

## **DDW: Hepatitis Patients at Risk for Accidental Acetaminophen Toxicity**

LOS ANGELES, May 22 - Over-the-counter flu remedies such as Nyquil or Theraflu are often used for relief of the flu-like symptoms of acute hepatitis, a choice that may trigger acute liver failure because those agents contain acetaminophen.

Serum samples from 72 patients with fulminant hepatitis detected evidence of acetaminophen toxicity in 12.5% of patients, said William M. Lee M.D., of the University of Texas Southwestern Medical Center in Dallas, who reported the findings at Digestive Disease Week sessions here today.

Dr. Lee and colleagues used a high-pressure liquid chromatography with electrochemical detection to assess acetaminophen levels. They studied 10 patients with liver failure due to confirmed acetaminophen overdose as a positive control group.

The average serum concentration of acetaminophen adducts was 0.45 nmol/mL versus 5.58 nmol/mL in the control group. Nonetheless, Dr. Lee said the evidence of acetaminophen adducts was "a second insult to the liver cells on top of hepatitis."

Importantly, the toxicity occurred when the patients used the over-the-counter flu medicines at therapeutic doses. "None reported doses that would exceed 4 g/day," he said. That is lower than previously reported toxic doses, he said.

Acetaminophen toxicity occurs in a dose-related fashion. Seven or eight grams consumed over the course of three to four days can be fatal, Dr. Lee said.

An online check of ingredients in cold and flu products found acetaminophen listed as an ingredient in 26 OTC remedies, including Coricidin D, Triaminic, NyQuil, DayQuil, and Dristan as well as Midol and Pamprin.

In this series, 67% of patients who had detectable acetaminophen-protein adducts in their blood died within three weeks of hospital admission versus 27% of patients who had no evidence of acetaminophen use (P=0.017).

Liver toxicity is a well known side-effect of acetaminophen, he said, noting that acetaminophen overdose is a leading cause of liver failure and liver transplants "I am surprised it is still on the market," Dr. Lee said.

He later qualified that statement saying that but the drug is so popular, and is sold under so many different brands-the most popular being Tylenol-that he doubts it would ever be removed from the market.

That said, he noted that people with liver disease are frequently unaware that they are using acetaminophen-containing compounds, which could put them at risk for liver failure.

"Vicodin and Percocet are the two most popular prescription compounds containing acetaminophen and these are often prescribed for pain relief in people with liver disease," he said. "Unbundling of both of these drugs, which might be done at some point, would be significant in terms of reducing accidental acetaminophen overdose."

He said that in 2002 a FDA advisory committee recommended that labels of over-the-counter cold and flu medicines be changed so that the front label would list acetaminophen as an ingredient. "But that was in 2002 and the FDA has yet to act on that recommendation."

John M. Vierling, M.D., president of the American Society for the Study of Liver Diseases, a professor of medicine at Baylor in Houston, said the hallmarks of acetaminophen toxicity are "a change in mental state and alteration in clotting ability."

Dr. Vierling called acetaminophen an "excellent drug" but added that Dr. Lee's study suggests the need to advise patients with chronic liver disease to avoid not only Tylenol and other acetaminophen products but also to be cautious when selecting cold and flu medicines.

The patients were included in the National Institutes of Health Acute Liver Failure Study (1999-2004), a national registry of acute liver failure cases. Dr. Lee said there are roughly 2,000 cases of acute liver failure annually and about 500 of those are fatal.

Primary source: Digestive Disease Week Source reference: Lee, WM et al "Acetaminophen as a co-factor in acute liver failure due to viral hepatitis determined by measurement of acetaminophen-protein adducts" Abstract S1002.