to10 day course of treatment is recommended in:

Diabetics
Recurrent urinary tract infection (UTI)
Symptoms lasting for 7 days
Age > 65 years
Recent use of contraceptive diaphragm

In pregnant females cotrimoxazole is best avoided and fluroquinalones are contraindicated.

Sterile pyuria

Symptomatic culture negative pyuria may be due to organisms including Chlamydia, Ureaplasma. Should be treated with azithromycin 1 g daily **Or** doxycycline 100 mg daily for 7 days.If there is no response a diagnosis of tuberculosis should be considered.

Acute pyelonephritis

A urine culture should always be done.Iif the patient is vomiting or is septicaemic treatment consists of:

Ampicillin 2 g iv 6 hourly for 14 days and gentamicin 4 to 6 mg/ kg daily

Or ciprofloxacin 400 mg iv b.d. for 14 days
Or ceftriaxone 1 g iv daily for 14 days
Or cefotaxime 1 g 8 hourly for 14 days

With response to therapy change to suitable oral treatment depending on the culture results.

Acute pyelonephritis without vomiting or sepsis should be treated as for cystitis with the same antibiotics but the duration should be 7 to 10 days.

Asymptomatic bacteriuria

Comprises the presence of 10^5 organisms/ ml in urine culture on 3 consecutive days.

Eradicative therapy is indicated according to antibiotic sensitivity results in: pregnancy
preschool child
men under 60 years of age
In pregnancy repeated cultures are necessary

Recurrent cystitis
Invariably occurs in women.
Treatment:
If related to coitus give single dose post-coital prophylaxis with:
Co-trimoxazole 960 mg **Or** nitrofurantoin 100 mg **Or** cefalexin 500 mg
Culture done after 5 days should be sterile.
If > 3 infections per year give:
Low dose continuous prophylaxis as above
The other option is to advise the patient on self administered short course of antiobiotics
For 3 days on development of symptoms
If there is a relapse always look for an underlying abnormality and treat as an uncomplicated UTI.

Once urine culture is negative, give continuous prophylaxis with co-trimoxazole 960 mg daily **Or** nitrofurantoin 50 mg daily for 6 – 8 months

Acute prostatitis
It is best managed by an urologist. Ciprofloxacin 500 mg orally b.d. for 1 month **Or** co-trimoxazole 960 mg orally b.d. for 1 month is recommended.

Chronic prostatitis
Give 3 months of treatment as for acute prostatitis together with prostatic massage.

Further reading
1. M.Yaqoob. Renal Disease. In: Kumar and Clark eds. Clinical Medicine, 6th edition. 2005; 637 – 643. W B Saunders

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Chapter 20

URINARY TRACT INFECTIONS IN CHILDREN

Urinary tract infection (UTI) is one of the common infections in childhood and it is defined as invasion of the urinary tract with multiplying bacteria. There is a risk of permanent scarring following urinary tract infection in children which may lead to end stage renal failure later in life. It is extremely important to make an early diagnosis, especially in children under 5 years of age and manage appropriately.

Often UTI in children is over-diagnosed and this results in the prolonged use of antibiotics, parental suffering, and exposure of the child to unnecessary and potentially harmful investigations.
Clinical assessment should be done to determine

- lower urinary tract infection from upper urinary tract infection
- evidence of urinary tract abnormalities (congenital or acquired)
- the presence of risk factors
- evidence of renal impairment

Symptoms of UTI are specific or non-specific
Non-specific (especially during infancy): fever, irritability, unexplained late onset jaundice, failure to thrive, vomiting. Specific: dysuria (crying during micturition), incontinence, haematuria, increased frequency, lower abdominal/ suprapubic/loin pain

Signs
Fever, palpable bladder/kidneys, suprapubic/loin tenderness,
Phimosis/labial adhesions should be looked for because they may be a cause of the symptoms or they may give rise to positive cultures even without UTI.

Symptoms and signs suggestive of lower UTI include dysuria, increased frequency, urgency, turbid urine, and suprapubic pain and tenderness

Investigations

Acute stage

Urine: full report – albumin, pus cells, red cells (in an uncentrifuged specimen number must be interpreted carefully) cultures – colony count, pure growth of 10^5

- with symptoms even a pure growth of 10^3 or 10^4 is significant
- repeat the culture when the results are inconclusive

Collection of urine for examination – midstream clean catch, sterile urine bags, supra pubic punctures, and rarely catheter specimens, and strict aseptic technique must be observed.

