

Emerging Diseases

Biosciences in the 21st Century

Dr. Amber Rice

November 23, 2015

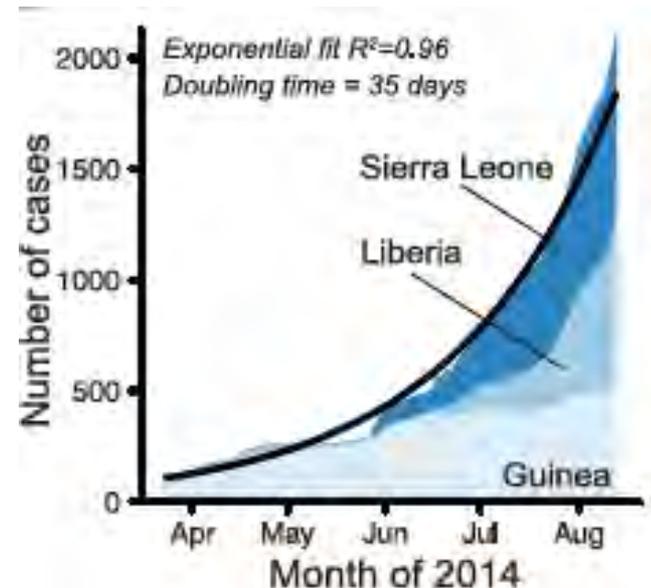
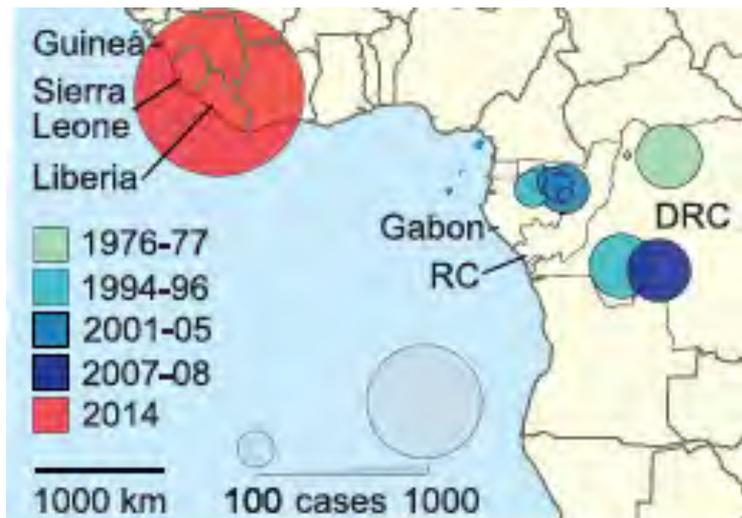
Outline

- Disease emergence: a case study
- How do pathogens shift hosts?
- Evolution within hosts: The evolution of virulence
- Treatments: the evolution of drug resistance

