
La-Net
PAE 511
SPECIFIC
INFECTIOUS
DISEASES
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Course code: PAE 511

Course title: Specific Infectious Diseases

Course credit load: 2 Units

Series 1: Malaria in Children

- **Part 1.1: Introduction, Epidemiology, and Types of Malaria**
    - Sub Part 1.1.1: Introduction to malaria
    - Sub Part 1.1.2: Species and types of malaria
    - Sub Part 1.1.3: Epidemiology of malaria in children
- **Part 1.2: Pathophysiology of Malaria**
    - Sub Part 1.2.1: The malaria life cycle
    - Sub Part 1.2.2: Mechanisms of illness in uncomplicated malaria
    - Sub Part 1.2.3: Pathophysiology of severe malaria
- **Part 1.3: Clinical Features and Diagnosis of Malaria**
    - Sub Part 1.3.1: Clinical features of uncomplicated malaria
    - Sub Part 1.3.2: Clinical features of severe malaria
    - Sub Part 1.3.3: Diagnosis and investigation of malaria
- **Part 1.4: Management, Prevention, and Control of Malaria**
    - Sub Part 1.4.1: Management of uncomplicated malaria
    - Sub Part 1.4.2: Management of severe malaria
    - Sub Part 1.4.3: Prevention and control of malaria

Introduction

Picture a three year old brought to a rural clinic with three days of fever, chills, and vomiting, in a region where malaria transmission occurs year round. This presentation, one of the most common reasons a child is brought to a health facility across much of sub-Saharan Africa, opens the PAE 511 course, since malaria remains one of the leading causes of childhood illness and death in Nigeria and the wider region despite being both preventable and treatable when recognised promptly.

The aim of this Series is to equip you with the knowledge required to understand the epidemiology and pathophysiology of malaria, recognise its clinical features, including the features of severe disease, and diagnose, manage, and prevent malaria in children.

This Series begins with an **introduction to the epidemiology and types of malaria**, before turning to its **pathophysiology**. Next, we examine the **clinical features and diagnosis of malaria**, including severe malaria, before concluding with its **management, prevention, and control**.

Series Learning Outcomes

At the end of this Series, you should be able to:

- **SLO 1.1:** describe the epidemiology of malaria in children,
- **SLO 1.2:** list the species of malaria parasite and distinguish uncomplicated from severe malaria,
- **SLO 1.3:** describe the pathophysiology of malaria,
- **SLO 1.4:** describe the clinical features of uncomplicated malaria,
- **SLO 1.5:** describe the clinical features and diagnostic criteria for severe malaria,
- **SLO 1.6:** describe the diagnosis and investigation of malaria,
- **SLO 1.7:** describe the management of uncomplicated and severe malaria, and
- **SLO 1.8:** describe the prevention and control of malaria.

1.1 Introduction, Epidemiology, and Types of Malaria

1.1.1 introduction to malaria

A single mosquito bite begins the whole process

Malaria is a **parasitic infection** transmitted to humans through the bite of an infected female **Anopheles mosquito**, and remains one of the leading causes of childhood morbidity and mortality in **sub-Saharan Africa**, including Nigeria, where transmission is frequently **year-round** in many regions rather than confined to a specific season, meaning malaria must be actively considered in the differential diagnosis of almost any febrile child presenting from an endemic area.

The disease is caused by parasites of the genus ***Plasmodium***, with **five species** known to infect humans, and, while all can cause clinically significant illness, one species in particular is responsible for the overwhelming majority of severe disease and death, discussed further in the

next sub-Part, making accurate species identification, where possible, clinically relevant to anticipating disease severity and appropriate management.

Fill in the blank: Malaria is transmitted to humans through the bite of an infected female _____ mosquito.

1.1.2 species and types of malaria

The five species of ***Plasmodium*** that infect humans are **Plasmodium falciparum**, **Plasmodium vivax**, **Plasmodium ovale**, **Plasmodium malariae**, and **Plasmodium knowlesi**, with **Plasmodium falciparum** responsible for the great majority of severe disease and death in sub-Saharan Africa, reflecting both its predominance in the region and its distinct capacity to cause the severe complications discussed later in this Series.

Clinically, malaria is broadly classified into **uncomplicated malaria**, in which the child is generally systemically well aside from fever and related symptoms, and **severe malaria**, in which one or more specific, serious clinical or laboratory features are present, a distinction of central importance since it directly determines the urgency and setting of required treatment, discussed in detail later in this Series.

Fill in the blank: Plasmodium falciparum is responsible for the great majority of _____ disease and death in sub-Saharan Africa.

1.1.3 epidemiology of malaria in children

Malaria disproportionately affects **young children**, particularly those **under five years of age**, who lack the partial immunity that develops gradually with repeated exposure in malaria-endemic regions, meaning this age group bears a substantial share of both malaria illness episodes and malaria-related deaths despite representing a smaller proportion of the overall population in affected areas.

Transmission intensity varies considerably between regions and seasons, generally correlating with rainfall and temperature patterns that favour mosquito breeding, and children living in areas of **high transmission intensity** typically experience their most severe disease episodes earlier in life, before partial immunity has had the opportunity to develop, in contrast to children in **lower transmission** settings, who may experience severe disease at a somewhat older age.

Fill in the blank: Malaria disproportionately affects children under _____ years of age.

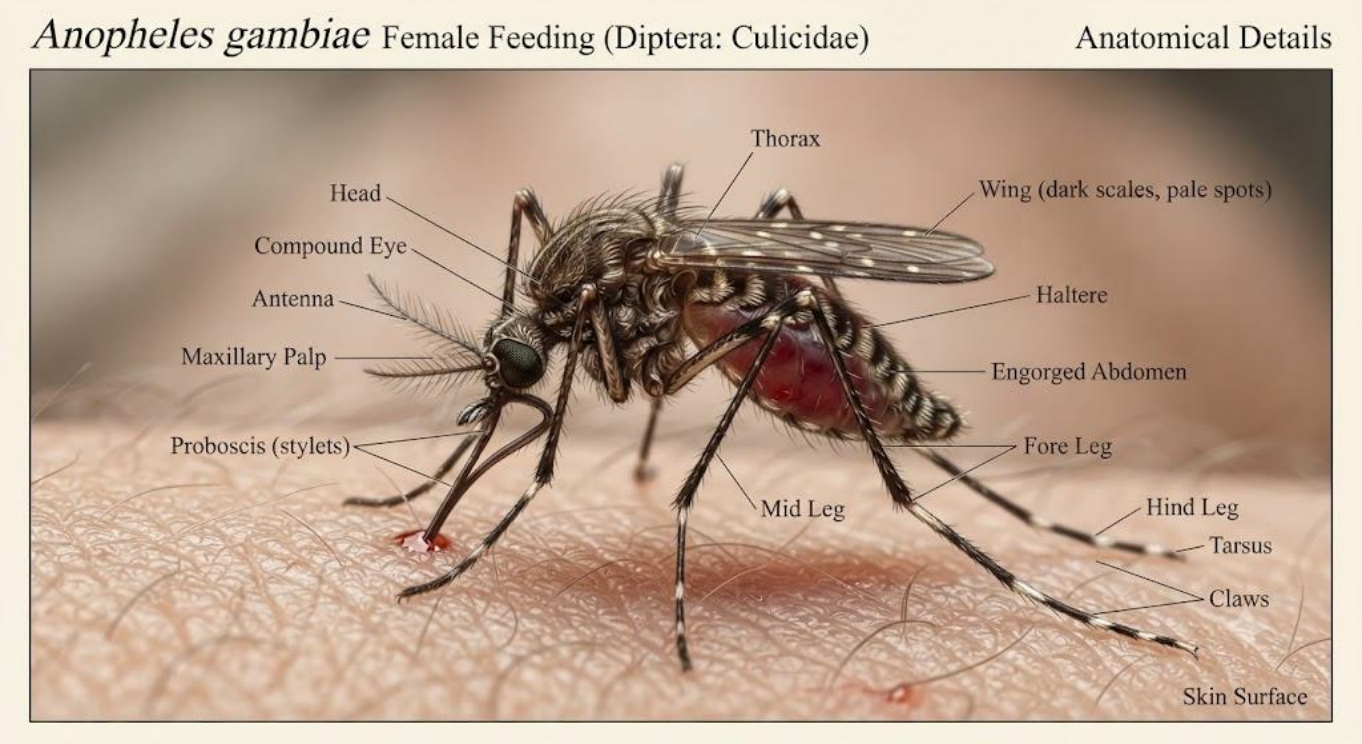

Figure 1.1: An Anopheles mosquito feeding, the vector responsible for malaria transmission.

Pilot questions 1.1

1. Describe how malaria is transmitted to humans. (Linked to SLO 1.1)
2. List the five species of Plasmodium that infect humans. (Linked to SLO 1.2)
3. Name the species responsible for the majority of severe malaria in sub-Saharan Africa. (Linked to SLO 1.2)
4. Distinguish uncomplicated from severe malaria. (Linked to SLO 1.2)
5. Explain why children under five years bear a disproportionate burden of malaria. (Linked to SLO 1.3)

1.2 Pathophysiology of Malaria

1.2.1 the malaria life cycle

Two hosts, two very different phases

The malaria parasite has a complex **life cycle** involving both the **human host** and the **Anopheles mosquito vector**. Following an infected mosquito bite, **sporozoites** are injected into the bloodstream and travel to the **liver**, where they invade hepatocytes and undergo asexual

multiplication during the **liver**, or **hepatic**, **stage**, which is clinically **silent**, producing no symptoms during this initial phase of infection.

After several days, the liver stage parasites rupture and release **merozoites** into the bloodstream, initiating the **blood stage** of infection, in which merozoites invade **red blood cells**, multiply, and cause the cells to rupture, releasing further merozoites to invade additional red cells in a repeating cycle, and it is this **blood stage** that is directly responsible for the clinical symptoms of malaria, discussed further in the next Part of this Series.

Fill in the blank: Following an infected mosquito bite, sporozoites travel to the _____, where they undergo asexual multiplication.

1.2.2 mechanisms of illness in uncomplicated malaria

The **cyclical rupture** of infected red blood cells releases **parasite antigens** and cellular debris into the circulation, triggering a **host immune and inflammatory response**, including release of **pyrogenic cytokines**, which is directly responsible for the characteristic **fever**, and often periodic fever pattern, together with the associated symptoms of **headache**, **myalgia**, and general malaise experienced by a child with uncomplicated malaria.

The destruction of red blood cells during the blood stage also contributes to the development of **anaemia**, both through direct destruction of infected cells and, to a lesser extent, through **increased splenic clearance** of both infected and uninfected red cells, with the degree of anaemia generally related to the duration and intensity of infection.

Fill in the blank: The cyclical rupture of infected red blood cells triggers release of _____ cytokines, causing fever.

1.2.3 pathophysiology of severe malaria

Severe malaria, almost exclusively caused by **Plasmodium falciparum**, results from additional pathophysiological mechanisms beyond those seen in uncomplicated disease, most importantly **cytoadherence**, in which infected red blood cells develop surface changes that cause them to **adhere to the walls of small blood vessels**, particularly in the brain and other vital organs, a process that obstructs normal microvascular blood flow and contributes to the organ dysfunction characteristic of severe disease.

This microvascular obstruction, combined with the **inflammatory response** and resulting **metabolic derangement**, including **hypoglycaemia** and **lactic acidosis**, underlies the specific severe manifestations of falciparum malaria, including **cerebral malaria**, in which

cytoadherence and inflammation within the cerebral microvasculature produce impaired consciousness and, often, seizures, discussed further in the next Part of this Series.

Fill in the blank: Cytoadherence describes infected red blood cells adhering to the walls of small _____ vessels.

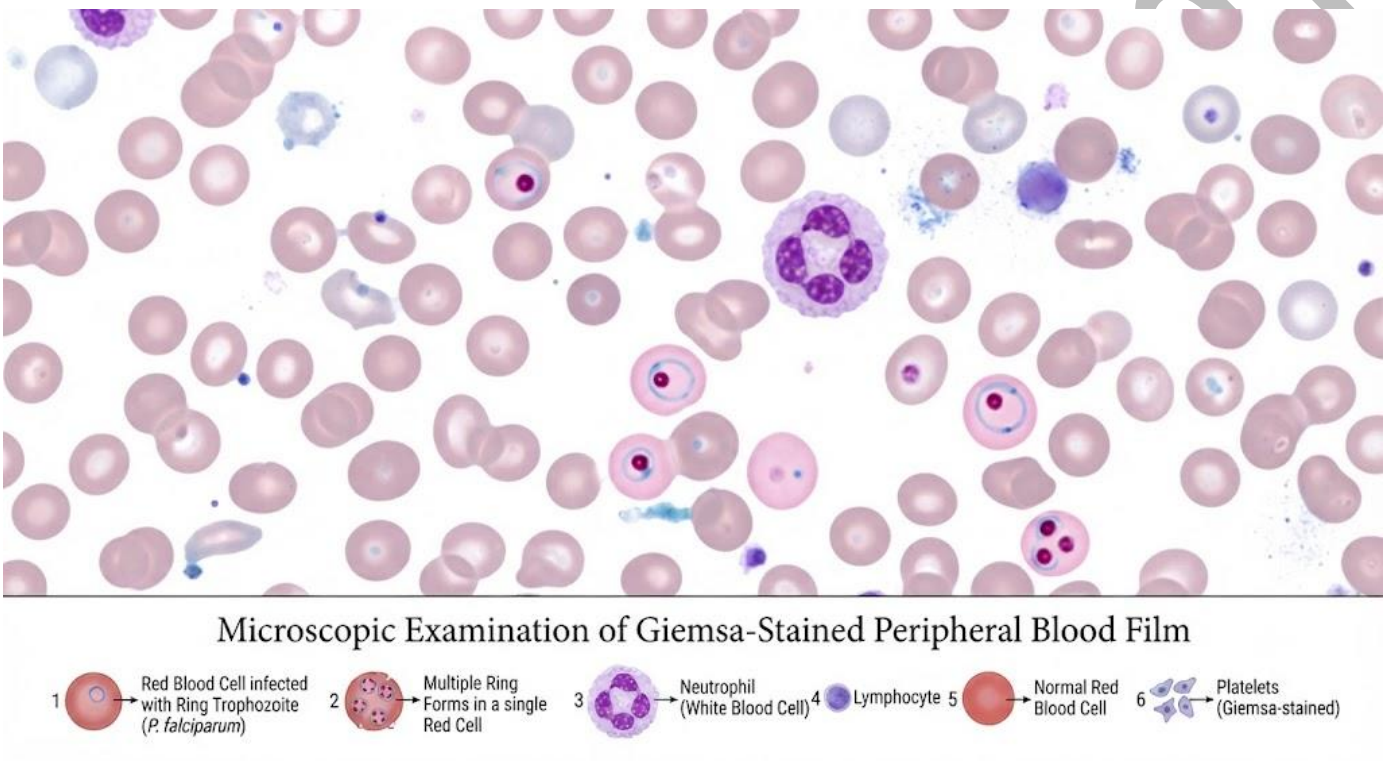

Figure 1.2: A blood film showing red blood cells infected with malaria parasites.

Pilot questions 1.2

1. Describe the liver and blood stages of the malaria life cycle. (Linked to SLO 1.3)
2. Explain what directly causes fever in uncomplicated malaria. (Linked to SLO 1.3)
3. Describe two mechanisms contributing to anaemia in malaria. (Linked to SLO 1.3)
4. Define cytoadherence and its role in severe malaria. (Linked to SLO 1.3)
5. Explain how cytoadherence contributes to cerebral malaria. (Linked to SLO 1.3)

1.3 Clinical Features and Diagnosis of Malaria

1.3.1 clinical features of uncomplicated malaria

A classic, but easily mistaken, presentation

Uncomplicated malaria typically presents with **fever**, often but not always following a **periodic pattern** related to the timing of synchronised red cell rupture, together with **chills** or **rigors**, **headache**, **myalgia**, **anorexia**, and, particularly in young children, **vomiting** and **abdominal pain**, a presentation that overlaps considerably with numerous other common childhood febrile illnesses, meaning malaria testing should be considered a routine part of evaluating any febrile child from an endemic area rather than reserved only for children with a specific, highly suggestive pattern of symptoms.

On examination, findings in uncomplicated malaria are often relatively **non-specific**, though **mild splenomegaly** may be present, particularly in children with repeated prior infections, and the child generally remains **alert** and without the specific warning signs discussed in the next sub-Part, a distinction that is central to correctly classifying a given presentation as uncomplicated rather than severe.

Fill in the blank: Fever in uncomplicated malaria often, but not always, follows a _____ pattern related to red cell rupture.

1.3.2 clinical features of severe malaria

Severe malaria is defined by the presence of one or more specific clinical or laboratory features indicating significant organ dysfunction, including **impaired consciousness** or **coma**, termed **cerebral malaria**, **repeated seizures**, **severe anaemia**, **respiratory distress**, often reflecting significant metabolic acidosis, **hypoglycaemia**, **circulatory collapse** or **shock**, and **jaundice**, with the presence of any one of these features indicating a genuine medical emergency requiring urgent, intensive treatment rather than standard outpatient management.

Recognising these warning signs promptly is essential, since severe malaria can progress rapidly, and a child presenting with early features of severe disease who is not recognised and treated urgently can deteriorate significantly within a matter of hours, underscoring the importance of actively and specifically screening for these features in every child with confirmed or suspected malaria rather than assuming uncomplicated disease by default.

Fill in the blank: Impaired consciousness or coma resulting from severe malaria is specifically termed _____ malaria.

1.3.3 diagnosis and investigation of malaria

Diagnosis of malaria requires **parasitological confirmation** wherever possible, most commonly using either **microscopy** of a **thick and thin blood film**, which allows both detection and species identification along with an estimate of **parasite density**, or a **rapid diagnostic test**, detecting specific parasite antigens and providing a result within minutes, particularly valuable in settings without immediate access to reliable microscopy.

In a child with features suggestive of **severe malaria**, further investigations are required to assess the extent of organ involvement, including **full blood count** to assess for anaemia, **blood glucose** given the risk of hypoglycaemia, and, where available, **serum lactate** or other markers of **acidosis**, together with any other investigations directed by the child's specific clinical presentation, since a purely parasitological diagnosis alone is insufficient to guide the intensity of treatment required.

Fill in the blank: A rapid diagnostic test for malaria detects specific parasite _____.

Table 1.3: World Health Organization criteria for severe malaria.

