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MED 406

INFECTIOUS AND TROPICAL DISEASES

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Course code: MED 406

Course title: Infectious and Tropical Diseases

Course credit load: 2 Units

Series 1: Foundations of Infectious Diseases

- **Part 1.1: Epidemiology and Transmission of Infectious Diseases**
    - Sub Part 1.1.1: Definitions and key concepts
    - Sub Part 1.1.2: Routes of transmission
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Introduction

Infectious diseases remain the leading cause of morbidity and mortality in Nigeria and across sub-Saharan Africa. From childhood diarrhoeal illnesses and respiratory infections to malaria, tuberculosis, and HIV/AIDS, the spectrum of infectious and tropical diseases that clinicians encounter in Nigeria is broad, complex, and consequential. A sound understanding of the foundations of infectious diseases, including how pathogens cause disease, how they spread through populations, and how they can be prevented and controlled, is the essential starting point for effective clinical practice.

The aim of this Series is to equip you with the fundamental knowledge needed to understand the epidemiology, pathogenesis, prevention, and laboratory diagnosis of infectious diseases. We shall commence by examining the key epidemiological concepts underlying infectious disease transmission and spread. Next, we will explore the pathogenesis of infectious diseases, covering aetiological agents, host-pathogen interaction, and the inflammatory response. Moving on, we will consider the strategies for prevention and control, including immunisation, infection control practices, and antimicrobial stewardship. Finally, we will address laboratory diagnosis, covering microbiological, serological, and molecular techniques.

Series Learning Outcomes

Upon completing this Series, you should be able to:

- **SLO 1.1:** define key epidemiological terms and describe the major routes of transmission of infectious diseases,
- **SLO 1.2:** describe the key epidemiological measures used in outbreak investigation,
- **SLO 1.3:** classify the major aetiological agents of infectious diseases and describe their key characteristics,
- **SLO 1.4:** describe host-pathogen interaction, virulence factors, and the pathogenesis of the systemic inflammatory response syndrome,

- **SLO 1.5:** describe the principles of immunisation, infection prevention and control, and antimicrobial stewardship, and
- **SLO 1.6:** describe the major microbiological, serological, and molecular techniques used in the laboratory diagnosis of infectious diseases.

1.1 Epidemiology and Transmission of Infectious Diseases

1.1.1 Definitions and key concepts

Infectious disease epidemiology studies the distribution and determinants of infectious diseases in populations. Key definitions: **incubation period** is the time between exposure to a pathogen and the onset of symptoms (during which the pathogen replicates); **communicable disease** is one that can be transmitted from person to person or from animals, insects, or the environment to humans; **endemic** describes a disease that is constantly present in a population at a predictable rate (for example, malaria in Nigeria); **epidemic** describes a higher than expected number of cases of a disease in a defined area and time period; and **pandemic** describes an epidemic that spreads across countries or continents.

The basic reproduction number (R0) quantifies the average number of secondary cases generated by one infectious case in a fully susceptible population: an R0 above 1 indicates that the disease will spread, while an R0 below 1 indicates that it will decline. Herd immunity is achieved when a sufficient proportion of the population is immune (through vaccination or prior infection) to interrupt transmission and protect unimmunised individuals. The herd immunity threshold is calculated as 1 minus the reciprocal of R0.

A disease that is constantly present in a population at a predictable rate is described as _____. The basic reproduction number R0 describes the average number of _____ cases generated by one infectious case in a fully susceptible population.

1.1.2 Routes of transmission

Infectious diseases are transmitted by several routes. Direct contact transmission involves physical contact between an infected and a susceptible person (skin-to-skin in scabies; sexual contact in gonorrhoea and HIV; droplet spray from coughing or sneezing landing on mucous membranes in influenza, COVID-19, and meningococcal disease). **Indirect contact transmission** involves a contaminated intermediate object or **fomite** (door handles, medical equipment, bed linen). **Airborne transmission** occurs when infectious particles remain suspended in the air for extended periods and are inhaled (tuberculosis, measles, varicella).

Faecal-oral transmission occurs when food or water is contaminated with faecal material containing pathogens (cholera, typhoid, hepatitis A, amoebic dysentery, polio). **Vector-borne transmission** occurs through an intermediate arthropod vector: mosquitoes transmit malaria, dengue, yellow fever, and Zika virus; tsetse flies transmit African sleeping sickness; sandflies transmit leishmaniasis. **Zoonotic transmission** occurs when pathogens are acquired from animals: Lassa fever (rodents), rabies (dog bites), brucellosis (cattle and goats), and monkeypox.

Tuberculosis, measles, and varicella are transmitted by the _____ route (infectious particles suspended in air). Malaria, dengue, and yellow fever are transmitted by the _____ route through mosquitoes.

1.1.3 Epidemiological measures and outbreak investigation

Key epidemiological measures: incidence (the number of new cases in a defined population over a defined time period: measures the rate of occurrence of new disease), prevalence (the proportion of the population with the disease at a given time: includes both new and existing cases), attack rate (the proportion of exposed individuals who develop the disease: useful in outbreak investigation), and case fatality rate (CFR: the proportion of confirmed cases who die: measures disease severity).

Outbreak investigation follows a systematic sequence: confirm the diagnosis and existence of an outbreak, establish a case definition, identify and count cases, describe the outbreak by time (epidemic curve), place, and person, generate and test hypotheses about the source and mode of transmission, implement control measures, and communicate findings. The epidemic curve (a histogram of cases by time of onset) distinguishes a common-source outbreak (a sharp peak from

a single exposure) from a propagated outbreak (a gradual rise from person-to-person transmission).

_____ measures the proportion of a population with a disease at a given time (both new and existing cases). A sharp peak on an epidemic curve suggests a _____ outbreak from a single exposure.

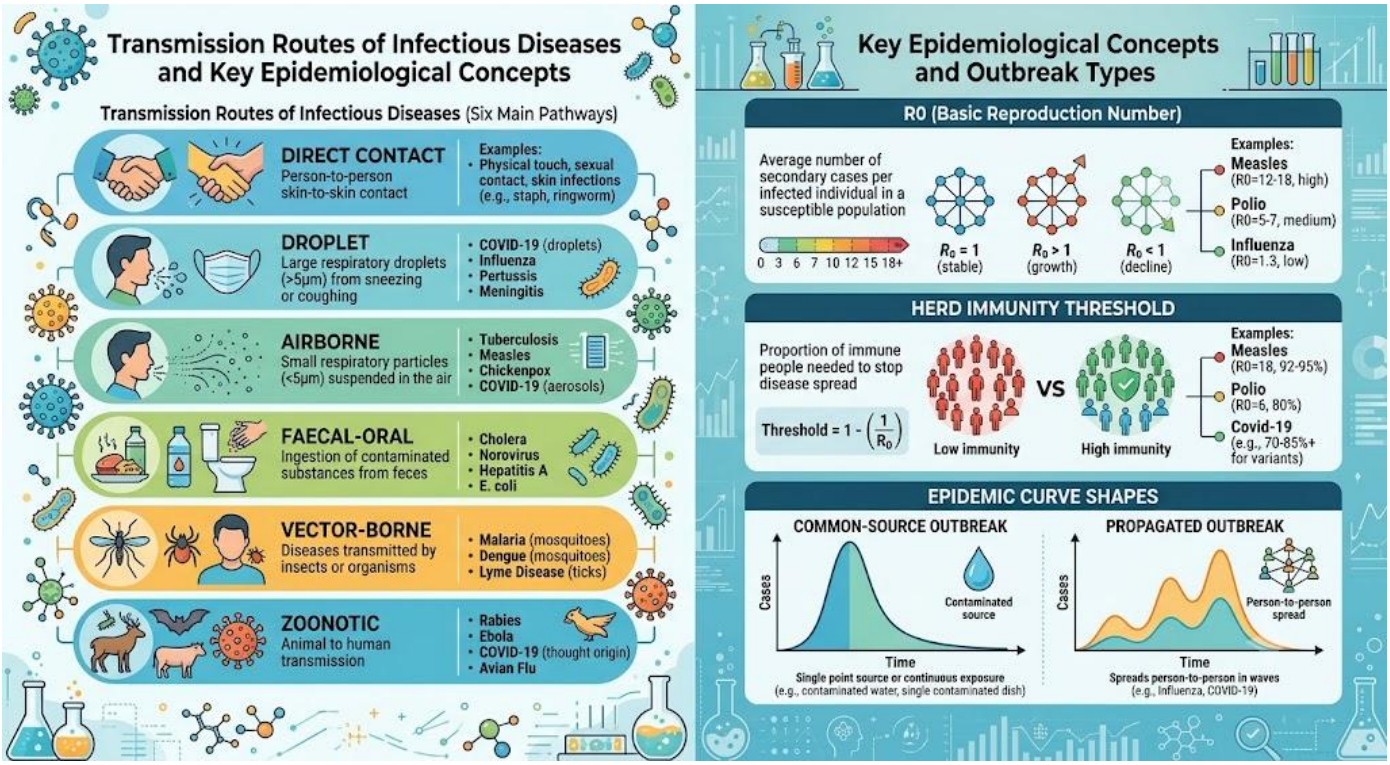

Figure 1.1: Routes of transmission of infectious diseases and key epidemiological concepts

Pilot questions 1.1

1. Define incubation period, endemic, epidemic, and pandemic. (Linked to SLO 1.1)
2. Describe the six major routes of transmission of infectious diseases with one example each. (Linked to SLO 1.1)
3. Explain the basic reproduction number R0 and state its significance for disease control. (Linked to SLO 1.1)
4. Define incidence, prevalence, attack rate, and case fatality rate. (Linked to SLO 1.2)

5. Describe the steps of an outbreak investigation. (Linked to SLO 1.2)

1.2 Pathogenesis of Infectious Diseases

1.2.1 Aetiological agents and their characteristics

Bacteria are prokaryotic organisms classified by Gram staining (Gram-positive: thick peptidoglycan cell wall staining purple; Gram-negative: thin peptidoglycan with outer lipopolysaccharide membrane staining pink), morphology (cocci, bacilli, spirochaetes), and oxygen requirement (aerobic, anaerobic, or facultative). **Viruses** are obligate intracellular parasites consisting of nucleic acid (DNA or RNA) enclosed in a protein capsid, which may be enveloped (HIV, influenza, hepatitis B) or non-enveloped (poliovirus, rotavirus). Enveloped viruses are more sensitive to drying and disinfectants.

Fungi are eukaryotic organisms that cause superficial infections (dermatophytes causing tinea), subcutaneous infections (Sporothrix), and systemic infections in immunocompromised patients (Cryptococcus neoformans causing meningitis; Pneumocystis jirovecii causing PCP; Aspergillus causing invasive aspergillosis). **Parasites** include protozoa (Plasmodium species causing malaria; Entamoeba histolytica; Giardia lamblia; Trypanosoma; Leishmania) and helminths (roundworms such as Ascaris; tapeworms such as Taenia solium; flukes such as Schistosoma mansoni).

Gram-positive bacteria have a _____ peptidoglycan cell wall and stain purple. Enveloped viruses such as HIV and influenza are more sensitive to drying and disinfectants than _____ viruses such as poliovirus.

1.2.2 Host-pathogen interaction and virulence

Virulence refers to the ability of a pathogen to cause disease in the host and is determined by specific **virulence factors**: adhesins (surface molecules that mediate attachment to host cells), invasins (proteins that facilitate entry into host cells), toxins (exotoxins: proteins secreted by bacteria that cause specific damage such as the cholera toxin causing secretory diarrhoea or the

tetanus toxin causing spastic paralysis; endotoxin: the lipopolysaccharide of Gram-negative bacteria, which triggers the systemic inflammatory response), and enzymes that degrade host tissues (coagulase, hyaluronidase, proteases).

Host defences against infection include physical barriers (intact skin and mucous membranes, mucociliary clearance, gastric acid), innate immunity (neutrophils, macrophages, natural killer cells, complement, interferon), and adaptive immunity (B lymphocytes producing specific antibodies; T lymphocytes mediating cell-mediated immunity, which is critical for intracellular pathogens such as Mycobacterium tuberculosis, Leishmania, and HIV). The balance between pathogen virulence and host defences determines the outcome of infection: elimination, latency, chronic infection, or death.

_____ are surface molecules on bacteria that mediate attachment to host cells. The _____ (LPS) of Gram-negative bacteria acts as an endotoxin triggering the systemic inflammatory response.

1.2.3 The inflammatory response and sepsis

Systemic inflammatory response syndrome (SIRS) is defined by two or more of: temperature above 38 degrees C or below 36 degrees C, heart rate above 90 beats per minute, respiratory rate above 20 per minute or PaCO2 below 32 mmHg, and white cell count above 12,000 or below 4,000 per microlitre or above 10 percent band forms. **Sepsis** is life-threatening organ dysfunction caused by a dysregulated host response to infection (Sepsis-3 definition), recognised clinically by a SOFA score increase of 2 or more points. **Septic shock** is a subset of sepsis with persisting hypotension requiring vasopressors to maintain MAP above 65 mmHg and serum lactate above 2 mmol/L despite adequate fluid resuscitation.

Management of sepsis follows the Surviving Sepsis Campaign Hour-1 bundle: measure serum lactate; obtain blood cultures before antibiotics; administer broad-spectrum antibiotics within 1 hour of recognition; begin 30 mL per kg IV crystalloid for hypotension or lactate above 4 mmol/L; apply vasopressors (noradrenaline: first choice) if the patient remains hypotensive after fluid resuscitation. Source control (drainage of abscess, removal of infected catheter, or surgical debridement) is an essential component of sepsis management.

Septic shock is defined as sepsis with persisting hypotension requiring _____ to maintain MAP above 65 mmHg and serum lactate above 2 mmol/L. The first-line vasopressor in septic shock is _____.

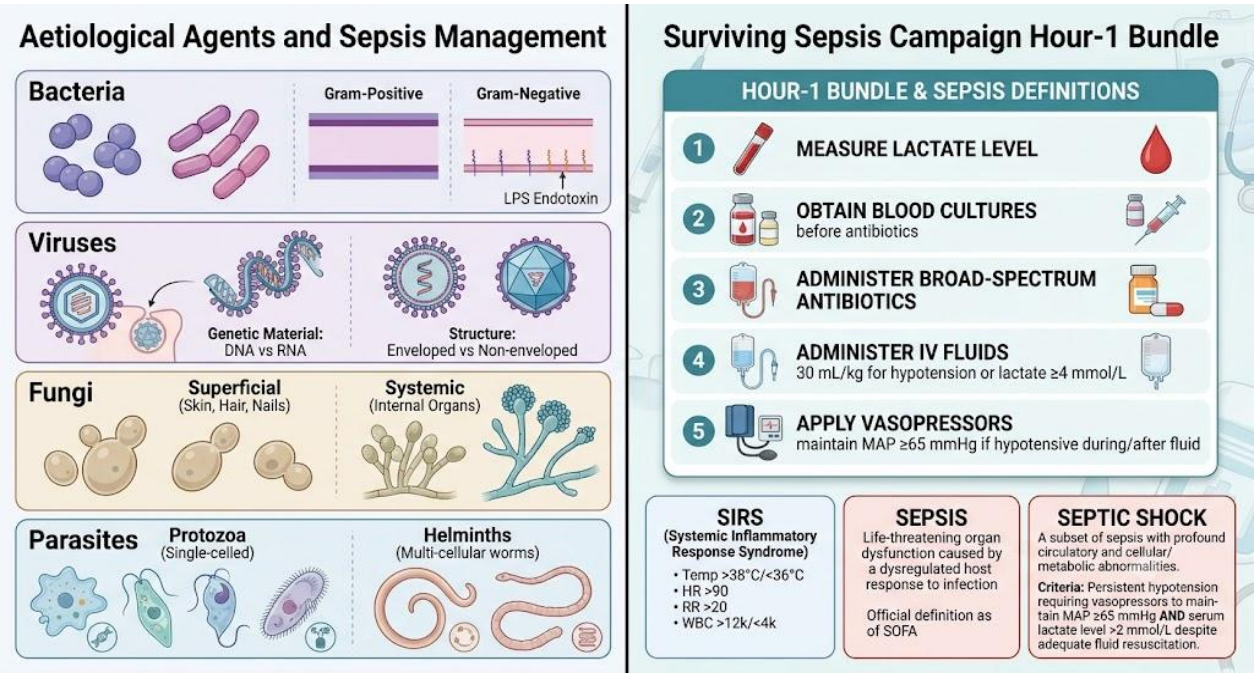

Figure 1.2: Aetiological agents of infectious diseases and the sepsis Hour-1 management bundle

Pilot questions 1.2

1. Classify the major aetiological agents of infectious diseases and give two examples of each. (Linked to SLO 1.3)
2. Describe the Gram stain and explain its clinical relevance in guiding antibiotic therapy. (Linked to SLO 1.3)
3. Define virulence and describe four types of virulence factors. (Linked to SLO 1.4)
4. Define SIRS, sepsis, and septic shock. (Linked to SLO 1.4)
5. Describe the Surviving Sepsis Campaign Hour-1 bundle. (Linked to SLO 1.4)

1.3 Prevention and Control of Infectious Diseases

1.3.1 Immunisation and vaccines

Immunisation is the process of conferring immunity against infectious diseases, either by vaccination (active immunisation: stimulating the immune system to produce its own antibodies and memory cells) or by administration of preformed antibodies (passive immunisation: immunoglobulins providing immediate but short-lived protection). Vaccines are classified by type: **live attenuated vaccines** (BCG, MMR, OPV, yellow fever: produce strong, long-lasting immunity but are contraindicated in immunocompromised patients), **inactivated vaccines** (hepatitis A, influenza, IPV: safer in immunocompromised patients but may require booster doses), **subunit vaccines** (hepatitis B, pneumococcal, meningococcal, HPV), and **toxoid vaccines** (tetanus, diphtheria: use inactivated bacterial toxins).

Nigeria's Expanded Programme on Immunisation (EPI) includes: BCG (birth), hepatitis B (birth dose), OPV (birth, 6, 10, 14 weeks), Pentavalent vaccine (Hib, diphtheria, pertussis, tetanus, hepatitis B: 6, 10, 14 weeks), PCV13 (6, 10, 14 weeks), IPV (14 weeks), rotavirus vaccine, yellow fever (9 months), measles-rubella (9 months and 15 to 18 months), and meningococcal A vaccine. Vaccine hesitancy, cold chain failures, and geographical inaccessibility remain important barriers to achieving full coverage in Nigeria.

Live attenuated vaccines such as BCG and MMR are contraindicated in _____ patients. Toxoid vaccines such as tetanus and diphtheria use inactivated bacterial _____ to stimulate immunity.

1.3.2 Infection prevention and control

Standard precautions are applied to all patients regardless of their infectious status and include: hand hygiene (the single most effective infection prevention measure: using soap and water or alcohol-based hand rub at the five WHO moments: before patient contact, before aseptic procedure, after body fluid exposure, after patient contact, after touching patient surroundings), **personal protective equipment (PPE)** (gloves, aprons, masks, eye protection as appropriate), safe handling and disposal of sharps, and safe disposal of infectious waste.

Transmission-based precautions are added for patients with known or suspected transmissible infections: contact precautions (gloves and apron: for MRSA, Clostridium difficile, norovirus), droplet precautions (surgical mask: for influenza, meningococcal disease, mumps), and airborne precautions (N95 respirator, negative pressure room: for tuberculosis, measles, varicella). Hand hygiene compliance among healthcare workers in Nigerian hospitals is often below the WHO target, and improvement requires system-level interventions including alcohol-based hand rub availability, education, and auditing.

_____ precautions are applied to all patients regardless of their infectious status, with hand hygiene being the single most effective measure. _____ precautions requiring an N95 respirator are used for tuberculosis, measles, and varicella.

1.3.3 Antimicrobial stewardship

Antimicrobial resistance (AMR) arises when microorganisms develop the ability to survive in the presence of antimicrobials that would normally kill or inhibit them. Mechanisms of resistance include: production of drug-inactivating enzymes (beta-lactamases destroying penicillins and cephalosporins; extended-spectrum beta-lactamases or ESBLs in Gram-negative bacteria), altered drug targets (MRSA: altered penicillin-binding protein PBP2a; penicillin-resistant Streptococcus pneumoniae), reduced drug uptake or increased efflux (Pseudomonas aeruginosa), and acquisition of resistance genes on plasmids.

Antimicrobial stewardship (AMS) programmes aim to optimise antimicrobial use to improve patient outcomes while minimising adverse effects and reducing AMR. Core principles include: prescribing the right drug at the right dose and duration for the right indication, de-escalation (switching from broad-spectrum to narrow-spectrum antibiotics when culture results are available), and avoiding antibiotics for viral infections. In Nigeria, antimicrobial stewardship is challenged by over-the-counter antibiotic dispensing without prescription, self-medication, and inadequate laboratory infrastructure for culture and sensitivity testing.

Extended-spectrum beta-lactamases (ESBLs) are enzymes produced by Gram-negative bacteria that inactivate _____ and cephalosporins. De-escalation in antimicrobial stewardship means switching from _____ to narrow-spectrum antibiotics when culture results are available.

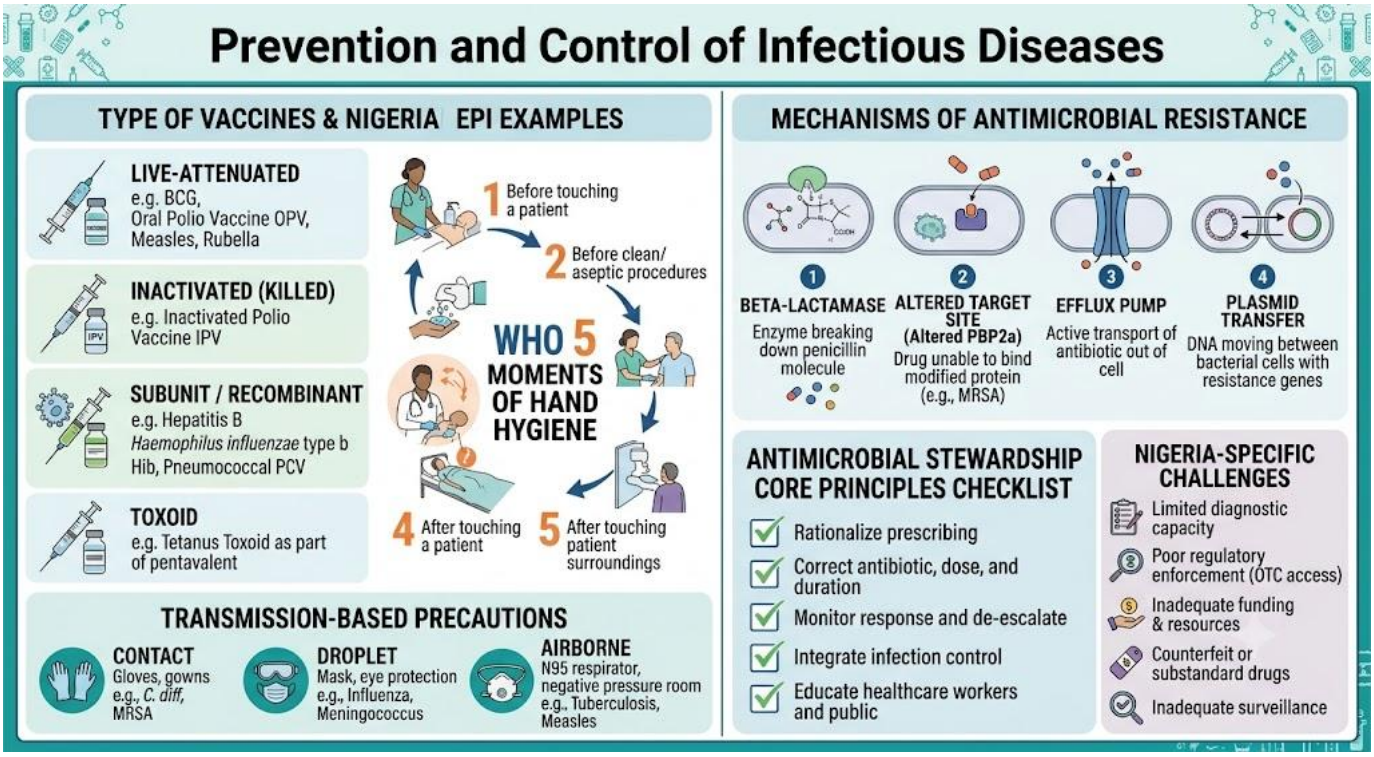

Figure 1.3: Prevention and control of infectious diseases: immunisation, infection control, and antimicrobial stewardship

Pilot questions 1.3

1. Classify vaccines by type and give two examples of each type. (Linked to SLO 1.5)
2. Describe the Nigeria EPI schedule and state three barriers to vaccine coverage. (Linked to SLO 1.5)
3. Describe the WHO 5 Moments of Hand Hygiene and state why hand hygiene is the most important infection prevention measure. (Linked to SLO 1.5)
4. Describe the transmission-based precautions and the pathogens that require each type. (Linked to SLO 1.5)
5. Describe the mechanisms of antimicrobial resistance and the principles of antimicrobial stewardship. (Linked to SLO 1.5)

1.4 Laboratory Diagnosis of Infectious Diseases

1.4.1 Microbiological techniques

Direct microscopy is the simplest and most rapid diagnostic technique: a specimen is examined under a microscope to identify organisms. Examples include Ziehl-Neelsen staining (acid-fast staining of sputum for Mycobacterium tuberculosis: the red bacilli appear against a blue background), Gram staining (to classify bacteria by cell wall type and guide empirical antibiotic therapy), potassium hydroxide (KOH) preparation (for fungal hyphae and spores), and peripheral blood film (for malaria parasites, trypanosomes, and microfilariae).

Culture and sensitivity testing involves inoculating a specimen onto culture media and incubating it under specific conditions to allow organisms to grow, followed by identification (by colony morphology, biochemical tests, or mass spectrometry using MALDI-TOF) and antibiotic sensitivity testing (disc diffusion or minimum inhibitory concentration). Blood culture (for bacteraemia and fungaemia), sputum culture (for respiratory infections), urine culture (for urinary tract infections), and cerebrospinal fluid culture (for meningitis) are standard investigations. Cultures require 24 to 72 hours for bacterial growth and up to 8 weeks for Mycobacterium tuberculosis on solid media.

Ziehl-Neelsen staining identifies _____ tuberculosis in sputum as red bacilli against a blue background. Culture of Mycobacterium tuberculosis on solid media (Lowenstein-Jensen medium) takes up to _____ weeks.

1.4.2 Serological and molecular diagnosis

Serological tests detect antibodies in the patient's serum produced in response to a specific antigen. IgM antibodies indicate recent or acute infection (IgM appears within days of infection and wanes after weeks to months), while IgG antibodies indicate previous exposure or immunity. Examples include: ELISA (enzyme-linked immunosorbent assay: used for HIV, hepatitis B and C serology, dengue, and Lassa fever antibody detection), rapid diagnostic tests (RDTs: lateral flow immunoassays used at point of care for malaria, HIV, and hepatitis B surface antigen), and

the Widal test (agglutination test for typhoid fever antibodies: limited specificity in endemic areas).

Molecular techniques detect pathogen nucleic acid directly in clinical specimens with very high sensitivity and specificity. **Polymerase chain reaction (PCR)** amplifies specific DNA or RNA sequences, allowing detection of minute quantities of pathogen nucleic acid. Quantitative PCR (qPCR) measures viral load and is used to monitor HIV treatment response and assess hepatitis B and C viral replication. GeneXpert MTB/RIF (a cartridge-based automated PCR system) simultaneously detects M. tuberculosis and rifampicin resistance within 2 hours and is the WHO-recommended first-line TB diagnostic test.

IgM antibodies indicate _____ infection, while IgG antibodies indicate previous exposure or immunity. GeneXpert MTB/RIF detects Mycobacterium tuberculosis and rifampicin resistance within _____ hours.

1.4.3 Interpretation of laboratory results

Laboratory results must always be interpreted in the clinical context. A positive culture does not always indicate pathogenic infection: skin organisms may contaminate blood cultures (coagulase-negative staphylococci are a common contaminant), respiratory flora may contaminate sputum cultures, and some organisms colonise without causing disease. A negative culture does not exclude infection: prior antibiotic use reduces culture sensitivity, and some pathogens do not grow on standard media (viruses, mycoplasma, rickettsia, treponema, and anaerobes require specific conditions).

Common pitfalls in laboratory interpretation: the Widal test is frequently false-positive in Nigeria due to high background antibody titres from prior typhoid exposure or vaccination; malaria rapid diagnostic tests may remain positive for weeks after treatment due to persistent circulating antigen; blood culture contamination rates above 3 percent indicate inadequate sterile technique. Reporting of infectious disease results must comply with Nigeria's disease surveillance and notification system, which requires compulsory notification of specified

diseases including cholera, Lassa fever, meningococcal disease, poliomyelitis, viral haemorrhagic fevers, and yellow fever.

A positive blood culture with coagulase-negative staphylococci most likely represents _____ rather than true bacteraemia. Prior _____ use reduces the sensitivity of cultures by inhibiting organism growth.

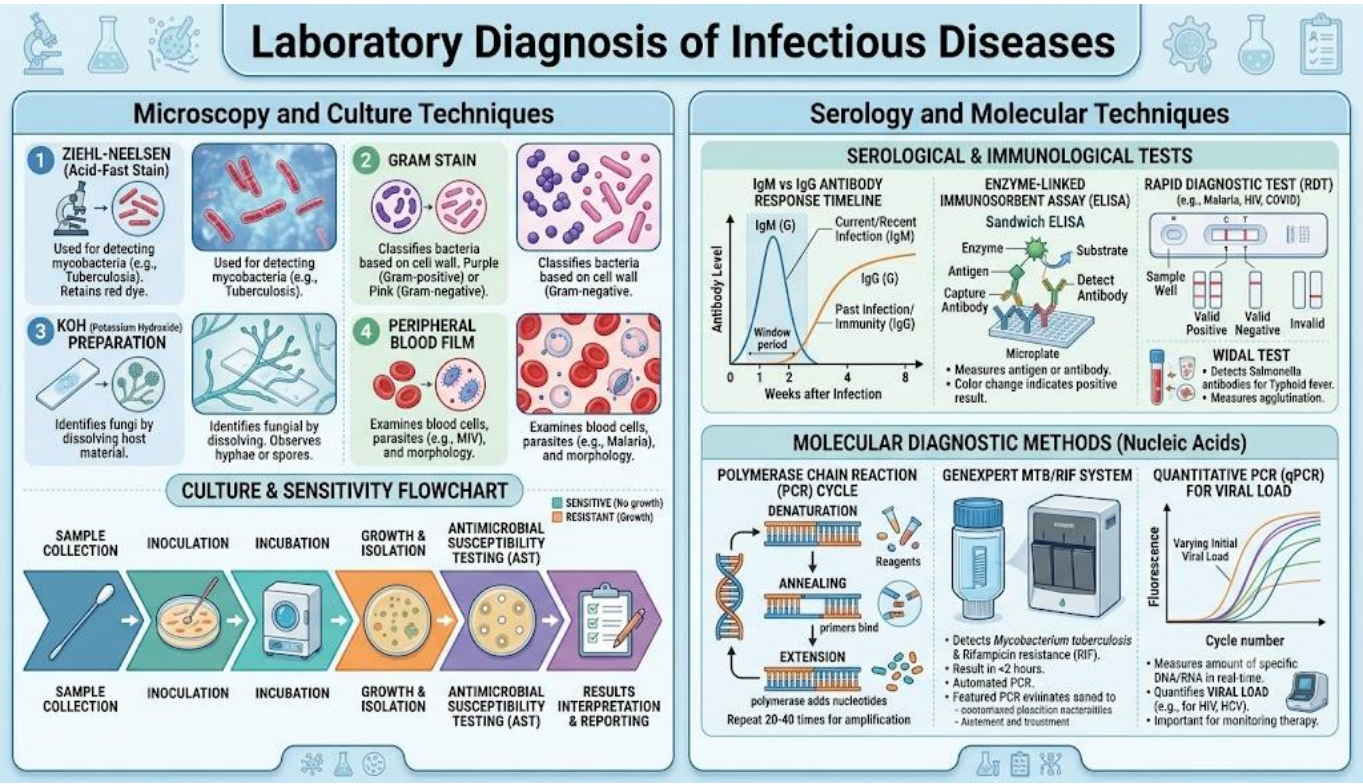

Figure 1.4: Laboratory diagnosis of infectious diseases: microscopy, culture, serology, and molecular techniques

Pilot questions 1.4

1. Describe the Ziehl-Neelsen stain and state what it is used to diagnose. (Linked to SLO 1.6)
2. Describe the culture and sensitivity testing process for a patient with suspected septicaemia. (Linked to SLO 1.6)

3. Distinguish between IgM and IgG antibodies and state the clinical significance of each. (Linked to SLO 1.6)
4. Describe GeneXpert MTB/RIF and state why it is the WHO-recommended first-line TB diagnostic test. (Linked to SLO 1.6)
5. Describe two common pitfalls in the interpretation of laboratory results in infectious disease diagnosis. (Linked to SLO 1.6)

Series Summary

This Series has established the foundations of infectious diseases. We began with epidemiology and transmission, defining key concepts including incubation period, endemic, epidemic, pandemic, R0, and herd immunity, and describing the six major routes of transmission (direct contact, droplet, airborne, faecal-oral, vector-borne, and zoonotic) and the steps of outbreak investigation including the epidemic curve. Next, we explored pathogenesis, classifying aetiological agents (bacteria by Gram stain and morphology, viruses by nucleic acid type and envelope status, fungi, and parasites), describing virulence factors (adhesins, invasins, toxins, and tissue-degrading enzymes), and defining SIRS, sepsis, and septic shock with the Hour-1 management bundle. Moving on, we covered prevention and control through immunisation (live attenuated, inactivated, subunit, and toxoid vaccines; Nigeria EPI schedule), infection prevention and control (standard precautions, WHO 5 Moments of Hand Hygiene, transmission-based precautions), and antimicrobial stewardship (AMR mechanisms and the principles of responsible prescribing). Finally, we addressed laboratory diagnosis, covering direct microscopy (Ziehl-Neelsen, Gram stain, peripheral blood film), culture and sensitivity testing, serological tests (ELISA, RDT, Widal), and molecular techniques (PCR and GeneXpert MTB/RIF).

By completing this Series, you should now be able to define key epidemiological terms and describe the major routes of transmission, describe the aetiological agents and pathogenesis of infectious diseases, outline the principles of immunisation and infection control, and describe the laboratory techniques used to diagnose infectious diseases. These abilities align with the Series Learning Outcomes (SLOs 1.1 to 1.6) and provide the essential foundation for the clinical and disease-specific content in the subsequent Series.

Glossary of Terms

- **Attack rate:** the proportion of exposed individuals who develop the disease during an outbreak; used to measure the transmissibility of the pathogen and identify the mode of transmission.

- **Basic reproduction number (R0):** the average number of secondary cases generated by one infectious case in a fully susceptible population; R0 above 1 indicates the disease will spread; R0 below 1 indicates decline.
- **Case fatality rate (CFR):** the proportion of confirmed cases of a disease who die; measures the severity of the disease in those who are infected.
- **Endemic:** describes a disease that is constantly present in a defined population at a predictable baseline rate, such as malaria in Nigeria.
- **GeneXpert MTB/RIF:** a cartridge-based automated PCR system that simultaneously detects Mycobacterium tuberculosis and rifampicin resistance in sputum within 2 hours; WHO-recommended first-line TB diagnostic test.
- **Herd immunity:** the indirect protection of unimmunised individuals when a sufficient proportion of the population is immune, interrupting transmission of the pathogen.
- **Incubation period:** the interval between exposure to a pathogen and the onset of symptoms; during this period the pathogen replicates in the host.
- **Prevalence:** the proportion of a defined population with a disease at a specific point in time; includes both new and existing cases.
- **Sepsis:** life-threatening organ dysfunction caused by a dysregulated host response to infection; recognised clinically by a SOFA score increase of 2 or more points.
- **Septic shock:** a subset of sepsis with persistent hypotension requiring vasopressors to maintain MAP above 65 mmHg and serum lactate above 2 mmol/L despite adequate fluid resuscitation.
- **Virulence:** the ability of a pathogen to cause disease in a host; determined by virulence factors including adhesins, invasins, exotoxins, endotoxin, and tissue-degrading enzymes.
- **Zoonosis:** an infectious disease transmitted from vertebrate animals to humans; examples include Lassa fever (rodents), rabies (dog bites), brucellosis (cattle and goats), and monkeypox.

