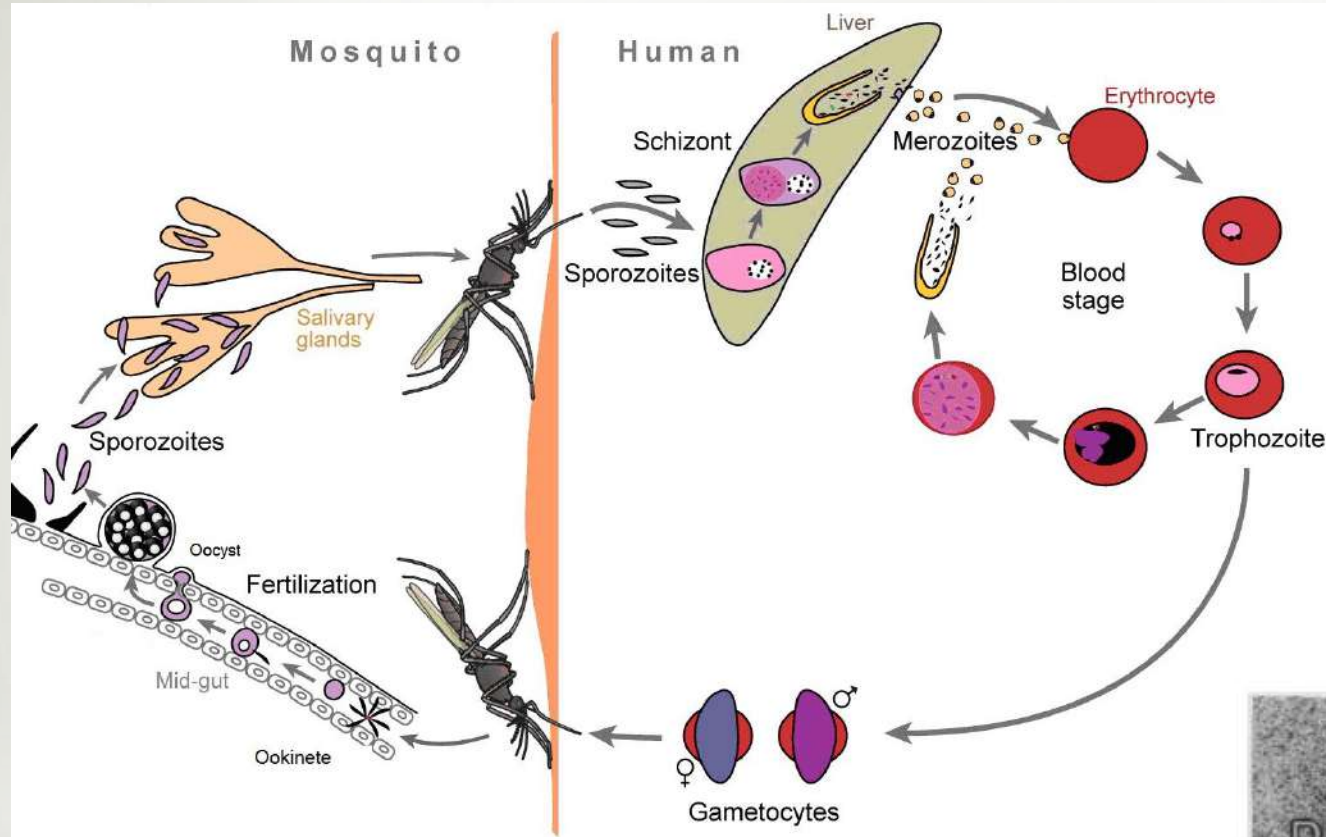


“Other” pathogens

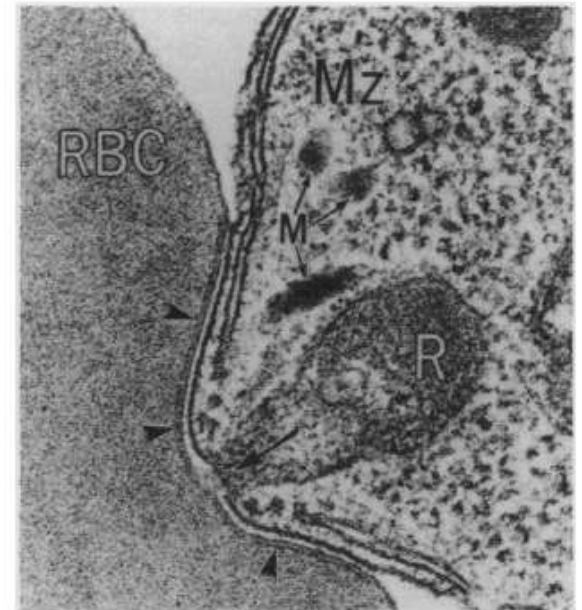
Name of pathogen	Type of organism	Disease caused	Disease causing mechanism	Examples
Fungi	Eukaryotic	Meningitis, Respiratory failure, Aspergillosis	Infect immunocompromised individuals, produce toxins (Aflatoxins, alkaloids)	<i>Candida albicans</i> , <i>Aspergillus fumigatus</i> , <i>Cryptococcus</i>
Protozoa	Eukaryotic, unicellular	Malaria, Sleeping sickness, intestinal disorder	Acquired through mosquito bites, contaminated food/water, has many stages in the life cycle	<i>Plasmodium falsiparum</i> , <i>Giardia lamblia</i> , <i>Trypanosoma brucei</i>
Helminth	Multicellular vertebrates	Schistosoma, heart failure, muscle pain	Spread through fecal-oral route, eggs can remain in environment for a long time, drugs are toxic	<i>Trichinella Spiralis</i>
Prion diseases	Protein (no genome)	Lethal neurodegenerative disorders	“infectious” version of protein causes large aggregation in CNS	Kuru, Scrapie, Bovine spongiform encephalopathy

