Chapter 9:

INFECTIOUS DISEASES

Student Authors: Efosa Ohonba, Zamandwandwe Ndima and Amy Stickells

Specialist Advisor: Dr Julie Copelyn

This chapter covers the following topics:

- Tuberculosis
- HIV
- Measles
- Mumps
- Chicken pox
- Pertussis (whooping cough)
- Rubella (German measles)
- Influenza
- Poliomyelitis
- Meningitis
- Malaria
- Diphtheria
- Rabies
- Typhoid
- Cholera
- Bilharzia
- Antibiotic Stewardship

TUBERCULOSIS (TB)

Pulmonary TB

Pathophysiology

Mycobacterium tuberculosis is the organism that causes TB. Infection occurs through exposure of the lungs or mucous membranes to infected aerosols i.e. droplet spread/airborne transmission. The inhaled droplets are deposited in the alveoli, where they form Ghon foci that drain to regional lymph nodes. The organisms grow for 2-12 weeks until the colony is of a size significant enough to elicit a cellular immune response. It is at this stage that the patient will have a positive tuberculin skin test reaction.

The infection can be cleared by the host's immune system, suppressed (latent TB) or develop into active TB infection. Only patients with active TB can spread the disease. Latent TB can develop into active TB should the host's immunity be suppressed, therefore becoming less effective at containing the infection.

The risk of developing TB disease is highest in the first year following exposure. Young children (<5 years old), especially those under 1 year of age, are at a particularly high risk for developing severe forms of disease e.g. miliary TB, TB meningitis.

Clinical Features

Younger patients with primary TB often present with non-specific symptoms and signs:

- FTT
- Cough
- Weight loss
- Fever
- Lymphadenopathy
- Disinterest in play

Adolescents with primary or reactivated TB may present with:

- Cough
- Chest pain
- Weakness and fatigue
- Loss of appetite

- Night sweats
- Fever

Investigations

If TB is suspected, one should perform the following investigations:

- Tuberculin skin test (see related image here)
- Sputum microscopy and culture (with staining for acid-fast bacilli and TB culture)
- TB GeneXpert (a polymerase chain reaction/PCR test which may be done on induced sputum or gastric aspirate)
- HIV test

See related image here.

Other Clinical Manifestations of TB

Pleural Effusion

It is more common in those older than 5 years. Smear microscopy and culture is usually negative.

Disseminated (Miliary) TB

In these patients, the immune response was unable to control the infection leading to occult, haematogenous dissemination of TB bacilli to other sites. Patients are usually wasted with generalised lymphadenopathy and hepatosplenomegaly. They may also present with fever, poor feeding and lethargy. There may be cutaneous manifestations (inflammatory papules, verrucous plaques, suppurative nodules, ulcers and other lesions) which can be biopsied for further investigations.

Respiratory symptoms may be limited (e.g. only tachypnoeic). The patient may have the typical “snowstorm”, reticulonodular pattern throughout both lung fields. The radiograph may also be normal. In these cases, the diagnosis can be confirmed with liver or bone marrow biopsy.

TB meningitis (TBM)

TBM is often associated with disseminated TB and occurs because the TB bacilli usually embed themselves in the meninges during the primary infection. Other less common routes of infection include transmission from disease affecting the middle ear, mastoid or spine. The bacilli create tuberculous granulomata in the brain (Rich foci) which undergo caseation and discharge into the CSF. This elicits an inflammatory response which causes a thick exudate to cover the base of the brain. This may result in obstructive hydrocephalus.

Clinical Features and Diagnosis

Patients with TBM usually present with non-specific signs, such as irritability, lethargy, headache and vomiting. In South Africa, TBM is divided into three stages based on the clinical features with which the patient presents:

- Stage 1 – non-specific signs, conscious, no focal neurological signs, no hydrocephalus
- Stage 2 – signs of meningeal irritation, confusion, and/or focal neurological signs
- Stage 3 – stupor, delirium, coma and/or neurological signs e.g. hemiplegia

Early diagnosis and treatment at Stage I carries the best prognosis. Diagnosis may be made based on suggestive:

- History and examination
- Neuroimaging e.g. infarctions, hydrocephalus, tuberculoma, basal enhancement
- Cerebrospinal fluid (CSF) findings i.e. low glucose, lymphocyte predominance, high protein (but CSF findings can be variable)
- CXR (may show features of primary TB)

A positive TST supports the diagnosis but a negative TST does not rule out infection, even in severe disseminated disease. If in doubt, one should start anti-TB therapy until TB has been excluded.

Superficial Lymphadenitis

TB lymphadenitis is usually cervical but is occasionally inguinal or axillary.

Abdominal TB

It may develop because the patient swallowed sputum containing TB bacilli or because there was haematogenous spread. Abdominal TB may manifest as intestinal TB, abdominal lymphadenopathy, peritoneal disease or solid organ TB e.g. liver, spleen.

TB Pericarditis

The pericardium may become involved due to spread from adjacent lymph nodes or haematogenous dissemination. Pericarditis and pericardial effusion develop because of fibrous organisation or calcification of the pericardium. The patient with TB pericarditis may have a pericardial friction rub, increased cardiac dullness, impalpable apex and muffled heart sounds. If there is tamponade or constriction, the patient will have a raised JVP, hepatomegaly and oedema.

TB of the Upper Respiratory Tract

The mouth and tonsils may be infected via a contaminated pacifier or contaminated milk. Infection may spread to the middle ear (through the Eustachian tube), adenoids and larynx.

Ocular TB

TB can affect the conjunctiva, cornea, lacrimal gland, iris, uvea and retina. However, involvement of the eye is rare.

TB of the Ears and TB Mastoiditis

The most common ear manifestation is otorrhea but TB can also cause conductive hearing loss (due to perforation of the tympanum) or facial nerve palsy (due to local lymph node enlargement. From the ear, the infection can spread to CNS.

