Immunology II: Disease Ecology

Human Anatomy and Physiology
Outline

• Darwin: A Case Study
• Epidemiological Triangle
  – Agent
  – Environment
  – Host
• Evolution of Disease
  – Hunter Gatherers vs. Modern Man
• Industrialization and the Eradication of Disease
• Zoonotic Diseases and Animal Domestication
Charles and William Darwin

William’s drawing on a manuscript of *The Origin of Species*
Scarlet fever in 1849 at the age of 8 (along with Henrietta and Elizabeth). After recovery, declining health and vigor, recurrent fevers, wasting. Final illness in the spring of 1851 at Dr. James Manby Gully’s hydrotherapy spa in Great Malvern. Darwin suspected an inherited predisposition. The likely cause was tuberculosis.
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THE EPIDEMIOLOGICAL TRIANGLE

AGENT

HOST

ENVIRONMENT
Agent Factors

• Virulence

• Transmission (route and probability)

• Life Cycle

• Evasion
Evasion

- Outrun
- Lay low
- Outwit
- Disable
Evasion

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Host Factors

• Passive & Acquired Immunity

• Nutritional Status

• Age

• Reproductive Status

• Co-morbidity
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Overfeeding, acute-phase response, inflammation (IL-1 and TNF) and insulin

Central effects

- Stomach, skeletal muscle and placenta
- Adipose tissue
- Fasting, reduced food intake and testosterone

Peripheral effects

- T-cell function
- Haematopoiesis
- Angiogenesis
- Pancreatic β-cell function
- Reproductive function
- Basal metabolism

Central nervous system and hypothalamus

- Food intake
- HPA hormones
- Bone formation and remodelling

CRH → ACTH → Glucocorticoids

HPA axis

Peripheral circulation

IL-1, IL-6, TNF and leptin

Lymph node

Thymus

T cells
Host Factors

• Passive & Acquired Immunity

• Nutritional Status

• Age

• Reproductive Status

• Co-morbidity
Anouk Caraux, Bernard Klein, Bruno Paiva, Caroline Bret, Alexander Schmitz, Gwenny M. Fuhler, Nico A. Bos, Hans E Johnsen, Alberto Orfao, Martin Perez-Andres,
Haematologica June 2010 95: 1016-1020; Doi:10.3324/haematol.2009.018689
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## Common Comorbidities in COPD

### Cardiovascular Disorders
- Pulmonary hypertension
- Right heart failure, Cor pulmonale
- Vascular disease
  - Coronary artery disease
  - Cerebrovascular disease
  - Peripheral vascular disease
- Systemic hypertension

### Nutritional Disorders, Cachexia

### Musculoskeletal Disorders
- Muscle dysfunction
- Osteoporosis

### Cancer

### Other
- Sleep disorders
- Sexual dysfunction
- Diabetes
- Depression, anxiety
- Anaemia
- Peptic ulcer
- Glaucoma
Environmental Factors

• Encounter rates with agent

• Encounter rates with susceptibles

• Vectors

• Reservoirs

• Seasonality
Environmental Factors

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- Vectors
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- Seasonality
Environmental Factors

• Encounter rates with agent

• **Encounter rates with susceptibles**

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Environmental Factors

• Encounter rates with agent

• Encounter rates with susceptibles

• Vectors

• Reservoirs

• Seasonality
The tick, *Ixodes scapularis*, has a two-year life cycle in which it requires three blood meals. The tick is infected by its first blood meal, and can pass on the infection to a human in its second.
Environmental Factors

• Encounter rates with agent

• Encounter rates with susceptibles

• Vectors

• Reservoirs

• Seasonality
West Nile virus

mosquito vector

incidental hosts

humans

West Nile virus

horses

bird reservoir host

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Environmental Factors

- Encounter rates with agent
- Encounter rates with susceptibles
- Vectors
- Reservoirs
- Seasonality
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Hunting and Gathering

• Directly transmittable diseases rare

• Pathogens with long latencies, dormant life cycle stages, non-human reservoirs and transmission vectors were probably more common.
Most directly transmittable diseases in humans appear to have originated in domestic animals and have increased as our intimate contact with these species has increased.
Transfer of diseases from animals to humans (zoonotic diseases) continues to occur when humans and animals come into frequent, intimate contact.
Agriculture

Adoption of agriculture as a subsistence base led to larger populations, fixed residence, seasonality in workload and food abundance, and alteration of local ecology.
The emergence of long range sea and land based trade routes facilitated the spread of epidemic disease in the ancient and medieval worlds.
Conquest, invasion, and migration have also often introduced new diseases to previously unexposed populations.
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Industrialization

Modern urban-industrial societies have brought further changes in the degree of crowding, nutritional status, and the rate and extent of population mixing.
Smallpox

Death Rate, per million

England and Wales

England and Wales

Bronchitis, pneumonia, influenza

England and Wales

Whooping Cough

Death Rate, per million children

Causal organism identified

Immunization generally available

England and Wales

What caused the epidemiological transition?

\[ R = (r_{\text{encounter}} * r_{\text{transmission}}) - r_{\text{death}} - r_{\text{recovery}} \]
Figure 1
Cluster Map of Fatal Cholera Cases in London, 1854

Source: Adapted from John Snow, Snow on Cholera (New York: Hafner, 1965).
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Zoonotic Diseases

• Definition – a disease that can pass between animal and humans.

• Examples
  – HIV
  – Ebola
  – Avian Flu
  – SARS
  – Bubonic Plague
HIV
Ebola virus

*Ebola virus* transmission dynamics

**Spillover dynamics**

**Intra- and inter-species transmission**

**Reservoir dynamics**

Olival and Hayman. *Viruses* 2014;6(4):1759-1788
Avian Flu

THE NEXT PANDEMIC?
Although the H5N1 virus, known as the avian flu virus, does not usually infect humans, new mutated forms of this virus could represent a realistic risk of a flu pandemic, experts say.

Shorebirds
Are natural carriers of the avian flu virus in the wild.

Domestic birds
Intermediate hosts and easily infected by the virus through contact with nasal or fecal material. Contact with other domestic animals favors the spread of the disease.

Mammals
Intermediate hosts. Hogs can also be infected by human flu virus, which increases the risk of mutated human compatible viruses.

Natural cycle

Pandemic cycle

Waterfowl
Infected by shared water sources.

Humans
Rarely infected by unaltered strains of the avian flu virus. Experts think that mutated viruses could spread from human to human.

OUTCOME OF AVIAN FLU INFECTIONS
(Reported by WHO 2007/03/20)

- People who recovered from infection (39.9%)
- People who died (60.1%)

MAJOR FLU PANDEMICS
Number of deaths in the USA:

- Spanish Flu (1918): 500,000
- Asian Flu (1957): 70,000
- Hong Kong Flu (1968): 34,000

Global killer: The [A(H1N1)] strain of the flu virus, commonly known as the “Spanish Influenza” killed more than 50 million people worldwide.

Sources: Centers for Disease Control, World Health Organization
SARS – Severe Acute Respiratory Syndrome

Phylogeny of SARS virus strains

- infects bats
- infects civets
- infects humans
Thought Question

• What are some other zoonotic diseases and what are their hosts?
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Study Guide Questions

• Be able to describe in details the epidemiological triangle and the categories that contribute to host, agent and environmental factors using examples.

• How have disease changed as human populations have evolved?

• What contributed to the eradication of potentially life threatening diseases?

• What is a zoonotic infection? Be able to describe the zoonotic infections we discussed in class and their hosts.