Laboratory safety

Personal protection

1. Laboratory coveralls, gowns or uniforms must be worn at all times for work in the laboratory.

2. Appropriate gloves must be worn for all procedures that may involve direct or accidental contact with blood, body fluids and other potentially infectious materials or infected animals. After use, gloves should be removed aseptically and hands must then be washed.

3. Personnel must wash their hands after handling infectious materials and animals, and before they leave the laboratory working areas.

4. Safety glasses, face shields (visors) or other protective devices must be worn when it is necessary to protect the eyes and face from splashes, impacting objects and sources of artificial ultraviolet radiation.

5. It is prohibited to wear protective laboratory clothing outside the laboratory, e.g. in canteens, coffee rooms, offices, libraries, staff rooms and toilets.

6. Open-toed foot wear must not be worn in laboratories.

7. Eating, drinking, smoking, applying cosmetics and handling contact lenses is prohibited in the laboratory working areas.

8. Storing human foods or drinks anywhere in the laboratory working areas is prohibited.

9. Protective laboratory clothing that has been used in the laboratory must not be stored in the same lockers or cupboards as street clothing.

Specimen Collection

- Lab request and lab report forms:

Lab request form: it fills computerize or paper filled by the doctor then send it to the lab. The lab request contains a list of tests to be performed on specimen of patient. Each lab has its specific request; for example, chemistry request, hematology request… etc.

Lab report form: it contains the result of patient.

Laboratory work flow cycle:

The flow cycle includes the entire steps of laboratory test, starting from test ordering by a doctor until reporting the results.

Three phases of laboratory testing:

- *Pre-analytical*: test ordering, specimen collection, transport and processing
- *Analytical-testing*
- *Post-analytical:* testing results transmission, interpretation, follow-up, retesting.

Phlebotomy :

Phlebotomy or blood collection:

The term phlebotomy refers to blood draw from a vein, artery, or the capillary bed for lab analysis or blood transfusion.

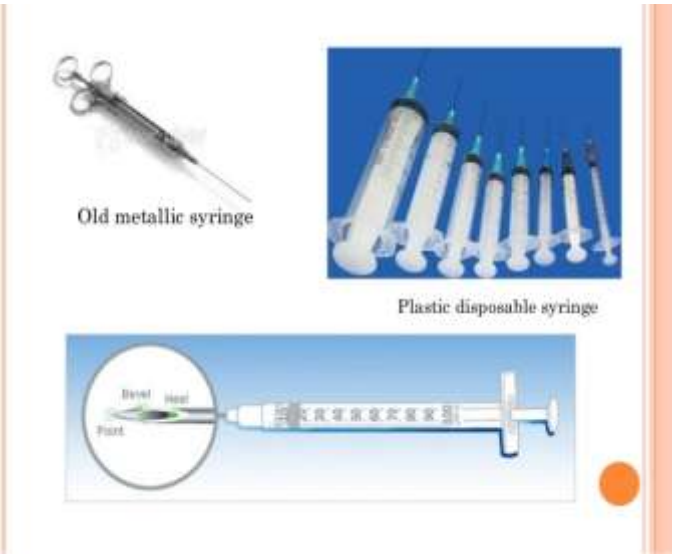
The phlebotomy equipment's:

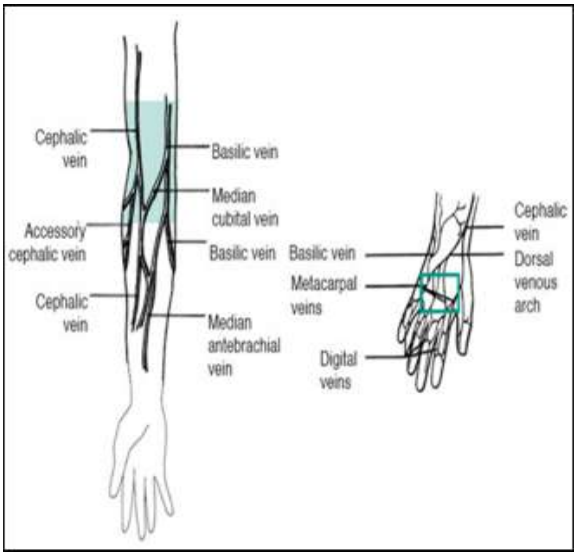
For specimen collection, the following materials will be required:

Selecting vein site:

Usually vein is used to collect blood by veinpuncture procedure.
In adults: most venipuncture procedure use arm vein.
On arm, one of three arm veins is used: median cubital vein "located on the middle", cephalic vein or basilic vein "located on both sides".

Median capital vein is the best choice (why?) because it has good blood flow than cephalic and basilica which has slower blood flow. However if vein puncture procedure is unsuccessful in median capital; cephalic or basilica is used.
Artery blood is rarely used in special cases as when blood gases, pH, PCO2, PO2 and bicarbonate is requested. It is usually performed by physicians.





Preparation of Blood Sample

One of three different specimens may be used:

Whole blood, **Serum**, **Plasma**

First: **Whole-blood specimen**:

It must be analyzed within limited time (why?)

Over time, cells will lyse in whole-blood which will change the conc. of some analytes as potassium, phosphate and lactate dehydrogenase. Some cellular

metabolic processes will continuo which will alter analytes conc. like glucose and lactate.

Second Serum:

Difference between Serum and plasma:

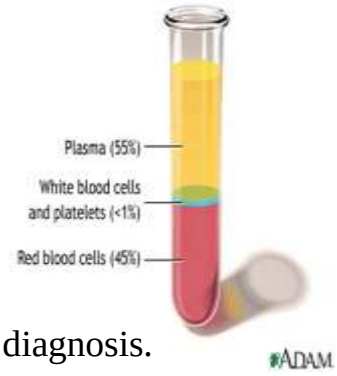
- Serum is the same as plasma except it doesn't contain clotting factors (as fibrin).
- Plasma contains all clotting factors.
- So, serum and plasma all has the same contents of electrolytes, enzymes proteins, hormones except clotting factors
- Serum is mainly use in chemistry lab & serology.

Procedure of Serum preparation:

- Draw blood from patient. Select vacutainer with no anticoagulant.
- Allow to stand for 20-30min for clot formation.
- Centrifuge the sample to speed separation and affect a greater packing of cells. Clot and cells will separate from clean serum and settle to the bottom of the vessel.
- The supernatant is the serum which can be now collected by
- Dropper or pipette for testing purposes or stored (-20°C to -80°C) for subsequent analysis or use.

Third Plasma:

The tube will have anti-coagulation after centrifugation the blood sample got separated into three layers



URINE SPECIMEN:-

Urine specimen remains an important tool for clinical diagnosis.

- A correct urine result is influenced by the collection method, timing and handling.

The laboratory test ordered determines the type of container to be used for collecting a specimen

TYPES OF COLLECTION

Laboratory urine specimens are classified by the type of collection conducted or by the collection procedure used to obtain the specimen.

- **RANDOM SPECIMEN**: This is the specimen most commonly sent to the laboratory for analysis, primarily because it is the easiest to obtain and is readily available. This specimen is usually submitted for urinalysis and microscopy analysis. Although there are no specific

- **FIRST MORNING SPECIMEN**: This is the specimen of choice for urinalysis and microscopic analysis, since the urine is generally more concentrated due to the length of time urine is allowed to remain in the bladder and, therefore, contains relatively higher levels of cellular elements and analytes such as protein, if present.

NOTE: any urine that is voided from the bladder during the eight hour collection period is pooled and refrigerated, so that a true 8hour specimen is obtained.

MIDSTREM CLEAN CATCH SPECIMEN: This is the preferred type of specimen for culture and sensitivity testing because of the reduced incidence of cellular and microbial contamination into a clean container, (any excess urine should be voided into the toilet). This method of collection can be conducted at any time of day or night.

TIMED COLLECTION SPECIMEN

Among the most commonly performed

CATHETER COLLECTION SPECIMEN

This assisted procedure is conducted when a patient is bedridden or cannot urinate independently. The healthcare provider inserts a Foley catheter into the bladder through the urethra to collect the urine specimen.

Specimen may as well be collected through an existing Foley catheter.

DEEP SPECIMEN COLLECTION

- Specimens for wound, lesion, abscess drainage, effusions, exudates, boils, incisions or ulcerations are best collected by aspirating with a syringe and needle.

- Using aseptic technique, clean the area in and over the lesions with sterile saline and sterile gauze prior to collection.

- Debride skin lesions, removing the crust and any purulent exudates with the moistened gauze.

SPUTUM SPECIMEN

- Preferably, the specimen should be a first morning collection. If more than one specimen is collected, they should be obtained one per day on consecutive mornings. To properly collect a sputum specimen, ask the patient to

i. Remove the container from the package and lift the top hinged

FECES SPECIMEN

Collect feces specimens in containers provided by the laboratory. Specimen should be well covered and labeled.

For culture only or both culture and parasite examination the specimen must be returned to the laboratory within one hour of collection.

i. Remove the container from the package and lift the top hinged
- ii. Do not spit into the container as saliva and postnasal secretions are not the maternal.
- iii. Close the lid, label the specimen.
- Bring the specimen to the clinical laboratory as soon as possible for best results.
- If there is a delay in transport, refrigerate specimen. Patients name, ID.

GENITAL SPECIMEN

Patients should not use or be exposed to vaginal medications for 24hours prior to collection.

- In female – insert swabs slowly into vaginal opening. For endocervical collections remove excess mucus from the endocervix and discard it. Rotate swab vigorously for 30seconds, allowing absorption to occur swab comes into contact

with all urethral surfaces. Allow swab to remain inserted for 2-3 seconds. Replace the swabs in the tube label and deliver to laboratory promptly.

CERVICAL SMEAR

- It's a screening test that helps a doctor diagnose and prevent cervical cancer in women. This test is also known as a

- **THROAT CULTURE**

- Use a tongue depressor to hold the tongue down.

- Carefully yet firmly rub swab over areas of exudate or over the tonsils and posterior pharynx, avoiding the cheeks, teeth, and gums

- Insert swab into packet and follow directions for handling the transport medium.

