

## Primary HIV infection

The first few weeks after an individual becomes infected with HIV are known as primary HIV infection, or acute HIV infection. When HIV first enters the body the immune system is unprepared to attack it, so HIV can reproduce at very high levels. A viral load test at this stage will usually show extremely high levels of HIV in the blood – often higher than at any other stage of HIV infection.

Levels of HIV elsewhere in the body, such as the lymph nodes and possibly semen and vaginal fluids, may also be very high. This may mean that the risk of transmitting HIV to other people may also be greatest during primary infection.

It takes several weeks after infection for the body to start to produce antibodies against HIV, and to generate immune cells that can recognise and destroy HIV-infected cells. The time at which antibodies to HIV appear is called seroconversion. When these immune responses against HIV develop, viral load drops to a much lower level known as the set point, which varies from person to person. However, the immune system is not able to eradicate HIV from the body altogether or to stop it from causing illness.

### Symptoms of primary infection

The high levels of HIV reproduction can cause a range of symptoms, which can be very similar to the flu or other common viral illnesses. These symptoms are sometimes called seroconversion illness, or acute retroviral syndrome, and usually only last for one or two weeks.

The symptoms may include fever, swollen glands, sore throat, rash, mouth or throat ulcers, and aching muscles or joints. At least 50% of newly infected people are thought to experience some such symptoms, and the true figure may be higher, but most people probably do not realise that their symptoms are HIV-related.

Several studies suggest that the more serious and prolonged the symptoms an individual experiences during primary infection, the faster he or she is likely to develop AIDS.

### Treating primary infection

Some doctors think that people who are identified during primary HIV infection should start an aggressive anti-HIV

regimen immediately. They argue that the drugs may help to control the high rates of HIV reproduction and limit its spread throughout the body. Studies have shown that in the vast majority of cases, taking a triple combination during very early HIV infection can suppress HIV to levels that are too low to be measured with current viral load tests.

Not so long ago, the most optimistic researchers believed that several years of intensive anti-HIV therapy might eradicate HIV from the body altogether. Nowadays, after many studies and much research, this possibility has been insofar ruled out as the current therapies have only proved, in many cases, to keep the virus undetectable (virus not found on blood); lengthening, nonetheless the lifetime of PWAS and endowing them with a better quality of life.

At present, there is no hard evidence that starting treatment during primary infection is better, in the long-term, than delaying treatment until later in the course of infection. Also, no-one knows whether there will be any real benefit from treating primary infection if the treatment is later stopped.

Indeed, some doctors are worried that suppressing HIV with drugs very soon after infection may make it harder for the body to generate strong anti-HIV immune responses. Other potential disadvantages include the risk of developing drug-resistant HIV strains, and the side-effects and inconvenience of taking the drugs throughout the entire duration of HIV infection.

The benefits of treatment may be greater for people who experience severe or prolonged symptoms during primary infection, since they are at a greater risk of disease progression.

## HIV 's lifecycle

HIV is a virus. Viruses are microscopic germs that are unable to reproduce (replicate) by themselves. Instead they need to find and infect a cell that will act as a host in which new viruses can be made. When HIV is outside a cell it is known as a virion and is surrounded by a protective envelope. The envelope surrounds a number of viral proteins and some genetic material - a 'blueprint' containing all the information necessary to make new viruses.

Viruses can be divided into two forms: those whose genetic material is made of DNA, and those whose genetic material consists of RNA (such as HIV). RNA viruses are called retroviruses. Their reproductive process involves an additional step that is not needed by DNA viruses.

### Fusion

Viruses often have a specific cell in the host human, animal or plant that they particularly like to infect. The main cells that HIV infects are those carrying a molecule called CD4 on their surface. CD4 is found on immune cells, most particularly on T-helper cells, which co-ordinate the immune system, and on macrophages, cells which roam the body engulfing bacteria and other germs.

HIV gets inside these cells by binding to the CD4 receptor using a molecule on the surface of the virus called gp120. Once HIV has bound to CD4, it activates other proteins on the surface of the human cell known as CCR5 and CXCR4 in order to complete its fusion with the cell.