Cutaneous TB

The skin may be involved through:

- Direct contact with the skin and subsequent infection (can cause a warty lesion)

- Haematogenous spread (can produce multiple nodular lesions, a large plaque, ulcers, multiple abscesses or chronic, indurated, destructive lesions)
- Hypersensitivity reactions to TB resulting in cutaneous lesions (tuberculids) e.g. papules (ears, elbows) and erythema nodosum

Osteoarticular TB

It may involve the spine (most commonly), hips, knees, other joints and other bones. X-rays will show decreased bone density, cysts and periostitis.

Urogenital TB

It can affect any organ along the urinary tract or reproductive tracts. However, urogenital TB is rare in children.

Management

When one suspects that a child has TB, one must ask oneself:

- Why does the child have TB?
    - Is s/he malnourished?
    - Is s/he immunocompromised?
    - Is s/he a close contact of someone with TB?
- What implications does this diagnosis have for those around the child?
    - Does the child attend a creche?
    - Are there other children (and adults) at home who are at risk for developing TB?

General and Supportive Measures

They include:

- Regularly monitoring the child's neurological status (to detect hydrocephalus early)
- Ensuring adequate nutrition (nasogastric feeding may be required)
- Rehabilitation (most patients will need physiotherapy and/or occupational therapy)

- Counselling and educating the child's family and caregivers

Specific Treatment

Drug-Sensitive TB (DS-TB)

DS-TB is treated with isoniazid (INH or H), rifampicin (RIF), pyrazinamide (PZA or Z) and ethambutol (EMB or E) (see also diagram available here). Isoniazid competes with vitamin B6 (pyridoxine) and can result in peripheral neuropathy, ataxia and paresthesia. For this reason, Isoniazid should always be prescribed with a pyridoxine supplement.

For the child <8 years or <30 kg with:

- Uncomplicated TB (i.e. HIV negative) – treat for 6 months
    - Intensive phase (first 2 months) – PZA, INH and RIF
    - Continuation phase (subsequent 4 months) – RIF and INH
- Complicated (HIV positive) – treat for 6 months
    - Intensive phase (first 2 months) – RIF, INH, PZA and E
    - Continuation phase – RIF and INH
- TBM/miliary TB – treat with RIF, INH, PZA and E for 6-9 months (duration depending on response to treatment)

For the child >8 years and >30kg

- Treat all TB that is not MDR-TB for 6 months
- Give RIF, INH, PZA, and E for 2 months and then RIF and INH for 4 months

Drug-Resistant TB (DR-TB)

The treatment of DR-TB in children should always be done in consultation with a clinician experienced in managing DR-TB in children.

HIV & TB Co-Infection

If the HIV and TB are diagnosed at the same time, one must treat as follows (to prevent immune reconstitution inflammatory syndrome):

- If non-neurological TB, start ART as soon as the patient is tolerating TB treatment, i.e. within the first 2 weeks of starting anti-TB treatment
- If TBM, defer ART initiation for 4 to 8 weeks

Table 9.1: Note on Steroid Use in TB Patients

Co-Administration of Steroids
Steroids are used in TB meningitis or if there are large intrathoracic lymph nodes causing airway compression. In these cases, one will give oral prednisone (2mg/kg daily) for 4 weeks, then taper to stop.

HUMAN IMMUNODEFICIENCY VIRUS (HIV) INFECTION

HIV is an enveloped RNA retrovirus which can be transmitted from mother to child in-utero, during labour or postnatally (through breastfeeding). It can also be transmitted through sexual contact or contact with contaminated blood e.g. needlestick injuries, infected blood splashing on an open wound. Fortunately, childhood HIV infection has been significantly reduced with the success of the Prevention of Mother to Child Transmission (PMTCT) programme. See related image here.

Pathogenesis

The virus (see structure here) primarily infects CD4 T lymphocytes, replicates within these T lymphocytes and subsequently kills these cells. This loss of T lymphocytes leads to impaired immunity.

Clinical Features

Children infected in early childhood may present with persistent generalised lymphadenopathy, recurrent infections, FTT or opportunistic infections e.g. TB. Many children of HIV-infected mothers receive prophylaxis or are diagnosed in the early asymptomatic stages due to the PMTCT program.

Diagnosis

In children under 18 months, a PCR test is done because maternal antibodies persist for up to 18 months i.e. antibody tests can give false positive results. From 18 months until 2 years of age, a rapid HIV antibody screening test can be done (see HIV rapid test kit available here). If this antibody test is positive it needs to be confirmed with a PCR.

From the age of 2 years, two positive rapid HIV antibody tests are needed in order to confirm the diagnosis of HIV.

Management

Early initiation of ART is important. The family (and the child, if appropriate) must be counselled as treatment, once commenced, must be continued lifelong. Baseline investigations should be done before initiating treatment e.g. full blood count (FBC), alanine transaminase (ALT), CD4 count. Thereafter, regular follow up is needed to assess adherence and treatment response.

General Measures

HIV-positive children on ART are encouraged to continue breastfeeding (even if mixed feeding) until 2 years of age. The healthcare worker must support ongoing treatment adherence in the child and mother.

Specific Treatment

The specific drugs and dosages used to treat the child with HIV are determined based on the child's age and weight. One should always refer to the most updated dosing chart provided by the Department of Health. At the time of publication, first line treatment for children:

- >4 weeks old and <20kg – abacavir (ABC) + lamivudine (3TC) + lopinavir/ritonavir (LPV/r)
- 20-35kg or <10 years old – ABC + 3TC + dolutegravir (DTG)
- ≥ 35kg and ≥10 years old – tenofovir (TDF) + 3TC + DTG

MEASLES

Measles is caused by the measles/rubeola virus, which is an RNA paramyxovirus. Measles is an acute and highly contagious disease. Its incidence has been greatly reduced by immunisation programs.

Transmission and Pathogenesis

Measles spread is through the inhalation of infected respiratory droplets. The virus replicates within respiratory epithelial cells before migrating to lymphatic tissue via the bloodstream, from where it spreads to other organs (see related image here).

