Introduction to Mathematical Models of Infectious Disease in Livestock

Lecture 2: Disease fundamentals

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Overview

Basic knowledge required for modelling infectious disease dynamics:

- Infection versus disease
- Why worry about infectious disease in livestock?
- The role of pathogens on infectious disease
- The role of the host on infectious disease
- Infection routes
- Infectious disease control

Definition: Infectious Disease

Diseases caused by parasites

- **Organism colonising a host**
  - **e.g. Viruses, bacteria, protozoa, worms, flies, ticks**

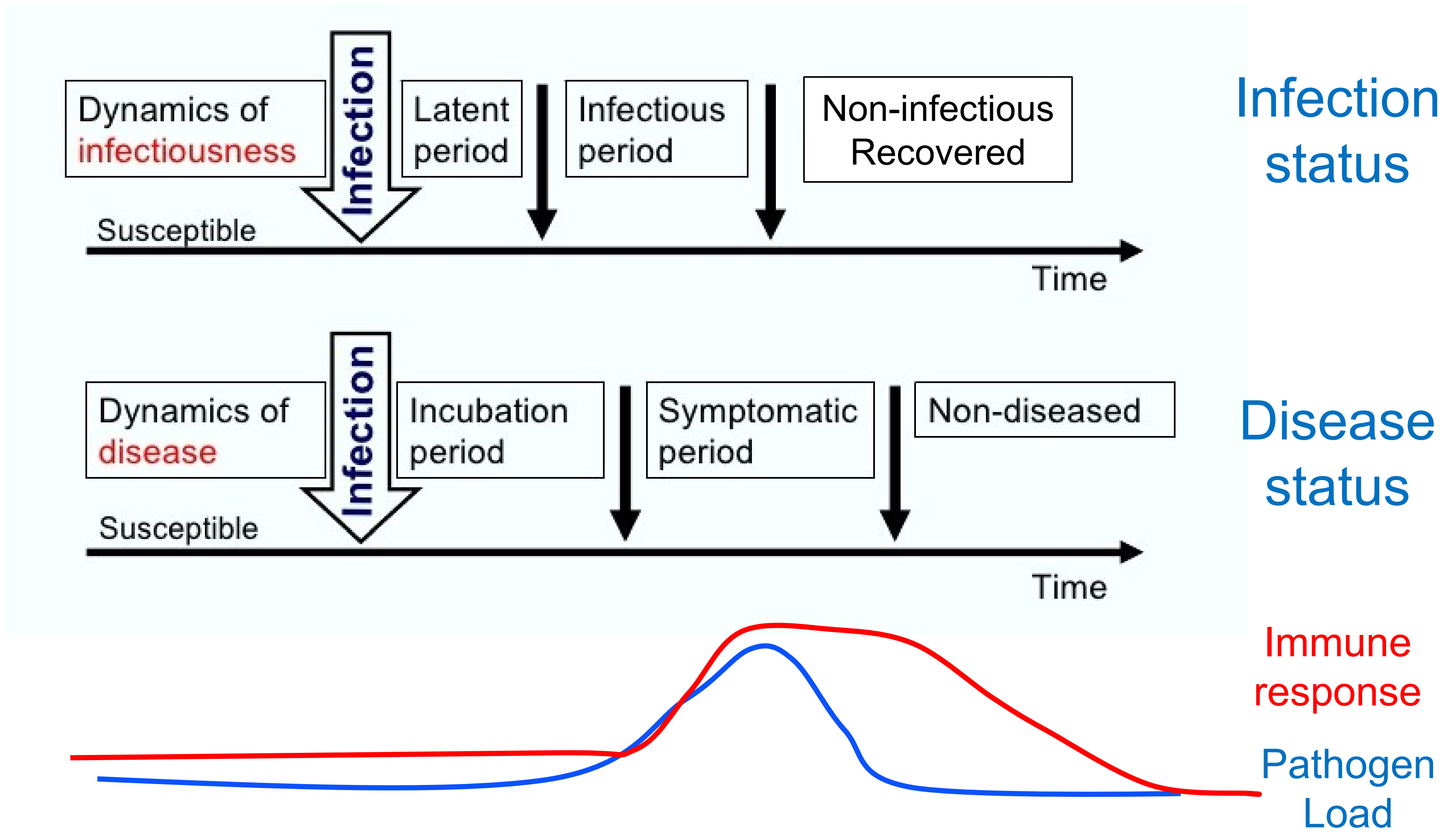
Infection vs Disease

- **Infection**
  - Colonization of host by parasite
- **Disease**
  - Side-effects of infection by parasite or immune response
  - Many forms:

    acute, chronic, latent, asymptomatic…

Infection need not cause disease!

Infection vs disease status



Why worry about infectious disease in livestock?

Huge impact on:

1. Animal welfare: Part of 5 Freedoms

Animal Welfare Act of 1966

1. Freedom from hunger or thirst by ready access to fresh water and a diet to maintain full health and vigour
2. Freedom from discomfort by providing an appropriate environment including shelter and a comfortable resting area
3. Freedom from pain, injury or disease by prevention or rapid diagnosis and treatment
4. Freedom to express (most) normal behaviour by providing sufficient space, proper facilities and company of the animal's own kind
5. Freedom from fear and distress by ensuring conditions and treatment which avoid mental suffering

Why worry about infectious disease?

Huge impact on:

2. Economics

- 10-20% of turnover in developed countries
- 35-50% in developing countries

Foresight report: Brownlie et al., 2006

Source: FAO (2002,2004); EU (2005).

