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viral load & CD4

sixth edition 2006

acknowledgments

Edited by Michael Carter **Sixth edition 2006**

NAM is a charity that publishes information for people affected by HIV and those working with them. We believe information helps people to make decisions about, and be in control of, their lives, health and treatment options.

Thanks for the assistance of

Dr Fiona Boag
Chelsea & Westminster
Hospital, London

Dr Ray Brettle
Western General Hospital,
Edinburgh

Professor Janet Darbyshire
Medical Research Council,
Clinical Trials Unit, London

Dr Martin Fisher
Royal Sussex County Hospital,
Brighton

Henry Grahame-Smith

Roy Kilpatrick

Professor Clive Loveday
Royal Free Hospital, London

Lisa Power

Terrence Higgins Trust, London

Dr Ian Williams

Mortimer Market Centre, London

Dr Mike Youle

Royal Free Hospital, London

Funders

NAM is grateful to the funders of this booklet series:

Department of Health, London
HIV & GUM Commissioning
Consortium and the Derek
Butler Trust



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viral load & CD4

This booklet focuses on blood tests called viral load and CD4 counts. These tests are crucial in helping you decide when to start treatment, and to monitor the effects of your treatment. This booklet is not intended to replace discussion with your doctor about your treatment or test results. However, it may help you to decide what questions to ask your doctor about any course of treatment you may be considering.

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What is the CD4 count?

CD4 cells, or T-helper cells, are white blood cells which organise the immune system's response to some micro-organisms, including bacteria, fungal infections and viruses.

The CD4 count is the measurement of the number of CD4 cells, in a cubic millimeter of blood (not the whole of your body). This is sometimes written as CD4 cells/mm³.

The CD4 count of a person who is not infected with HIV may lie anywhere between 500 and 1200. HIV can infect CD4 cells and use them to produce more HIV copies.

Even while a person with HIV feels well and has no symptoms, millions of CD4 cells are infected by HIV and are destroyed each day, and millions more CD4 cells are produced to replace them.

What CD4 counts predict

Most people with HIV find that their CD4 count usually declines over a number of years.

A CD4 count between 500 and 200 indicates that some damage to the immune system has occurred. If your CD4 count drops below 350, or starts falling rapidly, your doctor should talk with you about whether you need to start anti-HIV treatment.

If your CD4 count falls below 250-200 you are recommended to start treatment with anti-HIV drugs because this is the level at which the risk of AIDS-related illness is greatly increased.

The most important information that your CD4 count can give you is the overall trend of your immune system's health – whether it is declining or improving.

Changes in the CD4 count

Your CD4 count can go up and down in response to infections, stress, smoking, exercise, the menstrual cycle, the contraceptive pill, the time of day and even

the seasons of the year. Different types of CD4 counting-machines also give different readings.

This is why it is important to monitor its trend over time, rather than to focus too much on individual test results. It's also best to have your CD4 count measured at the same clinic and at roughly the same time of day wherever possible. If you have an infection like flu or herpes it is best to delay having a CD4 count until you are feeling better.

If you have a relatively high CD4 count, no symptoms and you are not taking anti-HIV drugs, you only need to measure your CD4 count once every three months.

However, if your count has been falling rapidly, or you are taking part in a clinical trial, or you have just started new treatment, your doctor may suggest that your count should be monitored more often.

If you are experiencing very wide variations in your CD4 count then it could be because your overall white blood cell count has changed, possibly in response to an infection. In these circumstances your doctor may look at other test results which give an indication of the state of the immune system, such as the CD4/CD8 ratio, or CD4 percentage to decide if the wide variation in CD4 count is important.

CD4 percentages

Instead of counting the number of CD4 cells per mm^3 , doctors sometimes assess what proportion of all white blood cells are CD4 cells. This is called the CD4 cell percentage; in HIV-negative people, a normal result is about 40%. A CD4 percentage below about 20% is thought to reflect the same risk of becoming ill because of HIV as a CD4 count of about 200.

4 Viral load

Viral load is the term used to describe the amount of HIV in your blood. The more HIV in your blood, the faster your CD4 cells are likely to disappear, and the greater your risk of developing symptoms or further illness within the next few years.

What is the viral load test?

Viral load tests estimate the number of HIV particles in the liquid, or plasma part of the blood. They do this by looking for HIV's genes, which are called HIV RNA.

The result of a viral load test is described as the number of copies of HIV RNA per millilitre.

