

# TREATMENT UPDATE

## April - May, 2007

Welcome to the 15th Queensland Positive People (QPP) Treatment Update Newsletter!

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*The information, comments and editing in this newsletter do not necessarily represent the views of those involved in direct medical care...  
...Always seek the opinion of your doctor.*

### HIV Infection doubles risk of heart attack in US patients, risk trebled in women

HIV infection doubled the risk of a heart attack for patients receiving care at Boston's two largest hospitals between 1996 and 2004, even after controlling for all the accepted risk factors for heart disease, researchers from Massachusetts General Hospital report in an article released early online by the *Journal of Clinical Endocrinology and Metabolism*.

Are people with HIV at higher risk of heart disease? Further research suggesting an elevated risk was published this week, and its conclusions are sobering.

HIV-positive people receiving treatment at two major US hospitals were 75% more likely to experience a heart attack, and women were almost three times as likely to experience a heart attack as their HIV-negative counterparts.

The findings could not be entirely explained by the presence of elevated cholesterol levels, high blood pressure or diabetes.

There are several reasons to think that the findings of the study, carried out by Steven Grinspon and colleagues at Massachusetts General Hospital, are robust.

Firstly, the study had a very large control group of HIV-negative patients (to compare with), and a substantial number of patient-years of HIV-positive followup.

Secondly, the researchers chose one hard endpoint - myocardial infarction - rather than the spectrum of cardiovascular disease investigated in some other studies.

Thirdly, the study had a higher proportion of African-Americans than other studies, and one-third of the HIV-positive patients were women, making its findings more representative of the HIV-positive population in the US than other studies, such as review of the Kaiser Permanente database in California.

Analysis of the DAD study group, which looked at HIV-positive patients in Europe and Australia also found that the elevation in risk might be as much as threefold, but they also found that the year-on-year risk of heart attack was probably around 1% based on their data.

In other words, although these findings are sobering, they shouldn't discourage anyone from taking antiretroviral therapy.

What they should do is encourage far greater discussion of risks for heart disease between doctors and patients. The Boston researchers found that they had data on the smoking habits of only 22% of their HIV-positive patients, despite the fact that patients were followed until 2004, when the risk of cardiovascular disease was already being widely discussed by HIV doctors.

More research is clearly needed in this area, but the findings add further weight to the case for choosing antiretroviral regimens that don't add to the risk of heart disease, and for smoking cessation advice to be given high priority in the work of any HIV clinic.

#### Treatment Officer's Note:

This new report reminds us once again of the strong linkages between smoking and its significant additive risk to cardiovascular disease.

QPP hopes to be able to offer a program for smoking cessation in the latter half of this year, and in doing so encourages PLWHA to call and register their interest in such a program with Peter Health Promotion & Treatments Officer on 3013-5505

**Reference:** Triant VA et al. *Increased acute myocardial infarction rates and cardiovascular risk factors among patients with HIV disease.* J Clin Endocrin Metab 2007 (advance online publication).

**Source:** [www.aidsmap.com](http://www.aidsmap.com) Article by Keith Alcorn.



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## Sculptra Access Trail Underway in Queensland

Queensland Health has provided substantial funding for a new trial of Sculptra (Poly Lactic Acid - PLA) for experimental rectification of *facial lipoatrophy* (fat loss in the face) as occurs via HIV and HIV treatment. The trial is called "QFLASH". This Queensland based trial has also been made available through the generous support of *Sanofi-Aventis* (manufacturers of Sculptra), in conjunction with NAPWA (National Association of People Living with AIDS) who have arranged a nationwide *Special Access Scheme* (SAS) with the company.

### Trial Sites

The trial is due to commence late April, 2007. In other words, it is enrolling – fast - now! There are **66 places** allocated for the whole state, between the following trial sites:

Cairns Sexual Health Clinic  
Townsville Sexual Health Clinic  
Rockhampton Sexual Health Clinic  
Nambour Clinic 87  
Gladstone Road Medical Centre  
Central Brunswick Medical Centre  
Royal Brisbane Hospital  
Princess Alexandra Hospital  
AIDS Medical Unit (AMU), Brisbane  
Brisbane Sexual Health Clinic  
Gold Coast Sexual Health Clinic  
Stonewall Medical Centre  
Toowoomba Sexual Health Clinic

### Getting In

For those people who regularly attend these clinics, please raise your interest with your treating doctor at those locations. For those people outside these areas, I encourage you to make enquiries with the study co-coordinator:

**Mr. Paul Negus**  
**AIDS Medical Unit**  
**Phone: 3837-5622.**

Paul can discuss with you ways in which you may be able access support schemes to avail your attendance at the sites for the treatment (every two weeks for 4 sessions – two weeks apart), and to assist your initial assessment as to whether you meet the entry criteria. The entry criteria are:

- 1) Patient and Doctor assessment for severity of your individual condition
- 2) Financial hardship to being unable to afford such treatment in the absence of a trial of this sort or through private means.

It is important to note, however, that there is a limitation to the level of extra funding and amounts for this purpose, which is unfortunate, but a reality of

the true cost of conducting such a trial with limited places available and limitations to the funding. This does not mean, however, that you should not enquire and personally advocate for your potential assessment and selection into the trial. I strongly encourage those of you who do feel you are deeply at the effect of lipoatrophy to do so.

### How is the trial structured?

50% of the patients will be allocated to immediate treatment, and 50% will be randomised to begin treatment 3 months down the track. All people will receive the same level of treatment. There are up to four injection treatments available two weeks apart for each patient.

The unique feature of this trial is the collection of information about your personal feelings and visual responses to the treatment, and any change you feel attributed to the treatment to your quality of life (i.e. sense of well-being and self image). You will be asked to fill out a self-assessment questionnaire in relation to this at the completion of the trial at 24 weeks and at 48weeks.

