Many of the diseases and parasites/pathogens we have discussed are human parasites or zoonotic diseases for which we know the reservoir hosts and transmission.

Zoonotic pathogens can hide for long periods: they reside where they do, and are opportunistic, and may move to humans (Chagas disease).

Spanish influenza (bird flu); *Diphyllobothrium latum* (broad fish tapeworm of bears); Plague; Bovine TB; Lyme disease, West Nile virus, Marburg virus, Lassa fever, Rift Valley fever, Rabies

Others are new, inexplicable, claim a few lives and disappear
Nipah, Sars, new virus
Hendra virus 1994

Machupo virus Bolivia 1960 case fatality 40%: studies to ID virus, id reservoir, reduce mouse population and epidemic


These represent continuous outbreaks- are they connected?

Are they happening to us or to other animals

Are they the unintended result of what we are doing

They reflect the convergence of crises: ecological and medical. As these broad areas intersect we get a weird, unpredictable new diseases from unexpected or unknown sources.

How do these jump from animals to humans. Why does this appear to be getting more and more frequent?
Human activities affect ecological pressures and disruptions; pathogens jump from animals to humans and humans spread these more widely

1) We cause disintegration of natural ecosystems: logging, slash and burn, hunting/eating wild animals, clear forest for agriculture, mining, etc. Not new activities, but 7 billion have more influence than 7 million. Tropical forests jeopardized, and their contents (viruses, bacteria, fungi, worms) move on

2) Millions of these organisms are parasitic. The virosphere is now a term to describe the realm of organisms in these areas, each parasitic on a bacterium, fungus, invertebrate, vertebrate, never before seen or identified by us. If they kill something, it probably is processed in the forest

3) Trees demolished, what was 50 m high is now at ground level; animals captured and eaten; pathogen deprived of preferred or natural host- jumps to new, available host- man. They do not target us- they exploit our availability and abundance
Ebola

What do we know, what do we not know, how can we find out more…

Abdominal pain; fever, headache, sore throat. Vomiting, nausea, joint and muscle pain, fast breathing, diarrhea, hemorrhaging, bleeding from gums, bleed out
The name Ebola

August 26, 1976 in Yambuku, a town in the north of Zaïre. A 44-year-old school teacher returned from a small hike. His went to the doctor and because of his high fever they gave him quinine (anti-malarial).

A week later, he had uncontrolled vomiting, bloody diarrhea, trouble breathing and then bleeding from his nose, mouth, and anus.

He died ~14 days after the onset of symptoms.

He started an epidemic that killed 280 of the 313 infected persons (88%).
History

- First appeared in Africa 1976
- “African Hemorrhagic Fever”
  - acute, mostly fatal disease
  - causes blood vessel “bursting”
  - systemic (all organs/tissues)
  - humans and nonhuman primates
- Excluding ‘2000 outbreak
  - 1,500 cases
  - over 1,000 deaths
  - It kills 50 to 90 percent of the infected
Ebola hemorrhagic fever

Ebola is a severe, often-fatal disease that affects people, as well as monkeys, gorillas and chimpanzees.

Origins of the disease
- Infection with Ebola virus, named after river in Congo, where disease was first recognized in 1976

Symptoms
1. Fever, headache, joint and muscle pain, sore throat, weakness
2. Followed by diarrhea, vomiting
3. Rash, internal and external bleeding

Confirmed human cases
Since 1976

How it spreads
- Direct contact with blood, secretions of infected person
- Contact with contaminated objects, such as needles
- Contact with infected animal; possibly eating contaminated meat

Treatment
- No standard treatment; sick person isolated, given fluids, oxygen; treatment for secondary infections

Source: U.S. Centers for Disease Control and Prevention
Graphic: Pat Carr

© 2004 KRT
Major Ebola Outbreaks

Confirmed cases and years

- Guinea (2014)
- Liberia (2014)
- Côte d’Ivoire (1994)
- Democratic Republic of Congo
- Sudan, South Sudan (2004, 1979, 1976)
- South Africa (1998)

Legend:
- Total infections
- Total deaths
On the move. The outbreak in West Africa has killed more than 100 people and is still spreading.

