

Concepts of Infectious Diseases



Open air treatment of tuberculosis (a reemerging disease), 1932

Subjects to be Covered

- Historical perspective
- Terminology and concepts of infectious diseases
- Pathway to and patterns of infection
- Sequence of steps necessary for infection
- Microbial virulence and strategies to evade the host

Historical Perspective The Concept of Contagion

"Those who cannot remember the past
are condemned to repeat it."

George Santayana



**Girolamo Fracastoro
(1478-1553)**

Among the first to theorize on
the principle of "contagion"
by direct contact, fomites
(contaminated particles) and air





Louis Pasteur (1822-1895)

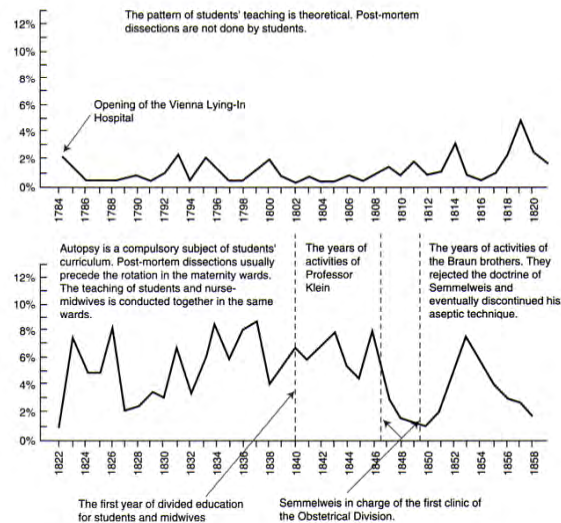
- Battled the concept of “spontaneous generation”
 - Microbes, *etc.*, arise from putrefying matter
- Discovered the role of anthrax in fatal illness of sheep
 - Demonstration of attenuation for vaccine development
- Development of a vaccine to treat rabies again using the concept of attenuation



**Ignaz Semmelweis
1818-1865**

- 1844 appointed as lecturer at the Univ. of Vienna Allgemeines Krankenhaus
- Found increased mortality from puerperal fever among the first vs. second clinic
- Suspected “cadaverous particles” from the autopsy room
- Instituted handwashing with chlorinated lime solution
- Mortality reduced from ~12% to 3%
- After he left his work was discounted and ignored

Maternal Mortality Statistics 1784-1858 Vienna Lying-In Hospital



Hand-Washing Patterns in a Medical Intensive Care Unit

<u>Group</u>	<u>No. Contacts Followed by Washing / Total No. Contacts (%)</u>
Physicians	90/236 (28)
Nurses	301/701 (43)
Respiratory therapists	91/120 (76)
Radiology technicians	7/16 (44)
Others	5/49 (10)
Total	494/1212 (41)