Blood: FBC, blood cultures, CRP, electrolytes, blood urea

Ultra sound scan of abdomen during the acute stage when there is evidence of obstructive uropathy.

Management

Symptomatic: Fever – antipyretics
Correction or prevention of dehydration
Maintenance of nutrition

Specific: In young children with UTI commonest pathogen isolated is *Esch.coli*. *Klebsiella* and *Proteus* are the other pathogens identified.

Antibiotics

Choice, route of administration, dose, and duration of treatment depends on: age of the patient, presence of fever, other factors such as congenital abnormalities and obstruction

In paediatric upper urinary tract infections

- use systemically effective antibiotics
- do not use urinary antiseptics

For febrile patients with urinary tract infections treatment should be started with intravenous antibiotics

Neonates and children up to 2 years

Intravenous antibiotics should be 3rd generation cephalosporins

Ceftriaxone: 50-100 mg/kg/day either single or divided doses 12 hourly, Cefotaxime: 150mg/kg/day (50- 200mg/kg/day) in divided doses 6-8 hourly, Co-amoxiclav: neonates 30mg/kg/day in divided

doses 12 hourly, older children 50 - 75 mg/kg/day in divided doses 8 hourly, Gentamicin: 5-7.5 mg/kg/day neonates in divided doses12 hourly, older children in divided doses 8 hourly for 24 - 48 hours (in neonates 72 hours) after fever has subsided change over to an oral antibiotic depending on the culture report. Duration of treatment is 10-14 days.
(Cefotaxime is preferred for children with hyperbilirubinaemia as unlike ceftriaxone it is not excreted in bile or displaces bilirubin from albumin).
Gentamicin should be used with care in children with renal insufficiency.
Intravenous antibiotics are also recommended for older children who are very ill, or have renal scars or congenital abnormalities.

For older children and children with a febrile upper UTI oral antibiotics can be used.
Oral cephalosporins: cephalexin: 25-50 mg/kg/day in divided doses 8 hourly
Co-trimoxazole : 40 mg/kg/day in divided doses 12 hourly
Co-amoxiclav: 20-40 mg/kg/day in divided doses 8 hourly
Cefuroxime: 10-25 mg/kg/day in divided doses12 hourly
Start immediately after collecting the urine for culture and change antibiotic if necessary depending on the ABST report and response to treatment
Duration - 7 – 10 days followed by antibiotic prophylaxis
(Co-trimoxazole is contraindicated when there is G6PD deficiency)

Lower urinary tract infection - (acute uncomplicated cystitis)
Older children, with classical symptoms of dysuria, suprapubic pain and tenderness, increased frequency, cloudy urine or haematuria.
Co-trimoxazole : 40 mg/kg/day in divided doses 12 hourly
Cephalexin: 25-50 mg/kg/day in divided doses 8 hourly
Nitrofurantoin : 5-7mg/kg/day in divided doses 6 hourly
Nalidixic acid : 50mg/kg/day in divided doses 6 hourly
Antibiotics are to be changed depending on the result of the antibiotic sensitivity test
Duration of treatment is 5 - 7 days

Subsequent management

Antibiotic prophylaxis

Choice of the antibiotic, dosage, and duration of treatment depends on age of the child and presence of urinary tract abnormalities

Neonatal period

Cephalosporin – 12mg/kg once daily

Infancy

Co-trimoxazole - 10 mg/kg once daily (except during neonatal period)

Nitrofurantoin: 1 mg/kg once daily

Older children

Nalidixic acid – 12.5mg/kg/day once daily at night,

Nitrofurantoin - 1mg/kg/day once at night,

Co trimoxazole

(Nalidixic acid is known to cause benign intracranial hypertension in infancy)

Duration of prophylaxis

- 6 months initially, till investigations are completed
- up to 5 years of age or longer if there are abnormalities such as vesico- ureteric reflux, renal scars, and obstructive lesions.

Further investigations must be carried out in children less than 5 years of age with febrile, culture positive urinary tract infections to exclude congenital abnormalities like vesico-ureteric reflux, obstructive lesions and renal scars.