WOUND CULTURE

- Specimens are culture for aerobic and anaerobic organisms.
- Using a sterile swab supplied by the laboratory, collect as much exudate as possible from the advancing margin of the lesion.
- Avoid swabbing surrounding skin.
- Place the swab immediately in appropriate transport culture tube and take to the laboratory.
- Label with the specific anatomic site

Lecture 2

General Urine Examination

Urine and urinalysis (The Composition of Urine)

Urinalysis can reveal diseases that have gone unnoticed because they do not produce striking signs or symptoms. Examples include diabetes mellitus, various forms of glomerulonephritis, and chronic urinary tract infections.

Urine (from Latin *Urina, ae, f.*) is a liquid by-product of the body secreted by the kidneys through a process called urination (or micturition) and excreted through the urethra. Cellular metabolism generates numerous by-products, many rich in nitrogen that require clearance from the blood stream. These by-products are eventually expelled from the body during urination, the primary method for excreting water-soluble chemicals from the body. These chemicals can be detected and analyzed by urinalysis. Human urine, together with human feces, are collectively referred to as human waste or human excreta.

- Urine is formed in nephron by three processes of glomerular filtration, tubular reabsorption, and tubular secretion.
- Any factors that affect the three processes of urine formation will influence components in urine.
- Various diseases are characterized by abnormal metabolism, which causes abnormal by-products to appear in the urine.
- An analysis of urine can yield valuable information about the health of the kidney and the body in general health of the kidney and the body in general.

Sample of human urine

Human urine consists primarily of water, with organic solutes including urea, creatinine, uric acid, and trace amounts of enzymes, carbohydrates, hormones, fatty acids, pigments, and mucus, and inorganic ions such as sodium (Na^+), potassium (K^+), chloride (Cl^-), magnesium (Mg^{2+}), calcium (Ca^{2+}), ammonium (NH_4^+), sulfates (SO_4^{2-}), and phosphates (e.g., PO_4^{3-}). A representative chemical composition would be:

water 95%, **urea** 9.3 g/l, **chloride** 1.87 g/l, **sodium** 1.17 g/l, **potassium** 0.750 g/l, **creatinine** 0.670 g/l, with lesser amounts **of other ions and compounds.**

The amount of urine your body produces in a day can be directly related to your health. The kidneys' main function is to maintain the correct balance of water and various chemicals in your blood. If your kidneys aren't functioning properly, an increase or decrease in urinary output could indicate the presence of kidney disease. As of 2013, kidney disease is the eighth leading cause of death in the U.S., according to the Centers for Disease Control and Prevention.

Urine Formation

The kidneys remove waste products from blood and expel them in urine. They accomplish this by filtering blood. Kidneys reabsorb the molecules, nutrients and water body needs and excrete concentrated waste products. When the kidneys aren't functioning properly, waste and fluid that are typically removed from body in the urine can accumulate and cause disease.

Normal Urinary Output

The normal range for an adult urinary output is between 400 to 2,000 mL of urine daily -- with a normal fluid intake of about 2 liters per day. Values for normal

urinary output may vary slightly between laboratories. A urine output of 500 mL per day is generally considered adequate for normal function.

Factors other than kidney disease that can influence how much urinate in a day include how much water you consume, the amount of fluid lost in perspiration, caffeine and alcohol intake and any medications you've taken. If doctor is concerned about kidneys, a 24-hour urine collection test is typically ordered.

Physical characteristics

Physical characteristics that can be applied to urine include color, turbidity (transparency), smell (odor), pH (acidity - alkalinity) and density.

Color: Typically yellow-amber, but varies according to recent diet and the concentration of the urine. Drinking more water generally tends to reduce the concentration of urine, and therefore causes it to have a lighter color.

Smell: The smell of urine may provide health information. For example, urine of diabetics may have a sweet or fruity odor due to the presence of ketones (organic molecules of a particular structure). Generally fresh urine has a mild smell but aged urine has a stronger odor similar to that of ammonia.

Acidity: pH is a measure of the acidity (or alkalinity) of a solution. The pH of a substance (solution) is usually represented as a number ranging from 0 (strong acid) to 14 (strong alkali, also known as a "base"). Pure water is "neutral" in the sense that it is neither acid nor alkaline; it therefore has a pH of 7. The real significance of pH in terms of physical chemistry is that it measures the activity of hydrogen ions (H+) in a solution.

The pH of normal urine is generally in the range 4.6 - 8, with a typical average being around 6.0. Much of the variation occurs due to diet. For example, high

protein diets result in more acidic urine, but vegetarian diets generally result in more alkaline urine (both within the typical range of 4.6 - 8).

Density: Density is also known as "**specific gravity**". This is the ratio of the weight of a volume of a substance compared with the weight of the same volume of distilled water. The density of normal urine ranges from 0.001 to 0.035.

Turbidity: The turbidity of the urine sample is gauged subjectively and reported as clear, slightly cloudy, cloudy, opaque or flocculent. Normally, fresh urine is either clear or very slightly cloudy. Excess turbidity results from the presence of suspended particles in the urine, the cause of which can usually be determined by the results of the microscopic urine sediment examination. Common causes of abnormal turbidity include: increased cells (RBC, WBC), numerous crystals, bacteria, lipiduria (lipids often raise to the surface), mucus, semen or fecal contamination.

ABNORMAL CONSTITUENT:	**ASSOCIATED CAUSES:**
Protein (albumin)	Albumin is normally too large to pass through glomerulus. Indicates abnormal increased permeability of the glomerulus membrane. *Non-pathological causes are: pregnancy, physical exertion, increased protein consumption. Pathological causes are: glomerulonephritis bacterial toxins, chemical poisons.*
Glucose –	Glycosuria is the condition of glucose in urine. Normally the filtered glucose is reabsorbed by the renal tubules and returned to the blood by carrier molecules. If blood glucose levels exceed renal threshold levels, the untransported glucose will spill over into the urine. *Main cause: diabetes mellitus*
Ketones –	Ketone bodies such as acetoacetic acid, beta-hydroxybutyric acid, and acetone can appear in urine in small amounts. These intermediate by-products are associated with the breakdown of fat. *Causes: diabetes mellitus, starvation, diarrhea*
Bilirubin –	Bilirubin comes from the breakdown of hemoglobin in red blood cells. The globin portion of hemoglobin is split off and the heme groups of hemoglobin is converted into the pigment bilirubin. Bilirubin is secreted in blood and carried to the liver where it is conjugated with glucuronic acid. Some is secreted in blood and some is excreted in the bile as bile pigments into the small intestines. *Causes: liver disorders, cirrhosis, hepatitis, obstruction of bile duct*
Urobilinogen –	Bile pigment derived from breakdown of hemoglobin. The majority of this substance is excreted in the stool, but small amounts are reabsorbed into the blood from the intestines and then excreted into the urine. *Causes: hemolytic anemias, liver diseases*
Hemoglobin –	Hemoglobinuria is the presence of hemoglobin in the urine. *Causes: hemolytic anemia, blood transfusion reactions, massive bums, renal disease*
Red blood cells –	Hematuria is the presence of intact erythrocytes. Almost always pathological. *Causes: kidney stones, tumors, glomerulonephritis, physical trauma*
White blood cells	The presence of leukocytes in urine is referred to as pyuria (pus in the urine). Causes: urinary tract infection
Nitrite –	Presence of bacteria. *Causes: urinary tract infection*

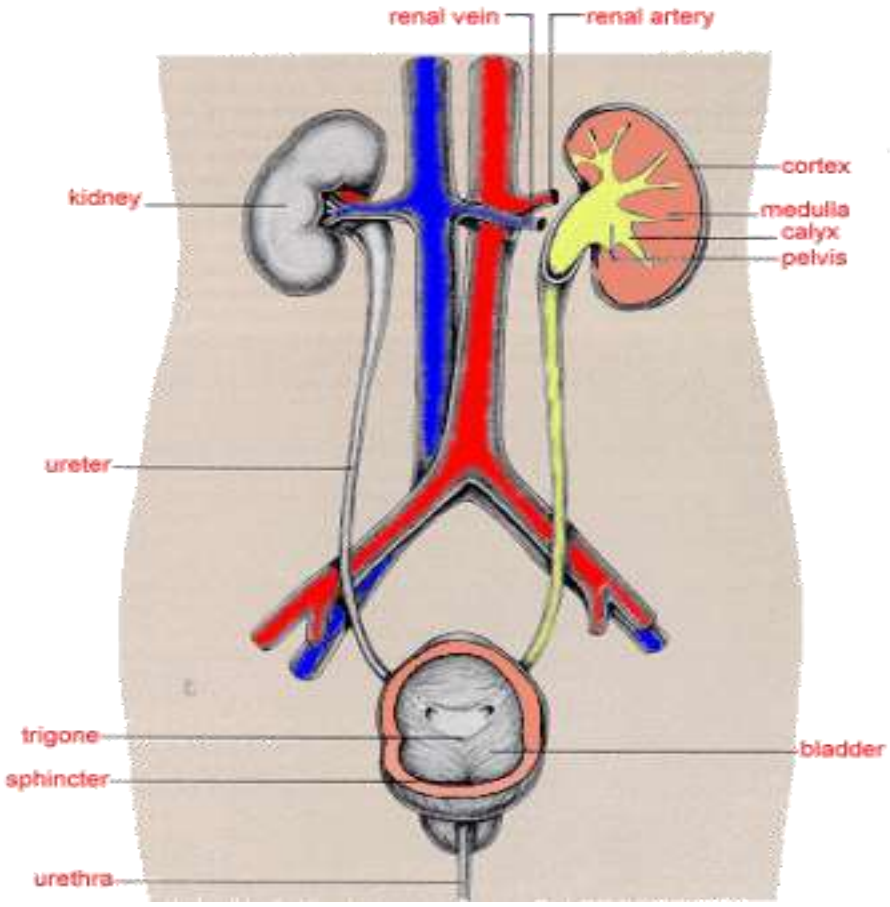
Lecture 3

What is a urinary tract infection (UTI)?

A UTI is an infection in the urinary tract. Infections are caused by microbes—organisms too small to be seen without a microscope—including fungi, viruses, and bacteria. Bacteria are the most common cause of UTIs. Normally, bacteria that enter the urinary tract are rapidly removed by the body before they cause symptoms. However, sometimes bacteria overcome the body's natural defenses and cause infection. An infection in the urethra is called **urethritis**. A bladder infection is called **cystitis**. Bacteria may travel up the ureters to multiply and infect the kidneys. A kidney infection is called **pyelonephritis**. An infection in the prostate (men) is called **prostatiti**s.