Disease emergence: a case study

Ebola Virus

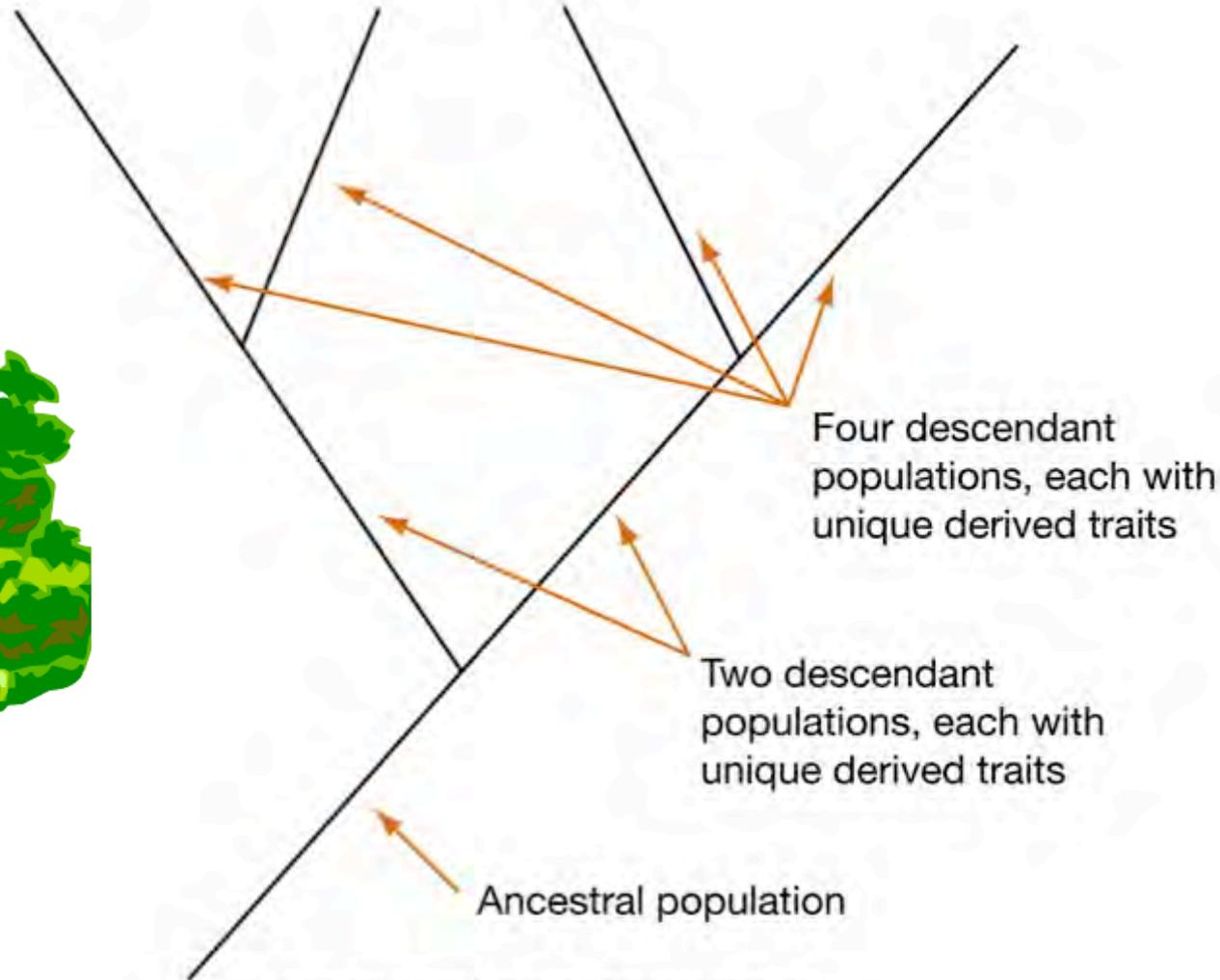
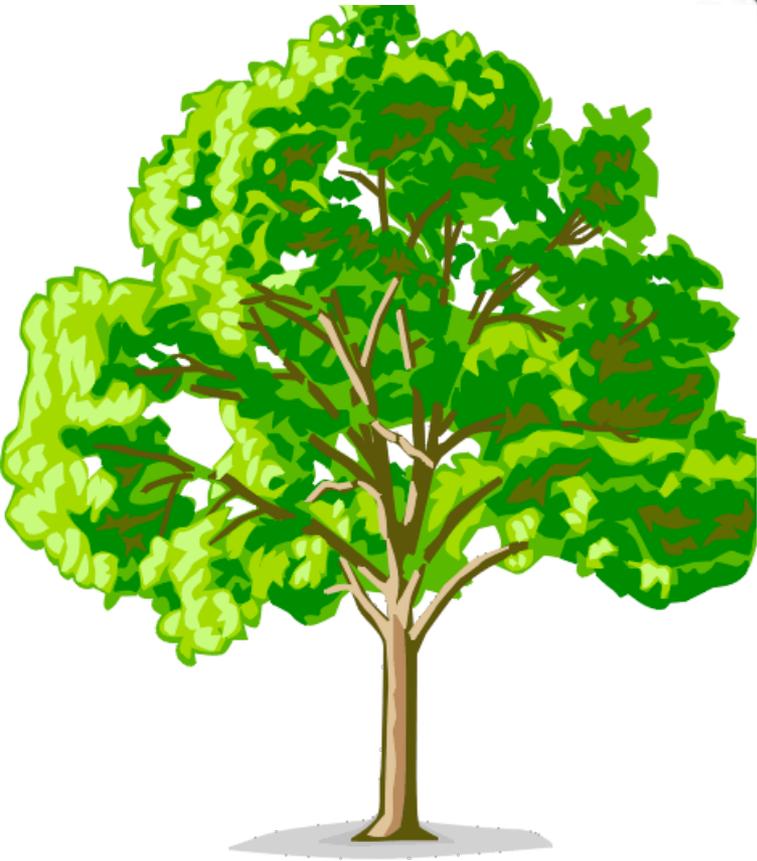
- First identified in Zaire, 1976
- Outbreaks in mid-90s, early 2000s, mid 2000s, 2014
- Average 50% fatality rate



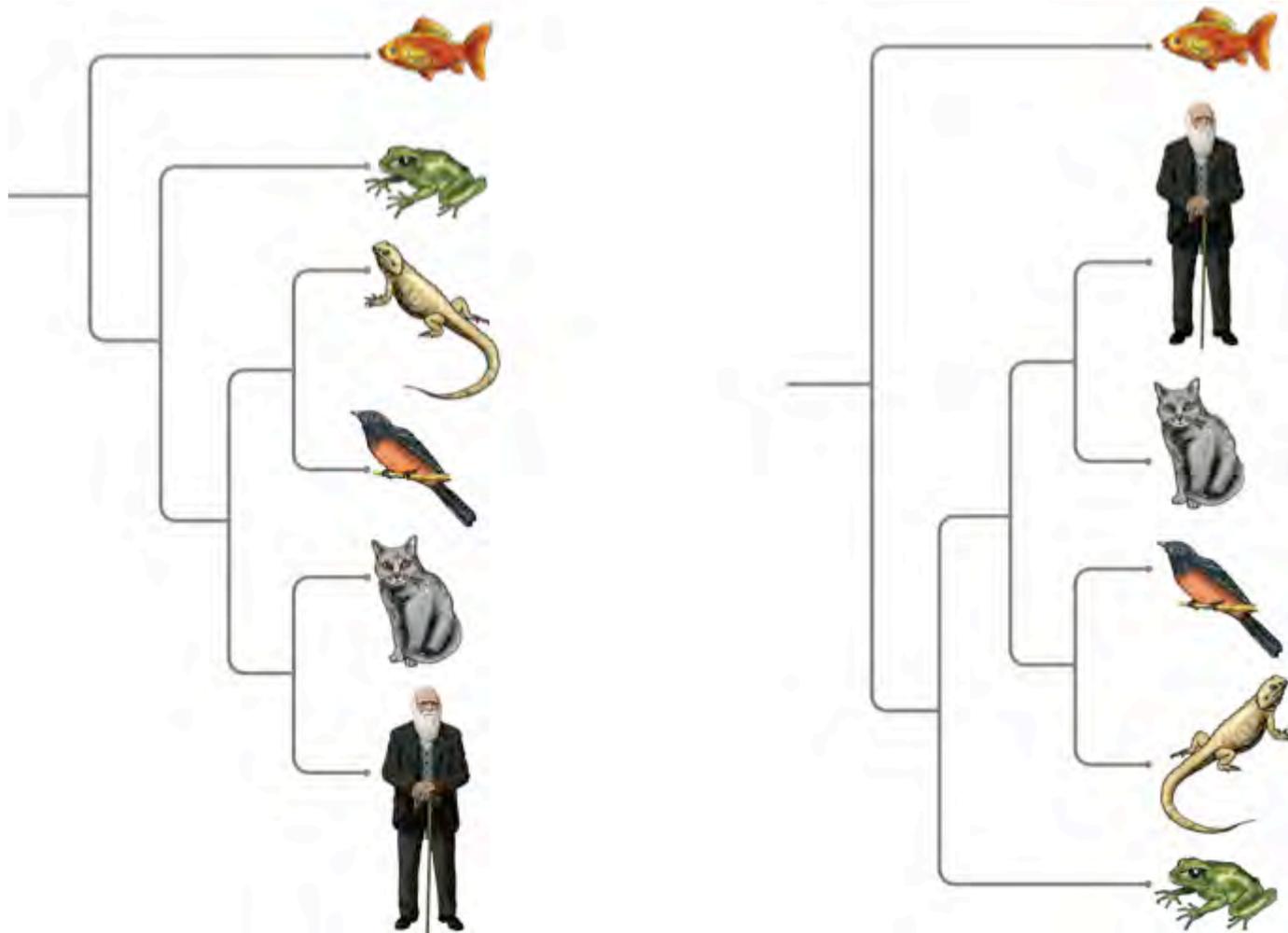
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Reading a phylogenetic tree

