IDHAYA COLLEGE FOR WOMEN, KUMBAKONAM

DEPARTMENT OF MICROBIOLOGY

Year : II MSc

Semester : IV

Topic : Unit-V

Subject Name : Medical Microbiology

Subject code : P16MB41

Prepared by

Mrs.K.PRIYA M.Sc.,M.Phil.,SET.,

Assistant Professor,

PG&Research department of Microbiology.

Entamoeba histolytica

Introduction

- ***Entamoeba histolytica*** is an anaerobic parasitic amoebozoan, part of the genus *Entamoeba*. Predominantly infecting humans and other primates causing amoebiasis.
- *E. histolytica* is estimated to infect about 35-50 million people worldwide.
- *E. histolytica* infection is estimated to kill more than 55,000 people each year
- The word *histolysis* literally means disintegration and dissolution of organic tissues.
- *E. histolytica*, as its name suggests (*histo–lytic* = tissue destroying), is pathogenic; infection can be asymptomatic or can lead to amoebic dysentery or amoebic liver abscess.

Transmission

- The active (trophozoite) stage exists only in the host and in fresh loose feces;
- cysts survive outside the host in water, in soils, and on foods.
- The infection can occur when a person puts anything into their mouth that has touched the feces of a person who is infected with *E. histolytica*, or swallows cysts (eggs) picked up from contaminated surfaces or fingers.
- The cysts are readily killed by heat and by freezing temperatures, and survive for only a few months outside of the host.
- When cysts are swallowed they cause infections by excysting (releasing the trophozoite stage) in the digestive tract. . Symptoms can include fulminating dysentery, bloody diarrhea, weight loss, fatigue, abdominal pain, and amoeboma.

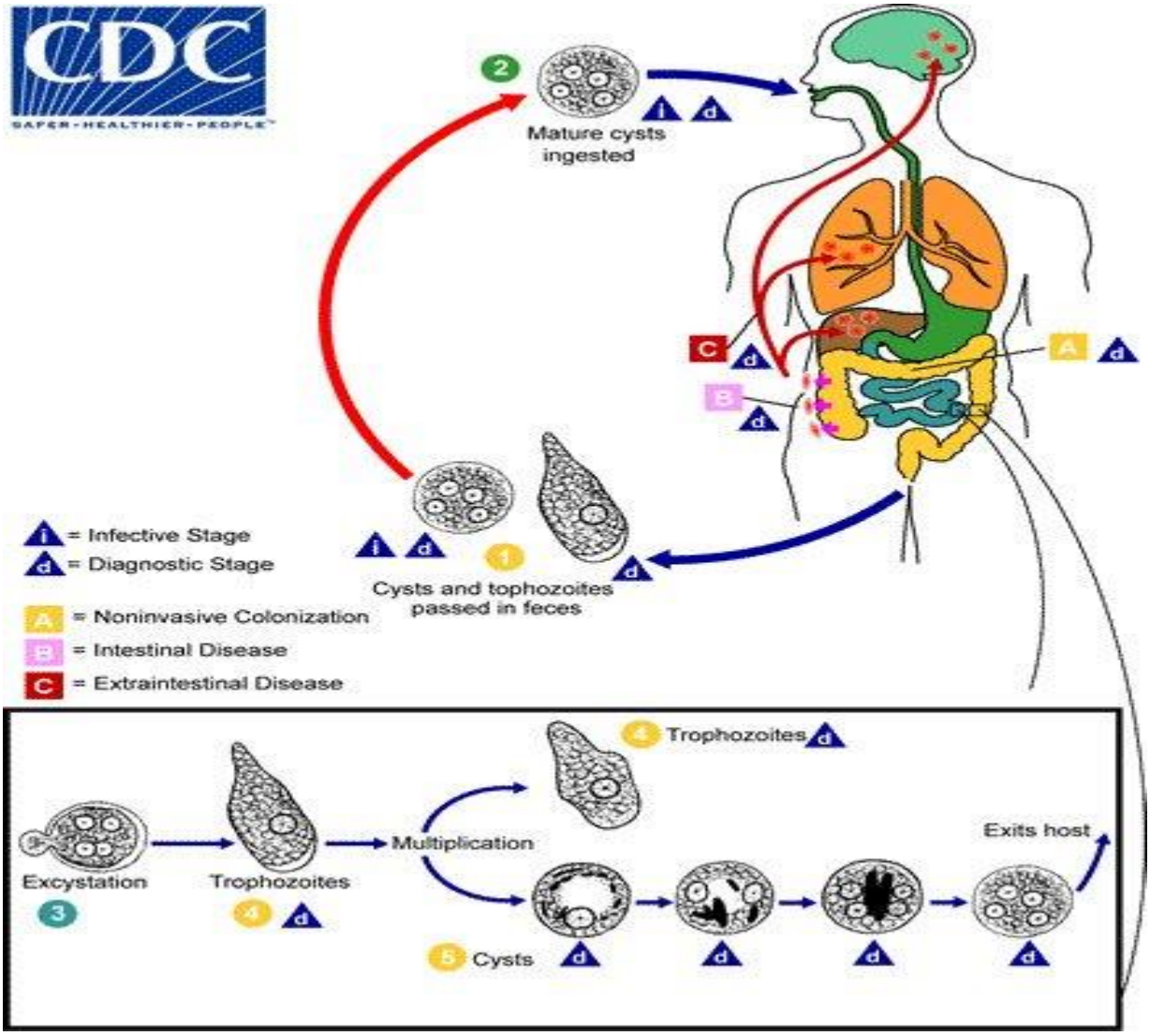
The amoeba can actually 'bore' into the intestinal wall, causing lesions and intestinal symptoms, and it may reach the blood stream. From there, it can reach different vital organs of the human body, usually the liver, but sometimes the lungs, brain, spleen, etc

. A common outcome of this invasion of tissues is a liver abscess, which can be fatal if untreated. Ingested red blood cells are sometimes seen in the amoeba cell cytoplasm.

Pathogenesis

E. histolytica causes tissue destruction which leads to clinical disease. *E. histolytica*–induced tissue damage by three main events:

I.direct host cell death II Inflammation III. parasite invasion



Pathology:

The trophozoites are excysted in the terminal ileum region, they colonize the large bowel, remaining on the surface of the mucus layer and feeding on bacteria and food particles.

- Occasionally, and in response to unknown stimuli, trophozoites move through the mucus layer where they come in contact with the epithelial cell layer and start the pathological process.
- *E. histolytica* has a lectin that binds to galactose and N-acetylgalactosamine sugars on the surface of the epithelial cells, The lectin normally is used to bind bacteria for ingestion.
- The parasite has several enzymes such as pore forming proteins, lipases, and cysteine proteases, which are normally used to digest bacteria in food vacuoles .
- Enzymes released allow penetration into intestinal wall and blood vessels, sometimes on to liver and other organs.
- The trophozoites will then ingest these dead cells. This damage to the epithelial cell layer attracts human immune cells and these in turn can be lysed by the trophozoite, which releases the immune cell's own lytic enzymes into the surrounding tissue, creating a type of chain reaction and leading to tissue destruction.
- This destruction manifests itself in the form of an 'ulcer' in the tissue, typically described as flask-shaped because of its appearance in transverse section. This tissue destruction can also involve blood vessels leading to bloody diarrhea, amebic dysentery.
- Occasionally, trophozoites enter the bloodstream where they are transported typically to the liver via the portal system.
- In the liver a similar pathologisequence ensues, leading to amebic liver abscesses. The trophozoites can also end up in other organs, sometimes via the bloodstream, sometimes via liver abscess rupture or fistulas. In all locations, similar pathology can occur.

Diagnosis

- Diagnosis is confirmed by microscopic examination for trophozoites or cysts in fresh or suitably preserved faecal specimens, smears of aspirates or scrapings obtained by proctoscopy, and aspirates of abscesses or other tissue specimen.

- A blood test is also available but is only recommended when a healthcare provider believes the infection may have spread beyond the intestine (gut) to some other organ of the body, such as the liver. However, this blood test may not be helpful in diagnosing current illness because the test can be positive if the patient has had amebiasis in the past, even if they are not infected at present.

- Stool antigen detection and PCR are available for diagnosis, and are more sensitive and specific than microscopy.

- Immunohistochemical staining of trophozoites (brown) using specific anti–E*ntamoeba histolytica* macrophage migration inhibitory factor antibodies in a patient with amebic colitiS

Treatment

Generally several antibiotics are available to treat *Entamoeba histolytica*.

Intestinal infection: Usually nitroimidazole derivatives (such as metronidazole) are used against the trophozoite form of the amoeba. Since they have little effect on amoeba cysts, usually this treatment is followed by an agent (such as paromomycin or diloxanide furoate) that acts on the organism in the lumen.

Liver abscess: Drugs like metronidazole and chloroquine, treatment of liver abscess must include agents that act in the lumen of the intestine (as in the preceding paragraph) to avoid re-invasion. Surgical drainage is usually not necessary except when rupture is imminent.

People without symptoms: For people without symptoms (otherwise known as carriers, with no symptoms), non endemic areas should be treated by paromomycin, and other treatments include diloxanide furoate and iodoquinol.

There have been problems with the use of iodoquinol and iodochlorhydroxyquin, so their use is not recommended. Diloxanide furoate can also be used by mildly symptomatic persons who are just passing cysts.

Prevention

- ✓ Amoebiasis can be prevented by stopping the fecal contamination of food and water by the Centers for Disease Control personnel by correcting poor sanitation.
- ✓ Identification and treatment of food handlers or other carriers of the parasite can reduce the chance of getting food-borne amebiasis.
- ✓ Avoiding sexual practices that involve fecal-oral contact also may reduce the chance of getting the disease.
- ✓ Avoiding malnutrition and alcohol use can reduce risk of the disease.
- ✓ Gal-lectin, an antigen from the parasite, has been used as a vaccine to protect animals against intestinal amebiasis and against amoebic liver abscesses.
- ✓ Other parasitic components are being tried as possible vaccine components to use in humans. Unfortunately, amebiasis doesn't result in any long-term immunity so that individuals can be reinfected multiple times.

****

Giardia lamblia

Introduction

- ❖ *Giardia lamblia* is a flagellated, microaerophilic microorganism, first discovered by Van Leeuwenhoek in 1681, who found it in his own diarrheal stool.
- ❖ The *G. lamblia* trophozoite, vegetative, motile form of *G. lamblia* is pear-shaped and have unique morphology The cyst is the reproductive form, and consists of a protective cyst wall as well as four nuclei.
- ❖ The genus *Giardia* has been isolated from more than 40 species. The species *G. lamblia* is known to infect human, mammals, reptiles, and birds, cows, sheeps and pigs, depending on the strain (Adam 2001).
- ❖ *G. lamblia* is one of the major cause of waterborne diseases worldwide (CDC, 2004), and infection results in giardiasis (characterized by malabsorption and severe diarrhea).
- ❖ Giardia-induced intestinal infection is particularly severe in developing world, where giardiasis occurrence relates heavily to water source contamination
- ❖ *Giardia lamblia* is also known as *intestinilis* or *G.duodenalis.*

- ❖ It was first observed by Antony von Leewenhoek (1681) while examining his own stool and Lambi (1859) describe the parasite and named it as Giardia labmlia
- ❖ Giardia is the only intestinal flagellate known to cause endemic and epidemic diarrhea in hum

Morphology:

G. lamblia exists in two morphological form- trophozoite and cyst

Trophozoite:

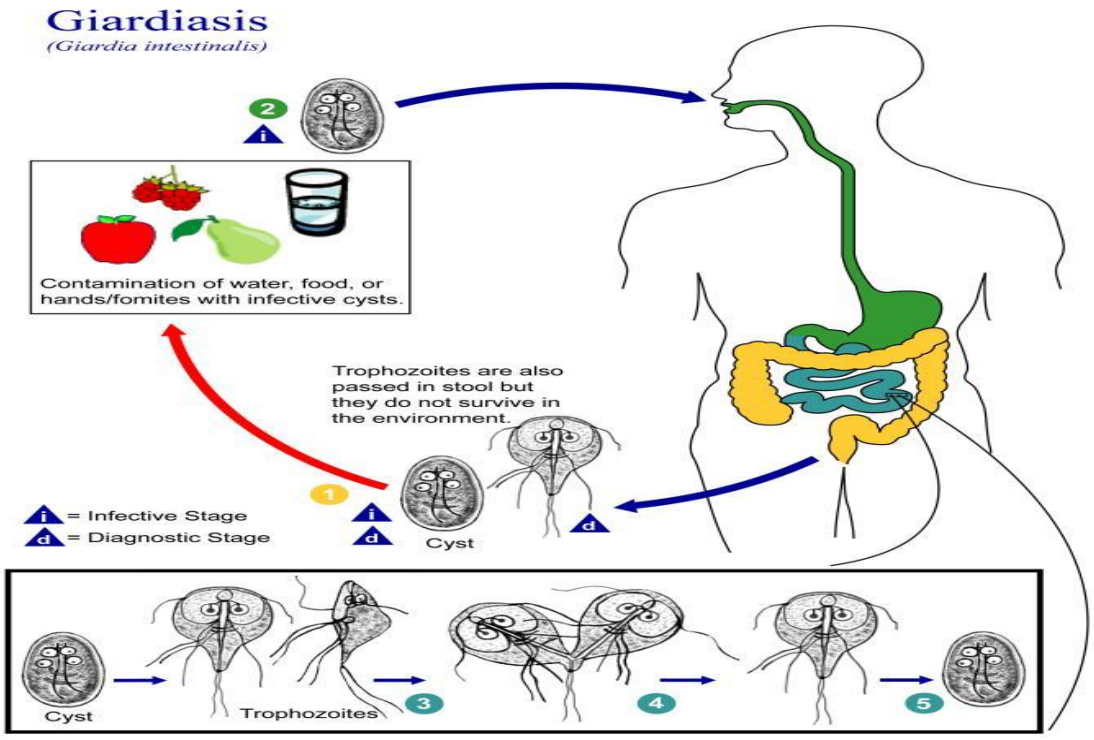
- o It is the active feeding stage of parasite which is responsible for colonization in intestine.
- o The shape of trophozoite is pear shape or tennis racket shape with broad round anterior end and a tapering posterior end.
- o It measures 9-21 µm in length and 5-5µm in breadth.
- o The dorsal surface is convex while ventral surface is concave with a sucking disc (adhesive disc) which acts as an organ for attachment.
- o Behind the adhesive disc lies a pair of large curved and transverse median bodies, unique to
- o It is bilaterally symmetrical and all organs of body are paired. They have two median bodies, two axostyle, two nuclei and four pairs of flagella.
- o Each nucleus consists of large central karyosome giving a characteristic face like appearance to the parasite in stained preparation.
- o Cytoplasm is uniform and finely granulated.
- o Motility shown typical ‘fallling leaf type’ motility.

