HIV and its long-term impact on the gut

By Heather Ellis, Positive Women Victoria

With the gut the largest part of our immune system, HIV hits this area the hardest in those early days of transmission before diagnosis and before antiretroviral therapy (ART) – but even with ART, what does this mean for the long-term health of people living with HIV? Heather Ellis, communications and engagement coordinator with Positive Women Victoria, who was diagnosed with HIV in 1995, spoke to infectious diseases and HIV Cure expert Professor Sharon Lewin, as part of Positive Women Victoria's health promotion webinar series.

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The impact of HIV on my gut (gastrointestinal tract) has interested me for many years, particularly as I was diagnosed with HIV in 1995 and later developed AIDS while travelling in developing countries in 1996 without knowing effective HIV treatments had just been discovered. I started ART in late 1997. With our gut making up the largest part of our immune system, and the home of our CD4 T-cells, which are killed by HIV as it replicates itself, this is where much of the damage was done in those early days. But that was nearly 30 years ago and today with an undetectable viral load thanks to ART, a healthy diet, exercise and avoiding foods that irritate my gut microbiome (gut bacteria), I can happily say, I have a healthy gut and suffer no side effects from my HIV meds. But with 'low level inflammation' the new buzz word in HIV science, I'd like to know, for my long-term health (and the long-term health of all people living with HIV), what is really going on in my gut.

In my role with Positive Women Victoria, I host a series of health promotion webinars and for our HIV and Gut Health webinar, I spoke to infectious diseases specialist and HIV cure researcher Professor Sharon Lewin. You can listen to the recording here.

So what is the gut and what does it do beside digest our food and turn it into energy? The gut, which starts at our mouth all the way down to our anus, has several layers, which have a selective permeability that form a barrier between the body and potentially harmful substances so that only nutrients can pass through into the bloodstream. The outer layer is made up of a trillion different types of good bacteria, which live in us in a symbiotic relationship. The other inner layers are made up of mucous membranes and connective tissue.

Professor Sharon Lewin explains that while most people just think about the gut as transporting food as nutrients to be used by the body

as energy, the very inner layer of our gut wall is lined with our immune system's CD4 T-cells in lymphoid tissue, noting "and everyone knows the CD4 T-cells are the favorite place for HIV to replicate."

It is understandable that we, as humans, have evolved with a large portion of our immune system in our gut. Back when we lived in caves and hunted and gathered our food, we consumed all kinds of toxins, pathogens and bacteria – some good, some bad – as we went about our daily struggle to survive. And our body is still basically the same today as when we rolled around in the dirt about five million years ago.

Sharon adds that it was about 20 years ago when researchers discovered that enormous amounts of viral replication happened inside the gastrointestinal tract. "It was from this research that scientists discovered that the viral load measured in blood was really just virus spilling over from T-cells that were infected in lymphoid tissue, and the biggest lymphoid organ in the body is the gut, so HIV kills T-cells in the blood as well as the gut. But if someone's been infected with HIV for a while, say years before they are diagnosed, there is usually a quite significant depletion of T-cells from the gut and this disrupts the gut barrier," Sharon says.

Sharon explains that in most people, T-cells in blood will recover to normal levels, but the gut T-cells never really recover back to completely normal levels, "and that means that the gut barrier is not as tight for people living with HIV. Normally, these tight junctions are where the cells stick really tightly together, but if there's a disruption or a break, then fragments of the bacteria can move through and into the bloodstream."

In medical terms in HIV science this is known as 'microbial translocation' and means pieces of bacteria can cross the gut barrier and these fragments can activate the immune system and thereby creating inflammation. Another condition affecting the gut of both those with and without HIV, is 'Leaky gut syndrome' in *which the gut barrier also becomes permeable to toxins that leak into your bloodstream*. Leaky gut syndrome is believed to be caused by many other diseases and health conditions. Some medical and nutrition experts believe leaky gut may also be a factor in the cause of other metabolic disorders such as obesity, diabetes, arthritis, chronic fatigue syndrome and asthma. Leaky gut can also be fairly common in older people with HIV. As a person living with HIV, when I'm sharing a meal with others from the HIV community, many of us have dietary restrictions and it is not unusual for us to discuss these. In order to find the right diet for you, it is important to speak with a nutrition expert.

Sharon explains that doctors can measure the bacterial products in the blood, but in HIV research, scientists take it a step further and measure fragments of bacteria called LPS (lipopolysaccharide), which is the shell of the bacteria. The amount of these fragments in the bloodstream shows just how permeable the gut barrier has become due to damage by HIV.

As Sharon explains, "we know that in people with HIV, even when they're on antiretrovirals, LPS will be elevated compared to people that don't have HIV. And this damage to the gut may contribute to ongoing inflammation in the body, which we are always worried about, because that's associated with increased risks of heart disease and other health conditions."

Sharon says that HIV is still there in our gut, even after it is controlled by ART, by way of the hidden HIV reservoir that embedded itself into our gut as well as other parts of our body in those early days of transmission.

"While ART is fantastic, we ideally want the immune system to get back to normal, but we haven't yet got something that does that. We don't know if the virus sitting inside a cell as a HIV reservoir, hiding intermittently and inactivated, drives some inflammation, or does inflammation in the gut drive HIV to persist? And this is a very active area of research so we will see more innovative ideas about how to improve gut permeability in people with HIV. But in order to protect your gut, staying fit and healthy and having a good diet and lots of exercise and sleep and not being stressed - all the things that all of us need to do as we get older - that's really important too," Sharon says.

One of these innovative ideas on HIV and gut research is by Melbourne researcher, Matthew Pitman, a PhD student of Professor Sharon Lewin at the University of Melbourne. Matthew investigated

the role of high dose Vitamin D at reducing inflammation by tightening gaps in the gut barrier, which may then lead to reducing the HIV reservoir in the gut. However, while results were promising, more research is needed. You can read Mathew Pitman's research here: HIV persistence, inflammation and the gut.

The International AIDS Society's, 12th IAS *Conference* on *HIV Science* is in *Brisbane* and virtually from 23 to 26 July 2023. At IAS 2023, HIV researchers from around the world will present their latest findings on many aspects of HIV science, including the complex relationship between HIV infection, the gut microbiome, inflammation and HIV reservoirs in the gut, which is increasingly gaining more attention among HIV scientists.

Professor Sharon Lewin is a leading infectious diseases expert, and Director of the Doherty Institute. She is also a Professor of Medicine at The University of Melbourne and a National Health and Medical Research Council (NHMRC) Practitioner Fellow. As an infectious diseases physician and basic scientist, her focus is on HIV cure research. Sharon is also the incoming IAS President (International AIDS Society) and leads the IAS HIV Science Conference in Brisbane from 22 to 26 July 2023.

Heather Ellis has lived with HIV since 1995. She a communications specialist in the HIV sector with Positive Women Victoria, an HIV advocate, journalist, motorcycle adventurer, single mother to three teenage boys and author of two bestselling books: *Ubuntu* and *Timeless On The Silk Road*. For details visit: www.heather-ellis.com