IAVI VACCINE LITERACY LIBRARY

2022

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Translating **science** into **global** health impact

About IAVI

IAVI is a non-profit scientific research organization dedicated to addressing urgent, unmet global health challenges including HIV, tuberculosis, and emerging infectious diseases. Its mission is to translate scientific discoveries into affordable, globally accessible public health solutions.

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And many other generous individuals and partners around the world

As of April 2022

Abbreviations

AE	Adverse event
AIDS	Acquired immunodeficiency syndrome
APC	Antigen-presenting cell
BCG	Bacillus of Calmette and Guerin
CAB	Community advisory board
CBO	Community-based organisation
CD	Cluster of differentiation
CDC	Centers for Disease Control and Prevention
CEPI	Coalition for Epidemic Preparedness Innovations
COVID-19	Coronavirus Disease 2019
CRF	Circulating recombinant forms
CTL	Cytotoxic T lymphocyte
DNA	Deoxyribonucleic acid
DOT	Directly observed therapy
EMA	European Medicines Agency
ERC	Ethics Review Committee
FDA	U.S. Food and Drug Administration
GCLP	Good Clinical Laboratory Practice
GCP	Good Clinical Practice
HIV	Human immunodeficiency virus
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IEC	Independent Ethics Committee
IGRA	Interferon-gamma release assays
IRB	Institutional Review Board
LASV	Lassa virus
LMIC	Low- to middle-income countries
LTBI	Latent tuberculosis infecton
MDR-TB	Multidrug-resistant tuberculosis
M.tb	Mycobacterium tuberculosis
NAT	Nucleic acid test
NGO	Non-governmental organisation
NK	Natural killer cells
NP	Nucleoprotein
NRA	National Regulatory Authority
POD	Prevention of disease
POI	Prevention of infection
POR	Prevention of reinfection
RNA	Ribonucleic acid
SAE	Serious adverse event
SAHPRA	South African Health Products Regulatory Authority
TB	Tuberculosis
TPP	Target product profile
TST	Tuberculin skin test
UNAIDS	Joint United Nations Programme on HIV/AIDS
VISP	Vaccine-induced seropositivity
VL	Viral load
VMMC	Voluntary medical male circumcision
WHO	World Health Organization
XDR-TB	Extensively drug-resistant TB

Introduction

The **IAVI Vaccine Literacy Library** contains basic information about HIV, TB, and Lassa virus vaccines, explained in simple language and in a user-friendly format. The text is divided into eight modules covering a range of topics, from basic science and clinical trials to social and ethical issues related to vaccine development and testing, as well as future access to and use of vaccines. The resource also includes a list of abbreviations used and a glossary with definitions of key terms.

Audience

The **IAVI Vaccine Literacy Library** is targeted to a broad range of stakeholders involved in HIV, TB, and Lassa virus vaccine-related work. While all the modules can be adapted for use at the local community level, they are generally written for individuals who provide education and information related to HIV, TB and Lassa virus.

Use of the IAVI Vaccine Literacy Library

The **IAVI Vaccine Literacy Library** is meant for use by individuals and organisations that are providing education and information related to HIV, TB and Lassa virus vaccine research and development.

Groups that may use this material include, but are not limited to:

- Clinical vaccine trial site staff.
- Non-Governmental Organisation (NGO) staff, to incorporate vaccine messages into their existing work.
- Medical professionals or institutions, to provide vaccine information to patients or to incorporate into advocacy efforts.
- Health Centres, to provide clients with vaccine information.
- Academic or religious leaders, to provide information and/or informed advice.
- Community Advisory Boards.

The **IAVI Vaccine Literacy Library** is designed for multiple uses to serve a variety of needs. For certain audiences, it may be used as reference information, such as background reading for training workshops. It can also be used as a reference document to develop educational materials or tools, or to incorporate vaccine information into existing tools, such as:

- Fact sheets on specific vaccine topics.
- Brochures to be given to potential vaccine trial participants.
- Informational videos to be shown in community settings.
- Street plays to be performed in community settings.
- Radio programmes.

The **IAVI Vaccine Literacy Library** can also be used directly for recruitment of trial participants or may be used to engage communities or national-level stakeholders to build understanding of and support for clinical trials and an eventual vaccine.

Using and Navigating the Core Content

The **IAVI Vaccine Literacy Library** is divided into eight modules covering a range of topics, from basic science and clinical trials to social and ethical issues related to vaccine development and testing, as well as future access and use.

Each module can be read and used as a standalone document.

Certain issues or concepts are covered in more than one module. These "cross-cutting issues" are cross referenced to other modules in capitalised text. All scientific and technical terms are defined in a comprehensive glossary that provides definitions for technical and scientific terms and expressions.

Acknowledgement of IAVI and Materials Review

As described, the **IAVI Vaccine Literacy Library** is designed primarily as a reference on HIV, TB, and Lassa virus vaccines that can be used to develop or adapt materials or messages.

If IAVI has not been involved in production of materials or tools based on the **IAVI Vaccine Literacy Library**, no review by IAVI is required. IAVI does request that appropriate acknowledgement of the **IAVI Vaccine Literacy Library** be given, but the IAVI logo should not be used.

IAVI requests that it be notified of any tools or materials produced, in order that they be added to the **IAVI Vaccine Resource Library**, which is a public resource serving the entire HIV, TB, and Lassa virus-vaccine field. Proper credit will be given for all resources included in the **IAVI Vaccine Literacy Library**.

Disclaimer

IAVI assumes no responsibility or liability for any errors or omissions in the content of the **IAVI Vaccine Literacy Library**. The information contained in this Resource Library is provided on an 'as is' basis with no guarantees of completeness, accuracy, usefulness, or timeliness.

How to Cite the IAVI Vaccine Literacy Library

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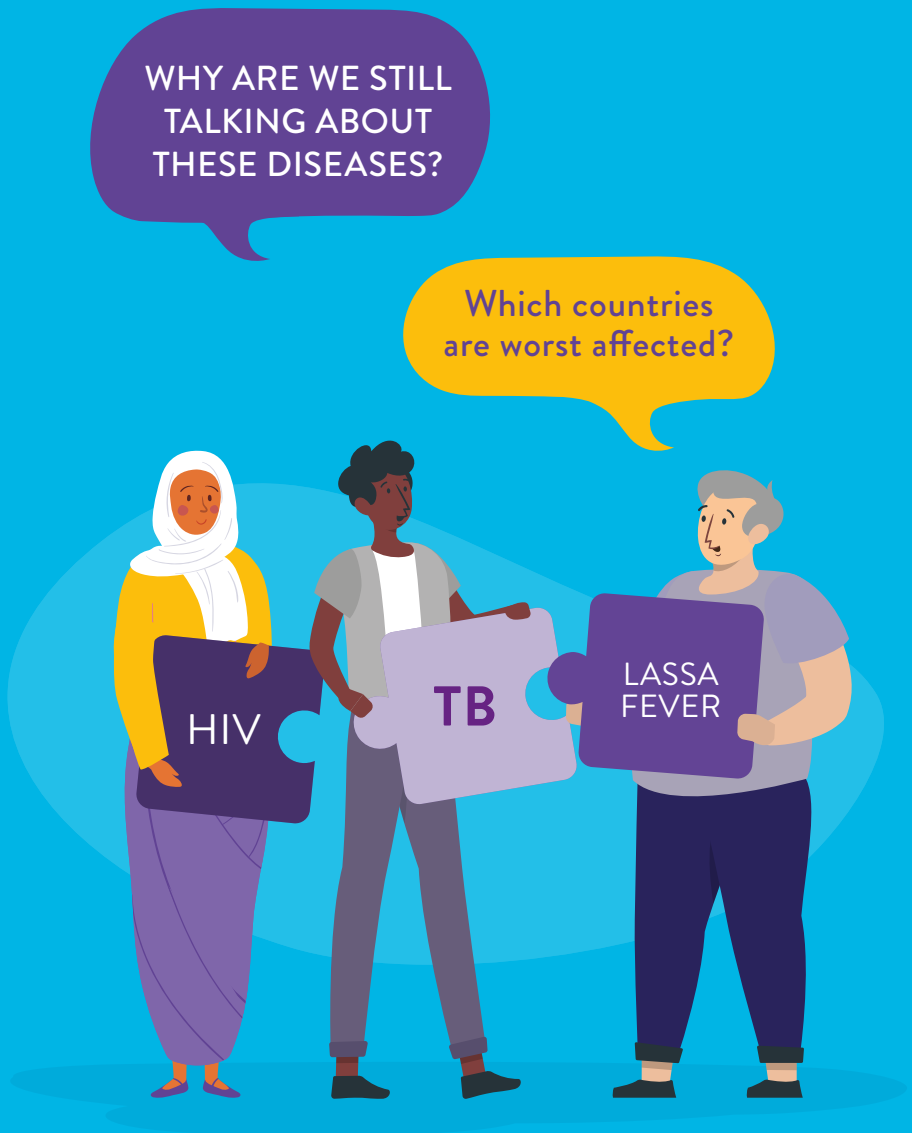
MODULE 2:
INTRODUCTION TO HIV, TUBERCULOSIS, AND LASSA FEVER



MODULE 2

INTRODUCTION TO HIV, TUBERCULOSIS, AND LASSA FEVER

CONTENTS 21

1. HIV

1.1 A Brief History

The origin of the human immunodeficiency virus (HIV) has been extensively researched and it is accepted that the infection spread from non-human primates to humans in Africa sometime in the early 20th century. The virus did not come to widespread public attention until 1981 when an unexplained illness was reported in men who have sex with men in the USA, now known as acquired immune deficiency syndrome (AIDS).

Within two years, in 1983, the virus that causes AIDS was discovered by two teams of researchers based in France and the USA who were awarded the Nobel Prize in Medicine in 2008. Since then, HIV and AIDS have been extensively studied leading to significant progress in diagnosis, prevention, and treatment.