2. Cyst:

- o It is an infective stage of parasite.
- o A fully mature cyst is oval or ellipsoidal in shape and measures 8-12µm in length and 7-10µm in breadth.

- Cyst is surrounded by a thick cyst wall. Cytoplasm is granulated and is separated from the cyst wall by clear space.
- The axostyle lies more or less diagonally.
- A cyst contains 4 nuclei.
- The remaining of flagella and the margins of sucking disc may be seen inside the cytoplasm.

Life cycle of *Giardia lamblia*:



- Life cycle of G. lamblia is simple and completes in a single host, man. No intermediate host is required.
- Infection is acquired orally by ingestion of cyst from contaminated hand or water or food.
- Excystation occurs in th stomach and in the duodenum in the presence of gastric acid, pancreatic enzymes (chymotrypsin and trypsin). An acidic environment with a pH 1.3-2.7 is required for excystation.

- Each cyst excysts to produce two trophozoites in the duodenum within 30 minutes of ingestion.
- These trophozoites multiplies in the intestine by bunary fission. Then they adhere to enterocytes through their ventral sucker mediated possibly through surface mannose-binding lectin present on the surface of trophozoites.
- Some of the trophozoites then pass down on the large intestine where they again encyst in the presence of neutral pH and bile salts.
- The process of encystation begins with the appearance of encystation specific secretory vesicles (ESVs) in the cytoplasm of trophozoites, followed by production of cyst wall within 15 hours.
- Within 24 hours after appearance of ESVs, the trophozoite is covered with these cyst wall proteins, resulting in formation of cyst.
- Formation of cyst begins by shortening of flagella followed by condensation of cytoplasm and finally secretion of thick hyline cyst wall.
- These encysted trophozoites then undergo another phase of nuclear division and produces quadrinucleated mature cyst.
- The cysts which are the infective form of parasite are excreted in faeces and life cycle is repeated.

Pathogenesis and pathology:

Mode of transmission:

- Man is the main reservoir of Giardia.
- Infection is acquired due to-
    - Ingestion of contaminated food and water
    - Person to person transmission due to poor hygiene in day care centers, nursing homes, mental asylums
    - Sexual transmission-oral-anal and oral-genital sex
- Immunocompromised individuals such as AIDS patients, X-linked gammaglobulinaemia, patients with protein energy malnutrition are more susceptible for giardiasis

Virulence factors:

- Cytoskeleton:
    - Giardia contains microtubules (MT) cytoskeletion which is essential for motility, attachment, intracellular transport, cell division and encystation/excystation.
- Cysts:
    - Cysts are resistant and responsible for transmission of parasite

Pathogenesis of *Giardia lamblia*:

- *Giardia* is intestinal parasite and it is non-invasive.
- Once excystation occurs, trophozoites are releases and they uses their flagella to 'swim' to the microvilli covered surface of duodenum and jejunum where they attach to the enterocytes using their adhesive disc.
- Lectins present on the surface of *Giardia* binds to receptor present on surface of enterocytes. This attachment process damage microvilli, which interfere with nutrition absorption by villi.
- Rapid multiplication of trophozoites eventually creates a physical barriers between the enterocytes and intestinal lumen, further interfering with nutrition absorption. This process leads to enterocytes damage, villi atropy, crypt hyperplasia, intestinal hyperpermeability and brush boarder damage that causes a reduction in disaccharide enzyme secretion.
- Lectins and othere cytopathic substance secreted by parasite also causes indirect damage to intestinal epithelium.
- Trophozoites do not invade or penetrate surrounding tissue or enter blood stream. So, infection is generally restricted to intestinal lumen.
- Giardiasis results in decreased jejunal electrolyte water and glucose absorptiom, and damages to intestinal epithelium leads to malabsorption of electrolyte and fluids, resulting in osmotic diarrhea known as giardiasis.

Clinical manifestation of *Giardia lamblia*:

- Incubation varies from 1-3 weeks
- In majority of cases infection remains asymptomatic.
- Symptomatic infection is more common in children than adults because of their lower immunity.

1. Acute giardiasis:

- It is characterized by acute watery diarrhea, abdominal cramp, bloating and flatulence. Occasionally nausea, vomiting, fever, rashes or constipation in some.
- Pus, blood and mucus are not seen in stool.
- The condition lasts for 5-7 days.

2. Chronic giardiasis:

- Symptoms includes chronic diarrhea with malabsorption of fat (steatorrhoea) and malabsorption of vitamin A, protein and D-xylose, weight loss, malaise, nausea, anorexia
- Protuberance of abdomen, spindly extremities and stunted growth are most common sign in children.
- It lasts for several weeks

3. Extra-intestinal are rare and sometimes urticarial and reactive arthritis are seen in rare case

- **Complication:**
- **In adults, malabsorption syndrome and weight loss**
- In children, growth retardation, delayed milestones achievements
- Giardiasis is self-limited disease and progression to chronic state is only 5% of infected people and death is rare.

Laboratory diagnosis of *Giardia lamblia*:

- **Specimen:**
    - Stool, duodenal contents, bile stained mucus, duodenal/jejunal biopsy

- **Stool examination:**
    - Microscopy:
        - Direct wet mount preparation: trophozoites are identified by their characteristic falling leaf motility
        - Iodine wet mount preparation: cyst can be observed
    - Examination of stained stool smear for demonstration of trophozoitse
    - Concentration method: formalin-ethyl acetate and zinc sulfate concentration method is used to concentrate stool and increase parasite yield for microscopy
    - Stool antigen detection: ELISA, IFA
- **Stool culture**
- **Entero-test:**
    - In entero-test, a gelatin capsule containing a nylon string with a weight attached to it is swallowed by patients.
    - When it reaches to stomach, the gelatin capsule is diddolved and nylon string moves down to duodenum and jejunum due to its attached weight.
    - The string is allowed to remain there for 4-6 hours or overneight.
    - After removal of string, bile stained mucus is collected on glass slide and examined for living trophozoites.
- **Serology**
- **Molecular methods**

Treatment for giardiasis:

- Metronidazole, trinidazole, nitroimidazole derivatives
- Nitrofurans- furazolidine
- * metronidazole is drug of choice. Dose- orally 250mg, 3 times daily for adults, 15mg/kg /day in three divided dose for children for 7 days

Prevention of giardiasis:

Improve water supply

- Proper disposal of human faeces
- Maintenance of good and proper personal hygiene
- Health education at individual as well as community levels
- Identifying the source of infection, particularly in outbreak situation.

****

Trichomonas vaginalis

Introduction

- *Trichomonas vaginalis* is an anaerobic, flagellated protozoan parasite and the causative agent of trichomoniasis.
- It is the most common pathogenic protozoan infection of humans in industrialized countries.
- Infection rates between men and women are similar with women usually being symptomatic, while infections in men are usually asymptomatic.
- Transmission usually occurs via direct, skin-to-skin contact with an infected individual, most often through vaginal intercourse.
- The WHO has estimated that 160 million cases of infection are acquired annually worldwide.
- The estimates for North America alone are between 5 and 8 million new infections each year, with an estimated rate of asymptomatic cases as high as 50%.Usually treatment consists of metronidazole and tinidazole.

Description

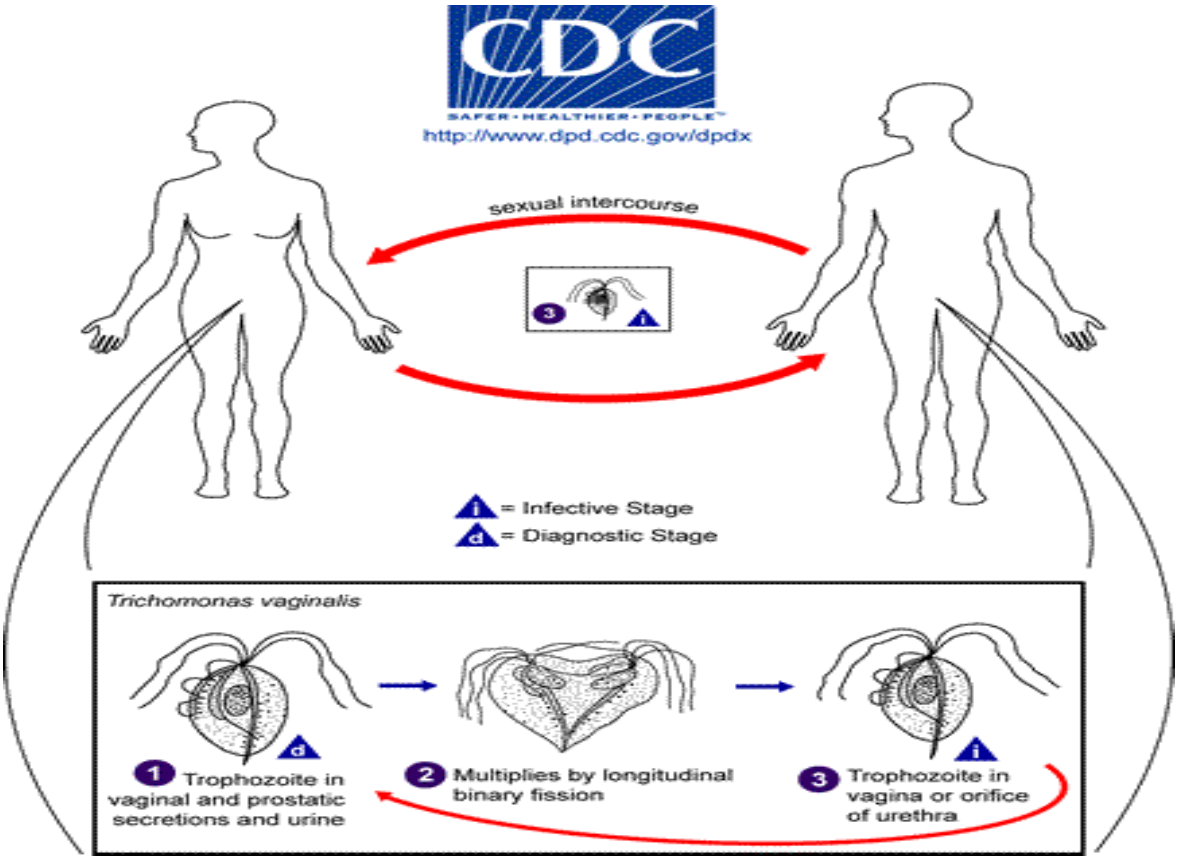
- *Trichomonas vaginalis* exists in only one morphological stage, a trophozoite, and cannot encyst.
- The *T. vaginalis* trophozoite is oval as well as flagellated, or "pear" shaped as seen on a wet-mount.
- It is slightly larger than a white blood cell, measuring 9 × 7 μm.

- Five flagella arise near the cytostome; four of these immediately extend outside the cell together, while the fifth flagellum wraps backwards along the surface of the organism. The functionality of the fifth flagellum is not known.
- In addition, a conspicuous barb-like axostyle projects opposite the four-flagella bundle. The axostyle may be used for attachment to surfaces and may also cause the tissue damage seen in trichomoniasis infections.