There are several different viral load tests in use at the moment. Each test uses a different technique to measure the number of HIV particles, but all the tests are equally reliable at determining whether your viral load is low, medium or high.

By and large, all the 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.

However, HIV strains in different parts of the world are always changing and mixing with one another, and there is a risk that the tests will be unable to pick up new strains of HIV. If your viral load result

does not seem right (for example, low when your CD4 count is also low), several different viral load tests may be used to get a more accurate picture.

Natural variations

Viral load measurements can rise and fall from one blood sample to the next but this may have no long-term impact on the health of the person being tested.

Researchers have investigated viral load changes in people not on treatment and found that two separate tests on the same sample of blood can give results which differ by as much as threefold. For

example, this means that you shouldn't necessarily be worried if your viral load goes up from 5,000 to 15,000 at a time when you are not on treatment.

Similarly, a rise from 50,000 to 100,000 if you aren't on treatment may not be significant, although it may seem like a big increase. Viral load appears to have doubled, but it's within the margins of error for this test.

Your viral load should ideally only be measured when you are well. If you have an infection or have recently had a vaccination, your viral load could temporarily increase.

The time to be concerned is when viral load results over several months show an upward trend, or when the increase is greater than threefold.

For example, a rise from 5,000 to 25,000 is significant. It represents a five-fold increase in the amount of virus in your blood since your last viral load test.

However, it is still best to confirm this trend on a repeat test.

The effects of vaccinations and infections

If you currently have an infection or have recently received a vaccination, you may

have a temporary increase in your viral load. In these cases it is best to avoid having a viral load test for at least one month after a vaccination or illness.

Why do I need to know my viral load and CD4 count?

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If you are not currently taking anti-HIV treatment

If you are not taking anti-HIV drugs, your viral load can provide information on the likely course of HIV infection if left untreated.

A study of viral load levels in untreated people suggests that, in combination with your CD4 count, they may help you to predict your risk of developing symptoms in the future.

Among people with the same CD4 count, research shows that those with higher viral load tend to develop symptoms more quickly than those with lower viral load.

Among people with the same viral load, those with lower CD4 counts tend to develop symptoms more quickly.

As the table on the following page shows, taken together, both CD4 count and viral load provide valuable information to predict the likelihood of developing AIDS in the short to medium term.

If you look at the column for people whose CD4 counts were between 351 and 500, there is a big difference in the risk of disease progression, depending on their viral load.

8 Table 1

Predicting progression

% of people who develop AIDS within 3 years (assuming no treatment)

Viral load	CD4				
	below 200	201-350	351-500	501-750	above 750
below 1,500	**	**	**	3.7	0
1,500-7,000	**	**	2.0	2.0	2.0
7,000-20,000	**	8.1	8.1	8.1	3.2
20,000-55,000	40.1	40.1	16.1	16.1	9.5
above 55,000	85.5	64.4	42.9	32.6	32.6

** indicates lack of data

Researchers have also looked at the risk of developing AIDS or dying for people taking treatment. Monitoring a very large number of people over a number of years they found that people who did less well on anti-HIV therapy tended to have the following characteristics when they started anti-HIV therapy:

- A CD4 count below 200.
- A viral load above 100,000 copies.
- Age over 50 years.
- Being an injecting drug user.
- Already had an AIDS-defining illness.

It is possible to calculate individual disease progression risk by visiting <http://www.art-cohort-collaboration.org>

and entering individual characteristics such as CD4 count, viral load, age, drug use history and past HIV-related illnesses.

Deciding whether to start treatment

The level of your viral load, along with other indicators, may help you to decide whether to start anti-HIV treatment.

At the moment, research evidence which helps doctors make decisions about when people with established (more than six months) HIV infection should start treatment places emphasis on CD4 count rather than viral load. It is recommended that people start treatment before their

CD4 count falls below 200, as people who start treatment with a CD4 count below 200 face a greater risk of death, in the short-term, than those who start before their CD4 count drops below this level.

At higher CD4 counts the picture is much less clear, and in these circumstances timing will depend on the level of viral load, the speed at which CD4 count is falling, the likelihood of achieving good adherence, the presence of symptoms, and the patient's wishes.

People who are advised to start treatment, but decide not to, should review their decision regularly, and have their CD4 and viral load monitored more regularly.

If you do not receive anti-HIV treatment, the table on page 8 shows that a high viral load, regardless of your CD4 cell count, increases your risk of AIDS-related illness.

