The first lecture (natural defense)

- antibacterial enzymes: lysozymes, secretory phospholipase A2 (Paneth cells).
- antimicrobial peptides: defensins, cathelicidins, and histatins
  and they are both considered as chemical barriers.
- The First line of defense is the epithelial layer of and if it is breached some chemical and enzymes will defense against microbe (ex: defensins) and if they fail to eradicate the pathogen then the innate immune system will work and again if it is failed, finally the adaptive immune system will do its function.
- Cell mediate immunity includes:
  1-inflammatory inducers (PAMPs and DAMPs)
  2-sensor cells
  3-mediators
  4- target tissues do specific function (according to the type of pathogen) to kill it.

- crypts of Lieberkuhn: it is an invagination located between villi, and it contains many cells which are stem cells (differentiate into intestinal epithelial cells), goblet cells (mucus secreting cells), and Paneth cells.
- There is something called Peyer's patches which are lymphoid nodules located beneath the epithelial layer (in the LAMINA PROPRIA) and the epithelial cells above them called M cells (allowing microbes to encounter ABCs
- There are intraepithelial lymphocytes (IELs), MOST OF THEM ARE T LYMPHOCYTES(CD8)
  In the lamina propria B CELLS predominate.

- The mucosal immune system has distinctive features:
  1-MALTs (Mucosa-Associated Lymphoid Tissues): collection of lymphoid tissues in the GIT, the most important example about that is payer's patches.
  2-GALTs (Gut-Associated Lymphoid Tissue): it is a type of MALTs.
- Main lymphocyte type in the isolated follicle: B cells
- Main lymphocyte type in Peyer's patches and the mesenteric lymph nodes: T cells
  3-mucus (glycosylated mucins) which is a protective layer from pathogens and it contains type-2 mucin,
  and holds IgA on it and it is a buffer layer.
  4- uptake and transport of antigens across the epithelial layer to be caught by M cells
  5-Transcytosis of IgA

- Microbiome: commensal microorganisms since they have symbiotic relation with the host, the relation between them and the can be considered as a mutualistic
- The colon contains the greatest number of microbiota.

- Two types of microbiota:
  -resident microbiota: fixed types that are regularly found in the body
  -transient microbiota: non-pathogenic but they are potentially pathogenic

- What influences microbiota?
  Nutrition, hormones, genetic composition, antibiotics and foreign objects.
- Bifidobacterium is the commonest commensal bacteria living in infants
- When are the harmful effects of the microbiome?
  -if introduced into sterile sites (blood)
  -if the immunity changed
  -imbalance between various species of bacteria

- Hygiene theory: is lack of early childhood exposure to infectious agents and that leads to
- Increase the susceptibility to allergic diseases by suppressing the natural development of the immune system.
- -obese people have a lower diversity of bacteria and higher levels of enzymes
- There is an association between microbiome and diabetes, oral diseases, GI cancers
- There is correlating link between microbiome and allergy-like diseases.
- PSUDOMEMBRANOUS COLITIS: fecal transport has shown its effectiveness
- We can manipulate microbiome by:
  1-propiotics (lactobacilli)
  2-prepiotics (sugars)
  3-immunomodulators
  4-antibiotics
  5-phage therapy
  6-fecal transplantation

The 2nd lecture (bacillus and clostridium -gram +)

Bacillus species (anthracis and cereus)

- Some of bacillus species are insect pathogen (ex: B thuringiensis)
- The most harmful ones are anthracis and cereus
- B.Thuringiensis is used as natural insecticide and B.subtilis is used in genetic studies
- Bacillus anthracis causes anthrax in 3 clinical forms 1. Cutaneous anthrax (most common form) 2. Inhalational anthrax (woolsorter's disease) 3. GI anthrax (extremely rare).

Bacillus cereus:

- They are motile, spore formers.
- Bacillus cereus is associated mainly with food poisoning.

