Rift Valley Fever Rears Its Head

Epidemic on the Senegal River indicates the wider reach, increased human involvement of the serious viral disease

LAST OCTOBER, two French army doctors working in a hospital in the Mauritanian river town of Rosso on the Senegal River made tests that led to a diagnosis of Rift Valley Fever among patients there. It was the first confirmed outbreak of the dangerous viral disease in humans in West Africa.

By the time the outbreak subsided, 28 deaths were recorded among the 245 cases seen at the hospital. Public health data in the area is very sketchy and the exact dimensions of the epidemic cannot be documented. After follow-up epidemiological work, however, the Pasteur Institute of Dakar estimated the total number of cases in Mauritania at 1264 with 224 deaths.

Although the disease was confined to a fairly limited area, increasing concern about the future seems warranted. A dam downriver at Diama in the Senegal River delta had begun operation 2 years before. Now there is circumstantial evidence, at least, that fears that impoundment of water behind the dam would lead to a worsening of waterborne diseases are being realized. The incident has prompted international efforts led by French and U.S. scientists to establish the status of the disease in the region and to frame countermeasures.

RVF, as the disease is known in virologists' shorthand, affects both animals—particularly ruminants—and humans. It is a febrile viral disease that in severe cases in humans may cause eye effects leading to blindness and fatal complications of hemorrhagic fever or encephalitis. It is also called enzootic hepatitis because of its effects on animals. RVF, caused by a virus of the *Phlebovirus* genus of the Bunyaviridiae family, can be transmitted by direct contact—especially by infected blood in aerosol form. But the major vector is insects, particularly mosquitoes.

Vaccines have been developed for both humans and animals. But the most commonly used vaccine for humans requires three inoculations spaced over a month and protects for less than a year. It is, therefore, regarded as impractical for large-scale immunization campaigns in the poor, developing countries of sub-Saharan Africa.

The RVF virus was originally isolated in the early 1930s in Kenya's Rift Valley, as the name of the disease indicates. In the following decades, outbreaks were confined to sub-Saharan Africa, occurring most frequently in East Africa and Southern Africa. The disease was known for its serious economic effect on cattle and other domestic animals—it causes abortions in virtually all pregnant females affected—but was regarded as nonfatal in humans.

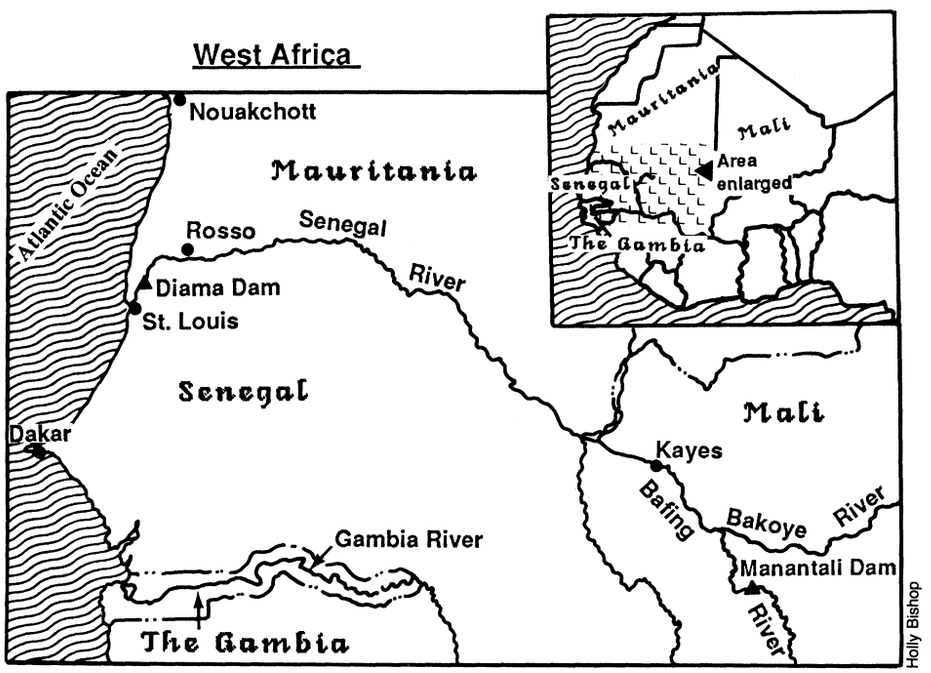
That changed in 1977 when a serious outbreak was reported in Egypt in the Nile Valley and Delta. Some 598 deaths occurred among the 18,000 clinical cases that were reported; medical opinion at the time interpreted the substantial human mortality rate as indicating increased virulence. Israel mounted a precautionary control campaign, vaccinating livestock and establishing a cordon sanitaire in the Sinai. The possibility that RVF would spread to the Middle East and southern Europe attracted international attention.