### How Does Sculptra Work?

*Poly-L-lactic acid* (polylactic acid/PLA), has been used in medicine and surgery for over 30 years. When injected into tissue, PLA does not cause inflammation or an immune system reaction in the tissue as often happens with other 'foreign substances'. When injected under the skin just below the cheek bone, polylactic acid is thought firstly to "fill-out" the cheek due to the volume injected. This first phase is followed by the formation of new collagen (a natural binding matrix in skin that 'knits' skin and associated fibres together), which thickens the lower level of the skin. Thus, both the first reaction and the secondary thickening are thought to make up for the lack of fat layers and, as a result, the skin 'rises' back to a more 'normal' appearance. Several small studies of polylactic acid for HIV facial lipoatrophy have shown both the treatment and the procedure are well tolerated. However at present the duration of the benefit is not known, but tends to be estimated to be around 3 years; and sometimes requires 'top-ups' within, or after, this period.

### The Future

This QFLASH trial does not allow for future top-up treatment after the trial has ended. People entering the trial therefore should understand that the trial is for once-off treatment only (comprising up to 4 injection sessions - 2 weeks apart each), and any future treatment with PLA (Sculptra) would be at your own expense.

PLA is registered in Australia (but not on the Pharmaceutical Benefits Scheme – PBS – which generally allows for low-cost co-payment of



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treatments). However, access is a different matter to cost. Access is not difficult (i.e. commonly available from many cosmetic physician clinics) - just expensive, in the absence of free trial programs like this. Although you will be treated fully within this access trial (being given the injections in areas of your face which are unique to your individual need), the durability (i.e. how long it will last for you, or any positive effects which may reduce over time) and the availability of future trial programs to further treat facial lipoatrophy, are not guaranteed.

Although some older antiretroviral HIV treatments have been noted to cause lipoatrophy at a greater rate and severity, newer and evolving treatments are tending to less contribute to this condition. Many doctors are now switching to these newer HIV treatments and combinations, although some people have needed to remain on the older treatments for various clinical reasons. Regardless, lipoatrophy still exists for many, and may be difficult to reverse in the absence of future counter treatments, other than PLA. There are, however, some potential alternative treatments which may be studied for lipoatrophy further down the track, but these investigational new treatments may more specifically have application to mitigating or reversing *peripheral* lipoatrophy (i.e. fat loss in the arms and legs, giving a 'veiny' look to them), rather than facial lipoatrophy. A roundup of these was provided in a previous edition of this Newsletter: *January – February 2006 (That newsletter reported on the 7<sup>th</sup> International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV. Newer research about lipoatrophy and lipodystrophy will be discussed in the next upcoming 9<sup>th</sup> Conference of the same name, to be held in Sydney this year 19<sup>th</sup>-21<sup>st</sup> July, 2007, so stay tuned!*

#### **What's important to know now?**

For those people entering the study it is important you understand why the study is being done, the procedures and assessments you will undergo, possible risks and benefits of the study and other important study information. A "*Participant/Patient Information Sheet*" will be provided to inform you of this and your written consent for involvement will also be sought once you have understood all the known current information about the product and what the trial is for. Further discussion and any queries you may have about Sculptra and this trial can be obtained from the specific trial sites; the Study Coordinator (contact info above); or the QPP Treatments Officer (contact info on front page of this newsletter).

## **New Treatments signal potential new treatment paradigm**

Several new medications have entered "Expanded Access Programs" in the USA, and likely soon here in Australia also. EAP programs are for people who have generally exhausted other medication options. Formal approval usually follows these programs within 6-12 months.

The following antiviral medications are currently available through new Expanded Access Programs (EAP) in the US:

#### **Raltegravir (MK-0518): An Integrase Inhibitor**

The Merck integrase inhibitor (MK-0518) is now available to individuals who have documented resistance to at least one drug in each of the three major drug classes (RTIs, NNRTIs, & PIs). Raltegravir is the first of a new class of drugs called Integrase Inhibitors (IIs) that most people's viral strain has not been exposed to. It inhibits HIV at a completely different part of HIV reproduction inside CD4 cells. Raltegravir is to be combined with the other current HIV medications which should include at least two medications to which an individual's virus is still sensitive to.

#### **Maraviroc: A CCR5 Antagonist/Viral Entry Inhibitor**

Maraviroc was designed by Pfizer to prevent HIV from entering the cells by blocking CCR5; one of two CD4 cell co-receptors which HIV uses to gain entry into CD4 cells. CXCR4 is the other co-receptor that HIV can use to gain entry into healthy cells. Since most people have never taken a drug from the CCR5 antagonist class, it is considered a new class that most HIV-infected individuals have not developed resistance to. This is true even if you have developed resistance to Fuzeon (T-20), which is another type of entry inhibitor called a fusion inhibitor.

This new treatment is intended to be added to an existing combination treatment regimen which is working reasonably well (stable). A test called - a viral tropism test - is used to determine which receptor your particular strain of virus is currently using to tell if the drug would work for you. We will probably see this drug available on an EAP soon in Australia.

#### **TMC-125: A Second Generation NNRTI**

First generation NNRTI HIV treatments include Stocrin (efavirenz), Viramune (nevirapine), and Rescriptor (delavirdine). While these are highly effective treatments, the first generation NNRTIs are known to have a low barrier to developing resistance. For this reason, many people have developed resistance to this entire class of medications.



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The Tibotec company has created an EAP for its investigational agent known as TMC-125. This antiviral medication is a 2nd generation NNRTI. TMC-125, and other 2nd generation NNRTI's currently in development, appear to be effective even when high level resistance to the first generation NNRTI's has occurred. They also appear to have relatively few side effects.