While *T. vaginalis* does not have a cyst form, organisms can survive for up to 24 hours in urine, semen, or even water samples**.**

Mechanism of infection

- *Trichomonas vaginalis*, a parasitic protozoan, is the etiologic agent of trichomoniasis, and is a sexually transmitted infection. More than 160 million people worldwide are annually infected by this protozoan.



- Trichomoniasis, a sexually transmitted infection of the urogenital tract, is a common cause of vaginitis in women, while men with this infection can display symptoms of urethritis. 'Frothy', greenish vaginal discharge with a 'musty' malodorous smell is characteristic.

Signs

Only 2% of women with the infection will have a "strawberry" cervix (*colpitis macularis*, an erythematous cervix with pinpoint areas of exudation) or vagina on examination. This is due to capillary dilation as a result of the inflammatory response.

Complications

- complications of *T. vaginalis* in women include: preterm delivery, low birth weight, and increased mortality as well as predisposing to HIV infection, AIDS, and cervical cancer.
- *T. vaginalis* has also been reported in the urinary tract, fallopian tubes, and pelvis and can cause pneumonia, bronchitis, and oral lesions. Condoms are effective at reducing, but not wholly preventing, transmission.
- *Trichomonas vaginalis* infection in males has been found to cause asymptomatic urethritis and prostatitis. It has been proposed that it may increase the risk of prostate cancer; however, evidence is insufficient to support this association as of 2014.

Diagnosis

- ✓ Classically, with a cervical smear, infected women may have a transparent "halo" around their superficial cell nucleus but more typically the organism itself is seen with a slight cyanophilic tinge, faint eccentric nuclei, and fine acidophilic granules.
- ✓ It is unreliably detected by studying a genital discharge or with a cervical smear because of their low sensitivity.
- ✓ *T. vaginalis* was traditionally diagnosed via a wet mount, in which "corkscrew" motility was observed.

- ✓ Currently, the most common method of diagnosis is via overnight culture, with a sensitivity range of 75–95%.
- ✓ Newer methods, such as rapid antigen testing and transcription-mediated amplification, have even greater sensitivity, but are not in widespread use.

✓ The presence of *T. vaginalis* can also be diagnosed by PCR, using primers specific for GENBANK/L23861

Prevention

- If you've had trichomoniasis and it's been treated, you won't be immune to the infection and could get it again.
- Like any sexually transmitted infection (STI), the best way to prevent trichomoniasis is to have safe sex. Use condoms (male or female) every time you have vaginal or anal sex

- If you have oral sex, cover the penis with a condom or the female genitals with a latex or polyurethane square (a dam)
- If you're a woman and rub your vulva against your female partner's vulva, one of you should cover your genitals with a dam
- Avoid sharing sex toys – if you do share them, wash them or cover them with a new condom before anyone else uses them.

Treatment

- ❖ Infection is treated and cured with metronidazole or tinidazole.
- ❖ The CDC recommends a one time dose of 2 grams of either metronidazole or tinidazole as the first-line treatment; the alternative treatment recommended is 500 milligrams of metronidazole, twice daily, for seven days if there is failure of the single-dose regimen.
- ❖ Medication should be prescribed to any sexual partner(s) as well because they may be asymptomatic carriers.

****

Plasmodium vivax

Introduction

Plasmodium vivax is a protozoal parasite and a human pathogen.

- This parasite is the most frequent and widely distributed cause of recurring malaria.
- *P. vivax* malaria infections can lead to severe disease and death, often due to splenomegaly (a pathologically enlarged spleen).
- *P. vivax* is carried by the female *Anopheles* mosquito; the males do not bite.

Epidemiology

- *Plasmodium vivax* is found mainly in Asia, Latin America, and in some parts of Africa.
- *P. vivax* is believed to have originated in Asia, but latest studies have shown that wild chimpanzees and gorillas throughout central Africa are endemically infected with parasites that are closely related to human *P. vivax.*These findings indicate that human P. vivax is of African origin.
- *Plasmodium vivax* accounts for 65% of malaria cases in Asia and South America.
- Central Asia is responsible for 82% of global population at risk .
- South East Asia has areas of high endemicity in Indonesia and Papua New Guinea and overall contributes 9% of global population at risk

P. vivax is carried by at least 71 mosquito species. Many vivax vectors live happily in temperate climates—as far north as Finland.

Pathogenesis

- Pathogenesis results from rupture of infected red blood cells, leading to fever.
- Infected red blood cells may also stick to each other and to walls of capillaries.

- ❖ *Plasmodium vivax* can cause a more unusual form of malaria with atypical symptoms. It has been known to debut with hiccups, loss of taste, lack of fever, pain while swallowing, cough and urinary discomfort.
- ❖ The parasite can go dormant in the liver for days to years, causing no symptoms and remaining undetectable in blood tests. They form what are called hypnozoites, a small stage that nestles inside an individual liver cell. This name derives from "sleeping organisms".

Life cycle

Like all malaria parasites, *P. vivax* has a complex life cycle. It infects a definitive insect host, where sexual reproduction occurs, and an intermediate vertebrate host, where asexual amplification occurs. In *P. vivax*, the definitive hosts are Anopheles mosquitoes (also known as the vector), while humans are the intermediate asexual hosts. During its life cycle, *P. vivax* assumes many different physical forms.

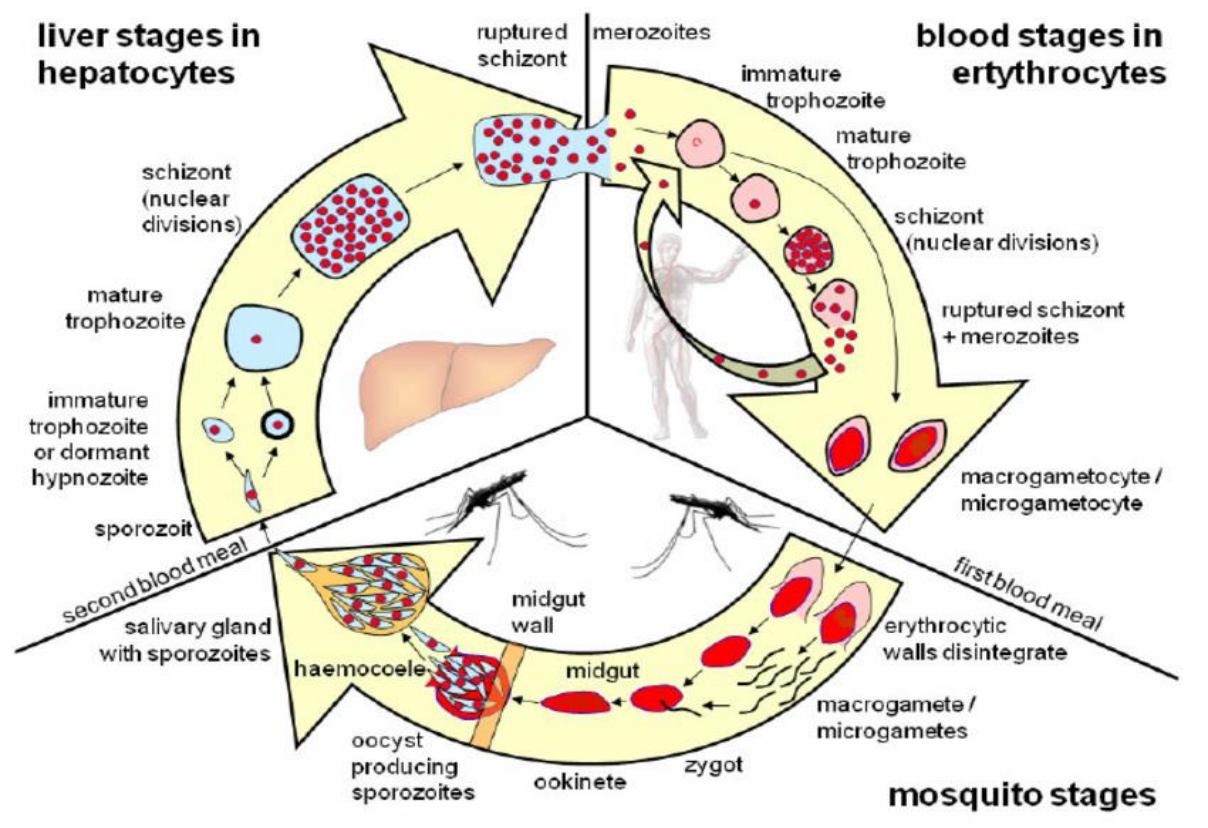
Asexual forms:

- Sporozoite: Transfers infection from mosquito to human
- Immature trophozoites (Ring or signet-ring shaped), about 1/3 of the diameter of a RBC.
- Mature trophozoites: Very irregular and delicate (described as *amoeboid*); many pseudopodial processes seen. Presence of fine grains of brown pigment (malarial pigment) or hematin probably derived from the haemoglobin of the infected red blood cell.
- Schizonts (also called meronts): As large as a normal red cell; thus the parasitized corpuscle becomes distended and larger than normal. There are about sixteen merozoites.

Sexual forms:

- Gametocytes: Round. *P. vivax* gametocytes are commonly found in human peripheral blood at about the end of the first week of parasitemia.
- Gametes: Formed from gametocytes in mosquitoes.
- Zygote: Formed from combination of gametes

- Oocyst: Contains zygote, develops into sporozoites



Liver stage

The *P. vivax* sporozoite enters a hepatocyte and begins its exoerythrocytic schizogony stage. This is characterized by multiple rounds of nuclear division without cellular segmentation. After a certain number of nuclear divisions, the parasite cell will segment and merozoites are formed.

Erythrocytic cycle

P. vivax preferentially penetrates young red blood cells (reticulocytes), unlike *Plasmodium falciparum* which can invade erythrocytes. In order to achieve this, merozoites have two proteins at their apical pole (PvRBP-1 and PvRBP-2). The parasite uses the Duffy blood group antigens (Fy6) to penetrate red blood cells. The parasite within it is often wildly irregular in shape (described as "amoeboid"). Schizonts of *P. vivax* . have up to twenty merozoites within them

Mosquito stage

Parasite life cycle in mosquitoes includes all stages of sexual reproduction:

1. Infection and Gametogenesis
    - Microgametes
    - Macrogametes
2. Fertilization
3. Ookinite
4. Oocyst
5. Sporogony

Mosquito Infection and Gamete Formation

When a female Anopheles mosquito bites an infected person, gametocytes and other stages of the parasite are transferred to the mosquito stomach. Gametocytes ultimately develop into gametes, a process known as gametogony.

The cytoplasm develops long thin flagella like projections, then a nucleus enter into each one of these extensions. These cytoplasmic extensions later break off as mature male gametes (microgametes). This process of formation of flagella-like microgametes or male gametes is known as exflagellation. They develop a cone of reception at one side and becomes mature as macrogametocytes (female gametes).

Fertilization

Male gametes move actively in the stomach of mosquitoes in search of female gametes. Male gametes then enter into female gametes through the cone of reception. The complete fusion of 2 gametes results in the formation of zygote. Here, fusion of 2 dissimilar gametes occurs, known as anisogamy.

The zygote remains inactive for sometime but it soon elongates, becomes vermiform (worm-like) and motile. It is now known as **ookinete**

. The pointed ends of ookinete penetrate the stomach wall and come to lie below its outer epithelial layer. Here the zygote becomes spherical and develops a cyst wall around itself.

The cyst wall is derived partly from the stomach tissues and partly produced by the zygote itself. At this stage, the zygote is known as an **oocyst**

. The oocyst absorbs nourishment and grows in size. Oocysts protrude from the surface of stomach, giving it a blistered appearance. In a highly infected mosquito, as many as 1000 oocysts may be seen.

Sporogony

The oocyst nucleus divides repeatedly to form large number of daughter nuclei. At the same time, the cytoplasm develops large vacuoles and forms numerous cytoplasmic masses. These cytoplasmic masses then elongate and a daughter nuclei migrates into each mass. The resulting sickle-shaped bodies are known as sporozoites. This phase of asexual multiplication is known as sporogony and is completed in about 10–21 days. The oocyst then bursts and sporozoites are released into the body cavity of mosquito

Diagnosis

- *P. vivax* has been sitting in EDTA for more than 30 minutes before the blood film is made will look very similar in appearance to *P. malariae,*
- . Blood films are preferably made within 30 minutes of the blood draw and must certainly be made within an hour of the blood being drawn.
- Diagnosis can be done with the strip fast test of antibodies**.**

Prevention:

The main way to prevent malaria is through vector control. There are mostly three main forms that the vector can be controlled:

(1) Insecticide-treated mosquito nets,

(2)Indoor residual spraying

(3) Antimalarial drugs.

