Identification of Infectious Disease

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D. Choi Bio

Daniel has been the dedicated infection preventionist for the Subacute unit at O'Connor hospital for approximately 2 years. Prior to starting in his current role, he spent over 8 years as a nurse in acute care setting, but his passion for patient care and safety leads him to the field of infection prevention and control where he felt he could affect change on a bigger scale. Despite being relatively new to the field, under the guidance of the O'Connor infection control team, he has grown tremendously, taking on various leadership roles and projects such as co-leading the Hand Hygiene subcommittee for the Healthcare-Associated Infection (HAI) taskforce at O'Connor hospital as well as successfully implementing Enhanced Barrier Precautions (formerly Enhanced Standard Precautions) in the Subacute unit.

He recently obtained the CBIC CIC and LTC-CIP certifications, continuing to show his passion and dedication to the field. He continues to strive to learn and grow to reduce patient harm and increase patient safety.

Objectives

- Identify risk factors as well as clinical signs and symptoms that can help identify infectious disease
- Review diagnostic and radiologic procedures that assist in the identification of infectious disease
- Explain general guidelines of specimen collection, transportation, handling and storage of laboratory specimens
- Review the basic microbiology of the human immune system, bacteria, viruses, prions, fungi, and parasites
- Examine the role of epidemiological significant organism including *Clostridioides difficile (C. diff),* multidrug resistant organisms (MDROs), carbapenemase producing organisms (CPO), and *Candida auris (C. auris)* in the healthcare setting

Risk Factors

Outside Environmental Factors

- Prevalence of a given organism in the community
- Climatic factors
  - Warmer/More Humid climates
- Travel
  - https://wwwnc.cdc.gov/travel/notices

Inside Environmental Factors

- Include nearly everything inside the healthcare facility
  - High-touch surfaces and medical equipment
  - Plumbing system design and operation
  - Heating, ventilation, and air conditioning (HVAC) system design and operation
  - Compliance with hand and respiratory hygiene
  - Population density in a facility
  - Organism prevalence in a facility

Immunocompromised Status

- Number and type of immunocompromised hosts are constantly increasing for several reasons
  - Medical advances
  - Aging of population
  - Homelessness
  - Obesity epidemic
  - Recreational drug abuse
  - Diminishing access to primary care

Vaccination Status

- Important strategy for preventing disease
- The CDC's Advisory Committee on Immunization Practices (ACIP) provides guidance regarding many vaccine-preventable diseases

Clinical Signs and Symptoms

Clinical Signs and Symptoms

- Bacteremia: fever/chills, nausea/vomiting, diarrhea, cough, and shortness of breath
- Gastroenteritis: diarrhea, pain or cramping in the abdomen, nausea, vomiting, and dehydration
- Influenza-like Illness: fever, cough, headache, sore throat, and muscle pain
- Meningitis: headache, lethargy, vomiting, irritability, fever, neck stiffness, cranial nerve signs (facial drooping, somnolence), seizures, and coma
- Pneumonia/pulmonary infection: fever, chills, cough, increased sputum, shortness of breath, hypoxia, tachycardia, malaise, and weakness

Clinical Signs Symptoms

- Urinary tract infection (UTI): fever, urgency, frequency, and burning with urination
- Sepsis: high heart rate or weak pulse; fever, shivering, or feeling very cold; confusion or disorientation; shortness of breath; extreme pain or discomfort; and clammy or sweaty skin
- Surgical site infection/Wound infection: fever, pain or tenderness, localized swelling, redness, and heat

