

**HIV  
TREATMENT  
BREAKS?**



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The Treatments Breaks Campaign is a joint campaign of the Australian Federation of AIDS Organisations (AFAO), The National Association of People With AIDS (NAPWA) and the Australasian Society for HIV Medicine (ASHM).

All of these organisations consider that the issue of 'treatments breaks' is an important one for people with HIV to be informed about. At the time of producing this campaign a lot of further research is being conducted which will better inform people with HIV in their decision making.

We urge people with HIV who are considering a treatment break to get the latest information from their doctor or local AIDS organisation, and to read the information in this booklet.

## ABOUT THIS BOOKLET

This booklet is for people who are HIV-positive. It provides information about the issues associated with taking a break from your HIV antiviral treatments.

It has now been over six years since combinations of three or more drugs were shown to be highly effective in treating HIV disease. This heralded an era of optimism and it was hoped that after long periods on these drugs it might be possible to 'eradicate' HIV from the body. With the currently available treatments in 2002 it is not possible to eradicate HIV from the body.

For some people there are significant toxicities associated with using the current drugs for long periods. It is not surprising then that one of the most pressing questions facing people with HIV is the issue of taking a break from treatments.

There is not a simple answer to the question, 'Can I safely take a break from my HIV treatments?' Everyone is different. The issues to be considered for someone who started treatments twelve months ago just after becoming infected with HIV and who has a good immune system are very different than those for someone who started treatments years ago when their immune system showed some damage.

There are however some bottom lines that apply to all people with HIV.

## SOME BOTTOM LINES

- 1. The benefit of "structured treatment" breaks has not yet been established in any setting and stopping therapy involves numerous potential risks.***
- 2. Taking a treatment break should always be done in partnership with your medical practitioners. Even if you started a break without telling your medical practitioner informing a medical practitioner and monitoring your health is very important.***

When some people stop treatments their viral load can rise ("rebound") very rapidly and their CD4 (T-cell) count start decreasing quickly. For this reason it is very important that there be frequent monitoring of your viral load and T-cell counts after stopping treatment because you can't necessarily tell from how you feel.

- 3. Everyone is different – there is not one simple answer to the question of 'Can I safely take a break from my HIV treatments?'.***

The medical and scientific answers depend on when you started treatment and the underlying state of your immune system. The questions relating to taking a break from treatments faced by a person with HIV who started treatment soon after getting infected with HIV are very different from those faced by someone who has been on antiviral treatment for a number of years and has a relatively low CD4 cell count.

## TREATMENT BREAKS, DRUG HOLIDAYS, GOING OFF ANTIVIRALS, TREATMENT IMMUNISATION, STRATEGIC TREATMENT INTERRUPTIONS...

#### **4. So called "Drug holidays" and unplanned treatment interruptions are different from planned or strategic treatment interruptions**

There have been a lot of words and phrases used to describe treatments breaks that have become popular in PLWHA communities. 'Drug holiday' is one such phrase. It initially referred to taking breaks from treatments for short periods to enjoy special events like Mardi Gras. **Stopping therapy for a weekend (what is commonly meant by a "drug holiday") every now and then is not strategic or structured and will almost certainly increase the risk of developing anti-HIV drug resistance.**

#### **5. "Compliance" or "adherence" – that is following the recommended dosing schedule for your HIV medications – remains important in getting the most benefit from your HIV medications while you are on them.**

Numerous studies have shown the importance of following the recommended dosing schedule for your HIV antiviral drugs. When you first start treatments or start a new treatment combination, taking them continuously according to the recommended schedule is necessary to get the most from your anti-HIV drugs.

These terms have been used quite a lot in relation to taking a break from your HIV treatment. The term "drug holiday" was initially used to refer to choosing to take a "holiday" from your antiviral pills for any reason. "Structured" implied that the break was done in consultation with your doctor.

"Structured treatment interruptions" or STIs has a particular meaning. It involves taking a break from your treatment for a pre-determined period of time or taking a break from your treatments and only restarting treatments when your viral load or CD4 cell count reaches a certain level.

## THE CURRENT HIV ANTI-VIRAL TREATMENT GUIDELINES

When the effectiveness of multiple combinations of antiviral drugs was proven, the HIV antiviral treatments guidelines were 'hit hard, hit early'. The belief was that most people could benefit from suppressing the viral replication. As experience with the drugs grew, knowledge about some of the longer-term toxicities associated with these drug combinations increased. The theoretical advantage of early treatment to maintain immune function has to be weighed against the toxicities of long-term exposure to anti-retrovirals.

