ENV H 451/541c

ExposureRoutes/ Infectious Disease Epidemiology

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Today's Objectives

1. Recognize the various routes of exposure and portals of Entry/Exit
2. Become familiar with terminology of infectious disease epidemiology
3. Learn to calculate incidence and prevalence
4. Recognize a common source outbreak
5. Learn types, progression, and outcomes of infection

FACTORS INFLUENCING EXPOSURE AND INFECTION: Agent Factors

Sources, Reservoirs, Transport and Persistence (in the Environment)

Ability to Enter a Portal in the Human or Other Host

Ability to Reach and Proliferate at Site(s) of Infection in the Host

Excretion of the Agent from the Host

Quantity and "Quality" (including virulence) of the Infectious

Factors Influencing Exposure and Infection: Environmental Factors

- Reservoirs: where organisms can live, accumulate or persist outside of the host of interest; could be another organism or the inanimate environment.

- Vehicles: inanimate objects/materials by which organisms get from one host to another; includes water, food, objects (called fomites) and biological products (e.g., blood).

- Amplifiers: Types of reservoirs where organisms proliferate; often applied to organisms transmitted by the airborne route.

Factors Influencing Exposure and Infection: Environmental Factors

- Vectors: Living organisms bringing infectious organisms to a host.
  - Mechanical vectors: Microbes do not multiply in the vector
    - ex: biting insects infected with the infectious organism
  - Biological vectors: Microbes must propagate in the vector before they can be transmitted to a host.

Environmental Factors Influencing Survival or Proliferation of Infectious Agents

- Physical: temperature, relative humidity, sunlight, moisture content or water activity, climate and weather, etc.

- Chemical and Nutritional: Antimicrobial chemicals, nutrients for microbial proliferation.

- Biological: Antagonistic activity by other organisms: antimicrobial agents, parasitism, etc.; presence and state of a vector

Factors Influencing Exposure and Infection: Host Factors and Host Susceptibility

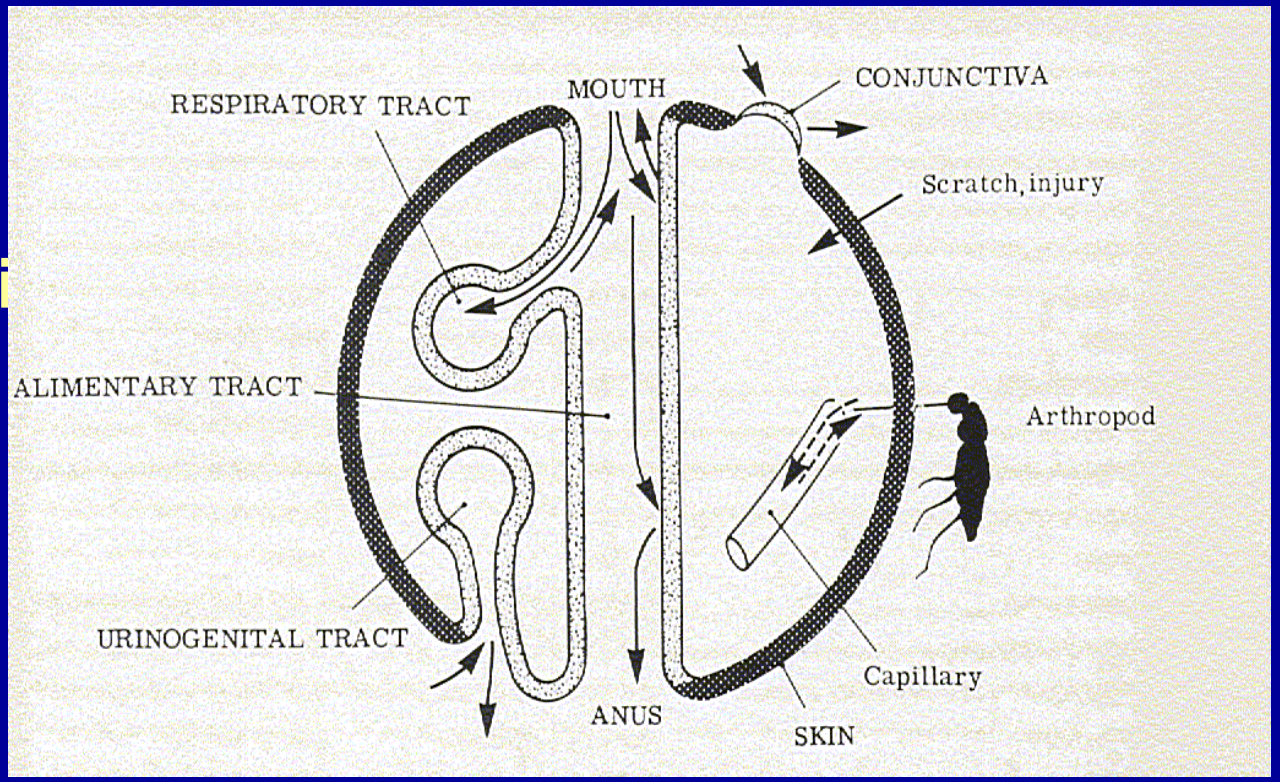
- **Opportunities for host exposure**
  - **transmission routes**
  - **host availability**
- **Susceptibility factors**
  - **Dosage (quantity) and "quality" of infectious organisms, including their "virulence";**
  - **age**
  - **immunity**
  - **nutritional status**
  - **immunocompetence and health status,**
  - **genetics**
  - **behavior (personal habits) of host.**

Routes of Transmission

- Direct Personal Contact: Person (animal)-to-Person
- Indirect Personal Contact: Droplet, Fomites, Other Vehicles
- Water and Food (Gastrointestinal Tract)
- Vector-borne: often insects
- Intrauterine or Transplacental
- Organ Transplants, Blood and Blood Products

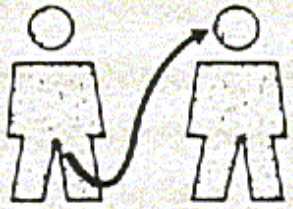
Sites or Portals of Entry to and/or Exit From the Body

- Respiratory
- Enteric or Gastrointestinal
- Skin: especially i skin barrier is penetrated
- Genitourinary
- Eye

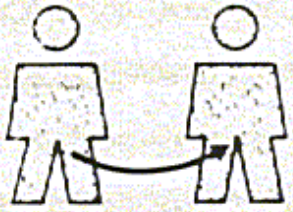


Pathogenesis of Infectious Disease

Respiratory or salivary spread



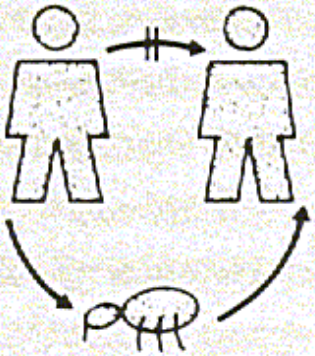
Faecal-oral spread



Venereal spread

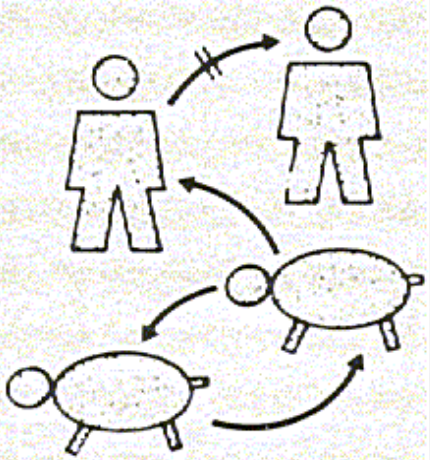
ZOONOSES

Infections acquired from animals (arthropods, vertebrates).
Human infection controlled by controlling animal infection.



