Why do we vaccinate?

A primer on Herd Immunity

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What is a vaccine?

- Passive – borrowing some one else's immunity
  - Blood donation
  - Cloning antibodies
- Active
  - Attenuated Vaccine
    - Diluted
    - Augmented
    - Vector
  - In-activated Vaccine
    - Destroyed
    - Parts of an Organism
  - Toxoid Vaccine
    - Selected chemical markers

- Risk of Vaccinating versus risk of Infection
  - Yellow Fever Vaccine
  - Smallpox
  - Rabies
  - Measles

- Not every vaccine is needed in every situation…
  - Exception is always made for organisms that are highly communicable *e.g. Measles*

Nelson, K. E., & Williams, C. M. (Eds.). (2012). *Infectious disease epidemiology*. Jones & Bartlett Publishers.

Ranheim, T., Mozier, N., & Egan, W. (2015). Vaccine Potency Assays. In*Vaccine Analysis: Strategies, Principles, and Control* (pp. 521-541). Springer Berlin Heidelberg.

Active Vaccination Controls Outbreaks

- Vaccination can:
  - Remove people from the susceptible pool
  - Reduce infectious period
  - Limit outbreak potential
  - Protect those that the vaccine will fail
- Vaccine is rarely a treatment
  - Immunity takes time to develop
  - Vaccination is usually prevention and not treatment
  - Vaccines are most effective when administered prior to exposure

Majumder, M. S., Cohn, E. L., Mekaru, S. R., Huston, J. E., & Brownstein, J. S. (2015). Substandard Vaccination Compliance and the 2015 Measles Outbreak. *JAMA pediatrics*.

Crowcroft, N. S., Deeks, S. L., & Upshur, R. E. (2015). Do we need a new approach to making vaccine recommendations?. *BMJ*, *350*, h308.

No Vaccine is 100%

- Host characteristics
  - Auto-immune diseases
  - Medications that suppress immune function
  - Immunocompromised status
    - HIV
  - Rotten luck
    - No able to make antibodies for that specific organism
- Organism characteristics
  - Antigenic Shifting
  - Weakly Antigenic
  - Dozens of serotypes
  - Virulence factors that suppress antibody response or binding

Heininger, U., Bachtiar, N. S., Bahri, P., Dana, A., Dodoo, A., Gidudu, J., & dos Santos, E. M. (2012). The concept of vaccination failure. *Vaccine*, *30*(7), 1265-1268.

Communicable Diseases

- There are three types of people
  - Susceptible
  - Infectious
  - Recovered (Immune)
    - Vaccination
    - Exposure
    - Dead
- A communicable disease is by definition
  - Spreadable! Infectious!

- Reproductive Value (RO)
  - How many cases will be generated from one case of disease?
- What influences a RO?
  - Transmission parameter
    - Blood, Droplet, ID 50
  - Population of Susceptible
    - Lack of vaccination or waning vaccination protection
  - How long is the person infectious?

McLean, A. R. (2013). Infectious Disease Modeling. In *Infectious Diseases* (pp. 99-115). Springer New York.

Examples of RO Values

- Often outbreak specific
- ROs appear to be somewhat stable over time, but population dynamics can shift the RO
- Observational Case Studies
  - We do not lock people up who are unvaccinated and expose them to evaluate the RO for specific diseases!

Disease	Geographical Location	RO
Diphtheria	New York & Maryland	4 – 5
Scarlet Fever	New York, Pennsylvania, & Maryland	5 – 8
Mumps	Maryland, England/Wales, Netherlands	7 – 14
SARS	Hong Kong	2 – 5
EBOLA	Africa 1976-2006	2 – 7
HIV	Male Homosexuals (Europe) Nairobi (Female Prostitutes) Kampala (Heterosexuals)	2 – 5 11 – 12 10 – 11
Rubella	Europe	6 – 15