Affected districts and number of reported cases in Guinea and Liberia

- 5–10
- 11–30
- 31–90
- Neighboring areas under investigation

Situation as of 7 April

G Vogel Science 2014;344:140

Published by AAAS
Ebola outbreak in West Africa spreading rapidly
Number of countries with cases: 5 (Guinea, Liberia, Sierra Leone, Nigeria, Senegal)
Number of cases as of Sept. 16: 4,985
Number of deaths as of Sept. 16: 2,461

Of the 4,985 cases (confirmed, probable or suspected) as of Sept. 16, 2014, half — 50 per cent — had been reported in the previous 21 days, a clear indication the disease had been spreading rapidly, the UN said. The disease is spreading most rapidly in Liberia, "driven by a surge of cases in the capital, Monrovia," the WHO says.

On a positive note, four districts in Guinea, three in Sierra Leone, and one in Liberia reported no new cases during the 21 days ending Sept. 7. However, one area in Liberia and one in Guinea had been Ebola-free but reported their first cases during the week ending Sept.
How one person spread the Ebola virus in Nigeria

One person infected with Ebola flew from Liberia to Nigeria, leading to 21 cases and eight deaths in Nigeria. Nigerian port health officials wait to screen passengers at the arrivals hall of the airport in Lagos, Nigeria in August.

The Ebola numbers for Nigeria show how the virus spreads, because all 21 cases, which include eight deaths, are believed to have followed a transmission chain that began when Liberian government official Patrick Sawyer travelled from Liberia to Lagos, Nigeria on July 20.

Number of people monitored in Lagos: 353

One man who evaded the monitoring travelled to Port Harcourt. That man later recovered but the doctor who treated him died of Ebola.

Number of people monitored in Port Harcourt: 451

Senegal has reported one case of Ebola, a person who travelled there from Guinea on Aug. 20. That led to the monitoring of 67 people twice daily. None had tested positive as of Sept. 7. The initial case has now fully recovered.
The other Ebola outbreak: Democratic Republic of Congo
Number of cases in DRC, as of Sept. 9: 62
Number of new cases, Sept. 3-9: 31
Number of deaths, as of Sept. 9: 35

The WHO says all the cases are linked to an initial case reported to the WHO on Aug. 26. **This outbreak is not connected to the one in West Africa.**
Disease projections
Total number of cases predicted by the WHO: **20,000** (WHO hopes to control the outbreak within nine months.)

Midas* projection of the number of cases through Oct. 12:

If control of the epidemic stays about the same: **18,406**
If control improves: **7,861**
If control worsens: **54,895**

(*Midas, Models of Infectious Disease Agent Study, is sponsored by the U.S. National Institutes of Health.)

Eurosurveillance projection: **77,181 to 277,124** additional cases by the end of 2014 (This projection, from a report in the peer-reviewed journal's, assumes continued exponential growth, which the authors say is unlikely.)
## Annual Morbidity & Mortality of Selected Parasitic Diseases

<table>
<thead>
<tr>
<th>Disease</th>
<th>Number Infected</th>
<th>Number deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>African Sleeping Sickness</td>
<td>300 thousand</td>
<td>&gt; 30 thousand (10%)</td>
</tr>
<tr>
<td>Malaria</td>
<td>500 million</td>
<td>2.7 million (0.5%)</td>
</tr>
<tr>
<td>Ascariasis</td>
<td>1.2 billion</td>
<td>60 thousand (0.005%)</td>
</tr>
<tr>
<td>Ebola</td>
<td>&lt;1000</td>
<td>&gt;80%</td>
</tr>
</tbody>
</table>

WHO (1997)
The Symptoms

• Symptoms are abrupt and unexpected.
• Incubation between 2 and 21 days.