Clinical Presentation

Once exposed, there is an incubation period of 10-11 days after which a prodrome of fever, cough, coryza and conjunctivitis occurs. Koplik spots (small red spots with white centres which appear on the buccal and labial mucous membranes) are pathognomonic for measles infection and appear on day 2 of the prodrome. A maculopapular rash, which affects the face, trunk and limbs, also appears.

Symptoms usually resolve after a few days provided that no complications arise.

Complications

Croup, diarrhoea and/or pneumonia may occur as a result of measles or may predispose the child to a secondary bacterial or viral infection. Otitis media and corneal ulceration may also occur. Rarely, encephalitis (acute and subacute sclerosing panencephalitis), nephritis, myocarditis and pericarditis can occur.

Management

The infection is usually self-limiting and supportive care is all that is required. This includes maintaining nutrition and hydration, early diagnosis and treatment of complications. Administration of vitamin A (100 000-200 000 IU) has been shown to reduce the risk of complications. Lifelong immunity develops following infection.

MUMPS

Mumps is caused by the mumps virus which is an RNA paramyxovirus. It is highly contagious but is less common due to the effect of the combined measles, mumps and rubella (MMR) vaccine (see related image here). Unfortunately, this vaccine is only available in the private sector in South Africa.

Transmission and Pathogenesis

Humans are the sole host of the mumps virus. The virus spreads via airborne droplets and direct contact with infected saliva. It has an affinity for the parotid glands and causes parotitis. Infected individuals are contagious for 3 days before and up to 9 days after disease onset (onset of parotitis).

Clinical Features

Once exposed, there is an incubation period of 14-21 days. Parotitis will then develop and may be unilateral or bilateral. The parotitis is characterized by tender swelling of the parotid, which may impair mouth opening and displace the ear lobe. This is accompanied by headache, malaise, low-grade fever and anorexia. Submandibular and sublingual lymphadenopathy may also occur.

Symptoms usually resolve after a week and the disease is self-limiting. There may be further dissemination of the virus to the lacrimal and mammary glands, pancreas, testes, ovaries and CNS.

Complications

Complications of mumps include:

- Epididymo-orchitis (can cause infertility)
- Oophoritis
- Meningoencephalitis
- Pancreatitis
- Thyroiditis
- Mastitis

Investigations

Viral serology can be done but the diagnosis of mumps is usually clinical. Positive serum IgM confirms the diagnosis. Alternatively, the pathogen can be detected through real-time reverse transcriptase PCR (rRT-PCR) or viral culture from infected body fluids.

Management

Treatment is supportive because mumps is usually self-limiting and has a good prognosis. The patient is, therefore, treated with:

- Paracetamol (for pain and fever)
- Bedrest
- Fluids
- Ice packs (to soothe parotitis)

Mumps can be prevented with the MMR vaccine (which is not part of the EPI). Lifelong immunity develops following mumps.

CHICKEN POX

Chicken pox is caused by primary infection with the varicella-zoster virus (VZV)/human herpesvirus type 3 (HHV-3). Infection usually occurs in childhood.

Transmission and Pathogenesis

VZV is highly contagious and the virus spreads through droplets or direct contact with vesicular fluid. It can also spread across the placenta. After infection of the mucosa and regional lymph nodes, there is viraemia with viral replication within the epidermis. This causes the characteristic vesicular rash.

Chicken pox only occurs once as the VZV antibodies persist for life (see related image available here). However, the virus can lie dormant in ganglion cells for many years and become reactivated if the immune system is compromised. This results in shingles (herpes zoster) which follows the affected dermatome.

Clinical Features

Following an incubation period of 13-17 days, a mild prodrome of fever, headache and malaise occurs. After 1-2 days, a crop of red papules appear and then turn into clear vesicles. The rash starts on the trunk and spreads over the face, scalp, conjunctivae and mucous membranes. The vesicles progress from clear to cloudy, develop a central

depression and eventually dry to scabs. Once scabs have formed, the patient is no longer contagious. The rash is severely pruritic (see *Dermatological Conditions* chapter for more information).

Investigations

The diagnosis is usually made clinically, based on the presence of the characteristic rash. However, a Tzanck smear, PCR, viral culture or viral serology can be performed if the diagnosis is unclear. These investigations may be performed in older, immunosuppressed or pregnant patients and are not commonly performed in children.

Complications

More common complications include:

- Secondary bacterial infection (with staphylococci and streptococci)
- Reactivation of latent VZV (causing shingles/herpes zoster)
- Scarring

Thrombocytopenia, pneumonia, hepatitis and encephalitis are rarer complications of VZV infection.

Management

Drying lotions and antipruritics can be prescribed for the rash. Calamine lotion or pramoxine gel may help to relieve the itch. If there is severe pruritus, oral antihistamines may be useful. Acyclovir can be prescribed for severe disease or in immunocompromised patients. Antibiotics may be prescribed if there is a secondary bacterial infection.

A live attenuated vaccine has been developed but is not part of the EPI.

PERTUSSIS (WHOOPING COUGH)

Pertussis is caused by infection with *Bordetella pertussis*.

Transmission and Pathogenesis

Bordetella pertussis is spread via droplets. The organism causes necrosis of ciliated respiratory epithelium, which leads to sloughing of cells and mucous production. This leads to micro-aspiration and coughing.

Clinical Features

There is an incubation period of 7 days followed by a catarrhal stage characterised by a low-grade fever, nasal secretions and a mild cough. The paroxysmal stage then follows. During this stage, patients have a paroxysmal cough (sudden and occurring at any time) followed by a forceful inspiration and ‘whoop’. This cough is often accompanied by vomiting of mucus or feeds. In young infants the cough is atypical. These children may present with apnoea or cyanosis. The paroxysmal stage lasts 2-4 weeks.
It is followed by the convalescent phase which lasts 2-4 weeks and is characterised by a decrease in severity and frequency of the cough. However, the cough can persist for 3 months or more.