Anti-HIV drugs which are designed to attack this stage of the HIV lifecycle are called fusion inhibitors. There are no drugs in this class which are licensed as yet, though T-20 (pentafuside) is currently being distributed through an expanded access programme. (Ask your doctor about it)

### Reverse transcription

Once fusion has occurred, the inside of the virus (the RNA and some important enzymes) is absorbed into the human cell. A viral enzyme called reverse transcriptase performs the process required to translate HIV's genetic material (RNA) into DNA.

Three classes of anti-HIV drugs target this stage: nucleoside analogues (AZT, ddI, 3TC, d4T, ddC, abacavir); non nucleoside reverse transcriptase inhibitors (efavirenz, nevirapine), and nucleotide analogues (tenofovir).

### Integration

The newly formed viral DNA is then integrated with the DNA of

the human host cell using a viral enzyme called integrase. This allows HIV to reprogramme the human cell to make more HIV.

New drugs called integrase inhibitors, which impede this stage of HIV's lifecycle, are in the very early stages of development.

### Transcription

In this stage, the two strands of DNA divide and form a new strand of viral RNA, sometimes called messenger RNA. Drugs called antisense nucleotides are being developed to target this stage.

### Translation

Next the protein building blocks which will go on to form the new HIV particle are assembled within the human cell. These blocks are laid out in turn through the translation of the information contained in the messenger RNA.

### Viral assembly

The protein building blocks are then cut into smaller pieces by a viral enzyme called protease. These pieces form the structure of the new HIV particle, including each of the enzymes and proteins needed to repeat the reproductive process. Once this assembly has occurred, the new viral particle buds off the human cell, floats off into the bloodstream and is able to infect other cells. It is estimated that about 10.3 billion new HIV virions are produced every day in people who are not on HAART.

The protease inhibitors (indinavir, ritonavir, saquinavir, nelfinavir, amprenavir, lopinavir) target this stage of the HIV lifecycle.

### Viral load

Viral load tests count the number of HIV particles in a sample of blood. The result of a viral load test is described as the number of 'copies' of HIV RNA per millilitre (copies/ml). 10,000 copies/ml or lower is generally considered 'low' and 50,000 copies/ml or greater is 'high'.

Each test has a limit below which it cannot reliably detect HIV RNA. For tests used in the past this limit was 400 or 500 copies. However, 'ultrasensitive' tests with a lower limit of 50 copies are now more widely used. Any sample with HIV levels below this threshold is said to have a viral load that is 'below the limit of detection', or simply 'undetectable'. This does not necessarily mean that there is no HIV in that sample; just that in the case of tests with a lower limit of 50 copies the number is somewhere between zero and 49.

If you currently have an active infection or recently received a vaccination, you may have a temporary increase in your viral load. In these cases it is best to leave a couple of months before having your viral load measured.

All viral load tests are now equally accurate at measuring types of HIV which are common in Africa and Asia. In the past, some tests couldn't always pick up these HIV strains.

#### Assessing prognosis

If you are not taking anti-HIV drugs, your viral load will be monitored at your regular clinic visits because this provides clues to the likely course of the HIV infection if left untreated. Amongst people who have the same CD4 count, those with higher viral load tend to have more rapid disease progression than those with lower viral load.

Changes in your viral load over time, along with other indicators such as your CD4 count and symptoms, can help you to decide whether or not to start anti-HIV treatment.

#### Monitoring treatment

Treatment with an effective anti-HIV regimen results in a fall in viral load. If you are starting treatment, or switching from one regimen to another, you should have a 'baseline' viral load test before you start or change drugs, followed by a second test a month or so later. The difference between the two may indicate the short-term anti-viral effects of the drugs.

According to current medical practice, your next viral load test should be twelve weeks after starting your new combination, and subsequent tests should then recur every twelve weeks. Additional tests may be needed from time to time, for example if you develop symptoms.

For some people, drug combinations can reduce viral load to below the limits of detection, even among people with low CD4 counts or who have taken anti-HIV drugs before. If your viral load is 'undetectable', HIV may be less likely to develop resistance to the drugs. It is recommended that an initial combination should lower viral load below 50 copies by 24 weeks after starting it. Subsequent combinations are less likely to meet this goal.

Routine viral load testing does not measure the amount of HIV inside cells, or in other body compartments beyond the blood, such as genital fluids or the brain, and the effects of anti-HIV drugs in these places may vary. It's important to remember therefore that HIV virus transmission is still possible in spite of its 'undetectable' status.

