PUBLIC HEALTH

Russian Chaos Breeds Diphtheria Outbreak

GENEVA—Since the fall of the Communist regime 4 years ago, the former Soviet Union has become a land of opportunity—for better or worse—for many of its inhabitants. One opportunist is *Corynebacterium diphtheriae*, the micro-organism responsible for diphtheria. Slipping through rents in Russia's tattered health system and gaps in its population's immunity against the disease, this bug has taken advantage of a newly mobile population to kindle an epidemic that so far has affected about 80,000 people and killed more than 2000 throughout the former Soviet Union.

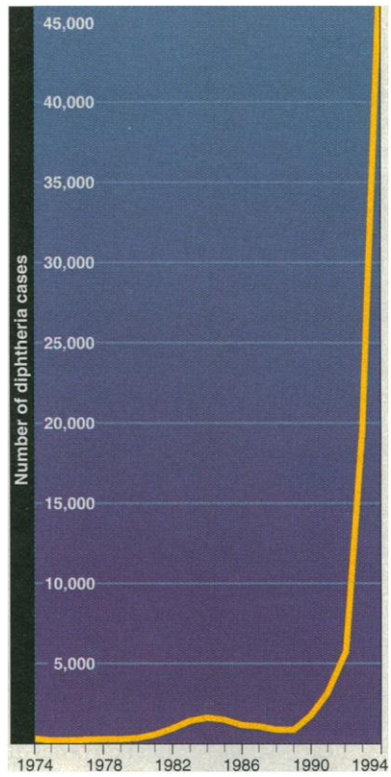
The epidemic has swept swiftly westward across Russia and moved into Ukraine, Belarus, and the Baltic states. By last December it had spread to all 15 states of the ex-Soviet empire. "It's one vast epidemic and it's escalating off the graph paper," says Nick Ward, acting head of the World Health Organization's (WHO's) Expanded Program on Immunization (EPI). Vadim Ivanov, who was head of the diphtheria department at Moscow's Tushinskaya Pediatric Hospital in the early days of the epidemic, recalls how "people reacted with shock and disbelief—this was a disease most people in the street thought had been wiped out."

Last week a group of specialists including an epidemiologist from the Centers for Disease Control and Prevention (CDC) in Atlanta visited Ukraine to help plan the containment of its epidemic. Western health agencies have every reason to get involved: The outbreak has begun to leak cases to a few Western countries—including the United States—via infected travelers, and populations in several countries may be vulnerable because levels of immunity in adults have decined in recent decades. Says Ward: "We're worried and believe me, the Russians and their new neighbors are worried."

Breeding ground. In many ways, Western health experts say, Russia's diphtheria outbreak was an accident waiting to happen. Too few Russian children were getting a full three-dose series of anti-diphtheria shots—only 68% in 1990 compared with more than 80% in 1980—and WHO says that at least 95% coverage is needed to prevent an epidemic. In some places, like St. Petersburg, only 45% of children had been fully vaccinated, according to WHO figures.

In addition, too few Russian adults had protective immunity against the disease—only about 20% of those between 30 and 50 years old, according to surveys carried out by researchers at Moscow's Gabrichevsky Institute. The reason is that in most countries widespread vaccination of children in the 1970s virtually wiped out *C. diphtheriae*, so that by the 1980s there was not enough around to boost adults' immunity naturally. "In Russia, with such a large pool of susceptible people—both in children and in adults—there was a real potential for an epidemic," says Artur Galazka, the EPI's diphtheria expert.

All it took to spark the epidemic was the arrival in Moscow in 1990 of a few infected paramilitary recruits from southern Russia, where *C. diphtheriae* is commonplace but only causes a mild skin disease. (The more serious throat diphtheria of the current epidemic begins with flulike symptoms which can eventually cause fatal damage to the heart and central nervous system.) In Moscow—and later in St. Petersburg—the infection quickly took hold in a large, immunologically weakened population of homeless, ill-nourished people, many of them alcoholics or drug users.



Off the chart. There have been over 80,000 cases since the epidemic began.