What is the urinary tract?

The urinary tract is the body's drainage system for removing wastes and extra water. The urinary tract includes two kidneys, two ureters, a bladder, and a urethra. The kidneys are a pair of bean-shaped organs, each about the size of a fist and located below the ribs, one on each side of the spine, toward the middle of the back. Every minute, a person's kidneys filter about 3 ounces of blood, removing wastes and extra water. The wastes and extra water make up the 1 to 2 quarts of urine a person produces each day. The urine travels from the kidneys down two narrow tubes called the ureters. The urine is then stored in a balloon like organ called the bladder and emptied through the urethra, a tube at the bottom of the bladder. When the bladder empties, a muscle called the sphincter relaxes and urine flows out of the body through the urethra. The opening of the urethra is at the end of the penis in males and in front of the vagina in females.



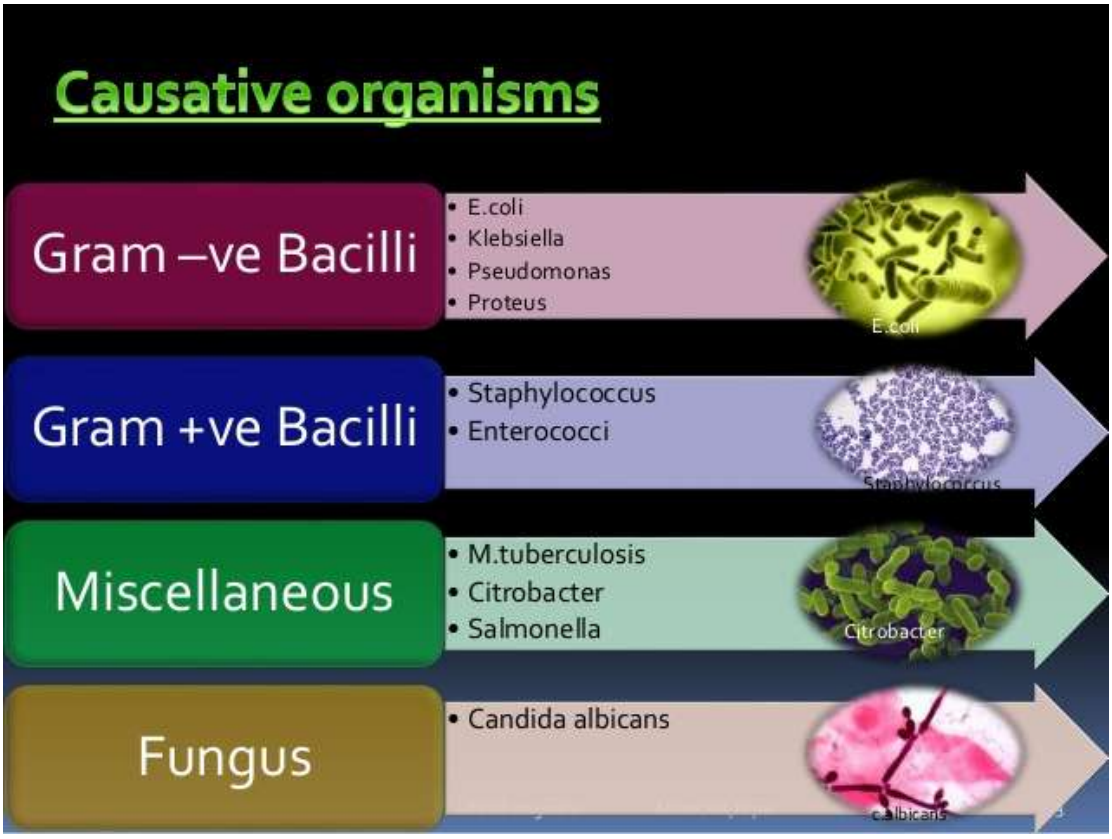
What causes UTIs?

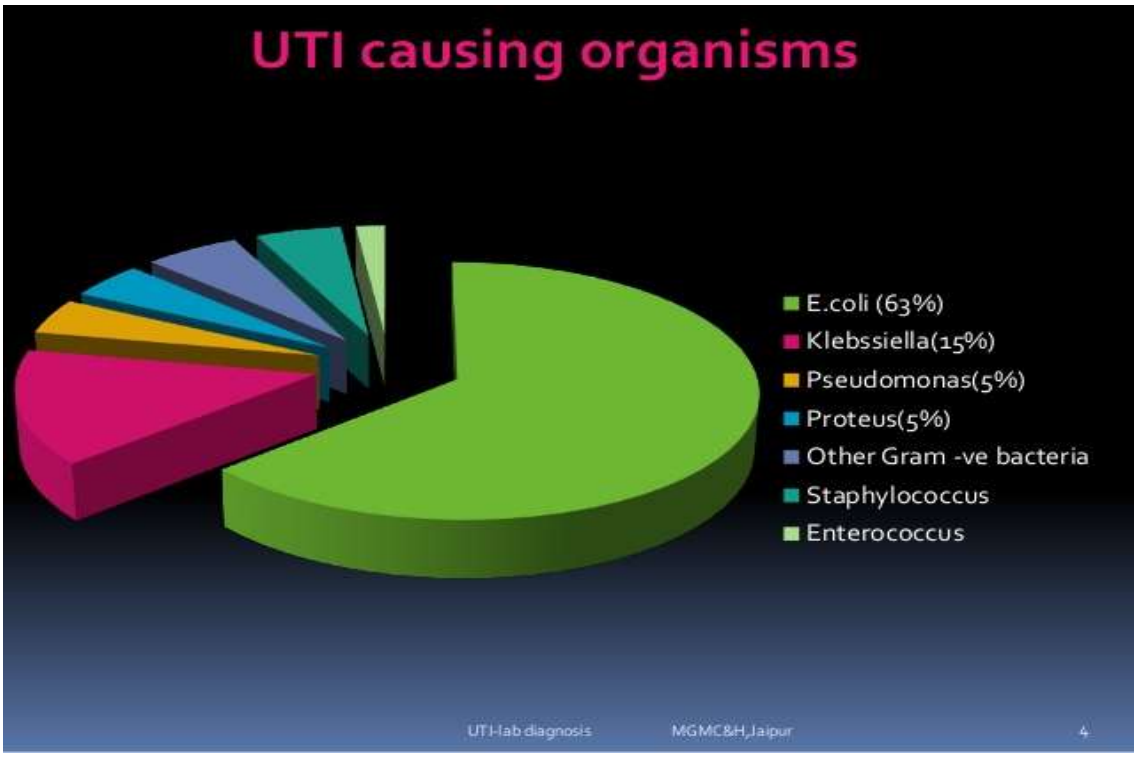
Most UTIs are caused by bacteria that live in the bowel. The bacterium *Escherichia coli* (*E. coli*) causes the vast majority of UTIs. Microbes called Chlamydia and Mycoplasma can infect the urethra and reproductive system but not the bladder. Chlamydia and Mycoplasma infections may be sexually transmitted and require treatment of sexual partners. The urinary tract has several systems to prevent infection. The points where the ureters attach to the bladder act like one-way valves to prevent urine from backing up toward the kidneys, and urination washes microbes out of the body. In men, the prostate gland produces secretions

that slow bacterial growth. In both sexes, immune defenses also prevent infection. But despite these safeguards, infections still occur. Certain bacteria have a strong ability to attach themselves to the lining of the urinary tract.

How are UTIs diagnosed?

To find out whether a person has a UTI, the health care provider will ask about urinary symptoms and then test a sample of urine for the presence of bacteria and white blood cells, which are produced by the body to fight infection. Because bacteria can be found in the urine of healthy individuals, a UTI is diagnosed based both on symptoms and a laboratory test. The person will be asked to give a "clean catch" urine sample by washing the genital area and collecting a "midstream" sample of urine in a sterile container. This method of collecting urine helps prevent bacteria around the genital area from getting into the sample and confusing the test results. Usually, the sample is sent to a laboratory, although some health care providers' offices are equipped to do the testing. For people with recurring infections and patients in the hospital, the urine may be cultured. The culture is performed by placing part of the urine sample in a tube or dish with a substance that encourages any bacteria present to grow. Once the bacteria have multiplied, which usually takes 1 to 3 days, they can be identified. The health care provider may also order a sensitivity test, which tests the bacteria for sensitivity to different antibiotics to see which medication is best for treating the infection. If a person has recurrent UTIs, the health care provider may order some additional tests to determine if the person's urinary tract is normal.


Causative organisms
Gram –ve Bacilli
• E.coli
• Klebsiella
• Pseudomonas
• Proteus
E.coli
Gram +ve Bacilli
• Staphylococcus
• Enterococci
Staphylococcus
Miscellaneous
• M.tuberculosis
• Citrobacter
• Salmonella
Citrobacter
Fungus
• Candida albicans
c.albicans


UTI causing organisms
E.coli (63%)
Klebssiella(15%)
Pseudomonas(5%)
Proteus(5%)
Other Gram -ve bacteria
Staphylococcus
Enterococcus
UTI-lab diagnosis
MGMC&H,Jaipur
4

Treatments and drugs

Antibiotics usually are the first line treatment for urinary tract infections. Which drugs are prescribed and for how long depend on your health condition and the type of bacteria found in your urine.

Simple infection

Drugs commonly recommended for simple UTIs include:

- Trimethoprim/sulfamethoxazole (Bactrim, Septra, others)
- Fosfomycin (Monurol)
- Nitrofurantoin (Macrodantin, Macrobid)
- Ciprofloxacin (Cipro)
- Levofloxacin (Levaquin)
- Cephalexin (Keflex)
- Ceftriaxone (Rocephin)
- Doxycycline (Monodox, Vibramycin, others)

Often, symptoms clear up within a few days of treatment. But you may need to continue antibiotics for a week or more. Take the entire course of antibiotics as prescribed. For an uncomplicated UTI that occurs when you're otherwise healthy, your doctor may recommend a shorter course of treatment, such as taking an antibiotic for one to three days. But whether this short course of treatment is enough to treat your infection depends on your particular symptoms and medical history.

Your doctor may also prescribe a pain medication (analgesic) that numbs your bladder and urethra to relieve burning while urinating, but pain usually is relieved soon after starting an antibiotic. One common side effect of urinary tract analgesics is discolored urine — orange or red.

