

What You Should Know About Ebola



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Ebola

- Outbreak began in December, 2013
- Captured the world media at the end of July with the news that two Americans who had been helping to treat patients in Liberia had caught the disease, and were subsequently brought to Emory University Hospital, Atlanta, GA, USA, for treatment
- So far, the largest recorded outbreak of Ebola

Ebola

- On Aug 8, WHO declared the outbreak to be a public health emergency of international concern, a decision that activates numerous recommendations for WHO member countries under the International Health Regulations

Ebola Cases – As of 31 Oct 2014

- 13 567 confirmed, probable, and suspected cases of Ebola virus disease (EVD) have been reported in 6 affected countries-
(Guinea, Liberia, Mali, Sierra Leone, Spain, and the United States of America) and 2 previously affected countries (Nigeria, Senegal) up to the end of 29 Oct 2014

Ebola Cases – As of 31 Oct 2014

- 4951 reported deaths (CFR- 36.4%)
- Intense transmission continues in Guinea, Liberia and Sierra Leone.
- All 83 contacts of the health-care worker infected in Spain have completed the 21-day follow-up period.

Why does Ebola elicit fear

- High case fatality rate
- Severe haemorrhagic symptoms
- Lack of vaccine or cure
- Fear of the Unknown

Ebola False Alarms

- Number of Ebola false alarms mounts as panic grows
- Australia: a plane made emergency landing when passenger vomited blood
- Czech Republic: Tests show man with symptoms of Ebola does not in fact have virus

Ebola False Alarms

- Taiwan: woman tested negative for Ebola after showing symptoms of virus
- UK: Scare at Liverpool coach station after passenger collapsed and vomited, medical staff boarded coach in protective gear and removed the woman. Doctors at Royal Liverpool Hospital confirmed she did not have Ebola.