Complications

They include:

- Pneumonia
- Atelectasis
- Encephalopathy
- FTT
- Subconjunctival haemorrhage (see related image here)
- Epistaxis

Investigations

Performing a PCR test on nasal swabs is the preferred investigation to detect the causative organism. One may perform an FBC as leucocytosis may be present.

Management

Hospital admission is warranted in severe cases where supplemental oxygen or mechanical ventilation is required, or if the child has apnoeic or cyanotic spells. The cough is best controlled by avoiding stimuli such as unnecessary suctioning, throat examinations and NGT insertion.

Antibiotics are administered with the aim of eradicating *Bordetella pertussis* and preventing secondary transmission. Macrolide antibiotics (e.g. clarithromycin, azithromycin and erythromycin) are highly effective at eradicating *Bordetella pertussis* from the nasopharynx.

The incidence of pertussis has largely been reduced due to immunisations (the vaccine is part of the EPI).

RUBELLA (GERMAN MEASLES)

It is caused by the rubella virus, which is an RNA virus.

Transmission and Pathogenesis

Rubella is transmitted via airborne droplets. It invades the respiratory epithelium and spreads via the blood (primary viraemia) to regional and distal lymphatics and replicates within the reticuloendothelial system. There is a second viraemia ~6 days after infection, causing the virus to spread to many different sites. The second viraemia peaks just before the rash develops.

Clinical Features

The incubation period lasts 14-21 days and is followed by a prodrome of malaise, coryza, conjunctivitis and tender lymphadenopathy (sub-occipital, post-auricular and cervical). There is then an exanthem phase in which a pink-red, maculopapular rash appears on the face. The rash typically starts behind the ears and then progresses distally to cause a generalized maculopapular rash that spares the palms and soles. The rash usually lasts 2-3 days (see *Dermatological Conditions* chapter for more information).

Complications

They include:

- Arthralgia
- Encephalitis
- Thrombocytopenic purpura

Investigations

The diagnosis is usually clinical. However, viral serology can be performed to confirm the diagnosis.

Management

Management is mostly supportive (symptom control). Generally, immunity develops after infection. Rubella can be prevented with the MMR vaccine (not on the EPI).

POLIOMYELITIS (POLIO)

It is caused by the poliovirus, which is an RNA virus.

Transmission and Pathogenesis

The poliovirus is spread via the faeco-oral route but may also be spread via oral-to-oral transmission. The virus multiplies in the gastrointestinal tract (GIT) and produces an immune response. If this response is adequate, the virus is neutralised. However, if the response is inadequate the virus continues to proliferate and gains access to the central nervous system (CNS) via the bloodstream or along nerve pathways from the GIT. It then attacks anterior horn cells, resulting in acute flaccid paralysis.

Clinical Features

The clinical presentation is variable and may include:

- Subclinical disease

- Mild, non-paralytic disease – fever, sore throat, abdominal pain, nausea and vomiting
- Meningism
- Various patterns of paralytic disease – weakness of the neck, trunk, abdomen, diaphragm and limbs (spinal) or muscles innervated by cranial nerves (bulbar) or a combination (bulbospinal)
- Encephalopathy – irritability, drowsiness, a tremor and disorientation

During the recovery period, those with paralytic disease may recover some muscle strength but there is often residual weakness and resultant deformities.

Investigations

All cases of suspected polio must be investigated as per the acute flaccid paralysis protocol. This involves sending two stool samples to the National Institute of Communicable Diseases (NICD) for viral isolation within fourteen days of onset of paralysis.

Management

Management in the acute phase is mainly supportive, with a major aim being the prevention of secondary respiratory tract infections. The patient may also require assisted ventilation if s/he has respiratory muscle paralysis. In the recovery phase, physiotherapy is key to facilitating muscle strengthening and preventing contractures and deformities. If the residual weakness results in deformities, orthopaedic surgery may be required.

Polio (see related image here) has been eradicated in most parts of the world due to vaccination programmes. It is part of the EPI.

INFLUENZA

Influenza is caused by the influenza virus, which is an RNA virus with three types – A, B and C.

Transmission and Pathogenesis

The influenza virus is spread via airborne droplets and has hemagglutinin and neuraminidase surface proteins. The hemagglutinin binds to respiratory epithelial cells which allow it to infect the host and replicate. The neuraminidase allows newly replicated virions to break free from the cell membrane and spread.

Clinical Presentation

The child may present with a sudden onset of fever, headache, myalgia, malaise, sore throat, rhinitis, vomiting and respiratory symptoms (e.g. coughing). Recovery usually occurs over a few days. However, the malaise may persist for a few weeks.

Complications

They include:

- Febrile seizures, encephalitis
- Reye's syndrome
- Pericarditis
- Myocarditis
- Secondary bacterial infection (causing pneumonia or otitis media)

Management

Management is mainly supportive but antiviral agents can be used e.g. oseltamivir, zanamivir (zanamivir is rarely used in South Africa and is only licensed for use in people >7 years). Some children may require hospitalisation and oxygen therapy if they are hypoxic or have secondary pneumonia.
Influenza may be prevented by annual vaccination (as there is new strain every year).

MENINGITIS

Aetiology

Meningitis may be caused by:

- Bacteria e.g. Group B streptococci (GBS), *Neisseria meningitidis* (infants and older children), *Haemophilus influenzae* type b (Hib; now uncommon because of vaccination), *E. coli*, *Listeria monocytogenes*, Klebsiella (neonates)
- Mycobacteria e.g. TB
- Viruses e.g. herpes simplex virus (1+2), Epstein-Barr virus (EBV), adenovirus, mumps, coxsackie, echovirus, poliovirus
- Fungi e.g. *Cryptococcus neoformans* (also causes a chronic basal meningitis; characterised by high CSF pressures)

Transmission and Pathogenesis

The route of transmission depends on the causative organism but is usually via haematogenous spread.

Inflammation and damage are largely due to the inflammatory response and release of inflammatory cytokines, as opposed to direct damage caused by the organism. This is particularly true for bacterial meningitis. Viral meningitis has a more benign self-limiting course and full recovery usually occurs. TBM and cryptococcal meningitis have a more chronic course.