Concept Check Questions [Series 1]

Objective questions

1. A disease constantly present in a population at a predictable rate is described as _____, while a higher than expected number of cases in a defined area and time is described as an epidemic. (Linked to SLO 1.1)
2. Tuberculosis, measles, and varicella are transmitted by the _____ route, requiring an N95 respirator and negative pressure room for infection control. (Linked to SLO 1.1)
3. Live attenuated vaccines such as BCG and MMR are contraindicated in _____ patients because the attenuated organism may cause disease. (Linked to SLO 1.5)
4. GeneXpert MTB/RIF detects Mycobacterium tuberculosis and rifampicin resistance within _____ hours and is the WHO-recommended first-line TB diagnostic test. (Linked to SLO 1.6)
5. _____ antibodies indicate recent or acute infection, while IgG antibodies indicate previous exposure or immunity. (Linked to SLO 1.6)

Short-answer questions

6. Define incidence and prevalence and explain the difference between them. (Linked to SLO 1.2)
7. Describe the Gram stain result for Staphylococcus aureus and Escherichia coli and explain its clinical relevance. (Linked to SLO 1.3)
8. Define sepsis according to the Sepsis-3 definition and describe two features of septic shock. (Linked to SLO 1.4)
9. Describe the WHO 5 Moments of Hand Hygiene. (Linked to SLO 1.5)
10. Describe two limitations of the Widal test for typhoid diagnosis in Nigeria. (Linked to SLO 1.6)

Long-answer questions

11. Describe the major routes of transmission of infectious diseases and give examples of diseases transmitted by each route. (Linked to SLO 1.1)
12. Classify the major aetiological agents of infectious diseases, describe their key characteristics, and explain how virulence factors contribute to pathogenesis. (Linked to SLOs 1.3 and 1.4)
13. Describe the types of vaccines, the Nigeria EPI schedule, and the barriers to achieving full vaccine coverage in Nigeria. (Linked to SLO 1.5)
14. Describe the mechanisms of antimicrobial resistance and the principles of antimicrobial stewardship. (Linked to SLO 1.5)
15. Describe the laboratory techniques used to diagnose tuberculosis, from direct microscopy through culture to molecular diagnosis. (Linked to SLO 1.6)

Answers to Concept Check Questions [Series 1]

Objective questions

1. Endemic.
2. Airborne.
3. Immunocompromised.
4. 2.
5. IgM.

Short-answer questions

6. Incidence measures the number of new cases of a disease in a defined population over a defined time period and reflects the rate at which new disease is occurring. Prevalence measures the proportion of a population with the disease at a given point in time and

includes both new and existing cases. A disease with a long duration will have a high prevalence relative to incidence, even if few new cases occur.

7. Staphylococcus aureus is a Gram-positive coccus: it has a thick peptidoglycan cell wall that retains the crystal violet stain and appears purple. Escherichia coli is a Gram-negative bacillus: its thin peptidoglycan cell wall and outer lipopolysaccharide membrane do not retain the crystal violet and it appears pink after counterstaining with safranin. Clinically, Gram staining guides empirical antibiotic therapy: Gram-positive infections are typically treated with beta-lactams or vancomycin, while Gram-negative infections require agents active against LPS-containing organisms such as cephalosporins or fluoroquinolones.
8. Sepsis (Sepsis-3 definition) is life-threatening organ dysfunction caused by a dysregulated host response to infection, recognised clinically by a SOFA score increase of 2 or more points. Septic shock is a subset of sepsis characterised by persistent hypotension requiring vasopressors to maintain mean arterial pressure above 65 mmHg despite adequate fluid resuscitation, and serum lactate above 2 mmol/L.
9. The WHO 5 Moments of Hand Hygiene: before patient contact (to prevent transferring organisms to the patient), before an aseptic procedure (to prevent introducing organisms into the patient), after body fluid exposure or risk (to protect the healthcare worker and prevent transmission), after patient contact (to prevent transferring organisms from the patient to the environment), and after touching patient surroundings (to prevent indirect transmission via contaminated surfaces).
10. The Widal test has poor specificity in Nigeria because high background antibody titres from prior subclinical typhoid infection or vaccination result in many false-positive results, making it unreliable as a diagnostic test in endemic areas. In addition, a single positive result cannot distinguish between acute infection and past exposure; paired sera showing a four-fold rise in titre are required to confirm acute infection, but this is rarely done in clinical practice.

Long-answer questions

11. **Basic response:** Direct contact (skin-to-skin: scabies; sexual contact: gonorrhoea, syphilis, HIV). Droplet (infectious particles above 5 microns landing on mucous membranes within 1 to 2 metres: influenza, COVID-19, meningococcal disease). Airborne (infectious particles below 5 microns suspended in air: tuberculosis, measles, varicella). Faecal-oral (contaminated food or water: cholera, typhoid, hepatitis A, hepatitis E, amoebic dysentery, polio, giardiasis). Vector-borne (through an arthropod intermediate: malaria and dengue and yellow fever via mosquito, sleeping sickness via tsetse fly, leishmaniasis via sandfly). Zoonotic (from animals: Lassa fever from rodents, rabies from dog bites, brucellosis from cattle and goats, monkeypox).

Value-added response: In Nigeria, vector-borne and faecal-oral transmission routes account for the majority of the infectious disease burden, because the combination of endemic malaria, inadequate access to safe drinking water, and poor sanitation infrastructure creates the conditions for sustained transmission of both mosquito-borne and waterborne pathogens.

12. **Basic response:** Bacteria: prokaryotes classified by Gram stain (Gram-positive: thick peptidoglycan, stains purple; examples: Staphylococcus aureus, Streptococcus pneumoniae; Gram-negative: thin peptidoglycan with LPS, stains pink; examples: E. coli, Salmonella, Neisseria), morphology (cocci, bacilli, spirochaetes), and oxygen requirement. Viruses: obligate intracellular parasites with DNA or RNA genome; enveloped (HIV, influenza, hepatitis B: sensitive to disinfectants) or non-enveloped (poliovirus, rotavirus: more resistant). Fungi: eukaryotes causing superficial, subcutaneous, or systemic infections (Cryptococcus neoformans causing meningitis in HIV patients; PCP from Pneumocystis jirovecii). Parasites: protozoa (Plasmodium causing malaria; Entamoeba histolytica; Trypanosoma) and helminths (Ascaris, Schistosoma, Taenia). Virulence factors: adhesins (attachment to host cells), invasins (entry into host cells), exotoxins (specific damage: cholera toxin causes secretory diarrhoea; tetanus toxin causes spastic paralysis), endotoxin or LPS (triggers SIRS in Gram-negative infections), and tissue-degrading enzymes (coagulase, hyaluronidase, proteases).

Value-added response: Understanding the classification of aetiological agents is clinically essential because it directly guides empirical antimicrobial therapy: a Gram stain result allows the clinician to narrow antibiotic choice immediately, before culture results are available, which is critical in life-threatening infections where delays in appropriate therapy worsen mortality.

13. **Basic response:** Vaccine types: live attenuated (BCG, MMR, OPV, yellow fever: strong long-lasting immunity; contraindicated in immunocompromised patients and pregnancy in some cases), inactivated (hepatitis A, influenza, IPV: safe in immunocompromised; may require boosters), subunit (hepatitis B, PCV13, HPV, meningococcal: safe, highly purified antigens), and toxoid (tetanus, diphtheria: inactivated bacterial toxins). Nigeria EPI schedule includes BCG and hepatitis B birth dose, OPV and pentavalent vaccine and PCV13 at 6, 10, and 14 weeks, IPV at 14 weeks, rotavirus vaccine, and yellow fever and measles-rubella vaccines at 9 months. Barriers to coverage: vaccine hesitancy from misinformation (false rumours of vaccine harm in the Kano polio vaccine boycott), cold chain failures (maintaining vaccines at 2 to 8 degrees C from manufacturer to point of delivery in a country with unreliable electricity), and geographical inaccessibility of nomadic and rural populations.

Value-added response: Achieving above 95 percent vaccination coverage for measles and polio in all local government areas is essential to maintain herd immunity thresholds; sub-threshold coverage in even small geographic pockets allows sustained transmission and outbreaks, as seen in the return of wild poliovirus in northern Nigeria following the 2003 to 2004 vaccine boycott.

14. **Basic response:** AMR mechanisms: beta-lactamase enzymes (destroy the beta-lactam ring of penicillins and cephalosporins; ESBLs in E. coli and Klebsiella confer resistance to most cephalosporins), altered drug targets (MRSA: altered penicillin-binding protein PBP2a with low affinity for all beta-lactams; penicillin-resistant pneumococcus), reduced drug uptake or increased efflux pumps (Pseudomonas aeruginosa), and acquisition of resistance genes on plasmids (which allow rapid spread of resistance between different bacterial species). AMS principles: prescribe the right drug for the right indication at the right dose and duration; perform culture and sensitivity testing before starting antibiotics in severe infections; de-escalate from broad-spectrum to narrow-spectrum antibiotics

when culture results are available; avoid antibiotics for viral upper respiratory infections; monitor and audit prescribing practice. Nigeria-specific challenges: over-the-counter antibiotic dispensing without prescription, patient self-medication and early cessation of treatment, and inadequate laboratory infrastructure for culture and sensitivity in many facilities.

Value-added response: AMR is a global emergency that disproportionately affects low-income countries like Nigeria: when first-line antibiotics such as ampicillin and cotrimoxazole fail due to resistance, patients require more expensive second-line drugs (cephalosporins, fluoroquinolones, carbapenems) that may not be available or affordable in the public health sector, and infections that were once easily treatable become life-threatening.

15. **Basic response:** Sputum microscopy (Ziehl-Neelsen stain): early morning sputum sample is smear-prepared on a glass slide, fixed, and stained with carbol fuchsin; after acid-alcohol decolorisation, Mycobacterium tuberculosis appears as red acid-fast bacilli against a blue background; three samples are recommended for maximum sensitivity (positive in 50 to 70 percent of pulmonary TB). GeneXpert MTB/RIF: the preferred first-line test in Nigeria (WHO-recommended); a sputum specimen is placed in a cartridge; automated PCR detects M. tuberculosis DNA and probes for rifampicin resistance mutations (rpoB gene) within 2 hours; sensitivity approximately 88 percent for smear-negative TB; simultaneously identifies MDR-TB potential. Culture on Lowenstein-Jensen solid medium: gold standard; detects organisms at lower concentrations than smear; essential for drug susceptibility testing to guide MDR-TB management; requires 4 to 8 weeks. MGIT liquid culture system: faster (10 to 14 days) but requires specialised equipment.

Value-added response: The introduction of GeneXpert in Nigeria has transformed TB diagnosis by enabling same-day diagnosis and rifampicin resistance detection in a single test, reducing the diagnostic delay that previously allowed continued community transmission; however, access to GeneXpert is still not universal across all health facilities, particularly at the primary healthcare level.

Answers to Pilot Questions [Series 1]

Part 1.1

1. Incubation period: the interval between exposure to a pathogen and onset of symptoms. Endemic: a disease constantly present in a population at a predictable rate. Epidemic: a higher than expected number of cases in a defined area and time period. Pandemic: an epidemic spreading across countries or continents.
2. Direct contact (skin-to-skin or sexual: scabies, gonorrhoea, HIV). Droplet (coughing or sneezing within 1 to 2 metres: influenza, COVID-19, meningococcal disease). Airborne (particles suspended in air: tuberculosis, measles, varicella). Faecal-oral (contaminated food or water: cholera, typhoid, hepatitis A, polio). Vector-borne (arthropod intermediate: malaria via mosquito, sleeping sickness via tsetse fly). Zoonotic (from animals: Lassa fever from rodents, rabies from dog bites).
3. R0 is the average number of secondary cases generated by one infectious case in a fully susceptible population. R0 above 1: the disease will spread in the population. R0 below 1: the disease will decline and eventually die out. It determines the herd immunity threshold needed to interrupt transmission: threshold equals 1 minus the reciprocal of R0.
4. Incidence: the number of new cases in a defined population over a defined time period (measures the rate of new disease occurrence). Prevalence: the proportion of the population with the disease at a given time (includes new and existing cases). Attack rate: the proportion of exposed individuals who develop the disease (used in outbreak investigation). Case fatality rate: the proportion of confirmed cases who die (measures disease severity).
5. Confirm the diagnosis and existence of an outbreak. Establish a case definition. Identify and count cases. Describe the outbreak by time (epidemic curve), place (spot map), and person (attack rates by age, sex, and exposure). Generate hypotheses about the source and

mode of transmission. Test hypotheses using analytical epidemiology. Implement control measures. Communicate findings to public health authorities.

Part 1.2

1. Bacteria (prokaryotes: examples S. aureus, E. coli, M. tuberculosis, V. cholerae). Viruses (obligate intracellular parasites: examples HIV, influenza, hepatitis B, SARS-CoV-2, measles). Fungi (eukaryotes: examples Candida albicans, Cryptococcus neoformans, Aspergillus fumigatus, Pneumocystis jirovecii). Parasites (protozoa: Plasmodium species, Entamoeba histolytica; helminths: Ascaris lumbricoides, Schistosoma mansoni).
2. Gram stain procedure: smear preparation, heat fixation, crystal violet primary stain, iodine mordant, acetone or alcohol decoloriser, safranin counterstain. Gram-positive result: thick peptidoglycan wall retains crystal violet and appears purple (Staphylococcus, Streptococcus, Clostridium). Gram-negative result: thin peptidoglycan with LPS does not retain crystal violet and appears pink (E. coli, Salmonella, Klebsiella, Pseudomonas). Clinical relevance: Gram staining allows empirical antibiotic choice within minutes of obtaining a specimen, well before culture results are available.
3. Virulence is the ability of a pathogen to cause disease in a host. Four virulence factors: adhesins (surface molecules mediating attachment to host cells, enabling colonisation: pili of E. coli), invasins (proteins facilitating entry into host cells: internalins of Listeria), exotoxins (secreted proteins causing specific damage: cholera toxin causes secretory diarrhoea by activating adenylate cyclase; tetanus toxin blocks glycine release at inhibitory synapses), and endotoxin (LPS of Gram-negative bacteria: triggers SIRS and septic shock).
4. SIRS: systemic inflammatory response syndrome; 2 or more of: temperature above 38 degrees C or below 36 degrees C, heart rate above 90 bpm, respiratory rate above 20 per minute or PaCO2 below 32 mmHg, white cell count above 12,000 or below 4,000 per microlitre. Sepsis (Sepsis-3): life-threatening organ dysfunction from a dysregulated host response to infection; recognised by SOFA score increase of 2 or more points. Septic

shock: subset of sepsis with persistent hypotension requiring vasopressors to maintain MAP above 65 mmHg and lactate above 2 mmol/L despite adequate fluids.

5. Hour-1 bundle: measure serum lactate (above 4 mmol/L: aggressive fluid resuscitation required); obtain blood cultures before antibiotics (ideally 2 sets from different sites); administer broad-spectrum IV antibiotics within 1 hour of recognition of sepsis; begin 30 mL per kg IV crystalloid bolus for hypotension or lactate above 4 mmol/L; apply vasopressors (noradrenaline: first choice) if MAP remains below 65 mmHg after adequate fluid resuscitation.

Part 1.3

1. Live attenuated (BCG, MMR, OPV, yellow fever, varicella: strong immunity; contraindicated in immunocompromised and pregnancy). Inactivated (hepatitis A, influenza, IPV, rabies: safe in immunocompromised; may need boosters). Subunit (hepatitis B, PCV13, HPV, meningococcal A: highly purified antigens; safe). Toxoid (tetanus, diphtheria: inactivated bacterial toxins; require primary series and boosters).
2. EPI schedule: BCG (birth), hepatitis B (birth dose), OPV (birth, 6, 10, 14 weeks), Pentavalent DTP-HBV-Hib (6, 10, 14 weeks), PCV13 (6, 10, 14 weeks), IPV (14 weeks), rotavirus vaccine (6 and 10 weeks), yellow fever (9 months), measles-rubella (9 months and 15 to 18 months), meningococcal A. Three barriers to coverage: vaccine hesitancy from misinformation, cold chain failures from unreliable electricity, and geographical inaccessibility of rural and nomadic populations.
3. Moment 1: before patient contact (transfers organisms from environment to patient). Moment 2: before an aseptic procedure (prevents introduction of organisms into a sterile site). Moment 3: after body fluid exposure or risk (protects healthcare worker and prevents transmission to environment). Moment 4: after patient contact (prevents transfer of patient organisms to healthcare worker or next patient). Moment 5: after touching patient surroundings (prevents indirect transmission via contaminated surfaces). Hand

hygiene is the most effective measure because hands are the main vehicle of cross-infection transmission in healthcare settings.

4. Contact precautions (gloves and apron: for MRSA, ESBL-producing organisms, Clostridium difficile, norovirus, scabies: prevents transmission by direct and indirect contact). Droplet precautions (surgical mask: for influenza, COVID-19, meningococcal disease, mumps, rubella: prevents large droplet transmission within 1 to 2 metres). Airborne precautions (N95 or FFP3 respirator, negative pressure isolation room if available: for tuberculosis, measles, varicella, smallpox: prevents inhalation of airborne particles).

5. AMR mechanisms: beta-lactamase production (destroys beta-lactam ring: ESBLs in Klebsiella and E. coli), altered drug targets (MRSA: PBP2a; penicillin-resistant pneumococcus: altered penicillin-binding proteins), efflux pumps (actively remove drugs from the bacterial cell: Pseudomonas aeruginosa), reduced membrane permeability (decreased outer membrane porins in Gram-negative bacteria), and plasmid-mediated resistance (allows rapid transfer of resistance genes between species). AMS principles: right drug, right dose, right duration, right indication; culture before antibiotics; de-escalate when results available; avoid antibiotics for viral infections; audit prescribing practice.

Part 1.4

1. Ziehl-Neelsen (acid-fast) staining: a sputum smear is prepared on a glass slide; carbol fuchsin dye is applied and heated; the slide is decolorised with acid-alcohol (mycobacteria resist decolorisation due to their mycolic acid-rich cell wall: they are acid-fast); safranin counterstain is applied; Mycobacterium tuberculosis appears as red (acid-fast) bacilli against a blue background. Used to diagnose pulmonary TB (sensitivity 50 to 70 percent in sputum; three samples maximise yield) and Mycobacterium leprae in skin smears.

2. Collect two blood culture bottles (aerobic and anaerobic) from two different venepuncture sites using strict aseptic technique before administering antibiotics. Inoculate blood directly into culture bottles at the bedside. Send to the laboratory: bottles are incubated in an automated system (BACTEC or BacT/ALERT) that detects CO2 production from bacterial growth, flagging positive bottles within 12 to 24 hours. Positive bottles are Gram-stained and subcultured onto solid media for identification and antimicrobial sensitivity testing (disc diffusion or MIC). Results guide antibiotic de-escalation.

3. IgM antibodies: appear within days of acute infection, peak at 1 to 2 weeks, and wane after 3 to 6 months; indicate recent or acute infection; clinically used to diagnose acute viral hepatitis A (anti-HAV IgM), acute hepatitis B (anti-HBc IgM), and acute EBV infection. IgG antibodies: appear after IgM, persist for years to decades, and indicate past infection or vaccination-induced immunity; used to assess immunity to hepatitis B (anti-HBs IgG), rubella, varicella, and to confirm previous infection with Entamoeba histolytica and Lassa fever in convalescent serum.

4. GeneXpert MTB/RIF is a cartridge-based automated real-time PCR system. A sputum specimen is mixed with a sample reagent and loaded into a single-use cartridge; the system performs cell lysis, nucleic acid extraction, amplification, and detection automatically within 2 hours. It detects M. tuberculosis DNA with sensitivity approximately 88 percent for smear-negative TB (compared with 50 to 70 percent for ZN smear) and identifies mutations in the rpoB gene conferring rifampicin resistance (a proxy for MDR-TB). It is WHO-recommended as the first-line TB diagnostic test because it provides same-day diagnosis and resistance information in a single test.

5. False-positive blood cultures from skin contamination: coagulase-negative staphylococci (Staphylococcus epidermidis) are a common blood culture contaminant from inadequate skin decontamination; a true bacteraemia is suggested by growth in both bottles, a short time to positivity, and clinical correlation. False-positive Widal test in Nigeria: high background anti-typhoid antibody titres from prior subclinical infection or prior typhoid vaccination cause false-positive Widal tests in a large proportion of the population, so a

single positive Widal test cannot diagnose acute typhoid fever without a fourfold rise in paired sera.

References and Attributions [Series 1]

Textual References

- Mandell, G. L., Bennett, J. E. and Dolin, R. (2015). Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases (8th ed.). Philadelphia: Elsevier.
- World Health Organization. (2020). Infection Prevention and Control in Health Care: Time for Much Greater Urgency. Geneva: WHO.
- Singer, M., Deutschman, C. S., Seymour, C. W. et al. (2016). The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA, 315(8), 801 to 810.
- Nigeria Centre for Disease Control. (2021). National Antimicrobial Resistance Action Plan 2017 to 2022. Abuja: NCDC.

Figures, Plates, Tables, and Boxes

- Figure 1.1: Routes of transmission and key epidemiological concepts. AI-generated using the prompt: "Create a professional medical infographic titled Transmission Routes of Infectious Diseases and Key Epidemiological Concepts. Left panel: six transmission routes with icons and examples. Right panel: R0, herd immunity threshold, and epidemic curve shapes." Suggested OER search string: "infectious disease transmission routes epidemiological concepts R0 herd immunity epidemic curve infographic OER."
- Figure 1.2: Aetiological agents and sepsis Hour-1 bundle. AI-generated using the prompt: "Create a professional medical infographic with bacteria, viruses, fungi, and parasite classification on the left and the Surviving Sepsis Campaign Hour-1 Bundle on the right." Suggested OER search string: "aetiological agents infectious diseases bacteria viruses fungi parasites sepsis hour-1 bundle infographic OER."
- Figure 1.3: Prevention and control: immunisation, infection control, and antimicrobial stewardship. AI-generated using the prompt: "Create a professional medical infographic

with vaccine types and Nigeria EPI schedule, WHO 5 Moments of Hand Hygiene, transmission-based precautions, and AMR mechanisms with AMS principles." Suggested OER search string: "infection prevention control immunisation antimicrobial stewardship AMR mechanisms infographic OER."

- Figure 1.4: Laboratory diagnosis of infectious diseases. AI-generated using the prompt: "Create a professional medical infographic with microscopy techniques (Ziehl-Neelsen, Gram stain, KOH, blood film), culture and sensitivity flowchart, serology (IgM vs IgG, ELISA, RDT, Widal), and molecular techniques (PCR, GeneXpert, viral load)." Suggested OER search string: "laboratory diagnosis infectious diseases microscopy culture serology PCR GeneXpert infographic OER."

Series 2: Clinical Evaluation and Diagnosis

- **Part 2.1: The Febrile Patient**
    - Sub Part 2.1.1: Approach to fever
    - Sub Part 2.1.2: History taking in the febrile patient
    - Sub Part 2.1.3: Physical examination and clinical patterns of fever
- **Part 2.2: Investigation of Infectious Diseases**
    - Sub Part 2.2.1: First-line investigations
    - Sub Part 2.2.2: Specific diagnostic investigations
    - Sub Part 2.2.3: Imaging in infectious diseases
- **Part 2.3: Systemic Inflammatory Response and Sepsis**
    - Sub Part 2.3.1: Recognition of sepsis in clinical practice
    - Sub Part 2.3.2: Management of sepsis
    - Sub Part 2.3.3: Complications of sepsis
- **Part 2.4: Antimicrobial Therapy**
    - Sub Part 2.4.1: Principles of antibiotic prescribing
    - Sub Part 2.4.2: Major antibiotic classes
    - Sub Part 2.4.3: Antiviral, antifungal, and antiparasitic therapy

Introduction

The clinical evaluation of a patient with a suspected infectious disease is a systematic process that begins at the bedside. Fever is the most common presenting feature of infectious disease and its accurate assessment, combined with a thorough history and physical examination, generates a

focused differential diagnosis before any investigation is ordered. In Nigeria, where the range of possible infections is broad and laboratory resources are often limited, clinical skills are particularly important.

This Series develops your clinical approach to the febrile patient from history taking through examination, investigation, and treatment. We shall commence by examining the approach to fever and the clinical evaluation of the febrile patient. Next, we will explore first-line and specific investigations used to diagnose infectious diseases, including the role of imaging. Moving on, we will consider the recognition and management of sepsis. Finally, we will address the principles of antimicrobial therapy, covering the major antibiotic classes and antiviral, antifungal, and antiparasitic agents.

Series Learning Outcomes

Upon completing this Series, you should be able to:

- **SLO 2.1:** describe the physiological basis of fever and conduct a systematic clinical evaluation of the febrile patient,
- **SLO 2.2:** select and interpret appropriate first-line and specific investigations for infectious diseases,
- **SLO 2.3:** recognise sepsis and septic shock and describe their immediate management,
- **SLO 2.4:** describe the major classes of antibiotics and their mechanisms of action, and
- **SLO 2.5:** describe the principles of antiviral, antifungal, and antiparasitic therapy.

2.1 The Febrile Patient

2.1.1 Approach to fever

Fever is defined as a core body temperature above 38.0 degrees C (axillary above 37.5 degrees C), resulting from the action of endogenous **pyrogens** (interleukin-1, interleukin-6, and tumour necrosis factor released by activated macrophages) on the hypothalamic thermoregulatory centre, which raises the temperature set point via prostaglandin E2. Fever is a non-specific host defence response that enhances immune function and inhibits pathogen replication. **Hyperpyrexia** (temperature above 41.5 degrees C) and hypothermia (temperature below 36 degrees C) in the context of infection both indicate severe disease and demand urgent assessment.

The differential diagnosis of fever in Nigeria is broad and must include malaria (the most important cause to exclude in any febrile patient), typhoid fever, septicaemia, meningitis, pneumonia, urinary tract infection, viral haemorrhagic fevers, and tuberculosis. Non-infectious causes of fever include malignancy, connective tissue disease, drug fever, and deep venous thrombosis. Fever of unknown origin (FUO) is defined as fever above 38.3 degrees C on at least three occasions over more than 3 weeks that remains undiagnosed after initial assessment.

Fever is mediated by endogenous pyrogens including interleukin-1 and _____ acting on the hypothalamus via prostaglandin E2. The most important cause to exclude in any febrile patient in Nigeria is _____.

2.1.2 History taking in the febrile patient

A systematic history in the febrile patient covers: onset and duration of fever (acute: hours to days suggests bacterial infection or malaria; subacute: days to weeks suggests typhoid, tuberculosis, or viral illness; chronic: weeks to months suggests tuberculosis, HIV, or malignancy), fever pattern (continuous, remittent, intermittent, relapsing), associated symptoms (rigors, night sweats, weight loss, cough, diarrhoea, rash, headache, altered consciousness, dysuria), and severity indicators (inability to eat, drink, or walk; altered consciousness; difficulty breathing).

The exposure history is critical: recent travel (within and outside Nigeria), contact with a confirmed infectious case, animal or vector exposure (mosquito bites, rodent contact, dog bites), water or food exposure (well water, raw food, unpasteurised dairy), immunisation status, sexual history (for sexually transmitted infections), and current medications. In Nigeria, the malaria risk is perennial and must be assessed in every febrile patient regardless of anti-malarial prophylaxis or prior negative tests.

Fever lasting days to weeks in a Nigerian patient should raise suspicion for _____ fever or tuberculosis. The exposure history must always include travel, animal or vector contact, water and _____ exposure, and immunisation status.

2.1.3 Physical examination and clinical patterns of fever

Physical examination of the febrile patient begins with vital signs: temperature (route and method of measurement), heart rate (tachycardia in sepsis; relative bradycardia in typhoid fever: **Faget's sign**), blood pressure, respiratory rate, and oxygen saturation. General examination includes nutritional status, hydration, level of consciousness (Glasgow Coma Scale), and the presence of jaundice, lymphadenopathy, or rash.

Specific examination findings guide the diagnosis: neck stiffness and photophobia (meningitis), chest signs (pneumonia), right upper quadrant tenderness (hepatitis or liver abscess), splenomegaly (malaria, typhoid, leishmaniasis, infective endocarditis), rose spots on the abdomen (typhoid), petechiae or purpura (meningococcal disease, dengue, viral haemorrhagic fever), and skin rash (measles: maculopapular starting at the hairline; chickenpox: vesicular in varying stages; secondary syphilis: involving the palms and soles).

Relative bradycardia in a febrile patient (Faget's sign) is a feature of _____ fever. _____ and photophobia on examination indicate meningeal irritation and meningitis.

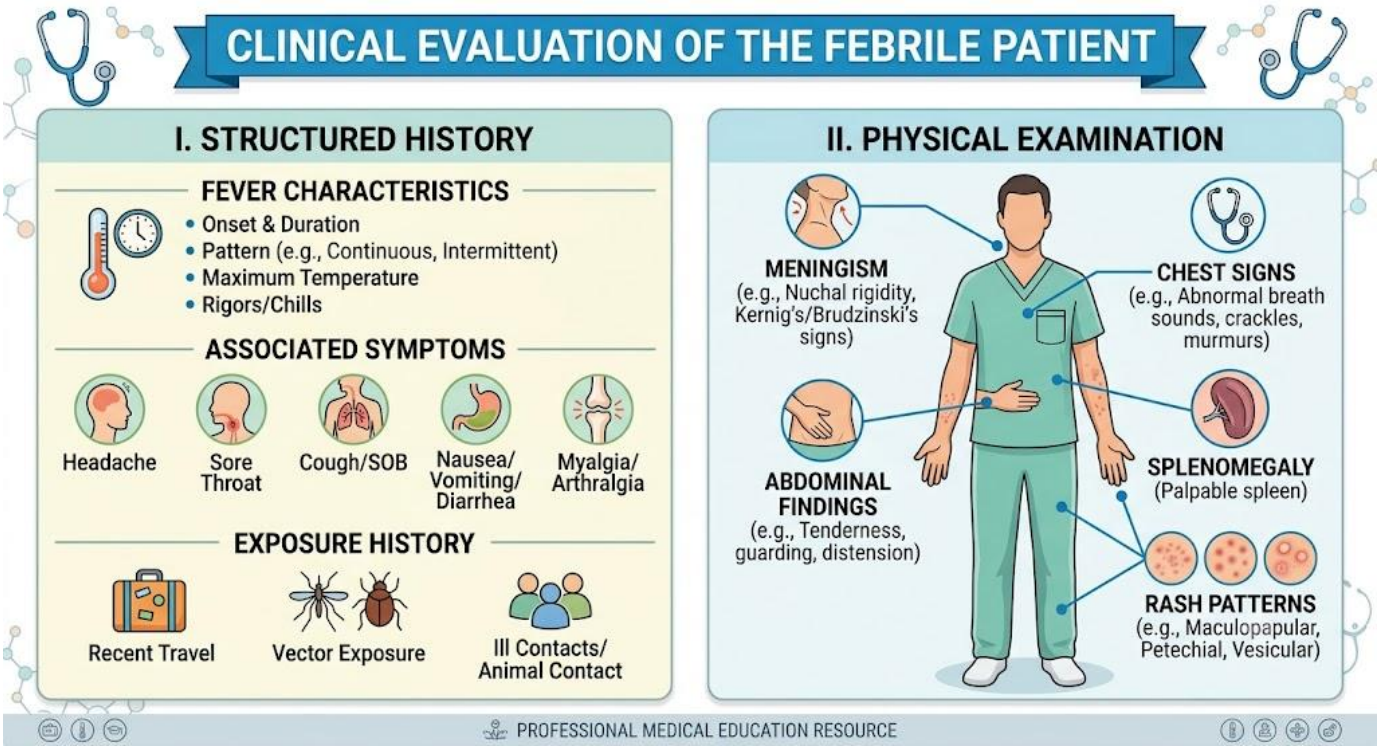

Figure 2.1: Clinical evaluation of the febrile patient: history taking and physical examination findings

Pilot questions 2.1

1. Define fever and describe its physiological mechanism. (Linked to SLO 2.1)
2. Describe the key elements of the history in a febrile patient. (Linked to SLO 2.1)
3. State the significance of Faget's sign and describe the rash of meningococcal disease. (Linked to SLO 2.1)
4. Describe the features of the fever in malaria compared with typhoid fever. (Linked to SLO 2.1)
5. Define fever of unknown origin and state three categories of causes. (Linked to SLO 2.1)

2.2 Investigation of Infectious Diseases

2.2.1 First-line investigations

First-line investigations in a febrile patient include: full blood count (leucocytosis with neutrophilia in bacterial infection; leucopenia in typhoid, dengue, and viral infections; thrombocytopaenia in malaria, dengue, and severe sepsis; anaemia in malaria and chronic infection), C-reactive protein and erythrocyte sedimentation rate (non-specific markers of inflammation elevated in infection), blood glucose (hypoglycaemia in severe malaria), serum electrolytes and renal function (renal impairment in sepsis, malaria, and leptospirosis), liver function tests (elevated transaminases in viral hepatitis, typhoid, and yellow fever), and urinalysis (leucocytes and nitrites: urinary tract infection; haematuria: schistosomiasis or leptospirosis).

Malaria rapid diagnostic test (RDT) or peripheral blood film is mandatory in every febrile patient in Nigeria: the RDT detects Plasmodium antigen within 15 minutes (sensitivity above 95 percent for P. falciparum); the peripheral blood film (thick film for sensitivity, thin film for species identification) remains the gold standard. Blood cultures (two sets, aerobic and anaerobic) before starting antibiotics are essential in all moderate to severely ill febrile patients to identify the causative organism and guide de-escalation.

Malaria RDT detects Plasmodium _____ within 15 minutes and has sensitivity above 95 percent for P. falciparum. _____ (two sets, aerobic and anaerobic) must be collected before starting antibiotics in all moderately to severely ill febrile patients.

2.2.2 Specific diagnostic investigations

Cerebrospinal fluid (CSF) analysis is the cornerstone investigation for meningitis. Normal CSF: clear, colourless, protein 0.15 to 0.45 g/L, glucose above two-thirds of plasma glucose, white cell count below 5 per microlitre (all lymphocytes). Bacterial meningitis: turbid or purulent CSF, markedly elevated protein (above 1 g/L), very low glucose (below one-third of plasma glucose), high white cell count (above 1000 per microlitre, predominantly neutrophils). Viral meningitis: clear CSF, mildly elevated protein, normal glucose, moderate white cell count

(predominantly lymphocytes). Cryptococcal meningitis: India ink stain positive (in HIV-positive patients); cryptococcal antigen lateral flow assay (CrAg LFA: highly sensitive and specific).

Stool microscopy and culture for diarrhoeal illness (identify parasites, ova, and cysts; culture for Shigella, Salmonella, Campylobacter, and ETEC). Sputum Gram stain and culture for respiratory infections. Urine microscopy and culture for urinary tract infection (significant bacteriuria: above 100,000 colony-forming units per millilitre of a single organism in a midstream urine specimen). Widal test for typhoid fever (limited by poor specificity in Nigeria: a fourfold rise in titre in paired sera is required to confirm acute infection). Dengue NS1 antigen (detectable in the first 5 days of illness) and dengue IgM/IgG serology.

Bacterial meningitis produces turbid CSF with markedly elevated _____ and very low glucose (below one-third of plasma glucose). Cryptococcal meningitis in HIV-positive patients is diagnosed by India ink stain or _____ lateral flow assay.

2.2.3 Imaging in infectious diseases

Chest X-ray is the most important first-line imaging investigation in infectious diseases: it identifies lobar consolidation in pneumonia (air bronchogram), bilateral perihilar infiltrates in PCP, military nodules in miliary tuberculosis, pleural effusion in empyema or TB, and cardiomegaly in viral myocarditis or pericarditis. Abdominal ultrasound identifies hepatomegaly (viral hepatitis, malaria), splenomegaly (typhoid, malaria, infective endocarditis), liver abscess (amoebic: single, right lobe; pyogenic: multiple), and free fluid (TB peritonitis, ruptured viscus).

