Unit-4

i) Plasmodium species (Malaria) (Protozoal disease)

Malaria is an infectious disease caused by a parasite, *Plasmodium*, which infects red blood cells. Malaria is characterized by cycles of chills, fever, pain, and sweating. Historical records suggest malaria has infected humans since the beginning of mankind. The name "mal aria" (meaning "bad air" in Italian) was first used in English in 1740 by H. Walpole when describing the disease. The term was shortened to "malaria" in the 20th century. C. Laveran in 1880 was the first to identify the parasites in human blood. In 1889, R. Ross discovered that mosquitoes transmitted malaria. Of the four common species that cause malaria, the most serious type is *Plasmodium falciparum* malaria. It can be life-threatening.

The common four species of malaria

Plasmodium falciparum
P. vivax,
P. malariae,
P. ovale

- **Malaria symptoms and signs**

The period between the mosquito bite and the onset of the malarial illness is usually one to three weeks (seven to 21 days). This initial time period is highly variable as reports suggest that the range of incubation periods may range from four days to one year. The usual incubation period may be increased when a person has taken an inadequate course of malaria prevention medications.

Certain types of malaria (*P. vivax* and *P. ovale*) parasites can also take much longer, as long as eight to 10 months, to cause symptoms. These parasites remain dormant (inactive or hibernating) in the liver cells during this time. Unfortunately, some of these dormant parasites can remain even after a patient recovers from malaria, so the patient can get sick again. This situation is termed relapsing malaria.

The symptoms characteristic of malaria include

i. Flu like illness with fever, chills, muscle aches, and headache.
ii. Some patients develop nausea, vomiting, cough, and diarrhea.

iii. Cycles of chills, fever, and sweating that repeat every one, two, or three days are typical.
iv. There can sometimes be vomiting, diarrhea, coughing, and yellowing (jaundice) of the skin and whites of the eyes due to destruction of red blood cells and liver cells.
v. People with severe *P. falciparum* malaria can develop bleeding problems, shock, liver or kidney failure, central nervous system problems, coma, and can die from the infection or its complications.
vi. Cerebral malaria (coma, or altered mental status or seizures) can occur with severe *P. falciparum* infection. It is lethal if not treated quickly; even with treatment, about 15%-20% die.

Life cycle

The malaria parasite has a complex, multistage life cycle occurring within two living beings, the vector mosquitoes and the vertebrate hosts.

All the *Plasmodium* species causing malaria in humans are transmitted by mosquito species of the genus *Anopheles*. The life cycle of *Plasmodium* was discovered by Ross. .

Sporozoites from the saliva of a biting female mosquito are transmitted to either the blood or the lymphatic system of the recipient

Life cycle in Human (Schizogony in the Human Host)

Man is the intermediate host for malaria, wherein the asexual phase of the life cycle occurs. The sporozoites inoculated by the infested mosquito initiate this phase of the cycle from the liver, and the latter part continues within the red blood cells, which results in the various clinical manifestations of the disease.

I) Pre-erythrocytic Phase - Schizogony in the Liver:

With the mosquito bite, tens to a few hundred invasive sporozoites are introduced into the skin.The sporozoites that find a blood vessel reach the liver within a few hours.

The sporozoites then negotiate through the liver sinusoids, and migrate into a few hepatocytes, and then multiply and grow within parasitophorous vacuoles. Each sporozoite develop into a schizont containing 10,000–30,000 merozoites (or more in case of *P. falciparum*).

The entire pre-eryhrocytic phase lasts about 5–16 days depending on the parasite species: on an average 5-6 days for *P. falciparum*, 8 days for *P. vivax*, 9 days for *P. ovale*, 13 days for *P. malariae* and 8-9 days for *P. knowlesi.* The pre-erythrocytic phase remains a "silent" phase, with little pathology and no symptoms, as only a few hepatocytes are affected.

These merozoites are eventually released into the blood stream at the lung capillaries and initiate the blood stage of infection thereon.

