

Doctors test latest attempt at artificial liver

By LAURAN NEERGAARD – February 2, 2009

WASHINGTON (AP) — There's help for failing kidneys and failing hearts. But there's no fix for a dying liver. Doctors are trying to change that at a few hospitals around the country, testing a machine packed with human liver cells as a last-ditch chance to survive sudden liver failure.

The experiment is the latest in a decades-long quest for an artificial liver, a device that could temporarily take over some of the liver's jobs much like dialysis helps kidneys work and cardiac pumps squeeze a flabby heart.

Unlike those organs, a damaged liver sometimes regenerates if it has enough recovery time. If it's too far gone, a transplant is the only option — but a dying liver starts a fast chain reaction where kidneys shut down, bleeding begins and patients fall into a coma, often too sick to try a transplant even if an organ could be found soon enough.

The goal: To help such patients stabilize enough for a transplant, or even to avoid one.

"It doesn't replace a liver," cautions Dr. Todd Frederick of California Pacific Medical Center.

But, "if we could buy some time while the liver is recovering, that potentially would be a great advance," says Dr. Lena Napolitano of the University of Michigan, who like Frederick is helping test the ELAD, or "extracorporeal liver assist device."

Elizabeth Blaj of San Diego credits the machine with doing just that.

"I believe that machine kept me alive for five days," says Blaj, 40, whose doctors at the Scripps Clinic expected her to die before a liver arrived for emergency transplant last October.

"I'm just eternally grateful," she said.

The problem: Previous attempts have seemed promising, too, only to fizzle later. A Mayo Clinic review last year found half a dozen different methods under development but none yet proven to reduce death. In fact, the maker of an earlier version of the ELAD went bankrupt in the midst of a 2002 study that gave some hints the device might help at least sometimes.

Early on, scientists focused on just one of the organ's jobs, to filter poisons out of blood. One such filter is sold today to help treat drug overdoses.

But a liver does more than filter. It also creates a stew of different chemicals crucial for such things as metabolism and blood-clotting. So scientists are trying to add living liver cells — from pigs or people — to filtering machines in hopes of better mimicking the full organ.

The first pig cell-powered machine failed to win Food and Drug Administration approval despite some tentative evidence that it improved outcomes.

Now enter the ELAD, powered by human liver cells. It "comes closer to replacing the amount of liver" people need, says Dr. Robert Brown of New York-Presbyterian Hospital and Columbia University, who has helped test most of the devices to date.

Proving whether the machine makes a difference is tough: Doctors have to choose patients sick enough to benefit but not so sick "that a little bit of liver won't do the trick," Brown says.

There are nearly 28,000 deaths a year in the U.S. from liver disease, and fewer than 6,000 liver transplants. Eligible for the experiment are a subgroup: People with conditions slowly damaging their livers, such as hepatitis or cirrhosis, when something — an infection, often — abruptly pushes them over the edge into full-fledged liver failure. About half die.

The FDA is asking if three to 10 days of ELAD liver support improves 30-day survival over the similarly ill who get today's standard supportive care. Among the safety issues to get close scrutiny: The device's cells initially were derived from a liver tumor and are encased to ensure none of those cells enter a patient's body. Doctors also will ask if any benefit is big enough to cover what could be a \$30,000 price tag.

Manufacturer Vital Therapies Inc. says that among the first 49 patients it studied in China, where liver failure is more rampant, 85 percent given ELAD therapy survived short-term compared with half of patients given regular care.

In the U.S., the study just began in October, too soon for any conclusions. But Michigan's Napolitano notes that kidney dialysis had a similarly rocky start in tests of the dying before doctors could determine how it best worked and use it on the less sick — an ultimate goal for whatever artificial liver scientists eventually develop.

"It's a challenging technology to test. It's a very challenging cohort of patients because they're so sick," agrees Dr. Winfred Williams of Massachusetts General Hospital. But he's testing ELAD again because of a 2002 patient, Kevin Fitzmaurice of Boston who started emerging from a five-day coma after a day of the liver-supporting therapy.

"The nurses fairly accosted me at the door to say he was waking up," Williams recalls, and a few days later Fitzmaurice was stable enough to transplant. "Had he not gotten onto the ELAD support, he would not have survived."

Now 55, Fitzmaurice says his donated liver is doing great.

EDITOR'S NOTE _ Lauran Neergaard covers health and medical issues for The Associated Press in Washington.