

Hepatotoxicity

What is hepatotoxicity?

Hepatotoxicity is a general term for liver damage. Medications, including those used to treat HIV infection, may cause hepatotoxicity. Hepatotoxicity has developed in HIV infected people taking anti-HIV medications from three classes: **nucleoside reverse transcriptase inhibitors (NRTIs)**, **non-nucleoside reverse transcriptase inhibitors (NNRTIs)**, and **protease inhibitors (PIs)**.

There are several specific conditions that all fall within the general category of hepatotoxicity. These conditions include:

- hepatitis—inflammation of the liver
- hepatic necrosis—death of liver cells
- hepatic steatosis—too much fat in the liver; may be associated with a life-threatening condition called *lactic acidosis* (see [Lactic Acidosis Fact Sheet](#))

What are the symptoms of hepatotoxicity?

The first sign of damage to the liver is an increase in liver **enzyme** levels in the blood. When the liver is damaged, its enzymes are released into the bloodstream, where the levels can be measured by blood tests. These are called **liver function tests (LFTs)**. Enzyme levels that are routinely checked as part of LFTs include:

- alanine aminotransferase (ALT)
- aspartate aminotransferase (AST)
- gamma-glutamyltransferase (GGT)

The signs and symptoms of hepatotoxicity vary depending on how badly the liver is damaged. Symptoms of liver damage include:

- nausea
- vomiting
- abdominal pain
- loss of appetite
- diarrhea

Terms Used in This Fact Sheet:

Enzyme: a special protein that speeds up chemical reactions.

Liver function tests (LFTs): tests that measure the blood levels of liver enzymes (proteins made and used by the liver) to determine if your liver is working properly.

Non-nucleoside reverse transcriptase inhibitor (NNRTI): class of anti-HIV medication. NNRTIs work by blocking reverse transcriptase, a protein that HIV needs to make copies of itself. The NNRTIs approved by the FDA are Rescriptor, Sustiva, and Viramune.

Nucleoside reverse transcriptase inhibitor (NRTI): class of anti-HIV medication. NRTIs are faulty versions of the building blocks (nucleosides) used by reverse transcriptase, a protein that HIV needs to make copies of itself. The NRTIs approved by the FDA are Combivir, Emtriva, Epivir, Epzicom, Retrovir, Trizivir, Truvada, Videx, Viread, Zerit, and Ziagen.

Protease inhibitor (PI): class of anti-HIV medication. PIs work by blocking protease, a protein that HIV needs to make copies of itself. The PIs approved by the FDA are Agenerase, Aptivus, Crixivan, Fortovase, Invirase, Kaletra, Lexiva, Norvir, Reyataz, and Viracept.

- feeling tired or weak
- jaundice (yellowing of the skin and eyes)
- hepatomegaly (liver enlargement)

Which anti-HIV medications cause hepatotoxicity?

All FDA-approved NRTIs, NNRTIs, and PIs are associated with hepatotoxicity.

NRTIs, especially Zerit (stavudine), Videx (didanosine), and Retrovir (zidovudine), are associated with lactic acidosis and hepatic steatosis.

NNRTIs, especially Viramune (nevirapine), are associated with hepatitis and hepatic necrosis. If you and your doctor decide to use Viramune in your HIV treatment regimen, you will likely be instructed to take only one pill a day for the first 14 days, then to increase

Hepatotoxicity (continued)

to two pills a day. This dosing schedule may decrease your risk of developing hepatotoxicity. Viramune-associated hepatotoxicity usually occurs within the first 12 weeks of taking the drug. Women appear to be at increased risk of liver damage. All patients starting therapy with Viramune should have LFTs every 2 weeks for the first month, then every month for the next 2 months, and then every 1 to 3 months throughout treatment.

PIs, especially full-dose Norvir (ritonavir) and Norvir-boosted Atrivus, are also associated with hepatotoxicity. Unlike Viramune, PIs may cause hepatotoxicity at any time. Patients infected with both HIV and hepatic C virus (HCV) may be at particular risk for developing hepatotoxicity while taking PIs.

Are there other risk factors for developing hepatotoxicity?

Yes. Other risk factors include:

- infection with hepatitis B or C virus
- high levels of certain liver enzymes prior to starting anti-HIV medications
- alcohol use
- use of other medications that damage the liver
- pregnancy

Can hepatotoxicity be prevented?

Because hepatotoxicity is poorly understood, it is not clear how it can be prevented. If you are worried about hepatotoxicity, one of the most important things you can do is to get checked for liver disease before starting anti-HIV medications. If you have liver disease or any risk factors for developing hepatotoxicity, you and your doctor may choose an HIV treatment regimen that minimizes the risk of liver damage. You should have LFTs performed frequently, especially when you first start your HIV treatment regimen.

What should I do if I develop hepatotoxicity?

Call your doctor if you develop any of the symptoms of hepatotoxicity. In some cases, hepatotoxicity goes away without changes in anti-HIV medications. Most cases, however, require that medications be stopped or changed. It is important that you do not stop or make any changes to your treatment regimen before talking with your doctor.

For more information:

Contact your doctor or an *AIDSinfo* Health Information Specialist at 1-800-448-0440 or <http://aidsinfo.nih.gov>.