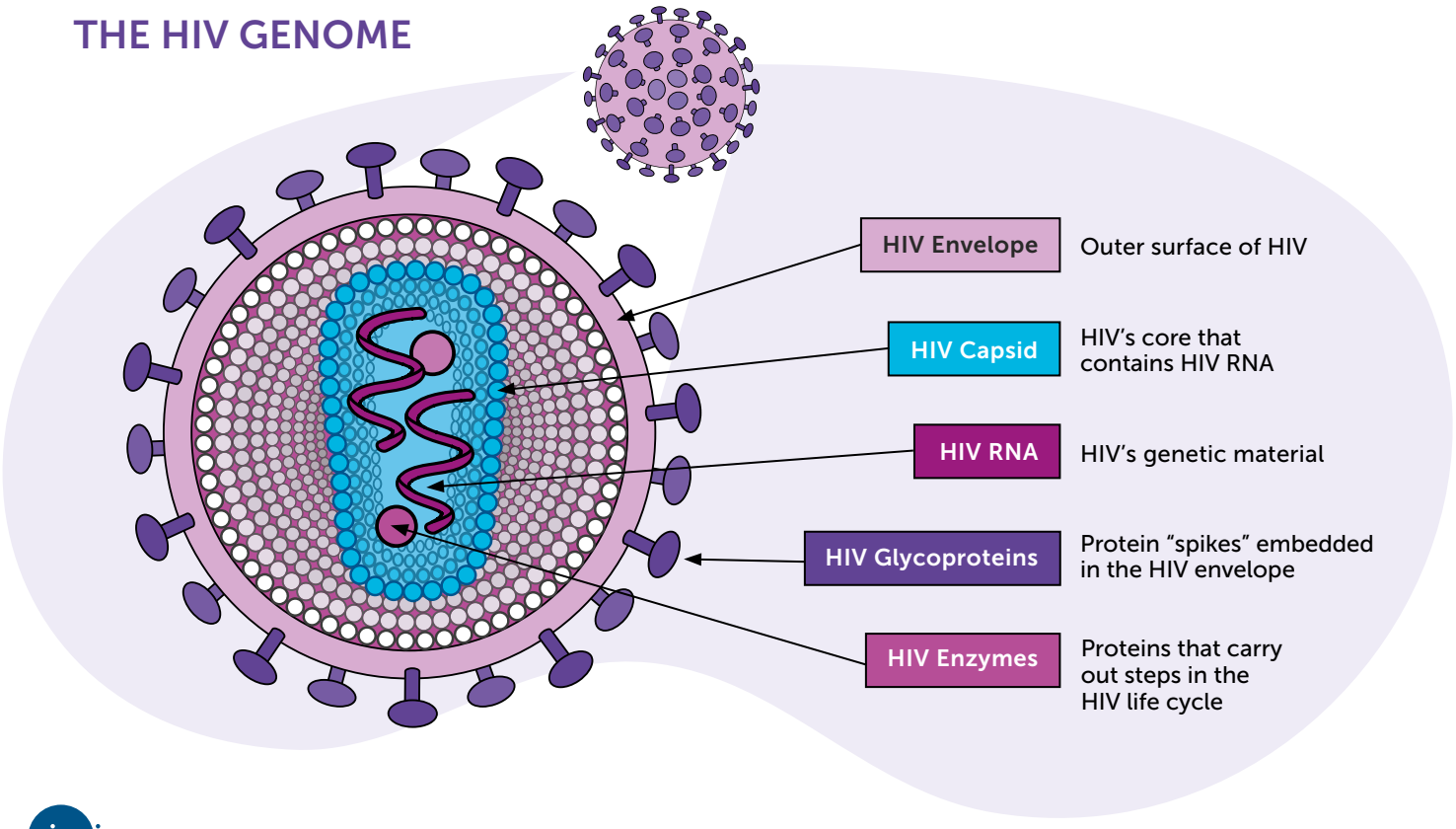
Despite these worldwide efforts, HIV remains a major global public health issue, having claimed 40 million lives since it was first reported (see **MODULE 1** for more information).

1.2 Human Immunodeficiency Virus

HIV is a retrovirus — this type of virus leads to multi-organ disease characterised by long incubation periods and long-lasting (persistent) infection. The HIV genome, which is made of RNA, contains nine genes that encode 15 viral proteins including structural proteins, enzymes, and envelope glycoproteins.

There are two types of HIV: HIV-1 and HIV-2. HIV-1 is responsible for most infections worldwide, whilst HIV-2 is less infectious, takes longer to cause AIDS and is mostly confined to West Africa and countries with links to West Africa.

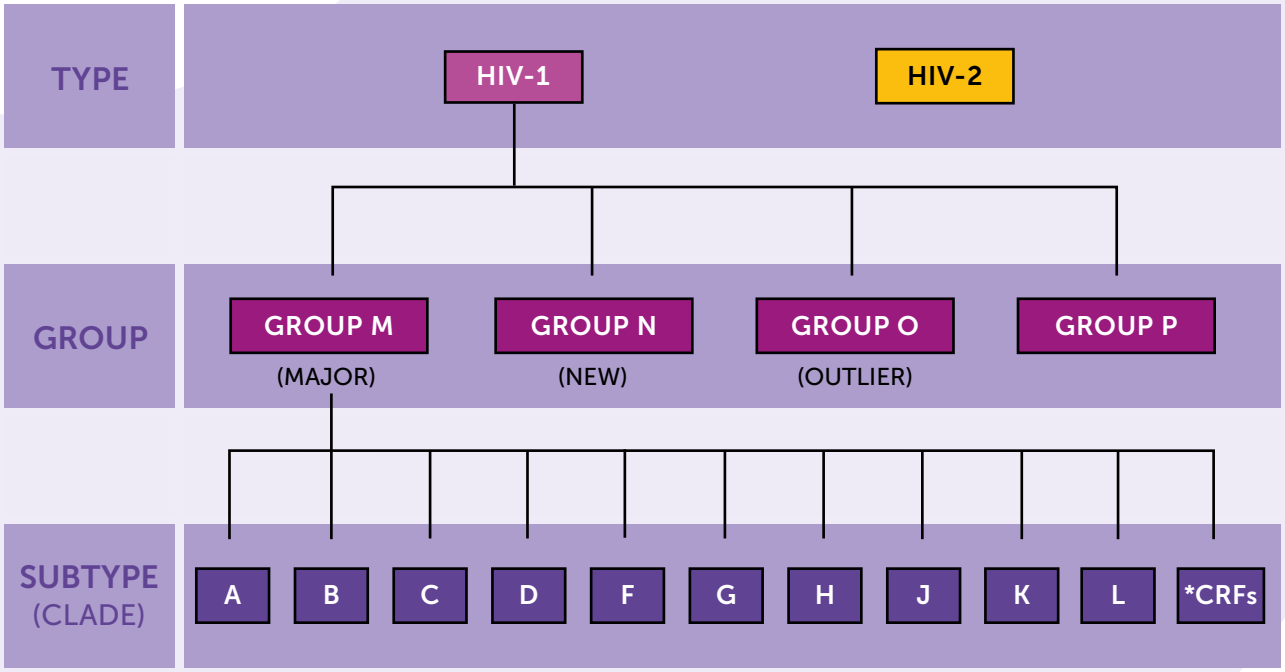
THE HIV GENOME



HIV-1 can be classified in four groups, with group M being the group responsible for the global HIV epidemic. Within group M, there are 10 distinct subtypes of viruses called clades, and hybrid viruses known as circulating recombinant forms (CRFs). The wide diversity of types of HIV makes prevention and treatment challenging.

HIV-1 GROUPS AND SUBTYPES

There are two types of HIV: HIV-1 and HIV-2. HIV-1 can be classified in four groups: M, N, O, and P with M being the group responsible for the global HIV epidemic. Within group M, there are 10 distinct subtypes, or clades, of viruses (A, B, C, D, F, G, H, J, K and L), and hybrid viruses known as circulating recombinant forms, CRFs.



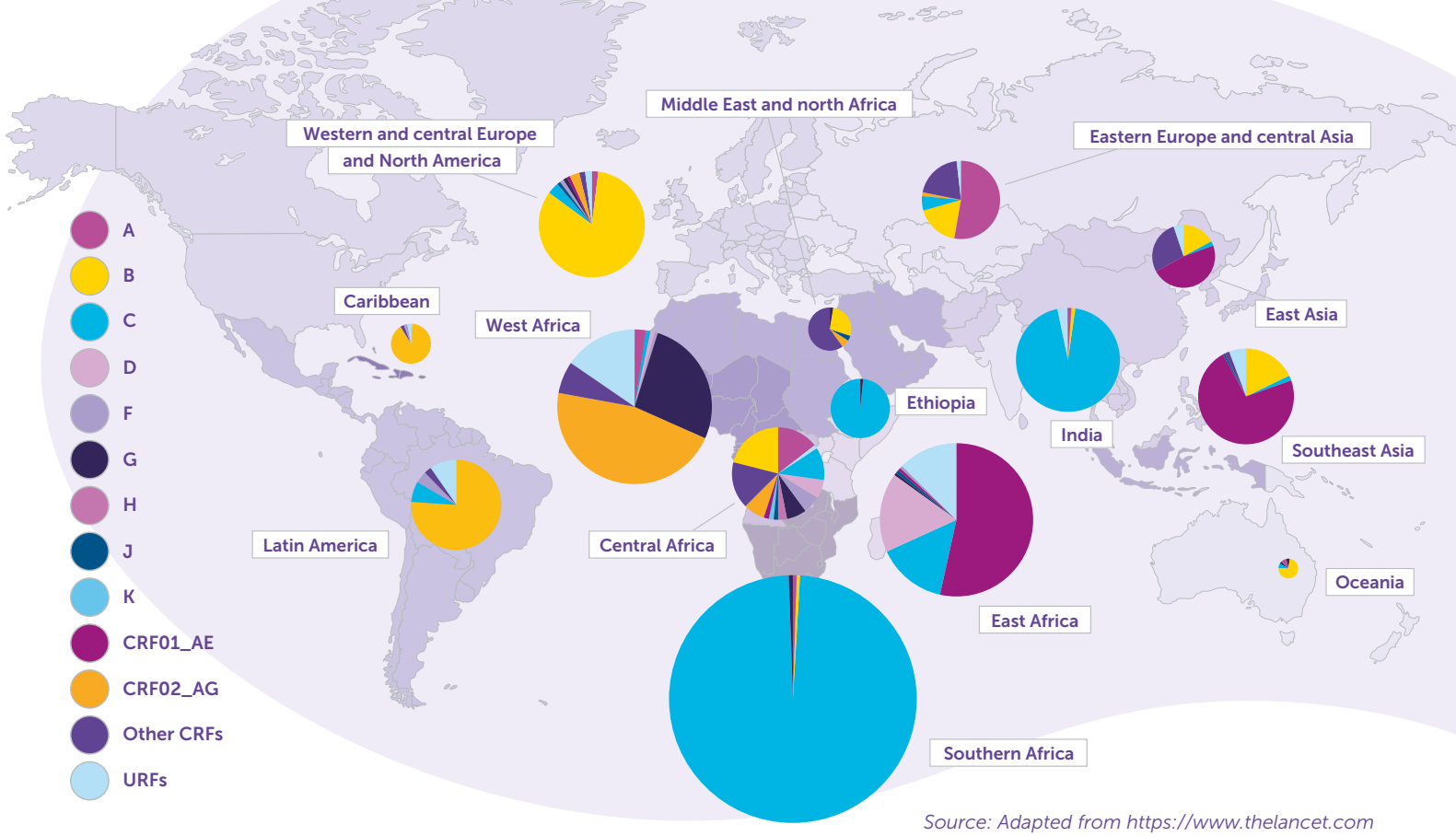
*CRFs = Circulating Recombinant Forms

HIV-1 Group M is the strain that is responsible for 90% of the global HIV pandemic.

Within group M, there are 10 distinct subtypes, or clades, of viruses (A, B, C, D, F, G, H, J, K and L).

The greatest diversity of HIV subtypes is found in Central Africa where the virus originated. Virus subtypes are distributed to varying degrees across different regions of the world. Subtype C is responsible for almost half of all HIV-1 infections worldwide. Subtype B is most common in the Americas, Western Europe, and Australasia. Virus diversity plays an important role in vaccine design and vaccine efficacy (see **MODULE 4**).

GEOGRAPHICAL DISTRIBUTION OF HIV-1 SUBTYPES



Source: Adapted from https://www.thelancet.com

1.3 HIV Life Cycle

HIV infection occurs via direct contact with the bodily fluids from a person with HIV with a detectable viral load. People with HIV who take HIV medicine consistently and do not have a detectable viral load have effectively no risk of sexually transmitting HIV to their HIV-negative partners (this is known as U=U, Undetectable = Untransmissible).