- It can cause localized and systemic infection, and the most common extra-intestinal infection caused by B.cereus is ocular infections (endophthalmitis).
- They are arranged in long chains or pairs
- We can differentiate them from B.anthracis on the bases of:
  1-colony morphology: B.anthracis have "medusa head" on culture and they have bamboo stick appearance under microscope, while B.cereus have more of feathery appearance with large square ends.
  2-hemolytic activity: anthracis is generally non-hemolytic, while cereus is hemolytic.
  3-motility: they are both motile (peritrichous flagella) but B.anthracis is described as slower or non-motile.
  4-antimicrobial susceptibility: B.cereus is more resistant.

- One of the toxins of B.cereus is heat-labile toxin which can survive "flash frying"
- According to the clinical presentation of B.cereus, we classify them into:
  1.emitic type (Chinese food poisoning) which is associated with fried rice and cereals and it is caused by ingestion of preformed heat-stable toxin(exotoxin, hemolysin, cereulide).
- Since it is caused by the ingestion of the toxin, the incubation period will be shorter than the diarrheal form which is characterized by long incubation period
  2-diarrheal type which is associated with meat dishes and sauces and it is caused by Ingestion of the food contaminated with bacteria itself and then it germinates in the gut producing the heal-labile toxin (enterotoxin).
  The patient with diarrheal form presented with abdominal cramps and diarrhea mainly
- The emetic type manifestations are similar to staph aureus
- The diarrheal type manifestations are similar to C.perferringes
  Both types are self-limiting …..(fever is absent)
- We isolate B.cereus from the suspect food as well as the stool and vomitus
  B cereus is resistant to a variety of antimicrobial agents so the trx is supportive.

Clostridium species:

Clostridia are strictly anaerobes and they are motile except C. perferringen.

Clostridium botulinum:

- is characterized by symmetrical (bilateral), descending, flaccid paralysis of motor and autonomic nerves usually beginning with cranial nerves.
- Ascending paralysis (guillain barre syndrome) is caused by shigella and campylobacter

- Is caused by canned alkaline food and we said it is like B.cereus poisoning
- It results in a reversible flaccid paralysis
- There are five clinical categories of botulism:
  1-foodporne botulism (most common): ingestion of preformed toxin
  2- wound botulism: injection of heroine since the bacteria grows in it.
  3-infant botulism: honey contaminated with spores
  4-Adult infectious botulism(rare): ingestion of spores
  5-Inadvertent, following botulinum IM toxin injection
- Manifestations of botulinum infection is characterized by 4ds
  Dry mouth, and diplopia, dysarthria, dysphagia and in severe cases respiratory muscle will be affected.
- If it affects the babies, they will develop poor feeding and signs of floppy baby will rise.
- the definitive diagnosis is by identifying the toxin producing strains by using gastric, serum, or stool from the patient.
- Mouse bioassay is the test of choice for the confirmation of botulism
- Trx: supportive treatment initially and surgical debridement in wound botulism
  And antitoxin (A trivalent) should be prompted IV with supportive care.
  NO ANTIBIOTIC TREATMENT
  Prevention: canned food must be avoided and NO honey for infants

Clostridium perferringins:

- The main risk factor for C.P food poisoning is the consumption of foods contaminated with this bacteria.
- It is the most common in invasive disease (myonecrosis and gas gangrene)
- It can elaborate a toxin in the gut and causes food poisoning that resembles that of B.cereus (diarreheal type)
- We have 2 types of C.perfringens depending on the toxin they produce:
  1-Type A; produces (alpha, theta, epsilon) and causes necrotizing fasciitis, gas gangrene and foodborne illness
  2-Type c; produces beta toxin and causes necrotic enteritis (necrotic enterocolitis) or Pig-bell disease (more serious but rare illness)

- Distinguishing features:
  They are anaerobic and form "stormy fermentation" in milk media.
  It has double zone of hemolysis (alpha and beta)
  Reservoir: human and soil
  It is transmitted by foodborne and traumatic implantation.
  What are the clinical findings?

- In wound infection, the bacteria spreads to deep tissues to produce crepitation, foul-smelling discharge.
- Food poisoning usually follows the ingestion of large numbers of clostridia.