Feature	Description
Impaired consciousness	Reduced level of consciousness or coma (cerebral malaria)
Repeated seizures	More than two convulsions within 24 hours
Severe anaemia	Haemoglobin below 5 g/dL in high transmission settings
Respiratory distress	Often reflecting significant metabolic acidosis
Hypoglycaemia	Blood glucose below 2.2 mmol/L
Circulatory collapse	Shock, with poor perfusion and hypotension

Pilot questions 1.3

1. List five clinical features of uncomplicated malaria. (Linked to SLO 1.4)
2. List four features that define severe malaria. (Linked to SLO 1.5)
3. Explain why prompt recognition of severe malaria features is critical. (Linked to SLO 1.5)
4. Describe the two main methods of parasitological confirmation of malaria. (Linked to SLO 1.6)
5. List two investigations performed in a child with suspected severe malaria. (Linked to SLO 1.6)

1.4 Management, Prevention, and Control of Malaria

1.4.1 management of uncomplicated malaria

Effective oral therapy has transformed outpatient treatment

Management of **uncomplicated malaria** in an area with **Plasmodium falciparum** resistance to older antimalarials, as is now the case across most of sub-Saharan Africa, relies on **artemisinin-based combination therapy**, or **ACT**, combining a rapidly acting **artemisinin derivative** with a **longer-acting partner drug**, a combination that both clears the infection quickly and reduces the risk of resistance developing to either individual component.

Alongside antimalarial treatment, **supportive care**, including **antipyretics** for fever and adequate **oral fluid intake**, is provided, and the child should be reassessed after treatment to confirm clinical improvement and actively monitor for any evolving features of severe disease, since a child initially classified as uncomplicated can occasionally deteriorate, particularly if treatment is delayed or an alternative diagnosis is subsequently identified.

Fill in the blank: Management of uncomplicated malaria relies on artemisinin-based _____ therapy.

1.4.2 management of severe malaria

Severe malaria requires urgent **hospital admission** and treatment with **parenteral antimalarial therapy**, with **intravenous artesunate** now the preferred first-line agent in most settings, having been shown to reduce mortality compared with older intravenous quinine-based regimens, together with **supportive care** directed at the specific complications present, including correction of **hypoglycaemia**, careful **fluid management** given the risk of both dehydration and fluid overload, and **blood transfusion** where severe anaemia is present.

Children with **cerebral malaria** require particularly close **neurological monitoring**, careful management of **seizures** should they occur, and general supportive intensive care, and, once the child has clinically improved and can tolerate oral intake, treatment is typically completed with a full oral course of artemisinin-based combination therapy to ensure complete parasite clearance.

Fill in the blank: Intravenous _____ is now the preferred first-line parenteral treatment for severe malaria in most settings.

1.4.3 prevention and control of malaria

Prevention of malaria centres on **vector control**, most importantly the use of **insecticide-treated bed nets**, which have been shown to substantially reduce malaria transmission and child mortality where used consistently, together with **indoor residual spraying** of insecticide in some settings, and appropriate **environmental management** to reduce mosquito breeding sites, such as eliminating areas of stagnant water near dwellings.

Chemoprevention strategies, including **seasonal malaria chemoprevention** in areas of highly seasonal transmission, and, more recently, the introduction of an effective **malaria vaccine** in a phased programme across several endemic countries, provide additional layers of protection, and effective malaria control ultimately depends on a **combination of interventions** delivered consistently at the population level, rather than reliance on any single measure in isolation.

Fill in the blank: Insecticide-treated bed nets are a key measure of _____ control in malaria prevention.

Figure 1.4: A child sleeping safely under an insecticide-treated bed net.

Pilot questions 1.4

1. Describe the first-line treatment for uncomplicated malaria and its rationale. (Linked to SLO 1.7)
2. Describe the first-line parenteral treatment for severe malaria. (Linked to SLO 1.7)
3. List two components of supportive care in severe malaria. (Linked to SLO 1.7)
4. Describe the role of insecticide-treated bed nets in malaria prevention. (Linked to SLO 1.8)
5. List two additional strategies for malaria prevention beyond bed nets. (Linked to SLO 1.8)

Series Summary

This Series introduced **malaria in children**, beginning with its epidemiology and the types of malaria parasite, before turning to its **pathophysiology**, including the mechanisms underlying severe disease.

We then examined the **clinical features and diagnosis of malaria**, including the specific features of severe malaria, before concluding with its **management, prevention, and control**. Having worked through this Series, you should now be able to recognise, diagnose, manage, and help prevent malaria in children. The next Series turns to **measles and pertussis**.

Glossary of Terms

- **Plasmodium falciparum:** the malaria species responsible for the majority of severe disease and death in sub-Saharan Africa.
- **Sporozoite:** the form of the malaria parasite injected into the bloodstream by a mosquito bite.
- **Merozoite:** the form of the malaria parasite released from infected liver or red blood cells to invade further cells.
- **Cytoadherence:** the adherence of infected red blood cells to small blood vessel walls, central to severe malaria pathophysiology.
- **Cerebral malaria:** severe malaria with impaired consciousness or coma resulting from cerebral microvascular involvement.
- **Uncomplicated malaria:** malaria in a systemically well child, without features of severe disease.
- **Severe malaria:** malaria with one or more specific features of significant organ dysfunction.
- **Rapid diagnostic test:** a test detecting malaria parasite antigens, providing a result within minutes.

- **Artemisinin-based combination therapy:** the first-line oral treatment for uncomplicated malaria in areas of drug resistance.
- **Intravenous artesunate:** the preferred first-line parenteral treatment for severe malaria.
- **Insecticide-treated bed net:** a key vector control intervention for malaria prevention.
- **Seasonal malaria chemoprevention:** a preventive medication strategy used in areas of highly seasonal malaria transmission.

Concept Check Questions [Series 1]

Objective questions

1. Malaria is transmitted to humans through the bite of an infected female _____ mosquito.
2. Plasmodium falciparum is responsible for the great majority of _____ disease and death in sub-Saharan Africa.
3. Cytoadherence describes infected red blood cells adhering to the walls of small _____ vessels.
4. Impaired consciousness or coma resulting from severe malaria is specifically termed _____ malaria.
5. Intravenous _____ is now the preferred first-line parenteral treatment for severe malaria in most settings.

Short-answer questions

6. List the five species of Plasmodium that infect humans.
7. Describe the liver and blood stages of the malaria life cycle.
8. List four features that define severe malaria.
9. Describe the two main methods of parasitological confirmation of malaria.
10. Describe the role of insecticide-treated bed nets in malaria prevention.

Long-answer questions

11. Discuss the epidemiology and types of malaria affecting children. (Linked to SLO 1.1, SLO 1.2)
12. Discuss the pathophysiology of uncomplicated and severe malaria. (Linked to SLO 1.3)
13. Discuss the clinical features and diagnosis of malaria, including severe malaria. (Linked to SLO 1.4, SLO 1.5, SLO 1.6)
14. Discuss the management of uncomplicated and severe malaria. (Linked to SLO 1.7)
15. Discuss the prevention and control of malaria. (Linked to SLO 1.8)

Answers to Concept Check Questions [Series 1]

Objective questions

1. Anopheles.
2. Severe.
3. Blood.
4. Cerebral.
5. Artesunate.

Short-answer questions

6. Plasmodium falciparum, vivax, ovale, malariae, and knowlesi.
7. The liver stage is a silent, asexual multiplication phase, while the blood stage involves red cell invasion, rupture, and the resulting clinical symptoms.
8. Impaired consciousness, repeated seizures, severe anaemia, and respiratory distress.
9. Microscopy of a blood film, and rapid diagnostic testing for parasite antigens.
10. They substantially reduce malaria transmission and child mortality when used consistently as a vector control measure.

Long-answer questions

11. **Basic response:** Malaria disproportionately affects children under five, particularly in high transmission areas, and is caused by five Plasmodium species, with falciparum responsible for most severe disease.

Value-added response: Uncomplicated and severe malaria are distinguished clinically, a distinction with direct implications for the urgency and setting of treatment required.

12. **Basic response:** The liver stage is clinically silent, while the blood stage causes fever through cytokine release from cyclical red cell rupture; severe disease involves cytoadherence causing microvascular obstruction.

Value-added response: Cytoadherence in the cerebral microvasculature underlies cerebral malaria, while metabolic derangements such as hypoglycaemia and acidosis contribute to the broader picture of severe disease.

13. **Basic response:** Uncomplicated malaria presents with fever, chills, and malaise, while severe malaria is defined by features such as impaired consciousness, severe anaemia, and hypoglycaemia, confirmed by microscopy or rapid testing.

Value-added response: Prompt recognition of severe features is critical since deterioration can occur within hours, and further investigations assess the extent of organ involvement once severe disease is suspected.

14. **Basic response:** Uncomplicated malaria is managed with artemisinin-based combination therapy, while severe malaria requires hospital admission and intravenous artesunate with supportive care.

Value-added response: Supportive care in severe malaria addresses specific complications, including hypoglycaemia correction, careful fluid management, and transfusion for severe anaemia.

15. **Basic response:** Prevention centres on vector control, particularly insecticide-treated bed nets, alongside indoor residual spraying and environmental management.

Value-added response: Chemoprevention strategies and the malaria vaccine provide additional protection, with effective control depending on a combination of interventions rather than any single measure.

Answers to Pilot Questions [Series 1]

Part 1.1

1. Malaria is transmitted through the bite of an infected female Anopheles mosquito.
2. Plasmodium falciparum, vivax, ovale, malariae, and knowlesi are the five species.
3. Plasmodium falciparum is responsible for the majority of severe malaria in sub-Saharan Africa.
4. Uncomplicated malaria is systemic illness without severe features; severe malaria has specific organ dysfunction features.
5. They lack the partial immunity that develops with repeated exposure over time.

Part 1.2

1. The liver stage is a silent phase of asexual multiplication; the blood stage involves red cell invasion and rupture causing symptoms.
2. Cyclical rupture of infected red cells releases pyrogenic cytokines, causing fever.
3. Direct destruction of infected red cells and increased splenic clearance contribute to anaemia.
4. Cytoadherence is infected red cells adhering to small vessel walls, obstructing microvascular flow in severe malaria.
5. Cytoadherence within the cerebral microvasculature obstructs flow and contributes to cerebral malaria.

Part 1.3

1. Fever, chills, headache, myalgia, and vomiting are features of uncomplicated malaria.
2. Impaired consciousness, repeated seizures, severe anaemia, and respiratory distress define severe malaria.
3. Severe malaria can progress rapidly, so delayed recognition risks significant deterioration within hours.
4. Microscopy of a blood film and rapid diagnostic testing are the two main confirmation methods.
5. Full blood count and blood glucose are investigations performed in suspected severe malaria.

Part 1.4

1. Artemisinin-based combination therapy is first-line, combining rapid and longer-acting components to clear infection and limit resistance.
2. Intravenous artesunate is the preferred first-line parenteral treatment for severe malaria.
3. Correction of hypoglycaemia and careful fluid management are components of supportive care.
4. Insecticide-treated bed nets substantially reduce transmission and child mortality as a vector control measure.
5. Indoor residual spraying and chemoprevention strategies are additional prevention measures.

- Kliegman, R. M., St Geme, J. W., Blum, N. J., Shah, S. S., Tasker, R. C. and Wilson, K. M. (2020). Nelson Textbook of Pediatrics (21st ed.). Elsevier.
- World Health Organization (2023). Guidelines for Malaria. WHO Press.
- World Health Organization (2015). Severe Malaria. Tropical Medicine and International Health, 19(Supplement 1), 7 to 131.
- Federal Ministry of Health, Nigeria (2020). National Guidelines for Diagnosis and Treatment of Malaria.

Figures, Plates, Tables, and Boxes

- Figure 1.1: An Anopheles mosquito feeding, the vector responsible for malaria transmission. AI-generated using the prompt: "A realistic, detailed biological illustration of a single female Anopheles mosquito shown feeding, with clear anatomical detail of its wings, legs, and characteristic tilted feeding posture. Single clean scientific illustration, plain neutral background, no text overlays, no multiple panels, accurate entomological detail."
- Figure 1.2: A blood film showing red blood cells infected with malaria parasites. AI-generated using the prompt: "A realistic microscopy-style illustration of a Giemsa-stained peripheral blood film showing red blood cells, several containing visible ring-form malaria parasites. Single clean scientific illustration in the style of a microscope image, plain neutral background, no text overlays, no multiple panels, accurate haematological detail."
- Table 1.3: World Health Organization criteria for severe malaria. AI-generated using the prompt: "Create a clean reference table titled WHO Criteria for Severe Malaria, listing feature and description. Simple clinical reference table style with outside border."
- Figure 1.4: A child sleeping safely under an insecticide-treated bed net. AI-generated using the prompt: "A warm, realistic illustration of a young child sleeping peacefully on a simple bed, fully covered and protected by a properly hung insecticide-treated mosquito net. Single clean illustration, soft calm lighting, no text overlays, no multiple panels, respectful and accurate depiction."

Course code: PAE 511

Course title: Specific Infectious Diseases

Course credit load: 2 Units

Series 2: Measles and Pertussis

- **Part 2.1: Measles: Aetiology, Epidemiology, and Clinical Phases**
  - Sub Part 2.1.1: Aetiology and epidemiology of measles
  - Sub Part 2.1.2: Clinical phases of measles
  - Sub Part 2.1.3: Complications of measles
- **Part 2.2: Evaluation, Management, and Prevention of Measles**
  - Sub Part 2.2.1: Differential diagnosis and evaluation of measles
  - Sub Part 2.2.2: Management of measles
  - Sub Part 2.2.3: Prevention of measles using the five levels of prevention
- **Part 2.3: Pertussis: Aetiology, Pathophysiology, and Clinical Features**
  - Sub Part 2.3.1: Aetiology, epidemiology, and pathophysiology of pertussis
  - Sub Part 2.3.2: Clinical phases of pertussis
  - Sub Part 2.3.3: Differential diagnosis and complications of pertussis
- **Part 2.4: Diagnosis, Management, and Prevention of Pertussis**
  - Sub Part 2.4.1: Investigation and diagnosis of pertussis
  - Sub Part 2.4.2: Management of pertussis
  - Sub Part 2.4.3: Prevention of pertussis

Introduction

In the last Series, we explored malaria, one of the most common causes of childhood febrile illness. We now turn to two highly contagious, vaccine-preventable respiratory infections, measles and pertussis. Picture a two year old, unimmunised, presenting with several days of fever and cough, who then develops a characteristic rash spreading from the face downward, alongside a different infant with weeks of a distinctive, severe coughing illness ending in a characteristic whooping sound. Both conditions, though caused by different organisms, remain

important causes of childhood morbidity and mortality where vaccination coverage is incomplete.

The aim of this Series is to equip you with the knowledge required to recognise, diagnose, manage, and prevent measles and pertussis in children.

This Series begins with the **aetiology, epidemiology, and clinical phases of measles**, before turning to its **evaluation, management, and prevention**. Next, we examine the **aetiology, pathophysiology, and clinical features of pertussis**, before concluding with its **diagnosis, management, and prevention**.

Series Learning Outcomes

At the end of this Series, you should be able to:

- **SLO 1.1:** describe the aetiology of measles infection,
- **SLO 1.2:** enumerate the risk factors and epidemiology of measles, and identify the measles rash,
- **SLO 1.3:** list the clinical phases of measles and the features seen in each phase,
- **SLO 1.4:** list the differential diagnosis of measles, and assess and manage a child with measles,
- **SLO 1.5:** enumerate the prevention of measles using the 5 levels of prevention,
- **SLO 1.6:** describe the aetiology, epidemiology, pathophysiology, phases, and clinical features of pertussis,
- **SLO 1.7:** list the differential diagnosis and complications of pertussis, and
- **SLO 1.8:** describe the investigation, diagnosis, management, and prevention of pertussis.

2.1 Measles: Aetiology, Epidemiology, and Clinical Phases

2.1.1 aetiology and epidemiology of measles

One of the most contagious diseases known

Measles is caused by the **measles virus**, a member of the **Morbillivirus** genus, and is transmitted through **respiratory droplets** and **airborne spread**, making it one of the most highly **contagious** infectious diseases known, with a single infected child capable of transmitting the virus to a large proportion of susceptible contacts in a shared environment.

Measles remains an important cause of childhood morbidity and mortality in settings with **incomplete vaccination coverage**, with **risk factors** for infection and severe disease including **lack of immunisation**, **young age**, particularly infants too young to have completed the routine vaccination schedule, **malnutrition**, and **vitamin A deficiency**, the last of which is specifically associated with more severe disease and a higher risk of complications.

Fill in the blank: Measles is transmitted through respiratory droplets and _____ spread.

2.1.2 clinical phases of measles

The clinical course of measles progresses through recognisable **phases**. The **incubation period**, typically **10 to 14 days**, is followed by the **prodromal phase**, lasting 2 to 4 days and characterised by fever together with the classic triad of **cough**, **coryza**, and **conjunctivitis**, sometimes remembered as the three **Cs**, during which the pathognomonic **Koplik spots**, small white spots on an erythematous base on the buccal mucosa, may be seen shortly before the rash appears.

The **exanthem phase** follows, marked by the appearance of a characteristic **maculopapular rash**, which classically begins on the **face** and **hairline** before spreading **downward** to involve the trunk and limbs over several days, with fever often peaking around the time the rash appears, and the rash itself typically **fading in the same order it appeared**, from face to extremities, over the following week as the child recovers.

Fill in the blank: The prodromal phase of measles is characterised by the three Cs: cough, coryza, and _____.

2.1.3 complications of measles

Complications of measles are relatively common and include **otitis media**, the most common complication overall, **pneumonia**, the leading cause of measles-related death, **diarrhoea**, and, less commonly but more seriously, **acute encephalitis**, and, as a rare, delayed complication occurring years after the initial infection, **subacute sclerosing panencephalitis**, a progressive and fatal neurological condition.

Complications are considerably more common and more severe in children who are **malnourished**, **vitamin A deficient**, or otherwise **immunocompromised**, underscoring why measles, despite often being perceived as a mild, self-limiting childhood illness, remains a genuinely significant cause of death in vulnerable populations, particularly where vaccination coverage and general nutritional status are suboptimal.

Fill in the blank: Pneumonia is the leading cause of measles-related _____.

Figure 2.1: The characteristic maculopapular rash of measles.

