Cholera Hides a Sinister Stowaway

Cholera has come nearly full circle, again. Beginning in Indonesia in 1961, the tireless traveler has almost completed its seventh circumnavigation of the globe since 1817, leaving freshly dug graves as evidence of its passage. In Latin America alone, cholera has claimed more than 10,000 lives since its landfall in Peru less than 6 years ago.

Now, scientists trying to determine what makes *Vibrio cholerae* so deadly and unstoppable have discovered that the virulent bacterium does not travel alone. Deep inside it resides a viral stowaway packing all the genes needed to turn even harmless strains of cholera into killers.

The virus—known as a bacteriophage, or phage—leaps readily from one cholera strain to the next, a capability that had been postulated for phages but never demonstrated before in the laboratory or in nature.

The cholera-infecting phage attaches itself to slender receptors called pili, which, in the human intestine, bristle from the cholera bacterium like a bad haircut. The phage then slips into the bacterium and deposits into its chromosome a tidy package of genes that code for cholera toxin. Without these genes, the bacterium is harmless.

"We are a hospitable environment for the infection of *Vibrio* by phage," says Matthew K. Waldor of the Tupper Research Institute of New England Medical Center in Boston, who, with John J. Mekalanos of Harvard Medical School's Shipley Institute of Medicine, reported the finding in the June 28 SCIENCE.

Waldor and Mekalanos began by removing cholera toxin genes from the prevalent El Tor strain and substituting genes that confer resistance to antibiotics. They showed that a phage carried the resistance genes as it moved from the infected strain to a strain that lacked the virulence genes. In this experiment, the gene that usually switches on toxin production conferred resistance instead.

Under favorable conditions, each phage with resistance genes infected millions of cholera bacteria. If conditions were changed so that the bacteria didn't produce pili, the transfer didn't take place at all.

"That's the proof that the pili are the receptors for the phage," says Stephen Richardson of the Bowman Gray School of Medicine at Wake Forest University in Winston-Salem, N.C.

Scientists say the work clarifies why some cholera bacteria cause disease while others of the same strain do not. It also promises to open new avenues of study into the virulence factors of other microorganisms (SN: 12/2/95, p. 383).

The findings have also disclosed a hidden pitfall of efforts to develop a live cholera vaccine. Phages may infect the deliberately weakened vaccine bacterium, turning it into a microbial Trojan horse full of cholera toxin.

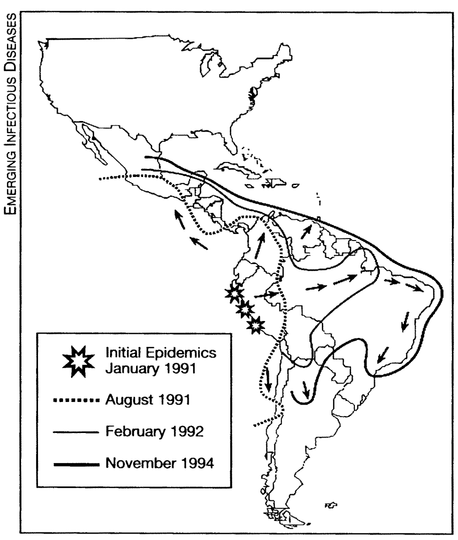
In a sense, the work also brings bacteriophage research full circle, to the era when phage discoverer Felix d'Hérelle of the Pasteur Institute in Paris thought he could use these viruses to cure cholera (SN: 6/1/96, p. 350). Soon after d'Hérelle reported his find in 1917, he began following cholera around the globe, trying to mitigate its impact.

He was unable to improve upon the accomplishment of physician John Snow, who in 1856 traced an outbreak of cholera in London to an area surrounding a communal pump. Removing the pump handle, Snow ended the epidemic, proved that cholera is waterborne, and inspired the preventive strategy used successfully today in the United States and other developed nations.

D'Hérelle's phage work, however, provided the basis for the new findings, which may help scientists prevent future pandemics. "They certainly could lead to some interesting approaches to breaking the infectious cycle," Richardson says.

— *S. Sternberg*

EMERGING INFECTIOUS DISEASES



Spread of cholera through Latin America.

Cutting the energy of communicating bits

Dash-dot, dot, dot-dash-dash, dot-dot-dot.

A century ago, Morse code represented a quick, efficient way of sending information over long distances. A telegraph operator tapped a key that opened and closed a switch to generate a string of electric pulses encoding the news, which was then transmitted over wires to its destination. Nowadays, digital communication involves analogous signals representing 1s and 0s, or bits, to convey information.

All of these forms of communication require a certain amount of energy to produce the electric pulses, radio signals, or photons that transmit an intelligible message.

Information handling invariably involves something physical—whether it's generating an electric pulse or a photon, marking a piece of paper, punching a hole in a card, or magnetizing a spot on a spinning disk—and must therefore conform to the laws of physics.

Rolf Landauer of the IBM Thomas J. Watson Research Center in Yorktown Heights, N.Y., has looked closely at whether the laws of physics mandate that sending a bit requires a certain minimal amount of energy. In the June 28 SCIENCE, he concludes that there is no such requirement, and he suggests alternative communication methods that, in theory, offer the possibility of transmitting information without dissipating energy.

"My message is that energy and matter used in sending information need not be thrown away at the receiving end," Landauer says. "They can, in principle, be recycled."

In the usual view of information transfer, researchers typically have argued that the minimum energy needed to send a bit is roughly equal to the energy of motion of an electron or molecule at the given temperature. Otherwise, the signal, whether electric pulses in a wire or photons in an optical fiber, gets drowned out by the background noise of jiggling molecules, atoms, or electrons of any material.

However, these limits don't necessarily apply to all conceivable forms of communication, Landauer insists. For instance, a great amount of information can be stored on a floppy disk and carried from one place to another, demanding considerably less energy expenditure per bit than if those bits travel through a wire.

Landauer has worked out more detailed schemes for moving bits that involve very little consumption of energy. He likens one of his proposed communication links to a ski lift—on a quantum scale. Instead of chairs, it has mov-