The current treatment guidelines recommend commencement of treatment whenever

- There are symptoms of HIV disease
- There is neurological HIV disease
- The CD4 count drops below 200
- Women with HIV are pregnant (in order to reduce the risk of transmission)

And

- Where the baseline CD4 cell count and viral load levels indicate a significant chance of disease progression in the absence of treatment. (see table 1 – as a rough guide it is recommended treatment to commence when CD4 count is less than 350 or viral load is greater than 50,000 copies).

These changes in treatment guidelines from the "hit hard, hit early" approach to a more cautious approach means that many people with HIV who commenced treatment some years ago would not currently be recommended to commence treatment under the changed guidelines.

**TABLE 1  
– RISK OF AIDS IN  
6 YEARS (%)**

Viral Load	CD4 Count		
	← 350	350-500	→ 500
→ 55,000	<b>93%</b>	<b>79%</b>	<b>67%</b>
20,000-55,000	<b>73%</b>	<b>57%</b>	50%
7,000-20,000	42%	40%	26%
← 7,000	19%	22%	1%

Where the chance of progression in six years is over 50% then treatment is recommended.

For example, with a CD4 count of 350 - 500 and a viral load of 755,000 there is a 79% chance of progression in 6 years so treatment is recommended.

# TREATMENT BREAKS AND DISEASE STAGE – A BRIEF SUMMARY

The table below summarises some of the issues and what is known as they relate to stage of HIV disease.

DISEASE STAGE	GOALS OF ANTIVIRAL TREATMENT	WHAT'S KNOWN AND NOT KNOWN
People who have been recently infected with HIV	<ul style="list-style-type: none"> <li>To preserve key components of the immune system until the body's own immune response to HIV can provide similar protection</li> </ul>	<p>Commencing treatments for a period and then stopping is the recommended strategy.</p> <p>The best method of stopping is not yet known.</p> <p>By using existing treatments in a structured way it may be possible to improve the body's own ability to fight HIV in the long term.</p>
People who are on treatment, doing well and whose immune system is still functioning well.	<ul style="list-style-type: none"> <li>To prevent progression of HIV disease AND</li> <li>to minimise the long term toxicities that may be associated with current HIV antiviral drugs</li> </ul>	<p>Treatment breaks are now under examination for this group of people with HIV.</p> <p>There is so far only limited information from small trials from which it is not yet possible to draw firm conclusions about the best treatments break strategy or the long term impact of structured treatments breaks.</p> <p>The possibility of structured treatments interruptions aimed at stimulating a stronger immune response so that HIV may be better controlled without the continual use of anti-HIV drugs is under investigation.</p>
People who are on treatment whose CD4 cell count is low	<ul style="list-style-type: none"> <li>To prevent progression of HIV disease, to minimise the long term toxicities that may be associated with current HIV antiviral drugs AND</li> <li>to minimise symptoms of advanced HIV disease</li> </ul>	<p>Treatment breaks are not recommended for people with advanced HIV disease because the existing evidence and clinical experience with people with advanced HIV disease is that the risks of taking a break from treatments outweigh any possible benefits.</p> <p>There may, however, still be reasons for people with advanced HIV disease to have a structured break such as experiencing treatment fatigue or severe side effects.</p>

## **SIDE EFFECTS - SOMETIMES YOU DON'T ALWAYS JUST HAVE TO PUT UP WITH THEM.**

Most people who have been or are on HIV antiviral medications are aware of the side effects that come with them. This booklet is not primarily about side effects and how to deal with them. But side effects are one of the most common reasons that people with HIV nominate for choosing to take a break from their HIV medications.

Sometimes people respond to complaints about side effects by saying things like 'but your laboratory results are so good' (i.e. your viral load and CD4 count). The implication is that the antiviral medications are keeping your immune system in shape so side effects are 'just something you should put up with.' But sometimes people with HIV are experiencing side effects such as constant diarrhoea that could be better treated or that may be better managed by swapping their antiviral treatments or individually tailoring the dose of their treatments.

Doctors may be able to give some useful tips in treating side effects. Often other allied health practitioners like dieticians are very knowledgeable and useful people in providing tips about minimising the side effects of these drugs.