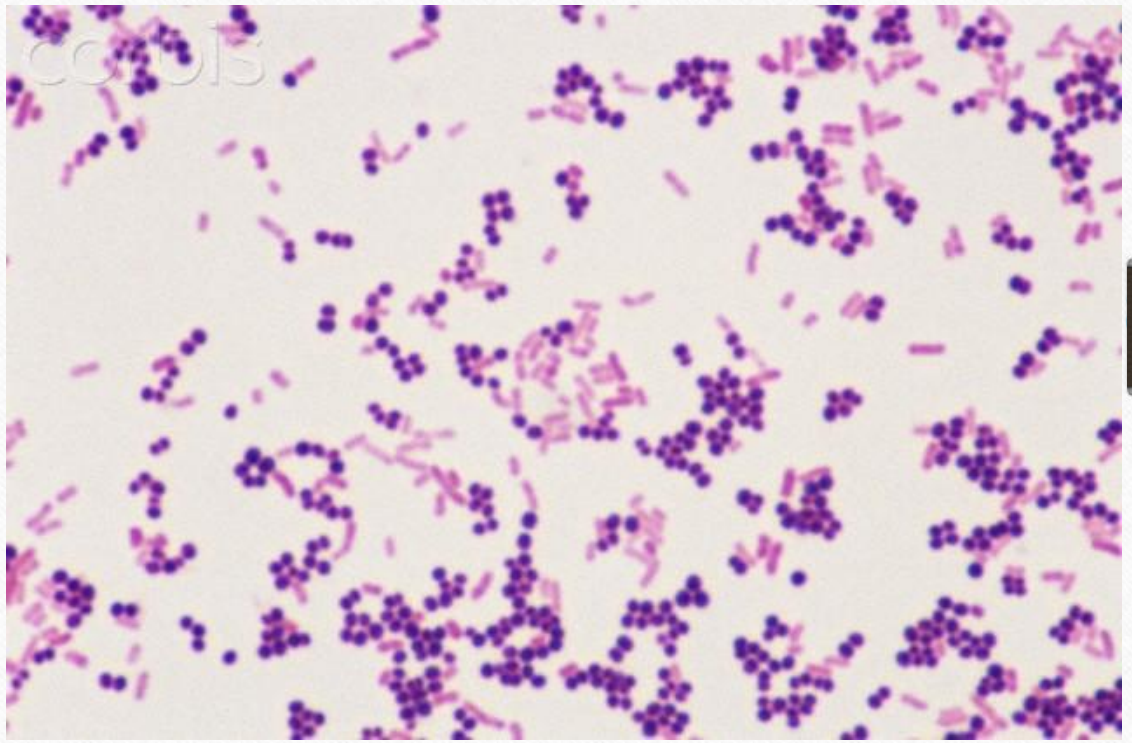
Colonization

- Presence of microorganisms in or on a host with growth and multiplication without causing any symptoms or disease
- An estimated 500 to 1,000 different bacterial species are considered normal flora
- Does not require treatment in most cases
- In some cases, decolonization strategies may be employed to reduce the chance for progression to active infection

Diagnostic, Radiologic, and Laboratory Reports

Gram Stain

- The most common procedure to directly examine a clinical specimen for the presence of microorganisms (i.e., bacteria or fungi)
- Involves a sequential staining process using crystal violet, iodine, acetone/alcohol, and safranin.



Gram-positive vs Gram-negative Bacteria

- Gram-positive bacteria
  - Thick peptidoglycan cell wall does not allow the crystal violet/iodine complex to be removed during the acetone/alcohol wash.
  - Under the microscope, appear dark violet, purple, or blue
- Gram-negative bacteria
  - Thin peptidoglycan cell wall. The acetone/alcohol wash disrupts this layer, and the crystal violet/iodine complex is rinsed out. As a result, cells are colorless until counterstained with a red dye. (Safranin is usually used.)
  - Under the microscope, appear pink or red

What determines whether an organism is classified as Gram-positive or Gram-negative in Gram staining?

a. Peptidoglycans

b. Lipids

c. Polysaccharides

d. Mycolic acids

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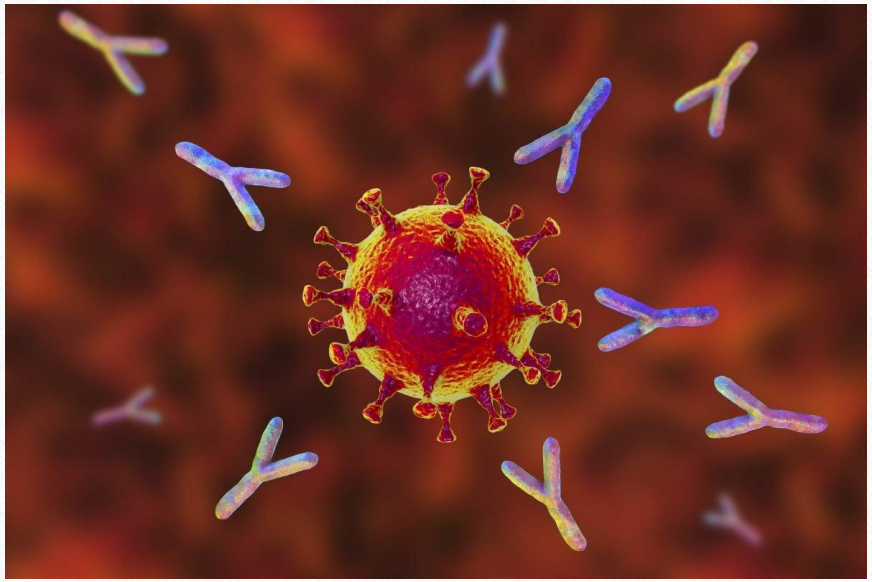
Antigen Detection

- Molecular structures, usually proteins or polysaccharides, that are capable of stimulating the production of antibodies (Immunoglobulins)
- Antigen detection is a direct method to test for the presence of infectious agents

Antibody Detection

- Antibodies are produced by B lymphocytes
- Detection is an indirect method of identifying infection
- Results may be reported qualitatively (positive or negative) or quantitatively (titers)



Hepatitis B

Test outcome	Interpretation
Hepatitis B Surface Antigen (HBsAG): **Positive** Total Hepatitis B Core Antibody(anti-HBc): **Positive** IgM anti-HBc: **Positive*** Hepatitis B Surface Antibody (Anti-HBs): **Negative**	Acute infection
HBsAg: **Positive** Total anti-HBc: **Positive** IgM anti-HBc: **Negative** Anti-HBs: **Negative**	Chronic infection
HBsAg: **Negative** Total anti-HBc: **Positive** Anti-HBs - **Positive**	Resolved infection
HBsAg: **Negative** Total anti-HBc: **Negative** Anti-HBs: **Positive**	Immune from receipt of prior vaccination (if documented complete series)

A paramedic has been exposed to a patient's blood. The patient is HBsAg positive and the paramedic is Anti-HBc and Anti-HBs positive. What is the risk of the paramedic acquiring Hepatitis B infection from the source patient?

a. There is no risk of infection for the paramedic because the paramedic was previously infected and is now immune.

b. There is no risk of infection for the paramedic because the patient is not infected.

c. The paramedic has been previously vaccinated and is immune.

d. There is a high risk of infection for the paramedic and he should be treated with Hepatitis B immune globulin.