Pathogenic protozoa - *Plasmodium falsiparum*

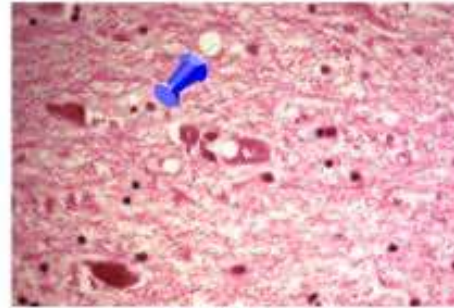


Vaccine targets:

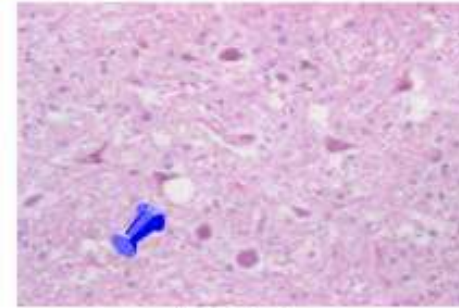
1. Pre-erythrocytic stage: CS protein of Sporozoite, RTS,S vaccine
1. Liver Stage: Liver stage antigen (LSA-1)
2. Blood stage: Merozoite Surface Protein (MSP-1)



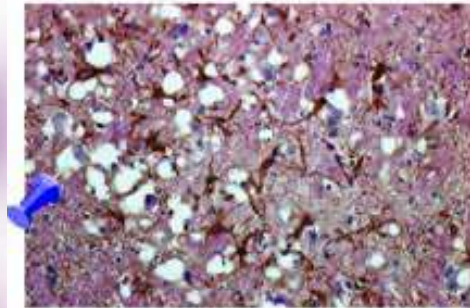
Prion diseases - Transmissible spongiform encephalopathies