Frequent infections

If you have frequent UTIs, your doctor may make certain treatment recommendations, such as:

- Low dose antibiotics, initially for six months but sometimes longer
- Self-diagnosis and treatment, if you stay in touch with your doctor
- A single dose of antibiotic after sexual intercourse if your infections are related to sexual activity
- Vaginal estrogen therapy if you're postmenopausal

Severe infection

For a severe UTI, you may need treatment with intravenous antibiotics in a hospital.

Lecture 4

Human Intestinal Parasites

Parasitic infections, caused by intestinal helminths and protozoan parasites, are among the most prevalent infections in humans. Protozoan parasites more commonly cause gastrointestinal infections compared to helminths. Intestinal parasites cause a significant **morbidity and mortality** in endemic countries. Helminths are worms with many cells. **Nematodes** (roundworms), **cestodes** (tapeworms), and **trematodes** (flatworms) are among the most common helminths that inhabit the **human gut**. Usually, helminths cannot multiply in the human body. **Protozoan** parasites that have only one cell can multiply inside the human body. There are four species of intestinal helminthic parasites, also known as **geohelminths** and soil-transmitted helminths : *Ascaris lumbricoides* (roundworm), *Trichiuris trichiuria* (whipworm), *Ancylostoma duodenale*, and *Necator americanicus* (hookworms). These infections are most prevalent in **tropical** and **subtropical regions** of the developing world where adequate water and sanitation facilities are lacking. Recent estimates suggest that *A. lumbricoides* can infect over a billion, *T. trichiura* 795 million, and hookworms 740 million people. Other species of intestinal helminths are not widely prevalent. Intestinal **helminths rarely cause death**. The most common intestinal protozoan parasites are: ***Giardia intestinalis, Entamoeba histolytica, Cyclospora cayetanenensis,* and *Cryptosporidium* spp**. The diseases caused by these intestinal protozoan parasites are known as ***giardiasis, amoebiasis, cyclosporiasis,* and *cryptosporidiosis*** respectively, and they are associated with **diarrhoea**.

Symptoms	Parasite
Abdominal pain and distension	*Giardia*, *Cryptosporidium*, Amoebiasis, *Ascaris*, hookworm, *taenia*
Diarrhoea +/- malabsorption	*Giardia*, *Cryptosporidium*, *Strongyloides*
Diarrhoea with blood loss	Amoebiasis, *Trichuris*, Hookworm
Tenesmus, prolapsed rectum	*Trichuris*

Infections & Diagnosis

The following list of parasites and what to look for may be of help in identifying some of the most common parasitic infections:

Amebiasis: Amoebas cause **irregular ulcers** in the **rectum with red borders** and **gray bases**. They can be found in fresh stool specimens and on biopsy specimens **taken from rectal ulcers.**

Balantidiasis: Diarrhea, dysentery, and occasional **ulceration** of the large **intestine characterize this disease**. *Balantidium coli* **cysts found in stools are diagnostic**.

Fascioliasis: Fasciola organisms can cause an enlarged and **painful liver accompanied** by fever. **Eggs of these organisms** can be found in **stools**.

Giardiasis: Infection with *Giardia lamblia* can cause **diarrheic** and/or **dysenteric symptoms. Cysts and trophozoites** can be found in **stools.**

Hookworm: Severe symptoms such as **iron-deficiency anemia**, **physical and mental** retardation, and **cardiac complication sometimes** occur. Diagnosis is made by the **finding of ova in stools**.

Pinworm: Although the most **common complaint** caused by pinworms is **perianal itching**, they may also cause **intestinal abscesses** and **bleeding. Eggs** may be found in the perianal area; they can be transferred with a **cellophane tape swab** to a slide for microscopic inspection. Worms may also be seen **in stools**, and sometimes **around the anus.**

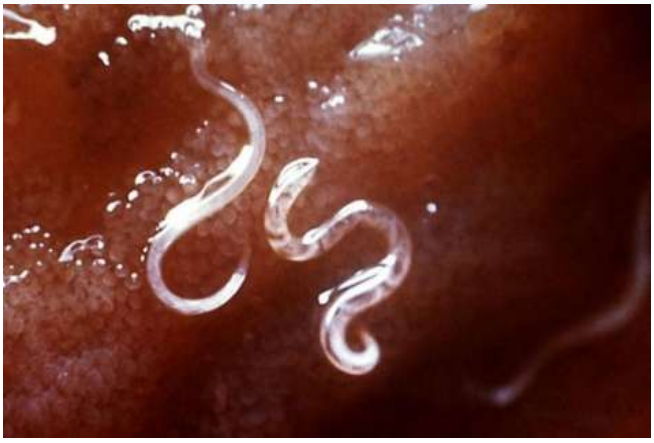
Roundworm: Severe symptoms-such as intestinal, **biliary, or pancreatic obstruction**; or **appendicitis**-may occur. Eggs may be diagnosed by a simple **smear of stools**.

Strongyloidiasis: The infectious agent is the nematode *Strongyloides stercoralis*. It **causes diarrhea**. **Larvae can be found in stools**.

Tapeworm: Segments of beef, pork, and fish tapeworms can be **found in stools**. Eggs can be **swabbed from perianal areas and examined.**

Trichinosis: Severe trichinosis infestation may result in **death** within six weeks. **Muscle biopsy,** to determine the presence of **encysted larvae** of *Trichinella spiralis*, is the only reliable diagnostic procedure, since neither **eggs nor worms occur in stools**.

Whipworm: Blood-streaked stools, **rectal prolapse**, **iron-deficiency anemia**, and **malnutrition may occur. Stool examination for eggs and parasites is indicated** for an accurate diagnosis.



Helminths

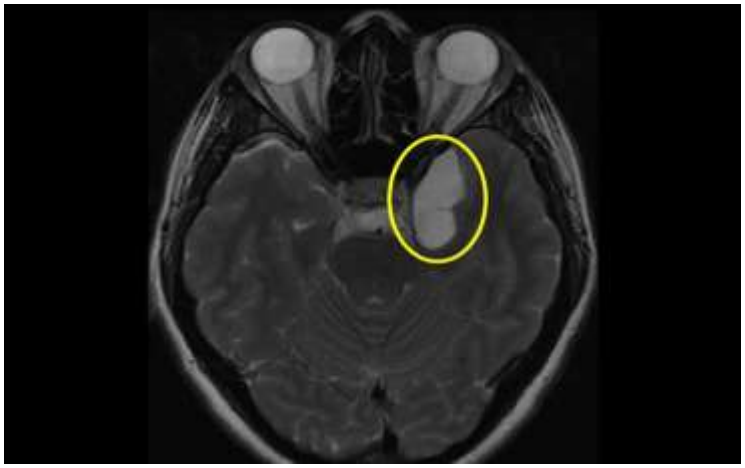
Cestodes

Tapeworms are long, segmented worms of the class Cestoda, which includes the genera ***Taenia, Diphyllobothrium, Hymenolepis, Dipylidium, Echinococcus,*** **and *Spirometra***. Adult tapeworms lack an intestinal tract and absorb **all nutrients through their integument**. The adults have a head (termed a **scolex**), a **neck**, and a **segmented body** with both male and female **gonads**. Tapeworms require one or more intermediate hosts in their life cycle. Typically, the eggs are passed from the **host** into the **environment**, where they are ingested by an intermediate host. In the intermediate host, the eggs hatch, and the larvae enter the host tissues and encyst. The primary host then ingests the cysts by consuming the flesh of the intermediate host.

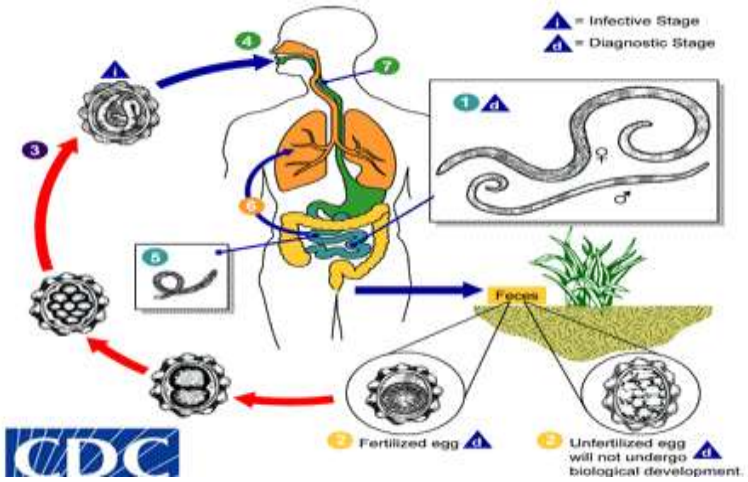
Humans are the **primary** hosts for *Taenia*, *Diphyllobothrium*, and *Hymenolepis*, but they may be **intermediate** hosts for *Echinococcus* and *Spirometra*. Infection is typically from either **fecal-oral transmission** or the ingestion of **contaminated**, undercooked meat. *Hymenolepis nana* the most commonly diagnosed parasitic intestinal infection with helminths and/or protozoa can lead to significant morbidity and mortality if not recognized and treated appropriately.

Many **cestode** infestations are **asymptomatic**. The most common symptoms are **abdominal pain**, **anorexia**, **weight loss**, and **malaise**. *Diphyllobothrium* **absorbs** large quantities of vitamin **B12**, causing **megaloblastic** anemia in hosts. *Taenia solium* may deposit cysts in the central nervous system, leading to the development of **seizures** from neurocysticercosis.

Echinococcus granulosus (shown) may deposit cysts slowly over years, eventually precipitating a mass effect on the involved organ; the alveolar form of the disease may not manifest until 5-15 years after infection. Rupture of these cysts may cause fever, pruritus, urticaria, eosinophilia, and anaphylaxis. Untreated symptomatic liver involvement carries a fatality rate greater than 2%-4%; untreated alveolar echinococcosis has an estimated mortality rate above 90% at 10-15 years.



Tapeworm infections can typically be diagnosed by **collecting two to three stool samples and checking for ova and parasites**. Enzyme-linked immunosorbent assay (**ELISA**), immunoblot, and polymerase chain reaction (**PCR**) assay may help confirm a diagnosis; sensitivities and specificities vary, depending on the species involved.