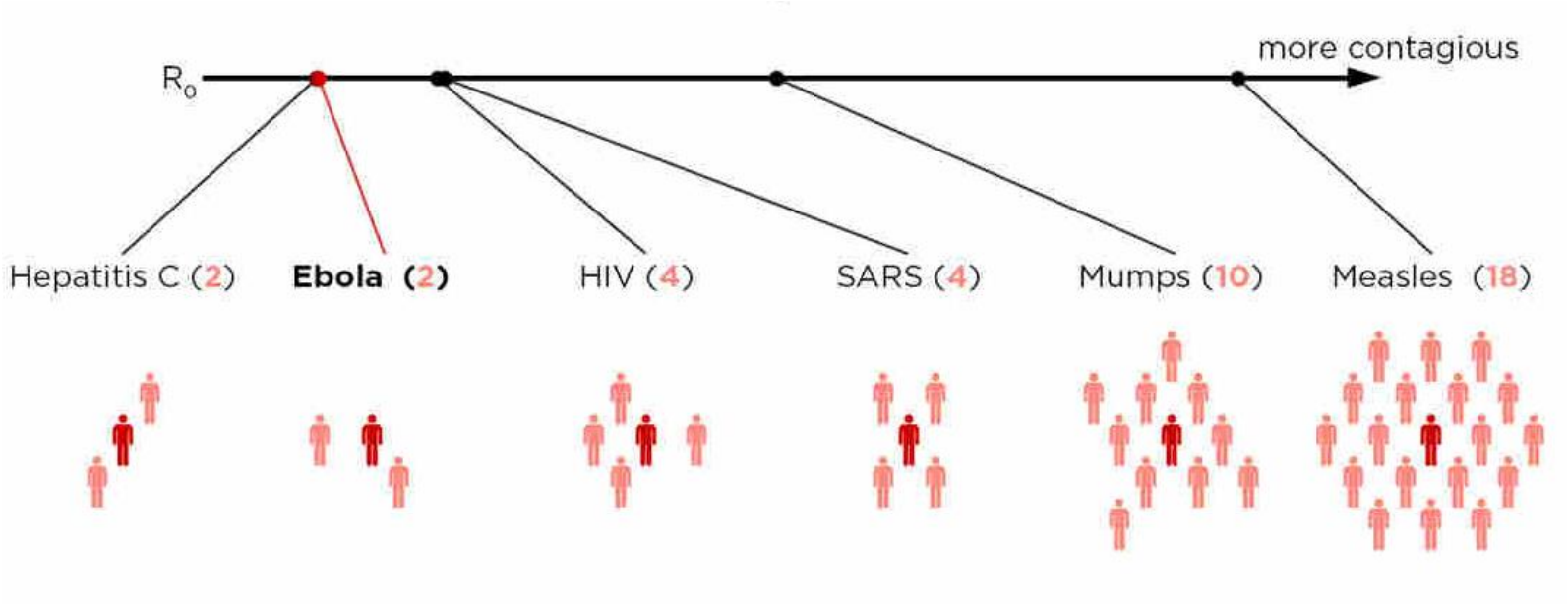
Nelson, K. E., & Williams, C. M. (Eds.). (2012). *Infectious disease epidemiology*. Jones & Bartlett Publishers.
McLean, A. R. (2013). Infectious Disease Modeling. In *Infectious Diseases* (pp. 99-115). Springer New York.

What impact does behavior have on a reproductive value (Ro)?

- Depends on the mode of transmission:
  - Airborne
  - Airborne Droplet
  - Fecal-oral route
  - Intimate contact
    - Saliva exchange
    - Sexual Activities
  - Bodily Fluids
    - EBOLA vs. Hepatitis B or C
- Number susceptible
  - Vaccination and recovery with immunity remove these people from the Ro calculation and limit the spread
- Length of infectivity Impact
- Severity of Disease

Nelson, K. E., & Williams, C. M. (Eds.). (2012). *Infectious disease epidemiology*. Jones & Bartlett Publishers.