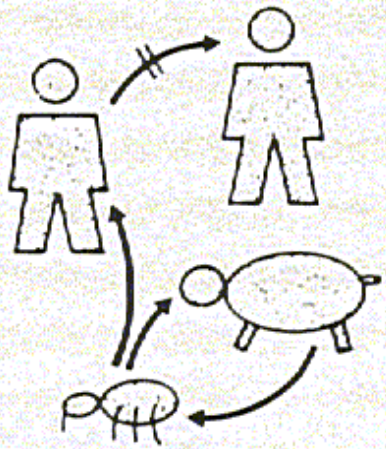
Vector (biting arthropod)

Malaria
Sandfly fever
Typhus (louse-borne)



Vertebrate reservoir

Brucellosis; rabies
Q fever; lassa fever
Salmonellosis



Vector-vertebrate reservoir

Plague
Trypanosomiasis
Yellow fever

Possible Outcomes of Exposure

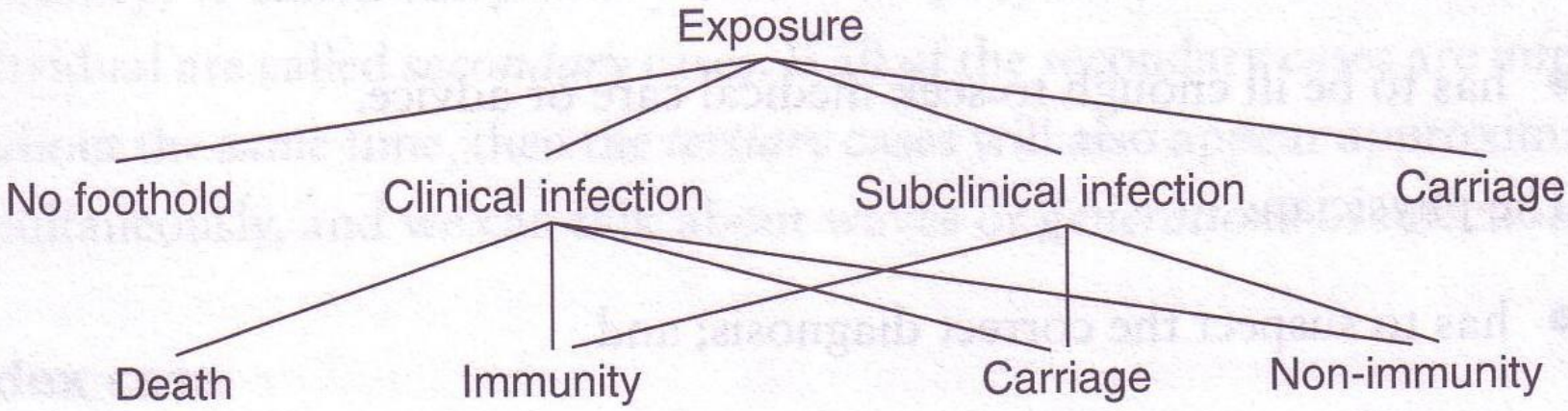


Figure 2.1 The possible outcomes of exposure to an infectious agent.

THE PROCESS OF INFECTION

- The growth/multiplication of a microbe in a host
- Infection does not always result in injury of the host (disease)
- Two main classes of infection by site:
  - localized
  - generalized (disseminated; systemic)

Localized Infections

- Organism enters the body and reaches target site of infection
- Organism adheres to or enters host cells and multiplies at site of infection
- Infection spreads within the site (e.g., respiratory tract; intestines)
- Symptoms of illness appear
- Organism does not spread through the lymphatic system or reach the bloodstream
- Infection subsides due to host defenses (e.g., immunity)
- Agent eliminated from the body; infected cells replaced; "cure"