### **Induction side effects**

There are side effects that seem to only occur soon after starting a new drug or drugs. These are known as 'induction' side effects – and they generally go away after you've been on the drug for a while.

### **Dose-related side effects**

Then there are persistent side effects that can occur all the time such as diarrhoea or disturbed sleep. These persistent side effects tend to be dose related – that is the higher the dose the more likely the side effect. There are four possible ways that persistent side effects may be managed:

- You decide to just 'live with them'
- You get treatment for them (including complementary therapy)
- You change your antiviral medications
- You take new tests (TDM) to see if the dose of one or more of your medications can be altered safely

Persistent diarrhoea may also be better managed by changes in diet. HIV experienced dieticians can offer good advice for better managing diarrhoea associated with HIV antiviral medications.

One new test being evaluated in HIV medical management for some drugs is a test called 'therapeutic drug monitoring' or TDM. This is still new (as at 2002) for HIV and can only be used for some drugs. Everyone is different, but the doses of drugs used for most HIV antivirals are the same for everyone. It may be the case that the dose of one of your pills is too high for you making side effects more likely or, conversely, too low for you making resistance more likely. The goal of TDM is to test your drug levels to see if your dose may need changing. Currently TDM is only used for some drugs and is not available everywhere in Australia. This may change – so ask your doctor about it.

## Long-term side effects

The last group of side effects are those that tend to develop over time. These include lipoatrophy and lipodystrophy (changes in the distribution of fat in your body) and osteopenia (bone disease). Quite often there are long-term elevated levels of cholesterol seen in people who have been on HIV antiviral medications for long periods. It is not yet known whether this will be associated with cardiovascular problems in the longer term. It is these long-term side effects that are giving the question of treatments breaks a higher priority. It is hoped that by adopting an appropriate program of structured breaks, the chances of long term side effects will be decreased without significantly increasing the chances of HIV disease progression.

Many of these long-term side effects have 'lifestyle' risk factors associated with them, – such as smoking, lack of exercise and inappropriate diet. The increased survival time as a result of improved treatments has put many of these 'other' health issues back on the personal agenda of people with HIV. Talk to your doctor about changes you can make that not only may decrease the chances of getting long term side effects but may have the added benefit of improving your overall health.

## PEOPLE RECENTLY INFECTED AND “TREATMENTS BREAKS”

People who start treatments around seroconversion or relatively soon after infection are in a very different situation than for people who started treatments after they had been infected for some years.

When you are first infected with HIV, your viral load can rise to very high levels before the body's own immune system response kicks in. Once the body's own immune response kicks in HIV viral load decreases over time to a 'baseline' level. This process may take some months. During this initial burst of HIV infection it is believed that key elements of your immune system can sometimes be overwhelmed and lost – diminishing the capacity of your body to control HIV on its own in the long term.

The theory is that if you can treat HIV infection very early, you can preserve these key elements of the immune system.

In early infection it is theoretically possible to use 'structured treatments interruptions' to enhance the body's own response to HIV. This is supported by some case reports – but whether this is always possible is not proven.

The theory behind structured interruptions to therapy in people treated very early is this: if therapy is stopped for a short period, the virus will begin to replicate, and the immune system, recognising the virus, will respond, and mount an attack on HIV-infected cells. If viral load begins to rise again, antiviral therapy can be used to suppress the virus again. Over a period of

time the immune system may become so effective at fighting HIV on its own that the need for antiviral suppression becomes less and less. It is sort of like treatments are being used in pulses (hence the name 'pulse therapy') to 'immunise' the body to HIV – hence 'treatments immunisation'.

However, this mechanism only applies in people very recently infected – and the issues for people with longer term or chronic HIV infection and treatments breaks are different.

## PEOPLE CURRENTLY ON TREATMENTS AND “DOING WELL” AND “TREATMENTS BREAKS”

Many people with HIV in Australia started treatments when there was convincing evidence about the effectiveness of combinations of three or more HIV antiviral drugs in controlling HIV infection. The guidelines produced soon after this evidence in Australia were 'hit hard, hit early'. The guidelines have now changed to more conservative ones. As a result many people with HIV commenced treatments some years ago who, under the current guidelines, would not be recommended to start HIV antiviral treatments.

Many of these people have been on treatments for some years, and have low or undetectable HIV viral load.

The medical reasons for considering a break are the possibility of decreasing the incidence and severity of the long-term side effects associated with HIV antiviral drugs and additionally the possibility of improving

the body's own capacity to control HIV. This has to be balanced against the possibility of less control of HIV replication and consequent damage to the immune system.