Diagnostic laboratory tests:

specimens from wounds, pus, and tissues

- Remember we are looking for the toxin not the bacteria itself
- Nagler test is used and it has lecithinase activity

Treatment and prevention:

- surgical debridement of the infected tissues
- antimicrobial drugs (start with penicillin)
- Hyperbaric oxygen may for detoxification
- Food poisoning is self-limiting and supportive treatment is required.

Clostridium difficle:

- A major cause of healthcare-associated infection
- People who take antibiotics especially clindamycin are at increased risk for developing C. difficile antibiotic associated diarrhea and of course immunocompromised patients also at higher risk.

- They can be transmitted from person to person through the fecal-oral route
- It produces two major toxins:
  Toxin A induces cytokine production with hypersecretion of fluid.
  Toxin B induces depolymerization of actin with loss of cytoskeleton
- Pseudomembranous colitis (fulminant colitis) is the severe form of this bacterial infection
- Diagnosis is done by combination of clinical criteria:
  1-pseudomembranous seen in the colon (by endoscopy)
  2-toxin A or B or both of them by using ELISA or PCR
  3- CULTURING ON SELECTIVE AGAR
  4-diarrhea with no other recognized cause

Treatment and prevention:

- IV and oral administration of metronidazole and if it not effective oral vancomycin is suggested.

The 3rd lecture (Enterobacteriaceae or coliform):

- Some of them part of your microbiota, and some are not and considered as strictly Pathogenic (salmonella and shigella).
  The part that is found in our microbiota waiting you to be compromised to establish the infection.
- Some of them are motile (peritrichous flagella) and some are non-motile (shigella. Klibeslla and yersinia)
- All ferment glucose, some ferment lactose ex: E coli (except one type STEC), others don't exa: Salmonella & Shigella.
- Thy are oxidase- and catalase+
- They are all have (Heat-stable somatic O) lipopolysaccharide (endotoxin activity).
- They also have Heat-labile K (capsular) antigens
- H (flagellar) antigens agglutinate with IgG
- They tend to produce bacteriocins (inhibitory peptides that kill the bacteria)
  NOTE: the capsular antigen of the salmonella typhi is called Vi antigens

E coli–associated diarrheal diseases:

- We said it is part of our normal microbiota of the upper respiratory and genital tracts and the GIT.
- They tend to Produce Green sheen colonies on EMB
- We have two differential media
  1-MacConkey agar: differentiating agar for lactose and non-lactose fermenters
  Lactose fermenters will produce pink colonies (E.coli do that) and non-lactose fermenters will form colorless area
  2- EMB agar (Eosin methylene blue): it will form black dots known as black nucleated colonies with a green sheen appearance

Enteropathogenic E coli (EPEC):

- A major cause of infantile diarrhea (associated with an outbreak in nurseries)
- Its pathogenicity requires two factors: attachment and effacement

- Attachment (EAF – Enteropathogenic E coli ADHERENCE FACTOR): forming pilus to attach to mucosal surface.
- Effacement: Chromosomal locus of enterocyte effacement (LEE):
  mainly achieves effacement by degeneration of brush border
- EPEC does not infect adults because it needs a large inoculum
  So, patient to patient transmission is much more common in children
- The result of this infection in infants is watery diarrhea and if it is sustained, we can shorten the duration of diarrhea by antibiotics (not for enterohemorrhagic)
- Regardless if it is acute or chronic, fluid restoration (supportive treatment) should be done.
- NOTE: EPEC DOES NOT LEAD TO IMMUNITY

Enterotoxigenic E coli (ETEC):

- A common cause of "traveler's diarrhea"
- ETEC use colonization factor to attach to mucosa to elaborate the toxin
- It produces two toxins
  Heat-stable toxin (not immunogenic) (increase cGMP), heat-labile toxin (immunogenic-short lived immunity-) (increase cAMP), and both toxins are hypersecretory of fluids and electrolytes.
- LT (labile toxin) is antigenic and cross-reacts with the enterotoxin of Vibrio cholerae.