Pilot questions 2.1

- Describe the causative organism and mode of transmission of measles. (Linked to SLO 2.1)
- List three risk factors for severe measles. (Linked to SLO 2.1)
- Describe the prodromal phase of measles, including Koplik spots. (Linked to SLO 2.2)
- Describe the distribution and evolution of the measles rash. (Linked to SLO 2.2)
- List three complications of measles. (Linked to SLO 2.1)

2.2 Evaluation, Management, and Prevention of Measles

2.2.1 differential diagnosis and evaluation of measles

Other rash-causing illnesses can mimic measles closely

The **differential diagnosis** of measles includes other causes of a **febrile rash illness** in children, such as **rubella**, generally milder with less prominent prodromal symptoms, **roseola infantum**,

in which the rash typically appears as the fever resolves rather than during the febrile period, **scarlet fever**, and **drug reactions**, meaning careful attention to the specific **pattern and timing** of fever, prodromal symptoms, and rash evolution is important in distinguishing measles from these alternative diagnoses.

Evaluation of a child with suspected measles should establish **immunisation status**, the **timing and pattern** of symptoms, and actively assess for evidence of **complications**, particularly examining for signs of pneumonia or otitis media, together with assessment of **nutritional status**, given the strong relationship between malnutrition, vitamin A deficiency, and complication risk discussed in the previous Part.

Fill in the blank: Roseola infantum typically has the rash appear as the fever _____, unlike measles.

2.2.2 management of measles

Management of uncomplicated measles is largely **supportive**, including **antipyretics**, adequate **hydration**, and continued **nutritional support**, and **vitamin A supplementation** is recommended for all children diagnosed with measles, regardless of apparent nutritional status, since it has been shown to reduce the severity of illness and the risk of measles-related complications and mortality, particularly in vitamin A deficient populations.

Children with identified **complications**, such as pneumonia or otitis media, require **specific treatment** directed at that complication, and any child with **severe disease**, evidence of **encephalitis**, or significant **dehydration** requires **hospital admission** for closer monitoring and more intensive supportive care, with isolation precautions maintained throughout given the highly contagious nature of the infection.

Fill in the blank: Vitamin _____ supplementation is recommended for all children diagnosed with measles.

2.2.3 prevention of measles using the five levels of prevention

Primordial and primary prevention of measles centre on **routine childhood immunisation** with the **measles-containing vaccine**, generally given as part of a combined vaccine, at the recommended schedule ages, together with broader public health measures to maintain high population **vaccination coverage**, since sustained high coverage is required to achieve **herd immunity** and interrupt ongoing transmission within a community.

Secondary prevention includes prompt recognition and, where indicated, **post-exposure prophylaxis** with vaccine or immunoglobulin in susceptible contacts, **tertiary prevention**

focuses on managing complications to minimise lasting harm, and **quaternary prevention** involves avoiding unnecessary intervention in straightforward, uncomplicated cases, together forming a comprehensive framework for reducing the overall burden of measles at both the individual and population level.

Fill in the blank: Sustained high vaccination coverage is required to achieve _____ immunity and interrupt measles transmission.

Table 2.2: The five levels of prevention applied to measles.

Level of prevention	Example applied to measles
Primordial	Public health measures supporting high population vaccination coverage
Primary	Routine measles-containing vaccine immunisation
Secondary	Post-exposure prophylaxis in susceptible contacts
Tertiary	Treatment of complications such as pneumonia or otitis media
Quaternary	Avoiding unnecessary intervention in uncomplicated cases

Pilot questions 2.2

1. List two conditions in the differential diagnosis of measles. (Linked to SLO 2.4)
2. Describe the key components of evaluating a child with suspected measles. (Linked to SLO 2.4)
3. Describe the general management of uncomplicated measles. (Linked to SLO 2.4)
4. Explain the rationale for vitamin A supplementation in measles. (Linked to SLO 2.4)
5. List the five levels of prevention as applied to measles. (Linked to SLO 2.5)

2.3 Pertussis: Aetiology, Pathophysiology, and Clinical Features

2.3.1 aetiology, epidemiology, and pathophysiology of pertussis

A toxin-mediated cough illness of striking duration

Pertussis, or **whooping cough**, is caused by ***Bordetella pertussis***, a **Gram-negative bacterium** transmitted through **respiratory droplets**, and remains an important cause of prolonged cough illness in children, particularly severe and potentially life-threatening in **young, incompletely immunised infants**, who are at greatest risk of the severe complications discussed later in this Series.

The organism attaches to and damages the **ciliated respiratory epithelium**, impairing normal mucus clearance, while its **pertussis toxin** and other **virulence factors** contribute to the characteristic, prolonged cough illness through a combination of direct local tissue damage and systemic effects, a pathophysiological process that explains why the cough of pertussis is typically far more prolonged and severe than that of a straightforward viral upper respiratory infection.

Fill in the blank: Pertussis is caused by Bordetella pertussis, a _____-negative bacterium.

2.3.2 clinical phases of pertussis

Pertussis progresses through three recognisable clinical phases. The **catarrhal phase**, lasting 1 to 2 weeks, resembles a mild upper respiratory infection with coryza and a mild cough, during which the child is highly **contagious** but not yet recognisably unwell with pertussis specifically, making early identification and isolation genuinely difficult at this stage.

The **paroxysmal phase** follows, lasting several weeks, and is characterised by severe, **paroxysmal coughing fits**, often ending in a characteristic **inspiratory whoop** as the child gasps for air after a coughing spell, and frequently followed by **post-tussive vomiting**, with young infants at particular risk of **apnoea** during severe paroxysms rather than the classic whoop, which is less commonly heard in this age group. The **convalescent phase** follows, over subsequent weeks to months, during which the frequency and severity of coughing episodes gradually diminish.

Fill in the blank: The paroxysmal phase of pertussis often ends in a characteristic inspiratory _____.

2.3.3 differential diagnosis and complications of pertussis

The **differential diagnosis** of a prolonged cough illness resembling pertussis includes other causes of **chronic cough** in children, such as **viral bronchiolitis** or **bronchitis**, **foreign body aspiration**, particularly where cough has a sudden onset, and infection with other organisms capable of producing a similar pertussis-like syndrome, such as ***Bordetella parapertussis*** or certain **adenoviruses**, meaning a careful history of the specific cough pattern and its evolution over time is important in distinguishing these possibilities.

Complications of pertussis include **pneumonia**, the most common serious complication and leading cause of pertussis-related death, **seizures**, related to hypoxia during severe coughing paroxysms or apnoeic episodes, and, less commonly, **encephalopathy**, with young, unimmunised or incompletely immunised infants again facing the highest risk of these severe

complications, reinforcing the particular clinical importance of pertussis in this specific age group.

Fill in the blank: Pneumonia is the most common serious complication and leading cause of pertussis-related _____.

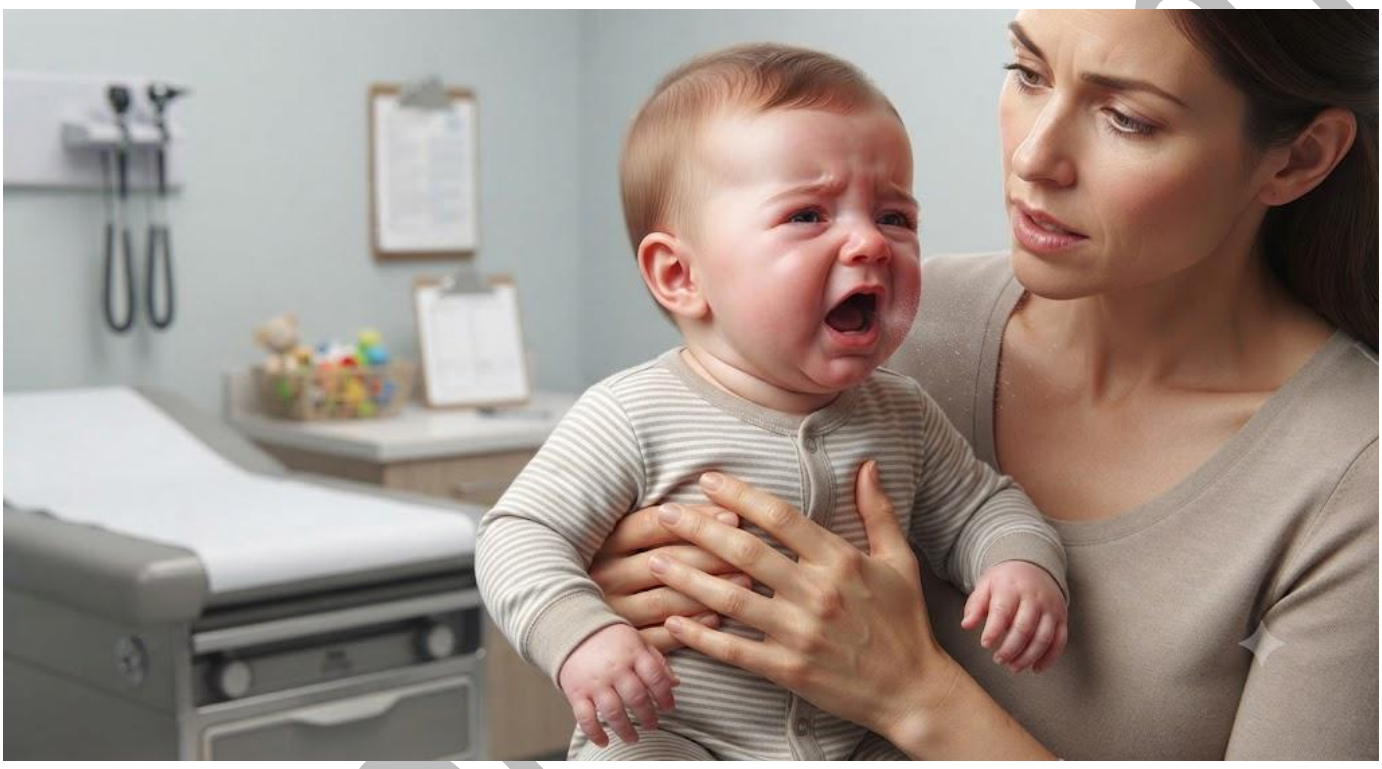

Figure 2.3: An infant experiencing a paroxysmal coughing episode characteristic of pertussis.

Pilot questions 2.3

1. Describe the causative organism and mode of transmission of pertussis. (Linked to SLO 2.6)
2. Describe the mechanism by which pertussis toxin contributes to the clinical illness. (Linked to SLO 2.6)
3. List and describe the three clinical phases of pertussis. (Linked to SLO 2.6)
4. Explain why young infants may present with apnoea rather than the classic whoop. (Linked to SLO 2.6)
5. List two complications of pertussis. (Linked to SLO 2.7)

2.4 Diagnosis, Management, and Prevention of Pertussis

2.4.1 investigation and diagnosis of pertussis

Timing of testing strongly affects diagnostic yield

Diagnosis of pertussis is supported by **nasopharyngeal swab** testing, with **polymerase chain reaction**, or **PCR**, now the preferred laboratory method given its greater sensitivity compared with traditional **bacterial culture**, particularly important since culture sensitivity declines considerably as the illness progresses beyond the early catarrhal phase, meaning the timing of sample collection relative to symptom onset significantly affects diagnostic yield.

A **full blood count** may show a characteristic **lymphocytosis**, particularly in young children, providing additional supportive evidence, though the diagnosis in a child with a classic clinical history and known local pertussis activity is often made **clinically**, particularly where laboratory confirmation is delayed or unavailable, since a strong clinical suspicion should not be dismissed simply because a specific test result is pending or negative given the described limitations of testing sensitivity over time.

Fill in the blank: Polymerase chain reaction, or PCR, is the preferred laboratory method for diagnosing _____.

2.4.2 management of pertussis

Antibiotic therapy, typically with a **macrolide** such as azithromycin, is used to treat pertussis and reduce the period of **infectivity**, though it has limited effect on the duration or severity of the cough itself once the paroxysmal phase has been established, meaning antibiotics are most beneficial for reducing transmission to others rather than providing dramatic symptomatic relief to the affected child at this stage of illness.

Supportive care is central to management, particularly in young infants, who often require **hospital admission** for close monitoring given their risk of **apnoea** and significant respiratory compromise during severe paroxysms, together with careful attention to **hydration** and **nutrition**, given the impact of frequent coughing and post-tussive vomiting on adequate oral intake in an unwell infant.

Fill in the blank: A macrolide antibiotic such as azithromycin reduces the period of _____ in pertussis.

2.4.3 prevention of pertussis

Prevention of pertussis relies principally on **routine childhood immunisation** with a **pertussis-containing vaccine**, given as part of the combined vaccination schedule, together with a **maternal pertussis vaccination** strategy during pregnancy in many settings, which provides passive antibody protection to the infant during the particularly vulnerable early months of life before the infant's own vaccination series has been completed.

Post-exposure prophylaxis with antibiotics may be offered to close contacts, particularly young infants and pregnant women, following exposure to a confirmed case, and, given the recognised phenomenon of **waning immunity** over time following both natural infection and vaccination, **booster doses** at defined intervals throughout childhood and adolescence remain an important component of a comprehensive, sustained prevention strategy.

Fill in the blank: A booster dose strategy addresses the recognised phenomenon of waning _____ over time.

Figure 2.4: An infant receiving a routine pertussis-containing vaccine.

Pilot questions 2.4

1. Describe the preferred laboratory method for diagnosing pertussis and its limitation. (Linked to SLO 2.8)
2. Describe the role of antibiotic therapy in the management of pertussis. (Linked to SLO 2.8)
3. Explain why young infants with pertussis often require hospital admission. (Linked to SLO 2.8)
4. Describe the role of maternal pertussis vaccination during pregnancy. (Linked to SLO 2.8)
5. Explain the rationale for booster doses of pertussis-containing vaccine. (Linked to SLO 2.8)

Series Summary

This Series examined **measles**, beginning with its aetiology, epidemiology, and clinical phases, before turning to its **evaluation, management, and prevention** using the five levels of prevention.

We then examined **pertussis**, its aetiology, pathophysiology, and clinical phases, before concluding with its **diagnosis, management, and prevention**. Having worked through this Series, you should now be able to recognise, diagnose, manage, and help prevent measles and pertussis in children. The next Series turns to **poliomyelitis and tetanus**.

Glossary of Terms

1. **Koplik spots:** small white spots on an erythematous base on the buccal mucosa, pathognomonic for measles.
2. **Exanthem phase:** the phase of measles marked by the appearance of the characteristic maculopapular rash.
3. **Subacute sclerosing panencephalitis:** a rare, delayed, progressive, and fatal neurological complication of measles.
4. **Herd immunity:** population-level immunity sufficient to interrupt ongoing disease transmission.

5. **Bordetella pertussis:** the Gram-negative bacterium that causes pertussis.
6. **Catarrhal phase:** the first phase of pertussis, resembling a mild upper respiratory infection.
7. **Paroxysmal phase:** the phase of pertussis characterised by severe coughing fits, often ending in a whoop.
8. **Inspiratory whoop:** the characteristic gasping sound following a pertussis coughing paroxysm.
9. **Post-tussive vomiting:** vomiting following a coughing episode, common in pertussis.
10. **Polymerase chain reaction:** the preferred laboratory method for diagnosing pertussis.
11. **Macrolide:** a class of antibiotic, such as azithromycin, used to treat pertussis and reduce infectivity.
12. **Maternal pertussis vaccination:** vaccination during pregnancy that provides passive antibody protection to the infant.

Concept Check Questions [Series 2]

Objective questions

- Measles is transmitted through respiratory droplets and _____ spread.
- The prodromal phase of measles is characterised by the three Cs: cough, coryza, and _____.
- Vitamin _____ supplementation is recommended for all children diagnosed with measles.
- Pertussis is caused by Bordetella pertussis, a _____-negative bacterium.
- The paroxysmal phase of pertussis often ends in a characteristic inspiratory _____.

Short-answer questions

1. List three risk factors for severe measles.
2. Describe the distribution and evolution of the measles rash.
3. List the five levels of prevention as applied to measles.
4. List and briefly describe the three clinical phases of pertussis.
5. Describe the role of antibiotic therapy in the management of pertussis.

Long-answer questions

6. Discuss the aetiology, epidemiology, and clinical phases of measles. (Linked to SLO 2.1, SLO 2.2)
7. Discuss the evaluation, management, and prevention of measles. (Linked to SLO 2.4, SLO 2.5)
8. Discuss the aetiology, pathophysiology, and clinical phases of pertussis. (Linked to SLO 2.6)
9. Discuss the differential diagnosis and complications of pertussis. (Linked to SLO 2.7)
10. Discuss the diagnosis, management, and prevention of pertussis. (Linked to SLO 2.8)

Answers to Concept Check Questions [Series 2]

Objective questions

11. Airborne.
12. Conjunctivitis.
13. A.
14. Gram.
15. Whoop.

Short-answer questions

16. Lack of immunisation, young age, and malnutrition or vitamin A deficiency.
17. The rash begins on the face and hairline, spreads downward to the trunk and limbs, and fades in the same order it appeared.
18. Primordial, primary, secondary, tertiary, and quaternary prevention.
19. The catarrhal phase resembles a mild respiratory infection; the paroxysmal phase has severe coughing fits with whoop; the convalescent phase shows gradual improvement.
20. Antibiotics reduce the period of infectivity but have limited effect on cough duration once the paroxysmal phase is established.

Long-answer questions

21. **Basic response:** Measles is caused by the measles virus, spread by respiratory droplets, and progresses through incubation, prodromal, and exanthem phases, with Koplik spots and a characteristic descending rash.

Value-added response: Risk factors for severe disease include malnutrition and vitamin A deficiency, and complications include otitis media, pneumonia, and rare but serious encephalitis or subacute sclerosing panencephalitis.

22. **Basic response:** Evaluation of measles establishes immunisation status and assesses for complications, with management being largely supportive alongside vitamin A supplementation.

Value-added response: Prevention spans the five levels, from population vaccination coverage as primary prevention to treatment of complications as tertiary prevention.

23. **Basic response:** Pertussis is caused by Bordetella pertussis, damaging ciliated respiratory epithelium, and progresses through catarrhal, paroxysmal, and convalescent phases.

Value-added response: Young infants may present with apnoea rather than the classic whoop, reflecting their particular vulnerability to severe disease and complications.

24. **Basic response:** Differential diagnosis includes other causes of chronic cough, and complications include pneumonia, seizures, and encephalopathy, particularly in young, incompletely immunised infants.

Value-added response: PCR testing on a nasopharyngeal swab is the preferred diagnostic method, though sensitivity declines with time since symptom onset, so clinical diagnosis remains important.

25. **Basic response:** Management combines macrolide antibiotics to reduce infectivity with supportive care, particularly hospital admission for young infants at risk of apnoea.

Value-added response: Prevention relies on routine and maternal vaccination, post-exposure prophylaxis for contacts, and booster doses to address waning immunity over time.

Answers to Pilot Questions [Series 2]

Part 2.1

1. Measles virus is transmitted through respiratory droplets and airborne spread.
2. Lack of immunisation, young age, and malnutrition or vitamin A deficiency are risk factors.
3. The prodromal phase has fever, cough, coryza, and conjunctivitis, with Koplik spots appearing before the rash.