• Starts with red eyes, then leads to fever, headache, flu-like symptoms, fatigue, internal/external bleeding, massive hemorrhage (uncontrollable bleeding).

• The infected body is also hemorrhaging internally. A cadaver's internal organs have been compared to black and red tapioca pudding.
• Destruction of the Immune System

1. Infects mononuclear phagocytes and fibroblastic reticular system (associated with lymph nodes)
   - Failure of early T-cell activation
   - Disrupts antigen trafficking and cytokine production
   - Extensive apoptosis of blood leukocytes
   - Lymphocyte numbers are reduced and severe damage to lymphoid tissue

2. Macrophages and circulating monocytes help transmit virus to other tissues
Filoviridae or “Filoviruses”

- Mysterious virus group
- Pathogenesis poorly understood
- Ebola
  - natural history/reservoirs unknown
  - exist throughout the world
  - endemic to Africa
  - filamentous ssRNA^- (antisense) viruses

Image courtesy of the Centers for Disease Control
Cures and Treatments

• There is no cure for Ebola ***.
• Due to the extreme biohazard, doctors must wear Level 4 containment suits.
• Infected people sometimes are put in a straw hut, and burned. Simple yet effective.
Epidemiology

- Reservoirs in Nature
  - largely unknown
  - possibly infected animals (primates?)

- Transmission
  - direct contact blood/secretions of infected person
  - possible airborne (Reston primate facility)

- Onset of illness abrupt
  - incubation period: 2 to 21 days
  - infections are acute and mostly deadly
Geography

- The link between human infection by the Ebola virus and their proximity to primates is clear.

- Outbreaks occurred in countries that house 80 percent of the world’s remaining wild gorilla and chimpanzee populations.

- The outbreaks coincided with the outbreaks in wild animals.

- The same distinct viral strains were isolated in animal carcasses and in the bodies of those who handled those carcasses.

- These outbreaks were preceded by an abnormally large death in wild Gorilla populations.
Transmission

• Ebola Virus
  – No carrier state (reservoir Unknown)
  – Researchers Hypothesize that it is Zoonotic
  – Unpopular theory that plant may be the reservoir of the virus
  – Human to Human Transmission through contact of contaminated secretions.

• Ebola-Reston
  – Occurred in the U.S (Reston, VA)
  – Occurred in African Green Monkeys
  – Why only to non-human primates?
    • Four scientists found to have antibody for the disease
  – Circumstantial Evidence of airborne transmission
    • Spread within and between rooms (national center for Infectious Diseases)

• Marburg Virus
  – Transmission from animal host unknown
  – Human to Human (Close Contact and change of fluids highly suspect source of transmission)
Transmission

• Direct contact with the blood, secretions, organs or semen of infected persons:
  – study of risk factors among family members in Kikwit. 27 surviving members were interviewed. Determined that those who had direct contact or who were exposed during late hospital phase were at very high risk. Those who had no physical contact with infected members remained uninfected.
  – Transmission through semen occurs up to 80 days after clinical recovery.
• Handling ill or dead infected people or chimpanzees
• Health care workers have frequently been infected while attending patients- Kikwit outbreak.
• Neonatal
• Droplets or small filovirus particle aerosols confirmed in alveoli of monkeys during Reston outbreak.

Where is the virus?
Reservoir does it exist?

- Not known
- May be
  - A rare species
  - One that usually does not contact clinical host
  - If contact is made the virus may not be easily transmitted
- Hypothesize..................What is going on here?
Ebola

The virus kills gorillas and chimpanzees and other monkeys. Because it kills apes in such high percentage – they are not considered to be the reservoir host.
Three trapping expeditions in areas close to infected gorilla and chimpanzee carcasses in Gabon and in Congo.

1,030 animals were tested including 679 bats, 222 birds and 129 small terrestrial vertebrates (PCR).