After 2 years, no more cases of RVF were reported and no further significant RVF activity was documented until the recent Mauritanian outbreak. The Egyptian epidemic, however, established RVF as one of the nastier arboviruses. Because of its widening geographic reach and increased human involvement, researchers have pressed work on the disease.

After the outbreak in Mauritania, the 19 February World Health Organization (WHO) *Weekly Epidemiological Record* concluded a description of the epidemic with the comment that "Further studies are needed to determine whether RVFV (Rift Valley Fever virus) is endemic in this region or was imported, to assess the extent of the affected area and to identify the cause of the epizootic [epidemic in animals] which was revealed by the cases among the human population, in particular the possible role of the recently inaugurated Diama dam in changing the vector population and thereby favoring the transmission of RVFV among livestock."

Answers to these questions are now being sought, with WHO focusing on RVF and French and American researchers collaborating with health authorities in Mauritania and Senegal. On the American side, the effort has centered in the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) at Fort Detrick, Frederick, Maryland. The immediate question in circumstances like those in Mauritania, according to Colonel C. J. Peters, chief of USAMRIID's disease assessment division is, "Where did the virus come from?"

As to whether the virus was "imported," as WHO puts it, the odds seem strongly against it. Early this year and well before the outbreak, scientists from the Pasteur Institute of Dakar and from the veterinary services of Mauritania and Senegal identified



an important "focus" of RVF circulation in southern Mauritania. Their serological survey of shepherds showed that 13% had antibodies against the RVF virus. In the 28 February 1987 issue of *Lancet*, they noted that the presence of this endemic focus raises "the possibility of epizootic and zoonotic disease" as humans and animals migrate through the region. They concluded that "Developments in the region, including the construction of dams on the Senegal River, have encouraged migration into this endemic focus, and the risk of RFV may be increasing."

The work was part of a larger Pasteur survey that also covered four other West African countries—the Gambia, Mauritania, Burkina Faso, and Niger. In all of these, blood samples taken from both domestic animals and man tested positive for RVF, but a substantially lower percentage showed antibodies to the disease than in Mauritania.

The presence of RVF virus activity in the area is not entirely surprising. In 1977, a team from the Yale Arbovirus Research Unit began fieldwork to assess the health implications of the projected dams on the Senegal River valley. The Yale team took blood samples from 1000 people on both the Mauritanian and Senegalese sides of the river. Wilbur G. Downs, the arbovirus lab's former director, who participated in the fieldwork, says they found "quite high antibody rates in the human population."

The team's report to their sponsor, the U.S. Agency for International Development was explicit in putting RVF on a list of diseases likely to pose a greater problem after the dams went into operation.

In the 1987 Mauritanian outbreak, the prime suspect both as a vector and reservoir for RVF is the *Aedes* mosquito. A USAMRIID entomologist, Major Kenneth G. Linthicum, who has worked on the subject in Kenya with a U.S. research team, explains the basis of the suspicion. Scientists have established that eggs laid by infected *Aedes* can maintain the RVF virus for several years; hatching occurs when conditions are favorable. In Kenya, *Aedes* are often found in so-called *dambos*, shallow depressions that fill with water during the rainy season and then dry out. *Aedes* eggs containing the virus are able to survive dry years and produce infected mosquitoes when conditions permit.

The favored scenario for an outbreak of RVF features abundant rains producing large numbers of mosquitoes. Other mosquitoes besides *Aedes* can serve as vectors for RVF and also thrive in the *dambos*. The process that leads to disease in humans apparently starts with *Aedes* introducing the virus to susceptible animals. Other mosquitoes, as secondary vectors, help to widen the circle. Substantial epizootics seem to lead to human infection.