There are a number of case reports of people taking breaks and a few small trials from which it is not possible to draw firm conclusions. A number of much larger trials are underway around the world trying to ascertain the impact of structured treatments breaks in the longer term. In general these trials are of two types:

- i) Comparing a strategy of regular set periods on and off treatments (eg a month on and a month off) to continuous treatment; and
- ii) Stopping treatment until viral load and/or CD4 cell count reaches a predetermined level at which time treatment is recommenced and this is compared to continuous therapy.

What can be tentatively observed from the small trials done so far is that in people who took breaks their levels of cholesterol and triglycerides (associated with long term side effects) were on average slightly lower and their HIV viral load was on average slightly higher. Further, there is quite a variation in what happens when people take a break, highlighting the importance of monitoring.

Many people with HIV have taken a break from their treatments in the past, are currently taking a break or considering taking a break. Treatment breaks have been a fact a life for some time. It just hasn't been that openly talked about until recently.

What is most important in taking a break is to remember the bottom lines.

Some people who stop have a big HIV viral load rebound, their viral load remains high and their CD4 cell count keeps falling rapidly. Others have an initial rebound that settles and their CD4 cell count doesn't fall as quickly. You can't tell unless you monitor carefully which group you will be in – **and you can't tell by how you feel.** Often people with HIV report feeling great after taking a break – but feeling great does not protect you from rapidly falling CD4 cells. While you have an effective immune system the choice to incorporate treatments breaks into your treatments strategies is always there. However, if you progress to advanced HIV disease then you tend to be more reliant on treatment to keep you well and have less ability to safely take a break from your treatments.

## PEOPLE WITH ADVANCED HIV DISEASE AND “TREATMENTS BREAKS”

It is often the case for people with advanced HIV disease that antiviral treatments play a significant role in maintaining their immune system and in preventing symptoms directly caused by HIV.

When current treatments are being tolerated, treatment breaks are not currently recommended for people with advanced HIV disease. A number of small studies seem to indicate that the risk of symptoms of HIV disease or getting opportunistic illnesses outweighs any potential benefits from stopping.

There may still be reasons that people with advanced HIV disease take or consider

breaks such as treatments fatigue or drug related toxicities.

One possible reason for taking a break that has been suggested is that for people who have ‘resistant virus’ (i.e. HIV that is resistant to the currently available antiviral drugs) taking a break may allow the virus in the body to become ‘re-sensitised’ to HIV drugs. While this a theoretical possibility, it has not been proven – and even though the virus may be somewhat resistant – it appears that generally combinations of drugs continue to provide partial protection.

## RESISTANCE AND “SLOPPY TREATMENTS INTERRUPTIONS”

Resistance is always serious in the context of HIV because of the potential for virus that is resistant to some drugs being resistant to other drugs in that same class (“cross-resistant”). All resistance, but especially cross-resistance, limits future treatments options.

One of the reasons that multiple (three or more) combinations of drugs have proved more effective in treating HIV disease is that it is much harder for the virus to develop resistance to three drugs at once – whereas HIV was able to develop resistance to one or two drugs – and often in a relatively short time.

However, if the recommended dosing schedule is not followed (known as “non-compliance” or “non-adherence”) then the chances of resistance developing increase a lot.

When you miss a dose of your combination, the drug levels will fall and HIV may begin to multiply. There are still some levels of drugs in your body but they are at too low levels (known as sub-therapeutic or sub-optimal levels). If there were no drugs present the virus would just multiply and resistance would not develop. But when there are drugs present at levels too low to suppress the virus, then the virus that can multiply the best is the virus that is most resistant to some of the drugs in your body. And with each missed dose the same thing happens – and over time the virus in your body will become more and more resistant.

For this reason a well planned and monitored break from your treatments is quite different to taking your drugs in an erratic or sporadic manner.

## **SOME OTHER ISSUES THAT MAY BE RELATED TO TAKING A BREAK FROM YOUR TREATMENTS**

Taking a break from your treatments may not be done for solely medical reasons. There may be other factors, such as work or travel plans that may make adhering or complying to your treatments regime difficult – so instead you may choose a complete break. Women with HIV who are trying to become pregnant may take a break in order to minimise any possible harmful effects of anti-HIV drugs on the foetus in early pregnancy (although later in the pregnancy HIV antiviral treatments will be recommended in order to minimise the risk of mother to child transmission). And you may just be ‘over treatments’ and psychologically need a break.

