# Infection, Infectious Disease, & Epidemiology

Dr. Melanie Meyer Microbiology CCV

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## **Biological Associations** *Symbiosis* or "living together," is an association between two or more species

1) Mutualism— a condition in which both species benefit (*E. coli* in colon—Vitamin K synthesis!)

**2)** Commensalism—one species benefits but the other neither benefits nor is harmed (most normal flora)

3) **Parasitism**—an association in which the parasite lives at the expense of the other species, the host (all microbial pathogens)







- Parasites are the cause of infectious disease
  - live at the expense of the host
  - cause damage or death to the host
- Parasitism results in a constant negotiation between the parasite and the host, as each evolves in response to the other
- Encompasses all microbes, including viruses, and worms that produce disease in the host



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### Koch's Postulates

- **1.** Association: The causative agent must be present in every case of a specific disease.
- 2. Isolation: The causative agent must be isolated in every case of the disease and grown in pure culture.
- **3.** Causation: The causative agent in the pure culture must cause the disease when inoculated into a healthy and susceptible laboratory animal.
- 4. **Re-isolation:** The causative agent must be re-isolated from the laboratory animal and be identical to the original causative agent.



### Exceptions to Koch's Postulates

- 1) Some pathogens cannot be cultured in the lab
- Some diseases are caused by a combo of pathogens or by a combination of pathogens and physical, environmental or genetic cofactors.
- 3) Ethical violations prevent application of Koch's postulates in humans in many cases.
- Some diseases can be caused by more than one pathogen (ie meningitis, hepatitis, pneumonia)
- 5) Some pathogens have been historically overlooked (ie *H. pylori*)



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2) 2) Offensive strategies that result in damage to the host



Structure or Secretion	Function	Examples
Defensive strategi	es	
Adhesins	Fixation to cell surfaces and linings	Neisseria gonorrhoeae (attachment to urethral lining); Streptococcus mutans (causes tooth decay and sticks to surface of teeth)
Capsules	Interfere with uptake of bacteria (phagocytosis)	Anthrax, plague, streptococcal diseases (e.g., scarlet fever, "strep" throat, pneumococcal infection)
Miscellaneous	Interfere with uptake of bacteria (phagocytosis)	"Waxy coat" of tubercle bacilli; M protein in streptococcal cell walls
Offensive strategie	s	
Enzymes	Destroy integrity of tissue structure	Hyaluronidase (breaks down hyaluronic acid of connective tissue), hemolysins (bring about lysis of red blood cells), collagenases (break down collagen in connective tissue), leukocidins (destroy white blood cells)
Exotoxins	Specific activities that interfere with vital host functions	Botulinum toxin (one of the most potent toxins known; interferes with transmission of nerve impulse, resulting in flaccid paralysis); tetanus toxin (interferes with transmission of nerve impulses, resulting in irreversible muscle contraction)
Endotoxins	Produces shock-like symptoms, chills, fever, weakness	Structural components of gram- negative cells





### Offensive Strategys: Exoenzymes

- Enzymes are proteins with activities that allow the invading bacteria to spread throughout host tissues, causing damage in the process.
- These enzymes are useful to the pathogen in breaking down tissue barriers in the host
- Examples:
  - Hyaluronidase breaks down hyaluronic acid content of connective tissues
  - Collagenase breaks down collagen which can result in necrotic (dead) tissue that requires debridement
  - Hemolysins destroy red blood cells
  - Kinases break down clots
  - Leukocidins destroy white blood cells





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### Offensive Strategy: Endotoxins

- Gram-negative bacteria have an outer membrane composed mainly of lipopolysaccharide (LPS)
- Endotoxin (aka lipid A) is the lipid portion of the menbrane's LPS.
- Many endotoxins stimulate the body to release chemicals that cause fever, inflammation, diarrhea, hemorrhaging, shock, and blood coagulation.
- Although exotoxin producing bacteria can produce more serious disease states, endotoxin-producing (gramnegatives) can produce life-threatening
- Endotoxin can be released when gram-negative bacteria:
  - Dividing
  - Disintegrating or dying naturally
  - Being digested by phagocytic cells

roperty	Exotoxins	Endotoxins
Site	Released from cell during growth and metabolism	Retained (for the most part) within outer membrane and released when cell disintegrates
Cell source	Primarily gram-positive cells	Gram-negative cells
Activity	Specific for each toxin	Essentially similar for all endotoxins
Chemical nature	Protein	Lipopolysaccharide
loxicity	High toxicity	Minimal toxicity
leat stability	Unstable; usually destroyed at about 60°C	Stable; can withstand temperatures of 100°C
Examples of diseases	Tetanus, scarlet fever, diphtheria, gangrene, botulism	Meningococcal meningitis, typhoid fever, salmonellosis

### Host response to endotoxins

Regardless of their source, endotoxins produce the same host response characterized by:

- Shock-like symptoms
- Chills
- Fever
- Weakness
- Formation of small blood clots
- Possible death

\*Individuals with gram-negative infections may experience exaggerated symptoms during antibiotic treatment because of the release of endotoxins from dead cells.