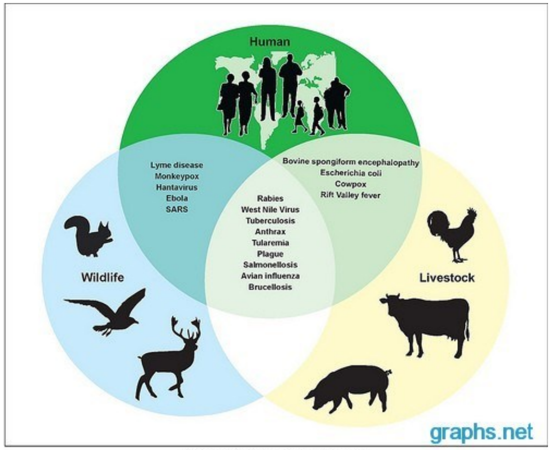
Disease	Total costs (£ billion)
BSE, UK 1996/1997	2.3
FMD, Chinese Province of Taiwan 1997	4
CSF, Netherlands 1997/1998	1.4
FMD, UK 2001	7
AI, Vietnam 2003/2004	0.32
AI, Netherlands 2003	0.4

Why worry about infectious disease?

Huge impact on:

3. Human Health

- Zoonotic threats & food poisoning
- Emergence of anti-microbial resistance



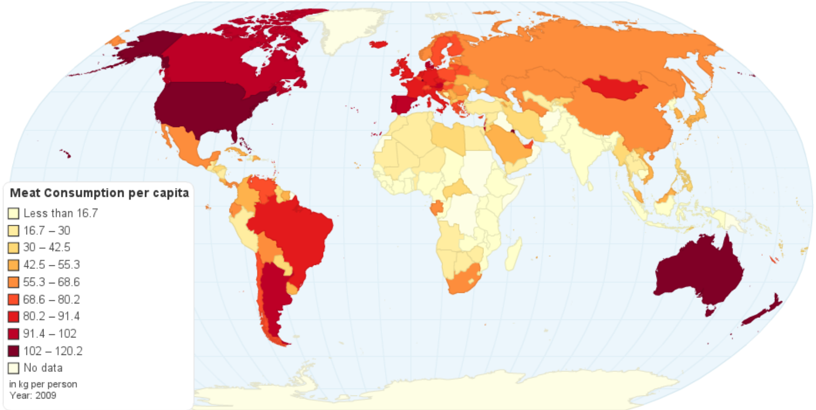
Source: GAO analysis of USGS data (data); Art Explosion (images).

Why worry about infectious disease?

Huge impact on:

4. Food security

- By 2050 over 9 billion people need to be fed
- Animal products are an important food source and supplier of protein
- All production systems at risk



Source: National Geographic 2011

Impact of infection on host fitness & performance

Infection-induced drop in animal (re)productive performance is a major problem to livestock production:

- Reduction in growth

  most micro- & macro-parasite infections; affects all host species

- Reduction in milk or wool production in ruminants

  e.g. mastitis, foot and mouth disease, bovine tuberculosis, gastro-intestinal parasite infections…

- Reduction in fertility

  e.g. Porcine Reproductive and Respiratory Syndrome, others

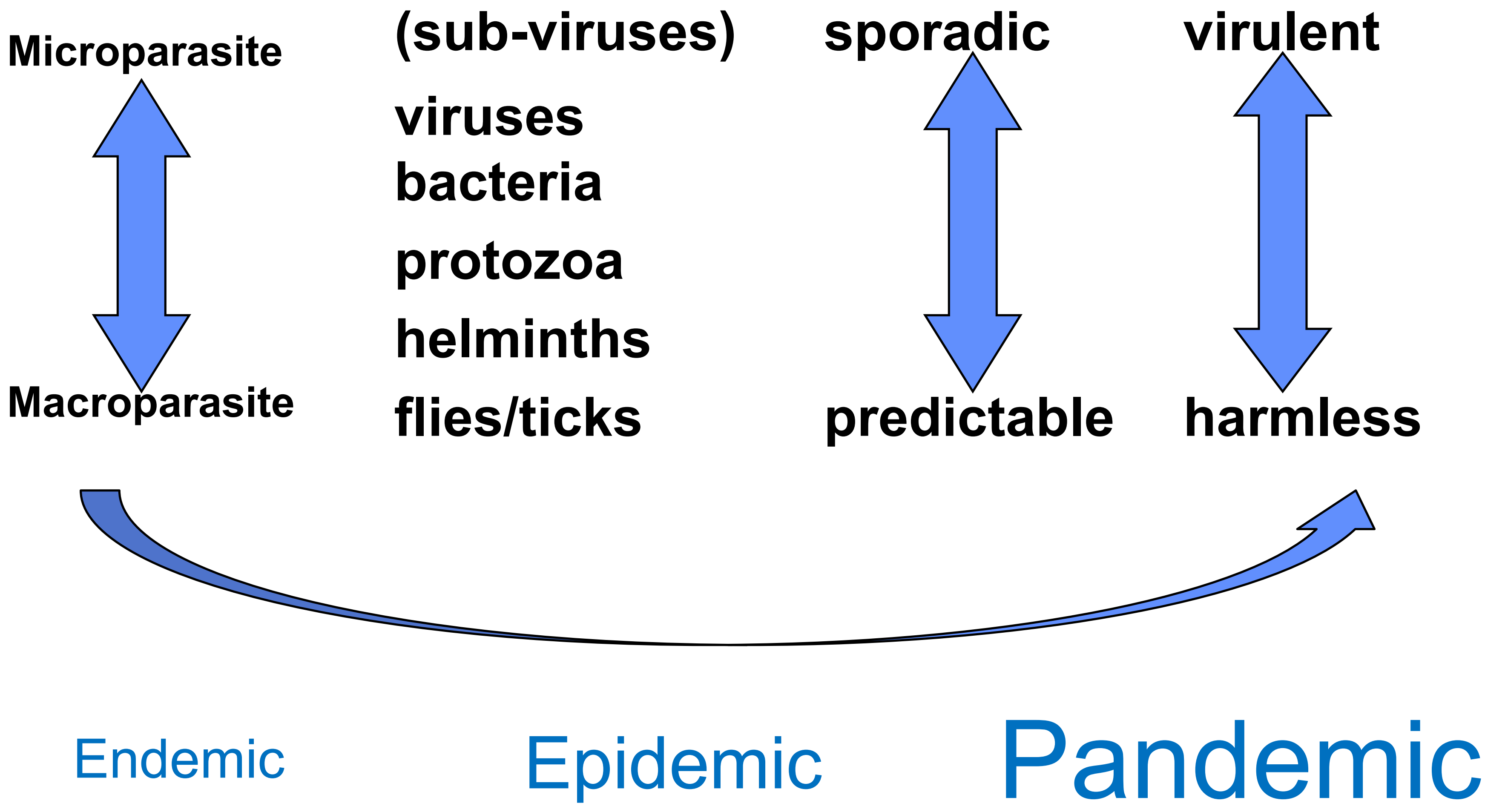
Mechanisms for infection-induced production losses: Resource allocation theory