- Long-lasting insecticidal nets (LLNs) are the preferred method of control because it is the most cost effective.
- The WHO is currently strategizing indoor residual spraying and has been proven effective if at least 80% of the homes are sprayed. However, such method is only effective for 3-6months.
- A drawback to these two methods, unfortunately, is that mosquito resistance against these insecticides has risen.
- Lastly, antimalarial drugs can also be used to prevent infection from developing into a clinical disease. However, there has also been an increase resistance to antimalarial medicine.
- In 2015 the World Health Organization (WHO) drew up a plan to address vivax malaria, as part of their Global Technical Strategy for Malaria.

Treatment

- Chloroquine remains the treatment of choice for *vivax* malaria.
- When chloroquine resistance is common or when chloroquine is contraindicated, then artesunate is the drug of choice, except in the U.S., where it is not approved for use Where an artemisinin-based combination therapy used for P. vivax malaria in combination with primaquine for radical cure.
- An exception is artesunate plus sulfadoxine-pyrimethamine (AS+SP), which is not effective against P. vivax in many places
- Mefloquine is a good alternative and in some countries is more readily available.
- Atovaquone-proguanil is an effective alternative in patients unable to tolerate chloroquine.

- Quinine may be used to treat *vivax* malaria but is associated with inferior outcomes.32–100% of patients will relapse following successful treatment of *P. vivax* infection if a radical cure (eradication of liver stages) is not given.
- Eradication of the liver stages is achieved by giving primaquine.
- In 2013 a Phase IIb trial was completed that studied a single-dose alternative drug named tafenoquine.

****

Leishmania donovani

Introduction

- *Leishmania donovani* is a species of intracellular parasites belonging to the genus *Leishmania*, a group of haemoflagellate kinetoplastids that cause the disease leishmaniasis.
- It is a human blood parasite responsible for visceral leishmaniasis or *kala-azar*, the most severe form of leishmaniasis.
- It infects the mononuclear phagocyte system including spleen, liver and bone marrow. Infection is transmitted by species of sandfly
- The parasite is prevalent throughout tropical and temperate regions including Africa , China, India, Nepal, southern Europe, Russia and South America
- *L. donovani* was independently discovered by two British medical officers William Boog Leishman in Netley, England, and Charles Donovan in Madras, India, in 190
- .. The parasite requires two different hosts for a complete life cycle, humans as the definitive host and sandflies as the intermediate host. In some parts of the world other mammals, especially canines, act as reservoir hosts

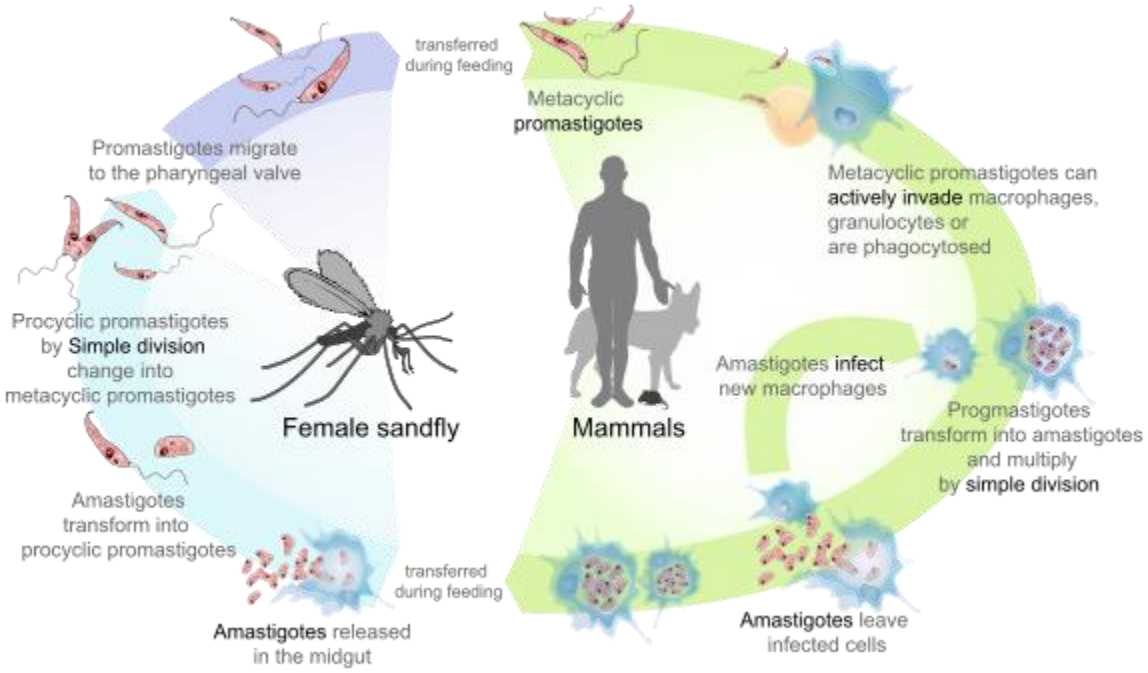
Structure:

Leishmania donovani is a unicellular eukaryote having a well-defined nucleus and other cell organelles including a kinetoplast and a flagellum.

Depending on its host it exists in two structural variants, as follows:

1. **Amastigote form** found in the mononuclear phagocyte and circulatory systems of humans. It is an intracellular and non-motile form, being devoid of external flagellum embedded in the anterior end without projecting out. It is oval in shape, and measures 3–6 μm in length and 1–3 μm in breadth.
2. **Promastigote** is formed in the alimentary tract of the sandfly. It is an extracellular and motile form. It is considerably larger and more highly elongated, measuring 15–30 μm in length and 5 μm in width,spindle-shaped, tapering at both ends. A long flagellum (about the body length) is projected externally at the anterior end. The nucleus lies at the centre, and in front of which are kinetoplast and basal body.

Life cycle:



Life cycle of *Leishmania donovani*

Leishmania donovani is a digenetic parasite passing its life cycle in two different hosts.

Definitive host

- In humans the metacyclic promastigotes are injected by sandfly through the skin during its blood meal. When sandfly bites using its proboscis it ejects the parasites that are stored inside the hollow tube. Some promastigotes may enter the blood stream directly where some are destroyed by macrophagic cytolysis. But many are also taken up through phagocytosis by mononuclear phagocytes in liver, spleen and bone marrow.
- Inside the cells they undergo spontaneous transformation into oval-shaped amastigotes. Granulocytes selectively kill the promastigotes by oxidative mechanism, while amastigotes are resistant.
- Then the surviving amastigotes undergo cell division using simple binary fission. Multiplication continues until the host cell can no longer hold and ruptures.
- In a fully congested cell there can be as many as 50 to 200 amastigotes, which are released into tissue cavities. Each individual amastigote is then capable of invading fresh cells. As a result, the entire tissue is progressively infected and destroyed.
- A number of free amastigotes then enters the blood stream where many are phagocytosed by macrophages. These free and phagocytosed amastigotes in peripheral blood are then sucked up by blood-feeding sandfly.

Intermediate host:

- *L. donovani* undergo further development only in the digestive tract of the female sandfly. Hence only females are responsible for transmitting the infection.
- Once the amastigotes are ingested, they enter the midgut of the sandfly. Then they undergo structural modification into flagellated promastigotes, becoming larger and considerably elongated.
- They get attached to the gut epithelial lining where they multiply rapidly by binary fission.
- They then migrate back towards the anterior part of the digestive system such as pharynx and buccal cavity. This process is known as anterior station development, which is unique in *Leishmania*.
- A heavy infection of pharynx can be observed within 6 to 9 days after initial blood meal. The promastigotes become infective only by this time, and the event is called the metacyclic stage.

Reservoir host

- Dogs are known to be susceptible to *L. donovani* infection.
- Especially in the New World, infection is a zoonotic disease, involving different canine species, including domestic dog and the two fox species, *Lycalopex vetulus* and *Cerdocyon thous*.
- In the Mediterranean region domestic dogs and fox. In Africa and Brazil, some marsupials and rodents are also reported to harbour *L. donovani*.

Epidemiology:

It is estimated that visceral leishmaniasis (VL) affects more than 100 million people worldwide, with 500,000 new cases and more than 50,000 deaths each year.

In India it is prevalent in the eastern region including Bihar, West Bengal, eastern Uttar Pradesh, Assam and foothills of Sikkim. It is responsible for tens of thousands of mortality

Pathogenicity

L. donovani is the causative agent of visceral leishmaniasis, traditionally known as *kala-azar* ("black fever", particularly in India), because of its characteristic symptoms.

The disease is highly lethal if not treated properly.

The incubation period generally ranges from 3 to 6 months, and in some cases may be over a year. In Indian leishmaniasis, incubation can be as short as 10 days.

The target cells are those of mononuclear phagocyte system. The two main tissues of infection are spleen and liver.

Clinical symptoms

- Include pyrexia (recurring high fever which may be continuous or remittent), enlargement of spleen and liver, and heavy skin pigmentation which darkens the physical appearance (the reason for naming "black fever").
- To a lesser extent mucosa of the small intestine and lymph nodes are also invaded by the parasite.
- Morphological symptoms are noticeable particularly on facial and abdominal regions. Skin becomes coarse and hard.
- In African infections, warty eruptions are common. In a fully developed stage, the patient shows emaciation and anaemia. Where medical facilities are poor, mortality can be as high as 75–95% within 2 years of epidemics.
- The disease is often accompanied by complications with dysentery, tuberculosis, septicaemia and even HIV infection.

Treatment:

The conventional treatment method is an intravenous injection with antimony compounds, such as pentostam. Unfortunately, these chemotherapeutics are so poisonous that about 15% of the patients die from the treaments.

1. Another antimicrobial drug amphotericin B is also commonly used. Liposomal amphotericin B (L-AmB) has been a drug of choice in India.Further, amphotericin B has severe adverse effects. Its acute effects includes nausea, vomiting, rigors, fever, hypertension or hypotension, and hypoxia, and its chronic effect is nephrotoxicity.
2. In 1999 an anticancer drug miltefosine was demonstrated to be highly effective (95% cure rate) among Indian patients,this oral drug is effective for visceral leishmaniasis.
3. Clinical trials showed that the new drug is relatively harmless. The most adverse effects were only vomiting and diarrhoea in 20–28% patients, which were rather mild. The drug has been officially approved in India. The recommended dosage is 100 mg per day over a period of four weeks.

Prevention & Control

- No vaccines or drugs to prevent infection are available.
- The best way for travelers to prevent infection is to protect themselves from sand fly bites.
- To decrease the risk of being bitten, follow these preventive measures:
- Avoid outdoor activities, especially from dusk to dawn, when sand flies generally are the most active.

When outdoors (or in unprotected quarters):

- Minimize the amount of exposed (uncovered) skin.
- To the extent that is tolerable in the climate, wear long-sleeved shirts, long pants, and socks; and tuck your shirt into your pants.
- Apply insect repellent to exposed skin and under the ends of sleeves and pant legs. The most effective repellents generally are those that contain the chemical DEET (N,N-diethylmetatoluamide.

When indoors:

- Stay in well-screened or air-conditioned areas.
- Keep in mind that sand flies are much smaller than mosquitoes and therefore can get through smaller holes.
- Spray living/sleeping areas with an insecticide to kill insects.
- If you are not sleeping in a well-screened or air-conditioned area, use a bed net and tuck it under your mattress
- . If possible, use a bed net that has been soaked in or sprayed with a pyrethroid-containing insecticide.
- The same treatment can be applied to screens, curtains, sheets, and clothing (clothing should be retreated after five washings).

Taenia solium

Introduction

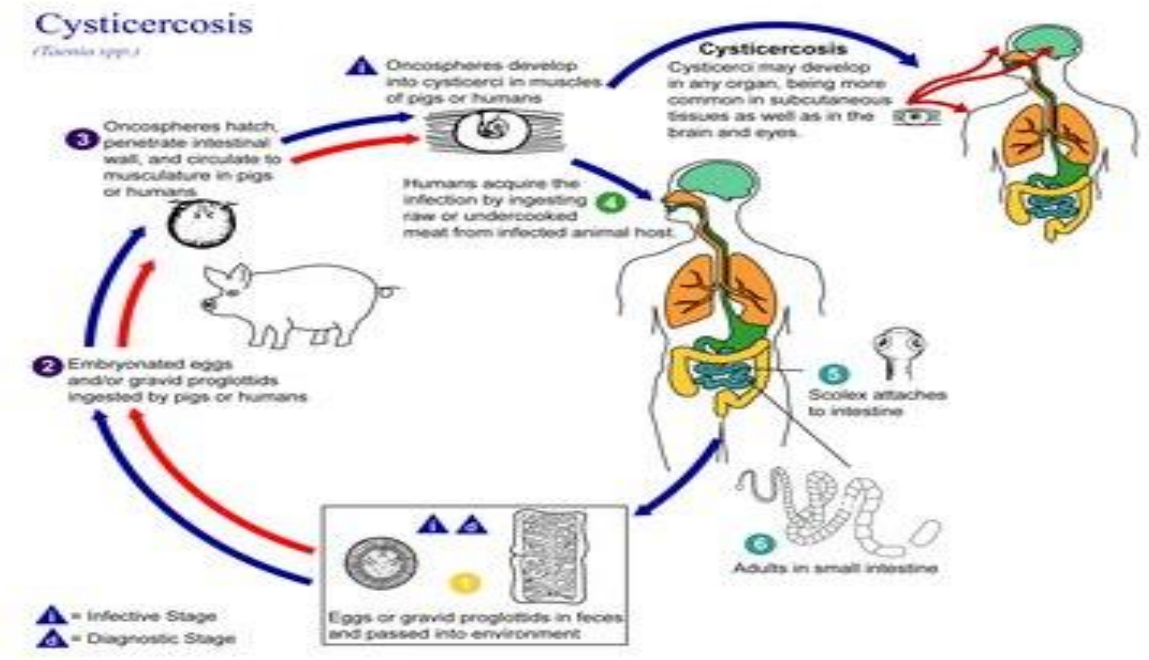
- *Taenia solium* is the pork tapeworm, a tapeworm belonging to the cyclophyllid cestode family Taeniidae.
- It is found throughout the world and is most common in countries where pork is eaten.
- There are two forms. One is due to eating undercooked pork that contains the cysts and results in adult worms in the intestine.The other, known as cysticercosis, is due to eating food or water contaminated with feces from someone infected by the adult worms.
- The adult worm has humans as its main host and has a flat, ribbon-like body which is white and measures 2 to 3 metres long or more.
- Its tiny long attachment, the scolex, contains duodenum wall-suckers and a rostellum as organs of attachment. The main body, the strobila, consists of a chain of segments known as proglottids.

