AFRICAN EPIDEMIC:

An explosive 1977 human epidemic in Egypt arose from a new, more virulent form of a virus that previously affected animals in other areas. Medical surveys now suggest the virus has spread throughout Africa and across to the Sinai peninsula.

During the first week of October in 1977 cases of fever sometimes followed by a fatal bleeding disease were reported from a group of Egyptian villages 70 kilometers northeast of Cairo. That area, which grows peanuts, fruit trees and rice, is irrigated by a canal that runs from the Nile. In the next two weeks additional cases of the disease were reported in many villages along the canal, both to the north and to the south. That was the start of a surprising new epidemic that swept Egypt, infecting up to 200,000 persons and killing 600 that year. Severe complications included encephalitis, loss of visual acuity and jaundice with bleeding. The disease along with the complications recurred in 1978 and 1979, and health authorities now fear that it may reach into the Mediterranean area and other regions of the world.

Blood samples from some of the first fever victims, patients in a town called Zagazig, were sent to the U.S. Naval Medical Research Unit in Cairo. There James M. Meegan and colleagues isolated a virus that did not match any of the viruses in their collection. Meegan took the specimen to Yale University, which houses the World Health Organization's Arbovirus Reference Center. Working with Robert E. Shope and others there, Meegan rapidly identified the disease agent, but he was startled by his finding. The virus was the same as that which caused Rift Valley Fever, formerly a disease primarily affecting livestock and only found in sub-Sahara Africa.

How that Rift Valley Fever virus jumped to Egypt and changed its pattern of infection is a puzzle to medical investigators. The virus was first studied in the Rift Valley in Kenya in 1930, where it distressed animal breeders by causing abortions in ewes and deaths among lambs. In the young animals, a short incubation period was followed by a fever, then liver degeneration and death frequently associated with bleeding. Goats, cattle and a wide variety of other domestic, wild and laboratory animals since have been found susceptible to the virus.

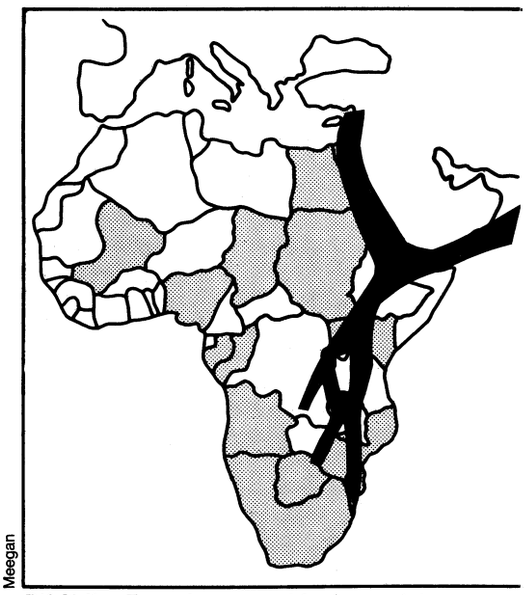
The Rift Valley Fever virus is promiscuous in its choice of carriers as well as in its mammalian hosts. Investigations since 1930 established that at least 26 arthropods, including 18 mosquito species, are potential carriers of the Rift Valley Fever virus.

With its wide range of hosts and carriers, the virus is able to circulate in a variety of ecological settings. It has caused major outbreaks of animal disease in Kenya, South Africa and the Sudan and minor ones in Nigeria, Uganda and Rhodesia. Outbreaks coincide with the increase in mosquito population following the rainy season and generally occur on a 2- to 8-year cycle. Only a small number of human infections were documented in Sub-Sahara Africa, generally among persons who had close contact with animals. Those affected suffered only a mild fever lasting about a week. Therefore, the appearance of Rift Valley Fever in Egypt as a disease with severe clinical manifestations and numerous human fatalities was "astounding," according to Shope.

Shope and Meegan recently reported on progress in characterizing Rift Valley Fever and on the precautions underway to halt its spread. In New York at the Gustav Stern Symposium on Perspectives in Virology, Shope said he has found that the virus is related to the Phlebotomus fever group of virus (including sandfly fever virus), which is itself a subset of the Bunyaviridae family. That family includes both the California and La Crosse encephalitis viruses.