In the Mauritanian outbreak the case against the *Aedes*, however, is not open and shut. The comparison to Kenya still falls short because it is not certain that the *Aedes* is in the area of the new outbreak to play the leading role. Linthicum says the *Aedes* is known to be present in southern Senegal, but it is not clear if it is present in the Senegal River region. Knowledge of the taxonomy of the mosquitoes is very important in the effort to understand the disease there, and Linthicum acknowledges, "We don't have the information."

Kenneth G. Linthicum

Hospital at Rosso. *Basic care is available here in the Mauritanian town where Rift Valley Fever was identified. In the epidemic, 28 patients died.*

Efforts to repair the deficiency are under way, however, with ORSTOM, the French government overseas science and technology research organization, undertaking a study of the taxonomy of mosquitoes in the region. This summer, a U.S.–sponsored team is also scheduled to go to Mauritania and Senegal in the rainy season there to focus specifically on the *Aedes*.

Another sort of evidence, however, both bolsters the Kenya analog and suggests that the new dams are implicated. Those familiar with the region say that in the 2 years since the Diama dam was put into operation, standing water after the rainy season has been more extensive and lasted longer than in the days of natural flooding by the river. According to Linthicum, observers on a flight over the region in January, about 2 months after the end of the rainy season, noted many persisting areas of standing water. In particular, there was a large lake not far from Rosso.

In satellite imagery provided by a NASA team headed by C. J. Tucker, there was no comparable lake in the area in 1985 before the Diama dam went into operation, says Linthicum. Even pictures from 1981, when rains were relatively heavy, indicated no standing water there at all. They also showed a marked expansion in irrigated agriculture along the river. These new irrigation perimeters could harbor mosquitoes.

The dam at Diama and a high dam far upriver at Manantali on a tributary of the Senegal, are products of a massive program, involving Mali as well at Mauritania and Senegal, aimed at developing the Senegal River valley. (*Science*, 30 May 1986, p. 1081).

Before the dam went into operation, no epidemics of RVF were reported in the area. The disease may have been endemic in the region, but if cases occurred in animals and humans they did not attract attention outside and were not diagnosed. Even the identification of RVF in the recent outbreak seems to have been fortuitous. Mauritania, one of the poorest and least populous of African countries, is part of a region rich in infectious diseases, but very poor in medical resources. Mortality from fever is frequent, the assumption usually being that malaria is responsible.

At Rosso it appears that without the French connection in West Africa—a carryover from the colonial past—the diagnosis might not have been made, or at least made as promptly. The French army had, in effect, loaned two physicians to the government of Mauritania. If they had not happened to be working in the Rosso hospital where they were alerted by cases of hemorrhagic fever and sent blood samples to the Pasteur Institute of Dakar, in the capital of neighboring Senegal, the incident might well have been written off as attributable to yellow fever which occurs sporadically in the region.

While a good deal is known about the ecology of RVF, the details of transmission and a causal connection between the dams and the disease have not been nailed down. Also, Peters, for one, is not convinced that the virus has grown more lethal. He acknowledges that there "may be variations in virulence," but regards the case as still not proved.

Since the flare-up, RVF is getting renewed attention. USAMRIID, which con-

ducts militarily relevant research on infectious agents as part of its mission to provide a defense against potential biological warfare agents, has focused seriously on RVF since the Egyptian outbreak. Now it has a new human vaccine against RVF that also can be used in domestic animals and is ready for field testing. Tests on monkeys indicate that a single shot of the live attenuated virus vaccine will protect for several years.

Such testing is ideally carried out where the disease occurs; the plan is to mount field trials in the Senegal River valley. Arranging vaccine trials in the Third World can be a delicate matter. The new vaccine has the blessings of WHO, which should help smooth the way, and U.S. researchers are cooperating as consultants with the Pasteur scientists in all work on RVF in the region in deference to French experience and status there.

Finding a better vaccine is important because, once a patient is ill with the disease, therapies are limited to providing general support. In most rural areas in sub-Saharan Africa, such support is minimal. Advances in treatment are being made, but remain mostly in the experimental stage. Peters says that decided promise for treating RVF is shown by the antiviral medication ribavirin, which is also used against AIDS. In addition, new testing techniques make it easier to obtain accurate antibody levels and to make much more rapid diagnoses of RVF by detecting viremia in patients with the disease.