It completes its life cycle in humans as the definitive host and often pigs as intermediate or secondary host.

Epidemiology

- *T. solium* is found worldwide, but its two distinctive forms rely on eating undercooked pork or on ingesting feces-contaminated water or food (respectively).
- . High prevalences are reported among many places with poorer than average water hygiene or even mildly contaminated water especially with a pork-eating heritage such as Mexico, Latin America, West Africa, Russia, India, Manchuria, and Southeast Asia
- The secondary host form, human cysticercosis, predominates in areas where poor hygiene allows for mild fecal contamination of food, soil, or water supplies
- Rates in the United States have shown immigrants from Mexico, Central and South America, and Southeast Asia bear the brunt of cases of cysticercosis caused by the ingestion of microscopic, long-lasting and hardy tapeworm egg

Life cycle



Lifecycle of *T. solium*

- The life cycle of *T. solium* is indirect. It passes through pigs or other animals, as intermediate hosts, into humans, as definitive hosts.
- In humans the infection can be relatively short or long lasting, and in the latter case if reaching the brain can last for life.
- From humans, the eggs are released in the environment where they await ingestion by another host.
- In the secondary host, the eggs develop into oncospheres which bore through the intestinal wall and migrate to other parts of the body where the cysticerci form. The cysticerci can survive for several years in the animal.[11]

Definitive host:

- Humans are colonised by the larval stage, the cysticercus, from undercooked pork or other meat. Each microscopic cysticercus is oval in shape, containing an inverted scolex (specifically "protoscolex"), which everts once the organism is inside the

small intestine. This process of evagination is stimulated by bile juice and digestive enzymes (of the host).

- ❖ Then, the T. Solium lodges in the host's upper intestine by using its crowned hooks and 4 suckers to enter the intestinal mucosa.
- ❖ Then, the scolex is fixed into the intestine by having the suckers attached to the villi and hooks extended. It grows in size using nutrients from the surroundings.
- ❖ Its strobila lengthens as new proglottids are formed at the foot of the neck. In 10–12 weeks after initial colonization, it is an adult worm.
- ❖ The exact life span of an adult worm is not determined; however, evidences from an outbreak among British military in the 1930s indicate that they can survive 2 to 5 years in humans.

Intermediate host:

- Pigs are the most common host who ingest such eggs in traces of human faeces, mainly from vegetation contaminated with it such as from water bearing traces of it.
- The embryonated eggs enter intestine where they hatch into motile oncospheres.
- The embryonic and basement membranes are removed by the host's digestive enzymes (particularly pepsin).
- Then the free oncospheres attach on the intestinal wall using their hooks. With the help of digestive enzymes from the penetration glands, they penetrate the intestinal mucosa to enter blood and lymphatic vessels.
- They move along the general circulatory system to various organs, and large numbers are cleared in the liver.
- The surviving oncospheres preferentially migrate to striated muscles, as well as the brain, liver, and other tissues, where they settle to form cysts — cysticerci.
- A single cysticercus is spherical, measuring 1–2 cm in diameter, and contains an invaginated protoscolex.

Humans are also accidental secondary hosts when they are colonised by embryonated eggs, either by auto-colonisation or ingestion of contaminated food. As in pigs, the oncospheres hatch and enter blood circulation.

Signs and symptoms

Taeniasis

Taeniasis is infection in the intestines by the adult *T. solium*. It generally has mild or non-specific symptoms. This may include abdominal pain, nausea, diarrhea and constipation. S

symptoms continue until the tapeworm dies from the course of treatment but otherwise could continue for many years, as long as the worm lives. If untreated it is common that the infections with *T. solium* last for approximately 2–3 years. It is possible that infected people may show no symptoms for years

Cysticercosis

- Ingestion of *T. solium* eggs or egg-containing proglottids which rupture within the host intestines results in the development and subsequent migration of larvae into host tissue to cause cysticercosis.
- In pigs, there are not normally pathological lesions as they easily develop immunity. But in humans, infection with the eggs causes serious medical conditions. This is because *T. solium* cysticerci have a predilection for the brain.
- In symptomatic including headaches, dizziness, and seizures. Brain infection by the cysticerci is called neurocysticercosis and is the leading cause of seizures worldwide.
- In more severe cases, dementia or hypertension can occur due to perturbation of the normal circulation of cerebrospinal fluid.
- In many cases, cysticercosis in the brain can lead to epilepsy, seizures, lesions in the brain, blindness, tumour-like growths, and low eosinophil levels. It is the cause of major

neurological problems, such as hydrocephalus, paraplegy, meningitis, convulsions, and even death.

Diagnosis

Stool tests

The microscopic examination of stools to determine the amount of eggs.

Stool tapeworm antigen detection:

Using ELISA increases the sensitivity of the diagnosis.

The downside of this tool is it has high costs, an ELISA reader and reagents are required and trained operators are needed.

Stool PCR:

This method can provide a species-specific diagnosis when proglottid material is taken from the stool. This method requires specific facilities, equipment and trained individuals to run the tests. This method has not yet been ested in controlled field trials.

Serum antibody tests:

Using immunoblot and ELISA, tape-worm specific circulating antibodies have been detected. The assays for these tests have both a high sensitivity and specificity.

Prevention

- The best way to avoid getting tapeworms is to not eat undercooked pork or vegetables contaminated with feces.
- Moreover, a high level of sanitation and prevention of faecal contamination of pig feeds also plays a major role in prevention.

- ❖ Infection can be prevented with proper disposal of human faeces around pigs, cooking meat thoroughly or freezing the meat at −10 °C for 5 days.
- ❖ For human cysticercosis, dirty hands are attributed to be the primary cause, and especially common among food handlers.

Treatment

- Treatment of cysticercosis must be carefully monitored for inflammation reactions to the dying worms, especially if they have moved into the brain.
- In some cases the worms can be surgically removed, and in others albendazole with steroids is given to reduce the inflammation.
- A vaccine to prevent cysticercosis in pigs has been studied.
- The life-cycle of the parasite can be terminated in their intermediate host, pigs, thereby preventing further human infection. The large scale use of these vaccine, however, is still under consideration.]

****

Ascaris lumbricoides

INTRODUCTION

- Ascaris lumbricoides, an intestinal roundworm, is one of the most common helminthic human infections worldwide.
- Highest prevalence in tropical and subtropical regions, and areas with inadequate sanitation. Ascariasis occurs in rural areas of the southeastern United States.
- In United States, ascariasis is the third most frequent helminth infection, exceeded only by hookworm and Trichuris trichiura (whipworm)
- *A. lumbricoides* is the largest intestinal nematode of man.

- The female worms are larger than the males and can measure 40 cm in length and 6 mm in diameter.
- They are white or pink and are tapered at both ends.

EPIDEMIOLOGY

- ❖ It is estimated that more than 1.4 billion people are infected with A. lumbricoides, representing 25 percent of the world population.
- ❖ A number of features account for its high prevalence including a ubiquitous distribution, the durability of eggs under a variety of environmental conditions, the high number of eggs produced per parasite, and poor socioeconomic conditions that facilitate its spread.
- ❖ Transmission is enhanced by the fact that individuals can be asymptomatically infected and can continue to shed eggs for years, yet prior infection does not confer protective immunity

- ❖ Although ascariasis occurs at all ages, it is most common in children 2 to 10 years old, and prevalence decreases over the age of 15 years.
- ❖ Infections tend to cluster in families, and worm burden correlates with the number of people living in a home .
- ❖ Infection rates for ascariasis have not been reported to be higher in patients infected with the human immunodeficiency virus (HIV)

The highest prevalence of ascariasis occurs in tropical countries where warm, wet climates , this contrasts to the situation in dry areas where transmission is seasonal, occurring predominantly during the rainy months .The prevalence is also greatest in areas where suboptimal sanitation practices lead to increased contamination of soil and water.

Transmission

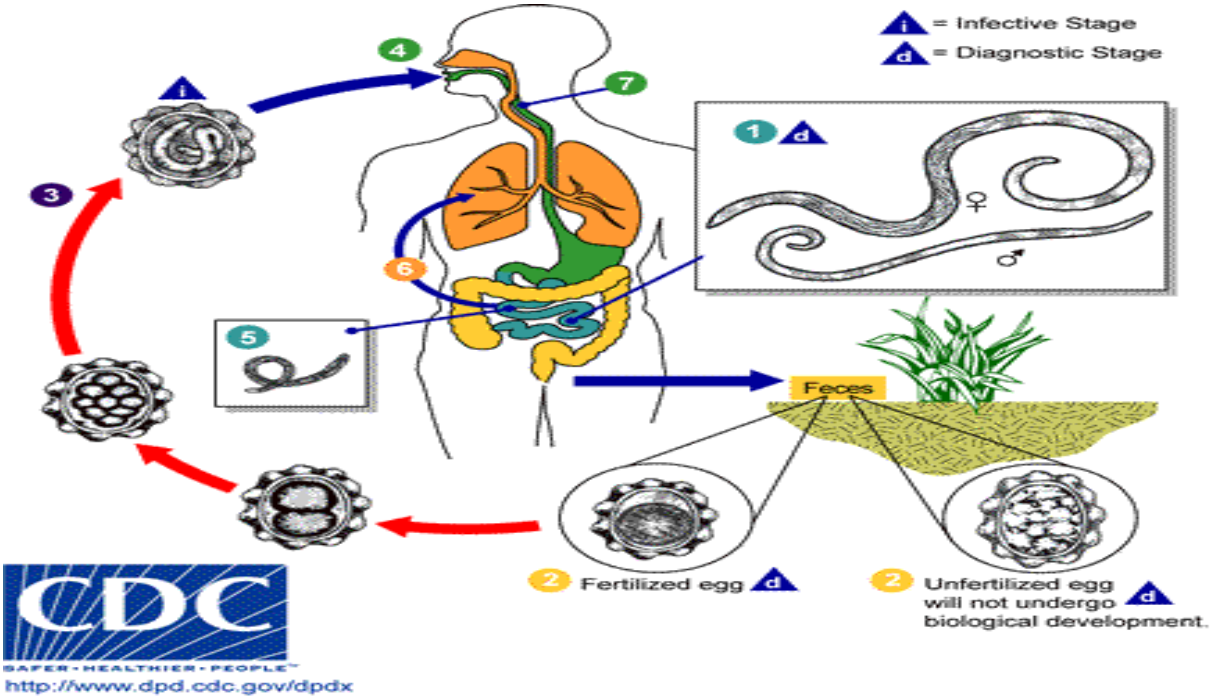
- Transmission occurs mainly via ingestion of water or food (raw vegetables or fruit in particular) contaminated with A. lumbricoides eggs and occasionally via inhalation of contaminated dust.
- Children playing in contaminated soil may acquire the parasite from their hands.
- Transplacental migration of larvae has also occasionally been reported . Coinfection with other parasitic diseases occurs with some regularity because of similar predisposing factors for transmission.

LIFE CYCLE

- Adult worms inhabit the lumen of the small intestine, usually in the jejunum or ileum. They have a life span of 10 months to 2 years and then are passed in the stool.
- When both female and male worms are present in the intestine, each female worm produces approximately 200,000 fertilized ova per day.
- When infections with only female worms occurs, infertile eggs that do not develop into the infectious stage are produced. With male-only worm infections, no eggs are formed.
- The ova are oval, have a thick shell, a mamillated outer coat, and measure 45 to 70 μm by 35 to 50 μm. The ova are passed out in the feces, and embryos develop into infective second-stage larvae in the environment in two to four weeks (depending upon environmental conditions).
- When ingested by humans, the ova hatch in the small intestine and release larvae, which penetrate the intestinal wall and migrate hematogenously or via lymphatics to the heart and lungs. Occasionally, larvae migrate to sites other

than the lungs, including to the kidney or brain.