People eligible for this expanded access program should be failing their current regimen or currently be on a treatment interruption, and have resistance to the first generation of NNRTI's.

...Stay tuned for updates on these drugs as they may avail themselves to Australia in this fashion soon.

Source: [www.jonkaiser.com/](http://www.jonkaiser.com/) Adapted article by Jon Kaiser.

## Prezista (darunavir) Approved in Australia

**Prezista (darunavir)**, formerly known under the experimental title as "TMC114", has now been given marketing approval on the 15<sup>th</sup> March, 2007, by Therapeutic Goods Administration (TGA). However, a further Pharmaceutical Benefits (PBS) listing is yet to arise for the medication in order that it can be provided under the co-payment PBS subsidy scheme.

Nonetheless, the drug is **now available to all people** (not just those participating in current and ongoing trials of this drug). However, it is **limited for prescription to only those people who have run out of other viable treatment options** (i.e. people who have had long term ongoing previous treatment with anti-HIV drugs)

This new treatment, whilst not a new class of treatment, is an important new Protease Inhibitor (PI) treatment when other drugs might not be working as well as they could for you, and your CD4 counts are low.

It is to be taken twice daily (600mg tablet) in conjunction with ritonavir (100mg) in order to keep its levels up high enough in the blood to make it work. Without ritonavir to boost it, its levels may be too low and HIV might develop further resistance to the drug leading to drug failure to work properly. This is especially important for people who have run out of most previous options for treatment.

Side effects are considered to be low, but in very rare cases a severe skin rash can develop, as is the case with other existing NNRTIs.

Readers might also be interested to know that the company who have developed this drug



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(Tibotec/Janssen-Cilag), being a new entrant in the HIV treatment field, are also now developing and trialling two (2) other very long awaited new NNRTIs. Currently, there are only 3 types of that class of drug (but with only 2 in general use) which has long been not enough - i.e. efavirenz [Stocrin] and nevirapine [Viramune].

The first new experimental NNRTI is called TMC278 (no name yet) and is currently in early trial stages for people first starting treatments - comparing it to efavirenz (which may be a very useful change as the central nervous system effects - mood and sleep disturbances - which occur more commonly with efavirenz can be particularly hard to cope with for some people first starting treatment - even though those side-effects tend to diminish after 6-8 weeks). If this treatment further proves fruitful, it may likely soon emerge as a direct competitor to efavirenz for first starting treatment.

The second new NNRTI drug is TMC125, and it is intended (like TMC114) for treatment-experienced people, where the current limited number of NNRTIs is not enough if they begin to stop working well, rather than needing to switch to PIs (which tend to bring along with them greater metabolic side-effects, such as lipodystrophy), despite their potent effectiveness.

## NEW HCV Monograph of Hep C Treatment Experiences

A new research report developed by the National Centre for HIV Social Research (NCHSR) has been produced. The report explores people's experiential issues with hepatitis C treatment and its Management, and what some patients (on treatment) and health professionals (providing the treatment) say. The report is available for downloading from the NCHSR website:

[http://nchsr.arts.unsw.edu.au/publications\\_drugs.html](http://nchsr.arts.unsw.edu.au/publications_drugs.html)

Monograph 4/2006

Max Hopwood, Carla Treloar, Louise Redsull.

For Hepatitis treatment to be effective it requires daily and weekly treatment for at least six months (sometimes 12 months). Some of the side effects of treatment can be hard to deal with such as constant heavy flu like symptoms, and at times a strong depression specifically caused by the treatment. Various people may experience this in lesser or greater ways. It's important to prepare for Hepatitis treatment and seek support whilst taking it, if not for the side effects, but for the emotional support of waiting for the likely outcome as to whether the treatment will be successful or not. However, rates of success for people with HIV/HCV coinfection can be up to 60+%, but some people can't clear the virus, either spontaneously or via treatment.

The report explores some in depth issues about things such as:

- Contemplating treatment
- Side effects and resilient coping strategies
- Support during hepatitis C treatment
- Disclosure of being in treatment, and hepatitis-C-related discrimination
- Unrealistic optimism

## High Lung Cancer Risk in HIV, Smoking Not ONLY Factor

The risk of lung cancer is "substantially elevated" among people living with HIV, according to new data published by researchers at the National Cancer Institute. While the report in the January 11 issue of *AIDS* indicates that a large percentage of HIV-positive people are smokers, tobacco use could not entirely account for the increased risk, especially among younger adults.

Previous research has established that lung cancer is the third most frequently seen cancer among HIV-positive people in the United States, with [Kaposi's sarcoma](#) (KS) and [non-Hodgkin's lymphoma](#) (NHL) being the most common. The risk of lung cancer has been estimated to be two to seven times higher among HIV-positive people, compared to those in the general population. What's more, especially among HIV-positive people, survival following a diagnosis of lung cancer is especially poor.

Because cigarette smoking is very common among HIV-positive people in the U.S. – one analysis indicated that 60% to 80% of those living with the virus are smokers (compared to smoking rates of 20% to 30% in the general population) – higher-than-average lung cancer rates in this population do not come as a surprise. However, researchers have also questioned whether or not HIV infection itself further increases the risk of lung cancer.

To better understand lung cancer risk in HIV-positive people, Anil Chaturvedi, PhD, and his colleagues at the NCI reviewed records on 397,927 people living with AIDS linked to cancer registries in six U.S. states and five metropolitan areas.

The analysis published in *AIDS* included adolescents and adults with AIDS – aged 15 years or older at AIDS onset – diagnosed between 1980 and 2002. Data from the cancer registries were used to identify lung cancer cases in the period spanning five years before to five years after AIDS onset. However, the analysis mostly focused on lung cancer diagnoses within four to 27 months after an AIDS diagnosis.