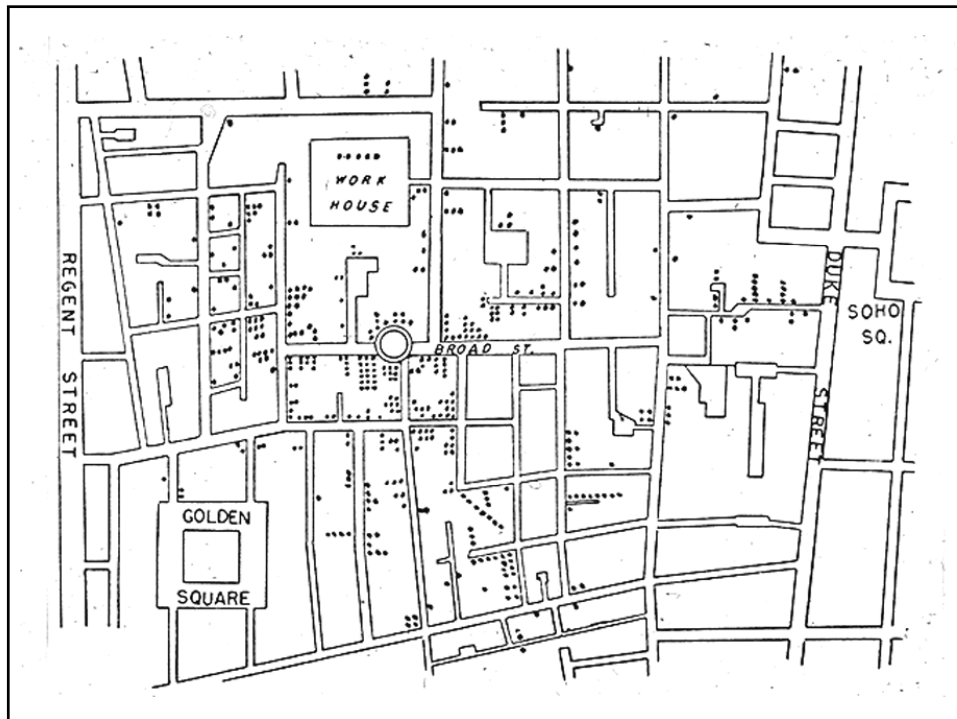
Albert and Condie, NEJM 1981

The Tale of the Broad Street Pump

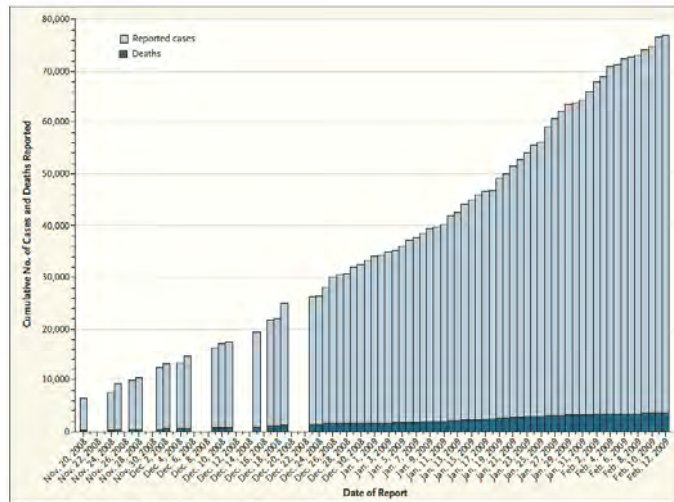


John Snow
1813-1858

- Outbreak of cholera in London - 1854
- > 500 fatalities within a radius of 250 yards and within 10 days
- Snow investigated 77 cases - of these 59 used the Broad street pump
- The epidemic was interrupted when the handle of the pump was removed



Cholera Cases in Zimbabwe 2008-2009



Cholera Cases and Deaths in Zimbabwe (November 20, 2008–February 12, 2009).