The bodily fluids involved in HIV transmission are:

- Blood
- Semen and pre-seminal fluid
- Rectal fluids
- Vaginal fluids
- Breast milk

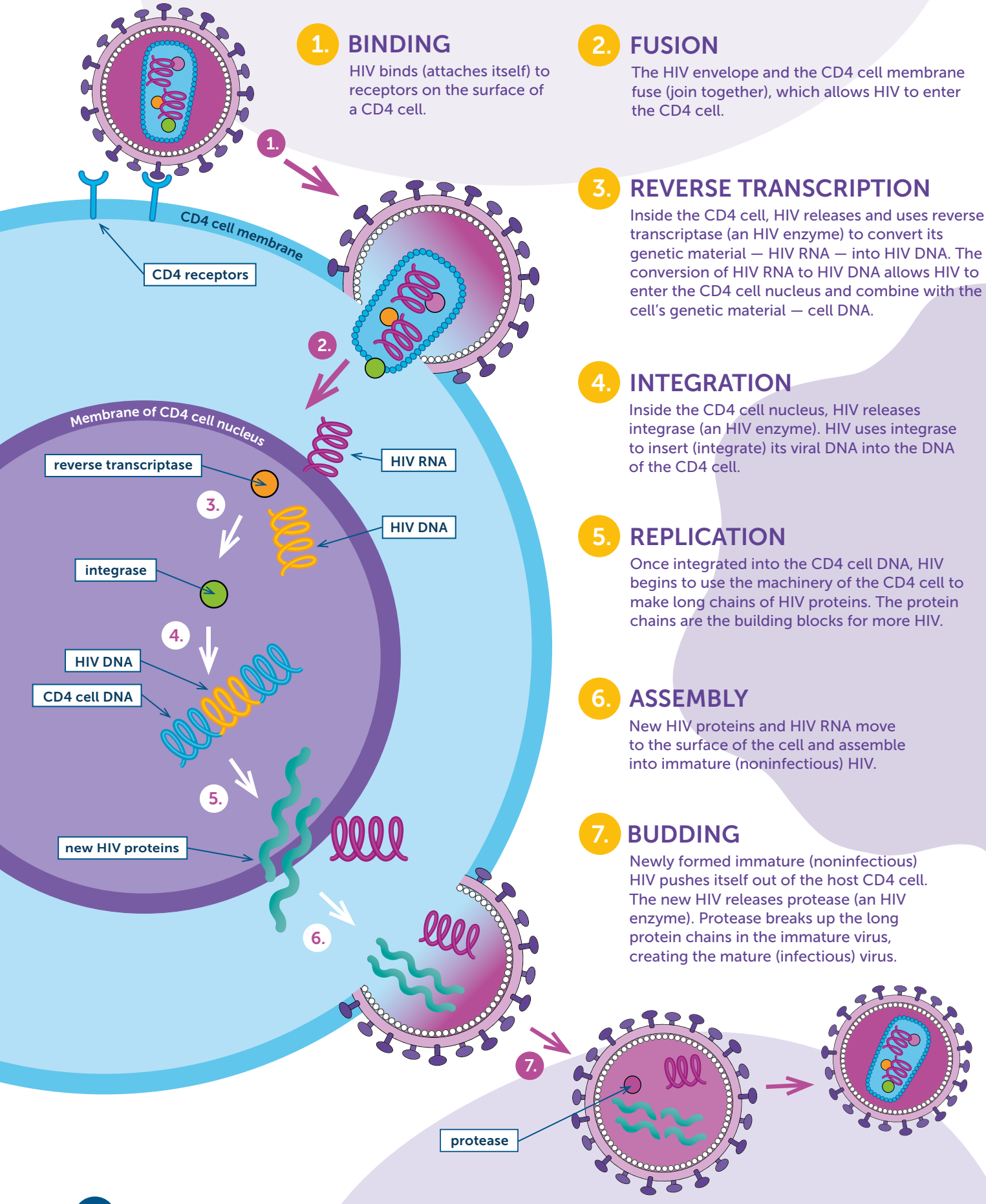
Ways HIV is not transmitted: sharing dishes; saliva; tears; sweat; shaking hands.

HIV enters cells using a 'lock and key' mechanism. Spikes on its outer surface (envelope glycoprotein) lock onto receptors on the cell's surface. The most frequent target cells for HIV infection are immune cells known as CD4+ T-cell lymphocytes.

After entering a cell, HIV RNA is transcribed into DNA by an enzyme called reverse transcriptase. HIV viral DNA can then be part of the genome of the host where it can hide in a dormant state for several years, creating a 'reservoir' of infected cells.

Once in the cell, the virus takes advantage of the cell machinery to produce viral RNA and other different viral components. The viral RNA is then packaged into mature 'virions' that are released by infected cells, killing the cells in the process.

THE HIV LIFE CYCLE



1. BINDING

HIV binds (attaches itself) to receptors on the surface of a CD4 cell.

2. FUSION

The HIV envelope and the CD4 cell membrane fuse (join together), which allows HIV to enter the CD4 cell.

3. REVERSE TRANSCRIPTION

Inside the CD4 cell, HIV releases and uses reverse transcriptase (an HIV enzyme) to convert its genetic material — HIV RNA — into HIV DNA. The conversion of HIV RNA to HIV DNA allows HIV to enter the CD4 cell nucleus and combine with the cell's genetic material — cell DNA.

4. INTEGRATION

Inside the CD4 cell nucleus, HIV releases integrase (an HIV enzyme). HIV uses integrase to insert (integrate) its viral DNA into the DNA of the CD4 cell.

5. REPLICATION

Once integrated into the CD4 cell DNA, HIV begins to use the machinery of the CD4 cell to make long chains of HIV proteins. The protein chains are the building blocks for more HIV.

6. ASSEMBLY

New HIV proteins and HIV RNA move to the surface of the cell and assemble into immature (noninfectious) HIV.

7. BUDDING

Newly formed immature (noninfectious) HIV pushes itself out of the host CD4 cell. The new HIV releases protease (an HIV enzyme). Protease breaks up the long protein chains in the immature virus, creating the mature (infectious) virus.

Source: Adapted from https://hivinfo.nih.gov/understanding-hiv/fact-sheets/hiv-life-cycle

1.4 Diagnosis

Many people with HIV do not have symptoms at first and are unaware of their infection status until much later. The incubation period, the time from exposure to the virus to when the first symptoms develop, can last several years. The most common way to diagnose an HIV infection is through a blood or saliva test.

There are three types of HIV tests available:

- Nucleic acid tests (NAT) that can detect HIV RNA in the blood.
- Antigen/antibody tests to detect parts of the virus, for example the viral capsid protein along with antibodies generated in response to the infection.
- Tests to detect antibodies generated by the body in response to the infection.

Antigen and/or antibody HIV tests can be performed with blood or saliva samples (oral test).

HIV testing can be performed by professionals in various settings (hospitals, local clinics, community health organisations) and by people using self-sampling or self-testing. In self-sampling the individual takes their own blood sample and sends it to a laboratory for testing; the results are returned a few days later. With self-testing, the individual collects a sample of saliva, then performs, and interprets the test themselves.

Tests work differently depending on the type of test and when it is carried out. HIV tests have a 'window period' between exposure to the virus and when a test can detect the infection. Laboratory tests are the most sensitive and the most accurate. No single test can provide a full HIV diagnosis and all positive tests require confirmation, while negative tests require regular testing.

1.5 Disease progression

Without treatment, HIV infection progresses in three stages, worsening over time: acute HIV infection, chronic HIV infection, and AIDS.

Acute Infection

During the first few weeks of the infection, HIV multiplies rapidly and spreads through the body. The amount of virus in the blood (viral load) increases exponentially and quickly becomes detectable. The body responds with an 'adaptive' immune response that involves two kinds of responses (these are described in detail in **MODULE 3**). When the first antibodies are produced and detectable this is called seroconversion. This phase may or may not be accompanied by symptoms. Some people may develop fever, generalised enlarged lymph nodes, a non-specific rash, muscle pain, and/or malaise. Others have a short flu-like illness called "seroconversion illness." People are most infectious during this phase.

Chronic Infection

During chronic infection, also called asymptomatic infection, HIV multiplies less rapidly, and HIV viral load decreases. This phase can last several years during which infected individuals show no symptoms or health problems. However, HIV continues to affect the immune system and other systems in the body. During this phase, viral load and CD4 counts indicate how well the body is responding to the infection.

CD4 Count and Viral Load

- CD4 cells are white blood cells of the immune system that fulfil various functions, notably they help coordinate the immune response by stimulating other cells of the immune system. A normal CD4 count ranges from 500 to 1,400 cells per cubic millimetre of blood. HIV weakens the immune system by destroying CD4 cells. The CD4 count is the most important indicator of immune function and the strongest predictor of HIV progression.
- **Viral load** (VL) measures the quantity of HIV in the blood and refers to the number of HIV RNA copies per millilitre of blood.

Over time, the virus rapidly changes and escapes the body's immune response. As the CD4 count decreases, the immune system becomes weaker, and symptomatic infections, such as severe bacterial and viral infections like chicken pox and tuberculosis, can start to occur. Further opportunistic infections, illnesses that the immune system can usually fight, such as fungal diseases begin to occur.

AIDS

In absence of treatment, the HIV infection develops into AIDS, the most advanced stage of the disease. AIDS (acquired immune deficiency syndrome) describes a number of potentially life-threatening infections and illnesses that happen when the immune system has been severely damaged by HIV. AIDS is characterised by a range of illnesses including cancers such as Kaposi sarcoma, certain lymphomas, invasive cervical cancers, and other infectious diseases. People diagnosed with AIDS have a very high viral load and can transmit HIV to others very easily. Without treatment, people with AIDS typically live for only about three years.

Elite Controllers

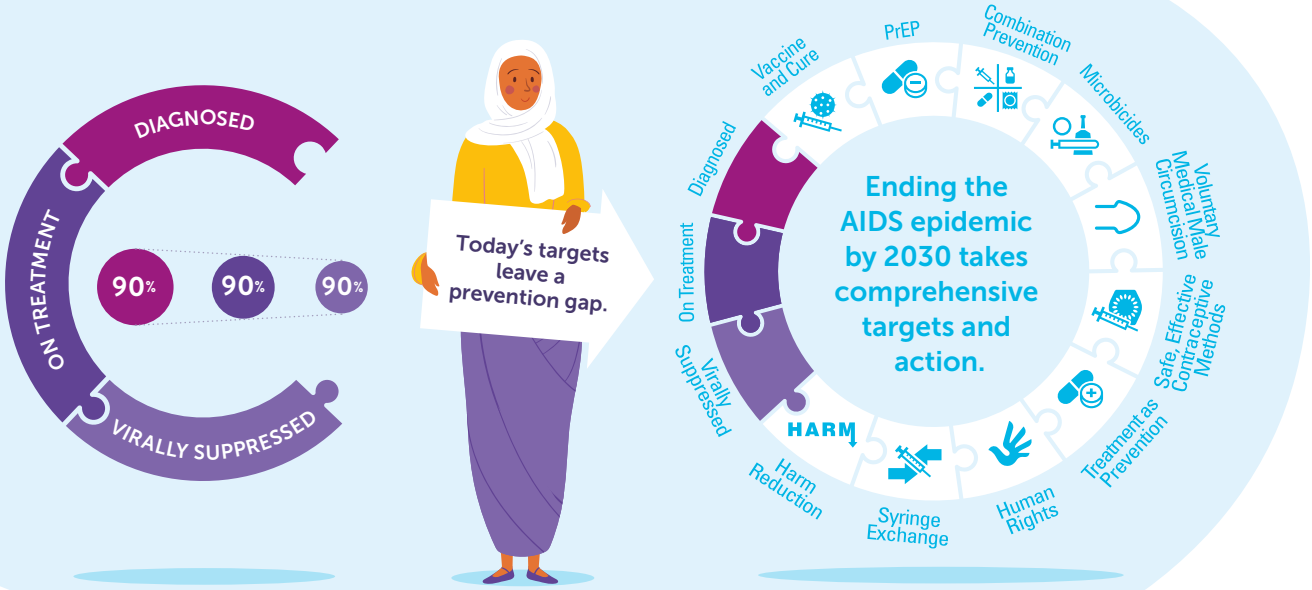
Elite controllers are people who naturally control HIV without antiretroviral therapy (ART). The study of their immune system and immune responses provides new information and directions for prevention, treatment, and cure research.