Shiga toxin-producing E coli (STEC):

- They are liked to consumption of fresh products (ex: lettuce, spinach), and of undercooked contaminated ground beef
- It has been associated with hemorrhagic colitis (BLOODY DIARREHEA), and with HUS (HEMOLYTIC UREMIC SYNDROME) which is a disease resulting in micro-angiopathic hemolytic anemia, acute renal failure and thrombocytopenia.
  Sorry but I should add these details since I don't know the scenario of cases in the exam.
- O157:H7 is the most common serotype that produce shiga-toxin
- STEC causes bloody diarrhea without mucosal invasion
- ANTIBIOTICS are contraindicated here since it puts the patient at higher risk to develop HUS
- The clinical picture of this infection is presented initially by non-bloody diarrhea and then it develops into bloody diarrhea.
- Fever is absent
- It is usually self-limited

- Diagnosis is done by EIA through stools and by cell culture cytotoxin testing using Vero cells
- It can be prevented by cooking ground beef and avoiding unpasteurized products such as apple cider.

Enteroinvasive E coli (EIEC):

- It produces a disease very similar to shigellosis.
- Unlike shigella, EIEC require large inoculum to induce the infection.
- They invade (as their name imply) the intestinal mucosal surface
- EIECs don't ferment sorbitol unlike other E.coli species, so they are negative on sorbitol plate culturing,
- They are late lactose (non-lactose) fermenters.

Enteroaggregative E coli (EAEC):

- It is associated with persistent diarrhea in patients with HIV.
- They have stacked-brick appearance on the cell culture
- They produce shiga-like toxin, enterotoxin and hemolysin
- Its diagnosis is very difficult
  Keep in mind that EIEC and STEC cause inflammatory diarrhea (bloody diarrhea)
- The general treatment of gram-negative infection is restoration of fluid and electrolyte balance, and institution of antimicrobial therapy.
- TMP-SMX is a drug of choice
- Prevention: prevention of traveler's diarrhea, including daily ingestion of bismuth subsalicylate and doxycycline.
- Their control depends on handwashing, rigorous asepsis, sterilization of equipment and it is difficult since they are normal flora

Shigellosis (Bacillary dysentery):

- ONLY infect humans so there is no human reservoir
- Non-motile, non-lactose fermenters, do not produce H2S, and produce a colorless colony in EMB
- Age of risk: any age but commonly under 5 y/o
- There are 4 species of shigella:
  1- Group A Shigella Dysenteriae (most potent producer of shiga toxin)
  2- Group B Shigella flexneri (the most common worldwide and in the developing countries)

3- Group C Shigella boydii
4- Group D Shigella sonnei (most common in developed countries)

- Micro abscesses, superficial ulceration and formation of "pseudomembrane" on the ulcerated area are all characteristic of shigellosis.
- S dysenteriae produces neurotoxic, cytotoxic and enterotoxin.
- After a short incubation period (1–2 days), there is a sudden onset of abdominal pain, fever, and watery diarrhea and then it is followed by invasion and yield bloody diarrhea
- bowel movement is accompanied by straining and tenesmus.

Diagnostic laboratory tests:

- culturing: you put them in enrichment media then on differential media (ex: MacConkey agar), then on selective media (Hektoen enteric agar or Salmonella –Shigella agar).
- Serology is not used to diagnose Shigella infections (FP)
- Opioids should be avoided in Shigella dysentery
- Antibiotics are mandatory
- IgA antibodies in the gut are important in limiting the infection
- Serum antibodies to somatic Shigella antigens are IgM
- Shigellae are transmitted by "food, fingers, feces, and flies. (4 F's)

The 4th lecture(salmonella):

- They are motile and produce H2S
  Serovars of salmonella:
  1- S. enterica subsp. Typhi
  2- S. enterica subsp. Enteritidis: (most common worldwide)
  3- S. enterica subsp. Typhimurium:(most common also)
  4- S. enterica subsp. Choleraesuis (most implicated in bacteremia and focal lesions in the bone (OM). NO GIT SYMPTOMS
  5- S. enterica subsp. Paratyphi
  6- S. enterica subsp.Dublin that causes cattle infection
- Sickle cell disease or trait are risk group