- Larvae usually reach the lungs by four days after ingestion of eggs. Within the alveoli of the lungs, the larvae mature over a period of approximately 10 days, then pass up via bronchi and the trachea, and are subsequently swallowed.
- Once back in the intestine, they mature into adult worms. Although the majority of worms are found in the jejunum, they may be found anywhere from the esophagus to the rectum.
- After approximately two to three months, gravid females will begin to produce ova which, when excreted, complete the cycle.
- Adult worms do not multiply in the human host, so the number of adult worms per infected person relates to the degree of continued exposure to infectious eggs over time.



Life Cycle Figure – Adult worms (1) live in the lumen of the small intestine. A female may produce

approximately 200,000 eggs per day, which are passed with the feces (2). Unfertilized eggs may be ingested but are not infective. Fertile eggs embryonate and become infective after 18 days to several weeks (3), depending on the environmental conditions (optimum: moist, warm, shaded soil). After infective eggs are swallowed (4), the larvae hatch (5), invade the intestinal mucosa, and are carried via the portal, then systemic circulation to the lungs (6). The larvae mature further in the lungs (10 to 14 days), penetrate the alveolar walls, ascend the bronchial tree to the throat, and are swallowed (7). Upon reaching the small intestine, they develop into adult worms (1). Between 2 and 3 months are required from ingestion of the infective eggs to oviposition by the adult female. Adult worms can live 1 to 2 years. Source: CDC's Parasite and Health Page about intestinal ascariasis

CLINICAL FEATURES

- The majority of infections with A. lumbricoides are asymptomatic. However, the burden of symptomatic disease worldwide is still relatively high because of the high prevalence of disease.
- Clinical disease is largely restricted to individuals with a high worm load .
- When symptoms do occur, they relate either to the larval migration stage or to the adult worm intestinal stage.

Pathophysiologic mechanisms include

- Direct tissue damage
- The immunologic response of the host to infection with larvae, eggs or adult worms
- Obstruction of an orifice or the lumen of the gastrointestinal tract by an aggregation of worms
- Nutritional sequelae of infection

The symptoms and complications of infection can be classified into the following

1. Pulmonary and hypersensitivity manifestations
2. Intestinal symptoms
3. Intestinal obstruction
4. Hepatobiliary and pancreatic symptoms

1. **Pulmonary and hypersensitivity manifestations —** Transient respiratory symptoms can occur in sensitized hosts during the stage of larval migration through the lungs.. Symptoms associated with the pneumonitis, which are known as Loffler's syndrome, tend to occur one to two weeks after ingestion of the eggs. The severity of symptoms tends to correlate with larval burden, but pulmonary symptoms are also less common in countries with continuous transmission of A. lumbricoides.

   Urticaria and other symptoms related to hypersensitivity usually occur toward the end of the period of migration through the lungs.

2. Intestinal symptoms

- Heavy infections provide abdominal discomfort, anorexia, nausea and diarrhea
- With relatively heavy infections, impaired absorption of dietary proteins, lactose and vitamin A has been noted, and steatorrhea may occur.

3. Intestinal obstruction

- A mass of worms can obstruct the bowel lumen in heavy Ascaris infection, leading to acute intestinal obstruction. The obstruction occurs most commonly at the ileocecal valve. Symptoms include colicky abdominal pain, vomiting and constipation. Vomitus may contain worms.
- Approximately 85 percent of obstructions occur in children . Complications including volvulus, ileocecal intussusception, gangrene,

and intestinal perforation occasionally result.

4.Hepatobiliary and pancreatic symptoms

- The migration of adult worms into the biliary tree can cause abdominal pain, biliary colic, acalculous cholecystitis, ascending cholangitis, obstructive jaundice, or bile duct perforation with peritonitis.
- Hepatic abscesses can also result . Retained worm fragments can serve as a nidus for recurrent pyogenic cholangitis. The pancreatic duct may also be obstructed, leading to pancreatitis, and the appendix resulting in appendicitis.
- Occasionally, migrating adult worms emerge from the mouth, nose, lacrimal ducts, umbilicus or inguinal canal. High fever, diarrhea, spicy foods, anesthesia and other stresses have all been associated with an increased likelihood of worm migration.

DIAGNOSIS

The diagnosis of ascariasis is usually made via stool microscopy. Other forms of diagnosis are through eosinophilia, imaging, ultrasound, or serology examination.

- **Microscopy** — Characteristic eggs may be seen on direct examination of feces or following concentration techniques. However, eggs do not appear in the stool for at least 40 days after infection; thus, the main drawback of relying upon eggs in feces as the sole diagnostic marker for Ascaris infection is that an early diagnosis cannot be made, including during the phase of respiratory symptoms.
- In addition, no eggs will be present in stool if the infection is due to male worms only. Sometimes an adult worm is passed, usually per rectum. If an Ascaris worm is found in the feces, a stool specimen can be checked for eggs to document whether or not additional worms are present prior to instituting

therapy .

Prevention

Preventing any fecal-borne disease requires educated hygienic habits/culture and effective fecal treatment systems. This is particularly important with *A. lumbricoides* because its eggs are one of the most difficult pathogens to kill , and the eggs commonly survive 1–3 years.

lumbricoides lives in the intestine where it lays eggs. Infection occurs when the eggs, too small to be seen by the unaided eye, are eaten. The eggs may get onto vegetables when improperly processed human feces of infected people are used as fertilizer for food crops.

A. Infection may occur when food is handled without removing or killing the eggs on the hands, clothes, hair, raw vegetables/fruit, or cooked food that is (re)infected by handlers, containers, etc.

B. Bleach does not readily kill *A. lumbricoides* eggs, but it will remove their sticky film, to allow the eggs to be rinsed away.

C. *A. lumbricoides* eggs can be reduced by hot composting methods, but to completely kill them may require rubbing alcohol, iodine, specialized chemicals, cooking heat, or "unusually" hot composting (for example, over 50 °C (122 °F) for 24 hours¨

TREATMENT

Treatment consists of choosing the right drugs, therapy, follow-up, and supportive care for each patient.

Choice of Drugs — A number of drugs can be used in the treatment of ascariasis. These include: pyrantel pamoate, mebendazole, albendazole, ivermectin, piperazine citrate, and levamizole.

* **Pyrantel pamoate —** Pyrantel pamoate (11 mg/kg up to a maximum of 1 g) is administered as a single dose. Adverse effects include gastrointestinal (GI) disturbances, headaches, rash, and fever.

* **Mebendazole —** Mebendazole (100 mg BID for 3 days or 500 mg as a single dose) is an alternative. Adverse effects include transient GI discomfort, headache, and rarely leukopenia. The three-day regimen is approximately 95 percent effective, and the single dose seems to have similar results.

* **Albendazole —** A single dose of albendazole (400 mg) is effective in almost 100 percent of cases, although reinfection commonly occurs . Albendazole causes the same adverse effects as mebendazole.

* **Ivermectin —** Ivermectin causes paralysis of adult worms and is approximately as effective as other available therapies but is not generally used.

* **Piperazine citrate —** Piperazine citrate (50 to 75 mg/kg QD up to a maximum of 3.5 g for 2 days) was a frequent treatment regimen.

* **Levamisole —** Levamisole (150 mg for adults and 5 mg/kg for children) is safe and is effective in 77 to 96 percent of cases of ascariasis.

Choice of therapy

The mainstays of treatment currently are the benzimidazoles, mebendazole and albendazole. However, they should not be given

during pregnancy because of possible teratogenic effects.Thus, pyrantel pamoate should be used in pregnancy.

Supportive care

In addition to specific anthelminthic therapy, supportive therapy for complications of ascariasis may be required, including potential surgical intervention for intraabdominal complications.

In biliary infections, conservative therapy with anthelminthics, often combined with antispasmodics, is often successful. However, surgical or endoscopic interventions may be required.

****

Ancylostoma duodenal

Introduction

- *Ancylostoma duodenale* is a species of the roundworm genus *Ancylostoma*.
- It is a parasitic nematode worm and commonly known as the Old World hookworm.
- It lives in the small intestine of hosts such as humans, cats and dogs, where it is able to mate and mature. *Ancylostoma duodenale* and *Necator americanus* are the two human hookworm species that are normally discussed together as the cause of hookworm infection.
- *Ancylostoma duodenale* is abundant throughout the world, including Southern Europe, North Africa, India, China, southeast Asia, some areas in the United States, the Caribbean, and South America.

Characteristics:

A. *A.duodenale* is small, cylindrical worm, greyish-white in color.

B. It has two ventral plates on the anterior margin of the buccal capsule. Each of them has two large teeth that are fused at their bases.

C. A pair of small teeth can be found in the depths of the buccal capsule. Males are 8–11 mm long with a copulatory bursa at the posterior end.

D. Females are 10–13 mm long, with the vulva located at the posterior end; females can lay 10,000 to 30,000 eggs per day. The average lifespan of *A. duodenale* is one year

Epidemiology

A.duodenale is prevalent in Southern Europe, North Africa, India, China, Southeast Asia, small areas of United States, the Caribbean islands, and South America.

- This hookworm is well known in mines because of the consistency in temperature and humidity that provides an ideal habitat for egg and juvenile development.
- An estimated 1 billion people are infected with hookworms

Transmission

* *A. duodenale* is by contact of skin with soil contaminated with larvae

Infection

A light hookworm infection causes abdominal pain, loss of appetite, and geophagy.

Heavy infection causes severe protein deficiency or iron-deficiency anemia.

Protein deficiency may lead to dry skin, edema, and abdominal extension from edema (potbelly), while iron-deficiency anemia might result in mental dullness and heart failure.

Women who are pregnant and infected should be aware that this parasite is able to infect the fetus and can cause complications such as low birth weight, maternal anemia, and infant mortality

Life cycle:

Hookworm infection begins when the worm is in the larval stage. The infective stage of hookworm is known as filariform larva (fig. 9.21). It penetrates the skin and migrates during its life cycle through the liver and the lungs, and it attaches to the mucosa of the small intestine.

The larva matures into adult in the small intestine, where the female worms may produce several thousand eggs a day. The eggs are released into the faeces and live on soil. Embryonated egg on soil hatch into juvenile 1 stage (rhabddtiform or noninfective stage) and mature into filariform larvae. It starts a new reproductive cycle.

The filariform larvae penetrate exposed skin of human host, usually that of the foot by the sweat glands and hair follicles. They invade the lymph and blood vessels, reach the lungs, and pass up the respiratory tract to reach the mouth. In mouth it is swallowed by the host reaches the small intestine. Hookworms deplete the body of nutrients, and a major effect is severe chronic iron-deficiency anemia.

Hookworm infection results into acute anaemia. In children, it retards growth of body and brain. The infection of Ancylostoma duodenale can be checked effectively by improving the sanitary conditions to avoid the contamination of faeces with the soil and other edibles, by protecting feet and ands from being touched with the soil. Children should be directed to keep their hands and feet clean.

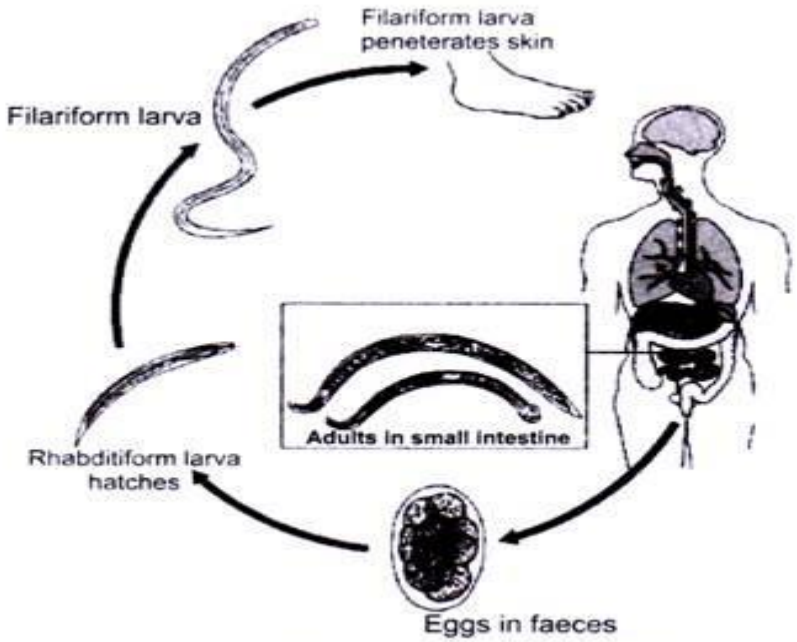


Fig. 9.21 Life Cycle of *A. duodenale*

Treatment:

*Education, improved sanitation, and controlled disposal of human feces are important.