4. The rash begins on the face and hairline, spreads downward, and fades in the same order it appeared.
5. Otitis media, pneumonia, and diarrhoea are common complications of measles.

Part 2.2

6. Rubella and roseola infantum are conditions in the differential diagnosis.
7. Evaluation establishes immunisation status, symptom timing, and screens for complications and nutritional status.
8. Management of uncomplicated measles is supportive, with antipyretics, hydration, and nutritional support.
9. Vitamin A reduces the severity of illness and the risk of complications and mortality.
10. Primordial, primary, secondary, tertiary, and quaternary prevention are the five levels.

Part 2.3

11. Bordetella pertussis, a Gram-negative bacterium, is transmitted by respiratory droplets.
12. Pertussis toxin damages ciliated respiratory epithelium and contributes to the prolonged cough illness.
13. Catarrhal phase resembles a mild cold; paroxysmal phase has severe coughing fits with whoop; convalescent phase shows gradual recovery.
14. Young infants may have reduced respiratory reserve, presenting with apnoea rather than a classic whoop.
15. Pneumonia and seizures are complications of pertussis.

Part 2.4

1. PCR on a nasopharyngeal swab is preferred; sensitivity declines as illness progresses beyond the catarrhal phase.
2. Antibiotics reduce infectivity but have limited effect on established cough symptoms.
3. Young infants are at risk of apnoea and significant respiratory compromise during paroxysms.
4. Maternal vaccination during pregnancy provides passive antibody protection to the infant in early life.
5. Booster doses address waning immunity from natural infection or vaccination over time.

References and Attributions [Series 2]

1. Kliegman, R. M., St Geme, J. W., Blum, N. J., Shah, S. S., Tasker, R. C. and Wilson, K. M. (2020). Nelson Textbook of Pediatrics (21st ed.). Elsevier.
2. World Health Organization (2023). Measles Fact Sheet. WHO Press.
3. American Academy of Pediatrics (2021). Red Book: Report of the Committee on Infectious Diseases (32nd ed.). American Academy of Pediatrics.
4. World Health Organization (2015). Pertussis Vaccines: WHO Position Paper. Weekly Epidemiological Record, 90(35), 433 to 460.

Figures, Plates, Tables, and Boxes

1. Figure 2.1: The characteristic maculopapular rash of measles. AI-generated using the prompt: "A realistic, respectful clinical illustration of a child's face and upper body showing a widespread red maculopapular rash characteristic of measles. Single clean medical illustration, soft clinical lighting, no text overlays, no multiple panels, accurate and sensitively depicted."
2. Table 2.2: The five levels of prevention applied to measles. AI-generated using the prompt: "Create a clean reference table titled The Five Levels of Prevention Applied to Measles, listing level and example. Simple clinical reference table style with outside border."
3. Figure 2.3: An infant experiencing a paroxysmal coughing episode characteristic of pertussis. AI-generated using the prompt: "A realistic, respectful clinical illustration of a young infant experiencing a coughing episode while being gently supported upright by a caregiver in a clinical setting. Single clean medical illustration, soft clinical lighting, no text overlays, no multiple panels, sensitively and accurately depicted."
4. Figure 2.4: An infant receiving a routine pertussis-containing vaccine. AI-generated using the prompt: "A warm, realistic clinical illustration of a healthcare worker gently administering a vaccine injection to an infant's thigh, while the infant is comfortably held by a caregiver. Single clean medical illustration, soft warm lighting, no text overlays, no multiple panels, respectful and accurate depiction."

Course code: PAE 511

Course title: Specific Infectious Diseases

Course credit load: 2 Units

Series 3: Poliomyelitis and Tetanus

- **Part 3.1: Poliomyelitis: Aetiology, Epidemiology, and Pathophysiology**
  - Sub Part 3.1.1: Aetiology and epidemiology of poliomyelitis
  - Sub Part 3.1.2: Pathophysiology of poliovirus infection
  - Sub Part 3.1.3: Forms of poliovirus infection
- **Part 3.2: Clinical Features, Diagnosis, and Management of Poliomyelitis**
  - Sub Part 3.2.1: Clinical features and differential diagnosis of polio
  - Sub Part 3.2.2: Investigation and diagnosis of polio
  - Sub Part 3.2.3: Management and prevention of polio
- **Part 3.3: Tetanus: Aetiology, Types, and Pathophysiology**
  - Sub Part 3.3.1: Aetiology of tetanus
  - Sub Part 3.3.2: Types of tetanus
  - Sub Part 3.3.3: Pathology and pathophysiology of tetanus
- **Part 3.4: Clinical Features, Management, and Prevention of Tetanus**
  - Sub Part 3.4.1: Clinical features and differential diagnosis of tetanus
  - Sub Part 3.4.2: Principles of management of tetanus
  - Sub Part 3.4.3: Prevention of tetanus using the five levels of prevention

Introduction

In the last Series, we explored measles and pertussis. We now turn to two further vaccine-preventable diseases, poliomyelitis and tetanus, both capable of causing severe, disabling, or life-threatening neurological illness. Picture a young child with sudden onset of weakness in one leg following a febrile illness, in a community where polio vaccination coverage has been incomplete, alongside an older child who develops progressive jaw stiffness and muscle spasms following an unclean wound. Both conditions remain important causes of preventable childhood

disability and death in settings where vaccination and wound care practices are not consistently applied.

The aim of this Series is to equip you with the knowledge required to recognise, diagnose, manage, and prevent poliomyelitis and tetanus in children.

This Series begins with the **aetiology, epidemiology, and pathophysiology of poliomyelitis**, before turning to its **clinical features, diagnosis, and management**. Next, we examine the **aetiology, types, and pathophysiology of tetanus**, before concluding with its **clinical features, management, and prevention**.

Series Learning Outcomes

At the end of this Series, you should be able to:

- **SLO 1.1:** describe the aetiology, epidemiology, and risk factors for poliovirus infection,
- **SLO 1.2:** describe the pathophysiology and forms of poliovirus infection,
- **SLO 1.3:** describe the clinical features and differential diagnosis of poliomyelitis,
- **SLO 1.4:** describe the investigation, diagnosis, management, and prevention of polio using the 5 levels of prevention,
- **SLO 1.5:** describe the aetiology and types of tetanus infection,
- **SLO 1.6:** describe the pathology and pathophysiology of tetanus,
- **SLO 1.7:** recognise the clinical features and differential diagnosis of tetanus, and
- **SLO 1.8:** describe the principles of management and prevention of tetanus using the 5 levels of prevention.

3.1 Poliomyelitis: Aetiology, Epidemiology, and Pathophysiology

3.1.1 aetiology and epidemiology of poliomyelitis

A virus that mostly hides, but sometimes strikes the spinal cord

Poliomyelitis, or **polio**, is caused by **poliovirus**, an **enterovirus** transmitted primarily through the **faecal-oral route**, though respiratory droplet transmission can also occur, and remains a disease of continued global concern given the potential for **outbreaks** in areas with incomplete vaccination coverage, even as wild poliovirus transmission has been eliminated from the majority of countries worldwide through sustained immunisation efforts.

Risk factors for poliovirus infection and its more severe manifestations include **lack of immunisation**, **young age**, and residence in or travel to areas with **ongoing wild poliovirus transmission** or, less commonly, circulating **vaccine-derived poliovirus** in settings of low vaccination coverage, meaning a careful travel and immunisation history remains an important part of evaluating any child with a clinical presentation consistent with polio.

Fill in the blank: Poliovirus is an enterovirus transmitted primarily through the _____ route.

3.1.2 pathophysiology of poliovirus infection

Following ingestion, poliovirus initially replicates in the **oropharynx** and **gastrointestinal tract**, and in the majority of infected individuals, infection remains confined to this level, producing either **no symptoms** at all or a mild, non-specific illness, without the virus ever reaching the central nervous system, an outcome that occurs in the overwhelming majority of infections.

In a small proportion of infected individuals, the virus enters the **bloodstream** and subsequently invades the **central nervous system**, where it demonstrates a particular tropism for the **anterior horn cells** of the spinal cord, the motor neurons responsible for voluntary muscle control, and destruction of these specific cells produces the characteristic **flaccid paralysis** that defines paralytic poliomyelitis, discussed further in the next Part of this Series.

Fill in the blank: Poliovirus demonstrates a particular tropism for the anterior horn cells of the _____.

3.1.3 forms of poliovirus infection

Poliovirus infection presents across a spectrum of clinical severity. **Asymptomatic infection**, accounting for the great majority of cases, produces no clinical illness at all, while **abortive poliomyelitis** produces a mild, non-specific febrile illness without any neurological involvement, and **non-paralytic**, or **aseptic meningitis**, poliomyelitis involves the central nervous system and produces features of meningeal irritation without weakness.

Paralytic poliomyelitis, the least common but most feared form, occurs in only a small minority of infections and is characterised by **asymmetric flaccid paralysis**, typically affecting the **lower limbs** more than the upper limbs, and, in the most severe cases, can involve the **respiratory muscles**, producing life-threatening respiratory failure, or, rarely, the **bulbar muscles**, affecting swallowing and airway protection.

Fill in the blank: Paralytic poliomyelitis typically produces asymmetric flaccid paralysis affecting the _____ limbs more than the upper limbs.

Table 3.1: Forms of poliovirus infection by clinical severity.

Form	Description
Asymptomatic infection	No clinical illness; accounts for the majority of infections
Abortive poliomyelitis	Mild, non-specific febrile illness without neurological involvement
Non-paralytic poliomyelitis	Aseptic meningitis features without weakness
Paralytic poliomyelitis	Asymmetric flaccid paralysis, occurring in only a small minority of infections

Pilot questions 3.1

- Describe the causative organism and mode of transmission of polio. (Linked to SLO 3.1)
- List two risk factors for poliovirus infection. (Linked to SLO 3.1)
- Describe why most poliovirus infections do not involve the central nervous system. (Linked to SLO 3.2)
- Explain why poliovirus destruction of anterior horn cells causes flaccid paralysis. (Linked to SLO 3.2)
- List the four forms of poliovirus infection by severity. (Linked to SLO 3.3)

3.2 Clinical Features, Diagnosis, and Management of Poliomyelitis

3.2.1 clinical features and differential diagnosis of polio

Asymmetry and preserved sensation are important clues

Paralytic poliomyelitis classically presents with a **preceding febrile illness**, followed after a period of apparent improvement by the sudden onset of **asymmetric**, **flaccid weakness**, with **reduced or absent deep tendon reflexes** in the affected limb, and, importantly, **preserved sensation**, since polio affects only motor neurons and does not involve the sensory pathways, a feature that helps distinguish it from certain other causes of acute weakness.

The **differential diagnosis** of acute flaccid paralysis in a child includes **Guillain-Barré syndrome**, generally producing more symmetric weakness with sensory involvement, **transverse myelitis**, and **traumatic neuritis**, meaning careful clinical assessment of the **pattern** of weakness, presence or absence of sensory involvement, and relevant history is important in

distinguishing these possibilities, alongside appropriate laboratory confirmation discussed in the next sub-Part.

Fill in the blank: Polio characteristically causes weakness with preserved _____, since only motor neurons are affected.

3.2.2 investigation and diagnosis of polio

Any child presenting with **acute flaccid paralysis** should be investigated as a potential polio case given the public health importance of prompt identification, with **stool samples** collected for **viral culture** and, where available, **molecular testing**, ideally within 14 days of symptom onset when viral shedding is most reliably detected, since diagnostic yield declines considerably beyond this window.

Acute flaccid paralysis surveillance is a core component of global polio eradication efforts, meaning any case meeting the clinical case definition should be promptly reported to relevant public health authorities regardless of the eventual laboratory result, since timely reporting and investigation of every potential case is essential to detecting and responding to any ongoing or reintroduced poliovirus transmission.

Fill in the blank: Stool samples for polio testing should ideally be collected within _____ days of symptom onset.

3.2.3 management and prevention of polio

There is **no specific antiviral treatment** for poliovirus infection, meaning management is entirely **supportive**, including **respiratory support**, potentially including mechanical ventilation, where respiratory muscle involvement is present, and **rehabilitation**, including **physiotherapy**, for children with residual limb weakness, since many children with paralytic polio experience at least some degree of **permanent disability** despite optimal supportive care.

Prevention relies principally on **routine childhood immunisation** with either **oral polio vaccine** or **inactivated polio vaccine**, depending on local programme design, as **primary prevention**, together with sustained **surveillance** for acute flaccid paralysis as an important form of **secondary prevention**, and **tertiary prevention** through rehabilitation services for children with residual paralysis, together forming the comprehensive framework that has brought the world close to global polio eradication.

Fill in the blank: There is no specific _____ treatment for poliovirus infection, meaning management is entirely supportive.

Figure 3.2: A child receiving physiotherapy for residual limb weakness following poliomyelitis.

Pilot questions 3.2

1. Describe the classic clinical presentation of paralytic poliomyelitis. (Linked to SLO 3.3)
2. List two conditions in the differential diagnosis of acute flaccid paralysis. (Linked to SLO 3.3)
3. Describe the investigation of a child with suspected polio. (Linked to SLO 3.4)
4. Explain the importance of acute flaccid paralysis surveillance. (Linked to SLO 3.4)
5. Describe the general management and prevention of polio. (Linked to SLO 3.4)

3.3 Tetanus: Aetiology, Types, and Pathophysiology

3.3.1 aetiology of tetanus

A ubiquitous soil organism with a specific route of entry

Tetanus is caused by ***Clostridium tetani***, an **anaerobic**, **spore-forming** bacterium widely distributed in **soil** and animal faeces, which enters the body through a **wound**, most classically a **puncture wound** or an area of **devitalised tissue** that provides the anaerobic environment

required for spore germination and subsequent toxin production, though in some cases no clear entry wound can be identified.

Unlike many infectious diseases, tetanus is **not transmitted from person to person**, since the disease results entirely from **local toxin production** at the site of wound contamination rather than from systemic bacterial spread, meaning isolation of an affected child is not required, though wound care and, where appropriate, immunisation of contacts remain relevant preventive considerations.

Fill in the blank: Clostridium tetani requires an _____ environment, such as a devitalised wound, for spore germination.

3.3.2 types of tetanus

Generalised tetanus, the most common and classic form, presents with widespread muscle rigidity and spasms affecting the whole body, while **localised tetanus** produces persistent muscle rigidity confined to the muscles near the wound site, generally a milder presentation that can occasionally progress to the generalised form if not adequately treated.

Cephalic tetanus, a rare form, results from a wound to the head or face and can affect cranial nerve function, sometimes producing facial weakness alongside trismus, and **neonatal tetanus**, discussed in detail in an earlier Series of this course in the context of umbilical cord contamination, represents a distinct and particularly serious presentation given the vulnerability of the newborn.

Fill in the blank: Cephalic tetanus results from a wound to the head or _____.

3.3.3 pathology and pathophysiology of tetanus

Once **Clostridium tetani** spores germinate within an anaerobic wound environment, the resulting vegetative bacteria produce the potent **exotoxin tetanospasmin**, which travels along **peripheral motor nerve axons** in a **retrograde** direction to reach the **central nervous system**, a transport process that explains the characteristic **incubation period** between wound contamination and the onset of clinical symptoms.

Within the central nervous system, tetanospasmin blocks release of the **inhibitory neurotransmitters glycine** and **gamma-aminobutyric acid**, removing normal inhibitory control over motor neurons and producing the **sustained, unopposed muscle contraction** that underlies the generalised rigidity and severe, often stimulus-triggered spasms characteristic of the disease, a mechanism essentially identical to that described for neonatal tetanus earlier in this course.

Fill in the blank: Tetanospasmin travels along peripheral motor nerve axons in a _____ direction to reach the central nervous system.

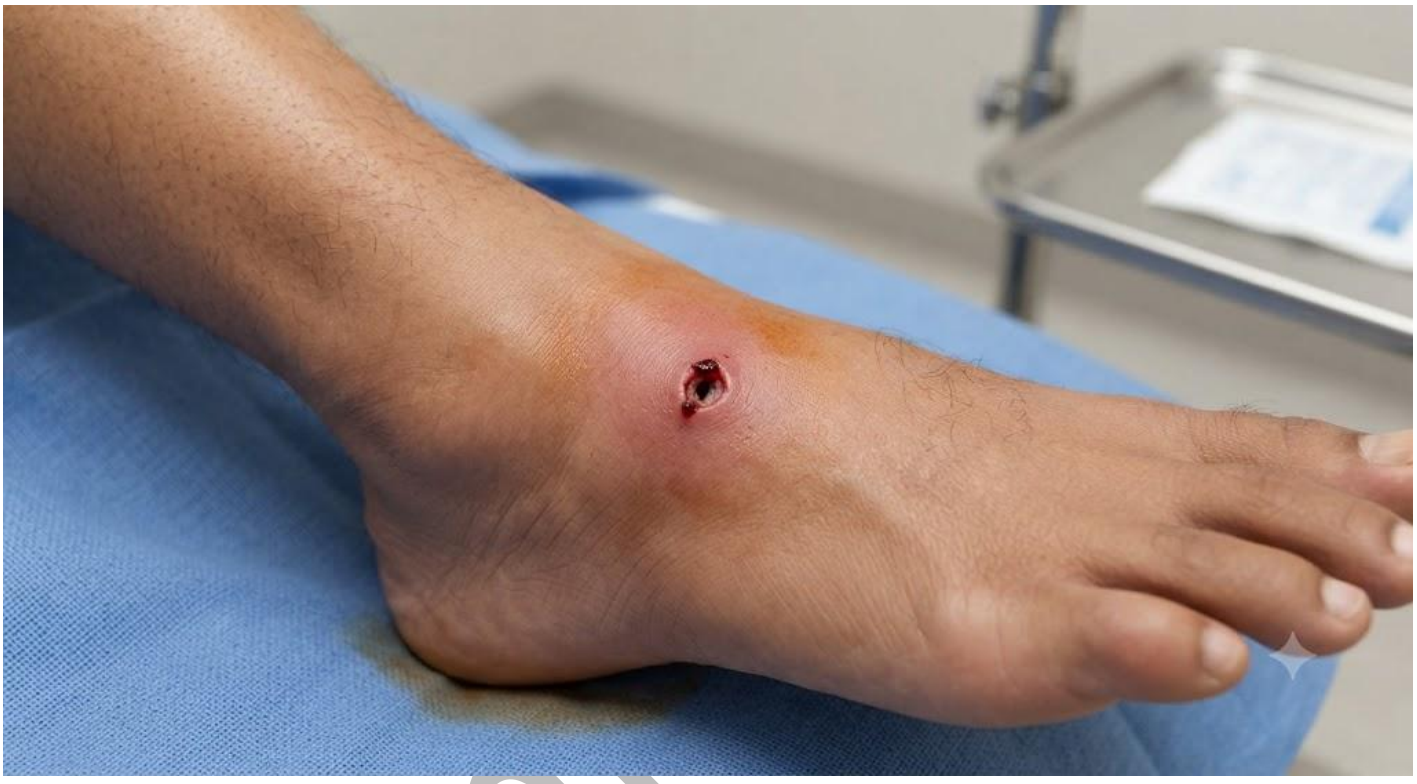

Figure 3.3: A deep puncture wound of the type associated with tetanus risk.