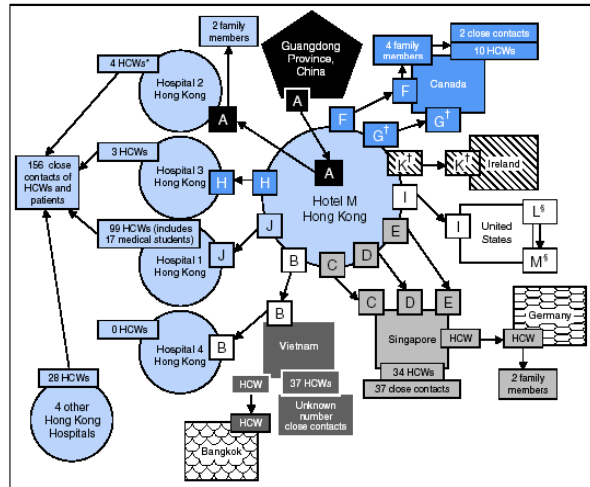
Mintz and Guerrant, NEJM 2009

Cholera – a Continuing Threat

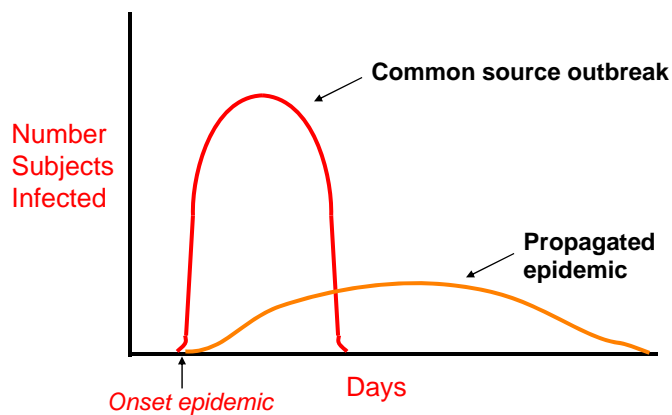


- More cases in Zimbabwe than were seen in previous years worldwide
- Complete breakdown in the sanitation and water supply systems
- Case fatality rate of >4.7%
- Secondary spread to neighboring countries

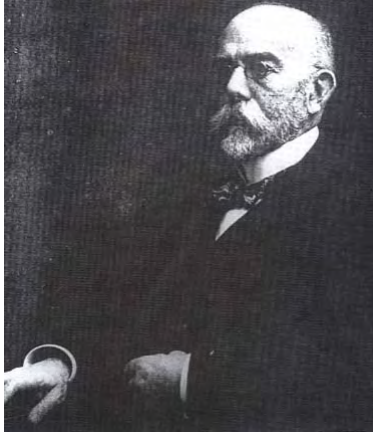
Severe Acute Respiratory Syndrome (SARS)!



Epidemic Curves



Henle-Koch Postulates



Robert Koch (1843-1910)

- The organism is regularly found in the lesions of the disease
- It can be isolated in pure culture on artificial media
- Inoculation of the pure culture into a susceptible animal reproduces the disease
- The organism can be recovered from the lesions in the infected animal

Terminology and concepts of infectious diseases

Terminology and Concepts (1)

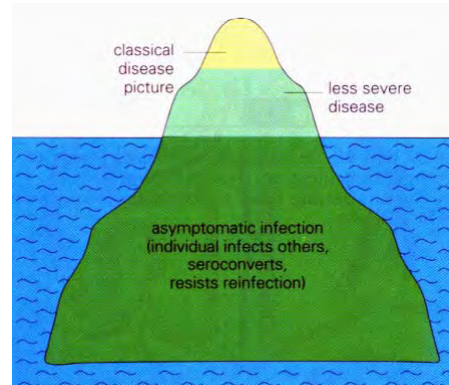
- **Pathogen:** any microorganism that is capable of causing disease in a susceptible host
 - Primary vs. opportunistic pathogens
- **Colonization:** establishment of an “ecological niche” for an organism, survival and replication without actual tissue invasion
- **Infection:** the ability of an organism to invade tissue, replicate and stimulate an immune response
- **Intoxication:** agents that cause disease by elaboration of toxin sometimes without the presence of viable bacteria

Terminology and Concepts (2)

- **Virulence:** the severity of the disease caused by the agent
 - e.g. rabies (uniformly fatal) vs. the common cold (minor symptoms)
- **Virulence determinant:** a bacterial component or product that contributes to the ability of a pathogen to cause disease
 - may be chromosomal or on movable genetic elements such as plasmids, transposons or phages

Terminology and Concepts (3)

- **Infections:** may vary from subclinical to fulminant
- **The iceberg model of infection**
 - In many infections > 90% are asymptomatic e.g., enterovirus infections
- Different pathogens cause a different frequency of **clinically apparent illness**
 - Gonorrhea (99%) vs. Polio (0.1-1.0%)



Terminology and Concepts (4)