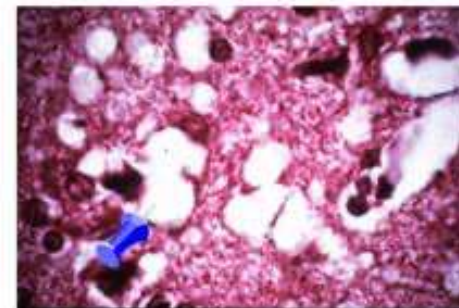
CJD



BSE

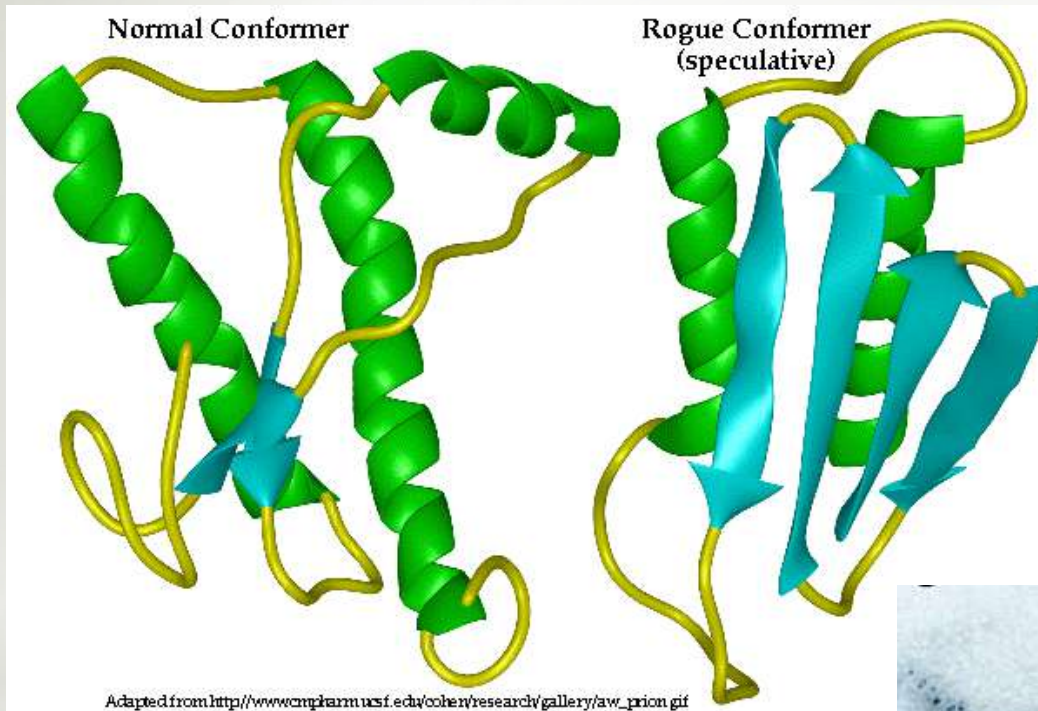


Scrapie



Kuru

Prion protein conformations



Adapted from http://www.cmp.karm.ucl.ac.uk/cohen/research/gallery/aw_prion.gif

Source: web.stanford.edu

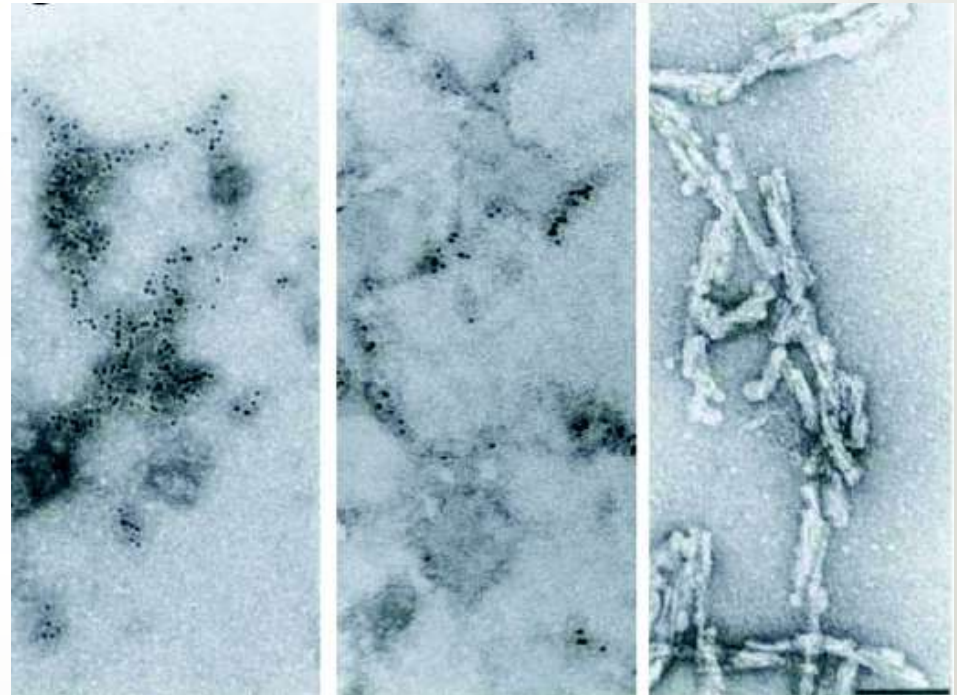
PrP^c - cell surface glycoprotein
found in all mammals and birds

Imposes own conformation onto
cellular prion protein (PrP^c) of host

Conformational conversion of PrP^c to
PrP^{Sc}, insoluble, partially protease
resistant isoform, aggregation prone

Infectious agent - abnormally
folded and aggregated protein

Capable of propagating itself,
described by Stanley B. Prusiner



Source: Adriano Aguzzi, and Anna Maria Calella, *Physiol Rev*, 2009

Evolution and disease



The future of humanity and microbes likely will unfold as episodes of a suspense thriller that could be titled “Our Wits Versus Their Genes”

Joshua Lederberg, “Infectious History” (2000)

How do microbes become virulent?