- **All biological processes** (e.g. maintenance, growth, milk / wool production, reproduction, fighting infections) **require nutritional resources** (protein, energy, minerals, …)
- Infection
  - Reduces resource intake; 'infection-induced anorexia'
  - Diverts available resources away from (re)production towards fighting infections

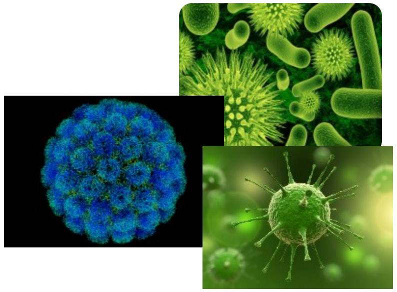
➢ Fewer resources available for (re)production

Lochmiller & Deerenberg; Rauw 2012

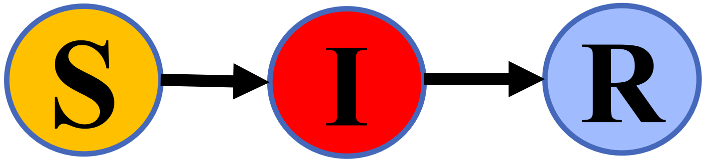
Classification of pathogens

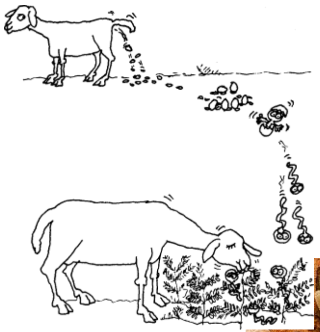


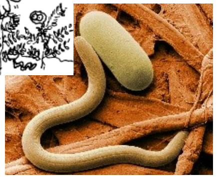
Micro-parasites



- All parasites that have direct reproduction within the host
  - E.g. virus, bacteria, some protozoa, fungi
- Characterised by small size, high reproduction rates & short generation time
- Hosts that recover usually acquire immunity over some time
- Duration of infection is usually short compared to life span of the host
- Lends itself to classification of hosts into susceptible, infected, recovered & immune / remover category







Macro-parasites

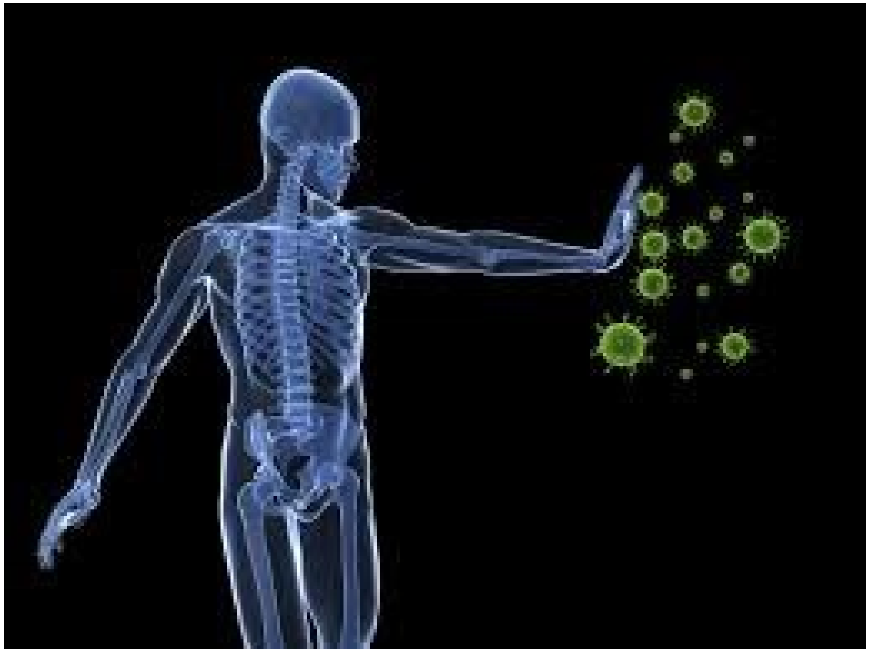
- Parasites with no direct reproduction within the host
  - E.g. most helminths and arthropods
- Typically larger & longer generation times
- Typically of persistent nature, with host being continually re-infected
- Factors influencing disease progression usually depend on the number of parasites in a given host
- Mathematical models need to take account of parasite life-cycle & parasite burden within / outside the host

Host traits affecting disease prevalence & impact

- Resistance
  - Ability of host to control parasite lifecycle
    - Ability to fully resist infection is an example
- Infectivity
  - Ability of host to transmit infection
    - Blocking transmission is an example
- Tolerance / Resilience
  - Ability of host to maintain fitness despite infection
    - Ability to not develop disease when infected is an example

Traits can be binary (e.g. not resistant / fully resistant) or continuous

Resistance



= ability to block pathogen entry or restrict within host pathogen replication

High resistance corresponds to:

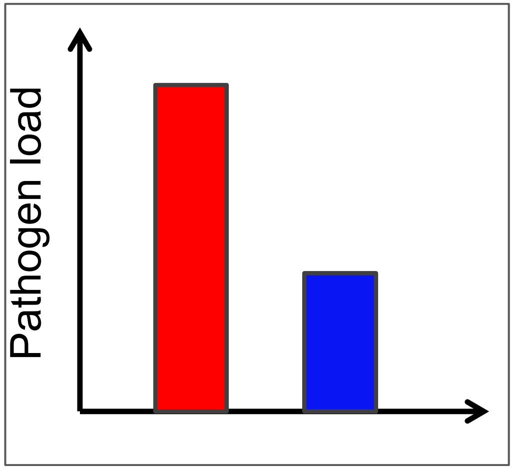
- Low pathogen burden
- Low risk of disease transmission
- High health and production

Desirable target trait for reducing disease prevalence and maintaining high health & production

How may an animal be resistant?

- Lack of binding proteins / receptors
- Immunocompetence
  - i.e. good & appropriate immune response
- Physical obstruction
- Avoidance
  - e.g. grazing behaviour

How to measure resistance?

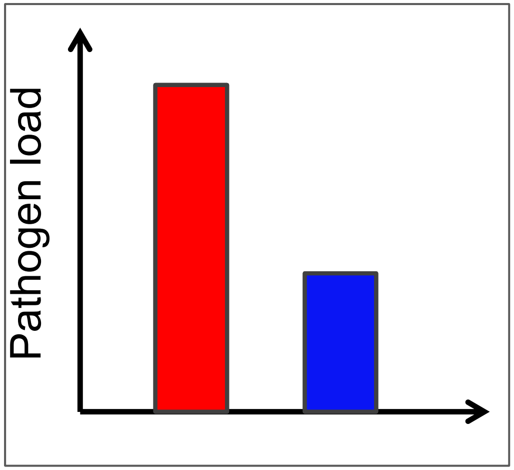


Resistance measures:

- Pathogen load (ideally)
- Immune response
- Infection status (healthy / diseased)
- Production or health trait

Are these accurate biomarkers for resistance?

How to measure resistance?



Resistance measures:

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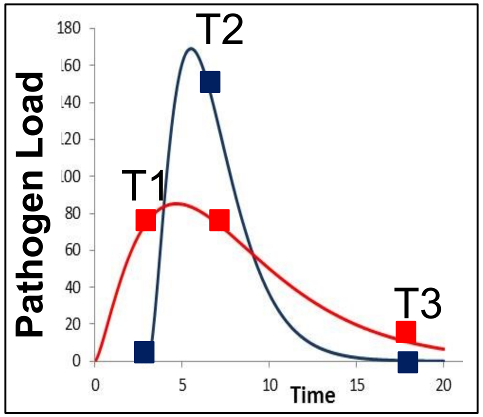


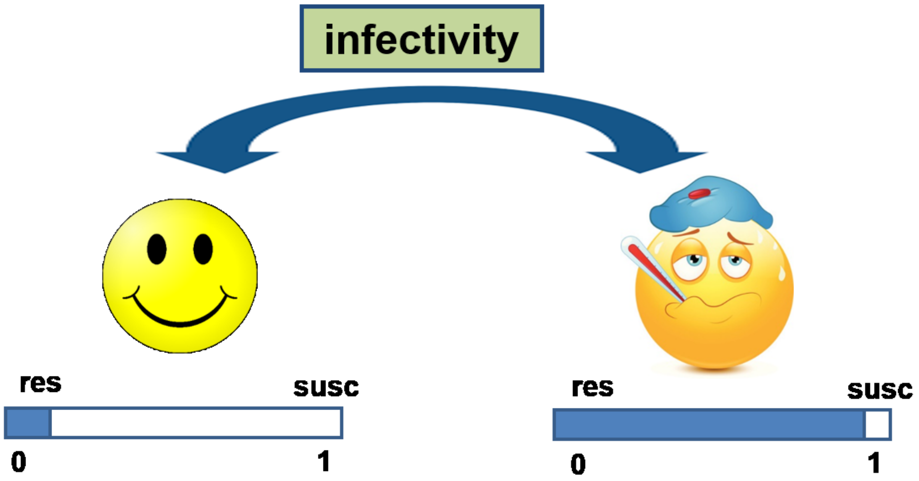
- Risk of confounding resistance with other factors is particularly high in field data

  Not all animals infected at same time / with same dose

- Uncertainty in identifying high risk individuals

Susceptibility

- **Susceptible individuals in epidemiology:** individuals **yet to be** infected
- **Susceptible individuals in genetics:** individuals **more likely to** be infected, i.e. with a higher liability to infection
  - Often considered as the inverse of resistance



Tolerance / Resilience

= ability of to limit the impact of infection on health or performance

High tolerance if:

- Increase of pathogen load has little impact on health / performance

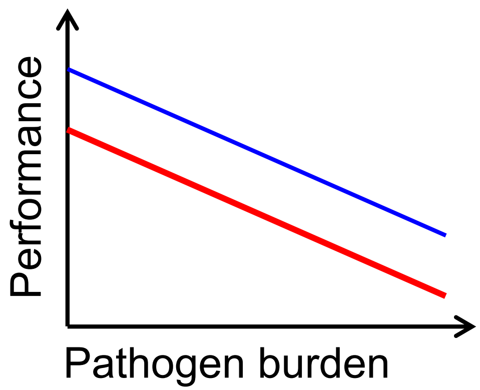
- Desirable target trait to maintain high health / production throughout infection
- But does not limit disease spread!

How may an animal be tolerant?