The investigations include ultra sound scan of the urinary tract, MCUG, DMSA and DTPA scans.

Children over 5 years of age without structural abnormalities in the urinary tract and older children with lower UTI need not be given prophylactic antibiotics.

Further reading

1. Jacobsson B, Berg U, Svenson L. Renal scarring after acute pyelonephritis. *Arch Disease Child* 1994; **70**:111-15

2. Management of Urinary tract infections in children – Practice Guideline, Child Health Network for the Greater Toronto Area, June 2002
3. Clinical Practice Guidelines, Use of antibiotics in paediatric care, Singapore. Ministry of Health Clinical Practice Guidelines, March 2002
4. McIntosh N, Helms PJ, Smyth RL, eds. Forfar & Arneil's Textbook of Paediatrics. 6th ed. 2003. Churchill Livingstone

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Chapter 21

WOUND INFECTIONS

Scope:
1. Surgical site wound infections
2. Infection in chronic ulcers
3. Septic foot in diabetics

Surgical site infections

Source:
1. Patient's own bacterial flora, from operating theater environment or from skin lesions of hospital staff
2. Spillage during surgery
3. Contributory causes such as haematoma, foreign bodies (non absorbable sutures, retained swabs), immune compromised patients including diabetics, and entero- cutaneous fistula

Micro-organisms, antibiotic preference, dose
1. *S. aureus*- cloxacillin 500 mg 6 hourly iv or orally
2. *Coliform sp*. – cefuroxime 750 mg iv 8 hourly or co-amoxiclav 1.2 g iv 12 hourly or 625 mg b.d. orally
3. *Streptococcus sp* – Benzylpenicillin 0.6-1.2 gm iv 6 hourly
4. *P. aeruginosa*. – ciprofloxacin 200 mg iv b.d. or 500 mg orally b.d. or gentamicin 80 mg iv b.d.

5. Anaerobes – metronidazole 500mg iv 8 hourly or 400mg t.d.s. orally.

Recommended drugs for infected wounds following:
Clean surgery (hernia, thyroid, breast): cloxacillin
Clean contaminable surgery (open cholecystectomy): co-amoxiclav
Clean contaminated surgery (colorectal): cefuroxime and metronidazole

Additional measures
Swabs or pus sent for culture and antibiotic sensitivity
Blood culture if febrile
Grade 1 – Erythema, pain, afebrile – observe, no antibiotics
Grade II – Erythema, pain, fever – antibiotics and remove some sutures
Grade III – As in Grade II plus discharge of pus from one site – antibiotics, remove sutures from site, express pus
Grade IV – Fever and pus exuding from entire wound – antibiotics, remove all sutures clean and dress with antiseptic (povidone iodine) and look for a contributory cause.

Infections in chronic ulcers
Source:
Almost all chronic ulcers contain a mixed flora of bacteria (at least 3 species) and wound healing can still occur in their presence. It is not the presence of bacteria but their interaction with the host that determines the organisms' influence on wound healing.
Contamination: non-replicating organisms cleared by host responses-no antibiotics indicated
Colonization: replicating organisms adherent to wound eg *Staph epidermidis*, *Corynebacterium sp* may enhance wound healing – no antibiotics.
Critical colonization or local infection: increasing bacterial burden characterized by poor wound healing/increase in size, excess exudates – local antiseptics and antibiotics beneficial

Wound infection: replicating organisms with host response characterized by pain, delayed wound healing increased exudates, friable granulation, absent granulation, odour, accompanied by systemic signs:

swelling, redness, warmth, pain, tender lymphadenopathy and fever. Antibiotics are essential.

Rationale for antibiotics

Antibiotics are not routinely recommended in treatment of chronic ulcers and they may even be harmful. Bacteria should be identified as reason for the impaired wound healing. Bacterial burden reduction could be achieved by use of local antiseptics alone, or antibiotics locally or systemically. Bacterial resistance develops more rapidly and more often with topical antibiotics than with antiseptics. Common antiseptics recommended are povidone iodine, 0.25% or 0.5% acetic acid, silver sulphadiazine. Local antibiotics recommended are neomycin, bacitracin, metronidazole, Evidence for efficacy of this treatment is not strong.