- Many bacteria can produce the same infectious disease syndrome, sometimes by completely different pathogenetic mechanisms - e.g. the sepsis syndrome
- A single bacterial or viral species can cause a multitude of different diseases
- A bacterial virulence determinant may be species, organ or disease specific

Pathways to and Patterns of Infection

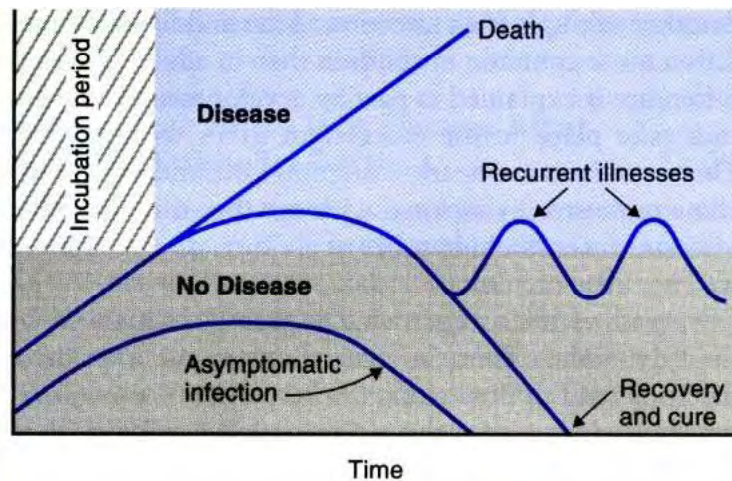
“Disease usually results from inconclusive negotiations for symbiosis, an overstepping of the line by one side, a biologic misinterpretation of borders”

Lewis Thomas
Germs, 1974

Categories or Stages of Human Infection

- **Asymptomatic:** HIV, salmonella, commensals
 - Also a source of nosocomial infections
- **Active:** subject with overt disease
- **Incubatory:** Subject incubating but without symptoms of disease
- **Latent:** pathogen persists in tissue without symptoms for much of the time - e.g. HIV, tuberculosis, herpes

Natural History of Infection



Host Factors That Increase Susceptibility to Infection

- Extremes of age
- Malnutrition
- Genetic defects in immunity (*e.g.*, WBC disorders)
- Acquired defects in immunity (*e.g.*, AIDS)
- Medical diseases: diabetes, liver disease
- Chemotherapy, immunosuppressive agents
- Implantation of prosthetic material
- Organ transplantation

Pathways to Infection

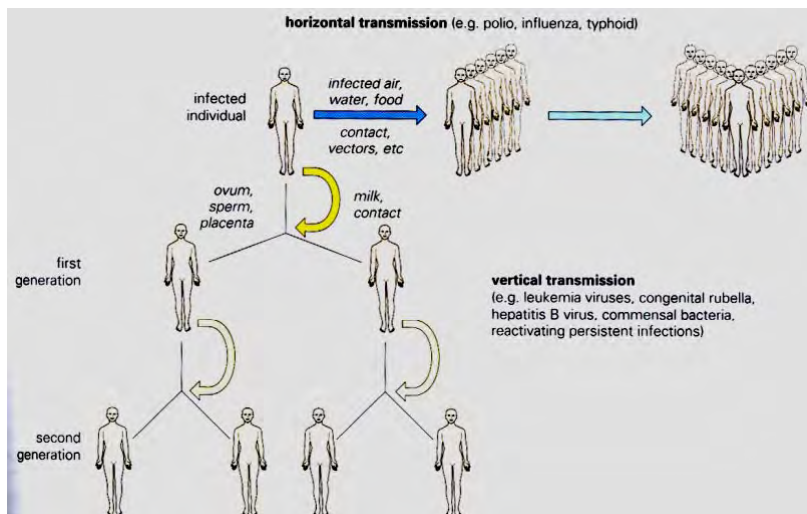
- Reservoirs of bacterial pathogens
- Means of pathogen transmission
 - Exogenous versus endogenous infection
 - Horizontal versus vertical transmission
- Portals of pathogen entry
- Host-response – host-pathogen interactions

