Koch Keeps New Watch on Infections

Germany is shoring up its infectious-disease surveillance systems, and it has enlisted the venerable Koch Institute to investigate outbreaks when state authorities ask for help

BERLIN—Early this year, health officials in Bavaria were bewildered by a puzzling pattern of bacterial infections that killed seven children in widely scattered villages and sent dozens of others into renal failure. The German federal health ministry's center for infectious diseases, the Robert Koch Institute, quickly dispatched a team of epidemiologists to the region to investigate the unusual outbreak, which was caused by an enterotoxic strain of *Escherichia coli* bacteria (*E. coli* 0157:H7). After 5 months of painstaking work, the Koch team is now closing in on the source, probably a local food product.

This swift federal response might seem routine to Americans who are used to the aggressive investigative methods of the Centers for Disease Control and Prevention (CDC) in Atlanta. But for Germany, it was a highly unusual move. "This was the first time in decades that Koch sent epidemiologists into a state to investigate an outbreak," explains Bernhard Schwartländer, director of Koch's Division of Infectious-Disease Epidemiology.

Germany's federal government has traditionally left most public health initiatives to its 16 states, but concern about new infectious diseases and the re-emergence of old ones is sparking a more active federal response when states request help to investigate outbreaks like the one in Bavaria. The venerable Koch Institute is playing a central role in this new approach: Over the past 2 years, the health ministry has begun "reorienting" it toward epidemiology and applied research, with less emphasis on the institute's basic research.

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Robert Koch's legacy. The institute is emphasizing epidemiology.

These German initiatives are being matched by similar efforts in other European countries, where researchers are intensifying their efforts to coordinate outbreak surveillance (see box, below). Over the past few years, European disease-control organizations have linked to form "surveillance networks" of experts in specialties such as *Salmonella*, Legionnaires' disease, and HIV/AIDS. In the United States, too, the CDC is attempting to bolster surveillance efforts in individual states, as well as forging links across the Atlantic and Pacific (see p. 1413).

The driving force behind these efforts is the growing international threat from infectious diseases. Last month—marking 200 years since Edward Jenner administered the first-ever vaccination—the World Health

A Shared European Concern

The rising tide of infectious diseases around the world, coupled with the spread of HIV, has prompted European public health agencies to combine forces in detecting and handling outbreaks that might spread quickly across national borders. "High-quality surveillance systems are extremely important for public health success," says Christopher Bartlett, director of the United Kingdom's Communicable Disease Surveillance Centre (CDSC). "And factors such as the increase in world travel make international cooperation essential."

The 1991 Maastricht Treaty gave the European Union some jurisdiction over public health issues, and that paved the way for more international cooperation. Disease-control experts in the 15 member nations formed a loose-knit organization called the "Charter Group," which first met in Rome last year. "We found overlaps, but also remarkable gaps in European epidemiological surveillance," says Bartlett, whose CDSC—part of the U.K.'s Public Health Laboratory Service—has taken the lead in Charter Group efforts. The group briefly considered establishing a centralized, European version of the American Centers for Disease Control and Prevention, but opted instead to expand a system of "networks of experts" in special fields such as *Salmonella*, *Legionella* infections, and HIV/AIDS. A small support unit at the CDSC's London headquarters helps coordinate the work of those surveillance networks.

Such cooperative efforts—including the exchange and "genetic fingerprinting" of new viral and bacterial strains—have already helped track down outbreaks. "In the last 5 years, our European surveillance network has detected 28 outbreaks of Legionnaires' disease that otherwise may not have been found," Bartlett says. *Legionella* is a prime candidate for such surveillance, as national efforts might never track down the source of infection: Typically, tourists contract the disease at hotels in warm climates and are not properly diagnosed until they return to their home nations.

In another success attributed to Europe's new disease-surveillance networks, Bartlett says British experts and their continental counterparts helped identify the source of an outbreak of a rare *Salmonella* (*S. agona*, phage type 15) that infected two dozen Britons last year. Researchers eventually pinpointed the source as an Israeli-made corn snack, which had also caused outbreaks in Israel and the United States. "By finding the source so quickly," Bartlett says, "many other cases were prevented."

European disease-control agencies have also established a new training program for European epidemiologists—coordinated by the Institute for Hygiene and Epidemiology in Brussels—and are producing a pilot Europe-wide disease-surveillance bulletin. In addition, the Charter Group plans stronger ties with disease-control agencies in the United States and Canada, as well as in eastern Europe. **–R.K.**

Organization (WHO) issued a report documenting the deadly toll: Infectious diseases killed an estimated 17 million people worldwide last year, the report noted, and the numbers are rising. "We are standing on the brink of a global crisis in infectious diseases," warned WHO director-general Hiroshi Nakajima.