Clinical Presentation

In neonates and infants, the presentation is non-specific.

Table 9.2: Clinical Features of Meningitis Categorised by Age Group

Neonates and Infants	Older Children
● Irritability ● Lethargy ● Poor feeding ● Bulging fontanelle ● Hyper/hypothermia	● Fever ● Nausea and vomiting ● Features of meningism (headache, neck stiffness, photophobia, and positive Kernig and Brudzinski signs)

In severe cases there may be signs of encephalopathy or coma. Meningococcal meningitis is usually more rapid in onset and has a characteristic petechial, purpuric rash.

Complications

Venous thrombosis is the main complication. It can lead to:

- Infarctions
- Subdural effusions
- Epileptic fits
- Cerebral oedema
- Hydrocephalus
- SIADH
- Cranial nerve palsies
- Brain abscesses

Investigations

One should perform a lumbar puncture (LP). One may find results similar to those outlined in the table below.

Table 9.3: CSF Findings in Infectious Meningitis

	Bacteria	Viruses	TB	Cryptococcus
Cells	100-50000 cells with neutrophil-predominance	25-500 cells with lymphocyte-predominance	25-100 cells of lymphocyte predominance (may have an early neutrophil-predominance)	Similar to TBM
Glucose	Low	Normal	Very low	

Protein	Mild-to-moderately increased	Mildly increased	Moderately increased	
Other tests	Gram stain and culture will reveal the causative organism			India Ink staining, culture and cryptococcal latex agglutination test (CLAT) will be positive for cryptococcus

Management

If there is high clinical suspicion of bacterial meningitis, antibiotics should be started immediately after the LP and blood culture samples have been taken. Other investigations which may be performed include CXR, FBC and urea and electrolyte levels.

Management of Bacterial Meningitis

For Infants <2 Months Old

Initial therapy is with cefotaxime 50mg/kg 8 hourly (12 hourly if <7 days old) AND ampicillin 50mg/kg 6 hourly (8 hourly if <7 days old).

If the child has GBS, treat with cefotaxime or ampicillin for 14 days. An aminoglycoside may be added to either drug. If the meningitis is caused by Gram-negative. enteric bacilli, treat with cefotaxime and an aminoglycoside for 31 days. If the meningitis is caused by *L. meningitis*, treat with ampicillin or penicillin for 14 days.

For Children > 2 Months Old

Initial therapy is with ceftriaxone 100mg/kg stat then 80-100mg/kg daily or 40-50mg/kg twice daily. If the meningitis is due to:

- Hib infection, treat for 7-10 days
- *S. pneumoniae*, treat for 10-14 days
- *N. meningitidis*, treat for 7 days

If the causative organism is a penicillin-resistant pneumococcus, add vancomycin.

Management of TBM

Treat with RIF, INH, PZA and E for 6-9 months (duration of treatment depending on the child's response to treatment).

Management of Cryptococcal Meningitis

Treat with amphotericin B 1mg/kg/day and 5-fluorocytosine 150mg/kg/day divided into 6-hourly doses for 1 week, followed by high dose fluconazole.

MALARIA

Aetiology

Malaria is caused by protozoa species of the *Plasmodium* genus, namely *P. falciparum, P. vivax, P. ovale, P. malariae and P. knowlesi. P. falciparum* is the most prevalent species and causes the most severe disease.

Transmission and Pathogenesis

Malaria is spread via a vector, namely the female *Anopheles* mosquito (see related image here). When bitten by the mosquito, sporozoites (immature protozoa produced during the sexual phase that occurs within the mosquito) of the protozoa are injected into the bloodstream. These sporozoites develop in the liver before invading circulating red blood cells (RBCs). They mature and multiply in the RBCs until these cells rupture. The sporozoites go on to infect other RBCs. Gametocytes form in the RBCs and are sucked up by a feeding mosquito. Once in the mosquito, the sexual phase is completed and the life cycle starts again. See also the life cycle of the malaria parasite here.

Clinical Features

The patient may have a history of recent travel to an endemic area. After an incubation period of 7-12 days in *P. falciparum* malaria and 10-30 in the other species, a fever develops. The fever is classically intermittent (occurs in 48-72-hour cycles depending on the species). This fever may be associated with rigor, headache, myalgia, arthralgia, nausea, vomiting, malaise and sweating. Splenomegaly is usually present and there may also be anaemia, leucopaenia and thrombocytopenia.

Complications

Complicated malaria may have any one of the following features and should be treated as an emergency:

- Severe anaemia (Hb <7 g/dl)
- Parasitaemia (>10000/μ or >5% infected RBCs)
- Renal failure
- Pulmonary oedema
- Circulatory collapse
- Hypoglycaemia
- Disseminated intravascular coagulation (DIC)
- Repeated generalised convulsions
- Severe metabolic acidosis
- Hepatic necrosis (will present jaundiced)
- Haemoglobinuria
- Features of cerebral malaria e.g. apathy, disorientation, psychotic behaviour, focal neurological signs, extrapyramidal signs, convulsions, coma

Investigations

They may include:

- Peripheral blood smear – will show infected erythrocytes.
- Rapid dipstick antigen test (to detect *P. falciparum*)
- FBC
- Renal function tests (RFTs; urea, electrolytes and creatinine)

- Liver function tests (LFTs)
- Blood glucose
- Urine dipsticks

Management

Treatment of Uncomplicated Malaria

It is treated with artemether/lumefantrine (20 mg/120 mg e.g. CoArtem®). The child should be given a stat dose and then a second dose 8 hours later. This should be followed by 12-hourly doses for the next two days. Therefore, the child should be given 6 doses in total.

The number of tablets that the child is given is dependent on her/his weight. If s/he weighs:

- 5-14.9 kg – 1 tablet/dose
- 15-24-9 kg – 2 tablets/dose
- 25-34.9 kg – 3 tablets/dose
- ≥35 kg – 4 tablets/dose

The CoArtem® must be administered with fat-containing food or full-cream milk to ensure adequate absorption.