Pilot questions 3.3

1. Describe the causative organism of tetanus and its typical route of entry. (Linked to SLO 3.5)
2. Explain why tetanus is not transmitted from person to person. (Linked to SLO 3.5)
3. List and briefly describe the four types of tetanus. (Linked to SLO 3.5)
4. Describe the mechanism by which tetanospasmin reaches the central nervous system. (Linked to SLO 3.6)
5. Explain how tetanospasmin causes muscle rigidity and spasm. (Linked to SLO 3.6)

3.4 Clinical Features, Management, and Prevention of Tetanus

3.4.1 clinical features and differential diagnosis of tetanus

Trismus is often the first and most telling clue

The earliest and most characteristic feature of generalised tetanus is **trismus**, or **lockjaw**, resulting from rigidity of the muscles of mastication, followed by progressive **generalised muscle rigidity**, the characteristic facial appearance of **risus sardonicus**, and **opisthotonus**, together with intermittent, often severely painful **muscle spasms**, which may be spontaneous or triggered by minimal external stimuli such as noise, light, or touch.

The **differential diagnosis** of tetanus includes other causes of **trismus** or generalised rigidity, such as **dystonic drug reactions**, certain **strychnine poisoning**, and, in a child with prominent spasms, **hypocalcaemic tetany**, though the characteristic **preserved consciousness** throughout the illness, together with a relevant history of a recent wound and incomplete immunisation, generally allows a confident clinical diagnosis of tetanus to be made.

Fill in the blank: The earliest and most characteristic feature of generalised tetanus is trismus, or _____.

3.4.2 principles of management of tetanus

Management of tetanus requires **hospital admission**, ideally to an **intensive care setting** in significant disease, with care provided in a **quiet, minimally stimulating environment** to reduce the frequency of triggered spasms, together with **wound debridement** to remove the source of ongoing toxin production and **human tetanus immunoglobulin**, where available, to neutralise circulating, unbound toxin before it can bind to additional nerve tissue.

Antibiotic therapy, typically **metronidazole**, is given to eliminate the causative organism, **muscle relaxants**, such as **benzodiazepines**, are used to control rigidity and spasms, and, in the most severe cases with significant respiratory muscle involvement, **mechanical ventilation** may be required, with the overall duration of intensive supportive care often extending over several weeks given the prolonged natural course of established disease.

Fill in the blank: Human tetanus immunoglobulin is given to neutralise circulating, unbound _____.

3.4.3 prevention of tetanus using the five levels of prevention

Primary prevention of tetanus centres on **routine childhood immunisation** with a **tetanus-containing vaccine**, given as part of the combined vaccination schedule with periodic **booster doses** throughout childhood and into adulthood, since protective immunity from tetanus vaccination, unlike some other vaccines, does **wane over time** without ongoing boosting, together with appropriate **wound care** for any injury with tetanus risk.

Secondary prevention includes appropriate **post-exposure prophylaxis** following a tetanus-prone wound, guided by the individual's prior immunisation status and the nature of the wound itself, **tertiary prevention** focuses on intensive supportive care to minimise complications and mortality once disease has developed, and **quaternary prevention** involves avoiding excessive or unnecessary intervention once a child is recovering, together forming a comprehensive framework spanning the full course of potential tetanus exposure and illness.

Fill in the blank: Protective immunity from tetanus vaccination wanes over time without ongoing _____ doses.

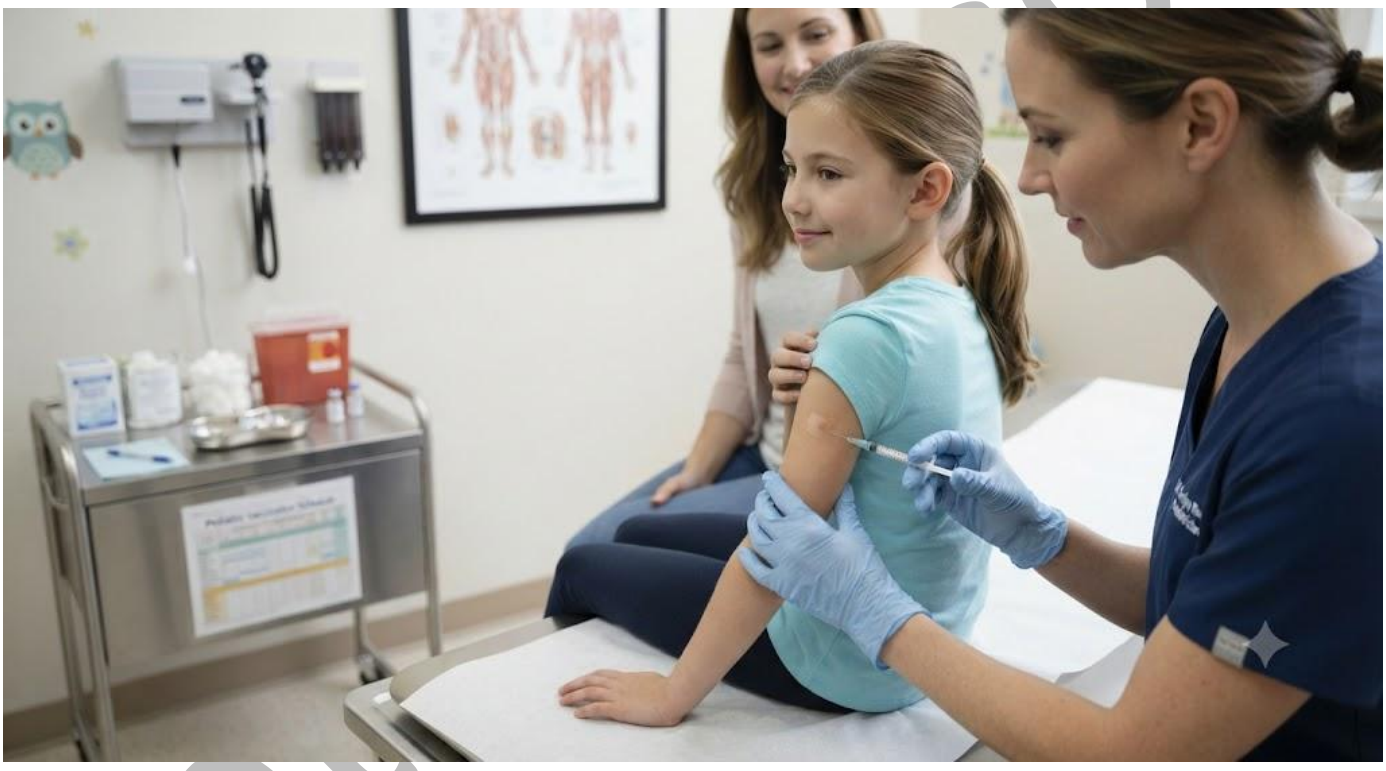

Figure 3.4: An older child receiving a routine tetanus-containing booster vaccine.

Pilot questions 3.4

1. Describe the classic clinical features of generalised tetanus. (Linked to SLO 3.7)
2. List two conditions in the differential diagnosis of tetanus. (Linked to SLO 3.7)
3. Describe the role of human tetanus immunoglobulin in management. (Linked to SLO 3.8)
4. Describe the supportive care required for severe tetanus. (Linked to SLO 3.8)
5. Explain why booster doses of tetanus vaccine are required throughout life. (Linked to SLO 3.8)

Series Summary

This Series examined **poliomyelitis**, beginning with its aetiology, epidemiology, and pathophysiology, before turning to its **clinical features, diagnosis, and management**.

We then examined **tetanus**, its aetiology, types, and pathophysiology, before concluding with its **clinical features, management, and prevention** using the five levels of prevention. Having worked through this Series, you should now be able to recognise, diagnose, manage, and help prevent poliomyelitis and tetanus in children. The next Series turns to **tuberculosis in children**.

Glossary of Terms

1. **Poliovirus:** the enterovirus that causes poliomyelitis, transmitted primarily via the faecal-oral route.
2. **Anterior horn cells:** the motor neurons of the spinal cord destroyed by poliovirus, causing flaccid paralysis.
3. **Paralytic poliomyelitis:** the form of polio infection producing asymmetric flaccid paralysis.
4. **Acute flaccid paralysis:** sudden onset limb weakness, the clinical case definition prompting polio investigation.
5. **Oral polio vaccine:** a live attenuated vaccine used in routine polio immunisation programmes.
6. **Clostridium tetani:** the anaerobic, spore-forming bacterium that causes tetanus.
7. **Generalised tetanus:** the most common form of tetanus, with widespread muscle rigidity and spasms.
8. **Cephalic tetanus:** a rare form of tetanus resulting from a wound to the head or face.
9. **Tetanospasmin:** the exotoxin produced by Clostridium tetani, responsible for the clinical features of tetanus.
10. **Trismus:** lockjaw, the earliest and most characteristic feature of generalised tetanus.
11. **Human tetanus immunoglobulin:** a treatment given to neutralise circulating, unbound tetanus toxin.
12. **Tetanus-containing vaccine:** a vaccine used for primary prevention of tetanus, requiring periodic booster doses.

Concept Check Questions [Series 3]

Objective questions

- Poliovirus is an enterovirus transmitted primarily through the _____ route.
- Paralytic poliomyelitis typically produces asymmetric flaccid paralysis affecting the _____ limbs more than the upper limbs.
- There is no specific _____ treatment for poliovirus infection, meaning management is entirely supportive.
- The earliest and most characteristic feature of generalised tetanus is trismus, or _____.
- Protective immunity from tetanus vaccination wanes over time without ongoing _____ doses.

Short-answer questions

1. Explain why most poliovirus infections do not involve the central nervous system.
2. List the four forms of poliovirus infection by severity.
3. List two conditions in the differential diagnosis of acute flaccid paralysis.
4. List and briefly describe the four types of tetanus.
5. Describe the role of human tetanus immunoglobulin in management.

Long-answer questions

6. Discuss the aetiology, epidemiology, and pathophysiology of poliomyelitis. (Linked to SLO 3.1, SLO 3.2)
7. Discuss the clinical features, diagnosis, and management of poliomyelitis. (Linked to SLO 3.3, SLO 3.4)
8. Discuss the aetiology, types, and pathophysiology of tetanus. (Linked to SLO 3.5, SLO 3.6)
9. Discuss the clinical features and differential diagnosis of tetanus. (Linked to SLO 3.7)
10. Discuss the management and prevention of tetanus using the five levels of prevention. (Linked to SLO 3.8)

Answers to Concept Check Questions [Series 3]

Objective questions

11. Faecal-oral.

12. Lower.
13. Antiviral.
14. Lockjaw.
15. Booster.

Short-answer questions

16. In most infections, the virus remains confined to the oropharynx and gastrointestinal tract without reaching the central nervous system.
17. Asymptomatic infection, abortive poliomyelitis, non-paralytic poliomyelitis, and paralytic poliomyelitis.
18. Guillain-Barré syndrome and transverse myelitis.
19. Generalised, localised, cephalic, and neonatal tetanus, differing by extent and site of involvement.
20. It neutralises circulating, unbound toxin before it can bind to additional nerve tissue.

Long-answer questions

21. **Basic response:** Poliovirus is a faecal-orally transmitted enterovirus that mostly causes asymptomatic or mild illness, but in a small proportion invades the CNS and destroys anterior horn cells.

Value-added response: This produces the four recognised forms of infection, from asymptomatic through to paralytic poliomyelitis, with asymmetric flaccid paralysis being the hallmark of the most severe form.

22. **Basic response:** Paralytic polio presents with asymmetric flaccid weakness and preserved sensation, diagnosed by stool sampling within 14 days, and managed supportively with rehabilitation for residual weakness.

Value-added response: Acute flaccid paralysis surveillance is essential for global eradication efforts, and prevention relies on routine immunisation as primary prevention.

23. **Basic response:** Tetanus is caused by Clostridium tetani entering through a wound, with generalised, localised, cephalic, and neonatal forms differing by extent and site of involvement.

Value-added response: Tetanospasmin travels retrograde along motor nerve axons to block inhibitory neurotransmission, causing the sustained muscle contraction characteristic of the disease.

24. **Basic response:** Generalised tetanus presents with trismus, rigidity, risus sardonicus, and opisthotonus, distinguished from other causes of rigidity by preserved consciousness and a relevant wound history.

Value-added response: Differential diagnoses include dystonic drug reactions and hypocalcaemic tetany, though the classic clinical picture usually allows confident diagnosis.

25. **Basic response:** Management includes wound debridement, human tetanus immunoglobulin, antibiotics, muscle relaxants, and supportive care in a minimally stimulating environment.

Value-added response: Prevention relies on routine and booster vaccination as primary prevention, since immunity wanes over time, together with post-exposure prophylaxis and wound care.

Answers to Pilot Questions [Series 3]

Part 3.1

1. Poliovirus is transmitted primarily through the faecal-oral route.
2. Lack of immunisation and residence in areas of ongoing transmission are risk factors.
3. The virus usually remains confined to the oropharynx and gastrointestinal tract without reaching the CNS.
4. Destruction of anterior horn cells, the spinal motor neurons, removes voluntary muscle control, causing flaccid paralysis.
5. Asymptomatic, abortive, non-paralytic, and paralytic poliomyelitis are the four forms.

Part 3.2

6. Preceding febrile illness followed by sudden asymmetric flaccid weakness with preserved sensation.
7. Guillain-Barré syndrome and transverse myelitis are in the differential diagnosis.
8. Stool samples are collected for viral culture or molecular testing, ideally within 14 days of onset.
9. It enables timely detection and response to ongoing or reintroduced poliovirus transmission.

10. Management is supportive, including respiratory support and rehabilitation; prevention relies on routine immunisation.

Part 3.3

11. Clostridium tetani, entering through a wound such as a puncture wound or devitalised tissue.
12. Disease results from local toxin production rather than systemic bacterial spread or person to person transmission.
13. Generalised, localised, cephalic, and neonatal tetanus, differing in extent and site of involvement.
14. Tetanospasmin travels along peripheral motor nerve axons in a retrograde direction to the CNS.
15. It blocks inhibitory neurotransmitters, causing sustained, unopposed muscle contraction.

Part 3.4

1. Trismus, generalised rigidity, risus sardonicus, opisthotonus, and painful spasms are classic features.
2. Dystonic drug reactions and hypocalcaemic tetany are in the differential diagnosis.
3. It neutralises circulating, unbound toxin before it binds to further nerve tissue.
4. A quiet, minimally stimulating environment, muscle relaxants, and, in severe cases, mechanical ventilation.
5. Protective immunity wanes over time, so booster doses maintain adequate protection throughout life.

References and Attributions [Series 3]

1. Kliegman, R. M., St Geme, J. W., Blum, N. J., Shah, S. S., Tasker, R. C. and Wilson, K. M. (2020). Nelson Textbook of Pediatrics (21st ed.). Elsevier.
2. World Health Organization (2023). Poliomyelitis Fact Sheet. WHO Press.
3. World Health Organization (2019). Tetanus Vaccines: WHO Position Paper. Weekly Epidemiological Record, 92(6), 53 to 76.
4. American Academy of Pediatrics (2021). Red Book: Report of the Committee on Infectious Diseases (32nd ed.). American Academy of Pediatrics.

Figures, Plates, Tables, and Boxes

1. Table 3.1: Forms of poliovirus infection by clinical severity. AI-generated using the prompt: "Create a clean reference table titled Forms of Poliovirus Infection, listing form and description. Simple clinical reference table style with outside border."
2. Figure 3.2: A child receiving physiotherapy for residual limb weakness following poliomyelitis. AI-generated using the prompt: "A respectful, realistic clinical illustration of a physiotherapist gently assisting a child with a leg exercise on a mat in a bright rehabilitation room. Single clean medical illustration, soft natural lighting, no text overlays, no multiple panels, dignified and accurate depiction."
3. Figure 3.3: A deep puncture wound of the type associated with tetanus risk. AI-generated using the prompt: "A realistic clinical illustration of a deep puncture wound on a person's foot or lower leg, shown clearly but without excessive graphic detail, appropriate for an educational medical context. Single clean medical illustration, neutral clinical lighting, no text overlays, no multiple panels, accurate and tastefully depicted."
4. Figure 3.4: An older child receiving a routine tetanus-containing booster vaccine. AI-generated using the prompt: "A realistic clinical illustration of a healthcare worker administering a vaccine injection into the upper arm of a calm older child seated on an examination table. Single clean medical illustration, soft clinical lighting, no text overlays, no multiple panels, respectful and accurate depiction."

Course code: PAE 511

Course title: Specific Infectious Diseases

Course credit load: 2 Units

Series 4: Tuberculosis in Children

- **Part 4.1: Definition, Classification, and Pathology of Tuberculosis**
  - Sub Part 4.1.1: Definition and classification of tuberculosis
  - Sub Part 4.1.2: Basic pathology of tuberculosis
  - Sub Part 4.1.3: Pathophysiology and immune response in tuberculosis
- **Part 4.2: Natural History and Clinical Features of Tuberculosis in Children**
  - Sub Part 4.2.1: Natural history of tuberculosis: the Wallgren timetable
  - Sub Part 4.2.2: Peculiarities of tuberculosis in children
  - Sub Part 4.2.3: Clinical features suggestive of tuberculosis in children
- **Part 4.3: Investigation and Diagnosis of Tuberculosis**
  - Sub Part 4.3.1: The tuberculin skin test and interferon-gamma release assay
  - Sub Part 4.3.2: Bacteriological and molecular investigation of tuberculosis
  - Sub Part 4.3.3: Clinical and radiological diagnosis of tuberculosis in children
- **Part 4.4: Management, Including DOTS, and Prevention of Tuberculosis**
  - Sub Part 4.4.1: Drugs used in the management of tuberculosis
  - Sub Part 4.4.2: Principles of management and DOTS
  - Sub Part 4.4.3: Prevention and control of tuberculosis using the five levels of prevention

Introduction

In the last Series, we explored poliomyelitis and tetanus. We now turn to tuberculosis, a disease that presents distinct diagnostic and management challenges in children compared with adults, since children often lack the classic, easily recognised features seen in adult pulmonary disease. Picture a four year old with several weeks of poor weight gain, low-grade fever, and a persistent cough, whose father was recently diagnosed with sputum-positive pulmonary tuberculosis.