Systemic antibiotics

First line drugs of choice are*:* benzylpenicillin 600 mg units iv 6 hourly or if patient is allergic, erythromycin 500mg 6 hourly/ clarithromycin 250mg bd. This is for spreading streptococcal infection characterized by swelling redness, erysipelas, cellulitis, lymphangitis.

Ciprofloxacin 200mg iv b.d. or 500mg b.d. orally for *Pseudomonas aeruginosa i*nfection (evidenced by greenish discharge).

Additional measures

- Surgical debridement/ drainage of pus especially in diabetics
- Once wound is clean, less frequent dressings e.g. once in 3 to 5 days is recommended.
- 4 layer compression bandage (venous ulcers).
- Oclusive dressings with hydrocolloid, hydrogels, alginates, foams and films.
- Newer methods include: topical recombinant human platelet derived wound healing factor, human skin equivalent, pneumatic compression pumps, vacuum suction therapy.

Septic wounds of diabetics

Source:

Inadequately treated plantar ulcer/ infected callosity
Web space fungal infection
Superficial skin abrasion

Secondary infection of gangrenous tissue usually toes.
Complicating factors include vascular insufficiency (macro or micro angiopathy), peripheral neuropathy, poor glycaemic control.

Microorganisms, recommended antibiotics and dose
Gram +ve aerobes:
Staphylococcus aureus/epidermidis – cloxacillin 500 mg iv 6 hourly
Streptococcus pyogenes – benzyl penicillin 0.6 to 1.2 gm iv 6 hourly

Gram –ve aerobes:
Enterococci – co-amoxiclav 1.2 g iv b.d. or 625mg orally bd.
Pseudomonas sp – gentamicin 80 mg iv b.d. if renal function is not affected
Esch. coli and *Klebsiella sp*: cefuroxime 750mg iv 8 hourly or ciprofloxacin 200mg iv b.d. or 500mg orally b.d.
In severe infections, 3rd generation antibiotics such as, meropenem 500 mg to 1g 8 hourly or teicoplanin 200 mg iv once or twice daily depending on renal function may be considered in limb/ life threatening situations.

Anaerobes:
Gram +ve: (*Clostridia) and Gram –ve – (Bacteroide sp.)* Sensitive to metronidazole 500mg iv 8 hourly or benzyl penicillin 0.6g or 1.2 g 8 hourly

Note. Organisms deep in tissues may be significantly different to isolates from the surface of the wound.

First line drugs:
Co-amoxiclav 1.2 gm iv b.d. or 625mg orally b.d.
Cefuroxime 750 mg iv 8 hourly
Benzylpenicillin 1.2 gm iv 6 hourly in suspected streptococcal infections.

Additional measures:
A septic wound in a diabetic is a surgical emergency.

Antibiotics alone could be disastrous – even contribute to death by giving a false sense of security. *Measures to be taken include:*
Rapid glycaemic control
Adequate hydration

Early surgical debridement *is an essential step in the management*

SUMMARY OF RECOMMENDED ANTIBIOTICS IN WOUND INFECTIONS

Condition	**Organism**	**Suggested Antibiotics**	**Reserve Antibiotics**	**Comments**
Following Clean surgery	*Staph aureus*	Cloxacillin add Gentamicin if septicaemic	Vancomycin for MRSA	Around 50% due to S. aureus. High dose Cloxacillin best
	Strep. pyogenes other beta haemolytic Strep.	High doses of Penicillin. Erythro/ Clarithro if allergic		Could be life threatening. May need clindamycin
	Other organisms			Choice depends on culture/ABST
Following contaminated surgery	Gram negatives Enterococci Anaerobes S. aureus	Gentamicin Ampicilin Metronidazole Cloxacillin	Newer Cephalosporins Newer Aminoglycosides Vancomycin for MRSA	Surgical drainage and antiseptics may suffice if not septicaemic

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Further reading:

1. Townsend CM Jr, Beauchamp RD, Evers BM, Mattox KL eds. Sabiston Textbook of Surgery 16th edition 2003; W.B.Saunders Co. Philadelphia.
2. Cushieri A, Giles GR, Moosa AR, eds.Essential Surgical Practice 2nd Edition 1998;.John Wright, London
3. Rutherford RB ed. Vascular Surgery. 5th Edition 2000; W.B.Saunders Co.Philadelphia.
4. Postgraduate Medicine online, Successful methods of treating leg ulcers.http://www.postgradmed.com/issues/1999/05 01 99/ Phillips.htm