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Molecular Testing

- Include the polymerase chain reaction (PCR), the first test developed using a nucleic acid amplification test (NAAT) method and is the most widely used.
- Tests for SARS-CoV-2 and enteroviral meningitis infections are common applications
- Unable to perform susceptibility testing

Cerebrospinal Fluid (CSF)

- For the diagnosis of infection, four basic components are considered:
  - Color/ clarity, protein, glucose and WBCs
- Suspected meningitis is a common reason to order a CSF test.
  - Bacterial meningitis typically results in a cloudy CSF sample, low glucose, high protein, and increased WBC
  - Gram-negative diplococci seen on a Gram stain of CSF analysis requires immediate initiation of droplet isolation precautions
- A lab order for a 14-3-3 protein test on a CSF sample may indicate that the ordering physician suspects Creutzfeldt-Jakob disease (CJD).

An infection preventionist (IP) is reviewing the cerebrospinal fluid (CSF) results from a patient admitted the previous night. The results indicate that the CSF is cloudy and has an elevated white blood cell count, markedly increased neutrophils, low glucose level, and elevated protein concentration. What type of meningitis should the IP suspect?

a. Bacterial

b. Viral

c. Fungal

d. Aseptic

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WBC Count

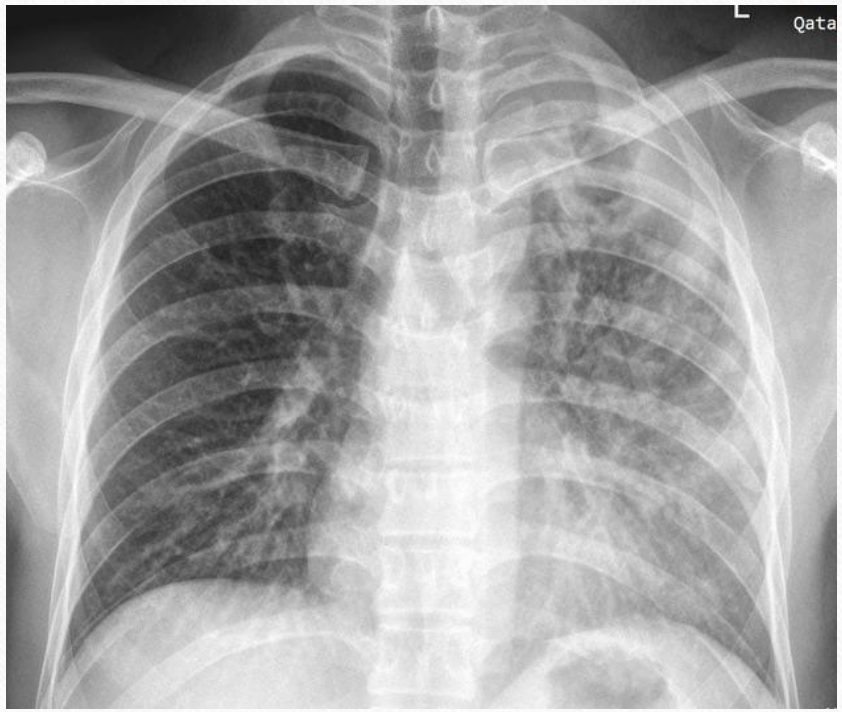
- The total number of WBCs (leukocytes) in one cubic millimeter of peripheral blood.
- Normal range 4000 to 11,000 cells/mm^3
- An increased count usually indicates infection, inflammation, or leukemia
- A decreased WBC count can occur in cases of overwhelming infection, AIDS, viral hepatitis, mononucleosis, and Legionnaires' disease.

Urine

- Frequently used screening test to assess health of the urinary tract
- Urinalysis includes assessment of
  - Color and clarity
  - The presence of proteins, glucose, ketones, blood, nitrite, and leukocyte esterase
  - In addition, may be examined microscopically for the presence of RBCs, WBCs, casts, crystals, bacteria, or yeast
- Urine Culture
  - Used to identify the causative organism of a UTI
  - Helps choose the most effective antibiotic therapy

X-ray

- Imaging of the chest is used to show potential issues including issues in the lungs.
- Particularly useful in the diagnosis of tuberculosis (cavitation on a chest X-ray is a hallmark result for pulmonary TB), which may present with nonspecific issues, and pneumonia.
- Results that may indicate these issues will show white cloudy areas in otherwise clear lungs.