In the ten-year period spanning five years before to five years after AIDS onset, 1,489 lung cancer

cases were documented. Compared to the general population, people with AIDS had a significantly increased risk of lung cancer, expressed statistically in the study using what is known as a "standardized incidence ratio."

Although the incidence increased appreciably with age, it was found that the risk was remarkably high in young people with AIDS. Among adolescents and adults between 15 and 29 years of age and diagnosed with AIDS, the risk of lung cancer was significantly higher relative to the age-matched general population.

As for sex, the incidence was higher in men than in women and increased with age. However, standardized incidence ratios indicated that the risk relative to the general population was higher for women.

Lung cancer risk was also elevated for all HIV risk groups, particularly injection drug users, and in all [CD4 \(T4 cell\) count](#) categories.

According to Dr. Chaturvedi's group, the alarming incidence of lung cancer in young people with AIDS suggests that the risk cannot be tied exclusively to the prevalence of cigarette smoking. However, it is possible that the effects of smoking – not just the duration of tobacco use – could be more severe in HIV-positive individuals.

The authors point to studies indicating an accelerated form of smoking-related emphysema – a risk factor for lung cancer – in HIV-positive people. Other types of lung damage, including significant inflammation, have also been documented in those living with the virus (including non-smokers).

Dr. Chaturvedi's group also indicate that HIV-positive people are more susceptible to lung infections and pneumonia caused by a wide range of organisms, such as [Streptococcus pneumoniae](#), Chlamydia pneumoniae, [Pneumocystis jiroveci](#), and Mycobacteria species (such as [Mycobacterium tuberculosis](#)). Repeated or chronic lung infections, they suggest, could increase the risk of lung cancer through chronic inflammation.

"In conclusion," Dr. Chaturvedi and his colleagues write, "the results of the present study indicate that lung cancer risk is significantly elevated among PLWHA and that smoking does not readily explain all of the excess lung cancer risk. Additional research is needed to understand the etiology of lung cancer among HIV-infected individuals."

**Reference:** Chaturvedi AK, Pfeiffer RM, Chang L, et al. Elevated risk of lung cancer among people with AIDS. *AIDS* 21:207-13, 2007.

**Source:** [www.aidsmap.com](http://www.aidsmap.com). Article by Tim Horn, Senior Writer & Editor, AIDSmeds.com



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## The limits of PEP: Saturation knowledge does not mean saturation use.

Knowledge of post-exposure prophylaxis (PEP) among HIV-negative gay men in Sydney, Australia, has reached virtual saturation point, with 97% aware of it, a study presented at the Sixteenth International AIDS Conference in Toronto reveals (Grulich).

However, the study also reveals that near-universal knowledge has not translated into universal use after HIV risk incidents. Just under a quarter incidents of the very highest-risk, namely unprotected receptive anal intercourse with a positive partner, resulted in men seeking PEP.

Some of the reasons gay men may not use PEP after a risk incidents were highlighted by another study from Toronto of so-called 'Easy PEP' (ePEP) which gave gay men 'starter packs' of tenofovir/FTC (*Truvada*) (Cretic). In this study gay men used their starter packs after 26% of cases of unprotected anal intercourse.

However young gay men (under 25) were better at using PEP: a slim majority of them used PEP after unprotected anal intercourse.

The first study was of the HIM cohort, a group of 1427 HIV-negative gay men enrolled between June 2001 and December 2004 via community venues in Sydney. Researchers conduct one phone and one in-person interview a year with researchers about their sexual behaviour and HIV risk factors. The yearly interviews have included asking cohort members if they knew about PEP and had ever received it.

Baseline knowledge of PEP was already high in 2001, with 79% of participants being aware of it following the PEP-NOW campaign that year (see this article for more). However, by 2004 this had risen to near-saturation level with 97% of participants being aware of PEP. This may be higher than the level of knowledge in the gay community at large, as HIM cohort members are informed and motivated enough to put themselves forward for research, but this still implies very high levels of knowledge of PEP in the gay community.

In contrast, as we were reminded by another poster at Toronto (Dodds), the UK has a lot of catching up to do: after the Terrence Higgins Trust's campaign on PEP, levels of knowledge in the annual UK Gay Men's Sex Survey (GMSS) increased from 24% in 2003 to 40% in 2005.

A comparatively large proportion of the cohort had used PEP, too: 6% a year, compared with 1% *ever* in the GMSS.

However, the question must be, why didn't even more men use PEP, considering this high level of knowledge? PEP was being sought appropriately and men graduated their level of use accurately according to the perceived risk. For instance, 1% of men sought PEP after incidents involving no anal sex but 10% sought it after unprotected anal intercourse (UAI) with a casual partner and 26% sought it if that partner was known to be HIV-positive (all these figures are annual incidence, i.e. the proportion who sought PEP within the last year).

They did seek PEP a lot less often with regular partners: whereas 11% of those who'd had UAI with casual partners of unknown HIV status sought PEP, only 5% of those who'd had UAI with regular partners of unknown status sought it, and only 18% of those who knew their regular partner was positive.

In terms of the type of anal sex, 8% sought PEP when they had been the active partner in casual sex, 9.8% when the passive partner without ejaculation, but 23% when a casual partner had ejaculated inside them.

In an interesting contrast when it came to regular partners 8% sought PEP when they had been the passive partner without ejaculation, but only 4% when ejaculation had occurred, suggesting that when regular partners do go "that far", conscious and willed risk-taking may be involved.

Use of PEP was not associated with any change, either positive or negative, with subsequent sexual risk behaviour with either regular or casual partners.