Microbes are accumulating mutations/new genetic material all the time
(viruses more than bacteria)

Horizontal gene transfer

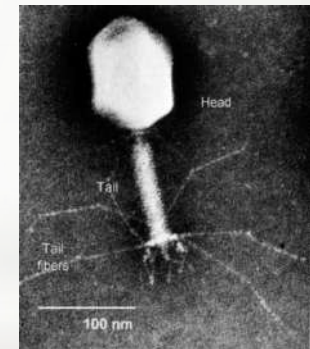
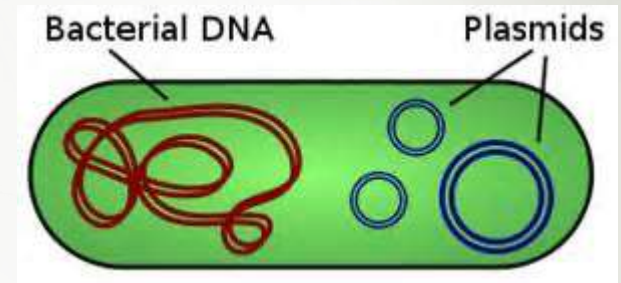
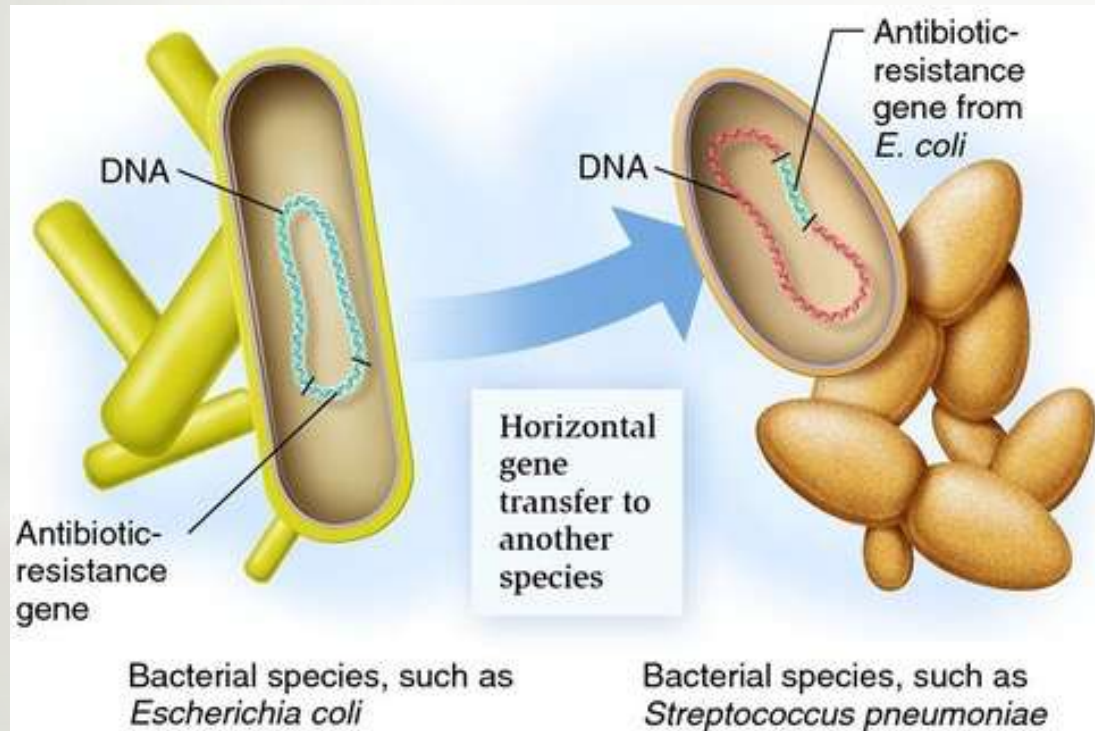
Looking for new reservoirs