One mystery of Rift Valley Fever is how it spread into Egypt. Evidence from blood tests indicates that the disease was brand new to the area in 1977. Antibody to the virus, an indication of previous exposure, was virtually absent in human blood samples taken before that year, but by early 1978 more than a third of the inhabitants of the Nile delta region had detectable antibody in their blood. "The explosive nature of the 1977 epidemic is most likely the result of a new virus moving into a totally virgin population," Shope says.

Shope now suspects that camels and perhaps other animals carried the virus into Egypt from Sudan. An outbreak of animal disease presumed to be Rift Valley Fever occurred in Sudan in 1976. Between 50,000 and 100,000 Sudanese camels enter Egypt each year, where they are slaughtered for food or used as draught animals or as mounts. Meegan and colleagues in Cairo collected blood samples from camels just after they crossed the Egyptian border. More than 30 percent of the animals contained antibody to Rift Valley Fever virus, indicating previous exposure to the disease. Therefore, camels are a likely source of the virus. When first introduced into Egypt, the disease probably spread among domestic animals and then attacked humans. In retrospect, the investigators find evidence that in the months before the first human cases were reported, there was increased abortion and mortality in camels, sheep, cattle and domestic buffalo.



Meegan

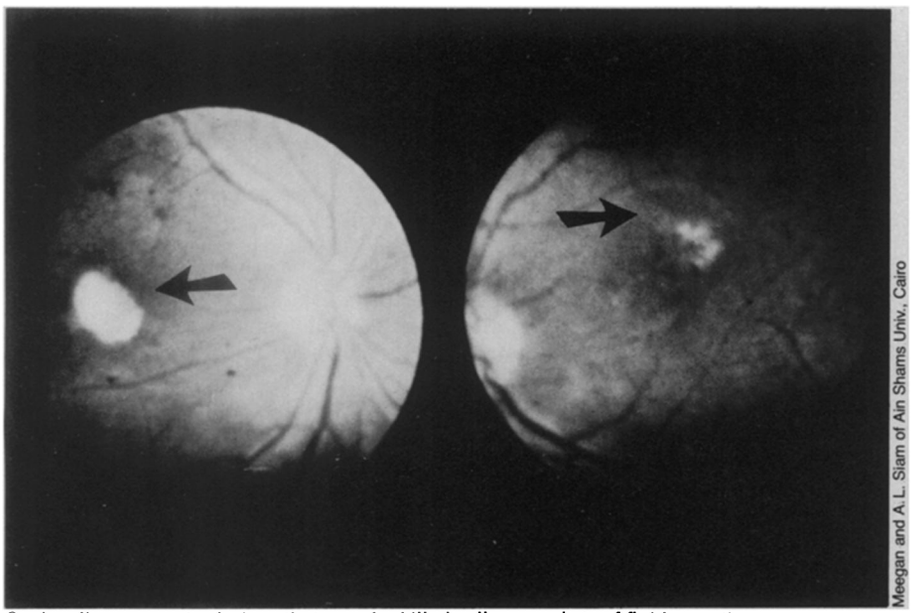
Rift Valley Fever has spread far beyond the Rift Valley (in black). All the countries shaded have reported evidence of the virus in mosquitoes, animals or humans.

Why does the Rift Valley Fever virus affect people in Egypt so much more severely than it did in the more southern countries? There is surprisingly little difference between the viral strains, the scientists find. The surface characteristics of the virus have not changed dramatically. A vaccine prepared to combat the old Rift Valley Fever virus and frozen in 1969 still is able to protect against the new "Zagazig" strain. The only difference that has shown up so far is that the Zagazig strain can kill certain laboratory animals that survive infection with the earlier viral strain. Meegan suggests that the increased virulence, and increased incidence of human complications, are due to an exchange of genes between viruses. Scientists are currently examining in more detail the genes of the different strains. They are also asking whether virus isolated from a 1978 Rhodesian epidemic, which killed one person and caused one reported case of encephalitis, is of the old or the new type.