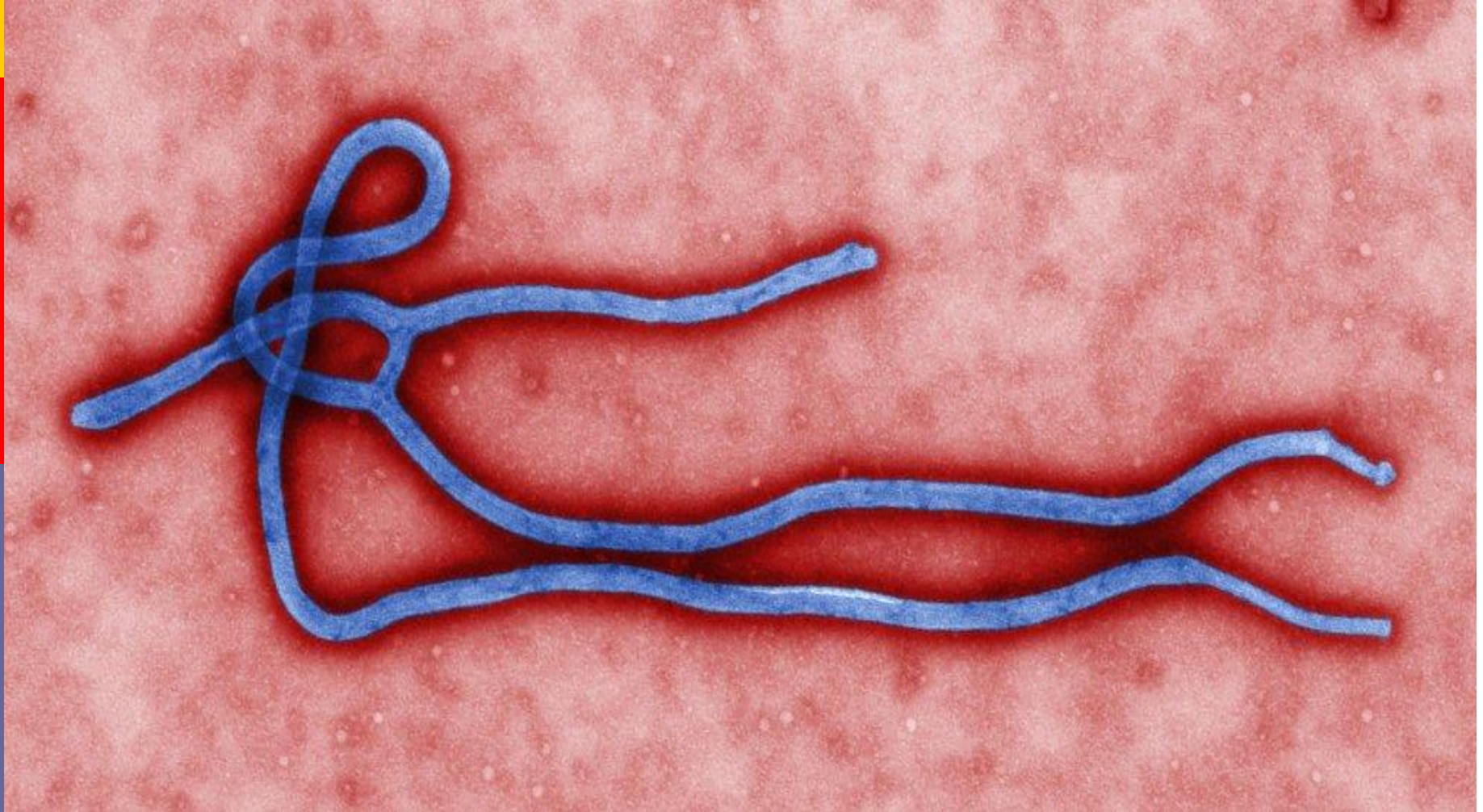
Ebola False Alarms

- USA: Another scare when man yelled 'I have Ebola!' on flight from Philadelphia
- USA: CDC is handling more than 800 false alarms a day from worried Americans

Ebola

- Ebola virus and Marburg virus constitute the family Filoviridae in the order of Mononegavirales.
- Filoviruses are enveloped, non-segmented, negative-stranded RNA viruses of varying morphology
- These viruses have characteristic filamentous particles that give the virus family its name

