# 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).

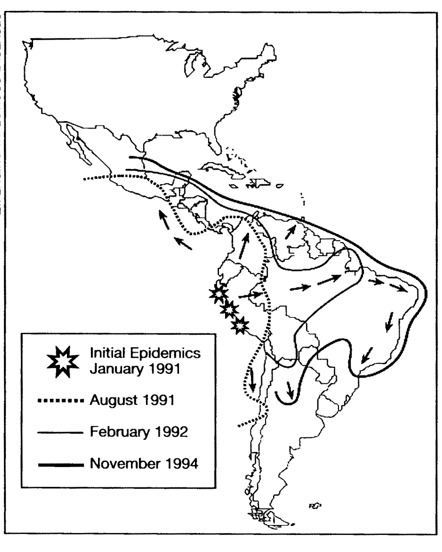
The findings have also disclosed a hidden pitfall of efforts to develop a live cholera vaccine. Phages may infect the deliberately weakened vaccine bacterium, turning it into a microbial Trojan horse full of cholera toxin.

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 moving compartments, or potential wells. Adjustable vertical barriers divide these wells in half. A particle loaded into, say, the left half of a well corresponds to 0 and into the right half to 1.

In the downhill loading step, an incoming bit (0 or 1) waits in its own well to meet a well returning from the top of the ski lift. This returning well is initially in the 0 state. If the incoming bit is 1, its well induces the barrier in the returning well to lower temporarily and forces the particle in the returning well to pass from the left to the right half. Then, the original incoming well is reset so the value of its bit is 0.

The freshly loaded well next travels back up the ski lift to the unloading area, where its bit is copied to a receiving well. The unloaded well is reset to 0 and returns downhill to repeat the information transfer cycle.

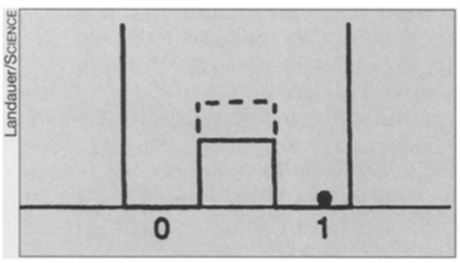
In principle, each of the operations involved in this scenario and in his other proposals involves no expenditure of energy, Landauer argues. Instead of getting thrown away, the bits are, in effect, recycled. Moreover, the basic setup does not require that the signals overcome background noise.

"These are not practical schemes," Landauer admits. They may, however, stimulate others to invent communication systems that make better use of energy than those now available.

For example, it may be possible to use the timing or angle of polarization of photons to achieve an effect similar to that underlying Landauer's quantum ski lift model of a communication link.

Even if his theoretical models are unachievable in practice, Landauer notes, it is still worthwhile knowing that no physical law prohibits extremely low energy communication. — *I. Peterson*

Landauer/Science




*Potential well divided in two by an adjustable barrier, with a particle loaded into the right side to represent 1.*

# Romanian cave contains novel ecosystem

A cavern isolated from the rest of the world under a Romanian cornfield nourishes the first known ecosystem of its kind, three biologists report this week. The 48 animal species—including 33 new ones—found in Movile Cave are part of a food chain that draws sustenance solely from energy-rich molecules in rocks instead of from the power packed in the sun's rays.

Almost all life systems on Earth depend on photosynthesis—directly or indirectly—to fill their metabolic needs. Most animals that live only in caves rely to some extent on photosynthesis because they consume decayed plants swept down from the surface, says Brian K. Kinkle, a microbiologist at the University of Cincinnati.

Scientists have discovered other ecosystems that derive their energy purely from chemical sources, such as bacteria living underground (SN: 10/21/95, p. 263) or deep-sea communities that feed off mineral-rich hydrothermal vents. However, the Romanian cave is unique, Kinkle says, in that it contains the first known land animals not tied to photosynthesis.

The biologists analyzed the animals' diet by taking specimens of bacteria, fungi, and small invertebrates and comparing the ratios of four nonradioactive carbon and nitrogen isotopes. The results showed that the animals live on fungi and bacteria floating on water that partially fills the cave, Kinkle and his colleagues report in the June 28 SCIENCE. These microorganisms consume hydrogen sulfide from the rocks.

The scientists see Movile Cave as a biological time capsule. It was sealed off more than 5.5 million years ago, they say, and its creatures have evolved into specialized, self-sufficient forms. The only thing they need from above is oxygen, which leaks into the cave via minute cracks.

Thomas C. Kane, a biologist at the University of Cincinnati and report coauthor, said he was excited by "not just finding a new species—that happens every day—but finding 33 new species."

The discoveries include grazers such as four species of isopods, or pillbugs, six springtails, a millipede, and a bristletail. Among the new species of carnivores are two pseudoscorpions, a 2-inch-long centipede, a worm-sucking leech, four spiders, and a water scorpion.

That such a diverse community can feed itself in a cave's perpetual night is news to other scientists, too. Larry Lemke of NASA's Ames Research Center in Mountain View, Calif., says Movile qualifies as an excellent "Mars analog site."

Lemke works on the design of new missions to search for life on the Red Planet. Scientists now hold that life may have existed there 3.5 billion years ago, when the planet was warmer and wetter (SN: 8/27/94, p. 137). If that life still survives, it would have to be underground, where liquid water could exist, as it does in Movile Cave.

"Movile Cave is interesting because it seems to be truly closed to outside sources of organic material," notes Lemke. — *E. Skindrud*

# Ancient world gets precise chronology

Scholarly debate and uncertainty have dogged efforts to specify precisely the years when various ancient civilizations thrived in the lands bordering the eastern Mediterranean Sea. An ongoing analysis of tree-ring evidence, described in the June 27 NATURE, promises to bring unprecedented exactitude to the calendar of ancient history.

New data from this project yield an exact chronology of eastern Mediterranean cultures from 2220 B.C. to 718 B.C., a time span that encompasses the rise and fall of early urban centers in Mesopotamia and Egypt, as well as the emergence of societies in Greece and Rome.

"Tree-ring dating now offers the route to a new, absolute chronology of the Old World that is independent of existing assumptions, gaps in evidence, and debates," asserts a scientific team headed by Peter Ian Kuniholm, an archaeologist at Cornell University.

Although this line of investigation will probably generate a reliable time line for archaeological sites in the eastern Mediterranean, doubts still remain about the dating sequence currently proposed by Kuniholm's group, writes Colin Renfrew of the McDonald Institute for Archaeological Research in Cambridge, England, in an accompanying comment.

Prior attempts to devise chronologies for early civilizations in the Near East and Egypt relied largely on recovered documents, such as clay tablets, which outline regional successions of kings and other royal figures. Three different chronologies have been proposed on the basis of such information.

Kuniholm and his colleagues aimed to calibrate a sequence of radiocarbon dates using tree rings from a variety of ancient timbers, most of which came from modern-day Turkey. They identified what they called a floating chronology of 1,503 years, a slice of time from around the second millennium B.C. that could not be pinned to exact years.

The scientists then obtained 18 high-precision radiocarbon dates from a juniper log at a Turkish archaeological site. A statistical comparison of these measurements to radiocarbon measurements from Europe and North America, all of which have established calendar dates, resulted in a chronological sequence for the eastern Mediterranean.

That estimate still contained a slight margin of error. Confirmation of the new chronology emerged with the observation at another Turkish site of exceptional growth in tree rings that correspond

*Continued on p. 406*