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## Virulence Mechanisms of Non-bacterial Pathogens

- Viruses
  - Defensive: antigenic variation (influenza), etc.
- Offensive: death (lysis) of host cell from
  - Production of large numbers of replicating viruses
  - Inhibiting host protein synthesis
  - Damage to plasma membrane
  - Inhibiting host cell metabolism

• Eukaryotic Microbes (including helminths)

• Combination of offensive and defensive strategies described for bacteria (adhesins, toxins, antigenic variation, etc.)

Stage	Description
ncubation	Period between initial infection and appearance of symptoms; considerable variation among diseases
Prodromal	Period in which early symptoms appear; usually short and not always well characterized
llness	Period during which the disease is most acute and is accompanied by characteristic symptoms
Decline	Period during which the symptoms gradually subside
Convalescence	Period during which symptoms disappear and recovery ensues

## Epidemiology and Cycle of Microbial Disease

**Epidemiology** = an investigative branch of medicine that deals with the source, cause, and possible control of infectious disease and other public health problems

**Epidemiologists** attempt to determine why an outbreak of disease occurs at a particular time and/or particular place

• Dispatched by the CDC when the threat of an outbreak occurs anywhere in the world

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### Epidemiology has a long and interesting history

- **Hippocrates** (460–377 B.C.) linked malaria, yellow fever, and swamps
- Edward Jenner's late 1700s observations regarding cowpox led to smallpox vaccine
- **Ignaz Semmelweis** (mid 1800s) proved that childbed fever resulted from physicians not washing their hands after dissections (remember how sad the outcome was for Semmelweis!)
- John Snow's 1849 detective work in London showed that most with cholera got water from the Broad Street pump, thus ending the epidemic





- Sporadic—occur only occasionally and in an unpredictable fashion (tetanus, etc.)
- Endemic—regularly found at a steady level in a particular location (common cold, etc.)
- · Epidemic-sudden increase in morbidity (illness rate) and mortality (death rate) above the norm (plague, etc.)
- **Pandemic**—epidemics that spread across continents (1918 influenza, HIV/AIDS)

### 1849 Cholera Outbreak, London







Figure 08.02: "Monster Soup," commonly called the Thames water.

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### Tracking Disease--terminology

Two measures to track occurrence of disease by epidemiologists:

**Incidence =** the number of *new* cases of a disease in a given area or population during a given period of time

**Prevalence =** *total number of cases,* both new and already existing, in a given area or population during a given period of time (a cumulative number)

### 2 Epidemic Types:

**1) Common-source** epidemics involve contact with a single contamination source (contaminated water)

**2) Propagated** epidemics result from person-to-person contact (mumps and chicken pox)



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## Herd Immunity (Group Immunity)

- Refers to the proportion of immunized individuals in a population
  - The smaller the number of susceptible individuals, the less opportunity for contact between them and infected individuals.
- Public health officials strive to maintain high levels of herd immunity
- Basis for mass vaccination/immunization programs

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### Reproduction rate ( $\mathbf{R}_0$ or **R-nought**)

- Measure of the potential for transmission of a particular disease
- Mathematical equation
- Mean number of secondary cases, occurring in a susceptible population in the wake of a particular infection.
  - Population density, duration of contagiousness, other factors considered
  - R<sub>0</sub> must be greater than 1 to spread; if less, it will die out.