Viral load in women

When HIV-positive women and men with the same CD4 cell counts are compared, women tend to have slightly lower viral load on average. However, this doesn't translate into any differences in response to treatment.

CD4 counts and viral load in children

Normal CD4 counts tend to be much higher in very young children than adults.

On average the CD4 cell count in a six-month old baby is about 3,000, and is about 1,500 in one year-olds and often over 1,000 in infants under six. However, CD4 cell counts stabilise at similar levels to those seen in adults when a child is aged between about six and twelve.

In HIV-positive babies, HIV viral load can rise to very high levels (over 1 million copies/ml) within a few weeks and gradually decline over the first few years of life. The exact reason for this is not known.

The effect of treatment

Effective anti-HIV treatment results in a reduction in viral load. If you start

anti-HIV treatment your doctor will test your viral load after four to twelve weeks of treatment to see by how much your viral load has gone down.

Changes in viral load are sometimes expressed using a logarithmic (log) scale.

■ example

If your viral load falls from 100,000 to 10,000, this is a 1 log reduction.

■ example

If your viral load falls from 100,000 to 1,000, this is a 2 log reduction.

■ example

If your viral load falls from 100,000 to 100, this is a 3 log reduction.

12 Undetectable viral load

What is undetectable viral load?

All viral load tests have a cut-off point below which they cannot reliably detect HIV. This point is called *the limit of detection* and varies from one testing kit to another.

However, just because the level of HIV is too low to be measured by these tests, it does not necessarily mean that the virus has disappeared entirely. The virus may still be present in your blood, but in amounts too low for the test to pick it up. Viral load tests only measure the amount of HIV in the blood. Even if you have an undetectable viral load this does not mean that your viral load in other parts of your body, such as your lymph nodes, is undetectable.

What are the limits of detection of current tests?

For tests used in the past, the lower limit of detection was 400 or 500 copies. However, *ultrasensitive* tests that measure down to 50 copies are now routinely used. Some tests can measure even lower and are mainly used in research.

The value of having undetectable viral load

Having undetectable viral load is desirable for two reasons:

- a very low risk of developing AIDS.
- a very low risk of developing resistance to the drugs you are taking now.

Doctors now think that undetectable viral load (below 50 copies) should be the aim of treatment.

Some people take three to six months to reach this point, while others go below the limit of detection within four to twelve weeks, and others may never achieve this goal.

People taking anti-HIV drugs for the first time are more likely to reduce their viral load to these very low levels than those who have taken treatment previously.

Some doctors will recommend changing your combination or adding another drug (after they have done a resistance test and found that this drug will work) if you don't have undetectable viral load after three months on a new combination of drugs.

However, doctors differ in their view of how quickly treatment should be changed. Some favour switching 'early' to reduce the risk of resistance. Others argue that this approach may cause you to stop treatments from which you were still benefiting. See *Viral load blips* below for further information about when to consider switching.

Changing treatment should ideally involve switching to a combination involving drugs which you haven't taken before, and which are unlikely to be cross resistant to those you've taken previously. This may pose more of a challenge the more drug experience you have.

It may also be the case that the quicker your viral load falls below 50 copies, the

longer it should stay there, providing you keep taking the drugs as instructed.

After six months on a first-line combination, your viral load should ideally have gone below 50 copies. Some people do not respond this well, however.

Viral load blips

People with undetectable viral load are likely to experience small blips in their viral load from time to time. Typically, viral load may rise from below 50 copies to above 100 or 200 copies on a single test, and be undetectable on the next test. This is common and does not necessarily indicate that your treatment

is failing. Most viral load blips seem to be due to testing errors at the laboratory.

However, if viral load continues to rise on each test, or if it stays above 50 copies without rising above 500 copies, this indicates that your treatment may fail and you may develop resistance.

At this point you should discuss switching treatment with your doctor. The longer that your viral load remains detectable while you take your current drug combination, the more likely you are to develop resistance to the drugs.

However, current resistance tests cannot detect resistance until your viral load is above 1,000 copies.

Developing resistance

If HIV develops resistance to the drugs you are taking, this means that they will be unable to suppress HIV efficiently, and viral load usually begins to rise.

Keeping viral load below the level of detection is associated with a very low risk of developing resistance to the anti-HIV drugs you are taking.

This is because the chance of developing resistance when you are taking anti-HIV drugs depends on the amount of HIV which is still being produced in your body.