Enteric Fevers (Typhoid Fever):

- Four serotypes that cause enteric fevers which are Paratyphi A, Paratyphi B, typhi and Choleraesuis
- Main presentation: febrile systemic illness with GIT symptoms
- Febrile systemic illness is caused by (S.Typhi & S.Paratyphi)

- It is strictly human pathogenic so the infection will be transmitted either from an infected patient or an asymptomatic carrier
- It is part of the normal flora in animals ONLY
- Persons with S/S hemoglobin (sickle cell disease) are exceedingly susceptible to Salmonella infections

Pathogenesis:

The salmonella invades payer's patches and transported to other intestinal L.N. where they multiply in Mononuclear cells to mesenteric L.N. to blood through thoracic duct (transient bacteraemia)

- After the stage of bacteremia, It can reach the reticule-endothelial cells in liver, spleen and bone marrow and cause prolonged fever
- Infectious dose is higher than shigella and it causes bloody diarrhea also.
- Chronic carriers often harbor the pathogen in their gallbladder, this is why sometimes cholecystectomy is needed.
- Typhoid Salmonella's modes of transmission: Food, water contaminated with human feces (mainly feco-orally), vertical transmission (trans- placental)
- Why does salmonella need high inoculum to establish a disease?
  Salmonella is highly sensitive to stomach acidity's so high inoculum is required to pass through the stomach to small intestine.
- Patients who take anti acid pills (reducing stomach's acidity) regularly are more susceptible to progressing Salmonella
- Salmonella, Shigella, Yersinia use M-cells to reach their target until they reach the blood Circulation.

Clinical manifestations:

- 1st week: blood is positive in the 1st week and the complications are
  Fever, headache, abdominal pain, diarrhea, and the temp increase in a stepwise (saddleback fever) matter
  (high platuea)
- 2nd week: High fever, rose spots and rash
- 3-4 weeks: if there no complications, signs gradually resolve
- In enteric fevers, the stools yield positive results from the second or third week on; in enterocolitis, the stools yield positive results during the first week.
- Blood culture results are usually negative, but stool culture results are positive
- Don't give antibiotics for patients with salmonella but it is recommended for immunocompromised patients (they are at higher risk to develop bacteremia)

- Enterocolitis and gastroenteritis are the most common manifestation of salmonella infection

- Culture: positive in the Blood (primary diagnostic method and used with typhoid fever and bacteremia with focal lesions), ü Bone marrow (in bacteremia with focal lesions) ü Stool (usually used when there is gastroenteritis or enteric fever in week two)

- Bacteriologic culturing for Isolation of Salmonellae:

  Enrichment media (tetrathionate broth which inhibits replication of normal intestinal bacteria and permit multiplication of salmonellae → Differential and Selective (EMB, MacConkey, salmonella-shigella (SS) agar, Hektoen enteric agar) →final identification (biochemical reactions and slide agglutinations to know which serotype is it)

- One of the serological methods that is not used anymore since it gives FP is tube dilution agglutination test (Widal test) and the alternatives to it include rapid colorimetric and EIA methods
- If reinfection occurs it will be milder.
- Secretory IgA antibodies may prevent attachment of salmonellae to intestinal epithelium

Treatment:

- enteric fevers and bacteremia's with focal lesions require antimicrobial treatment, the vast majority of cases of enterocolitis do not
- replacement of fluids and electrolytes is essential

prevention and control:

- Infected poultry, meats, and eggs must be thoroughly cooked
- Two typhoid vaccines are currently available: an oral live, attenuated vaccine and a Vi capsular polysaccharide vaccine for intramuscular use

Yersinia:

- Yersinia is primarily an animal pathogen with occasional transmission to humans (zoonosis)
- They grow best at 25ΣC and are motile at 25C but nonmotile at 37C
- we will focus on 3 species of yersinia:

1- Y pestis-plague-transmitted to humans through bite of an infected flea (inhalation also)
2- Y. enterocolitica is associated with terminal ileitis (it can cause mesenteric adenitis)
3- Y. pseudotuberculosis is associated with mesenteric adenitis

- Yersinosis is confused with appendicitis (similar symptoms)
- It is related to the consumption or preparation of raw meat, products milk (pasteurized, unpasteurized, and chocolate-flavored)
- The usual route of infection is oral
- They have type III secretion systems
- Virulence factors include: Yersinia outer membrane proteins.
- Gastrointestinal complications include granulomatous appendicitis
- yersinia infection is one of those infections which have a post infectious sequelae which is called REITER SYNDROM which involves the triad of reactive arthritis, conjunctivitis and urethritis. (C jejuni also involved)
- The number of Yersinia in stool may be small and can be increased by cold enrichment
- most clinical laboratories use a Yersinia selective agar such as CIN.
- They have bull's eye appearance
- Most cases are self-limiting and clinical trials do not support antimicrobial treatment
- No vaccines are available
- Consumption of food made from raw meat should be discouraged

The 5th lecture (Vibrio cholerae, Campylobacter jejuni, Helicobacter pylori)

- Vibrio cholerae produces an enterotoxin that causes cholera, a profuse watery diarrhea.
- Campylobacter jejuni and Campylobacter Coli are the most common bacterial causes of gastro-enteritis in humans. (as common as Salmonella and Shigella)
- Helicobacter pylori has been associated with peptic ulcer, adenocarcinoma in stomach and MALT lymphoma

Vibrios:

- the most common bacteria in surface waters
- V cholerae serogroups O1 and O139 (produce cholera toxin and cause pandemics)
- O139 have a capsule while O1 do not.
- Non-01 and non O139 cause Cholera-like diarrhea (Gastroenteritis)
- Other important Vibrio species that associated primarily with gastrointestinal include:
  1- V. parahaemolyticus (the most common cause of Sea-foodborne)
  2- V. vulnificus (oysters) (a cause of severe sepsis(septicemia) in patients with cirrhosis and primary wound infection)

3- v. alginolyticus occasionally causes eye, ear, and wound infections

- Vibrio cholera is comma shaped(curved) and they are motile by means of a polar flagellum.
- Vibrio grow at a very high alkaline pH
- Needs high dose to cause infection since it is sensitive to acidity (anti acids increase the risk)
- V. cholera grows well on thiosulfate-citrate-bile-sucrose (TCBS) agar producing yellow colonies
- They are oxidase+ and this is what differentiate them from enteric gram-negative bacteria
- they are susceptible to the compound O/129, which differentiates them from Aeromonas.
- Most Vibrio species are halotolerant
- They share a single heat-labile flagellar H antigen
- Two biotypes of V. cholerae O1, (classical and El Tor) and each one of them is subdivided into Inaba and ogawa.
- Eltor: infection higher rate, severity less.
- The genes for V cholerae enterotoxin (the toxin contain 2 subunits A and B) are on the bacterial chromosome
- The toxin increases the level of cAMP and results in prolonged hypersecretion of water and electrolytes.
- toxin-coregulated pilus (TCP): it is used for establishing v. cholera in small intestines (attachment), thus it can secrete toxins.
- Stools, which resemble "rice water" contain mucus, epithelial cells, and large numbers of vibrios.

Treatment:

- water and electrolyte replacement to correct the severe dehydration
- Oral tetracycline and doxycycline tend to reduce stool output in cholera and in children and pregnant women, alternatives to the tetracyclines include erythromycin and furazolidone.
- Prevention: two oral killed cholera vaccines

CAMPYLOBACTER:

- The most common cause of bacterial gastroenteritis in the developed world
- Reservoir: the GIT of many animals used for foods (poultry, swine)
- Campylobacters cause both diarrheal and systemic diseases

- Species that cause extraintestinal disease include Campylobacter fetus (immunocompromised patients are at higher risk)
- C. jejuni infects the jejunum & small intestine, however C. coli infects the colon (from their names) (laboratories generally do not differentiate between the two species)