Specimen Collection, Transportation, Handling, and Storage

- Specimen collection and transport to the laboratory is an essential part of the culture and identification process.
- Improperly selected, collected, or transported specimens can generate misleading data or specimen rejection
- In general, all specimens should be collected aseptically and placed in a sterile container

General Criteria

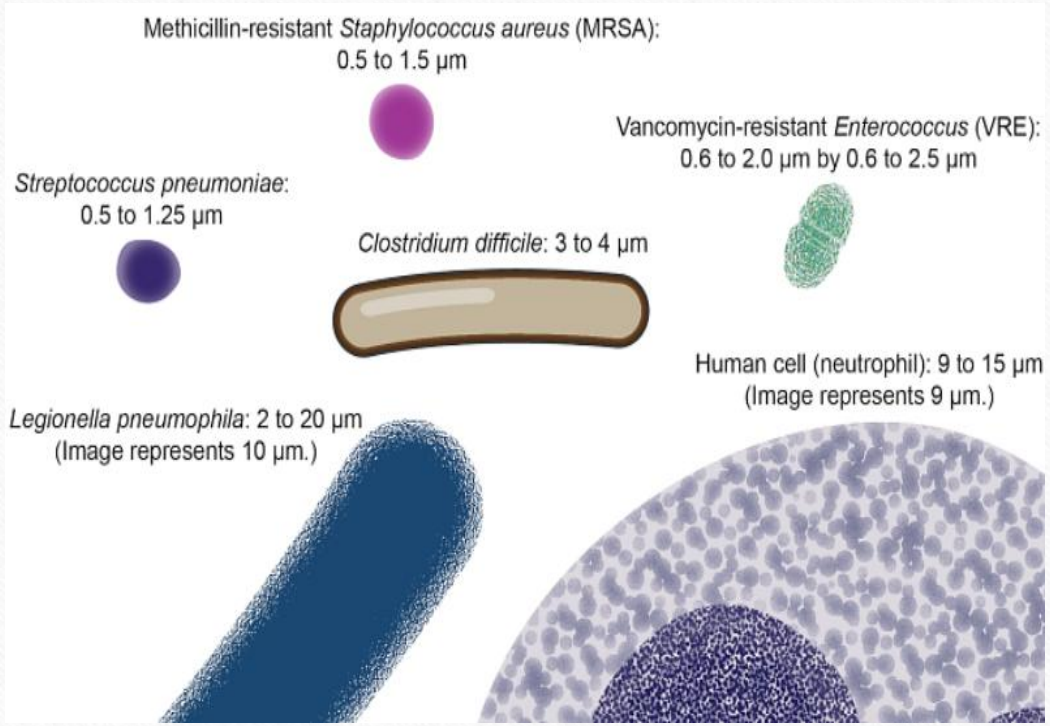
- Correct site in which the etiologic agent will most likely be found.
- At the optimum time
- Prior to administration of antibiotics (whenever possible).
- Minimize or eliminate contamination
- Appropriate collection devices
- Clearly labeled specimen
- Deliver the specimen promptly to the laboratory

Specimen Storage

- If transport is delayed, some specimens may be refrigerated (e.g., urine, stool, sputum)
- Do not refrigerate spinal fluid or genital, eye, or internal ear specimens