CT scanning provides greater detail: CT chest (for complex pneumonia, lung abscess, bronchiectasis, and TB cavitation), CT brain (for cerebral abscess, cerebral toxoplasmosis in HIV, cerebral malaria complications, and before lumbar puncture to exclude raised intracranial pressure). CT abdomen identifies complications of typhoid fever including intestinal perforation and mesenteric lymphadenopathy. Echocardiography is essential for suspected infective endocarditis (detects vegetations on cardiac valves).

Military nodules on chest X-ray suggest _____ tuberculosis. CT brain is performed before lumbar puncture to exclude raised _____ pressure.

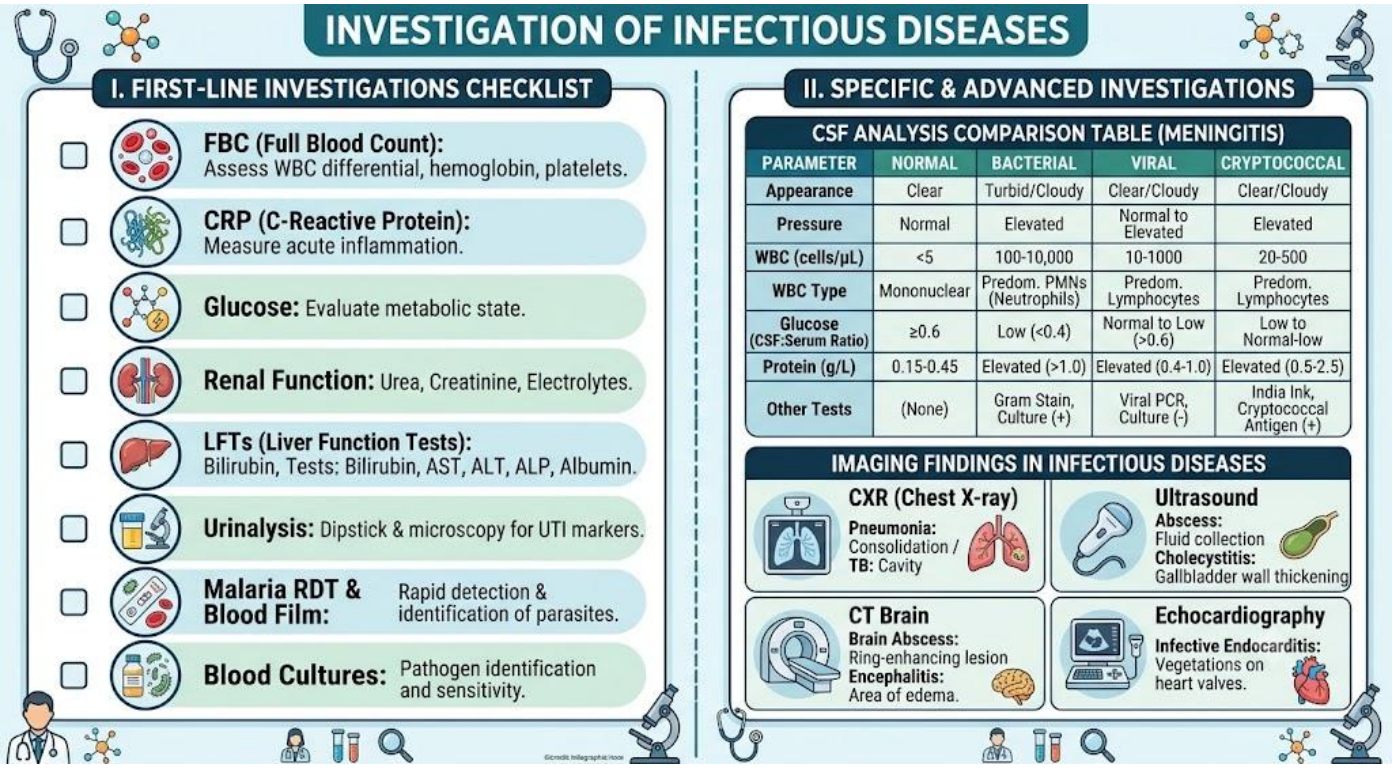

Figure 2.2: Investigation of infectious diseases: first-line investigations, CSF analysis, and imaging

Pilot questions 2.2

1. Describe the full blood count findings in bacterial septicaemia and in malaria. (Linked to SLO 2.2)
2. Describe the role of malaria RDT and peripheral blood film in the febrile patient in Nigeria. (Linked to SLO 2.2)
3. Describe the CSF findings in bacterial meningitis. (Linked to SLO 2.2)
4. Describe the chest X-ray findings in pulmonary tuberculosis. (Linked to SLO 2.2)
5. State the investigation of choice for suspected amoebic liver abscess and infective endocarditis. (Linked to SLO 2.2)

2.3 Systemic Inflammatory Response and Sepsis

2.3.1 Recognition of sepsis in clinical practice

Sepsis (Sepsis-3 definition) is life-threatening organ dysfunction from a dysregulated host response to infection, identified by a **SOFA score** increase of 2 or more points (Sequential Organ Failure Assessment: scores 6 organs: PaO2/FiO2 ratio, GCS, MAP, bilirubin, creatinine, and platelet count). The bedside **quick SOFA (qSOFA)** screen uses three criteria: altered mental status (GCS below 15), respiratory rate above 22 per minute, and systolic BP below 100 mmHg; two or more points identifies patients at high risk of sepsis-related organ dysfunction who need prompt assessment.

In Nigerian clinical practice, sepsis must be considered in any patient with suspected or confirmed infection who has any of: altered consciousness, tachycardia (HR above 100 bpm), tachypnoea (RR above 20 per minute), hypotension (systolic BP below 90 mmHg), reduced urine output (below 0.5 mL/kg/hour), or elevated serum lactate (above 2 mmol/L). Common sources of sepsis in Nigeria include malaria (the most frequent), urinary tract infection, pneumonia, typhoid perforation, meningitis, skin and soft tissue infection, and post-partum infection.

The qSOFA criteria for bedside sepsis screening are altered _____ status, respiratory rate above 22, and systolic BP below 100 mmHg. Serum _____ above 2 mmol/L indicates tissue hypoperfusion in sepsis.

2.3.2 Management of sepsis

The Surviving Sepsis Campaign Hour-1 bundle: (1) measure serum lactate (lactate above 4 mmol/L: resuscitate aggressively); (2) obtain blood cultures before antibiotics; (3) administer broad-spectrum IV antibiotics within 1 hour; (4) begin 30 mL per kg IV crystalloid for hypotension or lactate above 4 mmol/L; (5) apply vasopressors (noradrenaline: first choice, targeting MAP above 65 mmHg) if the patient remains hypotensive after adequate fluid resuscitation. Source control is essential: drain any abscess, remove infected IV cannulae or urinary catheters, and arrange surgical debridement as needed.

Antibiotic selection in sepsis without a known source: broad-spectrum coverage targeting Gram-positive and Gram-negative organisms. In Nigeria: piperacillin-tazobactam or a third-generation cephalosporin (ceftriaxone or cefotaxime) plus metronidazole (for anaerobic cover) is a practical first-line regimen. In severely immunocompromised patients or when Pseudomonas is suspected, antipseudomonal coverage (ceftazidime, piperacillin-tazobactam, or meropenem) is used. De-escalate to a targeted narrow-spectrum antibiotic when culture results are available.

The first vasopressor of choice in septic shock is _____, targeting a mean arterial pressure above 65 mmHg. _____ control (drainage of abscess, removal of infected catheter) is an essential component of sepsis management.

2.3.3 Complications of sepsis

Sepsis-induced organ dysfunction involves multiple organ systems: acute respiratory distress syndrome (ARDS: bilateral pulmonary infiltrates from non-cardiogenic pulmonary oedema, managed by protective lung ventilation with tidal volumes of 6 mL per kg), **acute kidney injury (AKI)** (managed by fluid optimisation and avoiding nephrotoxins; renal replacement therapy in severe cases), **disseminated intravascular coagulation (DIC)** (consumption of clotting factors and platelets causing simultaneous bleeding and thrombosis: prolonged PT and APTT, low fibrinogen, elevated D-dimer; managed by treating the underlying infection and replacing clotting factors with FFP and cryoprecipitate), and **hepatic dysfunction** (elevated bilirubin and transaminases from hepatic hypoperfusion).

Sepsis-induced immunosuppression follows the initial hyperinflammatory phase: prolonged lymphocyte apoptosis and monocyte deactivation increase susceptibility to secondary infections (hospital-acquired pneumonia, Candida bloodstream infection, Clostridium difficile colitis). Glycaemic control (target blood glucose 7.8 to 10 mmol/L) reduces infections and organ dysfunction. Early enteral nutrition (within 48 hours) preserves gut mucosal integrity and reduces bacterial translocation.

ARDS is managed by _____ lung ventilation with low tidal volumes of 6 mL per kg. DIC is characterised by prolonged PT and APTT, low _____, and elevated D-dimer from consumption of clotting factors.

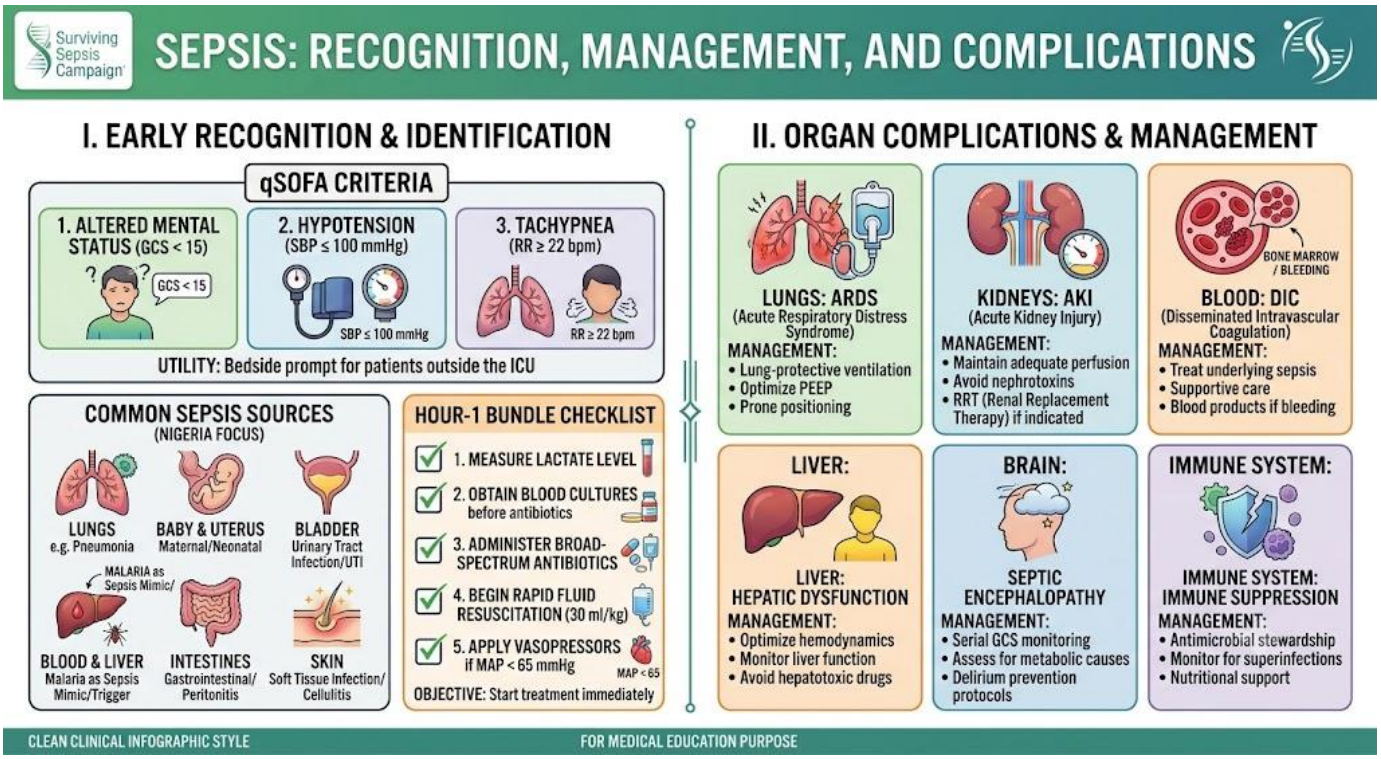

Figure 2.3: Sepsis recognition, Hour-1 management bundle, and organ complications

Pilot questions 2.3

1. Define sepsis using the Sepsis-3 definition and describe the qSOFA screen. (Linked to SLO 2.3)
2. List the five steps of the Surviving Sepsis Campaign Hour-1 bundle. (Linked to SLO 2.3)
3. Describe the first-line antibiotic regimen for community-acquired sepsis of unknown source in Nigeria. (Linked to SLO 2.3)
4. Describe the features and management of DIC in sepsis. (Linked to SLO 2.3)
5. Describe two organ complications of sepsis and their management. (Linked to SLO 2.3)

2.4 Antimicrobial Therapy

2.4.1 Principles of antibiotic prescribing

Effective antibiotic prescribing requires: selecting the right drug (based on the most likely pathogen, the likely antimicrobial susceptibility, and the site of infection), at the right dose and

route (IV for severe infections to achieve adequate tissue concentrations; oral for mild infections and step-down therapy), for the right duration (completing the prescribed course prevents recurrence and reduces resistance; unnecessarily long courses increase adverse effects and resistance). The pharmacodynamic properties of antibiotics guide dosing: time-dependent killing (beta-lactams: maintain drug concentration above the MIC for a sufficient proportion of the dosing interval) versus concentration-dependent killing (aminoglycosides, fluoroquinolones: maximise peak concentration above the MIC).

Before prescribing antibiotics: always obtain appropriate cultures (blood, urine, sputum, CSF as appropriate) before the first dose; assess for drug allergies (a history of anaphylaxis to penicillin contraindicates all beta-lactams; a simple rash does not); check renal function (dose reduction of renally excreted antibiotics in renal impairment: gentamicin, vancomycin, piperacillin-tazobactam); and check drug interactions (rifampicin induces liver enzymes reducing levels of many drugs including oral contraceptives and antiretrovirals).

Beta-lactam antibiotics use _____ killing and must maintain drug concentration above the MIC for most of the dosing interval. _____ induces liver enzymes, reducing levels of many drugs including antiretrovirals.

2.4.2 Major antibiotic classes

Beta-lactams (penicillins, cephalosporins, carbapenems, monobactams) inhibit cell wall synthesis by binding to penicillin-binding proteins (PBPs). Penicillins: amoxicillin (oral: community-acquired pneumonia, otitis media), flucloxacillin (S. aureus infections), piperacillin-tazobactam (broad-spectrum: hospital-acquired infections, Pseudomonas). Cephalosporins: ceftriaxone (3rd generation: meningitis, typhoid, severe community-acquired infections). Carbapenems: meropenem (ESBL infections, severe hospital-acquired infections). **Aminoglycosides** (gentamicin, amikacin): inhibit 30S ribosomal subunit; concentration-dependent killing; nephrotoxic and ototoxic: monitor levels and avoid in renal impairment.

Fluoroquinolones (ciprofloxacin, levofloxacin): inhibit DNA gyrase and topoisomerase IV; broad-spectrum; useful for urinary tract infection, typhoid (where sensitive), atypical pneumonia, and Gram-negative infections. **Macrolides** (azithromycin, clarithromycin): inhibit 50S ribosomal

subunit; used for atypical pneumonia (Mycoplasma, Chlamydophila, Legionella), pertussis, and typhoid. **Metronidazole** and tinidazole: active against anaerobes and protozoa (amoebic dysentery, giardiasis, Clostridium difficile, bacterial vaginosis). **Vancomycin** inhibits peptidoglycan synthesis; used for MRSA and severe Gram-positive infections.

Ceftriaxone is a _____ generation cephalosporin used for meningitis and severe community-acquired infections. _____ and tinidazole are active against anaerobes and protozoa including Entamoeba histolytica.

2.4.3 Antiviral, antifungal, and antiparasitic therapy

Antivirals act by inhibiting specific viral replication steps. Aciclovir inhibits herpes virus DNA polymerase (used for herpes simplex and varicella-zoster). Antiretrovirals: see Series 4. Oseltamivir (Tamiflu) inhibits influenza neuraminidase (reduces duration of influenza by approximately 1 day if started within 48 hours). Ribavirin is used for Lassa fever and some viral haemorrhagic fevers.

Antifungals: azoles (fluconazole: Candida and Cryptococcus infections; itraconazole: dermatophytes and Aspergillus; voriconazole: invasive Aspergillus), amphotericin B deoxycholate or liposomal amphotericin B (broadest spectrum antifungal: used for severe systemic fungal infections including cryptococcal meningitis in HIV-positive patients), and echinocandins (caspofungin: for invasive Candida infections). **Antiparasitic therapy** includes artemisinin-based combination therapy (ACT: the first-line treatment for uncomplicated P. falciparum malaria in Nigeria), IV artesunate (for severe malaria), metronidazole (amoeba, Giardia), albendazole or mebendazole (helminths), and praziquantel (schistosomiasis and tapeworms).

Aciclovir inhibits herpes virus _____ polymerase and is used for herpes simplex and varicella-zoster infections. _____ based combination therapy (ACT) is the first-line treatment for uncomplicated P. falciparum malaria in Nigeria.

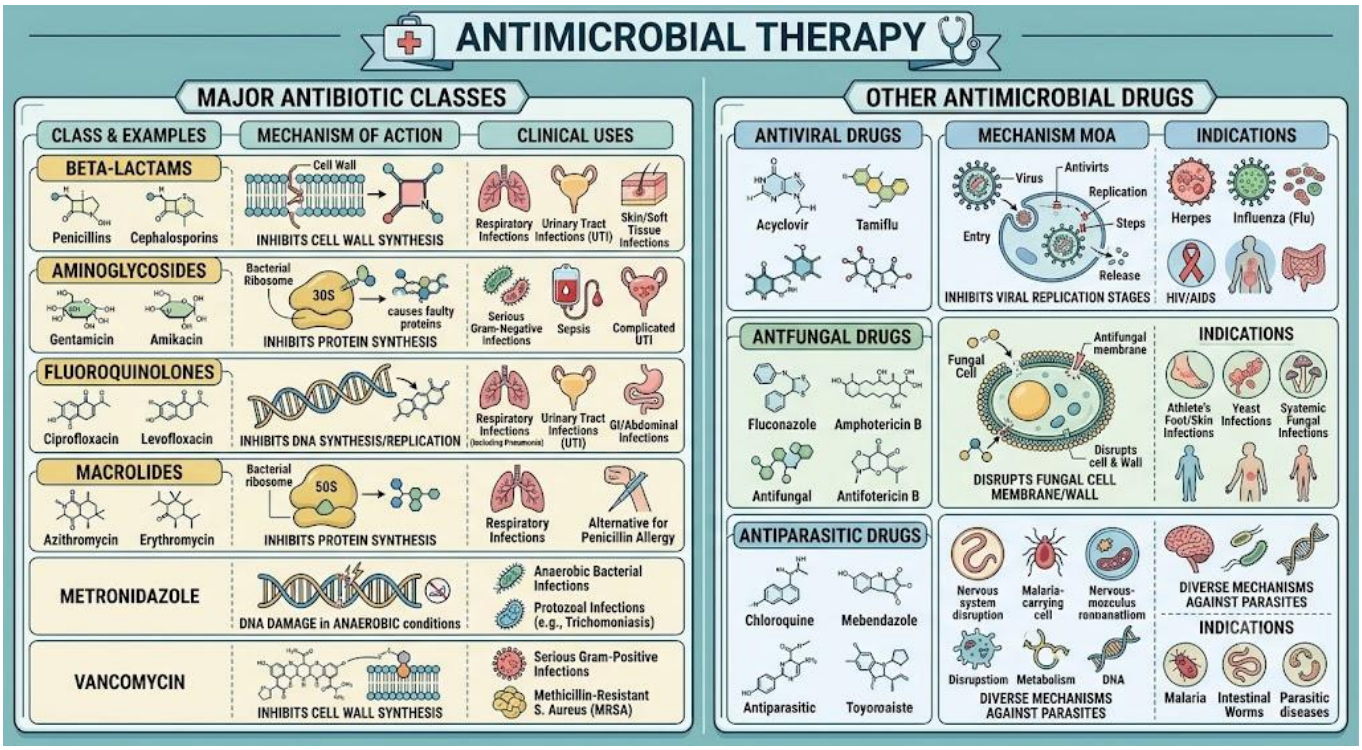

Figure 2.4: Major antibiotic classes and antiviral, antifungal, and antiparasitic therapy

Pilot questions 2.4

1. Describe the principles of antibiotic prescribing. (Linked to SLO 2.4)
2. Describe the mechanism of action and clinical uses of beta-lactam antibiotics. (Linked to SLO 2.4)
3. State the mechanism of action and clinical uses of fluoroquinolones and macrolides. (Linked to SLO 2.4)
4. Describe the first-line treatment for uncomplicated and severe falciparum malaria in Nigeria. (Linked to SLO 2.5)
5. State the antifungal of choice for cryptococcal meningitis in an HIV-positive patient and explain why. (Linked to SLO 2.5)

Series Summary

This Series developed your clinical approach to the evaluation and treatment of infectious diseases. We began with the febrile patient: fever defined as temperature above 38 degrees C, mediated by endogenous pyrogens acting on the hypothalamus; the history covering fever pattern, associated symptoms, and exposure history; and the examination identifying specific signs including Faget's sign (typhoid), neck stiffness (meningitis), splenomegaly (malaria, typhoid), and rash patterns. Next, we explored investigations: first-line tests (FBC, malaria RDT and blood film, blood cultures), CSF analysis (bacterial meningitis: turbid, low glucose, neutrophilic pleocytosis), and imaging (CXR miliary nodules in miliary TB; abdominal ultrasound for liver abscess; CT brain before LP for raised ICP; echocardiography for infective endocarditis). Moving on, we covered sepsis: Sepsis-3 definition (SOFA increase of 2 or more points), qSOFA screen (altered mental status, RR above 22, systolic BP below 100), Hour-1 bundle (lactate, cultures, antibiotics, fluids, vasopressors), and complications (ARDS, AKI, DIC, hepatic dysfunction). Finally, we addressed antimicrobial therapy: major antibiotic classes (beta-lactams, aminoglycosides, fluoroquinolones, macrolides, metronidazole, vancomycin) and antiviral, antifungal (fluconazole, amphotericin B), and antiparasitic therapy (ACT for malaria, metronidazole for amoeba, praziquantel for schistosomiasis).

By completing this Series, you should now be able to conduct a systematic clinical evaluation of the febrile patient, select and interpret appropriate investigations, recognise and initiate management of sepsis, and describe the major antimicrobial agents and their indications. These abilities align with SLOs 2.1 to 2.5 and equip you for the disease-specific content in the subsequent Series.

Glossary of Terms

- **Arterial blood gas (ABG):** a blood test measuring PaO2, PaCO2, pH, and bicarbonate; used in sepsis to assess oxygenation, ventilation, and acid-base status, and to calculate the PaO2/FiO2 ratio in ARDS.

- **Disseminated intravascular coagulation (DIC):** a pathological activation of the coagulation cascade in sepsis causing simultaneous clotting and bleeding; characterised by prolonged PT and APTT, low fibrinogen, and elevated D-dimer.
- **Faget's sign:** relative bradycardia (lower heart rate than expected for the degree of fever) seen in typhoid fever, yellow fever, and brucellosis; aids clinical diagnosis.
- **Fever of unknown origin (FUO):** fever above 38.3 degrees C on at least three occasions over more than 3 weeks that remains undiagnosed after initial assessment; causes include infection, malignancy, and connective tissue disease.
- **Peripheral blood film:** microscopic examination of a stained blood smear; thick film detects malaria parasites with high sensitivity; thin film allows species identification; also identifies trypanosomes and microfilariae.
- **Protective lung ventilation:** mechanical ventilation strategy for ARDS using low tidal volumes (6 mL per kg predicted body weight) and positive end-expiratory pressure to prevent ventilator-induced lung injury.
- **qSOFA:** quick Sequential Organ Failure Assessment; a bedside screening tool for sepsis using three criteria: altered mental status, respiratory rate above 22 per minute, and systolic BP below 100 mmHg; a score of 2 or more warrants urgent assessment.
- **Source control:** removal or drainage of the infection focus in sepsis; includes drainage of abscess, removal of infected IV cannulae or urinary catheters, and surgical debridement of necrotic tissue.
- **Time-dependent killing:** the pharmacodynamic property of beta-lactam antibiotics: efficacy depends on maintaining drug concentration above the MIC for a sufficient proportion of the dosing interval.
- **Vancomycin:** a glycopeptide antibiotic that inhibits peptidoglycan synthesis in Gram-positive bacteria; used for MRSA, coagulase-negative staphylococci, and severe Gram-positive infections; requires therapeutic drug monitoring.

Concept Check Questions [Series 2]

Objective questions

1. Fever is mediated by endogenous pyrogens including interleukin-1 and TNF acting on the hypothalamus via prostaglandin _____. (Linked to SLO 2.1)
2. Relative bradycardia (Faget's sign) in a febrile patient is a characteristic feature of _____ fever. (Linked to SLO 2.1)
3. Bacterial meningitis produces turbid CSF with very low glucose (below one-third of plasma glucose) and predominantly _____ in the white cell count. (Linked to SLO 2.2)
4. The first vasopressor of choice in septic shock is _____, targeting a mean arterial pressure above 65 mmHg. (Linked to SLO 2.3)
5. Artemisinin-based combination therapy (ACT) is the first-line treatment for uncomplicated P. _____ malaria in Nigeria. (Linked to SLO 2.5)

Short-answer questions

6. State the most important cause to exclude in any febrile patient in Nigeria and describe the two diagnostic tests available. (Linked to SLO 2.1)
7. Describe the CSF findings that distinguish bacterial from viral meningitis. (Linked to SLO 2.2)
8. Describe the qSOFA criteria and state what a score of 2 or more indicates. (Linked to SLO 2.3)
9. State the mechanism of action of beta-lactam antibiotics and give three examples used in Nigeria. (Linked to SLO 2.4)
10. State the antifungal of choice for cryptococcal meningitis and explain its mechanism of action. (Linked to SLO 2.5)

Long-answer questions

11. Describe the clinical approach to a febrile patient, including the key elements of history taking and the important physical signs. (Linked to SLO 2.1)
12. Describe the first-line investigations for a febrile patient presenting with suspected sepsis in Nigeria. (Linked to SLO 2.2)
13. Describe the immediate management of a patient with septic shock. (Linked to SLO 2.3)
14. Describe the major antibiotic classes and give a clinical indication for each. (Linked to SLO 2.4)
15. Describe the treatment of severe falciparum malaria and the management of its complications. (Linked to SLO 2.5)

Answers to Concept Check Questions [Series 2]

Objective questions

1. E2.
2. Typhoid.
3. Neutrophils.
4. Noradrenaline.
5. Falciparum.

Short-answer questions

6. The most important cause to exclude is malaria. The malaria rapid diagnostic test (RDT) detects P. falciparum antigen within 15 minutes with sensitivity above 95 percent. The peripheral blood film (thick film for maximum sensitivity, thin film for species identification) remains the gold standard and should always be performed alongside the RDT.

7. Bacterial meningitis: turbid or purulent CSF, markedly elevated protein (above 1 g/L), very low glucose (below one-third of plasma glucose), and high white cell count (above 1000 per microlitre predominantly neutrophils). Viral meningitis: clear CSF, mildly elevated protein, normal glucose, and moderate lymphocytic pleocytosis (predominantly lymphocytes, usually below 500 per microlitre).

8. qSOFA uses three criteria: altered mental status (GCS below 15), respiratory rate above 22 per minute, and systolic blood pressure below 100 mmHg. A score of 2 or more identifies patients at high risk of sepsis-related organ dysfunction who require prompt clinical assessment, investigation, and initiation of sepsis management.

9. Beta-lactam antibiotics inhibit bacterial cell wall synthesis by binding to penicillin-binding proteins (PBPs), preventing cross-linkage of peptidoglycan chains. Three examples: amoxicillin (community-acquired pneumonia and urinary tract infection), ceftriaxone (meningitis and severe community-acquired infections), and piperacillin-tazobactam (hospital-acquired infections and Pseudomonas coverage).

10. Amphotericin B (liposomal preferred to reduce nephrotoxicity) is the antifungal of choice for cryptococcal meningitis in HIV-positive patients. It binds to ergosterol in the fungal cell membrane, forming pores that cause leakage of cellular contents and cell death. It has the broadest antifungal spectrum and is fungicidal (kills rather than inhibits), making it the most effective agent for this life-threatening infection.

Long-answer questions

11. **Basic response:** History: fever onset and duration (acute: bacterial or malaria; subacute: typhoid or TB; chronic: TB, HIV, malignancy), fever pattern, associated symptoms

(rigors, night sweats, weight loss, rash, headache, altered consciousness), and exposure history (travel, mosquito bites, rodent contact, water and food, immunisation status). Examination: vital signs (temperature, HR: relative bradycardia in typhoid; BP; RR; SpO2), level of consciousness (GCS), signs of meningism (neck stiffness and photophobia), chest signs (pneumonia), splenomegaly (malaria, typhoid), rose spots (typhoid), and rash (petechiae or purpura: meningococcal or dengue; maculopapular from hairline: measles; vesicular: varicella).

Value-added response: The exposure history is the most discriminating element in Nigeria: a patient who has not taken malaria prophylaxis and lives in or has travelled through an endemic area almost certainly has malaria until proven otherwise, and a malaria test should be the first investigation regardless of the clinical presentation.

12. **Basic response:** Full blood count (leucocytosis with neutrophilia: bacterial sepsis; leucopenia: typhoid, dengue; thrombocytopaenia: severe sepsis, malaria). Malaria RDT and peripheral blood film (mandatory in Nigeria in all febrile patients). Blood cultures (two sets before antibiotics). Serum lactate (elevated above 2 mmol/L: tissue hypoperfusion). Renal function and electrolytes (AKI is common in sepsis). Liver function tests (elevated in hepatic sepsis, malaria, typhoid). Urinalysis (leucocytes and nitrites: UTI as source). Chest X-ray (identify pneumonia or empyema as source).

Value-added response: In Nigeria, the single most important investigation is the malaria blood film or RDT because malaria is the most frequent cause of severe febrile illness, and missing the diagnosis or delaying treatment significantly increases mortality from severe malaria.

13. **Basic response:** Hour-1 bundle: (1) measure serum lactate; (2) collect blood cultures before antibiotics; (3) administer IV broad-spectrum antibiotics within 1 hour; (4) give 30 mL per kg IV crystalloid if MAP below 65 mmHg or lactate above 4 mmol/L; (5) start noradrenaline if MAP remains below 65 mmHg after fluids. Source control: drain abscess, remove infected catheter or IV cannula. Antibiotic choice in Nigeria: ceftriaxone plus metronidazole (community-acquired source) or piperacillin-tazobactam (hospital-acquired). De-escalate to narrow-spectrum antibiotics when culture results available.

Value-added response: In resource-limited settings, early administration of the correct antibiotic within 1 hour is the intervention that most reduces septic shock mortality; the vasopressor and ventilatory support components of the bundle require ICU infrastructure, but antibiotic treatment can and must be started immediately in any clinical setting.

14. **Basic response:** Beta-lactams: inhibit PBP and cell wall synthesis; ceftriaxone for meningitis and typhoid; amoxicillin for community respiratory infections; piperacillin-tazobactam for hospital-acquired and Pseudomonas infections. Aminoglycosides: inhibit 30S ribosome; concentration-dependent killing; gentamicin for Gram-negative infections; nephrotoxic and ototoxic; monitor levels. Fluoroquinolones: inhibit DNA gyrase; ciprofloxacin for UTI, typhoid (where sensitive), and Gram-negative infections. Macrolides: inhibit 50S ribosome; azithromycin for atypical pneumonia and typhoid. Metronidazole: anaerobes and protozoa; amoebic dysentery, Giardia, and C. difficile. Vancomycin: inhibits peptidoglycan; MRSA and severe Gram-positive infections.

Value-added response: Ceftriaxone remains the most versatile antibiotic in the Nigerian hospital setting, covering meningitis, typhoid, pneumonia, and urinary tract infection with once-daily IV dosing; understanding its spectrum and limitations is essential for rational empirical prescribing.

15. **Basic response:** Severe falciparum malaria: IV artesunate 2.4 mg per kg at 0, 12, 24 hours then daily until oral therapy is tolerated; switch to artemisinin-based combination therapy (ACT) to complete the course when oral intake is possible. Manage complications: hypoglycaemia (IV dextrose 50 percent); severe anaemia (packed red cell transfusion when Hb below 7 g/dL or below 10 g/dL in children); cerebral malaria (nurse flat, avoid sedatives, treat seizures with diazepam, lumbar puncture to exclude bacterial meningitis); ARDS (protective lung ventilation); AKI (fluid balance, dialysis if severe); hyperparasitaemia (above 10 percent parasite density: consider exchange transfusion).

Value-added response: IV artesunate is superior to IV quinine for severe malaria (demonstrated in the AQUAMAT trial with 22 percent reduction in mortality); wherever artesunate is available

it must be used in preference to quinine, and advocacy for its stocking in all Nigerian hospitals managing severe malaria is important.

Answers to Pilot Questions [Series 2]

Part 2.1

1. Fever is defined as a core body temperature above 38.0 degrees C (axillary above 37.5 degrees C). Mechanism: pathogens or their products stimulate macrophages to produce endogenous pyrogens (interleukin-1, interleukin-6, and TNF); these act on the hypothalamic thermoregulatory centre, which raises the temperature set point via prostaglandin E2; the body responds by increasing heat generation (shivering) and reducing heat loss (vasoconstriction).
2. Fever pattern and duration (continuous, remittent, intermittent, or relapsing), associated symptoms (rigors, night sweats, weight loss, cough, diarrhoea, rash, headache, altered consciousness), and exposure history (travel, mosquito bites, rodent contact, water and food exposure, immunisation status, sexual history, and medications).
3. Faget's sign is relative bradycardia: the heart rate is lower than expected for the degree of fever (normally HR rises by 10 bpm per degree C of fever). It is a characteristic feature of typhoid fever and also seen in yellow fever and brucellosis. Meningococcal disease produces petechiae or purpura (non-blanching, dark red or purple spots from microhaemorrhages) which, in the context of fever and meningism, indicate a medical emergency requiring immediate IV benzylpenicillin.
4. Malaria fever is classically intermittent and paroxysmal: P. vivax and P. ovale cause tertian periodicity (fever every 48 hours); P. malariae causes quartan periodicity (every 72 hours); P. falciparum causes irregular fever without a clear periodicity. Typhoid fever classically shows a stepwise rise over the first week, reaching a sustained plateau in the second week, accompanied by relative bradycardia and rose spots on the trunk.

5. FUO is fever above 38.3 degrees C on at least three separate occasions over more than 3 weeks that remains undiagnosed after initial assessment. Three categories of causes: (1) infections (tuberculosis is the most common infectious cause in Nigeria; others include typhoid, infective endocarditis, deep-seated abscess, brucellosis, and HIV); (2) malignancy (lymphoma, leukaemia, solid tumours); (3) non-infectious inflammatory causes (adult-onset Still's disease, SLE, vasculitis, inflammatory bowel disease, drug fever).