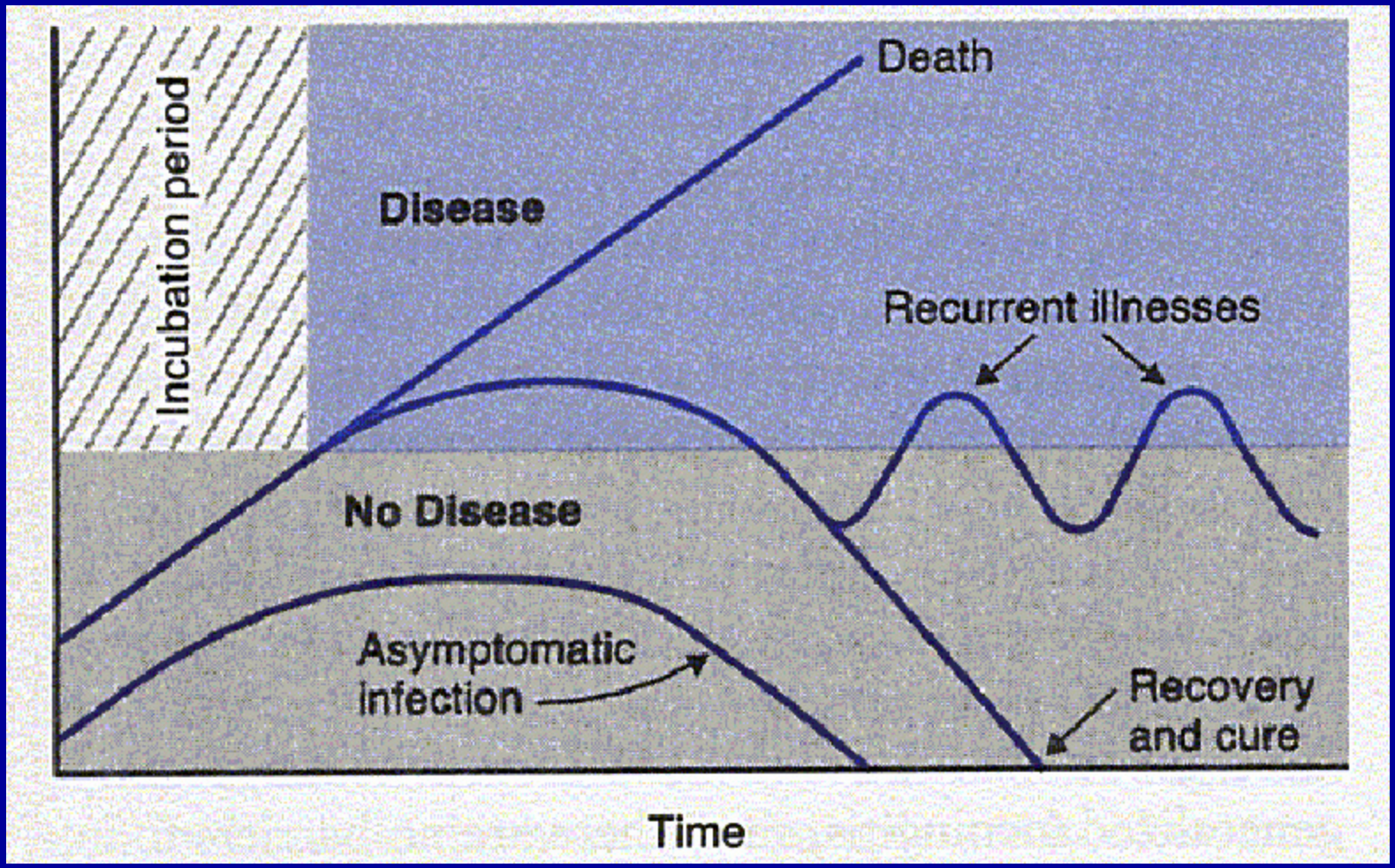
Generalized Infections

- Organism enters the body and reaches target site of initial infection
- Organism adheres to or enters host cells and multiplies at initial site of infection
- Infection spreads within site and to other sites via tissues, lymphatic system, bloodstream (bacteremia, viremia, etc.) and possibly other routes
- Symptoms of illness may appear
- Organisms infect other organs, tissues and cells; more spread via bloodstream
- Symptoms of illness become severe
- Host defenses eliminate organisms leading to cure or disease continues, possibly leading to irreversible damage or death

Outcomes of Infection

Microbes differ in their ability to produce the different outcomes of infection:

- (i) infection without illness;
- (ii) infection with illness; (with or without long-term sequelae) and
- (iii) infection, illness and then death


Death
Disease
Incubation period
Recurrent illnesses
No Disease
Asymptomatic infection
Recovery and cure
Time

Infectious Dose and Dose-Response

- Probability of infection is dose-dependent
  - Higher dose gives higher probability of infection and illness
- Shape (mathematical model) of the dose-response relationship is of major interest
  - esp. at low dose range
  - estimated by extrapolation

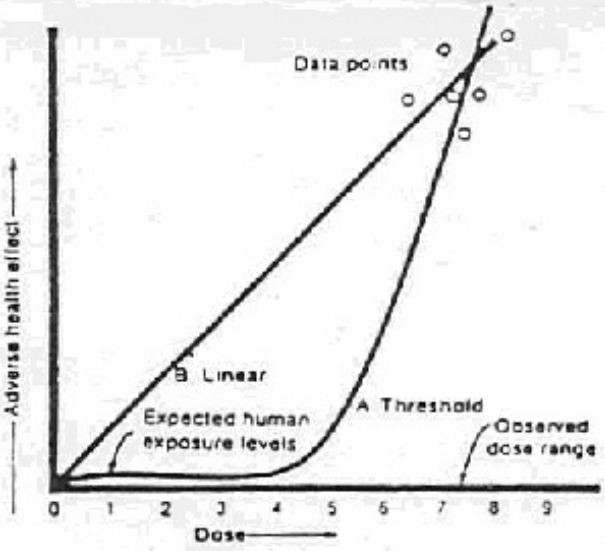


Figure 1. Linear vs. Threshold Dose-response Relationships

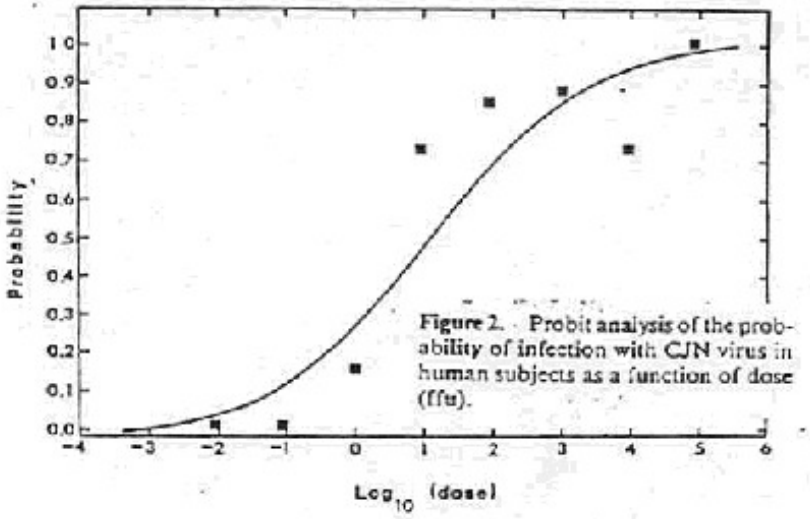


Figure 2. Probit analysis of the probability of infection with CJN virus in human subjects as a function of dose (ffu).

Infectious Dose

- Microbes differ in their infectious dose.
- Enteric and respiratory viruses are infectious at very low doses
  - as little as one cell culture infectious dose has a high probability of infecting an exposed human.
  - But, this may still require exposure to many virus particles.
- Most enteric bacteria are infectious at moderate (10s-100s of cells) to high (1,000 cells) doses.
- Protozoan cysts may be infectious at low doses
  - A few as 1-10 cysts of *Giardia lamblia*) or oocysts of *Cryptosporidium parvum*