The lower your viral load, the lower your risk of developing resistance to the drugs you are taking.

So, suppressing viral load to undetectable levels (below 50 copies) is likely to delay the development of resistance for longer.

Cross-resistance

HIV that has developed resistance to one drug that you are taking may also be resistant to some other similar drugs which you have not taken yet. This is called cross-resistance.

Cross-resistance can limit the range of drugs you can take in the future. In order to keep as many options open as possible, some doctors argue that treatment should always aim for undetectable viral load.

However, other doctors take the view that if you switch drugs every time your viral load rises above the limit of detection, you may run out of drugs relatively quickly. For more information, see another NAM booklet in this series, *Resistance*.

If you have high levels of HIV in the blood, you may also have high levels of HIV in semen or vaginal fluid. People with high viral load are likely to be more infectious.

Anti-HIV treatment that reduces viral load in the blood usually also reduces HIV levels in semen and in vaginal fluid.

However, even if the viral load in your blood becomes undetectable after treatment, this doesn't mean that HIV has disappeared from your semen or vaginal fluid. You still risk passing on the virus during sexual intercourse if you aren't using a condom with your partner.

Untreated sexually transmitted infections, most notably gonorrhoea, can increase

viral load in sexual fluids and mean that the risk of passing on HIV to your partner is greater if you are not using a condom.

Anti-HIV treatment has been proven effective in reducing mother-to-baby HIV transmission. If you are pregnant or planning to conceive, discuss your treatment options with your doctor. If you have undetectable viral load whilst pregnant, the risk of passing HIV to your baby will be very low.

18 How often should I have my viral load tested?

If you are not on treatment

As the table on page 8 shows, there's a big difference in the risk of developing AIDS between having a low viral load of 5,000 compared with a high viral load of 50,000, even when you have a CD4 count above 500.

If your CD4 cell count is between 350 and 200 and is falling quickly, you should attend your clinic every month or even more frequently for closer monitoring, because a fast decline in CD4 cell count indicates a higher risk of AIDS-related illness.

Even if your CD4 count is currently above 500, it is a good idea for you to attend your clinic for viral load testing every four to six months, and to get the results back quickly.

If you are about to start treatment

Get two 'baseline' viral load measurements before starting, so that later you will be able to see just how well your treatment has worked.

If you have started treatment

It is possible to get an indication of how well your combination therapy is working by testing your viral load after a month or so, and again after three months of treatment. Subsequent tests should occur every twelve weeks. Additional tests may be needed from time to time, for example if you develop symptoms. You should get

these results within a week if they are to provide an accurate picture of the current effect of your treatment. The level your viral load has reached at these points usually predicts how long this particular combination will keep your viral load low, or undetectable.

The initial fall in viral load after four months is also an accurate indicator of how much benefit you'll get from this combination in the next few years in terms of a reduced risk of developing AIDS or further illness. The greater the fall in viral load at this point, the better your outlook in the medium to long term.

If you have just had an increase in viral load on treatment

Another test should be carried out within two to four weeks to confirm this result. You should always have viral load and CD4 counts tested at the same time.

20 Summary

- Your CD4 cell count gives an impression of the health of your immune system.
- Monitoring your CD4 cell count can help you and your doctor decide when you need to start HIV treatment.
- Viral load is the term used to describe the amount of HIV in your blood.
- CD4 cell counts and viral load can vary naturally - you should look at trends, not single results.
- The aim of anti-HIV treatment for people who have never taken HIV drugs before is a viral load below 50 copies, this is usually called an undetectable viral load.

CD4 A molecule on the surface of some cells onto which HIV can bind. The CD4 count roughly reflects the state of the immune system.

cross resistance The mechanism by which HIV that has developed resistance to one drug may also be resistant to other similar drugs.

gene A DNA sequence which determines the structure of a protein.

immune system The body's mechanisms for fighting infections and eradicating infections and eradicating dysfunctional cells.

resistance A drug resistant HIV strain is one which is less susceptible to the effects of one or more anti-HIV drugs because of its genotype.

strain A variant characterised by a specific genotype.

viral load Measurement of the amount of virus in a sample. HIV viral load indicates the extent to which HIV is reproducing in the body.

viral load rebound An increase in viral load, often from below the level of detection on a viral load test.

Notes



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Sixth Edition 2006
© NAM
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photography Photos.com
print Litosphere

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