Part 2.2

1. Bacterial septicaemia: leucocytosis with neutrophilia (white cell count above 12,000 per microlitre, above 10 percent band forms), thrombocytopaenia in severe sepsis, and elevated CRP. Malaria: leucopenia or normal white cell count (leucocytosis suggests superadded bacterial infection), thrombocytopaenia (a characteristic feature: platelet count below 100,000 per microlitre), anaemia (haemolytic: progressive with severity), and in severe malaria, hypoglycaemia.
2. Malaria RDT: detects Plasmodium falciparum-specific histidine-rich protein 2 (HRP2) antigen; results available within 15 minutes; sensitivity above 95 percent for P. falciparum; does not require laboratory equipment; widely available at primary care level in Nigeria. Peripheral blood film: thick film (multiple microscope fields examined: highest sensitivity for detecting any parasite); thin film (allows morphological identification of Plasmodium species: ring forms, trophozoites, schizonts); remains the gold standard and should always confirm a positive or negative RDT in a moderately to severely ill patient.
3. Bacterial meningitis CSF: turbid or frankly purulent appearance; markedly elevated protein (above 1 g/L, often above 3 g/L); very low glucose (below one-third of simultaneous plasma glucose or below 2.2 mmol/L); high white cell count (above 1000 per microlitre, predominantly neutrophils); Gram stain positive in approximately 60 to 80

percent; culture and sensitivity are essential for species identification and antimicrobial guidance.

4. Pulmonary tuberculosis CXR findings: upper lobe infiltrates (most common: the upper lobes have the highest V/Q ratio favouring mycobacterial growth), cavitation (thick-walled cavities from caseous necrosis), hilar lymphadenopathy (primary TB and military TB), military pattern (1 to 2 mm uniformly distributed nodules in both lung fields: military TB), and pleural effusion (exudative lymphocytic in TB pleuritis). Fibrocalcific changes indicate healed prior TB.
5. Amoebic liver abscess: abdominal ultrasound is the investigation of choice (single large abscess in the right lobe of the liver with low echogenicity; aspirate yields anchovy sauce pus); confirmed by positive amoebic serology (ELISA: highly sensitive and specific). Infective endocarditis: transthoracic echocardiography (TTE) is the first-line investigation (detects vegetations on cardiac valves, valve perforation, and perivalvular abscess); transoesophageal echocardiography (TOE) is more sensitive (detects smaller vegetations, particularly on prosthetic valves) and is performed when TTE is inconclusive.

Part 2.3

1. Sepsis (Sepsis-3): life-threatening organ dysfunction caused by a dysregulated host response to infection, identified by a SOFA score increase of 2 or more points. qSOFA screen: altered mental status (GCS below 15: one point), respiratory rate above 22 per minute (one point), systolic BP below 100 mmHg (one point); a score of 2 or more identifies patients at high risk of sepsis-related organ dysfunction who need prompt evaluation and management.
2. Hour-1 bundle: (1) measure serum lactate (lactate above 4 mmol/L: aggressive fluid resuscitation); (2) obtain blood cultures before antibiotics (two sets from different sites); (3) administer broad-spectrum IV antibiotics within 1 hour; (4) begin 30 mL per kg IV crystalloid for hypotension or lactate above 4 mmol/L; (5) apply vasopressors

(noradrenaline first choice) if MAP remains below 65 mmHg after adequate fluid resuscitation.

3. Community-acquired sepsis without a known source in Nigeria: ceftriaxone 2 g IV once daily (covers S. pneumoniae, Gram-negative organisms, meningococcus) plus metronidazole 500 mg IV every 8 hours (adds anaerobic cover for a possible intra-abdominal or pelvic source). If malaria is excluded and a urinary source is likely: ceftriaxone alone is appropriate. If hospital-acquired sepsis or Pseudomonas is suspected: piperacillin-tazobactam or meropenem is used instead.
4. DIC in sepsis: pathological activation of the coagulation cascade causing simultaneous consumption of clotting factors and platelets, resulting in bleeding (petechiae, oozing from venepuncture sites, GI bleeding) and microvascular thrombosis (organ ischaemia). Laboratory findings: prolonged PT and APTT, low fibrinogen (consumed), elevated D-dimer (fibrin degradation products), and thrombocytopaenia. Management: treat the underlying infection (the definitive treatment), replace depleted clotting factors with FFP (for elevated PT and APTT), cryoprecipitate (for low fibrinogen), and platelet transfusion (for severe thrombocytopaenia with active bleeding).
5. ARDS: bilateral pulmonary infiltrates from non-cardiogenic pulmonary oedema; managed by protective lung ventilation with tidal volume 6 mL per kg predicted body weight, PEEP of 5 to 10 cmH2O, and target SpO2 of 88 to 95 percent; prone positioning for severe ARDS. AKI: acute decline in renal function (rising creatinine and reduced urine output below 0.5 mL per kg per hour); managed by fluid optimisation (correct hypovolaemia without fluid overload), avoidance of nephrotoxic drugs (NSAIDs, aminoglycosides, IV contrast), and renal replacement therapy (haemodialysis or haemofiltration) for severe AKI with fluid overload, severe hyperkalaemia, or uraemia.

Part 2.4

1. Right drug: based on the most likely pathogen, likely susceptibility, and site of infection; cultures should be obtained before the first dose. Right dose and route: IV for severe

infections to achieve adequate tissue concentrations; oral for step-down therapy. Right duration: sufficient to eradicate the infection but not unnecessarily long to reduce adverse effects and resistance. De-escalate from broad-spectrum to narrow-spectrum antibiotics when culture and sensitivity results are available.

2. Beta-lactams inhibit bacterial cell wall synthesis by binding to penicillin-binding proteins (PBPs) and preventing cross-linkage of peptidoglycan. They use time-dependent killing (efficacy depends on maintaining drug concentration above the MIC). Sub-classes: penicillins (amoxicillin for community-acquired pneumonia; flucloxacillin for S. aureus; piperacillin-tazobactam for Gram-negative and Pseudomonas infections), cephalosporins (ceftriaxone for meningitis, typhoid, and severe community-acquired infections), and carbapenems (meropenem for ESBL-producing organisms and severe hospital-acquired infections).

3. Fluoroquinolones (ciprofloxacin, levofloxacin): inhibit DNA gyrase (topoisomerase II) and topoisomerase IV, preventing bacterial DNA replication and transcription; concentration-dependent killing; used for UTI, typhoid (where sensitive), atypical pneumonia (levofloxacin), Gram-negative bone and joint infections, and traveller's diarrhoea. Macrolides (azithromycin, clarithromycin): inhibit the 50S ribosomal subunit, preventing bacterial protein synthesis; used for atypical pneumonia (Mycoplasma, Chlamydophila, Legionella), pertussis, typhoid (azithromycin: oral alternative to ceftriaxone), and sexually transmitted infections (chlamydia, gonorrhoea in combination).

4. Uncomplicated falciparum malaria (able to take oral medication): artemisinin-based combination therapy (ACT): artemether-lumefantrine (Coartem: the most widely used ACT in Nigeria: 6 doses over 3 days) or artesunate-amodiaquine. Severe falciparum malaria (impaired consciousness, seizures, severe anaemia, respiratory distress, hypoglycaemia, hyperparasitaemia, AKI, or unable to take oral medication): IV artesunate 2.4 mg per kg IV at 0, 12, and 24 hours, then daily; switch to oral ACT when the patient can swallow.

5. Amphotericin B (liposomal formulation preferred: less nephrotoxic than amphotericin B deoxycholate) is the antifungal of choice for cryptococcal meningitis in HIV-positive patients. Mechanism: binds to ergosterol in the fungal cell membrane, creating pores that

cause leakage of intracellular contents and fungal cell death. It is fungicidal (kills the organism) rather than fungistatic, which is critical in cryptococcal meningitis where a rapid reduction in fungal burden prevents further cerebrospinal fluid pressure rise and brain herniation.

References and Attributions [Series 2]

Textual References

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Figures, Plates, Tables, and Boxes

- Figure 2.1: Clinical evaluation of the febrile patient. AI-generated using the prompt: "Create a professional medical infographic titled Clinical Evaluation of the Febrile Patient. Left panel: structured history. Right panel: body diagram with labelled

examination findings." Suggested OER search string: "febrile patient clinical evaluation history physical examination infectious disease infographic OER."

- Figure 2.2: Investigation of infectious diseases. AI-generated using the prompt: "Create a professional medical infographic with first-line investigations checklist, CSF analysis comparison table, and imaging findings." Suggested OER search string: "investigation infectious diseases CSF analysis imaging meningitis malaria RDT infographic OER."
- Figure 2.3: Sepsis recognition, management, and complications. AI-generated using the prompt: "Create a professional medical infographic with qSOFA criteria, Hour-1 Bundle checklist, and six organ complication boxes." Suggested OER search string: "sepsis recognition management complications qSOFA hour-1 bundle ARDS DIC infographic OER."
- Figure 2.4: Antimicrobial therapy. AI-generated using the prompt: "Create a professional medical infographic with major antibiotic classes in a structured grid and antiviral, antifungal, and antiparasitic therapy sections." Suggested OER search string: "antibiotic classes mechanisms antiviral antifungal antiparasitic therapy infographic OER."

Series 3: Major Bacterial and Viral Infections

- **Part 3.1: Typhoid Fever and Bacterial Meningitis**
    - Sub Part 3.1.1: Typhoid fever
    - Sub Part 3.1.2: Bacterial meningitis
    - Sub Part 3.1.3: Management
- **Part 3.2: Tuberculosis**
    - Sub Part 3.2.1: Epidemiology and pathogenesis
    - Sub Part 3.2.2: Clinical features and diagnosis
    - Sub Part 3.2.3: Treatment
- **Part 3.3: Common Viral Infections**
    - Sub Part 3.3.1: Measles
    - Sub Part 3.3.2: Viral hepatitis
    - Sub Part 3.3.3: Respiratory viral infections
- **Part 3.4: Sexually Transmitted Infections**
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Introduction

Bacterial and viral infections account for the vast majority of the infectious disease burden in Nigeria. Typhoid fever, bacterial meningitis, and tuberculosis are among the most consequential bacterial infections, while measles, viral hepatitis, and respiratory viral infections remain major

causes of death. Sexually transmitted infections serve as a gateway for HIV transmission and carry serious reproductive health consequences.

We shall commence with typhoid fever and bacterial meningitis, covering their pathogenesis, clinical features, and management. Next, we will examine tuberculosis in depth from pathogenesis through treatment. Moving on, we will consider the major viral infections. Finally, we will address sexually transmitted infections and syndromic management.

Series Learning Outcomes

Upon completing this Series, you should be able to:

- **SLO 3.1:** describe the pathogenesis, clinical features, diagnosis, and management of typhoid fever and bacterial meningitis,
- **SLO 3.2:** describe the epidemiology, pathogenesis, clinical features, diagnosis, and treatment of tuberculosis,
- **SLO 3.3:** describe the clinical features, diagnosis, and management of measles, viral hepatitis, and respiratory viral infections, and
- **SLO 3.4:** describe the clinical features, diagnosis, and syndromic management of the major sexually transmitted infections.

3.1 Typhoid Fever and Bacterial Meningitis

3.1.1 Typhoid fever

Typhoid fever is caused by **Salmonella enterica serotype Typhi**, transmitted by the faecal-oral route through contaminated food and water. After ingestion, organisms penetrate the intestinal mucosa, enter mesenteric lymph nodes, and seed the bloodstream producing a sustained bacteraemia.

Clinical course: Week 1 brings stepwise rising fever, headache, malaise, and relative bradycardia (Faget's sign). Week 2 sees fever plateau, hepatosplenomegaly, and rose spots on the trunk in approximately 30 percent of patients. Week 3 brings the feared complications: intestinal perforation (sudden peritonitis and free gas on erect chest X-ray), intestinal haemorrhage, and encephalopathy.

Fill in the blank: Typhoid fever is caused by Salmonella enterica serotype _____, transmitted by the _____ route.

3.1.2 Bacterial meningitis

Bacterial meningitis carries a case fatality rate of 10 to 40 percent. The most common causative organisms in Nigeria are **Neisseria meningitidis** (serogroup A: epidemic in the meningitis belt; petechial or purpuric rash), **Streptococcus pneumoniae** (the most common in adults; high mortality), and **Haemophilus influenzae type b** (children; largely preventable by vaccine).

The classic clinical triad is fever, neck stiffness, and photophobia. Kernig's sign (inability to extend the knee with the hip flexed) and Brudzinski's sign (involuntary hip flexion on neck flexion) indicate meningeal irritation. A non-blanching petechial or purpuric rash in the context of fever and meningism indicates meningococcal disease and is a medical emergency.

Fill in the blank: The classic triad of bacterial meningitis is fever, neck _____, and photophobia. A non-blanching _____ rash with fever indicates meningococcal disease.

3.1.3 Management

Typhoid: first-line in Nigeria is ceftriaxone 2 g IV or oral for 10 to 14 days due to widespread resistance to ciprofloxacin, chloramphenicol, and ampicillin. Azithromycin is an oral alternative. Prevention: safe water, sanitation, and Vi polysaccharide typhoid vaccine.

Bacterial meningitis: give IV ceftriaxone 2 g every 12 hours immediately without waiting for CSF results. Add dexamethasone 0.15 mg per kg IV every 6 hours for 4 days before or with the

first antibiotic dose to reduce neurological complications in pneumococcal meningitis. Isolate under droplet precautions and arrange chemoprophylaxis for close contacts of meningococcal cases.

Fill in the blank: First-line treatment for typhoid in Nigeria is _____ due to widespread resistance to older agents. _____ reduces neurological complications in pneumococcal meningitis when given before or with the first antibiotic dose.

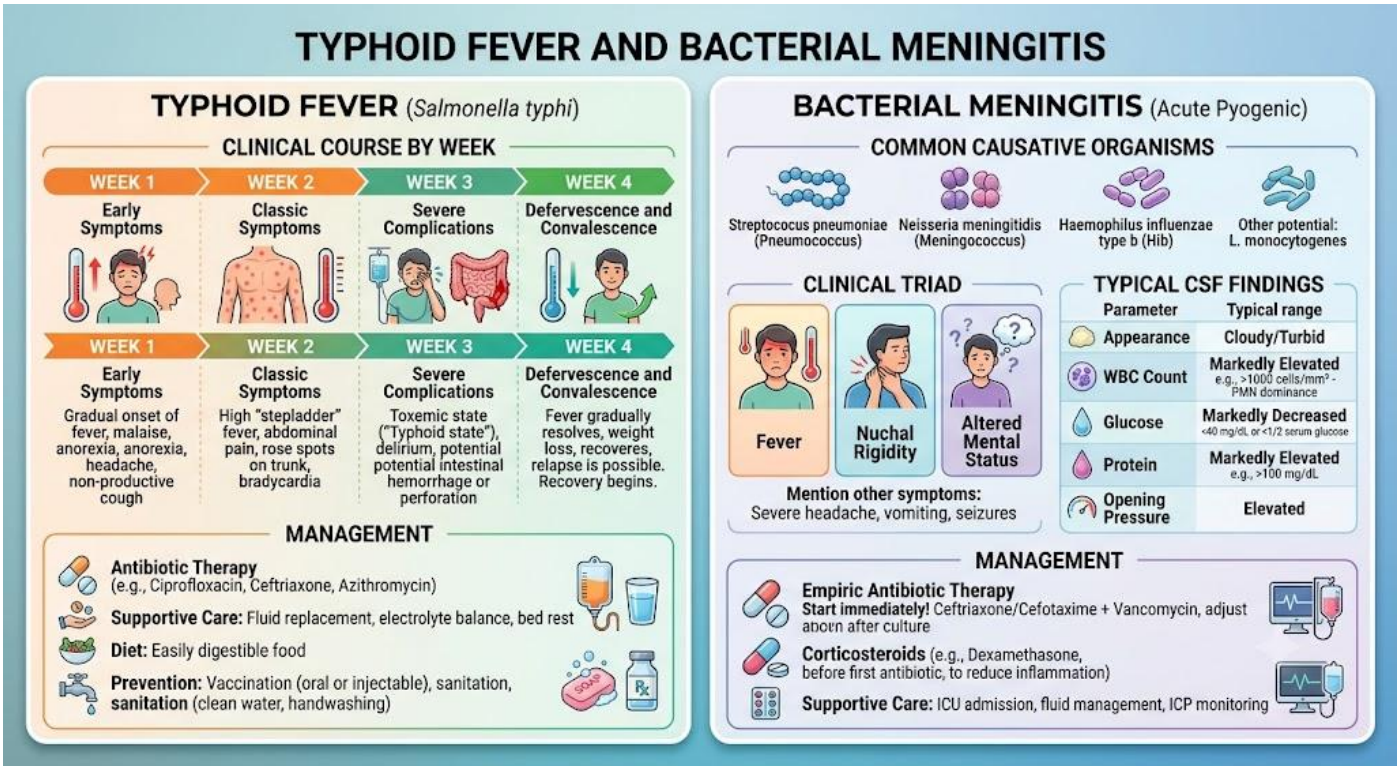

Figure 3.1: Typhoid fever and bacterial meningitis: clinical features and management

Pilot questions 3.1

1. Describe the clinical course of typhoid fever by week. (Linked to SLO 3.1)
2. State three common causative organisms of bacterial meningitis in Nigeria. (Linked to SLO 3.1)
3. Describe the immediate management of suspected bacterial meningitis. (Linked to SLO 3.1)

4. State why ceftriaxone is preferred for typhoid in Nigeria. (Linked to SLO 3.1)
5. Describe the CSF findings in bacterial meningitis. (Linked to SLO 3.1)

3.2 Tuberculosis

3.2.1 Epidemiology and pathogenesis

Mycobacterium tuberculosis is an aerobic acid-fast bacillus transmitted by airborne droplet nuclei. Nigeria is among the top 10 high-burden TB countries globally. After inhalation, macrophages phagocytose but fail to kill mycobacteria. CD4 T-lymphocytes form granulomas containing the infection as **latent TB** in most immunocompetent individuals. Reactivation to active disease occurs in approximately 10 percent of immunocompetent and up to 50 percent of HIV-positive individuals.

The primary complex (Ghon focus in the lung plus hilar lymphadenopathy) represents the initial infection. Risk factors for progression from latent to active TB include HIV infection (20 to 30-fold increased risk), malnutrition, diabetes mellitus, immunosuppressive therapy, and extremes of age. HIV is the single most important risk factor for TB in Nigeria.

Fill in the blank: Tuberculosis is transmitted by airborne _____ nuclei. The risk factor that most increases TB reactivation in Nigeria is _____ infection.

3.2.2 Clinical features and diagnosis

Pulmonary TB: cough lasting more than 2 weeks (initially dry, then productive and blood-stained), night sweats, significant weight loss, low-grade fever, and haemoptysis in cavitary disease. Extrapulmonary TB includes cervical lymphadenopathy (scrofula: the most common form), TB meningitis (the most lethal), TB pericarditis, TB peritonitis, and Pott's disease (vertebral TB).

GeneXpert MTB/RIF is the WHO first-line test: detects M. tuberculosis and rifampicin resistance within 2 hours with approximately 88 percent sensitivity for smear-negative TB.

Ziehl-Neelsen smear has sensitivity of 50 to 70 percent. Culture on Lowenstein-Jensen medium (4 to 8 weeks) is the gold standard. CXR shows upper lobe infiltrates and cavitation in post-primary pulmonary TB.

Fill in the blank: Pulmonary TB classically presents with cough above _____ weeks, night sweats, weight loss, and haemoptysis. GeneXpert MTB/RIF detects M. tuberculosis and _____ resistance within 2 hours.

3.2.3 Treatment

Standard first-line regimen 2HRZE/4HR: intensive phase of 2 months with isoniazid (H), rifampicin (R), pyrazinamide (Z), and ethambutol (E), followed by 4 months of isoniazid and rifampicin. Directly observed therapy (DOT) is recommended throughout. Stop all four drugs if transaminases exceed five times the upper limit of normal.

Key side effects: isoniazid (peripheral neuropathy: prevent with pyridoxine; hepatotoxicity), rifampicin (orange body fluids; CYP450 inducer reducing OCP and antiretroviral levels; hepatotoxicity), pyrazinamide (hyperuricaemia; hepatotoxicity), and ethambutol (optic neuritis: monitor visual acuity monthly). **MDR-TB** is resistance to isoniazid and rifampicin; treated with second-line drugs for 18 to 24 months.

Fill in the blank: The standard TB regimen is 2HRZE/4HR. Isoniazid causes peripheral neuropathy prevented by _____ supplementation. MDR-TB is resistance to isoniazid and _____.

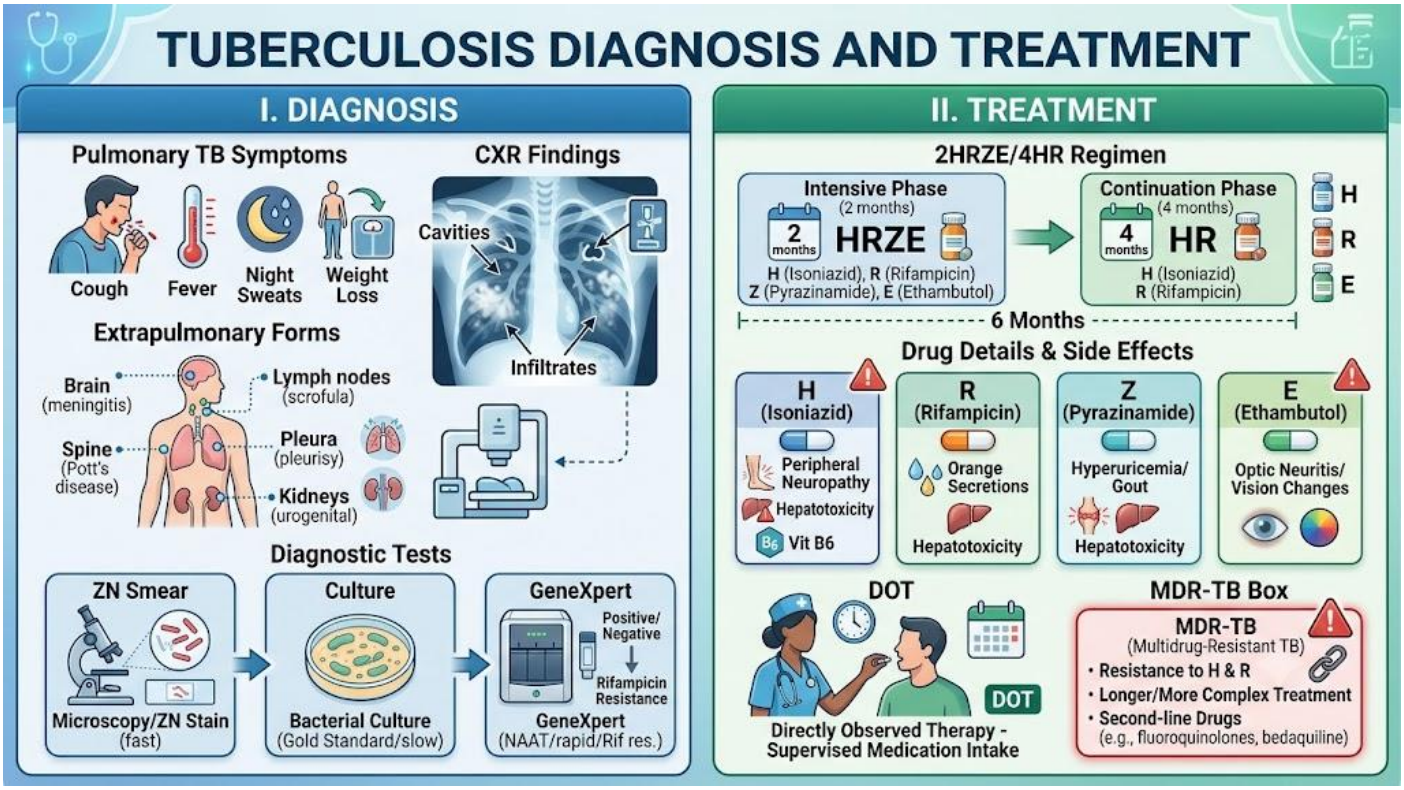

Figure 3.2: Tuberculosis: clinical features, diagnosis, and 2HRZE/4HR treatment regimen

Pilot questions 3.2

1. Describe the pathogenesis of TB from inhalation to latent infection. (Linked to SLO 3.2)
2. Describe the clinical features of pulmonary TB. (Linked to SLO 3.2)
3. Compare GeneXpert MTB/RIF with ZN smear for TB diagnosis. (Linked to SLO 3.2)
4. Describe the 2HRZE/4HR regimen and the side effects of each drug. (Linked to SLO 3.2)
5. Define MDR-TB and state its management. (Linked to SLO 3.2)

3.3 Common Viral Infections

3.3.1 Measles

Measles is caused by a paramyxovirus with an R0 of 12 to 18 (the highest of any known infection), transmitted by airborne droplet nuclei. The prodrome consists of the three Cs: **cough, coryza, and conjunctivitis** for 2 to 4 days, followed by **Koplik's spots** (white spots on red

buccal mucosa: pathognomonic of measles, appearing before the rash) and a maculopapular rash spreading from the hairline downwards.

Complications: pneumonia (the most common cause of measles death), diarrhoea and dehydration, corneal ulceration and blindness (vitamin A deficiency in malnourished children), and encephalitis. Treatment is supportive with vitamin A supplementation (two doses at presentation reduce mortality and severity). Prevention: MR vaccine at 9 months and 15 to 18 months in the Nigeria EPI.

Fill in the blank: Measles is characterised by the three Cs (cough, coryza, _____) and _____ spots on the buccal mucosa before the rash.

3.3.2 Viral hepatitis

Hepatitis A (HAV): faecal-oral transmission; self-limiting acute hepatitis; anti-HAV IgM confirms acute infection; prevention by vaccine and improved sanitation. Hepatitis B (HBV): blood, sexual, and vertical transmission; highly endemic in Nigeria (surface antigen prevalence 10 to 15 percent); chronic in up to 90 percent of perinatally infected infants; complications include cirrhosis and hepatocellular carcinoma; treatment with tenofovir or entecavir; prevention by 3-dose vaccination with birth dose. Hepatitis C (HCV): blood-borne; no vaccine; chronic in 80 percent; cure with direct-acting antivirals above 95 percent. Hepatitis E (HEV): faecal-oral; self-limiting but causes fulminant hepatic failure in pregnant women with up to 25 percent mortality.

Acute viral hepatitis presents with a prodrome of nausea, vomiting, anorexia, and right upper quadrant pain followed by jaundice, dark urine, and pale stools. LFTs show a hepatocellular pattern with markedly elevated ALT and AST. All hepatitis viruses can cause fulminant hepatic failure (encephalopathy plus coagulopathy within 8 weeks), which carries high mortality and may require liver transplantation.

Fill in the blank: Hepatitis E causes _____ hepatic failure in pregnant women with mortality up to 25 percent. Chronic HBV is defined as HBsAg positive for more than _____ months.

3.3.3 Respiratory viral infections

Influenza viruses undergo antigenic drift (minor mutations causing seasonal epidemics) and antigenic shift (major gene segment reassortment causing pandemics). Clinical features: sudden onset high fever, rigors, myalgia, headache, and dry cough. Complications: primary viral pneumonia, secondary bacterial pneumonia, and exacerbation of underlying cardiorespiratory disease. Treatment: oseltamivir within 48 hours reduces duration. Prevention: annual influenza vaccination for high-risk groups.

COVID-19 (SARS-CoV-2) presents across a clinical spectrum from asymptomatic to ARDS and septic shock. Dexamethasone 6 mg daily for 10 days reduces mortality in patients requiring oxygen or ventilation. Other important respiratory viruses: **RSV** (the most common cause of bronchiolitis in infants) and **rhinovirus** (the most common cause of the common cold).

Fill in the blank: Influenza antigenic _____ causes seasonal epidemics while antigenic _____ causes pandemics. Dexamethasone reduces mortality in COVID-19 patients requiring oxygen or _____.

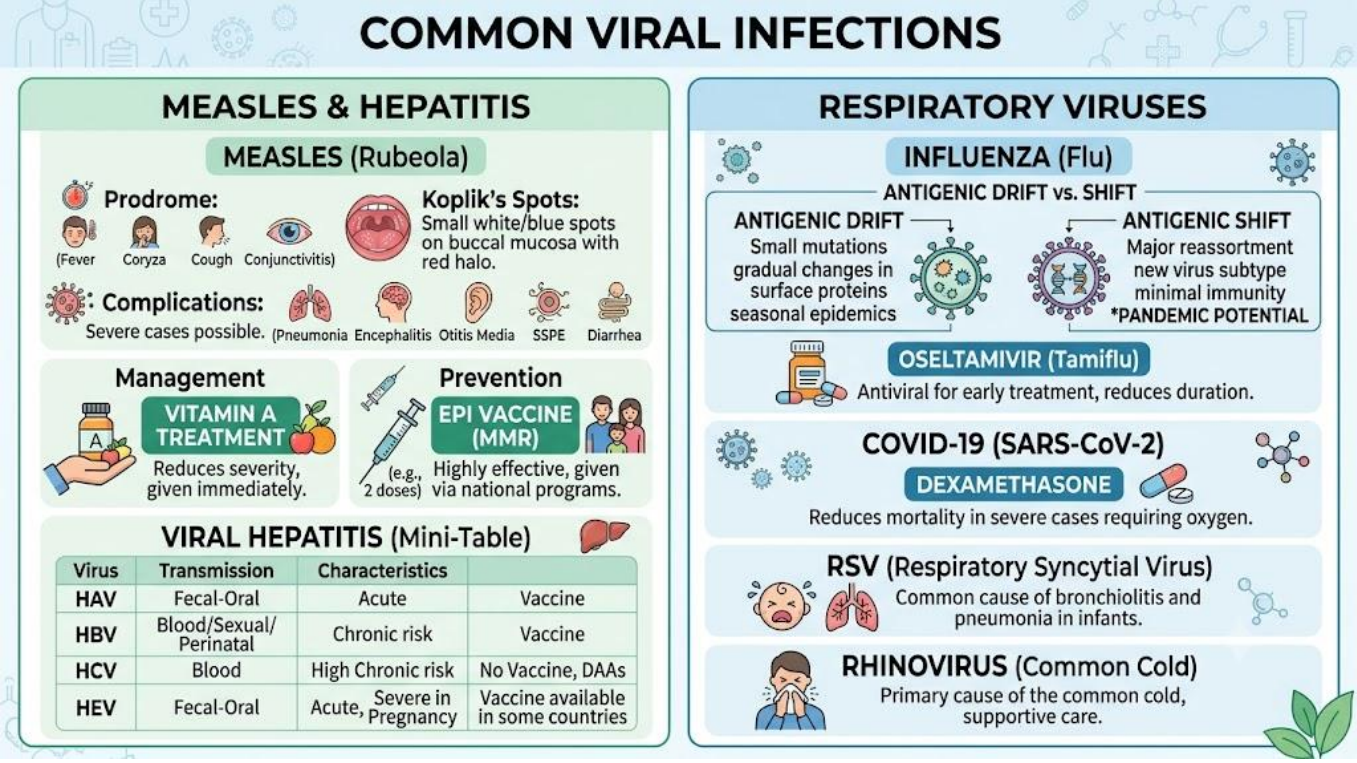

Figure 3.3: Common viral infections: measles, viral hepatitis, and respiratory viruses

Pilot questions 3.3

1. Describe the clinical features of measles and its most common complication. (Linked to SLO 3.3)
2. Describe the clinical features of acute viral hepatitis and state the most dangerous form in pregnancy. (Linked to SLO 3.3)
3. Distinguish antigenic drift from antigenic shift in influenza. (Linked to SLO 3.3)
4. Describe the treatment of COVID-19 that reduces mortality. (Linked to SLO 3.3)
5. State the most common cause of bronchiolitis in infants and the most common cause of the common cold. (Linked to SLO 3.3)

3.4 Sexually Transmitted Infections

3.4.1 Gonorrhoea and chlamydia

Gonorrhoea (Neisseria gonorrhoeae: Gram-negative diplococcus): in men presents with dysuria and purulent urethral discharge; in women is often asymptomatic or causes cervicitis and pelvic inflammatory disease (PID). Diagnosis by Gram stain (Gram-negative intracellular diplococci) and culture. **Chlamydia** (Chlamydia trachomatis: obligate intracellular bacterium) is often asymptomatic; diagnosed by NAAT (nucleic acid amplification test). Both cause PID in women, a major cause of tubal infertility and ectopic pregnancy.

Treatment: ceftriaxone 500 mg IM single dose (gonorrhoea: due to fluoroquinolone resistance) plus doxycycline 100 mg twice daily for 7 days or azithromycin 1 g single dose (chlamydia). Dual treatment covers both organisms given frequent co-infection. Partner notification and treatment is essential.

Fill in the blank: Gonorrhoea in men presents with dysuria and purulent _____ discharge. The most sensitive diagnostic test for chlamydia is _____ (NAAT).

3.4.2 Syphilis

Syphilis is caused by Treponema pallidum, a spirochaete. **Primary syphilis**: painless indurated genital ulcer (chancre) at the inoculation site, healing in 3 to 6 weeks. **Secondary syphilis**: generalised maculopapular rash involving the palms and soles, condylomata lata, mucous patches, and generalised lymphadenopathy. **Latent syphilis**: asymptomatic (early: within 1 year; late: after 1 year). **Tertiary syphilis**: gummas, neurosyphilis (meningovasculitis, general paresis, tabes dorsalis), and cardiovascular syphilis (aortitis).

Diagnosis: treponemal tests (TPHA, TPPA: confirm syphilis exposure; remain positive for life) and non-treponemal tests (VDRL, RPR: titre falls with treatment; used to monitor treatment response; may be false-positive in pregnancy and SLE). Treatment: benzathine benzylpenicillin 2.4 million units IM single dose for primary, secondary, and early latent syphilis; three weekly doses for late latent and tertiary.

Fill in the blank: Primary syphilis presents as a painless indurated genital _____ at the inoculation site. Secondary syphilis produces a rash involving the palms and _____.

3.4.3 Other STIs and syndromic management

Other STIs: HSV-2 (painful recurrent genital ulcers; treated with aciclovir), HPV (low-risk types 6 and 11: genital warts; high-risk types 16 and 18: cervical carcinoma; prevented by HPV vaccine), chancroid (Haemophilus ducreyi: painful ulcers with undermined edges; treated with azithromycin or ceftriaxone), and LGV (Chlamydia trachomatis serovars L1 to L3: treated with doxycycline for 21 days).

Syndromic management is the standard approach in Nigerian primary care where laboratory diagnosis is unavailable. Urethral discharge syndrome: treat for gonorrhoea and chlamydia. Vaginal discharge syndrome: treat for bacterial vaginosis, trichomoniasis, and gonorrhoea and chlamydia. Genital ulcer syndrome: treat empirically for syphilis (benzathine penicillin) and HSV-2 (aciclovir). Partner notification and HIV testing are integral to all syndromic management pathways.

Fill in the blank: HPV types 16 and _____ cause cervical carcinoma. Genital ulcer syndrome is treated empirically for syphilis and _____.