1.6 Prevention and Treatment

Today several prevention options are available to avert HIV acquisition in various settings and for different transmission routes including:

- Male and female condom use.
- Testing and counselling for HIV and STIs.
- Voluntary medical male circumcision (VMMC).
- Antiretroviral drugs (ARVs) for prevention, also known as PrEP (pre-exposure prophylaxis) or post-exposure prophylaxis (PEP).
- Harm reduction for people who use drugs.
- Elimination of mother-to-child transmission (MTCT) of HIV.
- Treatment of people living with HIV to prevent further transmission.

MIND THE GAP



Source: Adapted from AVAC Report 2014/15: Prevention on the Line
www.avac.org/report2014-15/graphics

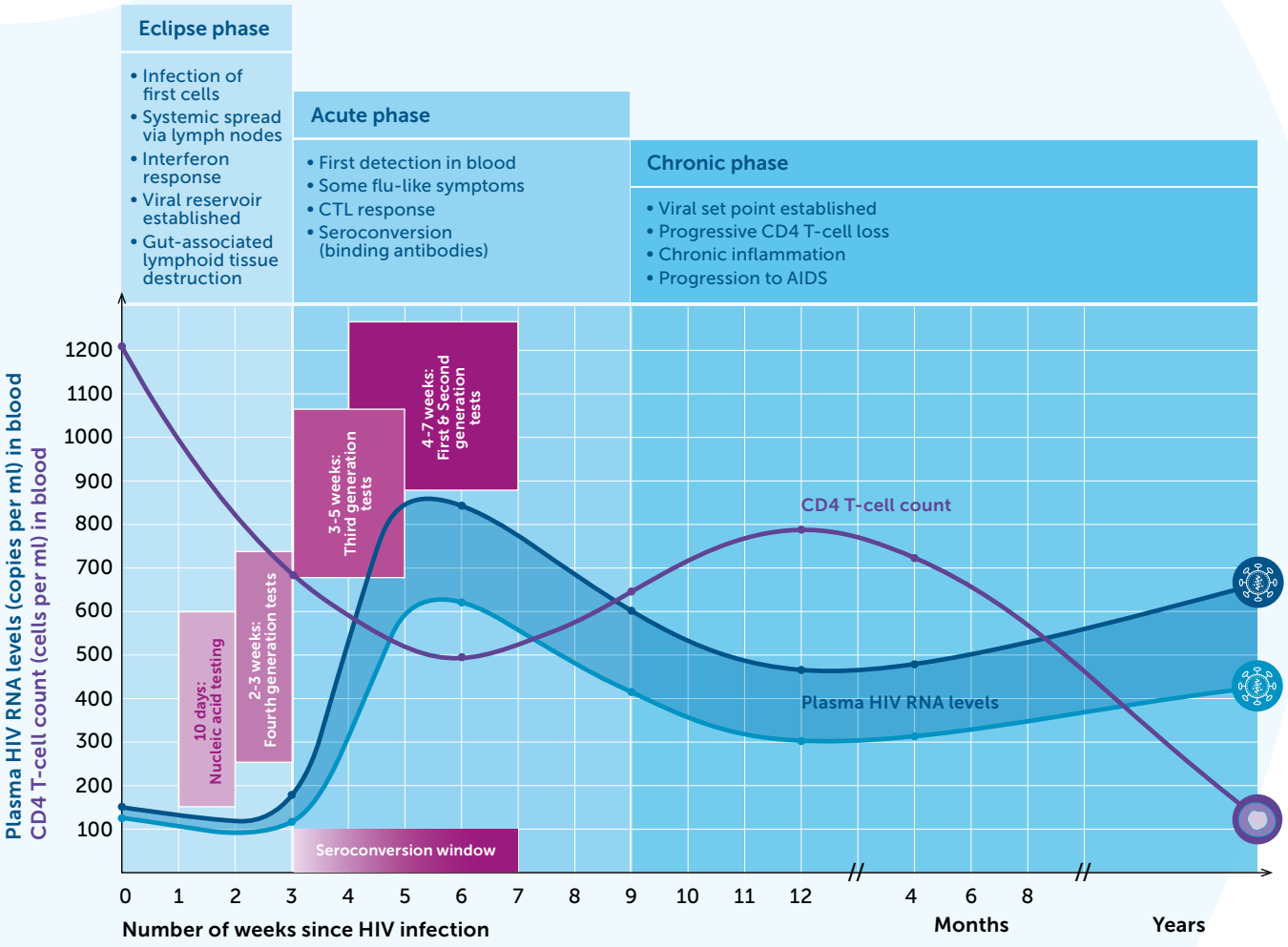
There is no cure for HIV and treatment requires taking a combination of ARVs that reduce the amount of virus in the body. There are now more than 30 ARVs that can be used in first- second-, and third-line therapy. Treatment requires a combination of at least two different drugs that can be made into one pill that must be taken daily for life. New long-acting drugs are being developed that will not require taking pills daily.

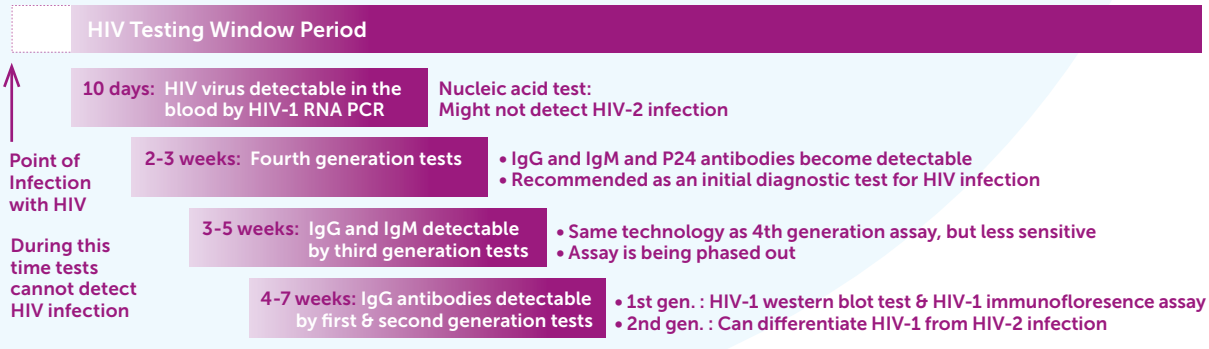
Resistance to treatment can occur, especially when people are not taking treatment as prescribed. This can lead to people needing to change to a different drug regimen, which can be more difficult to take.

People living with HIV on treatment lead healthy, productive lives. Effective treatment also prevents the transmission of HIV from mother to child, and someone who is on antiretroviral therapy and has an undetectable viral load will not pass HIV to their sexual partners.

HIV PROGRESSION

KEY:
- CD4 T-cell count (cells per ml) in blood
- Plasma HIV RNA levels (copies per ml) in blood (higher set point)
- Plasma HIV RNA levels (copies per ml) in blood (lower set point)
- HIV testing window period





FIND OUT MORE...

- Centers for Disease Control and Prevention: *https://www.cdc.gov/hiv/default.html*
- World Health Organization: *https://www.who.int/health-topics/hiv-aids*
- AVERT: *https://www.avert.org/professionals/hiv-science/overview*
- Deeks, S., Overbaugh, J., Phillips, A. et al. HIV infection. Nat Rev Dis Primers 1, 15035 (2015): *https://doi.org/10.1038/nrdp.2015.35*

2. Tuberculosis

2.1 A Brief History

Tuberculosis (TB) has affected humans for thousands of years. It is caused by *Mycobacterium tuberculosis (M.tb)* a bacteria discovered in 1882 by Dr Robert Koch who was awarded the Nobel Prize of Medicine in 1905 for this discovery.

Over two billion people are infected with M.tb worldwide, but only 5–10% will develop tuberculosis during their lifetime. Although anyone can develop TB, the risk is much higher among people living with HIV, as well as people with other risk factors including undernourishment, diabetes, alcoholism, and smoking. Although most cases of active TB disease occur in adolescents and adults, and in men more than women, 1.2 million children also get sick with TB each year.

Before the COVID-19 pandemic, TB was the leading infectious disease killer worldwide and the leading infectious cause of death among people living with HIV. TB remains a major cause of morbidity and mortality, primarily in low- and middle-income countries.

TB is treatable and curable. However, multidrug-resistant TB (MDR-TB) can develop when the TB bacteria become resistant to the ordinary drugs used to treat the disease. This occurs for various reasons:

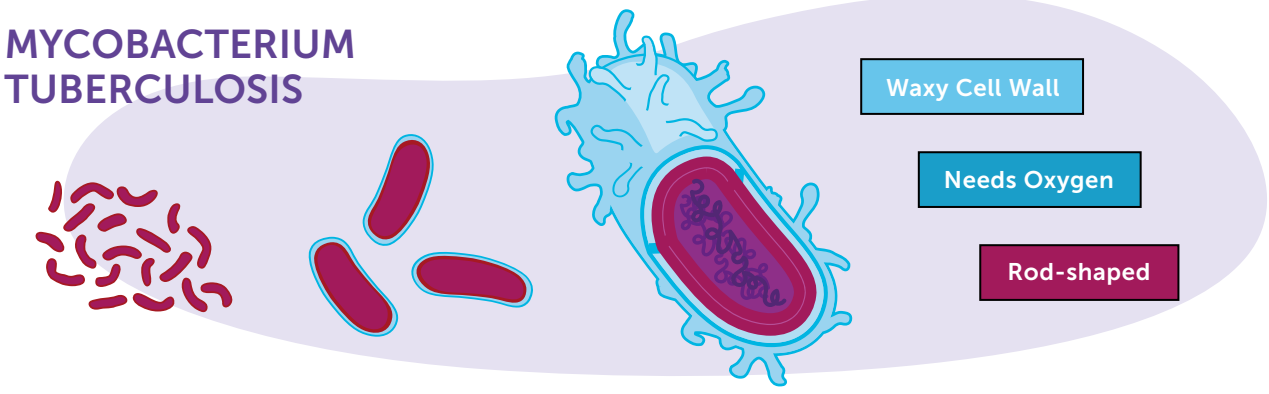
- TB drugs are not prescribed or taken as prescribed.
- Routine TB treatment is not completed.
- Routine TB treatment is stopped and restarted.

A person can also be exposed to someone already infected with MDR-TB. MDR-TB has a huge impact on the cost of treatment and is a public health crisis and a health security threat.

2.2 Mycobacterium tuberculosis (M.tb)

M.tuberculosis is a member of the Mycobacterium family, which includes other bacteria that can be responsible for diseases in humans. Able to survive for several weeks in a dormant state, it grows slowly compared to other bacteria and has unique features that makes it difficult to diagnose, treat, and to develop a vaccine against it. The organism is also able to survive and evolve within its human host.

M.tb is not highly infectious compared to other bacteria and viruses. It spreads primarily through the air from individuals with active pulmonary TB when they speak, cough, spit, or sing.



