



Dominican Hospital

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NEWS RELEASE

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Landmark drug trial underway at Dominican Hospital

Physicians developing protocol to manage deadly mushroom poisoning

SANTA CRUZ – Two physicians on Dominican Hospital’s Medical Staff are working to save lives locally and around the world from one of nature’s most deadly poisons. Todd Mitchell, MD, MPH and Alan Buchwald, MD, are the Principal and co-Investigators of the first FDA sanctioned clinical trial of a comprehensive protocol for treating patients with amatoxin mushroom poisoning.

Amatoxin refers to a family of peculiar bicyclic octapeptides that are impervious to freezing, drying, and cooking. The toxin is unfazed by the acidic environment of the stomach, human digestive enzymes, and the metabolic efforts of the liver. It destroys rapidly dividing cells in the gut, liver, and kidneys by shutting down protein synthesis. Amatoxin mushroom poisoning occurs on every inhabited continent, and is responsible for many deaths annually in Eastern Europe and Asia. Cases in the USA are much less frequent but no less deadly, particularly after a large ingestion.

Once a generally delicious amatoxin mushroom is consumed, it takes anywhere from six to 24 hours for the toxin to make its presence known through severe diarrhea and vomiting. Meanwhile, some of the poison is absorbed into the bloodstream, while the rest travels with bile salts into the liver.

The kidneys are able to effectively clear amatoxin from the bloodstream as long as urine output is maintained. However, the kidneys are at risk if urine output stalls from dehydration.

Amatoxin in the liver is excreted into bile where it can flow into the intestine and back again to the liver by a process called enterohepatic circulation. A poisoning may result in acute kidney and liver failure within days of ingestion.

Dr. Mitchell became an unlikely amatoxin investigator in January 2007. He and Wendy Knapp, MD, admitted an immigrant family of six who had foraged for wild mushrooms at Wilder Ranch. They ate tacos containing Death Caps (*Amanita phalloides*) which are often mistaken for edibles.

Dr. Mitchell obtained a special waiver from the FDA allowing the first American use of intravenous silibinin (Legalon-Sil), a European antidote derived from the common Milk Thistle. The drug was delivered by courier from Germany. An 83-year-old grandmother succumbed to kidney failure, but the others, including three with life threatening liver failure, all recovered following treatment.

Dr. Mitchell researched the amatoxin literature in preparation for a required report to the FDA on the Dominican cases. He learned of a 1996 case in St. Louis, Mo., where biliary drainage was performed in order to remove amatoxin laden bile from a deathly ill 18-year-old. The boy made a rapid recovery, and the bile was later found to contain a fatal dose of the poison. An obscure reference from a nursing journal described the first time biliary drainage had been undertaken. Dr. Mitchell was astonished to learn that the case had been managed here at Dominican Hospital in 1982, by former and now retired Chief Medical Officer, Larimore Cummins, MD.

Dr. Mitchell and toxicologist Dr. Buchwald are now spearheading the first-ever FDA-approved clinical trial for the prevention and treatment of amatoxin induced renal and liver failure.

“Dominican Santa Cruz Hospital and its Institutional Review Board are hosting an International effort to prevent death and/or liver transplantation after the most severe amatoxin mushroom poisonings,” said Dr. Mitchell. “It is virtually unprecedented for a community hospital, rather than an academic tertiary care center, to assume the leading role in a study like this. Dominican has been on the cutting edge of so many advances in medical practice over the past decade (eliminating ventilator associated pneumonia in the ICU, reduction of hospital associated bloodstream infections, *da Vinci* minimally invasive robotic surgery) that perhaps it isn’t as strange it might seem.”

The protocol is based on three treatment principles. First, patients receive aggressive intravenous hydration to preserve and protect the kidney’s filtering function. Second, Legalon-Sil, the milk thistle antidote, is administered intravenously. Finally, a biliary drainage procedure may be performed by a GI doctor or radiologist. Bile that is collected will undergo quantitative mass spectroscopy analysis for amatoxin content at UC Davis and San Francisco General Hospital.

This study is not double blinded and lacks a placebo control group. The exception was readily agreed to by the FDA as these poisonings are rare but often fatal or result in liver transplant. The data that is accumulated will have to be compelling in order to persuade a skeptical medical community.

The doctors hope to enroll both American and overseas cases into the trial. Patients (14 so far) who have received Legalon-Sil on the treatment protocol have universally done well. The first patient ever to undergo percutaneous biliary drainage for this indication was recently managed at a CHW affiliate in Arroyo Grande, Calif.

Drs. Mitchell and Buchwald intend to publish their results. As interventional radiology and GI endoscopic procedures are available at tertiary hospitals around the world, they hope to demonstrate that the protocol is applicable not only in the West, but in developing countries as well where the majority of cases occur.