Killer Viruses: The Why and The How

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Disclosures

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Purpose

• New, unrecognized infectious diseases continue to emerge
• Major potential for disruption
  • Societal
  • Healthcare
• Chance favors the prepared mind
• Endlessly fascinating
Outline

• A Snapshot of the Current Situation
• Causes
  • It’s a Small World
  • Human - human interactions
  • Human - animal interactions
  • Human – environmental interactions
  • Vectors
• Surveillance and the Tools of discovery
Snapshot

- MERS
- Yellow Fever
- Zika
- Ebola
- Powassan
- SFTS (Severe Fever with Thrombocytopenia Syndrome)
- West Nile
- SARS
- Measles
- Monkeypox
- Chikungunya
- Dengue
- Avian Influenza (H5, H7)
- Swine Influenza
- Hepatitis A
Global Examples of Emerging and Re-Emerging Infectious Diseases

- Antimicrobial-resistant threats
  - CRE
  - MRSA
  - *C. difficile*
  - *N. gonorrhoeae*
  - H3N2 influenza
  - Cyclosporiasis
  - *E. coli* O157:H7
  - Measles
  - Human monkeypox
  - Listeriosis
  - Bourbon virus
  - 2009 H1N1 influenza
  - Adenovirus 14
  - Anthrax bioterrorism
  - Chikungunya
  - Hantavirus pulmonary syndrome
  - Dengue
  - Zika virus
  - Yellow fever
  - Human African trypanosomiasis
  - Cholera
  - Marburg hemorrhagic fever
  - MDR/XDR tuberculosis
  - Plague

- New emerging
- Re-emerging/resurging
- “Deliberately emerging”

October 2015
The Trend
A little bit of mathematical reasoning

• Incubation period
• Period of contagiousness
• Travel Time

➔ If travel time < incubation period and/or period contagiousness
➔ Importation of disease
YELLOW JACK
Global Flight Map
it's a small world!
Origins of Globalization

The Columbian Exchange

AMERICAS TO EUROPE, AFRICA, AND ASIA

EUROPE, AFRICA, AND ASIA TO AMERICAS

Disease
- Smallpox
- Influenza
- Typhus
- Measles
- Malaria
- Diphtheria
- Whooping Cough

Livestock
- Cattle
- Sheep
- Pigs
- Horses

Grains
- Wheat
- Rice
- Barley
- Oats

Onions

Citrus Fruits

Pineapples

Peanuts
Potatoes
Tomatoes
Corn

Turkeys

Cacao
Beans
Vanilla
Honeybees

Pumpkins
Squash

Peaches, Pears
Coffee Beans

Grasses

Sweet Potatoes

Tobacco

Tobacco

Onions

Olives

Turnips
Top identified specific causes for gastrointestinal, febrile, dermatologic, and respiratory illnesses by region among ill returned travelers. More than 5 diagnoses are shown if >1 cause had equal numbers of cases. These graphs represent proportions, and there is variability in the number of ill travelers represented from panel to panel (shown from largest to smallest traveler numbers). CLM = cutaneous larva migrans; D. fragilis = Dientamoeba fragilis; E. histolytica = Entamoeba histolytica; P. falciparum = Plasmodium falciparum; P. vivax = Plasmodium vivax; PEP = postexposure prophylaxis; SF = spotted fever; TB = tuberculosis.
Human Factors
Epidemiological Transitions and Ages

• 3 major transitions from Neolithic to modern area
  1. Nomadic → Agriculture 10,000 years ago (Age of Pestilence and Famine)
  2. Industrial Revolution (Age of Receding Epidemics)
  3. Globalization, Urbanization, Aging (Age of Degenerative and Manmade diseases)
Nomadic → Stationary Transition

- Population density increases
- Human to human interaction increases
- Waste management
- Agriculture
- Lifestyle changes
- Evolution
Agriculture ➔ Zoonosis
Definitions

• **Zoonotic** = “zoo” meaning “animal” and “nosis” meaning “disease”

• **Reservoir** = animal where etiologic agent is maintained

• **Vector** = the medium (insect or other) transferring the etiologic agent between the animal reservoir and the human host.