These reasons for taking a break may be just as legitimate and important for you as the medical ones. However, regardless of the reason for taking a break – the bottom lines remain the same – it is still important to monitor your health and inform your doctor.

## WHAT HAPPENS WHEN YOU STOP TREATMENTS – THE IMPORTANCE OF MONITORING

Each individual can react differently if they stop antiviral treatment.

In most people HIV soon starts to multiply more and quite quickly. Some people begin to see obvious signs of immune damage (eg their T-cell count begins to fall). In other people, evidence of immune damage may take longer (their T-cells can remain relatively stable for months).

Some people report feeling really well – particularly if they were experiencing drug related side effects. In some people, the virus begins to multiply very rapidly. Quite often this can sweat, fever and fatigue due to HIV itself.

You can't predict how you will react. Which is why monitoring is so important.

## YOUR DOCTOR(S) AND YOU

Until recently treatments breaks were hard to talk about – and many people with HIV reported difficulty in talking about this with their medical practitioner(s). However, most HIV-experienced doctors realise that treatments breaks are now a fact of life in the management of HIV. It is still the case that some doctors do not wish to discuss or countenance the possibility of treatments breaks. If this is the case then there is often the possibility of seeking a second medical opinion. While your doctor may not recommend a treatments break they will usually be prepared to discuss it – and it is much better for your medical management if they know what you choose.

While the evidence on treatments breaks is not clear enough to make firm recommendations what is clear is that stopping treatments without advice, monitoring, support or contingency plans is far more dangerous than a well-planned and monitored break from your treatments.

## TAKING A BREAK – SOME SUGGESTED GUIDELINES

### 1. Know how to stop

Viral load rebounds after stopping treatment. It is important that all drugs are stopped at once – i.e. if you're on a triple combination don't stop one drug one week and another drug a week later. However, different medications have different lengths of time that they are active in the body (their "half-life"). Drugs with a longer half-life will stay in the body when the other drugs have been cleared. Thus viral load may have started increasing while there is still one drug in your body – increasing the chances of developing resistance to that drug. This means that if you are on something such as nevirapine that has a longer half-life it's important to stop that earlier.

### 2. Monitor carefully

Maintaining a close watch on CD4 cell counts and viral load is the crucial thing to decide to do if you decide to take a break from your treatments. The rebound in viral load can occur quite soon after stopping. In some people this settles down to a reasonable baseline level and in others it stays too high – which is why it's important to monitor. It's probably not a good idea to respond to the viral load results taken very soon after stopping.

### 3. Plan your next treatment strategy

The word 'break' implies something with a beginning and an end. Unfortunately some people go on breaks, don't monitor and then only start treatments again when they get sick and their immune systems have been damaged quite a lot. So when starting a break it's a good idea to have your next combination already decided. If you're not taking a break that is part of a clinical trial then decide in advance with your doctor at what viral load levels and/or CD4 cell levels you will restart therapy.

### 4. Share the experience

This doesn't mean write the novel about it – though that might be fun. However, there are clinical trials that you can participate in that are evaluating different treatment breaks strategy. These may not be for everyone but it is certainly the case that we need more information from these sorts of studies to better inform our decisions.

# FOR FURTHER INFORMATION

## **NSW**

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AIDS Council of NSW (02) 9206 2000

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PLWHA(NSW) (02) 9361 6011

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## **VICTORIA**

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Victorian AIDS Council (03) 9865 6700

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PLWHA Vic (03) 9865 6772

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## **QUEENSLAND**

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Queensland AIDS Council (07) 3017 1777

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Queensland Positive People (07) 3017 1777

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## **SOUTH AUSTRALIA**

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AIDS Council of SA (08) 8362 1611

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PLWHA SA (08) 8293 3700

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## **WESTERN AUSTRALIA**

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Western Australian AIDS Council (08) 9482 0000

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HIV/AIDS Peer Advisory Network (08) 9482 0012

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## **TASMANIA**

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Tasmanian Council on AIDS,  
Hepatitis C and related Diseases (03) 6234 1242

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## **NORTHERN TERRITORY**

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Northern Territory AIDS Council (08) 8941 1711

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Positive Services (08) 8941 1711

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## **ACT**

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AIDS Action Council of the ACT (02) 6257 2855

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PLWHA ACT (02) 6257 4985

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