Organism Titer in Host

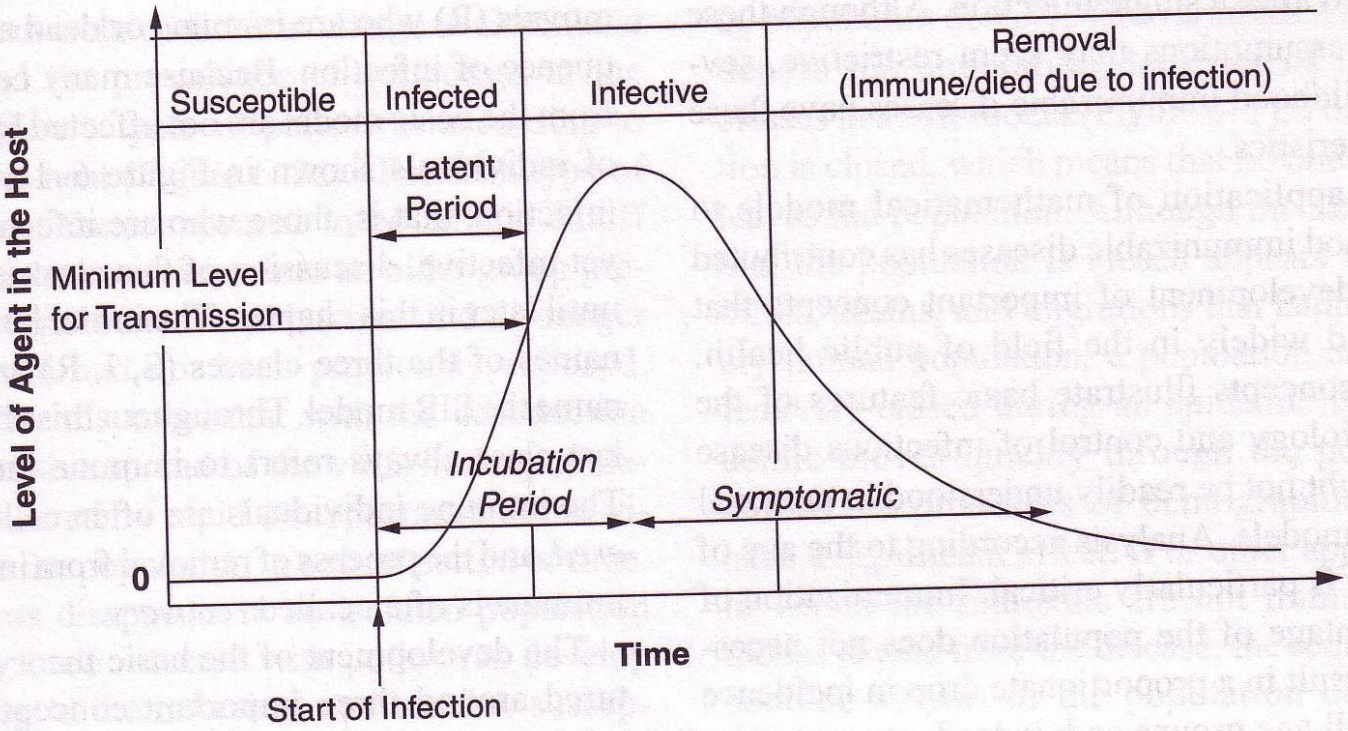


Figure 6–1 Population size of an infectious agent replicating inside a host and classification of stages of infection

TABLE 19.2 Concentration of Enteric Pathogens in Feces

Organism	Per gram of feces
Protozoan parasites	10^6–10^7
Helminths	
Ascarus	10^4–10^5
Enteric viruses	
Enteroviruses	10^3–10^7
Rotavirus	10^{10}
Adenovirus	10^{11}
Enteric bacteria	
Salmonella spp.	10^4–10^{10}
Shigella	10^5–10^9
Indicator bacteria	
Coliform	10^7–10^9
Fecal coliform	10^6–10^9

Epidemiology - Definition

- Literally – "the study of epidemics"
- The logic of observation and the methods to quantify these observations in populations (groups) of individuals.
- The study of the distribution of health-related states or events in specified populations and the application of this study to the control of health problems.
- Characterization of Disease
  - Temporally
  - Spatially
  - Demographically

Epidemiology includes:

- 1) methods for measuring the health of groups and for determining the attributes and exposures that influence health;
- 2) study of the occurrence of disease in its natural habitat rather than the controlled environment of the laboratory (exception: clinical trails); and
- 3) methods for the quantitative study of the distribution, variation, an determinants of health-related outcomes in specific groups (populations) of individuals, and the application of this study to the diagnosis, treatment, and prevention of these states or events.

Infectious Disease Epidemiology: Classical Epidemiology

- the study of epidemics
- the study of the dynamic factors involved in the transmission of infectious agents in populations
- the natural history of disease
  - how a disease spreads through groups or a population
  - how a case of that disease develops in an individual

Special Features of Infectious Disease Epidemiology

- A case may be a risk factor
- People may be immune
- A case may be a source without being recognized as a case
- There is sometimes a need for urgency
- Preventative measures usually have a good scientific basis

- **Infectious Diseases**-All diseases caused by microorganisms

- **Communicable Diseases**-Diseases that can be transmitted person to person, directly or indirectly

- **Transmissible Diseases**-Diseases that can be transmitted by unnatural routes

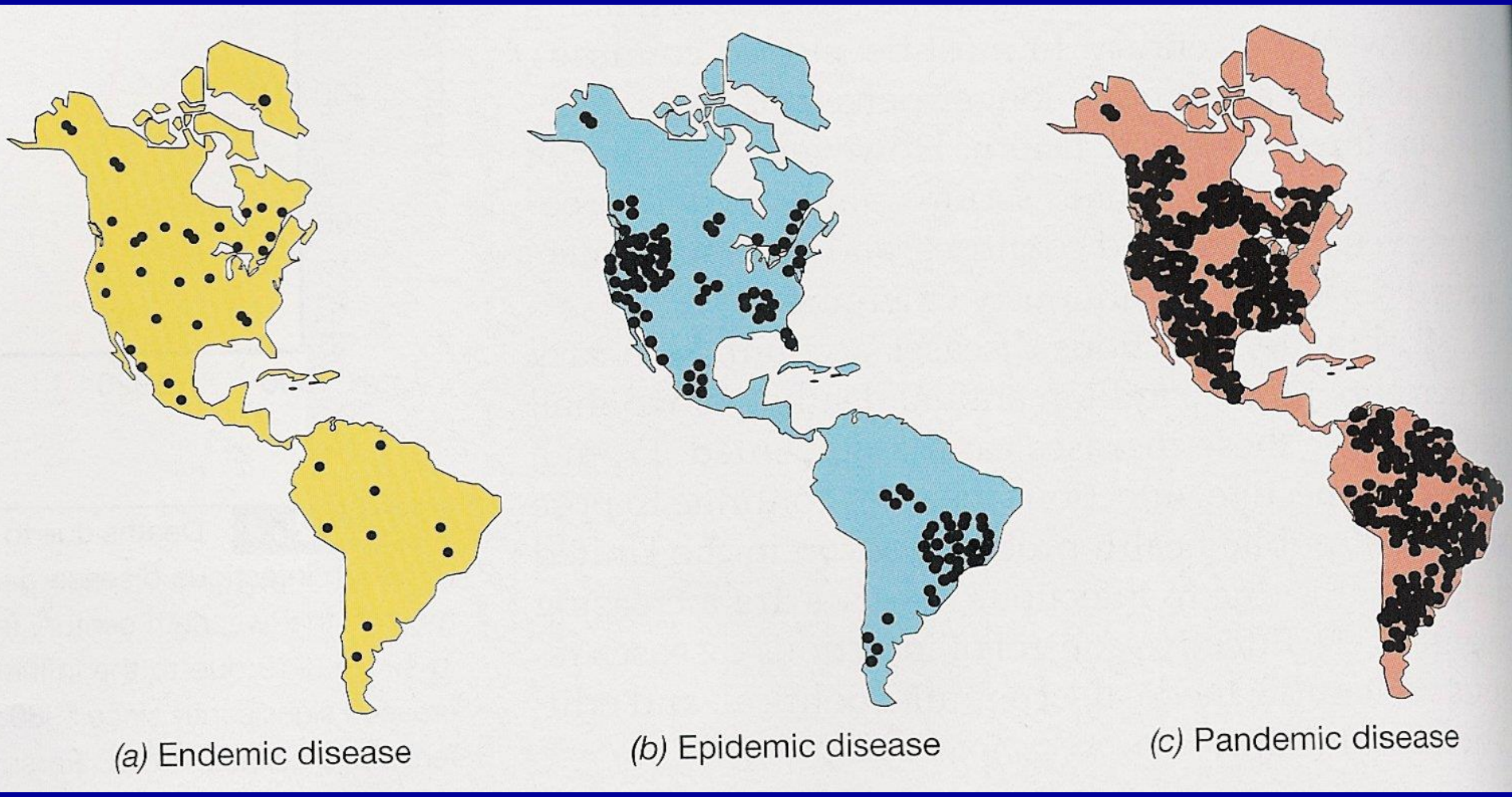
- **Morbidity**-the measure of the proportion of illness within a population for a particular disease