Ro in Practice

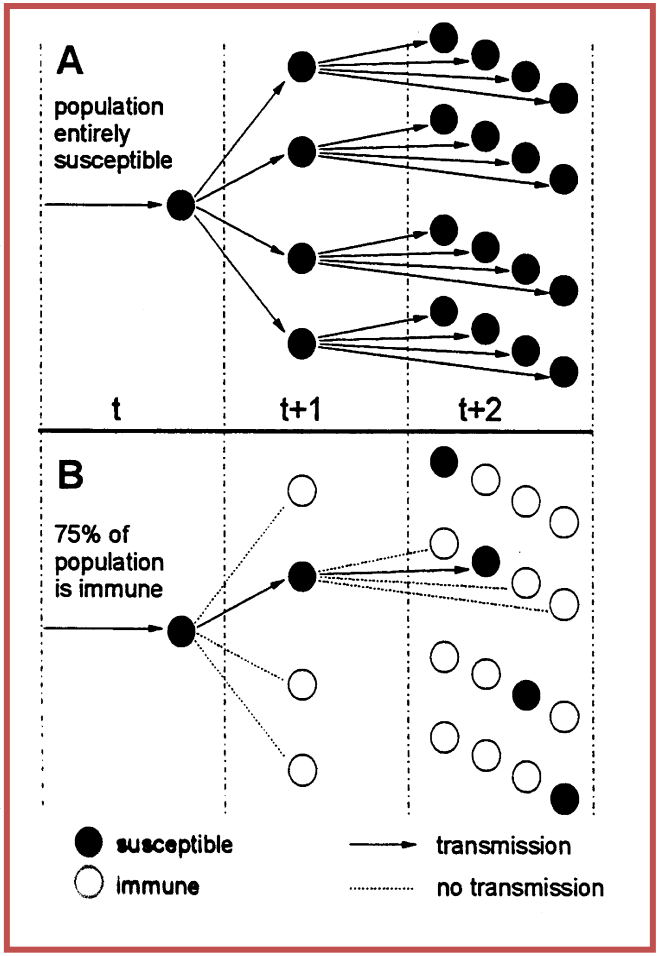


http://www.npr.org/blogs/health/2014/10/02/352983774/no-seriously-how-contagious-is-ebola

Evaluation of the potential for spread of an infection

$R_0 = 4$
with whole population susceptible

$R_0 = 4$
with 75% population immune
(25% susceptible)

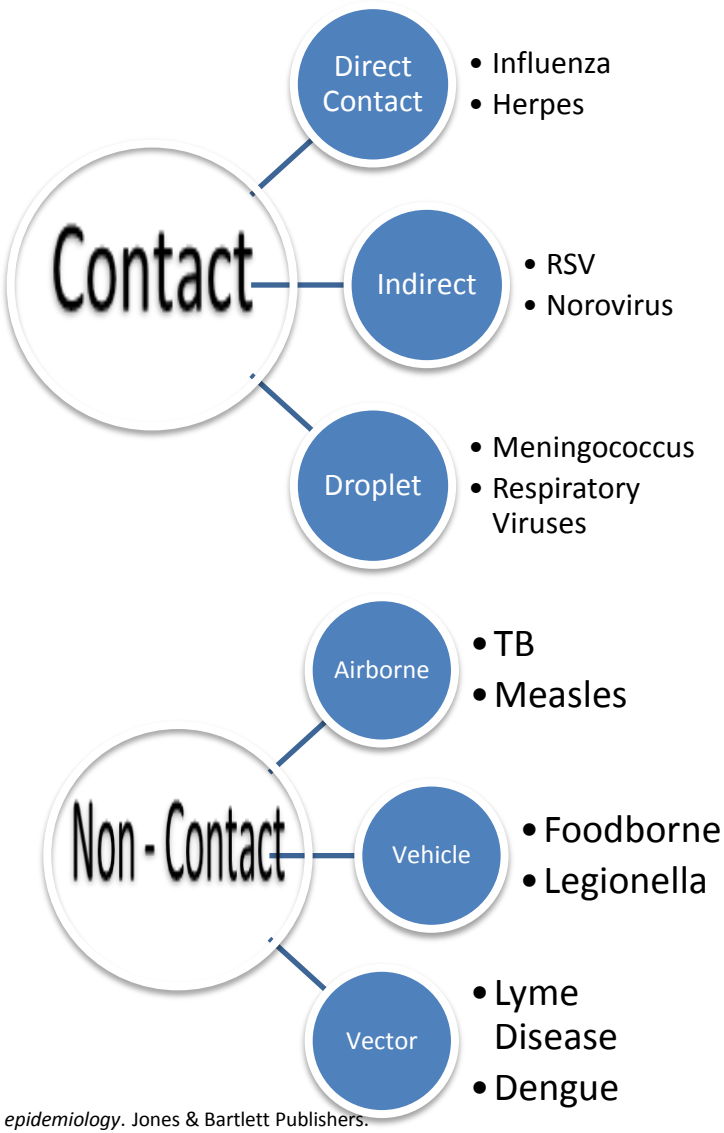


(Dr. Effelterre, GSK, 2008)

Examples of Infectious Doses (ID 50) & Modes of Transmission

Organism	Mode Of Transmission	ID50
*B. anthracis**	Inhaled	10,000 to 20,000
F. tularensis	Inhaled, direct contact	10
Ebola	Direct Contact with Bodily Fluids	1
Norovirus	Fecal-oral	2,740
Measles	Airborne	500
Influenza A	Airborne Droplet	3 - 66

