Predicting the ups and downs of chest pain

Imagine coronary arteries choked with a bumpy layer of atherosclerotic plaque. Suddenly, the plaque ruptures and a swarm of platelets rushes to the scene in an attempt to heal the injured artery wall. A gelatinous blood clot forms at the site of the rupture.

This microdrama causes an unpredictable chest pain that can strike even while a person is resting. In medical parlance, such pain is called unstable angina. It's a dangerous condition that may signal an impending heart attack.

New findings suggest that people hospitalized with unstable angina face a higher risk of suffering a heart attack during their hospital stay if they have a telltale protein circulating in their bloodstream. Other new research demonstrates the down side of an anticoagulant drug commonly prescribed for unstable angina. Investigators describe both studies in the July 16 NEW ENGLAND JOURNAL OF MEDICINE.

In the first study, Christian W. Hamm of the University Hospital of Hamburg in Germany and his colleagues focused on cardiac troponin T, a protein that helps the heart contract. Although cardiac troponin T is not normally found in the bloodstream, it does escape into the circulation when heart cells are damaged. Thus, Hamm's group speculated that a blood test for the protein might help predict the outcome for people with unstable angina.

The investigators studied 109 people who were admitted to the hospital with unstable angina. Troponin T showed up in the blood serum of 33 (39 percent) of the 84 patients who had reported ongoing chest pains even while resting – the more serious form of unstable angina. Of these 33 people, 10 went on to have a heart attack, and five of the 10 died during hospitalization.

By contrast, the researchers found no troponin T in blood serum from the 25 patients with the less severe form of angina, in which pain subsided somewhat after hospitalization. None of these patients suffered a heart attack or died during hospitalization.

The presence of troponin T in the bloodstream suggests trouble ahead for patients with unstable angina, concludes James H. Chesebro of the Mayo Clinic in Rochester, Minn., in a commentary accompanying the research report. The test for troponin T "can detect small amounts of damage to heart muscle and thus is a warning sign," he told SCIENCE NEWS. Such patients may need greater protection from blood clots, which can block the coronary arteries, causing a heart attack, he adds.

In most cases, doctors treat unstable angina by giving patients anticoagulant drugs such as heparin. During an attack of unstable angina, blood clots may form in an attempt to heal the damaged artery. With heparin preventing the formation of new clots, the body's own enzymes can begin to dissolve any existing blood clots, Chesebro explains.

While heparin is considered the gold standard of unstable angina therapy, a second study hints that recurrent chest pain – and even heart attacks – may arise when patients stop taking the drug.

A team at the Montreal Heart Institute, led by cardiologist Pierre Théroux, made this discovery after conducting a clinical trial comparing the efficacy of heparin, aspirin, a combination of heparin and aspirin, and a placebo in the treatment of unstable angina. The researchers focused on 403 people who had been hospitalized with unstable chest pains and who received a six-day course of their assigned treatment. After therapy ended, the team monitored all patients closely for several days, recording any problems.

In analyzing the data, they were surprised to note a greater number of serious setbacks among people who had received heparin alone than among people assigned to any of the other treatment groups.

Of the 107 people who received heparin alone, 14 developed complications – such as another bout with chest pain or a heart attack – within hours after they were taken off the drug. Only five patients in each of the other three study groups developed such problems.

Furthermore, 11 of the 14 heparin patients with complications went on to require urgent intervention, such as cardiac bypass surgery. Only two other patients – one in the aspirin group, the other in the placebo group – needed such drastic care after their unstable angina flared up again.

No one knows why post-heparin patients are at heightened risk. However, Théroux speculates that once the drug is stopped, the body's clot-producing machinery may become hyperactive. The body metabolizes heparin quickly, he notes, and within hours new blood clots can start to form. In contrast, aspirin's effect lingers for days after treatment is stopped. Study participants who received aspirin along with the heparin may enjoy some residual protection, Théroux says, because aspirin discourages platelets from clumping together – a key step in the clotting process.

Chesebro advises cardiologists to monitor angina patients carefully after discontinuing heparin therapy and to consider giving them a second anticoagulant drug at that time.