Ebola Virus

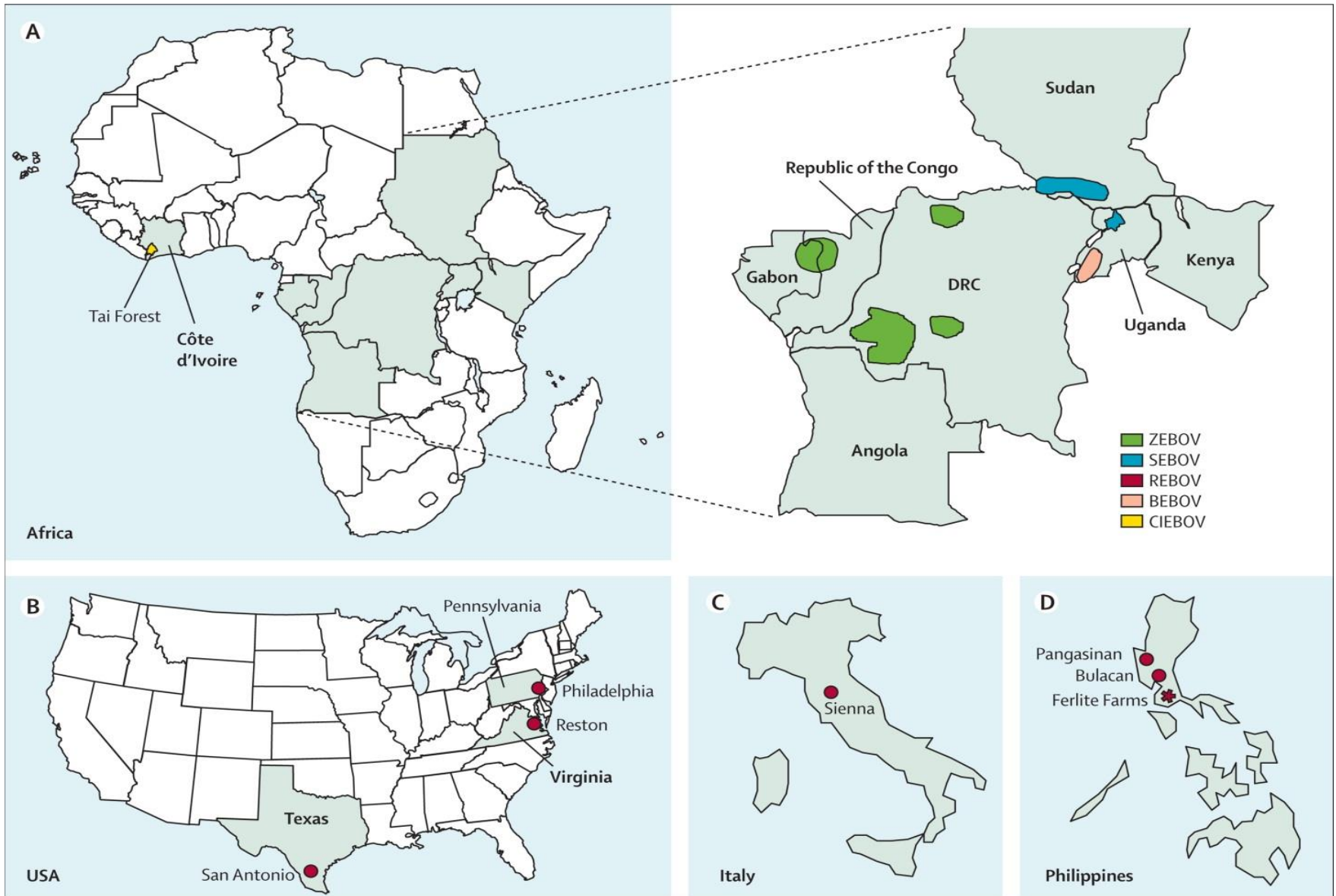


Genus Ebolavirus

- Bundibugyo ebolavirus*
- Zaire ebolavirus*
- Reston ebolavirus**
- Sudan ebolavirus*
- Tai Forest ebolavirus

* associated with large outbreaks in Africa

** found in the Philippines and PROC with no illness or death in humans



Ecology

- Thought to be a classic zoonosis with persistence of the Ebola virus in a reservoir species generally found in endemic areas
- Apes, man, and perhaps other mammalian species that are susceptible to Ebola virus infection are regarded as end hosts and not as reservoir species

Ecology

- Ebola viruses (EBOV) cause often fatal hemorrhagic fever in several species of simian primates including human.
- While fruit bats are considered natural reservoir, involvement of other species in EBOV transmission is unclear.
- In 2009, Reston-EBOV was the 1st EBOV detected in swine with indicated transmission to humans.

Ecology

- ❑ In-contact transmission of Zaire-EBOV (ZEBOV) between pigs was demonstrated experimentally.
- ❑ ZEBOV transmission from pigs to cynomolgus macaques without direct contact was also shown.
- ❑ Piglets inoculated oro-nasally with ZEBOV were transferred to the room housing macaques in an open inaccessible cage system.
- ❑ All macaques became infected.

Ecology

- Infectious virus was detected in oro-nasal swabs of piglets, and in blood, swabs, and tissues of macaques.
- This is the 1st report of experimental interspecies virus transmission, with the macaques also used as a human surrogate.

Virulence – Ability to cause disease

- Virulence of Ebola virus in man is variable and is dependent on the species or strain; a similar variability seems to recapitulate well in non-human primates
- Within the genus Ebola virus, infections with the Zaire Ebola virus species have the highest case-fatality rates (60—90%) followed by those for the Sudan Ebola virus species (40—60%)

Virulence

- On the basis of one outbreak, case-fatality rates for Bundibugyo strain infections are estimated to be only 25%.