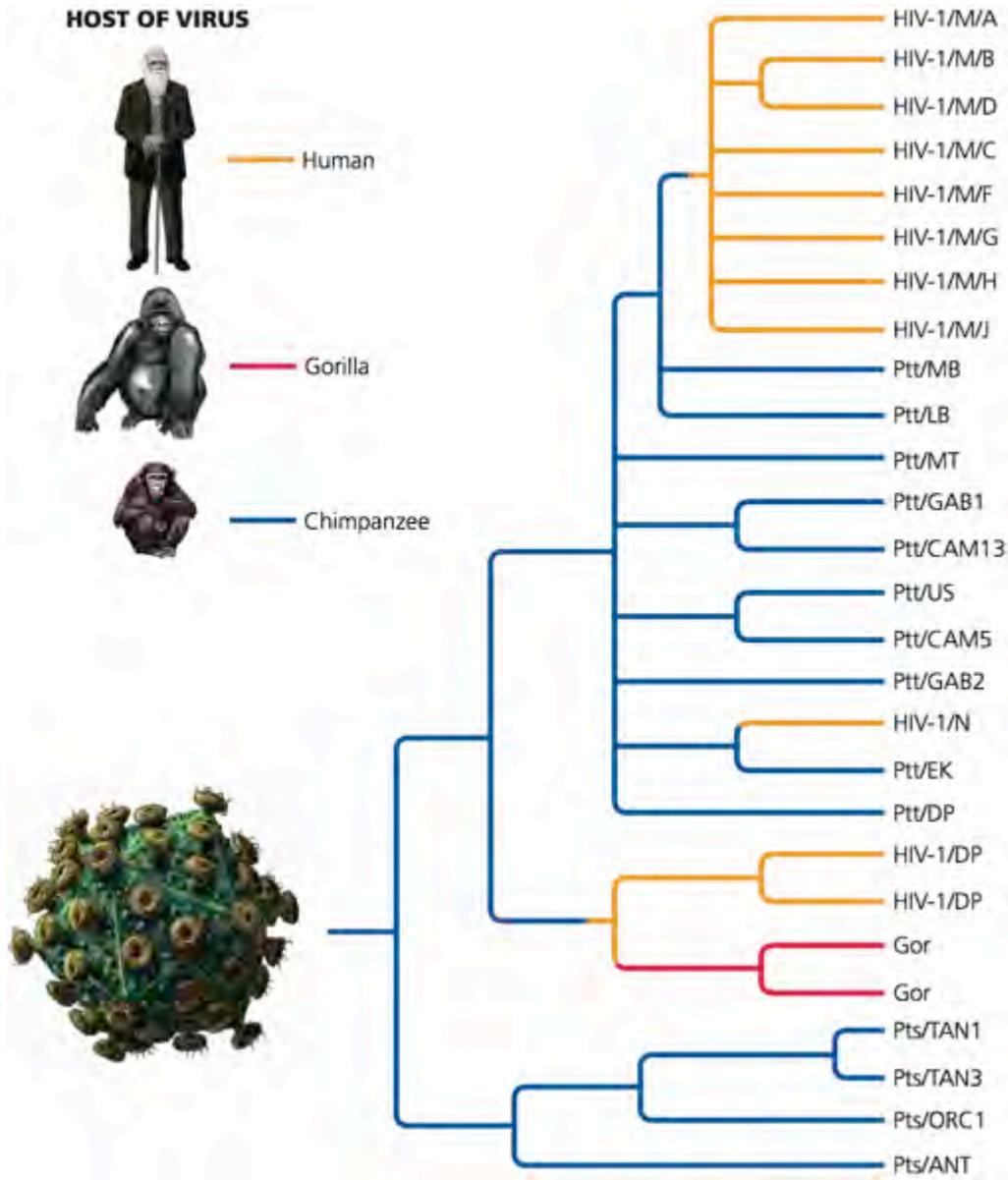


No currently existing species is ancestral to any other



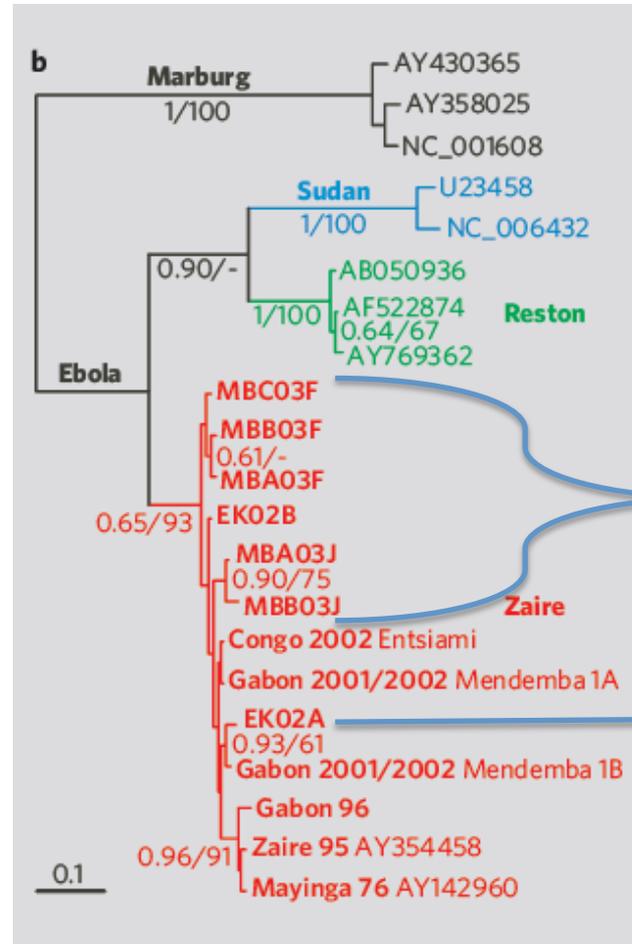
There is no linear ancestor-descendent relationship! Humans did not evolve from cats or fish!

Phylogeny of HIV



Three separate introductions from chimpanzees

Back to our case study: Ebola's natural reservoir

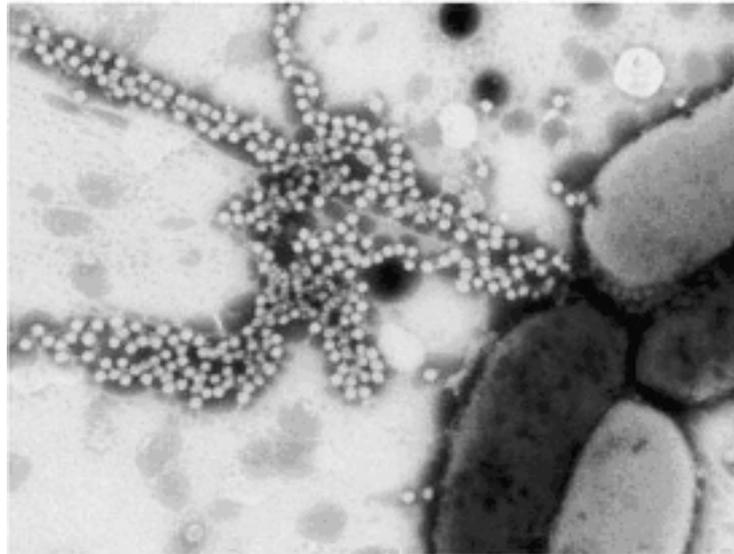


Ebola isolates from fruit bats

Ebola isolate from fruit bats

