



Ebola risk assessment in the pig value chain in Uganda



RESEARCH
PROGRAM ON
Agriculture for
Nutrition
and Health

LED BY IFPRI

Ebola risk assessment in the pig value chain in Uganda

Christine Atherstone, Kristina Roesel and Delia Grace

© 2014 International Livestock Research Institute (ILRI)



This publication is copyrighted by the International Livestock Research Institute (ILRI). It is licensed for use under the Creative Commons Attribution-Noncommercial-Share Alike 3.0 Unported Licence. To view this licence, visit <http://creativecommons.org/licenses/by-nc-sa/3.0/>. Unless otherwise noted, you are free to copy, duplicate or reproduce, and distribute, display, or transmit any part of this publication or portions thereof without permission, and to make translations, adaptations, or other derivative works under the following conditions:

- ① **ATTRIBUTION.** The work must be attributed, but not in any way that suggests endorsement by ILRI or the author(s).
- ② **NON-COMMERCIAL.** This work may not be used for commercial purposes.
- ③ **SHARE ALIKE.** If this work is altered, transformed, or built upon, the resulting work must be distributed only under the same or similar licence to this one.

NOTICE:

For any reuse or distribution, the licence terms of this work must be made clear to others.
Any of the above conditions can be waived if permission is obtained from the copyright holder.
Nothing in this licence impairs or restricts the author's moral rights.
Fair dealing and other rights are in no way affected by the above.
The parts used must not misrepresent the meaning of the publication.
ILRI would appreciate being sent a copy of any materials in which text, photos etc. have been used.

Edited by Tezira Lore

Design and layout—ILRI Editorial and Publishing Services, Addis Ababa, Ethiopia.

Cover photo—ILRI/Charlie Pye-Smith

ISBN 92-9146-350-7

Citation: Atherstone, C., Roesel, K. and Grace, D. 2014. *Ebola risk assessment in the pig value chain in Uganda*. ILRI Research Report 34. Nairobi, Kenya: International Livestock Research Institute.

ilri.org
Better lives through livestock
ILRI is a member of the CGIAR Consortium

Box 30709, Nairobi 00100, Kenya
Phone: + 254 20 422 3000
Fax: +254 20 422 3001
Email: ILRI-Kenya@cgiar.org

Box 5689, Addis Ababa, Ethiopia
Phone: +251 11 617 2000
Fax: +251 11 617 2001
Email: ILRI-Ethiopia@cgiar.org

Contents

Tables	v
Figures	vi
Abbreviations and acronyms	vii
Acknowledgements	viii
Executive summary	ix
Introduction and background	1
Methodology	2
Hazard identification	3
Can it cause harm?	3
Can it be present in food?	4
Hazard characterization	5
What harm does it cause?	5
How does harm depend on dose?	6
Stability and viability	7
Classification and history	7
Summary of outbreaks in Uganda	11
Significance	12
Spatial distribution	13
Ecology	13
Clinical symptoms, diagnosis and treatment	21
Exposure assessment	26
Possible transmission routes if fruit bats are involved	27
Possible transmission routes if pigs are involved	28

Human-to-human transmission	31
Other considerations	36
Conclusions	37
Recommendations	39
References	41

Tables

Table 1. Recent naming convention of <i>Ebolavirus</i> and case fatality rates	7
Table 2. Known cases and outbreaks of EVD, in chronological order	8
Table 3. Known cases and outbreaks of EVD in Uganda in chronological order	11
Table 4. Source of infection for confirmed EVD cases	20
Table 5. Treatment and prophylaxis of EVD	25
Table 6. Pig populations in the districts of reported EVD outbreaks in Uganda	29
Table 7. Date of first suspected EVD cases and proximity to national holidays	30

Figures

Figure 1. Risk analysis framework developed by the ILRI-led Safe Food, Fair Food project	3
Figure 2. Deceased EVD patient removed from home	6
Figure 3. Incidence and mortality of EVD outbreaks in Uganda	12
Figure 4. Geographic distribution of EVD outbreaks in sub-Saharan Africa, 1979–2008	13
Figure 5. <i>Ebolavirus</i> ecology	14
Figure 6. Geographic range of <i>E. franqueti</i>	15
Figure 7. Geographic range of <i>E. helvum</i>	15
Figure 8. Geographic range of <i>E. gambianus</i>	16
Figure 9. Geographic range of <i>E. labiatus</i>	16
Figure 10. Geographic range of <i>E. wahlbergi</i>	17
Figure 11. Geographic range of <i>H. monstrosus</i>	17
Figure 12. Geographic range of <i>M. torquata</i>	18
Figure 13. Geographic range of <i>R. aegyptiacus</i>	18
Figure 14. Model of <i>Ebolavirus</i> pathogenesis in humans	22
Figure 15. Hypothesis of transmission of <i>Reston ebolavirus</i>	28
Figure 16. Seasonal pork consumption patterns overlaid with <i>Ebolavirus</i> outbreaks in Uganda	30
Figure 17. EVD isolation ward, Lacor Hospital, Gulu	31
Figure 18. EVD sensitization team	32
Figure 19. Entrance to the containment unit at Kagadi Hospital, Kibaale District	34
Figure 20. Burial team disinfecting the coffin of an EVD patient	35

Abbreviations and acronyms

ASF	African swine fever
CDC	Centers for Disease Control and Prevention
DRC	Democratic Republic of the Congo
ELISA	enzyme-linked immunosorbent assay
EMPRES	Emergency Prevention System
EVD	Ebola virus disease
FAO	Food and Agriculture Organization of the United Nations
HIV	human immunodeficiency virus
IgG	immunoglobulin G
IgM	immunoglobulin M
ILRI	International Livestock Research Institute
MSF	Médecins sans Frontières
PCR	polymerase chain reaction
RNA	ribonucleic acid
RT-PCR	real time polymerase chain reaction
WHO	World Health Organization

Acknowledgements

Many people contributed to this report with their expert knowledge of Ebola, swine, bats, nonhuman primates and zoonotic diseases. Their insight and expertise was invaluable in drafting this report.

Jonathan Towner and Luke Nyakarahuka from the Centers for Disease Control and Prevention (CDC), Entebbe, Uganda;

Noelina Nantima, Deo Ndumu, Chris Ayebazibwe and Benard Ssebide from the Ministry of Agriculture, Animal Industries and Fisheries, Entebbe, Uganda;

Joseph Wamala and Winnie Kaboyo from the Ministry of Health, Kampala, Uganda;

Patrick Atimnedi and Patrick Tushabe from the Uganda Wildlife Authority;

Charles Masembe, Robert Kityo and Francis Ejobi from Makerere University;

Herbert Kazoora and Melissa Dahlke from the African Field Epidemiology Network, Kampala, Uganda;

Solomon Ssekitoleko from the Uganda Tourism Board;

Thomas Easley from the PREDICT project, Kampala, Uganda; and

Sally Lahm from George Washington University, Washington, DC, USA.

Executive summary

In Uganda, the frequency of Ebola virus disease (EVD) outbreaks is increasing, with many of the index case patients unable to account for their source of infection. Recent epidemiological work has revealed swine as a host for *Ebolavirus*.

Agriculture is the backbone of Uganda's economy, providing livelihoods to 80% of its citizens. The predicted fourfold population explosion in the next 40 years will place pressure on livestock production to address infections that affect production outputs in order to safeguard food security and human health. A more thorough understanding of how *Ebolavirus* infection impacts the health and welfare of pigs, and hence the health and livelihoods of pig farmers, will help prioritize how limited resources can be efficiently expended to ensure human health, livelihoods, food safety and food security.

The rising demand for pork in Uganda has sparked a massive expansion of pig production in the country. Pigs are preferred to other livestock species due to their relatively rapid growth rate, large litter sizes and potential to provide financial returns over a relatively short time. These higher pig populations, particularly those reared under tethering or free-range systems, overlap with fruit bat habitats. Where these pigs scavenge for food, they come in contact with dropped fruit, excrement, saliva, urine and faeces from suitable fruit bat hosts of *Ebolavirus*.

Furthermore, this intensification of pig production coupled with poor pig husbandry practices increases pig-human contact, a risk for direct transmission of *Ebolavirus*. In order to strengthen the pig value chain in Uganda, further research is warranted to determine what role pigs play in *Ebolavirus* transmission and specific risk factors for infection in pigs and from pigs to humans. Such foresight will help identify interventions that would minimize food instability, public health consequences, social stigma, mass public panic and negative economic impact from trade and travel restrictions associated with EVD outbreaks.

Introduction and background

During the last decades, the demand for meat and milk has increased in the world, particularly in developing countries. Consumption of meat increased almost three times more in developing countries than in developed countries from early 1970 to the mid-1990s (Delgado and Narrod 2002). The trend is expected to continue. The need for fast maturing sources of animal protein which require low cereal inputs places nonruminant animals in prime position for fulfilling this growing demand (Thomas et al. 2013). To this end, pig production is becoming increasingly popular, with pork and poultry contributing 76% of the increased meat consumption in the developing world between 1982 and 1998 (Delgado et al. 2001).

In sub-Saharan Africa, millions of small-scale farmers efficiently supply the great majority of the meat, milk and fish markets. Animal-source food products have a high nutritional value which enhances public health, while the production, transportation, processing and retailing of these products provide income and employment to millions.

On the other hand, animal-source foods are the single most important source of foodborne disease. About 80% of the animal-source foods are distributed through informal markets without adequate safety inspection. As a result, most of the people living in the region are exposed to a variety of foodborne agents which can cause diarrhoea, fever, chronic wasting, abortions or even epilepsy and cancer. These infections can have severe negative impacts on the population, including a high infant mortality, and may contribute significantly to the region's poverty.

In Uganda, the International Livestock Research Institute (ILRI)-led Safe Food, Fair Food project aims to support development of the pig value chain through risk-based approaches to ensure food safety. A systematic literature review resulting in a risk assessment to determine the threat of *Ebolavirus* in the pig value chain in Uganda was warranted, considering the increase in pig numbers and pig density in areas of Uganda where EVD outbreaks have been recorded. This preliminary risk assessment served as a foresight study to determine whether further research resource mobilization was needed to ensure public health and food safety in the pig value chain.

Methodology

In order to determine the risk of *Ebolavirus* in the pig value chain in Uganda, articles in published and grey literature related to *Ebolavirus* in pigs were identified through online databases, visiting university libraries and interviewing experts within Uganda. The following criteria were used to exclude publications from the study: date of publication, language of publication, animal species and content (with respect to prevalence, impact and control).

Thus, for this risk assessment, a publication was excluded if it was produced before 1990, it was not written in English, the species was not porcine and the study did not refer to prevalence (presence of level of hazard in pigs, pork and pig products, people, or wildlife interacting with pigs), impact (economic cost, disability-adjusted life years, social or other burdens or environment) and control (risk factors, knowledge and control methods).

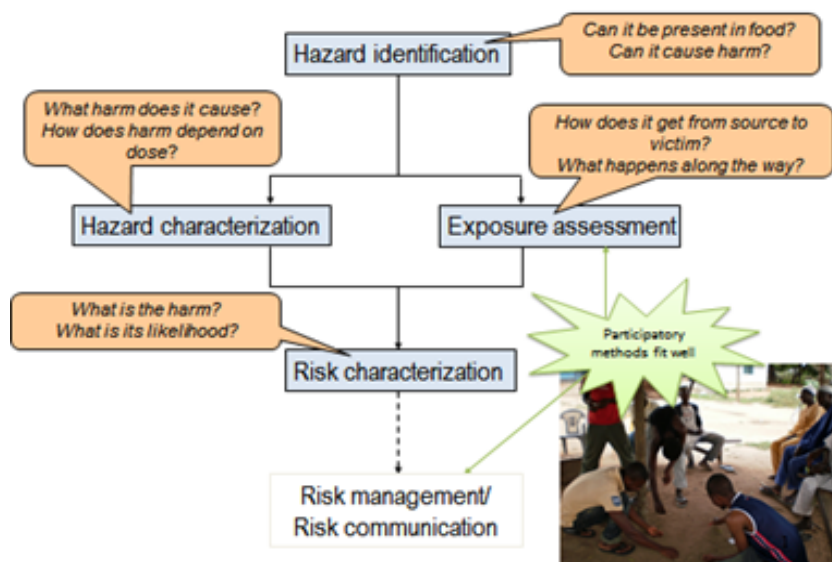
Databases searched included PubMed, CAB Direct, Web of Science, African Journals Online, Makerere University library, World Bank, World Health Organization (WHO) global burden of disease, World Animal Health Information Database, HealthMap, International Symposia on Veterinary Epidemiology and Economics proceedings, Tropentag proceedings, ILRI institutional repository, International Food Policy Research Institute resources, WHO library database, International System for Agricultural Science and Technology, CDC and two national daily newspapers (Daily Monitor and New Vision). Relevant searches using the search terms 'Uganda' AND 'Ebola', 'Ebola' AND 'pig' OR 'pork' OR 'porcine' OR 'swine' were carried out on all the above databases and websites.

An additional 15 expert interviews were conducted using a semi-structured questionnaire. Finally, unpublished Bachelor's, Master's and PhD theses from 1990 to the present at Makerere University, College of Veterinary Medicine, Animal Resources and Biosecurity were reviewed for relevant content on *Ebolavirus* in swine or diseases in swine that shared symptoms or histological changes similar to *Ebolavirus* infection in pigs.

Hazard identification

Using the Codex Alimentarius Commission framework for risk assessment, the Safe Food, Fair Food project adapted the framework for participatory risk assessments. The framework process is shown in Figure 1.

Figure 1. Risk analysis framework developed by the ILRI-led Safe Food, Fair Food project.



Can it cause harm?

EVD is a severe, often-fatal zoonotic disease in humans, nonhuman primates (gorillas, chimpanzees, mandrills, guenon and other monkeys), duikers and bush pigs (The Center for Food Security and Public Health 2009) that has appeared sporadically since its initial recognition in 1976. The disease is caused by infection with *Ebolavirus*, named after a river in the Democratic Republic of the Congo (DRC) in Africa, where it was first recognized. The ribonucleic acid (RNA) virus is one of two members in the family Filoviridae. There are five identified subtypes of *Ebolavirus* with a sixth waiting to be named from an outbreak currently ongoing in Guinea and Liberia (ProMED-mail 2014). Five of the six strains have caused disease in humans: *Zaire ebolavirus*, *Sudan ebolavirus*, *Côte d'Ivoire ebolavirus*, *Bundibugyo ebolavirus* and the new strain causing the outbreak in Guinea and Liberia that has yet to be named. The sixth, *Reston ebolavirus*, has caused disease in nonhuman primates but not in humans (CDC 2009b).

Can it be present in food?

Humans often become infected with *Ebolavirus* after handling sick and dead animals found in the forest, especially nonhuman primates, duikers (forest antelope) and fruit bats (CDC 2009a; The Center for Food Security and Public Health 2009; Feldmann and Geisbert 2011). *Zaire ebolavirus* transmission to humans has been clearly documented in central Africa through the hunting, butchering and consumption of bushmeat, especially gorillas and chimpanzees. Handling and consumption of freshly killed bats was associated with an outbreak of *Zaire ebolavirus* in DRC (Feldmann and Geisbert 2011). This close contact with organs and body fluids while hunting and consuming bushmeat and fruit bats puts people at risk of infection with *Ebolavirus*.

However, the *Ebolavirus* lipid envelope renders it relatively unstable in the environment. Infection in persons whose sole contact is with meat procured by others has not been reported and is probably rare, if it occurs at all. The greatest risk is probably among butchers and others who handle organs and body fluids of infected animals as a part of their occupation. Proper cooking of foods should inactivate infectious *Ebolavirus* although ingestion of contaminated food cannot be wholly ruled out as a possible route of exposure in natural infections (Feldmann and Geisbert 2011). It should be noted, however, that these observations come from remote African settings where there is little or no cold storage. The more reliable cold storage conditions typically involved in commercial pig farming could help preserve the virus (Bausch 2011).

Hazard characterization

To identify the risk of *Ebolavirus* in pigs in Uganda, EVD ecology, significance, spatial distribution and prevalence are discussed below.

What harm does it cause?

In humans, *Ebolavirus* causes severe disease and high case fatality rates of 25–90%, depending on the strain (CDC 2009a). During convalescence, which can be slow, some patients develop joint pain, deafness, pericarditis and orchitis (The Center for Food Security and Public Health 2009). Reports of intense familial and social stigma in recovered human patients are also common (Kinsman 2012).

In wildlife, *Ebolavirus* causes death in gorillas (*Gorilla gorilla*), chimpanzees (*Pan troglodytes*), mandrills (*Mandrillus spp.*), guenon (*Cercopithecus spp.*) and other monkeys as well as duikers (*Cephalophus dorsalis*) and bush pigs (*Potamochoerus porcus*) (Leroy et al. 2004; The Center for Food Security and Public Health 2009).

In domestic livestock, pigs are the only species, at present, found to be naturally infected with *Ebolavirus* (CDC 2009b). The disease course in pigs depends on the infective strain; *Reston ebolavirus* causes asymptomatic infection to mild respiratory symptoms (Barrette et al. 2009) and *Zaire ebolavirus* causes severe lung pathology (Kobinger et al. 2011).