By the end of 2005 there had been 42 seroconversions among the HIM cohort participants, giving an overall HIV incidence of 1% a year (in the UK, the last estimate of incidence among gay men attending GUM clinics – who may be a higher-risk group – was 3% a year in 2004). However use of PEP was not associated with reduced incidence: rather the opposite. Ten men who had ever sought PEP seroconverted, yielding an annual incidence among this group of 3% a year.

This doesn't mean that PEP, when taken, didn't work, but that, as the figures suggest, the men were also involved in HIV risk incidents (indeed a majority of incidents) where they didn't seek PEP.

So why, despite saturation knowledge, do gay men still not use PEP? A study from Canada looked at reasons for not using PEP after a risky episode.

This small study used the concept of giving men three-day "starter packs" of *Truvada* to take in case of a risk episode. The participants were gay men aged 18-60 who were not in a monogamous relationship and reported unprotected anal sex at



least once in the last six months but less than once a week. They had access to the starter packs for six months and were told to call researchers via a 24-hour helpline if they initiated PEP. They then got the remaining 25 days of PEP from their clinic.

The starter packs were withdrawn after six months but participants were followed for an additional three months to chart any further changes in behaviour or PEP use.

The subjects were split between a youth group of 23 men aged below 25 and an adult group aged 25 and over.

Sexual risk behaviour declined in both groups during the study from two-thirds of participants reporting sexual risk behaviour at baseline to less than half at nine months. The youth group had higher baseline rates of sexual risk with nearly three-quarters reporting risk behaviour at baseline, but their risk behaviour declined more during the study, to around 45%. However whereas adult risk behaviour continued to fall after the ePEP packs were withdrawn, among youth it rose again and stood at 60% at nine months.

Nearly all the adult group (89%) reported at least one episode of UAI during the study but fewer of the youths (73%). Furthermore the youth were better at using PEP; nearly half (47%) of incidents of UAI were accompanied by PEP use in the youth group compared with only 29% of incidents in the adult group. However only a third of participants said that the availability of PEP had changed their sexual behaviour (in either direction) by the end of the study, though this proportion did increase as the study went on.

There was a high rate of seroconversion in the study; five men (three youth and two adults) became infected during the nine months, yielding an annual incidence of 11%. Four of the five never used ePEP and the fifth did not use it during the three-month period he became infected.

So why did the men not take the pills in their bathroom cabinet after a risky episode? The poster supplies a revealing list of reasons:

- "I just have a feeling about which partner I can trust"
- "I'm not at risk because my partner gets tested"
- "I'm lucky and probably won't get HIV"
- "I was in love with him and didn't want to think about it"
- "It wasn't risky because it was very brief"
- "Pulling out is relatively safe"

- "As long as my partner does not cum in me I can be certain I won't get infected"

One of the five took PEP twice but still became infected: he was a heavy drinker and took PEP after two incidents of blacking out at a bathhouse and coming to 'with memories of being barebacked'. He did not take PEP the third time this happened because he 'didn't think anything risky had happened' and then seroconverted.

Since only one of the people who seroconverted said they had changed their sexual risk behaviour during the nine months, this study may document the limits of that a purely biomedical prevention intervention can do for 'high-risk' gay men without additional cognitive or behavioural help.

Two other studies of PEP (Mayer, Lunding) showed better results. In March 2005 the HIV clinic in Boston switched its PEP combination to *Truvada* from *Combivir* (AZT/3TC). Since then 57 people have taken it, the same number as in the Canadian study, but with no seroconversions (and lower rates of side effects than with Combivir).

PEP has been available in Denmark since 1998, and the country operates a registry documenting every prescription. So far PEP has been prescribed 257 times, and to eleven individuals more than once. Only one seroconversion during PEP has been documented, of a gay man who started PEP 15 hours after the risk incidents and completed his course, but who later admitted to having risky sex again during the period he was on PEP.

Denmark's guidelines state that PEP can only be prescribed within 24 hours of the risk incident, and the average length of time is only 10 hours; in the UK, where guidelines say it can be prescribed within 72 hours, the average waiting time is 23 hours.

Lastly, there was a presentation (Ende) from somewhere where PEP is much more patchily documented and offered: New York State. PEP has been available in hospital emergency departments since December 2004 but New York guidelines state that the source partner *must* have HIV and that PEP will only be prescribed within 36 hours of exposure. A survey revealed that only 60% of hospitals have a protocol for prescribing PEP after what is called 'voluntary sex' (i.e. not sexual assault). PE was prescribed two-thirds of the time after a report of sexual assault but only 43% of the time after voluntary sex. Thirty per cent of emergency departments, despite the state guidelines, did not prescribe PEP, only a third follow-up patients and only 23% review seroconversion rates.

#### References:

Creticos C et al. *Feasibility of easy post-exposure prophylaxis (PEP) for HIV prevention in high-risk men*. Sixteenth international AIDS conference, Toronto, abstract THPE0449, 2006.



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Grulich A et al. *Non-occupational post-exposure prophylaxis against HIV (NPEP) and subsequent HIV infection in homosexual men: data from the HIM cohort*. Sixteenth international AIDS conference, Toronto, abstract TUPE0434, 2006.

Lunding S et al. *Danish postexposure prophylaxis (PEP) registry: use and failure of antiretroviral chemoprophylaxis following sexual exposure to HIV*. Sixteenth international AIDS conference, Toronto, Abstract TUPE0433, 2006.

Mayer K et al. *Tenofovir-based regimens for Non-Occupational Post-Exposure Prophylaxis (NPEP): improved tolerability and adherence compared to AZT-based regimens*. Sixteenth international AIDS conference, Toronto, Abstract TUPE0432, 2006.