Shifting to another host species

- phi 6: virus that infects bacteria (bacteriophage)
- phi 6 only infects *Pseudomonas syringae*



Shifting to another host species

- Could phi 6 switch hosts?
- Plated on 14 different *Pseudomonas* species
- A few viruses infected and survived
- All had mutation in protein for attaching to host



Shifting to another host species

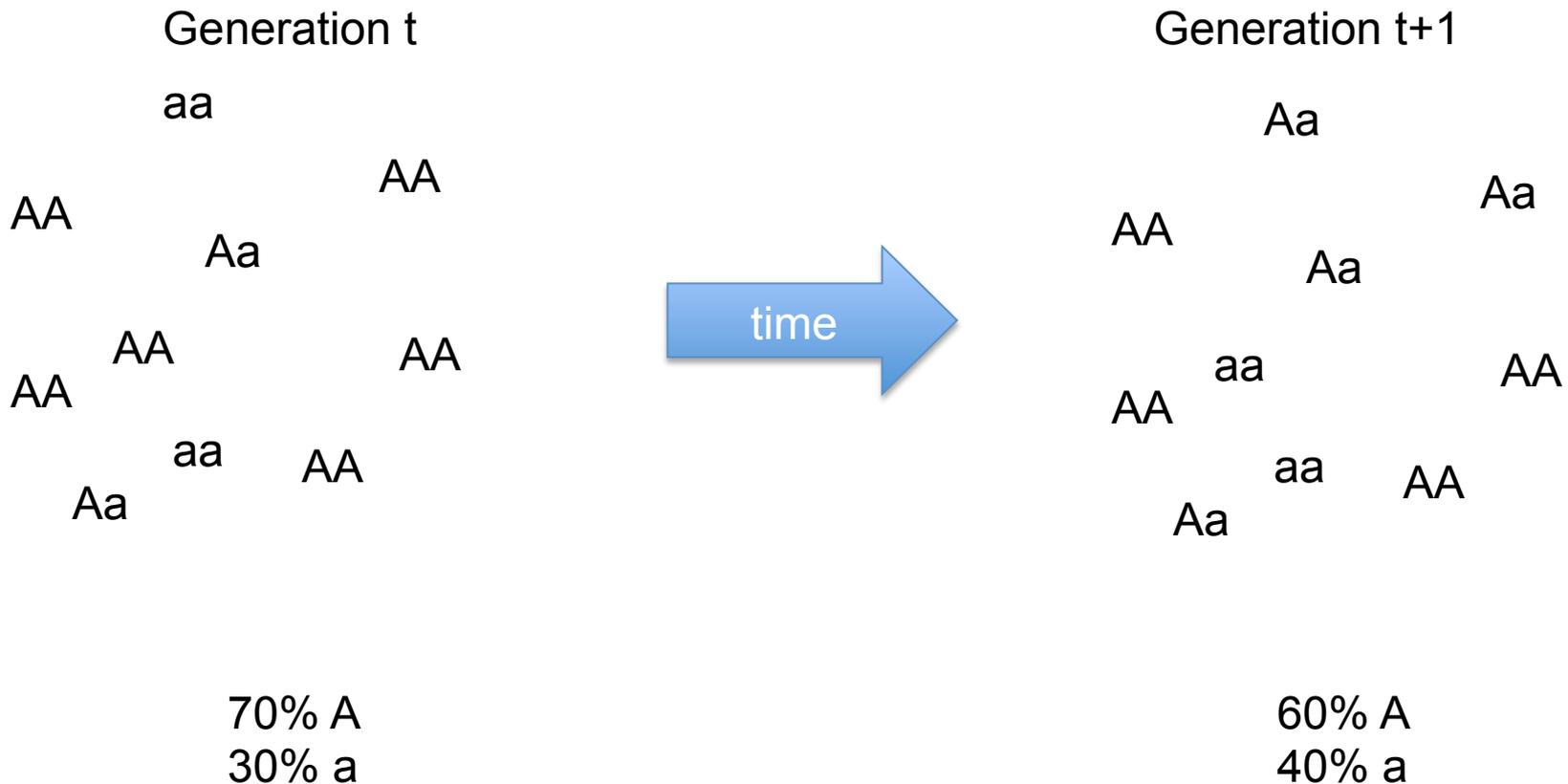
- Once in a new host, must adapt quickly
- Slow growth can lead to extinction