Disease	Type of Causative Agent	Ro
Measles	Virus	12-18
Pertussis	Bacterium	12–17
Diphtheria	Bacterium	6–7
Smallpox	Virus	5–7
Poliomyelitis	Virus	5–7
Rubella	Virus	5–7
Mumps	Virus	4–7
HIV/AIDS	Virus	2-5
Influenza A	Virus	2–3
Ebola hemorrhagic fever	Virus	1
Rabies	Virus	<1



Frequency and distribution of disease includes monitoring of the following re: a disease-afflicted population:

- Age
- Gender
- Diet
- Lifestyle

The above are used as starting points to establish a strategy for halting an outbreak

Center for Disease Control (CDC), The World Health Organization (WHO), and local and state agencies are responsible for ongoing surveillance of disease (See Table 8.2 for list of Nationally Notifiable Diseases, 2011)

Graphs, charts, and maps are used by epidemiologists to illustrate the frequency and distribution of diseases HME HGE/



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TABLE 8.2 Major Infectious Disea National Level, United	ises Designated as Notifiable at the I States, 2011		
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Hepatitis A Hepatitis B Hepatitis C	Toxic shock syndrome (staphylococcal) Trichinellosis	Table 08.02: Major Infectious Diseases	
HIV infection Influenza-associated pediatric mortality Jamestrian Camon virus	Tuberculosis Tularemia Typhoid fever	Designated as Notifiable at the	_
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Reproduced from the Cl Notifiable Disease, 2011	DC. Summary of L.		1':

### Cycle of Microbial Disease

• For infectious dz to exist at the community level, a chain of linked factors (reservoirs, modes of transmission, portals of entry and exit) contributes to the cycle of microbial disease



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### **Reservoirs of Infection**

- Active carriers are individuals who have a microbial disease
- **Chronic carriers** harbor the pathogen for long periods of time after recovery, without ever becoming ill again
- **Healthy carriers** have no symptoms and may unwittingly pass the disease on to others
  - Chronic carriers continue to harbor the microbe after recovery, this state can continue indefinitely without illness (Typhoid Mary)
  - Carriers play a significant role in spread of TB.
- Zoonoses are diseases in which animals serve as

### **Reservoirs of Infection**

**Reservoir** is a site in nature in which microbes survive (and possibly multiply) and from which they may be transmitted

- All pathogens, to exist, must have one or more reservoirs
- Reservoirs are prime targets for preventing, minimizing, and eliminating existing and potential epidemics
- Humans are the only known reservoir for pathogens that cause smallpox, gonorrhea, measles, polio, among others.

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**Zoonoses** are diseases of animals that can affect humans. Animals act as reservoirs of pathogen.

### TABLE 8.3 Selected Zoonotic Diseases

Transmission by Arthropod Bites	Transmission Via Food, Water, or Animal Bites Bacteria
Ehrlichiosis Relapsing fever Lyme disease Rocky Mountain spotted fever Plague Typhus fever Viruses	Undulant fever Leptospirosis Anthrax Cat scratch fever Tularemia <b>Viruses</b> Rabies
Yellow fever Eastern equine encephalitis West Nile virus disease La Crosse encephalitis Rift Valley fever Dengue fever <b>Protozoans</b> Babesiosis Sleeping sickness Malaria American trypanosomiasis Leishmaniasis	Hantavirus disease Viral gastroenteritis Severe acute respiratory syndrome (SARS) <b>Diservirus</b> Giardiasis <i>Cyclospora</i> infection Toxoplasmosis

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### Nonliving Reservoirs

Some organisms are able to survive and multiply in nonliving environments, such as soil and water

• Spore formers, like the group of *Clostridium* bacteria (cause of tetanus and botulism) can survive for many years in soil



Figure 08.07: Soil can be a nonliving reservoir for microbes and helminth egg

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### Transmission

**Transmission** = the mechanism by which an infectious agent is spread to a susceptible person

#### TABLE 8.5 Modes of Transmission

#### Direct

Contact (e.g., kissing, sneezing, coughing, singing, sexual contact) Animal bites Indirect Vehicles (fomites, e.g., doorknobs, eating utensils, toys, facial tissue) Airborne (via aerosols created by, e.g., shaking bedsheets, sweeping, mopping) Vectors (e.g., mosquitoes, ticks, flies)

Transplacental

Table 08.05: Modes of Transmission.

TABLE 8.4 Wat	er and Food as Reservoirs of Infection
<b>Type of Microbe</b> Bacteria Viruses Protozoa Worms	<b>Examples of Waterborne and Foodborne Infections</b> Salmonellosis, shigellosis, cholera, gastroenteritis Hepatitis A, poliomyelitis, viral gastroenteritis (e.g., norovirus) Giardiasis, amebiasis, cryptosporidiosis Ascariasis, trichinellosis, <i>Trichuris</i> infection
Tal	ole 08.04: Water and Food as Reservoirs of Infection.