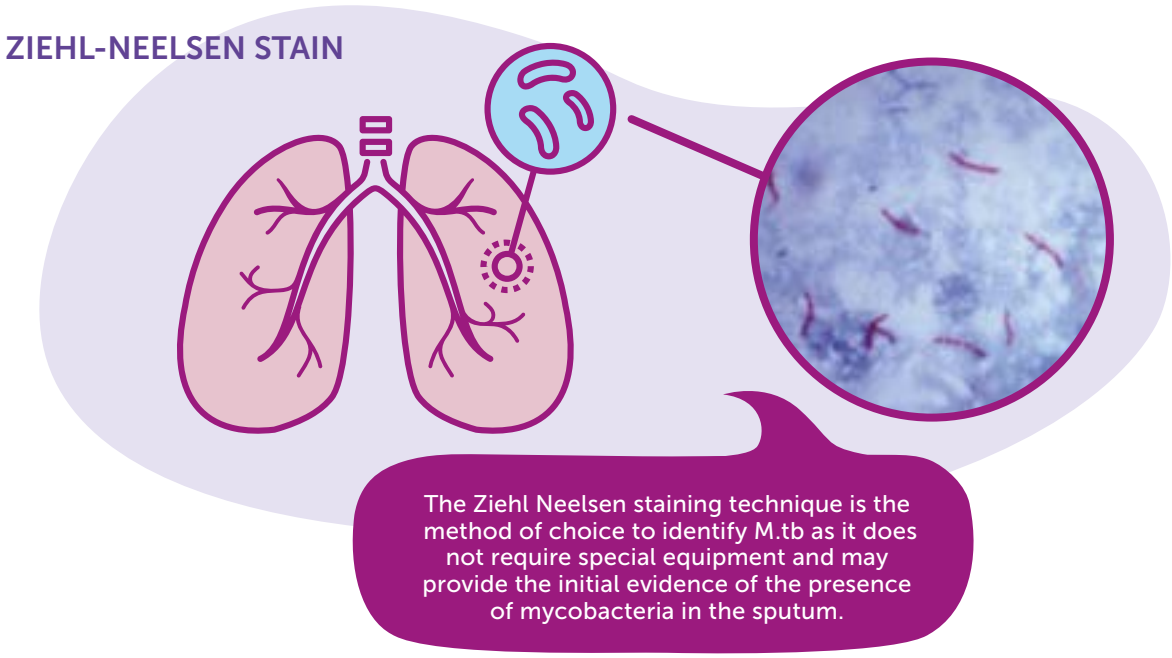
2.3 Diagnosis

TB presents in people in two forms, active and latent TB. The symptoms of a TB infection are diverse depending on where the bacteria are in the body. M.tb most often affects the lungs, causing pulmonary TB. Common signs and symptoms include coughing with sputum (phlegm) and blood at times, chest pain, weakness, weight loss, fever, and night sweats. A person with latent TB disease may have no symptoms. It is important to screen for TB when individuals experience common signs for TB.

Diagnosing TB requires a clinical examination and confirmatory diagnostic tests. In some cases, diagnostic tests are also used to determine if a person has a latent TB infection or the TB disease. Tuberculosis is very difficult to diagnose in children as it can be difficult to distinguish from other respiratory diseases that cause fever.

Diagnostic tests for TB include-

- Mantoux tuberculin skin test (TST) can be performed in the clinic and tells if a person has been infected with M.tb, but not whether the person has latent TB infection or has progressed to TB disease.
- Interferon Gamma Release Assay (IGRA), a blood test performed in a laboratory to assess a person's immune system reaction to M.tb. Additional tests are needed to determine whether the person has latent TB infection or TB disease.
- Imaging techniques (mainly chest X-ray, Positron emission tomography-computed tomography).
- In a laboratory, by visualising the bacteria in phlegm smear with a microscope using special staining techniques (the Ziehl-Neelsen staining).
- In a laboratory, by detecting components of M.tb in the sputum using rapid molecular tests. These tests can also be used to detect if an infecting strain of M.tb is resistant to rifampin, an important drug used in treating active TB.
- M.tb antigen detection in a laboratory, especially for people living with HIV.
- Growing the bacteria in a laboratory from sputum samples. This is considered as the most accurate test but takes up to eight weeks to provide results.



2.4 Disease Progression

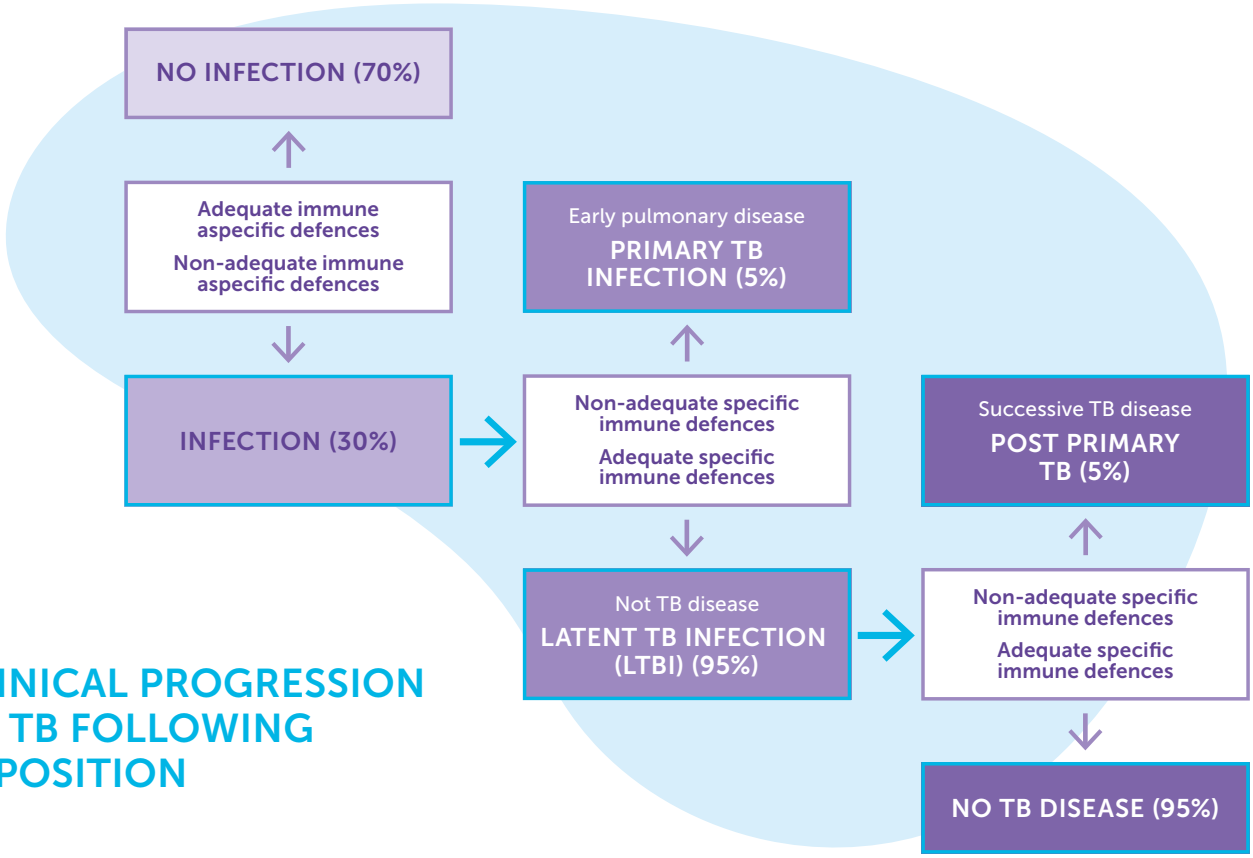
M.tb enters the lungs via inhalation and infects lung macrophages, lung-based scavenger cells that normally ingest and destroy the infecting bacteria. M.tb can prevent its destruction in the macrophages and can survive in these cells where they multiply, infect other cells, and eventually establish new infections in other areas, most commonly the upper parts of the lungs.

If the body can control the infection at this point, and no symptoms develop, the person is said to have latent TB infection (LTBI). People with LTBI are not infectious, but the bacteria can become active, multiply and progress from LTBI to TB disease depending on the person's immunity and comorbidities (for example HIV).

Approximately 5% of all persons infected with M.tb develop active TB disease within the first 18–24 months following initial infection. Another 5% will develop TB at some time later in life. The other 90% of persons infected with M.tb maintain the infection in a latent stage for the rest of their lives (LTBI); an unknown percentage of these M.tb-infected individuals may eradicate the organism completely.

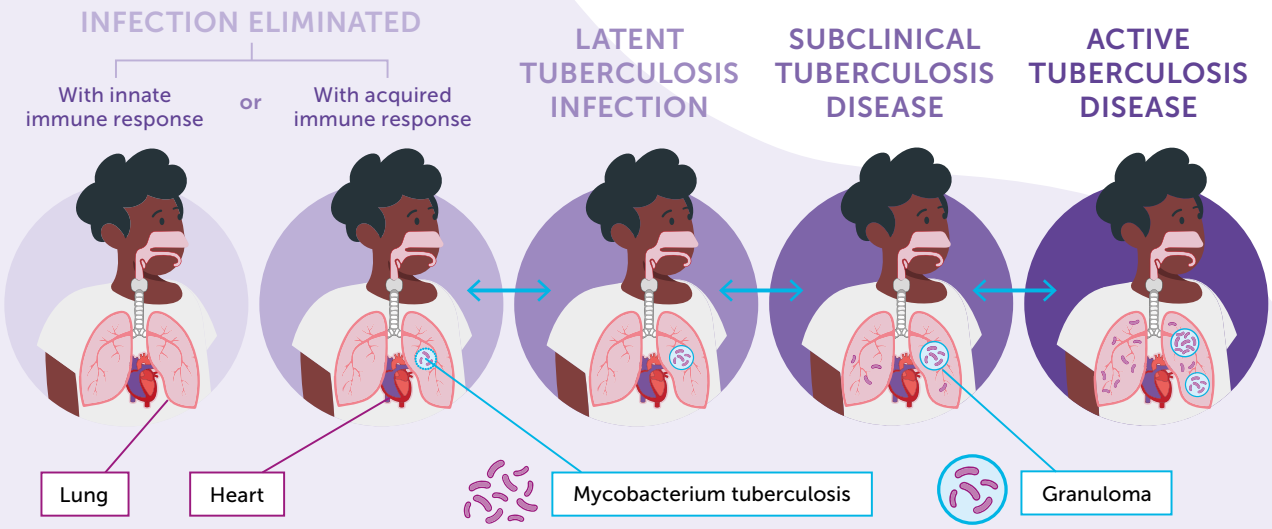
Active TB disease can develop in the lung, or the bacteria may disseminate further in the body and reach other organs and cause active TB in other organs, including the brain and the kidneys. Individuals who have active TB disease are symptomatic and infectious.

- TB disease: after infection, the bacteria persist in the body in an active state. The individual shows a variety of symptoms and can infect others.
- TB latent infection: the bacterium lives in the person's body without making them sick. People are not infectious, but the bacterium can become active, multiply and trigger TB disease.