– K.A. Fackelmann

'Baked Alaska' cooked up in liquid helium

Baked Alaska seems an unlikely term to encounter in physics, but this culinary surprise, consisting of meringue baked around ice cream, serves as an apt description of an exotic, theoretical model accounting for a curious aspect of liquid-helium behavior. The model, proposed in 1984 by Anthony J. Leggett of the University of Illinois at Urbana-Champaign, suggests that high-energy particles produced by cosmic rays can trigger the otherwise inexplicable formation of one form of superfluid helium-3 at the expense of another.

In the baked Alaska scenario, high-energy electrons, created by the passage of cosmic-ray-generated muons through the supercooled liquid, deposit significant amounts of energy in spots less than a micron in diameter. Each intensely heated microball of liquid helium expands into a hot shell, leaving behind a pocket of cold superfluid helium. Isolated from the rest of the liquid, this cold core provides a protected environment in which a bubble of a different type of superfluid helium-3 can nucleate and start to grow.

Now researchers have obtained experimental evidence establishing the plausibility of Leggett's scenario. "Our results are certainly consistent with the [baked Alaska] model, though there are still some unanswered questions," says Peter E. Schiffer of Stanford University.

"The Stanford results show that at least the idea of nucleation by high-energy particles isn't totally crazy," Leggett notes.

Schiffer, Douglas D. Osheroff, and co-workers report their findings in the July 6 PHYSICAL REVIEW LETTERS.

Helium-3, a rare isotope of helium, becomes a superfluid – a liquid that flows without friction – at temperatures below 2.5 millikelvins. In this chilly state, helium atoms tend to form pairs. Because these pairs can arrange themselves in two different ways, helium-3 has two distinct superfluid states. Depending on the pressure and the magnetic field applied to a sample, the so-called A phase is more stable than the B phase at higher temperatures, whereas the B phase takes over at lower temperatures.

In 1977, Osheroff (then at AT&T Bell Laboratories) and co-worker Michael Cross showed that the superfluids had characteristics implying that the A phase, even when supercooled well below the temperature at which a transition from the A to the B phase should occur, cannot by itself spontaneously make the change. Because such phase transitions actually do occur, this puzzling feature led to a search for a mechanism that would explain how the transition happens.

"I played around with various ideas, and it eventually sank into my mind that no mechanism based on a thermal equilibrium distribution of energy was going to explain this," Leggett recalls. His baked Alaska model emerged out of this line of reasoning.

"I had to convince myself you couldn't apply the normal laws of hydrodynamics or thermal transport under these conditions because you're so far from equilibrium," he says. "It really matters how the heat spreads out."

To check whether radiation can indeed trigger the nucleation of the B phase within the A phase of superfluid helium-3, the Stanford group used a specially designed, long, thin, silica glass tube with microscopically smooth surfaces. Within this tube, the team discovered it could dramatically supercool samples of the A phase to temperatures as low as 0.37 millikelvins, much lower than temperatures achieved by other groups.

In addition, by placing sources of radiation near the sample cell, they discovered that they could greatly reduce the length of time before nucleation occurs in the supercooled A phase. Both gamma rays and neutrons produced comparable effects.

"It's clear that radiation does play a part," Osheroff says.

These findings indirectly suggest that the presence of surface irregularities or defects also has a strong influence on the nucleation of phase B. This factor may have thwarted previous attempts to detect radiation-induced nucleation.

Moreover, the Stanford experiment demonstrates the conditions necessary for observing the A phase at lower temperatures and lower magnetic fields than previously possible. "Now that we've got it pinned down, I think there's going to be a burst of activity," Leggett says. "A lot of people would love to have [A-phase] helium-3 in low magnetic fields at low temperatures. There are all sorts of things you can do with it."

Precisely how surface roughness and the presence of minute traces of such impurities as radioactive tritium contribute to the nucleation of phase B remains unclear. Osheroff and his team are now discussing the design of sample containers specially fabricated to have a certain roughness. The researchers would also like to observe nucleation at different pressures and magnetic fields.

"Helium-3 is an ideal system for understanding physics that would be completely masked in any other system," Osheroff says.