Histopathology on the lungs of the infected pigs showed inflammatory cells in the bronchiolar epithelium, alveolar septae, the lumen of the bronchiole and the nearby alveolar spaces. Additionally, alveoli were filled with oedema fluid, the bronchiole with luminal inflammatory exudates and the expansion of the pleura with fibrin. Immunohistochemical staining showed heavy staining throughout the lobule.

In 2012, Ugandan Muslims were banned from travel to Mecca for the Hajj pilgrimage for fear of importing *Ebolavirus* into Saudi Arabia. Also, due to the similarity in name between Kibaale District and Kibale National Park, a popular tourist destination for chimpanzee trekking in Uganda, many tourists from Western countries cancelled their summer holiday travel plans to Uganda. Travel alerts and restrictions issued by Western countries did nothing to help curb the fear of tourists becoming infected. This was particularly hard on the tourism sector as Lonely Planet had named Uganda 'Best Country to Visit' in 2012. Despite the accolades by Lonely Planet, tourist numbers decreased by 13% in 2012 over 2011, with the month of September particularly hard hit with 50% fewer tourists than in 2011. This would coincide with the airing of news of an EVD outbreak in Kibaale District in international media outlets and tourists cancelling plans for wildlife tourism activities in Uganda (Uganda Wildlife Authority and Tushabe 2013).

During EVD outbreaks in Uganda, a case management team is organized that develops a response plan and mobilizes resources for the government and its partners. Essentially, all care is provided at no cost to the patients or their families. During burial, the relatives provide the coffin and passively participate in the burial which is presided over by a trained burial team. Survivors and their families are followed up by the psychosocial team to ensure smooth integration into the communities. All cases are also compensated for the materials destroyed by the infection control and burial teams. Presently, no targeted studies to determine the cost per patient have been undertaken (J.F. Wamala,

personal communication, 17 May 2013). This type of case management approach relies on patients presenting to health centres, overlooking those who rely on traditional healers for healthcare or do not have the means to access health centres as evidenced in Figure 2 which shows a deceased EVD patient removed directly from home.

Figure 2. Deceased EVD patient removed from home.



Photo courtesy of www.ifrc.org.

While most of the supportive care of infected patients takes place in healthcare centres in Uganda, at least one patient instituted his own infection control standards using buckets of Jik (bleach or sodium hypochlorite) (Oketch 2012).

How does harm depend on dose?

There is growing concern over transmission of *Ebolavirus* through the air between species (McGrath 2012) after Canadian scientists demonstrated that the virus was transmitted from pigs to monkeys without any direct contact between them (Kobinger et al. 2011). One to 10 aerosolized organisms are sufficient to cause infection in humans (Franz et al. 2001).

There is little research linking dose to disease course and outcome. However, in humans, the route of infection seems to affect the disease course and outcome. For contact exposure, the mean incubation period for cases of *Zaire ebolavirus* via infection by injection was 6.3 days versus 9.5 days for direct contact exposure. Additionally, the case fatality rate in the 1976 DRC outbreak of *Zaire ebolavirus* was 100% (85 of 85) in cases associated with injection compared to 80% (119 of 149) in cases of known contact exposure (Feldmann and Geisbert 2011).

For nonhuman primates infected with *Zaire ebolavirus*, the disease course seems to progress faster in animals exposed by intramuscular or intraperitoneal injection than in animals exposed by aerosol droplets (Feldmann and Geisbert 2011).

Stability and viability

The virus can survive in liquid or dried material for a number of days (Leroy et al. 2004). Infectivity is found to be stable at room temperature or at 4°C for several days and indefinitely stable at –70°C (Evans and Kaslow 1997; Mwanatambwe et al. 2001). Infectivity can be preserved by lyophilization (Public Health Agency of Canada 2010).

Ebolavirus is susceptible to sodium hypochlorite, lipid solvents, phenolic disinfectants, peracetic acid, methyl alcohol, ether, sodium deoxycholate, 2% glutaraldehyde, 0.25% Triton X-100, β-propiolactone, 3% acetic acid (pH 2.5), formaldehyde and paraformaldehyde and detergents such as sodium dodecyl sulphate (Elliott et al. 1982; Mitchell and McCormick 1984; Evans and Kaslow 1997; Loutfy et al. 1998; Franz et al. 2001).

Ebolavirus is moderately thermolabile and can be inactivated by heating for 30–60 minutes at 60°C, boiling for five minutes, gamma irradiation (1.2×10^6 rads to 1.27×10^6 rads) or ultraviolet radiation (Elliott et al. 1982; Mitchell and McCormick 1984; Evans and Kaslow 1997).

Classification and history

Ebolavirus belongs to a virus family called Filoviridae and can cause severe haemorrhagic fever in humans and nonhuman primates. So far, only two members of this virus family have been identified: *Marburgvirus* and *Ebolavirus*. The disease was originally named Ebola haemorrhagic fever, but due to the misconception that all infected patients develop haemorrhage, it was renamed EVD. Table 1 presents the recent naming convention of *Ebolavirus*. *Ebolavirus* is comprised of six species, namely, *Sudan ebolavirus*, *Zaire ebolavirus*, *Côte d'Ivoire ebolavirus* also known as *Tai Forest ebolavirus*, *Bundibugyo ebolavirus*, *Reston ebolavirus* and a sixth strain yet to be named from the ongoing outbreak in Guinea. *Reston ebolavirus* is the only known filovirus that does not cause severe disease in humans but it can be fatal in monkeys (CDC 2012a). The *Ebolavirus* is a single-stranded, RNA virus, the type of virus known to have the widest range of gene expression strategies (Bruce and Brysiewicz 2002).

Table 1. Recent naming convention of *Ebolavirus* and case fatality rates

Genus/species	Virus	Abbreviation	Human case fatality rate
<i>Tai Forest ebolavirus</i>	Tai Forest virus	TAFV	Non-fatal (one case)
<i>Reston ebolavirus</i>	Reston virus	RESTV	Non-fatal
<i>Sudan ebolavirus</i>	Sudan virus	SUDV	41–100%
<i>Zaire ebolavirus</i>	Zaire virus	ZEBV	47–100%
<i>Bundibugyo ebolavirus</i>	Bundibugyo virus	BDBV	25–55%

Source: CDC (2009a); Barrette et al. (2011).

Table 2 lists a chronology of known cases and outbreaks of EVD. *Ebolavirus* was first identified in 1976 when two outbreaks of EVD occurred in northern Zaire (now DRC) and southern Sudan. The outbreaks involved what eventually proved to be two different species of *Ebolavirus*. The outbreaks were named after the nations in which they were discovered. Both viruses showed themselves to be highly lethal, as 90% of the Zairian cases and 50% of the Sudanese cases resulted in death (CDC 2012a).

Table 2. Known cases and outbreaks of EVD, in chronological order

Year(s)	Country	Ebola subtype	Reported number of human cases	Reported number (%) of deaths among cases	Situation	Confirmatory laboratory analysis
1976	Zaire (now DRC)	Ebola-Zaire	318	280 (88%)	Occurred in Yambuku and surrounding area. Disease was spread by close personal contact and by use of contaminated needles and syringes in hospitals and clinics. This outbreak was the first recognition of the disease	Serology
1976	Sudan	Ebola-Sudan	284	151 (53%)	Occurred in Nzara, Maridi and the surrounding area. Disease was spread mainly through close personal contact within hospitals. Many medical care personnel were infected	Antibody detection by immunofluorescence; virus isolation, histopathology
1976	England	Ebola-Sudan	1	0 (0%)	Laboratory infection by accidental stick of contaminated needle	Virus isolation by electron microscopy
1977	Zaire	Ebola-Zaire	1	1 (100%)	Noted retrospectively in the village of Tandala	Antibody detection by immunofluorescence
1979	Sudan	Ebola-Sudan	34	22 (65%)	Occurred in Nzara, Maridi. Recurrent outbreak at the same site as the 1976 Sudan epidemic	Virus isolation; antibody detection by indirect immunofluorescence
1989	United States of America	Ebola-Reston	0	0 (0%)	Ebola-Reston virus was introduced into quarantine facilities in Virginia and Pennsylvania by monkeys imported from the Philippines	Virus isolation by electron microscopy
1990	United States of America	Ebola-Reston	4 (asymptomatic)	0 (0%)	Ebola-Reston virus was introduced once again into quarantine facilities in Virginia and Texas by monkeys imported from the Philippines. Four humans developed antibodies but did not get sick	Serology: immunofluorescence and Western blot test
1989–90	Philippines	Ebola-Reston	3 (asymptomatic)	0 (0%)	High mortality among cynomolgus macaques in a primate facility responsible for exporting animals into the United States of America. Three workers in the animal facility developed antibodies but did not get sick	Indirect fluorescent antibody test; Western blot test
1992	Italy	Ebola-Reston	0	0 (0%)	Ebola-Reston virus was introduced into quarantine facilities in Sienna by monkeys imported from the same export facility in the Philippines that was involved in the episodes in the United States of America. No humans were infected	Sera tests against viruses isolated in monkeys from previous outbreak in the Philippines
1994	Gabon	Ebola-Zaire	52	31 (60%)	Occurred in Mékouka and other gold-mining camps deep in the rain forest. Initially thought to be yellow fever; identified as EVD in 1995	Indirect immunofluorescence assays, IgM and IgG ELISA

Year(s)	Country	Ebola subtype	Reported number of human cases	Reported number (%) of deaths among cases	Situation	Confirmatory laboratory analysis
1994	Côte d'Ivoire	Ebola-Côte d'Ivoire	1	0 (0%)	Scientist became ill after conducting an autopsy on a wild chimpanzee in the Taï Forest. The patient was treated in Switzerland	Immunofluorescence assay and electron microscopy
1995	DRC (formerly Zaire)	Ebola-Zaire	315	250 (81%)	Occurred in Kikwit and surrounding area. Traced to index case-patient who worked in forest adjoining the city. Epidemic spread through families and hospitals	Ebola antibody and antigen ELISA, viral RNA RT-PCR
1996 (Jan–Apr)	Gabon	Ebola-Zaire	37	21 (57%)	Occurred in Mayibout area. A chimpanzee found dead in the forest was eaten by people hunting for food. Nineteen people who were involved in the slaughter of the animal became ill; other cases occurred in family members	Indirect immunofluorescence assays, IgG and IgM ELISAs
Jul 1996–Jan 1997	Gabon	Ebola-Zaire	60	45 (74%)	Occurred in Booué area with transport of patients to Libreville. Index case-patient was a hunter who lived in a forest camp. Disease was spread by close contact with infected persons. A dead chimpanzee found in the forest at the time was determined to be infected	Indirect immunofluorescence assays, IgG and IgM ELISAs
1996	South Africa	Ebola-Zaire	2	1 (50%)	A medical professional travelled from Gabon to Johannesburg, South Africa, after having treated Ebola virus-infected patients and thus having been exposed to the virus. He was hospitalized and a nurse who took care of him became infected and died	Immunofluorescence and serology
1996	United States of America	Ebola-Reston	0	0 (0%)	Ebola-Reston virus was introduced into a quarantine facility in Texas by monkeys imported from the Philippines. No human infections were identified	Immunohistochemistry; sandwich ELISA, IgG and IgM ELISA, RT-PCR
1996	Philippines	Ebola-Reston	0	0 (0%)	Ebola-Reston virus was identified in a monkey export facility in the Philippines. No human infections were identified	Antigen capture ELISA
2000–01	Uganda	Ebola-Sudan	425	224 (53%)	Occurred in Gulu, Masindi and Mbarara districts of Uganda. The three most important risks associated with <i>Ebolavirus</i> infection were attending funerals of EVD case-patients, having contact with case-patients in one's family and providing medical care to Ebola case-patients without using adequate personal protective measures	RT-PCR for IgG antibodies and Ebola genome

Year(s)	Country	Ebola subtype	Reported number of human cases	Reported number (%) of deaths among cases	Situation	Confirmatory laboratory analysis
Oct 2001–Mar 2002	Gabon	Ebola-Zaire	65	53 (82%)	Outbreak occurred over the border of Gabon and the Republic of the Congo	Antigen detection, IgG antibody ELISA, RT-PCR
Oct 2001–Mar 2002	Republic of the Congo	Ebola-Zaire	57	43 (75%)	Outbreak occurred over the border of Gabon and the Republic of the Congo. This was the first time that EVD was reported in the Republic of the Congo	Antigen detection, IgG antibody ELISA, RT-PCR
Dec 2002–Apr 2003	Republic of the Congo	Ebola-Zaire	143	128 (89%)	Outbreak occurred in the districts of Mbomo and Kéllé in Cuvette Ouest Department	IgG antibody ELISA, antigen detection by ELISA and RT-PCR
2003 (Nov–Dec)	Republic of the Congo	Ebola-Zaire	35	29 (83%)	Outbreak occurred in Mbomo and Mbandza villages located in Mbomo District, Cuvette Ouest Department	IgG antibody ELISA, antigen detection by ELISA and RT-PCR
2004	Sudan	Ebola-Sudan	17	7 (41%)	Outbreak occurred in Yambio county of southern Sudan. This outbreak was concurrent with an outbreak of measles in the same area, and several suspected EVD cases were later reclassified as measles cases	Antigen ELISA, RT-PCR of Ebola genome
2007	DRC	Ebola-Zaire	264	187 (71%)	Outbreak occurred in Kasai Occidental Province. The outbreak was declared over on 20 November. Last confirmed case on 4 October and last death on 10 October	IgG and IgM antibody detection and antigen detection by ELISA, RT-PCR to detect genome
Dec 2007–Jan 2008	Uganda	Ebola-Bundibugyo	131	42 (37%)	Outbreak occurred in Bundibugyo District in western Uganda. First reported occurrence of a new strain	Antigen capture; IgG and IgM ELISA
Nov 2008	Philippines	Ebola-Reston	6 (asymptomatic)	0 (0%)	First known occurrence of Ebola-Reston in pigs. Strain closely similar to earlier strains. Six workers from the pig farm and slaughterhouse developed antibodies but did not become sick	IgG antibody detection
Dec 2008–Feb 2009	DRC	Ebola-Zaire	32	15 (47%)	Outbreak occurred in the Mweka and Luebo health zones of Kasai Occidental Province	
May 2011	Uganda	Ebola-Sudan	1	1 (100%)	Single case in Luwero District, Uganda	RT-PCR, antigen detection ELISA
Jul–Aug 2012	Uganda	Ebola-Sudan	11*	4* (36.4%)	Outbreak occurred in the western district of Kibaale; 20 of the patients were from the same family	
Aug–Nov 2012	DRC	Ebola-Bundibugyo	36*	13* (36.1%)	Outbreak occurred in northeastern Orientale Province	

Year(s)	Country	Ebola subtype	Reported number of human cases	Reported number (%) of deaths among cases	Situation	Confirmatory laboratory analysis
Nov 2012	Uganda	Ebola-Sudan	6*	3* (50%)	Outbreak occurred in the central district of Luwero and carried by an infected patient to the capital city, Kampala. Many of the patients were from the same family	
Feb 2014—ongoing as of this report	Guinea, Liberia	New strain yet to be named at publication of this report	203 (ongoing as of this report)	129 (63.5%) (ongoing as of this report)	First outbreak in Guinea and Liberia; outbreak began in southern Guinea and was carried by infected patients to the capital, Conakry, and Liberia. Consumption of bats, a local delicacy, was implicated in starting the outbreak. First reported occurrence of a new strain	RT-PCR, virus isolation

*Laboratory confirmed cases.

ELISA: enzyme-linked immunosorbent assay; EVD: Ebola virus disease; IgG: immunoglobulin G; IgM: immunoglobulin M; RNA: ribonucleic acid; RT-PCR: real time polymerase chain reaction.

Source: CDC (2009a).

As journal articles are published from the more recent EVD outbreaks, laboratory analysis used to confirm the outbreaks should become available.

Summary of outbreaks in Uganda

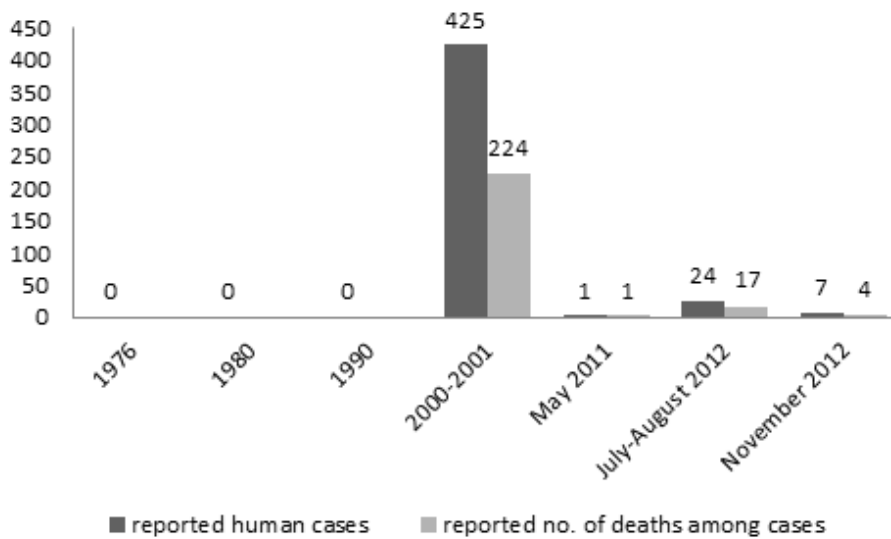
Table 3 presents a summary of EVD outbreaks in Uganda. While many of the outbreaks in Uganda were caused by the Sudan strain, in 2007 a new strain of *Ebolavirus*, Bundibugyo, was discovered. This new strain was named after the region where the outbreak occurred.