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CHAPTER 22

POINTS TO REMEMBER WHEN ADMINISTERING INTRAVENOUS ANTIBIOTICS

1. Intravenous antibiotics should be used only if the patient is ill enough to need them.
2. It is best to admit the patient to hospital, if intravenous antibiotics are required. With improved pharmacokinetics and pharmacodynamics there are antibiotics, which have long plasma half-lives, which could be administered once a day. The patient could visit the hospital or healthcare unit daily to receive such antibiotics. In developed countries, intravenous antibiotic administering teams go to homes to administer them, if the patient is unable to visit the hospital daily.
3. Venous access could be via peripheral veins or central veins, the former being the preferred access. Long term peripheral access could be obtained by subclavian vein tunnels, so that the patient has free mobility of his hands. Most beta-lactam antibiotics cause thrombophlebitis and periodical re-siting of the intravenous cannulae in desirable.
4. A reason to use more than one antibiotic is to achieve synergy. When combinations such as beta-lactams and aminoglycosides are used synergy is achieved in vivo. It is important to know that these antibiotics inactivate each other in vitro and should not be mixed during administration. To overcome this vital drug interaction and also to achieve synergy, it is best that these antibiotics are administered at different times.
5. Peripheral intravenous cannulae must be re-sited every 3-4 days to avoid canula-associated infections.
6. With response to intravenous antibiotics, 'step down' to oral route is recommended if antibiotics need to be continued.
7. All intravenous antibiotics are best administered as an infusion over 20-30 minutes.
   However, they may be given as a slow iv bolus over 10-15 minutes.

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CHAPTER 23

A PHARMACOKINETIC AND PHARMACODYNAMIC APPROACH TO ANTIBIOTIC THERAPY

Introduction

Pharmacokinetic (PK) and pharmacodynamic (PD) aspects influence antimicrobial efficacy. Predictions of antimicrobial efficacy have focused on PK factors and particularly the serum concentration profile of a drug over time as well as its penetration into the site of infection. Presently PD properties which describe the relationship between serum concentrations and drug action and toxicity have assumed greater importance. The integration of PK and PD parameters are used to design effective dose regimens which counteract or prevent development of antimicrobial resistance.

Pharmacokinetic and pharmacodynamic predictors of efficacy

The primary measure of antibiotic activity is the minimum inhibitory concentration (MIC). The MIC is the lowest concentration of an antibiotic that completely inhibits the growth of a microorganism in vitro. Although the MIC is a good indicator of the potency of an antibiotic, it does not indicate the duration of antimicrobial activity. PK parameters quantify the serum level / time course of an antibiotic. The three pharmacokinetic parameters that are important for evaluating antibiotic efficacy are the peak serum level (Cmax), the trough level (Cmin), and the area under the serum concentration time curve (AUC). These parameters quantify the serum level time course, but they do not describe the killing activity of an antibiotic.

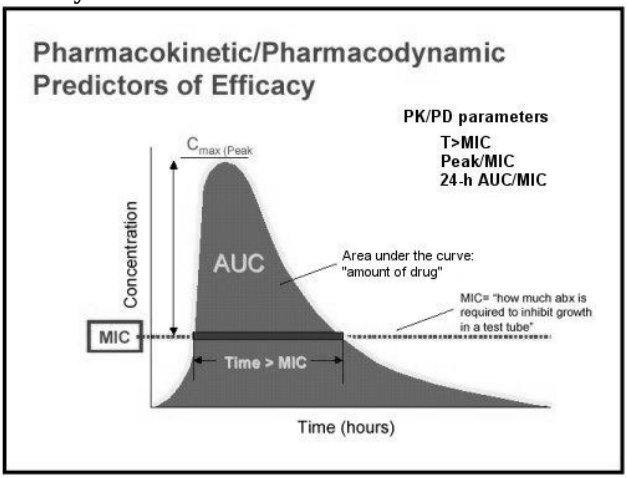
PK/PD parameters

Integrating the PK parameters with the MIC gives us three PK/PD parameters which quantify the activity of an antibiotic: the Peak/MIC ratio, the Time>MIC (time above MIC), and the 24hour-AUC/MIC ratio. The Peak/MIC ratio is the Cmax divided by the MIC.