Basic Microbiology

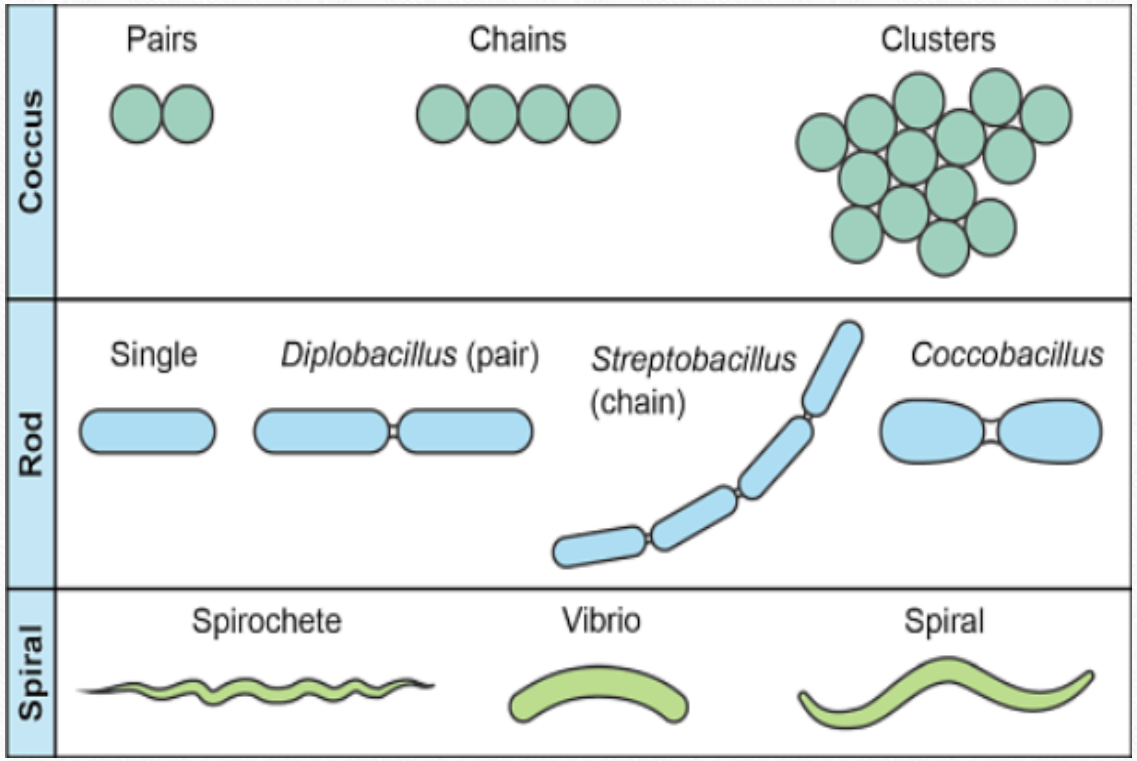
Bacteria



- Single-celled organisms that normally live benignly in and on the human body
- Only a small fraction of species are known to cause human disease
- Most range in size from 0.2 to 2.0 µm in diameter and 2 to 8 µm in length
- Reproduce by binary fission, with one cell dividing into two

Bacteria Shape

- Coccus or cocci
  - Round shaped
  - Pairs (Diplococci)
  - Chains (Streptococci)
  - Clusters (Staphylococci)
- Bacillus or bacilli
  - Rod shaped
  - Some are oval and look like cocci called coccobacilli
- Spiral
  - Curved (vibrios)
  - Corkscrews (spirilla)
  - Helical (spirochetes).



Bacterial Toxins

- Classified as either exotoxins or endotoxins
- Exotoxins are secreted mainly gram-positive bacteria
  - Organisms include *Clostridioides difficile* and *Staphylococcus aureus*
- Endotoxins are surface components of gram-negative bacteria.
  - Organisms include *Escherichia coli* and Salmonella

Which of the following is unique to gram-negative bacteria?

a. They contain endotoxins

b. They contain a thick peptidoglycan layer

c. They contain flagella

d. They produce endospores

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Endospores

- Formed by certain gram-positive bacteria
- Composed of nuclear material and protein
- Able to survive in water heated to above boiling, extreme drying, and exposure to some toxic chemicals
- When conditions permit, can transforms into the vegetative form

Biofilm

- Preferred method of growth for many microorganisms
- Can contain multiple species of microorganisms
- Notorious for attaching to the inside of lumens, to central line tubing, and to the lumens of endoscopes.
- Result in unique characteristics for the involved microbes
  - Higher organism concentration
  - Loss of antibiotic susceptibility
  - Enhanced virulence
  - Altered cellular expression

What is the name for a substance that prevents water-soluble elements such as antibiotics and disinfectants from reaching pathogens?

a. Cell wall

b. Biofilm

c. Sludge

d. Biocarbon

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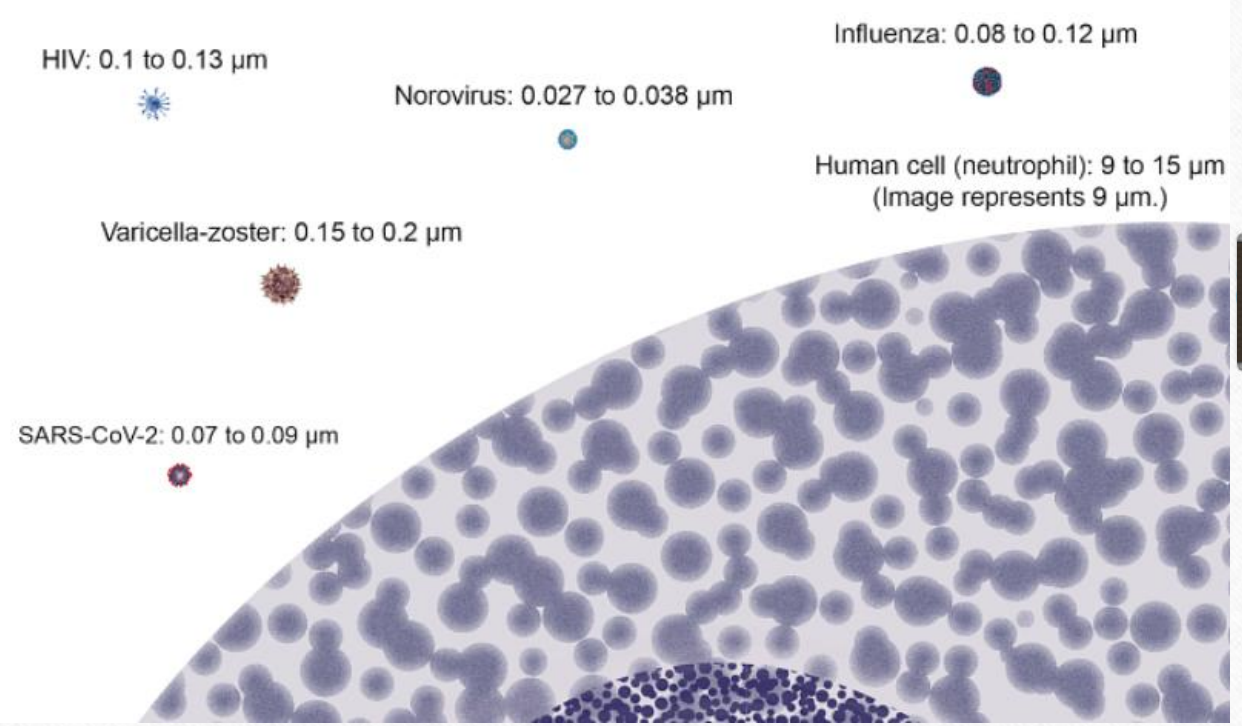
Viruses