*Varies depending on mode of transmission



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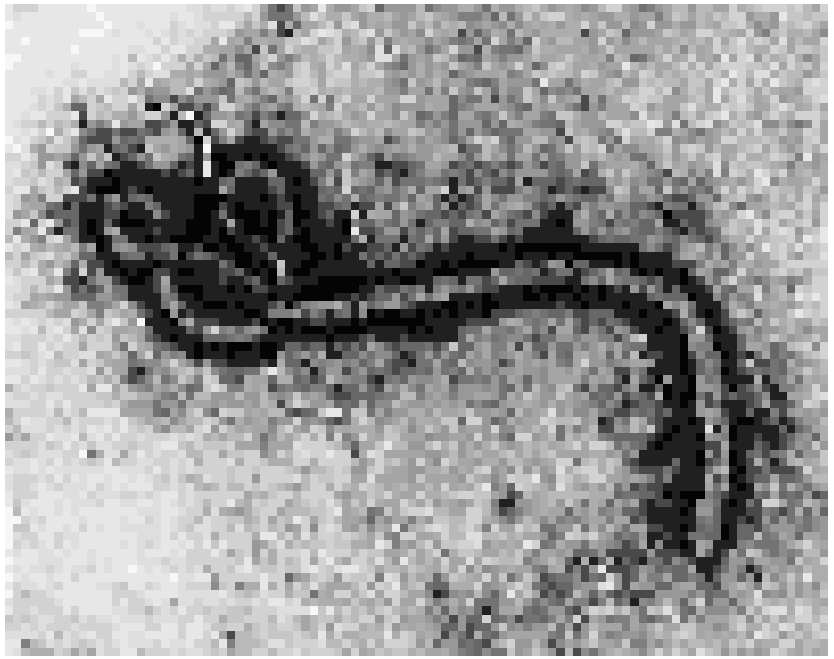
New and Exciting Vaccination News: EBOLA Overview