CLINICAL PROGRESSION OF TB FOLLOWING EXPOSITION

TB CLINICAL PROGRESSION



TST	Negative	Positive	Positive	Positive	Usually positive
IGRA	Negative	Positive	Positive	Positive	Usually positive
Culture	Negative	Negative	Negative	Intermittently positive	Positive
Sputum smear	Negative	Negative	Negative	Usually negative	Positive or negative
Infectious	No	No	No	Sporadically	Yes
Symptoms	None	None	None	Mild or none	Mild to severe
Preferred treatment	None	None	Preventative therapy	Multidrug therapy	Multidrug therapy

Source: Adapted from https://www.nature.com/articles/nrdp201676

2.5 Prevention and Treatment

TB is preventable. Prevention involves both preventing infection and preventing latent TB infection from progressing to TB disease. Important strategies to prevent initial M.tb infection include:

- Avoidance as much as possible of crowded, poorly ventilated spaces in areas where TB disease is endemic (e.g., microbuses, crowded trains, factories, classrooms, camps for displaced persons, barracks for migrant workers).
- Reducing crowding and improving ventilation in locations such as these.
- Active case finding, early diagnosis and treatment; community education and awareness; and the development of vaccines capable of preventing TB disease, particularly in adolescents and adults.
- Early diagnosis and implementation of effective drug treatment of new TB cases is a critically important strategy in preventing the spread of M.tb.
- Emphasising the importance of screening when symptoms are experienced.

The Bacillus of Calmette and Guerin (BCG) is the only vaccine currently available against TB. It was first used in 1921 and is made from a weakened form of *Mycobacterium bovis*, responsible for TB in cattle. BCG vaccination offers variable levels of protection and prevents severe forms of TB in children. It has not been able to prevent the epidemic of global M.tb infection and TB disease and there is currently no vaccine that is effective in preventing TB disease in adolescents and adults, who are responsible for most M.tb transmission.

Not everyone infected with TB bacteria becomes sick. Without treatment however, latent TB infection can progress to TB disease, and result in death. TB infection and active TB disease are treated with different combinations of drugs and different duration of treatment. Drug-sensitive TB is curable with a four- to six-month course of currently available TB treatment. MDR-TB is also treatable, but with a much longer course of multiple drugs that can cause many side-effects.

Standard treatment for TB disease is based on first-line antimicrobials (isoniazid, rifampicin, pyrazinamide, and ethambutol). Resistance to treatment can occur and second-line antimicrobials are then needed, usually administered for up to 20 months based on level of resistance and previous treatment received and may involve daily injections for six months. If treatment fails, extensively drug-resistant TB (XDR-TB) can develop. Treatment of XDR-TB is lengthier, more complex, and more expensive. In resource-limited settings, XDR-TB is extremely difficult to treat, and at times impossible to treat.

There are several treatment regimens recommended for LBTI, and to avoid the development of drug resistant TB, Directly Observed Therapy (DOT) can be used with people who are at high risk for TB disease and who are either taking an intermittent regimen or who may have difficulty with taking treatment regularly.

Drug interactions should be considered when treating people who are also living with HIV.

FIND OUT MORE...

- World Health Organization: *https://www.who.int/health-topics/tuberculosis*
- Centers for Disease Control and Prevention: *https://www.cdc.gov/tb/default.htm*
- Medscape: *https://emedicine.medscape.com/article/230802-overview*
- TB Alliance: *https://www.tballiance.org/*
- TB Vaccine Initiative: *https://www.tbvi.eu/*
- Pai, M., Behr, M., Dowdy, D. et al. Tuberculosis. Nat Rev Dis Primers 2, 16076 (2016).

3. Lassa Fever Virus

3.1 A Brief History

Lassa haemorrhagic fever (Lassa fever) was first described in the 1950s. The virus responsible for the disease, Lassa mammarenavirus (LASV), was identified in 1969 after the death of two missionary nurses in the town of Lassa in Nigeria. The disease is spread by rats and mice that live in large numbers in West Africa where the disease is endemic.

People can get Lassa fever through ingestion of food or inhalation of air contaminated with urine or faeces from infected rodents. Person-to-person transmission may occur after exposure to Lassa virus in the blood, tissue, secretions, or excretions of a Lassa-infected individual, often in health care settings where protective equipment is not available or medical equipment is contaminated. Lassa fever is not spread through direct contact (like hugging, shaking hands, or sitting near someone) but sexual transmission has been reported.

Nearly 60 million people are estimated to be at risk of infection. The proportion of people who die from a confirmed Lassa fever infection is estimated at 1% but among patients who are hospitalised with severe Lassa fever, the fatality rate is estimated at around 15%. The World Health Organization (WHO) has listed Lassa as a high priority pathogen for the development of new prevention and treatment options.

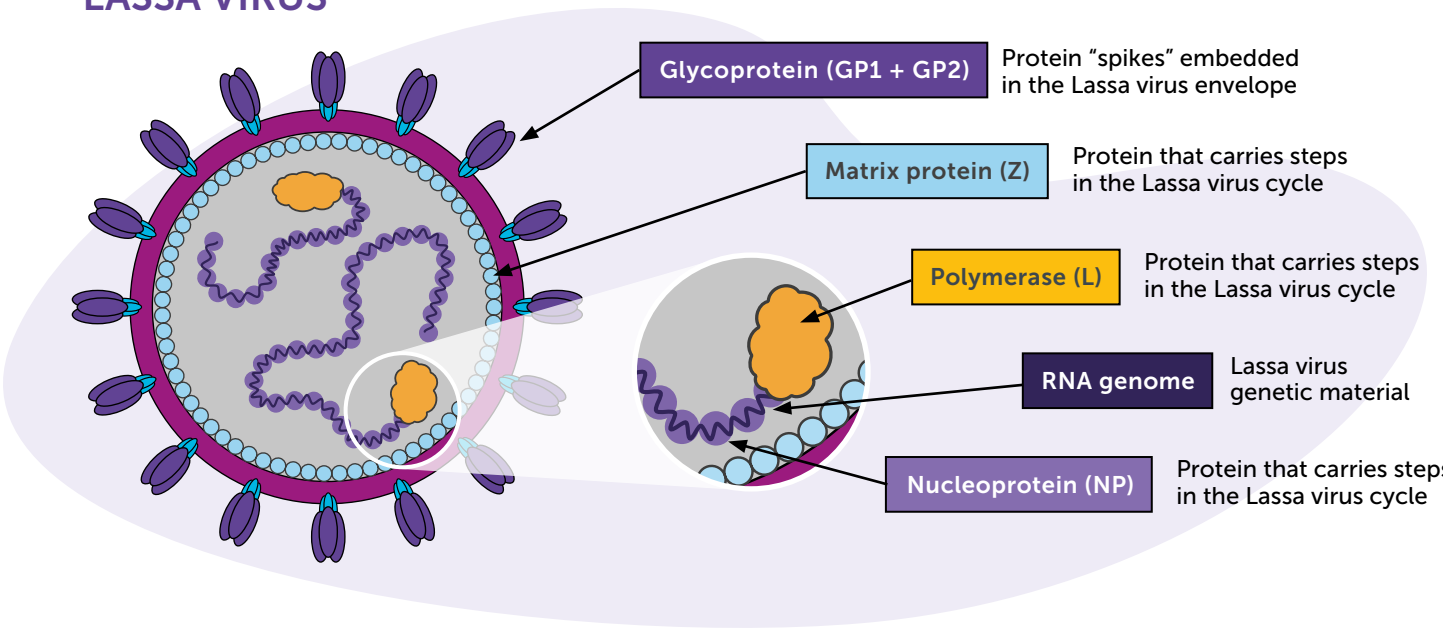
3.2 The Lassa Virus

LASV is a retrovirus, generally spread by rodents that act as the virus' natural reservoir. The LASV genome is made of two single-strand RNA that contains genes for four viral proteins including structural proteins, enzymes, and envelope glycoproteins.

There are six types of LASV identified so far with different geographic localisation. The Josiah strain from Sierra Leone is the most studied and is widely used in vaccine research.

Little is known about the replication and life cycle of the Lassa virus. The virus enters human cells using its envelope glycoprotein and a receptor present at the surface of human cells. Once in the cell, the viral genome is replicated in the cytoplasm using the cell machinery to produce new viral RNA and the different viral components. Viral RNA is then packaged into mature virions that bud out of the infected cells.

LASSA VIRUS



3.3 Diagnosis

Clinical diagnosis of Lassa fever is often difficult due to the variety of non-specific symptoms, many of which are like those observed with other viral haemorrhagic fever such as Ebola.

Definitive diagnosis requires testing only available in specialised laboratories using the following tests:

- Nucleic acid tests (NAT) that detect RNA from the virus in the blood.
- Tests to detect antibodies generated by the body in response to the infection.
- Antigenic tests to detect parts of the virus.
- Virus isolation by cell culture.

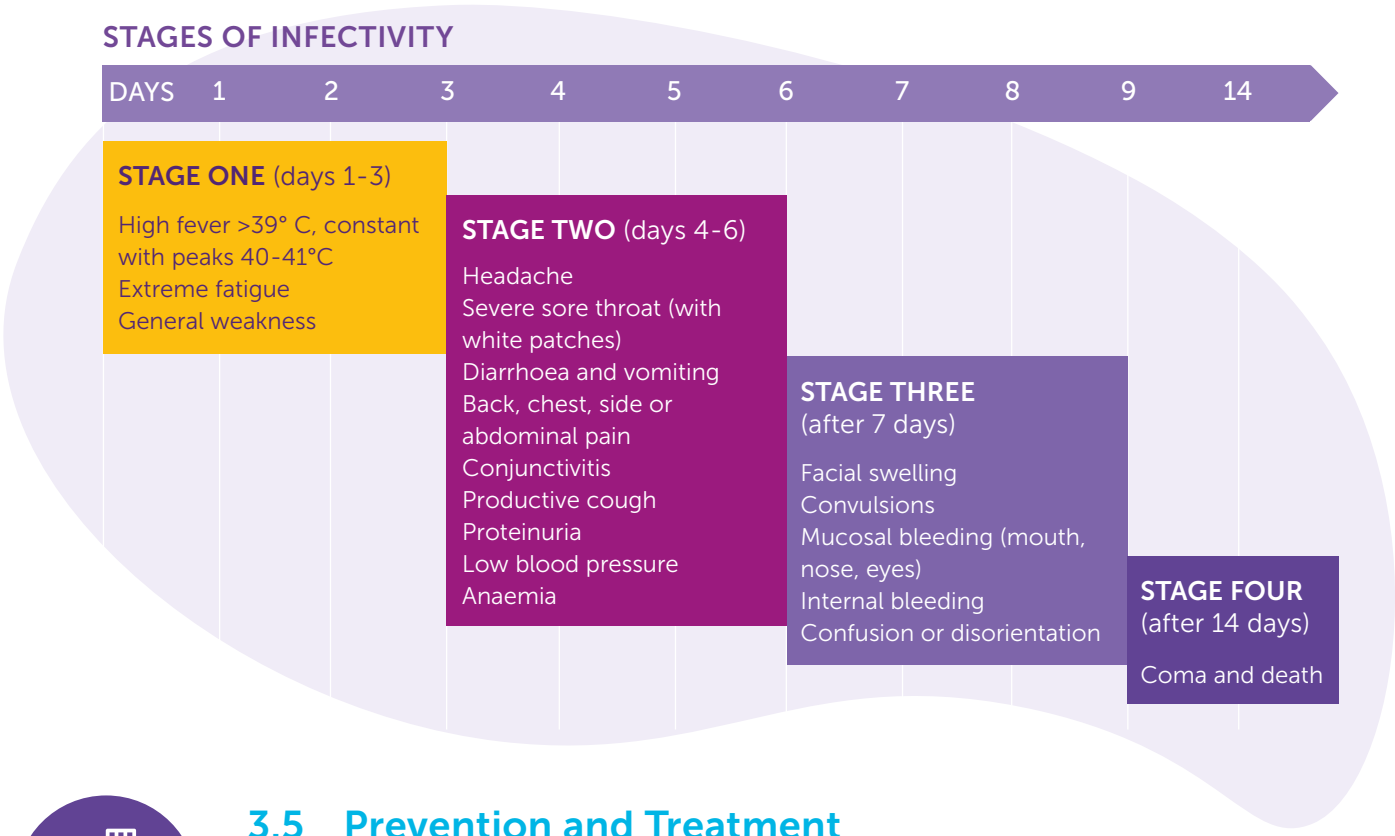
3.4 Disease Progression

Lassa fever is an acute viral haemorrhagic fever that is often mild or has no observable symptoms for most of the infections (approximately 80%). Symptoms include slight fever, general malaise and weakness, and headache.