The T>MIC is the percentage of a dosage interval in which the serum level exceeds the MIC.

The 24hour-AUC/MIC ratio is determined by dividing the 24-hour-AUC by the MIC.

Figure 1. PK/PD parameters used in determining antibiotic efficacy



Antimicrobial patterns

The specific PK/PD parameter correlating with efficacy is mostly dependent on whether bacterial killing of an antibiotic is concentration or time dependent. For time dependent agents, such as betalactams and macrolides it is important that the dosing regimen maximizes the duration of time above the MIC (T>MIC) of the agent against the target pathogen. Persistent effects include the post-antibiotic effect (PAE). PAE is the persistant suppression of bacterial growth following antibiotic exposure.

Using these parameters, antibiotics can be divided into 3 categories:

Table 1. PK/PD parameters predictive of antimicrobial efficacy

Pattern of Activity	**Antibiotics**	**Goal of Therapy**	**PK/PD Target**
Type I Concentration-dependent killing and prolonged persistent effects	Aminoglycosides Fluoroquinolones Azithromycin Ketolides	Maximize concentration	24h-AUC/MIC >25 -30 or Peak/MIC >3 (immunocompetent) or 24h-AUC/MIC > 100 or Peak/MIC >12 (immunocompromised)

Type II Time-dependent killing and Minimal /Moderate persistent effects	Penicillins Cephalosporins Carbapenems Erythromycin Clindamycin Cotrimoxazole Linezolid	Maximize duration of exposure	T>MIC should be >40% - 50% of the dosing interval
Type III Time-dependent killing and prolonged persistent effects.	Azithromycin Tetracyclines Vancomycin Teicoplanin	Maximize amount of drug	24h-AUC/MIC > 25 – 30 (immunocompetent) or 24h-AUC/MIC > 100 (immunocompromised)

For **Type I** antibiotics, the ideal dosing regimen would maximize **concentration**, because the higher the concentration, the more extensive and faster are the cidal effects. Therefore, the 24hour-AUC/MIC ratio, and the Peak/MIC ratio are significant predictors of antibiotic efficacy. For aminoglycosides, it is best to have a Peak/MIC ratio of at least 10 - 12 to prevent development of resistance and once daily dosing is adequate except in burns patients and in infective endocarditis. For fluoroquinolones against Gram negative bacteria, the optimal 24h-AUC/MIC ratio is > 125 and against Gram positive bacteria, such as *S. pneumoniae* 40 is optimal. Therefore once or twice daily dosing with fluoroquinolones is adequate.

Type II antibiotics demonstrate the complete opposite properties. The ideal dosing regimen for these antibiotics should maximize the **duration** of exposure. The T>MIC is the parameter that correlates best with efficacy. For betalactams and erythromycin, maximum cidal effect is seen when the time above MIC is at least 50% of the dosing interval. Frequent doses are required to maintain the appropriate serumlevel.

Type III antibiotics have mixed properties. They have time-dependent killing and prolonged persistent effects. Therefore, the 24h-AUC/MIC ratio is the parameter that correlates with efficacy. For vancomycin a 24h-AUC/MIC ratio of >125 should be achieved.

Further reading

1. Jacobs MR. How can we predict bacterial eradication. *International Journal of Infectious Diseases.* 2003; **7:** S13 – 20.
2. Li RC, Zhu ZY. The integration of four major determinants of antibiotic action: bactericidal activity, postantibiotic effect, susceptibility, and pharmacokinetics. *Journal of Chemotherapy*. 2002; **14(6)**:579-83
3. Frimodt-Moller N. How predictive is PK/PD for antibacterial agents? *International Journal of Antimicrobial Agents*. 2002; **19(4)**:333-9.
4. Van Bambeke F, Tulkens PM. Macrolides: pharmacokinetics and pharmacodynamics. *International Journal of Antimicrobial Agents*. 2001;**18 (Suppl 1):**S17-23.
5. Nicolau D P. Optimizing outcomes with antimicrobial therapy through pharmacodynamic profiling. *Journal of Infection and Chemotherapy*. 2003; c **9(4):** 292 -6.

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