Reservoirs for Bacterial Pathogens

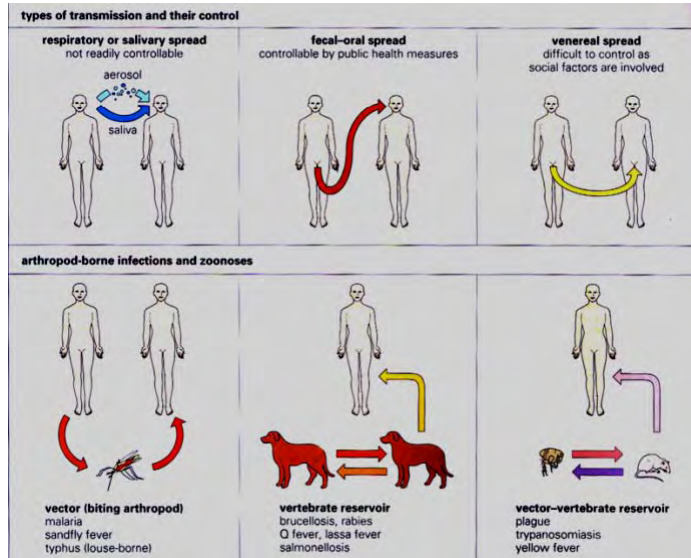
Source/Reservoir	Pathogens
Human*	<i>T. pallidum</i> , Hepatitis B, HIV, Commensals
Animals	Rabies, Leptospira, Brucella
Soil	<i>Clostridium tetani</i> and <i>botulinum</i> , Histoplasma
Water	Legionella, Cholera, Shigella

* Single most important reservoir

Transmission of Microbial Pathogens



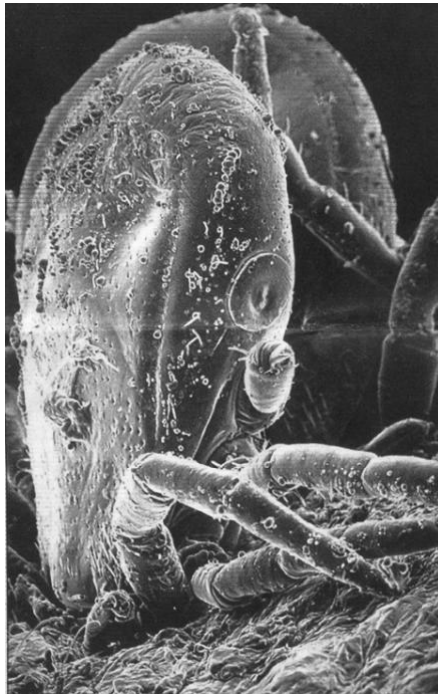
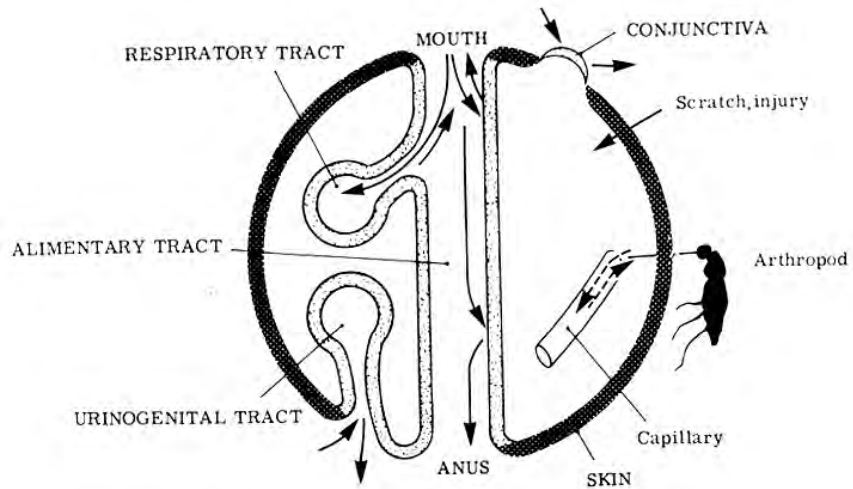
Transmission of Microbial Pathogens