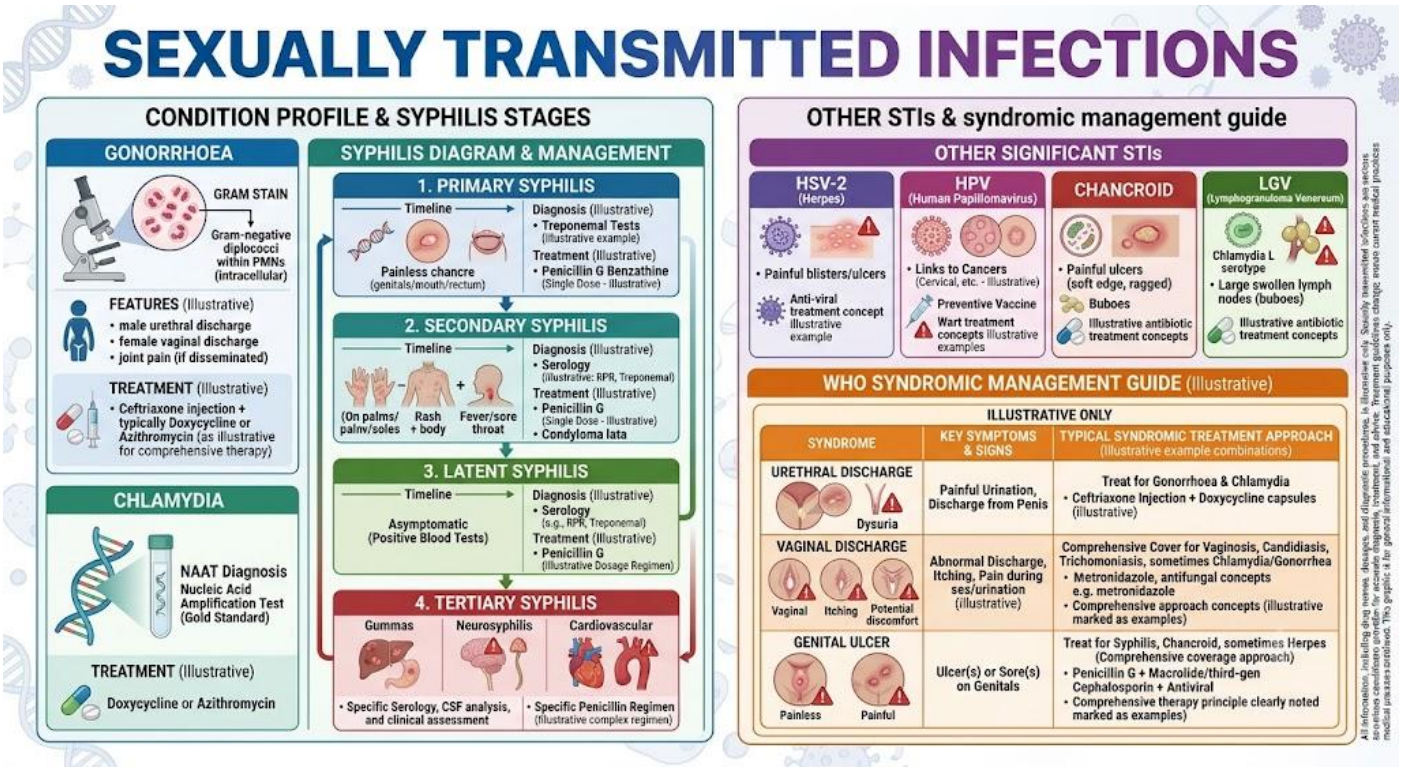

Figure 3.4: Sexually transmitted infections and syndromic management

Pilot questions 3.4

1. Describe the clinical features of gonorrhoea in men and women. (Linked to SLO 3.4)
2. Describe the four stages of syphilis. (Linked to SLO 3.4)
3. Explain the difference between treponemal and non-treponemal tests for syphilis. (Linked to SLO 3.4)
4. Describe the syndromic management of genital ulcer syndrome. (Linked to SLO 3.4)
5. State the HPV types causing genital warts and cervical carcinoma. (Linked to SLO 3.4)

Series Summary

This Series covered the major bacterial and viral infections. Typhoid fever (Salmonella Typhi: faecal-oral; stepwise fever week 1, rose spots week 2, intestinal perforation week 3; ceftriaxone first-line in Nigeria) and bacterial meningitis (N. meningitidis, S. pneumoniae, Hib; fever, neck stiffness, photophobia; non-blanching rash in meningococcal disease; immediate ceftriaxone; dexamethasone reduces neurological complications). Tuberculosis (M. tuberculosis: airborne; latent TB in most; reactivation in HIV; GeneXpert MTB/RIF first-line diagnostic; 2HRZE/4HR regimen; DOT; MDR-TB: second-line drugs). Common viral infections: measles (three Cs, Koplik's spots, maculopapular rash; vitamin A; MR vaccine), viral hepatitis (HEV: fulminant hepatic failure in pregnancy; HBV: birth-dose vaccine), influenza (antigenic drift: epidemics; antigenic shift: pandemics; oseltamivir within 48 hours), and COVID-19 (dexamethasone reduces mortality). STIs: gonorrhoea and chlamydia (ceftriaxone plus doxycycline), syphilis (four stages; benzathine penicillin), and syndromic management (urethral discharge, vaginal discharge, and genital ulcer syndromes).

By completing this Series, you should now be able to describe the pathogenesis and management of typhoid and meningitis, the diagnosis and treatment of TB, the features and management of major viral infections, and the syndromic management of STIs. These abilities align with SLOs 3.1 to 3.4.

Glossary of Terms

- **2HRZE/4HR:** the standard first-line TB treatment: 2 months of isoniazid, rifampicin, pyrazinamide, and ethambutol (intensive phase) followed by 4 months of isoniazid and rifampicin (continuation phase).
- **Antigenic drift:** minor incremental mutations in influenza surface antigens causing seasonal influenza epidemics as immunity from prior strains wanes.

- **Antigenic shift:** major reassortment of influenza gene segments producing a novel haemagglutinin or neuraminidase subtype to which no population has prior immunity, causing pandemics.
- **Chancre:** the painless indurated genital ulcer of primary syphilis; heals spontaneously in 3 to 6 weeks.
- **DOT (directly observed therapy):** a strategy in which a health worker observes each TB drug dose being swallowed to ensure adherence and prevent acquired drug resistance.
- **Faget's sign:** relative bradycardia in the context of fever; characteristic of typhoid fever, yellow fever, and brucellosis.
- **GeneXpert MTB/RIF:** cartridge-based PCR system detecting M. tuberculosis and rifampicin resistance within 2 hours; the WHO first-line TB diagnostic test.
- **Koplik's spots:** white spots on red buccal mucosa appearing 1 to 2 days before the measles rash; pathognomonic of measles.
- **MDR-TB:** multidrug-resistant tuberculosis: resistance to at least isoniazid and rifampicin; requires 18 to 24 months of second-line drugs.
- **PID (pelvic inflammatory disease):** infection of the upper female genital tract from N. gonorrhoeae and C. trachomatis; a major cause of tubal infertility and ectopic pregnancy.
- **Rose spots:** salmon-coloured blanching maculopapular spots on the trunk in approximately 30 percent of typhoid patients in week 2.
- **Syndromic management:** treatment of STIs based on symptom and sign patterns rather than laboratory diagnosis; the standard approach in Nigerian primary healthcare.

Concept Check Questions [Series 3]

Objective questions

1. Typhoid fever is caused by Salmonella enterica serotype Typhi, transmitted by the _____ route; the most feared week 3 complication is intestinal perforation. (Linked to SLO 3.1)
2. The classic triad of bacterial meningitis is fever, neck stiffness, and photophobia; a non-blanching petechial rash indicates _____ meningitis. (Linked to SLO 3.1)
3. Tuberculosis is caused by Mycobacterium tuberculosis; the standard first-line treatment is the _____ regimen. (Linked to SLO 3.2)
4. Measles is characterised by Koplik's spots and a maculopapular rash; the prodrome includes cough, coryza, and _____. (Linked to SLO 3.3)
5. Primary syphilis presents as a painless indurated genital _____; secondary syphilis produces a rash involving the palms and soles. (Linked to SLO 3.4)

Short-answer questions

6. Describe the management of severe typhoid fever with altered consciousness. (Linked to SLO 3.1)
7. State two extrapulmonary forms of tuberculosis and describe one clinical feature of each. (Linked to SLO 3.2)
8. Describe the clinical features of acute viral hepatitis. (Linked to SLO 3.3)
9. Describe the treatment of gonorrhoea and explain why dual therapy is recommended. (Linked to SLO 3.4)
10. Describe the syndromic management of urethral discharge syndrome. (Linked to SLO 3.4)

Long-answer questions

11. Describe the diagnosis and treatment of pulmonary tuberculosis. (Linked to SLO 3.2)
12. Describe the clinical features and management of measles. (Linked to SLO 3.3)
13. Describe the four stages of syphilis and the treatment for each. (Linked to SLO 3.4)
14. Describe the management of bacterial meningitis in a Nigerian adult. (Linked to SLO 3.1)
15. Describe the approach to a patient with genital ulcers in a primary care setting in Nigeria. (Linked to SLO 3.4)

Answers to Concept Check Questions [Series 3]

Objective questions

1. Faecal-oral.
2. Meningococcal.
3. 2HRZE/4HR.
4. Conjunctivitis.
5. Chancre.

Short-answer questions

6. Severe typhoid with altered consciousness requires IV ceftriaxone 2 g daily plus dexamethasone, which reduces mortality in patients with shock or altered consciousness. Dexamethasone is given as 3 mg per kg IV loading dose then 1 mg per kg every 6 hours for 48 hours. Supportive care includes IV fluids, nasogastric feeding if unable to eat, and monitoring for complications.

7. Scrofula (cervical TB lymphadenopathy) presents as painless, firm, rubbery enlarged cervical nodes that may become fluctuant and discharge. TB meningitis (the most lethal form) presents with fever, headache, neck stiffness, and altered consciousness; CSF shows lymphocytic pleocytosis, elevated protein, and very low glucose.
8. Acute viral hepatitis presents with a prodrome of nausea, vomiting, anorexia, fatigue, and right upper quadrant discomfort. This is followed by the icteric phase with jaundice, dark urine, and pale stools. Liver function tests show a hepatocellular pattern with markedly elevated ALT and AST.
9. Gonorrhoea is treated with ceftriaxone 500 mg IM as a single dose. Dual therapy with doxycycline 100 mg twice daily for 7 days (or azithromycin 1 g single dose) is added because co-infection with Chlamydia trachomatis is common (occurring in up to 30 to 40 percent of gonorrhoea cases) and treating both organisms simultaneously prevents treatment failure and ongoing transmission.
10. Urethral discharge syndrome is treated with a single-dose combination covering both gonorrhoea and chlamydia: ceftriaxone 500 mg IM and doxycycline 100 mg twice daily for 7 days (or azithromycin 1 g orally as a single dose). Counsel the patient on partner notification, adherence to the full course, abstinence until treatment is completed, and HIV testing.

Long-answer questions

11. **Basic response:** Diagnosis: GeneXpert MTB/RIF (first-line: detects M. tuberculosis and rifampicin resistance within 2 hours; 88 percent sensitivity for smear-negative TB), ZN smear (three early morning samples; 50 to 70 percent sensitivity; rapid and cheap), and culture (gold standard; 4 to 8 weeks; essential for drug susceptibility testing). Treatment: 2HRZE/4HR regimen with DOT throughout. Intensive phase 2 months: isoniazid (pyridoxine to prevent neuropathy), rifampicin (orange urine; CYP450 inducer), pyrazinamide (hyperuricaemia), ethambutol (optic neuritis: monitor vision monthly). Continuation phase 4 months: isoniazid and rifampicin only.

Value-added response: Stop all four drugs if transaminases exceed five times normal and re-introduce sequentially once liver function recovers. In HIV-positive patients on antiretrovirals, rifampicin reduces antiretroviral levels; efavirenz-based regimens are preferred as efavirenz is least affected.

12. **Basic response:** Clinical features: prodrome of three Cs (cough, coryza, conjunctivitis) for 2 to 4 days, followed by Koplik's spots (pathognomonic) and maculopapular rash spreading from the hairline downwards. Complications: pneumonia (most common cause of measles death), corneal ulceration and blindness (vitamin A deficiency in malnourished children), diarrhoea and dehydration, and encephalitis. Management: vitamin A supplementation (two doses at presentation reduces mortality), supportive care for complications, nutritional support.

Value-added response: Measles mortality in Nigeria remains high because vaccination coverage is below the 95 percent herd immunity threshold; cold chain failures, vaccine hesitancy, and geographical inaccessibility of remote communities sustain coverage gaps and allow outbreaks.

13. **Basic response:** Primary: painless indurated chancre at inoculation site; heals in 3 to 6 weeks; treat with benzathine penicillin 2.4 million units IM single dose. Secondary: maculopapular rash on palms and soles, condylomata lata, mucous patches, lymphadenopathy; treat with benzathine penicillin single dose. Latent: asymptomatic; early latent (within 1 year): single dose; late latent (after 1 year): three weekly doses. Tertiary: gummas, neurosyphilis, cardiovascular aortitis; neurosyphilis requires IV benzylpenicillin for 14 days.

Value-added response: All stages of syphilis respond to penicillin with no documented resistance; the Jarisch-Herxheimer reaction (fever and rigors within hours of the first dose from rapid spirochaete killing) should be anticipated and managed symptomatically with paracetamol.

14. **Basic response:** Give IV ceftriaxone 2 g every 12 hours immediately without waiting for CSF results. Add dexamethasone 0.15 mg per kg IV every 6 hours for 4 days before or with the first antibiotic dose to reduce neurological complications in pneumococcal

meningitis. Isolate under droplet precautions. Perform lumbar puncture when safe (after CT brain to exclude raised ICP). Arrange chemoprophylaxis for close contacts of confirmed meningococcal meningitis.

Value-added response: The single most important intervention is immediate antibiotics: every hour of delay worsens neurological outcomes and increases mortality; IM ceftriaxone is acceptable if IV access is difficult.

15. **Basic response:** In a primary care setting without laboratory diagnosis, genital ulcers are managed syndromatically. Treat empirically for syphilis (benzathine penicillin 2.4 million units IM single dose) and HSV-2 (aciclovir 400 mg three times daily for 7 days). If the ulcer has undermined edges with an inguinal bubo (suggesting chancroid), add azithromycin 1 g as a single oral dose. Counsel on partner notification, HIV testing, condom use, and abstinence until healed.

Value-added response: Genital ulcers are a major risk factor for HIV transmission because they disrupt mucosal barriers; prompt syndromic management of genital ulcer disease in Nigeria is therefore both treatment and HIV prevention.

Answers to Pilot Questions [Series 3]

Part 3.1

1. Week 1: stepwise rising fever, headache, malaise, anorexia, and relative bradycardia (Faget's sign). Week 2: fever plateau, hepatosplenomegaly, abdominal distension, and rose spots on the trunk in approximately 30 percent of patients. Week 3: complications including intestinal perforation (sudden peritonitis and free gas on erect CXR), intestinal haemorrhage, encephalopathy, and myocarditis.
2. Neisseria meningitidis (meningococcus): serogroup A causes epidemic meningitis in the meningitis belt with a characteristic petechial or purpuric rash. Streptococcus pneumoniae: the most common cause in adults, associated with high mortality and

neurological sequelae. Haemophilus influenzae type b (Hib): most common in children, now largely preventable by vaccine.

3. Give IV ceftriaxone 2 g every 12 hours immediately without waiting for CSF results. Add dexamethasone 0.15 mg per kg IV every 6 hours for 4 days before or with the first dose. Isolate under droplet precautions. Perform lumbar puncture when safe (after CT brain to exclude raised ICP). Arrange chemoprophylaxis for close contacts.

4. Salmonella Typhi strains in Nigeria show widespread resistance to the older first-line agents (chloramphenicol, ampicillin, and cotrimoxazole: multidrug-resistant typhoid) and increasing fluoroquinolone resistance. Ceftriaxone, a third-generation cephalosporin, remains active against most strains and achieves high concentrations in blood, bile, and tissues, making it the reliable first-line option in Nigeria.

5. Bacterial meningitis CSF: turbid or frankly purulent appearance; markedly elevated protein (above 1 g/L); very low glucose (below one-third of plasma glucose or below 2.2 mmol/L); high white cell count (above 1000 per microlitre) with predominantly neutrophils; Gram stain positive in approximately 60 to 80 percent of cases; culture and sensitivity essential for species identification.

Part 3.2

1. M. tuberculosis is inhaled as airborne droplet nuclei reaching the alveoli. Alveolar macrophages phagocytose the bacilli but fail to kill them because mycobacteria resist phagosome-lysosome fusion. CD4 T-lymphocytes are activated, forming granulomas (the hallmark of TB pathology) that contain the infection as latent TB with no symptoms in most immunocompetent individuals. The Ghon focus (lung lesion) plus hilar lymphadenopathy forms the primary complex.

2. Cough lasting more than 2 weeks (initially dry, then productive and blood-stained), drenching night sweats, significant unintentional weight loss, low-grade afternoon fever, fatigue, and haemoptysis from cavitary disease. Examination may show apical crackles

and signs of pleural effusion or be normal in early disease. Constitutional symptoms are often present for weeks to months before diagnosis.

3. GeneXpert MTB/RIF: cartridge-based automated PCR; results within 2 hours; detects M. tuberculosis DNA and simultaneously identifies rifampicin resistance mutations; sensitivity approximately 88 percent for smear-negative TB. ZN smear: requires three early morning sputum samples; sensitivity only 50 to 70 percent; rapid and cheap but misses up to half of smear-negative cases. GeneXpert is preferred because it is faster, more sensitive, and provides resistance information in the same test.

4. Intensive phase 2 months (HRZE): isoniazid (hepatotoxicity; peripheral neuropathy: give pyridoxine prophylactically), rifampicin (hepatotoxicity; orange body fluids; CYP450 inducer reducing OCP and antiretroviral levels), pyrazinamide (hepatotoxicity; hyperuricaemia and gout), ethambutol (optic neuritis: monitor visual acuity and colour vision monthly). Continuation phase 4 months (HR): isoniazid and rifampicin only. DOT throughout. Stop all drugs if transaminases exceed five times the upper limit of normal.

5. MDR-TB is M. tuberculosis resistant to both isoniazid and rifampicin, the two most potent first-line drugs. It develops through inadequate or incomplete treatment selecting for pre-existing resistant mutants. Management requires second-line drugs including bedaquiline, linezolid, clofazimine, and other agents based on drug susceptibility testing, for 18 to 24 months. The BPaL regimen (bedaquiline, pretomanid, linezolid) can achieve cure in 6 months in XDR-TB.

Part 3.3

1. Prodrome: three Cs (cough, coryza, and conjunctivitis) for 2 to 4 days, followed by Koplik's spots (pathognomonic white spots on red buccal mucosa appearing before the rash) and a maculopapular rash spreading from the hairline downwards to the trunk and extremities. The most common complication is pneumonia (either primary measles pneumonia or secondary bacterial pneumonia from S. pneumoniae or S. aureus), which is the leading cause of measles-related death.

2. Prodrome: nausea, vomiting, anorexia, right upper quadrant pain, and fatigue. Icteric phase: jaundice, dark urine (conjugated bilirubinaemia), pale stools, and yellow sclerae. LFTs show a hepatocellular pattern with markedly elevated ALT and AST. The most dangerous form in pregnancy is hepatitis E (HEV), which causes fulminant hepatic failure in the third trimester with mortality up to 20 to 25 percent.
3. Antigenic drift: minor incremental point mutations in haemagglutinin or neuraminidase surface antigens from errors in RNA polymerase replication, accumulating gradually and causing seasonal epidemics as immune protection from prior strains wanes gradually. Antigenic shift: a major reassortment of gene segments between two different influenza A strains (for example an animal and human strain co-infecting the same cell) generating a novel haemagglutinin or neuraminidase subtype to which no human population has prior immunity, causing pandemics.
4. Dexamethasone 6 mg orally or IV daily for 10 days reduces mortality by approximately one-third in patients requiring supplemental oxygen and by approximately one-half in mechanically ventilated patients. It suppresses the dysregulated immune-mediated lung inflammation that drives ARDS in severe COVID-19. It should be given to all patients with SpO2 below 94 percent or requiring ventilation.
5. RSV (respiratory syncytial virus) is the most common cause of bronchiolitis in infants (presenting with wheeze, tachypnoea, subcostal recession, and difficulty feeding; managed supportively with oxygen and fluids). Rhinovirus is the most common cause of the common cold (presentation with nasal congestion, rhinorrhoea, mild sore throat, and low-grade fever; self-limiting; managed symptomatically).

Part 3.4

1. Men: dysuria and purulent yellow-green urethral discharge, which is usually present in the morning before micturition; epididymo-orchitis (unilateral scrotal pain and swelling) may develop if untreated. Women: often completely asymptomatic (making screening important); symptomatic presentations include vaginal discharge, intermenstrual or post-

coital bleeding from cervicitis, lower abdominal pain from PID, and complications of PID including tubal factor infertility and ectopic pregnancy.

2. Primary: painless indurated genital chancre at the inoculation site, appearing 9 to 90 days after exposure and healing spontaneously in 3 to 6 weeks. Secondary: generalised maculopapular rash classically involving the palms and soles, condylomata lata in moist skin folds, mucous patches, and generalised lymphadenopathy, appearing 4 to 8 weeks after the chancre heals. Latent: asymptomatic; early latent within 1 year; late latent after 1 year. Tertiary: gummas (destructive granulomatous lesions in skin, bone, or viscera), neurosyphilis (meningovasculitis, general paresis, tabes dorsalis), and cardiovascular syphilis (aortitis causing aortic regurgitation).

3. Treponemal tests (TPHA and TPPA and rapid treponemal assays): detect antibodies specifically against T. pallidum antigens; highly sensitive and specific; remain positive for life after successful treatment so they confirm exposure to syphilis but cannot be used alone to diagnose active infection or monitor treatment. Non-treponemal tests (VDRL and RPR): detect cardiolipin antibodies produced in response to tissue damage; titre correlates with disease activity and falls with successful treatment; a fourfold fall in titre at 3 to 6 months confirms adequate treatment response; false-positive results occur in pregnancy, SLE, and antiphospholipid syndrome.

4. Genital ulcer syndrome in the syndromic approach: treat empirically for both syphilis (benzathine penicillin 2.4 million units IM single dose) and HSV-2 (aciclovir 400 mg three times daily for 7 days) because laboratory differentiation is unavailable at primary care level. If the ulcer has undermined edges with a tender inguinal bubo suggesting chancroid, add azithromycin 1 g orally as a single dose. Counsel on partner notification and treatment, HIV testing, condom use, and abstinence until the ulcers have healed.

5. HPV types 6 and 11 (low-risk oncogenic types) cause condylomata acuminata (anogenital warts: soft pedunculated flesh-coloured lesions). HPV types 16 and 18 (high-risk oncogenic types) cause cervical carcinoma (responsible for approximately 70 percent of cervical cancer cases worldwide), as well as anal, oropharyngeal, vulval, vaginal, and penile carcinoma. Prevention: HPV vaccine (given to girls aged 9 to 14 before sexual

debut for maximum efficacy; also recommended for boys to prevent anogenital and oropharyngeal malignancies).

References and Attributions [Series 3]

Textual References

- World Health Organization. (2022). WHO Consolidated Guidelines on Tuberculosis: Diagnostic Testing. Geneva: WHO.
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- Mandell, G. L., Bennett, J. E. and Dolin, R. (2015). Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases (8th ed.). Philadelphia: Elsevier.
- Nigeria Centre for Disease Control. (2021). National Tuberculosis and Leprosy Control Programme Annual Report 2021. Abuja: NCDC.

Figures, Plates, Tables, and Boxes

- Figure 3.1: Typhoid fever and bacterial meningitis. AI-generated using the prompt: "Two-panel infographic: left typhoid clinical course by week and management; right meningitis organisms, triad, CSF findings, and management." Suggested OER search string: "typhoid fever bacterial meningitis clinical features management infographic OER."
- Figure 3.2: Tuberculosis diagnosis and treatment. AI-generated using the prompt: "Two-panel infographic: left pulmonary TB symptoms and CXR findings, extrapulmonary forms, diagnostic methods; right 2HRZE/4HR regimen with drug side effects and MDR-TB box." Suggested OER search string: "tuberculosis diagnosis 2HRZE treatment regimen GeneXpert MDR-TB infographic OER."
- Figure 3.3: Common viral infections. AI-generated using the prompt: "Two-panel infographic: left measles (prodrome, Koplik's spots, complications, vitamin A, EPI) and viral hepatitis mini-table; right influenza (antigenic drift vs shift), COVID-19 (dexamethasone), RSV and rhinovirus." Suggested OER search string: "measles viral hepatitis influenza COVID-19 RSV respiratory viruses infographic OER."

- Figure 3.4: Sexually transmitted infections and syndromic management. AI-generated using the prompt: "Two-panel infographic: left gonorrhoea, chlamydia, and four-stage syphilis diagram; right other STIs (HSV-2, HPV, chancroid, LGV) and syndromic management table." Suggested OER search string: "sexually transmitted infections syphilis gonorrhoea chlamydia HSV HPV syndromic management infographic OER."

Series 4: HIV/AIDS and Opportunistic Infections

- **Part 4.1: Virology and Epidemiology of HIV**
    - Sub Part 4.1.1: HIV virology and transmission
    - Sub Part 4.1.2: Epidemiology of HIV in Nigeria
    - Sub Part 4.1.3: Natural history and staging
- **Part 4.2: Clinical Features and Diagnosis of HIV**
    - Sub Part 4.2.1: Acute HIV infection and asymptomatic phase
    - Sub Part 4.2.2: Symptomatic HIV and AIDS-defining illnesses
    - Sub Part 4.2.3: Diagnosis of HIV
- **Part 4.3: Antiretroviral Therapy**
    - Sub Part 4.3.1: Principles of ART
    - Sub Part 4.3.2: First-line and second-line ART in Nigeria
    - Sub Part 4.3.3: Monitoring ART and managing side effects
- **Part 4.4: Opportunistic Infections**
    - Sub Part 4.4.1: Respiratory opportunistic infections
    - Sub Part 4.4.2: Neurological opportunistic infections
    - Sub Part 4.4.3: Other opportunistic infections and prophylaxis

Introduction

HIV/AIDS remains one of the most significant infectious disease challenges in Nigeria. With an estimated 1.9 million people living with HIV, Nigeria accounts for approximately 9 percent of the global HIV burden. The introduction and scale-up of antiretroviral therapy has transformed HIV from a uniformly fatal illness into a manageable chronic condition. Understanding the virology, epidemiology, clinical features, diagnosis, and treatment of HIV, as well as the recognition and management of opportunistic infections, is essential for every clinician in Nigeria.

This Series examines HIV/AIDS comprehensively. We shall commence with HIV virology, transmission, epidemiology, and natural history. Next, we will explore the clinical features and laboratory diagnosis. Moving on, we will cover antiretroviral therapy including first-line regimens and monitoring. Finally, we will address the major opportunistic infections affecting the respiratory, neurological, and other organ systems.

Series Learning Outcomes

Upon completing this Series, you should be able to:

- **SLO 4.1:** describe the virology, routes of transmission, and natural history of HIV infection,
- **SLO 4.2:** describe the clinical features of HIV infection from acute seroconversion through to AIDS-defining illnesses,
- **SLO 4.3:** describe the laboratory diagnosis of HIV and interpret CD4 count and viral load results,
- **SLO 4.4:** describe the principles of antiretroviral therapy, the first-line regimen used in Nigeria, and the monitoring of ART, and

- **SLO 4.5:** describe the clinical features, diagnosis, and management of the major opportunistic infections in HIV-positive patients.

4.1 Virology and Epidemiology of HIV

4.1.1 HIV virology and transmission

HIV (human immunodeficiency virus) is a retrovirus (RNA virus) belonging to the lentivirus family. It has two main types: **HIV-1** (the dominant global strain responsible for the AIDS pandemic) and **HIV-2** (less pathogenic; confined mainly to West Africa). The HIV genome encodes three key structural genes: gag (core proteins: p24 capsid antigen), pol (reverse transcriptase, integrase, and protease), and env (envelope glycoproteins: gp120 and gp41). HIV infects cells bearing the **CD4 receptor**, primarily CD4 T-lymphocytes, macrophages, and dendritic cells.

Routes of transmission: sexual contact (unprotected vaginal and anal intercourse: the most common route in Nigeria), blood and blood products (sharing injection needles, blood transfusions, needlestick injuries), and vertical transmission (mother to child: during pregnancy, labour and delivery, or breastfeeding; accounts for approximately 90 percent of childhood HIV infections). HIV is not transmitted by casual contact, insect bites, sharing utensils, or airborne routes.

Fill in the blank: HIV infects cells bearing the _____ receptor, primarily CD4 T-lymphocytes. The most common route of HIV transmission in Nigeria is _____ contact.

4.1.2 Epidemiology of HIV in Nigeria

Nigeria has the largest HIV burden in Africa and the second largest in the world (after South Africa), with an estimated 1.9 million people living with HIV. The adult HIV prevalence is approximately 1.4 percent, with significant variation by state. The epidemic in Nigeria is predominantly heterosexually driven, with key affected populations including female sex workers, men who have sex with men, people who inject drugs, and clients of sex workers.

Prevention of mother-to-child transmission (PMTCT) is a critical programme in Nigeria: without intervention, the risk of MTCT is 15 to 45 percent; with optimal PMTCT (ART for the mother throughout pregnancy and breastfeeding plus nevirapine syrup for the infant for 6 weeks), MTCT can be reduced below 5 percent. Despite scale-up, PMTCT coverage in Nigeria remains below the 95 percent target, leaving many infants at risk.

Fill in the blank: Nigeria has approximately 1.9 million people living with HIV, making it the country with the largest HIV burden in _____. Without PMTCT intervention, the risk of mother-to-child transmission is _____ to 45 percent.

4.1.3 Natural history and staging

The WHO clinical staging system classifies HIV disease into four stages based on clinical features: Stage 1 (asymptomatic or persistent generalised lymphadenopathy), Stage 2 (minor mucocutaneous manifestations: seborrhoeic dermatitis, recurrent oral ulcers, herpes zoster, fungal nail infections), Stage 3 (severe conditions: oral candidiasis, pulmonary TB, severe bacterial infections), and Stage 4 (AIDS-defining conditions: Pneumocystis pneumonia, cryptococcal meningitis, cerebral toxoplasmosis, oesophageal candidiasis, Kaposi's sarcoma, HIV wasting syndrome).

The CD4 count is the most important laboratory marker of immune status. Normal CD4 count is 500 to 1500 cells per microlitre. A CD4 count below 200 cells per microlitre defines AIDS in the United States classification (regardless of symptoms) and marks the threshold at which Pneumocystis pneumonia prophylaxis with cotrimoxazole is essential. The CD4 count guides the urgency of ART initiation and the risk of specific opportunistic infections.

Fill in the blank: WHO HIV Stage 4 includes AIDS-defining conditions such as PCP, cryptococcal meningitis, and _____. A CD4 count below _____ cells per microlitre defines AIDS and marks the threshold for cotrimoxazole prophylaxis.

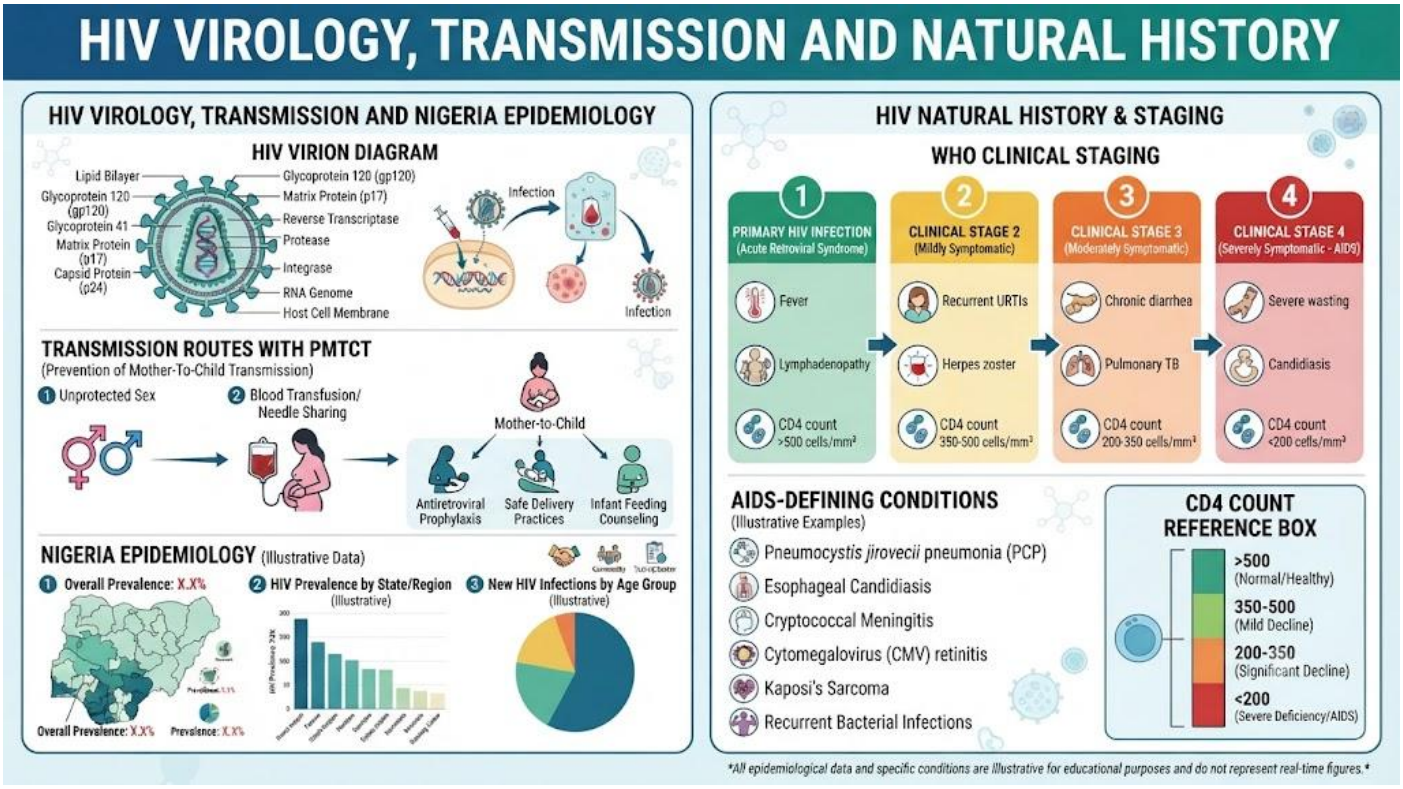

Figure 4.1: HIV virology, transmission, natural history, and WHO clinical staging

Pilot questions 4.1

1. Describe the structure of HIV and name the three key structural genes. (Linked to SLO 4.1)
2. Describe the routes of HIV transmission and state the most common route in Nigeria. (Linked to SLO 4.1)
3. Describe the PMTCT programme and state the risk of MTCT with and without intervention. (Linked to SLO 4.1)
4. Describe the WHO clinical staging system for HIV disease. (Linked to SLO 4.1)
5. State the CD4 count threshold for AIDS diagnosis and for cotrimoxazole prophylaxis. (Linked to SLO 4.1)

4.2 Clinical Features and Diagnosis of HIV

4.2.1 Acute HIV infection and asymptomatic phase

Acute HIV infection (primary HIV infection) occurs 2 to 4 weeks after exposure and represents the initial viraemic phase. It presents as an acute retroviral syndrome resembling infectious mononucleosis: fever, pharyngitis, generalised lymphadenopathy, myalgia, headache, and a maculopapular rash. Oral ulcers and aseptic meningitis may occur. This phase lasts 2 to 4 weeks. HIV antibody tests may be negative at this stage (the window period before seroconversion) because antibodies have not yet developed; **HIV RNA PCR (viral load)** is the most sensitive test during acute infection.

The asymptomatic phase follows seroconversion and may last 8 to 10 years without treatment. During this phase the patient is infectious. The CD4 count declines gradually (by approximately 50 to 100 cells per microlitre per year) while the viral load remains detectable. Persistent generalised lymphadenopathy (enlarged lymph nodes in two or more extra-inguinal sites lasting more than 3 months without another cause) is a common finding in the asymptomatic phase.

Fill in the blank: Acute HIV infection presents 2 to 4 weeks after exposure as an acute _____ syndrome with fever, pharyngitis, and rash. HIV antibody tests may be negative during this phase because the patient is in the _____ period before seroconversion.

4.2.2 Symptomatic HIV and AIDS-defining illnesses

As the CD4 count falls below 350 cells per microlitre, symptomatic HIV disease develops. Early symptomatic features (WHO Stage 2 to 3): oral candidiasis (white plaques on the buccal mucosa and tongue: the most common oral manifestation of HIV), herpes zoster (shingles: vesicular dermatomal rash; its occurrence in a young adult is a strong indicator of HIV infection), recurrent bacterial pneumonia, pulmonary tuberculosis, and unexplained weight loss above 10 percent of body weight.

AIDS-defining illnesses (WHO Stage 4) occur when the CD4 count falls below 200 cells per microlitre and include: **Pneumocystis jirovecii pneumonia (PCP)** (bilateral interstitial infiltrates; subacute onset; treated with high-dose cotrimoxazole), **cryptococcal meningitis** (the

most common cause of meningitis in HIV-positive adults in Nigeria), **cerebral toxoplasmosis** (multiple ring-enhancing lesions on CT brain), **oesophageal candidiasis** (dysphagia and odynophagia), **Kaposi's sarcoma** (purple skin lesions from HHV-8 infection), and **HIV wasting syndrome** (above 10 percent involuntary weight loss with diarrhoea or fever).