The international problem of infectious disease is worsening, in part, because some nations' outbreak-surveillance apparatus atrophied during the 1960s and '70s—a period when the sustained success of vaccination campaigns and antibiotic drugs had lessened concern about communicable diseases. In Germany, this was compounded by the fact that the public health system is highly fragmented. As in the United States, Germany's states, or Länder, have authority over public health, but Germany's more than 500 local health departments have greater autonomy than their U.S. counterparts. "Under the German system, if something big happens, you have limited capacity to deal with it," says Lyle R. Petersen, a CDC epidemiologist who is on assignment to the Koch Institute. "And up until now, there was no federal agency here that could deal effectively with major outbreaks."

Germany's answer is to enlist the Koch Institute in meeting that challenge. Franz-Josef Bindert, who heads the German health ministry's communicable-diseases section, says the field study in Bavaria is "a good example" of the sort of work that Koch can do to help German state and local health departments detect and fight outbreaks of infectious diseases.

The Koch Institute has a rich heritage in science's struggle against disease. Founded in 1891 as the Prussian Royal Institute for Infectious Diseases, its first director was Robert Koch, the famous German bacteriologist who traveled the globe seeking out the causes of epidemics and ways to help contain them. The institute was the site of some important research by Koch, who won the 1905 Nobel Prize in medicine. Allied bombs badly damaged the institute's laboratories during World War II, and its reputation suffered when some of its Nazi-era scientists were accused of unethically testing vaccines on humans.

After the war, Koch rebuilt itself by concentrating on basic research in fields such as electron microscopy, virology, and bacteriology—rather than on the applied techniques of epidemiology. Now the federal health ministry is changing Koch's focus again, more toward disease epidemiology and surveillance. The changes began a couple of years ago, when Koch's core HIV/AIDs section was expanded to encompass other infectious diseases. Koch's team of epidemiologists started analyzing state data more

U.S. Beefs Up CDC's Capabilities

In 1967, U.S. Surgeon General William Stewart announced that the United States could "close the book on infectious disease." U.S. health officials, like those in other developed countries, believed that the astounding success of vaccines and antibiotics would continue and eventually beat infectious disease into submission. That confidence has proved to be at best premature, however: Diseases such as tuberculosis, cholera, and typhus, for decades considered under control, have resurfaced with a vengeance and, along with AIDS and new food- and water-borne infections, have caused deaths from infectious diseases to increase by 58% between 1980 and 1992 in the United States alone.

Researchers at the U.S. Centers for Disease Control and Prevention (CDC) in Atlanta admit that they let their guard down. "There was a general complacency," explains Ruth L. Berkelman of CDC's National Center for Infectious Diseases. Much of CDC's expertise in the field was lost as infectious-disease experts retired and were not replaced. All in all, there was "a major erosion of CDC's capability to deal with these problems," agrees Jon Counts, a microbiologist at Washington State's Department of Health in Seattle.

Two years ago, spurred in part by three reports between 1987 and 1992 from the Institute of Medicine critical of the U.S. public health system, CDC took steps to try to reverse the slide. The agency drew up an ambitious $125-million-a-year plan—Addressing Emerging Infectious Disease Threats: A Prevention Strategy for the United States—which called for increased monitoring for emerging infections, improvements in local and state public health facilities, and enhancement of international efforts to control the spread of these pathogens and to watch out for the development of infectious agents resistant to existing treatments.

The U.S. Congress responded by allocating $6.7 million in 1995 and $10.7 million this year, a sum President Clinton wants to increase to $27 million in 1997. "It's the first money for emerging infectious diseases [excluding AIDS] that we've had," says Berkelman. Already, with about $2.5 million of those funds, Connecticut, Minnesota, Oregon, and northern California have set up programs to monitor known emerging infectious diseases, such as a tick-borne illness called ehrlichiosis and the *Escherichia coli* strain 0157:H7, and to look for new threats. The CDC has also agreed to provide $200,000 a year to 13 states, as well as to New York City and Los Angeles, to bolster local public health efforts to combat infectious diseases. But this level of federal support is a far cry from what the CDC plan called for. "The additional funding to states is a good beginning, but we still have major problems," Counts says. Most public health efforts will still be directed to dealing with crises, even though catching outbreaks early and preventing the spread of an epidemic is far more cost-effective, explains Mike Osterholm, an epidemiologist at the Minnesota Department of Health in Minneapolis.

In parallel with its efforts to bolster domestic disease surveillance, CDC, along with other federal agencies, has been pursuing international cooperation. In mid-April, the United States and Japan signed an agreement to work together for the first time to improve global efforts to prevent and control the spread of emerging and re-emerging diseases. Similarly, the most recent Trans-Atlantic Alliance agreement between the United States and the European Union calls for a global communicable-disease network. Next week, the two parties will announce the creation of three subcommittees that will develop goals for expanding surveillance and response, research and training, and the capacity to deal with emerging infections.

But such international agreements face an uphill struggle. With U.S. national programs in such disarray, for CDC "the focus thus far has been on domestic programs," says Robert Pinner, an epidemiologist at CDC's National Center for Infectious Diseases. And WHONET, a computerized database designed to monitor for resistant microbes across the globe, has only about 30 countries contributing data and many developed nations are just beginning to get involved, says clinical microbiologist Thomas O'Brien, who runs WHONET from Brigham and Women's Hospital in Boston.