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**Direct transmission**—infectious agent is directly and immediately transferred from a port of exit into a port of entry

- Horizontal: person-to-person, touch (including sex), droplets, etc.
- Vertical: mother-to-child (transplacental, breast milk, birth canal)

#### Means of transmission:

- Contact (kissing, sneezing, sex, etc.) < horizontal>
- Animal Bites <horizontal>
- Transplacental <vertical>

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Indirect transmission = microbes pass from reservoir (or source) to an intermediate agent and then to a host 1) Vehicle-borne: via food, water, biological products (organs, blood, blood products), and fomites (inanimate

objects)
2) Airborne: aerosols of water or dust particles (less than 4 μm) in the air; unlike droplets (10 μm or larger) aerosols remain airborne for extended periods

**3) Vector-borne**: Arthropods (i.e., ticks, flies, mosquitoes, lice, and fleas) or insects (Chagas' kissing bug, etc.)

- Mechanical passive transmission on feet, etc.; microbes do not invade, multiply, or develop in the vector
- **Biological vectors** are a necessary part of the life cycle of a pathogen, transmission is an active process

### Transmission





Figure 08.08: Droplet transmission (sneezing)--DIRECT

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Figure 08.09: Exercise machines can b reservoirs for microbes--FOMITES

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Disease	Type of Microbe	Genus of Microbe	Arthropod Vector	Distribution
Plague	Bacterium	Yersinia pestis	Fleas	Southeast Asia, Central Asia, South America, western North America
Relapsing fever	Bacterium	Borrelia sp.	Lice or ticks	South America, Africa, Asia, western North America
yme disease	Bacterium	Borrelia sp.	Ticks	Europe, North America, Australia, Japan
yphus fever endemic)	Bacterium	<i>Rickettsia</i> sp.	Fleas	Worldwide
yphus fever epidemic)	Bacterium	<i>Rickettsia</i> sp.	Lice	Eastern Europe, Asia, Africa, South America
astern equine encephalitis	Virus	Alphavirus	Mosquito ( <i>Culex,</i> <i>Coquillettidia, Aedes</i> )	North and South America
apanese encephalitis	Virus	Flavivirus	Mosquito (Culex)	Asia, Pacific Islands, Torres Strait of Australia, Papua New Guinea
a Crosse encephalitis	Virus	Bunyavirus	Mosquito ( <i>Ochlerotatus</i> )	United States
St. Louis encephalitis	Virus	Flavivirus	Mosquito (Culex)	North and South America
Vest Nile encephalitis	Virus	Flavivirus	Mosquito ( <i>Culex</i> )	Africa, North America, Caribbean, South and Central America, India, Australia, Middle East, Russia, Europe, Southeast Asia
Vestern equine encephalitis	Virus	Alphavirus	Mosquito (Aedes)	North and South America

Disease	Type of Microbe	Genus of Microbe	Arthropod Vector	Distribution
Dengue fever	Virus	Flavivirus (Dengue 1, 2, 3 and 4)	Mosquito ( <i>Aedes</i> )	India, Southeast Asia, Pacific, Mexico, South America, Caribbean, United States (Texas/ Mexico border)
Rift Valley fever	Virus	Phlebovirus	Mosquito (Aedes)	Africa, Arabia
Yellow fever	Virus	Flavivirus	Mosquito (Aedes)	Tropical South America, Africa
Chikungunya fever	Virus	Alphavirus	Mosquito (Aedes)	Africa, Southeast Asia, Philippines
O'nyong-nyong fever	Virus	Alphavirus	Mosquito (Anopheles)	Africa
Ross River fever	Virus	Alphavirus	Mosquito ( <i>Culex,</i> Aedes)	Australia, South Pacific
/enezuelan encephalitis	Virus	Alphavirus	Mosquito ( <i>Culex,</i> Aedes)	North and South America
Murray Valley or Australian encephalitis	Virus	Flavivirus	Mosquito ( <i>Culex</i> )	Australia, New Guinea
Barmah Forest fever	Virus	Alphavirus	Mosquito ( <i>Culex,</i> Aedes)	Australia
California encephalitis Colorado tick fever	Virus Virus	Bunyavirus Orbivirus	Mosquito ( <i>Aedes</i> ) Tick	United States United States and Canada
Malaria	Protozoan	Plasmodium sp.	Mosquito (Anopheles)	Africa, Southwestern Pacific, South America, Southeastern Asia, India
Babesiosis	Protozoan	Babesia sp.	Ticks	United States, Europe
American rypanosomiasis (Chagas disease)	Protozoan	<i>Trypanosoma</i> sp.	Kissing bug	South and Central America
African trypanosomiasis (sleeping sickness)	Protozoan	<i>Trypanosoma</i> sp.	Tsetse flies	West, Central, and East Africa
Leishmaniasis	Protozoan	<i>Leishmania</i> sp.	Sand flies	Central and South America, Africa, India, and other parts of Asia, Europe
Filariasis or elephantiasis	Worm	<i>Wuchereria</i> sp. <i>Brugia</i> sp.	Mosquito ( <i>Culex,</i> Anopheles, Aedes, Mansonia, Coquillettidia)	Central and South America, Africa, India, and other parts of Asia
Onchocerciasis	Worm	Onchocerca sp.	Black flies	Central America, tropical South America, Africa

