



DMS's Henry Bernstein, D.O., published in the journal *Pediatrics* the first prospective study of post-childbirth discharge decisions; 17% of patients were deemed not ready to go home.

A simple recipe for cerebral disaster

What do you get when you mix a pinch each of normal prions and polyanions with a dash of copurified lipid molecules? A brew of infectious prions.

A DMS team led by biochemist Surachai Supattapone, M.D., Ph.D., has published the first report of spontaneous generation of infectious prions in a test tube. The paper was in the June *Proceedings of the National Academy of Sciences*.

Prions are normal proteins found in the brain that become infectious when they misfold. As they slowly convert from the normal to the infectious form, they can cause rare, deadly brain disorders called transmissible spongiform encephalopathies, such as mad cow disease in cows, scrapie in sheep, and Creutzfeldt-Jakob disease (CJD) in humans.

Rare: The Dartmouth work provides a biochemical model of the naturally occurring, but very rare, sporadic CJD, says Supattapone. And, adds his lab manager Nathan Deleault, the first author on the study, "it gives us a glimpse as to how this process occurs in the brain."

The findings, Supattapone notes, also provide the best support to date for the protein-only hypothesis—that unlike other pathogens, which rely on nucleic acid

containing DNA or RNA to replicate, a prion can propagate without nucleic acid. Some scientists are critical of this idea and think prion diseases are caused by an as-yet-unidentified slow virus. But others—like Supattapone, who trained in the lab of Nobel Laureate Stanley Prusiner, M.D., a prion pioneer at the University of California, San Francisco (UCSF)—prefer the protein-only hypothesis.

The study was also important in that it was "the first time that an infectious agent has been created from noninfectious components," says Supattapone. It was "very surprising." Surprising enough that he wanted to be sure the samples hadn't been contaminated with infectious prions from other research. So his team ran the experiments again in a colleague's prion-free lab—and reproduced the results.

At DMS since 2001, Supattapone has been slowly unraveling the mysteries of prion disease. Next, his team hopes to determine how the interaction between polyanions—molecules with repeated, negatively charged ions that are found naturally in the brain—may contribute to spontaneous infectious prion formation.

Patent: Prion researchers are seeking ways to prevent, diagnose, and treat prion disease. And they're trying to "develop ways to break the transmission cycle," says Supattapone. He and Prusiner recently received a patent for an antiseptic compound they developed at UCSF. Called PrioX, it can inactivate infectious prions on surgical blades and other surfaces.

Still, Supattapone is modest about his achievements. So far, he says "all we've done is create a biochemical model, which mimics what occurs naturally in the brain." But he doesn't plan to stop there. LAURA STEPHENSON CARTER



JON GILBERT FOX

Deleault, left, and Supattapone generated prions in the lab.

Affected by CF

DMS scientists have identified a gene named *cif* that, with its corresponding protein, may contribute to cystic fibrosis (CF). The group previously reported that *Pseudomonas aeruginosa*, a pathogen that often colonizes CF-affected lungs, secretes a protein (the one just identified) that may contribute to the disease. Writing in *Infection and Immunity*, principal investigator George O'Toole, Ph.D., and colleagues "demonstrate that the *cif* gene is expressed in the cystic fibrosis lung," and propose a model by which *P. aeruginosa* colonizes a CF lung.



Bone of contention

A hip fracture increases an elderly person's risk of dying, but only in the first six months after the injury, a DMS study concluded. After six months, pre-fracture frailty and illness are more important predictors of death than the fracture itself or age, sex, race, or socioeconomic status. "Our study indicates that fracture prevention may be of limited benefit in extending overall life expectancy," wrote Anna Tosteson, Sc.D., and colleagues in *Osteoporosis International*. Since "hip fracture is one of the most highly visible and devastating consequences of osteoporosis," they note, the finding has implications for the "economic value" of "costly new osteoporosis treatments."