Table 3. Known cases and outbreaks of EVD in Uganda in chronological order

Year(s)	Ebola subtype	Reported number of human cases	Reported number (%) of deaths among cases	Situation	Confirmatory laboratory analysis
2000–01	Ebola-Sudan	425	224 (53%)	Occurred in Gulu, Masindi and Mbarara districts of Uganda. The three most important risks associated with Ebola virus infection were attending funerals of Ebola virus disease case-patients, having contact with case-patients in one's family and providing medical care to Ebola case-patients without using adequate personal protective measures	RT-PCR for IgG antibodies and Ebola genome
Dec 2007–Jan 2008	Ebola-Bundibugyo	131	42 (37%)	Outbreak occurred in Bundibugyo District in western Uganda. First reported occurrence of a new strain	Antigen capture; IgG and IgM ELISA
May 2011	Ebola-Sudan	1	1 (100%)	Single case in Luwero District, Uganda	RT-PCR, antigen detection ELISA
July–Aug 2012	Ebola-Sudan	24	17 (71%)	Outbreak occurred in the western district of Kibaale; 20 of the patients were from the same family	
Nov 2012	Ebola-Sudan	7	4 (57%)	Outbreak occurred in the central district of Luwero and carried by an infected patient to the capital city, Kampala; many of the patients were from the same family	

ELISA: enzyme-linked immunosorbent assay; IgG: immunoglobulin G; IgM: immunoglobulin M; RT-PCR: real time polymerase chain reaction.

Figure 3. Incidence and mortality of EVD outbreaks in Uganda.



From Figure 3, it is clear that the frequency of EVD outbreaks is increasing in Uganda.

Significance

The significance of EVD cannot be overstated. Although the incidence of EVD may be low compared to other infectious diseases in Africa, its high index of illness severity together with the profound human suffering and agonizing death (Bruce and Brysiewicz 2002) triggers public panic nationally and globally.

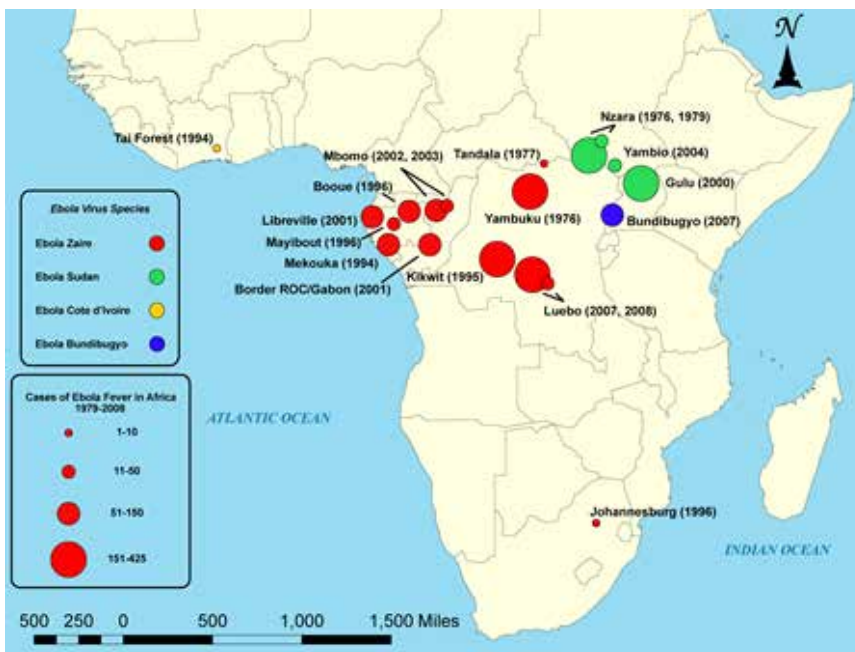
Ebolavirus is highly pathogenic to human and nonhuman primates, with lethality rates of up to 90% for humans and no current pre- and post-exposure treatment options. The emergence and re-emergence in epidemic regions of Africa, the potential for introductions into non-endemic countries through international travel and the global trade in wildlife and the possible use as a bioweapon make *Ebolavirus* a worldwide public health concern. The recently reported decline of Central African wildlife, particularly the great apes, has further extended the threats posed by this virus to include fear of extinguishing one of the world's largest populations of gorillas and chimpanzees (Feldmann et al. 2004; Groseth et al. 2007).

In addition to the risk to human and animal health, the public fear and stigma associated with EVD cannot be overstated. Retrospective analysis of media reports found that responses to an EVD outbreak can be very dramatic, disproportionate to the actual danger present. Responses included confusion, anger, serious stigma in affected communities, medical staff working themselves to exhaustion, medical staff quitting their posts, patients fleeing from hospitals, calls to spiritual forces for protection against infection, imposition of some international travel restrictions and a coordinated national control strategy (Kinsman 2012).

Spatial distribution

Zaire ebolavirus, *Sudan ebolavirus*, *Côte d'Ivoire ebolavirus* and *Bundibugyo ebolavirus* are endemic in several countries in sub-Saharan Africa. The pattern of outbreaks seems to suggest they each may have a distinct geographic range (Figure 4). *Côte d'Ivoire ebolavirus* has been reported only in West Africa, while *Sudan ebolavirus* tends to occur in eastern Africa (Sudan and Uganda) and *Zaire ebolavirus* has been seen mainly in the west-central region of Africa (DRC, Gabon and Republic of the Congo). *Bundibugyo ebolavirus* was reported from two outbreaks: one in Uganda and the other in DRC (The Center for Food Security and Public Health 2009).

Figure 4. Geographic distribution of EVD outbreaks in sub-Saharan Africa, 1979–2008.

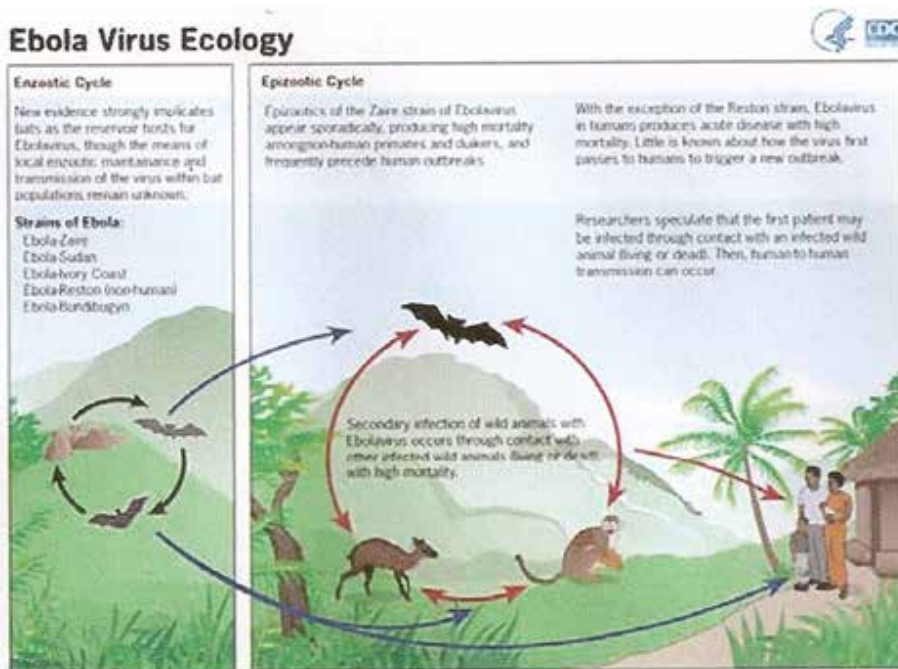


Source: CDC (2012b).

However, recent serological surveys suggest that some of these strains may be more widespread. Antibodies to *Zaire ebolavirus* have been found in nonhuman primates and bats in much of central Africa. Seropositive animals were found in some countries, such as Cameroon, where outbreaks of EVD have never been reported (Becker et al. 1992; The Center for Food Security and Public Health 2009).

Ecology

Although *Ebolavirus* emerged more than three decades ago, the reservoirs of this zoonotic pathogen and the routes of primary transmission to humans and nonhuman primates remain inconclusive. Recent outbreaks have been associated with multiple introductions into the population, indicating the circulation of distinct strains that have evolved in reservoir species that occupy different ecological niches (Feldmann et al. 2004). Considering the restricted geographical region in which EVD is found and the tremendous efforts invested over the past three decades to identify a reservoir, it seems probable that whatever the reservoir, it is rarely encountered and/or transmission is inefficient or perhaps regulated by specific conditions (Groseth et al. 2007). Figure 5 shows a pictorial representation of *Ebolavirus* ecology.

Figure 5. *Ebolavirus* ecology.

Source: Rousseau (2010).

Bats

Anecdotal evidence has linked contact with bats to *Ebolavirus* infection. For instance, in the 1976 outbreak of Sudan *ebolavirus*, the first six human cases were cotton factory employees who worked in a room where bats roosted. In 1994 in Côte d'Ivoire, chimpanzees which developed EVD had been feeding in a fig tree together with fruit bats for two weeks before developing the disease. The 1989–90 and 1996 Reston *ebolavirus* outbreaks in primate facilities were linked back to a single export facility in the Philippines which was a former fruit orchard where animals were potentially exposed to fruit bats (Rousseau 2010). Additionally, the first human victim in the 2007 Zaire *ebolavirus* outbreak in DRC was linked to direct exposure to freshly killed bats bought from hunters (Leroy et al. 2009).

Antibodies to *Ebolavirus* have been found in several fruit bat species in Ghana: African straw coloured fruit bat (*Eidolon helvum*), Franquet's epauletted fruit bat (*Epomops franqueti*), Gambian epauletted fruit bat (*Epomophorus gambianus*), Hammer-headed fruit bat (*Hypsignathus monstrosus*) and Veldkamp's bat (*Nanonycteris veldkampii*) (Hayman et al. 2012). However, serology and virus isolation carried out on 539 bats captured during the 1995 Kikwit Zaire *ebolavirus* outbreak were all negative for antibodies and virus isolation was unsuccessful (Leirs et al. 1999). Experimental infection of captured bats in and around the 1995 Kikwit Zaire *ebolavirus* outbreak found that several species supported replication and circulation of high titres of virus: Angola free-tailed bat (*Tadarida condylura*), Wahlberg's epauletted fruit bat (*Epomophorus wahlbergi*) and little free-tailed bat (*Tadarida pumila*). Furthermore, virus was recovered from faecal samples 21 days post-inoculation (Swanepoel et al. 1996).

During the Zaire *ebolavirus* outbreaks that occurred between 2001 and 2003 in DRC and Gabon, numerous animals were captured in the search for reservoir species, including 222 birds, 129 small terrestrial vertebrates and 679 bats. Of the 1024 small mammals sampled, *Ebolavirus* specific antibodies were detected in the serum of 16 (8%) of 192 fruit bats belonging to three species: *H. monstrosus*, *E. franqueti* and *M. torquata*. *Ebolavirus* RNA was detected in pooled liver and spleen samples from 13 (5%) of 279 such bats (Leroy et al. 2005). A large-scale serological survey of bats belonging to these three species was then conducted, with 1390 specimens captured between 2003 and 2006 in three regions of Gabon and in the epidemic border region with DRC. The prevalence of *Ebolavirus* specific immunoglobulin G (IgG) was about 5% in bats from all four regions (Pourrut et al. 2009). Antibodies to Zaire *ebolavirus* were found in six bat species captured: *E. franqueti*, *H. monstrosus*, *M. torquata*, *Micropteropus pusillus*, *Mops condylurus* and *Rousettus*

aegyptiacus. Zaire ebolavirus RNA was isolated from three of these species: *E. franqueti*, *H. monstrosus* and *M. torquata* (Pourrut et al. 2009) but the extent to which *Ebolavirus* causes disease in these species is still not known.

In the Greater Accra Region of Ghana, fruit bats have also been found to be positive for IgG antibody to Zaire ebolavirus. *E. franqueti*, *Epomops gambianus*, *H. monstrosus* and *N. veldkampii* all had IgG *Ebolavirus* specific antibody (Hayman et al. 2012).

In Uganda, *Ebolavirus* antibody has also been found in *Epomophorus labiatus*, *R. aegyptiacus* and *Eidolon helvum* (Reed 2012; Shoemaker 2013). In addition to these bat species, *E. franqueti*, *E. gambianus*, *E. wahlbergi*, *H. monstrosus* and *M. torquata* can all be found in Uganda and have all been found infected with either *Ebolavirus* or *Ebolavirus* specific antibodies.

Figure 6. Geographic range of *E. franqueti*.



Source: Mickleburgh et al. (2008c).

Figure 7. Geographic range of *E. helvum*.



Source: Mickleburgh et al. (2013).

Figure 8. Geographic range of *E. gambianus*.



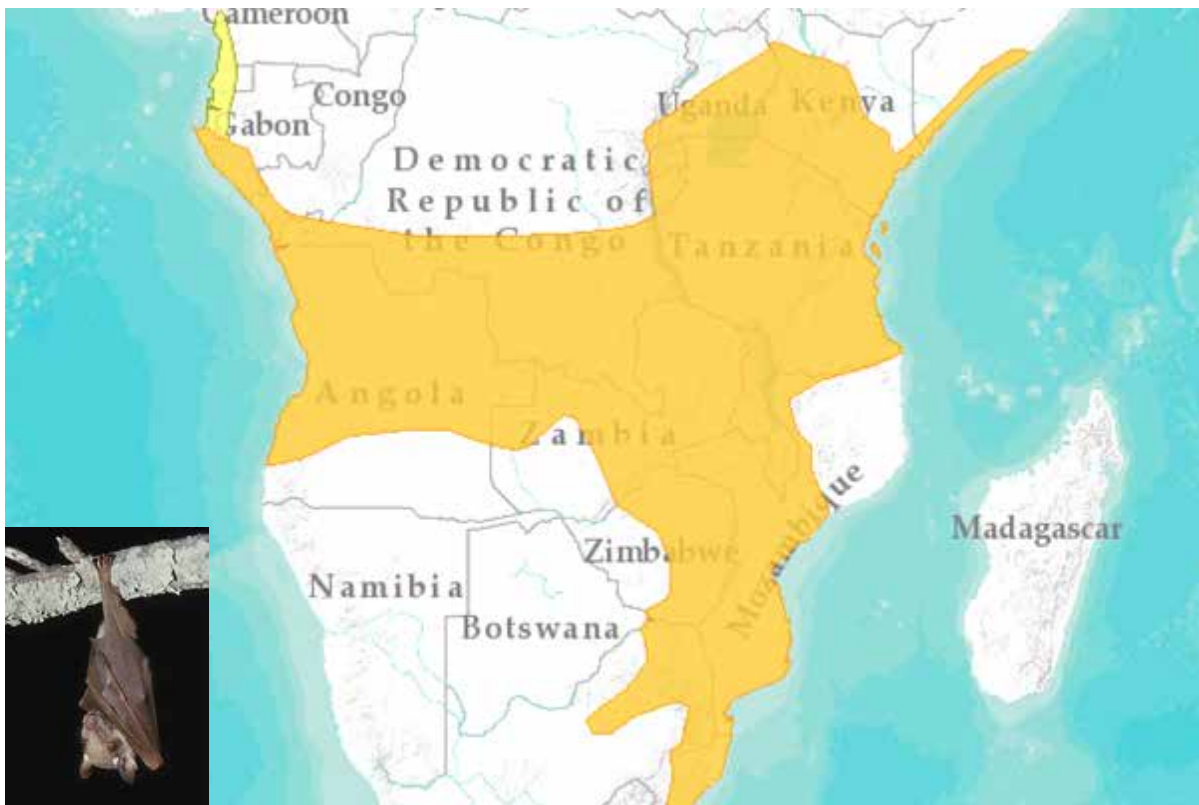
Source: Mickleburgh et al. (2008f).

Figure 9. Geographic range of *E. labiatus*.



Source: Mickleburgh et al. (2008a).

Figure 10. Geographic range of *E. wahlbergi*.



Source: Mickleburgh et al. (2008b).

Figure 11. Geographic range of *H. monstrosus*.



Source: Mickleburgh et al. (2008d).

Figure 12. Geographic range of *M. torquata*.

Source: Mickleburgh et al. (2008e).

Figure 13. Geographic range of *R. aegyptiacus*.

Source: Benda et al. (2008).

From the maps in Figures 6 to 13, it is clear that many of the bat species found with either *Ebolavirus* or circulating antibodies are found in Uganda. The many different species and habitats make it a challenge to identify best-bet interventions for controlling bat-pig contact.

If we assume, as now seems likely, that bats have a role as a reservoir species for *Ebolavirus*, it will be important to examine the role that seasonal, environmental or temporal physiological factors (for example, pregnancy or other stresses) have in facilitating virus replication and subsequent transmission to other susceptible hosts (Groseth et al. 2007). While bats have been presumptively considered the natural reservoirs of *Ebolavirus*, it is interesting to note that there are many human cases of EVD that cannot be directly linked to contact with bats.

