# IDENTIFICATION OF INFECTIOUS DISEASE PROCESS

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### Disclosures

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### Objectives

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Infectious disease process (aka. Pathogenesis) Clinical signs/symptoms of infection (aka. Immune process) Diagnostics and laboratory reports including specimen handling Infection vs. colonization vs. contamination Antimicrobial Use

### **Disclosures** (2)

I cannot teach you all of infectious diseases and microbiology in 90 minutes.

I will address each core principle broadly and add context.

To illustrate the core principles I'll add a specific scenario.

Try to hit key pathogens from each of the (38!) chapters I'm supposed to cover

Average 2.4 minutes per chapter



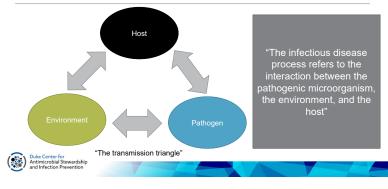


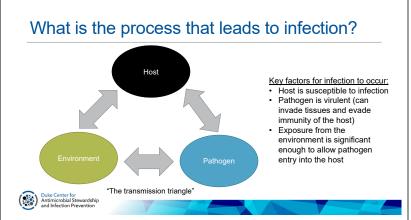


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### What is the process that leads to infection?





### Environmental risk factors

People, places/physical structure/space, time

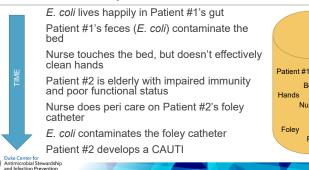
Healthcare environments (e.g. Hospitals, OR, Clinic, ED, SNF/ALF) or community settings

Each setting and practice/procedure has it's own unique environmental risks to consider

- Examples:
- Likelihood of needle sticks? Likelihood of significant contamination events?
- Likelihood of an encounter with a returning traveler presenting with fever?
- What infections are circulating at this time of year?

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### Transmission: linear in time, multidimensional in space



#### Reservoirs and intermediaries The Environmental component may include multiple intermediate steps for transmission to occur: Reservoir Portal of Exit (from the reservoir) Fece Mode of Transmission E.g. surface/skin contact, airborne, fecal-oral large droplet, sex, vector-borne Hands Portal of Entry (to the host) Patient #2 https://www.cdc.gov/malaria/about/biology/index.html Antimicrobial Stewardship

### Transmissibility

Inoculum: number of organisms needed to cause disease during an exposure

Ability of the pathogen to survive in the environment

Method of transmission (move from a reservoir to other hosts)

Reproductive number (R0) measure of infectivity: average number of people that one sick person will infect





Bed

Nurse

### **Practice Question**

Which of the following statements about influenza is FALSE?

A. Influenza is primarily spread between individuals via respiratory secretions (droplets)

B. Viral shedding starts 48-72 hours after infection and typically 48 hours before the onset of symptoms

C. Viral shedding normally persists for less than 5 days but can be longer in children and in immunocompromised persons

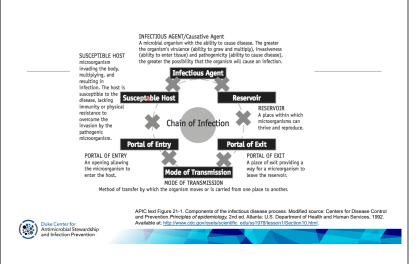
D. The typical influenza symptomology is not always predictive of influenza in elderly or immunocompromised persons.





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### Mitigation of transmission risks

There are MANY things we can do to reduce transmission (examples):

- Environmental engineering, cleaning/disinfection Occupational health, avoidance of presenteeism
- Appropriate use of transmission based precautions
- Hand hygiene!
- Cohorting; staffing ratios

Some things are NOT modifiable with facility-level IP (examples):

- Host factors, complexity of patient population
- External factors, e.g. geographic and regional epidemiology · Cannot wholly avoid risky things like surgery, chemotherapy, and central lines (aka competing
- risks)

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### Practice Question

An IP is conducting an educational session to help the nursing staff understand infectious disease transmission. She explains that an initial element in transmission is the ability of an organism to survive in the external environment during transit between hosts. What is the second element?