To Leggett, the A-B transition in superfluid helium-3 represents a particularly clear example of how locally concentrated energy that can't dissipate through normal channels can induce events that by any other, reasonable, statistical measure would seem astronomically improbable. *– I. Peterson*

Courts challenge feds on health rules

Last week, an appeals court struck down a 1989 federal air-pollution standard that set new or lower workplace-exposure limits on 428 toxic chemicals. The next day, a second federal appeals court upheld a classical interpretation of the nation's food-additives law – a move that effectively revokes Environmental Protection Agency regulations allowing trace levels of certain carcinogenic pesticides in processed foods.

Science proved pivotal in both decisions, though in distinctly different ways. In the first case, the court argued that the Occupational Safety and Health Administration (OSHA) failed to justify scientifically not only that each new exposure limit was feasible, but also that it would substantively reduce workers' health risks.

In the second case, the court argued that improved analytical methods and toxicological data gave EPA no right to reinterpret how it administers a 34-year-old law.

At press time, neither OSHA nor EPA had decided whether to appeal the ruling affecting it to the Supreme Court.

Between its founding in 1970 and its promulgation of the now-contested air-contaminants rule, OSHA issued just 24 chemical-specific health regulations. To tackle a growing backlog of toxic substances needing new or revised limits, OSHA issued a "generic" standard for widely diverse agents. OSHA can do that if it provides separate scientific studies and economic analyses to justify the limits on each agent, notes Peter T. Fay in an opinion he issued for the 11th Circuit Court of Appeals, in Atlanta. But OSHA did not provide such backup.

For instance, Fay notes, OSHA cited no scientific studies to justify its new limits on vegetable-oil mists or fumes from aluminum welding. The agency did cite data establishing risks for carbon tetrachloride and vinyl bromide, two carcinogens.

However, even OSHA acknowledged that those new limits would allow hazardous exposures. OSHA's argument for why it didn't set lower limits – time and resource constraints – "is unpersuasive," Fay argued, and appears to violate the law under which the new limits were promulgated.

"Given OSHA's history of slow progress in issuing standards, we can easily believe OSHA's claim that going through detailed analysis for each of the 428 different substances regulated was not possible, given the time constraints set by the agency," Fay wrote. However, current law does not permit the scientific shorthand and analytic shortcuts presented by OSHA as justification for the new limits, the court ruled.

"We agree that the way OSHA arrived at some of its permissible-exposure limits was less than ideal," observes Colleen M. O'Neill, a spokesperson for unionized workers with the AFL-CIO in Washington, D.C. However, she adds, "We were dismayed that the court chose to throw all [those limits] out and revert back to the 1971 limits."

The Washington, D.C.-based Chemical Manufacturers Association (CMA) also called the ruling "a major disappointment." OSHA's shorthand approach "permitted the agency to set exposure standards for individual substances years quicker than it could by conducting chemical-by-chemical reviews," according to CMA Vice President Morton L. Mullins. Rewriting separate limits for all 428 chemicals "is simply too much of a burden for the agency's limited resources," he says.

EPA's reinterpretation of the "Delaney clause" – a section of the amended Food, Drug, and Cosmetic Act dealing with food additives – came under equal attack. The Delaney clause prohibits the sale of processed foods containing higher levels of carcinogens than the raw foods from which they were made – regardless of whether those carcinogens represent a health risk at the levels present in processed foods.

In 1988, after learning that four approved pesticides can accumulate in processed foods to levels higher than those in raw produce, grains, and oils, EPA decided to reinterpret the Delaney clause: It would allow concentrated residues in foods – if they posed only a "de minimis" (negligible) cancer risk.

Last week, however, the U.S. Court of Appeals for the Ninth Circuit, in San Francisco, ruled that regardless of how reasonable that approach might be, revising existing law "is neither our function nor the function of EPA."

"We hope EPA will seek and the Supreme Court will agree to review this decision," says C. Manly Molpus, president of the Grocery Manufacturers of America in Washington, D.C. Calling the Delaney clause "bad science and bad public policy," he argues that since 1987, "every major scientific organization, including the prestigious National Academy of Sciences, has called for the federal government to adopt a . . . 'de minimis' approach" to regulating pesticide residues in foods.

Congress has a chance to undo, at least partially, what the court rulings have wrought. One bill currently before the House and Senate would formally incorporate a de minimis provision in the Delaney clause. Another would require that OSHA regularly update its air-exposure limits for workers. *– J. Raloff*