Viral nucleotides were discovered in some species.
Leading suspect. Researchers have found evidence of Ebola infections in the little collared fruit bat, *Myonycteris torquata*, but the bats don't seem to get sick from the virus.
In a worst-case hypothetical scenario, should the outbreak continue with recent trends, the case burden could gain **an additional 77,181 to 277,124 cases** by the end of 2014. That is a jaw-dropping number.

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**Figure 1**


**A.** Cumulative number of confirmed or probable cases.

- Guinea
- Liberia
- Sierra Leone

**B.** Estimated daily number of cases.

- Guinea
- Liberia
- Sierra Leone

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A) Cumulative number of confirmed or probable cases of EVD reported to the World Health Organization [10]. Solid lines are the smoothing spline fits to cumulative curves for each country with a coefficient of variation $R^2$ at 0.995.

B) Estimated daily incidence curves based on the smoothing spline model. Data from Nigeria and Senegal have been omitted due to the limited number of cases recorded in these countries thus far.
The Mathematics of Ebola Trigger Stark Warnings: Act Now or Regret It

There are two possible future chapters to this story that should keep us up at night.

The first possibility is that the Ebola virus spreads from West Africa to megacities in other regions of the developing world. This outbreak is very different from the 19 that have occurred in Africa over the past 40 years. It is much easier to control Ebola infections in isolated villages. But there has been a 300 percent increase in Africa’s population over the last four decades, much of it in large city slums...

The second possibility is one that virologists are loath to discuss openly but are definitely considering in private: that an Ebola virus could mutate to become transmissible through the air… viruses like Ebola are notoriously sloppy in replicating, meaning the virus entering one person may be genetically different from the virus entering the next.

The current Ebola virus’s hyper-evolution is unprecedented; there has been more human-to-human transmission in the past four months than most likely occurred in the last 500 to 1,000 years. Each new infection represents trillions of throws of the genetic dice.
Glamour disease of the 1990s
Koch's postulates are as follows:

The bacteria must be present in every case of the disease.

The bacteria must be isolated from the host with the disease and grown in pure culture.

The specific disease must be reproduced when a pure culture of the bacteria is inoculated into a healthy susceptible host.

The bacteria must be recoverable from the experimentally infected host.

However, Koch's postulates have their limitations and so may not always be the last word. They may not hold if:

1) The particular bacteria (such as the one that causes leprosy) cannot be "grown in pure culture" in the laboratory.

2) There is no animal model of infection with that particular bacteria.
Tekmira Establishes Regulatory Framework for Emergency Use of TKM-Ebola

Tekmira Pharmaceuticals Corporation (TKMR) (TKM.TO), a leading developer of RNA interference (RNAi) therapeutics, today announced that the FDA has authorized Tekmira to provide TKM-Ebola for treatment under expanded access protocols to subjects with confirmed or suspected Ebola virus infections.

"Tekmira is reporting that an appropriate regulatory and clinical framework is now in place to allow the use of TKM-Ebola in patients. We have worked with the FDA and Health Canada to establish this framework and a treatment protocol allowing us to do what we can to help these patients." "We have insisted on acting responsibly in the interest of patients and our stakeholders," added Dr. Murray. "Today we are reporting that, working closely with regulators in the United States and Canada, we have established a framework for TKM-Ebola use in multiple patients. In the US, the FDA has granted expanded access use of TKM-Ebola under our Investigational New Drug application (IND) and Health Canada has established a similar framework, both of which allow the use of our investigational therapeutic in more patients."

TKM-Ebola is an investigational therapeutic, being developed under an FDA approved IND, which is currently the subject of a partial clinical hold under which the FDA has allowed the potential use of TKM-Ebola in individuals with a confirmed or suspected Ebola virus infection.
You have been given a contract to study Ebola transmission in Bisc 318 region of Gv bvghghv in central Africa.

What do you do?
How do you do it?
How do you prepare to do it?
Logistics?
Scientific approaches.....