No Time to Lose
Lessons from Ebola & Aids

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No future in infectious diseases!? (1974)
Preliminary Communications

ISOLATION AND PARTIAL CHARACTERISATION OF
A NEW VIRUS CAUSING ACUTE HÄMORRHAGIC FEVER IN ZAIRE

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An outbreak of hæmorrhagic fever with an exceptionally high mortality-rate occurred in southern Sudan and northern Zaire with peak case-rates in September, 1976. A W.H.O. International Commission operated in Sudan and Zaire from October onward.\textsuperscript{1,2} Blood and tissue specimens from persons with hæmorrhagic disease were sent to laboratories in Belgium and England, and findings from these laboratories appear in the accompanying reports.\textsuperscript{3,4} While these specimens were being studied, Mr E. T. W. Bowen (Microbiological Research Establishment, Porton Down) sent an aliquot of an acute blood specimen from a patient in Zaire (no. 718, patient M.E.) to the Center for Disease Control, Atlanta, for additional study.

This specimen, and all subsequent acute specimens, were inoculated into Vero (African green monkey) cells. Three days later a distinct cytopathic change (focal rounding and refractility) was evident, and an aliquot of supernatant fluid was removed for negative contrast electron microscopy.
The Ebola River
SCHEMATIC OF ONSET AND DURATION OF PREDOMINANT CLINICAL FEATURES OF PATIENTS DYING WITH AFRICAN HEMORRHAGIC FEVER IN ZAIRE - 1976

- fever
- headache
- myalgia
- abdominal pain
- arthritis
- sore throat
- nausea
- conjunctivitis
- vomiting/diarrhea
- bleeding

Day of illness: 0, 1, 2, 3, 4, 5, 6, 7, 8
Fig. 2 Cases of Ebola Hemorrhagic Fever, by day of onset, Equateur Region, Zaire, Africa, Sept. 1 - Oct. 30, 1976
Age and sex distribution of cases, Zaire 1976

My lessons from Ebola, 1976

• Anything can happen!
• Time, place, person
• Poverty driving disease
• The power and challenges of international collaboration
• EIS: US field epidemiology
• Good intentions can be dangerous
• This is what I want to do!
Ebola haemorrhagic fever in Zaire, 1976

Report of an International Commission

Between 1 September and 24 October 1976, 318 cases of acute viral haemorrhagic fever occurred in northern Zaire. The outbreak was centred in the Bumba Zone of the Equateur Region and most of the cases were recorded within a radius of 70 km of Yambuku, although a few patients sought medical attention in Bumba, Abumombazi, and the capital city of Kinshasa, where individual secondary and tertiary cases occurred. There were 280 deaths, and only 38 serologically confirmed survivors.

The index case in this outbreak had onset of symptoms on 1 September 1976, five days after receiving an injection of chloroquine for presumptive malaria at the outpatient clinic at Yambuku Mission Hospital (YMH). He had a clinical remission of his malaria symptoms. Within one week several other persons who had received injections at YMH also suffered from Ebola haemorrhagic fever, and almost all subsequent cases had either received injections at the hospital or had had close contact with another case. Most of these occurred during the first four weeks of the epidemic, after which time the hospital was closed, 11 of the 17 staff members having died of the disease. All ages and both sexes were affected, but women 15–25 years of age had the highest incidence of disease, a phenomenon strongly related to attendance at prenatal and outpatient clinics at the hospital where they received injections. The overall secondary attack rate was about 5%, although it ranged to 20%, among close relatives such as spouses, parent or child, and brother or sister.

Active surveillance disclosed that cases occurred in 35 of some 550 villages which were examined house-by-house. The disease was hitherto unknown to the people of the affected region. Intensive search for cases in the area of north-eastern Zaire between the Bumba Zone and the Sudan frontier near Nzara and Maridi failed to detect definite evidence of a link between an epidemic of the disease in that country and the outbreak near Bumba. Nevertheless it was established that people can and do make the trip between Nzara and Bumba in not more than four days: thus it was regarded as quite possible that an infected person had travelled from Sudan to Yambuku and transferred the virus to a needle of the hospital while receiving an injection at the outpatient clinic.

Both the incubation period and the duration of the clinical disease averaged about one week. After 3–4 days of non-specific symptoms and signs, patients typically experienced progressively severe sore throat, developed a maculopapular rash, had intractable abdominal pain, and began to bleed from multiple sites, principally the gastrointestinal tract. Although laboratory determinations were limited and not conclusive, it was concluded that pathogenesis of the disease included non-icteric hepatitis and possibly acute pancreatitis as well as disseminated intravascular coagulation.