- A. Secretion of enzymes that enhance spread through tissues
- B. A mechanism for transmission to a new host
- C. Invasion and dissemination in the host
- D. Avoidance of host resistance

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# Host Defenses Physiologic barriers: Secretions, Fever, normal flora

Mechanical barriers: Mucosa or skin

#### Immune system

- Non-specific "Innate" immunity: Phagocytic cells (neutrophils, monocytes), hormones, fibronectin
- Complement system: protein pathways that poke holes and ramp up inflammatory response
- Pathogen-specific "Adaptive" immunity: Cellular immunity (T cells), Humoral immunity (B cells, antibodies)

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### Practice Question

The IP is teaching nurses how to assess infection risks in patients. Depletion of what cell type provides the best indication of susceptibility to most bacterial infections?

- A. monocyte
- B. Eosinophil
- C. neutrophil
- D. lymphocyte



### Immunity

#### Terms and numbers to know:

- Normal WBC : 4,000 10,000 cells/mm<sup>3</sup>
- Leukocytosis: WBC >10,000 cells/mm3
- Leukopenia: WBC <4,000 cells/mm3</p>
- Neutropenia: PMN or band forms <500 cells/mm3 or absolute neutrophil count less than 1000 cells/mm3
- Absolute count = total WBC count x % of PMN leukocytes
- Polys: PMNs: mature or segmented neutrophils
- Bands: Immature or nonsegmented neutrophils
- Infection risk is high when absolute neutrophil count is <500 cells/mm





Non-specific defenses against invading pathogens

### Immunity = Defense

# Host

#### Active

- Acquired through prior exposure (+/- resolved infection) or vaccination
- Memory of prior antigens and previously produced humoral reaction (antibodies)

#### Passive

- Antibodies acquired through other means than a patient's own immune system
- Maternal (first 6mo of life)

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- IVIG (all types of immune globulin)
- Can be specific: e.g. rabies Ig, VZIg



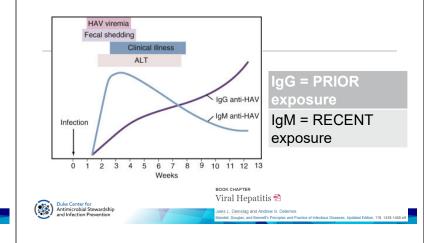
#### ΙgΜ Appears FIRST in adaptive response, Circulating free in blood plasma; too big to go into goes away by ~6mo after exposure, tissues pentamer MAJOR antibody, 4 subclasses lgG Circulating free in blood plasma; moves easily into tissues SECRETORY, histamine release, allergic IgA Mucous membranes and secretions reactions, dimer lgD On lymphocytes, small amt circulating in plasma ALLERGY-inducing, "reagin", increased lgE Mucous membranes, incr in seasonal allergies with parasites laG IqA ( IaM I InD e chain A bat 88 Antimicrobial Stewardship and Infection Prevention 4

Host

### **Practice Question**

The first immoglobulin response after exposure to a communicable disease pathogen or vaccine is production of:

- A. Immunoglobulin G (IgG)
- B. Immunoglobulin M (IgM)
- C. Immunoglobulin A (IgA)
- D. Immunoglobulin C (IgC)



#### воок снартег Viral Hepatitis 🔁

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Antimicrobial Stewardship

Jules L. Dienstag and Andrew S. Delemos Mandell, Douglas, and Bennet's Principles and Practice of Infectious Diseases, Updated Edition, 119, 1439