- **Mortality**- the measure of the proportion of the entire population that die from a particular disease each year

- **Lethality (Case Fatality Rate)-** the portion of people that will die if contracting a particular disease

Basic Epidemiological Concepts and Terms

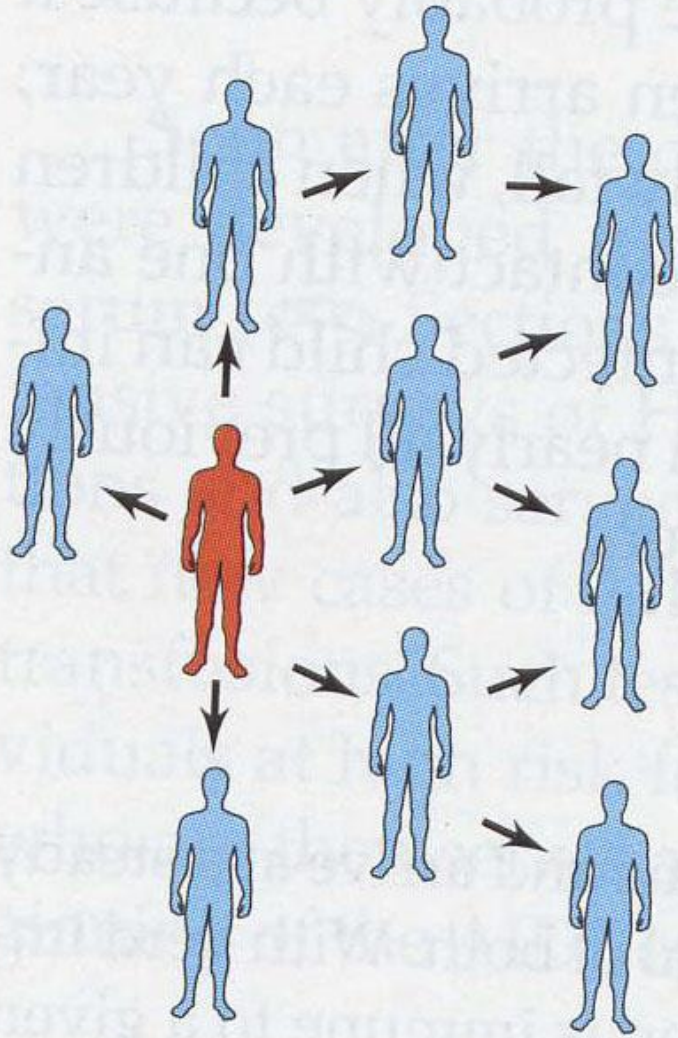
- Epidemic:
  - # cases in excess of expected # for population
  - the uncontrolled spread of a disease (or condition) in a community.
- Herd immunity: cumulative # of immune persons in population or % of population immune.
- Seasonality: temporal distribution of incidence