CAMPYLOBACTER JEJUNI:

- Gull-wing shape
- darting motility
- They are microaerophilic and thermophilic and they are susceptible to gastric acid.
- Feco-oral route of transmission
- Pathogenesis: invasion of the mucous & submucosa of the small intestine (intracellular infection) which will lead to bloody diarrhea (like salmonella & shigella)

HELICOBACTER PYLORI:

- spiral-shaped
- It has multiple flagella at one pole and is actively motile.
- They have urease activity
- Microaerophilic
- Humans are the only important reservoir of H. pylori
- Initial colonization is facilitated by the blockage of acid production by a bacterial acid–inhibitory protein and neutralization of gastric acids with the ammonia produced by bacterial urease activity.
- Diagnosis depends on high acute inflammatory markers with or without H. pylori seen
- It is a risk factor for gastric carcinoma and lymphoma.
- Culture is difficult
- urea breath tests are done to detect H.pylori.
- Gastric biopsy material can also be placed onto a urea-containing medium with a color indicator. If H pylori is present, the urease rapidly splits the urea (1–2 hours), and the resulting shift in pH yields a color change in the medium. • Another test: stool antigen test, detection of H pylori antigen in stool specimens is appropriate as a test of the cure for patients with known H pylori infection who have been treated.

Treatment:

- Triple therapy: clarithromycin, amoxicillin and PPI
- Quadruple therapy: metronidazole, amoxicillin and PPI (also bismuth subsalicylate

The 6th lecture (BRUCELLAE):

- They are animal pathogens (zoonosis) transmitted to humans by accidental contact with infected animal or their products, The common sources of infection for humans are unpasteurized milk, milk products, and cheese (is common vehicle)
- They are gram negative, non-spore forming, non -motile, aerobic (except abortus it favors microaerophilic environment), unencapsulated, obligate or facultative intracellular bacteria and they don't ferment carbohydrates
- Catalase and oxidase positive
- They have endotoxin activity only (exotoxin is not detectable)
- Urease negative (to differentiate them from H.pylori)
  Each one of these species has a preferred host but they can infect both animals and humans
- Brucella melitensis: typically infects goat
- Brucella suis: swine
- Brucella canis: dogs
- Brucella abortus: cattle
- The disease is called brucellosis and characterized by undulant fever; Malta fever is characterized by an acute bacteremic phase followed by a chronic stage.
- Brucella melitensis is the most pathogenic, it is responsible for many clinical cases
- They are killed by boiling and pasteurization but are resistant to freezing and drying
- Human-human transmission and vertical transmission are rare
- Common routes of infection:
  1-ingestion (most common) 2-mucous membranes (droplets) 3-direct contact

- One of the hallmarks features of Brucellosis is the formation of Granulomatous nodules that may progress into abscesses in the parenchymatous organs (liver, spleen, etc.)
- The granulomas form and consist of epithelioid and giant cells, with central necrosis
- When brucella is found in the blood it forms the acute presentation of brucellosis (bacteremic phase), and the chronic stage starts when brucella shunts out into reticuloendothelial organs.
- Brucella are responsible for recurrent chills and fever (similar to salmonella typhi)
- The incubation period ranges from 1–4 weeks
- fever usually rises in the afternoon; its fall during the night is accompanied by drenching sweat (associated with MSS symptoms)
- usually fever and acute monoarthritis of the hip or knee in a young child and lower back pain in adults
- Specimens: blood and biopsy material
- Culturing is difficult (false negative)

- The typical virulent organism forms a smooth, transparent colony; upon culture

Serology:

- IgM levels rise during the first week, reach the peak at 3 months, IgG and IgA antibody levels rise about 3 weeks after onset of acute disease, peak at 6– 8 weeks, and remain high during chronic disease
- Agglutination test: IgG agglutinin titers above 1:80 indicate active infection
  EXTRA from me: An SAT titer above 1:80 in the context of Brucellosis means that the patient's serum has been diluted more than 80 times and still shows agglutination (clumping) of Brucella bacteria.