Children <5 kg should be given oral quinine 10 mg/kg 8 hourly for 7-10 days and clindamycin 10 mg/kg 12 hourly for 7 days.

Complicated Malaria

Those with complicated malaria (have the features listed above, are vomiting or are unable to tolerate oral medication) should ideally be treated with IV artesunate. If the child weighs <20 kg, s/he should be given 3 mg/kg IV artesunate at 0, 12 and 24 hours and then once daily until s/he can tolerate oral CoArtem®. The full Coartem® course should be completed thereafter. If the child weighs >20 kg, s/he should be given 2.4 mg/kg IV artesunate and the same schedule followed as above.

However, IV artesunate may be difficult to acquire and IV quinine may need to be used as an alternative. The child should be given a loading dose of IV quinine (20 mg/kg; 20 mg salt/kg mixed with 5-10 mL/kg of 5% dextrose or dextrose saline) over 4 hours. The

maintenance dose should be given 8 hourly (10 mg/kg slow IV quinine over 4 hours). Once the patient can tolerate oral therapy, CoArtem® OR oral quinine and clindamycin (10 mg/kg/dose 12 hourly orally for 7 days) may be given.
Note: Patients on IV quinine should have regular blood glucose and ECG monitoring.

Prevention

If possible, children <5 years of age should not be taken to high-risk areas. Measures should be taken to prevent mosquito bite, such as:

- Only visiting malaria areas in the dry season
- Staying indoors after dark
- Using mosquito nets and mosquito repellants
- Sleeping under bed nets where available
- Dressing the child in long-sleeved shirts and trousers

Antimalarial prophylaxis is also effective in limiting the risk of malaria.

TETANUS

It is caused by the bacterium *Clostridium tetani*, an obligate anaerobe that exists in spore-form and is found in soil and animal faeces. It is also called ‘lockjaw’ as this characteristic clinical feature is sometimes present.

Transmission and Pathogenesis

The spores enter the body via wounds exposed to contaminated dirt, faeces or saliva. As *C. tetani* is an anaerobe, it generally requires wounds with compromised blood supplies in order for it to germinate and multiply. Thus, deep, penetrating wounds, open fractures, surgical procedures and burns are ideal replicating environments because of the associated ischaemia and necrosis. However, any wound can be tetanus prone. The spores multiply and produce neurotoxins called tetanospasmin and tetanolysin. Tetanospasmin reaches the central nervous system (CNS) via retrograde axonal transport, where the toxin binds to the peripheral nerve receptors and is transported to interneurons in the CNS via vesicles. It prevents the action of inhibitory

neurotransmitters (GABA and glycine), leading to uninhibited activation of α-motor neurons, muscle spasms, rigidity and autonomic instability. Tetanolysin causes haemolysis and also has cardiotoxic effects.

Clinical Features

There is an incubation period of 3-21 days. Early signs include trismus (lockjaw) progressing to generalised muscle rigidity and intermittent spasms. Risus sardonicus is a term used to describe the sustained facial muscle spasms that produce a characteristic sardonic (mocking) grin and raised eyebrows. Dysphagia and odynophagia can also occur. A generalised tetanic posture is classically that of opisthotonus (abduction and flexion of the shoulders, flexion of the elbows and wrists, clenched fists and extension of the legs). Autonomic disturbance also commonly occurs, with the patient developing labile hypertension, episodes of hypotension, tachycardia, arrhythmias, peripheral vasoconstriction and sweating.

Complications

They include:

- Upper airway obstruction or diaphragmatic spasm leading to respiratory failure
- Autonomic instability with sudden cardiac death
- Venous thrombo-embolism
- Stress ulcers
- Contractures
- Joint dislocations

Diagnosis

The diagnosis is clinical and is made based on history and examination i.e. muscle spasms with rigidity in the context of a susceptible wound and inadequate immunisation.

Management

Treatment

Management is supportive and aims to control infection, eliminate toxin production and neutralise the toxins already present. Therefore, the wound should be cleaned and debrided. Patients should be allowed to recover in quiet environments with minimal external stimuli, as these can trigger spasms. Intubation and ventilation may be required in some.

Pharmacological management includes the administration of:

- Tetanus immunoglobulin 500–2 000 IU IM as a single dose
- Metronidazole 7.5 mg/kg/dose IV 8 hourly for 10 days (alternatively use penicillin G)
- Diazepam 0.1–0.2 mg/kg/dose IV 4–6 hourly (to control spasms)

After recovery, patients should be fully immunised.

Prevention

Most cases are prevented through immunisation. As tetanus immunisation is included in the EPI, the incidence of tetanus is low. In children with major wounds, tetanus toxoid (0,5 mL IM) can be administered. If the wound is seriously contaminated or older than 6 hours, tetanus immunoglobulin (250 U IM into the limb opposite to the one exposed to the toxoid) can also be given. Additionally, 5 days of antibiotics (penicillin/metronidazole/erythromycin/cephalosporin) may be given. Tetanus toxoid can be given every 5 years to prevent tetanus infection.

DIPHTHERIA

Diphtheria is caused by *Corynebacterium diphtheriae* (see related image here).

Transmission and Pathogenesis

Corynebacterium diphtheriae is transmitted through droplet spread. The virulent diphtheria bacilli lodge in the nasopharynx where they multiply and produce a toxin. This toxin causes local tissue necrosis and an anti-inflammatory and exudative process,

which results in the formation of a pseudomembrane. Once the toxin enters the blood, it can affect other organs. However, it has an affinity for myocardial and neural tissue. This organism can occasionally infect skin and the patient may present with leg ulcers.

