

LASSA FEVER (ARENAVIRUSES) AS A PUBLIC HEALTH PROBLEM¹Akinyele Fabiyi²

Lassa fever, a disease observed in Africa for the first time in 1969, is highly infectious, presenting a particular threat to hospital personnel and medical scientists. The recorded outbreaks have had case-fatality rates of from 36 to 67 per cent.

Two "new" viruses have recently been shown to have caused severe epidemics with high mortality, especially among hospital personnel and medical scientists. One of them, Marburg virus, is morphologically unlike any other known virus family.³ The other has been classified with the arenaviruses, a group that includes the agent of lymphocytic choriomeningitis and other members of the Tacaribe complex, including the agents of Argentine and Bolivian hemorrhagic fever.

In 1969 an epidemic of undiagnosed infectious virus disease occurred in northern Nigeria. This was followed a year later by another epidemic in the same area; 23 patients were hospitalized and 13 died. The virus isolated from these infections was named "Lassa fever" virus because the index case of the 1969 epidemic came from the town of Lassa in the northeast of Nigeria. In Nigeria a total of four epidemics of Lassa fever have been confirmed—1969, 1970, 1974, and 1975. In other West African countries epidemics have been reported from Liberia, in 1972 (2), and from Sierra Leone, in 1970, 1974 (2,3). In addition, serologic evidence has confirmed existence of the disease in Guinea and Senegal (2).

These epidemics have had case-fatality rates ranging from 36 to 67 per cent.

Lassa fever is characterized by insidious onset with fever, chills, malaise, and aching pains. Its symptoms have been described as "nonspecific," and clinical diagnosis can be entertained only after a number of similar cases have been observed. Persistently high temperature is usually common in severe or fatal cases. The incubation period of Lassa fever is from seven to 16 days (average 10). Pathologically, this is a systemic disease in which many organs and tissues are involved, which probably accounts for the toxic condition of the patient. An infected person has been shown to shed virus up to 32 days from the development of symptoms. Some patients who survived Lassa fever showed evidence of impaired hearing and total nerve deafness. In general the course of Lassa fever resembles that of yellow fever and typhoid fever, with which it has been confused.

Evidence is accumulating to show that Lassa fever induces premature births and abortions in pregnant women. Most pregnant female patients abort within four days after admission to hospital; in mild cases, however, abortion usually takes longer to occur. The question of transplacental infection of the fetus has not been investigated, and so far no attempt has been made to determine whether or not the aborted fetuses are infected with the virus.

In the 1972 Sierra Leone epidemic several strains of the virus were isolated from the

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³See Dowdle communication above.

multimammate rodent *Mastomys natalensis* caught in homes of patients (2). Recently other isolations from rodents of the same species caught in several areas of northern Nigeria (4) have been reported. The fact that these latter isolations have been from animals caught in a "nonepidemic" period strongly confirms that rodents are reservoirs of the virus. Isolations from rodents other than *Mastomys* have also been reported from animals caught in the same general area of Nigeria (4).

The mode of transmission from rodents to man is still not clear. Contamination of foodstuffs, grains, and water with infected feces, urine, or saliva is suspected. Human transmission probably occurs from respiratory droplets, urine, or feces. Respiratory transmission has been confirmed from the following data based on clinical and laboratory evidence from epidemics of the disease: 65 per cent of patients have cough, 82 per cent have pharyngitis, and 65 per cent have pulmonary rales; virus has been recovered from the pharynx in 73 per cent of the cases (2). Parenteral transmission by accidental inoculation from infected needles and instruments has occurred in a number of instances. Indirect transmission from handling of contaminated hospital utensils (bedpans, etc.) can occur, and insect transmission by bites cannot be ruled out.

Sera from patients who have recovered from Lassa fever have been shown to have high levels of complement-fixing antibody. Persistent CF antibody has been reported more than two years after recovery (3). In addition, silent infections in hospital personnel who have had contacts with Lassa fever patients have been confirmed by demonstration of antibody to the virus. Plasma from recovered Lassa fever patients has been used in treatment of the disease. To date five patients have been treated and only one has died. However, the effectiveness of antibody-positive plasma in the treatment of the disease still needs further evaluation.

Recommendations

The following approaches are proposed in regard to the study and control of Lassa fever:

- **Diagnosis:**
 - Establishment of laboratory diagnostic services at local and regional levels;
 - Special research to develop rapid and improved means of diagnosis; and
 - Provision of a supply of killed virus antigen and control sera for diagnosis.
- **Continuous surveillance:**
 - Checks for individuals with positive Lassa fever virus antibody in the population;
 - Large-scale banking of positive plasma for use in epidemics; and
 - Serologic surveys in *both* endemic and nonendemic areas.
- Establishment of special laboratory facilities for biochemical (chemical pathology) and hematologic studies of the disease (*not* the virus). Information in this area may be of value in early diagnosis.
 - Special training of hospital personnel (as a task force) specifically to deal with outbreaks of Lassa fever. There should ultimately be task forces at three levels: local, regional, and central (international).
 - Establishment of contingency plans at all levels with international coordination, to deal with epidemic outbreaks.
 - Consideration of provision for isolation centers for the care of Lassa fever patients.
 - General and basic studies of the virus(es) for understanding and elucidation of agent-host interactions and for vaccine development. While this may not be readily feasible in view of the highly infectious nature of the virus, some special laboratory, as suggested above, might be allowed to carry out such studies provided all the necessary precautions are undertaken.
 - Eradication of known reservoir hosts and other conditions conducive to the maintenance and perpetuation of the disease.

SUMMARY

Two "new" virus infections, Marburg and Lassa fever, now constitute diseases of public health importance in several countries of Africa, especially West Africa. Lassa fever has an insidious onset, is initially difficult to diagnose, has "nonspecific" clinical symptoms which have been confused with yellow fever and typhoid, shows evidence of persistent infection, is tremendously contagious, has a high mortality rate, and in particular exhibits unusual nosocomial

propensity. It has also been shown to be the cause of premature births and spontaneous abortions in pregnant women. The virus is transmitted by the respiratory route and by direct contact with contaminated materials. Persistent complement-fixing antibodies have been demonstrated in patients recovered from the disease. The causative agent, a member of the arenavirus group, is known to be enzootic in rodents, especially *Mastomys natalensis*.

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ENTEROVIRUSES OTHER THAN POLIOVIRUS¹Reisaku Kono²

Research is underway to elucidate the role of enteroviruses in certain specific conditions—cardiac disease, nephritis, diabetes, hemorrhagic conjunctivitis. Heart disease has been definitely linked to five types of Coxsackievirus B; also, two types of Coxsackievirus A, along with two echoviruses, are strongly suspected.

There are now 71 known types of enteroviruses, including poliovirus types 1, 2, and 3. The apparent role of enteroviruses in certain specific disorders will be discussed.

Cardiac Diseases

According to the WHO yearly virus report, 1,295 cases of viral cardiac disease were reported in the five-year period 1969-1973. In 300 of these cases (23.3 per cent), the most prevalent agent was Coxsackievirus B (CBV). These data, together with other published reports, provide good justification for believing that CBV plays a central

¹Working paper, WHO Scientific Group on Virus Diseases (Geneva, 1-5 September 1975); also appearing in *Bol Of Sanit Panam*, 1977.

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