Host adaptation/virulence strategies

Most do not succeed in becoming pathogenic

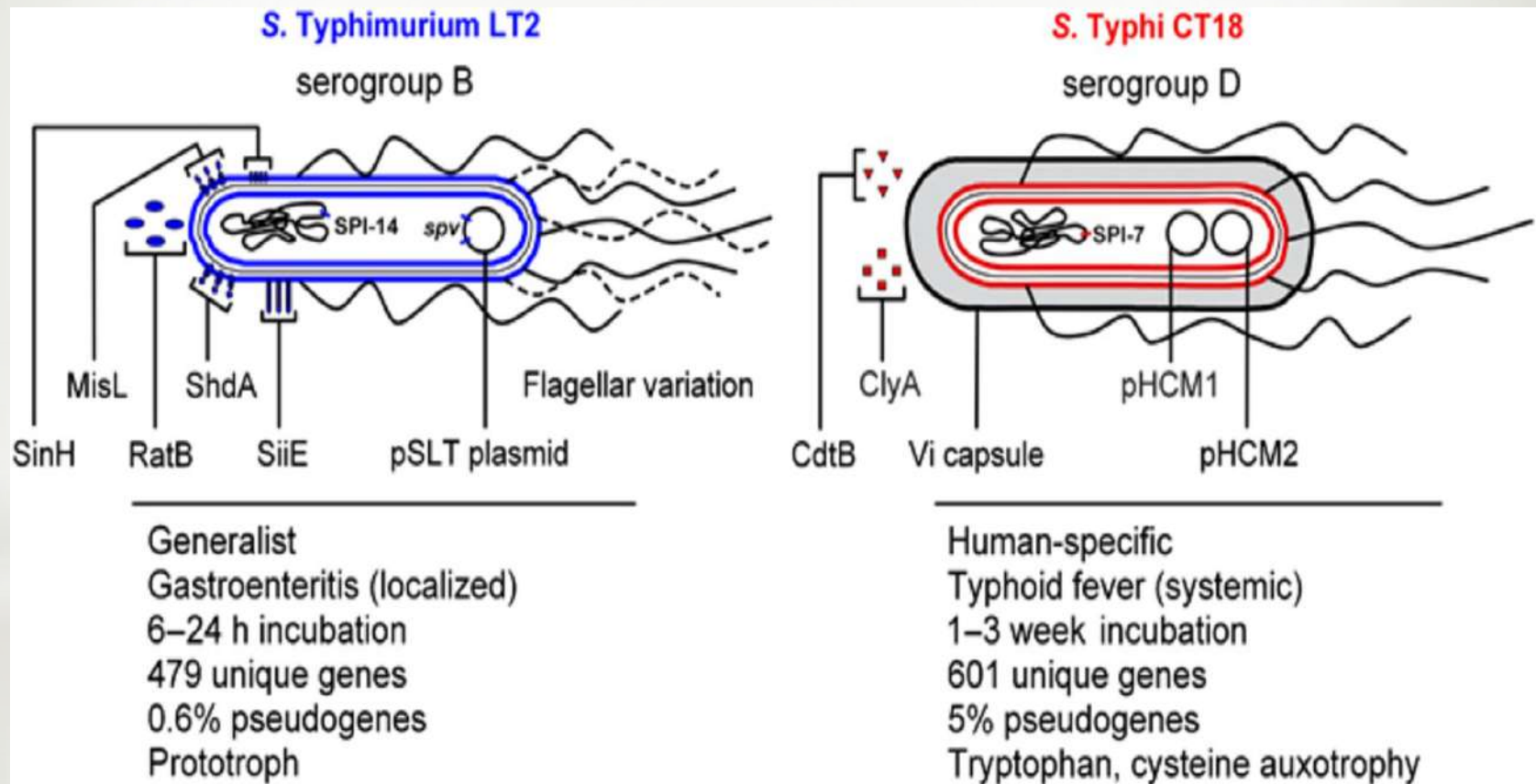
Strong biological/ecological barrier at every step

Horizontal gene transfer



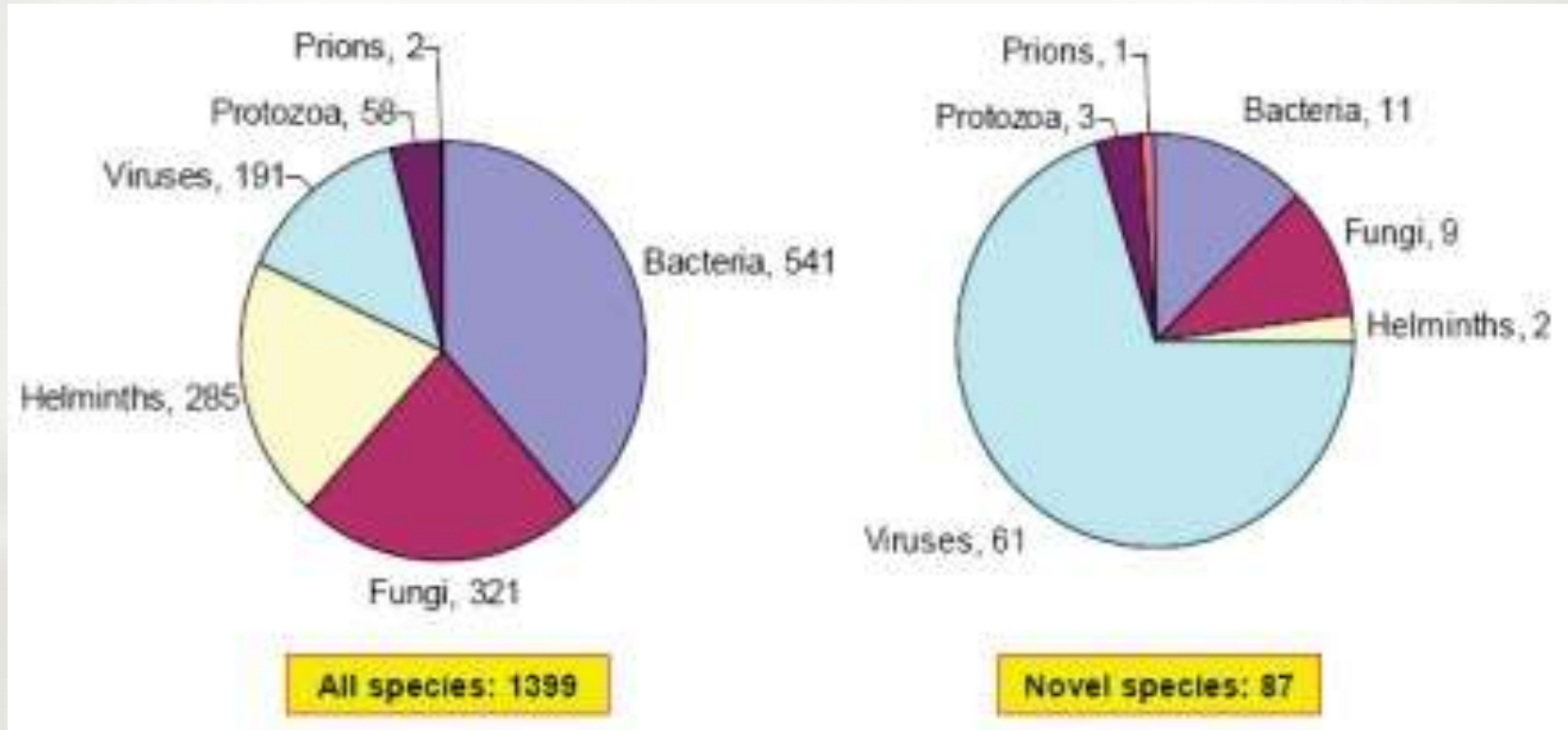
Transfer of pathogenicity islands through plasmids, bacteriophages, transposable elements