Clinical Features

Patients initially present with a sore throat, fever, malaise and non-specific symptoms of an upper respiratory tract Infection (URTI). There is subsequent development of a white-grey pseudomembrane in the nose, pharynx, tonsils, palate and/or glottis. Cervical lymphadenopathy can give a ‘bull neck’ appearance.
If myocarditis develops the child may present 1-2 weeks later with signs and symptoms of cardiac failure. 3-6 weeks after the initial onset of symptoms, neuritis may manifest as dysphagia, nasal speech, regurgitation, strabismus, diplopia and, in extreme cases, respiratory muscle paralysis. Weakness of the limbs can also occur if peripheral nerves are involved.

Complications

They may include:

- Myocarditis
- Congestive cardiac failure
- Neuritis and its manifestations
- Pneumonia
- Renal failure
- Disseminated intravascular coagulopathy
- Thrombocytopenia

Investigations

Nose and throat cultures can be done to confirm the diagnosis. However, one must not wait for confirmation before initiating treatment if diphtheria is suspected.

Management

The dose of anti-diphtheria serum (ADS; antitoxin) depends on the extent of infection (20 000-100 000 U IM or IV). One must be wary of anaphylaxis when administering this medication. Procaine penicillin (50 000 IU/kg/day IM in 2 doses for 10 days) or erythromycin (50 mg/kg/day oral in 4 doses for 10 days) should also be given.
Bed rest is warranted if the patient has myocarditis. One should restrict fluids, diurese and use digoxin as necessary, if the patient has congestive cardiac failure (CCF). Nasogastric feeds and supportive therapy with physiotherapy may be required. The patient should be isolated and airborne precautions should be implemented.

Prevention

Isolation and airborne precautions should be enforced. Contacts need nose and throat cultures followed by antibiotic treatment for those with a positive result.
An infected person will also require immunisation after recovery. Immunisation in childhood has largely reduced the incidence of diphtheria.

RABIES

It is caused by the rabies virus, which is a single-stranded RNA virus that is bullet shaped.

Transmission and Pathogenesis

Rabies is transmitted when a wound is contaminated with saliva from a rabid animal, such as a stray dog, bat or meerkat. The principle vector may vary in different countries but it is widespread in warm-blooded animals. Once the virus gains entry through the skin, it multiplies in the striated muscles. It then enters peripheral nerves, and travels along axons until it reaches the CNS where it multiplies and causes severe damage within the brainstem, pyramidal cells, cranial nerves, posterior horns of the spinal cord and other CNS structures. The virus then migrates to the salivary glands.

Clinical Features

There is an initial incubation period ranging from a few weeks to 2-3 months where the patient is asymptomatic. This is followed by the prodromal phase when the patient may present with fever, malaise, anorexia, vomiting, headaches and paraesthesia at the site of the wound (pathognomonic but may not always occur).

An acute neurologic phase (furious rabies) occurs after a few days of the prodrome. It is characterised by hydrophobia, aerophobia and alternating periods of hyperactivity, hallucinating, biting and bizarre behaviours. There are then periods of calm, co-operation and normal behaviour. Eventually, there is ascending symmetrical paralysis, areflexia, coma and death (due to respiratory muscle paralysis or arrhythmias). In some cases, there is ascending symmetrical paralysis without the furious phase.

Complications

Death is almost inevitable as only a handful of people have survived rabies.

Investigations

One should perform serum antibody tests, nuchal skin biopsies and tests on the saliva for the rabies virus (see rabies vaccine related image here).

Management

Treatment – Post-Exposure Prophylaxis

In patients with a suspected bite by a rabid animal, clean the wound with soap and water and apply a virucidal solution e.g. 10% povidone iodine.

Administer rabies immunoglobulin (RIG) at the wound and the rest at a distant site (20 IU total dose). Administer human diploid cell vaccine on days 0, 3, 7, 14, 30 and 90 at a separate site from where the RIG was given.

Give supportive management if the patient presents with symptoms.

Prevention

Rabies may be prevented by vaccinating all domestic animals and eliminating stray animals. High-risk individuals (e.g. vets, health inspectors, cave explorers, those who work with wildlife) should receive regular vaccinations.

TYPHOID

It is caused by infection with *Salmonella typhi* (bacteria).

Transmission and Pathogenesis

Salmonella is spread via the faeco-oral route – contaminated food/water and poor hand hygiene. During the incubation period (usually 7-14 days but up to 30 days), organisms multiply in the reticuloendothelial system of the small bowel before invading the bloodstream. The disease can disseminate to various organs and cause focal liver necrosis, inflammation within the biliary tract and reinvasion of the small bowel with ulceration, perforation or haemorrhage. The organism also releases an endotoxin which causes multisystem reactions.

Clinical Features

Typhoid classically has three clinical stages. After the incubation period, there is an onset of fever, with anorexia, headaches, malaise, diarrhoea and vomiting. This usually lasts about one week (see related diagram here).

In the second week, there is persistent fever, abdominal pain with diarrhoea and rose-coloured spots on the abdomen. Complications may develop in the third week, namely hepatosplenomegaly, perforation and intestinal bleeding, secondary bacteraemia and peritonitis. Multiple organ systems can be involved, thus patients can have a wide range of clinical presentations (cough, delirium, meningeal irritation, myalgia, arthralgia, abdominal pain).

Complications

They include but are not limited to:

- GI haemorrhage/perforation (most common)
- Myocarditis
- Meningitis
- Delirium
- Psychosis

Investigations

One may order:

- Blood tests, which will show:
    - Anaemia
    - Leucopaenia/leucocytosis
    - Abnormal liver functions
    - *S. typhi* grown on blood culture
- Urine and stool cultures

Management

Treatment

Antibiotics are given in addition to supportive management and early diagnosis and treatment of complications. Uncomplicated disease may be treated with fluoroquinolones e.g. ciprofloxacin 30 mg/kg/day orally in two divided doses for 7-10 days. Severe infection may be treated with third-generation cephalosporins e.g. ceftriaxone 80 mg/kg IM/IV once daily for 10-14 days (maximum 4 g/day).

Prevention

Typhoid may be prevented with good hygiene and sanitation, and a vaccination before travelling to endemic areas.

CHOLERA

It is caused by *Vibrio cholerae*.

