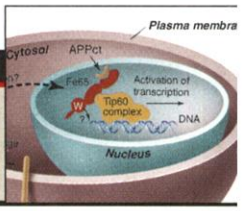
PAGE 27 Remembering a memory

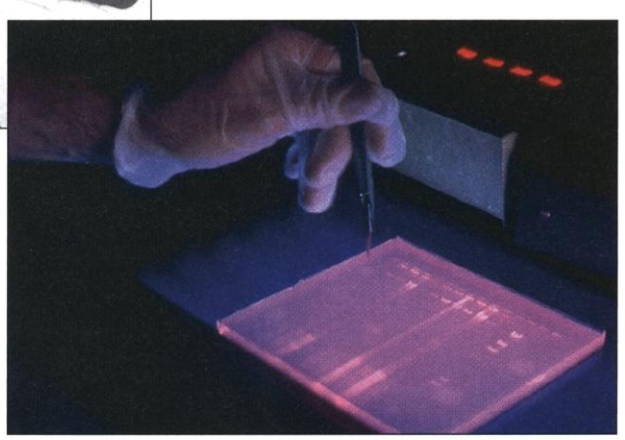
PAGE 28 APP and gene expression



VIROLOGY

Old Guard Urges Virologists To Go Back to Basics

When the dot-com bubble burst, many wondered how the old way of doing business—face to face—could have been written off so prematurely. Now, some say that in science, too, infatuation with modern technology has gone too far. In an impassioned plea published last week, a group of veteran virologists argues that the genetic techniques that have revolutionized their field can't answer some of the most urgent and basic questions.



Changing times. Some researchers worry that the genetic revolution is pushing out classic virological techniques.

The message to the younger generation, with its sleek polymerase chain reaction (PCR) robots, DNA sequencers, and high-speed computers: Without bricks-and-mortar virology, it will be much harder to understand and fight the next dangerous virus that comes along.

"We may be old farts, but I think we have something important to say," says Charles Calisher, 64, a virologist at Colorado State University in Fort Collins, who drafted the paper. Slated to be printed in the July/August issue of *Emerging Infectious Diseases*, it was posted online* last week.

Calisher has been worrying for years about the wholesale takeover by modern lab toys, fearing that the genetic code they spit out sheds much less light on a virus's workings than "classic" methods. Many senior scientists (some quite a bit younger) share his views: The 14 signatories include some of the most illustrious names in U.S. virology. Together, they have many decades of experience chasing exotic viruses across the globe.

Most of these virologists trace their professional roots to the 1950s, '60s, and '70s, when money was plentiful and new viruses were discovered by the dozen. The procedure was straightforward, recalls Calisher: Once you isolated a new virus, you'd produce a stock of it, induce antibodies by injecting the virus into mice, then send your virus and reagents to one of several viral repositories around the world. Local health labs could use antibody tests to detect these new viruses, and other researchers could inject them into animals to study how they caused disease.

Nowadays, scientists can detect a virus simply by searching for and amplifying snippets of its DNA in human or animal samples. Indeed, they have identified and described quite a few new viruses without ever isolating them. Thanks to techniques such as PCR and sequencing, diagnostic labs everywhere can perform high-sensitivity tests for a battery of viruses in a matter of hours. By comparing viral genomes, researchers can even construct complete phylogenetic trees. That, for instance, is how they found out that the West Nile virus strain that invaded the United States in 1999 probably came from Israel.

Although all that is terrific, says Calisher, a string of DNA letters in a data bank tells little or nothing about how a virus multiplies, which animals carry it, how it makes people sick, or whether antibodies to other viruses might protect against it. Just studying sequences, Calisher says, is "like trying to say whether somebody has bad breath by looking at his fingerprint." Yet funding agencies, eager to promote cutting-edge science, prefer molecular virology, the group writes. "People think you're a dinosaur if you still use the old techniques," says co-author Robert Tesh, 65, of the University of Texas Medical Branch in Galveston.

The playing field is further tilted, the researchers say, because of safety rules restricting work with live viruses. As for stalking new viruses, today's PCR generation "doesn't wanna go to Venezuela, sweat, eat bad food, and get diarrhea," says Calisher. "But that's how you come home with tons of interesting samples."

Similar complaints can be heard in other fields of biology. But the trend is especially worrying in virology, Calisher asserts, because it might undermine the response to future public health threats. Other senior scientists agree. "This really needed to be said," notes Harvey Artsob, 56, of the Canadian Science Center for Human and Animal Health in Winnipeg.

But some (relative) youngsters are crying foul. "I don't think there's much to this argument," says Brian Hjelle, 45, of the University of New Mexico, Albuquerque. Within an hour after being asked to comment on this story, Hjelle shot back a two-page, 13-point memo defending molecular virology and criticizing classical methods. Modern techniques have delivered diagnostic tests for hantaviruses, HIV, and hepatitis C, which the old tools couldn't, and these have saved many lives. And techniques such as cloning and PCR are indispensable for studying viruses that are impossible to isolate.

