

- with non-steroidal anti-inflammatory drugs misdirected? *Lancet* 1993;341:353-4.
- 15 Liang MH, Fortin P. Management of osteoarthritis of the hip and knee (editorial). *N Engl J Med* 1991;325:125-7.
- 16 Bradley JD, Brandt KD, Katz BP, Kalasinski LA, Ryan SI. Comparison of an anti-inflammatory dose of ibuprofen, an analgesic dose of ibuprofen, and acetaminophen in the treatment of patients with osteoarthritis of the knee. *N Engl J Med* 1991;325:87-91.
- 17 March L, Irwig L, Schwarz J, Simpson J, Chock C, Brooks P. N of 1 trials comparing non-steroidal anti-inflammatory drug with paracetamol in osteoarthritis. *BMJ* 1994;309:1041-5.
- 18 Newman NM, Ling RSM. Acetabular bone destruction related to non-steroidal anti-inflammatory drugs. *Lancet* 1985;ii:11-4.
- 19 Rashad S, Revell P, Hemingway A, Low F, Rainsford K, Walker F. Effect of non-steroidal anti-inflammatory drugs on the course of osteoarthritis. *Lancet* 1989;2:111-3.
- 20 Bateman DN, Kennedy JG. Non-steroidal anti-inflammatory drugs and elderly patients. *BMJ* 1995;310:817-8.
- 21 Jobanputra P, Nuki G. Non-steroidal anti-inflammatory drugs in the treatment of osteoarthritis. *Curr Opin Rheumatol* 1994;6:433-9.
- 22 Schapira D, Nahir M, Scharf Y. Trochanteric bursitis: a common clinical problem. *Arch Phys Med Rehabil* 1986;67:815-7.
- 23 Amstruz HC, Kin WC. Osteoarthritis of the hip. In: Moskowitz R, Howell D, Goldberg V, Mankin H, eds. *Osteoarthritis*. 2nd ed. Philadelphia: Saunders, 1992:314-42.

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Review of cases of nosocomial Lassa fever in Nigeria: the high price of poor medical practice

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Abstract

Objective—To investigate two hospital outbreaks of Lassa fever in southern central Nigeria.

Setting—Hospitals and clinics in urban and rural areas of Imo State, Nigeria.

Design—Medical records were reviewed in hospitals and clinics in both areas. Patients with presumed and laboratory confirmed Lassa fever were identified and contacts traced. Hospital staff, patients, and local residents were questioned, records were carefully reviewed, and serum samples were taken. Serum samples were assayed for antibody specific to Lassa virus, and isolates of Lassa virus were obtained.

Results—Among 34 patients with Lassa fever, including 20 patients, six nurses, two surgeons, one physician, and the son of a patient, there were 22 deaths (65% fatality rate). Eleven cases were laboratory confirmed, five by isolation of virus. Most patients had been exposed in hospitals (attack rate in patients in one hospital 55%). Both outbreak hospitals were inadequately equipped and staffed, with poor medical practice. Compelling, indirect evidence revealed that parenteral drug rounds with sharing of syringes, conducted by minimally educated and supervised staff, fuelled the epidemic among patients. Staff were subsequently infected during emergency surgery and while caring for nosocomially infected patients.

Conclusion—This outbreak illustrates the high price exacted by the practice of modern medicine, particularly use of parenteral injections and surgery, without due attention to good medical practice. High priority must be given to education of medical staff in developing countries and to guidelines for safe operation of clinics and hospitals. Failure to do so will have far reaching, costly, and ultimately devastating consequences.

In early March 1989 three doctors from two different hospitals in Imo State, south central Nigeria (fig 1), died of suspected Lassa fever at the University of Nigeria Teaching Hospital, Enugu, within a period of 11 days. One doctor owned a small clinic (hospital A) in Aboh Mbaise (population 500 000), a densely populated agricultural area 20 km north of the Imo state capital, Owerri. The other two were a surgeon and the physician-owner of a hospital (hospital B) close to the crowded marketplace of Aba (population 1 000 000) 60 km south east of Owerri. Lassa fever is a severe haemorrhagic disease endemic in southern Nigeria, as in most of west Africa.^{1,2} It is caused by an

arenavirus that persistently infects a west African rodent, *Mastomys natalensis*.