How do microbes become virulent?



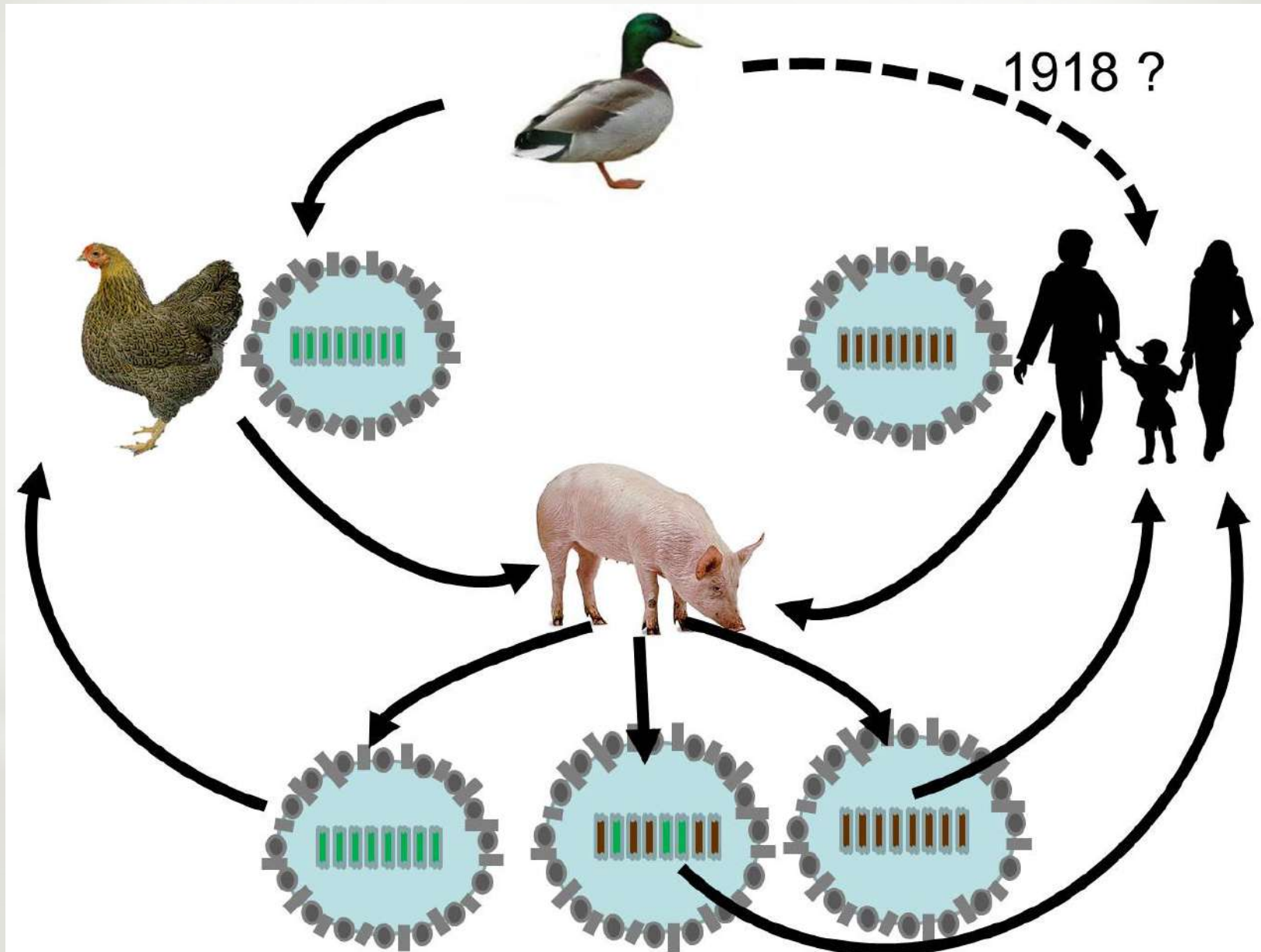
Acquisition of genes which confer virulence and antibiotic resistance
Loss of genes which control interaction with host cells
Loss of function leads to specialization
Offer selective advantage, selection done by host behaviour