Recognising the peculiarities of childhood tuberculosis, and understanding its diagnosis and management, is the focus of this Series.

The aim of this Series is to equip you with the knowledge required to define, classify, recognise, diagnose, manage, and help prevent tuberculosis in children.

This Series begins with the **definition, classification, and pathology of tuberculosis**, before turning to its **natural history and clinical features in children**. Next, we examine the **investigation and diagnosis of tuberculosis**, before concluding with its **management, including DOTS, and prevention**.

Series Learning Outcomes

At the end of this Series, you should be able to:

- **SLO 1.1:** define and classify tuberculosis infection,
- **SLO 1.2:** describe the basic pathology and pathophysiology of tuberculosis,
- **SLO 1.3:** describe the natural history of tuberculosis, including the Wallgren timetable,
- **SLO 1.4:** recognise the clinical features suggestive of tuberculosis in children,
- **SLO 1.5:** describe the investigation and diagnosis of tuberculosis,
- **SLO 1.6:** list the drugs used in the management of tuberculosis and their possible side effects,
- **SLO 1.7:** enumerate the principles of management of tuberculosis, including DOTS, and
- **SLO 1.8:** describe the prevention and control of tuberculosis using the 5 levels of prevention.

4.1 Definition, Classification, and Pathology of Tuberculosis

4.1.1 definition and classification of tuberculosis

Infection and disease are two distinct clinical states

Tuberculosis, or **TB**, is a chronic infectious disease caused by ***Mycobacterium tuberculosis***, an **acid-fast bacillus** transmitted primarily through inhalation of **respiratory droplet nuclei** from an infectious source case, typically an adult or older child with active pulmonary disease, and remains a leading cause of infectious disease morbidity and mortality worldwide, with children bearing a disproportionate share of the burden in high-incidence settings such as

Nigeria, where household exposure to an infectious adult is frequently the source of paediatric infection.

TB is classified into **latent tuberculosis infection**, in which the bacteria are present within the body in a **dormant state**, controlled by the host immune response, without any clinical illness or radiographic abnormality, and **active tuberculosis disease**, in which the bacteria are actively multiplying and causing clinical illness, a distinction of central importance since the two states differ considerably in their infectiousness, required investigation, and treatment approach, and since only a proportion of individuals with latent infection will ever progress to active disease over their lifetime.

Fill in the blank: Tuberculosis is caused by Mycobacterium tuberculosis, an _____-fast bacillus.

4.1.2 basic pathology of tuberculosis

Following inhalation, ***Mycobacterium tuberculosis*** organisms are engulfed by **alveolar macrophages**, within which the organism can survive and multiply owing to specific mechanisms that allow it to resist normal intracellular killing, and this initial host-pathogen interaction triggers a characteristic **granulomatous inflammatory response**, in which immune cells aggregate around the infected macrophages in an attempt to contain the infection, forming the pathological hallmark lesion known as the **granuloma**, or **tubercle**.

The combination of the initial **lung parenchymal lesion**, termed the **Ghon focus**, together with involvement of the draining **regional lymph nodes**, is collectively termed the **primary complex**, or **Ghon complex**, and this primary complex, together with the pattern of subsequent bacterial spread, whether contained or progressing to active disease, forms the essential pathological foundation for understanding the natural history of tuberculosis discussed in the next Part of this Series.

Fill in the blank: The pathological hallmark lesion of TB, formed by immune cells aggregating around infected macrophages, is called the _____.

4.1.3 pathophysiology and immune response in tuberculosis

The outcome of initial infection depends heavily on the balance between the **host immune response** and the **bacterial burden and virulence**, with an effective **cell-mediated immune response**, involving **T lymphocytes** and activated macrophages, generally succeeding in containing the infection within the granuloma, resulting in **latent infection** in the majority of immunocompetent individuals rather than progression to active, symptomatic disease at the time of initial exposure.

In a proportion of infected individuals, particularly **young children**, who have a relatively immature immune system compared with older children and adults, and **immunocompromised individuals**, including those with **HIV co-infection**, this initial containment fails, or, alternatively, latent infection can **reactivate** at a later point when host immunity becomes compromised for any reason, with young age at initial infection specifically associated with a substantially higher risk of rapid progression to disseminated or severe disease forms compared with infection acquired later in childhood.

Fill in the blank: Young children have a relatively immature _____ system compared with older children and adults, increasing their risk of disease progression.

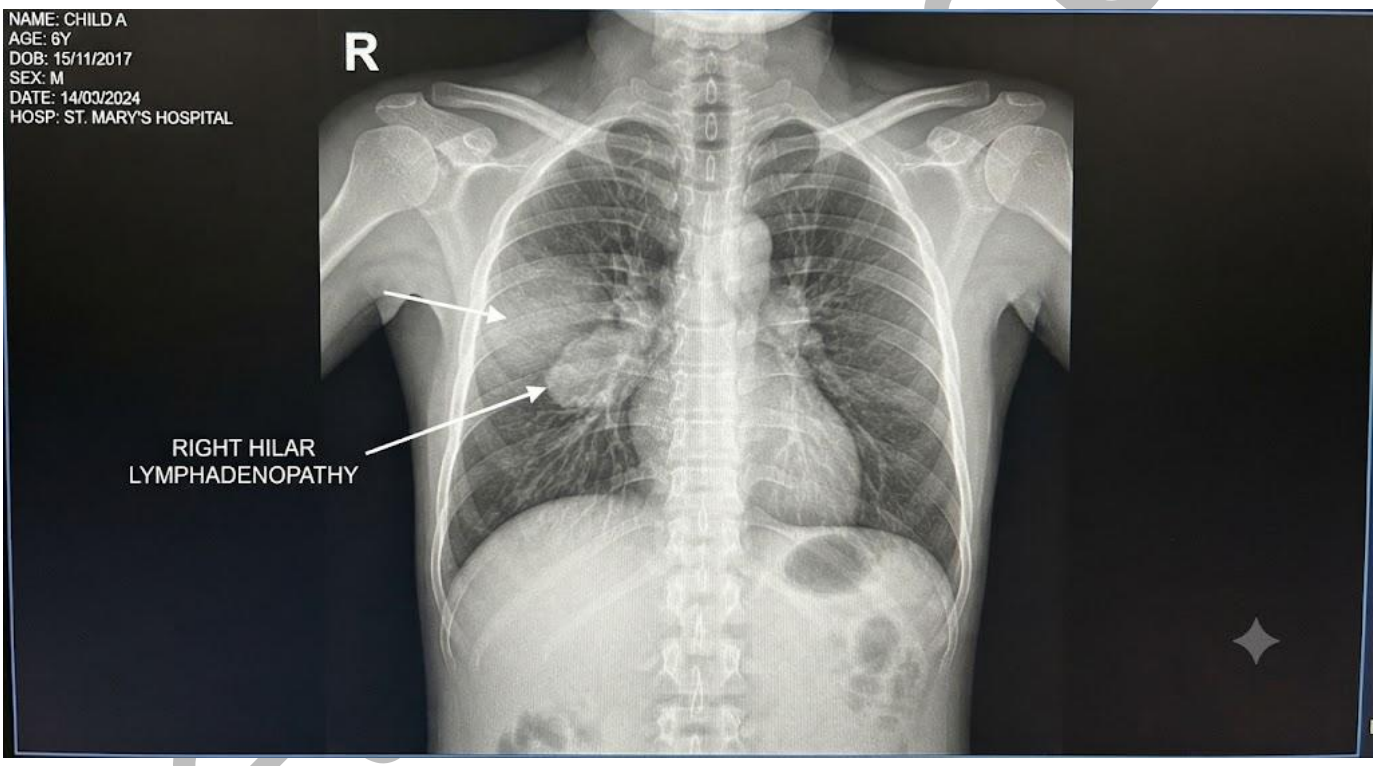

Figure 4.1: A chest radiograph showing changes consistent with primary pulmonary tuberculosis.

Pilot questions 4.1

- Describe the causative organism and mode of transmission of tuberculosis. (Linked to SLO 4.1)
- Distinguish latent tuberculosis infection from active tuberculosis disease. (Linked to SLO 4.1)
- Describe the initial pathological response following inhalation of Mycobacterium tuberculosis. (Linked to SLO 4.2)
- Define the primary complex, or Ghon complex. (Linked to SLO 4.2)

- Explain why young children are at increased risk of progression to active disease. (Linked to SLO 4.2)

4.2 Natural History and Clinical Features of Tuberculosis in Children

4.2.1 natural history of tuberculosis: the Wallgren timetable

Different complications appear at predictable intervals

The **Wallgren timetable**, based on detailed historical observational studies, describes the characteristic **chronological sequence** of events following primary tuberculosis infection in an untreated child, providing a useful conceptual framework for anticipating which complications are most likely to occur at a given point in time following exposure, and remains clinically relevant today for understanding the natural progression of untreated paediatric tuberculosis.

According to this timetable, a **positive tuberculin skin test** typically develops within **3 to 8 weeks** of infection, **pleural effusion** and **lymph node disease** typically occur within the following **3 to 9 months**, the most severe complications, **miliary** and **meningeal tuberculosis**, occur within the first **2 to 6 months**, reflecting early **haematogenous dissemination**, while **bone and joint tuberculosis** may not become clinically apparent for **1 to 3 years**, and renal tuberculosis considerably later still, illustrating how the risk of specific complications evolves in a broadly predictable pattern over an extended period following initial infection.

Fill in the blank: According to the Wallgren timetable, a positive tuberculin skin test typically develops within _____ to 8 weeks of infection.

4.2.2 peculiarities of tuberculosis in children

Tuberculosis in children differs considerably from the disease as it typically presents in adults, since children more often develop **primary disease**, occurring shortly after initial infection, rather than the **reactivation disease** more typical of adults, and are also considerably more prone to **disseminated forms** of the disease, including **miliary tuberculosis** and **tuberculous meningitis**, particularly in **young children under two years of age**, reflecting the relative immaturity of the immune response discussed in the previous Part of this Series.

Children with pulmonary tuberculosis are also frequently **paucibacillary**, meaning they have a relatively low bacterial burden in respiratory secretions compared with adults with cavitary disease, making bacteriological confirmation, discussed further in the next Part, considerably more challenging in children, and children are generally **less likely to produce sputum**

effectively, particularly younger children, further complicating standard diagnostic approaches that rely heavily on sputum-based testing in adult practice.

Fill in the blank: Children with pulmonary tuberculosis are frequently _____, meaning they have a relatively low bacterial burden.

4.2.3 clinical features suggestive of tuberculosis in children

Clinical features suggestive of tuberculosis in a child include **persistent cough** lasting more than **2 to 3 weeks** and not responding to standard treatment for other causes, **unexplained fever** persisting for more than **2 weeks**, **poor weight gain** or **weight loss**, and **failure to thrive**, particularly when accompanied by a relevant **history of contact** with an adult or adolescent with known or suspected infectious tuberculosis, which should always be actively sought in any child with a compatible clinical presentation.

Additional features vary depending on the specific site and extent of disease, and may include **lymphadenopathy**, particularly cervical, **hepatosplenomegaly** in disseminated disease, and, in tuberculous meningitis, **headache**, **irritability**, **neck stiffness**, and, in advanced cases, **altered consciousness**, meaning tuberculosis should be actively considered in the differential diagnosis of a child with any of these presentations, particularly in a setting of known local TB prevalence or a positive contact history.

Fill in the blank: A persistent cough lasting more than 2 to 3 weeks and not responding to standard treatment should raise suspicion for _____.

Figure 4.2: A child undergoing assessment for suspected tuberculosis, including growth monitoring.

Pilot questions 4.2

1. Describe the purpose and general structure of the Wallgren timetable. (Linked to SLO 4.3)
2. State the typical timing of miliary and meningeal tuberculosis according to the Wallgren timetable. (Linked to SLO 4.3)
3. Describe two ways childhood tuberculosis differs from adult tuberculosis. (Linked to SLO 4.4)
4. Explain why bacteriological confirmation of TB is more difficult in children than in adults. (Linked to SLO 4.4)
5. List four clinical features suggestive of tuberculosis in a child. (Linked to SLO 4.4)

4.3 Investigation and Diagnosis of Tuberculosis

4.3.1 the tuberculin skin test and interferon-gamma release assay

Two tests, similar purpose, different practical trade-offs

The **tuberculin skin test**, also called the **Mantoux test**, involves intradermal injection of **purified protein derivative**, with the resulting area of **induration**, not simply redness, measured after **48 to 72 hours**, and interpreted against age- and risk-specific thresholds, since a positive result indicates **immune sensitisation** to mycobacterial antigens, reflecting either latent infection or active disease, but does not, on its own, distinguish reliably between the two.

Interferon-gamma release assays, a newer blood-based alternative, measure the release of interferon-gamma by sensitised T cells in response to specific mycobacterial antigens, offering greater **specificity** in individuals previously vaccinated with **BCG**, since the antigens used are not shared with the BCG vaccine strain, though cost and laboratory infrastructure requirements limit their availability in many resource-limited settings where the tuberculin skin test remains the more widely accessible option.

Fill in the blank: The tuberculin skin test result is read by measuring the area of _____, not redness, after 48 to 72 hours.

4.3.2 bacteriological and molecular investigation of tuberculosis

Bacteriological confirmation remains the diagnostic gold standard where achievable, using **sputum microscopy** for acid-fast bacilli, **mycobacterial culture**, which, while more sensitive than microscopy, can take several weeks to yield a result given the slow growth rate of the organism, and **molecular testing**, such as **GeneXpert MTB/RIF**, which provides a considerably more rapid result and, importantly, simultaneously identifies **rifampicin resistance**, information that directly influences the choice of treatment regimen.

Given the diagnostic challenges specific to children discussed in the previous Part, alternative specimen collection methods are frequently required, including **gastric aspirate**, collecting swallowed respiratory secretions, particularly useful in young children unable to expectorate sputum voluntarily, and **induced sputum**, using nebulised hypertonic saline to stimulate productive coughing, both of which improve the yield of bacteriological testing in this challenging age group.

Fill in the blank: GeneXpert MTB/RIF testing simultaneously identifies resistance to the drug _____.

4.3.3 clinical and radiological diagnosis of tuberculosis in children

Given the frequent difficulty obtaining bacteriological confirmation in children, diagnosis is often made using a **composite clinical approach**, combining a **compatible clinical picture**, a

relevant history of contact with an infectious case, a **positive tuberculin skin test or interferon-gamma release assay**, and **suggestive chest radiograph findings**, such as hilar lymphadenopathy or a primary complex, since relying exclusively on bacteriological confirmation would result in a substantial proportion of genuinely affected children remaining undiagnosed and untreated.

Various **scoring systems** have been developed to help standardise this composite clinical diagnostic approach across different settings, assigning points to specific clinical, radiological, and contact history features to arrive at an overall probability of tuberculosis disease, though clinical judgement, informed by local disease prevalence and the specific individual clinical picture, remains essential alongside any such standardised scoring tool.

Fill in the blank: A composite clinical approach to TB diagnosis combines clinical picture, contact history, tuberculin testing, and _____ findings.

Table 4.3: Key investigations used in the diagnosis of tuberculosis in children.

Investigation	Key feature
Tuberculin skin test	Measures induration at 48 to 72 hours; indicates sensitisation, not necessarily active disease
Interferon-gamma release assay	Blood test with greater specificity in BCG-vaccinated children
Sputum or gastric aspirate microscopy	Rapid but lower sensitivity, particularly in children
GeneXpert MTB/RIF	Rapid molecular test; also detects rifampicin resistance
Chest radiograph	May show hilar lymphadenopathy or primary complex

Pilot questions 4.3

1. Describe how the tuberculin skin test is performed and interpreted. (Linked to SLO 4.5)
2. Explain the advantage of interferon-gamma release assays over the tuberculin skin test. (Linked to SLO 4.5)
3. Describe two methods of obtaining a specimen for bacteriological testing in a young child. (Linked to SLO 4.5)
4. Explain why GeneXpert MTB/RIF testing is clinically valuable beyond simply confirming diagnosis. (Linked to SLO 4.5)
5. Describe the composite clinical approach to diagnosing tuberculosis in children. (Linked to SLO 4.5)

4.4 Management, Including DOTS, and Prevention of Tuberculosis

4.4.1 drugs used in the management of tuberculosis

Multiple drugs working together reduce the risk of resistance

Standard treatment of drug-susceptible tuberculosis in children uses a combination of **first-line anti-tuberculosis drugs**, including **isoniazid**, **rifampicin**, **pyrazinamide**, and **ethambutol**, given together during an **intensive phase**, typically lasting **2 months**, followed by a **continuation phase**, typically with isoniazid and rifampicin alone for a further **4 months**, with the use of multiple drugs in combination specifically designed to reduce the risk of the organism developing **drug resistance** during treatment.

Each of these drugs carries specific, recognised **side effects** that should be actively monitored for during treatment, including **hepatotoxicity**, a risk with isoniazid, rifampicin, and pyrazinamide, **peripheral neuropathy** with isoniazid, which is generally preventable with co-administered **pyridoxine**, **visual disturbance**, specifically **optic neuritis**, with ethambutol, and a characteristic, generally harmless **orange discolouration** of body fluids with rifampicin, which is important to proactively explain to families to avoid unnecessary alarm or reduced treatment adherence.

Fill in the blank: The intensive phase of standard TB treatment in children typically lasts _____ months.

4.4.2 principles of management and DOTS

Directly Observed Treatment, Short-course, abbreviated **DOTS**, is a comprehensive treatment strategy in which each dose of anti-tuberculosis medication is administered under the **direct observation** of a trained healthcare worker or designated treatment supporter, a strategy specifically designed to maximise **treatment adherence**, since incomplete or interrupted treatment is a major driver of both treatment failure and the emergence of drug-resistant tuberculosis.

Beyond direct observation of dosing, the broader DOTS strategy encompasses **government commitment** to sustained TB control, access to **quality-assured diagnostic testing**, a **standardised treatment regimen** with reliable **drug supply**, and a robust **recording and reporting system** to monitor treatment outcomes at both the individual and programme level, reflecting the recognition that successful TB control requires a coordinated **health system approach** rather than simply prescribing appropriate medication to an individual patient in isolation.

Fill in the blank: DOTS stands for Directly Observed Treatment, _____-course.