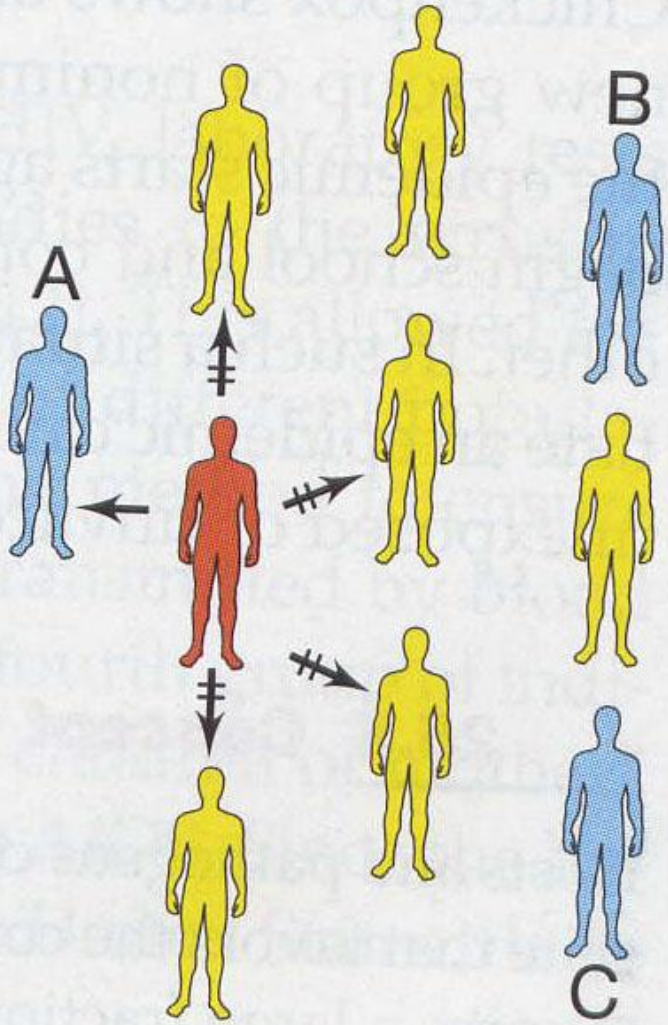
(a) Endemic disease

(b) Epidemic disease

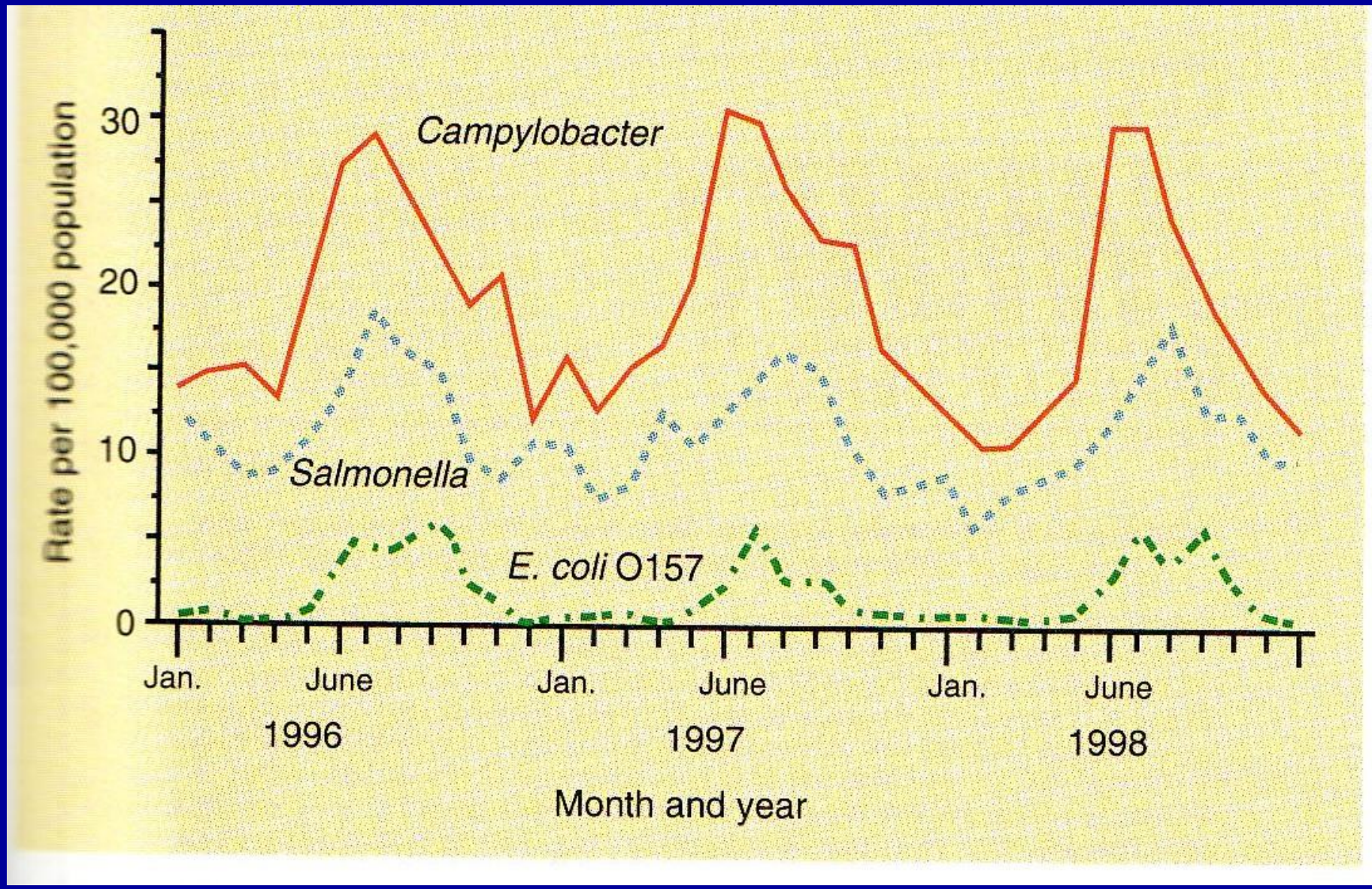
(c) Pandemic disease



(a)



(b)

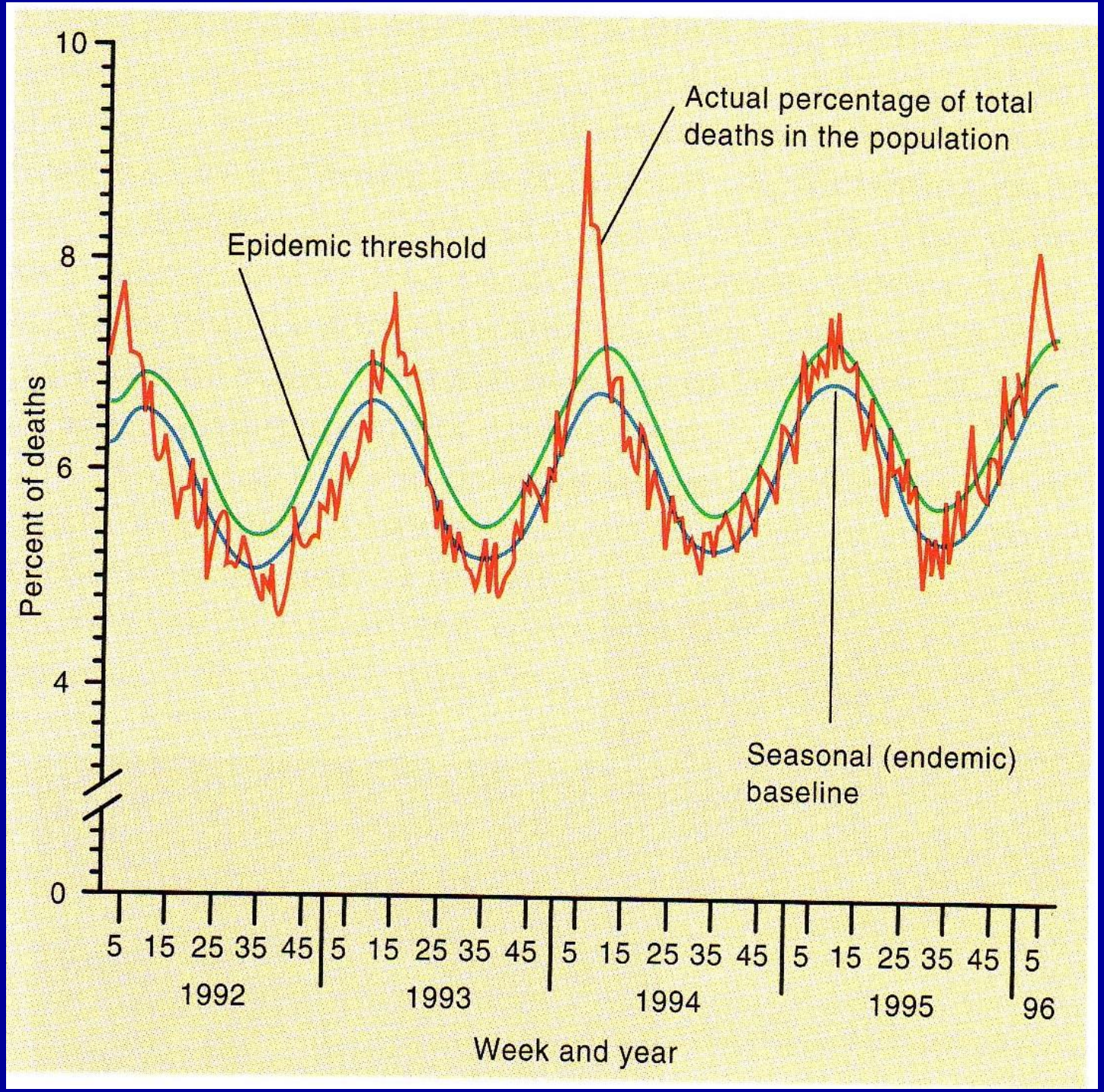

Rate per 100,000 population
30
20
10
0
Campylobacter
Salmonella
E. coli O157
Jan.
June
Jan.
June
Jan.
June
1996
1997
1998
Month and year

Outbreaks or Epidemics

A disease or condition at involves many or an excessive number of people at the same time and the same place

The occurrence of a disease or condition at a frequency that is unusual or unexpected

