

## The bones of the matter

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As people are living longer with HIV, due largely to the introduction of [HAART](#) [1] Highly Active AntiRetroviral Therapy ??? aggressive treatment of HIV infection using several different drugs together., we know that there are still likely to be some significant health impacts, both from the [virus](#) [2] A small infective organism which is incapable of reproducing outside a host cell. itself and from its treatments. One area that has raised concerns and some controversies for researchers and physicians is bone disorders.

Studies have shown markedly higher rates of osteopenia and osteoporosis in people with HIV compared with the general population and the exact causes of this and the best treatments to be used have been the subject of some debate.

Osteoporosis is the wasting of bone tissue due to mineral depletion and osteopenia is the moderate form of the condition. Like all body tissues, bones are in a constant state of flux with a process called bone remodelling or turnover. Bone tissue is destroyed or assimilated into the body (called resorption) to allow calcium and phosphates stored in the bones to enter the bloodstream to help with body functions such as blood clotting, nerve transmissions, and fluid movement between cells. Bone formation then occurs to replace this loss — at a rate of about 15% in healthy adults every year.

The body is less able to absorb the dietary calcium needed for healthy bone growth as you get older. When there are irregular rates of bone resorption and formation, and more bone loss, bone disease develops.

Osteoporosis is a common bone disorder in the aged – with approximately 25% of women and 13% of men over the age of 50 being affected in US studies. These people are at a high risk of bone fractures with thinner bones in the hip and fore- [arm](#) [3] Any of the treatment groups in a randomised trial. Most randomised trials have two "arms," but some have three "arms," or even more. being more likely to break with the condition. There is also the risk of spontaneous fractures of the spine leading to curvature in the back, often seen in older people.

Bone Mineral Density (BMD) is the main measure used to detect bone loss and it is generally assessed through a DEXA scan, although there are also blood and urine tests which can help with diagnosis. The extra risk factors for developing bone disorders, apart from ageing, include a family history of the disease, endocrine disorders, low sex hormone levels, gastrointestinal disease, rheumatoid arthritis, depression and alcoholism.

Additional factors include nutritional deficiencies (particularly low intake of calcium or Vitamin D), smoking, lack of exercise, low weight, use of corticosteroids and anti- convulsants, low body mass index and racial origin (with a greater risk in Caucasians and Asians).

### Osteopenia in HIV-positive people

While there have not yet been high numbers of reports of fractures related to osteopenia or osteoporosis reported in people with HIV, there is a much higher incidence of the conditions in HIV- positive people generally, even in young children, compared with the general population.

Brown and Qaqish from John Hopkins University summarised recent studies from around the world which showed 67% of the HIV+ population studied had reduced bone density (six times greater than uninfected controls) and 15% of HIV-positive population has osteoporosis (three times more prevalent than the controls) <sup>1</sup>.

As positive people get older, particularly those who already have some limb wasting, it seems likely that the incidence of bone disease and fractures related to falls, will become greater.

Professor Jenny Hoy from the Alfred Hospital in Melbourne was one of the early researchers to report on high levels of osteopenia in HIV-positive people. In a presentation to the CROI Conference in 2000, Professor Hoy found in 80 Australian patients with lipodystrophy [enrolled](#) [4] The act of signing up participants into a study.

Generally this process involves evaluating a participant with respect to the eligibility criteria of the study and going through the informed consent process. In the PIILR study 28% had evidence of osteopenia and 9% had osteoporosis. Other research papers since have put the prevalence of osteopenia at between 21 and 45% of people with HIV.

## Role of HAART?

What might be the cause of this high prevalence? There still does not seem to be consensus amongst researchers and physicians about this: early reports suggested a possible involvement of HAART in the problem. The early reports of bone mineral loss, including Professor Hoy's, were in people who had been on protease inhibitors (PIs) and there was some evidence cited at the 7th CROI by Tebas of Washington University in St Louis that, [in vitro](#) [5] (Latin: within the glass) refers to the technique of performing a given experiment in a controlled environment outside of a living organism; for example in a test tube. (test tube) some PIs inhibit the production of Vitamin D<sup>3</sup>.

At the Lipodystrophy Conference in Toronto in 2000, Dr Andrew Carr from St Vincent's Hospital in Sydney theorised that there might be a relationship with lactic acidemia induced by taking NRTIs as well as a lower body mass index prior to antiretroviral therapy. However these theories were not proven at the time and some other researchers since have failed to find this connection. As further research is done, some association with HAART may prove to be a co-factor along with other causes.

Some of the suggested causes include lower levels of sex hormones in both HIV-positive men and women, deficiencies in growth hormone, high cytokine levels (part of the body's response to inflammation) and some relationship with HIV wasting (as yet unclear).

