

## SECTION 1

# HIV AND VIROLOGY

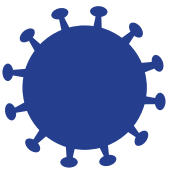
This section provides information about HIV as a virus. What kind of infection is HIV; what happens after you are infected and how is the virus monitored?



After reading this section, you will have a basic understanding of:

- » The definition of HIV.
- » The difference between different causes of illness: viruses, bacteria, fungi and parasites.
- » Viral load in early and chronic infection and the natural history of HIV.
- » The impact of coinfections on viral load.
- » Viral load tests and their accuracy.
- » Viral load in relation to whether or not you are taking HIV treatment (ART).
- » The HIV viral life cycle.

## DEFINITION OF HIV



HIV stands for Human Immunodeficiency Virus.

**Human** – means it is a virus that infects humans.

**Immunodeficiency** – means it reduces the immune system.

**Virus** – means that the infection is a virus!

- » A **virus** is genetic organism that can only reproduce inside cells of another living organism. Some viruses are harmless and others can cause illness. Anti-viral drugs are used to treat viral infections.
- » **Viral infections** that affect people with HIV include hepatitis A, B and C, herpes (HSV-1 and HSV-2), cytomegalovirus (CMV), and human papilloma virus (HPV).
- » HIV belongs to a family of viruses called **retroviruses**. This is why HIV drugs are called **antiretrovirals (or ARVs)**.
- » A retrovirus is a type of virus that needs to make a **'backward step'** in order to reproduce – hence 'retro'.

## OTHER CAUSES OF ILLNESS

As well as viruses, other things can affect your health. This includes bacteria, fungi, parasites and protozoa.

Different types of drugs are used for each infection. For example, antibiotics work against bacteria but they do not work against viruses.

The difference between viral, bacterial and fungal infections is not always clear.

But, sometimes drugs designed to treat one kind of infection also work against a another type. This is complicated because it applies only to individual drugs for specific infections.



### BACTERIA

Bacteria are single-cell microorganisms. Some bacteria are healthy and help your body. Some bacteria are dangerous and cause disease. Antibiotic drugs are used to treat bacterial infections.

Examples of bacterial infections that affect people with HIV include tuberculosis, bacterial pneumonia, sinusitis, gonorrhoea and some skin infections.



### FUNGI

Fungi are parasitic organisms that include moulds, mildews, mushrooms and yeast. Antifungal drugs are used to treat fungal infections.

Examples of fungal infections that affect people with HIV include candida (thrush) and cryptococcosis.



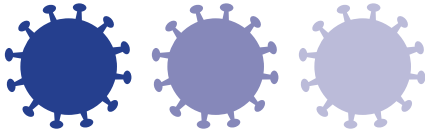
### PARASITES AND PROTOZOA

A parasite is an animal or plant that gets nutrients and support from another species. This includes protozoa which are single-celled animals that are larger and more complex than bacteria.

Examples of parasite-related infections are cryptosporidium and microsporidium. An example of an illness cause by protozoa is toxoplasmosis.

## HIV AND INFECTION: KEY FACTS

- » The **risk of HIV transmission** is related to how much virus is in the blood or infectious fluids. The risk is highest when the viral load is high. Levels of HIV are measured using viral load tests.
- » HIV is **not infectious** in saliva, spit, tears, urine or faeces.
- » Outside the body, HIV in blood or other bodily fluids is thought to die within a minute or so.
- » HIV is a difficult virus to catch from sexual exposure. But only one exposure is needed to become HIV positive. This is just good or bad **luck**.
- » HIV is much easier to catch from sharing **infected needles** or other IV drug taking equipment. This is because there is direct blood-to-blood contact.
- » HIV enters the blood by broken **skin** or through cells that are close to the surface of the skin. This can include contact with **mucous membranes** (the type of tissue that lines the inside of the vagina, rectum and inner foreskin).
- » **Without testing**, many people with HIV do not know they are HIV positive.
- » **Without treatment** (ART), some people (less than 5%) will become ill within 1 to 2 years. A few people (also less than 5%) can go for 15 years without symptoms.
- » Although a lot of information about your health and HIV comes from blood tests, **less than 2%** of the HIV in your body is in your blood.
- » Most HIV is in your **lymph system and lymph nodes**. These are the little lumps that sometimes get enlarged in your neck, under your arms, and in the crease between your legs and your body.



## THE NATURAL HISTORY OF HIV INFECTION

The natural history of any illness describes the pattern of a disease if it is not treated. It is very important to understand the natural history of HIV.

The natural history of HIV infection has several different stages. These stages include infection, seroconversion, primary infection, chronic infection and late-stage illness.