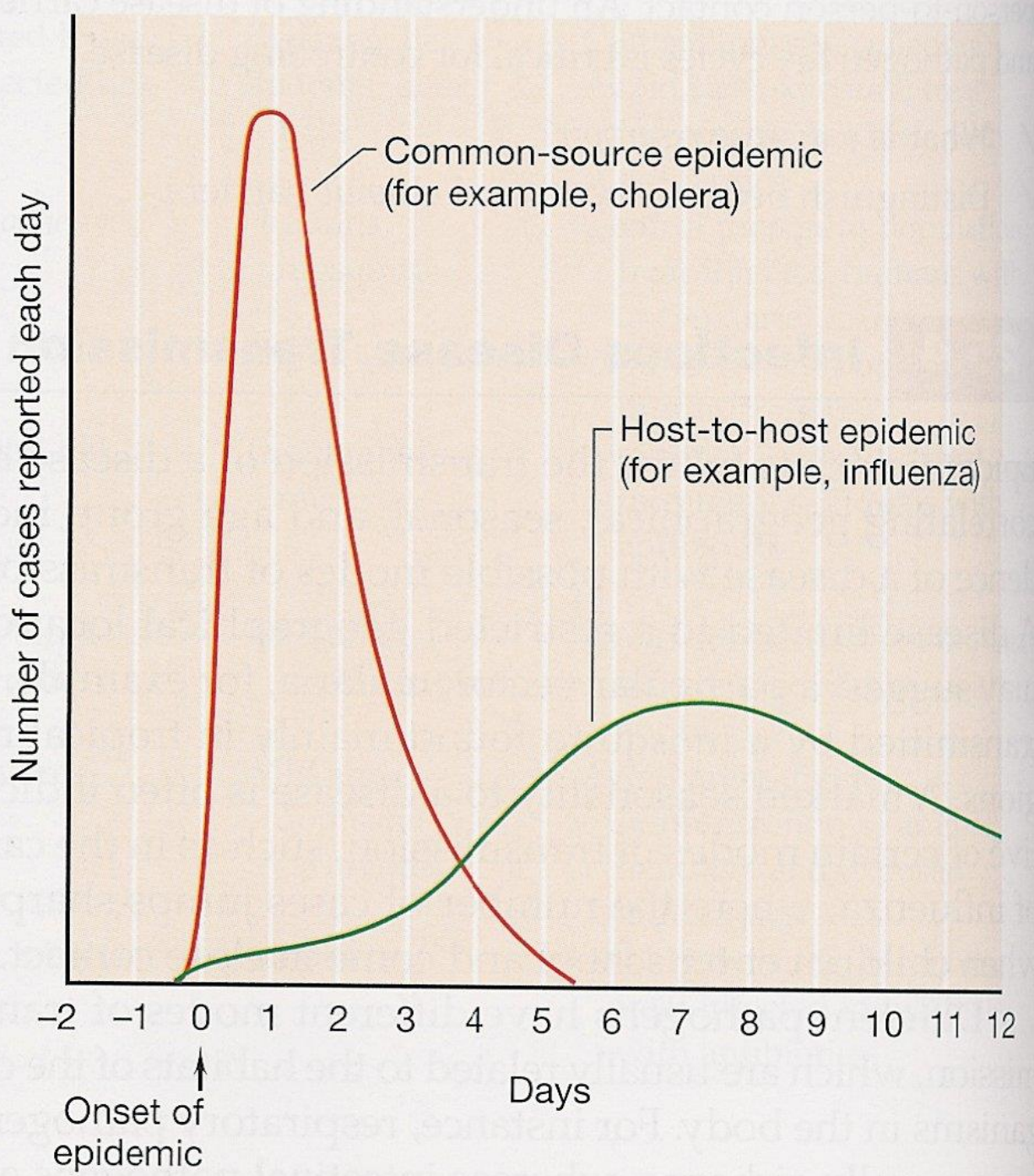
increase above background or endemic level


10
8
6
4
0
Percent of deaths
Actual percentage of total deaths in the population
Epidemic threshold
Seasonal (endemic) baseline
5 15 25 35 45 5 15 25 35 45 5 15 25 35 45 5 15 25 35 45 5
1992
1993
1994
1995
96
Week and year

Requirements for an Outbreak or Epidemic:

- (i) presence of an infected host or other source of infection.
- (ii) adequate number of susceptible individuals
- (iii) an effective method of contact for transmission to occur.

- Common Source Outbreak
  - Typical of food or waterborne outbreaks
- Host to Host (Propagated) Outbreak
  - High rates of secondary transmission
  - Person to person spread


Common-source epidemic
(for example, cholera)
Host-to-host epidemic
(for example, influenza)
Number of cases reported each day
–2 –1 0 1 2 3 4 5 6 7 8 9 10 11 12
Days
Onset of
epidemic

Basic Epidemiological Concepts and Terms

- Incidence: # of new cases of disease/total # at risk.
- Incidence rate: Incidence/unit of time.
  - Cumulative Incidence: Incidence measured over longer period

- Prevalence: # cases (or # with defined condition) existing at specific time.
- Prevalence rate: # of such cases/total # at risk.

- P = I X D, where D is duration

Basic Epidemiological Concepts and Terms

- **Risk**- The number of individuals who are exposed and become ill divided by the number of those exposed

- **Relative Risk**- The risk of illness for individuals exposed divided by the risk of illness for those not exposed

Example

	# Ill that did eat	Total # eating	# Ill that did not eat	Total # not Eating
Quice	2	10	3	5
Cheesecake	4	5	1	10
Swiss Roll	3	7	2	8
Chocolate Cake	1	3	4	12
Cheese Dip	4	11	1	4

What Are Relative Risks for Each Food Item???

Food	Relative Risk
Quice	0.33
Cheesecake	8
Swiss Roll	1.72
Chocolate Cake	0.93
Cheese Dip	1.44

Basic Epidemiological Concepts and Terms

- **Odds for Cases**- Number of cases exposed to a factor divided by the number of cases not exposed to the factor
- **Odds for Controls**- Number of controls exposed to a factor divided by the number of controls not exposed to the factor
- **Odds Ratio**- Odds for cases divided by odds for controls
  - **$OR = O_{cases}/O_{controls}$**

Example

	Cases	Controls
Exposed	a	b
Not Exposed	c	d

What is Odds Ratio???

OR = (a/c)/(b/d) = ad/bc

Koch's Postulates

- Organism must be consistently present in diseased state
- Organism must be isolatable and culturable
- Cultured organism must induce disease when introduced to susceptible host

Basic Epidemiological Concepts and Terms

- Confounding- when a factor is associated with the exposure one is studying and which at the same time is associated with the outcome

- Causation- nine criteria outlined by Sir Austin Bradford Hill in 1965.
  - **Strength** (is the risk so large that we can easily rule out other factors)
  - Consistency (have the results have been replicated by different researchers and under different conditions)
  - Specificity (is the exposure associated with a very specific disease as opposed to a wide range of diseases)
  - **Temporality** (did the exposure precede the disease)
  - **Biological gradient** (are increasing exposures associated with increasing risks of disease)
  - **Plausibility** (is there a credible scientific mechanism that can explain the association)
  - Coherence (is the association consistent with the natural history of the disease)
  - Experimental evidence (does a physical intervention show results consistent with the association)
  - Analogy (is there a similar result that we can draw a relationship to)

Temporal Elements of Transmission

- Attack Rate- Proportion of individuals exposed to an infectious agent who become clinically ill
- Waves or Generations of Infection
  - Primary Case- Individual that brings infection to a population
  - Secondary Case- People infected by primary case
- Index Case- First case identified by health care system

Temporal Elements of Transmission

- Reproductive Rate- Potential of contagious disease to spread within a population; R_0=# individuals infected when case enters population of susceptibles
  - Depends on risk/probability of transmission in contact, how common contacts are, how long person is infectious, and proportion of population that is immune
  - R_0<1 disease will eventually disappear
  - R_0=1 disease will become endemic
  - R_0>1 disease will be an epidemic

Temporal Elements of Transmission

- Incubation Period- Amount of time between exposure and showing of symptoms
- Serial Interval- Time between successive generations
- Infectious Period- Amount of time during which an individual can transmit infection
- Latent Period- Time between infection and beginning of infectious period