**Source:** [www.aidsmap.com](http://www.aidsmap.com). Article by Gus Cairns, Saturday, August 19, 2006

and HIV-positive MSM with partners of unknown HIV serostatus.

"Our data support the hypothesis that MSM are increasingly selecting HIV seroconcordant partners when engaging in unprotected anal intercourse," the investigators say. "The choice of HIV negative people as the insertive partner, referred to as strategic positioning (or 'seropositioning') may reflect a second strategy to decrease HIV risk."

"There are other reasons why people may choose partners of the same serostatus beyond the risk of HIV transmission," Dr. McFarland explained. "For example, HIV-positive persons may find more support in a relationship with another HIV-positive person because they share many more of the challenging aspects of living with HIV."

The investigator concluded: "Our observations and studies of serosorting may simply be documenting the rise of a community-generated HIV prevention strategy that is happening whether we have any control over it or not." Dr. McFarland said.

**Reference:** Sex Transm Infect 2006;82:461-466.

**Source:** [www.aidsmap.com](http://www.aidsmap.com) Article by Will Boggs, MD. January 15, 2007.

## 'Serosorting' Appears To Be Limiting Spread of HIV

Selection by men of sexual partners and behaviours according to HIV status, a phenomenon called "serosorting", influences the spread of HIV and other sexually transmitted infections, according to a report in the December 2006 issue of Sexually Transmitted Infections.

"Prevention with positives is a promising point of intervention to slow the epidemic by preventing further transmission," Dr. Willi McFarland from the San Francisco Department of Public Health, California told Reuters Health. "With respect to serosorting in particular, physicians should be ready to discuss the implications of HIV-positive patients having unprotected sex with other HIV-positives."

Dr. McFarland and colleagues attempted to assess whether increases in HIV serosorting contribute to preventing further expansion of the epidemic and have other effects on other sexually transmitted diseases.

Despite decreases in the incidence of HIV infection among men who have sex with men (MSM) in San Francisco, the authors report, cases of rectal gonorrhoea and early syphilis increased from 1998 to 2004.

Over this interval, there was an increase in unprotected anal intercourse, the results indicate, but the behaviour decreased among HIV-negative

## Study shows selenium has positive effect on HIV Viral Load and CD4 counts

Daily supplementation with 200µg of selenium stabilised viral load and modestly increased CD4 counts in both untreated (not taking HIV drugs) and treated (taking HIV drugs) PLWHA according to a recent nine-month randomised trial in the US. The researchers say their findings suggest a role for selenium supplementation as a simple, inexpensive and safe adjunct therapy for HIV, and that longer-term research into its use should be undertaken.

Selenium is a mineral essential for human health. Deficiencies can lead to immune dysfunction and cardiomyopathy (heart muscle disease), and are common in resource-limited settings and in countries with low selenium levels in soil\*.

### \* **Treatment Officer's Note:**

*Australia is generally noted to have selenium deficient soils.*

Selenium deficiency has been noted in HIV disease and predicts an increased risk of death. Test tube incubation of HIV-infected white blood cells (called "monocytes") with selenium results in the suppression of HIV replication.

Researchers from the University of Miami, who have extensive experience of investigating the relationship between HIV disease and micronutrient deficiencies, recruited 262 adult HIV-positive



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people, three quarters of whom were on HIV drug treatments when they started the study.

Participants were randomised to receive 200µg of selenium daily (Selenomax), or a placebo. Selenomax was chosen because it was considered most likely to provide high levels of bioavailable selenium - not all selenium supplements may be as effective in raising plasma selenium levels.

About half the group (141 people) were given selenium, and the rest (121 people) were given a placebo (fake) tablet. Adherence to the selenium was monitored by a computerised chip in the cap of the pill bottle (which basically counts and records each time the bottle is opened).

At the start of the trial people in both groups had similar selenium levels.

	Selenium Group	Placebo Group
Mean viral load (copies/ml)	24,558 (+/- 87,051)	10,491 (+/- 20,251)
Median viral load (copies/ml)	688	209
Median CD4 cell count	417	440
%Antiretroviral therapy	74.6%	71.7%
% undetectable viral load	37.6%	35.5%
Prior AIDS diagnosis	62.7%	60%
Mean selenium level (µg/L)	112	110

After nine months 174 participants remained in the study (91 selenium group, 83 placebo group). During this time mean selenium levels rose by 0.5µg/L in the placebo group and by 323.2 µg/L in the selenium group. A greater increase in selenium concentration was shown to predict decreased viral load ( $p < 0.02$ )\*, and indirectly, increased CD4 cell count ( $p < 0.04$ )\*.

**\*Treatment Officer's Note:**

The figures above are both modestly significant results, the best result being in reduction of viral load. There were some differences in non-responders v's responders in both groups, but basically the results showed that:

- Around half of those receiving antiretroviral therapy in this study had detectable viral load at the start of the study, and those with detectable viral load in the placebo group experienced a twofold greater increase in viral load than those in the selenium group. This finding led the authors to conclude that:
- The selenium effect on viral load was independent of any effect of antiretroviral therapy, but why selenium supplementation appears to have a suppressive effect on viral load is not known.

It is thought that Selenium may reduce the oxidative stress (free radicals) that is one stimulant of HIV replication, or it may directly suppress HIV replication, but the authors say that strong evidence for the latter is still lacking.

The authors note that the main limitation of their study is the limited follow-up. They have data on nine months follow-up at present, and have only measured selenium levels, viral load and CD4 cell counts at one time point after starting selenium supplementation. They recommend further research to examine how selenium exerts an effect on viral load, and to determine whether the effect of supplementation on the CD4 cell count is solely a consequence of viral load suppression, or whether selenium also has an additional immunological benefit in HIV disease.