Given what is known about the transmission of RVF, one possible strategy would be to rely on remote sensing for an early warning. Enough comparative data are available to spot changes in vegetative cover that would indicate conditions favorable to mosquito hatching. At that point, livestock in the area could be vaccinated to prevent an epizootic. Linthicum says it has also been suggested that breeding places could be seeded with persistent pesticides.

The growing potential for combating RVF clashes with the reality of the conditions prevailing in the region now and in the foreseeable future. Rosso, only about 50 miles upriver from the Atlantic port of St. Louis, is hardly the most remote place in that part of the world, but it took a full month for the suspicions about RVF in Rosso to be confirmed in the lab in Dakar.

Peters and others suggest that the RVF epidemic on the Mauritanian shore could serve as a paradigm for other outbreaks of the disease. Unfortunately, it could also serve as a paradigm for the predicament affecting developing countries when the scientific ability to prophesy misfortune far exceeds the capacity to avert it.

■ JOHN WALSH

U.S.-Soviet Science Pact Stalls

Negotiations between the United States and the Soviet Union over a draft agreement providing a framework for scientific cooperation have hit a snag. Talks with a Soviet delegation were proceeding last month in hopes that an agreement could be signed by President Reagan and General Secretary Gorbachev at the Moscow summit. But shortly before the summit, officials from the Office of Science and Technology Policy (OSTP) asserted that a provision of the proposal could be used by the Soviets to gain access to sensitive corporate technology. Though other American agencies disagree with OSTP's interpretation, the agreement was put on hold.

The draft agreement, if approved, would represent a modest step in renewing joint collaboration among Soviet and American scientists under the auspices of each government's agencies. Scientific cooperation between the two countries has been limping along since the Soviets invaded Afghanistan. The last general scientific agreement between the two countries was signed in 1972.

Under the new proposal, the areas of collaboration would be limited to basic science, although the Soviets have pressed for joint projects in applied science. The proposal would include study in life sciences, mathematics, theoretical physics, chemistry, and Arctic research. The National Science Foundation and the U.S. Geological Survey would be the main American agencies participating in the exchanges under this agreement. (These federal agencies and others already cooperate with individual Soviet institutions under separate accords.)

The provision that OSTP is worried about defines who can participate in the bilateral agreement and under what conditions. In a small, but significant, change from the past, the language now proposed by the U.S. delegation emphasizes that exchanges will take place between individuals rather than institutions. To the frustration of Americans, Soviets in the past have sometimes pulled their best scientists from a joint project and substituted more obscure researchers.

As it stands now, the provision says that the joint projects would be carried out by higher institutions, government agencies, and individual scientists. It contains a parenthetical note that individual scientists could include researchers from companies. Acting assistant secretary of state Richard Smith, after hearing no objections from a 21-member U.S. delegation, which included OSTP members, last month initialed the proposal along with the Soviets.

But OSTP is said to have asserted that this parenthetical note could provide the Soviets direct access to researchers at American companies. White House Science Adviser William Graham declined to discuss the specific language of the proposal, but told *Science* "OSTP and other agencies want to ensure that the U.S. government is aware of the contacts proposed or allowed under the agreement. We don't want to give the Soviets a hunting license to go to universities and corporate labs without the cognizance of the U.S. government."

Smith says, "Contacts between individual scientists could only take place pursuant to the scope and conditions specified by a particular project-related agreement" that is negotiated by government agencies. Smith also contends that the proposed agreement does not increase the chances of technology transfer, but would narrow them because all of the scientific contacts allowed under the proposal must be authorized by American agencies. In addition, Soviet scientists would be subject to normal visa procedures which require them to detail the purpose of their visit and their itineraries.

In a separate, but related matter, the United States and the Soviets are discussing the possibility of launching an American device for measuring stratospheric ozone from a Soviet rocket. The United States launched such an instrument, known as TOMS, nearly two decades ago, but the device is expected to fail in the next 6 to 8 months. Last month, officials at the National Aeronautics and Space Administration brought up the idea of a Soviet launch of a new TOMS during informal talks in Moscow. The device is made from 1960s technology, says NASA official Samuel Keller. He said, "It's speculative whether the joint project will actually go forward, but it looks like it might be doable."

Gorbachev had suggested before the summit that the Soviets and the U.S. might reach an agreement on a mission to Mars. But after the Moscow meeting, the two leaders issued a joint statement that merely said that missions to the moon and Mars are "areas of possible bilateral and international cooperation." ■ MARJORIE SUN