DIAGNOSTIC INTERPRETATION	SEROLOGIC TESTS OF PATIENT'S SERUM				
	HBsAg	IgM Anti-HAV	IgM Anti-HBc	Anti-HCV	
Acute hepatitis B	+	-	+	-	
Chronic hepatitis B	+	-	-	-	
Acute hepatitis A superimposed on chronic hepatitis B	+	+	-	-	
Acute hepatitis A and B	+	+	+	-	
Acute hepatitis A	-	+	-	-	
Acute hepatitis A and B (HBsAg below detection threshold)	-	+	+	-	
Acute hepatitis B (HBsAg below detection threshold)	-	-	+	-	
Acute hepatitis C	-	-	-	+	

### Practice question

Higher morbidity rates in chronic hepatitis B virus carriers are associated with a co-infection of which of the following:

- A. Hepatitis A
- B. Hepatitis D
- C. Hepatitis C
- D. Hepatitis E



All of the following are descriptions of patients with immunocompromised status EXCEPT:

- A. HIV with CD4 count <200
- B. Leukemia or lymphoma

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- C. Neutropenia (absolute neutrophil count <500/mm3)
- D. 1 year post bone-marrow transplant

### "Susceptible" Host

Can include a large variety of factors:

No prior exposures and thus no adaptive immunity

Invasive procedures (breaking through mechanical defenses)

Immunocompromise (partial list)

- Medications (e.g. high dose steroids, chemotherapy, transplant meds)
- Malignancy (e.g. real or functional neutropenia)
- Metabolic (e.g. diabetes, ESRD, ESLD)
   HIV/AIDS
- Asplenia (e.g. s/p MVA + splenectomy, sickle cell disease)
- Inherited immune deficiency

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### Pathogen Virulence

Pathogen

Factors about the pathogen that can contribute to its ability to invade the host, evade host immunity, or survive:

	Advantage	Example virulence factor	Pathogen/syndrome
	Enzymes to increase local tissue damage/spread	Toxin production	S. pyogenes and necrotizing fasciitis
	Invade, disseminate	Motility	E. coli swimming up a ureter
	Evade host defenses	Biofilms Attach or adhere to surfaces Alter cell wall or membrane Capsule prevents phagocytosis	Coag-neg Staph on IV line S. aureus on a prosthetic knee HIV S. pneumoniae
	Survive in harsh conditions	Spore-formation Lipid coat	C. difficile, Bacillus spp. M. tuberculosis
)	Antimicrobial Stewardship and Infection Prevention		

### Pathogen-specific features you must know

Type of microorganism: bacteria, virus, fungus, parasite Clinical features of infection

Laboratory diagnosis (e.g. culture, serology, PCR)

Precautions recommended in healthcare setting (e.g. contact, airborne, droplet, standard)

Key transmission data:

- Mode of transmission
- Timing: incubation period and "shedding"/contagious period (key for droplet, airborne, and some contact/viruses), typical duration of symptoms
- Vectors

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### List of pathogens/syndromes to know



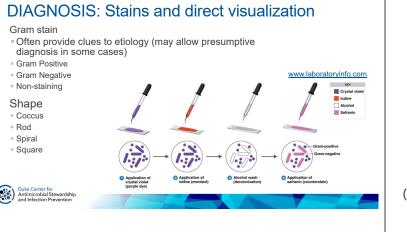
### Quick and Dirty Micro Classification

Gram positive – skin, lung, guts, devices Gram negative – guts, urine, some lung Atypicals – lung, STIs, ticks Anaerobes –gas- and abscess-forming, bad odors, guts Less commonly encountered: Mycobacterium (lung), spirochetes (Syphilis and Borrelia)

Fungal – guts, devices, really bad in immunosuppressed hosts







### Significance of the Gram Stain

By knowing the shape and gram staining reaction of the organisms, along with the body site involved; clinicians can make a reasonable guess as to the causative agent.

The reasonable guess can guide early empiric antibiotic choices.

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### Practice Question

When reviewing the Gram stain of a person with a wound infection, the IP sees Gram-positive organisms in clusters. Which organism would this most likely represent?