- Require living host cells to grow and reproduce
- Dependent on the cells' machinery
- Not considered to be cells
- Generally range in size from 20 to 400 nanometers

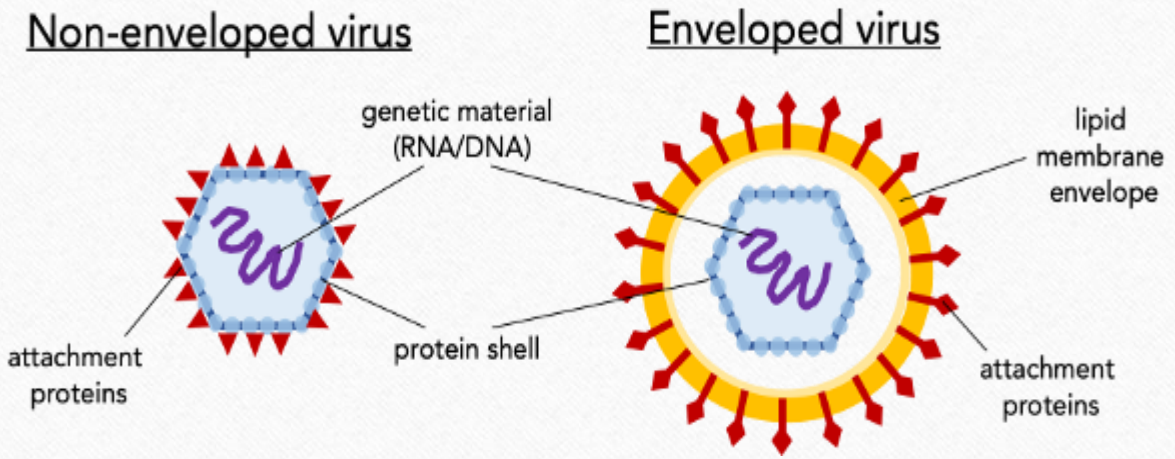


Viruses

- Reproduce through the spread of virions
- Virions are made up of RNA or DNA, a protein coat (capsid), and possibly an envelope
- Virions are taken in by living host cells where virus particles are assembled and released by the cell to invade other host cells
- May cause host cell damage that leads signs and symptoms of infection
- Can lie dormant in the host cell for months or years

Viral Envelope

- A lipid bilayer membrane surrounding protein capsid of many viruses
- Important for cleaning and disinfection
  - Alcohol has little effect against non-enveloped viruses



Spongiform Encephalopathies (Prions)

- Infectious particles of abnormally folded proteins that do not contain DNA or RNA
- Prion disease progress rapidly and are fatal
- Normal sterilization procedures are typically insufficient
- Prion disease can be:
  - Acquired through contaminated food or medical equipment
  - Familial by inheriting mutated gene from either biological parent
  - Sporadic which develops without any known cause
- Most common is Creutzfeldt-Jakob Disease (CJD)

A 70-year-old patient presents with symptoms of rapid neurological degeneration. The physician orders several diagnostic tests, including a 14-3-3 spinal fluid assay, an electroencephalogram (EEG), and magnetic resonance imaging (MRI). Which of the following is a possible diagnosis if the results are positive?

---

a. Meningitis

b. Alzheimer's disease

c. Multiple sclerosis

d. Creutzfeldt-Jakob disease

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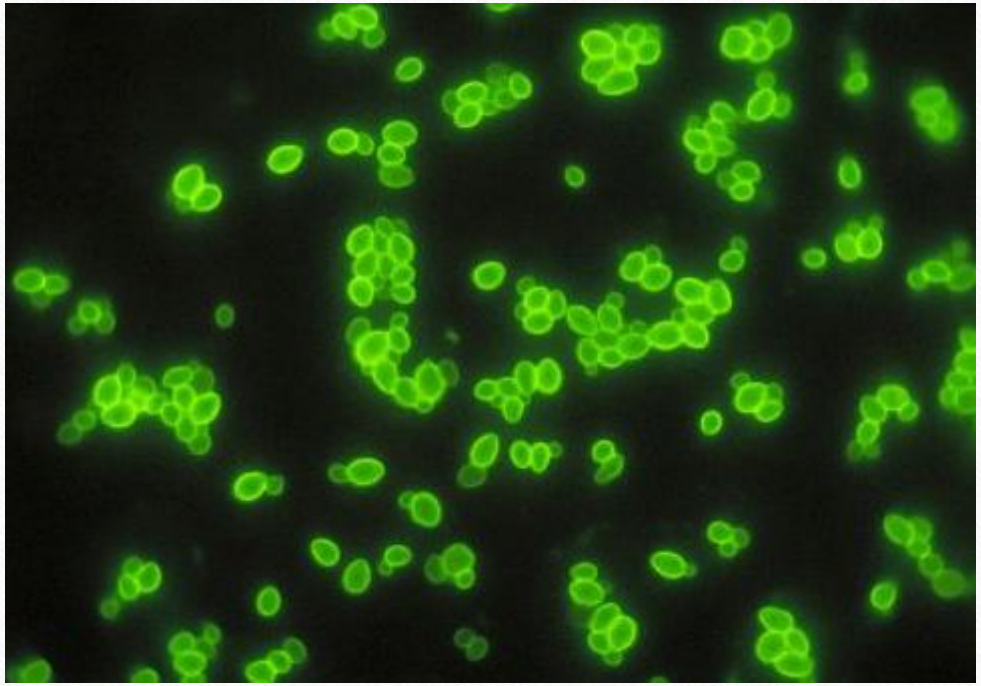
Fungus