Route of Infection – How does one get infected?

- Ebola virus seems to enter the host through mucosal surfaces, breaks, and abrasions in the skin, or by parenteral introduction
- Most human infections in outbreaks seem to occur by direct contact with infected patients or cadavers

Route of Infection

- ❑ Infectious virus particles or viral RNA have been detected in semen, genital secretions, and in skin of infected patients;
- ❑ they have also been isolated from skin, body fluids, and nasal secretions of experimentally infected non-human primates

Route of Infection

- ❑ Laboratory exposure through needlestick and blood has been reported.
- ❑ Reuse of contaminated needles played an important part in the 1976 outbreaks of Ebola virus in Sudan and Zaire

Route of Infection

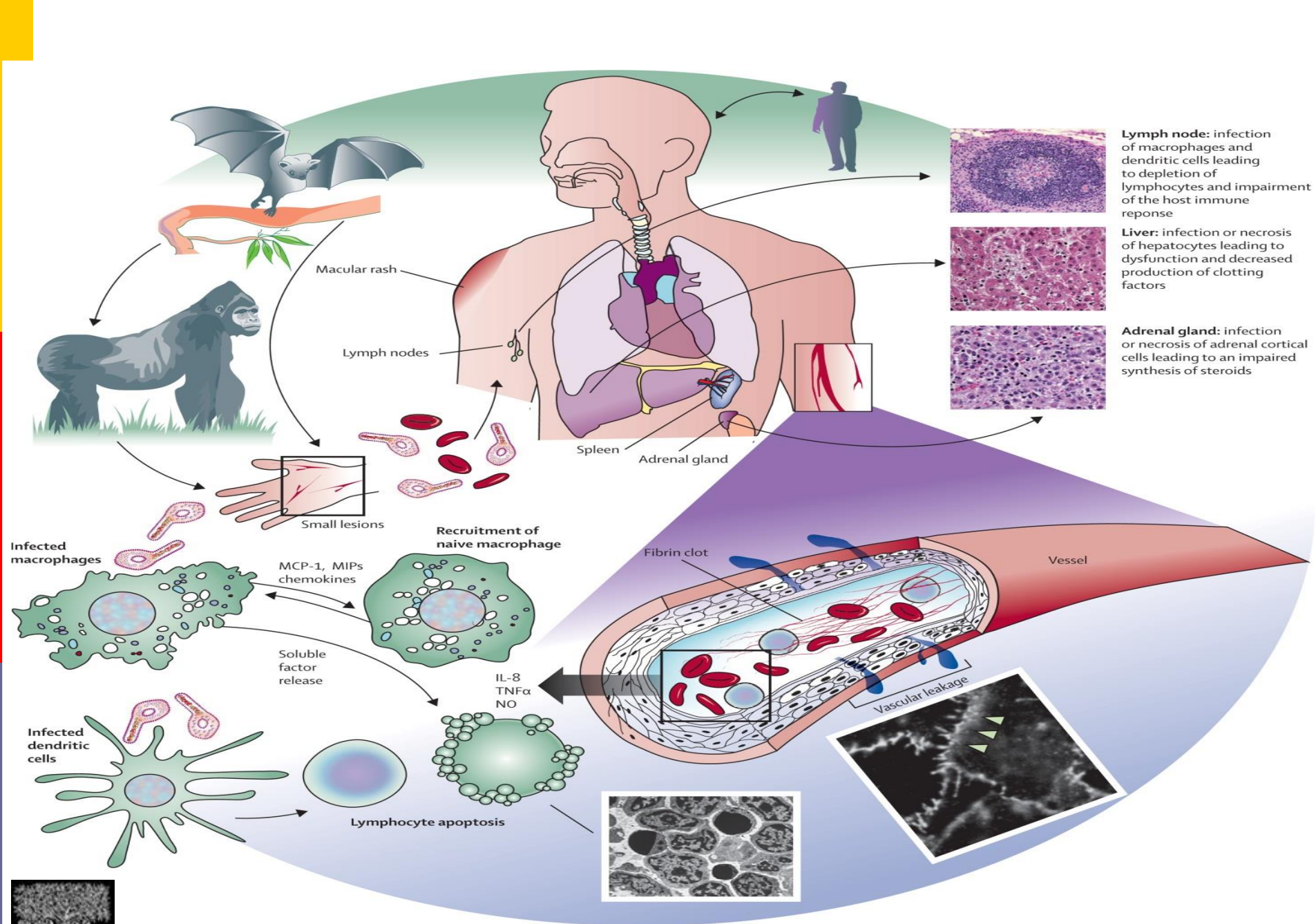
- ❑ Butchering of a chimpanzee for food was linked to outbreaks of Zaire Ebola virus in Gabon, and contact exposure was the probable route of transmission.
- ❑ Although proper cooking of foods should inactivate infectious Ebola virus, ingestion of contaminated food cannot wholly be ruled out as a possible route of exposure in natural infections