- A. Streptococcus
- B. Enterococcus
- C. Corynebacterium
- D. Staphylococcus

### **Microbiology**

Physical requirements for growth of bacteria

- -Nutrition (media)
- Temperature 35° for most bacteria
- Atmospheric conditions
- Aerobic (needs oxygen to survive)
- Anaerobic (needs absence of oxygen to survive)
- -Facultative anaerobes (with or without oxygen)
- Microaerophilic



### **Microbiology: Key words**

#### Growth media

- Blood agar = Multiple organisms Chocolate = Haemophilus, Neisseria
- Charcoal = Yeast, legionella
- MacConkey = Gram Negative
  Bile esculin = group D Strep
  Thayer-Martin = N. gonorrhoeae
  Lowenstein Jensen = Mycobacterium

#### **Biochemical tests**

Catalase: Strep (-) Staph (+) - Coagulase: Staph aureus (+)



### **Microbiology: Key words**

Hemolysis on Blood Agar

- Alpha = green
- Beta = clear Gamma = no hemolysis

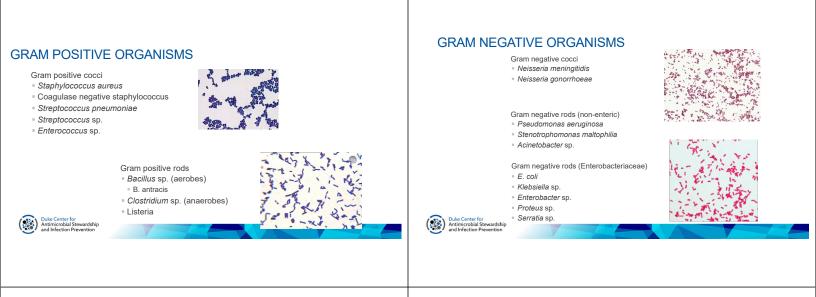




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https://microbiologyinfo.org/ and-its-types-with-example

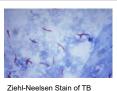


#### NON-STAINING/Special stain PATHOGENS

- Not stained by Gram's method
- Legionella sp.
- Chlamydia
- Rickettsia
- Mycobacteria

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- M. tuberculosis
- Non-tuberculous mycobacteria



Aka. Acid Fast

## Organism Diagnosis

- Fungal
- = Morphology
- Presence of hyphae
- Size of yeast Presence of capsule
- Virology
- Direct- electron microscopy
- Antigen detection
- Virus isolation from culture Antibody detection/serology
- PCR testing

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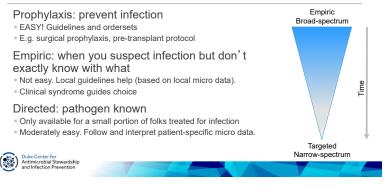
- Parasitology Direct exam
- Microscopy (oocytes)
- Antigen detection/serology

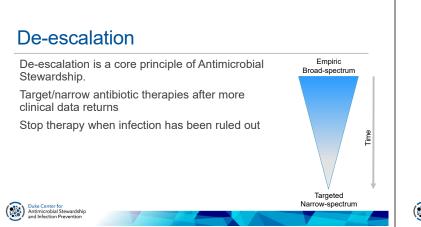
## **Choice of Empiric Antimicrobials**

- What class of pathogen am I likely to be treating? (Bacterial? Viral? Fungal? Other?)
- If bacterial, what organisms are most likely? (Gram positive? Gram negative? Anaerobe?)
- What information can I get to guide treatment? - Microbiology data?
- Do I need to order any other diagnostic tests?
- How sick is my patient? How risky would it be if I miss?