This syndrome was caused by a virus morphologically similar to Marburg virus, but immunologically distinct. It was named Ebola virus. The agent was isolated from the blood of 8 of 10 suspected cases using vero cell cultures. Titration of serial specimens obtained from one patient disclosed persistent viremia of 10^6–10^7 infectious units from the third day of illness until death on the eighth day. Ebola virus particles were found in formalin-
After Africa, America!
University of Washington, Seattle

Zen and the art of microbial maintenance. Stanley Falkow of Stanford University.
ACQUIRED IMMUNODEFICIENCY SYNDROME IN A HETEROSEXUAL POPULATION IN ZAIRE

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Summary

38 patients with the acquired immunodeficiency syndrome (AIDS) were identified in Kinshasa, Zaire, during a 3 week period in 1983. The male to female ratio was 1:1.1. The annual case rate for Kinshasa

AIDS in Africa: An Epidemiologic Paradigm

Thomas C. Quinn,* Jonathan M. Mann, James W. Curran, Peter Piot

The acquired immune deficiency syndrome (AIDS) has become recognized as a global health problem. Cases have now been reported in 74 countries with more than 1.5 million people infected. More than 2,000,000 people have

Cases of the acquired immune deficiency syndrome (AIDS) have been reported in countries throughout the world. The prevalence and incidence of AIDS are increasing rapidly, especially in Africa and South America.
PULMONARY TUBERCULOSIS IN HIV-INFECTED PATIENTS IN ZAIRE

A Controlled Trial of Treatment for Either 6 or 12 Months

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Abstract Background. We studied the efficacy of a Results. After six months, 260 of 335 HIV-seropositive
short-course regimen of chemotherapy for pulmonary tuberculosis in women of reproductive age studied for up to 36
months had normal serum VHS titers, and none had a history

Figure: Time trends in incidence of HIV and other STD among HIV-1-negative women followed up for a maximum of 36
months.
Isolation and characterization of a new chimpanzee lentivirus (simian immunodeficiency virus isolate cpz-ant) from a wild-captured chimpanzee

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Objective: To assess the prevalence of infection with simian immunodeficiency virus (SIV) isolate cpz, a lentivirus closely related to HIV-1, in chimpanzees, and to obtain new SIV<sub>cpz</sub> isolates.

Methods: Forty-four wild-captured chimpanzees in Belgium and Côte d'Ivoire were tested for HIV and SIV antibodies. Virus was isolated from the peripheral blood lymphocytes of positive animals and characterized by electron microscopy, Western blot and radioimmunoprecipitation assay.

Results: One animal had antibodies that cross-reacted with HIV-1. A lentivirus was isolated and referred to as SIV<sub>cpz-ant</sub>. With regard to molecular weight patterns, SIV<sub>cpz-ant</sub> differs from SIV<sub>cpz-gab</sub>, an HIV-1-related virus isolated from a wild-captured chimpanzee in Gabon. The major core protein, the transmembrane and outer membrane glycoproteins of the SIV<sub>cpz-ant</sub> strain consistently had higher molecular weights. Significantly more HIV-1-positive sera reacted with the envelope proteins of the Gabonese SIV<sub>cpz-gab</sub> strain than with the SIV<sub>cpz-ant</sub> strain.

Conclusions: This study shows that natural infection of wild-captured chimpanzees with an HIV-related virus may not be uncommon. The diversity of the two chimpanzee isolates, the different geographical origin and the absence of disease suggest that chimpanzees have not recently become SIV<sub>cpz</sub>-infected.

The Prevalence of Infection with Human Immunodeficiency Virus over a 10-Year Period in Rural Zaire

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The Nairobi STD Program
An International Partnership

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Retrospective Seroepidemiology of AIDS Virus Infection in Nairobi Populations

Peter Piot, Francis A. Plummer, Marie-Anne Rey, Elisabeth N. Ngugi, Christine Rouzioux, Josiah O. Ndinya-Achola, Gaby Vercauteren, Lourdes J. D’Costa, Marie Laga, Herbert Nsanze, Lieve Fransen, David Haase, Guido van der Groen, Robert C. Brunham, Allan R. Ronald, and Francoise Brun-Vézinet

PROPHYLAXIS OF GONOCOCCAL AND CHLAMYDIAL OPHTHALMIA NEONATORUM
A Comparison of Silver Nitrate and Tetracycline


Abstract We evaluated the use of silver nitrate drops and tetracycline ointment for the prophylaxis of ophthalmia neonatorum in a controlled trial involving 2732 newborns. In uncircumcised men, the incidence of genital ulcer disease plus uncircumcised (n=81) 52.6%.