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What is evolution?

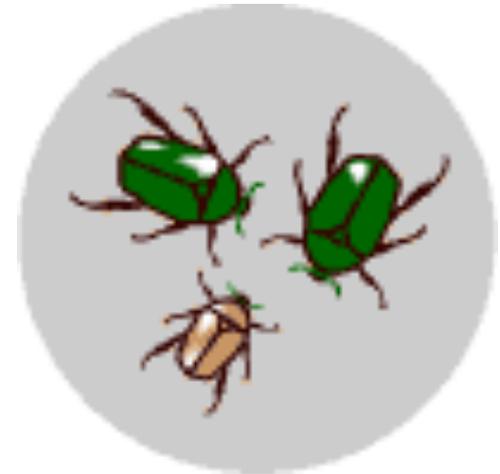
Evolution is a change in a population's allele frequencies over time.



Mechanisms of evolution: sources of variation

Mutation: a change in DNA sequence, gene order, or chromosome number

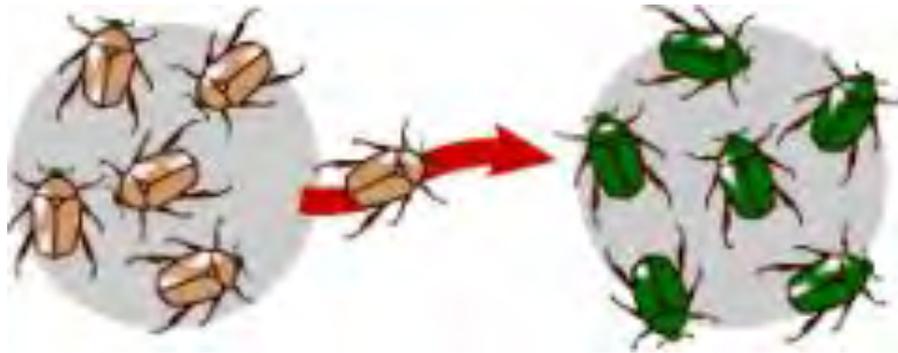
- Random
- Increases genetic variation within populations
- Types of mutations:
 - Point mutations
 - Insertions
 - Deletions
 - Gene duplications
 - Chromosomal inversions
 - Polyploidy



Mechanisms of evolution: sources of variation

Gene flow (or migration): movement of genes between populations

- Increases genetic variation within populations
- Makes populations more similar to each other



Mechanisms of evolution

Natural selection: differential reproductive success

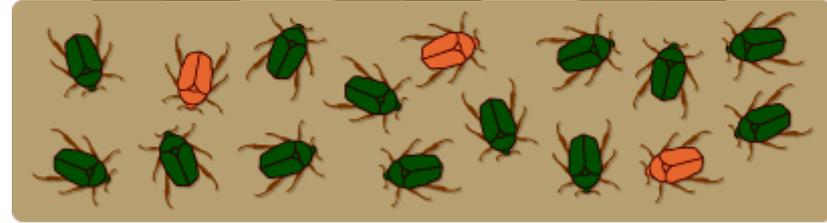
- Non-random
- Not forward-looking, can only work with existing variation
- Only adaptive mechanism of evolution



Evolution by natural selection

Ingredients needed for evolution by natural selection

- Variation in traits
- Inheritance
- Differential reproduction (natural selection)

