

a series of fact sheets written  
by experts in the field of liver  
disease

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## *The Liver: Acetaminophen and Your Liver*

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*The pain-reliever acetaminophen (also known as **paracetamol**) is one of the best-selling over-the-counter medications, used by more than 200 million Americans a year. It is sold under many brand names, including Tylenol, and is an ingredient in nearly 200 medications, both over-the-counter (such as Excedrin, Midol, NyQuil, and Sudafed) and prescription (such as Vicodin).*

Most people believe that acetaminophen is safe, but it can cause serious liver damage – and even acute liver failure – if it is taken in high enough doses. In fact, it is one of the leading causes of liver failure in the United States, accounting for more than 56,000 emergency room visits, 2,600 hospitalizations and an estimated 450 deaths per year.

### *Unsafe At Any Dose?*

Most people are only at risk for liver toxicity if they take more than the normal recommended amount of acetaminophen. Most cases of liver damage occur in people who have taken at least 10-15 grams—more than twice the recommended dose. Many of the emergency room visits and deaths linked to acetaminophen poisoning are due to accidental or intentional overdoses (for example, suicide attempts).

But some people are more susceptible to acetaminophen toxicity and can experience liver damage even at the recommended dose. A study by the U.S. Food and Drug Administration (FDA) showed that about 20% of people with acetaminophen-related liver toxicity had taken less than the recommended daily amount. For other people, a dangerous dose is not much higher than the recommended dose—that is, the “window” between a therapeutic dose and a toxic dose is smaller for acetaminophen than it is for many other drugs. Some experts also believe that taking acetaminophen for several days in a row may cause a dangerous build-up of the drug in the body.

Acetaminophen is more likely to cause liver toxicity at near-normal doses when used by people who drink alcohol. In fact, people who drink regularly may be more prone to liver damage even if they do not consume alcohol and acetaminophen at the same time. There appears to be added risk even if people take acetaminophen a few hours, or in some cases longer, before or after drinking. Since the mid-1990s, the Tylenol package has included a warning against drinking alcohol when using the drug. The current labeling of Tylenol has more specific language on the effects of combining acetaminophen and alcohol:

### *Warnings*

**Alcohol warning:** If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take acetaminophen or other pain relievers or fever reducers. Acetaminophen may can liver damage.

### *How Acetaminophen Harms the Liver*

Like many drugs, acetaminophen is metabolized by the liver. If the normal processing pathway is overwhelmed by a high dose, a different pathway known as the cytochrome P450 enzyme system kicks in. When this happens, a toxic metabolic byproduct called NAPQI is produced that can kill liver cells. Alcohol and many other drugs also use the cytochrome P450 processing system, and the risk of a “bottleneck” is greater if the liver has to deal with both acetaminophen and these other substances at the same time.

Acetaminophen poisoning has three stages. During the first 12-24 hours after taking the drug, a person may experience nausea and vomiting. During the second phase, from 24-48 hours, the person usually feels better. After 48-72 hours, however, liver enzyme (ALT and AST) levels start to rise, indicating liver injury. In the most severe cases, a person may develop acid buildup in

the blood, excessive bleeding, and coma. At this stage, only a liver transplant can prevent death.

Fortunately, there is an antidote for acetaminophen poisoning. NAPQI is normally detoxified by a naturally occurring antioxidant called glutathione. But if too much acetaminophen is present, the body's supply of glutathione can be used up. An amino acid called N-acetylcysteine (NAC), which restores glutathione in the cells, can be administered to reverse acetaminophen toxicity. NAC is most effective when used within 16 hours after taking acetaminophen; however, people often do not recognize that gastrointestinal symptoms could be an early sign of acetaminophen poisoning.

### *Fair Warning?*

An FDA advisory panel recommended several times (most recently in September 2002) that products containing acetaminophen should carry a warning on the label about the risk of liver toxicity. In January 2004, the FDA launched a new public education campaign warning consumers about the potential risks of acetaminophen and other pain-relievers. Some companies now clearly label their products containing acetaminophen. This is important because unintentional overdoses can occur when people take two or more medications together without realizing they all contain acetaminophen. However, the FDA still does not require that such products carry a warning label concerning liver toxicity.

### *Acetaminophen for People with Hepatitis*

What does all this mean for people with chronic hepatitis B or C? Doctors often recommend acetaminophen to relieve symptoms such as body aches and fever, which are common side effects of interferon therapy. For most people, acetaminophen is safe and effective. According to the FDA's Dr. John Senior, "It's very clear the average dose for the average person is very safe. But we are not all average people." For many individuals, acetaminophen is still a good choice, especially considering that other over-the-counter pain-relievers can cause problems of their own (such as stomach bleeding with aspirin and nonsteroidal anti-inflammatory drugs).

Many HCV providers now recommend that their patients with HCV take a somewhat lower dose than is generally recommended for people with healthy livers. It is also important that medical providers know what medications their patients are using (including over-the-counter and prescription medications) so that the medical provider

can best advise a person with hepatitis C on how much acetaminophen is safe.

### ***The following tips can help prevent acetaminophen-related liver toxicity:***

- Do not take more than the recommended dose of 4 grams within a 24-hour period (for example, 12 regular strength or 8 extra strength Tylenol tablets)
- Do not take the full day's dose at one time; space it out over the course of the day
- Do not take acetaminophen for more than 10 days in a row
- Avoid drinking alcohol; this is important for people with hepatitis whether or not they use acetaminophen
- People who do consume 2-3 alcoholic drinks per day should not take more than half the usual recommended dose of acetaminophen (2 grams within 24 hours)
- People with advanced liver fibrosis or cirrhosis should avoid acetaminophen
- Write down how much acetaminophen you take, and when, if you have trouble remembering
- Check the labels of all medications; small doses of acetaminophen in combination remedies can add up to big trouble.

**For more information about hepatitis C, hepatitis B and HCV coinfections, please visit [www.hcvadvocate.org](http://www.hcvadvocate.org).**

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A publication of the Hepatitis C Support Project

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