Fig 1—Survivorship plot of cumulative frequency of HIV-1 seroconversion in the presence of genital ulcer disease and in uncircumcised men.
UN Secretary-General Kofi Annan, Al Gore, Vice President of the USA, chaired the first debate on AIDS as a major security issue at the UN Security Council in January 2000.

UN Photo
Prices (US$/year) of antiretroviral regimen in Uganda: 1998-2003
Resources available for HIV in low- and middle-income countries, 1986-2010

Source: UNAIDS, 2010
Estimated new HIV infections and AIDS deaths, 1990–2013

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INSIDE THIS WEEK: TECHNOLOGY QUARTERLY

The trap for Turkey
Wall Street's plumbing problem
Lady Gaga, Mother Teresa and profits
Brazil's boiling economy
The farce that is FIFA

The end of AIDS?

How 5 million lives have been saved, and a plague could now be defeated

LONDON SCHOOL OF HYGIENE & TROPICAL MEDICINE
How AIDS invented Global Health (A. Brandt, NEJM 2013)

- Disrupted divide between prevention and treatment
- New forms of advocacy and activism
- New global funding
- Reduced cost of essential medicines
- Recognised basic human rights
- Major boost for global health research and academic interest
Ebola's perfect storm

The devastating Ebola epidemic in West Africa is the result of a perfect storm: dysfunctional health services as the result of decades of war, low public trust in government and Western medicine, traditional beliefs and even denials about the cause or existence of the virus, and burial practices that involve contact with contagious Ebola-infected corpses. There are now five affected West African countries: Guinea, Liberia, Nigeria, Sierra Leone, and most recently, Senegal. Ebola has killed around 2000 and infected more than 3500, with over 40% of cases occurring within the past few weeks. The World Health Organization (WHO) predicts that 20,000 may become infected. This fast pace of Ebola's spread is a grim reminder that epidemics are a global threat and that the only way to get this virus under control is through a rapid response at a massive global scale—much stronger than the current efforts.

West African governments and the international community have been slow to act in a way commensurate to a major threat to health, economies, and societal stability. It took nearly 4 months after the first patient died in December 2013 before the outbreak was confirmed as being caused by the Ebola virus. Despite multiple calls by Médecins Sans Frontières (MSF), WHO and the governments concerned only declared the epidemic a public health emergency in August 2014. Finally, national authorities and international organizations, including WHO, the populations in quarantine. This must be done while dealing with other endemic health challenges: Uninfected people are dying from treatable diseases because of closed or abandoned health facilities, the cancellation of international flights to the infected countries is creating an obstacle to international support, and there are growing concerns about sending medical help without a plan of treatment for these workers (around 150 doctors and nurses have died of Ebola, and 240 medical staff are infected).

This is an opportune time to accelerate clinical evaluation of experimental therapies, vaccines, and diagnostics, while respecting ethical and scientific standards for such trials. Human trials of Ebola vaccines and therapies are about to start. WHO has announced that compassionate use of experimental therapies is ethically justified, even if they have not been tested in humans. An exceptional crisis requires an exceptional response. One of the lessons from the AIDS response is that prevention has little credibility if treatment for those infected is not available. Let us hope that this is the last Ebola outbreak where all we have to offer is isolation and quarantine, instead of a vaccine and treatment.

The impact of this epidemic will last long after its end. Health systems will need to be rebuilt, disease surveillance systems established, trust in health services and authorities rebuilt, orphans educated and protected, and economic losses restored. More Ebola outbreaks will follow, because the popula-
Delayed Detection & Response

OUT OF CONTROL
The death toll from Ebola virus in West Africa continues to rise. Infectious-disease experts say that more health-care workers are needed to contain the outbreak.

8 August: The WHO declares outbreak a public-health emergency of international concern.

4 August: The World Bank pledges up to US$200 million to contain outbreak.


20 June: Médecins Sans Frontières says outbreak is "totally out of control".
Ebola: Some lessons

• Never assume things remain the same
• Above all, act promptly
• Massively invest in health services, public health systems & people
• Revise R&D model, incentives, funding, regulation
• Multiple disciplines needed
• Beware of rumors
• Global governance failing
• Shield IHR from politics
• As always in crises: best and worst behaviour...
Global Health 2.0

- PI = North America/Europe
- “My study site”
- Largely biomedical
- Infectious diseases, MCH
- Clinical trials, epidemiology
- Delivery of innovation
- Brain drain

- PI = global
- Collaborating centres
- Multi-disciplinary
- Broad health issues
- From discovery to translation
- Innovation of delivery
- Circular migration
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AIDS BETWEEN SCIENCE AND POLITICS
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NO TIME TO LOSE
A LIFE IN PURSUIT OF DEADLY VIRUSES
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