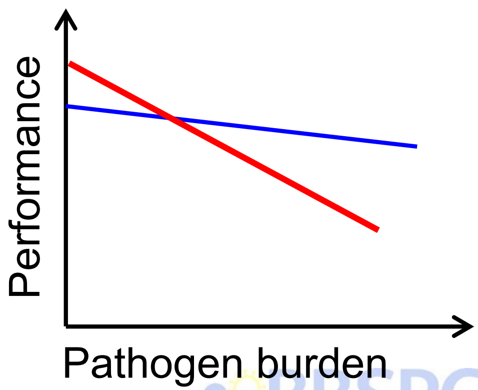
- Effective tissue damage control mechanisms
  - E.g. reduction of systemic inflammation
- Effective resource allocation
  - e.g. by timely allocation of resources to e.g. immune response
  - e.g. bats infected with Ebola virus minimize oxidative stress associated with activities of high metabolic costs (e.g. flight)
- Still much research to be done!

How to measure tolerance?

Same tolerance

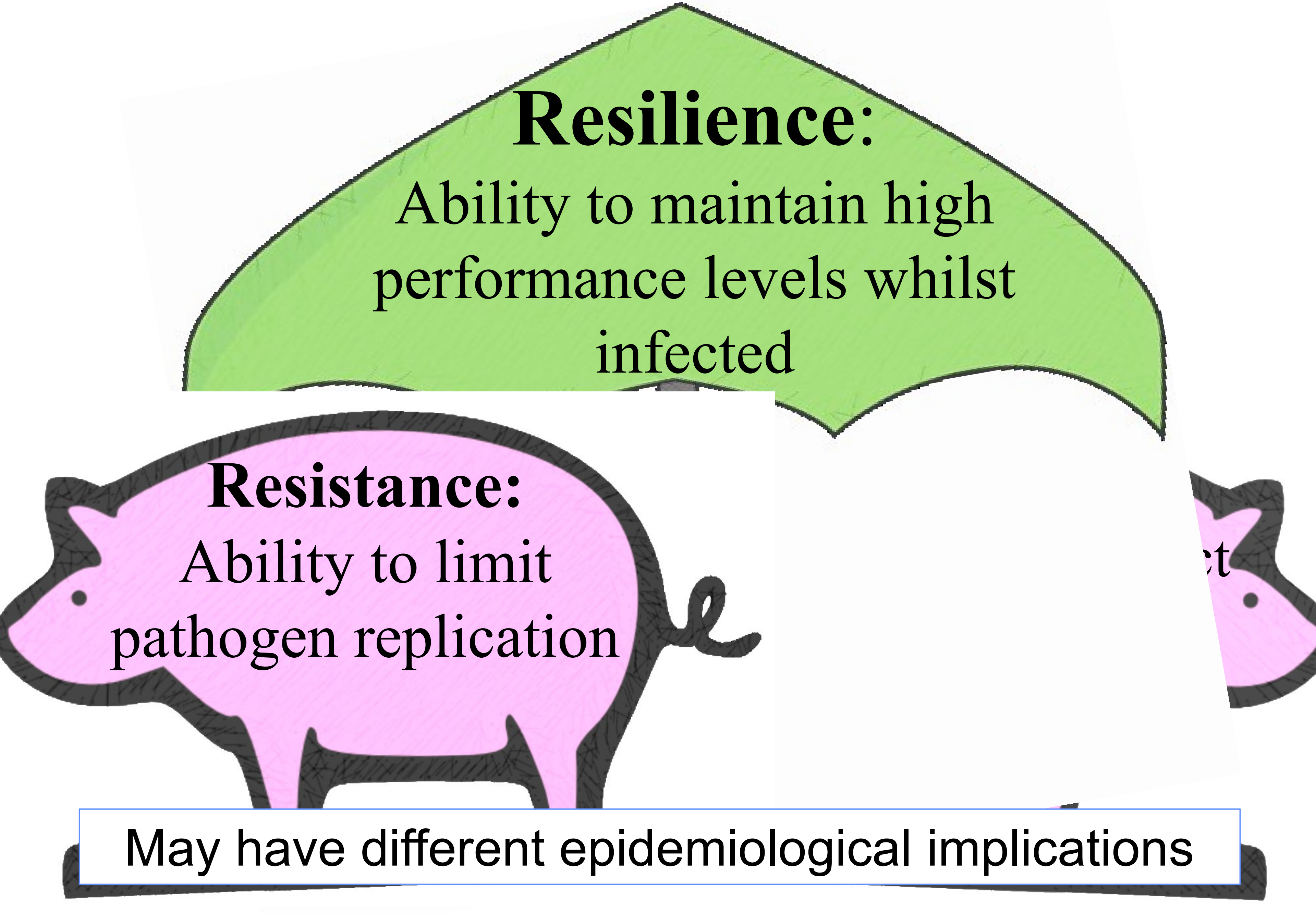


Different tolerance

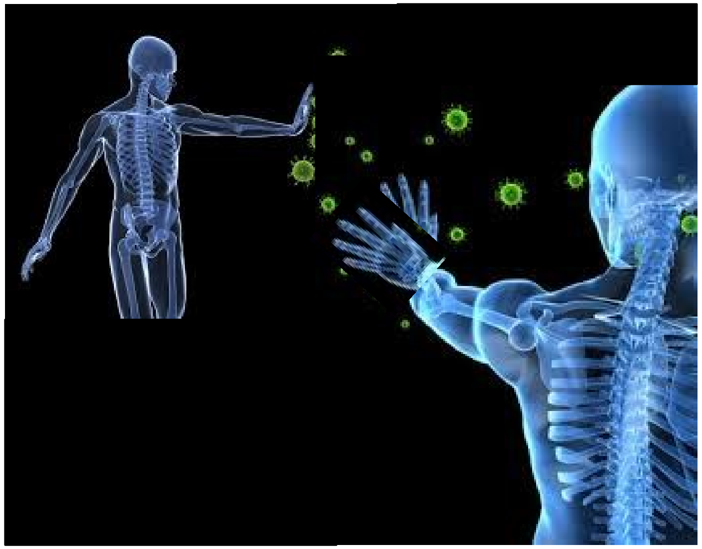


- Tolerance is usually measured as the reaction-norm of performance with respect to change in pathogen burden
- Requires lots of individual measurements
- Can usually only be determined on level of a group