- ELISA assays: IgG, IgA, and IgM antibodies may be detected. (it is more sensitive and specific)
- Treatment of choice: doxycycline and either streptomycin or rifampin (skip 😬)
- There are no human vaccinations for brucella.

Leptospira:

- They are motile, aerobic.
- They can be transmitted by the exposure to animal's or human's urine.
- Skin exposure (to urine) is the most common route, followed by mucosal and rarely ingestion.
- Two species:
  1- Leptospira interrogans (affect humans)
  2-Leptospira biflexa (free-living) (non-pathogenic)
- Leptospirosis has a broad spectrum of clinical manifestations, varying from asymptomatic infection to fulminant, fatal disease (Weil's Syndrome).
- Human urine may contain spirochetes in the second and third weeks of disease.
- Hepatitis and nephritis and pulmonary hemorrhage are clinical manifestations of leptospirosis.

Leptospira interrogans:

- They are actively motile and have a question mark appearance
- It survives in an alkaline pH
- Can best be seen microscopically by dark-field examination and after silver impregnation staining of tissues.

- Most cases are asymptomatic, some are mild, and around 1% can be severe which can lead to Weil's Syndrome (is characterized by bleeding, blood urea nitrogen retention (due to kidney injury) as well as jaundice.
- Pathogenesis: Transmission occurs through cuts, abraded skin, or mucous membranes, then they cross tissue barriers and disseminate hematogenously, then they establish themselves in the parenchymatous organ.
- It is a biphasic disease include:
  1-leptospiermic phase (bacteria in the blood)
  2-immune or parenchymatous phase (cleared from the blood)
- the second phase develops when the IgM antibody titer rises. It manifests itself often as "aseptic meningitis" with an intense headache, stiff neck, and pleocytosis of the CSF.
- Culture: they grow best under aerobic conditions in semisolid medium (eg, Ellinghausen-McCullough- Johnson- Harris EMJH) skip😐
- Serology: The diagnosis of leptospirosis in most cases is confirmed serologically with microscopic agglutination test (MAT) and ELIS.
- Severe leptospirosis should be treated with IV penicillin
- No human vaccine

Mycobacterium Tuberculosis (Mtb):

- Mtb is a slow growing, obligate aerobe, facultative intra- cellular bacterium
- Non-spore forming, non-motile acid fast bacilli
- Mycobacterium bovis is associated with abdominal Tb
- Two TB-related conditions exist (latent and disease), People who have latent TB infection do not feel sick, do not have any symptoms, and cannot spread TB to others
- TB is considered an airborne infectious disease and it can be spread through un-pasteurized milk, direct inoculation
- TB lymphadenitis is the most common form of extrapulmonary TB and the pluera TB is the second most cause
- The abdominal TB usually occurs in four forms: tuberculous lymphadenopathy, peritoneal tuberculosis (most common in abdomen), gastrointestinal (GI) tuberculosis and visceral tuberculosis involving the solid organs

Gastrointestinal (GI) tuberculosis pathogenesis:

- Tuberculosis of the abdomen may occur via reactivation of latent TB infection or by ingestion of tuberculous mycobacteria or by sputum (when it gets out of the lung and then you swallow it)

- It may develop via hematogenous spread or via contiguous spread of TB from adjacent organs
- Gastrointestinal TB clinical finding: abdominal pain and a palpable mass are common findings. (fever and night sweats also)
- Laboratory diagnostic methods:
  - Smear microscopy: Acid Fast Bacilli AFB or mycobacteria can be demonstrated by yellow fluorescence after staining with auramine

  -culture: Radiometric broth culture and MGIT … skip😮

- Treatment: isoniazid (INH), rifampin (RIF), pyrazinamide (PZA), and either ethambutol (EMB) or streptomycin (SM)
- Isoniazid preventive therapy IPT is the recommended treatment for LTBI
- Prevention: Mycobacterium bovis Bacillus Calmette–Guérin (BCG) (an attenuated vaccine)