Nonhuman primates and other wildlife

Although in many outbreaks the source of infection for the human index case was not identified, many have had documented contact with nonhuman primates known to be susceptible to *Ebolavirus* infection (gorillas, chimpanzees and duikers). Nonhuman primates are believed to be infected directly from the natural reservoir. Subsequently, the virus circulates or spreads by horizontal transmission (for example, ape to ape) within a primate population. Transmission can take place after direct contact with infected blood, secretions or excretions. Transmission is also possible through contact with contaminated inanimate objects or vegetation (Feldmann et al. 2004).

The epizootics caused by *Reston ebolavirus*, the only *Ebolavirus* of Asian origin, have raised the possibility that nonhuman primates might be a reservoir. This appears to be unlikely, at least for the *Ebolavirus* of African origins, which are highly pathogenic to nonhuman primates—a feature that is generally incongruous with the concept of a reservoir host. If not the reservoir, nonhuman primates could be indicator hosts for *Ebolavirus* circulation. This is supported by deaths in monkey species that occurred before human cases, as described in the outbreak of *Côte d'Ivoire ebolavirus* in the Taï Forest, several of the *Ebolavirus* outbreaks occurring after 1996 in Gabon and the recent outbreak of *Ebolavirus* in DRC (Feldmann et al. 2004; Leroy et al. 2004).

In a study designed to test animal mortality in regions of EVD in Gabon, 14 of the 34 animal carcasses found tested positive for *Zaire ebolavirus* RNA (10 gorillas, 3 chimpanzees and 1 duiker) (Groseth et al. 2007; Lahm et al. 2007).

Increased mortality as a result of *Zaire ebolavirus* in susceptible great apes at the end of the rainy season and/or the start of the dry season has previously been observed. Thus, it has been widely hypothesized that these seasonal changes might force different animal species into closer proximity. The dry season from November to February is in fact a time of high fruit abundance in Gabon, suggesting that increased interaction between the relevant species during feeding and/or altered dietary preference during these times might also have a role in spillover (Groseth et al. 2007).

Suggested modes of transmission between fruit bats and nonhuman primates include competition for fruit between fruit bats and nonhuman primates leading to spatiotemporal clustering of these frugivorous animals creating an increased likelihood of spillover (Rousseau 2010).

Detection of *Zaire ebolavirus* RNA in organ tissues of rodents and shrews captured in the Central African Republic suggested that a reservoir exists within small terrestrial mammals living in peripheral forest areas (Feldmann et al. 2004; Gonzalez et al. 2007). However, other ecological studies of captured rodents have found no evidence of *Ebolavirus* by serology and attempts at virus isolation have been unsuccessful (Swanepoel et al. 1996; Leirs et al. 1999).

Experimental *Ebolavirus* infections in newborn mice and guinea pigs have been successful (The Center for Food Security and Public Health 2009), but the results have not been confirmed by other research. Likewise, attempts to experimentally infect plants (Swanepoel et al. 1996) and isolate virus from arthropods (Reiter et al. 1999) have been unsuccessful.

Domestic livestock

Due to the number of human cases of EVD in previous outbreaks with no known contact with nonhuman primates or bats, there has been speculation that other reservoirs of infection cause spillover into human populations. Table 4 lists the source of infection for confirmed EVD cases. In the 1976 outbreak in Sudan, 14 (4.9%) of the 284 cases and 55 (17.4%) of the 315 cases during the 1995 outbreak in Kikwit, DRC had no direct physical contact with an infected person or known infected carcass (Roels et al. 1999; Allela et al. 2005). The source of infection remained unknown for 12 case-patients in the August 2000–January 2001 *Sudan ebolavirus* outbreak in Uganda (Francesconi et al. 2003).

Table 4. Source of infection for confirmed EVD cases

Virus strain	Year	Location	Source of infection	Number of cases	Case fatality rate (%)	
Zaire	1976	Zaire	Unknown	318	88	
	1977	Zaire	Unknown	1	100	
	1994	Gabon	Contact with NHPs	49	65	
	1995	DRC	Unknown	315	88	
	1996	Gabon	Contact with NHPs	37	57	
	1996	Gabon	Contact with NHPs	60	75	
	2001	Gabon/DRC	Contact with NHPs	123	79	
	2003	DRC	Contact with NHPs	143	90	
	2003	DRC	Contact with NHPs	35	83	
	2004	Russia	Lab accident	1	100	
	2005	DRC	Unknown	12	75	
	2007	DRC	Contact with bats	264	71	
	2008	DRC	Unknown	32	47	
	Sudan	1976	Sudan	Unknown	284	53
		1976	England	Lab accident	1	0
1979		Sudan	Unknown	43	65	
2000		Uganda	Unknown	425	53	
2004		Sudan	Unknown	17	42	
Côte d'Ivoire	1994	Côte d'Ivoire	Necropsy of chimp	1	0	
Bundibugyo	2007	Uganda	Unknown	102	42	

NHPs: nonhuman primates.

Source: Kortepeter et al. (2011).

These cases resulting from unknown sources of infection have led to searches for *Ebolavirus* reservoirs in species beyond fruit bats and nonhuman primates. At present, pigs are the only livestock species found naturally infected with *Reston ebolavirus* (FAO and EMPRES 2008; CDC 2009b). Of 141 tested humans, six individuals who worked on pig farms or with swine products had positive serum IgG titres to *Reston ebolavirus*, confirming the potential transmission between pigs and humans (Barrette et al. 2009). One theory suggests that fruit bats dropped partially eaten fruit into the areas where pigs scavenge for food. Pigs then ingested the contaminated fruit, serving as amplifying hosts, transmitting *Ebolavirus* to humans through direct contact.

Experimental infection of pigs with *Zaire ebolavirus* has also been successful. In this study, naïve pigs reared in contact with the infected pigs become infected, suggesting transmission via direct contact, probably through aerosols as virus was isolated from lung tissue in the experimentally infected pigs (Kobinger et al. 2011).

Finally, dogs in Ghana were also found to be seropositive to *Ebolavirus* with no clinical symptoms observed (Allela et al. 2005). Perhaps dogs could serve as sentinels for *Ebolavirus* circulation, as in many communities throughout Africa, including Uganda, they typically roam free and scavenge for their own food like bushmeat and slaughter waste.

Humans

It is clear that once humans become infected, subsequent *Ebolavirus* transmission is continued from person to person. After the first case patient in an outbreak setting is infected, the virus can be transmitted in several ways. People can be exposed to *Ebolavirus* from direct contact with the blood and/or secretions of an infected person. Thus, the virus is often spread through families and friends because they come in close contact with such secretions when caring for infected persons. People can also be exposed to *Ebolavirus* through contact with objects, such as needles, that have been contaminated with infected secretions.

Large outbreaks of EVD are usually driven by person-to-person contact. Virus has been detected in saliva, stool, semen, breast milk, tears, nasal blood and skin swabs during the acute phase of illness (Bausch et al. 2007). In particular, *Ebolavirus* was frequently found in saliva in the early course of disease. Hence, intimate contact and the sharing of food, particularly eating with the hands from a common plate, a custom common in many parts of Africa, could be possible transmission routes from person to person. Additionally, the presence of *Ebolavirus* in breast milk suggests the possibility of direct mother-to-child transmission via breastfeeding. Finally, the isolation of *Ebolavirus* in semen 40 days after the onset of illness underscores the risk of sexual transmission of during convalescence (Bausch et al. 2007).

Nosocomial transmission refers to the spread of a disease within a healthcare setting, such as a clinic or hospital. Nosocomial transmission occurs frequently during EVD outbreaks. In African healthcare facilities, patients are often cared for without the use of a mask, gown or gloves. Exposure to the virus has occurred when healthcare workers treated infected individuals without wearing these types of protective clothing. In addition, when needles or syringes are used, they may not be of the disposable type or may not have been sterilized but only rinsed before reinsertion into multi-use vials of medicine. If needles or syringes become contaminated with virus and are then reused, numerous people can become infected. Nosocomial transmission becomes more of a factor when there are low hygiene standards and poor healthcare practices, such as reusing syringes and needles and the lack of protective clothing (CDC 2009a). Environmental contamination and transmission via fomites in an isolation ward was low as long as recommended infection control guidelines were followed (Bausch et al. 2007).

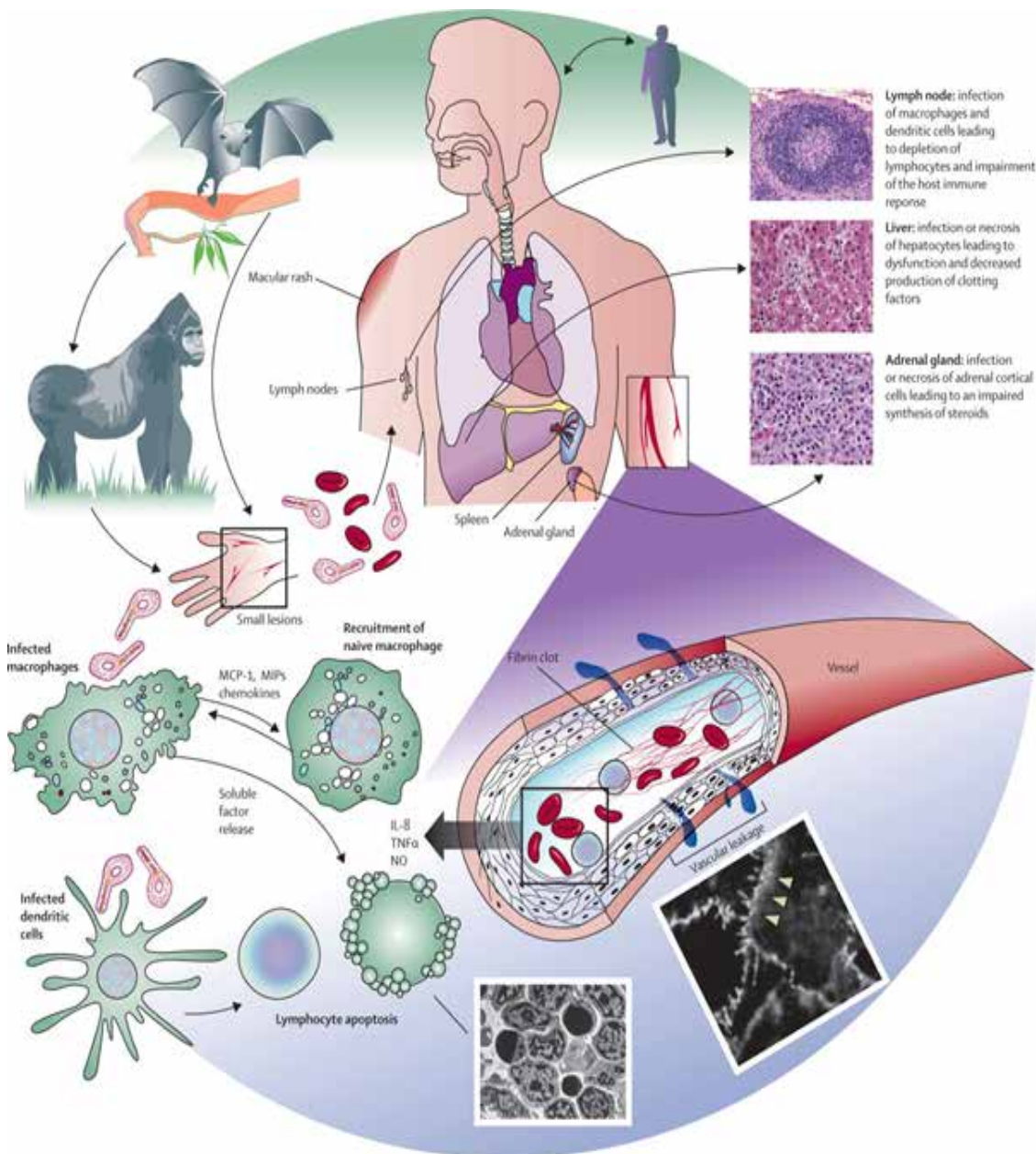
In addition to communal meals, washing of the deceased and hand washing, rituals common at the funerals, have also been found to be significant in the transmission of *Ebolavirus*. Ritual hand washing requires funeral goers to share a bowl of water that symbolizes unity with the dead and ancestral spirits (Bruce and Brysiewicz 2002).

During the *Sudan ebolavirus* outbreak in Uganda from August 2000 to January 2001, the introduction of the virus into the human community via one infected person was followed by dissemination by person-to-person transmission within medical facilities. Epidemiological investigations identified the three most important means of transmission as attending funerals of presumptive EVD case patients where ritual contact with the deceased occurred, and intrafamilial and nosocomial transmission. Fourteen (64%) of the 22 healthcare workers in Gulu were infected after establishing isolation wards. Two distance focal outbreaks were initiated by movement of infected contacts of EVD cases from Gulu to Mbarara and Masindi districts (CDC 2001).

Clinical symptoms, diagnosis and treatment

In humans

Infections with *Ebolavirus* are typically acute. There is no carrier state. There have been reports of asymptomatic *Ebolavirus* infection (Leroy et al. 2000; Leroy et al. 2001) but these reports are rare. The different species of *Ebolavirus* seem to cause somewhat different clinical syndromes, but opportunities for close observation of the diseases under good conditions have been rare. Figure 14 illustrates a model of *Ebolavirus* pathogenesis in humans. Generally, following an incubation period of 2–21 days, the onset of EVD is insidious with symptoms resembling a cold or influenza. However, within a few hours, the body temperature rises rapidly causing the victim to sweat and shiver uncontrollably, symptoms often associated with malaria, brucellosis and yellow fever. Within 48 hours, any movement of the eyes, jaws or head causes pain. Subsequently, haemorrhage from every orifice, including the victim's eyes and ears, manifests not only as a definitive sign of the disease but also of impending death (Bruce and Brysiewicz 2002). Patients with fatal disease develop clinical signs early during infection and die typically between day 6 and 16 with hypovolaemic shock and multiorgan failure. Haemorrhages can be severe but are only present in fewer than half of patients. In nonfatal cases, patients have fever for several days and improve typically around day 6–11, about the time that the humoral antibody response is noted. Convalescence is extended, often resulting in myelitis, recurrent hepatitis, psychosis or uveitis. Pregnant women have an increased risk of miscarriage (Feldmann and Geisbert 2011).

Figure 14. Model of *Ebolavirus* pathogenesis in humans.

Source: Feldmann and Geisbert (2011).

There has been little research into asymptomatic infection in humans. *Ebolavirus* infections without apparent disease were common among residents of the Central African Republic. Of 962 serum samples screened using an immunofluorescent antibody test, 561 (58.8%) were positive to either *Zaire ebolavirus* or *Sudan ebolavirus* (Johnson et al. 1993). During the 1996 *Zaire ebolavirus* outbreak in Gabon, there were asymptomatic infections in close contacts of symptomatic cases (Leroy et al. 2000; Leroy et al. 2001). Finally, as noted above, during the EVD outbreak in pigs in the Philippines and in monkey handlers in the United States of America, asymptomatic infection in the animal handlers was noted by seroconversion.

Diagnosing EVD in an individual who has been infected only a few days previously is difficult because early symptoms, such as red eyes and a skin rash, are nonspecific to the virus and are seen in other patients with diseases that occur much more frequently. However, if a person has the constellation of symptoms described above and infection with

Ebolavirus is suspected, isolation of the patient and notification of the relevant authorities is the recommended first course of action (CDC 2009a). The WHO has a handbook, *Viral haemorrhagic fever infection control in the African healthcare setting*, that outlines standard precautions with all patients, identifying suspect cases, isolating patients, wearing protective clothing, disinfecting reusable supplies and equipment, safe disposal of waste, safe burial practices, mobilizing community resources and conducting community education (WHO et al. 1998).

There is no standard treatment for EVD, just supportive therapy. This consists of balancing the patient's fluids and electrolytes, maintaining their oxygen status and blood pressure and treating them for any complicating infections (CDC 2009a).

Antigen-capture enzyme-linked immunosorbent assay (ELISA), Immunoglobulin M (IgM) ELISA, polymerase chain reaction (PCR) and virus isolation can be used to diagnose a case of EVD within a few days of the onset of symptoms. Persons tested later in the course of the disease or after recovery can be tested for IgM and IgG antibodies. The disease can also be diagnosed retrospectively in deceased patients by using immunohistochemistry testing, virus isolation or PCR (CDC 2009a).

In nonhuman primates

Ebolavirus infections have been intensively investigated in various species of nonhuman primates, but mainly in cynomolgus (*Macaca fascicularis*) and rhesus macaques (*Macaca mulatta*). African green monkeys (*Chlorocebus aethiops*) are resistant to *Ebolavirus* and baboons (*Papio hamadryas*) appear to be somewhat resistant to *Ebolavirus*. The viral dose and strain, the route of infection and the species of nonhuman primates infected all appear to influence the onset, duration and severity of the clinical signs.

For cynomolgus macaques infected with *Ebolavirus*, the onset of clinical signs is fairly rapid, occurring within 4–5 days. In other nonhuman primate models, the onset of symptoms is slower and thus more similar to that observed in humans. Usually macaques become febrile and lethargic 2–3 days after infection and fever persists throughout the course of the disease. A drop in body temperature usually precedes death. Animals also show weight loss of up to 10% of their body weight, which is probably primarily related to dehydration rather than mobilization of fat reserves and catabolism, although all of these factors probably contribute. In addition, some animals develop diarrhoea and intermittent bloody stool. As soon as the fourth day after infection, nonhuman primates generally develop a maculopapular rash that remains prominent until death (Bente et al. 2009).