### General Indications for Antibiotics





### **DIAGNOSIS:** Culture

- "Gold standard" to identify the pathogen
   Requires sampling of site of infection, best if collected \*prior to\* therapy
   Allows determination of antimicrobial
- susceptibility Can be "banked" for future tests if
- needed, e.g. outbreak investigations, strain typing, PFGE

**DIAGNOSIS:** Culture

- There are some key limitations to traditional culture methods:
- Time and resource intensive
- Typically have no info other than the stain for 2-3 days
- Highly reliant on specimen collection techniques
- Sometimes positive in absence of infection
- Sometimes negative when infection is
- present (e.g. in the setting of antibiotics) or get contaminated/mixed flora result



### **Practice Question**

Guidelines for transporting specimens include:

- 1) Transport within 2 hours of collecting a specimen
- 2) Transport in leakproof specimen containers and sealable leakproof bags
- 3) Transport specimen in the syringe used to collect it
- 4) Refrigerate all specimens prior to transport
  - A. 1,4
  - B. 2,3
  - C. 1,2
  - D. 3,4



### **Culture Contamination**

Inadequate specimen collection technique can lead to confusing results.

Best example: Contaminated blood cultures with skin flora – infection or not?

 Solutions: Collect blood cultures in pairs. Avoid drawing from existing lines. Hire/educate phlebotomists.

Other examples: Patients had clinical symptoms, are sick, but culture comes back "mixed flora" and pathogen remains unknown. Patient is treated with broad spectrum therapy.

- Example: urine cultures from existing foley catheter (doh!)
- Example: lower respiratory cultures



## Specimen Collection: Key points

Do not contaminate sterile specimens: Aseptic technique + sterile specimen carriers; Appropriate skin prep; Get more than 1

Tissue > Fluid >>>>> Swab (avoid!)

More volume is better (blood, fluids)

Send tissue from the OR to BOTH path and micro Label appropriately and include key clinical clues for the lab, esp for pathogens that are more difficult to culture

Don't send cultures from drains/foleys that are already in place

Don't let specimens sit around (to lab within 2h preferred)

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A patient has a nasal swab positive for methicillin-resistant Staphylococcus aureus (MRSA) in the absence of symptoms. This is an example of:

- A. Normal flora
- B. Colonization

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- C. Asymptomatic infection
- D. Symptomatic infection

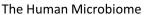
### Infection vs. Colonization

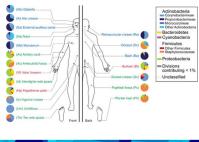
Human beings are not sterile. Clinicians have trouble NOT treating when they see a

positive culture. Clinical presentation is very important.

Clinical criteria for diagnosis of infection should lead to diagnostic testing (not the other way around).

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### Infection vs. Colonization



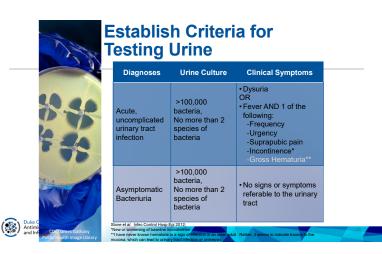
Diagnostic tests used indiscriminately lead to overdiagnosis, overtreatment, and associated negative consequences.

- Exhibit A: Asymptomatic bacteriuria
- Exhibit B: Patient colonized with C. difficile had only 1 loose BM after kayexalate = +PCR and classified as HO-CDI LabID event

Questions to ask before sending diagnostic test:

- "What is the pre-test probability that this patient has infection?"
- "What would I do differently if the test comes back positive? Negative?"





### **DIAGNOSIS:** Antigen Tests

- Identifies pathogen-specific proteins
- Very useful for diagnosing viral infections: HIV, HBV, COVID
- Occasionally useful for others: Cryptococcus antigen (CSF, blood), S. pneumoniae (urine), legionella (urine)



### **DIAGNOSIS:** Serologic testing



- Detects immune response to a pathogen, or prior exposure to a pathogen
- For bacterial infections, generally not useful in early diagnosis (may require acute and convalescent tests)
- For viral infections, IgM indicates early diagnosis or recent exposure (e.g., Hep A)
- Important for screening for prior exposure, documenting immunity, and ensuring vaccination
   e.g. Occupational health titers for varicella, HBV
- Once serology is positive, it is typically life-long