Doeschl-Wilson et al. 2012


Resilience:
Ability to maintain high performance levels whilst infected
Resistance:
Ability to limit pathogen replication
May have different epidemiological implications

Infectivity



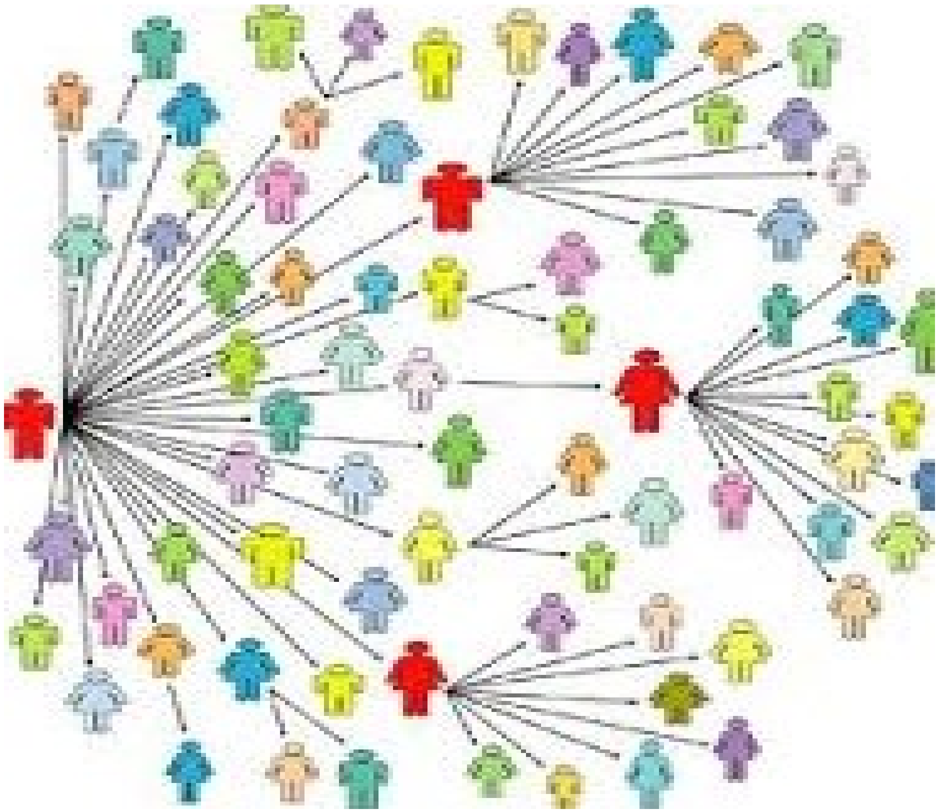
= ability of an infected individual to transmit the infection

High infectivity implies:

- High risk of transmission
- High risk of epidemic outbreaks
- Many recent epidemic outbreaks attributed to '**super-spreaders**' (Lloyd-Smith et al., Nature 2005)

Desirable target trait to reduce disease spread in populations

How to measure infectivity?