### HIV treatment (ART) prevents progression of the HIV disease.

#### STAGE 1: INFECTION

- » This is the point when HIV infects the first cells. It then takes several hours for these newly infected cells to carry HIV to the lymph nodes.
- » During the next few days or weeks, HIV continues to multiply in the lymph nodes. Lymph nodes are packed with CD4 cells, which HIV uses to reproduce.

#### STAGE 2: SEROCONVERSION

- » After building up in the lymph nodes, the nodes burst, sending HIV into the blood. This sends HIV throughout the body. HIV levels (viral load) become detectable in blood and reach very high levels (often millions of copies/mL).
- » As viral load increases, this high level of viral activity produces symptoms in up to 80% people. HIV can cause a range of symptoms that include night sweats, fevers, weakness and tiredness and, more rarely, mouth ulcers.
- » The immune system reacts to viral load in the blood by producing antibodies to fight HIV. It usually takes 1-3 months after infection for antibodies to HIV to be strong enough to be detected on an HIV antigen test. Occasionally it can take longer.

#### STAGE 3: PRIMARY (HIV) INFECTION

- » PHI is also called *early infection* or *acute infection*. Primary infection describes the first six months after infection.

#### STAGE 4: CHRONIC INFECTION

- » Chronic infection describes HIV infection after the first six months. Chronic infection can last for many years. It can take from 2 to 10 years until the majority of people get symptoms from having a damaged immune system. With ART, chronic infection can be life-long – ie 20, 30, or 40 or more years after infection.

#### STAGE 5: ADVANCED HIV DISEASE (AHD)

- » AHD is the most serious stage. AHD is seen in people who do not have access to treatment, who are only diagnosed very late. It is also seen when treatment has stopped working because HIV has become resistant to ARVs.



## EFFECT OF ARVs ON VIRAL DYNAMICS OF HIV INFECTION

After starting ART, viral load should go down by at least 90% (1 log) within the first week – mostly in the first few days.

After starting ART, viral load should then become undetectable (less than 50 copies/mL) within three months. Some people become undetectable after only a month. For some people this takes longer.

How quickly viral load becomes undetectable depends on three main factors.

1. How high viral load is when ART is started.
2. How good someone is at taking their meds and not missing doses.
3. Which HIV drugs are in the combination. Integrase inhibitors (including dolutegravir) reduce viral load quicker than other types of HIV drugs.

- » A few weeks after infection, HIV viral load shoots up to very high levels. This is when someone is most infectious.
- » Then your body fights back. Viral load drops to much lower levels in most people.
- » Without ART, over the next 2 to 10 years viral load increases slowly. Viral load usually becomes very high (around 50,000-200,000 copies/mL) by the time the CD4 count drops to 350 cells/mm<sup>3</sup>.
- » All guidelines recommend ART for all HIV positive people – at any CD4 count.
- » ART stops HIV reproducing once viral load becomes undetectable.
- » After ART brings viral load down to less than 50 copies/mL, ART can last for many years.



## WHAT IS A VIRAL LOAD TEST?

A viral load test is a measurement of the amount of HIV virus in a sample of blood. This is usually reported as the number of copies per millilitre (copies/mL). Even though less than 2% of HIV is in your blood, viral load is a good marker of how much HIV is in your body. Blood tests are also easier than trying to test lymph nodes or other body tissues.

Viral load tests can also check the amount of HIV in other kinds of sample like genital fluid, semen or spinal fluid.

### TYPES OF VIRAL LOAD TEST

There are three main types of viral load tests:

1. **PCR** – polymerase chain reaction (written as PCR RNA). This is the most widely used type of test.
2. **bDNA** – branched DNA
3. **NASBA** – nucleic acid sequence based amplification

These tests work in slightly different ways. PCR is the most widely used viral load test.

PCR technology is also used to measure levels of HIV DNA in some circumstances.

### HOW DO VIRAL LOAD TESTS WORK?

Viral load tests multiply virus found in a small sample of blood many times so that it can be counted more easily. But this means that the individual results from any one test are not very accurate.

Viral load tests can have a 3-fold margin of error. So, if your viral load result is 30,000, the real result could be anywhere between 10,000 and 90,000 copies/mL.

- » Each viral load test has a sensitivity cut off. This is the **lowest level of HIV** that the test can measure. It is a measure of how sensitive the test is.
- » The main cut-off limit for viral load tests is less than 50 copies/mL. Some tests now have a lower cut-off of 20 copies/mL.
- » Special tests can measure down to 5 copies/mL or even to 1 copy/mL. These are only used in research.

## USING VIRAL LOAD AND CD4 COUNT TO MONITOR HIV

Used together, CD4 counts and viral load results will tell a doctor nearly everything about the risk to your health from HIV. These tests also show how well treatment is working.