Temporal Elements of Transmission

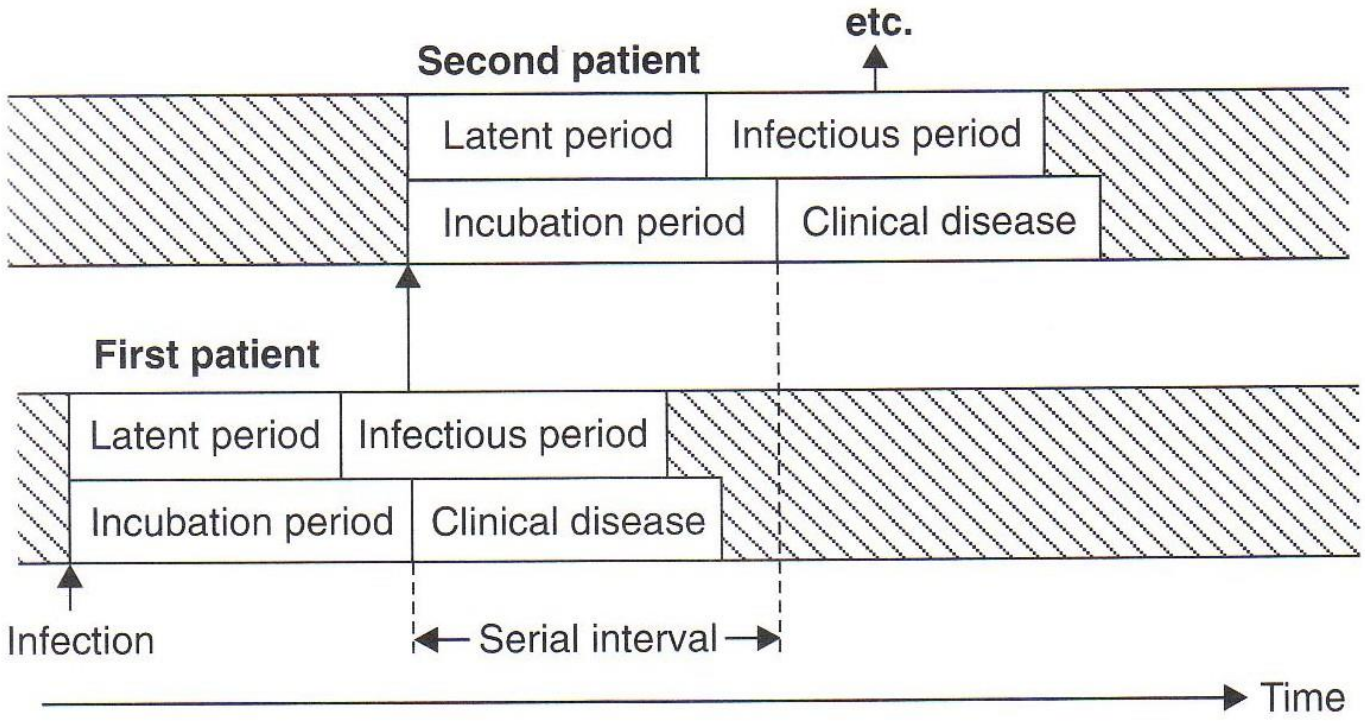


Figure 2.2 The relationships of some important time periods. The patient at the bottom is infected first, and transmits the infection to a second patient.

Dynamic Population Model

- SIR Model (n = S + I + R)
  - S= Susceptibles
  - I= Immune
  - R=Resistants

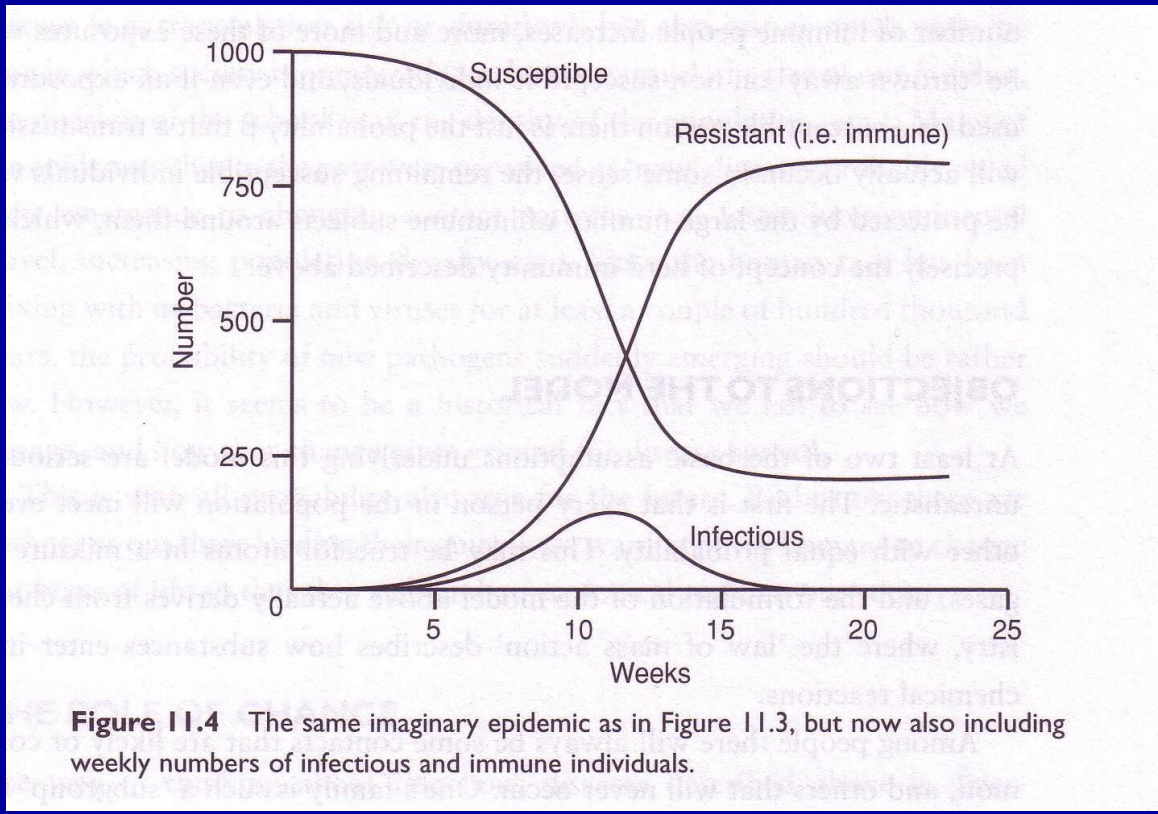


Figure 11.4 The same imaginary epidemic as in Figure 11.3, but now also including weekly numbers of infectious and immune individuals.

SIR Model

- Population in each of the categories changes with time
- $S_{t+1} = S_t – (\beta \times \kappa \times S_t \times I_t)$
  - β = risk of transmission from contact
  - K = number of contacts per unit time
- $I_{t+1} = I_t + (\beta \times \kappa \times S_t \times (I_t - I_t/D))$
  - D = period of time to immunity (or death)
- $R_{t+1} = R_t + I_t/D$