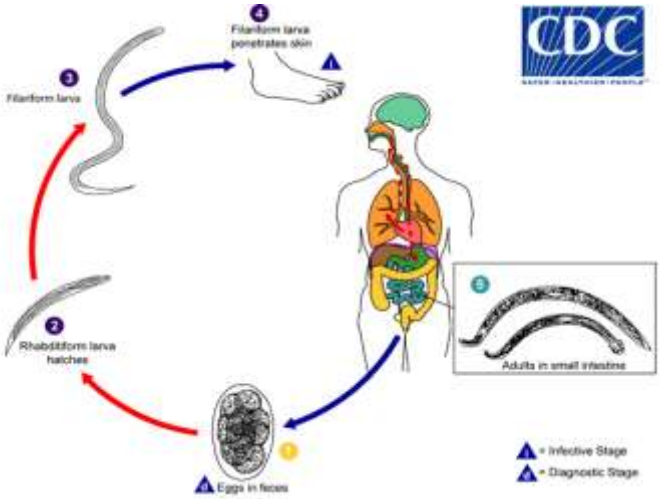


Ascaris

Ascariasis is the most **common** helminthic infection worldwide. *Ascaris lumbricoides* is the **largest** of the roundworms that infect humans, growing as long as 35 cm, and it may live for up to 2 years in the small intestine. Its life cycle is **complex** and involves multiple human organs.

Every day, a female worm will produce about 200,000 eggs, which are fertilized by nearby male worms. Fertilized eggs may remain **viable** for up to **17 months** in soil, where they cause infection through ingestion and subsequent hatching in the small intestine. **Second**-stage larvae pass through the **intestinal wall** and migrate through the portal system to the liver and lungs. Larvae may be expectorated and then swallowed into the digestive tract, where they mature into adults. Adults will feed on **digestive products**, which can **lead to protein, calorie, or vitamin A deficiency** in children at risk for malnutrition. Because pinworms do not multiply in the host, infection is limited to 2 years unless reexposure occurs. Although most infected individuals are asymptomatic, patients may develop growth retardation, pneumonitis, pneumonia, eosinophilia, intestinal or pancreatic obstruction, and hepatobiliary injury.

The diagnosis of **ascariasis** is typically made by means of **stool ova and parasite examination**. Abdominal **x-rays** may show signs of bowel obstruction, and ultrasonography may reveal a single worm or a mass of the worms with segmented sections and curling movements. Treatment with a single dose of albendazole, mebendazole, or ivermectin is usually effective for eradication. Medical therapy during active pulmonary infection is not indicated, not only because pulmonary ascariasis is a self-limited disease but also owing to the high risk of developing pneumonitis from the dying larvae. Endoscopic retrograde cholangiopancreatography may be used both to diagnose and to treat infection of the biliary system. Most worms will spontaneously migrate from the intestines and biliary system, but surgery may be needed for refractory cases. Preventive chemotherapy may be used as a short-term strategy, but improvements to water, sanitation, and hygiene are needed to prevent long-term reinfection



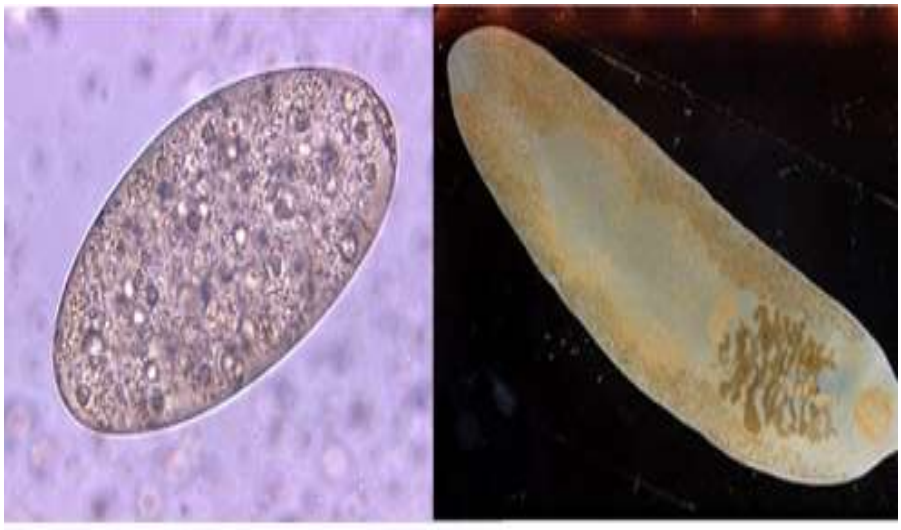
Hookworms

Human hookworms, predominantly *Ancylostoma duodenale* and *Necator americanus*, infect hundreds of millions of people (576-740 million) worldwide. They are the second most common cause of helminthic infections after ascariasis.

Hookworm larvae rapidly penetrate the skin of humans who are exposed to soil contaminated by human feces (life cycle shown). "Ground itch" (local skin manifestations involving severe allergic itching) at the site of penetration is common.

The larvae then burrow into venules and embolize into the lungs, where they penetrate into alveoli and cause an asymptomatic alveolitis with eosinophilia. Coughing and then swallowing transport the larvae into the intestines, where they mature into adults. Adult worms feed on blood from the mucosal capillaries. About 5 weeks after initial infection, female worms release thousands of eggs into the stool daily. If no reexposure occurs, the infection will disappear once the worms die; the lifespan of *Necator* is 3-10 years, and that of *Ancylostoma* is 1-3 years

Patients may report diarrhea, vague abdominal pain, colic, or nausea. The diagnosis is made by means of stool ova and parasite examination. Both iron-deficiency anemia and eosinophilia may be present on a complete blood cell count. Treatment with iron therapy is used to manage the anemia; a single dose of albendazole or mebendazole, or one dose daily of pyrantel pamoate for 3 days, is typically sufficient to eradicate the infection



Intestinal trematodes

Intestinal flukes are flat hermaphroditic worms (class Trematoda) that range in length from a few millimeters to several centimeters. The species that most commonly infect humans are *Fasciolopsis buski* (shown), which is the largest and most common human intestinal fluke, *Heterophyes heterophyes*, *Metagonimus yokogawai*, and *Echinostoma* species.

The life cycle of each species is very complex and can involve a number of intermediate hosts, such as snails, fish, tadpoles, or vegetables. Humans are typically infected after ingesting a raw or undercooked intermediate host. Developmental forms will attach to the small intestinal walls, where they develop into adults over a period of several months. Adult flukes will cause inflammation, ulceration, and mucus secretion at the site of attachment.

Most infected persons are asymptomatic, but some may develop loose stools, weight loss, malaise, and nonspecific abdominal pain. In severe infection, alternating diarrhea and constipation; edema of the face, abdominal wall, and lower extremities; anorexia; nausea; and vomiting may occur. The diagnosis is made by means of stool ova and parasite examination. Treatment with three doses of praziquantel over 1 day is typically sufficient to clear infection

Protozoa

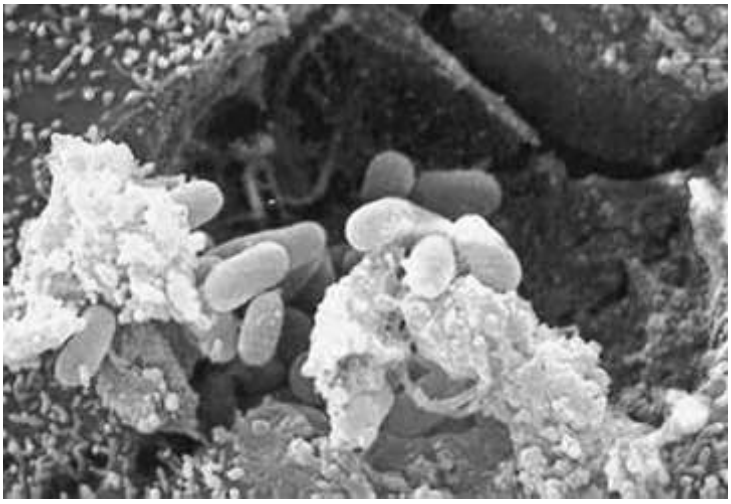
Balantidium coli

Balantidiasis is an intestinal infection caused by the **ciliated** protozoan *Balantidium coli* (shown).The primary reservoir is thought to be pigs. Thus, those who handle pigs or pig byproducts are at increased risk for infection.

After human ingestion of infective cysts via **contaminated food** or water, *B coli* organisms migrate to the large intestine, cecum, and terminal ileum. There, they develop into trophozoites, which replicate by binary fission and conjugation while consuming bacteria.They reside primarily within the intestinal lumen but may penetrate the mucosa and cause ulcers. Although most immunocompetent individuals will be

asymptomatic, patients may develop bloody, mucoid diarrhea; nausea; vomiting; abdominal pain; anorexia; weight loss; fever; colitis; and dehydration.

The diagnosis is made on the basis of wet smears of stool specimens (shown at 1000× magnification). Trophozoites can be recognized by their large size, ciliary covering, and spiraling motility. Treatment includes volume and electrolyte replacement, as well as antimicrobial coverage with tetracycline, metronidazole, or iodoquinol. There are no large-scale reports of antimicrobial resistance.

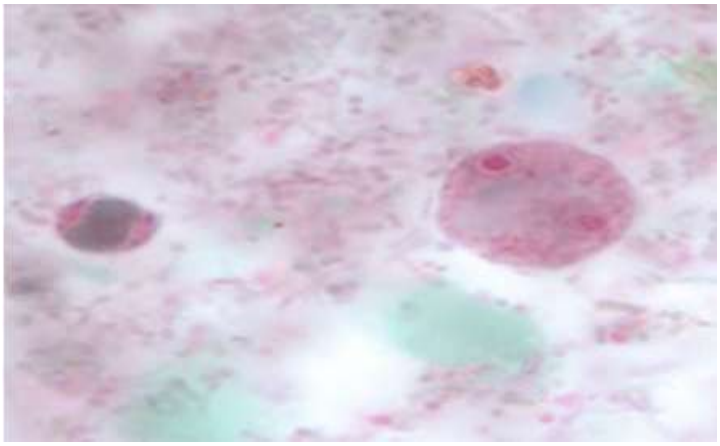


Microsporidia

Microsporidia are obligate, intracellular, spore-forming parasites. The phylum Microsporidia contains over 1200 fungal species, a large number of which cause infection in humans. Two of the most important of these species are *Encephalitozoon hellem* and *E intestinalis*. Most cases of infection are associated with human immunodeficiency virus (HIV) or other immunosuppressing illness, including organ transplant recipients, diabetics, children, and the elderly. Microsporidiosis occurs through ingestion or inhalation of microsporidial spores from human-to-human or waterborne transmission. The spores will extrude a polar tubule and inject an infective

sporoplasm into the host cell. Within the cell, the sporoplasm multiplies by binary fission and eventually ruptures the cell, releasing more spores (shown). Patients with intestinal microsporidiosis may develop chronic nonbloody diarrhea, weight loss, abdominal pain, nausea, vomiting, and malnourishment. With dissemination, cholecystitis and renal failure as well as infections of the muscles, brain, and respiratory tract may occur.

