Lassa Fever, Nigeria, 2005–2008

To the Editor: Lassa fever affects ≈100,000 persons per year in West Africa (1). The disease is caused by Lassa virus, an arenavirus, and is associated with bleeding and organ failure. The case-fatality rate in hospitalized patients is 10%–20%. The reservoir of the virus is multimammate mice (Mastomys natalensis). Investigations in the 1970s and 1980s pointed to the existence of 3 disease-endemic zones within Nigeria: the northeastern region around Lassa, the central region around Jos, and the southern region around Onitsha (2,3). The current epidemiologic situation is less clear because no surveillance system is in place.

In 2003 and 2004, we conducted a hospital-based survey in Irrua, which demonstrated ongoing transmission of the virus in Edo State, Nigeria (4). Since then, laboratory capacity at the University of Lagos for diagnosing Lassa fever has been improved and used for small-scale passive surveillance in other parts of the country. Public health officials or hospital staff reported suspected cases. Blood samples were sent to Lagos, or staff from Lagos collected samples on site. Confirmatory testing, sequencing, and virus isolation were performed at the Bernhard Nocht Institute for Tropical Medicine in Hamburg, Germany. Primary testing was done by reverse transcription–PCR (RT-PCR) that targeted the glycoprotein (GP) gene (5,6). An RT-PCR that targeted the large (L) gene was used as a secondary test (7), and PCR products were sequenced. Serologic testing for Lassa virus–specific immunoglobulin (Ig) G and IgM was performed by immunofluorescent antibody test using Vero cells infected with Lassa virus. Virus isolation with Vero cells was conducted in the BioSafety Level 4 laboratory in Hamburg.

From 2005 through 2008, 10 cases of Lassa fever were confirmed by virus detection (cases 3–10) or implicated by epidemiologic investigation and serologic testing (cases 1 and 2) (on-line Appendix Table, www.cdc.gov/EID/content/16/6/1040-appT.htm). Case-patients 1–4 were involved in a nosocomial outbreak that occurred in February 2005 at the Ebonyi State University Teaching Hospital (EB-SUTH) in Abakaliki. Retrospective investigation suggests the following transmission chain. The presumed index case-patient was a male nurse living in Onitsha, who became ill on January 21, 2005, and traveled ≈200 km to EB-SUTH for better medical treatment. The detection of Lassa virus–specific IgM during his convalescent phase indicates that he had Lassa fever. The second case-patient was a female nurse who had contact with the index case-patient on February 4. She was admitted on February 7 and died 6 days later. Her clinical features were compatible with Lassa fever, but laboratory confirmation is lacking because specimens were not collected.

Two additional case-patients among hospital staff (case-patients 3 and 4) were seen on February 21; each had had contact with case-patient 2. Case-

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ports on Lassa fever in southern and central parts of Nigeria. That healthcare workers are still at as high a risk of contracting and dying from the disease as they were 20 years ago (8) is alarming.

A key to solving this problem would be the establishment of diagnostic facilities that can provide rapid molecular testing at referral centers in the disease-endemic zones. This testing would facilitate appropriate case and contact management, including early treatment and postexposure prophylaxis with ribavirin, and eventually raise awareness that Lassa fever should be considered in every severe febrile illness in these regions.

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References


Laboratory Diagnosis of Lassa Fever, Liberia

To the Editor: Lassa fever is endemic in West Africa, with ≤300,000 Lassa virus (LASV) infections occurring annually (1). Persons on humanitarian missions and peacekeeping forces in regions comprising Sierra Leone and Liberia are at risk for Lassa fever (2–4). Reliable laboratory diagnosis, particularly in acute cases, is crucial for triage, implementation of barrier nursing, and contact tracing, as well as for initiation of treatment with ribavirin. Reverse transcription–PCR (RT-PCR) is routinely used for confirmation of cases, but few proven assay formulations are available, and these have not been evaluated on larger cohorts of patients (5).

We summarize our experiences from testing 184 patients from Liberia with suspected cases of Lassa fever with the most widely used LASV-specific RT-PCR assay (6). Patients were suspected of having Lassa fever on clinical grounds by physicians of the United Nations peacekeeping troops and other international relief organizations. Patients included local citizens as well as members of the mentioned organizations. EDTA-plasma samples or serum specimens packed on ice were sent to our laboratory in Hamburg, Germany, by international airfreight, taking 4–7 days for shipment. Information on clinical signs and symptoms or outcome was generally not available.