The particularly disturbing finding presented at the 8th CROI by researchers at St Luke's-Roosevelt Hospital in New York that there was a significant correlation between HIV status and loss of bone mineral density in children, and that this gets worse with age, shows a need for bone density to be monitored in all positive people. <sup>3</sup>

## Treatment and prevention

Calcium supplementation has long been recommended as a treatment for people with osteoporosis with the recommendations for a daily intake of 1200-1500 mg per day for post menopausal (over 50) being probably a good marker for people with HIV although this has not been firmly established in trials yet. Good sources of dietary calcium are dairy products, fruits and vegetables.

Vitamin D supplements can also be used to help with the absorption of calcium although people with HIV need to consult with their doctors around the dose as PIs can lift the levels of Vitamin D too high. Good dietary sources are fish- [liver](#) [6] A large organ, located in the upper right abdomen, which assists in digestion by metabolising carbohydrates, fats and proteins, stores vitamins and minerals, produces amino acids, bile and cholesterol, and removes toxins from the blood. oils, egg yolks as well as milk, breads and breakfast cereals which have been fortified with Vitamin D. Getting at least 15 minutes unclothed exposure to sunlight three times a week also helps with you gain your daily allowance of the vitamin.

Weight-bearing exercise is also highly recommended for people with low BMD. It stimulates bone formation and strengthens muscles attached to the bone, as well as improving balance and agility, reducing risks of falls and bone injuries. This kind of exercise includes lifting weights, brisk walking, hiking, jogging and stair-climbing. It should be carried out for one hour at least three times a week to gain maximum benefit.

Giving up smoking and reducing alcohol can help too as both have been linked with osteopenia.

There are other therapies suggested for osteoporosis which include testosterone replacement for men and possibly women although there is not a lot of [clinical](#) [7] Pertaining to or founded on observation and treatment of participants, as distinguished from theoretical or basic science. data of its use for this purpose in people with HIV. Studies of drugs called bisphosphonates, particularly alendronate, shows promise in treating people with HIV for this problem as they have been found not to interact with [antiretrovirals](#) [8] A medication or other substance which is active against retroviruses such as HIV..

Professor Jenny Hoy said that research into bone disorders in people with HIV is being conducted to look at changes over time in bone mineral density (most studies performed to date have been a single snapshot in time of a group of patients, all at different stages of their HIV infection journey). The impact of different antiretroviral agents on BMD in the short and long term needs to be evaluated, and the effect of HIV itself, or immune activation secondary to HIV infection, requires investigation.

We need to develop practical guidelines for monitoring of BMD in HIV-positive people, and find ways of funding the DEXA scans (not currently funded for monitoring in HIV infection). Professors Andrew Carr and Jenny Hoy have written a sub- study that will compare changes in BMD in patients enrolled in the START study, and they are currently applying for funding for this work to become a part of the main study when it is rolled out beyond the pilot phase.

Professor Hoy is also trying to find funding for Alfred patients with HIV at the highest risk of osteoporosis. Currently the hospital is seeing a number of fractures in patients particularly in the vertebrae and femur.

The longer we live with HIV the greater the risk, it seems, that we will develop a lower bone mineral density and possibly a bone disorder. It would seem that having a regular DEXA scan may become a recommendation for people with HIV as is eating a good diet, full of calcium and sufficient Vitamin D. The odd dose of sun doesn't hurt either. A brief lie in the sun—now that would be one of the better medicines a doctor could order!

Thanks to the HIV Hepatitis C and STI Education and Resource Centre at the Alfred Hospital and to Professor Jennifer Hoy for help with this article.

## References

1. Brown T, Qaqish RB, Antiretroviral therapy and the prevalence of osteopenia and osteoporosis: a meta-analytic review, *AIDS* 2006: 2165-2174.
2. Tebas. P et al, Accelerated bone mineral loss in HIV- infected patients receiving potent antiretroviral therapy, 7th CROI, Abstract 207.
3. Arpadi, S. et al, Decreases on total bone mineral content progress with age in HIV-infected children, 8th CROI, 2001, Abstract LB8.

- [bone disorders](#)
- [treatment side effects](#)

## Links:

- [1] <http://www.napwa.org.au/glossary/term/96>
- [2] <http://www.napwa.org.au/glossary/term/125>
- [3] <http://www.napwa.org.au/glossary/term/470>
- [4] <http://www.napwa.org.au/glossary/term/489>
- [5] <http://www.napwa.org.au/glossary/term/500>
- [6] <http://www.napwa.org.au/glossary/term/102>
- [7] <http://www.napwa.org.au/glossary/term/475>
- [8] <http://www.napwa.org.au/glossary/term/122>