Viral load test results can be used together with CD4 counts to monitor HIV infection. Never make any treatment decision based on the result of one test.

When using HIV treatment, viral load is important, not CD4 count, because not getting viral load below 50 copies/mL will limit how long ART will work.

Viral load tests are used in many countries, including South Africa, but are difficult to get in others.

Even if you do not have access to these tests, it makes a difference that you understand how CD4 count and viral load change.

## IMPACT OF CO-INFECTIONS ON VIRAL LOAD

Other infections can increase HIV viral load.

- » Having another virus can increase HIV viral load.
- » Some sexually transmitted infections (STIs) increase levels of HIV in genital fluids, but only by relatively small amounts. These STIs include herpes, gonorrhoea and syphilis. The higher viral load will make HIV slightly more infectious. This is one reason why having other STIs are related to a higher risk of HIV transmission.
- » Luckily, the results from the PARTNER study did not report HIV transmissions when a positive partner had an undetectable viral load in blood, even though some people had STIs that might have increased viral load a little.  
Link: [i-base.info/partner-study/](http://i-base.info/partner-study/)
- » Viral infections like the flu can increase your viral load while the infection is active.
- » Malaria can increase your viral load while the infection is active.
- » Some vaccinations may also increase viral load temporarily.
- » HIV can also increase the levels of other viruses in someone who has HIV and another infection.



## VIRAL LOAD ON AND OFF TREATMENT

### VIRAL LOAD WHEN NOT ON HIV TREATMENT (ART)

When not on ART, your CD4 count is more important than viral load.

Even though ART is now recommended for everyone, the CD4 count still shows if you have a low CD4 and are at risk for AHD

Viral load tests are still useful, but they are not as important at either predicting the risk of infections or when you should start treatment.

### VIRAL LOAD WHEN ON TREATMENT

If you are taking ART, viral load is more important than CD4 count.

This is because on ART, your CD4 count is probably already increasing.

Your viral load when on treatment is the best measure of how long you can expect treatment to last.

If viral load gets to less than 50 copies/mL then ART is likely to last for many years. When viral load is this low, resistance usually only develops if you are late or miss taking your medication.

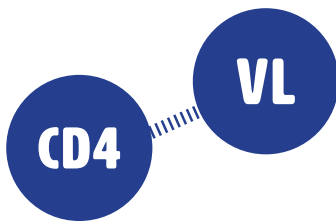
How quickly viral load becomes undetectable depends:

1. How high viral load is when you start ART.
2. How good you are at taking all your meds.
3. What drugs are in your combinations. Integrase inhibitors, like dolutegravir, reduce viral load more quickly than other types of HIV drugs.

## WHAT HAPPENS IF YOU DO NOT HAVE ACCESS TO A VIRAL LOAD TEST?

If you do not have access to a viral load test, then your nurse or doctor will manage you based either on CD4 tests or on clinical symptoms.

Not having access to viral load tests should not be used as a reason to not use ART. Not all countries have viral load tests in routine use, but still provide treatment effectively.



## HOW CD4 AND VIRAL LOAD ARE RELATED

Although the CD4 and viral load tests measure different things, the pattern of results between each test is usually related.

- » When viral load is low, CD4 counts will be high.
- » When CD4 counts are low, viral load will be high.

A few weeks after infection, HIV viral load is very high, and the CD4 count drops. Then as the immune system brings viral load down, CD4 counts go back up again. There is sometimes a time lag between viral load and CD4 changes:

- » After starting HIV treatment (ART) viral load drops very quickly. The CD4 count only increases slowly (often over several months).
- » If treatment fails and the viral load level starts to rebound, the CD4 count may take a while before it starts to fall.
- » As viral load gets higher, the CD4 count will nearly always start to fall within a few weeks.

You can now see how the CD4 count and viral load curves fit together.

### CD4 COUNT AND VIRAL LOAD WITHOUT ART

After infection, viral load levels are very high. Then your body fights back and it drops to much lower levels. Over time though, usually over several years, viral load increases again. Viral load continues to rise and the CD4 count continues to fall.

When the CD4 count is very low, the immune system is no longer strong enough to fight off infections – in other words you have AHD. This causes serious illnesses. Some of these infections can be fatal.

Without ART, for nearly everyone, HIV is likely to be fatal.

### EFFECT OF ARVs ON CD4 COUNT AND VIRAL LOAD

After starting treatment, viral load falls quickly and CD4 counts rise slowly.

If ART brings viral load down to less than 50 copies/mL, then ART can last for many years.



## QUESTIONS

Exercises – eg role play, quizzes, design a booklet

WE WILL WORK ON THESE AT TAC MEETING