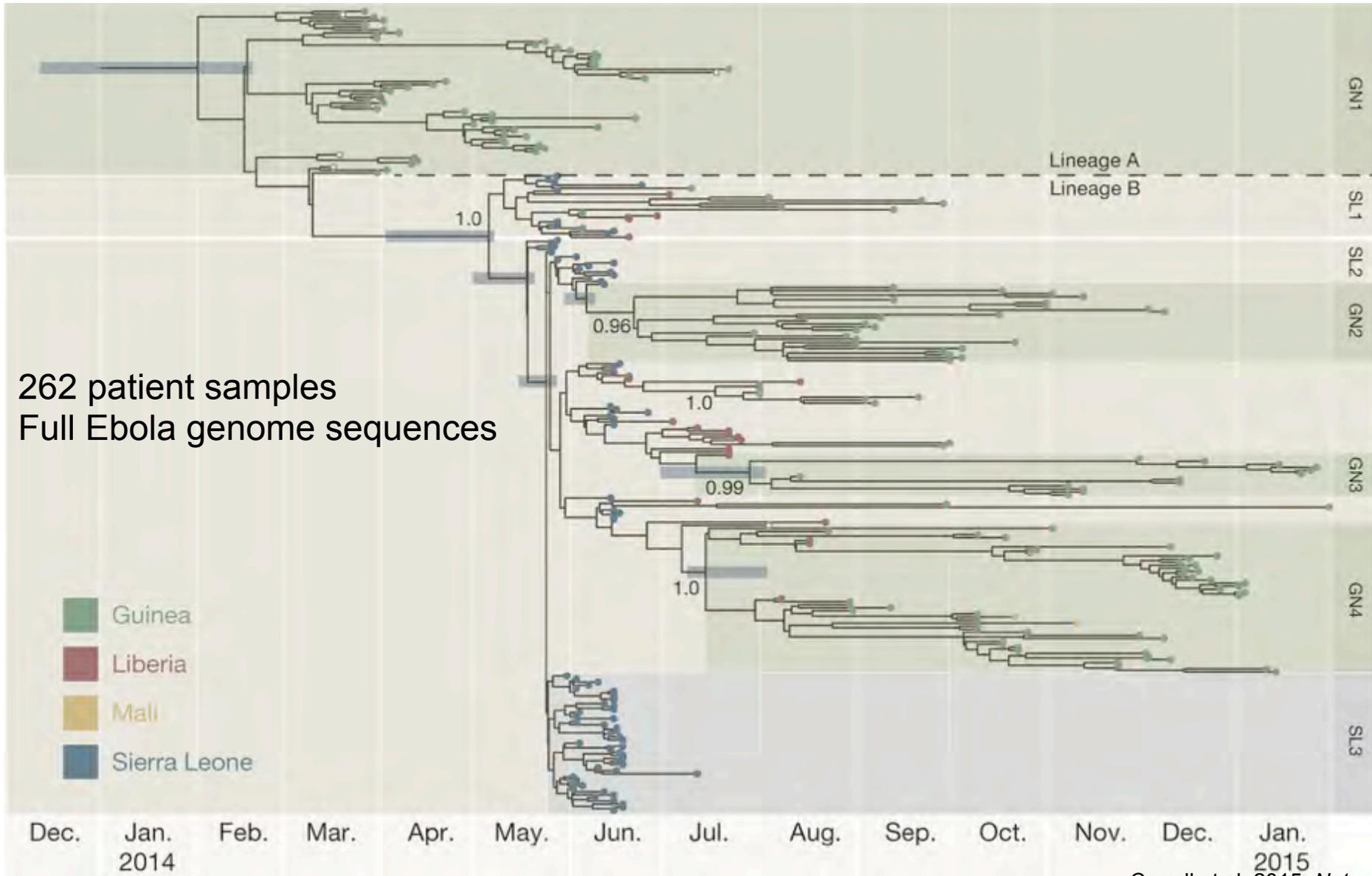


End result: Traits that increase reproductive success increase in frequency in a population.

Evolution within the host species

- Once in a new host, must adapt quickly
- Slow growth can lead to extinction
- Host switching leads to strong selection:
 - Infection
 - Evade immune system and replicate
- **What factors allow pathogens to evolve quickly?**

Back to our case study: the transmission of Ebola, 2014-15



Evolution of virulence: a trade-off

Selection **within host** favors rapid replication (increased virulence).

Competition within host



Transmission to new hosts

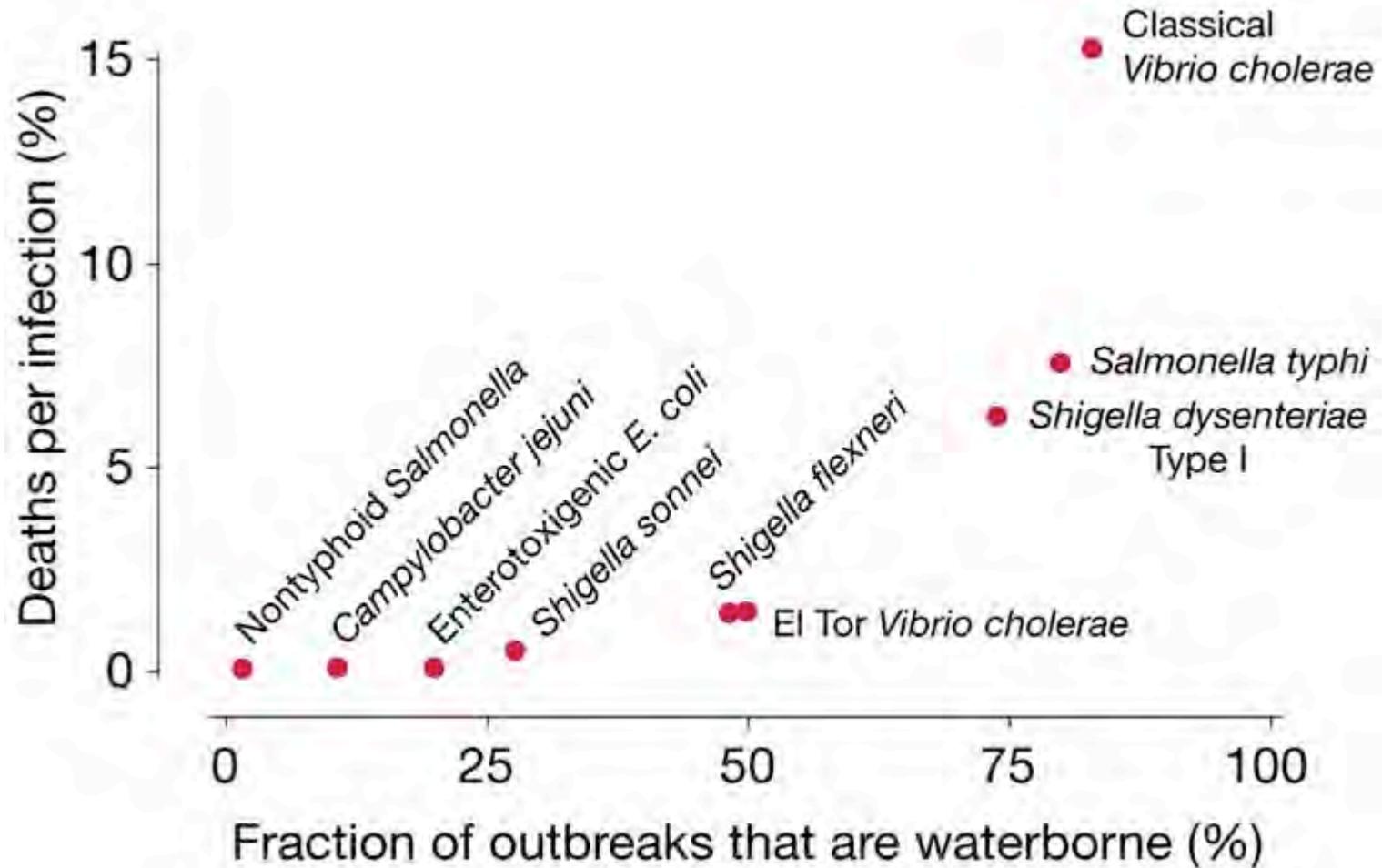
Selection **across hosts** favors reduced virulence.