Only a few studies have evaluated the pathogenesis of *Sudan ebolavirus* in nonhuman primates. In rhesus and cynomolgus macaques, *Sudan ebolavirus* disease course appears to be several days slower than that seen following *Zaire ebolavirus* infection and rates of survival appear to be higher (Bente et al. 2009).

At present, diagnosis and treatment in nonhuman primates is similar to that in humans. However, given that nonhuman primates are typically found dead in the forest from EVD, control and prevention measures have not been attempted in wildlife. Until a suitable vaccine is available, protection of wild nonhuman primates from *Ebolavirus* infection, particularly in vulnerable great ape populations, will remain elusive. At present, Uganda does not have a plan in place to protect the critically endangered mountain gorillas, a source of significant tourism revenue, from an EVD outbreak (P. Atimnedi, personal communication, 23 July 2013).

In pigs

Reston ebolavirus was accidentally discovered in pigs while investigating a particularly pathogenic *porcine reproductive and respiratory syndrome virus* outbreak, a respiratory and abortion disease syndrome in swine. Symptoms included a high fever of 41 °C, laboured breathing, thumping, coughing, nasal discharge, loss of appetite, diarrhoea, skin haemorrhage and reddish discolouration, with some pigs found in recumbent position. High nursery house and growing house mortalities were observed. Additionally, sows had previously been affected by high fever and abortions

(Rousseau 2010). A panviral microarray, PCR, Ebola-specific real time polymerase chain reaction (RT-PCR), ELISA, immunochemistry and virus isolation were used to confirm *Reston ebolavirus* in this outbreak (Barrette et al. 2009).

During experimental infection of pigs with *Zaire ebolavirus*, laboured breathing with an abdominal component, loss of interest in human presence, loss of appetite, reluctance to stand up and move and lack of interactions and play behaviour with cage mates were all observed. RT-PCR, histology, virus isolation and ELISA were all used to diagnose *Zaire ebolavirus* (Kobinger et al. 2011).

Measures to prevent infection of swine with *Reston ebolavirus* have not yet been established, but normal biosecurity measures, including quarantine of suspected animals and prevention of contact with bats and nonhuman primates, are appropriate. Eradication procedures, including quarantine, testing and culling, have been established in infected pigs and exports were suspended from affected areas (The Center for Food Security and Public Health 2009).

Case-fatality rates of EVD

The case-fatality rate of EVD has varied between outbreaks, ranging from 25–100%. Infections with *Zaire ebolavirus* have the highest case-fatality rates (60–100%) followed by those with *Sudan ebolavirus* (40–100%). On the basis of two outbreaks, case-fatality rates for *Bundibugyo ebolavirus* are estimated to be 25–55%. The current outbreak of *Ebolavirus* in Guinea and Liberia, with a strain that has yet to be named, has a case-fatality rate of 63.5% at the time of this report. The only reported person infected with *Côte d'Ivoire ebolavirus* became ill but survived. *Reston ebolavirus* is deemed non-pathogenic to humans, but laboratory tests have documented the occurrence of infection.

By comparison, case-fatality rates for *Marburg virus* in Africa are 70–85% but were much lower in the outbreak in Europe in 1967 which had a case-fatality rate of only 22%. This low case-fatality rate has led to speculation that proper intensive care with supportive therapy would increase the survival rate of infected patients. This hypothesis is hard to test because of austere field conditions and ethical dilemmas about not providing care to some patients (Feldmann and Geisbert 2011).

Prevalence and incidence data

Confirmed cases of EVD have been reported in Côte d'Ivoire, DRC, Gabon, Guinea, Liberia, the Republic of the Congo, Sudan and Uganda. No outbreaks of EVD in humans have ever been reported anywhere outside of Africa. *Reston ebolavirus* caused severe illness and death in monkeys imported to research facilities in Italy and the United States of America from the Philippines; during these outbreaks, several research workers became infected with the virus but did not become ill.

EVD typically appears in sporadic outbreaks, usually spread within a healthcare setting, a situation known as amplification. It is likely that sporadic, isolated cases occur as well but go unrecognized (CDC 2009a).

Therapy and vaccine research

Several therapies and vaccines are under investigation in rodent and nonhuman primate models. In view of the severe and rapid progression of EVD, no single therapy is likely to be sufficiently potent. Presently, the most promising strategy is to slow down virus replication and disease progression in order to allow the adaptive and innate immune responses to overcome infection (Feldmann and Geisbert 2011). A combination of therapies may be the best option (Table 5), something that makes application in rural African healthcare settings difficult where lack of cold storage, inadequately trained healthcare staff and inconsistent stocks of pharmaceuticals are routine occurrences.

Table 5. Treatment and prophylaxis of EVD

Approach	Success in animals	Issues and concerns
Treatment approach		
<i>Antibody therapy</i>	Efficacy in rodents but not in non-human primates	Escape mutants; genetic variability; antibody-dependent enhancement of infection
<i>Antisense oligonucleotides</i>		
Phosphorodiamidate morpholino oligonucleotides	Efficacy in rodents and non-human primates (latter prophylactic only)	Genetic variation; delivery
Small interfering RNAs	Efficacy in rodents and non-human primates	Genetic variation; delivery
<i>Inflammatory modulators</i>		
Type I interferons	Efficacy in rodents but not in non-human primates	Manipulation of immune system
S-adenosylhomocysteine hydrolase inhibitors	Efficacy in rodents but not in non-human primates	Manipulation of immune system
<i>Coagulation modulators</i>		
Heparin sulphate	Efficacy in humans questionable; not tested in animals	Manipulation of coagulation
Tissue factor pathway inhibitors	Not tested in rodents; partial protection in non-human primates	Manipulation of coagulation
Activated protein C	Not tested in rodents; partial protection in non-human primates	Manipulation of coagulation
Vaccination approach		
<i>Post-exposure vaccination</i>		
Vesicular stomatitis virus	Efficacy in rodents and non-human primates	Efficacy dependent on filovirus species and time of treatment start
<i>Post-exposure vaccination</i>		
Adenovirus type 5	Efficacy in rodents and non-human primates; one dose; clinical trials	Pre-existing immunity; high dose
Human parainfluenza virus type 3	Efficacy in rodents and non-human primates; two doses needed for non-human primates	Pre-existing immunity; safety (replication-competent)
Vesicular stomatitis virus	Efficacy in rodents and non-human primates; one dose	Safety (replication-competent)
Virus-like particles	Efficacy in rodents and non-human primates; three doses needed for non-human primates	Boost immunization needed; production
Recombinant <i>Ebolavirus</i> without VP35	Efficacy in rodents	Safety

Source: Feldmann and Geisbert (2011).

Exposure assessment

The exact origin, locations and natural habitat of *Ebolavirus* remain unknown. However, on the basis of available evidence and the nature of similar viruses, researchers believe that the virus is zoonotic with five of the six subtypes occurring in an animal host native to Africa. A similar host, most likely in the Philippines, is probably associated with *Reston ebolavirus*, which was isolated from infected cynomolgus monkeys that were imported to Italy and the United States of America from the Philippines. The virus is not known to be native to other continents (CDC 2009b).

Where information is available, it has frequently been observed that EVD index patients tend to be individuals whose work takes them into forests, caves or mines. In particular, several outbreaks have been traced back to hunters who had contact with infected wildlife. Furthermore, although it remains unclear what role direct human infection from bats might have in the initiation of outbreaks, studies of human behaviour as an indicator for *Ebolavirus* seropositivity in Cameroon have associated an increased risk of *Ebolavirus* infection with the consumption of bats and with logging activities. However, because for many index cases other causes (for example, contact with infected animal carcasses) have clearly contributed to infection, it is unclear to what extent these activities will actually have a role or if there are regional differences that affect local risk factors. Complicating our understanding of natural transmission are several seroepidemiological reports indicating high levels of seroprevalence in many areas of Africa in which notable disease is absent. Although these data are often used to suggest that *Ebolavirus* might be endemic in many areas of Africa, they could also suggest that, despite the usual association of *Ebolavirus* infection with high case-fatality rates, there might be co-circulation of antigenically cross-reactive but non-pathogenic *Ebolavirus* species, other related pathogens and/or mechanisms of resistance in humans that are currently not understood. It should be noted that earlier studies (in particular those before 1995) used approaches for serological detection that are subject to cross-reactivity, thus infection with *Ebolavirus* in these populations should be confirmed using newer and more reliable approaches before firm conclusions can be drawn (Groseth et al. 2007).

There are currently two theories to explain the transmission of *Ebolavirus* among susceptible hosts in nature. The first suggests that, as with many classical viral zoonotic pathogens, the virus has been maintained in endemic regions within a reservoir host and its episodic emergence has occurred owing to infrequent contact between the reservoir(s) and humans or nonhuman primates.

However, an alternative mechanism of spread has been proposed, whereby the virus has been more recently introduced into susceptible populations and spread in a wave-like fashion to each outbreak site through an undefined reservoir host.

Ebolavirus outbreaks are spreading into new regions either at the front of an advancing wave or in a series of jumps to each new location. With the evidence of viral genome stability within an individual outbreak coupled with the observation of multiple strains of *Ebolavirus* occurring in a single outbreak, as seen in the Gabon/Republic of Congo outbreak in 2001 with 2–3% variation, it seems likely that some outbreaks may have more diverse origins than originally thought. Likewise, a pattern of multiple, parallel introductions of *Reston ebolavirus* in swine in the Philippines in 2008 lends credence to the observation that multiple individual introductions of unique viruses originating from a viral reservoir may be an integral part of the viral transmission cycle (Barrette et al. 2011).

Similarly, some scientists believe that the genetic differences between *Ebolavirus* strains isolated from humans and apes during outbreaks suggest that apes are infected through multiple independent transmissions from the reservoir as opposed to a single outbreak directionally spreading through adjacent regions. Evidence of up to eight different strains circulating in humans and apes between 2001 and 2003 during outbreaks in Gabon and the Republic of Congo supports this theory. These were all associated with separate introductions into the human population following contact with infected animal carcasses and might, therefore, support the hypothesis of long-term maintenance and evolution of the virus in a reservoir species in an endemic area (Groseth et al. 2007).

Possible transmission routes if fruit bats are involved

There are some proposed mechanisms of *Ebolavirus* transmission to wildlife, domestic animals or humans from fruit bats:

- competition for fruit between bats and nonhuman primates leads to spatiotemporal clustering of frugivorous animals leading to an increased likelihood of spillover; or
- contact with infectious virus in saliva, faeces (guano), urine or birthing fluids such as blood and placental tissues (Rousseau 2010).

Given that the eight fruit bat species (*E. franqueti*, *E. helvum*, *E. gambianus*, *E. labiatus*, *E. wahlbergi*, *H. monstrosus*, *M. torquata* and *R. aegyptiacus*) assumed to be reservoirs of *Ebolavirus* are widely distributed across Uganda, the geographic range of these fruit bat species puts humans and susceptible wildlife and domestic livestock species at risk of direct contact with bats, their body fluids and shared fruit feeding sites. For instance, Kitaka mine in western Uganda is home to approximately 112,000 fruit bats. Research has shown that approximately 5000 bats could be infected at one time through horizontal transmission of *Ebolavirus* from pregnant female bats to their young (Groseth et al. 2007; Rousseau 2010). This large number of infected fruit bats in a geographically specific area places the livestock and people living in that area at risk of spillover through direct contact with dropped fruit and excretions from the large number of infected bats.

At present, the studies carried out on captured fruit bats or experimentally infected fruit bats have focused on serology and virus isolation from blood, tissues and body excretions. To date there have been no studies quantifying the risk of *Ebolavirus* infection from bat secretions and body fluids. It is notable that *Ebolavirus* was found to be shed in the faeces of experimentally infected fruit bats for up to three weeks (Swanepoel et al. 1996).

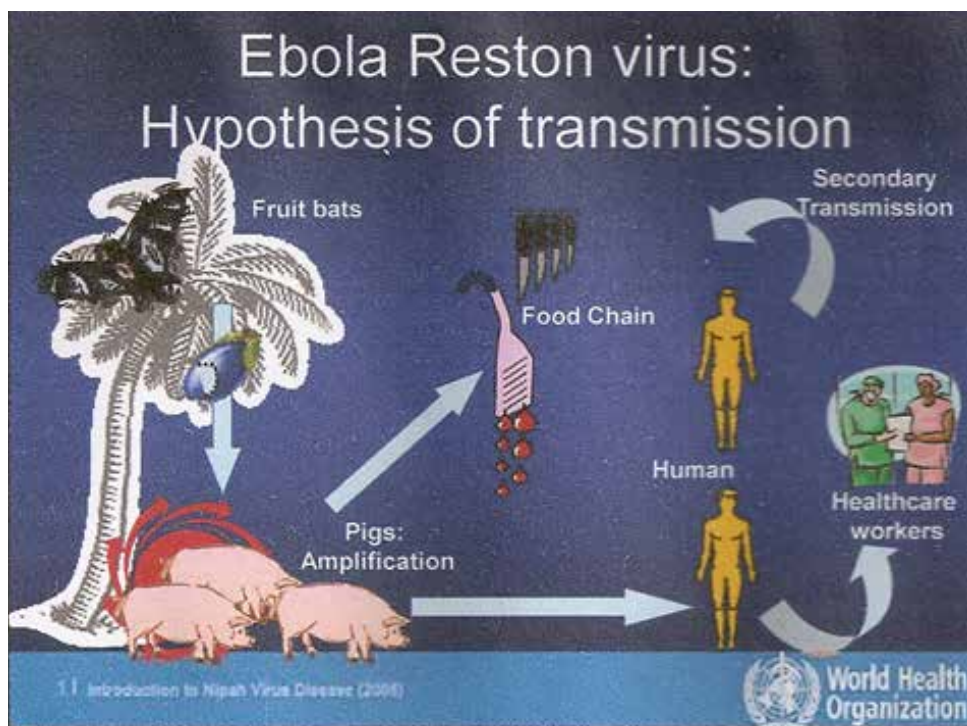
Considering the habitat overlap between pigs and bats, pigs may play a role as intermediary hosts, even amplifying the virus. Furthermore, assuming that bats are the reservoir for all species of *Ebolavirus*, and considering the long range migratory habits of some species, the area at risk for both human and animal infection could be vast. An example of this is the serologic evidence of *Ebolavirus* infection in bats caught in Ghana, hundreds of miles from the nearest reported human case (Bausch 2011).

Virus has been detected in human saliva, stool, semen, breast milk, tears, nasal blood and skin swabs during the acute phase of illness (Bausch et al. 2007). One could extrapolate that there is the possibility of the same being true in bat excretions and body fluids with virus titres high enough to be infective. This is an area of research that still needs elucidation.

Possible transmission routes if pigs are involved

During the *Reston ebolavirus* outbreak in pigs in the Philippines, the transmission cycle was hypothesized visually as shown in Figure 15.

Figure 15. Hypothesis of transmission of *Reston ebolavirus*.



Source: Rousseau (2010).

If pigs are involved in the transmission of *Ebolavirus*, possible routes include the following:

1. Direct contact with infected pigs by humans through daily care, butchering or hunting. Also, sick pigs are typically the first to be sold by farmers in Uganda (C. Masembe, personal communication, 18 April 2013). Additionally, rumours of outbreaks in communities cause pig farmers to sell off their stock. Both of these practices in Uganda increase the risk of spreading *Ebolavirus* to humans and other pig farms. In an ongoing African swine fever (ASF) project at Makerere University, it was shown that sick pigs and contact pigs were sold to other farmers, some of them transported 500 kilometres over several district borders within Uganda (C. Masembe, personal communication, 18 April 2013). The chance of these transported infected pigs and the pigs they had come in contact with expanding the geographic range of *Ebolavirus* outbreaks or creating secondary outbreaks would be quite high, given the large distance over which pigs are transported in Uganda.
2. Spread between wild and domestic pigs, potentially amplifying *Ebolavirus*. Uganda is the natural habitat for several widespread wild pig species: giant forest hogs (*Hylochoerus meinertzhageni*), Red River hogs (*Potamochoerus porcus*), bushpigs (*Potamochoerus larvatus*) and common warthogs (*Phacochoerus africanus*). Bushpigs in particular have a wide distribution throughout East Africa, where they live and move at the interface of national parks and farmland. This interaction increases pathogen sharing between wild and domestic pigs (Blomström et al. 2012). Personal communication with Charles Masembe confirms that there is phenotype evidence of breeding between wild and domestic pigs (C. Masembe, personal communication, 18 April 2013). Additionally, given the different production systems of pig rearing in Uganda, including tethering and free range, there is contact between wild and domestic pigs. While transmission dynamics of *Ebolavirus* have not been studied between wild and domestic pigs,

possible routes may be through direct contact, contact with urine and faeces in the environment and sharing of food via scavenging. Research on the spatial ecology of free-ranging domestic pigs in western Kenya revealed that the domestic pigs travelled an average of 4340 metres in a 12-hour period and had a mean home range of 10,343 square metres with pigs spending on average 47% of their time outside their homestead of origin (Thomas et al. 2013). There was a lack of significant difference between day and night time movements, indicating that the pigs were benefitting from a foraging strategy that involves both day and night scavenging. While the study tracked just 10 pigs, the information it revealed is helpful in highlighting the risk scavenging may play in *Ebolavirus* transmission. The study revealed that free-ranging domestic pigs travel large distances, both during the day and at night, and that almost half of the time is spent outside their homestead, extending the geographic range and habitats these pigs scavenge and travel in. This large range and lengthier scavenging could be risk factors for *Ebolavirus* infection.