Investigations of the outbreaks

The investigating team was assembled and travelled to the two hospitals following requests for help from physicians at the University of Nigeria Teaching Hospital and the Nigerian Ministry of Health. The two hospitals were deserted, and the investigations were conducted amid high levels of fear, suspicion, and rumour. It was not possible to obtain all the desired evidence, but we were able to identify cases of Lassa fever retrospectively in both epidemics. Most surviving hospital staff were traced and blood samples taken, but many surviving patients were unwilling to cooperate. We gathered information on these and missing staff members from records and interviews. We conducted a careful analysis of all available medical records and reviewed all inpatient deaths from December 1988 in outbreak hospitals and all other hospitals in Aboh Mbaise, Aba, and Owerri. Presumptive Lassa fever was defined by history of prolonged fever (more than five days), sore throat, proteinuria, oedema, bleeding or convulsions, and lack of response to antimicrobial and antimalarial agents between 1 January and 31 March 1989.³ Laboratory confirmation was by either or both the isolation of Lassa virus or the detection of IgG and IgM by immunofluorescent antibody assays against standard Lassa virus and isolates from this epidemic.⁴

Interviews were completed on 935 individuals and 814 serum samples were obtained. In Aboh Mbaise

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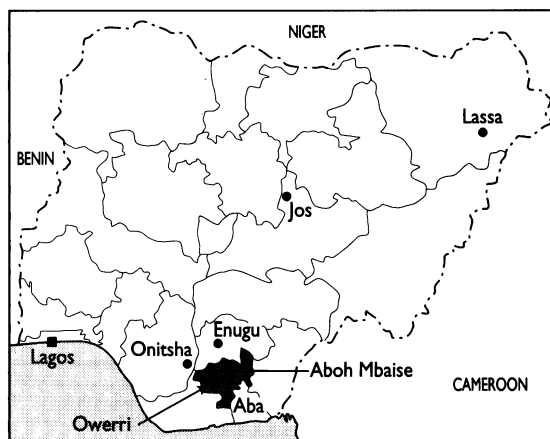


FIG 1—Location of the two outbreaks sites and previous reports of Lassa fever in Nigeria. Imo State is shaded

(hospital A) blood was taken from 527 of 569 individuals questioned (175 hospital staff and 352 community participants). Blood was taken from 240 of 319 hospital staff in Aba (hospital B) and from all of 47 staff from the University of Nigeria Teaching Hospital. Between 1 January and 31 March 1989 Lassa fever was presumed in 34 patients in the two hospitals, and laboratory confirmed in 11 as well as in two of 22 patients who died (65% fatality rate). Lassa virus was isolated in five cases, including two that were fatal.

Outbreak in hospital A

Hospital A consisted of a tiny outpatient office, two inpatient wards with 16 beds, and a tiny, sparsely equipped surgical room. It was deserted; taxi drivers would not stop in the village, and rumours abounded. The deceased physician-director had only undergraduate medical qualifications. Many of the "student nurses" were teenage girls with little formal schooling or training. There were a few incomplete patient charts and no records of surgery. Complete drug administration sheets, kept for accounting purposes, were the principal records. From these we abstracted individual parenteral administrations of drugs and fluids timed, dated, and signed by the administering nurse. Major events (convulsions, haemorrhage) were occasionally noted in the margin. The clinical course of Lassa fever could be inferred from sequential multiple antimicrobial drug regimens over 7-14 days with increasing use of antipyretic and antiemetic agents. The records also documented futile efforts to combat pulmonary oedema, convulsions, and haemorrhage with infusions, diuretics, corticosteroids, and anti-convulsants. Shortly before his final illness the physician requested assistance from local health authorities, who made a written record of his verbal account, which we reviewed.

The index case was the 25 year old nephew of the physician, admitted on 10 January 1989 with a sickle cell crisis. He received infusions and parenteral drugs and after three days was discharged well. He was readmitted 10 days later, on 23 January, with high fever, sore throat, and chest and abdominal pain and failed to respond to antimalaria and multiple microbial drugs. Severe vomiting and haematemesis preceded death on 28 January. A day patient who underwent herniorrhaphy on 23 January was readmitted on 29 January and died on 15 February with fever, tremors, and convulsions unresponsive to antimalarial and antimicrobial drugs. He and subsequent patients received the same parenteral drugs on the same drug rounds as had the first and subsequent cases (fig 2). The epidemic peaked in the third week of February when seven patients died. The physician-director fell ill on 25 February and died on 3 March and the hospital closed. All patients received multiple oral and parenteral drugs, including parenteral analgesics—often six or more drugs at a time (table). The 17 presumed cases totalled 167 inpatient days, during which the patients were given 826 doses of parenteral drugs, an average of five injections a day per person. Hospital staff confirmed that syringes were shared or reused. We documented between two and five generations of infection in patients from the drug charts (fig 2).