4.4.3 prevention and control of tuberculosis using the five levels of prevention

Primary prevention of tuberculosis includes **BCG vaccination**, given at birth in many high-burden settings including Nigeria, which provides meaningful protection against the most severe disseminated forms of childhood disease, particularly miliary tuberculosis and tuberculous meningitis, though it offers less reliable protection against pulmonary disease overall, together with broader **infection control** measures to reduce transmission within households and healthcare facilities.

Secondary prevention includes **contact tracing** and **isoniazid preventive therapy** for young, exposed children found to have latent infection without active disease, aiming to prevent progression to active disease before it occurs, **tertiary prevention** focuses on prompt, complete treatment of active disease to prevent complications and further transmission, and **quaternary prevention** involves avoiding unnecessary or excessive treatment once cure is confirmed, together forming a comprehensive strategy spanning from population-level vaccination programmes through to individual patient care.

Fill in the blank: Isoniazid preventive therapy is given to exposed children with latent infection to prevent progression to active _____.

Figure 4.4: A healthcare worker directly observing a child taking anti-tuberculosis medication.

Pilot questions 4.4

1. List the four first-line anti-tuberculosis drugs used in the intensive phase. (Linked to SLO 4.6)
2. Describe two specific side effects of first-line anti-tuberculosis drugs. (Linked to SLO 4.6)
3. Define DOTS and explain its purpose. (Linked to SLO 4.7)
4. List two components of the broader DOTS strategy beyond directly observed dosing. (Linked to SLO 4.7)
5. Describe the five levels of prevention as applied to tuberculosis. (Linked to SLO 4.8)

Series Summary

This Series examined **tuberculosis in children**, beginning with its definition, classification, and basic pathology, before turning to its **natural history and the peculiarities of clinical presentation in children**.

We then examined the **investigation and diagnosis of tuberculosis**, before concluding with its **management, including the DOTS strategy, and prevention** using the five levels of prevention. Having worked through this Series, you should now be able to recognise, diagnose, manage, and help prevent tuberculosis in children. The next Series turns to **paediatric HIV/AIDS and schistosomiasis**.

Glossary of Terms

1. **Latent tuberculosis infection:** a dormant state of TB infection controlled by the host immune response, without clinical illness.
2. **Ghon complex:** the primary complex of tuberculosis, comprising the initial lung lesion and regional lymph node involvement.
3. **Wallgren timetable:** a chronological framework describing the typical sequence of complications following untreated primary TB infection.

4. **Miliary tuberculosis:** a severe, disseminated form of tuberculosis, most common in young children.
5. **Paucibacillary:** having a relatively low bacterial burden, typical of childhood pulmonary tuberculosis.
6. **Tuberculin skin test:** a test measuring induration following intradermal injection of purified protein derivative.
7. **Interferon-gamma release assay:** a blood test with greater specificity than the tuberculin skin test in BCG-vaccinated individuals.
8. **GeneXpert MTB/RIF:** a rapid molecular test for tuberculosis that also detects rifampicin resistance.
9. **Directly Observed Treatment, Short-course (DOTS):** a TB treatment strategy in which each medication dose is administered under direct observation.
10. **Isoniazid preventive therapy:** preventive treatment given to exposed children with latent TB infection to prevent progression to active disease.
11. **BCG vaccination:** a vaccine given at birth in high-burden settings, protecting particularly against severe disseminated childhood TB.
12. **Hepatotoxicity:** liver toxicity, a recognised side effect of several first-line anti-tuberculosis drugs.

Concept Check Questions [Series 4]

Objective questions

- Tuberculosis is caused by Mycobacterium tuberculosis, an _____-fast bacillus.
- The pathological hallmark lesion of TB, formed by immune cells aggregating around infected macrophages, is called the _____.
- According to the Wallgren timetable, a positive tuberculin skin test typically develops within _____ to 8 weeks of infection.
- The tuberculin skin test result is read by measuring the area of _____, not redness, after 48 to 72 hours.
- DOTS stands for Directly Observed Treatment, _____-course.

Short-answer questions

1. Distinguish latent tuberculosis infection from active tuberculosis disease.
2. Describe two ways childhood tuberculosis differs from adult tuberculosis.

3. List four clinical features suggestive of tuberculosis in a child.
4. List the four first-line anti-tuberculosis drugs used in the intensive phase.
5. Describe two components of the broader DOTS strategy beyond directly observed dosing.

Long-answer questions

6. Discuss the definition, classification, and basic pathology of tuberculosis. (Linked to SLO 4.1, SLO 4.2)
7. Discuss the natural history of tuberculosis using the Wallgren timetable, and the peculiarities of TB in children. (Linked to SLO 4.3, SLO 4.4)
8. Discuss the investigation and diagnosis of tuberculosis in children. (Linked to SLO 4.5)
9. Discuss the drugs used in TB management, their side effects, and the DOTS strategy. (Linked to SLO 4.6, SLO 4.7)
10. Discuss the prevention and control of tuberculosis using the five levels of prevention. (Linked to SLO 4.8)

Answers to Concept Check Questions [Series 4]

Objective questions

11. Acid.
12. Granuloma.
13. 3.
14. Induration.
15. Short.

Short-answer questions

16. Latent infection is a dormant, controlled state without illness, while active disease involves actively multiplying bacteria causing clinical illness.
17. Children more often develop primary disease and disseminated forms, and are more often paucibacillary compared with adults.
18. Persistent cough over 2 to 3 weeks, unexplained fever, poor weight gain, and failure to thrive.
19. Isoniazid, rifampicin, pyrazinamide, and ethambutol.

20. Government commitment, quality-assured diagnostics, standardised regimens with reliable drug supply, and recording and reporting systems.

Long-answer questions

21. **Basic response:** TB is caused by Mycobacterium tuberculosis, classified as latent infection or active disease, with initial infection producing a granulomatous response and the Ghon complex.

Value-added response: Outcome depends on the balance between host immunity and bacterial burden, with young children and immunocompromised individuals at higher risk of progression to active disease.

22. **Basic response:** The Wallgren timetable describes the typical sequence of complications after untreated primary infection, with miliary and meningeal disease occurring earliest, within 2 to 6 months.

Value-added response: Children differ from adults by developing more primary and disseminated disease, being paucibacillary, and less able to produce sputum, complicating diagnosis.

23. **Basic response:** Diagnosis uses tuberculin skin testing or interferon-gamma release assays, bacteriological testing including GeneXpert, and chest radiography, combined in a composite clinical approach.

Value-added response: Gastric aspirate and induced sputum improve specimen yield in young children, and GeneXpert additionally detects rifampicin resistance, guiding treatment choice.

24. **Basic response:** Treatment uses isoniazid, rifampicin, pyrazinamide, and ethambutol in an intensive phase, followed by a continuation phase, with DOTS ensuring directly observed dosing to maximise adherence.

Value-added response: Each drug carries specific side effects requiring monitoring, and DOTS extends beyond dosing to encompass a coordinated health system approach to TB control.

25. **Basic response:** Prevention includes BCG vaccination as primary prevention, contact tracing and isoniazid preventive therapy as secondary prevention, and prompt treatment as tertiary prevention.

Value-added response: BCG particularly protects against severe disseminated forms such as miliary TB and meningitis, while isoniazid preventive therapy aims to prevent progression from latent infection to active disease.

Answers to Pilot Questions [Series 4]

Part 4.1

1. Mycobacterium tuberculosis, an acid-fast bacillus, transmitted through inhalation of respiratory droplet nuclei.
2. Latent infection is dormant and asymptomatic; active disease involves actively multiplying bacteria causing illness.
3. Alveolar macrophages engulf the organism, triggering a granulomatous inflammatory response forming the tubercle.
4. The primary complex is the initial lung lesion (Ghon focus) together with regional lymph node involvement.
5. Young children have a relatively immature immune system, increasing the risk of progression to active disease.

Part 4.2

6. It describes the chronological sequence of complications following untreated primary infection.
7. Miliary and meningeal tuberculosis typically occur within the first 2 to 6 months after infection.
8. Children more often develop primary and disseminated disease, and are paucibacillary compared with adults.
9. Children have lower bacterial burden and are less able to produce sputum, reducing diagnostic yield.
10. Persistent cough, unexplained fever, poor weight gain, and failure to thrive are suggestive features.

Part 4.3

11. Purified protein derivative is injected intradermally, and induration is measured after 48 to 72 hours.
12. Interferon-gamma release assays have greater specificity in BCG-vaccinated children.
13. Gastric aspirate and induced sputum are methods used to obtain specimens in young children.
14. It also detects rifampicin resistance, directly informing the choice of treatment regimen.
15. It combines clinical picture, contact history, tuberculin or IGRA testing, and radiograph findings.

Part 4.4

1. Isoniazid, rifampicin, pyrazinamide, and ethambutol are the four first-line drugs.
2. Hepatotoxicity with several drugs, and peripheral neuropathy with isoniazid, are recognised side effects.
3. DOTS is Directly Observed Treatment, Short-course, ensuring each dose is observed to maximise adherence.
4. Quality-assured diagnostics and reliable drug supply are components of the broader DOTS strategy.
5. Primary prevention with BCG, secondary prevention with contact tracing and preventive therapy, and tertiary prevention with prompt treatment.

References and Attributions [Series 4]

1. Kliegman, R. M., St Geme, J. W., Blum, N. J., Shah, S. S., Tasker, R. C. and Wilson, K. M. (2020). Nelson Textbook of Pediatrics (21st ed.). Elsevier.
2. World Health Organization (2022). WHO Consolidated Guidelines on Tuberculosis: Module 5, Management of Tuberculosis in Children and Adolescents. WHO Press.
3. Marais, B. J. et al. (2004). The natural history of childhood intra-thoracic tuberculosis. International Journal of Tuberculosis and Lung Disease, 8(4), 392 to 402.
4. Federal Ministry of Health, Nigeria (2021). National Tuberculosis, Leprosy and Buruli Ulcer Control Programme: Guidelines for TB Management.

Figures, Plates, Tables, and Boxes

1. Figure 4.1: A chest radiograph showing changes consistent with primary pulmonary tuberculosis. AI-generated using the prompt: "A realistic radiographic-style illustration of a paediatric chest X-ray showing a subtle lung opacity with enlarged hilar lymph nodes consistent with primary tuberculosis. Single clean medical illustration in the style of an X-ray image, plain neutral background, no text overlays, no multiple panels, accurate radiological detail."
2. Figure 4.2: A child undergoing assessment for suspected tuberculosis, including growth monitoring. AI-generated using the prompt: "A realistic clinical illustration of a clinician

gently examining a young child on a weighing scale in a clinic room, with a growth chart visible on the wall nearby. Single clean medical illustration, soft clinical lighting, no text overlays, no multiple panels, respectful and accurate depiction."

3. Table 4.3: Key investigations used in the diagnosis of tuberculosis in children. AI-generated using the prompt: "Create a clean reference table titled Key Investigations in Paediatric Tuberculosis Diagnosis, listing investigation and key feature. Simple clinical reference table style with outside border."
4. Figure 4.4: A healthcare worker directly observing a child taking anti-tuberculosis medication. AI-generated using the prompt: "A warm, realistic clinical illustration of a healthcare worker sitting with a child at a clinic desk, watching supportively as the child takes oral medication with a glass of water, with a caregiver present nearby. Single clean medical illustration, soft warm lighting, no text overlays, no multiple panels, respectful and accurate depiction."

Course code: PAE 511

Course title: Specific Infectious Diseases

Course credit load: 2 Units

Series 5: Paediatric HIV/AIDS and Schistosomiasis

- **Part 5.1: Epidemiology, Pathogenesis, and Natural History of Paediatric HIV**
  - Sub Part 5.1.1: Epidemiology and burden of paediatric HIV
  - Sub Part 5.1.2: Pathogenesis of HIV infection
  - Sub Part 5.1.3: Natural history and disease progression
- **Part 5.2: Clinical Features and Staging of Paediatric HIV**
  - Sub Part 5.2.1: Clinical features of paediatric HIV
  - Sub Part 5.2.2: Clinical staging of HIV disease
  - Sub Part 5.2.3: Immunological staging of HIV disease
- **Part 5.3: Diagnosis of HIV in Children and Antiretroviral Therapy**
  - Sub Part 5.3.1: Laboratory diagnosis of HIV in children
  - Sub Part 5.3.2: The national algorithm for early infant diagnosis and PITC
  - Sub Part 5.3.3: Pharmacology of antiretroviral therapy in children
- **Part 5.4: Care of the HIV-Exposed Child and Schistosomiasis**
  - Sub Part 5.4.1: Care of the HIV-exposed child
  - Sub Part 5.4.2: Introduction to schistosomiasis
  - Sub Part 5.4.3: Diagnosis and management of schistosomiasis

Introduction

In the last Series, we explored tuberculosis in children. We now turn to paediatric HIV and AIDS, a condition that, together with tuberculosis, represents one of the most significant chronic infectious disease burdens facing children in Nigeria and the wider region, before concluding this course with a brief introduction to schistosomiasis. Picture an infant born to a mother with HIV,

whose care from birth onward depends on a coordinated series of interventions to prevent infection or, where infection has occurred, to identify it as early as possible and begin effective treatment.

The aim of this Series is to equip you with the knowledge required to understand the natural history, clinical features, staging, and diagnosis of paediatric HIV, the pharmacology of antiretroviral therapy, the care of the HIV-exposed child, and the basics of schistosomiasis.

This Series begins with the **epidemiology, pathogenesis, and natural history of paediatric HIV**, before turning to its **clinical features and staging**. Next, we examine the **diagnosis of HIV in children and antiretroviral therapy**, before concluding with the **care of the HIV-exposed child and schistosomiasis**.

Series Learning Outcomes

At the end of this Series, you should be able to:

- **SLO 1.1:** describe the pathogenesis and natural history of HIV infection in children,
- **SLO 1.2:** categorise HIV infected children based on rate of disease progression, and list the factors that influence disease progression,
- **SLO 1.3:** discuss the clinical features of paediatric HIV infection,
- **SLO 1.4:** discuss the clinical and immunological staging of HIV disease in children,
- **SLO 1.5:** outline the criteria and methods for laboratory diagnosis of HIV in children,
- **SLO 1.6:** describe the national algorithm for early infant diagnosis of HIV infection and PITC, and the care of the HIV-exposed child,
- **SLO 1.7:** explain the pharmacology of antiretroviral therapy in children, and
- **SLO 1.8:** describe the aetiology, clinical features, and management of schistosomiasis.

5.1 Epidemiology, Pathogenesis, and Natural History of Paediatric HIV

5.1.1 epidemiology and burden of paediatric HIV

Most childhood infections trace back to the mother

Paediatric HIV infection remains a substantial public health burden in sub-Saharan Africa, including Nigeria, with the overwhelming majority of infections in young children resulting from **mother-to-child transmission**, occurring during **pregnancy**, **labour and delivery**, or through **breastfeeding**, rather than through other routes of transmission relevant in older children and adults.

Transmission risk without any intervention is substantial, but has been dramatically reduced in many settings through **prevention of mother-to-child transmission** programmes, combining maternal **antiretroviral therapy**, safer delivery practices, and infant **antiretroviral prophylaxis**, meaning the burden of new paediatric infections is heavily influenced by the reach and effectiveness of these programmes within a given population.

Fill in the blank: The overwhelming majority of paediatric HIV infections result from _____ transmission.

5.1.2 pathogenesis of HIV infection

HIV is a **retrovirus** that specifically targets and infects **CD4 positive T lymphocytes**, a central component of the cell-mediated immune system, using the enzyme **reverse transcriptase** to convert its **RNA genome** into **DNA**, which then integrates into the host cell genome, allowing the virus to persist and replicate within infected cells indefinitely.

Progressive infection and destruction of CD4 cells over time leads to a gradual decline in **immune function**, ultimately resulting in the susceptibility to **opportunistic infections** and **malignancies** that characterise **acquired immunodeficiency syndrome**, or **AIDS**, the advanced stage of untreated HIV infection, though this progressive decline occurs at markedly different rates between individuals, discussed further in the next sub-Part.

Fill in the blank: HIV uses the enzyme reverse transcriptase to convert its RNA genome into _____.

5.1.3 natural history and disease progression

In the absence of treatment, HIV infected children can be broadly categorised by their **rate of disease progression** into **rapid progressors**, who develop severe immunosuppression and AIDS within the first year or two of life, **typical progressors**, who develop advanced disease over several years, and **slow progressors**, or **long-term non-progressors**, who maintain relatively preserved immune function for many years without treatment.

Factors influencing disease progression include the **timing of infection**, with infection acquired early in utero generally associated with more rapid progression than infection acquired later, such as through breastfeeding, **maternal viral load** at the time of transmission, **viral characteristics**, and **host genetic factors**, meaning the clinical course of untreated paediatric HIV is genuinely variable rather than following a single, predictable trajectory.

Fill in the blank: Infection acquired early in utero is generally associated with more _____ disease progression than infection acquired later.

Figure 5.1: A mother and infant attending a prevention of mother-to-child transmission clinic.

Pilot questions 5.1

- Describe the main route of HIV transmission in young children. (Linked to SLO 5.1)
- List two components of a prevention of mother-to-child transmission programme. (Linked to SLO 5.1)
- Describe how HIV infects and replicates within CD4 cells. (Linked to SLO 5.1)
- Distinguish rapid, typical, and slow progressors of HIV disease. (Linked to SLO 5.2)
- List two factors that influence the rate of HIV disease progression. (Linked to SLO 5.2)

5.2 Clinical Features and Staging of Paediatric HIV

5.2.1 clinical features of paediatric HIV

Presentation ranges from subtle to severe

Clinical features of paediatric HIV infection are wide-ranging and can include **failure to thrive**, **generalised lymphadenopathy**, **hepatosplenomegaly**, **persistent or recurrent oral candidiasis**, **chronic or recurrent diarrhoea**, and **recurrent serious bacterial infections**,

reflecting the progressive immunosuppression that characterises untreated disease, with the specific combination and severity of features varying considerably between children.

As disease progresses, children may develop **opportunistic infections**, including **Pneumocystis jirovecii pneumonia**, particularly in young infants, **tuberculosis**, discussed in the previous Series, and, in more advanced disease, specific **AIDS-defining conditions**, together with **HIV encephalopathy**, presenting with developmental delay or regression, underscoring the wide-ranging systemic impact of untreated HIV infection in children.

Fill in the blank: Pneumocystis jirovecii pneumonia is a particularly important opportunistic infection in young _____.