### **DIAGNOSIS:** Molecular tests

PCR and other "molecular" tests

- Increasingly used allows diagnosis of non-culturable pathogens (e.g.,
- norovirus) and faster identification(e.g., pertussis, MRSA in blood);
- Subject to false positives due to sensitivity (e.g. C. difficile)



#### **DIAGNOSIS: Sterile fluid studies**

Evidence of infection due to inflammatory, chemical, and cellular changes in body fluids

Examples: synovial fluid, CSF, pleural, and peritoneal fluid Typically combined with GS/culture (which takes a while)



### **Practice Question**

An IP is reviewing the cerebrospinal fluid (CSF) result from a patient admitted the previous night. The CSF is cloudy and has an elevated White Blood Cell count (WBC), markedly elevated neutrophils, low glucose, and elevated protein. What type of meningitis should she suspect?

A. Bacterial

- B. Viral
- C. Fungal
- D. Aseptic

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#### ≥1,000/m Neutrophils Elevated Gram\* stain Bacteria, Elevated Normal to (early or partially (mild to very) m may show decreased "Septic" treated may GPC or have GNC/GNR lymphocyte predominance) Virus. Usually Usually normal <100 per Lymphocytes Normal to Gram stain. normal elevated negative mm "Aseptic" Variable Variable Lymphocytes Elevated India ink Fungi Low (Crypto), positive AFB stain, TB Variable Low (can be Variable Lymphocytes Elevated positive extremely low) (••

### Antibiotic susceptibility testing: Key Terms

- Antibiotic = A drug that kills or inhibits the growth of microorganisms
- Resistant = An antimicrobial will NOT inhibit bacterial growth at clinically achievable concentrations
- Susceptible = An antimicrobial WILL inhibit bacterial growth at clinically achievable concentrations
- Intermediate= An antimicrobial may not inhibit bacterial growth at typical doses

### Key Terms

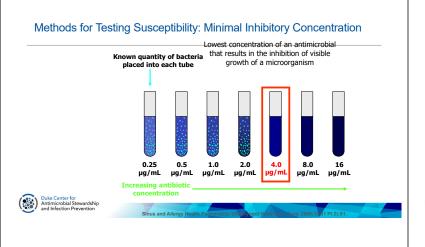
Table 74-1 APIC text

MIC = Minimal inhibitory concentration. Lowest concentration of antimicrobial that inhibits growth of bacteria. Commonly used in clinical lab

MBC = Minimal bactericidal concentration. Concentration of an antimicrobial that kills bacteria. Used clinically only in special circumstances

Breakpoint = The MIC that is used to designate between susceptible and resistant. Set by an expert committee (CLSI).

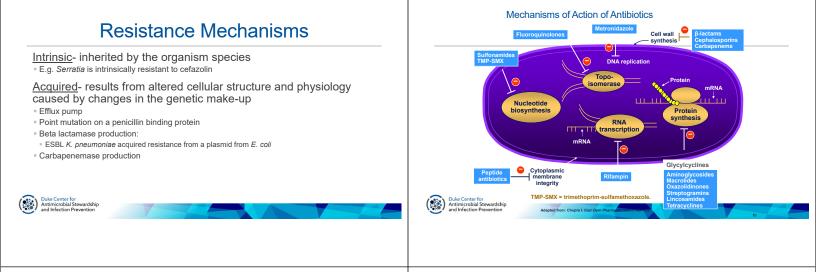




### Methods for Testing Susceptibility

- Broth dilution = MIC testing (Automated system) = a number
- Disc Diffusion = Kirby Bauer (Manual) = a zone size
- E test = "Strip" (Manual) = a number







# SELECTED PATHOGENS



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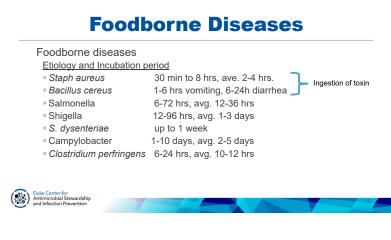


