

Pain pathway: New road for old foe?

It may not make you feel any better to know this, but the pain associated with tissue injury and inflammation may have a chemical pathway, other than the well-documented prostaglandin route, from hurtful impulse to your brain. Don't despair. The finding, researchers say, may offer new opportunities to block pain transmission.

Aspirin and acetaminophen block the synthesis of prostaglandins, which sensitize nerve cells to painful stimuli. Because these compounds don't block all pain, Jon Levine and colleagues at the University of California at San Francisco looked at the leukotrienes, similar in structure to prostaglandins and also active in inflammation.

They found that leukotriene B₄ (LTB₄) can, like prostaglandins and prostaglandin stimulators, cause pain. The leukotriene pathway may explain why prostaglandin inhibitors like aspirin and acetaminophen alleviate some but not all pain — why, for example, one person with arthritis may get relief with aspirin and another person may not.

"If we can find drugs that block this pathway, we could help the large number of people who don't get relief from aspirin-like drugs, or who get only moderate relief," says Levine. The goal is to avoid the drawbacks of currently available narcotics and steroids — addiction, tolerance and toxicity. He and his co-workers are working on interventions, but he's not saying at present just what or how.

LTB₄ injected into rats' paws makes the paws extremely tender, as do prostaglandin-related compounds, the researchers report in the Aug. 17 *SCIENCE*. When they used a prostaglandin inhibitor along with LTB₄, the acute sensitivity remained, indicating, says Levine, that the leukotriene pain system is independent of prostaglandins. But it does seem to depend on immune system cells called polymorphonuclear leukocytes: When they injected the rats with a leukocyte inhibitor, the LTB₄ no longer caused the extreme tenderness. Levine and colleagues Wai Lau, Geoffrey Kwiat and Edward J. Goetzl suggest that LTB₄ affects nerve cells indirectly by its effects on the immune system.

The California researchers have some work to do to prove the importance of LTB₄ in pain. Robert A. Lewis of Harvard Medical School in Boston, who has personal experience with the compound, doubts that it plays a major role in human pain. He and two co-workers injected themselves with LTB₄ several years ago, in amounts greater than what occurs in injured tissue. There was, he says, modest tenderness but no pain.

"Not to degrade the study, but based on

human experience with LTB₄, it seems unlikely to me that that's going to be a major mediator of pain," Lewis says. But Levine feels that tenderness itself is important from the point of view of the sufferer and for intervention. "Tenderness is what you see in most clinical situations," he says.

—J. Silberner

Scientists offer aid to Sakharovs

Last week the International Coalition of Scientists for Sakharov (ICSS) announced that it had cabled Soviet leader Konstantin Chernenko with the names of 55 scientists who have agreed to serve as potential "good faith witnesses." Each volunteer has offered to become part of a two-person team that would travel at their own expense for a week's stay in the Soviet Union while Yelena Bonner, wife of dissident physicist Andrei Sakharov, temporarily left that country for heart surgery. The scientists pledged to maintain a "continuous presence" in the Soviet Union through successive pairs of witnesses until Bonner returned home.

Sakharov's most recent hunger strike was initiated in May to protest his wife's being denied the exit visa she needs to obtain medical treatment abroad.

Bonner is expected to stand trial this fall for alleged anti-Soviet activities. Soviet officials have told her family and inquiring scientists that she is being denied the visa so that she cannot use access to foreign news media to denounce her government further. The officials further maintain that Bonner not only is healthy, but also has access to fine medical care at home.

At the ICSS news conference in Washington, D.C., last week, Sakharov's daughter, Tanya Yankelevich, denounced as "amoral" the Soviets' suggestion that her mother might speak out or politicize her trip — actions that could jeopardize Sakharov's status. Yankelevich said she had not received direct word from either of her parents since April 9. She added that the Soviets' inability to produce Sakharov, and thereby relieve growing concern over his health, "gives rise to grave and morbid suspicions that he may not be alive."

Among those concerned about the health of Sakharov, a 63-year-old Nobel Prize winner (for peace), are 33 North American Nobelists. On Aug. 16 they petitioned the United Nations, asking that it cable Chernenko of their concern. In addition, the North American scientists offered to serve as authorized United Nations observers in the Soviet Union "to ascertain the whereabouts and condition of the Sakharovs."

This week an English-language broadcast on Radio Moscow offered the first official word on Sakharov in two months. It maintained he was well and drawing a full pension.

—J. Raloff

Acidophilus: Milky bane to cholesterol?

Consumers have been offered a new dairy product in recent years: sweet acidophilus milk. A more palatable source of *Lactobacillus acidophilus* bacteria than its sour, fermented predecessor, this milk tastes no different from the ordinary low-fat pasteurized liquid to which the live organisms have been added. Long promoted as a health food, milk with these bacteria has been shown beneficial in controlling the growth of certain undesirable microorganisms, such as *Salmonella*, in the intestinal tract. And the growing popularity of acidophilus milk could skyrocket if preliminary research findings by animal scientists at Oklahoma State University in Stillwater are confirmed. Their studies show that under conditions that exist in the digestive tract, certain strains of these bacteria absorb cholesterol.

In the new study, pigs were fed a diet containing 1,000 milligrams (mg) of pure, crystalline cholesterol — a level that the researchers were confident would boost the animals' normal serum-cholesterol levels. Those animals whose milk had also been laced with a strain of cholesterol-loving *L. acidophilus* registered a gain in serum-cholesterol concentrations of only 9 mg per deciliter (dl) of blood, or half the 18 mg/dl increase experienced by pigs not receiving the bacterial additive. Explains Stanley Gilliland, who headed the project, "We picked the pig as an animal model because its intestinal and circulatory systems are similar to the human's."

The current research, Gilliland says, was spurred by the finding that certain strains of the bacteria would attack bile acids, cleaving off an amino acid from a steroid bile salt. Since bile salts are synthesized in the body from cholesterol, he says, the scientists decided to turn *L. acidophilus* loose against that target.

Gilliland's team has found that *L. acidophilus* not only varies among strains in its ability to assimilate cholesterol but also has evolved a certain host specificity — strains cultured from pigs don't thrive in humans, and vice versa. However, he says his research indicates there's at least one cholesterol-active strain specific to humans. Adding credence to the idea that the bacteria's cholesterol antagonism occurs in humans is other research that reported a reduction in cholesterol levels among infants fed a formula containing *L. acidophilus*.

Its potential effect on cholesterol is not acidophilus milk's only claim to fame. Research reported by Gilliland last year shows the bacteria supply an enzyme — deficient in many adults — needed to digest lactose. That appears to be why some individuals who had to avoid milk could drink this form without ill effect in his study.

—J. Raloff