Wearing shoes in endemic areas can reduce the prevalence of infection, as well.

**A. duodenale* can be treated with albendazole, mebendazole, and benzimidazoles. Pyrantel pamoate is an alternative. In severe cases of anemia, blood transfusion may be necessary.

****

Wuchereria bancrofti

Introduction

* *Wuchereria bancrofti* is a human parasitic worm (Filariworm) that is the major cause of lymphatic filariasis.

* It is one of the three parasitic worms, together with *Brugia malayi* and *B. timori*, that infect the lymphatic system to cause lymphatic filariasis.

* These filarial worms are spread by a variety of mosquito vector species.

* *W. bancrofti* is the most prevalent and affects over 120 million people, primarily in Central Africa and the Nile delta, South and Central America, the tropical regions of Asia including southern China, and the Pacific islands.

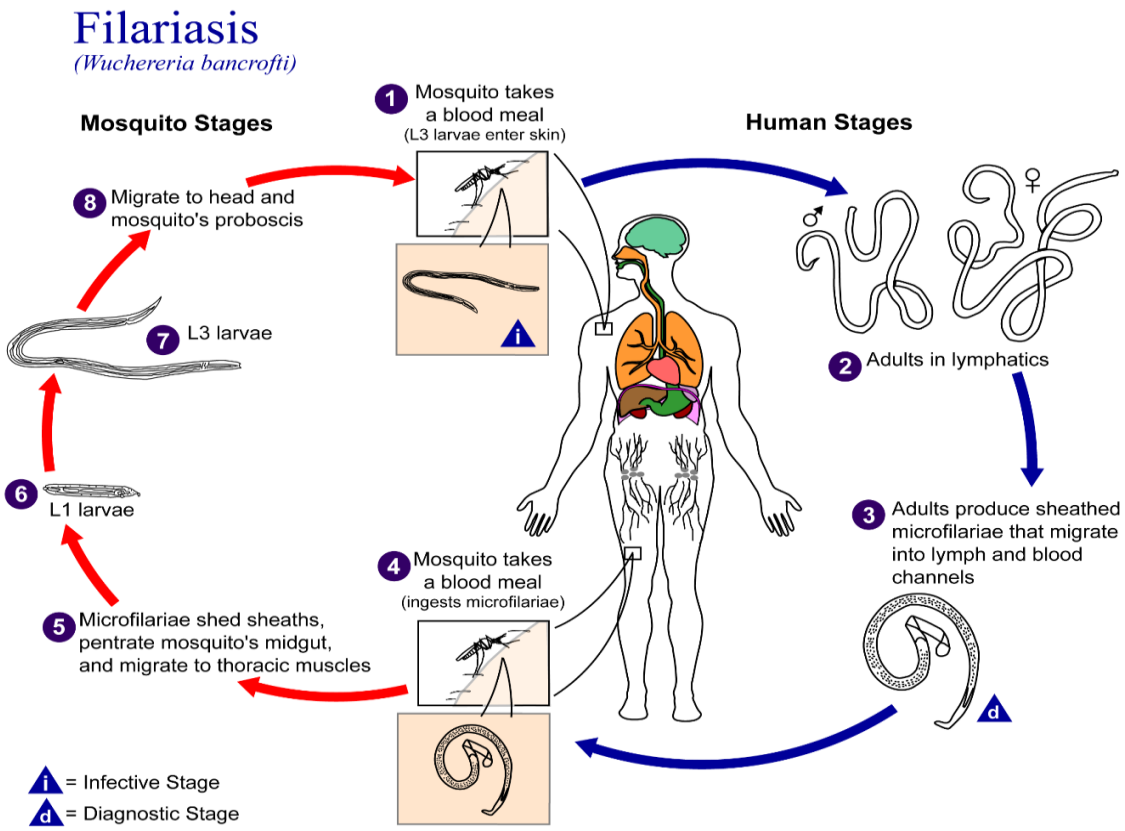
Morphology

- *W. bancrofti* exhibits sexual dimorphism. The adult worm is long, cylindrical, slender, and smooth with rounded ends.
- It is white in colour and almost transparent. The body is quite delicate, making removing it from tissues difficult.
- It has a short cephalic or head region connected to the main body by a short neck, which appears as a constriction.
- Dark spots are dispersed nuclei throughout the body cavity, with no nuclei at the tail tip. Males and females can be differentiated by size and structure of their tail tips.

- The male worm is smaller, 40 mm (1.6 in) long and 100 μm (0.0039 in) wide, and features a ventrally curved tail. The tip of the tail has 15 pairs of minute caudal papillae, the sensory organs.
- Adult males and females are most often coiled together and are difficult to separate. Females are ovoviviparous and can produce thousands of juveniles known as microfilariae.

LIFECYCLE

- *W. bancrofti* carries out its lifecycle in two hosts. Humans serve as the definitive host and mosquitos as the intermediate host. The adult parasites reside in the lymphatics of the human host.
- They are found mostly in the afferent lymphatic channels of the lymph glands in the lower part of the body.



- The first-stage larvae, known as microfilariae, are present in the circulation. The microfilariae have a membrane "sheath". This sheath, along with the area in which the worms reside, makes identification of the species of microfilariae in humans easier to determine.
- The microfilariae are found mainly in the peripheral blood and can be found at peak amounts from 10 pm to 4 am. They migrate between the deep and the peripheral, circulation exhibiting unique diurnal periodicity.

During the day, they are present in the deep veins, and during the night, they migrate to the peripheral circulation. The cause of this periodicity remains unknown, but the advantages of the microfilariae being in the peripheral blood during these hours may ensure the vector, the nighttime mosquito, will have a higher chance of transmitting them elsewhere.

- Physiological changes also are associated with sleeping, such as lowered body temperature, oxygen tension, and adrenal activity, and an increased carbon dioxide tension, among other physical alterations, any of which could be the signals for the rhythmic behavior of microfilarial parasites.
- If the hosts sleep by day and are awake at night, their periodicity is reversed.
- The microfilariae are transferred into a vector, which are most commonly mosquito species of the genera *Culex*, *Anopheles*, *Mansonia*, and *Aedes*. Inside the mosquito, the microfilariae mature into motile larvae called juveniles; these migrate to the labium after a period around 10 days.
- When the infected mosquito has its next blood meal, *W. bancrofti* larvae are deposited from the mouthparts onto the skin of the prospective host and migrate through microcuts in the dermis or the tract created by the proboscis into the blood stream of the new human host.
- The larvae move through the lymphatic system to regional lymph nodes, predominantly in the legs and genital area. The larvae develop into adult worms over the course of a year, and reach sexual maturity in the afferent lymphatic vessels. After mating, the adult female worm can produce thousands of microfilariae that migrate into the bloodstream.

- A mosquito vector can bite the infected human host, ingest the microfilariae, and thus repeat the lifecycle. The organism notably does not multiply within its intermediate host, the mosquito.

Diagnosis

1. A blood smear is a simple and fairly diagnostic tool, provided the blood sample is taken during the period in the day when the juveniles are in the peripheral circulation.
2. Blood smear must be able to distinguish between *W. bancrofti* and other parasites potentially present.
3. A polymerase chain reaction test can also be performed to detect a minute fraction, as little as 1 pg, of filarial DNA.
4. Ultrasonography can also be used to detect the movements and noises caused by the movement of adult worms Dead, calcified worms can be detected by X-ray examinations

Prevention

- Insect repellents and mosquito nets are useful to protect against mosquito bites.
- Public education efforts must also be made within the endemic areas of the world to successfully lower the prevalence of *W. bancrofti* infections

Treatment

- The severe symptoms caused by the parasite can be avoided by cleansing the skin, surgery, or the use of anthelmintic drugs, such as diethylcarbamazine, ivermectin, or albendazole.
- The drug of choice is diethylcarbamazine, which can eliminate the microfilariae from the blood and also kill the adult worms with a dose of 6 mg/kg/day for 12 days, semiannually or annually.
- A polytherapy treatment that includes ivermectin with diethylcarbamazine or albendazole is more effective than either drug alone.

- Protection is similar to that of other mosquito-spread illnesses; one can use barriers both physical (a mosquito net), chemical (insect repellent), or mass chemotherapy as a method to control the spread of the disease.

****

EMERGENCE OF MDR BACTERIAL AND FUNGAL PATHOGEN

Introduction

Some bacteria are resistant to many different antibiotics; they are multidrug-resistant. Multidrug-resistant bacteria can be difficult to treat and facilitates spread of antibiotic resistance.

Multidrug-resistant bacteria

When a single bacterium is resistant to more than one antibiotic it is said to be multidrug-resistant. This can occur in two distinct ways.

- A bacterium can have several different resistance genes, each providing resistance to a particular antibiotic. Accumulation of resistance genes often takes place on small DNA-pieces called plasmids that can be transferred between bacteria in a single event. Read more under Plasmids and co-selection.
- The other possibility is that a single resistance mechanism gives resistance to more than one antibiotic. For example, one resistance strategy bacteria use is to pump the antibiotic out of the cell. Sometimes such pumps can recognize many different molecules, including different types of antibiotics. That is, the bacteria use a single pump to pump out several different antibiotics. This is also called cross-resistance
- **Multidrug-resistant bacteria problems**:

- Infections with multidrug-resistant bacteria are hard to treat since few or even no treatment options remain. In some cases health care providers have to use antibiotics that are more toxic for the patient.

- Multidrug-resistance facilitates spread of antibiotic resistance. When multidrug-resistance plasmids are transferred to other bacteria, these become resistant to many antibiotics at once. In environments where bacteria are continuously exposed to antibiotics, like in hospitals or some large production animal farms, multidrug-resistance may be favorable and therefore selected and spread further.
- Multidrug-resistance complicates efforts to reduce resistance. When many different antibiotics select for the same resistant bacteria or plasmids, reducing use of one type of antibiotic is not enough to reduce resistance to that antibiotic.

Multidrug-resistant bacteria are increasing

There is an increasing prevalence of pathogenic multidrug-resistant bacteria globally. An example is ESBL (extended spectrum beta lactamase)-producing Gram-negative bacteria like *E. coli* and *Klebsiella pneumoniae*. ESBLs are enzymes that destroy many clinically important antibiotics. Infections with bacteria expressing ESBLs are hard to treat and are becoming increasingly common. A worrisome trend is that more and more people around the world are asymptomatic carriers of ESBL-producing bacteria[2]. For example, more than 50% of the community populations in some parts of Southeast Asia are colonized with ESBL-producing bacteria according to recent estimates [2]. Numbers are increasing also in other parts of the world. This puts many at risk for future antibiotic-resistant infections. Read more in Why should I care? – Risks for the individual and society.

Neisseria gonorrhoeae

- Fluoroquinolone resistance is associated with resistance to penicillin and tetracycline in *N. gonorrhoeae* .fluoroquinolone-resistant strains were more likely to be resistant to penicillin, tetracycline, and erythromycin than fluoroquinolone-sensitive strains (fluoroquinolone-resistant versus fluoroquinolone-sensitive, 98.4% versus 89.4% for penicillin, 98.0% versus 81.1% for tetracycline, and 66.2% versus 14.8% for erythromycin).
- We found that resistance to penicillin, tetracycline, and fluoroquinolones are positively correlated . (correlation coefficients of 0.371, 0.416, and 0.452 for penicillin and tetracycline, penicillin and ciprofloxacin, and tetracycline and ciprofloxacin, respectively

Mycobacterium tuberculosis

We calculated the correlation coefficients of resistance to different drugs used to treat tuberculosis (TB) by using the data from 114 countries in *Anti-Tuberculosis Drug Resistance in the World: Fourth Global Report* .We found strong positive correlations between

Staphylococcus aureus We found positive correlations between resistance to antibiotics used to treat *S. aureus* infection, including penicillin, erythromycin, clindamycin, tetracycline, levofloxacin, gentamicin, and trimethoprim, using data from a tertiary care hospital in the United States