The diagnosis is made via stool microscopy, but this does not allow species identification. Cytologic and histologic examination may also be helpful; additionally, immunofluorescence assays (IFA) and PCR are available. Typically, treatment with albendazole for 2-4 weeks is effective for most ocular, intestinal, and disseminated microsporidiosis.



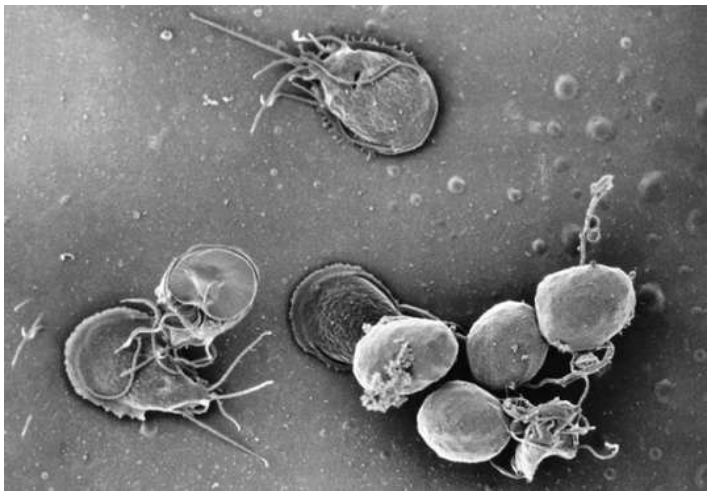
Dientamoeba fragilis

Dientamoeba fragilis is a nonflagellated protozoan (shown) that infects the large intestine. Transmission is thought to be via human-to-human fecal-oral spread or via coinfection with the eggs of *E vermicularis* (human pinworm); however, the life cycle is incompletely understood, and no cystic stage has been definitively identified.

Trophozoites infect the mucosal crypt cells of the large intestine, invoking an eosinophilic inflammatory response. Abdominal pain and nonbloody diarrhea are the

most common symptoms, but anorexia, weight loss, nausea, vomiting, flatulence, headaches, fever, malaise, and fatigue may also develop.

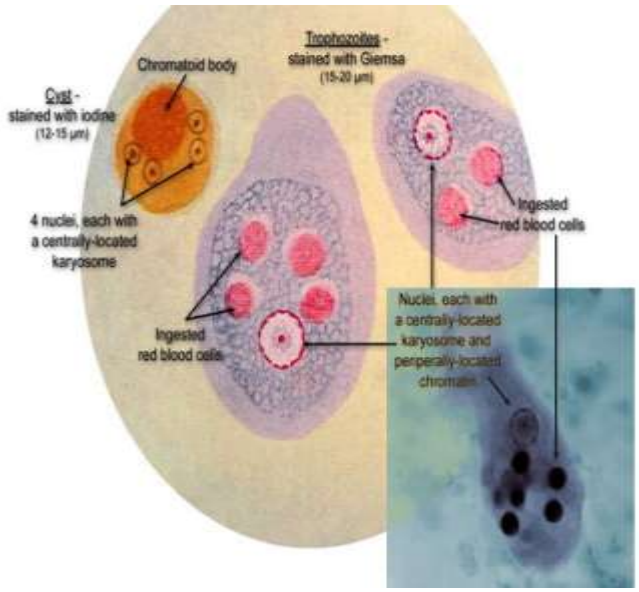
The diagnosis is typically made through microscopic evaluation of permanently stained fresh fecal smears (trichrome), which show a characteristic pleomorphic trophozoite with up to four nuclei (most commonly binucleate [shown]) that are distinctive for their clumped chromatin granules. Treatment typically involves the use of an anthelmintic medication such as iodoquinol (drug of choice), metronidazole, tetracycline, or paromomycin.



Giardia

Giardiasis is a major diarrheal illness found worldwide; in the United States, it is the most frequently diagnosed intestinal parasitic disease. It is most commonly caused by the flagellate protozoan *Giardia lamblia* (also known as *G intestinalis*). Infection is via the ingestion of *Giardia* cysts, typically from contaminated water, which then excyst, multiply, and colonize the upper small bowel. Cysts are able to retain viability for 2-3 months in cold water, and the infective dose is as low as 10-25 cysts. The exact pathophysiology is unclear. Most infections are asymptomatic, and asymptomatic carriage is quite common. Person-to-person transmission from poor hygiene and sanitation is a primary means of infection. Symptomatic individuals may report explosive, watery diarrhea; abdominal cramps; foul flatus; vomiting; fever; malaise; anorexia; lactose intolerance; and weight loss. Symptoms may last for up to 3 weeks,

and more than 50% of patients lose an average of 10 lb. Physical findings are typically unremarkable, and stools are usually heme negative. The diagnosis is made by means of stool examination for cysts or trophozoites, stool antigen detection with ELISA or IFA, or, rarely, duodenal sampling. Treatment typically involves aggressive fluid and electrolyte replacement plus administration of an antimicrobial agent such as albendezole or metronidazole.



Entamoeba histolytica

Amebiasis is caused by infection with the protozoan *Entamoeba histolytica*; this occurs after ingestion of cystic protozoa, typically in fecally contaminated soil, food, or water. Excystation into trophozoites occurs in the cecum, terminal ileum, or colon. The trophozoites then penetrate the colonic mucosal barrier and, with severe invasive disease, produce tissue destruction, secretory bloody diarrhea, and colitis. Hematogenous spread can cause trophozoite deposition into the liver, brain, and lungs, leading to abscess formation

The diagnosis can be made by means of stool microscopy for cysts and trophozoites, ELISA, IFA, indirect hemagglutination, or PCR. Treatment for asymptomatic amebiasis is with iodoquinol or paromomycin. Symptomatic intestinal and extraintestinal disease is treated with metronidazole or tinidazole, followed by

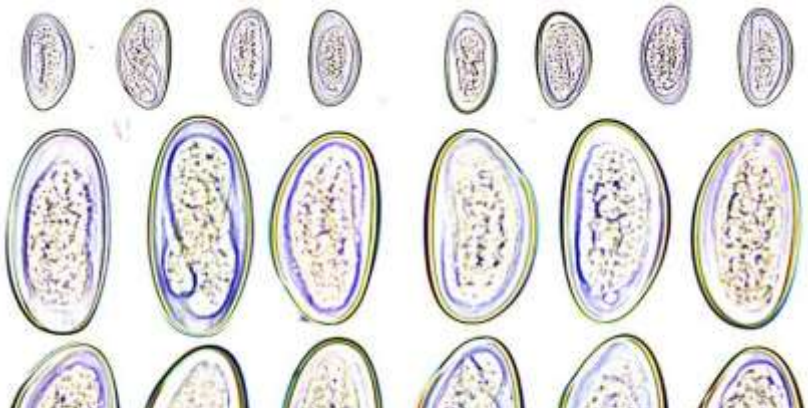
administration of iodoquinol or paromomycin. Extraintestinal abscesses generally require both drainage and metronidazole or tinidazole administration.

E. vermicularis

E. vermicularis, commonly referred to as the pinworm or seat worm, is a nematode, or roundworm, with the largest geographic range of any helminth. It is the most prevalent nematode in the United States. Humans are the only known host, and about 209 million persons worldwide are infected. More than 30 percent of children worldwide are infected. Adult worms are quite small; the males measure 2 to 5 mm, and the females measure 8 to 13 mm. The worms live primarily in the cecum of the large intestine, from which the gravid female migrates at night to lay up to 15,000 eggs on the perineum. The eggs can be spread by the fecal-oral route to the original host and new hosts. Eggs on the host's perineum can spread to other persons in the house, possibly resulting in an entire family becoming infected. Ingested eggs hatch in the duodenum, and larvae mature during their migration to the large intestine. Fortunately, most eggs desiccate within 72 hours. In the absence of host autoinfection, infestation usually lasts only four to six weeks.

Disease secondary to *E. vermicularis* is relatively innocuous, with egg deposition causing perineal, perianal, and vaginal irritation. The patient's constant itching in an attempt to relieve irritation can lead to potentially debilitating sleep disturbance. Rarely, more serious disease can result, including weight loss, urinary tract infection, and appendicitis.

Pinworm infection should be suspected in children who exhibit perianal pruritus and nocturnal restlessness. Direct visualization of the adult worm or microscopic detection of eggs confirms the diagnosis, but only 5 percent of infected persons have eggs in their stool. The “cellophane tape test can serve as a quick way to clinch the diagnosis.



Lecture 5

Human Intestinal infection

A range of viruses and bacteria (as well as parasites) can infect the human alimentary canal. Mixed infections of viruses and bacteria are not uncommon, and quite complex physiological changes can result from such infections. This chapter documents the main viruses and bacteria involved in mixed gastroenteritis infections and then survey the frequency and nature of mixed viral-bacterial infections in humans. The literature on the possible mechanisms of such mixed infections is then examined under four headings: (i) the occurrence of asymptomatic infections by viral and bacterial enteropathogens; (ii) the clinical features of natural mixed infections in humans; (iii) the nature of mixed infections in animal models; (iv) relevant in vitro studies of viral-bacterial interaction.

Bacterial Agents of Gastroenteritis in Humans

Ten main bacterial groups associated with human gastroenteritis have been identified in mixed viral-bacterial infections in humans or used in experiments to study such mixed infections. A brief description of their classification and sites of action follows.