If you are taking anti-HIV drugs correctly but your viral load starts to rise again, this probably indicates that the drugs' antiviral effects are waning, perhaps due to resistance or because you are not absorbing them properly. Doctors differ in their view of how quickly you should switch to a new combination if your viral load begins to rise. Some argue that the aim of treatment should always be to achieve and maintain undetectable viral load because the risk of resistance to drugs being taken increases as long as viral load is detectable. Others are concerned that with today's drugs this is unachievable for many people and will encourage them to change drugs too rapidly, until eventually they may run out of options.

## You and your doctor

During the course of infection, HIV-positive people are more likely than almost all other patient groups to maintain frequent contact with their doctor. The relationship you forge with your doctor is one of the most important you will have post-diagnosis.

Certain doctors may attract certain kinds of patients: some doctors will advocate aggressive therapy, whilst others will be more receptive should you wish to hold off treatment or use a range of complementary approaches in addition to conventional HIV care.

It's important that you find the right kind of doctor for you. Friends may be able to recommend a suitable doctor, but building up a relationship will take time. You may not develop a rapport with the first doctor you meet. Establishing a trusting relationship with your doctor is essential if you are to feel a sense of selfempowerment and control over your use of treatments.

### Effective doctors

It is essential that your doctor has well-developed interpersonal skills, and many do. The level of knowledge of your clinician is clearly important too. An effective doctor should take the trouble to explain things to you, be sensitive to personal issues raised by you, be a good listener and be able to provide you with a range of opinions.

All patients need their doctor to be open, frank and communicative, being clear when he or she does not know the answer to your questions.

### Effective patients

To be an effective patient you will need to be involved in your own care. Exactly what this means depends upon the type of person you are. Some people will want to take a more active role in their health care and have clear ideas about what kind of treatments they do or do not want to use. Others will be more inclined to look to their doctor for guidance.

Being prepared for your consultations is a joint responsibility. Ask questions until you understand. If you are likely to forget what your doctor tells you during the consultation, make notes. If you are likely to forget which questions you would like to ask, then write a letter to your doctor containing the questions you want to ask, and send it in advance of your appointment. It's

also worth remembering that if you attend your clinic without an appointment, your regular doctor may not be available.

### Participation and partnership

During the course of your relationship, it's likely there will occasionally be issues upon which you and your doctor do not agree. It's important that you learn how to manage these situations. If you become unhappy over a disagreement with your doctor, you may choose to invite a patient advocate to help you communicate your feelings.

In extreme cases, if you wish to pursue a complaint you should address this to the clinic director by letter. Should you need some help you may phone gTt 933020411 or Medicina Tropical 934412997. If you decide you are no longer happy to continue your relationship with your doctor, this need not be a reason to move to another clinic - most clinics allow switching between doctors.

It is important to be honest with your doctor about any risks you may be taking, or sexual practices, alcohol or drug use that may affect your long-term health.

Knowing the facts helps your doctor to consider appropriate care and treatment for you. If, however, you feel unable to confide in your doctor about certain issues, there may be other staff in the department which you might be able to talk to more easily.

Maintaining contact with the same doctor can be extremely difficult, as they are usually very busy, and staff change from time to time. Remember though, their time is no more valuable than your own. If getting access to your doctor is difficult, discuss ways of improving the situation. Would a short phone call, or email enquiry be acceptable? You will need to be organised to get the most from your doctor's time.

Learning about the roles of other staff at your treatment centre will also help you avoid using your doctor's time when another member of staff would be able to help, and can provide you with additional sources of support.

## Drug diary

Some people find drug diary sheets can help them remember to take treatments. It's very important when taking anti-HIV drugs that you don't miss doses or take them later than planned, as this can cause your treatment to fail. Keeping a drug diary may be a useful way of getting into a routine, particularly when starting a new course of treatment.

Ask your doctor or pharmacist to provide written information about your treatment when your drugs are dispensed.

Fill in the name of each drug in your combination at the top of the box below (use another sheet if you are taking more than four drugs). Tick off each dose that you take opposite the day of the week. This form allows you to record up to three daily doses. If your combination is dosed less frequently you may want to cross out surplus dose columns to avoid confusion.

Today's date	Drug name:											
	Dose 1	Dose 2	Dose 3	Dose 1	Dose 2	Dose 3	Dose 1	Dose 2	Dose 3	Dose 1	Dose 2	Dose 3
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