"We've never really had a strong national disease-surveillance program, and globally, [surveillance] has been fragmented," says Gail Cassell, a microbiologist at the University of Alabama, Birmingham. And she worries that the U.S. government is still not ready to commit to real change: "[The funding] is not nearly enough to fix the problems we have, and it doesn't even touch on the research needs." **–Elizabeth Pennisi**

thoroughly and began publishing weekly bulletins on communicable-disease issues. Recently, the health ministry also moved to strengthen Germany's network of national reference center laboratories.

Schwartländer, who worked at the CDC in 1990 to '91, says he used the Atlanta-based agency as a model for several changes being implemented at Koch. "We don't want to simply collect data on infectious disease; we want to translate those data into action," he says. "In some ways, we are going back to the work of Robert Koch."

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But the institute's new role rankles some of its research staff. Health ministry officials have said that they want more emphasis on applied research, with somewhat less focus on the sort of basic studies that many of Koch's 115 tenured scientists and four dozen untenured researchers have pursued in recent decades. Franz J. Fehrenbach—director of Koch's bacteriology and parasitology section—contends that basic research is essential "to foresee emerging problems in infectious diseases." He has no objections to bolstering Koch's disease-surveillance work, but does not think it should be done at the expense of basic research. At the same time, the director of Koch's virology section, Georg Pauli, says that he thinks Koch "is on a good track." While Koch scientists "still do quite a bit of research," Pauli says, "we now have to do more work for the [health] ministry and for the public."

The health ministry's Bindert says he appreciates the value of basic research, but insists that Koch's main emphasis should be on applied research. After all, other German institutions—including the Max Planck Society and universities—are engaged in basic science in infectious diseases. One prominent German scientist, who asked not to be named, says Koch's reputation for basic research has declined in recent years. "You can't compare Koch with [France's] Pasteur Institute," the scientist says. Koch officials respond that the Pasteur Institute has a different history and mission, with far less responsibility for public health. Among the burdensome public duties that Koch is saddled with, some say, is monitoring German genetic-engineering experiments.

Whether Koch adapts to its new role happily, the institute's services are certainly needed. Petersen, who headed the CDC's HIV Seroepidemiology Branch, had only just arrived in Berlin in January as a consultant to help bolster the Koch Institute's disease-control efforts when he was dispatched to Bavaria to head the institute's on-site team. He says he was astonished that the Bavarian outbreak, which probably involved hundreds of persons, "went completely undetected for months. It shows the pressing need for better infectious-disease surveillance and investigation."

Early this month, Koch epidemiologists were still at work on the Bavarian outbreak, trying to pinpoint its source. "It's an extremely difficult case, because the infections occurred in a large area and over a relatively long time span," says Schwartländer. "This outbreak is a good example of why Koch needs to get involved."

–Robert Koenig

Robert Koenig is a writer in Berlin.

THEORETICAL PHYSICS

Seoul Unveils Regional Center

TOKYO—Ten Pacific countries are laying claim to a larger Asian presence in theoretical physics this week at a conference in Seoul that marks the debut of a new research organization. The government entity, called the Asian Pacific Center for Theoretical Physics (APCTP), is intended to make the South Korean capital a mecca for researchers by assembling a world-class permanent faculty, offering workshops and meetings, and eventually awarding advanced degrees. "We want to create a truly international center that can compete with the best Western institutes," says Yong Min Cho, a professor of physics at Seoul National University and secretary-general of the center.

The center is a dream come true for many of the region's physicists. "Whenever [Asia-Pacific] physicists met at international conferences, we used to talk about the possibility [of such a center]," says Yoshio Yamaguchi, co-chair of the international planning committee and a former director of the University of Tokyo's Institute for Nuclear Physics. The center grew out of a 1989 meeting of physicists at Japan's National Laboratory for High-Energy Physics (KEK), which led in early 1993 to an international planning committee. The Korean government agreed to put up most of the initial cost of the center. In return, Seoul was chosen as the site, although support also comes from Australia, China, Japan, Malaysia, the Philippines, Singapore, Taiwan, Thailand, and Vietnam.

Realizing a dream. Scientists from 10 nations have been meeting in Seoul to plan the new Asian Pacific Center for Theoretical Physics, to be headed by C. N. Yang *(back row, center)*.

Organizers hope the center will become known not just for excellence in all areas of theoretical physics but also as a milestone in the region's scientific development. "Frankly speaking, in Asia there has never been a truly first-class international institute, not just in physics, but in any science," says Cho. Toward that end, the center has recruited Nobel laureate Chen Ning Yang as its first president and chair of the board of trustees, although his duties as director of the Institute of Theoretical Physics at the State University of New York, Stony Brook, and head of the Institute of Mathematical Sciences at the Chinese University of Hong Kong mean that someone else will handle the center's day-to-day affairs.

Achieving world-class status will hinge on becoming a permanent home for world-class researchers from all countries, as well as hosting visiting fellows and other part-time appointees. And Cho admits, "It's not easy to attract this kind of people." No resident senior fellows have been selected despite the lure of good pay and excellent support. In addition to what Cho calls