Rift Valley Fever, as experienced in Egypt, has four possible clinical forms: The infected person first experiences a fever with headache and back pain lasting less than two weeks. A small proportion of

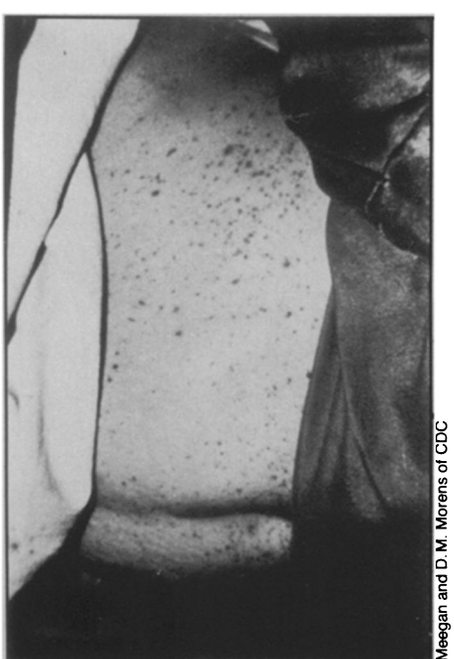
WHERE IS IT HEADING?

BY JULIE ANN MILLER



Meegan and A.L. Siam of Ain Shams Univ., Cairo

Ocular disease creates lesions that may be killed cells or pockets of fluid on retina.



Meegan and D.M. Morens of CDC

Bleeding spots under skin on abdomen are a symptom of hemorrhagic disease.

those affected then develop complications. In some cases it is encephalitis, with hallucinations and vertigo. Although most recover from the encephalitis, some are left with neurological damage. Other patients suffer from an ocular disease; they lose central vision and some suffer permanent loss of visual acuity. Finally, others experience the third type of complication, a hemorrhagic syndrome involving jaundice and severe bleeding. Investigators at the Naval Medical Research Unit estimate that less than 1 percent of the cases of fever later develop complications. Currently, those complications are thought to involve the body's immune system overreacting to the viral infection.

Concern now focuses on where the disease may spread next. It is one of only a few diseases that causes both severe loss of domestic animals and illness in humans. Its versatility is impressive both in host and carrier. Meegan believes that the mosquito *Culex pipiens* is probably the most important carrier of Rift Valley Fever in Egypt. Laboratory-reared mosquitoes fed on virus-infected hamsters transmitted the virus for seven to 36 days. Meegan and collaborators also isolated Rift Valley Fever viruses from wild mosquitoes collected in Egypt in 1978.

People can become infected by the virus from handling infected meat and inhaling aerosols containing the virus, as well as presumably by mosquito transmission. In Egypt, diseased animals are customarily slaughtered for human consumption. This practice was especially prevalent during the outbreak of Rift Valley Fever, when many animals were ill. Many people slaughtered and butchered sick sheep and distributed contaminated meat.

Evidence that breathing microscopic blood droplets containing the virus can cause disease came from a field trip taken by scientists at the Naval Medical Research Unit. In November 1977 six members of the unit clustered in a small room while two villagers slaughtered a sick sheep by the traditional throat-cutting method. All six observers came down with the fever three days later, apparently from inhaling blood droplets. The two villagers also became ill. Meegan and colleagues believe, however, that mosquitoes and contamination through skin cuts and abrasions are more significant sources of human infection than are aerosols. So far no direct person-to-person transmission of the fever has been observed.

Because most countries of the world have both potential vertebrate hosts and arthropod carriers for Rift Valley Fever, worldwide distribution is a clear possibility. In 1944 African horsesickness virus spread from Sudan north to Egypt and subsequently across the Suez canal into Asia. Considering that precedent, Meegan obtained blood samples from United Nations soldiers stationed on the Sinai peninsula to determine whether Rift Valley Fever had crossed the canal. He discovered that about 1 percent of the Swedish soldiers had been exposed to Rift Valley Fever during their 1978 tour of duty. In addition, a local inhabitant who had never traveled outside the Sinai also had evidence of viral exposure. These findings, Meegan says, make it "highly probable" that even the restricted movement of humans and animals has already spread the virus eastward from continental Africa.

Shope and Meegan are not "overly frightened" about the prospects of further Rift Valley Fever epidemics, but say that countries should be prepared. The limited amount of vaccine now available is being used to vaccinate troops in the Sinai. Israel is inoculating animals near its border and monitoring both animals entering from the Sinai and local arthropods. Three laboratories in the United States are undertaking production of a human vaccine, working to develop a veterinary vaccine and developing diagnostic methods. "Because of the high concentration of virus in the blood during viremia [infection], humans can become a vehicle for spreading the virus into new geographic areas," says the U.S. Center for Disease Control in the Jan. 4 MORBIDITY AND MORTALITY WEEKLY REPORT. "The extensive travel between this part of the world [Egypt] and North America emphasizes the possibility of importation of this disease." □