Other hard-core molecular virologists, although not completely embracing the statement, concede that the baby may have been thrown out with the bath water. "We

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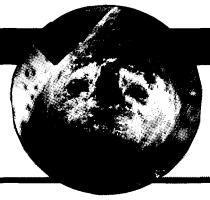
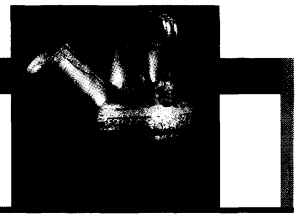
* www.cdc.gov/ncidod/eid/vol7no4/calisher.html





need both new and old techniques," says Gregory Ebel, 33, who studies West Nile virus at the New York State health lab in Guilderland. "I completely agree with most of Calisher's points," adds Robert Lanciotti, 41, who helped tease out the West Nile pedigree at the Centers for Disease Control and Prevention in Fort Collins, Colorado. (And "I'd love to go on field trips," he adds.)

Ab Osterhaus, 53, of Erasmus University in Rotterdam, the Netherlands, says he agrees with the authors' basic point, but he thinks they're overly pessimistic. There may be a little imbalance right now, but Osterhaus is certain that people will discover that good virology takes both fancy new tricks and time-honored methods. "I'm not worried that the field is going down the tubes," he says.

Calisher is not so sure. "I'll keep stirring this pot," he promises. "There's too many people who think they don't need this old-fashioned stuff." **–MARTIN ENSERINK**

WETLANDS RESTORATION

Recreated Wetlands No Match for Original

The assumption that an artificial wetland can replace a natural one has shaped U.S. policy for the past decade. Now, in unusually blunt language, a new report by the National Research Council* (NRC) says that the current approach, designed to ensure "no net loss" of wetlands, is a failure and that humanmade ecosystems are often a poor substitute for the real thing. What's needed, the report says, are major changes to the system for designing and regulating replacement wetlands.

Environmental groups that have long criticized the current wetlands approach are delighted at the report's assertive tone. "This report changes the landscape on wetlands," says Julie Sibbing, wetlands policy expert for the National Wildlife Federation in Reston, Virginia. "We can't pretend [the policy] is working anymore."

The existing policy gives developers the option of building a subdivision or a shopping center on top of a water-logged spot—if it's unavoidable and they restore or create a marsh nearby. That compromise was struck some 2 decades ago after government officials realized that the country was losing its wetlands at an alarming rate. What's more, these swamps or marshes, once regarded as unhealthy and worthless, were actually key wildlife habitat and valuable resources for cleaning water and controlling floods. In 1980, the Environmental Protection Agency (EPA) revised its guidance on the amended 1972 Clean Water Act to stipulate that landowners who get a permit from the U.S. Army Corps of Engineers or a state agency to build on a marsh may need to make up for the damage. Agencies began to promote this so-called mitigation policy after the first Bush Administration embraced a goal of "no net loss" of the area and function of wetlands in the continental United States, now estimated at 42 million hectares. The policy was continued under President Clinton.

Cheap imitation? Developers often take the easy way out, building cattail ponds instead of more complicated wetlands.

The NRC expert committee, formed at the request of EPA, found that although various factors, including less destruction of wetlands for agriculture, have stemmed their overall loss, mitigation isn't working. According to the corps, 17,000 hectares of wetlands have been created for 9500 lost between 1993 and 2000. Yet despite almost double the area, "the goal of no net loss is not being met," says panel chair Joy Zedler, an ecologist at the University of Wisconsin, Madison.

One problem, the panel found, is that the corps doesn't keep very close tabs on the projects, and many are abandoned or never begun. Also, many of the recreated wetlands don't function in the same way as the original ones, which often depend on intermittent water flows to support a specific mix of plant and animal species (*Science*, 17 April 1998, p. 371). Moreover, some developers construct easily imitated types of wetlands such as cattail-lined ponds where they're "not naturally occurring," Zedler says.

The report recommends that wetlands that can't easily be replicated—like fens and bogs—be left alone. Wetlands that must be harmed should first be studied so that permit holders know what they're trying to reproduce. And before issuing a permit, regulators should look at the entire watershed to see if creating a different, more distant wetland would do more good in the long run than building an identical one nearby. To help accomplish these goals, the panel recommends a new database to track permits, a research program to find out what works, stricter enforcement, and long-term monitoring.

It's now up to the younger Bush Administration and Congress to turn the report into action by beefing up the corps' regulatory budget for wetland mitigation, now $125 million a year, says panel vice chair Leonard Shabman, an economist at Virginia Polytechnic Institute and State University in Blacksburg. The watershed approach will also require better coordination among various agencies. "It's not an easy thing to do," says Jeanne Christie, executive director of the Association of State Wetland Managers in Berne, New York. "We've been talking about this for years." **–JOCELYN KAISER**

KENNEWICK MAN

Missing Thighbones Suddenly Reappear

In the latest twist in the interminable tale of Kennewick Man, four leg bones that disappeared 4 years ago have apparently resurfaced at the Benton County sheriff's storage facility in Kennewick, Washington. The Federal Bureau of Investigation (FBI) promptly took over the bones, which were rediscovered last week at the same time a court case resumed over disposition of the 9300-year-old remains.

The bones, found on the shore of Washington's Columbia River in 1996, have been the object of a long-running tug-of-war between scientists who want to study them and Native Americans who want to bury them. Several federal agencies have mediated the dispute, and scientists are hoping that a ruling due soon from U.S. District Judge John

*Compensating for Wetland Losses Under the Clean Water Act, NRC, June 2001, www.nap.edu/books/0309074320/html

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