Disease	Location	Year(s)
Yellow fever	Cuba	1900–1901
Yellow fever	Panama	1904
Yellow fever	Brazil	1932
Anopheles gambiae infestation	Brazil	1938
Anopheles gambiae infestation	Egypt	1942
Louseborne typhus	Italy	1942
Malaria	Sardinia	1946
Yellow fever	Americas	1947-1970
Yellow fever	West Africa	1950–1970
Malaria	Americas	1954–1975
Malaria	Global	1955–1975
Onchocerciasis	West Africa	1974–present
Bancroftian filariasis	South Pacific	1970s
Chagas disease	South America	1991-present
Reproduced from Duane J. Gu	bler and CDC, Emerging Infection	us Diseases, 4 (1998): 442–450.
	Mantaukawa Diasaa	







	Examples of Disease or Microbe
Portals of entry	
Mucous membranes	
Respiratory tract	Streptococcus pneumoniae, tuberculosis, Legionnaires' disease, influenza, hantavirus, common cold
Gastrointestinal tract	Cholera, salmonellosis, <i>E. coli,</i> rotavirus, norovirus, hepatitis A, poliomyelitis, guinea worm disease, giardiasis
Urogenital tract	Gonorrhea, chlamydia, AIDS, genital warts genital herpes
Skin (hair follicles, sebaceous glands, wounds, arthropod bites) Blood (transfusion, blood products, arthropod bites, placental transfer)	Boils, abscesses, cutaneous anthrax, rabies, warts, hookworm, schistosomiasis, malaria Congenital syphilis, AIDS, German measles, toxoplasmosis, Chagas disease, hepatitis C
Portals of exit	
Respiratory tract	Tuberculosis, Legionnaires' disease, influenza, common cold
Gastrointestinal tract	Cholera, salmonellosis, rotavirus, norovirus, hepatitis B and A, poliomyelitis, hookworm, guinea worm disease
Urogenital tract	Gonorrhea, chlamydia, HIV, schistosomiasis, genital herpes
Skin	Impetigo, boils, abscesses, warts, cold sores, fever blisters, guinea worm disease, candidiasis
Blood (transfusion, blood products, arthropod bites, placental transfer)	Congenital syphilis, toxoplasmosis, HIV, hepatitis B and C, rubella, malaria



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### Nosocomial Infections

= infections acquired by patients or health care workers while they are in a health care facility (including hospitals, dental offices, nursing homes, and waiting rooms in doctor's offices)

- CDC estimate: 10% of American patients acquire a nosocomial infection each year
- Result in 90,000 deaths annually.

#### 2 types of nosocomial infections:

- 1) Exogenous nosocomial infection
- 2) Endogenous nosocomial infection

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### Exogenous vs. Endogenous Nosocomial Infections

**Exogenous**= caused by pathogens acquired from the health care environment

**Endogenous**= situation in which the normal flora becomes a pathogen as a result of medical treatments or hospitalization (i.e. chemotherapy)

**latrogenic Infections** = subset of nosocomial infections that are the direct result of modern medical proceduressuch as use of catheters, invasive diagnostic procedures and surgery ("doctorinduced")

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### Nosocomial (Hospital-Acquired) Infections

#### **Control Measures**

#### TABLE 8.10 Nosocomial Infections Caused by Antibiotic-Resistant Bacteria

Most Common Type of Infection	Pathogen
Bloodstream infections	Acinetobacter baumannii
Surgical site infections	Staphylococcus aureus
Diarrhea	Clostridium difficile
Ventilator-associated pneumonia	Klebsiella pneumoniae
Pneumonia, urinary tract infections, and bloodstream infections	Pseudomonas aeruginosa
Catheter-associated urinary tract infections	Escherichia coli
Catheter-associated urinary tract infections	Enterococcus faecalis

All hospitals are required to have an infection-control officer and an infection control committee to maintain accreditation.