How do microbes become virulent?

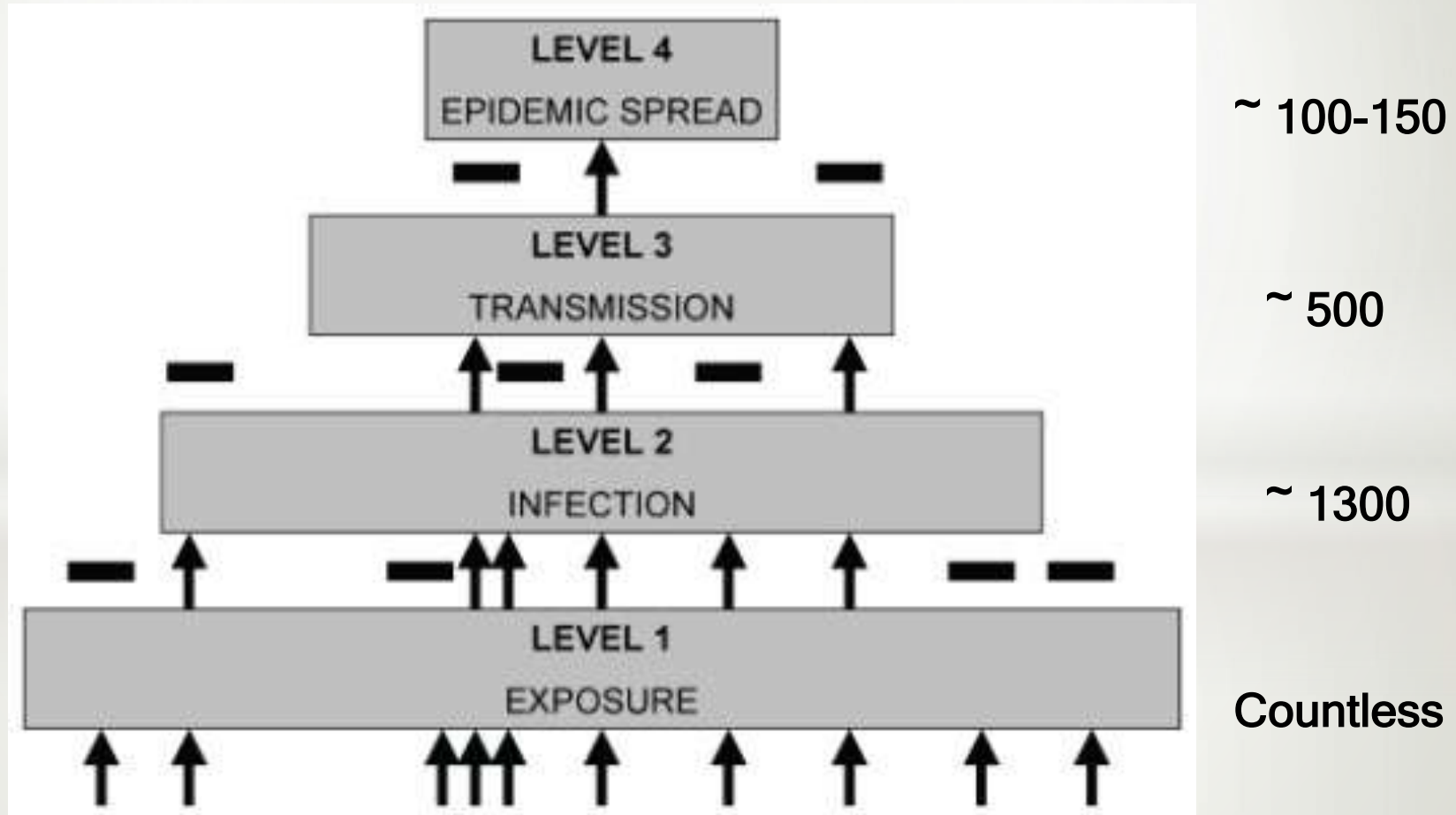


Viruses are better at accumulating mutations

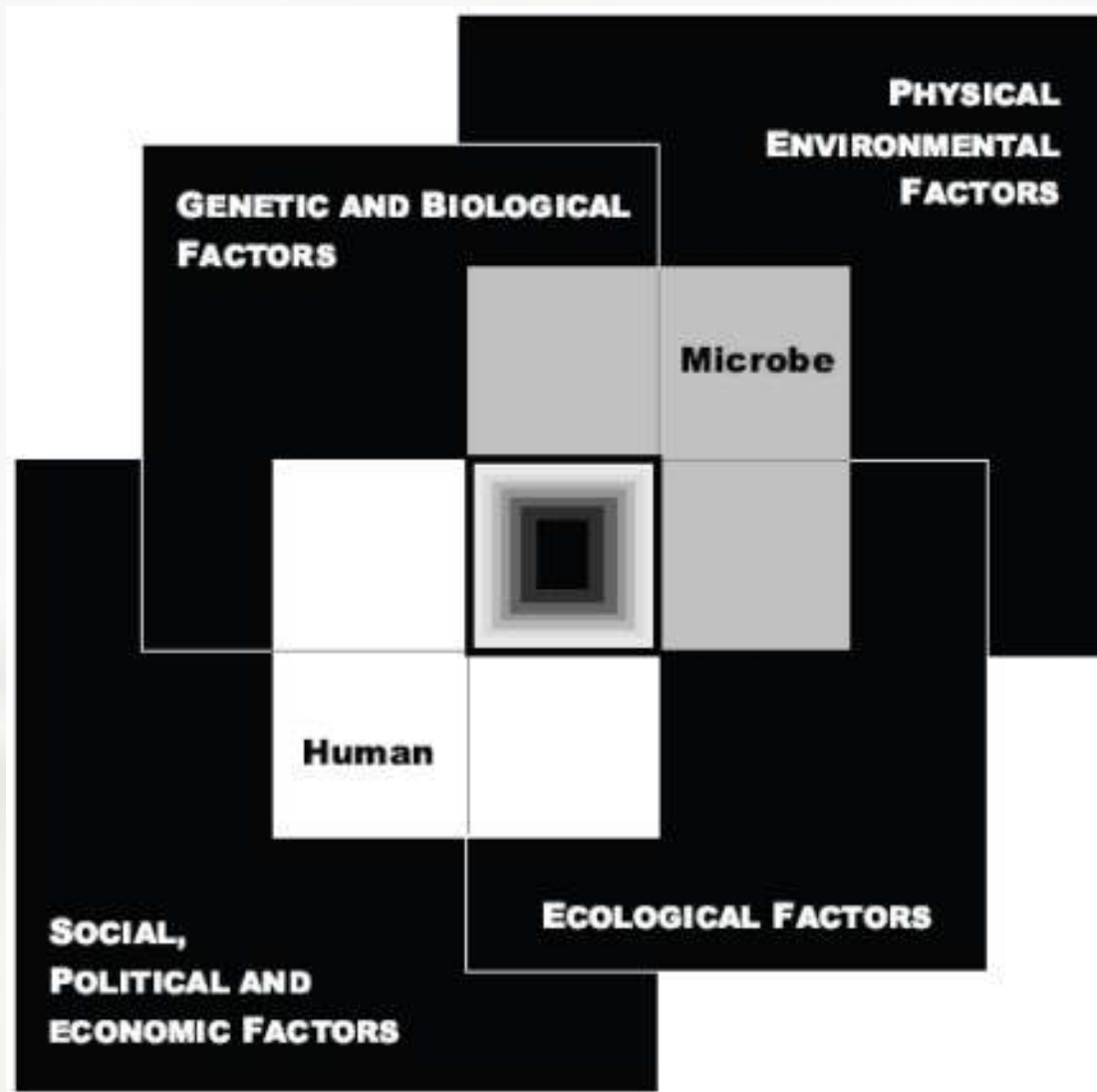
Accumulation of mutations/selective pressure



Biological barrier to establishment of virulence



The convergence model for emergence of an infectious disease



Perfect storm leads to pandemic

**“Both host and pathogen are learning from each other,
the goal is peaceful co-existence”**



Microbial adaptation strategies

Pathogenic organisms are in continuous strife with non-pathogenic Counterparts

Adaptation is to ensure continuous supply of nutrients, safety, multiplication

Extremely virulent pathogens may be replaced by benign ones

Major epidemics of syphilis, coevolution to benign strain

Scarlet fever causing bacteria (*Streptococcus pyogenes*) coevolved to milder strain

Diphtheria causing bacteria evolved to milder strains

Killing reservoirs not a good strategy!

Microbes with vector transmission pathways or “storage facilities” can afford to be more virulent e.g. microbes causing malaria, anthrax, cholera

Microbes spread by direct contact evolve to become less virulent

“The vast majority of microbes are yet to be identified”