3. The eight bat species presumed to be reservoirs of *Ebolavirus*—*E. franqueti*, *E. helvum*, *E. gambianus*, *E. labiatus*, *E. wahlbergi*, *H. monstrosus*, *M. torquata* and *R. aegyptiacus*—are all found in Uganda. Given the different preferred habitats of these bats and the increase in pig populations in Uganda over the past 30 years, increasing contact between pigs and fruit bats would be likely. In the districts where EVD outbreaks in Uganda have been recorded, the estimated pig populations are as shown in Table 6.

Table 6. Pig populations in the districts of reported EVD outbreaks in Uganda

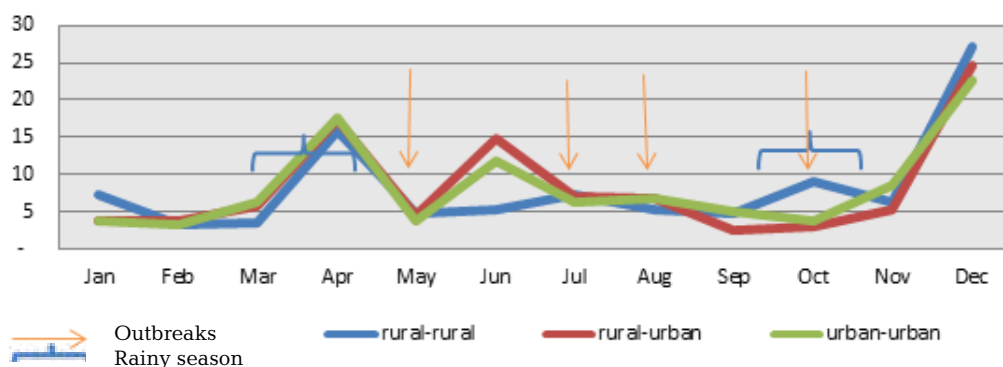
District	Households owning pigs	Average herd size	Pig population
Gulu	6200	2	26,570
Bundibugyo	3390	2	14,690
Luwero	22,850	2	59,040
Kibaale	53,360	2	153,510 (highest in Western region)

Source: Uganda Bureau of Statistics (2008).

The rising demand for pork in Uganda has sparked a massive expansion of intensive pig production in the country. Pigs are preferred to other livestock species due to their relatively rapid growth rate, large litter sizes and potential to provide financial returns over a relatively short time. This intensification of pig production increases pig-human contact and when added to the poor pig husbandry practices rampant throughout Uganda, potential public health consequences ensue, like pig-to-human *Ebolavirus* transmission.

4. Aerosol transmission between domestic pigs, between pigs and humans and between wild and domestic pigs cannot be overlooked. Experimentally infected pigs spread *Ebolavirus* to naïve pigs presumably through aerosols from the oronasal mucosa, which were found to have high titres of *Ebolavirus* (Kobinger et al. 2011). This study was interesting in that the contact pigs that became infected had a less severe disease course than those that had been experimentally infected. The risk of aerosol transmission needs further study, but the initial findings support the possibility of aerosol transmission of *Ebolavirus* by pigs.

Given that there are a number of human cases where the source of infection was unknown, it was interesting to note that during an ILRI-led assessment of Uganda smallholder pig value chains, the Safe Food, Fair Food project observed that producers and consumers ate pork especially during Easter and Christmas. It is typical for meat to be consumed on special occasions in Uganda. Overlaying outbreaks of *Ebolavirus* in Uganda with seasonal pork consumption patterns shows outbreaks near peak pork consumption periods, where increased handling, slaughter and transporting of pigs would happen (Figure 16).

Figure 16. Seasonal pork consumption patterns overlaid with *Ebolavirus* outbreaks in Uganda.

Source: Roesel and Carter (2013).

Outlining EVD outbreaks with their proximity to public holidays shows some association, given an incubation period of 2–21 days for infected patients to become symptomatic. This may be purely coincidental but it is worth noting (Table 7).

Table 7. Date of first suspected EVD cases and proximity to national holidays

Date of first suspected case	Location	Holiday	Incubation period
30 Aug 2000	Gulu	19 Aug: Eid ul Fitr (End of Ramadan)	11 days
6 May 2011	Luwero	1 May: Labour Day	5 days
Beginning of July 2012	Kibaale	3 June: Martyrs' Day 9 June: National Heroes' Day	2–3 weeks
25 Oct 2012	Luwero	9 Oct: Independence Day	16 days

Research to understand transmission dynamics of ASF in Uganda highlighted the role of the sale of sick pigs and the sale and consumption of pork from the dead pigs in spreading and extending an outbreak of ASF in Gulu (Tejler 2012). This outbreak of ASF happened around Independence Day, a national holiday during which meat is typically consumed. In addition, the research found that many of the pigs that died as a result of the ASF outbreak were consumed either on the farm or sold to the butcher in the local community. Both the practice of eating pigs that have died of unknown causes and the sale of sick pigs would spread and extend an outbreak of *Ebolavirus* in pigs and increase the risk of spillover into humans.

Most pig farmers sell their pigs live, using the money from the sale to cater for family needs and purchasing a kilogram of pork for their own consumption (Roesel and Carter 2013). Given that pork is a luxury item consumed on special occasions like public holidays, the risk of *Ebolavirus* infection from pigs to humans may be seasonal, linked with periods of greater pork consumption and hence live pig sales and movement. The highest risk is at farm level via direct contact with infected body fluids and during slaughter, where contact with blood, internal organs and other body fluids is a part of the process. At the household consumption level, the risk of *Ebolavirus* infection is most likely only if the raw pork is handled in preparation for cooking. Eating of processed pork does not pose a significant risk at present, based on current knowledge of *Ebolavirus* stability and pork cooking and preservation techniques.

Human-to-human transmission

Transmission from one person to another occurs by direct contact with infected body fluids such as blood, sweat, saliva, semen, vaginal fluids, urine and sputum or through direct inoculation by contaminated instruments such as needles, pins and razor blades. Nosocomial transmission through contaminated needles and syringes has been documented (Lamunu et al. 2004). Large outbreaks of EVD are usually driven by person-to-person transmission with caregivers both at home and in hospital at particular risk (Bausch et al. 2007).

Contact with body fluids, direct physical contact with an infected person and touching the body of an infected deceased person were practices of patients who became infected during the 2000 Gulu outbreak. In addition, indirect transmission from sleeping on the same mat, participating in ritual hand washing during the funeral ceremony and sharing a communal meal during the funeral service were significantly associated with disease. Risk tended to increase with an increasing number of different direct contacts. The risk of infection was higher among persons who were exposed through two or three different types of direct contact compared to those who had no direct contact (Francesconi et al. 2003).

In a different study carried out during the Gulu outbreak, the three most important means of transmission were identified as attending the funerals of presumptive EVD case patients where ritual contacts with the deceased occurred, and intrafamilial or nosocomial transmission (CDC 2001).

Gulu outbreak: During the 2000 Gulu outbreak, secondary outbreaks occurred in Masindi and Mbarara districts from infected individuals traveling from Gulu. A woman who had been treated at St. Mary's Hospital Lacor in Gulu for an unrelated chronic condition by a nurse, who later died of EVD, left the hospital and returned to her home in Masindi District (ProMED-mail 2000). During this secondary outbreak in Masindi, the index case patient became the origin of transmission within her own extended family (18 further cases), from index family members to Masindi healthcare workers (six cases) and from Masindi healthcare workers to their household contacts (one case). Because of multiple simultaneous contacts, transmission chains within the index family could not be established but this intrafamilial transmission is consistent with human-to-human transmission of *Ebolavirus*. It was also confirmed that two family members had been buried before the EVD outbreak in Masindi. Figure 17 shows the EVD isolation ward in Lacor Hospital.

Figure 17. EVD isolation ward, Lacor Hospital, Gulu.



Photo courtesy of www.nydailynews.com.

Breaches in barrier nursing by the nursing staff resulted in six of the occupational cases among the Masindi healthcare workers. The household contact of the Masindi healthcare worker was a two-year-old child who became infected after close contact with its hospitalized and infected mother (Borchert et al. 2011). This secondary outbreak confirmed the typical transmission dynamics in humans: nosocomial and intrafamilial.

The secondary outbreak in Mbarara was started by an infected soldier being transferred from Gulu to Mbarara. This secondary outbreak ended rather quickly with five cases and four deaths. The details of these cases are not known. Given the stigma in Uganda associated with EVD, protecting patients' privacy, including their identification, is understandable.

Survivors... in their own words

'People still shun me. I feel stigmatized. I have failed to resume my business.' (Mugerwa and Kalungi 2012)

'Whenever I go to buy goods, people run away from me.' (Mugerwa and Ssenkibirwa 2012)

'Neighbours have shunned my house... When I send a 'boda boda' (motorcycle taxi) to buy for me cement or any other materials, he doesn't return. No one is willing to give me a lift. I feel troubled.' (Mugerwa 2012a).

A follow-up of EVD patients seven years after the 2000 Gulu outbreak found that several still complained of chronic conditions such as headache, chest pain, problems with eyesight, pain in joints and other body parts, general body weakness, swelling in the legs and inability to do any heavy lifting (Ocowun and Wendo 2007). Survivors of the Bundibugyo outbreak also confirmed weakened hearing and vision (Croome 2011).

Bundibugyo outbreak: The Bundibugyo outbreak in 2007 was amplified by nosocomial transmission. Five healthcare workers who treated an EVD patient were infected and died. While early reports claimed that the initial cases had eaten a dead goat, the story later changed, confirming they had eaten a monkey (Butagira et al. 2007b). It should be noted that the hospital had no isolation ward or protective gear for this initial EVD patient (ProMED-mail 2007).

In an effort to avert the spread of *Ebolavirus* from Bundibugyo to other districts, many different measures were taken. In Fort Portal District, about 45 minutes from Bundibugyo, hotels were advised not to provide hand towels for drying over fear that the virus could be spread on these towels. In Hoima District, all visitors from Bundibugyo District were stopped. Additionally, oil workers at the Kingfisher oil site, a large oil well in Uganda managed by Heritage Oil and Gas Company at the time, were sensitized about the risks of contracting EVD. Figure 18 shows a member of the EVD sensitization team at work.

Figure 18. EVD sensitization team.



Photo courtesy of www.newvision.co.ug.

Two non-governmental organizations, World Wildlife Fund and Save the Children, suspended their operations and withdrew all of their personnel from Kasese and Bundibugyo. Furthermore, in Kasese District, which borders Bundibugyo District, the selling and drinking of 'mulwa', a drink brewed from millet, was banned for fear that sharing the straw could spread the virus. All public places and bars selling mulwa were closed. The transport of smoked fish from Bundibugyo to Kasese was halted because, according to the Kasese District vice-chairperson, 'the smoked fish business could contribute to the escalation of the disease'. Finally in Kibaale District, which shares a border with Bundibugyo District along Lake Albert, the local government banned all intra-district transactions with Bundibugyo, closed all businesses on the shore of Lake Victoria and had the police enforce the parking of all boats at landing sites, halting fishing activities and the transport of passengers from Congo and Bundibugyo (Kayizzi et al. 2007). An article published in a national newspaper during the Bundibugyo outbreak attempted to quell public panic over contracting *Ebolavirus* from handshakes, public pay phones, touching money, hugging, public toilets and spitting in public (Baguma 2007).

Students at Kyambogo University in Kampala caused such a scare on campus after returning from the funeral of a relative in western Uganda, that the Ministry of Health officials placed the students under medical observation (Butagira et al. 2007a).

In Hoima District, when a patient vomiting blood was admitted to Hoima Referral Hospital, medical workers scattered in disarray (Butagira et al. 2007c). The patient died a few hours later but not from EVD. The cause of this patient's death was never released.

The president of Uganda refused to shake hands with a visiting delegation from the DRC over fear of contracting EVD. He even urged Ugandans to avoid handshakes to 'minimize further dispersion of Ebola to the countryside' (Butagira and Matsiko 2007).

As the number of EVD cases declined in Bundibugyo, WHO reported on the measures that were most successful in control: safe burial of EVD patients, reducing the number of attendants providing food and medicines in the isolation ward, reducing visits to less than 10 minutes in the isolation ward and washing hands before entering and after leaving the isolation camp (Butagira et al. 2007c).

Many local people suspected that the EVD outbreak was started by infected monkeys, especially after dead monkey carcasses were reported to the Uganda Wildlife Authority in Rwenzori National Park in Bundibugyo District (Ainganiza 2008). These carcasses were not analysed for *Ebolavirus*.

Single case in Luwero: In the single case of EVD in Luwero in May 2011, a 12-year-old infected girl was transported by motorcycle taxi 35 kilometres to the hospital. At the time of transport she was experiencing vaginal bleeding and vomiting blood. However, despite infectious virus being found in blood during the acute phase of infection (Bausch et al. 2007), the driver of the motorcycle taxi and the girl's grandmother and father who helped transport her to the hospital did not become infected (Shoemaker et al. 2012). While anecdotal in evidence, this shows that infected individuals using public transport may not pose much of a risk of transmission, as long as passengers do not come in contact with body fluids.

Kibaale outbreak: The Kibaale outbreak in July–August 2012 was started by a three-month-old girl who was thought to have been bitten by a monkey. The infection spread when 15 people who attended her funeral later contracted the disease (ProMED-mail 2012b). As noted earlier, the communal rituals of burial in Uganda favour the spread of *Ebolavirus*.

One patient was infected when he sneaked into the isolation ward at Kagadi Hospital and stole a phone from an EVD patient (Mugerwa 2012b). This is not hard to imagine when a picture of the containment unit at Kagadi Hospital was released in the local newspapers (Figure 19).

Figure 19. Entrance to the containment unit at Kagadi Hospital, Kibaale District.



Photo courtesy of www.msf.org.

During the Kibaale outbreak, all public gatherings in the district were banned and markets, schools and other venues of social gatherings were closed from 28 July to 30 August (Kasooha 2012). Taxi operators noted a decline in passengers visiting the region, with few people boarding taxis to Kibaale District. Police intervention was also required to contain patients at Kagadi isolation ward over alleged neglect. The patients had been complaining of a shortage of food and clean water and that 'no doctor was attending to them' (Tumussime et al. 2012). Additionally, large groups were banned from visiting the Parliament in Kampala. Members of Parliament were also requested to suspend calling visits and arranging school visits in their constituencies. The Special Forces Group, the president's security group, was advised to avoid unnecessary movement to high-risk areas like Kibaale and neighbouring districts (Mugerwa et al. 2012). In a rather bizarre request, President Museveni even banned all physical contact after reports that the outbreak had spread to Kampala. He called on people 'not to shake hands to avoid the spread of the killer virus' and to 'avoid promiscuity because this sickness can also go through sex' (Agencies 2012). Finally, visits to prisons were suspended for two weeks in efforts to prevent infected people from coming into contact with prisoners and spreading *Ebolavirus* (Arinaitwe 2012).

A clinical officer who attended to the dead at Kagadi Hospital was transferred to Mulago Hospital in the capital city of Kampala (ProMED-mail 2012a). She died at Mulago Hospital. Doctors and nurses who attended to her while at Mulago Hospital were quarantined, creating mass panic that a secondary EVD outbreak would occur in Kampala. However, aside from the transferred clinical officer who died at Mulago Hospital, there were no additional EVD cases in Kampala.

Luwero outbreak: During the outbreak in November 2012, the initial case in Luwero was a motorcycle taxi driver. Presumably he would have had contact with many people due to the nature of his work. However, the only other confirmed cases originating from this index patient were two of his family members who assisted with his care once he became sick (ProMED-mail 2012c). This case also supports the role of intrafamilial transmission while also adding to evidence that sharing public transport with an infected person is not *per se* a high-risk practice. The risk is contact with infected body fluids. However, transporting infected patients would extend the geographic range of an EVD outbreak, complicating outbreak control.

Initial reports from the field communicated widespread panic among the health centres in Luwero, with patients abandoning the health units and medical personnel claiming they had not received protective gear (Wandera 2012).

During this outbreak, the burial team in Luwero narrowly escaped lynching by upset mourners who accused the burial team of violating Muslim burial rites (Ayebazibwe et al. 2012). According to Islamic burial rites, the body must be washed before burial. Figure 20 shows the burial team disinfecting the coffin of an EVD patient.

Figure 20. Burial team disinfecting the coffin of an EVD patient.



Photo courtesy of www.usatoday.net.

Traditional healers were also banned from admitting patients they did not know during the outbreak (Ayebazibwe et al. 2012). As the Ministry of Health relies on healthcare facilities to report suspected EVD cases, patients presenting to traditional healers would fall outside the surveillance activities established during EVD outbreaks.

A formal outbreak plan was announced by the Ministry of Health (Ayebazibwe 2012) and included the following measures:

1. A team of experts from the Ministry of Health, WHO, Médecins sans Frontières (MSF) and the African Field Epidemiology Network are already on the ground to support the response plan.
2. A national task force coordinated by the Ministry of Health has now refocused its attention to the Luwero epidemic since the Marburg situation in western Uganda is fully under control.
3. Plans are underway to create an isolation facility at Nyimbwa Health Centre IV or Bombo Military Hospital.
4. The Luwero District task force has been reactivated and is developing a response plan.
5. Active and sustained tracing and listing of all possible contacts that were exposed to the suspected and confirmed cases are in high gear. So far, a number of contacts have been recorded and are being closely monitored.
6. The isolation facility at Mulago National Referral Hospital, Kampala has already been reopened and has admitted two suspect cases.