Impact of Social and Environmental Factors on Risk of Disease Transmission

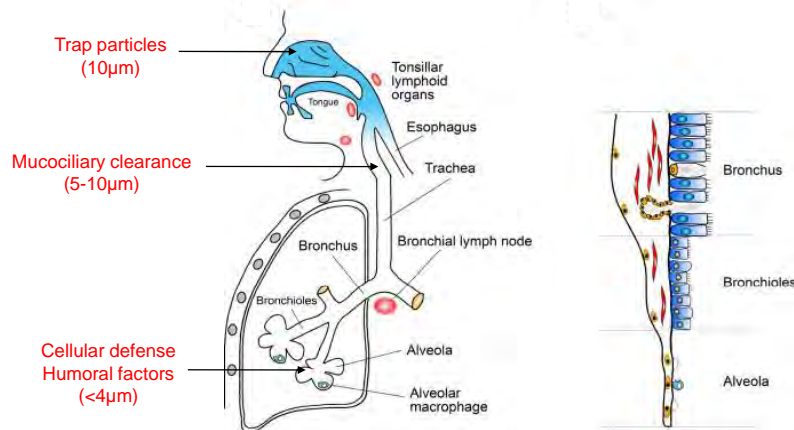
- Increased travel - opportunities for acquisition/spread of “exotic” infections e.g., malaria, H1N1 influenza
- Change in sexual habits - transmission of HIV, gonorrhea
- Change in animal food production with intensive exposure to antibiotics - coupled with fast foods - increase in listeria, salmonella
- Construction in previously forested regions increased exposure to vectors of lyme, RMSF

Portals of Pathogen Entry



Any Ideas?

Host Response: Barriers to Infection



A Man with a Cough

A 77 year old man returns from a visit with his grandchildren. He develops fever, a cough productive of yellow-green sputum and pleuritic chest pain. His X-ray reveals an infiltrate. His white blood cell count is elevated. His sputum and blood cultures grow *S. pneumoniae*. He has a history of smoking and heavy alcohol intake.

Pathways to Infection

- Reservoirs/Transmission
 - Patient or grandchildren
 - Nasopharyngeal colonization
- Sites of entry
 - Oropharyngeal aspiration
- Host response
 - Inflammatory response
 - Immune response
- Potential for complications

Sequence of steps necessary for pathogens to initiate infection

Sequence of Steps Necessary for Establishment of Infection

- Adherence and colonization of host surfaces
- Evasion of host defense mechanisms such as phagocytosis or intracellular killing
- Adaptation to the host environment, ability to undergo change such as antigenic variation
- Invasion of tissue both locally or systemically (dissemination)
- Host response - often responsible for tissue damage

Strategies Used by Pathogens to Cause Respiratory Tract Infections

- Target specific cellular receptors for adherence *e.g.*, rhinovirus and ICAM-1
- Interference or evasion of clearance mechanisms *e.g.*, droplet nuclei of *M. tuberculosis*, inhibition/destruction of ciliary activity by bordetella, influenza virus
- Evasion of phagocytosis - capsules, protein A (pneumococcus, hemophilus)
- Evade destruction by alveolar macrophages *e.g.*, *M. tuberculosis*

So What Do You Really Need to Know?

- Historical vignettes – Yes!
- Terminology and concepts of infectious diseases
- Vectors and different mechanisms of disease transmission
- The steps involved in development of infections