Fill in the blank: Oral _____ (white plaques on the buccal mucosa) is the most common oral manifestation of HIV. A young adult presenting with herpes _____ should be tested for HIV.

4.2.3 Diagnosis of HIV

HIV testing follows a serial testing algorithm. First test: rapid diagnostic test (RDT: lateral flow immunoassay detecting HIV antibodies; results within 20 minutes). A reactive first test is followed by a second test with a different RDT. If the second test is also reactive, the patient is diagnosed HIV-positive. If the two tests give discordant results, a third test (tiebreaker) using an alternative assay is used. In Nigeria, the standard algorithm uses three different RDTs. A 4th-generation combination antigen-antibody assay (Ag/Ab combo test) detects both p24 antigen and antibodies, shortening the window period to approximately 18 days.

CD4 count (measures immune status and guides ART initiation and OI prophylaxis) and HIV viral load (HIV RNA PCR: measures the amount of virus in the blood; used to monitor ART response: an undetectable viral load below 50 copies per mL indicates successful virological suppression; a viral load above 1000 copies per mL after 6 months of ART indicates treatment failure requiring investigation and regimen switch).

Fill in the blank: A reactive first HIV RDT must be confirmed with a _____ RDT using a different assay. A viral load above _____ copies per mL after 6 months of ART indicates virological failure.

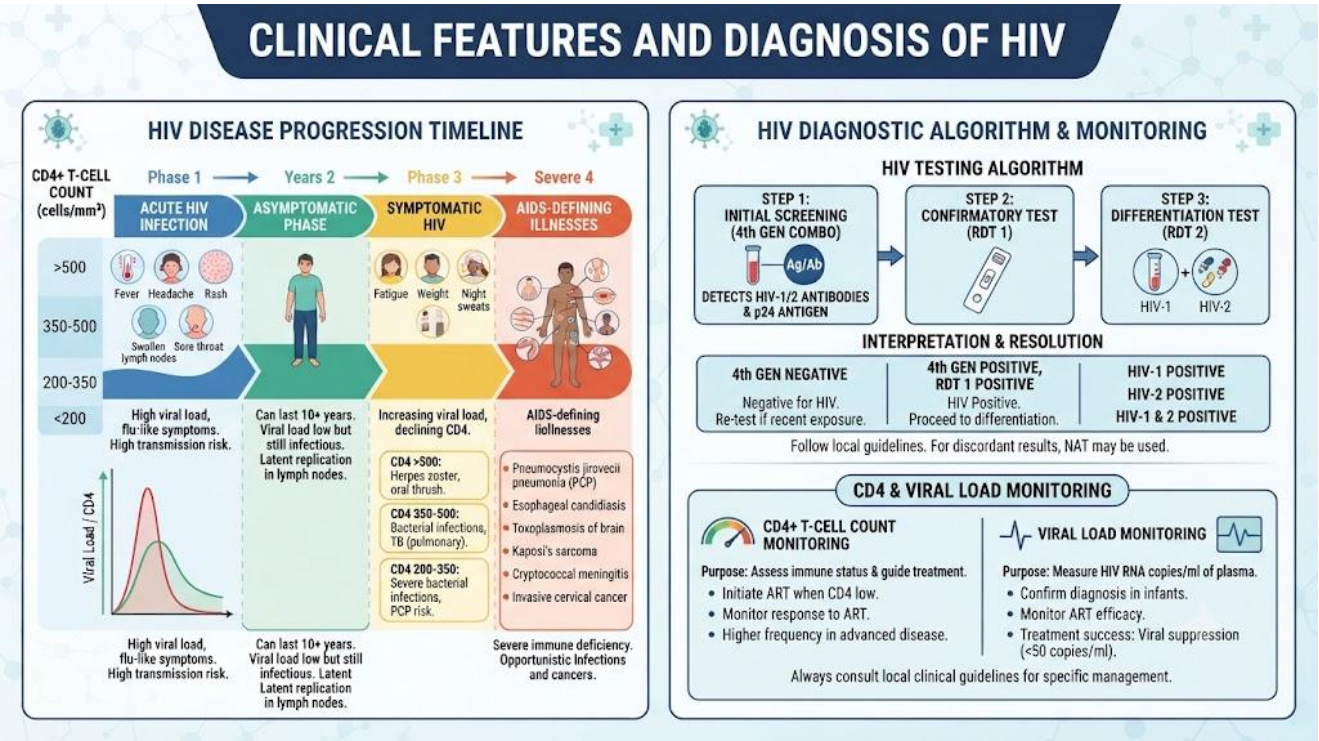

Figure 4.2: Clinical features of HIV disease and the HIV testing and monitoring algorithm

Pilot questions 4.2

1. Describe the clinical features of acute HIV infection. (Linked to SLO 4.2)
2. State three AIDS-defining illnesses and the CD4 count threshold at which they occur. (Linked to SLO 4.2)
3. Describe the HIV testing algorithm used in Nigeria. (Linked to SLO 4.3)
4. Explain the significance of CD4 count and viral load in managing HIV. (Linked to SLO 4.3)
5. Describe the clinical features of oral candidiasis and herpes zoster in HIV-positive patients. (Linked to SLO 4.2)

4.3 Antiretroviral Therapy

4.3.1 Principles of ART

ART works by suppressing HIV replication with combinations of drugs acting at different stages of the viral life cycle, preventing immune destruction and the development of AIDS. The goals of ART are: undetectable viral load (below 50 copies per mL: the primary treatment goal; prevents transmission and immune decline), immune reconstitution (rising CD4 count reducing OI risk), prevention of transmission (an undetectable viral load renders the patient non-infectious: Undetectable equals Untransmittable or U=U), and prevention of MTCT.

ART should be initiated in all HIV-positive individuals regardless of CD4 count (treat all: the current WHO and Nigeria guideline). Earlier initiation prevents immune decline, reduces transmission, and reduces non-AIDS morbidity including cardiovascular, renal, and liver disease. ART is also given as post-exposure prophylaxis (PEP: within 72 hours of high-risk exposure: 28-day course) and pre-exposure prophylaxis (PrEP: tenofovir-emtricitabine daily for HIV-negative individuals at high risk).

Fill in the blank: The primary goal of ART is an undetectable viral load below _____ copies per mL. ART should be initiated in _____ HIV-positive individuals regardless of CD4 count.

4.3.2 First-line and second-line ART in Nigeria

The Nigeria ART programme follows WHO guidelines. The preferred first-line regimen for adults and adolescents is **TLD: tenofovir disoproxil fumarate (TDF) + lamivudine (3TC) + dolutegravir (DTG)**, given as a single daily tablet. TDF and 3TC are nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) that inhibit HIV reverse transcriptase. DTG is an integrase strand transfer inhibitor (INSTI) with a high genetic barrier to resistance and an excellent tolerability profile.

Second-line ART (for patients failing first-line TLD): zidovudine (AZT) + lamivudine (3TC) + atazanavir/ritonavir (ATV/r) or lopinavir/ritonavir (LPV/r). Boosted protease inhibitors (ATV/r, LPV/r) are the backbone of second-line therapy: ritonavir inhibits CYP3A4, boosting the plasma levels of the companion protease inhibitor. Third-line ART is guided by genotypic resistance

testing. Special populations: pregnant women should receive TDF + 3TC + DTG (DTG is now recommended in pregnancy; previous concerns about neural tube defects have been resolved by updated data).

Fill in the blank: The preferred first-line ART regimen in Nigeria is TLD: tenofovir + lamivudine + _____. Boosted protease inhibitors use ritonavir as a pharmacokinetic _____ to increase drug levels.

4.3.3 Monitoring ART and managing side effects

ART monitoring: viral load at baseline, 6 months, and 12 months, then annually if suppressed. A viral load above 1000 copies per mL after 6 months of ART indicates treatment failure (after excluding adherence failure and drug interactions). CD4 count at baseline and every 6 months until above 350 per microlitre and stable. Full blood count, renal function (TDF is nephrotoxic: monitor creatinine and eGFR; switch to tenofovir alafenamide or TAF in renal impairment), and liver function tests at baseline and regularly.

Key ART side effects: TDF (nephrotoxicity: decline in eGFR; Fanconi syndrome: proximal tubular dysfunction; osteopenia), AZT (anaemia and neutropenia: check full blood count; lactic acidosis), nevirapine (severe cutaneous hypersensitivity reactions including Stevens-Johnson syndrome; hepatotoxicity: do not use when CD4 above 250 in women or above 400 in men due to increased hepatotoxicity risk), efavirenz (CNS side effects: vivid dreams, dizziness, mood disturbance: usually resolve after 2 to 4 weeks), and DTG (weight gain; insomnia; rarely immune reconstitution inflammatory syndrome or IRIS).

Fill in the blank: Viral load above 1000 copies per mL after 6 months of ART indicates _____ failure. TDF causes _____ toxicity; monitor creatinine and eGFR and switch to TAF in renal impairment.

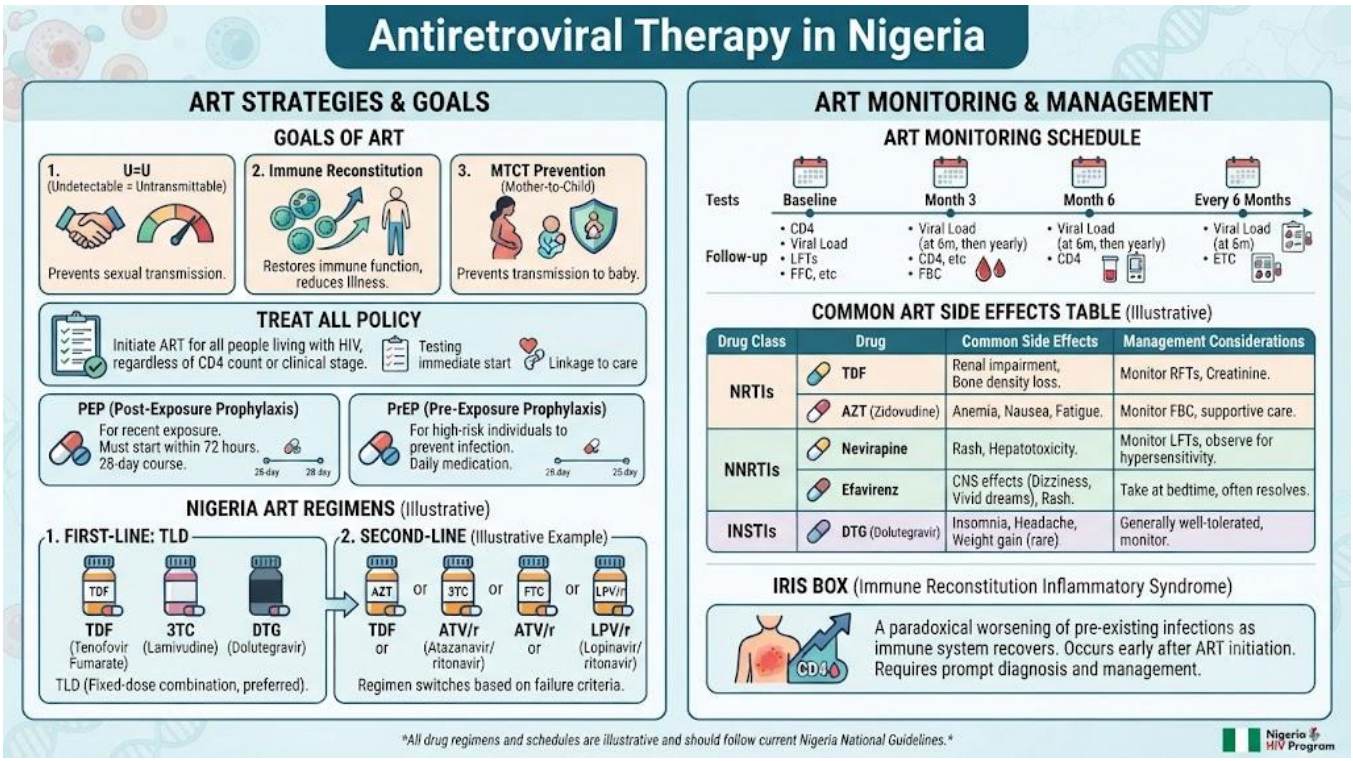

Figure 4.3: Antiretroviral therapy in Nigeria: goals, regimens, monitoring, and side effects

Pilot questions 4.3

1. State the goals of ART and explain the U=U concept. (Linked to SLO 4.4)
2. Describe the first-line ART regimen in Nigeria and the mechanism of action of each drug. (Linked to SLO 4.4)
3. Describe how ART response is monitored in Nigeria. (Linked to SLO 4.4)
4. Describe the side effects of TDF and nevirapine. (Linked to SLO 4.4)
5. Define IRIS and describe its management. (Linked to SLO 4.4)

4.4 Opportunistic Infections

4.4.1 Respiratory opportunistic infections

Pneumocystis jirovecii pneumonia (PCP) is an AIDS-defining illness occurring when CD4 falls below 200 per microlitre. It presents with subacute onset progressive exertional dyspnoea, dry cough, fever, and hypoxia disproportionate to chest findings. CXR shows bilateral perihilar

interstitial infiltrates (ground-glass appearance). Diagnosis: bronchoalveolar lavage (BAL) with silver staining or immunofluorescence; serum beta-D-glucan is elevated. Treatment: high-dose oral or IV cotrimoxazole (trimethoprim-sulfamethoxazole) for 21 days; adjunctive prednisolone when PaO2 below 70 mmHg. Primary prophylaxis: daily cotrimoxazole when CD4 below 200.

Pulmonary tuberculosis is the most common opportunistic infection in HIV-positive individuals in Nigeria and the leading cause of death in people living with HIV globally. HIV increases the risk of TB reactivation 20 to 30-fold and alters the clinical presentation: smear-negative TB is more frequent, the CXR may show atypical patterns (mid and lower zone infiltrates, intrathoracic lymphadenopathy, miliary pattern), and extrapulmonary TB is more common. GeneXpert MTB/RIF is the recommended first-line diagnostic test. TB treatment follows the standard 2HRZE/4HR regimen; ART should be started within 2 weeks of TB treatment if CD4 is below 50, and within 8 weeks for all others.

Fill in the blank: PCP presents with progressive _____ dyspnoea and bilateral perihilar infiltrates on CXR; it is treated with high-dose _____. TB should trigger ART initiation within 2 weeks if CD4 is below 50 per microlitre.

4.4.2 Neurological opportunistic infections

Cryptococcal meningitis is the most common cause of meningitis in HIV-positive adults in Nigeria and carries a high mortality. It is caused by **Cryptococcus neoformans**, an encapsulated yeast acquired by inhalation of pigeon or bird droppings. Presentation: subacute onset headache, fever, altered consciousness, and meningism; raised intracranial pressure (ICP) is common and is the primary cause of early death. Diagnosis: India ink stain (encapsulated yeast cells: positive in above 80 percent), cryptococcal antigen lateral flow assay (CrAg LFA: the most sensitive test; can also be performed on serum for screening at CD4 below 100). Treatment: amphotericin B deoxycholate plus flucytosine for 7 days (induction) followed by oral fluconazole 800 mg for 8 weeks (consolidation) then 200 mg daily (maintenance until CD4 above 200).

Cerebral toxoplasmosis is caused by reactivation of **Toxoplasma gondii** (acquired from cat faeces or undercooked meat) when CD4 falls below 100. Presentation: focal neurological deficits (hemiparesis, aphasia, cranial nerve palsies), headache, fever, and altered consciousness. CT or

MRI brain: multiple ring-enhancing lesions with surrounding oedema, classically at the basal ganglia. Treatment: pyrimethamine plus sulfadiazine plus folinic acid for 6 weeks; if pyrimethamine is unavailable, cotrimoxazole is used as an alternative.

Fill in the blank: Cryptococcal meningitis is diagnosed by India ink stain and _____ lateral flow assay; raised intracranial pressure is the primary cause of early death. Cerebral toxoplasmosis shows multiple _____ lesions on CT brain at the basal ganglia.

4.4.3 Other opportunistic infections and prophylaxis

Oesophageal candidiasis (Candida albicans): dysphagia and odynophagia in a patient with oral thrush; diagnosed by endoscopy (white plaques on oesophageal mucosa) or empirically; treated with fluconazole 200 mg daily for 14 to 21 days. Kaposi's sarcoma (KS): caused by HHV-8 (human herpesvirus 8); presents as violaceous or dark purple skin lesions that can also involve the oral mucosa, lymph nodes, and viscera; treated with ART (ART alone causes regression in early KS) and systemic chemotherapy (liposomal doxorubicin) for advanced KS. CMV retinitis (CD4 below 50): blurred vision and visual field loss; diagnosed by fundoscopy (haemorrhages and exudates in a brushfire pattern); treated with IV ganciclovir.

OI prophylaxis: cotrimoxazole prophylaxis (CPT) is the cornerstone of OI prevention in Nigeria. It prevents PCP, toxoplasmosis, and bacterial infections and reduces malaria morbidity. Indications: CD4 below 200 per microlitre, all HIV-positive pregnant women, and all HIV-positive children below 5 years of age. Fluconazole prophylaxis prevents cryptococcal meningitis in patients with CD4 below 100 in resource-limited settings. Isoniazid preventive therapy (IPT: isoniazid 300 mg daily for 6 months) prevents TB reactivation in HIV-positive individuals with latent TB.

Fill in the blank: Cotrimoxazole prophylaxis is indicated in all HIV-positive patients with CD4 below _____ per microlitre. Isoniazid preventive therapy (IPT) is given for _____ months to prevent TB reactivation in HIV-positive individuals.

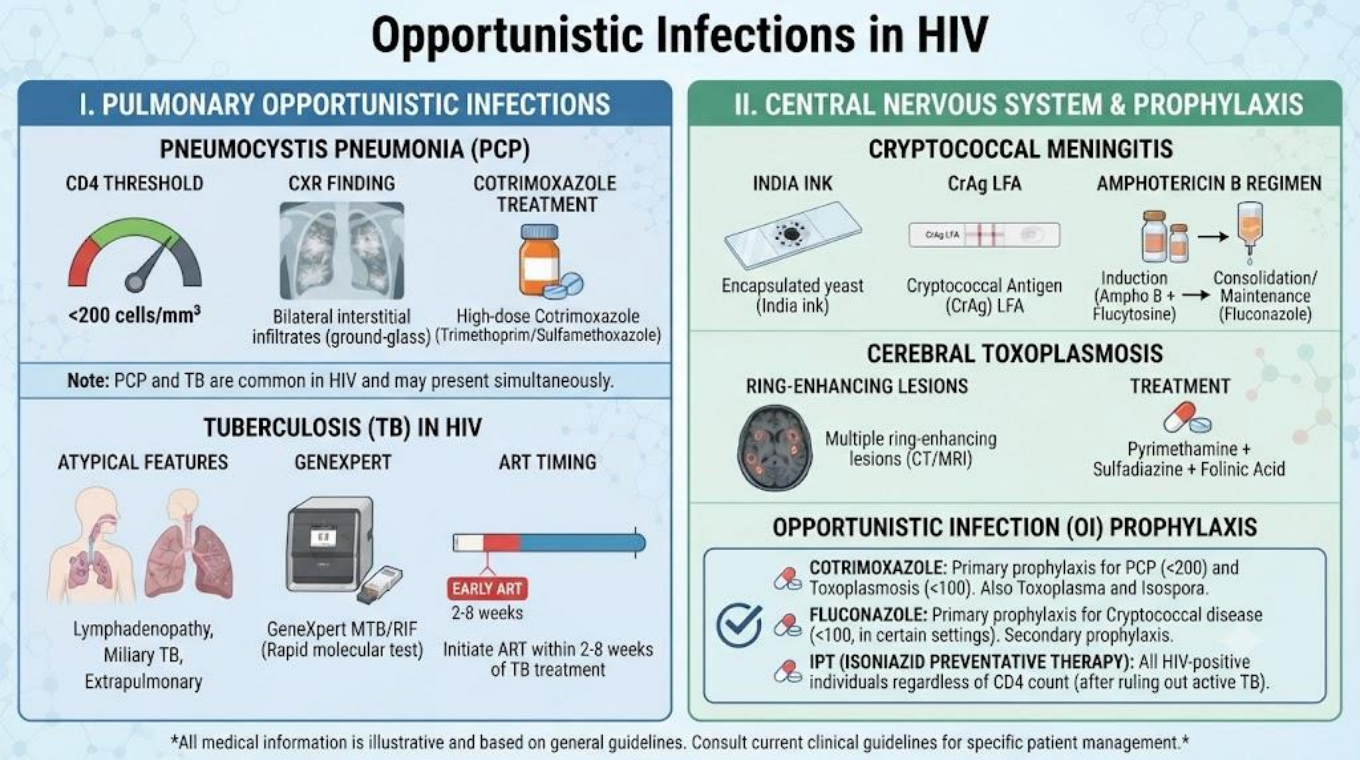

Figure 4.4: Opportunistic infections in HIV: PCP, TB, cryptococcal meningitis, cerebral toxoplasmosis, and OI prophylaxis

Pilot questions 4.4

1. Describe the clinical features and management of PCP. (Linked to SLO 4.5)
2. Describe the clinical features and diagnosis of cryptococcal meningitis. (Linked to SLO 4.5)
3. Describe the management of cryptococcal meningitis. (Linked to SLO 4.5)
4. Describe the clinical features and CT findings in cerebral toxoplasmosis. (Linked to SLO 4.5)
5. Describe the indications and drugs used for OI prophylaxis in Nigeria. (Linked to SLO 4.5)

Series Summary

This Series covered HIV/AIDS comprehensively. We examined HIV virology (retrovirus; gp120 binds CD4 receptor; gag, pol, env genes), transmission (sexual most common in Nigeria; vertical: 15 to 45 percent risk reduced below 5 percent with PMTCT), epidemiology (1.9 million in Nigeria; largest burden in Africa), and natural history (WHO stages 1 to 4; CD4 count below 200 defines AIDS). Clinical features progressed from acute retroviral syndrome (fever, rash, pharyngitis; window period: HIV RNA PCR most sensitive) through asymptomatic phase to symptomatic HIV (oral candidiasis, herpes zoster, TB) and AIDS-defining illnesses (PCP, cryptococcal meningitis, toxoplasmosis, KS). Diagnosis uses serial RDT algorithm and 4th-generation Ag/Ab assay; CD4 guides OI risk; viral load monitors ART response. ART goals are undetectable viral load (U=U) and immune reconstitution; Treat All policy: TLD (TDF plus 3TC plus DTG) is the preferred first-line single daily tablet; monitoring by viral load at 6 and 12 months. Opportunistic infections: PCP (cotrimoxazole 21 days), pulmonary TB (2HRZE/4HR; ART within 2 weeks if CD4 below 50), cryptococcal meningitis (amphotericin B plus flucytosine induction then fluconazole consolidation), toxoplasmosis (pyrimethamine plus sulfadiazine 6 weeks); OI prophylaxis: cotrimoxazole (CD4 below 200), fluconazole (CD4 below 100), IPT (6 months).

By completing this Series, you should now be able to describe the virology, transmission, and natural history of HIV, recognise the clinical features from acute infection to AIDS, describe the HIV testing algorithm and monitoring, describe the first-line ART regimen in Nigeria, and diagnose and manage the major opportunistic infections. These abilities align with SLOs 4.1 to 4.5.

Glossary of Terms

- **CD4 count:** a measure of the number of CD4 T-lymphocytes per microlitre of blood; the most important marker of immune status in HIV; normal 500 to 1500; below 200 defines AIDS and triggers cotrimoxazole prophylaxis.

- **CrAg LFA:** cryptococcal antigen lateral flow assay; a highly sensitive point-of-care test for cryptococcal antigen in CSF or serum; used for diagnosis and screening of cryptococcal infection in HIV-positive patients with CD4 below 100.
- **DTG (dolutegravir):** an integrase strand transfer inhibitor (INSTI); the third drug in the preferred first-line TLD regimen in Nigeria; high genetic barrier to resistance; excellent tolerability; given once daily.
- **IRIS (immune reconstitution inflammatory syndrome):** a paradoxical worsening or unmasking of an opportunistic infection after ART initiation, caused by the restored immune response targeting subclinical pathogens; managed by continuing ART and treating the underlying OI.
- **Kaposi's sarcoma:** an AIDS-defining malignancy caused by HHV-8, presenting as violaceous or dark purple skin lesions that can also involve oral mucosa, lymph nodes, and viscera; treated with ART and chemotherapy for advanced disease.
- **PMTCT:** prevention of mother-to-child transmission; a programme that reduces the risk of HIV transmission from an HIV-positive mother to her infant from 15 to 45 percent (without intervention) to below 5 percent (with ART for the mother and nevirapine for the infant).
- **PrEP:** pre-exposure prophylaxis; daily tenofovir-emtricitabine for HIV-negative individuals at high ongoing risk of HIV acquisition; reduces HIV risk by above 90 percent with consistent use.
- **TLD:** tenofovir disoproxil fumarate plus lamivudine plus dolutegravir; the preferred first-line ART regimen in Nigeria; given as a single daily tablet; highly effective with minimal side effects and high genetic barrier to resistance.
- **U=U (Undetectable equals Untransmittable):** the evidence-based principle that a person living with HIV who has achieved and maintains an undetectable viral load (below 50 copies per mL) on ART cannot sexually transmit HIV to a partner.
- **Viral load:** the quantitative measurement of HIV RNA in the blood (copies per mL), measured by PCR; the primary marker of ART response; an undetectable viral load below

50 copies per mL indicates virological suppression; above 1000 copies per mL after 6 months of ART indicates treatment failure.

- **Window period:** the interval between HIV infection and the development of detectable antibodies (approximately 23 to 90 days depending on the assay); during this period, HIV antibody tests may be negative despite active infection; HIV RNA PCR detects virus during the window period.

Concept Check Questions [Series 4]

Objective questions

1. HIV infects cells bearing the _____ receptor, primarily CD4 T-lymphocytes, macrophages, and dendritic cells. (Linked to SLO 4.1)
2. A CD4 count below _____ cells per microlitre defines AIDS and is the threshold for cotrimoxazole prophylaxis. (Linked to SLO 4.1)
3. The preferred first-line ART regimen in Nigeria is TLD: tenofovir, lamivudine, and _____. (Linked to SLO 4.4)
4. Cryptococcal meningitis is diagnosed by India ink stain and the cryptococcal antigen _____ assay; raised ICP is the primary cause of early death. (Linked to SLO 4.5)
5. Cotrimoxazole prophylaxis prevents PCP, toxoplasmosis, and bacterial infections in HIV-positive patients with CD4 below _____. (Linked to SLO 4.5)

Short-answer questions

6. Describe the routes of HIV transmission and state the most common route in Nigeria. (Linked to SLO 4.1)

7. Describe the clinical features of acute HIV infection and explain why antibody tests may be negative. (Linked to SLO 4.2)
8. Describe the HIV testing algorithm used in Nigeria. (Linked to SLO 4.3)
9. Describe the clinical features of PCP and state its treatment. (Linked to SLO 4.5)
10. State three drugs used for OI prophylaxis and the indication for each. (Linked to SLO 4.5)

Long-answer questions

11. Describe the natural history of HIV from transmission to AIDS, including the WHO staging system. (Linked to SLOs 4.1 and 4.2)
12. Describe the first-line ART regimen in Nigeria, including the mechanism of action of each drug and monitoring of treatment. (Linked to SLO 4.4)
13. Describe the clinical features, diagnosis, and management of cryptococcal meningitis. (Linked to SLO 4.5)
14. Describe the clinical features and management of cerebral toxoplasmosis. (Linked to SLO 4.5)
15. Describe the approach to an HIV-positive patient presenting with a subacute headache and fever. (Linked to SLOs 4.2 and 4.5)

Answers to Concept Check Questions [Series 4]

Objective questions

1. CD4.
2. 200.

3. Dolutegravir (DTG).
4. Lateral flow (CrAg LFA).
5. 200.

Short-answer questions

6. HIV is transmitted by sexual contact (unprotected vaginal and anal intercourse: the most common route in Nigeria), blood and blood products (needle sharing, blood transfusion, needlestick injury), and vertical transmission from mother to child during pregnancy, labour, or breastfeeding. The most common route in Nigeria is unprotected heterosexual intercourse.
7. Acute HIV infection presents 2 to 4 weeks after exposure as an acute retroviral syndrome: fever, pharyngitis, generalised lymphadenopathy, myalgia, headache, maculopapular rash, and oral ulcers. Antibody tests may be negative because the patient is in the window period: antibodies have not yet developed in sufficient quantity to be detected, even though the virus is actively replicating at high levels.
8. The Nigeria HIV testing algorithm uses three rapid diagnostic tests (RDTs). A reactive first RDT is followed by a second RDT using a different assay. If the second is reactive, the patient is HIV-positive. If the first and second are discordant, a third RDT (tiebreaker) is performed. A 4th-generation Ag/Ab combination test detects both p24 antigen and antibodies, shortening the window period to approximately 18 days.
9. PCP presents with subacute progressive exertional dyspnoea, dry cough, fever, and hypoxia disproportionate to clinical chest signs; CXR shows bilateral perihilar interstitial infiltrates. Treatment is high-dose oral or IV cotrimoxazole (trimethoprim-sulfamethoxazole) for 21 days, with adjunctive prednisolone when PaO2 is below 70 mmHg.
10. Cotrimoxazole (CD4 below 200: prevents PCP, toxoplasmosis, and bacterial infections in all HIV-positive patients with CD4 below this threshold). Fluconazole (CD4 below 100:

prevents cryptococcal meningitis in resource-limited settings where screening is not available). Isoniazid preventive therapy or IPT (for HIV-positive individuals with latent TB: isoniazid 300 mg daily for 6 months reduces active TB by approximately 60 percent).

Long-answer questions

11. **Basic response:** After sexual, blood-borne, or vertical transmission, HIV infects CD4 T-lymphocytes via gp120 binding to the CD4 receptor. Acute retroviral syndrome (2 to 4 weeks): fever, pharyngitis, rash, lymphadenopathy; high viraemia; antibodies absent (window period). Asymptomatic phase (8 to 10 years): CD4 declines 50 to 100 per microlitre per year; patient infectious. Symptomatic HIV (CD4 below 350): WHO Stage 2 to 3 conditions: oral candidiasis, herpes zoster, recurrent bacterial pneumonia, TB. AIDS (CD4 below 200): WHO Stage 4: PCP, cryptococcal meningitis, toxoplasmosis, KS, oesophageal candidiasis, wasting syndrome.

Value-added response: Without ART, median survival from AIDS diagnosis is approximately 1 to 2 years; with early ART achieving viral suppression, life expectancy approaches that of the HIV-negative population, demonstrating the transformative impact of antiretroviral therapy.

12. **Basic response:** First-line TLD: TDF (tenofovir disoproxil fumarate: NRTI; inhibits HIV reverse transcriptase by competing with the natural substrate and causing chain termination; nephrotoxic: monitor eGFR), 3TC (lamivudine: NRTI; same mechanism; well tolerated), DTG (dolutegravir: INSTI; inhibits HIV integrase preventing insertion of viral DNA into host genome; high genetic barrier to resistance; given as one tablet daily). Monitoring: viral load at baseline, 6 months, and 12 months; CD4 at baseline and 6-monthly; renal function and FBC and LFTs at baseline. Viral load above 1000 copies per mL at 6 months indicates treatment failure (after confirming adherence); switch to second-line AZT plus 3TC plus ATV/r.

Value-added response: DTG's high genetic barrier to resistance means that virological failure with DTG-based regimens is rare even with suboptimal adherence, making TLD more forgiving than earlier efavirenz-based regimens and improving long-term treatment durability.

13. **Basic response:** Cryptococcal meningitis is caused by Cryptococcus neoformans (encapsulated yeast; inhaled from pigeon droppings). Presentation: subacute onset headache (worsening over days to weeks), fever, altered consciousness, and meningism; raised intracranial pressure is common and is the primary cause of early death. Diagnosis: India ink stain of CSF (encapsulated budding yeast: positive in above 80 percent), CrAg LFA on CSF or serum (most sensitive), and CSF opening pressure on lumbar puncture. Treatment: amphotericin B deoxycholate plus flucytosine for 7 days (induction) then fluconazole 800 mg daily for 8 weeks (consolidation) then 200 mg daily until CD4 above 200 (maintenance). Raised ICP is managed by therapeutic lumbar puncture (daily drainage until pressure normalises).

Value-added response: ART should be delayed by 4 to 6 weeks after cryptococcal meningitis to allow ICP to stabilise and reduce the risk of severe IRIS; early ART initiation in cryptococcal meningitis increases mortality.

14. **Basic response:** Cerebral toxoplasmosis is caused by reactivation of latent Toxoplasma gondii when CD4 falls below 100 per microlitre. Presentation: subacute onset focal neurological deficits (hemiparesis, aphasia, cranial nerve palsies), headache, fever, and altered consciousness. CT or MRI brain: multiple ring-enhancing lesions with surrounding oedema, classically at the basal ganglia (highly characteristic). Treatment: pyrimethamine plus sulfadiazine plus folinic acid (leucovorin) for at least 6 weeks (folinic acid reduces pyrimethamine-induced bone marrow toxicity); cotrimoxazole is an effective alternative when pyrimethamine is unavailable.

Value-added response: A single ring-enhancing lesion on CT brain in an HIV-positive patient raises concern for primary CNS lymphoma rather than toxoplasmosis; empirical toxoplasmosis treatment is tried first, and failure to improve clinically and radiologically after 2 weeks should prompt brain biopsy to exclude lymphoma.

15. **Basic response:** An HIV-positive patient with subacute headache and fever should be assessed for meningitis. Check CD4 count (below 100: high risk for cryptococcal meningitis; below 200: risk for TB meningitis). Perform CT brain to exclude mass lesion or raised ICP before lumbar puncture. CSF analysis: opening pressure (raised in cryptococcal meningitis), cell count, protein, glucose, Gram stain and culture, India ink stain, CrAg LFA, AFB stain and GeneXpert, and VDRL for neurosyphilis. If CrAg LFA positive: start amphotericin B plus flucytosine induction. If ring-enhancing lesions on CT and CD4 below 100: empirical toxoplasmosis treatment.

Value-added response: Raised intracranial pressure in cryptococcal meningitis (opening pressure above 25 cmH2O) requires immediate therapeutic lumbar puncture to drain 20 to 30 mL of CSF, which rapidly reduces headache and prevents brainstem herniation; daily lumbar punctures may be needed until pressure normalises.

Answers to Pilot Questions [Series 4]

Part 4.1

1. HIV is a retrovirus with an RNA genome enclosed in a lipid envelope. The three key structural genes are: gag (encodes core proteins including p24 capsid antigen), pol (encodes reverse transcriptase, integrase, and protease), and env (encodes the envelope glycoproteins gp120 and gp41 that mediate CD4 receptor binding and viral entry).
2. Sexual contact (unprotected vaginal and anal intercourse: the most common route in Nigeria), blood and blood products (needle sharing, blood transfusion, needlestick injury in healthcare workers), and vertical or MTCT (mother to child during pregnancy, labour and delivery, or breastfeeding). HIV is not transmitted by casual contact, airborne routes, insect bites, or sharing food and utensils.
3. PMTCT involves giving ART to the HIV-positive mother throughout pregnancy and breastfeeding (to suppress her viral load to undetectable, preventing transmission) and nevirapine syrup to the infant for 6 weeks after birth. Without PMTCT, the risk of MTCT

is 15 to 45 percent; with optimal PMTCT, this is reduced to below 5 percent, and in settings where breastfeeding is replaced by formula feeding, to below 2 percent.

4. WHO Stage 1: asymptomatic or persistent generalised lymphadenopathy. Stage 2: minor mucocutaneous manifestations (seborrhoeic dermatitis, recurrent oral ulcers, herpes zoster, fungal nail infections). Stage 3: severe conditions (oral candidiasis, pulmonary TB, severe bacterial infections, unexplained weight loss above 10 percent). Stage 4: AIDS-defining conditions (PCP, cryptococcal meningitis, cerebral toxoplasmosis, oesophageal candidiasis, Kaposi's sarcoma, HIV wasting syndrome).