7. The necessary drug supplies and logistics for case management have been mobilized. The national medical stores have been requested to send the necessary logistics.
8. MSF is already on the ground to evaluate and mobilize the necessary requirements for setting up an appropriate isolation centre at Nyimbwa Health Centre IV or Bombo Military Hospital.
9. The ministry has already dispatched personal protective equipment and body bags to Luwero District.
10. Collection of samples from suspect and probable cases has already commenced. Last evening, two samples were taken from suspect cases admitted at Mulago National Referral Hospital.

In addition to the above mentioned action items, the Ministry of Health created national hotlines for people to report any suspect cases (Businge 2012) and briefed communities about EVD via radio talk shows (Mugerwa and Ayebazibwe 2012).

National newspaper articles have mentioned the proximity of EVD outbreaks to the Congo and Sudan borders and to large settlements of Rwandese, Congolese and Sudanese refugees. Particular blame seems to be towards infected Congolese refugees bringing EVD into Uganda, followed by infected soldiers in Congo or Sudan crossing into Uganda for healthcare. During the Gulu outbreak, several Ugandan soldiers were among the fatalities, raising fears that returning Ugandan troops and their Congolese wives had brought EVD into Uganda (WHO 2000). There have been no firm links between infected soldiers, immigrants or refugees bringing EVD into Uganda. However, given the porous borders between DRC, Sudan and Uganda, the threat of EVD being introduced by soldiers, refugees and immigrants cannot be ruled out.

Other considerations

Uganda has several important factors that favour increasingly higher EVD incidence in humans. First, Uganda's population is projected to quadruple in the next 40 years (Population Reference Bureau 2011). The pressure on land to produce food for the growing population will place people into greater contact with wildlife, including nonhuman primates and fruit bats, and domestic livestock.

Eighty per cent of Ugandans are engaged in agriculture (Uganda Bureau of Statistics 2007). Agriculture is the backbone of the economy, providing livelihood to many of Uganda's citizens. The predicted population explosion will place pressure on livestock production to address infections that affect production outputs. A more thorough understanding of how *Ebolavirus* infection impacts the health and productivity of pigs, and hence the livelihoods of pig farmers, will help prioritize how limited resources can be efficiently expended to ensure human health, livelihoods, food security and food safety.

In Uganda, human health is also affected by the dual burden of disease, battling a host of infectious conditions and chronic health problems. National malnutrition rates are abysmal; 39.1% of children below five years of age are stunted for their age (WHO 2010). Human immunodeficiency virus (HIV) prevalence stands at 6.5% (WHO 2010) though rumours around the medical community indicate that the rate is higher and rising (Maseruka and Asiimwe 2011). Malaria accounts for 11% of adult deaths each year. Tuberculosis prevalence is around 3% (WHO 2010). There is also a growing incidence of diabetes (Basudde 2011). Malnutrition and other chronic health conditions weaken the body's immune system, making the host particularly less likely to mount and sustain an immune response. The role that malnutrition and co-infection play in *Ebolavirus* infection and disease outcome is yet to be determined. Suffice it to say that Uganda has a segment of the population that is immunologically vulnerable to infection.

Conclusions

EVD has a tendency to create public panic locally, nationally, regionally and globally, disproportionate to the actual risk of infection. Since research into the role pigs play in maintaining and transmitting *Ebolavirus* is limited, and there is no need for rash decisions like the Reuters article (Mogato 2009) detailing the slaughter of pigs in the Philippines after the discovery of *Reston ebolavirus*, general risk factors favouring *Ebolavirus* infection in pigs in Uganda will be outlined.

1. Pig production in Uganda has significantly increased over the last 30 years. A higher density of pigs may favour *Ebolavirus* transmission between pigs and from pigs to humans due to increased direct contact.
2. These higher pig populations raised under tethering or free-range systems create overlap of fruit bat habitats (and their dropped fruit, excrement, saliva and urine) where these pigs scavenge for food.
3. The risk to commercial pig farming is poorly understood. It may be possible that fruit bats roost in pig structures and direct contact with their excrement and urine are the biggest risk factors. The website of the International Union for Conservation of Nature notes that *M. torquata* is adaptable and has been found in city gardens. Also, given that many farmers in Uganda engage in mixed farming, it is possible that pig operations are more at risk from having fruit trees within a certain geographic distance and pigs scavenging fruits. Perhaps the cultivation of fruit trees in addition to pig keeping creates suitable habitats for fruit bats to forage and structures to roost in, fostering direct contact.
4. The human population is experiencing dramatic growth in Uganda. In addition to the increasing contact between humans and wildlife, livestock follow these people as walking bank accounts. As humans encroach into new habitats, so will their livestock. Some of these new environments will include bat and nonhuman primate habitats. This may cause the incidence of EVD outbreaks to increase as infected hosts and their body fluids come in direct contact with suitable hosts at a higher frequency. It should also be noted that as more humans infringe into nonhuman primate and bat habitats, the human need for protein may drive an increase in hunting and bushmeat consumption. Pigs may become infected from scavenging the waste products of bushmeat hunting.
5. At present, the risk to pork products is very poorly understood. It is based on anecdotal evidence at best. Given the link between hunting and consumption of bushmeat with *Ebolavirus* infection, there is a chance that slaughtering pigs and certain methods of handling raw pork may pose a greater risk of *Ebolavirus* infection and pork contamination.
6. The disease course and outcome of different strains of *Ebolavirus* infection in pigs is also in its research infancy. To date, there is no research into natural or experimental infection in pigs with *Bundibugyo ebolavirus* or *Sudan ebolavirus*. Even the *Zaire ebolavirus* study was done under experimental conditions, where the pigs were kept in conditions dissimilar to those in Uganda.
7. The role pigs may play in *Ebolavirus* transmission is poorly understood. The present data suggest they may be amplifying hosts, but likely not reservoir hosts. This suggests the conditions under which pigs become infected with *Ebolavirus* and the role they play in transmission may have many variables that will have to be elucidated.

Likewise, perhaps the increasing pig densities, coupled with higher human densities and both pigs and humans in contact with nonhuman primates and fruit bats, will create highly favourable conditions for *Ebolavirus* amplification and maintenance, increasing both the frequency and incidence of *Ebolavirus* outbreaks.

8. While the 31 pig samples taken as part of an ecological study after the Kibaale outbreak were all negative by serology (IgG ELISA), the number of samples was very small and not representative enough to draw any conclusions. Additionally, the pigs sampled were all healthy. Dr Jonathan Towner of CDC Atlanta noted in his presentation (Towner 2013) that in fruit bats, virus isolation was more successful from liver and spleen tissue samples than from blood. This is something to consider if a field survey of pigs is undertaken in future.

Recommendations

There are still many unknowns about *Ebolavirus* and its ecology and transmission. However, what is established is that Uganda has had EVD in the past, so the pathogen is present. It is also home to suitable hosts—humans, nonhuman primates, fruit bats and pigs. These hosts have a number of different habitats and situations that place them in direct contact with each other and their infected body fluids. Some of these hosts are increasing in density and numbers, namely, humans and pigs. Given ILRI's commitment to food safety and food security while sustaining the millions of poor farmers who rely on livestock for income and employment, listed below are recommendations for further work:

1. Since the reservoir of *Ebolavirus* still has not been conclusively identified, the role pigs play in *Ebolavirus* maintenance and transmission needs further research. To help identify what role pigs play in *Ebolavirus* maintenance and transmission, a prevalence study to determine the percentage of pigs infected with *Ebolavirus* in Uganda would be a good first step. This will also determine the geographical areas of greatest infection as well as whether breed or sex of the pigs impacts infection. Dr Charles Masembe of Makerere University has offered ILRI pig serum samples collected during his ASF research for analysis and it would be worth checking with the National Animal Disease and Diagnostic Centre in Entebbe about utilizing stored pig serum samples from their ongoing disease outbreak investigations. This data could be compiled into risk maps to identify *Ebolavirus* hotspots in Uganda.
2. Administration of a questionnaire to pig farmers to determine whether links between housing, surrounding farm habitat and contact with wildlife, bats, domestic pets or other livestock increase or decrease the risk of infection. This will help determine specific risk factors to infection in pigs as well as form the basis for best-bet interventions to prevent and control infection.
3. Further research is also needed to determine whether *Ebolavirus* is activated or reactivated during certain periods of a pig's life cycle.
4. At present, animal samples must be sent either to South Africa or Atlanta, Georgia in the United States of America for analysis. Building capacity in Uganda for laboratories to be able to diagnose and confirm *Ebolavirus* in domestic livestock and wildlife and to develop field diagnostic kits will speed up diagnosis and its confirmation in animals.
5. The Ministry of Health already has a system for reporting suspected human EVD cases. However the Ministry of Agriculture, Animal Industries and Fisheries has no mechanism to report suspected *Ebolavirus* cases in animals. In addition to creating a reporting system for the Ministry of Agriculture, there is a need to link the reporting systems of the two ministries to ensure timely outbreak response and containment and efficient use of personnel and resources.

6. Identify best-bet interventions and tools to train pig farmers in the prevention of *Ebolavirus* in their pigs, households and communities.
7. Given that *Ebolavirus* has many different suitable hosts, ILRI will need to partner with different organizations in human and wildlife health to stay informed of new developments in the understanding of *Ebolavirus* ecology that will inform better interventions in the pig value chain in Uganda.

References

- Agencies. 2012, July 30. Uganda warns on contact as Ebola reaches capital, Kampala. *Daily Monitor*. Retrieved from <http://www.monitor.co.ug>
- Ainganiza, S. 2008, January 5. Ebola scare as dead monkeys found in Bundibugyo. *Daily Monitor*. Retrieved from <http://www.monitor.co.ug>
- Allela, L., Boury, O., Pouillot, R., Délicat, A., Yaba, P., Kumulungui, B., Rouquet, P., Gonzalez, J.P. and Leroy, E.M. 2005. Ebola virus antibody prevalence in dogs and human risk. *Emerging Infectious Disease* 11(3):385–390.
- Arinaitwe, S. 2012, August 2. Prisons officials suspend visits over Ebola. *Daily Monitor*. Retrieved from <http://www.monitor.co.ug>
- Ayebazibwe, A. 2012, November 15. Ebola: Five admitted, 15 under surveillance. *Daily Monitor*. Retrieved from <http://www.monitor.co.ug>
- Ayebazibwe, A., Wandera, D. and Kaweesa, S. 2012, November 19. Ebola deaths at five as 40 are monitored. *Daily Monitor*. Retrieved from <http://www.monitor.co.ug>
- Baguma, A. 2007, December. Can you contract Ebola from a handshake, pay phone? *New Vision*. Retrieved from <http://www.newvision.co.ug>
- Barrette, R.W., Metwally, S.A., Rowland, J.M., Xu, L., Zaki, S.R., Nichol, S.T., Rollin, P.E., Towner, J.S., Shieh, W.J., Batten, B., Sealy, T.K., Carrillo, C., Moran, K.E., Bracht, A.J., Mayr, G.A., Sirios-Cruz, M., Catbagan, D.P., Lautner, E.A., Ksiazek, T.G., White, W.R. and McIntosh, M.T. 2009. Discovery of swine as a host for the Reston ebolavirus. *Science* 325(5937):204–206.
- Barrette, R.W., Xu, L., Rowland, J.M. and McIntosh, M.T. 2011. Current perspectives on the phylogeny of Filoviridae. *Infection, Genetics and Evolution* 11(7):1514–1519.
- Basudde, E. 2011, November 24. Ignorance increases rate of diabetes in Uganda—World Diabetes Day. *New Vision*. Retrieved from <http://www.newvision.co.ug>
- Bausch, D. 2011. Ebola virus as a foodborne pathogen? Cause for consideration, but not panic. *Journal of Infectious Diseases* 204(2):179–181.
- Bausch, D.G., Towner, J.S., Dowell, S.F., Kaducu, F., Lukwiya, M., Sanchez, A., Nichol, S.T., Ksiazek, T.G. and Rollin, P.E. 2007. Assessment of the risk of Ebola virus transmission from bodily fluids and fomites. *Journal of Infectious Diseases* 196(Supplement 2):S142–S147.
- Becker, S., Feldmann, H., Will, C. and Slenczka, W. 1992. Evidence for occurrence of filovirus antibodies in humans and imported monkeys: Do subclinical filovirus infections occur worldwide? *Medical Microbiology and Immunology* 181(1):43–55.
- Benda, P., Aulagnier, S., Hutson, A.M., Amr, Z.S., Kock, D., Sharifi, M., Karataş, A., Mickleburgh, S., Bergmans, W. and Howell, K. 2008. *Rousettus aegyptiacus*. (Available from <http://www.iucnredlist.org>) (Accessed on 10 April 2014).
- Bente, D., Gren, J., Strong, J.E. and Feldmann, H. 2009. Disease modeling for Ebola and Marburg viruses. *Disease Models and Mechanisms* 2(1–2):12–17.
- Blomström, A.L., Ståhl, K., Masembe, C., Okoth, E., Okurut, A.R., Atmnedi, P., Kemp, S., Bishop, R., Belák, S. and Berg, M. 2012. Viral metagenomic analysis of bushpigs (*Potamochoerus larvatus*) in Uganda identifies novel variants of Porcine parvovirus 4 and Torque teno sus virus 1 and 2. *Virology Journal* 9:192.

- Borchert, M., Mutyaba, I., van Kerkhove, M.D., Lutwama, J., Luwaga, H., Bisoborwa, G., Turyagaruka, J., Pirard, P., Ndayimirije, N., Roddy, P. and van Der Stuyft, P. 2011. Ebola haemorrhagic fever outbreak in Masindi District, Uganda: outbreak description and lessons learned. *BMC Infectious Diseases* 11:357.
- Bruce, J. and Brysiewicz, P. 2002. Ebola fever: The African emergency. *International Journal of Trauma Nursing* 8(2):36–41.
- Businge, C. 2012, July 31. Ebola outbreak: Hotlines out. *New Vision*. Retrieved from <http://www.newvision.co.ug>
- Butagira, T. and Matsiko, G. 2007, December 17. Museveni shuns handshakes with Congolese over Ebola. *Daily Monitor*. Retrieved from <http://www.monitor.co.ug>
- Butagira, T., Bogere, H. and Mugisa, J. 2007a, December 8. Nation on Ebola alert. *Daily Monitor*. Retrieved from <http://www.monitor.co.ug>
- Butagira, T., Bogere, H. and Mugisa, J. 2007b, December 13. Museveni orders probe into Ebola origin. *Daily Monitor*. Retrieved from <http://www.monitor.co.ug>
- Butagira, T., Bogere, H., Mugisa, J., Ssebuyira, M., Balyesima, A. and Tumushabe, A. 2007c, December 14. Ebola cases declining. *Daily Monitor*. Retrieved from <http://www.monitor.co.ug>
- CDC (Centers for Disease Control and Prevention). 2001. Outbreak of Ebola hemorrhagic fever Uganda, August 2000–January 2001. *Morbidity and Mortality Weekly Report* 50(5):73–77.
- CDC (Centers for Disease Control and Prevention). 2009a. Ebola hemorrhagic fever information packet. (Available from http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/Fact_Sheets/Ebola_Fact_Booklet.pdf) (Accessed on 1 April 2013).
- CDC (Centers for Disease Control and Prevention). 2009b. Questions and answers about Ebola-Reston virus in pigs, Philippines. (Available from <http://www.cdc.gov/ncidod/dvrd/spb/outbreaks/qaEbolaRestonPhilippines.htm>) (Accessed on 1 April 2013).
- CDC (Centers for Disease Control and Prevention). 2012a. Filovirus fact sheet. (Available from <http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/filoviruses.htm>) (Accessed on 1 April 2013).
- CDC (Centers for Disease Control and Prevention). 2012b. Cases of ebola hemorrhagic fever in Africa, 1976–2008. (Available from <http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/ebola/ebolamap.htm>) (Accessed on 1 April 2013).
- Croome, P. 2011, June 5. Is Ebola an emerging pandemic? *Daily Monitor*. Retrieved from <http://www.monitor.co.ug>
- Delgado, C.L. and Narrad, C. 2002. *Impact of changing market forces and policies on structural change in the livestock industries of selected fast-growing developing countries*. Rome, Italy: FAO.
- Delgado, C.L., Rosegrant, M.W. and Meijer, S. 2001. *Livestock to 2020: The revolution continues*. Annual meetings of the International Agricultural Trade Research Consortium, Auckland, New Zealand. pp. 18–19.
- Elliott, L.H., McCormick, J.B. and Johnson, K.M. 1982. Inactivation of Lassa, Marburg, and Ebola viruses by gamma irradiation. *Journal of Clinical Microbiology* 16(4):704–708.
- Evans, A.S. and Kaslow, R.A. 1997. *Viral infections of humans: Epidemiology and control*. New York, USA: Springer.
- FAO (Food and Agriculture Organization) and EMPRES (Emergency Prevention System). 2008. *Ebola-Reston virus in pigs*. (Available from http://www.fao.org/ag/againfo/programmes/en/empres/ebola_111208.html) (Accessed on 1 April 2013).
- Feldmann, H. and Geisbert, T.W. 2011. Ebola haemorrhagic fever. *Lancet* 377(9768):849–862.
- Feldmann, H., Wahl-Jensen, V., Jones, S.M. and Ströher, U. 2004. Ebola virus ecology: A continuing mystery. *Trends in Microbiology* 12(10):433–437.
- Francesconi, P., Yoti, Z., Declich, S., Onek, P.A., Fabiani, M., Olango, J., Andraghetti, R., Rollin, P.E., Opira, C., Greco, D. and Salmaso, S. 2003. Ebola hemorrhagic fever transmission and risk factors of contacts, Uganda. *Emerging Infectious Diseases* 9(11):1430–1437.
- Franz, D.R., Jahrling, P.B., McClain, D.J., Hoover, D.L., Byrne, W.R., Pavlin, J.A., Christopher, G.W., Cieslak, T.J., Friedlander, A.M. and Eitzen, E.M. 2001. Clinical recognition and management of patients exposed to biological warfare agents. *Clinics in Laboratory Medicine* 21(3):435–473.
- Gonzalez, J.P., Pourrut, X. and Leroy, E. 2007. Ebolavirus and other filoviruses. *Current Topics in Microbiology and Immunology* 315:363–387.