• **Relatively infrequent cause of infection**
  • But, most infections were zoonoses at one time
Patterns of Zoonotic Infections

Animal reservoir ➔ Human reservoir

Direct skin penetration ➔ Inhalation ➔ Ingestion

Human-Animal ➔ Human-Human ➔ Vector

No Further Transmission

Transmission

Human Encounter

Colonization

Pathology (human disease)
Factors Affecting Zoonotic Infections

- Improved diagnostics
- Recreational travel to rural areas
- International travel
- Population displacement due to warfare
- Homelessness
- Interactions with animals
- High population of reservoir host
- New reservoir or transmission cycle
- Weather patterns + events
- Translocation of reservoir host and ectoparasites
- Newly emerged or recognized organism
Yosemite hantavirus outbreak has sickened 10, killed 3, CDC says

November 21, 2012 | By Eryn Brown | Los Angeles Times

To date, 10 people have fallen ill — and three have died — in the hantavirus outbreak at Yosemite National Park's "signature" cabins in Curry Village, according to the U.S. Centers for Disease Control and Prevention.

Hantavirus only infects a handful of people in the U.S. each year, but when it strikes it is deadly about a third of the time, killing by shutting down the respiratory system. Humans can catch the virus by getting bitten by infected deer mice, which carry the disease, or by inhaling virus particles that are shed in mouse feces or urine. Hantavirus cannot pass from person to person.
Cycle of Transmission: Hantavirus

Natural Reservoir

Dead End Host

Transmission (Urine)

Transmission (Urine)
Ebola

Reservoirs of ZEBOV & MARV: fruit bat species

Intermediary susceptible species: virus amplification in great apes and duikers
**Rousettus aegyptiacus**: Egyptian Fruit Bat

**Hypsignathus monstrosus**: Hammer-headed bat

**Epomops franqueti**: Franquet’s Epauletted Fruit Bat

**Myonycteris torquata**: Little Collared Fruit Bat

**Bat Zoonoses**
-- rabies
-- Nipah
-- Hendra
-- Marburg
-- SARS
-- MERS

### Why Bats?
-- most populous mammalian species
-- travel
-- world wide
Flu: H3N2v, H1N2v & Avian Influenza
Influenza
--RNA virus
--segmented genome
--multiple hosts
--reassortment
--respiratory transmission
This figure represents the genetic composition of a particular influenza virus lineage over time. In each chart, gene segments are shown along the left side, and dates from 1918 to 2009 are shown along the top. Color coding shows the avian origins and history of each gene segment in each influenza virus lineage. The influenza virus gene segment reassortments that gave rise to the H2N2 and H3N2 strains of human influenza A are shown on the left side of the diagram, along with human influenza A (H1N1) viruses or their descendants. Swine influenza A (H1N1) viruses are shown on the right side of the diagram.
Figure 2. Distribution of reported human influenza A(H7N9) cases in China by week, week 1/2013 to week 25/2017 (N=1,548)

H7N9
--more cases in 3rd wave
--some changes showing human tropism
--antiviral resistance
--change in strain – vaccine mismatch
--high pathogenicity variant in chickens
Box 1. Steps in pandemic emergence.

For an avian-adapted strain of influenza A to become a pandemic strain, several events are required:

1. The avian-adapted strain must become sufficiently widespread in wild or domestic birds, swine or other reservoir species to expose at least one human to infection.

2. One or more humans must acquire infection from the reservoir species.

3. The infection must replicate sufficiently in a zoonotic case to produce infectious virus in respiratory or other secretions.

4. The infection must be transmitted to additional humans, avoiding an "early" termination of the transmission chain due to chance. Such early termination is a significant risk given the relatively low infectiousness of influenza and the moderate degree of overdispersion in the number of secondary cases infected by each case, both of which contribute to the probability that a transmission chain will terminate by chance (Lloyd-Smith et al., 2005; Lipsitch et al., 2003). It must also avoid extinction due to deliberate control efforts put in place by public health authorities (Ferguson et al., 2006; Merler et al., 2013).