However, for 20% of infected individuals, severe illnesses are observed including bleeding (in gums, eyes, or nose, for example), respiratory distress, repeated vomiting, facial swelling, pain in the chest, back, and abdomen, and shock. Death may occur within two weeks after symptoms start due to multi-organ failure and although 1% case fatality has been reported, there is considerable uncertainty around this estimate with some believing that this is an underestimate. Various degrees of deafness have been seen to occur in 25% of recovered patients with hearing returning in half the cases after 1–3 months.

Lassa fever is especially severe in pregnant women, with an increased maternal mortality in the third trimester (greater than 30%) and spontaneous abortion with an estimated 90% mortality in foetuses of infected pregnant mothers. Lassa is also a significant cause of child hospitalisations in some areas of West Africa.

TIMELINE OF LASSA FEVER DISEASE FROM SYMPTOM ONSET



3.5 Prevention and Treatment

Community education in areas affected is an important part of the control and prevention of Lassa fever. Prevention relies on good 'community hygiene' to prevent rodents from entering homes and good public health practice to prevent transmission in health-care settings.

There is currently no approved treatment for Lassa fever. Off-label use of ribavirin, an antiviral medication used to treat chronic hepatitis C, fluid replacement, and dialysis are used for the treatment of severe Lassa fever.

Several treatments are under investigation including the antiviral favipiravir, plasma from convalescent people that contain antibodies against the virus, and a human monoclonal antibody cocktail that have shown some efficacy in preclinical research and a potential for use in clinical settings.

FIND OUT MORE...

- Centers for Disease Control and Prevention: *https://www.cdc.gov/vhf/lassa/index.html*
- World Health Organization: *https://www.who.int/health-topics/lassa-fever*
- Purushotham J, Lambe T, Gilbert SC. Vaccine platforms for the prevention of Lassa fever. Immunology Letter 215:1-11, (2019).

Glossary

A

Acquired immunity: immunity that develops during a person's lifetime.

Adjuvant: a substance added to its formulation to enhance or modify the immune response to the components of the vaccine.

Adverse event: an unexpected medical problem experienced by an individual in a clinical trial. The term is used whether the effect can be attributed to the vaccine under study or something else happening during the study.

Adverse reaction (also known as adverse event or side effect): in a clinical trial, an unwanted effect detected in participants and attributed to the study vaccine.

AIDS (acquired immunodeficiency syndrome): the most advanced stage of HIV infection, characterised by a deterioration of the immune system and a susceptibility to a range of opportunistic infections and cancers.

Antibody: a protein found in the blood or bodily fluids that binds, neutralises, and helps destroy pathogens (e.g., bacteria, viruses) or toxins. Antibodies are also known as immunoglobulins. Each antibody binds specifically to the antigen that stimulated its production.

Antibody-mediated immunity: immunity that results from the activity of antibodies. Also called humoral immunity.

Antigen: any substance that stimulates the immune system to trigger an immune response.

Antigen-presenting cell (APC): B cell, macrophage, dendritic cell or other cells that ingest and process pathogens such as bacteria and viruses. An APC displays fragments of the pathogen on its surface to attract and activate the cells of the immune system that respond specifically to that antigen (see also dendritic cell; macrophage).

Antiretrovirals: drugs that reduce the ability of HIV or other types of viruses to multiply in the body.

Apoptosis: cellular suicide. A possible mechanism used by HIV to destroy cells of the immune system. HIV may cause apoptosis in both HIV-infected and HIV-uninfected immune system cells. Also known as programmed cell death.

Arm: a group of participants in a clinical trial, all of whom receive the same treatment, intervention, or placebo.

Attenuated: weakened. Attenuated viruses are often used as vaccines because they can no longer produce disease but still stimulate a strong immune response, similar to that caused by the natural virus.

B

B lymphocyte (B cell): one of the two major classes of lymphocytes, B lymphocytes are white blood cells of the immune system that are derived from the bone marrow and spleen. B cells develop into plasma cells, which produce antibodies.

Baseline: the time point in a study just before initiation of an intervention (for example vaccination). Measurements taken at later time points may be compared with those taken at baseline to determine if the intervention makes a difference.

B

Binding antibody: an antibody that attaches to part of a pathogen. Binding antibodies may or may not lead to the killing of the pathogen.

Blinded study: a clinical trial in which participants are unaware as to whether they are in the experimental or control arm of the study. See also double-blind study.

Booster: a vaccine dose given after the first dose to increase the immune response to the vaccine antigen(s). A booster may be given shortly after the first dose or much later. The vaccine given as the booster dose may or may not be the same as the primary vaccine. See also prime-boost.

Breakthrough infection: an infection that occurs during a vaccine trial conducted to prevent that infection. Such an infection is caused by exposure to the infectious agent and may occur before or after the vaccine has taken effect or all doses have been given.

C

CD: abbreviation for 'cluster of differentiation,' referring to molecules at the surface of cells that are used to identify immune cells, for example, CD4+ T cells.

CD4+ T lymphocyte: cell of the immune system that carries a molecule on its surface known as 'cluster of differentiation 4' (CD4). These cells are the primary targets of HIV. Also known as helper T cells, CD4+ T cells help orchestrate the immune response, including antibody responses as well as CTL responses (see also T cell).

CD8+ T lymphocyte: cell of the immune system that carries a molecule on its surface known as 'cluster of differentiation 8' (CD8) (see also cytotoxic T lymphocyte (CTL); T cell).

Cell-mediated immunity (cellular immune response): the immune response coordinated by T cells. This branch of the immune system targets cells infected with microorganisms such as viruses, fungi, and certain bacteria.

Challenge: in vaccine research and development, the deliberate exposure of an immunised animal to the infectious agent. Challenge experiments are never done in human HIV vaccine research.

Circulating recombinant forms (CRFs): HIV made of different subtypes of the virus that have recombined.

Clade: a group of related viruses classified according to their degree of genetic similarity. Also called a subtype or strain.

Cohort: groups of individuals who share one or more characteristics in a research study and who are followed over time. For example, a vaccine trial might include two cohorts, a group at low risk for HIV and a group at higher risk for HIV.

Complement proteins: blood proteins that play an important role in the immune response. Generally, complement proteins amplify the effects of antibodies and inflammation.

Control arm: in vaccine clinical trials, the group of participants that is not given the experimental intervention. The control arm can be given an intervention that is considered effective (the standard of prevention), a placebo, or no intervention. The control group is compared with one or more groups of participants given experimental vaccines to measure any effects of the vaccines tested as well as to measure differences in safety.

C

Core: the section of a virus that contains the genetic information and other proteins needed for a virus to replicate.

Correlates of immunity (correlates of protection): the immune responses a vaccine or natural immunity need to trigger to protect an individual from a certain infection.

Cytokine: a hormone-like protein produced by white blood cells that acts as a messenger between cells. Cytokines can stimulate or inhibit the growth and activity of various immune cells. Cytokines are essential for a coordinated immune response and can also be used as immunologic adjuvants. HIV replication is regulated by a delicate balance among cytokines.

Cytotoxic T lymphocyte (CTL): a type of immune system cell that can destroy cancer cells and cells infected with viruses, fungi, or certain bacteria. Also known as killer T cells.

D

Deletion (genetic): elimination of a gene or portion of a gene. Genetic deletion can occur naturally or in the laboratory.

Dendritic cell: antigen-presenting cell with thread-like tentacles (called dendrites) used to surround antigen, which they present to T cells.

DNA (deoxyribonucleic acid): the double-stranded, helical molecular chain found within the nucleus of each cell. DNA carries the genetic information that encodes proteins and enables cells to reproduce and perform their functions.

Dose-ranging study: a clinical trial in which two or more doses (starting at a lower dose and proceeding to higher doses) of a vaccine are tested against each other to determine which dose works best and has acceptable side effects.

Dose-response relationship: the relationship between the dose of a vaccine and an immune or physiologic response. In vaccine research, a dose-response effect means that as the dose of the vaccine increases, so does the level of the immune response.

Double-blind study: a type of clinical trial in which neither the participants nor the research team know which intervention a specific participant is receiving. This helps prevent bias or expectations from influencing the results of the study.

Data and Safety Monitoring Board (DSMB): a committee of independent clinical research experts who review data while a clinical trial is in progress. The DSMB ensures that participants are not exposed to undue (unacceptable) risk and looks for any differences in effectiveness between the experimental and control groups. The DSMB may review the data in such a way that they know which group received the vaccine and which group did not. This group may also recommend that a trial be modified or stopped if there are safety concerns or if the trial objectives have been achieved or will not be achieved. See futility.

E

Effectiveness: the measurement of how well a vaccine works to reduce infection or disease in the overall population when used in the 'real world.'

Efficacy: the measurement of how well a vaccine works at producing a desired clinical effect in optimal conditions, that is, in clinical trials.

ELISA (enzyme-linked immunoabsorbent assay): a laboratory test to detect the presence of antibodies in the blood or other body fluid.

E

Endpoint: an outcome or event used to objectively measure the effect of a drug or other intervention being studied in a clinical trial. Common endpoints include infection, severe toxicity, relief of symptoms, and improvements in quality of life.

Envelope: outer surface of a virus, also called the coat. Not all viruses have an envelope.

Enzyme: a protein produced by cells to trigger a specific chemical reaction. Enzymes are generally named by adding the ending '-ase' to the name of the substance on which the enzyme acts (for example, the HIV reverse transcriptase converts HIV RNA into viral DNA)

Epidemic: a widespread outbreak of a disease in a large number of individuals over a particular period of time either in a given area or among a specific group of people.

Epidemiology: the study of the characteristics, frequency, and distribution of diseases in human populations.

Epitope: a specific part of an antigen that stimulates specific immune responses.

Experimental arm: in a clinical trial, the group of participants given the intervention being studied. Outcomes in the experimental arm are compared with those in the control arm to determine any differences, for example, in safety and effectiveness.

F

Functional antibody: an antibody that binds to an antigen and has an effect that can be demonstrated in laboratory tests. For example, neutralising antibodies are functional antibodies that inactivate HIV or prevent it from infecting other cells.

Futility: the inability of a clinical trial to achieve its objectives. A clinical trial can be stopped when an interim analysis of the results by the DSMB suggests that it is unlikely to achieve its objective and stopping it can save resources and time that could be used on more promising research.

G

Genetic engineering: the laboratory technique of recombining genes to produce proteins used for drugs and vaccines.

Genome: the complete genetic material of an organism, including all its genes. The genomes of viruses can exist as DNA or RNA.

Glycoprotein (gp): A protein that is coated with carbohydrates (sugars).

H

Healthy participant: someone with no known significant health conditions who participates in research to test a new drug, device, or intervention. Also known as 'Clinical Research Participant.'

Helper T cell: T-cell lymphocyte bearing the CD4 marker. Helper T cells regulate the functions of other cells of the immune response.