Mode of transmission affects virulence

Direct transmission, vectorborne, waterborne



Mode of transmission affects virulence



Evolution of virulence: implications for public health

Select for lower virulence by interfering with transmission

- Improve hygiene
- Wear masks
- Provide clean water
- Widespread vaccination

Selection **within host** favors rapid replication (increased virulence).



Selection **across hosts** favors reduced virulence.



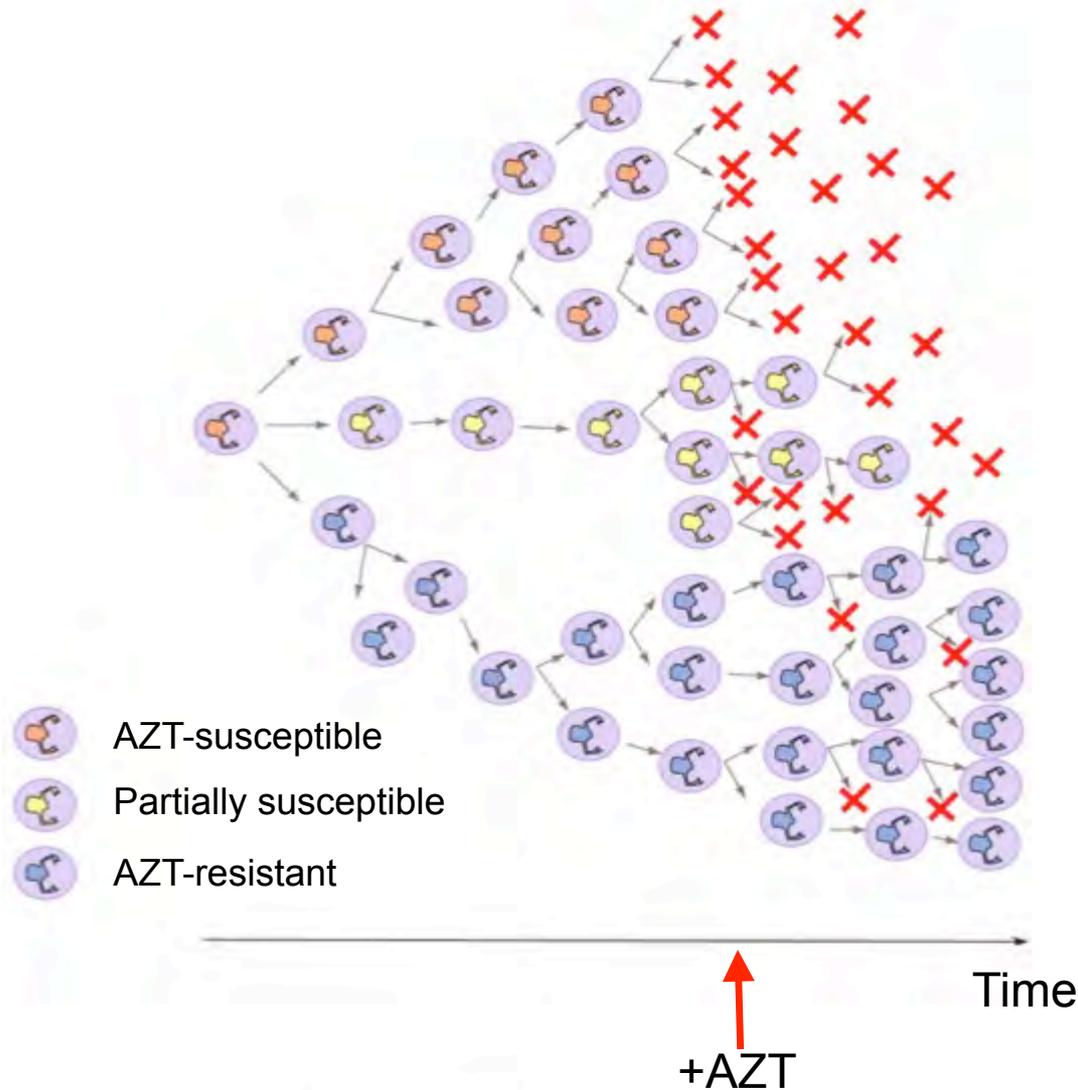
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Evolution within the host species

- Once in a new host, must adapt quickly
- Slow growth can lead to extinction
- Host switching leads to strong selection:
 - Infection
 - Evade immune system and replicate
- **What's another source of strong selection?**