- Widely distributed in nature with more than 100,000 species of fungi
- Fewer than 50 have been identified as causing infections in healthy persons
- Common cause of infection in individuals with altered immune systems
- Fungi can be yeasts and/or molds
- Several pathogenic species of fungi can grow as both yeast and mold; they are referred to as dimorphic
  - Examples include Histoplasma and Coccidioides species

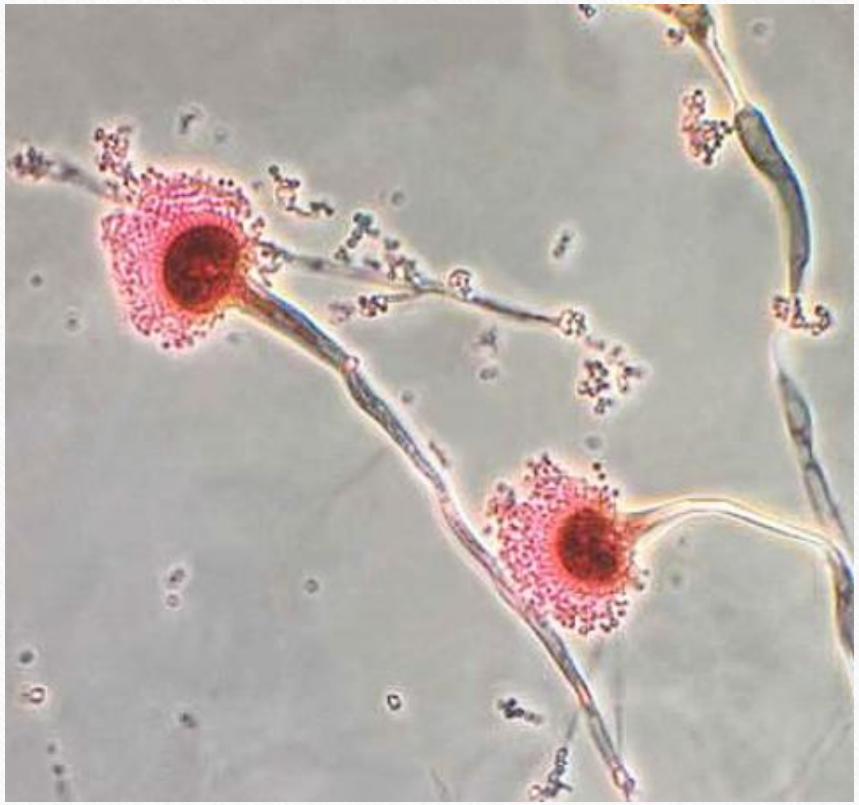
Yeasts

- Unicellular, round to oval organisms ranging in size from 2 to 6mm
- Reproduce by budding and the production of spores
- Produce moist, creamy, opaque, or pasty colonies
- Examples include Candida and Cryptococcus species



Molds

- Reproduce by elongation and fragmentation of their hyphae (or pseudohyphae)
- Can also reproduce sexually and asexually by the formation of spores
- Produce fluffy, cottony, wooly, or powdery colonies
- Examples include Aspergillus and Penicillium species



Parasites

- **Protozoa:** Include amoebas, flagellates, ciliates, and nonmotile tissue-dwelling organisms. They reproduce either sexually or asexually
- **Helminths:** Large, multicellular organisms. Adult stages are generally visible to the naked eye. Infection results from eggs that hatch into larvae in the jejunum and small intestine of humans
- **Microfilaria:** Microscopic filarial worms transmitted by mosquitoes
- **Arthropods:** Live on the outside of their hosts. Transmit parasitic, viral, bacterial, and rickettsial diseases while ingesting a blood meal

A patient has a nasal swab positive for methicillin-resistant Staphylococcus aureus (MRSA) in the absence of symptoms. Which of the following terms describes this situation?

a. Normal flora

b. Colonization

c. Asymptomatic infection

d. Symptomatic infection

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Immune Response

Innate Immunity

- Born with this type of immunity and is the first line of defense
- Activated by the presence of foreign antigens
- Includes:
  - Physical barriers such as the skin and mucous membranes
  - Defense mechanisms such as secretions, mucous saliva, tears and swear
  - General non-specific immune response