### Practice Question:

The ED reports 3 cases of cramping, abdominal pain, and diarrhea within a 24-hour period. All persons are from the same community, and onset of symptoms was within 12 to 36 hours of a picnic they all attended. The IP suspects which of the following foodborne illnesses:

- A. Salmonella
- B. Hepatitis A
- C. Staphylococcus aureus
- D. Clostridium perfringens





A patient is admitted with pruritic lesions on the hands, webs of fingers, wrists, the extensor surfaces of the elbows and knees, and the outer surfaces of the feet, armpits, buttocks, and waist. The most likely diagnosis is:

- A. Scarlet fever
- B. Herpes zoster
- C. Scabies
- D. Measles

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**Practice Question** 

A patient who was hospitalized for 2 days calls 3 days after discharge complaining that he has developed healthcare-associated scabies due to his recent inpatient stay. The IP knows that his scabies infestation is not healthcare-associated because:

A. Scabies is only transmitted through contaminated linens, and the IP confirmed that all linens the patient came into contact with had been properly laundered

B. the incubation period for scabies is longer than 5 days

C. the incubation period for scabies is shorter than 3 days

D. Scabies is only transmitted through direct contact and none of the healthcare personnel who cared for the patient are infested

### Quick and dirty on parasites

"any organism living within or on another living creature and deriving advantage from doing so while causing disadvantage to the host"



### **Practice Question**

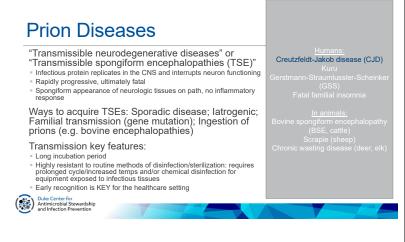
The causative organism of Creutzfeldt-Jakob disease is a:

- A. helminth
- B. diphtheroid

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- C. spirochete
- D. prion





Which is TRUE about a tuberculin skin test (TST):

- A. Positive TST indicates active tuberculosis (TB) infection
- B. Negative TST rules out active TB infection
- C. Positive TST indications past exposure to TB
- D. Negative TST indicates past exposure to TB

### **Practice Question**

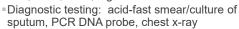
The optimal time to collect a sputum specimen for acid-fast bacilli (AFB) testing to rule out TB would be:

- A. First thing in the morning
- B. After a respiratory treatment
- C. Prior to the patient going to bed
- D. Prior to a respiratory treatment

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### Mycobacterium tuberculosis

- Acid-fast bacilli
- Clinical features of pulmonary disease: subacute onset, cough/congestion (sputum may be bloody), weakness, fatigue, weight loss, chills, fever, night sweats



TST/PPD or IGRA is a screening test for latent disease or prior exposure



tps://radiopaedia.org/cases/pulmonary-tuberculosis

### Mycobacterium tuberculosis

Transmission: airborne by inhalation of droplet nuclei

 Prevention: negative pressure isolation room, N95 mask, direct observed therapy for all new cases

 Treatment: 4-drug therapy: isoniazid (INH), rifampin (RIF), pyrazinamide (PZA), ethambutol (EMB); others if drug-resistant (streptomycin, bedaquiline, FQ)



https://radiopaedia.org/cases/pulmonary-tuberculosis-29



### **Practice Question**

A 14yo boy from rural Maryland was seen in the emergency department with fever, fatigue, chills, headache, and a large annular lesion on his left thigh. What is the most probable vector of this child's illness?

A. tick

- B. mosquito
- C. flea
- D. louse



### Spirochetes: spiral shaped bacteria

### Lyme (*Borrelia burgdorfori*): tick borne illness in the NE US (but expanding)

- Target lesions (erythema migrans), fever, headache, arthralgias; can also cause CNS disease and associated with Bell's palsy; cardiomyopathy
- Confusing diagnostics (serology and protein detection)
- Tick = Ixodes scapularis "black legged"
- Treatment = doxycycline, ceftriaxone for CNS