Route of Infection

- Notably, handling and consumption of freshly killed bats was associated with an outbreak of Zaire Ebola virus in DRC
- Organ infectivity titres in non-human primates infected with Ebola virus are frequently in the range of 10^7 to 10^8 pfu/g

Route of Infection

- Exposure through the oral route could invariably be associated with very high infectious doses. In fact, Zaire Ebola virus is highly lethal when given orally to rhesus macaques.
- Role of aerosol transmission in outbreaks is unknown, but is thought to be rare



Clinical Manifestations

- ❑ Incubation period of 2—21 days (mean 4—10)
- ❑ Characterised by fever, chills, malaise, and myalgia
- ❑ May also include systemic (prostration), gastrointestinal (anorexia, nausea, vomiting, abdominal pain, diarrhoea), respiratory (chest pain, shortness of breath, cough, nasal discharge), vascular (conjunctival injection, oedema), and neurological (headache, confusion, coma) manifestations

Clinical Manifestations

- Hemorrhagic manifestations arise during the peak of the illness and include petechiae, ecchymoses, uncontrolled oozing from venipuncture sites, mucosal hemorrhages, and post-mortem evidence of visceral haemorrhagic effusions

Clinical Manifestations

- ❑ Macropapular rash associated with varying severity of erythema and desquamation can often be noted by day 5–7 of the illness;
- ❑ This symptom is a valuable differential diagnostic feature and is usually followed by desquamation in survivors

Clinical Manifestations

- Abdominal pain is sometimes associated with hyperamylasaemia and true pancreatitis
- In later stages, shock, convulsions, severe metabolic disturbances, and, in more than half the cases, diffuse coagulopathy supervene

Lab Findings

- early leucopenia (as low as 1000 cells per μL) with lymphopenia and subsequent neutrophilia
- left shift with atypical lymphocytes, thrombocytopenia (50 000—100 000 cells per μL),
- highly raised serum aminotransferase concentrations (aspartate aminotransferase typically exceeding alanine aminotransferase),
- hyperproteinaemia, and proteinuria

Lab Findings

- Prothrombin and partial thromboplastin times are extended and fibrin split products are detectable, indicating diffuse intravascular coagulopathy.
- In a later stage, secondary bacterial infection might lead to raised counts of white blood cells

Clinical Course

- Patients with fatal disease develop clinical signs early during infection and die typically between day 6 and 16 with hypovolemic shock and multi-organ failure
- Hemorrhages can be severe but are only present in fewer than half of patients.

Clinical Course

- In non-fatal cases, patients have fever for several days and improve typically around day 6—11, about the time that the humoral antibody response is noted

Clinical Course

- Patients with non-fatal or asymptomatic disease mount specific IgM and IgG responses that seem to be associated with a temporary early and strong inflammatory response, including interleukin β , interleukin 6, and tumor necrosis factor α (TNF α).

