

EBOLA



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Center

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Improving People's Lives
through innovation in research, education and patient care

Sudan - June 27, 1976

- Nazra Township Cotton factory storekeeper became ill
 - 48 cases/ 27 deaths
 - Contact was admitted to local hospital in Maridi
- Unrelated cases continued in cotton factory workers July-Oct.



Content Provider: CDC/ Dr. Lyle Conrad; 1976

World Health Organization. Ebola haemorrhagic fever in Sudan, 1976. Report of a WHO/International Study Team. *Bulletin of the World Health Organization*. 1978;56(2):247-270.



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Sudan 1976



Content Provider: CDC/ Dr. Lyle Conrad; 1976

- Barrier nursing/disposable isolation equipment established early October
- WHO team arrived on October 20, 1976
 - Isolation precautions
- Last case occurred on November 20, 1976

284 cases, 151 deaths (mortality rate 53%)

World Health Organization. Ebola haemorrhagic fever in Sudan, 1976 . Report of a WHO/International Study Team . *Bulletin of the World Health Organization*. 1978;56(2):247-270.



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Zaire - September 1, 1976



- First Case in Yambuku hospital
- 5 syringes/needles
- Sept 30th- hospital closed
 - 11/17 HCW died
- Last case – Nov 5th

318 cases: 280 deaths
88% mortality

Content Providers: CDC/ Dr. Lyle Conrad; Photo Credit: Joel G. Breman, M.D., D.T.P.H; 1976

World Health Organization. Ebola haemorrhagic fever in Zaire, 1976. Report of an International Convention. *Bulletin of the World Health Organization*. 1978;56(2):271-293.



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Ebolavirus

- Sudan ebolavirus (SUDV)
- Zaïre ebolavirus (EBOV)
- Taï Forest (Ivory Coast) ebolavirus (TAFV)
- Bundibugyo ebolavirus (BDBV)

- Reston ebolavirus (RESTV)

Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, Seventh Edition. Gerald L. Mandell, John E. Bennett, and Raphael Dolin. 164, 2259-2263



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Guinea- December 2013

- Guéckédou, Guinea
 - 2yr old Child
 - Fever, black stool, vomiting
 - Onset Dec. 2, 2013; died Dec. 6, 2013
- Transmitted from HCW (patient #14) to neighboring towns
 - HCW died Feb. 10, 2014
- March 10, 2014 – Guinea Ministry of Health Notified
- March 14, 2014- Outbreak team in place

111 suspect cases: 79 deaths (71% mortality)

Transmission

- Zoonotic -introduced to humans through close contact with infected animal's bodily fluids
 - **Fruit bats**
 - Chimpanzees
 - Gorillas
 - Monkeys
 - Forest Antelope
 - Porcupines



Human to Human Transmission

- Direct contact with infected bodily secretions
- Indirect contact with contaminated environments
 - In lab study: Ebola can remain active for up to 6 days
 - Environmental cxs: 2/33 samples positive for Ebola
 - Blood stained physical glove
 - Bloody IV insertion site
- Direct contact with infected corpses
- Men who survive can transmit virus via semen for up to 7 weeks

<http://www.who.int/mediacentre/factsheets/fs103/en/>

Sagripanti JL, Rom AM, Holland LE. Persistence in darkness of virulent alphaviruses, Ebola virus, and Lassa virus deposited on solid surfaces. Arch Virol 2010; 155:2035-2039

Bausch DG et al. Assessment of the Risk of Ebola Virus Transmission from Bodily Fluids and Fomites The J of Infect Dis 2007; 196:S142-7



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High Risk Exposures

- Percutaneous
 - needle stick or mucous membrane exposure to body fluids
- Direct care or exposure to body fluids without appropriate personal protective equipment (PPE)
- Participation in funeral rites



Low Risk Exposures

- Household member or other casual contact with an EVD patient
- Providing patient care or casual contact without high-risk exposure with EVD patients



Ineffective Transmission

Previous epidemics have calculated that 1 primary human case of Ebola generates only 1 to 3 secondary cases on average.