- Groseth, A., Feldmann, H. and Strong, J.E. 2007. The ecology of Ebola virus. *Trends in Microbiology* 15(9):408–416.
- Hayman, D.T., Yu, M., Cramer, G., Wang, L.F., Suu-Ire, R., Wood, J.L. and Cunningham, A.A. 2012. Ebola virus antibodies in fruit bats, Ghana, West Africa. *Emerging Infectious Diseases* 18(7):1207–1209.
- Johnson, E.D., Gonzalez, J.P. and Georges, A. 1993. Haemorrhagic fever virus activity in equatorial Africa: Distribution and prevalence of filovirus reactive antibody in the Central African Republic. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 87(5):530–535.
- Kasooha, I. 2012, August 30. Ebola: Kibaale public gatherings ban lifted. *New Vision*. Retrieved from <http://www.newvision.co.ug>
- Kayizzi, F., Kisakye, B., Kasooha, I. and Colombus, T. 2007, December 4. How districts are handling Ebola cases. *New Vision*. Retrieved from <http://www.newvision.co.ug>
- Kinsman, J. 2012. 'A time of fear': Local, national, and international responses to a large Ebola outbreak in Uganda. *Globalization and Health* 8:15.
- Kobinger, G.P., Leung, A., Neufeld, J., Richardson, J.S., Falzarano, D., Smith, G., Tierney, K., Patel, A. and Weingartl, H.M. 2011. Replication, pathogenicity, shedding, and transmission of Zaire ebolavirus in pigs. *Journal of Infectious Diseases* 204(2):200–208.
- Kortepeter, M.G., Bausch, D.G. and Bray, M. 2011. Basic clinical and laboratory features of filoviral hemorrhagic fever. *Journal of Infectious Diseases* 204(Supplement 3):S810–S816.
- Lahm, S.A., Kombila, M., Swanepoel, R. and Barnes, R.F.W. 2007. Morbidity and mortality of wild animals in relation to outbreaks of Ebola hemorrhagic fever in Gabon, 1994–2003. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 101(1):64–78.
- Lamunu, M., Lutwama, J.J., Kamugisha, J., Opio, A., Namboozee, J., Ndayimirije, N. and Okware, S. 2004. Containing a haemorrhagic fever epidemic: The Ebola experience in Uganda (October 2000–January 2001). *International Journal of Infectious Diseases* 8(1):27–37.
- Leirs, H., Mills, J.N., Krebs, J.W., Childs, J.E., Akaibe, D., Woollen, N., Ludwig, G., Peters, C.J. and Ksiazek, T.G. 1999. Search for the Ebola virus reservoir in Kikwit, Democratic Republic of the Congo: Reflections on a vertebrate collection. *Journal of Infectious Diseases* 179(Supplement 1):S155–S163.
- Leroy, E.M., Baize, S., Debre, P., Lansoud-Soukate, J. and Mavoungou, E. 2001. Early immune responses accompanying human asymptomatic Ebola infections. *Clinical and Experimental Immunology* 124(3):453–460.
- Leroy, E.M., Baize, S., Volchkov, V.E., Fisher-Hoch, S.P., Georges-Courbot, M.C., Lansoud-Soukate, J., Capron, M., Debré, P., McCormick, J.B. and Georges, A.J. 2000. Human asymptomatic Ebola infection and strong inflammatory response. *Lancet* 355(9222):2210–2215.
- Leroy, E.M., Epelboin, A., Mondonge, V., Pourrut, X., Gonzalez, J.P., Muyembe-Tamfum, J.J. and Formenty, P. 2009. Human Ebola outbreak resulting from direct exposure to fruit bats in Luebo, Democratic Republic of Congo, 2007. *Vector-Borne and Zoonotic Diseases* 9(6):723–728.
- Leroy, E.M., Kumulungui, B., Pourrut, X., Rouquet, P., Hassanin, A., Yaba, P., Délicat, A., Paweska, J.T., Gonzalez, J.-P. and Swanepoel, R. 2005. Fruit bats as reservoirs of Ebola virus. *Nature* 438(7068):575–576.
- Leroy, E.M., Rouquet, P., Formenty, P., Souquière, S., Kilbourne, A., Froment, J.M., Bermejo, M., Smit, S., Karesh, W., Swanepoel, R., Zaki, S.R. and Rollin, P. 2004. Multiple Ebola virus transmission events and rapid decline of central African wildlife. *Science* 303(5656):387–390.
- Loutfy, M.R., Assmar, M., Hay Burgess, D.C. and Kain, K.C. 1998. Effects of viral hemorrhagic fever inactivation methods on the performance of rapid diagnostic tests for *Plasmodium falciparum*. *Journal of Infectious Diseases* 178(6):1852–1855.
- Maseruka, J. and Asiimwe, B. November 4, 2011. Rising numbers of new HIV cases worry experts. *New Vision*. Retrieved from <http://www.newvision.co.ug>
- McGrath, M. 2012. Growing concerns over 'in the air' Ebola transmission. BBC News. (Available from <http://www.bbc.co.uk/news/science-environment-20341423>) (Accessed on 1 April 2013).
- Mickleburgh, S., Hutson, A.M. and Bergmans, W. 2008a. *Epomophorus labiatus*. (Available from <http://www.iucnredlist.org>) (Accessed on 10 April 2014).
- Mickleburgh, S., Hutson, A.M. and Bergmans, W. 2008b. *Epomophorus wahlbergi*. (Available from <http://www.iucnredlist.org>) (Accessed on 10 April 2014).

- Mickleburgh, S., Hutson, A.M., Bergmans, W., Fahr, J. and Juste, J. 2008c. *Epomops franqueti*. (Available from <http://www.iucnredlist.org>) (Accessed on 10 April 2014).
- Mickleburgh, S., Hutson, A.M., Bergmans, W., Fahr, J. and Juste, J. 2008d. *Hypsignathus monstrosus*. (Available from <http://www.iucnredlist.org>) (Accessed on 10 April 2014).
- Mickleburgh, S., Hutson, A.M., Bergmans, W., Fahr, J. and Juste, J. 2008e. *Myonycteris torquata*. (Available at <http://www.iucnredlist.org>) (Accessed on 10 April 2014).
- Mickleburgh, S., Hutson, A.M. and Bergmans, W. 2008f. *Epomophorus gambianus*. (Available from <http://www.iucnredlist.org>) (Accessed on 10 April 2014).
- Mickleburgh, S., Hutson, A.M., Bergmans, W., Fahr, J. and Racey, P.A. 2013. *Eidolon helvum*. (Available from <http://www.iucnredlist.org>) (Accessed on 10 April 2014).
- Mitchell, S.W. and McCormick, J.B. 1984. Physicochemical inactivation of Lassa, Ebola, and Marburg viruses and effect on clinical laboratory analyses. *Journal of Clinical Microbiology* 20(3):486–489.
- Mogato, M. 2009. Manilla to slaughter 6,000 pigs to stop Ebola spread. (Available from <http://www.reuters.com/article/2009/02/23/idUSMAN392763>) (Accessed on 14 February 2014).
- Mugerwa, F. 2012a, August 8. Ebola claims nurse in line of duty. *Daily Monitor*. Retrieved from <http://www.monitor.co.ug>
- Mugerwa, F. 2012b, August 26. Phone thief contracts deadly Ebola. *Daily Monitor*. Retrieved from <http://www.monitor.co.ug>
- Mugerwa, F. and Ayebazibwe, A. 2012, July 30. Suspected Ebola carriers hunted. *Daily Monitor*. Retrieved from <http://www.monitor.co.ug>
- Mugerwa, F. and Kalungi, N. 2012, August 18. Ebola patients bounce back to good health but suffer stigma. *Daily Monitor*. Retrieved from <http://www.monitor.co.ug>
- Mugerwa, F. and Ssenkabirwa, A.-M. 2012, September 28. Muslims barred from travelling over Ebola. *Daily Monitor*. Retrieved from <http://www.monitor.co.ug>
- Mugerwa, F., Muzoora, G., Ndyasiima, E., Naturinda, S., Ssebuyira, M., Nalubega, F. and Butagira, T. 2012, August 30. Mulago on alert as Ebola cases hit 30. *Daily Monitor*. Retrieved from <http://www.monitor.co.ug>
- Mwanatambwe, M., Yamada, N., Arai, S., Shimizu-Suganuma, M., Shichinohe, K. and Asano, G. 2001. Ebola hemorrhagic fever (EHF): Mechanism of transmission and pathogenicity. *Journal of Nippon Medical School* 68(5): 370–375.
- Ocowun, C. and Wendo, C. 2007, December 14. Ebola survivors still sick after seven years. *New Vision*. Retrieved from <http://www.newvision.co.ug>
- Oketch, B. 2012, August 4. Surviving the deadly Ebola: A joyous tale shrouded in painful memories. *Daily Monitor*. Retrieved from <http://www.monitor.co.ug>
- Population Reference Bureau. 2011. 2011 population data sheet. (Available from http://www.prb.org/pdf1/2011population-data-sheet_eng.pdf) (Accessed on 29 March 2013).
- Pourrut, X., Souris, M., Towner, J.S., Rollin, P.E., Nichol, S.T., Gonzalez, J.P. and Leroy, E. 2009. Large serological survey showing cocirculation of Ebola and Marburg viruses in Gabonese bat populations, and a high seroprevalence of both viruses in *Rousettus aegyptiacus*. *BMC Infectious Diseases* 9:159.
- ProMED-mail. 2000. Ebola hemorrhagic fever—Uganda: Archive number: 20001016.1769. (Available from <http://www.promedmail.com>) (Accessed on 14 February 2014).
- ProMED-mail. 2007. Ebola hemorrhagic fever—Uganda (06): (Bundibugyo): Archive Number: 20071206.3933. (Available from <http://www.promedmail.com>) (Accessed on 14 February 2014).
- ProMED-mail. 2012a. Ebola hemorrhagic fever—Uganda (03): (KI) update: Archive Number: 20120730.1220418. (Available at <http://www.promedmail.com>) (Accessed on 14 February 2014).
- ProMED-mail. 2012b. Ebola hemorrhagic fever—Uganda (09): (KI): Archive Number: 20120803.1227357. (Available from <http://www.promedmail.com>) (Accessed on 14 February 2014).
- ProMED-mail. 2012c. Ebola virus disease—Uganda (27): (LO) family deaths: Archive Number: 20121116.1411532. (Available from <http://www.promedmail.com>) (Accessed on 14 February 2014).
- ProMED-mail. 2014. Ebola virus disease—West Africa (19): New Strain, Guinea new cases, Mali. (Available from <http://www.promedmail.com>) (Accessed on 18 April 2014).

- Public Health Agency of Canada. 2010. Ebola virus: Pathogen safety data sheet—Infectious substances. (Available from <http://www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/ebola-eng.php>) (Accessed on 10 April 2014).
- Reed, Z. 2012. A historical perspective and review of the evidence to support fruit bats as the natural reservoir for Ebola viruses. MPH thesis. Georgia, USA: Georgia State University.
- Reiter, P., Turell, M., Coleman, R., Miller, B., Maupin, G., Liz, J., Kuehne, A., Barth, J., Geisbert, J., Dohm, D., Glick, J., Pecor, J., Robbins, R., Jahrling, P., Peters, C. and Ksiazek, T. 1999. Field investigations of an outbreak of Ebola hemorrhagic fever, Kikwit, Democratic Republic of Congo, 1995: Arthropod studies. *Journal of Infectious Diseases* 179(Supplement 1):S148–S154.
- Roels, T.H., Bloom, A.S., Buffington, J., Muhungu, G.L., Mac Kenzie, W.R., Khan, A.S., Ndambi, R., Noah, D.L., Rolka, H.R., Peters, C.J. and Ksiazek, T.G. 1999. Ebola hemorrhagic fever, Kikwit, Democratic Republic of the Congo, 1995: Risk factors for patients without a reported exposure. *Journal of Infectious Diseases* 179(Supplement 1):S92–S97.
- Roesel, K. and Carter, N. 2013. Safe Food, Fair Food in Uganda: PigRisk project outcome mapping. (Available from <http://www.slideshare.net/ILRI/safe-food-fair-food-in-uganda>) (Accessed on 1 April 2014).
- Rousseau, D. 2010. *Ebola and Marburg viruses human-animal interfaces*. Second FAO-OIE-WHO consultation: Influenza and other emerging zoonotic diseases. Rome, Italy: FAO.
- Shoemaker, T. 2013. *Dissemination of VHF ecological investigation findings from Kibaale Ebola outbreak*. Kampala, Uganda: CDC.
- Shoemaker, T., MacNeil, A., Balinandi, S., Campbell, S., Wamala, J.F., McMullan, L.K., Downing, R., Lutwama, J., Mbidde, E., Ströher, U., Rollin, P.E. and Nichol, S.T. 2012. Reemerging Sudan Ebola virus disease in Uganda, 2011. *Emerging Infectious Diseases* 18(9):1480–1483.
- Swanepoel, R., Leman, P.A., Burt, F.J., Zachariades, N.A., Braack, L.E.O., Ksiazek, T.G., Rollin, P.E., Zaki, S.R. and Peters, C.J. 1996. Experimental inoculation of plants and animals with Ebola virus. *Emerging Infectious Diseases* 2(4):321–325.
- Tejler, E. 2012. Outbreaks of African swine fever in domestic pigs in Gulu district, Uganda. Veterinary Medicine thesis. Uppsala, Sweden: Swedish University of Agricultural Sciences.
- The Center for Food Security and Public Health. 2009. Viral hemorrhagic fevers—Ebola and Marburg. (Available from http://www.cfsph.iastate.edu/Factsheets/pdfs/viral_hemorrhagic_fever_filovirus.pdf) (Accessed on 14 April 2013).
- Thomas, L.F., de Glanville, W.A., Cook, E.A. and Fèvre, E.M. 2013. The spatial ecology of free-ranging domestic pigs (*Sus scrofa*) in western Kenya. *BMC Veterinary Research* 9(1):46.
- Towner, J. 2013. *Dissemination of VHF ecological investigation findings from Kibaale Ebola outbreak*. Kampala, Uganda: CDC.
- Tumussime, R., Mugerwa, F., Katusabe, R and Ayebazibwe, A. 2012, 2 August. Two new Ebola deaths as patients go on strike. *Daily Monitor*. Retrieved from <http://www.monitor.co.ug>
- Uganda Bureau of Statistics. 2007. *Uganda national household survey 2005/2006*. Kampala, Uganda: Uganda Bureau of Statistics.
- Uganda Bureau of Statistics. 2008. *National livestock census 2008*. Kampala, Uganda: Uganda Bureau of Statistics.
- Uganda Wildlife Authority and Tushabe, P. 2013. *Uganda wildlife visitor statistics 2005–2012*. Kampala, Uganda: Uganda Wildlife Authority.
- Wandera, D. 2012, November 18. Two more Ebola cases confirmed. *Daily Monitor*. Retrieved from <http://www.monitor.co.ug>
- WHO (World Health Organization). 2000. Ebola, Uganda. *Weekly Epidemiological Record* 75(42):337–338.
- WHO (World Health Organization). 2010. Uganda: Health profile. (Available from <http://www.who.int/gho/countries/uga.pdf>) (Accessed on 14 April 2013).
- WHO (World Health Organization), CDC (Centers for Disease Control and Prevention) and United States Department of Health and Human Services. 1998. *Infection control for viral haemorrhagic fevers in the African health care setting*. Geneva, Switzerland: WHO.

ISBN 92-9146-350-7



The International Livestock Research Institute (ILRI) works to improve food security and reduce poverty in developing countries through research for better and more sustainable use of livestock. ILRI is a member of the CGIAR Consortium, a global research partnership of 15 centres working with many partners for a food-secure future. ILRI has two main campuses in East Africa and other hubs in East, West and southern Africa and South, Southeast and East Asia. ilri.org



CGIAR is a global agricultural research partnership for a food-secure future. Its science is carried out by 15 research centres that are members of the CGIAR Consortium in collaboration with hundreds of partner organizations. cgiar.org