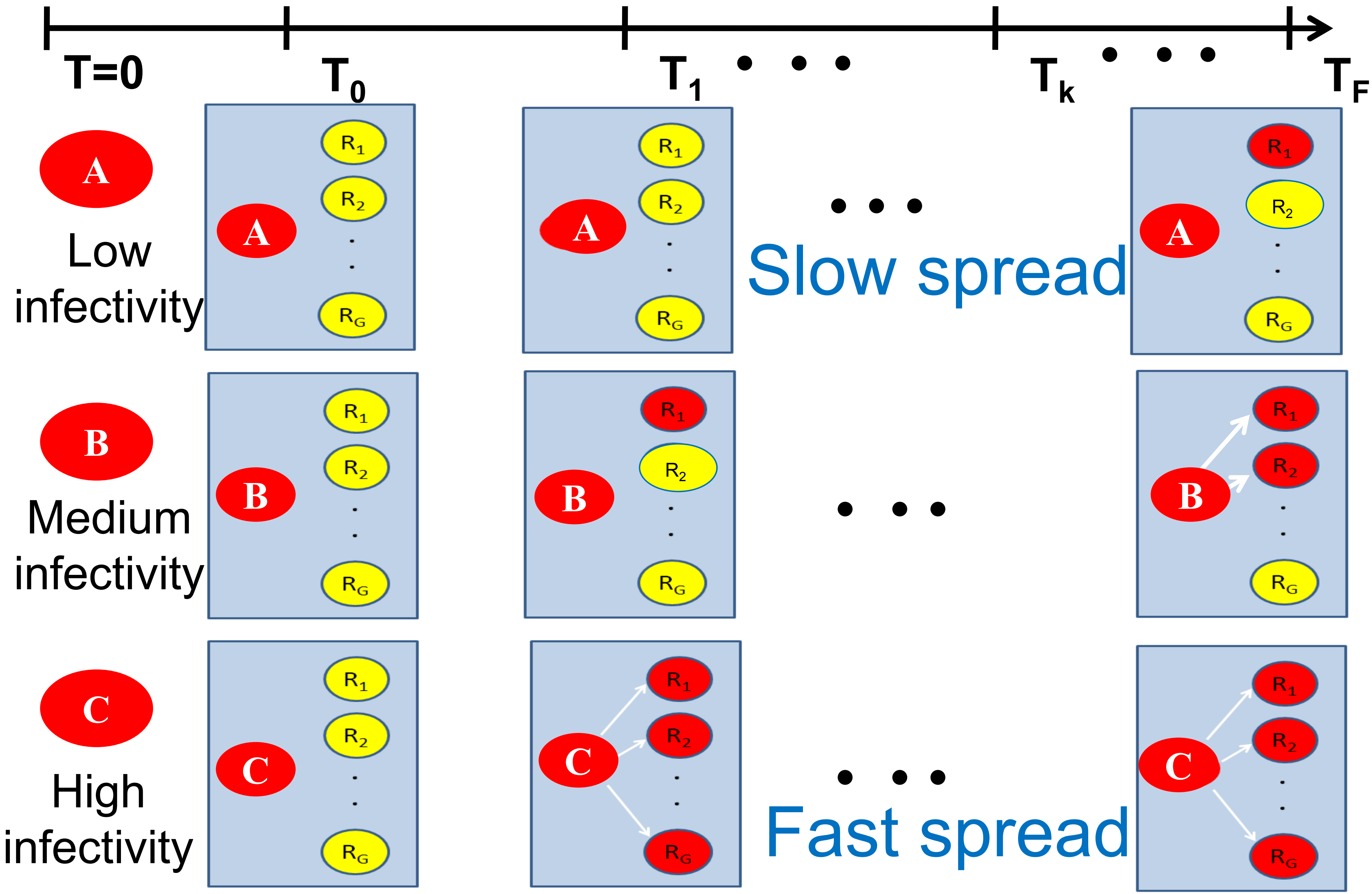


Requires knowledge of

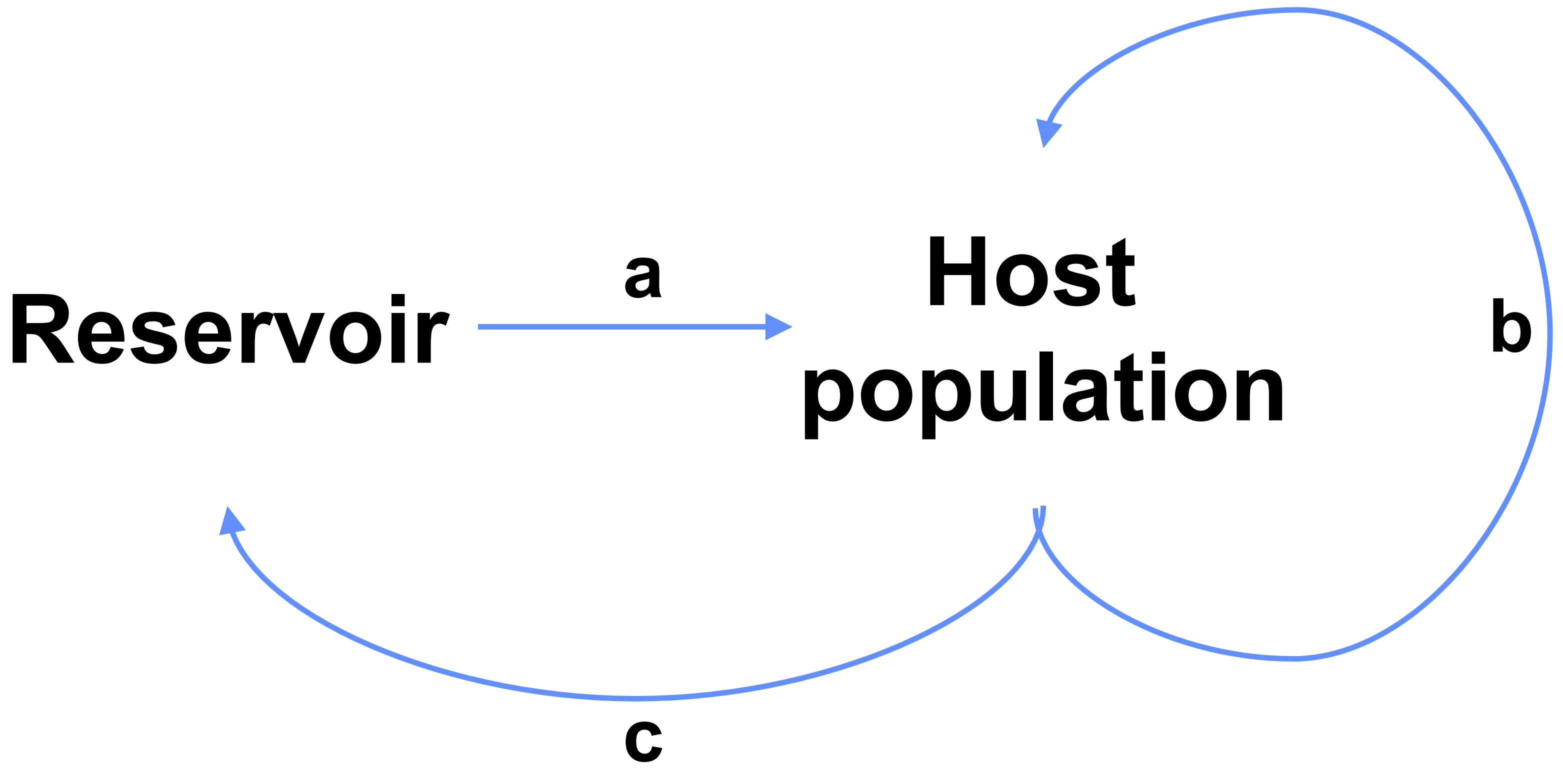
- Contact structure
- Infection status of individuals in contact

Measuring infectivity requires observations from contact individuals

How to identify a super-spreader?