Transmission and Pathogenesis

It is transmitted through the faeco-oral route – contaminated food/water and poor hand hygiene. The bacteria grow well in an alkaline medium, thus a high infective dose is required to cause disease in the acidic gastric environment. Once in the small bowel, the organism produces an enterotoxin that causes the secretion of large amounts of fluid and electrolytes (mainly chloride) into the gut lumen i.e. it causes a severe secretory diarrhoea.

Clinical Presentation

There is an incubation period of 1-5 days. Symptoms include fever, vomiting and diarrhoea. The diarrhoea in cholera (see image cholera patient here) quickly becomes colourless and mucoid, producing the characteristic 'rice water' appearance.
The diarrhoea is often complicated by severe dehydration, shock and electrolyte abnormalities. It usually lasts a few days and is self-limiting, but, if no interventions are instituted to mitigate the dehydration, death can occur.

Complications

They may include:

- Severe dehydration
- Shock
- Death

Pneumonia is also possible.

Management

Treatment

Rapid fluid and electrolyte replacement and rehydration are the mainstays of treatment. Antibiotics are not routine but ciprofloxacin (if <8 years old) or tetracycline (if >8 years old) can be given to shorten the duration.

Enteric precautions, regular weight, hydration and blood pressure (BP) checks, and input and output monitoring are essential. Regular electrolyte monitoring is also important.

Prevention

Good hygiene and sanitation and the availability of clean water are key components of prevention.

BILHARZIA

It is caused by schistosomes which are parasitic trematodes or flukes of the genus *Schistosoma*: *Schistosoma haematobium* affects the genitourinary tract, while *Schistosoma mansoni* and *Schistosoma japonicum* affect the intestine and liver. In SA, *S. haematobium* is more common than the others.

Transmission and Pathogenesis

The organism's life cycle involves freshwater snails (intermediate hosts) and humans (definitive host) (see related image here). Infected humans excrete schistosome eggs in urine and faeces. Eggs present in infected water hatch and infect freshwater snails. Once in a more mature form, they pass from the snail and penetrate the skin of humans who are in the water.

The schistosomes migrate to the portal vessels where they mature into adults. They mate and migrate either to the bladder's venous plexus (*S. haematobium*) or inferior mesenteric vessels (*S. mansoni* and *S. japonicum*). Eventually they migrate into the bladder and large intestine from where they can be excreted and the cycle begins again.

Eggs may deposit in other tissues, such as the lungs and CNS. They tend to stimulate an eosinophilic reaction which varies among individuals and also depends on the parasite load. Pathology is mainly linked to the degree of the host's hypersensitivity reaction and involves the formation of granulomas.

Clinical Features

Initially there is a pruritic, erythematous maculopapular rash at the site of entry with a local reaction, often called ‘swimmer’s itch’ or cercarial dermatitis. After 4-6 weeks patients may present with fever, rash, lymphadenopathy, oedema and hepatosplenomegaly (Katayama fever). Patients may also encounter bronchospasm, severe headache and features of encephalopathy and cardiac disease. In urogenital disease they may be asymptomatic or have terminal haematuria (pathognomonic). In some cases there may be dysuria or suprapubic pain. GIT disease often presents with abdominal pain and dysentery. If chronic there may be anaemia and ascites. If infection affects the liver it may lead to periportal fibrosis leading to Portal HPT and its sequelae. Deposition of eggs can lead to chronic inflammation with granuloma formation.

Complications

They usually develop in patients with chronic infection and may include:

- GI ulcers
- GI obstruction
- Pyelonephritis
- Chronic renal failure
- Chronic lung disease
- Pulmonary HPT
- Portal HPT
- Encephalitis
- Spinal cord lesions
- Urinary tract obstruction
- Bladder calcification

Investigations

Serology is the most sensitive diagnostic investigation for travellers but cannot distinguish between a current or past infection (not useful in patients from an endemic area). Direct visualisation of schistosome eggs via stool or urine microscopy is, thus, the gold standard and can also determine the schistosome subtype.

Management

Treatment

Corticosteroids are used to treat the acute syndrome as they dampen the immune system's inflammatory response. Prednisone (1-2 mg/kg) must be promptly administered if there is neuroschistosomiasis, to prevent irreversible tissue damage secondary to the inflammatory response.

After acute symptoms have resolved the patient should be given a single dose of praziquantel (30-45 mg/kg orally). This may be repeated after 1 month. One should also implement specific management of the complications if present.

Prevention

Good sanitation, avoidance of swimming or urinating in water, especially in endemic areas. Wear protective clothing if swimming in freshwater in endemic areas. Boil drinking water.

ANTIBIOTIC STEWARDSHIP

Antibiotic stewardship refers to a set of coordinated strategies that are employed to improve the use of antimicrobial medications. The goal is to enhance patient health outcomes, reduce antibiotic resistance and decrease unnecessary costs. It is important because resistance to antibiotics is on the rise and the rate at which new drugs are being produced is not sufficient.

Principles of Rational Antibiotic Prescribing

One must:

- Consider the indication for the antibiotic i.e. does the patient have a bacterial infection?
- Perform cultures before administering antibiotics (if appropriate) in hospitalised patients or outpatients with recurrent infections
- Choose an appropriate empiric antibiotic

- Ensure the correct dose and route are prescribed
- Quickly start antibiotics in patients with severe infections
- Ensure early and effective source control
- Evaluate appropriateness of continued antimicrobial therapy on a daily basis and use a narrow-spectrum drug if possible

It is also important to prevent the spread of resistant organisms with good infection control (hand hygiene is key).

See related image here.

IMMUNISATIONS

Table 9.4: Immunisations

According to the South African expanded programme on immunisation (EPI) schedule (which can be sourced from www.westerncape.gov.za), children are vaccinated against:

- Polio
- Measles
- Hepatitis B
- Haemophilus influenza B
- Pertussis
- Diphtheria
- Pertussis
- TB

The catch-up schedule can be sourced on the NICD website at www.nicd.ac.za