5. A CD4 count below 200 cells per microlitre defines AIDS (in the CDC classification) and marks the threshold at which Pneumocystis jirovecii pneumonia prophylaxis with daily cotrimoxazole is essential. Below 200, the risk of PCP, cryptococcal meningitis, toxoplasmosis, and disseminated fungal infections increases dramatically, making prophylaxis life-saving.

Part 4.2

1. Acute HIV infection presents 2 to 4 weeks after high-risk exposure as an acute retroviral syndrome resembling infectious mononucleosis: high fever, pharyngitis, generalised lymphadenopathy, myalgia, severe headache, and a maculopapular rash on the trunk. Oral ulcers and aseptic meningitis may also occur. The syndrome lasts 2 to 4 weeks and coincides with peak viraemia.

2. PCP (CD4 below 200): Pneumocystis jirovecii pneumonia; bilateral interstitial infiltrates on CXR. Cryptococcal meningitis (CD4 below 100): Cryptococcus neoformans; subacute headache, meningism, and raised ICP. Cerebral toxoplasmosis (CD4 below 100): Toxoplasma gondii; focal neurological deficits and multiple ring-enhancing lesions on CT brain. All three occur when the CD4 count falls below 200 (PCP) or below 100 (cryptococcal meningitis and toxoplasmosis).

3. Three-RDT serial algorithm: first RDT (reactive or non-reactive; non-reactive: HIV-negative or advise repeat testing if recent high-risk exposure); second RDT with a

different assay if first is reactive (reactive: proceed; non-reactive: discordant result); third RDT tiebreaker if results are discordant. Two reactive tests on different assays confirm HIV-positive diagnosis. A 4th-generation Ag/Ab combo test detecting p24 antigen plus antibodies shortens the window period to approximately 18 days.

4. CD4 count: measures the number of CD4 T-lymphocytes per microlitre; reflects the degree of immune suppression; determines when to start cotrimoxazole prophylaxis (below 200) and fluconazole prophylaxis (below 100); guides urgency of ART initiation. Viral load (HIV RNA PCR): measures the amount of virus in the blood; the primary marker of ART response; an undetectable viral load below 50 copies per mL indicates treatment success; a viral load above 1000 copies per mL at 6 months indicates virological failure requiring regimen change.
5. Oral candidiasis: white plaques on the buccal mucosa, tongue, or palate that can be scraped off leaving a red bleeding surface; the most common oral manifestation of HIV; treated with oral fluconazole or nystatin suspension. Herpes zoster: a vesicular rash in a dermatomal distribution (shingles), typically unilateral and painful; its occurrence in a young adult (particularly in the absence of other immunosuppressive conditions) is a strong clinical indicator of underlying HIV infection and should prompt HIV testing.

Part 4.3

1. Goals of ART: undetectable viral load below 50 copies per mL (the primary treatment goal); immune reconstitution with rising CD4 count; prevention of MTCT; prevention of non-AIDS morbidity (cardiovascular, renal, liver disease). The U=U (Undetectable equals Untransmittable) concept: a person living with HIV who has achieved and maintains an undetectable viral load on ART cannot sexually transmit HIV to a partner; this is supported by strong evidence from large clinical studies and has profound implications for reducing HIV stigma.
2. TLD: TDF (tenofovir disoproxil fumarate: NRTI; inhibits reverse transcriptase by competing with the natural nucleotide substrate and causing chain termination;

nephrotoxic), 3TC (lamivudine: NRTI; same mechanism as TDF; excellent tolerability), and DTG (dolutegravir: INSTI: integrase strand transfer inhibitor; inhibits HIV integrase, preventing the insertion of viral DNA into the host cell genome; high genetic barrier to resistance; given as a single tablet once daily).

3. Viral load at baseline, 6 months, and 12 months, then annually when suppressed; a viral load above 1000 copies per mL at 6 months indicates virological failure (after confirming adherence). CD4 count at baseline and every 6 months until above 350 and stable. Renal function and eGFR (TDF is nephrotoxic: decline in eGFR or rising creatinine requires switch to TAF). FBC (AZT causes anaemia and neutropenia). LFTs at baseline. Adherence counselling at every visit.

4. TDF side effects: nephrotoxicity (proximal tubular dysfunction: Fanconi syndrome; declining eGFR; haematuria; glycosuria with normal blood glucose); monitor creatinine and eGFR and switch to TAF (tenofovir alafenamide) in renal impairment; also causes osteopenia and osteoporosis. Nevirapine side effects: severe cutaneous hypersensitivity reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis (potentially life-threatening: stop immediately and never reintroduce); hepatotoxicity (particularly in the first 6 weeks: avoid nevirapine when CD4 is above 250 in women and above 400 in men due to significantly elevated hepatotoxicity risk).

5. IRIS (immune reconstitution inflammatory syndrome) is a paradoxical worsening or unmasking of an opportunistic infection after ART initiation, caused by the restored immune system mounting an inflammatory response against subclinical or treated pathogens. Presentation: fever, lymphadenopathy, or worsening of OI symptoms within weeks of ART initiation. Management: continue ART (do not stop), treat the underlying OI aggressively, and add corticosteroids (prednisolone) for severe or life-threatening IRIS (such as IRIS associated with cryptococcal meningitis or TB meningitis).

Part 4.4

1. PCP presents with subacute onset progressive exertional dyspnoea (worsening over days to weeks), dry non-productive cough, low-grade fever, and hypoxia disproportionate to the paucity of chest signs (a characteristic feature). CXR shows bilateral perihilar interstitial infiltrates (ground-glass appearance). Serum beta-D-glucan is elevated. Diagnosis is confirmed by BAL with silver staining or immunofluorescence. Treatment: high-dose cotrimoxazole (TMP-SMX 15 to 20 mg per kg per day of the TMP component in divided doses orally or IV for 21 days); add prednisolone 40 mg twice daily for 5 days then tapering when PaO2 is below 70 mmHg or A-a gradient above 35 mmHg.

2. Cryptococcal meningitis presents subacutely with worsening headache (typically the most prominent symptom), fever, altered consciousness, and signs of meningeal irritation (neck stiffness and photophobia). Raised intracranial pressure (ICP above 25 cmH2O) is very common and manifests as worsening headache, visual blurring, sixth nerve palsy (diplopia), and papilloedema. Diagnosis: CSF India ink stain (encapsulated budding yeast with a clear halo from the polysaccharide capsule: positive in above 80 percent), CrAg LFA on CSF or serum (most sensitive test), and CSF culture (gold standard but takes several days).

3. Induction phase (7 days): amphotericin B deoxycholate 0.7 to 1 mg per kg IV daily plus flucytosine 100 mg per kg per day orally in four divided doses (reduces early mortality compared with amphotericin B alone). Consolidation phase (8 weeks): fluconazole 800 mg daily orally. Maintenance phase (until CD4 above 200 for more than 6 months): fluconazole 200 mg daily. ICP management: therapeutic lumbar puncture to drain 20 to 30 mL of CSF daily until opening pressure normalises; acetazolamide and mannitol are not effective for raised ICP in cryptococcal meningitis.

4. Cerebral toxoplasmosis presents with subacute onset focal neurological deficits (hemiparesis, aphasia, hemianopia, or cerebellar signs depending on lesion location), headache, fever, and altered consciousness. Seizures may occur. CT brain with contrast: multiple ring-enhancing lesions with surrounding oedema, classically at the basal ganglia and corticomedullary junction (a characteristic location distinguishing toxoplasmosis from other ring-enhancing lesions). MRI brain is more sensitive than CT and may detect additional lesions.

5. Cotrimoxazole (trimethoprim-sulfamethoxazole): indicated when CD4 is below 200 per microlitre; prevents PCP, toxoplasmosis, and bacterial infections; also reduces malaria morbidity; given to all HIV-positive pregnant women and all children below 5 years regardless of CD4. Fluconazole 200 mg daily: indicated when CD4 is below 100; prevents cryptococcal meningitis in settings where CrAg screening is unavailable. IPT (isoniazid preventive therapy): isoniazid 300 mg daily plus pyridoxine for 6 months; prevents TB reactivation in HIV-positive individuals with latent TB (confirmed by positive tuberculin skin test or IGRA or empirically in high-burden settings).

References and Attributions [Series 4]

Textual References

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- Mandell, G. L., Bennett, J. E. and Dolin, R. (2015). Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases (8th ed.). Philadelphia: Elsevier.

Figures, Plates, Tables, and Boxes

- Figure 4.1: HIV virology, transmission, natural history, and WHO clinical staging. AI-generated using the prompt: "Two-panel infographic: left HIV virion diagram, transmission routes with PMTCT, and Nigeria epidemiology; right WHO clinical staging four-stage diagram and CD4 count reference box." Suggested OER search string: "HIV virology transmission natural history WHO staging CD4 count infographic OER."
- Figure 4.2: Clinical features of HIV and HIV testing algorithm. AI-generated using the prompt: "Two-panel infographic: left timeline of HIV disease progression from acute infection to AIDS; right HIV testing algorithm (three RDT steps and 4th-generation combo test) and CD4 and viral load monitoring box." Suggested OER search string: "HIV clinical features AIDS-defining illnesses HIV testing algorithm CD4 viral load infographic OER."
- Figure 4.3: Antiretroviral therapy in Nigeria. AI-generated using the prompt: "Two-panel infographic: left ART goals, Treat All policy, PEP and PrEP, and TLD first-line and

second-line ART regimen diagrams; right ART monitoring schedule and side effects table with IRIS box." Suggested OER search string: "antiretroviral therapy Nigeria TLD first-line ART monitoring side effects IRIS infographic OER."

- Figure 4.4: Opportunistic infections in HIV. AI-generated using the prompt: "Two-panel infographic: left PCP and TB in HIV; right cryptococcal meningitis, cerebral toxoplasmosis, and OI prophylaxis box (cotrimoxazole, fluconazole, IPT)." Suggested OER search string: "opportunistic infections HIV PCP tuberculosis cryptococcal meningitis toxoplasmosis OI prophylaxis infographic OER."

Series 5: Emerging Tropical and Vector-Borne Conditions

- **Part 5.1: Malaria**
    - Sub Part 5.1.1: Epidemiology and pathogenesis
    - Sub Part 5.1.2: Clinical features and diagnosis
    - Sub Part 5.1.3: Treatment and prevention
- **Part 5.2: Viral Haemorrhagic Fevers**
    - Sub Part 5.2.1: Lassa fever
    - Sub Part 5.2.2: Ebola virus disease and other VHFs
    - Sub Part 5.2.3: Management and infection control for VHFs
- **Part 5.3: Neglected Tropical Diseases**
    - Sub Part 5.3.1: Schistosomiasis and soil-transmitted helminths
    - Sub Part 5.3.2: Lymphatic filariasis and onchocerciasis
    - Sub Part 5.3.3: African trypanosomiasis and leishmaniasis
- **Part 5.4: Emerging and Re-emerging Infections**
    - Sub Part 5.4.1: Dengue fever and yellow fever
    - Sub Part 5.4.2: Monkeypox
    - Sub Part 5.4.3: Pandemic preparedness and One Health

Introduction

Nigeria's tropical climate and ecological diversity create ideal conditions for the transmission of vector-borne and tropical diseases. Malaria remains the single most important infectious disease in Nigeria, accounting for the greatest number of clinical encounters and deaths. Viral haemorrhagic fevers, particularly Lassa fever, present unique diagnostic and infection control challenges. Neglected tropical diseases continue to cause significant morbidity in rural communities, while emerging infections including dengue, monkeypox, and pandemic respiratory viruses underscore the need for robust surveillance and preparedness.

This Series covers the major tropical and vector-borne conditions systematically. We shall commence with malaria, examining its pathogenesis, clinical features, diagnosis, and treatment. Next, we will explore viral haemorrhagic fevers, focusing on Lassa fever and Ebola. Moving on, we will address neglected tropical diseases including schistosomiasis, filariasis, onchocerciasis, and trypanosomiasis. Finally, we will consider emerging infections and the principles of pandemic preparedness.

Series Learning Outcomes

Upon completing this Series, you should be able to:

- **SLO 5.1:** describe the epidemiology, pathogenesis, clinical features, diagnosis, and management of malaria in Nigeria,
- **SLO 5.2:** describe the clinical features, diagnosis, management, and infection control measures for viral haemorrhagic fevers,
- **SLO 5.3:** describe the epidemiology, clinical features, and treatment of the major neglected tropical diseases in Nigeria,
- **SLO 5.4:** describe the clinical features and management of dengue fever, yellow fever, and monkeypox, and

- **SLO 5.5:** describe the principles of pandemic preparedness and the One Health approach to emerging infections.

5.1 Malaria

5.1.1 Epidemiology and pathogenesis

Malaria is caused by intraerythrocytic protozoan parasites of the genus **Plasmodium**, transmitted by the bite of the female Anopheles mosquito. Five species infect humans: **P. falciparum** (the most dangerous: responsible for the vast majority of malaria deaths globally and for nearly all severe malaria in Nigeria), P. vivax (can cause relapse from dormant liver forms called hypnozoites), P. malariae (causes quartan fever: 72-hour periodicity), P. ovale (also causes relapse from hypnozoites), and P. knowlesi (zoonotic: primarily in South-East Asia).

Nigeria accounts for approximately 27 percent of global malaria cases and 31 percent of malaria deaths, making it the highest-burden country in the world. Pathogenesis: after a female Anopheles bite, sporozoites travel to the liver where they undergo asexual multiplication (exoerythrocytic schizogony) for 7 to 30 days without symptoms. Merozoites released from the liver infect red blood cells (erythrocytic cycle), causing the fever paroxysms from synchronised RBC rupture and release of merozoites, haemozoin, and pyrogenic cytokines.

Fill in the blank: P. falciparum causes the majority of malaria deaths in Nigeria. P. vivax and P. ovale can cause _____ from dormant liver forms called _____s.

5.1.2 Clinical features and diagnosis

Uncomplicated malaria: the classic malaria paroxysm consists of three stages: cold stage (rigors and shaking chills), hot stage (high fever above 40 degrees C, headache, myalgia, and vomiting), and sweating stage (profuse sweating with defervescence). P. falciparum malaria does not follow a regular periodicity. Anaemia (from haemolysis and dyserythropoiesis) and splenomegaly are common findings. Thrombocytopaenia is characteristic.

Severe falciparum malaria (WHO criteria) occurs when P. falciparum infection is complicated by any of: **cerebral malaria** (unarousable coma not explained by another cause: GCS below 11 in adults), severe anaemia (Hb below 7 g/dL or haematocrit below 21 percent), respiratory distress (ARDS from pulmonary oedema), hypoglycaemia (blood glucose below 2.2 mmol/L), acute kidney injury, hyperparasitaemia (above 10 percent parasitised RBCs), or circulatory collapse.

Diagnosis: malaria rapid diagnostic test (RDT: detects P. falciparum HRP2 antigen within 15 minutes; sensitivity above 95 percent for P. falciparum) and peripheral blood film (thick film: high sensitivity for detecting parasites; thin film: species identification and parasite density quantification: the gold standard). Both tests should be performed in all clinically suspected cases; a negative RDT does not exclude malaria, especially for non-falciparum species.

Fill in the blank: The classic malaria paroxysm consists of the cold, hot, and _____ stages. Cerebral malaria is defined as _____ coma not explained by another cause.

5.1.3 Treatment and prevention

Uncomplicated P. falciparum malaria: artemisinin-based combination therapy (ACT) is the WHO-recommended and Nigeria-endorsed first-line treatment. The preferred ACT in Nigeria is artemether-lumefantrine (Coartem: six doses over 3 days) or artesunate-amodiaquine. Artemisinin derivatives act rapidly, clearing parasitaemia within 48 hours. The partner drug (lumefantrine or amodiaquine) eliminates residual parasites and prevents recrudescence.

Severe falciparum malaria: IV artesunate 2.4 mg per kg at 0, 12, and 24 hours then daily until oral therapy is tolerated; switch to a full course of oral ACT on recovery. IV artesunate is superior to IV quinine in reducing mortality (AQUAMAT trial: 22 percent reduction in mortality). Manage complications: cerebral malaria (nurse in lateral position, treat seizures with IV diazepam, avoid hypoglycaemia), severe anaemia (packed red cell transfusion when Hb below 7 g/dL), and AKI (fluid balance and renal replacement therapy).

Prevention: long-lasting insecticidal nets (LLINs: the single most cost-effective malaria prevention intervention), indoor residual spraying (IRS) with insecticides, intermittent preventive

treatment in pregnancy (IPTp: sulfadoxine-pyrimethamine given at each antenatal visit from the second trimester), and seasonal malaria chemoprevention (SMC: monthly sulfadoxine-pyrimethamine plus amodiaquine for children 3 to 59 months during the malaria transmission season in the Sahel).

Fill in the blank: First-line treatment for uncomplicated P. falciparum malaria in Nigeria is _____ (ACT). IV _____ is the treatment of choice for severe malaria, superior to IV quinine.

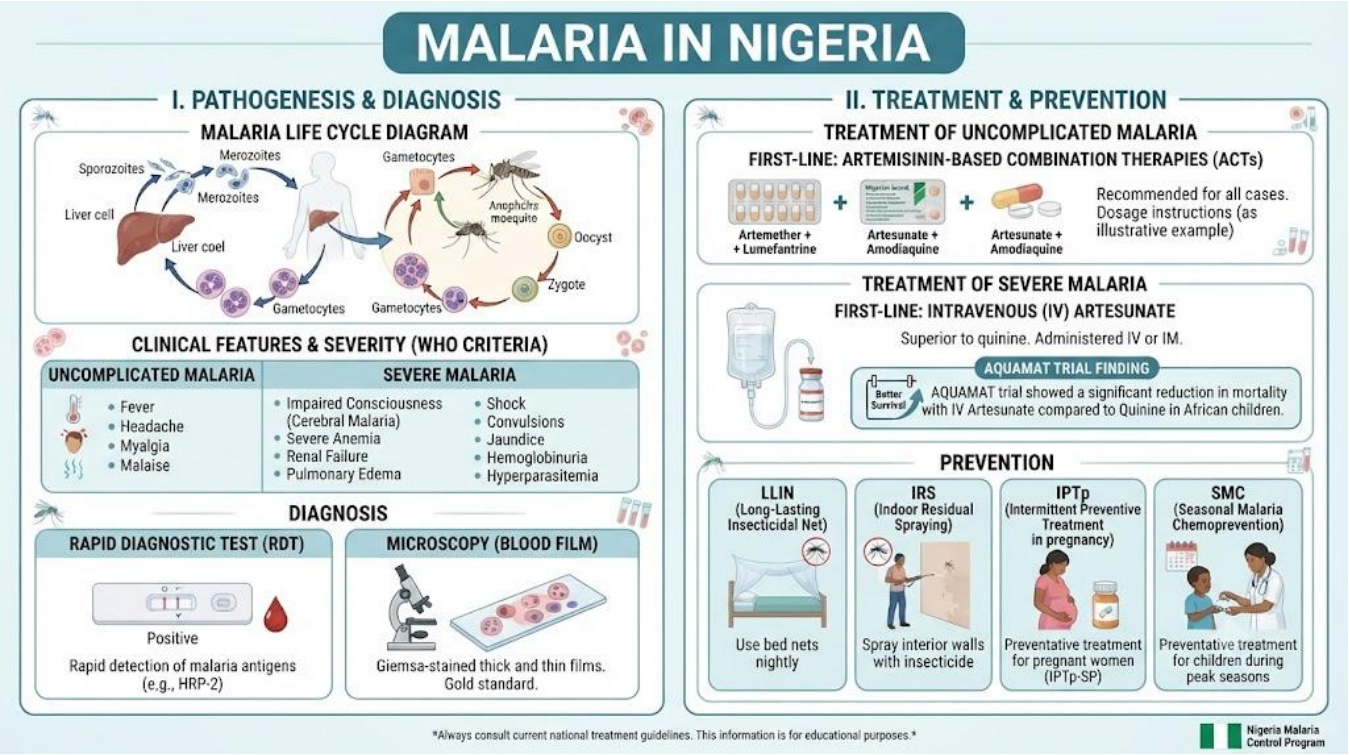

Figure 5.1: Malaria in Nigeria: life cycle, clinical features, diagnosis, treatment, and prevention

Pilot questions 5.1

1. Describe the malaria life cycle from mosquito bite to fever paroxysm. (Linked to SLO 5.1)
2. State five WHO criteria for severe falciparum malaria. (Linked to SLO 5.1)
3. Describe the diagnosis of malaria using RDT and peripheral blood film. (Linked to SLO 5.1)

4. Describe the treatment of uncomplicated and severe falciparum malaria in Nigeria. (Linked to SLO 5.1)
5. Describe four malaria prevention strategies relevant to Nigeria. (Linked to SLO 5.1)

5.2 Viral Haemorrhagic Fevers

5.2.1 Lassa fever

Lassa fever is caused by Lassa virus, an arenavirus transmitted to humans from the multimammate rat **Mastomys natalensis** through contact with rodent urine or faeces contaminating food or surfaces (zoonotic transmission), or by direct contact with blood or body fluids of infected humans (person-to-person transmission in healthcare settings). Nigeria is the most endemic country for Lassa fever globally, with thousands of confirmed cases annually, predominantly in the southern and central states.

Clinical features: most infections (approximately 80 percent) are mild or asymptomatic. Severe Lassa fever presents after an incubation period of 6 to 21 days with insidious onset fever, weakness, malaise, headache, sore throat, and retrosternal chest pain. Characteristic signs: exudative pharyngitis (white patches on the posterior pharynx), facial oedema, and bleeding manifestations (mucosal bleeding, haemorrhage) in about one-third of severe cases. The case fatality rate in hospitalised patients is approximately 15 to 25 percent; deafness (unilateral or bilateral sensorineural hearing loss) occurs in approximately 30 percent of survivors.

Fill in the blank: Lassa fever is transmitted from the _____ rat (Mastomys natalensis) through contact with rodent urine or faeces. Deafness occurs in approximately _____ percent of Lassa fever survivors.

5.2.2 Ebola virus disease and other VHFs

Ebola virus disease (EVD) is caused by Ebola virus (a filovirus), transmitted by direct contact with blood or body fluids of infected or deceased individuals. The 2014 to 2016 West Africa outbreak was the largest in history, killing over 11,000 people. Nigeria successfully contained an

importation in 2014. Clinical features: sudden onset fever, myalgia, and weakness followed by vomiting, diarrhoea, and haemorrhagic manifestations (in about 50 percent). The case fatality rate is 25 to 90 percent depending on the outbreak. Vaccination (rVSV-ZEBOV: a live-attenuated recombinant vaccine) is available for outbreak control.

Other VHFs of relevance to Nigeria: yellow fever (Flavivirus: transmitted by Aedes mosquito; presents with fever, jaundice, and haemorrhage; prevented by a highly effective live attenuated vaccine), dengue (Flavivirus: Aedes mosquito; breakbone fever with haemorrhagic complications: see Part 5.4), and Crimean-Congo haemorrhagic fever (CCHF: Nairovirus: tick-borne; presents with sudden fever and haemorrhage; treated with ribavirin). All VHFs share common features: fever, haemorrhage, and high infectivity in healthcare settings requiring strict infection control.

Fill in the blank: Ebola virus disease is caused by a _____ (filovirus) transmitted by contact with blood or body fluids of infected individuals. The rVSV-ZEBOV vaccine is used for _____ control of Ebola outbreaks.

5.2.3 Management and infection control for VHFs

Lassa fever treatment: ribavirin (an antiviral nucleoside analogue) given IV for 10 days (or oral for 10 days) reduces mortality in severe Lassa fever, particularly when started within the first 6 days. Supportive care: IV fluids to maintain perfusion (caution: over-hydration causes pulmonary oedema in Lassa fever), electrolyte correction, blood transfusion for haemorrhage, and analgesia. Experimental treatments including monoclonal antibodies are under evaluation for Ebola.

Infection prevention and control (IPC) for VHFs is critical to prevent nosocomial amplification. All patients with suspected VHF should be isolated immediately in a single room with a closed door. Healthcare workers must use full PPE: **gloves (double)**, **gown**, **N95 or higher respirator**, and **face shield or goggles**. Hand hygiene before donning and after doffing PPE is mandatory. Safe burial practices (avoiding contact with the body of VHF decedents) are essential for community transmission control. All suspected VHF cases must be notified to the Nigeria Centre for Disease Control (NCDC) immediately.

Fill in the blank: Ribavirin reduces mortality in Lassa fever when started within _____ days of illness onset. Suspected VHF patients must be isolated immediately and managed in full _____ including N95 respirator and face shield.

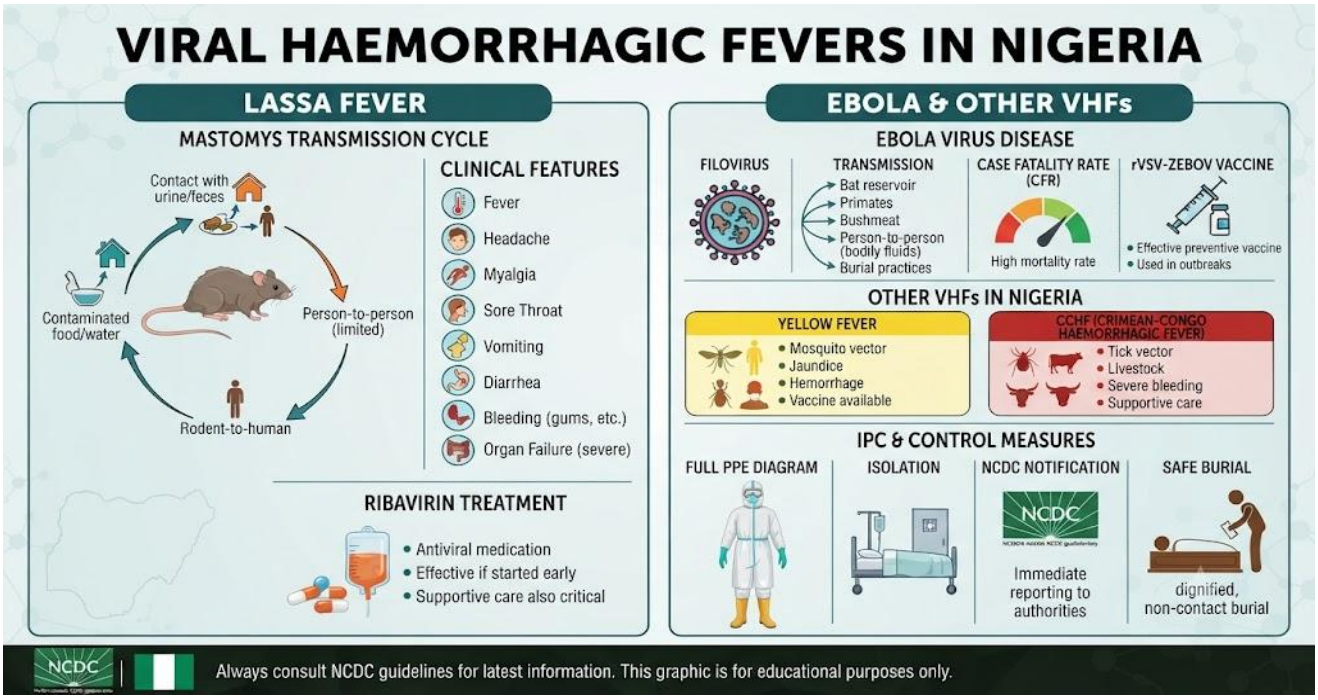

Figure 5.2: Viral haemorrhagic fevers in Nigeria: Lassa fever, Ebola, and infection prevention and control

Pilot questions 5.2

1. Describe the transmission and clinical features of Lassa fever. (Linked to SLO 5.2)
2. Describe the treatment of Lassa fever and state when ribavirin should be started. (Linked to SLO 5.2)
3. Describe the clinical features of Ebola virus disease and state its case fatality rate. (Linked to SLO 5.2)
4. Describe the IPC measures required for a patient with suspected VHF. (Linked to SLO 5.2)
5. State three VHFs of relevance to Nigeria and describe a distinguishing feature of each. (Linked to SLO 5.2)

5.3 Neglected Tropical Diseases

5.3.1 Schistosomiasis and soil-transmitted helminths

Schistosomiasis is caused by blood flukes of the genus **Schistosoma**. The two species endemic in Nigeria are **S. haematobium** (urogenital schistosomiasis: transmitted by freshwater snails of the Bulinus genus; cercariae penetrate the skin during water contact; adult worms live in the vesical plexus around the bladder; clinical features: haematuria, dysuria, obstructive uropathy, and increased risk of bladder carcinoma) and **S. mansoni** (intestinal schistosomiasis: adult worms in the mesenteric veins; presents with bloody diarrhoea, hepatosplenomegaly, and hepatic fibrosis leading to portal hypertension). Treatment: praziquantel 40 mg per kg as a single oral dose.

Soil-transmitted helminths (STHs) are intestinal roundworm infections caused by Ascaris lumbricoides (the most prevalent helminth infection globally: heavy infection causes malnutrition, growth faltering, and intestinal obstruction in children), Trichuris trichiura (whipworm: causes bloody diarrhoea and rectal prolapse in heavy infections), and hookworm (Ancylostoma duodenale and Necator americanus: causes iron deficiency anaemia from intestinal blood loss; larvae penetrate skin, causing ground itch). Treatment: albendazole 400 mg or mebendazole 500 mg as a single oral dose.

Fill in the blank: S. haematobium causes _____ schistosomiasis presenting with haematuria and obstructive uropathy. Hookworm causes iron deficiency _____ from intestinal blood loss; larvae penetrate skin at the site of soil contact.

5.3.2 Lymphatic filariasis and onchocerciasis

Lymphatic filariasis (LF) is caused by **Wuchereria bancrofti** (in Nigeria), transmitted by Culex mosquitoes. Adult worms live in the lymphatic vessels, causing lymphatic damage that leads to: lymphoedema (swelling of the lower limbs, scrotum, or arms), hydrocele (fluid accumulation around the testes: the most common clinical manifestation), and elephantiasis (massive chronic lymphoedema with skin thickening). Microfilariae circulate in the blood with nocturnal periodicity (peak at midnight). Diagnosis: blood film at night for microfilariae;

circulating filarial antigen (CFA) card test. Treatment: annual single-dose ivermectin plus albendazole (mass drug administration for elimination).

Onchocerciasis (river blindness) is caused by **Onchocerca volvulus**, transmitted by the blackfly **Simulium damnosum** (breeding in fast-flowing rivers in Nigeria). Microfilariae from adult worms migrate to the skin and eyes, causing: skin disease (onchodermatitis: intense pruritus, hypopigmentation, and skin thickening), and ocular disease (punctate keratitis progressing to sclerosing keratitis and ultimately corneal opacity and blindness). Onchocerciasis is the second leading infectious cause of blindness globally. Treatment: ivermectin annually (kills microfilariae but not adult worms; must be given for the 10 to 15 year lifespan of adult worms).

Fill in the blank: Lymphatic filariasis in Nigeria is caused by Wuchereria bancrofti, transmitted by _____ mosquitoes. Onchocerciasis (river blindness) is transmitted by the _____ fly breeding in fast-flowing rivers.

5.3.3 African trypanosomiasis and leishmaniasis

Human African trypanosomiasis (HAT) or sleeping sickness is caused by **Trypanosoma brucei gambiense** (West and Central Africa: chronic disease) and T. brucei rhodesiense (East Africa: acute disease), transmitted by the tsetse fly (Glossina species). Clinical features: Stage 1 (haemolymphatic): fever, headache, lymphadenopathy (Winterbottom's sign: enlarged posterior cervical lymph nodes in T.b. gambiense), and skin rash (trypanosomal chancre at the bite site). Stage 2 (meningoencephalitic): neurological involvement with altered sleep-wake cycle (daytime somnolence and nighttime insomnia: the origin of the name sleeping sickness), personality changes, motor signs, and coma if untreated.

Diagnosis of HAT: lymph node aspirate or blood film for trypanosomes (mini anion exchange centrifugation technique: MECT), CSF examination in Stage 2 (trypanosomes in CSF plus white cell count above 5 per microlitre confirms Stage 2). Treatment: Stage 1 (pentamidine for gambiense), Stage 2 (nifurtimox-eflornithine combination therapy: NECT for gambiense;

melarsoprol for rhodesiense: highly toxic with encephalopathic reaction in 5 to 10 percent). Leishmaniasis: caused by Leishmania species transmitted by sandflies; visceral leishmaniasis (kala-azar: hepatosplenomegaly, fever, and pancytopaenia) treated with liposomal amphotericin B or miltefosine.

Fill in the blank: Human African trypanosomiasis is transmitted by the _____ fly. Stage 2 HAT (sleeping sickness) involves _____ signs including altered sleep-wake cycle and coma if untreated.

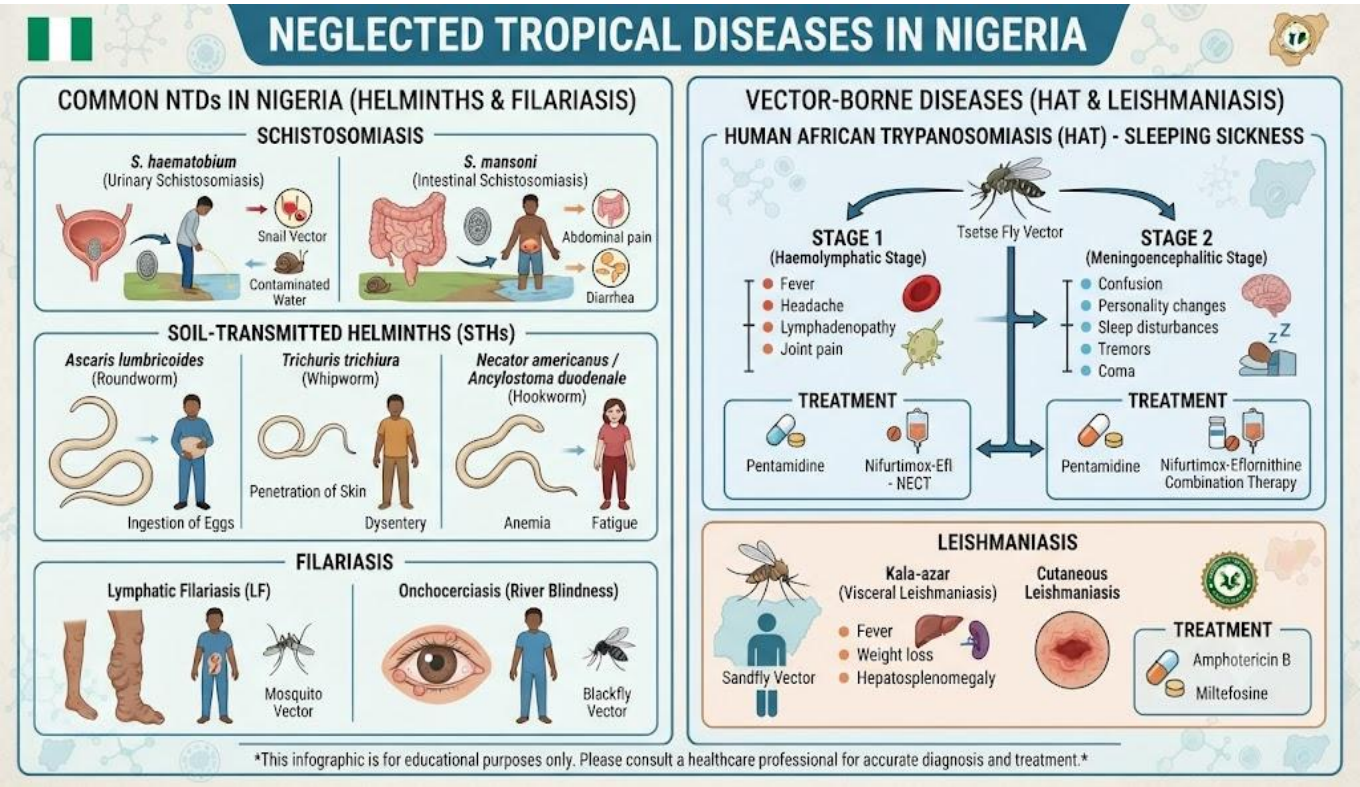

Figure 5.3: Neglected tropical diseases in Nigeria: schistosomiasis, STHs, filariasis, onchocerciasis, trypanosomiasis, and leishmaniasis

Pilot questions 5.3

1. Distinguish S. haematobium from S. mansoni in terms of site of infection and clinical features. (Linked to SLO 5.3)
2. Describe the clinical features of lymphatic filariasis and state the treatment. (Linked to SLO 5.3)

3. Describe the clinical features and ocular complications of onchocerciasis. (Linked to SLO 5.3)
4. Describe the two stages of human African trypanosomiasis. (Linked to SLO 5.3)
5. State the treatment for Stage 1 and Stage 2 gambiense HAT. (Linked to SLO 5.3)

5.4 Emerging and Re-emerging Infections

5.4.1 Dengue fever and yellow fever

Dengue fever is caused by dengue virus (DENV 1 to 4: four serotypes), a flavivirus transmitted by **Aedes aegypti** and Aedes albopictus mosquitoes. It is the most rapidly spreading arboviral infection globally, with Nigeria reporting increasing cases. Clinical spectrum: dengue fever (breakbone fever: sudden high fever, severe retro-orbital headache, myalgia, arthralgia, and a maculopapular rash: the dengue rash appears on days 3 to 5 and is described as islands of white in a sea of red); dengue haemorrhagic fever (DHF: thrombocytopaenia below 100,000 per microlitre, haemorrhagic manifestations, and plasma leakage: requires hospitalisation); and dengue shock syndrome (DSS: the most severe form: circulatory failure). Diagnosis: dengue NS1 antigen (days 1 to 5), dengue IgM/IgG serology (after day 5). Treatment is supportive.