Order: ***Mononegavirales***

Family: ***Filoviridae***

Genus: ***Ebola like viruses***

Species: ***Ebola***

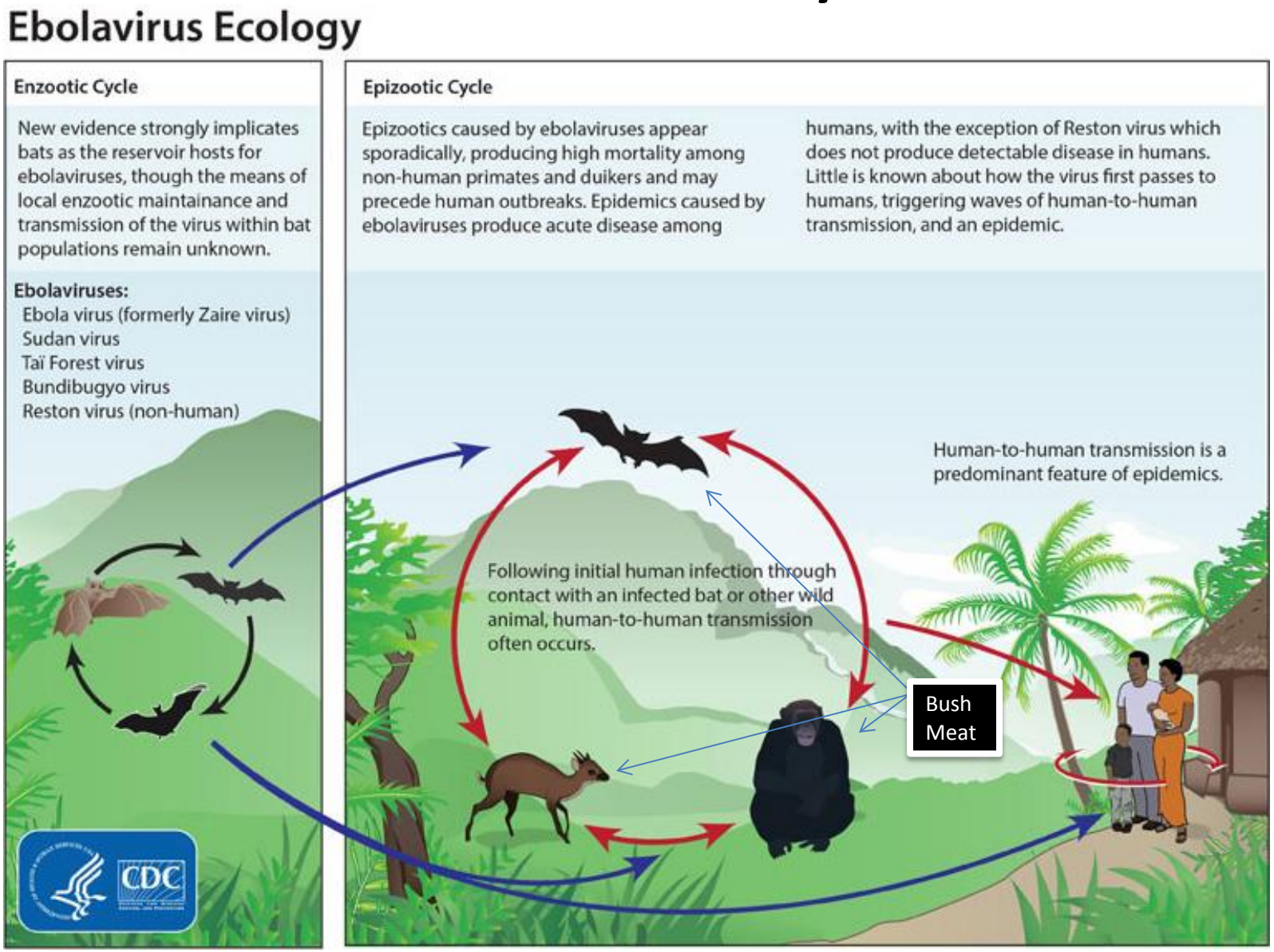
Subtypes

- Ebola-Zaire, Ebola-Sudan,Ebola-Ivory Coast
  - disease in humans
- Ebola-Reston
  - disease in nonhuman primates

EBOLA: Symptoms and Diagnostic Tests

- Early symptoms
  - muscle aches, fever, vomiting
  - red eyes, skin rash, diarrhea, stomach pain
- Acute symptoms
  - bleeding/hemorrhaging from skin, orifices, internal organs
- Early Diagnosis
  - very difficult
  - signs & symptoms very similar to other infections
- Laboratory Test
  - PCR detection
  - ELISA (enzyme-linked immuno-absorbant) assay

EBOLA: Life Cycle



Characteristics of EBOLA

- EBOLA outbreaks occur every 3 to 4 years
- Recent outbreak was largest on record and due to porous isolation procedures
- Bush meat will not stop being consumed by poorer African regions
  - Continuous vaccination would be the only way to prevent these epidemics from cycling

- Current Vaccine
  - rVSV (vector vaccine)
    - Vesicular stomatitis virus
  - Phase 1
    - No serious side effects
    - Immunogenic after 1 dose
  - Phase 2
    - Trials promising
  - Phase 3 – field testing
    - Begins the end of February

Agnandji, S. T., Huttner, A., Zinser, M. E., Njuguna, P., Dahlke, C., Fernandes, J. F., ... & Moorthy, V. (2015). Phase 1 Trials of rVSV Ebola Vaccine in Africa and Europe—Preliminary Report. *New England Journal of Medicine*.

Marzi, A., Ebihara, H., Callison, J., Groseth, A., Williams, K. J., Geisbert, T. W., & Feldmann, H. (2011). Vesicular Stomatitis Virus–Based Ebola Vaccines With Improved Cross-Protective Efficacy. *Journal of Infectious Diseases*,*204*(suppl 3), S1066-S1074.

http://apps.who.int/iris/bitstream/10665/149045/1/WHO_EVD_Meet_HIS_15.1_eng.pdf?ua=1

Fast Tracking the Vaccine

- Anti-viral therapies are approved and effective
  - In short supply
- A vaccine has shown
  - Strong immune response
  - Safe
- Ethical issues surrounding a person's ability to say no to a vaccine like this in face of a disease with a 60% Case Fatality Rate

- If successful:
  - The vaccine will have to be a mainstay of these populations
  - Vaccination could interrupt the cycle of EBOLA in Africa
  - Due to the wild animal reservoir it is unlikely that EBOLA will be eradicated
  - Persistent vaccination will eventually be pursued

Geisbert TW. Emergency Treatment for Exposure to Ebola Virus: The Need to Fast-track Promising Vaccines. *JAMA*.2015;313(12):1221-1222. doi:10.1001/jama.2015.2057.

So, why do we vaccinate?

- Do we vaccinate to protect the individual alone?
  - No, no vaccine is 100%
- Do we vaccinate to eradicate a disease?
  - Sometimes, it has been done with smallpox and it is possible to do it with measles and polio
- We vaccinate to remove those susceptible from the population to limit the impact of outbreaks