in several times," says Darrell Jackson of the University of Washington. Along with colleague James Ritcey, Jackson proposes a solution based on time-reversal with a twist: One submarine sends out a "probe" pulse, and multiple copies of it arrive at another sub's TRM. This turns all the signals around and sends them back, but this time with digital information encoded into them. All of these encoded signals should then arrive back at the original sub simultaneously, so that one path can't confuse the data stream arriving along another.

For all the practical uses of TRMs, Fink is not neglecting basic science. He has recently put together experiments to test the limits of acoustic time-reversal. He is totally scrambling sound pulses by passing them through a "forest" of thousands of scatterers, then reassembling the pulses with a TRM and sending them back through the forest to see how well the original signal survives. So far, none of his pulses has lost its reversibility in the forest. But Fink has still more severe tests planned for his acoustic pilgrims. If those pan out, growing numbers of physicists are likely to be saying "bonjour" to this technology.

–James Glanz

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INFECTIOUS DISEASES

E. coli Scare Spawns Therapy Search

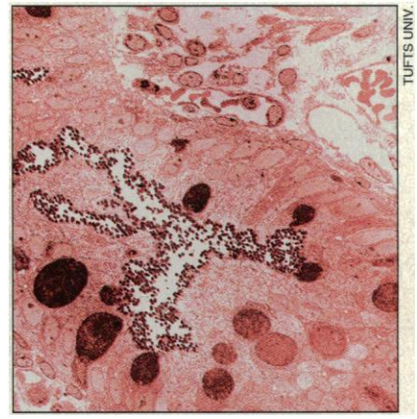
Research was overshadowed by radiation in the headlines last week after a panel of scientific experts met to forge a strategy for combating the bacterial pathogen *Escherichia coli* O157:H7. This strain has been responsible for an estimated 200 to 500 deaths per year, according to the federal Centers for Disease Control and Prevention in Atlanta. It usually makes its way into humans through ground beef, and the panel, which met in Washington, D.C., under the sponsorship of the American Gastroenterological Association Foundation, recommended irradiating that beef—a plan that prompted outcries from consumers and advocacy groups who see radiation itself as a health threat.

But the controversial call drew attention away from other reports at the meeting of research on treatments, including drugs to block the toxins released by the bacteria, and investigations of potential vaccines. "There is a lot of very interesting research going on," says conference attendee Gerald Keusch, an infectious-disease specialist at the New England Medical Center.

One reason more research is desperately needed is that the conventional anti-microbial strategy—antibiotics—may do more harm than good to those infected with O157:H7. Antibiotics typically kill bacteria by puncturing their cell walls, and in this case the ruptures could boost the release of the bugs' toxic cargo. This *E. coli* strain wreaks havoc by releasing either one or a pair of potent toxins, known as Shiga-like toxins (SLT) I and II, which enter intestinal and kidney cells, killing them and setting the stage for serious illness. Puncturing the bacteria could cause more poisonous contents to spill out, says James Kaper, a microbiologist at the University of Maryland School of Medicine, worsening the illness.

As an alternative, researchers are targeting the toxins themselves. One of the most promising experimental therapies involves making spongelike particles that mop up the toxins before they have a chance to bind to cells. SLT I and II each have a protein subunit that binds to a receptor on the host cell surface like a key in a lock and—through an unknown mechanism—clears the way for the toxin to enter the cell. Once inside, the toxins head for the ribosomes, the cells' protein factories, and cripple the cell by preventing the synthesis of new proteins.

To prevent this key, known as the B subunit, from encountering a healthy cell's lock in the first place, researchers are working on decoys that would bind the B subunit before it reached the cell. In one project, a team of Canadian researchers led by Glen Armstrong of the University of Alberta in Edmonton has fashioned a trio of sugar molecules into duplicates of the natural receptors and used them to attract free-floating toxins. These synthetic receptors are attached to the surface of inert clay particles that don't break down in the gut, and early lab tests indicated that the particles were able to attract and hold enough toxin to prevent the onset of disease.



A growing danger. A potentially lethal colony of *E. coli* O157:H7 (small, dark objects in center of micrograph) grows in a piglet colon.

Last month, at a conference on bacterial toxins in Bergamo, Italy, Armstrong reported the results of Phase I human trials, showing that the particles had no toxic side effects and that they retained their ability to sop up toxin even after passing through the intestines of healthy volunteers. Further trials are under way with infected children at 12 hospitals across Canada to see whether the treatment can block the toxins from causing intestinal hemorrhaging and hemolytic uremic syndrome (HUS), which can cause kidney failure, strokes, and death.

"This is the first potentially useful treatment for HUS," says Keusch. "Whether or not it translates to [an effective one], I don't know," he adds. The problem, he notes, is that there is usually a period of 3 to 4 days between the time someone is infected with the bacteria and the time they show symptoms of HUS. So by the time an accurate diagnosis is made, the toxins have likely already been released, and most of the significant damage to cells is done.

One solution is to stop the toxins earlier. So other researchers are attempting to create vaccines that prevent the toxins from getting a foothold in the body—a strategy that's the basis for successful vaccines against diphtheria and tetanus. At the conference in Italy, a team led by Ed Boedeker at the Walter Reed Army Institute of Research in Washington, D.C., reported producing a rabbit-infecting strain of *E. coli* that made SLT I. They then injected rabbits with a vaccine containing the B subunit of SLT I. The rabbits' immune systems generated antibodies to the subunit, which primed the immune system to protect the rabbits when they were later challenged with the toxin-producing bugs. Researchers believe this vaccine will block the toxin as it travels through the bloodstream, where antibodies are plentiful.

This approach has its own drawbacks, however. Blood-circulating antibodies are not often found in the intestinal lining, so this technique is not likely to prevent damage by bacterial colonies there. Keusch's group is working on a strategy to spark an intestinal antibody response, but it is very preliminary. "[Vaccines] aren't going to be a cure in the next 5 years," says Mitchell Cohen, a gastroenterologist at Children's Hospital Medical Center in Cincinnati.

Since researchers are not sure how to prevent the bacteria from infecting cattle in the first place, and because a wide-ranging food radiation program is likely to continue to be the subject of heated debate, the number of victims of *E. coli* O157:H7 will almost certainly grow. And that is likely to make the calls for new treatments grow ever louder.

–Robert F. Service