Yellow fever is caused by yellow fever virus (YFV: a flavivirus) transmitted by Aedes mosquitoes. Nigeria experienced major yellow fever outbreaks in 2017 to 2018 and 2019. Clinical features: most infections are mild; severe yellow fever presents with the toxic phase: fever, jaundice, haemorrhage (haematemesis: black vomit), and acute renal failure. Case fatality rate in the toxic phase is 20 to 50 percent. The **17D yellow fever vaccine** is one of the most effective vaccines ever developed (a single dose provides lifelong immunity in above 99 percent of recipients) and is part of the Nigeria EPI at 9 months. No antiviral treatment exists.

Fill in the blank: Dengue fever is caused by dengue virus serotypes 1 to 4, transmitted by _____ mosquitoes. The 17D yellow fever vaccine provides lifelong immunity in above 99 percent of recipients with a _____ dose.

5.4.2 Monkeypox

Monkeypox (now officially renamed mpox) is a zoonotic disease caused by monkeypox virus (MPXV), an orthopoxvirus. In Nigeria, it is primarily a zoonosis transmitted from rodents and squirrels to humans through direct contact with infected animals or their products. Person-to-person transmission occurs through direct contact with skin lesions, respiratory droplets (prolonged close contact), or fomites. The 2022 global mpox outbreak involved a distinct clade (Clade IIb) spreading mainly through sexual contact between men who have sex with men.

Clinical features: prodrome of fever, headache, myalgia, and lymphadenopathy (a distinguishing feature from smallpox), followed by a characteristic rash that progresses through stages: macules, papules, vesicles, pustules, and crusts, classically centrifugal (face and extremities more affected than trunk). Rash on the palms and soles is characteristic. Genital and perianal lesions predominate in the sexual transmission-associated outbreak. Diagnosis: PCR on vesicle fluid (the most sensitive test). Treatment: supportive; tecovirimat (an antiviral inhibiting viral morphogenesis) is licensed for severe cases.

Fill in the blank: Monkeypox is distinguished from other febrile rash illnesses by prominent _____ at the onset of illness. Diagnosis is confirmed by _____ on vesicle fluid.

5.4.3 Pandemic preparedness and One Health

Pandemic preparedness is the systematic development of plans, capacities, and responses to limit the impact of disease outbreaks that spread internationally. Core components: surveillance (early detection of unusual disease clusters through the Integrated Disease Surveillance and Response System: IDSR), laboratory capacity (rapid diagnosis of novel pathogens), risk communication (clear and timely public health messaging), health system surge capacity (sufficient ICU beds, ventilators, PPE stocks, and trained personnel), and international coordination (compliance with the International Health Regulations: IHR 2005, which require member states to notify WHO of potential public health emergencies of international concern: PHEIC).

The One Health approach recognises that human health, animal health, and ecosystem health are interdependent and must be addressed in an integrated manner to prevent and control diseases

at the human-animal-environment interface. Most emerging infections are zoonotic: they originate in animals and spill over to humans when ecological boundaries are disrupted (deforestation, urbanisation, agricultural intensification, and wildlife trade). Key One Health interventions in Nigeria: collaborative surveillance between the Nigeria Centre for Disease Control (NCDC), the Federal Department of Veterinary and Pest Control Services (FDVPCS), and the Federal Ministry of Environment; aflatoxin control at the human-animal-food interface; integrated vector management for malaria and NTDs.

Fill in the blank: The International Health Regulations (IHR 2005) require member states to notify _____ of potential public health emergencies of international concern. The One Health approach addresses disease control at the human-_____ environment interface.

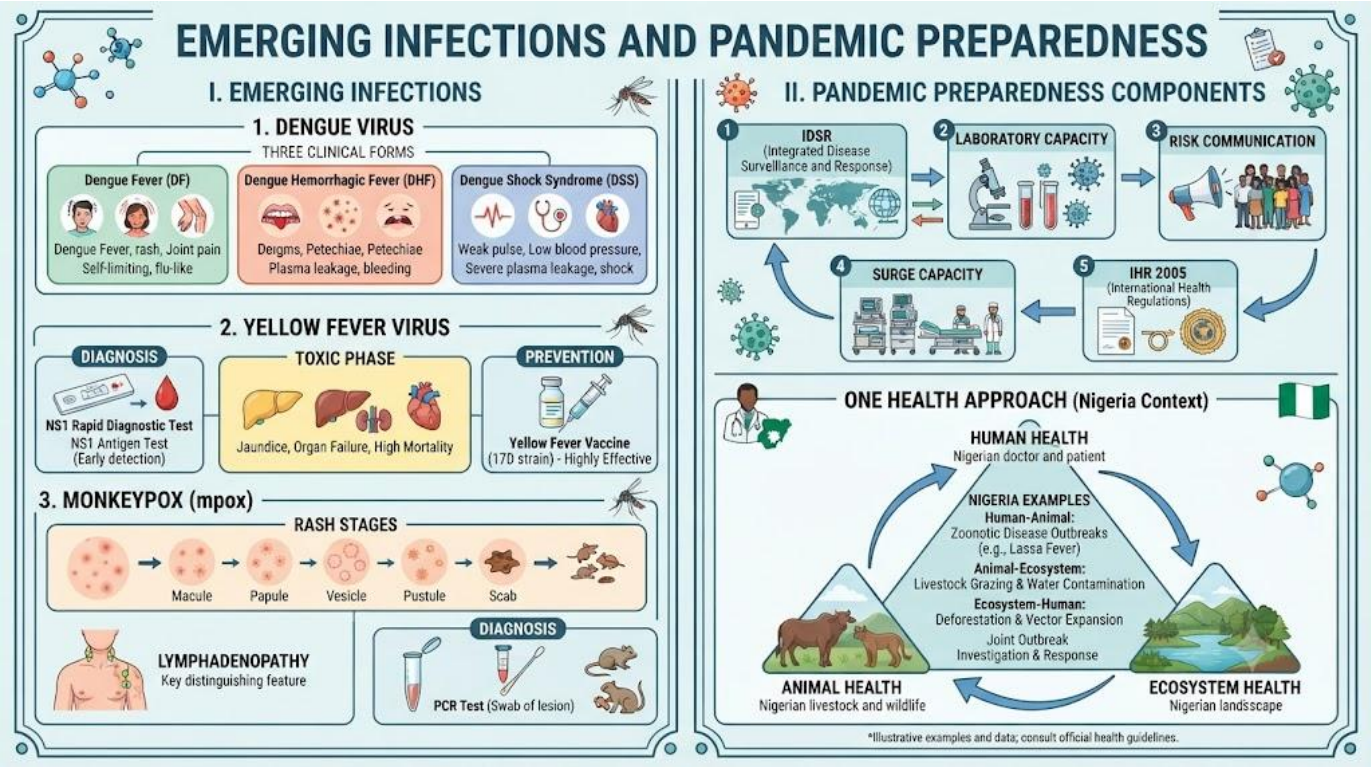

Figure 5.4: Emerging infections and pandemic preparedness: dengue, yellow fever, monkeypox, and One Health

Pilot questions 5.4

1. Describe the clinical spectrum of dengue fever and state the distinguishing features of dengue haemorrhagic fever. (Linked to SLO 5.4)
2. Describe the clinical features of severe yellow fever and state the prevention. (Linked to SLO 5.4)
3. Describe the clinical features of monkeypox and state how it is distinguished from other febrile rash illnesses. (Linked to SLO 5.4)
4. Describe the core components of pandemic preparedness. (Linked to SLO 5.5)
5. Explain the One Health approach and give two examples of its application in Nigeria. (Linked to SLO 5.5)

Series Summary

This Series covered the major tropical and vector-borne conditions relevant to Nigeria. Malaria (P. falciparum responsible for nearly all deaths; Nigeria has the highest global burden; paroxysm of cold, hot, and sweating stages; severe malaria: cerebral malaria, severe anaemia, ARDS, AKI; diagnosis by RDT and blood film; treatment: ACT for uncomplicated and IV artesunate for severe malaria; prevention: LLINs, IRS, IPTp, SMC). Viral haemorrhagic fevers: Lassa fever (Mastomys rat; ribavirin within 6 days; deafness in 30 percent of survivors; strict PPE and isolation and NCDC notification) and Ebola (filovirus; rVSV-ZEBOV vaccine). Neglected tropical diseases: schistosomiasis (praziquantel), STHs (albendazole), lymphatic filariasis and onchocerciasis (annual ivermectin), and sleeping sickness (two-stage: pentamidine for Stage 1 and NECT for Stage 2 gambiense). Emerging infections: dengue (NS1 antigen; supportive treatment), yellow fever (17D vaccine: lifelong immunity; no antiviral), and monkeypox (prominent lymphadenopathy; rash progressing to pustules; PCR diagnosis; tecovirimat for severe cases). Pandemic preparedness (IDSR, IHR 2005, laboratory capacity, surge capacity) and One Health (integrated human-animal-ecosystem approach to zoonotic disease control in Nigeria).

By completing this Series, you should now be able to describe the pathogenesis, diagnosis, and management of malaria, describe VHF management and IPC, describe NTDs and their treatment, describe dengue, yellow fever, and monkeypox, and explain pandemic preparedness and One Health. These abilities align with SLOs 5.1 to 5.5 and complete your preparation in MED 406.

Glossary of Terms

- **ACT (artemisinin-based combination therapy):** the WHO-recommended first-line treatment for uncomplicated P. falciparum malaria; artemisinin rapidly clears parasitaemia while the partner drug (lumefantrine or amodiaquine) eliminates residual parasites and prevents recrudescence.

- **Cerebral malaria:** an AIDS-defining WHO criterion for severe falciparum malaria: unarousable coma (GCS below 11 in adults) not explained by another cause, resulting from sequestration of parasitised red blood cells in cerebral microvasculature.
- **Elephantiasis:** massive chronic lymphoedema with skin thickening and fibrosis, most commonly of the lower limbs or scrotum, caused by long-standing lymphatic damage from Wuchereria bancrofti infection (lymphatic filariasis).
- **Haemorrhagic fever:** a clinical syndrome characterised by fever and bleeding manifestations from vascular damage; caused by a group of viruses including Lassa, Ebola, yellow fever, dengue, and CCHF viruses.
- **IHR 2005:** International Health Regulations (2005): a legally binding WHO framework requiring member states to develop core public health capacities and notify WHO of potential public health emergencies of international concern.
- **IPTp:** intermittent preventive treatment in pregnancy; sulfadoxine-pyrimethamine given at each antenatal care visit from the second trimester onwards to prevent malaria in pregnant women.
- **LLIN:** long-lasting insecticidal net; a bed net treated with a pyrethroid insecticide that retains insecticidal activity for at least 3 years; the most cost-effective malaria prevention intervention.
- **Onchocerciasis:** river blindness; caused by Onchocerca volvulus transmitted by Simulium blackflies breeding in fast-flowing rivers; microfilariae damage the skin and cornea, leading to sclerosing keratitis and blindness; treated annually with ivermectin.
- **One Health:** an integrated approach recognising that human, animal, and ecosystem health are interdependent; used to prevent and control diseases at the human-animal-environment interface including zoonoses, antimicrobial resistance, and food safety.
- **Ribavirin:** a broad-spectrum antiviral nucleoside analogue used to treat Lassa fever (IV or oral for 10 days, most effective when started within 6 days) and some other viral haemorrhagic fevers including CCHF.

- **Schistosomiasis:** a parasitic infection caused by blood flukes (Schistosoma species); S. haematobium causes urogenital disease with haematuria and bladder carcinoma risk; S. mansoni causes intestinal and hepatic disease; treated with praziquantel.
- **Winterbottom's sign:** enlarged posterior cervical lymph nodes in West African trypanosomiasis (T.b. gambiense infection); a characteristic early sign of haemolymphatic stage sleeping sickness used to identify cases in endemic communities.

Concept Check Questions [Series 5]

Objective questions

1. P. falciparum causes the majority of malaria deaths in Nigeria; P. vivax and P. ovale can cause relapse from dormant liver forms called _____. (Linked to SLO 5.1)
2. Lassa fever is transmitted from the Mastomys rat through contact with rodent urine or faeces; deafness occurs in approximately _____ percent of survivors. (Linked to SLO 5.2)
3. S. haematobium causes _____ schistosomiasis presenting with haematuria, obstructive uropathy, and increased risk of bladder carcinoma. (Linked to SLO 5.3)
4. The 17D yellow fever vaccine provides lifelong immunity in above 99 percent of recipients with a single dose and is part of the Nigeria EPI at _____ months. (Linked to SLO 5.4)
5. The One Health approach recognises that human health, _____ health, and ecosystem health are interdependent and must be addressed in an integrated manner. (Linked to SLO 5.5)

Short-answer questions

6. State five WHO criteria for severe falciparum malaria. (Linked to SLO 5.1)
7. Describe the IPC measures required for a patient with suspected Lassa fever. (Linked to SLO 5.2)
8. Distinguish lymphatic filariasis from onchocerciasis in terms of vector and clinical features. (Linked to SLO 5.3)
9. Describe the clinical features of monkeypox and state how lymphadenopathy distinguishes it from other rash illnesses. (Linked to SLO 5.4)
10. Explain the IHR 2005 and state the obligation it places on Nigeria. (Linked to SLO 5.5)

Long-answer questions

11. Describe the diagnosis and treatment of malaria in Nigeria, distinguishing uncomplicated from severe disease. (Linked to SLO 5.1)
12. Describe the clinical features, treatment, and infection control measures for Lassa fever. (Linked to SLO 5.2)
13. Describe the two stages of human African trypanosomiasis and state the treatment for each. (Linked to SLO 5.3)
14. Describe the clinical spectrum of dengue fever and outline its management. (Linked to SLO 5.4)
15. Explain the One Health approach and describe its relevance to the control of emerging infections in Nigeria. (Linked to SLO 5.5)

Answers to Concept Check Questions [Series 5]

Objective questions

1. Hypnozoites.
2. 30.
3. Urogenital.
4. 9.
5. Animal.

Short-answer questions

6. Five WHO criteria for severe falciparum malaria: cerebral malaria (unarousable coma, GCS below 11), severe anaemia (Hb below 7 g/dL or haematocrit below 21 percent), respiratory distress (ARDS or pulmonary oedema), hypoglycaemia (blood glucose below 2.2 mmol/L), and acute kidney injury. Other criteria include hyperparasitaemia (above 10 percent parasitised RBCs) and circulatory collapse.

7. Isolate the patient immediately in a single room with a closed door. Notify the NCDC immediately. Healthcare workers must don full PPE: double gloves, impermeable gown, N95 or higher respirator, and face shield or goggles. Hand hygiene is performed before donning and immediately after doffing PPE. Safe burial practices (avoiding contact with the body of the deceased) and contact tracing must be initiated.

8. Lymphatic filariasis is caused by Wuchereria bancrofti, transmitted by Culex mosquitoes; it causes lymphoedema, hydrocele, and elephantiasis from lymphatic vessel damage; microfilariae show nocturnal periodicity. Onchocerciasis is caused by Onchocerca volvulus, transmitted by Simulium blackflies breeding in fast-flowing rivers; it causes intense pruritus and skin changes from microfilariae in the skin, and corneal opacity and blindness from ocular microfilarial invasion.

9. Monkeypox presents with a prodrome of fever, headache, and myalgia followed by prominent lymphadenopathy (enlarged and tender lymph nodes), which is the distinguishing feature from smallpox and chickenpox (which do not cause significant lymphadenopathy). A rash then develops, progressing through macules, papules, vesicles, pustules, and crusts; it is centrifugal (face and extremities more affected than trunk) and involves the palms and soles.

10. The IHR 2005 is a legally binding WHO framework requiring all member states to develop and maintain core public health capacities including surveillance, laboratory diagnosis, risk communication, and health system response. It obligates Nigeria to notify WHO of any event that may constitute a Public Health Emergency of International Concern (PHEIC) within 24 to 48 hours of detection, enabling coordinated international response to potential pandemic threats.

Long-answer questions

11. **Basic response:** Diagnosis: malaria RDT (detects P. falciparum HRP2 antigen within 15 minutes; sensitivity above 95 percent) and peripheral blood film (thick film: high sensitivity; thin film: species identification and parasite density; gold standard; both should be performed). Uncomplicated malaria (able to take oral treatment): ACT first-line: artemether-lumefantrine (Coartem: 6 doses over 3 days) or artesunate-amodiaquine. Severe malaria (any WHO severity criterion): IV artesunate 2.4 mg per kg at 0, 12, and 24 hours then daily; switch to oral ACT when tolerating oral therapy. Manage complications: cerebral malaria (IV diazepam for seizures, avoid hypoglycaemia, nurse in lateral position), severe anaemia (packed RBC transfusion when Hb below 7 g/dL), AKI (fluid balance and renal replacement therapy).

Value-added response: IV artesunate is superior to IV quinine in reducing mortality from severe malaria (demonstrated in the AQUAMAT trial with a 22 percent reduction); wherever IV artesunate is available in Nigeria it must be used in preference to quinine, and its stocking in all hospitals managing severe malaria should be advocated.

12. **Basic response:** Lassa fever is caused by Lassa virus (arenavirus) transmitted from Mastomys natalensis rodents through contact with urine or faeces, or by person-to-person contact with blood and body fluids in healthcare settings. Clinical features: 80 percent are mild; severe disease presents with insidious fever, weakness, sore throat, retrosternal chest pain, exudative pharyngitis, facial oedema, and bleeding in one-third; CFR 15 to 25 percent in hospitalised patients; sensorineural deafness in 30 percent of survivors. Treatment: ribavirin IV for 10 days, most effective when started within 6 days. IPC: immediate isolation in a single room; full PPE (double gloves, gown, N95 respirator, face shield); hand hygiene before donning and after doffing; safe burial; NCDC notification and contact tracing.

Value-added response: Lassa fever disproportionately kills healthcare workers in Nigeria who are exposed without adequate PPE; strengthening healthcare worker training in VHF recognition

and IPC, and ensuring stock availability of PPE in endemic states, is the most important institutional prevention measure.

13. **Basic response:** Stage 1 (haemolymphatic): fever, headache, generalised lymphadenopathy, Winterbottom's sign (enlarged posterior cervical nodes in gambiense), trypanosomal chancre at the bite site, and skin rash. Treatment: pentamidine IM for T.b. gambiense; suramin for T.b. rhodesiense. Stage 2 (meningoencephalitic): neurological involvement with the characteristic altered sleep-wake cycle (daytime somnolence and nighttime insomnia), personality changes, motor signs, and coma if untreated; trypanosomes found in CSF with white cell count above 5 per microlitre. Treatment: NECT (nifurtimox-eflornithine combination therapy) for T.b. gambiense; melarsoprol for T.b. rhodesiense (highly toxic: encephalopathic reaction in 5 to 10 percent).

Value-added response: The distinction between Stage 1 and Stage 2 HAT is critical for treatment choice; all patients with confirmed HAT must have CSF examination because Stage 2 requires different and more toxic drugs, and treating Stage 2 with Stage 1 drugs will result in treatment failure and death from progressive encephalitis.

14. **Basic response:** Clinical spectrum: dengue fever (breakbone fever: sudden high fever, severe retro-orbital headache, myalgia, arthralgia, and a maculopapular rash on days 3 to 5 described as islands of white in a sea of red; self-limiting in most), dengue haemorrhagic fever (DHF: thrombocytopaenia below 100,000 per microlitre, haemorrhagic manifestations, and evidence of plasma leakage: rising haematocrit or pleural effusion or ascites), and dengue shock syndrome (DSS: circulatory failure: the most life-threatening form). Diagnosis: NS1 antigen (days 1 to 5), dengue IgM or IgG serology (after day 5). Management: supportive; IV fluid resuscitation is the cornerstone of DHF and DSS management (crystalloid to maintain perfusion without overload); monitor haematocrit, platelet count, and clinical signs of plasma leakage; blood transfusion only for significant haemorrhage; no specific antiviral.

Value-added response: The four dengue serotypes (DENV 1 to 4) are immunologically distinct; secondary infection with a different serotype increases the risk of DHF from antibody-dependent

enhancement, in which non-neutralising antibodies from prior infection facilitate entry of the new serotype into macrophages, amplifying viraemia and cytokine release.

15. **Basic response:** One Health recognises that human, animal, and ecosystem health are interdependent. Most emerging infections are zoonotic and originate in animals before spilling over to humans when ecological boundaries are disrupted. In Nigeria: Lassa fever (Mastomys rodents in human habitations; reduction of rodent-human contact through improved food storage is a One Health intervention); avian influenza (poultry-human interface; surveillance in both bird and human populations and rapid culling of infected poultry prevents human amplification); and antimicrobial resistance (antibiotic use in livestock agriculture drives resistance gene spread to human pathogens, requiring coordinated prescribing surveillance in human, veterinary, and agricultural sectors). One Health requires institutional collaboration between NCDC, the Federal Department of Veterinary and Pest Control Services, and the Federal Ministry of Environment.

Value-added response: The COVID-19 pandemic demonstrated the catastrophic consequences of inadequate pandemic preparedness; the Nigerian response was strengthened by the existing NCDC infrastructure built during Ebola and Lassa fever responses, illustrating how investment in One Health surveillance capacity for endemic zoonotic diseases directly enhances readiness for novel pandemic threats.

Answers to Pilot Questions [Series 5]

Part 5.1

1. A female Anopheles mosquito injects sporozoites during a blood meal. Sporozoites travel to the liver and undergo asexual multiplication (exoerythrocytic schizogony) for 7 to 30 days without symptoms. Merozoites released from the liver infect red blood cells. Inside RBCs, merozoites multiply through the erythrocytic cycle; synchronised rupture of infected RBCs every 48 hours (P. falciparum) releases merozoites, haemozoin, and pyrogenic cytokines (TNF, IL-1, IL-6), triggering the fever paroxysm.

2. Cerebral malaria (unarousable coma, GCS below 11), severe anaemia (Hb below 7 g/dL), respiratory distress (ARDS or pulmonary oedema), hypoglycaemia (blood glucose below 2.2 mmol/L), and acute kidney injury. Additional criteria: hyperparasitaemia (above 10 percent parasitised RBCs), circulatory collapse, abnormal bleeding, and jaundice with other organ dysfunction.

3. Malaria RDT: detects P. falciparum-specific HRP2 antigen; results within 15 minutes; sensitivity above 95 percent for P. falciparum; does not require laboratory equipment; available at primary care level. Peripheral blood film: thick film (multiple fields examined for maximum sensitivity: detects any species including non-falciparum); thin film (species identification by morphology of parasites within RBCs: ring forms, trophozoites, schizonts; also quantifies parasite density); the gold standard; both tests should always be performed together.

4. Uncomplicated P. falciparum malaria: artemether-lumefantrine (Coartem: 6 doses over 3 days: the most widely used ACT in Nigeria) or artesunate-amodiaquine. Severe falciparum malaria: IV artesunate 2.4 mg per kg at 0, 12, and 24 hours then daily until oral therapy is tolerated; switch to a full course of oral ACT on recovery. IV artesunate is superior to IV quinine, reducing mortality by 22 percent (AQUAMAT trial).

5. Long-lasting insecticidal nets (LLINs: most cost-effective intervention; treat insecticide-resistant mosquitoes as they rest on the net after feeding). Indoor residual spraying (IRS: spraying the interior walls of houses with residual insecticide kills mosquitoes resting after feeding). Intermittent preventive treatment in pregnancy (IPTp: sulfadoxine-pyrimethamine at each ANC visit from the second trimester: prevents malaria in pregnant women). Seasonal malaria chemoprevention (SMC: monthly sulfadoxine-pyrimethamine plus amodiaquine for children 3 to 59 months in the Sahel during the transmission season).

Part 5.2

1. Lassa fever is transmitted from Mastomys natalensis (multimammate rat) to humans through contact with rodent urine or faeces contaminating food or household surfaces (zoonotic: the main route in endemic areas) or through person-to-person contact with blood or body fluids of infected patients (nosocomial amplification in healthcare settings). Clinical features: 80 percent mild or asymptomatic; severe disease presents with insidious onset fever, weakness, malaise, headache, sore throat, retrosternal chest pain, exudative pharyngitis (white patches), facial oedema, and bleeding in one-third; CFR 15 to 25 percent hospitalised; sensorineural hearing loss in 30 percent of survivors.

2. Ribavirin (IV 2 g loading dose then 1 g every 6 hours for 4 days then 500 mg every 8 hours for 6 days, or oral equivalent for 10 days) reduces Lassa fever mortality, particularly when started within the first 6 days of illness onset. Starting after 6 days is still beneficial but less effective. Early identification and early treatment are therefore critical. Supportive care (IV fluids with caution to avoid pulmonary oedema, electrolyte correction, blood transfusion for haemorrhage) complements ribavirin.

3. Ebola virus disease presents with sudden onset fever, severe headache, myalgia, and weakness, followed within days by vomiting, diarrhoea (often profuse, leading to severe dehydration), and haemorrhagic manifestations in approximately 50 percent of cases (bleeding from mucous membranes, venepuncture sites, and body orifices). The CFR ranges from 25 to 90 percent depending on the outbreak strain, healthcare access, and quality of supportive care; the 2014 to 2016 West Africa outbreak had a CFR of approximately 40 percent.

4. Isolate the patient immediately in a single room with a closed door. Notify the NCDC immediately. Don full PPE before any patient contact: double gloves, impermeable fluid-resistant gown, N95 or higher respirator, and face shield or goggles. Perform hand hygiene before donning and immediately after doffing PPE (using the buddy system for safe doffing). Use dedicated single-use equipment. Handle blood and body fluids as high-risk biological material. Implement safe burial practices (trained burial teams; no touching of the body by family). Initiate contact tracing for all persons who had unprotected contact with the patient.

5. Lassa fever (Mastomys rat; West Africa; ribavirin treatment; deafness in survivors; Nigeria most endemic). Ebola virus disease (filovirus; direct contact transmission; CFR 25 to 90 percent; rVSV-ZEBOV vaccine for outbreak control; West Africa 2014 to 2016 outbreak). Yellow fever (Aedes mosquito-borne Flavivirus; toxic phase: jaundice and black vomit; 17D vaccine: highly effective; no antiviral; part of Nigeria EPI).

Part 5.3

1. S. haematobium: cercariae penetrate skin during freshwater contact; adult worms live in the vesical plexus around the bladder; clinical features: haematuria (terminal haematuria: blood at the end of micturition), dysuria, obstructive uropathy, and increased risk of squamous cell carcinoma of the bladder. S. mansoni: adult worms live in the mesenteric veins; clinical features: bloody diarrhoea, hepatosplenomegaly, and progressive hepatic periportal fibrosis leading to pre-sinusoidal portal hypertension with oesophageal varices. Treatment for both: praziquantel 40 mg per kg as a single oral dose.
2. Lymphatic filariasis (LF) caused by Wuchereria bancrofti presents with lymphoedema (progressive swelling of the lower limbs from lymphatic vessel damage), hydrocele (fluid accumulation around the testes: the most common clinical manifestation), and in chronic untreated cases elephantiasis (massive fibrotic lymphoedema). Microfilariae circulate in the blood with nocturnal periodicity. Treatment: annual single-dose ivermectin plus albendazole in mass drug administration programmes aimed at elimination.
3. Skin manifestations: intense generalised pruritus (the most distressing symptom), onchodermatitis (skin thickening, hypopigmentation giving a spotted leopard skin appearance, and loss of skin elasticity), and subcutaneous nodules (onchocercomas: fibrous nodules over bony prominences containing adult worms). Ocular complications: microfilariae that die in the cornea trigger an inflammatory response causing punctate keratitis progressing to sclerosing keratitis (opacification of the cornea leading to blindness: the cause of the name river blindness). Onchocerciasis is the second leading infectious cause of blindness globally after trachoma.

4. Stage 1 (haemolymphatic): fever, headache, generalised lymphadenopathy, Winterbottom's sign (enlarged posterior cervical lymph nodes in T.b. gambiense infection), trypanosomal chancre at the bite site (a red inflammatory reaction developing within a week of the tsetse fly bite), and maculopapular skin rash. The patient is clinically unwell but the central nervous system is not yet involved. Stage 2 (meningoencephalitic): the parasite crosses the blood-brain barrier; features include characteristic altered sleep-wake cycle (daytime somnolence and nighttime insomnia: the hallmark of sleeping sickness), personality and behavioural changes, motor abnormalities, seizures, and progressive coma leading to death if untreated.

5. Stage 1 T.b. gambiense: pentamidine isethionate 4 mg per kg IM daily for 7 days. Stage 2 T.b. gambiense: nifurtimox-eflornithine combination therapy (NECT): eflornithine 400 mg per kg per day IV in divided doses for 7 days plus nifurtimox 15 mg per kg per day orally in three divided doses for 10 days (NECT replaced melarsoprol as first-line for Stage 2 gambiense because of equivalent efficacy and a much lower rate of treatment-related encephalopathic reaction; melarsoprol causes fatal reactive encephalopathy in 5 to 10 percent).

Part 5.4

1. Dengue fever: sudden high fever (above 39 degrees C), severe retro-orbital headache, myalgia (breakbone fever), arthralgia, and a maculopapular rash appearing on days 3 to 5 (described as islands of white in a sea of red); leucopenia is characteristic. Dengue haemorrhagic fever (DHF) is distinguished by: thrombocytopaenia (platelet count below 100,000 per microlitre), haemorrhagic manifestations (petechiae, purpura, positive tourniquet test, mucosal bleeding), and evidence of plasma leakage (rising haematocrit above 20 percent of baseline, or pleural effusion or ascites on imaging); DHF requires hospitalisation for IV fluid management and close monitoring.

2. Severe yellow fever (toxic phase) presents with return of fever after brief remission, jaundice (from hepatic involvement), haemorrhagic manifestations including

haematemesis (black vomit from degraded blood in the vomitus), and acute renal failure; the CFR in the toxic phase is 20 to 50 percent. Prevention: the 17D yellow fever vaccine is one of the most effective vaccines ever developed; a single dose provides lifelong immunity in above 99 percent of recipients within 30 days; it is a live attenuated virus vaccine that is part of the Nigeria EPI at 9 months; it is also required for entry into many countries. No specific antiviral exists; management is supportive.

3. Monkeypox presents with a prodrome of fever, headache, myalgia, and prominent lymphadenopathy (enlarged, tender lymph nodes: a distinguishing feature from smallpox, which does not cause significant lymphadenopathy, and from chickenpox, which causes only mild lymphadenopathy); the lymphadenopathy often precedes the rash. The rash then develops, progressing sequentially through macules, papules, vesicles, pustules, and crusts; it is centrifugal (face and extremities more severely affected than the trunk) and characteristically involves the palms and soles. In the 2022 outbreak, genital and perianal lesions were predominant. Diagnosis is confirmed by PCR on vesicle fluid.

4. Surveillance (early detection of unusual disease clusters: IDSR system; genomic sequencing capacity for novel pathogen identification). Laboratory capacity (rapid diagnostic testing for novel pathogens; national and regional reference laboratories). Risk communication (clear, accurate, timely public health messaging to the population and healthcare workers; countering misinformation). Health system surge capacity (adequate ICU beds, ventilators, oxygen supplies, PPE stocks, and trained personnel). International coordination (compliance with IHR 2005: notifying WHO of PHEIC within 24 to 48 hours; sharing epidemiological data internationally).

5. The One Health approach recognises that human health, animal health, and ecosystem health are interdependent. Emerging infections originate at the human-animal-environment interface when ecological boundaries are disrupted. Application in Nigeria: Lassa fever control (rodent control through improved food storage and household hygiene; surveillance in Mastomys populations in endemic states; rapid human case detection and contact tracing: a collaborative NCDC and FDVPCS intervention). Avian influenza preparedness (joint surveillance in poultry markets and human populations; rapid culling protocols; healthcare worker training for case detection: requires

coordination between NCDC and veterinary authorities). AMR control requires simultaneous reduction of antibiotic use in human, animal, and agricultural settings.

References and Attributions [Series 5]

Textual References

- World Health Organization. (2021). WHO Guidelines for the Treatment of Malaria (3rd ed.). Geneva: WHO.
- Nigeria Centre for Disease Control. (2022). Lassa Fever: Situation Reports 2022. Abuja: NCDC.
- World Health Organization. (2019). Neglected Tropical Diseases: Progress Report 2010 to 2019 and Road Map 2021 to 2030. Geneva: WHO.
- Mandell, G. L., Bennett, J. E. and Dolin, R. (2015). Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases (8th ed.). Philadelphia: Elsevier.

Figures, Plates, Tables, and Boxes

- Figure 5.1: Malaria in Nigeria. AI-generated using the prompt: "Two-panel infographic: left malaria life cycle diagram, uncomplicated and severe malaria clinical features and WHO criteria, diagnosis (RDT and blood film); right ACT treatment and IV artesunate for severe malaria, and prevention (LLIN, IRS, IPTp, SMC)." Suggested OER search string: "malaria Nigeria life cycle clinical features diagnosis ACT treatment prevention infographic OER."
- Figure 5.2: Viral haemorrhagic fevers in Nigeria. AI-generated using the prompt: "Two-panel infographic: left Lassa fever (Mastomys transmission, clinical features, ribavirin treatment); right Ebola (transmission, CFR, rVSV-ZEBOV vaccine), other VHFs (yellow fever, CCHF), and IPC measures (full PPE diagram, isolation, NCDC notification, safe burial)." Suggested OER search string: "Lassa fever Ebola viral haemorrhagic fever Nigeria IPC PPE management infographic OER."
- Figure 5.3: Neglected tropical diseases in Nigeria. AI-generated using the prompt: "Two-panel infographic: left schistosomiasis, STHs, lymphatic filariasis, onchocerciasis; right

two-stage HAT sleeping sickness diagram and leishmaniasis box." Suggested OER search string: "neglected tropical diseases schistosomiasis filariasis onchocerciasis trypanosomiasis Nigeria infographic OER."

- Figure 5.4: Emerging infections and pandemic preparedness. AI-generated using the prompt: "Two-panel infographic: left dengue (three clinical forms), yellow fever (toxic phase, 17D vaccine), monkeypox (rash stages, lymphadenopathy, PCR); right pandemic preparedness components (IDSR, IHR 2005, surge capacity) and One Health triangle diagram." Suggested OER search string: "dengue fever yellow fever monkeypox pandemic preparedness One Health emerging infections infographic OER."