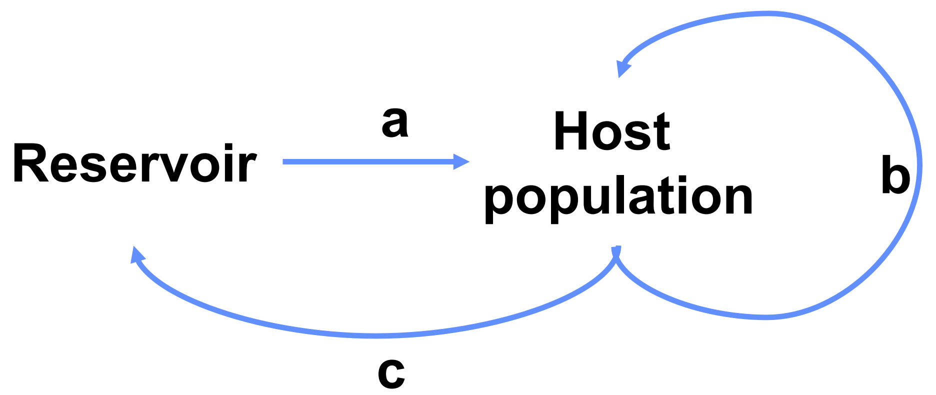
Infection Pathways



a) & b) Direct transmission

c) Indirect transmission

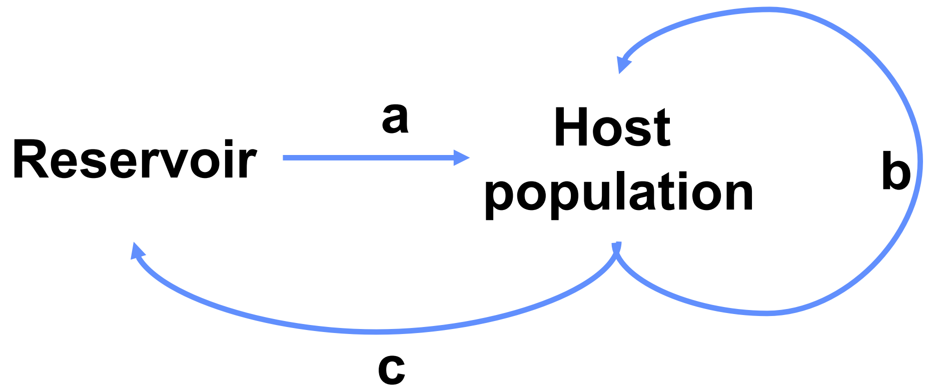
Example pathways



Pathway

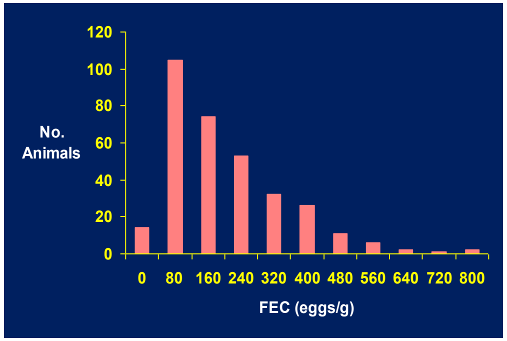
- Vector-borne diseases ?
  - e.g. ticks, tsetse flies
- Gastro-intestinal parasite infections ?
- Viral infections ?

Example pathways



	Pathway
• Vector-borne diseases	a
– e.g. ticks, tsetse flies	
• Gastro-intestinal parasite infections	a & c
• Viral infections	b

The 20:80 rule and the super-spreading phenomenon



- **Macro-parasites:**

Empirical evidence from plotting parasite distributions among hosts: ~20% of the population harbour ~80% of the parasites

- **Micro-parasites:**

Empirical evidence (supported by mathematical models) using contact tracing data: 20% of the population is responsible for 80% of transmissions

Disease Control

Reduce incidence

- Eliminate pathogens
- Improve host resistance / infectivity

Mitigate impact

- Decrease pathogen virulence
- Improve host resilience / tolerance

Strategies can have different impact on host-pathogen interaction and on epidemiology & pathogen evolution

Methods of disease control

- Chemical intervention (antibiotics, anthelmintics)

  Boost host resistance or tolerance
- Sanitation & disinfection
- Culling, isolation & control of movement
- Vaccination
- Genetic selection

Methods of disease control

- Chemical intervention (antibiotics, anthelmintics)

  Boost host resistance or tolerance
- Sanitation & disinfection

  Eliminate pathogens, reduce host infectivity
- Culling, isolation & control of movement

  Reduce host infectivity
- Vaccination

  Boost host resistance/tolerance, eliminate pathogens
- Genetic selection

  Improve host resistance, tolerance, infectivity

Efficacy of disease control methods

- **Chemical intervention (antibiotics, anthelmintics)**
  Dangerous side-effects (e.g. antibiotic resistance)
- **Sanitation & disinfection**
- **Culling, isolation & control of movement**
- **Vaccination**
- **Genetic selection**

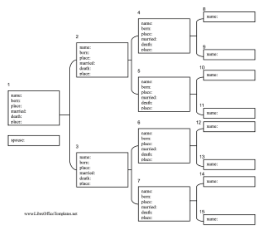
Efficacy of disease control methods

- **Chemical intervention (antibiotics, anthelmintics)**
  Dangerous side-effects (e.g. antibiotic resistance)
- **Sanitation & disinfection**
  Usually not fully effective
- **Culling, isolation & control of movement**
  Effective, but huge economic impact
- **Vaccination**
  Often only partially protective
  Risk of pathogen evolution
- **Genetic selection**
  Long-term, considered as complementary strategy

Infectious disease time scales

- **Short-term: duration of one infection / epidemic):**
  - Individual animal level: Impact on animal health and physiological state over time
  - Population level: impact on disease prevalence over time
  - Typical time window: days – months, sometimes years

- **Long-term (over several generations):**
  - Impact on host or pathogen evolution
  - Typical time window: months - years



Further reading

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