Conventional RT-PCR specific for the glycoprotein precursor gene was conducted as described (7). RT-PCR results positive for LASV were seen in 35 (19%) of 184 patients. Median time between onset of symptoms and sampling was 7 days. Median time from reception of samples to final RT-PCR or culture results was 1 day and 4 days, respectively.
<table>
<thead>
<tr>
<th>Locality (hospital)</th>
<th>Case no.</th>
<th>Date of admission</th>
<th>Age, y/sex</th>
<th>Symptoms</th>
<th>Treatment</th>
<th>Outcome</th>
<th>HCW</th>
<th>GP and L gene RT-PCR</th>
<th>IgM IFAT†</th>
<th>IgG IFAT†</th>
<th>Virus isolation</th>
<th>Lassa virus strain (GenBank accession nos.)‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abakaliki, Ebonyi State (EBSUTH)</td>
<td>1</td>
<td>2005 Feb 4</td>
<td>40/M</td>
<td>Fever</td>
<td>Antimicrobial drugs, antimalaria prophylaxis</td>
<td>Survived</td>
<td>Nurse</td>
<td>Neg§</td>
<td>1:160§</td>
<td>&gt;1:80§</td>
<td>ND</td>
<td>–</td>
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<tr>
<td></td>
<td>2</td>
<td>2005 Feb 7</td>
<td>54/F</td>
<td>Fever, vomiting, diarrhea, respiratory distress, oliguria</td>
<td>Antimicrobial drugs, corticoid</td>
<td>Died</td>
<td>Nurse/contact to case 1</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>2005 Feb 21</td>
<td>35/F</td>
<td>Fever, severe weakness</td>
<td>NA</td>
<td>Survived</td>
<td>Nurse/contact to case 2</td>
<td>Pos</td>
<td>Neg§</td>
<td>1:640§</td>
<td>&gt;1:5120§</td>
<td>Neg</td>
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<tr>
<td></td>
<td>4</td>
<td>2005 Feb 21</td>
<td>36/F</td>
<td>Fever, vomiting, nausea, spontaneous abortion, shock</td>
<td>Antimicrobial drugs, tracheotomy</td>
<td>Died</td>
<td>Nurse/contact to case 2</td>
<td>Pos</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
<td>Nig05-043 (GU481056, GU481057)</td>
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<td>5</td>
<td>2008 Jan 17</td>
<td>35/F</td>
<td>Fever, vomiting, diarrhea, abdominal tenderness, anuria, generalized seizure, unconsciousness</td>
<td>Antimicrobial drugs, antimalaria prophylaxis, dobutamine, dopamine, furosemide</td>
<td>Died</td>
<td>Jan 23</td>
<td>Doctor</td>
<td>Pos</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
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<td>6</td>
<td>2008 Mar 5</td>
<td>38/M</td>
<td>Fever, vomiting, hiccups, bloody diarrhea, abdominal tenderness, generalized seizure, unconsciousness</td>
<td>Antimicrobial drugs, antimalaria prophylaxis, assisted ventilation</td>
<td>Died</td>
<td>Mar 11</td>
<td>Doctor</td>
<td>1:20</td>
<td>1:20</td>
<td>Pos</td>
<td>Nig08-04 (GU481068, GU481069)</td>
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<tr>
<td>Abuja, FCT State (NHA)</td>
<td>7</td>
<td>2008 Jan 2</td>
<td>37/M</td>
<td>Fever, vomiting, diarrhea, abdominal tenderness, generalized seizure, unconsciousness</td>
<td>Antimicrobial drugs, ribavirin on day of death</td>
<td>Died</td>
<td>Jan 7</td>
<td>No</td>
<td>1:20</td>
<td>1:20</td>
<td>Neg</td>
<td>Nig08-02 (GU481063 to GU481065)</td>
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<tr>
<td>Jos, Plateau State</td>
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<td>2007 Dec</td>
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<td>Died</td>
<td>NA</td>
<td>Pos</td>
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<td>Nig07-05 (GU481060 to GU481062)</td>
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<td>30/M</td>
<td>NA</td>
<td>NA</td>
<td>Died</td>
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<td>Pos</td>
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<td>1:80</td>
<td>Pos</td>
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<td>NA</td>
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<td>No</td>
<td>Pos</td>
<td>1:80</td>
<td>1:80</td>
<td>Pos</td>
<td>Nig08-A19 (GU481072, GU481073)</td>
</tr>
</tbody>
</table>

*HCW, health care worker; GP, glycoprotein; L, large; Ig, immunoglobulin; RT-PCR, reverse transcription PCR; IFAT immunofluorescent antibody test; EBSUTH, Ebonyi State University Teaching Hospital; pos, positive; neg, negative; ND, not done; NA, data not available; FCT, Federal Capital Territory; NHA, National Hospital Abuja.
†Titer of IFAT (cut-off 1:20).
‡Partial GP and L gene sequences were obtained by sequencing the fragments amplified by the diagnostic RT-PCRs. Additional nucleoprotein gene sequences were generated for Nig07-05 and Nig08-02, and strains isolated in cell culture were completely sequenced (D. Ehichioya, unpub. data).
§Convalescent-phase serum sample.