**Reference:** Hurwitz BE et al. Suppression of human immunodeficiency virus type 1 viral load with selenium. A randomised controlled trial. Arch Int Med 167: 148-154, 2007.

**Source:** [www.aidsmap.com](http://www.aidsmap.com) Adapted from article by **Keith Alcorn**, Tuesday, January 23, 2007. *Selenium supplementation has positive effect on HIV viral load, CD4 counts in randomised study.*



## Understanding Lifespan

Dr Wohl, in your recent podcast interview, you mentioned a recent study that was done to try to find out the "cost of HIV treatment". The study also came up with an "average lifespan" number of **24.2 years** based on current treatments and starting treatment around the current guidelines of CD4~350, or a 15% ratio (of CD4 to CD8 cells).

This seems to be in conflict with the CDC's June 2005 update. Which states that there are about 1.1 million Americans who are HIV positive (between 1 and 1.2 million). The 18,000 annual AIDS deaths would be only 1.6% of this population. This means an annual remainder of 98.4%. A simple calculation ( $.984^{43}=.50$ ) shows that at this rate of attrition it would take about 43 years on average for the HIV positives to die from AIDS (i.e. for half of them to succumb to one of the 30 or so old diseases that are called AIDS if the patient is HIV positive).

I guess I'm finding it hard to understand the discrepancy in the two sets of numbers...

I understand that there are many many factors that go into these kind of "statistics", with the most important among these being how variable each individual person responds to the particular strain and subsequent mutations of their (their) virus.

I also understand that many of these "lifespan" numbers are just statistical mathematics, which covers things like averages of averages, etc.

To help understand this on a more personal level, can you tell me if I'm understand the following facts correctly (understanding that each one assumes "responds well"):

1) Based on current guidelines, treatment should start (and not see "interruptions") roughly around  $CD4 < (350/15\%)$ , especially if the VL is High ( $>100,000$ )

2) Those that have a "non-resistant" strain and maintain strict compliance with their treatment plan can HOPE to see VL become undetectable and see CD4 rise over time.

3) Those that start treatment around 350 and respond well could hope to see CD4 rise upwards of approx 500 with a few responding so well as to near the level of 800 (which is the lowest range of "normal").

4) Those that see VL not reaching undetectable are probably facing some amount of drug resistant strains of the virus in their system.

5) Those that reach undetectable VL, but don't see increases in CD4 may be experiencing a deeper level of infection of Latent HIV Reservoirs (marrow, brain, & CD4 "stem cells" that are infected) such that while not contributing new virus to the bloodstream, those long lived cells are passing HIV

via normal stem cell mitosis (transfer) and subsequent differentiation, meaning that the resulting "new" CD4 cells are often short lived and may not reach maturity.

6) People don't die from HIV, they die from Opportunistic Infections and basically what amounts to long term treatment toxicities. It's this one that I'm finding a degree of conflicting information around.

6a) Would it be correct to say that "Age", and thus lifespan, is predominately an effect of a cell's ability to maintain healthy mitochondria? We age because as the mitochondria in our cells replicate both oxidation as well as generational "errors in replication" result in depletion of mitochondria as well as less "healthy" mitochondria over time.

6b) So with treatment while we might maintain "near healthy" CD4 levels and undetectable VL which can prevent most OIs, there is still the combination of HIV's direct effect on cells (increased Apoptosis - cell death) which when combined with mitochondrial depletion being caused by most of today's HIV medications, will still result in shorter lifespans than might be considered "normal"?



Response from Dr.

Wohl

You raise many important points. It will be difficult to answer all of your excellent questions in detail as the text of such an answer would be the basis of a nice book reviewing much of what is known about HIV infection.

As far as the article I described in the podcast, the paper presented results generated from a computer simulation of a hypothetical cohort of patients starting therapy. It is not an accounting of what is happening now to the mix of HIV+ people who are at various stages of HIV infection and HIV treatment.

**The 24 year estimate is to be taken with a large grain of salt**

The computer can not take into account everything that influences life expectancy. It also does not incorporate major advances in HIV care that I think are inevitable.

The bottom line regarding treatment is that current HIV therapy is potent and in the majority of patients will drive the viral load to very low levels, permitting growth of the T-cells. How long this lasts depends on many factors - treatment adherence and pre-treatment drug resistance being major factors. How high the T-cell count can go is



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very individual but generally those starting with a T-cell count of 200+ will see increases that approach or enter into the normal range.

At present, most all people with HIV infection should start therapy before the T-cell count drops below 350. If HIV is detected at a lower count, therapy should start right away. There are data suggesting starting HIV therapy at higher T-cell counts may be even better. We will see if this translates into a tendency to initiate therapy even sooner in the course of infection - I think it might\*.

**\* Treatment Officer's Note:**

We are left to wonder does this statement suggest a return to the "hit-early" - at 500 CD count - old treatment paradigm?  
...Are we coming full circle again?

The causes of death among people with HIV are less and less related to opportunistic infections (in the US and Europe, at least). Liver disease, typically as a result of hepatitis, is a major cause of death as are cancers - some of which may be arguably related to immunosuppression from HIV but also from increasing age of those with HIV. Infections are a problem mostly in those with really low T-cell counts. Cardiovascular disease also accounts for some deaths among HIV+ folks, but this is also the major cause of death among people living in the US, Canada and Europe. The contribution of HIV therapy to heart disease developing among people living with HIV, so far, seems to be low.

There is more to life, and death, than mitochondria.