5.2.2 clinical staging of HIV disease

The **World Health Organization clinical staging system** classifies HIV disease in children into **four clinical stages**, from **Stage 1**, asymptomatic disease, through **Stage 2** and **Stage 3**, with progressively more significant clinical features, to **Stage 4**, representing **severe, AIDS-defining disease**, with staging based entirely on **clinical findings** rather than laboratory results, making it a practical tool usable even in settings without ready access to laboratory testing.

Clinical staging is used both to guide **treatment decisions** and to provide a standardised way of describing and comparing disease severity across children and settings, and, while modern guidelines increasingly recommend starting **antiretroviral therapy** in all HIV infected children regardless of clinical stage, staging remains clinically useful for monitoring disease course and anticipating specific complications.

Fill in the blank: The WHO clinical staging system for HIV classifies disease into _____ clinical stages.

5.2.3 immunological staging of HIV disease

Immunological staging, complementary to clinical staging, uses **CD4 count** or **CD4 percentage**, with percentage generally preferred in young children given greater age-related variability in absolute CD4 count, to classify the degree of immunosuppression into **not significant**, **mild**, **advanced**, and **severe** categories, providing an objective, laboratory-based measure of immune status alongside the clinical assessment.

Combining clinical and immunological staging provides the most complete picture of an individual child's disease status, since clinical and immunological findings do not always correlate perfectly, and both are used together to guide decisions around **treatment initiation**,

monitoring frequency, and the threshold for specific opportunistic infection prophylaxis in a given child.

Fill in the blank: CD4 percentage is generally preferred over absolute CD4 count in young children due to greater age-related _____.

Table 5.2: WHO clinical staging summary for paediatric HIV disease.

Stage	General description
Stage 1	Asymptomatic, or persistent generalised lymphadenopathy only
Stage 2	Mild symptoms, such as recurrent respiratory infections or dermatitis
Stage 3	Moderate symptoms, such as chronic diarrhoea or oral candidiasis
Stage 4	Severe, AIDS-defining conditions, such as Pneumocystis pneumonia or HIV encephalopathy

Pilot questions 5.2

1. List four clinical features suggestive of paediatric HIV infection. (Linked to SLO 5.3)
2. Name an important opportunistic infection particularly affecting young HIV infected infants. (Linked to SLO 5.3)
3. Describe the structure of the WHO clinical staging system for paediatric HIV. (Linked to SLO 5.4)
4. Explain why CD4 percentage is generally preferred over absolute CD4 count in young children. (Linked to SLO 5.4)
5. Explain why clinical and immunological staging are used together. (Linked to SLO 5.4)

5.3 Diagnosis of HIV in Children and Antiretroviral Therapy

5.3.1 laboratory diagnosis of HIV in children

Maternal antibodies complicate testing in young infants

Laboratory diagnosis of HIV in children differs by age because of **maternal antibody transfer** across the placenta, which persists in an infant's circulation for up to **18 months**, meaning standard **antibody-based tests**, reliable in older children and adults, cannot reliably distinguish a truly infected infant from one who has simply retained passively transferred maternal antibody without being infected themselves.

For children **under 18 months**, diagnosis therefore requires **virological testing**, most commonly **HIV DNA polymerase chain reaction**, which directly detects the virus itself rather than antibodies, while for children **over 18 months**, standard **antibody testing**, similar to that used in adults, becomes reliable, since any passively acquired maternal antibody has, by this age, been cleared from the infant's circulation.

Fill in the blank: Maternal antibody can persist in an infant’s circulation for up to _____ months.

5.3.2 the national algorithm for early infant diagnosis and PITC

Early infant diagnosis programmes typically use **dried blood spot** sampling, collected from an at-risk infant at a defined age, often around **6 weeks**, and transported to a centralised testing facility for **HIV DNA PCR** testing, since this approach allows testing to be extended to peripheral health facilities without on-site advanced laboratory capacity, considerably improving access to timely diagnosis for exposed infants.

Provider-initiated testing and counselling, abbreviated **PITC**, describes the routine offer of HIV testing to patients attending health facilities for other reasons, as a standard component of care rather than only in response to a specific patient request, an approach that has substantially increased HIV testing uptake and earlier diagnosis in many settings compared with relying solely on client-initiated testing.

Fill in the blank: Early infant diagnosis typically uses dried blood spot sampling collected from an infant around _____ weeks of age.

5.3.3 pharmacology of antiretroviral therapy in children

Antiretroviral therapy in children uses combinations of drugs from different classes, most commonly **nucleoside reverse transcriptase inhibitors**, **non-nucleoside reverse transcriptase inhibitors**, and **protease inhibitors**, or, increasingly, **integrase inhibitors**, combined to achieve durable **viral suppression** while minimising the risk of drug resistance developing through use of a single agent alone.

Paediatric **dosing** is generally calculated according to **body weight** or **body surface area**, requiring regular dose adjustment as the child grows, and available **formulations**, including liquid preparations and dispersible tablets for younger children who cannot swallow standard tablets, together with attention to **palatability** and **pill burden**, meaningfully influence a child's ability to adhere consistently to treatment over the long term.

Fill in the blank: Paediatric antiretroviral dosing is generally calculated according to body weight or body _____ area.

Figure 5.3: Dried blood spot sample collection from an infant for early infant HIV diagnosis.

Pilot questions 5.3

1. Explain why antibody-based HIV testing is unreliable in infants under 18 months. (Linked to SLO 5.5)
2. Describe the laboratory method used to diagnose HIV in a child under 18 months. (Linked to SLO 5.5)
3. Describe the process of early infant diagnosis using dried blood spot sampling. (Linked to SLO 5.6)
4. Define provider-initiated testing and counselling and explain its purpose. (Linked to SLO 5.6)
5. List two classes of antiretroviral drugs used in children. (Linked to SLO 5.7)

5.4 Care of the HIV-Exposed Child and Schistosomiasis

5.4.1 care of the HIV-exposed child

Every HIV-exposed infant needs a structured package of care

An **HIV-exposed infant**, born to a mother with HIV, requires a structured package of care regardless of eventual infection status, including **infant antiretroviral prophylaxis** for a defined period after birth, **cotrimoxazole prophylaxis**, starting at around **6 weeks** of age, to reduce the risk of Pneumocystis jirovecii pneumonia and other bacterial infections, and **early infant diagnosis testing** as described in the previous Part.

Infant feeding counselling is also essential, since current guidance in many high-burden settings recommends **exclusive breastfeeding** for HIV-exposed infants whose mothers are receiving effective antiretroviral therapy, given the substantial benefits of breastfeeding for overall infant health that generally outweigh the now considerably reduced transmission risk when maternal viral suppression is well maintained, together with ongoing **growth monitoring** and **routine immunisation** following the standard schedule.

Fill in the blank: Cotrimoxazole prophylaxis in an HIV-exposed infant typically starts at around _____ weeks of age.

5.4.2 introduction to schistosomiasis

Schistosomiasis, or **bilharzia**, is caused by parasitic **blood flukes** of the genus **Schistosoma**, transmitted through contact with **freshwater** containing infected **snail intermediate hosts**, and remains an important cause of chronic morbidity in children in endemic areas, including many parts of Nigeria, with **Schistosoma haematobium**, causing predominantly **urinary tract** disease, and **Schistosoma mansoni**, causing predominantly **intestinal and hepatic** disease, the two species of greatest regional importance.

Chronic infection can lead to significant morbidity over time, including **haematuria** and **bladder wall changes** with urinary schistosomiasis, and **hepatosplenomegaly** with **portal hypertension** in longstanding intestinal schistosomiasis, meaning children in endemic areas with relevant symptoms, particularly persistent haematuria, should be actively evaluated for this treatable parasitic infection.

Fill in the blank: Schistosoma haematobium causes predominantly _____ tract disease.

5.4.3 diagnosis and management of schistosomiasis

Diagnosis of schistosomiasis relies on demonstrating **parasite eggs** in **urine**, for Schistosoma haematobium, or **stool**, for Schistosoma mansoni, using standard **microscopy** techniques, and treatment is with **praziquantel**, a single-dose oral antihelminthic that is highly effective against the adult worm stage of the parasite responsible for ongoing egg production and tissue damage.

Prevention in endemic areas centres on **mass drug administration** programmes targeting school-age children, reducing infection intensity at a population level, together with longer-term measures such as improved **sanitation** and **access to safe water sources**, reducing both egg contamination of water bodies and ongoing human contact with infected water, reflecting a similar population-level prevention approach to several of the other infectious diseases discussed throughout this course.

Fill in the blank: Treatment of schistosomiasis is with a single dose of the oral antihelminthic _____.

Figure 5.4: A healthcare worker administering cotrimoxazole prophylaxis to an HIV-exposed infant.

Pilot questions 5.4

1. List three components of the care package for an HIV-exposed infant. (Linked to SLO 5.6)

2. Describe current infant feeding recommendations for HIV-exposed infants of mothers on effective treatment. (Linked to SLO 5.6)
3. Describe the causative organism and mode of transmission of schistosomiasis. (Linked to SLO 5.8)
4. Distinguish the disease caused by Schistosoma haematobium from that caused by Schistosoma mansoni. (Linked to SLO 5.8)
5. Describe the diagnosis and treatment of schistosomiasis. (Linked to SLO 5.8)

Series Summary

This Series examined **paediatric HIV/AIDS**, beginning with its epidemiology, pathogenesis, and natural history, before turning to its **clinical features and staging**.

We then examined the **diagnosis of HIV in children and antiretroviral therapy**, before concluding with the **care of the HIV-exposed child and schistosomiasis**. Having worked through this Series, and indeed this course, you should now be equipped with a systematic approach to the recognition, diagnosis, and management of the specific infectious diseases most significant to child health in Nigeria and the wider region.

Glossary of Terms

1. **Mother-to-child transmission:** the primary route of HIV transmission in young children, occurring during pregnancy, delivery, or breastfeeding.
2. **CD4 positive T lymphocyte:** the primary target cell of HIV infection, central to cell-mediated immunity.
3. **Rapid progressor:** an HIV infected child who develops severe immunosuppression and AIDS within the first year or two of life.
4. **WHO clinical staging:** a four-stage clinical classification system for paediatric HIV disease severity.
5. **CD4 percentage:** an immunological marker of HIV disease severity, generally preferred over absolute CD4 count in young children.
6. **HIV DNA PCR:** the virological test used to diagnose HIV in children under 18 months of age.

7. **Early infant diagnosis:** a programme using dried blood spot sampling to diagnose HIV in exposed infants.
8. **Provider-initiated testing and counselling (PITC):** the routine offer of HIV testing to patients attending health facilities for other reasons.
9. **Antiretroviral therapy:** combination drug treatment for HIV infection, aiming for durable viral suppression.
10. **HIV-exposed infant:** an infant born to a mother with HIV, requiring a structured package of prophylactic care.
11. **Schistosomiasis:** a parasitic infection caused by Schistosoma blood flukes, transmitted through contact with infected freshwater.
12. **Praziquantel:** the single-dose oral antihelminthic used to treat schistosomiasis.

Concept Check Questions [Series 5]

Objective questions

- The overwhelming majority of paediatric HIV infections result from _____ transmission.
- HIV uses the enzyme reverse transcriptase to convert its RNA genome into _____.
- The WHO clinical staging system for HIV classifies disease into _____ clinical stages.
- Maternal antibody can persist in an infant's circulation for up to _____ months.
- Treatment of schistosomiasis is with a single dose of the oral antihelminthic _____.

Short-answer questions

1. Distinguish rapid, typical, and slow progressors of HIV disease.
2. List four clinical features suggestive of paediatric HIV infection.
3. Describe the laboratory method used to diagnose HIV in a child under 18 months.
4. Define provider-initiated testing and counselling and explain its purpose.
5. Distinguish the disease caused by Schistosoma haematobium from that caused by Schistosoma mansoni.

Long-answer questions

6. Discuss the epidemiology, pathogenesis, and natural history of paediatric HIV infection. (Linked to SLO 5.1, SLO 5.2)

7. Discuss the clinical features and staging of paediatric HIV disease. (Linked to SLO 5.3, SLO 5.4)
8. Discuss the diagnosis of HIV infection in children, including early infant diagnosis. (Linked to SLO 5.5, SLO 5.6)
9. Discuss the pharmacology of antiretroviral therapy in children. (Linked to SLO 5.7)
10. Discuss the care of the HIV-exposed child and the basics of schistosomiasis. (Linked to SLO 5.6, SLO 5.8)

Answers to Concept Check Questions [Series 5]

Objective questions

11. Mother-to-child.
12. DNA.
13. Four.
14. 18.
15. Praziquantel.

Short-answer questions

16. Rapid progressors develop AIDS within 1 to 2 years; typical progressors over several years; slow progressors maintain immune function for many years.
17. Failure to thrive, generalised lymphadenopathy, hepatosplenomegaly, and recurrent oral candidiasis.
18. HIV DNA polymerase chain reaction testing is used, since it directly detects the virus rather than antibodies.
19. PITC is the routine offer of HIV testing to patients attending for other reasons, increasing testing uptake and earlier diagnosis.
20. Schistosoma haematobium causes predominantly urinary tract disease, while Schistosoma mansoni causes predominantly intestinal and hepatic disease.

Long-answer questions

21. **Basic response:** Paediatric HIV is predominantly acquired through mother-to-child transmission, with HIV targeting CD4 cells, and disease progression rate varying between rapid, typical, and slow progressors.

Value-added response: Prevention of mother-to-child transmission programmes and factors such as timing of infection and maternal viral load significantly influence both transmission risk and subsequent disease course.

22. **Basic response:** Clinical features range from failure to thrive to opportunistic infections, with WHO clinical staging classifying disease into four stages based on clinical findings alone.

Value-added response: Immunological staging using CD4 percentage complements clinical staging, together guiding treatment initiation and monitoring decisions.

23. **Basic response:** Diagnosis in children under 18 months requires HIV DNA PCR due to persistent maternal antibody, while early infant diagnosis uses dried blood spot sampling around 6 weeks of age.

Value-added response: Provider-initiated testing and counselling increases testing uptake by offering testing routinely rather than only on request, supporting earlier diagnosis.

24. **Basic response:** Antiretroviral therapy combines drugs from different classes to achieve viral suppression, with paediatric dosing based on weight or body surface area.

Value-added response: Available formulations and attention to palatability and pill burden meaningfully influence a child's ability to adhere to treatment over the long term.

25. **Basic response:** HIV-exposed infants require a structured care package including prophylaxis, feeding counselling, and early infant diagnosis; schistosomiasis is diagnosed by egg detection and treated with praziquantel.

Value-added response: Exclusive breastfeeding is recommended for HIV-exposed infants of mothers on effective treatment, while schistosomiasis prevention relies on mass drug administration and improved sanitation.

Answers to Pilot Questions [Series 5]

Part 5.1

1. Mother-to-child transmission during pregnancy, delivery, or breastfeeding is the main route in young children.

2. Maternal antiretroviral therapy and infant antiretroviral prophylaxis are components of PMTCT programmes.
3. HIV uses reverse transcriptase to convert RNA to DNA, which integrates into the host CD4 cell genome.
4. Rapid progressors develop AIDS within 1 to 2 years, typical progressors over several years, slow progressors over many years.
5. Timing of infection and maternal viral load are factors influencing disease progression.

Part 5.2

6. Failure to thrive, lymphadenopathy, hepatosplenomegaly, and recurrent oral candidiasis are suggestive features.
7. Pneumocystis jirovecii pneumonia is an important opportunistic infection in young infected infants.
8. WHO clinical staging has four stages, from asymptomatic Stage 1 to severe, AIDS-defining Stage 4.
9. CD4 percentage is preferred because absolute CD4 count varies considerably more with age in young children.
10. Clinical and immunological findings do not always correlate, so both are used together for a complete picture.

Part 5.3

11. Antibody tests cannot distinguish infection from passively transferred maternal antibody present until around 18 months.
12. HIV DNA polymerase chain reaction testing is used to diagnose HIV in children under 18 months.
13. Dried blood spot samples are collected around 6 weeks of age and sent for centralised HIV DNA PCR testing.
14. PITC is the routine offer of testing to patients attending for other reasons, increasing testing uptake.
15. Nucleoside and non-nucleoside reverse transcriptase inhibitors are examples of antiretroviral drug classes.

Part 5.4

1. Antiretroviral prophylaxis, cotrimoxazole prophylaxis, and early infant diagnosis testing are components of the care package.
2. Exclusive breastfeeding is recommended when the mother is receiving effective antiretroviral therapy.

3. Schistosoma blood flukes, transmitted through contact with freshwater containing infected snails, cause schistosomiasis.
4. Schistosoma haematobium causes urinary tract disease; Schistosoma mansoni causes intestinal and hepatic disease.
5. Diagnosis relies on egg detection in urine or stool, and treatment is with a single dose of praziquantel.

References and Attributions [Series 5]

1. Kliegman, R. M., St Geme, J. W., Blum, N. J., Shah, S. S., Tasker, R. C. and Wilson, K. M. (2020). Nelson Textbook of Pediatrics (21st ed.). Elsevier.
2. World Health Organization (2021). Consolidated Guidelines on HIV Prevention, Testing, Treatment, Service Delivery and Monitoring. WHO Press.
3. Federal Ministry of Health, Nigeria (2020). National Guidelines for HIV Prevention, Treatment and Care.
4. World Health Organization (2022). Schistosomiasis Fact Sheet. WHO Press.

Figures, Plates, Tables, and Boxes

1. Figure 5.1: A mother and infant attending a prevention of mother-to-child transmission clinic. AI-generated using the prompt: "A warm, realistic clinical illustration of a mother holding her infant while a healthcare worker reviews notes with her in a bright, calm clinic room. Single clean medical illustration, soft warm lighting, no text overlays, no multiple panels, respectful and accurate depiction."
2. Table 5.2: WHO clinical staging summary for paediatric HIV disease. AI-generated using the prompt: "Create a clean reference table titled WHO Clinical Staging of Paediatric HIV, listing stage and general description. Simple clinical reference table style with outside border."
3. Figure 5.3: Dried blood spot sample collection from an infant for early infant HIV diagnosis. AI-generated using the prompt: "A realistic, gentle clinical illustration of a healthcare worker collecting a small blood sample from an infant's heel onto a filter paper card, with the infant calm and supported by a caregiver nearby. Single clean

medical illustration, soft clinical lighting, no text overlays, no multiple panels, respectful and accurate depiction."

4. Figure 5.4: A healthcare worker administering cotrimoxazole prophylaxis to an HIV-exposed infant. AI-generated using the prompt: "A warm, realistic clinical illustration of a healthcare worker gently giving an infant a dose of oral liquid medication with a small syringe, while the infant is held comfortably by a caregiver. Single clean medical illustration, soft warm lighting, no text overlays, no multiple panels, respectful and accurate depiction."