5. Finally, the infection must spread beyond the local area to infect members of distant populations, a process accelerated by modern global travel (Cooper et al., 2006). This step and the one before are enhanced if the level of population susceptibility is high, as occurs when the surface proteins of the new strain are dissimilar to those on any currently or recently circulating human influenza A strains.
One Health

Environmental health

Ecology

Veterinary medicine

Public health

Human medicine

Molecular and microbiology

Health economics

Individual health

Population health

Ecosystem health

Comparative medicine / Translational medicine

Metabolic disorders in humans and animals

Cancer and cardiovascular disease in humans and animals

Joint and skeletal diseases in humans and animals

Human - animal bond

Environmental hazards exposure to humans and animals

Zoonotic infections

Bacterial infections

Viral infections

Vector-borne infections

Parasite infections

Antimicrobial resistance

Food safety

Intervention

Surveillance

Vaccines and therapeutics

Sanitation

Vector control

Global health
Vector-borne Diseases Strike Back

Urbanization
Complacency
Where They Lurk?

Approximate distribution of Aedes aegypti and Aedes albopictus in the United States.*

* Maps have been updated from a variety of sources. These maps represent CDC's current understanding of the distribution of these species.
Historical US Yellow Fever Outbreaks
Table 1. Vaccination Status of Measles Cases and Crude Measles Incidence Rate (IR) by Age Group in the United States, 2001-2015

<table>
<thead>
<tr>
<th>Age Group</th>
<th>No. of Measles Casesa</th>
<th>Vaccination Status, No. (%)b</th>
<th>Annual IR per Million Population (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Unvaccinated</td>
<td>Vaccinated</td>
</tr>
<tr>
<td>0-5 mo</td>
<td>31</td>
<td>31 (100.0)</td>
<td>0</td>
</tr>
<tr>
<td>6-11 mo</td>
<td>163</td>
<td>161 (98.8)</td>
<td>2 (1.2)</td>
</tr>
<tr>
<td>12-15 mo</td>
<td>106</td>
<td>95 (89.6)</td>
<td>7 (6.6)</td>
</tr>
<tr>
<td>16 mo-4 y</td>
<td>214</td>
<td>164 (76.6)</td>
<td>36 (16.8)</td>
</tr>
<tr>
<td>5-17 y</td>
<td>464</td>
<td>406 (87.5)</td>
<td>36 (7.8)</td>
</tr>
<tr>
<td>18-29 y</td>
<td>362</td>
<td>235 (64.9)</td>
<td>67 (18.5)</td>
</tr>
<tr>
<td>30-49 y</td>
<td>366</td>
<td>114 (31.1)</td>
<td>80 (21.9)</td>
</tr>
<tr>
<td>≥50 y</td>
<td>81</td>
<td>36 (44.4)</td>
<td>2 (2.5)</td>
</tr>
<tr>
<td>Overallc</td>
<td>1789</td>
<td>1243 (69.5)</td>
<td>230 (12.9)</td>
</tr>
</tbody>
</table>
Chance Favors the Prepared Mind
Tip of the Spear

• Bush meat hunters
• Abattoir workers
• Viral chatter
• Hot spots
Diagnostics

- Unknowns: Biological "dark matter"
- Viral testing
- New technologies
central Africa, for instance Dr Bila Kapita, chief of internal medicine at Hôpital Mama Yemo in Kinshasa, reported that, at least since the mid-1970s, they started seeing cases that in retrospect were very likely to have been AIDS. This would be consistent with some degree of dissemination of the virus during the mid-1960s, given the average ten-year interval between infection and symptomatic disease. But could the disease have been present even earlier?¹²

In most district or regional hospitals of countries inhabited by *P.t. troglodytes*, the diagnostic facilities during the colonial era (and even now) were so minimal that it would have been difficult, even for astute and experienced clinicians, to recognise the emergence of a new disease characterised by intermittent fevers and profound wasting. Most such institutions did not have any kind of half-decent microbiology laboratory. No cultures were done, either for common bacterial pathogens or the agent of tuberculosis, and diagnoses were based on stains made directly on the specimens, or solely on the combination of symptoms and signs found during the clinical examination. Fifty years later, I found the same situation at the Nioki hospital in Zaire: nothing had changed. This approach was relatively effective for diagnosing parasitic diseases (malaria, sleeping sickness, filariasis, intestinal parasites) but very insensitive for most bacterial diseases. Little radiological investigation was available either; only in the best hospitals was it possible to get something as elementary as a chest x-ray. The first x-ray machine in Brazzaville was
Eradication of Smallpox (1980)

• Led by Dr. DA Henderson (1928-2016)
• First and only eradication of a human infectious disease
• Predicted by Jenner
Thanks for your attention and interest

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