The evolution of drug resistance by natural selection



Estimates of Burden of Antibacterial Resistance

European Union *population 500m*

25,000 deaths per year

2.5m extra hospital days

Overall societal costs
(€ 900 million, hosp. days)
Approx. €1.5 billion per year



Source: ECDC 2007

Thailand *population 70m*

>38,000 deaths

>3.2m hospital days

Overall societal costs
US\$ 84.6–202.8 mill. direct
>US\$1.3 billion indirect



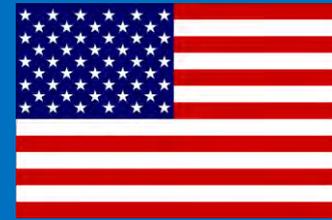
Source: Pumart et al 2012

United States *population 300m*

>23,000 deaths

>2.0m illnesses

Overall societal costs
Up to \$20 billion direct
Up to \$35 billion indirect



Source: US CDC 2013

Global information is insufficient to show complete disease burden impact and costs

Resistance to “last resort” antibiotics

THE LANCET Infectious Diseases

Articles

Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study

Yi-Yun Liu, BS[†], Yang Wang, PhD[†], Prof Timothy R Walsh, DSc, Ling-Xian Yi, BS, Rong Zhang, PhD, James Spencer, PhD, Yohei Doi, MD, Guobao Tian, PhD, Baolei Dong, BS, Xianhui Huang, PhD, Lin-Feng Yu, BS, Danxia Gu, PhD, Hongwei Ren, BS, Xiaojie Chen, MS, Luchao Lv, MS, Dandan He, MS, Hongwei Zhou, PhD, Prof Zisen Liang, MS, Prof Jian-Hua Liu, PhD  , Prof Jianzhong Shen, PhD  

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Published Online: 18 November 2015



WDIY news arts & life music programs

HEALTH

E. Coli Bacteria Can Transfer Antibiotic Resistance To Other Bacteria

Updated November 20, 2015 · 1:07 PM ET 



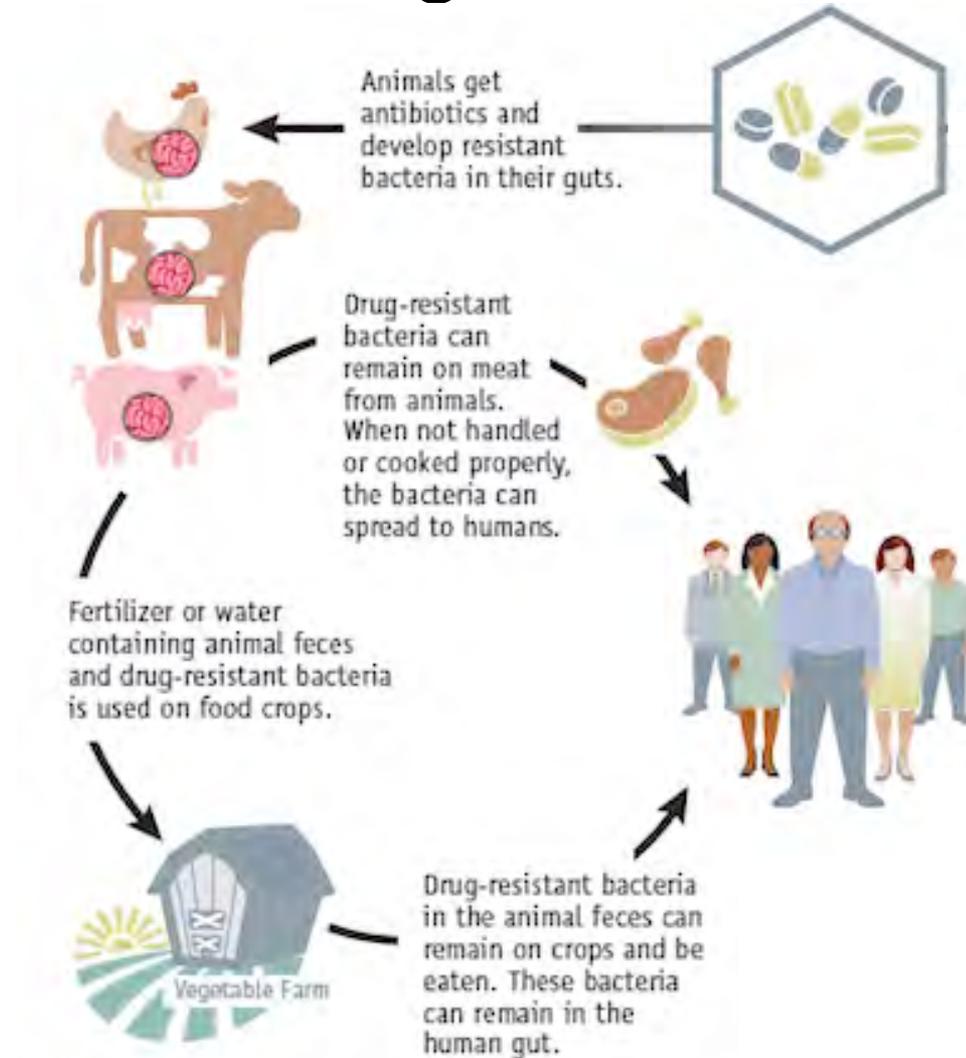
JASON BEAUBIEN



Avoiding more widespread resistance

1. Avoid contracting infections
2. Minimize transmission of resistant microbes
3. Improve use of antimicrobial drugs
 - Take only when appropriate (i.e., don't take an antibiotic for the flu!)
 - Use antibacterial soaps/cleaners ONLY around people with weakened immune systems
 - Avoid broad-spectrum antibiotics if possible.
 - Take ALL of the medication
 - Reduce agricultural use of antibiotics

Why can reducing inappropriate use of antimicrobial drugs combat resistance?



- Resistant bacteria escape livestock, spread to humans

Current research aims

- Can we predict which pathogens are more likely to shift to humans?
- What makes some strains so much more deadly than others?
- How can we develop effective new vaccines and drugs?
- What is the mechanism of resistance?
- How can we develop better and faster diagnostic tools?