Acquired (Adaptive) Immunity

- Expressed by proteins called antibodies
- Specific to foreign antigens
- Slower to respond
- Carried out by WBCs called lymphocytes which include:
  - B cells which secrete antibodies which bind to the antigen
  - T cells which can directly react with the foreign antigen or produce signal molecules that activate macrophages to destroy the pathogen

Types of Antibodies

- **Immunoglobulin G (IgG):** the major circulating antibody. It occurs late in the immune response process and lasts the longest
- **Immunoglobulin M (IgM):** the first antibody to react during immune response to an infection. Generally produced for no more than six months after the onset of the infection
- **Immunoglobulin A (IgA):** primarily produced in plasma cells residing in mucous membranes. It may cause the release of histamine, leading to an allergic clinical response
- **Immunoglobulin D (IgD):** trace amounts of this antibody circulate freely in plasma
- **Immunoglobulin E (IgE):** the principal allergy-inducing immunoglobulin.

Epidemiologically Significant Organisms

Multidrug-resistant organisms (MDROs)

- Microorganisms – predominantly bacteria – that are resistant to one or more classes of antimicrobial agents
- Usually resistant to all but a few commercially available antimicrobial agents
- Patient-to-patient transmission in healthcare settings, usually via hands of HCWs, has been a major factor accounting for the increase in MDRO incidence and prevalence
- Examples include:
  - Methicillin-Resistant Staphylococcus aureus (MRSA)
  - Vancomycin-Resistant Enterococcus (VRE)
  - Extended Spectrum Beta-Lactamases (ESBL)
  - Carbapenemase Producing Organism (CPO)

Carbapenemase Producing Organism (CPO)

- Gram-negative bacteria, commonly Enterobacterales (CRE), Acinetobacter baumannii (CRAB), Pseudomonas aeruginosa (CRPA)
- CPO produce a Carbapenemase enzyme that make carbapenem and other β-lactam antibiotics ineffective
- Commonly contain mobile genetic elements, such as plasmids, that can facilitate transmission of resistance genes between bacteria
- Examples of carbapenemase genes include
  - KPC, NDM, OXA-48, VIM, IMP

CPO

- Screen patients admitted from long-term acute care hospitals (LTACH), ventilator-equipped skilled nursing facilities (vSNF) or any other facility with known CPO outbreak
- Also consider screening patients with known risk factors such as patients with indwelling devices or patients with history of C.auris
- Implement Contact Precautions. In skilled nursing facilities (SNF), implement enhanced barrier precautions if there is no outbreak;
- Use an Environmental Protection Agency (EPA)-registered hospital-grade disinfectant effective against gram-negative bacteria Consider use of List P disinfectant effective against C. auris (List K or bleach, if not accessible) for daily and terminal cleaning and disinfection of patient care environment and reusable medical equipment
- Alcohol-based hand sanitizer as the preferred method for cleaning hands if not visibly soiled; if visibly soiled, wash with soap and water

Candida auris (C. auris)

- Yeast that are often multidrug-resistant
- Highly transmissible between patients through contact with contaminated surfaces or objects in healthcare facilities
- *C. auris* can live on surfaces for long periods of time making it harder to keep surfaces disinfected
- Can cause infection or colonization
- Laboratory testing with sequencing or mass spectrometry is required for accurate identification of *C. auris*.

C. auris

- Screen patients admitted from Long term acute care hospitals, ventilator-equipped skilled nursing facilities or any other facility with known C. auris outbreak
- Also consider screening patients with known risk factors such as patients with indwelling devices or patients with history of CPO
- Implement Contact Precautions. In Skilled Nursing Facilities, implement EBP if no outbreak;
- Use an Environmental Protection Agency (EPA)-registered hospital-grade List P disinfectant effective against C. auris (List K or bleach, if not accessible) for daily and terminal cleaning and disinfection of patient care environment and reusable medical equipment
- Alcohol-based hand sanitizer as the preferred method for cleaning hands if not visibly soiled; if visibly soiled, wash with soap and water

Clostridioides difficile (*C. diff*)

- Spore-forming, gram-positive bacillus that produces two exotoxins: toxin A and toxin B
- Major cause of healthcare-associated diarrhea and responsible for many large outbreaks in healthcare settings
- Transmitted among humans via the fecal-oral route
  - Any surface that is contaminated with feces can serve as a reservoir for *C.diff* spores
- Symptoms include watery diarrhea, fever, increase WBC count, abdominal pain

C.diff

If a patient has had three or more stools in 24 hours:

- Isolate patients with possible *C. diff* immediately, even if you only suspect
- Order a *C. diff* test if other etiologies of diarrhea such as stool softener or laxative were not used
- Wear gloves and a gown when treating patients with potential infectious diarrhea, including *C. diff*, even during short visits
- Consistent hand hygiene using of soap and water, rather than alcohol-based hand rubs for mechanical removal of spores from hands
- Perform daily cleaning and terminal cleaning upon discharge of C.diff patient rooms using a *C. difficile* sporicidal agent (EPA List K agent)