Injections received by patients who developed Lassa fever in hospital A

	Total	Median	Mean (SD)	Range
No of injections of antimicrobial agents	590	51	42 (27-13)	3-96
No of doses of steroids (oral and injectable)	69	4	3.7 (5.7)	0-21
Total injections (all drugs)	853	66	61 (35.48)	8-127
No of days of hospitalisation	156	11.5	115 (4.97)	2-19
Mean No of injections a day	71	4.85	5 (5.39)	1.0-10.6

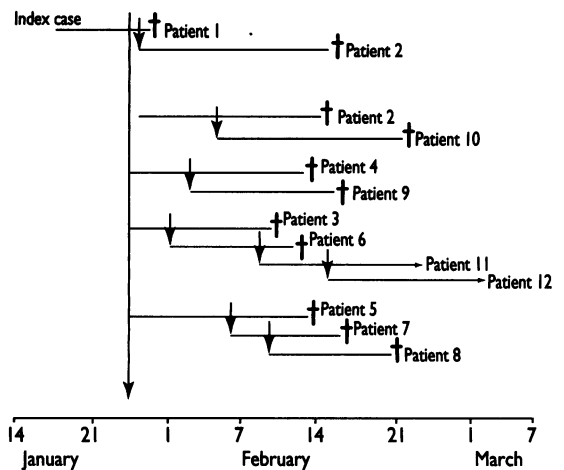


FIG 2—Sequence of drug sharing for 12 of 14 patients involved in hospital A outbreak of Lassa fever. Data were obtained from drug records signed by administering nurse. Vertical arrows show first occasion of sharing the same drug, at the same time of day, and administered by the same nurse; crosses indicate deaths

Outbreak in hospital B

Hospital B, opened two years previously, was also deserted. This busy hospital had 50 beds and was staffed by four physicians, a surgeon, and about 120 "student nurses" and support staff. The nurses had little schooling and minimal training or supervision. The theatre consisted of two rooms, each 4-5 m², in which three to five major operations were performed daily. The operation table was a modified gynaecological examination couch lit by a single domestic fluorescent strip. There was a sink, and on the floor were two domestic gas burners with large cooking pots for sterilisation.

Six of the nine patients with Lassa fever in hospital B died, including three of five infected medical staff. The single event associating four cases was an emergency operation on a 35 year old man referred from another hospital on 9 February with postoperative complications following "failed appendicectomy." Initially he improved with conservative treatment (nasogastric suction, parenteral fluids, and antibacterial agents by injection), becoming afebrile for several days. Subsequently he developed high fever, deteriorated, and was taken to theatre on 25 February for emergency abdominal surgery. He bled profusely and died later that night. Both surgeons became ill on 3 March; they were transferred together to University of Nigeria Teaching Hospital and both died on 15 March, when virus was isolated. The theatre nurse and a student nurse who washed blood soaked cloths both developed febrile illnesses on 7 March, and both had IgG and IgM for specific Lassa virus. The theatre nurse was traced to her village; she was almost totally deaf and severely ataxic.

Three other presumed cases were identified: the matron who became ill on 5 February and died on 26 February; a nurse who became ill on 5 March, was transferred to hospital C, and died on 15 March; and a patient transferred to hospital D, where he died on 7 March. No connection between any of these cases could be established since patient records were not available. No further cases were identified in hospital C or D, where conditions were much better than in hospital B.

Community and hospital surveys

In two Owerri hospitals we found two patients unconnected with the outbreak, from both of whom we isolated Lassa virus. One was a woman who had aborted a dead fetus and the other a travelling salesman.

Both survived. Despite intensive record searching and questioning in Aba and Aboh Mbaise we found no evidence of community based outbreaks of Lassa fever. Serum samples from six of 415 (1%) healthy individuals in Aboh Mbaise communities had antibodies to Lassa virus. One was a laboratory technician and one a farmer; the occupation of the others was unknown. In Aboh Mbaise, two of 175 hospital staff (1%) had IgG specific to Lassa virus and in Aba five of 240 (2%). None of the 47 staff at University of Nigeria Teaching Hospital who had been in contact with the three doctors had antibody to Lassa virus. We obtained histories of recent injections in 44 of 250 hospital staff, patients, and community members of Aboh Mbaise and found no cases of Lassa fever without history of injections, but 19 cases among 44 patients with injections.

Discussion

These outbreaks illustrate the high price exacted by introducing modern medicine, particularly parenteral drugs and surgery, without due attention to good medical practice. We observed the seeding of Lassa infection in hospital patients that initiated several generations of amplification, culminating in infection and death of medical staff. Lassa fever is endemic in this region, and the first documented outbreak of Lassa fever was hospital associated and took place in 1969 in Jos, northern Nigeria.¹ Subsequently Lassa virus antibodies were detected in 357 of 1677 (21.3%) serum samples from Nigeria.² Sporadically, patients with Lassa fever are admitted to local hospitals. High mortality may be due to large inocula of infecting virus, administration of steroids, or underlying illness.