Herd immunity: protection from an infectious disease happening when a significant percentage of a population is immune to the infection either through vaccination or immunity developed through previous infection.

Host: a plant or animal harbouring another organism.

Humoral immunity: see antibody-mediated immunity.

Hypothesis: a proposed explanation made based on limited evidence as a starting point for further investigation.

I

Immune complex: an antigen bound to its specific antibody.

Immune deficiency: a breakdown or inability of certain parts of the immune system to function, thus making a person susceptible to diseases that they would not ordinarily develop.

Immunisation: the process of inducing immunity by administering a vaccine.

Immunity: protection provided by the immune system to a specific disease. Immunity may be innate or acquired, partial or complete, specific or nonspecific, long-lasting, or temporary.

Immunocompetent: capable of developing an immune response; possessing a normal immune system.

Immunogen: a substance capable of provoking an immune response. Also called an antigen.

Immunogenicity: the ability of an antigen or vaccine to stimulate immune responses.

Immunoglobulin: a general term for antibody immunotherapy: a treatment that stimulates or modifies the body's immune response.

in vitro: an artificial environment outside a living organism (e.g., in a laboratory) used for the conduct of experimental research.

in vivo: research performed with a living organism, e.g., human or animal studies.

Incidence: the number of individuals who develop a specific disease or experience a specific health-related event during a particular period of time (such as a month or year).

Inclusion/exclusion criteria: factors used to determine whether a person is eligible (inclusion criteria) or not eligible (exclusion criteria) to participate in a clinical trial. Eligibility criteria may include disease type and stage, other medical conditions, previous treatment history, age, and gender.

Informed consent: a process between a person and a researcher to ensure that the person understands all relevant facts associated with their participation in a clinical trial. Participants into a clinical trial are required to sign an informed consent form before joining a clinical trial to show that they understand the risks and benefits of participating in the research. Informed consent includes the right to leave a clinical trial at any point during the study.

Innate immunity: immunity that is present at birth and lasts a person's entire life. Innate immunity is the first response of the body's immune system to a harmful foreign substance or pathogen.

Institutional Review Board (IRB): a committee of medical professionals, statisticians, community advocates, and others that reviews clinical trial protocols before they can be initiated. IRBs ensure that the trial is scientifically sound, ethical, and that the rights and safety of participants are adequately protected.

K

Key populations: groups of people such as sex workers, people who use drugs, prisoners, transgender people, and men who have sex with men that are at higher risk of HIV or TB, in part due to discrimination and social exclusion.

L

Latent TB infection (LTBI): a state of persistent immune response to stimulation by *Mycobacterium tuberculosis* antigens without evidence of active TB.

Live-vector vaccine: a vaccine in which a live pathogen is weakened (attenuated) through chemical or physical processes to produce an immune response without causing the severe effects of the disease.

Lymphadenopathy: enlargement of the lymph nodes in response to regional infection or inflammation.

Lymphocyte: a type of white blood cell primarily responsible for immune responses. Present in the blood, lymph, and lymphoid tissues. See also B cell and T cell.

Lymphoid tissue: the part of the body that plays an important role in the immune response and helps protect it from infection and pathogens. Lymphoid tissue is present throughout the body and includes the lymph nodes, spleen, tonsils, adenoids, and other organs.

Lymphomas: types of cancer that begin in the lymphatic system.

M

Macrophage: a large cell of the immune system that can ingest pathogens. Macrophages stimulate other immune cells by presenting them with small pieces of the pathogen. Macrophages also can harbour large quantities of HIV without being killed, acting as reservoirs of the virus.

Memory cell: a subset of T cells and B cells that help the body defend itself against disease by remembering prior exposure to specific pathogens. They can proliferate (recognise the antigen and divide) more readily when the immune system re-encounters the same pathogen.

Monoclonal antibody: a custom-made, identical antibody that recognises only one epitope.

Monocyte: a type of immune cell that is made in the bone marrow and travels through the blood to tissues in the body where it becomes a macrophage or a dendritic cell.

Monovalent vaccine: a vaccine that contains only one antigen.

Mucosal immunity: immune response pertaining to mucous membranes. Mucosal immunity relies on immune cells and antibodies present in the linings of the reproductive tract, gastrointestinal tract, and other moist surfaces of the body exposed to the outside world.

N

Natural killer cell (NK cell): a type of immune cell that can kill tumour cells or cells infected with a virus or bacteria. An NK cell is a type of white blood cell. NK cells are 'natural' killers because they do not need to recognise a specific antigen to attack and kill their target.

Neutralising antibody: an antibody that prevents a virus from infecting a cell in the body, usually by blocking receptors on the cell or the virus itself.

Nosocomial: an infection acquired or occurring in a hospital.

Nucleic acid: an important class of macromolecules found in all cells and viruses. Nucleic acids play an important role in how genetic information is stored and used.

Nucleic acid test (NAT): a laboratory test to detect the genetic material of a microorganism. The viral load (HIV RNA) test is a type of nucleic acid test.

O

Off-label use: the legal use of a prescription drug to treat a disease or condition for which the drug has not already been approved by the regulatory authority.

Open-label trial: a type of clinical study in which both the researchers and the participants are aware of the drug or treatment being given.

Opportunistic infection: an illness caused by an organism that usually does not cause disease in a person with a healthy immune system.

P

Pandemic: An epidemic occurring over a very wide area (several countries or continents) and usually affecting a large proportion of the population.

Parenteral: administered into the bloodstream or by injection.

Pathogen: organisms (e.g., bacteria, viruses, parasites, and fungi) that cause disease in human beings.

Pathogenesis: the origin and development of a disease. More specifically, the way a microbe (bacteria, virus, etc.) causes a disease.

Peptide: a short compound formed by linking two or more amino acids. Peptides that contain many amino acids are called polypeptides or proteins.

Phase I clinical trial: The first step in testing a new vaccine in humans. A Phase I clinical trial tests the safety, side effects, best dose, and timing of a new vaccine.

Phase II clinical trial: These trials measure safety and immunogenicity in a larger group (50–3000) of participants. Here the goal is also to find the best dose and regimen. Phase II trials may last up to two years or longer.

Phase III vaccine trial: A large study that tests the safety and how well a new vaccine works compared with a standard treatment.

Placebo: An inactive substance or other intervention that looks the same as, and is given the same way as, the vaccine being tested.

Plasma: The clear, yellowish, fluid part of the blood that carries the blood cells.

Preclinical: research often using animals to find out if a drug, procedure, or treatment is likely to be useful. Preclinical studies take place before any testing in humans is done.

Prevalence: the total number of individuals in a population who have a disease or health condition at a specific point in time, usually expressed as a percentage of the population.

Prime-boost: in HIV vaccine research, administration of one type of vaccine, such as a live-vector vaccine, followed by or together with a second type of vaccine, such as a recombinant subunit vaccine. The intent of this combination regimen is to induce different types of immune responses and enhance the overall immune response, a result that may not occur if only one type of vaccine were to be given for all doses.

Priming: the first dose of a vaccine given to induce a particular immune response, followed by or together with a second dose of vaccine. The intent of priming is to induce certain immune responses that will be enhanced by the booster dose(s).

Prophylaxis: the prevention of disease.

Protocol: the detailed plan for a clinical trial that states the trial's rationale, purpose, vaccine dosage, routes of administration, length of study, eligibility criteria and other aspects of trial design.

R

Randomised trial: a study in which participants are assigned by chance to one of two or more intervention arms or regimens. Randomisation minimises the differences among groups by equally distributing people with particular characteristics among all the trial arms.

Reactogenicity: physical reactions that occur soon after vaccination and are a physical manifestation of the inflammatory response to vaccination.

Reagent: any chemical used in a laboratory test or experiment.

Receptor: a molecule on the surface of a cell that can recognise and bind to other molecules such as antigens, antibodies.

Recombinant DNA technology: the technique by which genetic material from one organism is inserted into a cell to mass produce proteins.

Regulatory gene: genes that regulate the replication of pathogens.

Reservoir: HIV-infected cells that are not actively producing HIV.

Retrovirus: viruses that carry their genetic material in the form of RNA rather than DNA and have the enzyme reverse transcriptase that can transcribe it into DNA. In turn, this DNA will be used to create viral RNA in the infected cells.

Reverse transcriptase: the enzyme found in retroviruses that enables them to direct a cell to make DNA from their viral RNA.

RNA (ribonucleic acid): one of two types of nucleic acid made by cells. RNA contains information that has been copied from DNA (the other type of nucleic acid). Many forms of RNA have functions related to making proteins.

S

Seroconversion: the production of antibodies against a particular antigen in the blood of a person who did not have the antibodies before. When people develop antibodies, they 'seroconvert' from antibody-negative to antibody-positive (see also VISP).

Serostatus: the state of either having or not having detectable antibodies against a specific antigen, as measured by a blood test (serologic test).

Serum: the clear, yellowish liquid part of blood that remains after clotting. Serum is used for various laboratory tests.

Simian-Human Immunodeficiency Virus (SHIV): a genetically engineered hybrid virus with a human virus envelope and a simian virus core.

Side effect: see adverse reaction.

Simian Immunodeficiency Virus (SIV): a diverse group of viruses that naturally infect a wide range of African monkeys. This infection generally does not result in immunodeficiency in African monkeys, but Asian or Indian rhesus macaques will develop simian AIDS (SAIDS).

Statistical significance: a mathematical measure of difference between groups in a clinical study. The difference is said to be statistically significant if it is greater than what might be expected to happen by chance alone.

Sterilising immunity: an immune response that completely prevents the establishment of an infection.

Strain: a specific version of virus of bacteria. Many diseases, including HIV and Lassa fever virus have multiple strains.

S

Stratification: separation of a study cohort into subgroups or strata according to specific characteristics.

Subtype: a subgroup of genetically related HIV-1 viruses. Also called a clade.

Subunit vaccine: a vaccine that contains only part of the virus or other pathogen which have been specially selected for their ability to stimulate immune cells.

Surrogate marker: substitute measure of a clinical or biological endpoint. For example, CD4 count is a surrogate marker of disease progression.

T

T cell: a type of white blood cell critical to the immune response. Among these are CD4 T cells and CD8 T cells.

Therapeutic HIV vaccine: a vaccine designed to boost the immune response against HIV in a person living with the virus to slow the progression of HIV infection or delay the onset of AIDS.

V

Vaccine: a substance administered to trigger an immune response against a particular disease to prevent an infection.

Vector: a bacteria or virus that does not cause disease in humans and is used in genetically engineered vaccines to transport genes coding for antigens into the body to induce an immune response.

Viral Load (VL): the amount of HIV in a sample of blood. Viral load is reported as the number of HIV RNA copies per millilitre of blood.

Viremia: the presence of virus in the bloodstream.

Virion: a mature infectious virus particle that exists outside of a cell.

Virus: a microorganism that infects cells and may cause disease. To reproduce, a virus must infect a cell and direct its cellular machinery to produce new viruses.

Vaccine-Induced HIV Seropositivity (VISP): antibody induced by vaccination and that can confound the interpretation of HIV diagnostics tests. VISP may have implications in the everyday life of clinical trial participants (for example access to insurance, employment, or immigration).

W

Western blot: a laboratory test to detect antibodies to specific components of a virus such as HIV in the blood.

Window period: the period of time from exposure to HIV to when the body produces enough HIV antibodies to be detected by standard HIV tests.

RESOURCES

- NIH glossary of HIV/AIDS-related terms: *https://clinicalinfo.hiv.gov/en/glossary*
- CDC Vaccines and immunisation glossary: *https://www.cdc.gov/vaccines/terms/glossary.html*

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