1 case of Measles in West Africa generates 14-17 cases.

Chowell G, Hengartner NW, Castillo-Chavez C, Fenimore PW, Hyman JM. The basic reproductive number of Ebola and the effects of public health measures: the cases of Congo and Uganda. *J Theor Biol* 2004;229:119-126

Legrand J, Grais RF, Boelle PY, Valleron AJ, Flahault A. Understanding the dynamics of Ebola epidemics. *Epidemiol Infect* 2007;135:610-621



Clinical Manifestations

- Incubation period of 8-10 days (range 2-21)
- Abrupt onset of fever, with HA and myalgia
 - Nausea, vomiting, abdominal pain, and diarrhea
 - Maculopapular rash by day 5-7
 - Chest pain, shortness of breath
 - Hemorrhage
 - Confusion, seizures

Kortepeter MG, Bausch DG, Bray M. Basic clinical and laboratory features of filoviral hemorrhagic fever. *J Infect Dis.* 2011 Nov;204 Suppl 3:S810–6



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Differential Diagnosis

- Malaria
- Typhoid Fever
- Dengue
- Lassa Fever
- Shigellosis
- Meningococcal septicemia
- Plague
- Relapsing fever
- Marburg Virus
- Yellow fever
- Viral hepatitis
- Anthrax
- Chikungunya fever
- Leptospirosis
- Typhus



Pathogenesis

- Monocytes, macrophages, and dendritic cells are infected early
- Virus suppresses type 1 interferon responses and induces cytokine and chemokine release
- Virus replicates, released and migrates to local lymph nodes, travels through the lymphatic system to blood
- Virus disseminated throughout the body

Feldmann H, Geisbert TW. Ebola haemorrhagic fever. *Lancet*. 2011 Mar 5;377(9768):849-62.



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Pathogenesis (cont)

- Lymphocytes undergo apoptosis, which undermines adaptive immunity
- Hepatocellular necrosis → DIC
- Adrenal necrosis → Hypotension
→ Impaired Steroid Synthesis
- Extensive tissue necrosis and shock



Diagnostic labs tests

- Ebola virus is detectable in blood only after onset of symptoms
- Detectable by real-time RT-PCR between 3 to 10 days post-onset of symptoms



Lab Abnormalities

- Leukopenia
- Thrombocytopenia – 50 to 100K range
- Transaminitis: $AST > ALT$
- Proteinuria may be present
- PT and PTT prolonged
- Fibrin elevated



Fatal Illness

- LFTS and D-dimer higher in fatal illness.
- Calcium <6mg/dL associated with death
- Median survival of 9 days
- Most patients die during the second week
- Alive on day 14 portends >75% survival
- Fatally infected patients do not develop an AB response

Kortepeter MG, Bausch DG, Bray M. Basic clinical and laboratory features of filoviral hemorrhagic fever. *J Infect Dis.* 2011 Nov;204 Suppl 3:S810–6



Treatment

- Supportive care
- Antibiotics for secondary infections

- September 4-5, WHO scheduled conference on potential Ebola therapies and vaccines in Geneva



Experimental Therapeutics

- ZMapp™ - composed of three monoclonal antibodies directed against the Ebola Zaire virus strain.
- TkM-Ebola - small interfering RNAs targeting EV RNA polymerase L
- AVI-7537 - which targets EV protein VP24 through an RNA interference technology
- BCX-4430 - an adenosine analogue that is active against EV in rodents
- chloroquine and imatinib, have shown activity against EV in vitro and, in some cases, in rodent models.

Jesse L. Goodman, M.D., M.P.H. Studying “Secret Serums” — Toward Safe, Effective Ebola Treatments



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Additional References



Dr. Margaret Isaacson as she was tending to the needs of an Ebola patient in a Yambuku, Zaire hospital theatre block that was used as a temporary ICU for Ebola patients during the country's 1976 outbreak.

CDC Ebola Hemorrhagic Fever site: www.cdc.gov/ebola

WHO: <http://www.who.int/csr/disease/ebola/en/>

<http://www.nejm.org/page/ebola-outbreak>

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