The difficulties of carrying out formal scientific investigations in these conditions are well illustrated. We were not able to establish seroprevalence with any reliability, conduct aetiological studies, or even establish surveillance. Parenteral transmission of viral diseases has been implicated in several investigations in developing countries.^{6,7} Accidental inoculation and close contact with severely ill patients are known to be sources of hospital infection with Lassa virus, but transmission by use of injections has not previously been described.^{8,10} We could not obtain direct evidence for needle transmission, but the high association of infection with receiving injections, documented trails of sharing of injection, incubation periods, and absence of outbreaks in the community and in better managed hospitals are strongly suggestive. Though Lassa virus infection acquired during major surgery has been recognised in Sierra Leone (J McCormick, unpublished observations), this is its first documentation, though in 1974 a surgeon in Onitsha, 80 km north of Owerri, who performed a tracheotomy on a physician who died of Lassa fever was infected.⁹

Since Lassa fever was first described, medical practice in much of rural and urban Africa, including Nigeria, has grown substantially, with proliferation of small hospitals and clinics run often with emphasis on profit. In Nigeria these shoulder a large burden of the medical care of the most populous country in Africa. Need to conserve scant resources leads to sharing and reuse of disposable equipment. Some clinics and hospitals employ staff with little formal education or professional training outside of the meagre experience gained at their workplace. We found little knowledge of Lassa fever. Rampant polypharmacy and widespread use of parenteral treatment often for trivial indications is driven by patients who believe that injections have superior therapeutic value and by practitioners to generate revenue. Surgical facilities

are inadequate, and trained personnel and essential supplies are limited.

The potential for epidemics in countries with similar conditions is devastating, mirrored in the 1995 outbreak of Ebola haemorrhagic fever in Zaire, where introduction of the virus into a poorly run hospital led to several generations of infections. Only emergency operation on a patient during which several staff members were fatally infected gained public attention (L. Garrett, personal communication). Similarly, in this outbreak of Lassa fever only the simultaneous deaths of three doctors brought public notice.

The conditions we observed are rooted in systems where there is poor medical education, little attention to safety, no surveillance, no rules, and no safeguards and where profits are often the most powerful driving force. Ironically, improved socioeconomic conditions increase the ability of people to demand and pay for invasive procedures. Lassa fever, with its short incubation period and acute, severe clinical course, dramatises the menace of bloodborne viruses. Spread of other blood borne viruses with longer incubation periods (hepatitis C and HIV), is more difficult to document because they will not be observed until long after the events which transmitted them.^{7,10,11} High priority must be given to education of medical staff in developing countries and to guidelines for safe operation of clinics and hospitals. Efforts of the World Health Organisation to develop such guidelines and to assist developing countries in devising an effective way of promulgating and enforcing them must be supported. Failure to do so will have far reaching and costly consequences.

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Conflict of interest: None.

- 1 Frame JD, Baldwin JM Jr, Gocke DJ, Troup JM. Lassa fever, a new virus disease of man from West Africa. I. Clinical description and pathological findings. *Am J Trop Med Hyg* 1970;19:670-6.
- 2 McCormick JB, Webb PA, Krebs JW, Johnson KM, Smith ES. A prospective study of the epidemiology and ecology of Lassa fever. *J Infect Dis* 1987;155:437-44.
- 3 McCormick JB, King IJ, Webb PA, Johnson KM, O'Sullivan R, Smith ES, et al. A case-control study of the clinical diagnosis and course of Lassa fever. *J Infect Dis* 1987;155:445-55.
- 4 Johnson KM, McCormick JB, Webb PA, Smith ES, Elliott LH, King IJ. Clinical virology of Lassa fever in hospitalized patients. *J Infect Dis* 1987;155:456-64.
- 5 Tomori O, Fabiyi A, Sorungbe A, Smith A, McCormick JB. Viral haemorrhagic fever antibodies in Nigerian populations. *Am J Trop Med Hyg* 1988;38:407-10.
- 6 World Health Organisation. Ebola haemorrhagic fever in Zaire, 1976: report of an International Commission. *Bull World Health Organ* 1978;56:271-93.
- 7 Hersh BS, Popovici F, Apetrei RC, Zolotusca L, Beldescu N, Calomfirescu A, et al. Acquired immunodeficiency syndrome in Romania. *Lancet* 1991;338:645-9.
- 8 Fabiyi A, Tomori O, Pinneo P. Lassa fever antibodies in hospital personnel in the Plateau State of Nigeria. *Niger Med J* 1979;9:23-5.
- 9 Bowen GS, Tomori O, Wulff H, Casals J, Noonan A, Downs WG. Lassa fever in Onitsha, East Central State, Nigeria in 1974. *Bull World Health Organ* 1975;52:599-604.
- 10 Carey DE, Kemp GE, White HA, Pinneo L, Addy RF, Fom ALMD, et al. Lassa fever. Epidemiological aspects of the 1970 epidemic, Jos, Nigeria. *Trans R Soc Trop Med Hyg* 1972;66:402-8.
- 11 Alter MJ. Inapparent transmission of hepatitis C1. Footprints in the sand. *Hepatology* 1991;14:389-91.

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