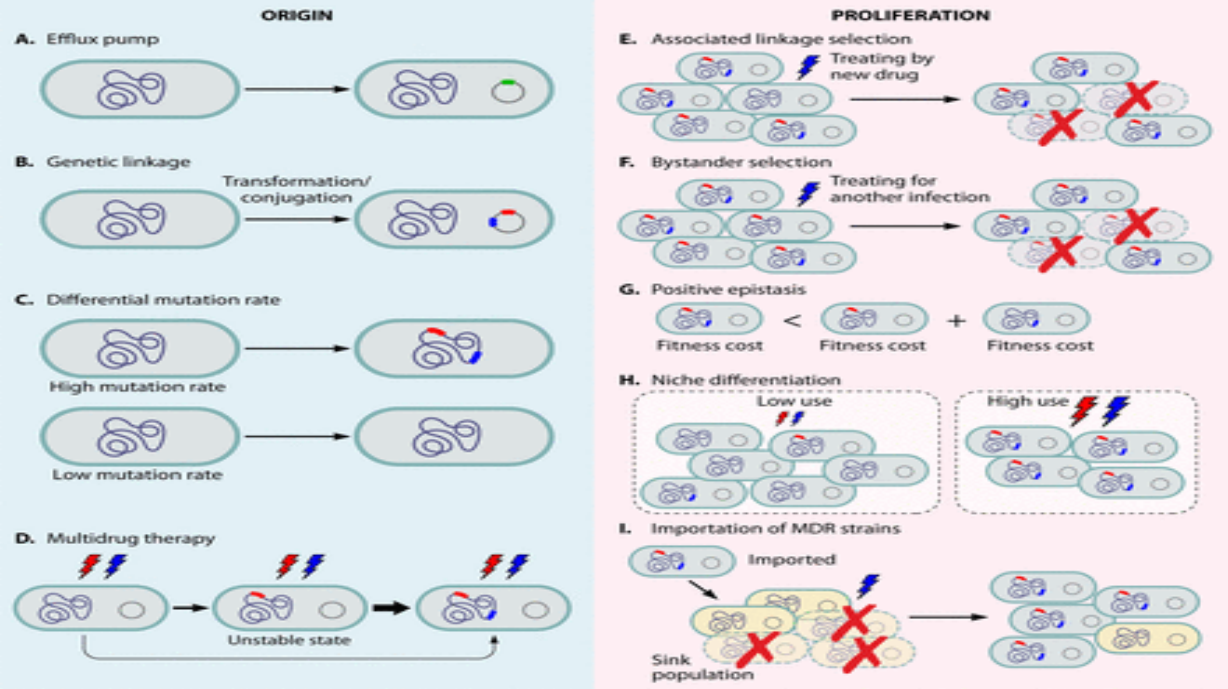
The significant positive correlations between resistance to drugs used to treat *S. aureus* infection were also identified in the province of British Columbia, Canada, in 2012 (15) (correlation coefficients of 0.229, 0.550, 0.054, and 0.052 for methicillin versus clindamycin, erythromycin, trimethoprim-sulfamethoxazole, and tetracycline, respectively [$n = 5{,}214$; $P < 0.001$ for all.

Explanations for the Origin of MDR Strains

- Single biochemical mechanism conferring resistance to multiple drugs.

The simplest explanation for observing an excess of MDR is that a single biochemical mechanism confers resistance to more than one drug

- An example is that of bacterial efflux pumps which etrude antibiotics out of cells such that the intracellular antibiotic concentration decreases and resistance to the antibiotics occurs.
- Some efflux systems are antibiotic specific, but others confer resistance to multiple drug classes . Typically, efflux pumps provide low-level drug resistance . Another example is cell wall thickening in *S. aureus* that resulted in resistance to vancomycin and daptomycin, antibiotics with relatively large molecular sizes .



MDR FUNGAL PATHOGEN

Introduction

- Resistance to antibiotics in pathogenic fungi is a problem of special importance in the control of infections caused by these organisms.
- The same extraordinary conservation of the basic eukaryotic cellular biology exhibited by fungal and animal cells that has allowed these smaller eukaryotes to serve as outstanding model organism limits the range of fungus-specific antibiotics that have been described.
- In addition, mutant fungi are readily isolated, both in the laboratory and in the clinic, that demonstrate resistance to a wide range of antibiotics beyond that initially used for treatment.

MDR Fungal pathogen characteristics:

- This broad-spectrum drug tolerance is referred to as multidrug resistance and occurs in organisms ranging from bacteria to humans
- . The limited number of antifungal drugs makes this phenotype an acute problem in the chemotherapeutic eradication of fungal infections.

- Much of our understanding of multidrug resistance in fungi comes from studies in the generally nonpathogenic yeast *Saccharomyces cerevisiae*, in which the multidrug-resistant phenotype is referred to as pleiotropic drug resistance or Pdr .
- Genes influencing this phenotype are typically designated *PDR* loci. With the development of powerful new genetic and molecular biological techniques, workers have provided important new insights into the physiology of multidrug resistance from experiments performed directly in pathogenic organisms.
- This review focuses on providing an introduction to the various pathways influencing multidrug resistance in *S. cerevisiae* and compares these pathways to similar ones from pathogenic fungi such as *Candida albicans*, *Candida glabrata*, and *Aspergillus fumigatus*
- Resistance to antibiotics in pathogenic fungi is a problem of special importance in the control of infections caused by these organisms.
- The same extraordinary conservation of the basic eukaryotic cellular biology exhibited by fungal and animal cells that has allowed these smaller eukaryotes to serve as outstanding model organism limits the range of fungus-specific antibiotics that have been described.
- In addition, mutant fungi are readily isolated, both in the laboratory and in the clinic, that demonstrate resistance to a wide range of antibiotics beyond that initially used for treatment. This broad-spectrum drug tolerance is referred to as multidrug resistance and occurs in organisms ranging from bacteria to humans .
- The limited number of antifungal drugs makes this phenotype an acute problem in the chemotherapeutic eradication of fungal infections.
- Much of our understanding of multidrug resistance in fungi comes from studies in the generally nonpathogenic yeast *Saccharomyces cerevisiae*, in which the multidrug-resistant phenotype is referred to as pleiotropic drug resistance or Pdr
- . Genes influencing this phenotype are typically designated *PDR* loci.
- With the development of powerful new genetic and molecular biological techniques, workers have provided important new insights into the physiology of multidrug resistance from experiments performed directly in pathogenic organisms.
- This review focuses on providing an introduction to the various pathways influencing multidrug resistance in *S. cerevisiae* and compares these pathways to simislar ones from pathogenic fungi such as *Candida albicans*, *Candida glabrata*, and *Aspergillus fumigatus.*

Extensively drug-resistant tuberculosis (TB)

XDR-TB

XDR-TB, an abbreviation for extensively drug-resistant tuberculosis (TB), is a form of TB which is resistant to at least four of the core anti-TB drugs. XDR-TB involves resistance to the two most powerful anti-TB drugs, isoniazid and rifampicin, also known as multidrug-resistance (MDR-TB), in addition to resistance to any of the fluoroquinolones (such as levofloxacin or moxifloxacin) and to at least one of the three injectable second-line drugs (amikacin, capreomycin or kanamycin).

MDR-TB and XDR-TB both take substantially longer to treat than ordinary (drug-susceptible) TB, and require the use of second-line anti-TB drugs, which are more expensive and have more side-effects than the first-line drugs used for drug-susceptible TB.

Transmission of XDR-TB

- People may get XDR-TB in one of two ways. It may develop in a patient who is receiving treatment for active TB, when anti-TB drugs are misused or mismanaged, and is usually a sign of inadequate clinical care or drug management.
- It can happen when patients are not properly supported to complete their full course of treatment; when health-care providers prescribe the wrong treatment, or the wrong dose, or for too short a period of time; when the supply of drugs to the clinics dispensing drugs is erratic; or when the drugs are of poor quality.
- The second way that people can develop XDR-TB is by becoming infected from a patient who is already ill with the condition.
- Patients with TB of the lungs can spread the disease by coughing, sneezing, or simply talking. A person needs only to breathe in a small number of these germs to become infected. However only a small proportion of people infected with TB germs develop the disease. A person can be infected by XDR-TB bacteria but not develop the active disease, just as with drug-susceptible TB.

- . The spread of TB bacteria depends on factors such as the number and concentration of infectious people in any one place together, and the presence of people with a higher risk of being infected (such as those with HIV/AIDS).
- The likelihood of becoming infected increases with the time that a previously uninfected person spends in the same room as an infectious case.
- The risk of spread increases where there is a high concentration of TB bacteria, such as can occur in poorly-ventilated environments like overcrowded houses, hospitals or prisons.
- The risk of spread is reduced if infectious patients receive timely and proper treatment.

Control measures of XDR-TB

- While patients with XDR-TB may be as infectious as those with ordinary TB, the chances of a TB infection being XDR-TB is lower due to the rarity of the condition. The measures to be taken are the same as those for the prevention of ordinary TB.
- Close contact with a patient with infectious TB is to be avoided especially in poorly ventilated spaces. The risk of becoming infected with TB is very low outdoors in the open air. TB patients should be encouraged to follow good cough hygiene, for example, covering their mouths with a handkerchief when they cough, or even, in the early stages of treatment, using a surgical mask, especially when in closed environments with poor ventilation

The most important thing is for the health care workers and community to provide all the means (information, counselling, and material support) that enable patients to continue taking all their treatment as prescribed.

No doses should be missed and above all, treatment should be taken right through to the end. If a patient finds that side-effects are a problem, for example, the tablets make them feel sick, then they should inform their doctor or nurse, because often there is a simple solution. If they need to go away for any reason, patients should make sure they have enough tablets with them for the duration of the trip.

Treatment

- XDR-TB patients can be cured, but with the current drugs available, the likelihood of success is much smaller than in patients with ordinary TB or even MDR-TB. Cure depends on the extent of the drug resistance, the severity of the disease and whether the patient's immune system is compromised.
- Patients infected with HIV may have a higher mortality. Early and accurate diagnosis are important so that effective treatment is provided as soon as possible.
- Effective treatment requires that a good selection of second-line drugs is available to clinicians who have special expertise in treating such cases

.Diagnosis of XDR

- If TB bacteria are found in the sputum, the diagnosis of TB can be made in a day or two. To confirm XDR-TB, however, it may take from 6 to 16 weeks.

****

Superbug

Introduction

A superbug refers to a microorganism that has adapted after being exposed to antibiotics. The proper terminology for this is a multiresistant bacterium; the term 'superbug' has been popularised by the media.

Resistance to an antibiotic occurs when a microorganism grows in the presence of a concentration of antibiotic which would usually be sufficient to inhibit or kill organisms of the same species

The severity of a superbug depends on the number of different antibiotics the microorganism is resistant to, with some being resistant to one or two, and others, resistant to multiple drug

It is estimated that antibiotic-resistant bacteria are responsible for more than 700,000 deaths worldwide, every year. A review by the UK government on antimicrobial resistance foresaw the number rising to 10 million by 2050

A major risk of superbugs is that if they spread, we could reach the point where it becomes too dangerous to perform routine surgeries such as c-sections and transplants due to the risks presented by infection

Cuase of superbug

- The major cause of drug resistance is the overuse of antibiotics.
- Almost all species of bacteria have developed some degree of resistance since the invention of antibiotics in the 1930s, but most are still sensitive to numerous classes of agents .
- A smaller subgroup of bacteria (known as multiresistant strains) are only susceptible to a very limited range of antibiotics .
- As antibiotics often cause unwanted side effects, it is not uncommon to be advised to change antibiotics more than once in the treatment of severe infection.
- If a person acquires a multi-strain bacterium, it is only a matter of time before treatment options become limited .
- Research has shown that just one course of antibiotics can affect the level of drug-resistant bugs in a person's body. It can also contribute to the wider issue of antibiotic-resistant disease in the community .
- Antibiotic-resistant strains are not exclusive to developing countries. Brazil, Greece and South Africa have major problems with superbugs
- There is a strong correlation between countries with high incidents of antibiotic-resistant strains and countries where antibiotics are available over the counter .
- Traditionally, hospitals have been known to be the breeding site of the most serious infections, however, superbug infections are developing outside of hospital environments at an increasing rate .

Keep in mind that while antibiotic resistance is a catalyst for superbug growth, the impact of a germ is not only dependant on whether there is an effective antibiotic available, but by the virulence of the organism, the volume the person is exposed to and the health of their immune system

The severity of a superbug depends on the number of different antibiotics the microorganism is resistant to. Antibiotics.

Research emerging

Carbapenem-resistant Enterobacteriaceae (CRE) A group of bacteria that appear to be resistant to carbapenems, which are very strong antibiotics:

  - The number of cases of infections resistant to carbapenems has risen by more than 14%.
  - Without treatment, roughly 40% of patients suffer death and many endure severe side effects.

- A yeast called *candida auris* is proving to be resistant to several antifungals and is thought to have come to Australia from overseas
- Strains of gonorrhoea are displaying resistance to treatments, they are thought to havecome from South-East Asia.
- It is said there is a current 'black hole in surveillance' in antibiotic resistance in Australia.

- ## Examples of superbug

- Carbapenem-resistant Enterobacteriaceae (CRE)
- Methicillin-resistant Staphylococcus aureus (MRSA)
- ESBL-producing Enterobacteriaceae (extended-spectrum β-lactamases)
- Vancomycin-resistant Enterococcus (VRE)
- Multidrug-resistant Pseudomonas aeruginosa.
- Multidrug-resistant Acinetobacter

Control procedures

A vital way to protect one's self from superbugs is to follow recommended infection control procedures, such as:

- Wash hands with warm water and soap regularly.
- Dry hands thoroughly after washing them.

- Avoid coughing or sneezing into hands.
- Wash hands well after handling any raw animal products.
- Washing hands well after coming into contact with someone who is sick.
- Avoid sharing personal items such as razors or towels.
- Practice safe sex to prevent antibiotic-resistant gonorrhoea.
- Cook foods to safe temperatures.

****