Galazka says the Russians could have stamped out the epidemic in its infancy, but did little or nothing at first. He was part of a WHO team that went to Moscow in February 1991 to warn government officials about the coming epidemic and to recommend urgent action. "In the early months of the epidemic most cases were confined to Moscow and St. Petersburg. The outbreak could have been snuffed out without too much trouble if they had acted quickly. But they denied there was a real problem."

Part of the reason for the delay, many health officials believe, is the fact that in the changeover from a Soviet to a federal system, Russia emerged with two health authorities in charge of infectious diseases—one in the health ministry, the other in one of the President's state committees. "The two just don't speak the same language," one official told *Science*. Arkady Yashinsky, chief of program development in the State Committee for Sanitary and Epidemiological Surveillance, says some protective measures were put into effect as soon as the epidemic started, but he admits that "really strong action was only taken in 1993."

Sieghart Dittmann, head of immunization at the Robert Koch Institute in Berlin, who is coordinating efforts by WHO's European office in Copenhagen, Denmark, to battle the epidemic, believes the Russians perceived the danger, but "this problem got buried under the huge pile of other problems the country was facing." Over the past 18 months, however, the Russians have finally begun to take effective action. Last year more than 30 million of the country's 150 million inhabitants were immunized with at least one dose of vaccine, according to Mikhail Narkevich, chief of the health ministry's infectious diseases department. "We hope to vaccinate another 40 or 50 million people this year," he says. If things go according to plan, he believes, "we could wipe out this epidemic in 2 years."

Other Russian scientists are skeptical. Maya Gasparyan, former professor of infectious diseases at Moscow's No. 1 Infectious Disease Hospital, says "We've got too many people on the move in Russia," spreading the disease and not easily brought into a vaccination program. "Our economic and ecologic problems have increased the numbers of our immunosuppressed children. I'm really pessimistic."

One hurdle most Russian officials recognize is the difficulty of convincing Russian pediatricians, especially in remote rural areas, to immunize their patients. In the 1980s, unconfirmed but widely publicized reports of brain damage and other side effects of childhood vaccines created resistance to immunization among the general public. Pediatricians were also reluctant to immunize because the health ministry had issued a very long list of conditions when vaccines should not be administered (WHO lists only five). Today, these barriers have been overcome, at least officially and in the big cities. But, Dittmann fears, "the message has still to get to the rest of the country."

Other newly independent states of the former Soviet bloc are also struggling to contain diphtheria epidemics that were not caught in time. In Ukraine, the next hardest-hit country, with over 8000 cases over the past 4 years, the epidemic seems to have

peaked. At last week's meeting in Kiev, Ukrainian health officials presented to experts and aid organizations a plan to vaccinate or complete the vaccination of the entire population of 52 million by the end of this year. Earlier this year, the other ex-Soviet republics approved an outbreak containment plan drawn up by WHO and UNICEF, involving rapid diagnosis and treatment of cases and their contacts, and mass vaccination campaigns.

But for most of these countries, the plan could be sunk by a desperate shortage of vaccine, particularly of the adult variety known as Td. There is also a dearth of antitoxin, a horse serum containing anti-C. *diphtheriae* antibodies that can prevent the cardiac and neural damage that kills between 3% and 10% of patients. The only production plants in the region are on Russian soil. Narkevich and Yashinsky say that because these plants can only supply Russia's own needs, the Russian government banned export of the vaccine and antitoxin after the breakup of the Soviet Union, leaving its neighbors to rely on international donors. Dittmann reckons that about 500 million doses of vaccine will be needed over the next 2 years at a cost of more than $50 million and at least 200,000 vials of antitoxin costing about $1 million—although prices are rising rapidly as world demand outstrips supply. Colette Roure, EPI adviser to WHO's European office, says funds are desperately needed.*

Heading west. Before the lifting of the Iron Curtain, such an outbreak would almost certainly have been contained within the Soviet Union. No longer. A few cases have cropped up in close neighbors such as Poland, Finland, and Norway. Further west, Germany has reported six cases, and in the last few months two Russian-born American citizens returned home to give the United States its first taste of the Russian epidemic.