Clinical Course

- However, whether this is the mechanism for protection from fatal disease remains to be proven
- Convalescence is extended and often associated with sequelae such as myelitis, recurrent hepatitis, psychosis, or uveitis

Diagnosis

- Measurement of host-specific immune responses to infection and detection of viral particles, or particle components in infected individuals.
- RT-PCR and antigen detection ELISA are the primary assays to diagnose an acute infection.
- Viral antigen and nucleic acid can be detected in blood from day 3 up to 7–16 days after onset of symptoms

Diagnosis - ELISA

- IgM antibodies can appear as early as 2 days post onset of symptoms and disappear between 30 and 168 days after infection
- IgG-specific antibodies develop between day 6 and 18 after onset and persist for many years
- IgM or rising IgG titre constitutes a strong presumptive diagnosis

Diagnosis

- Decreasing IgM, or increasing IgG titres (four-fold), or both, in successive paired serum samples are highly suggestive of a recent infection
- Nucleic acid can be amplified by purification of the virus RNA from materials treated with guanidinium isothiocyanate—a chemical chaotrope that denatures the proteins of the virus and renders the sample non-infectious

Treatment

- Mapp Biopharmaceutical - drug ZMapp
- Serum consists of three monoclonal antibodies that target different epitopes of the Ebola virus glycoprotein
- ZMapp cocktail rescued three (43%) of seven infected macaques when administered after the laboratory animals presented symptoms of infection

Treatment

- Before the outbreak the cocktail had never been used in human beings.
- Two of the three westerners who received the treatment survived, but this might also have been due to the high quality of care they received

Treatment

- Tekmira's TKM-Ebola is a small interfering RNA that blocks the expression of the L protein of Ebola's RNA polymerase
- Raised cytokine levels in healthy volunteers, but has since been cleared by the US FDA for use in infected patients

Treatment

- Biocryst and MediVector are both developing small molecule broad-spectrum viral polymerase inhibitors that could soon be ready for use in healthy volunteers or Ebola patients
- Experts are also debating whether statins and interferons, which have anti-inflammatory activity, could have a role in a treatment plan

Vaccine

- Public Health Agency of Canada (PHAC) donated up to 1000 doses of its experimental VSV-EBOV candidate
- Vaccine consists of transgenic vesicular stomatitis virus that expresses the Ebola glycoprotein
- Vaccine which has only been tested in animals, protected 100% of macaques when administered 21 days before an otherwise fatal infection

Vaccine

- US NIH and GSK are developing a second vaccine, a recombinant chimp adenovirus that expresses the glycoproteins of two different strains of Ebola virus.
- Vaccine provided 100% protection when used prophylactically in primates
- phase 1 trials in healthy volunteers as early as September

Preventive Measures after Exposure

- ❑ If an infected droplet does get on to your skin, it can be washed away immediately with soap and water or an alcohol-based hand sanitiser.
- ❑ Spray of droplets from a sneeze directly into the eye, for example, could let the virus in.
- ❑ Similarly, the mucous membranes of the mouth and inside of the nose are vulnerable areas, as is broken skin.

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- "It (Ebola) is the most extraordinary challenge that the world could possibly face..." said Dr. David Nabarro, who is heading the U.N. response to the Ebola epidemic.
 - Nabarro has said a "20-fold increase" in the global response is needed compared to efforts at the end of August [2014].

“Drugs and vaccines ought to only play a small part in an overall control strategy. This outbreak really is the outlier that proves that good infection control, good contact tracing, and good public health infrastructure are probably the most important components to limit this epidemic.”

Michael Kurilla, Director, Office of BioDefense, NIH

THE FIRST TIME
ONE OF THEM
SNEEZES,
CUT THE
ROPE



THANK YOU