Escherichia coli

Six main groups of pathogenic *E. coli* are now known: enteropathogenic *E. coli* (EPEC), enteroinvasive *E. coli* (EIEC), enterotoxigenic *E. coli* (ETEC),

enterohaemorrhagic *E. coli* (EHEC), enteroaggregative *E. coli* (EaggEC), and diffusely adherent *E. coli* (DAEC). Some pathogenic *E. coli* strains show a particular pattern of adherence to HEp-2 cells referred to as "localized adherence". Many, but not all, of these strains fall into the EPEC category so that strains classified as locally adherent cannot at this stage be further categorized. The pathogenesis of different strains of *E. coli* can vary; e.g., EIEC tends to invade epithelial cells and damage them through multiplication in the cytoplasm, whereas other strains such as ETEC and EHEC do not invade the cell. Toxin production is particularly important in the pathogenesis of noninvasive *E. coli* such as ETEC. Different strains of *E. coli* may also affect different parts of the intestine, e.g., ETEC tends to colonize the small intestine whereas EIEC and EPEC tend to infect both the small intestine and colon.

Shigella spp

Four main species of *shigellae* are commonly recognized in humans: *Shigella dysenteriae, Shigella flexneri, Shigella boydii,* and *Shigella sonnei. Shigellae* normally infect colonic epithelial cells. Shigellae can produce a toxin which contributes to their pathogenic effect.

Salmonella spp

Salmonella spp., which are all considered to be potentially pathogenic, currently number more than 2,370 recognized serological types. These bacteria bind to and penetrate the wall of the small intestine. Salmonellae produce toxins which contribute to their pathogenic effect.

Vibrio spp

Common species of *Vibrio* associated with food-borne infections include *Vibrio cholerae, Vibrio parahaemolyticus,* and *Vibrio vulnificus. V. cholerae,* the most studied of this group, colonizes the small intestine, where pathogenesis of several strains is assisted by the production of toxins.

***Campylobacter* spp**

The genus *Campylobacter* includes a number of species which can cause gastroenteritis, notably *C. jejuni. C. jejuni* principally infects the colon, but infection may also involve the small intestine. Bacterial toxin production may facilitate cell damage.

Yersinia enterocolitica

Bacteria related to *Y. enterocolitica* include many species which are usually referred to as the *Yersinia enterocolitica* group. These bacteria bind to and penetrate the small intestinal mucosa; they then colonize the Peyer's patches and can then spread to other organs. The pathogenesis of *Y. enterocolitica* is related in part to production of a toxin. *Y. enterocolitica* infection can cause a wide range of clinical symptoms, including diarrhea.

***Aeromonas* spp**

Infection with many species of the genus *Aeromonas* can be associated with gastroenteritis, particularly in children. Pathogenesis of the bacteria appears to be related to several factors, including toxin production in the host gut.

***Clostridium* spp**

Three main species are commonly associated with human disease: *Clostridium difficile, C. perfringens,* and *Clostridium botulinum*. *C. difficile* can colonize the colon and induce diarrhea following the production of toxins. *C. perfringens* is a common cause of food poisoning; these bacteria can secrete a toxin during the process of sporulation within the intestine. *C. botulinum* is also an important cause of food poisoning. This bacterium can multiply and produce a neurotoxin in the intestine.

***Bacillus* spp**

Some species of the genus *Bacillus* are occasionally associated with outbreaks of food-borne illness. *Bacillus cereus* infection can involve either the small intestine or the colon.

B. cereus produces a number of toxins which may contribute to the development of diarrhea.

Listeria spp

Two species of the genus *Listeria, Listeria monocytogenes* and *Listeria ivanovii,* are considered pathogenic in humans and can affect the gastrointestinal tract.

Viral Agents of Gastroenteritis in Humans

Nine main virus groups associated with human gastroenteritis have been identified in mixed viral-bacterial infections or have been used in studies of such mixed infections. A brief description of the classification and site of action of human gastroenteritis viruses follows.

Rotaviruses

Rotaviruses are a major cause of gastroenteritis, particularly in children. The virus, which measures about 70 nm in diameter, is classified in the genus *Rotavirus* in the family *Reoviridae*. Rotavirus infects villus epithelial cells in the small intestine; although recent evidence indicates rotavirus can also produce a toxin.

"Norwalk-like" Viruses

"Norwalk-like" viruses (NLV) are an important cause of gastroenteritis in humans and are currently classified in the genus "Norwalk-like viruses" in the family *Caliciviridae*. The particles measure about 35 nm in diameter. The virus appears to infect the epithelium of the small intestine.

Adenoviruses

Adenoviruses, particularly serotypes 40 and 41, are an important cause of gastroenteritis in humans, especially in children. These viruses are classified in the genus *Mastadenovirus* in the family *Adenoviridae* and measure about 70 to 90 nm in diameter. The viruses appear to infect the duodenal mucosa.

Astroviruses

Astroviruses are a major cause of gastroenteritis in humans, particularly children. These viruses, which measure about 27 nm in diameter, are classified in the genus *Astrovirus* in the family *Astroviridae.* Astroviruses appear to infect the duodenal epithelium in the lower third of the villi.

"Sapporo-like" Viruses

The "Sapporo-like" viruses comprise a genus within the family *Caliciviridae* and represent an important cause of illness, particularly in children. They measure about 31 nm in diameter. The term "human calicivirus" has also been applied to this group, although the term is now often used to collectively describe the Norwalk-like viruses and Sapporo-like viruses. The pathogenesis of this virus does not appear to have been described in detail.

Toroviruses

Toroviruses are pleomorphic particles, about 100 to 140 nm in diameter, often with surface projections about 10 nm in length. These viruses are classified in the genus *Torovirus* in the family *Coronaviridae*. The pathogenesis of toroviruses in humans is not well established, but the animal torovirus, Breda virus, replicates in intestinal epithelial cells. Toroviruses have been detected in children with gastroenteritis.

Coronaviruses

"Coronavirus-like particles" (CVLP), i.e., the fringed membranous particles sometimes detected in human feces, may be neither pathogenic in humans nor viral in nature. The occasional identification of true coronaviruses in humans with gastroenteritis appears to be the exception rather than the rule.

Picornaviruses

A series of studies by Yamashita and colleagues has established that Aichi virus, a member of the family *Picornaviridae,*is a cause of gastroenteritis in humans, Reports

have also linked infections with viruses of the genus *Parechovirus* within the family *Picornaviridae* with gastrointestinal symptoms in humans.

Herpesviruses

Herpesviruses, notably cytomegalovirus (CMV), have been found in humans with gastroenteritis, particularly patients infected with the human immunodeficiency virus (HIV). CMV can infect the human gastrointestinal tract with resultant gastrointestinal symptoms.

Lecture 6

Hematology

Hematology is a branch of medicine concerning the study of blood, the blood-forming organs, and blood diseases. The word "heme" comes from the Greek for blood. It involves treating diseases that affect the production of blood and its components, such as blood cells, hemoglobin, blood proteins, bone marrow, platelets, blood vessels, spleen, and the mechanism of coagulation.

Blood is a bodily fluid in animals that delivers necessary substances such as nutrients and oxygen to the cells and transports metabolic waste products away from those same cells. In vertebrates, it is composed of blood cells suspended in blood plasma, which constitutes 55% of blood fluid, is mostly water (92% by volume),[2] and contains dissipated proteins, glucose, mineral ions, hormones, carbon dioxide (plasma being the main medium for excretory product transportation), and blood cells themselves. Albumin is the main protein in plasma, and its function is to regulate the colloidal osmotic pressure of blood. The blood cells are mainly red blood cells (also called RBCs or erythrocytes), white blood cells (also called WBCs or leukocytes) and platelets. The most abundant cells in vertebrate blood are red blood cells. These contain hemoglobin, an iron-containing protein, which facilitates oxygen transport by reversibly binding to this respiratory gas and greatly increasing its solubility in blood. In contrast, carbon dioxide is almost entirely transported extracellularly dissolved in plasma as bicarbonate ion.

Blood is circulated around the body through blood vessels by the pumping action of the heart. In animals with lungs, arterial blood carries oxygen from inhaled air to the tissues of the body, and venous blood carries carbon dioxide, a waste product of metabolism produced by cells, from the tissues to the lungs to be exhaled.

Medical terms related to blood often begin with ***hemo-*** or ***hemato-*** (also spelled ***haemo-*** and ***haemato-***) from the Greek word (*haima*) for "blood". In terms of anatomy and histology, blood is considered a specialized form of connective tissue, given its origin in the bones and the presence of potential molecular fibers in the form of fibrinogen.

Two tubes of EDTA-anticoagulated blood.
Left tube: after standing, the RBCs have settled at the bottom of the tube.
Right tube: contains freshly drawn blood.

Blood eccupy for about 7% of the human body weight, with an average density of approximately 1060 kg/m^3, very close to pure water's density of 1000 kg/m^3. The average adult has a blood volume of roughly 5 litres (11 US pt), which is composed of plasma and several kinds of cells.

These blood cells (which are also called *corpuscles* or "**formed elements**") consist of erythrocytes (red blood cells, RBCs), leukocytes (white blood cells), and thrombocytes (platelets). By volume, the red blood cells constitute about 45% of whole blood, the plasma about 54.3%, and white cells about 0.7%.

Whole blood (plasma and cells) exhibits non-Newtonian fluid dynamics. If all human hemoglobin were free in the plasma rather than being contained in RBCs, the circulatory fluid would be too viscous for the cardiovascular system to function effectively.

Blood component

1- Cells (Erythrocyte, leukocyte and thrombocyte or platelets

2- Serum albumin

3- Blood-clotting factors (to facilitate coagulation)

4- Immunoglobulins (antibodies)

5-lipoprotein particles

6-Various other proteins

7- Various electrolytes (mainly sodium and chloride)

Hemoglobin

Hemoglobin is the principal determinant of the color of blood in vertebrates. Each molecule has four heme groups, and their interaction with various molecules alters the exact color. In vertebrates and other hemoglobin-using creatures, arterial blood and capillary blood are bright red, as oxygen imparts a strong red color to the heme group. Deoxygenated blood is a darker shade of red; this is present in veins, and can be seen during blood donation and when venous blood samples are taken. This is because the spectrum of light absorbed by hemoglobin differs between the oxygenated and deoxygenated states.[24]

Blood in carbon monoxide poisoning is bright red, because carbon monoxide causes the formation of carboxyhemoglobin. In cyanide poisoning, the body cannot utilize oxygen, so the venous blood remains oxygenated, increasing the redness. There are some conditions affecting the heme groups present in hemoglobin that can make the skin appear blue—a symptom called cyanosis. If the heme is oxidized, methaemoglobin, which is more brownish and cannot transport oxygen, is formed. In the rare condition sulfhemoglobinemia, arterial hemoglobin is partially oxygenated, and appears dark red with a bluish hue.