WHO's Galazka believes some industrialized countries may have the ingredients for an epidemic. Some have certainly let childhood immunization slip in recent years: In the United States, for example, only 44% of children were fully vaccinated in 1991–92, according to CDC estimates. More disturbing, says the CDC's Iain Hardy, is the large proportion of adults—between 30% and 60%, he reckons—whose immunity has fallen to low levels in many countries, including the United States, Canada, and Australia. In Europe, the proportion of unprotected adults ranges from as low as 20% in Finland and Denmark to 53% in Poland.

WHO has advised all European countries to ensure that at least 95% of children are immunized by 2 years of age and that they receive a booster on starting and another on leaving school. Most countries have begun implementing these measures, says Roure. States close to the Russian epidemic are taking special measures: Finland, for example, has already vaccinated 80% of its adult population, and Poland has immunized all adolescents aged 19 and all officials policing its eastern border.

In the United States, Hardy believes the risk of infection spreading from a few isolated cases "is real but not worrying: We have a fairly aggressive management approach to contact tracing, surveillance, diagnosis ... and rapid hospitalization of cases." But state public health authorities and physicians throughout the country "should be made more aware of this disease. Most American doctors have not seen a single case of diphtheria and could easily fail to diagnose it or could misdiagnose it."

Meanwhile, back in Russia, officials are understandably anxious to get the diphtheria epidemic out of the way so they can get on with the other problems of daily life, such as cholera, dysentery, tuberculosis, AIDS, and even malaria.

–John Maurice

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BIOTECHNOLOGY

European Parliament Axes Patent Policy

After 6 years in the drafting, a European Union (EU) directive seeking to set common standards of patent protection for biotechnological inventions was thrown out last week by the European Parliament in Brussels. The directive would have set ground rules for the patentability of genes, cells, and other biological material derived from humans, animals, and plants. Its demise means that the biotech industry will have to stick with existing legislation—which was not designed to deal with the complex issues of living inventions—and build up precedents on a case-by-case basis. It could also result in a patchwork of different regulations in different European countries.

The ethics of patenting biological organisms has long been controversial in Europe, and the Directive on the Legal Protection of Biotechnological Inventions had a stormy ride through Europe's legislative corridors. Indeed, at one point last year, the Parliament and the Council of Ministers were so deeply divided over the text and subsequent amendments that a conciliation procedure established by the 1992 Maastricht Treaty had to be invoked for the first time. But even that wasn't enough: Unexpected opposition from many new members of the European Parliament (MEPs) elected last year killed the directive by 240 votes to 188, with 23 abstentions.

The vote was hailed as a victory by environmentalists and animal-rights groups, who opposed the basic premise of the directive, that life is patentable. But genetics researchers are disappointed. They fear that without guidelines specifically designed to address genetic engineering inventions, the existing practice of patent offices may give commercial companies too much control over genetic data, thereby restricting research. The biotech industry, surprisingly, isn't hitting the panic button: It feels that in its final form the directive was too ambiguous and would have achieved few of its original aims.

"We'll see what comes out of EPO case law, and I think industry's happy to abide by that."

—Nick Scott-Ram

The biotech industry provided the initial impetus for the directive. It wanted to ensure that European patent regulations were generally in line with those of the United States and Japan, which have tended to be less restrictive in deciding what kinds of living inventions can be patented. Currently, applications in Europe can be filed with a national patent office for protection in that country only, or with the European Patent Office (EPO) in Munich, Germany, for protection in the 17 countries that signed the 1973 European Patent Convention (EPC). Each nation has been treating biotech patents slightly differently, and the EPO has been interpreting the EPC on a case-by-case basis. If the directive had been passed, all EU member states would have had to write its provisions into their patent laws.

It took more than 5 years of negotiations before the European Parliament and the Council of Ministers agreed on a draft text in December 1993. This was modified in February 1994 to address the biotech community's concern that the directive would have been more restrictive than the EPC. Then last May, MEPs requested several amendments, one of which—aiming to clarify exactly the instances in which a human body part can be patented—required conciliation proceed-