**In short, HIV therapy is good. All the data we have so far demonstrates that HIV meds prolong life - how long we just do not know at this point.**

There are side effects of these meds but it looks like the side effects of HIV itself trump these and are more life-threatening to more people. Starting HIV therapy before the T-cell count declines below 350 is beneficial. Taking meds that are potent and active against the virus an individual harbours and taking them as directed reduces the risk of their failure.

I hope this helps. DW

Source: [www.thebody.com](http://www.thebody.com) Jan 30 2007.

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## Are You Affected by Welfare to Work? Tell Your Story and Make a Difference!



Are you having problems with Centrelink or with an agency that is helping you to look for work or to get ready to look for work?

Have you been affected by the Federal Government's recent changes, called *Welfare to Work*?

Are you a person with a disability?

If so, the Australian Federation of Disability Organisations would love to hear from you.

We are collecting stories from people with disability about their experiences dealing with Centrelink and other agencies. We will use the stories to help the Government and the media to understand the impact of *Welfare to Work*.

You can find forms to help you to tell us your story on our website: [www.afdo.org.au/node/80](http://www.afdo.org.au/node/80), or you can call us on 03 9662 3324 and we can post them to you.

**If you would like to talk to someone about your story, or you need help to tell it, call us on (03) 9662 3324. If you live outside Melbourne we will call you back.**

*The AFDO gratefully acknowledge support from the Reichstein Foundation for this project*

## Scientists Explore Possible New Ways to Fight AIDS

A naturally occurring molecule saves vital immune system cells from cellular suicide during the onslaught of the AIDS virus and might help keep the body's natural defences working in HIV-infected people, a study found.

The findings represent a potential new avenue to fight the effects of the human immunodeficiency virus, HIV, according to U.S. National Institutes of Health scientists whose work was published on Monday in the Proceedings of the National Academy of Sciences.

Dr. Paolo Lusso and colleagues at the NIH's National Institute of Allergy and Infectious Diseases looked at the role played by interleukin 7 in averting the death of T cells, a kind of white blood cell important to the immune system.

Interleukin 7 is a substance important in maintaining proper functioning of the immune system.

AIDS has killed more than 25 million people since it was first recognized in 1981. About 40 million people now live with HIV, with sub-Saharan Africa hardest hit.

Lusso expressed "reasonable optimism" that treatment involving interleukin 7 may benefit people with AIDS, a disease for which no cure exists.

"I don't think one solution will be applicable to all the patients. It's possible that IL-7 (interleukin 7) may benefit some patients and do nothing in other cases," Lusso said in an interview.

"But I think we are moving in the right direction because we are starting to appreciate that antiretroviral therapy alone (existing AIDS drug treatment) is not sufficient to bring back a full immune competence, and we are starting to identify at least some strategies that may work."

### **Immune System Targeted**

An insidious aspect of HIV is that the virus attacks the body's natural defences -- the immune system.

In assaulting the immune system, HIV hides inside certain T cells. These cells, as the infection progresses, commit cellular suicide -- called apoptosis -- undermining the body's ability to combat infections and certain cancers. In fact, the virus manages to induce the suicide of many more T cells than it directly infects.

The researchers, who also included Dr. Lia Vassena and NIAID Director Dr. Anthony Fauci, used blood samples from 24 HIV-infected people. They added interleukin 7 to the blood samples and then gauged the survival of T cells.

The actual patients themselves were not treated with interleukin 7.

The samples with interleukin 7 displayed lower levels of T cell death. The benefits differed from sample to sample based on the person's stage of infection, the study found.

The researchers believe interleukin 7 potentially could be used alongside existing AIDS drugs to bolster the immune system.

Lusso noted that existing AIDS drugs can keep the virus at bay for years, but damage to the immune system commonly persists even after years of such treatment.

Scientists want to find new ways to remedy these immune defects, with the aim to make the immune system functional even in HIV-infected people.

Lusso said apoptosis may be a major mechanism through which T cells die in AIDS. The new study is important, he said, in that it identifies how interleukin 7 may help -- by preventing these cellular suicides.

He said the next step is a study in which monkeys with the simian equivalent of HIV are given interleukin 7 to see if it blocks immune system dysfunction and immune cell depletion.

### **Treatment Officer's Note:**

*This is exciting news which reinforces that medical researchers remain on a constant quest to find new and better ways to treat HIV.*

Source: <http://today.reuters.co.uk/> © Reuters 2007. All Rights Reserved. Mon 5 Feb 2007 22:00:19 GMT. By Will Dunham.

## **Website of the Month**

### **Social Network Website for PLWHA**

[HIVConnect.net](http://HIVConnect.net) is a new social network website for people with HIV/AIDS, and the people who support them: Community Based Organisations, AIDS Service Organizations, and the family / friends of HIV-positive people.

Whilst this website is US based, our experiences are often the same, or at least worthwhile to share and create new bonds and friendship. Long term survivors of HIV/AIDS are becoming isolated environments, where the extended use of medication and mutations of the virus are creating distinctive responses in many individuals. Doctors often face unique situations, yet sharing these experiences is often difficult and time prohibitive. Those that are newly diagnosed today have a completely different experience from those that were diagnosed over 20 years ago. It is imperative that the stories and experiences of the long term survivors are preserved and shared with this new generation and the organisations that serve to community. HIVConnect.net provides a place for authentic communication. The site hopes to make life easier for all who are affected by HIV/AIDS while educating those that seek to support them.

### **NEWS FLASH !!!**

QPP has a new Peer Support Officer:  
**Jarran Heywood.**

People who are interested in creating and contributing to new peer support groups and activities please feel free to contact Jarran by:  
Email: [jheywood@qpp.org.au](mailto:jheywood@qpp.org.au) , OR  
Phone: 3013-5504, OR  
Toll Free: 1800-636-241



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