Veins close to the surface of the skin appear blue for a variety of reasons. However, the factors that contribute to this alteration of color perception are related to the light-scattering properties of the skin and the processing of visual input by the visual cortex, rather than the actual color of the venous blood.[25]

Blood clotting

Coagulation or **clotting** is the process by which blood changes from a liquid to a gel, forming a clot. It potentially results in hemostasis, the cessation of blood loss from a damaged vessel, followed by repair. The mechanism of coagulation involves activation, adhesion, and aggregation of platelets along with deposition and maturation of fibrin. Disorders of coagulation are disease states which can result in bleeding (hemorrhage or

bruising) or obstructive clotting (thrombosis). In all mammals, coagulation involves both a cellular (platelet) and a protein (coagulation factor) component.

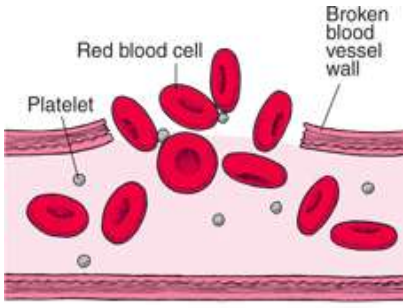
Coagulation begins almost instantly after an injury to the blood vessel has damaged the endothelium lining the vessel. Exposure of blood to the space under the endothelium initiates two processes: changes in platelets, and the exposure of sub-endothelial tissue factor to plasma Factor VII, which ultimately leads to fibrin formation. Platelets immediately form a plug at the site of injury; this is called primary hemostasis. Secondary hemostasis occurs simultaneousl. Hemostasis is the body's way of stopping injured blood vessels from bleeding. Hemostasis

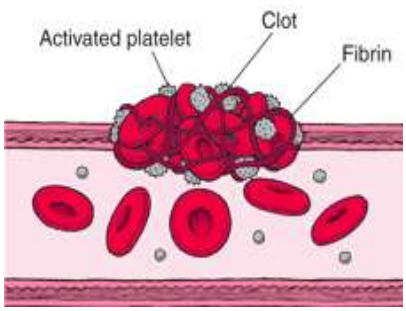
includes clotting of the blood. Too much clotting can block blood vessels that are not bleeding. Consequently, the body has control mechanisms to limit clotting and dissolve clots that are no longer needed. An abnormality in any part of this system that controls bleeding can lead to excessive bleeding or excessive clotting, both of which can be dangerous. When clotting is poor, even a slight injury to a blood vessel may lead to severe blood loss. When clotting is excessive, small blood vessels in critical places can become clogged with clots. Clogged vessels in the brain can cause strokes, and clogged vessels leading to the heart can cause heart attacks. Pieces of clots from veins in the legs, pelvis, or abdomen can travel through the bloodstream to the lungs and block major arteries there (pulmonary embolism).

Hemostasis involves three major processes:

- Narrowing (constriction) of blood vessels
- Activity of cell-like blood particles that help in blood clotting (platelets)
- Activity of proteins found in blood that work with platelets to help the blood clot (clotting factors)

Additional coagulation factors or clotting factors beyond Factor VII respond in a complex cascade to form fibrin strands, which strengthen the platelet plug.





Formation of a clot also involves activation of a sequence of blood clotting factors that generate thrombin. Thrombin converts fibrinogen, a blood clotting factor that is normally dissolved in blood, into long strands of fibrin that radiate from the clumped platelets and form a net that entraps more platelets and blood cells. The fibrin strands add bulk to the developing clot and help hold it in place to keep the vessel wall plugged.

The reactions that result in the formation of a blood clot are balanced by other reactions that stop the clotting process and dissolve clots after the blood vessel has healed. Without this control system, minor blood vessel injuries could trigger widespread clotting throughout the body—which actually happens in some diseases.

Blood disorder

1-Anemia

Anemia is the most common blood disorder, and according to the National Heart, Lung, and Blood Institute, it affects more than 3 million people daily. Red blood cells carry hemoglobin, an iron-rich protein that attaches to oxygen in the lungs and carries it to tissues throughout the body. Anemia occurs when you do not have enough red blood cells or when your red blood cells do not function properly. It is diagnosed when a blood test shows a hemoglobin value of less than 13.5 gm/dl in a man or less than 12.0 gm/dl in a woman. Normal values for children vary with age.

Anemia may characterised by several symptoms: Weakness, Shortness of breath, Dizziness , Fast or irregular heartbeat, Pounding or "whooshing" in your ears, Headache, Cold hands or feet, Pale or yellow skin, Chest pain.

There are several types of Anemia:

Iron-deficiency anemia: is the most common type of anemia. It happens when you do not have enough iron in your body. Iron deficiency is usually due to blood loss but may occasionally be due to poor absorption of iron. Pregnancy and childbirth consume a great deal of iron and thus

can result in pregnancy-related anemia. People who have had gastric bypass surgery for weight loss or other reasons may also be iron deficient due to poor absorption.

Vitamin-deficiency anemia may result from low levels of vitamin B12 or folate (folic acid), usually due to poor dietary intake. Pernicious anemia is a condition in which vitamin B12 cannot be absorbed in the gastrointestinal tract.

Aplastic anemia is a rare form of anemia that occurs when the body stops making enough red blood cells. Common causes include viral infections, exposure to toxic chemicals, drugs, and autoimmune diseases. Idiopathic aplastic anemia is the term used when the reason for low red blood cell production is not known.

Hemolytic anemia occurs when red blood cells are broken up in the bloodstream or in the spleen. Hemolytic anemia may be due to mechanical causes (leaky heart valves or aneurysms), infections, autoimmune disorders, or congenital abnormalities in the red blood cell. Inherited abnormalities may affect the hemoglobin or the red blood cell structure or function. Examples of inherited hemolytic anemias include some types of thalassemia and low levels of enzymes such as glucose-6 phosphate dehydrogenase deficiency. The treatment will depend on the cause.

Sickle cell anemia is an inherited hemolytic anemia in which the hemoglobin protein is abnormal, causing the red blood cells to be rigid and clog the circulation because they are unable to flow through small blood vessels.

Anemia caused by other diseases - Some diseases can affect the body's ability to make red blood cells. For example, some patients with kidney disease develop anemia because the kidneys are not making enough of the hormone erythropoietin to signal the bone marrow to

make new or more red blood cells. Chemotherapy used to treat various cancers often impairs the body's ability to make new red blood cells, and anemia often results from this treatment.

2- **Bleeding disorders** are a group of conditions that result when the blood cannot clot properly. In normal clotting, platelets, a type of blood cell, stick together and form a plug at the site of an injured blood vessel. Proteins in the blood called clotting factors then interact to form a fibrin clot, essentially a gel plug, which holds the platelets in place and allows healing to occur at the site of the injury while preventing blood from escaping the blood vessel. While too much clotting can lead to conditions such as heart attacks and strokes, the inability to form clots can be very dangerous as well, as it can result in excessive bleeding. Bleeding can result from either too few or abnormal platelets, abnormal or low amounts of clotting proteins, or abnormal blood vessels.

Hemophilia is perhaps the most well-known inherited bleeding disorder, although it is relatively rare. It affects mostly males. Many more people are affected by von Willebrand disease, the most common inherited bleeding disorder in America caused by clotting proteins. Von Willebrand disease can affect both males and females. Platelet disorders are the most common cause of bleeding disorder and are usually acquired rather than inherited.

3- Leukemia

Leukemia is a type of cancer found in your blood and bone marrow and is caused by the rapid production of abnormal white blood cells. These abnormal white blood cells are not able to fight infection and impair the ability of the bone marrow to produce red blood cells and platelets.

Leukemia can be either acute or chronic. Chronic leukemia progresses more slowly than acute leukemia, which requires immediate treatment. Leukemia is also classified as lymphocytic or myelogenous. Lymphocytic leukemia refers to abnormal cell growth in the marrow cells that become lymphocytes, a type of white blood cell that plays a role in the immune system. In myelogenous leukemia, abnormal cell growth occurs in the marrow cells that mature into red blood cells, white blood cells, and platelets. There are four broad classifications of leukemia:

- Acute lymphocytic leukemia (ALL)
- Acute myelogenous leukemia (AML)
- Chronic lymphocytic leukemia (CLL)

- Chronic myelogenous leukemia (CML)

Leukemia occurs in both adults and children. ALL is the most common form of*childhood* leukemia, and AML is the second most common. Decades of research have led to vastly improved outcomes for children diagnosed with ALL. The two most common *adult* leukemias are AML and CLL.

4- Lymphoma

About half of the blood cancers that occur each year are lymphomas, or cancers of the lymphatic system. This system - composed of lymph nodes in your neck, armpits, groin, chest, and abdomen - removes excess fluids from your body and produces immune cells. Abnormal lymphocytes, a type of white blood cell that fights infection, become lymphoma cells, which multiply and collect in your lymph nodes. Over time, these cancerous cells impair your immune system.

Lymphomas are divided into two categories: Hodgkin lymphoma and non-Hodgkin lymphoma. About 12 percent of people with lymphoma have Hodgkin lymphoma. Because of breakthrough research, this once fatal diagnosis has been transformed into a curable condition. Most non-Hodgkin lymphomas are B-cell lymphomas, and either grow quickly (high-grade) or slowly (low-grade). There are 14 types of B-cell non-Hodgkin lymphomas. The rest are T-cell lymphomas, named after a different cancerous white blood cell, or lymphocyte.

5- Myeloma

Myeloma is cancer of the plasma cells. Plasma cells are white blood cells that produce disease- and infection-fighting antibodies in your body. Myeloma cells prevent the normal production of antibodies, leaving your body's immune system weakened and susceptible to infection. The multiplication of myeloma cells also interferes with the normal production and

function of red and white blood cells. An abnormally high amount of these dysfunctional antibodies in the bloodstream can cause kidney damage. Additionally, the myeloma cells commonly produce substances that cause bone destruction, leading to bone pain and/or fractures. Myeloma cells are produced in the bone marrow, the soft tissue inside your bones. Sometimes myeloma cells will travel through your blood stream and collect in other bones in your body. Because myeloma frequently occurs at many sites in the bone marrow, it is often referred to as multiple myeloma.