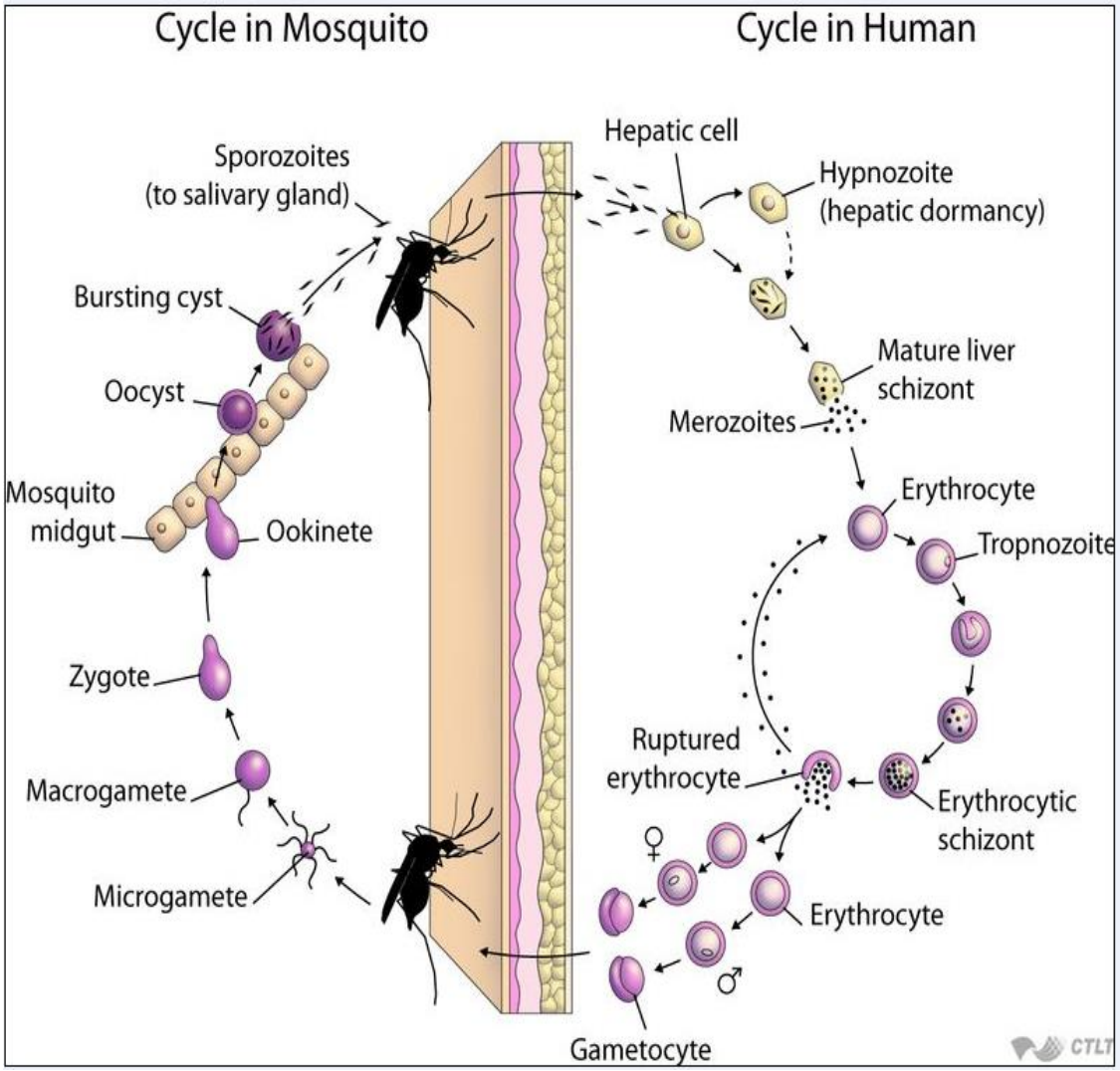
II) Erythrocytic Schizogony - Centre Stage in Red Cells

Red blood cells are the 'centre stage' for the asexual development of the malaria parasite. Within the red cells, repeated cycles of parasitic development occur with precise periodicity, and at the end of each cycle, hundreds of fresh daughter parasites are released that invade more number of red cells.

The merozoites released from the liver recognize, attach, and enter the red blood cells (RBCs). The erythrocytic cycle occurs every 24 hours in case of *P. knowlesi,* 48 h in cases of *P. falciparum, P. vivax* and *P. ovale* and 72 h in case of *P. malariae.*

During each cycle, each merozoite grows and divides within the vacuole into 8–32 (average 10) fresh merozoites, through the stages of ring, trophozoite, and schizont. At the end of the cycle, the infected red cells rupture, releasing the new merozoites that in turn infect more RBCs.

A small proportion of asexual parasites do not undergo schizogony but differentiate into the sexual stage gametocytes. These male or female gametocytes are extracellular and nonpathogenic and help in transmission of the infection to others through the female anopheline mosquitoes, wherein they continue the sexual phase of the parasite's life cycle.



Life cycle in mosquitoes (Sporogony Within the Mosquitoes)

Mosquitoes are the definitive hosts for the malaria parasites, wherein the sexual phase of the parasite's life cycle occurs. The sexual phase is called ***sporogony*** and results in the development of innumerable infecting forms of the parasite within the mosquito that induce disease in the human host following their injection with the mosquito bite.

When the female *Anopheles* draws a blood meal from an individual infected with malaria, the male and female gametocytes of the parasite find their way into the gut of the mosquito. The molecular and cellular changes in the gametocytes help the parasite to quickly adjust to the insect host from the warm-blooded human host and then to initiate the sporogonic cycle. The male and female gametes fuse in the mosquito gut to form zygotes, which subsequently develop into actively moving ookinetes that burrow into the mosquito midgut wall to develop into oocysts.

Growth and division of each oocyst produces thousands of active haploid forms called sporozoites. After the sporogonic phase of 8–15 days, the oocyst bursts and releases sporozoites into the body cavity of the mosquito, from where they travel to and invade the mosquito salivary glands. When the mosquito thus loaded with sporozoites takes another blood meal, the sporozoites get injected from its salivary glands into the human bloodstream, causing malaria infection in the human host.

- **Diagnosis**

The classic and most used diagnostic test for malaria is the blood smear on a microscope slide that is stained (Giemsa stain) to show the parasites inside red blood cells.

Other tests based on immunologic principles exist; including RDTs (rapid diagnostic tests) approved for use in the U.S. in 2007 and polymerase chain reaction (PCR) tests. These are not yet widely available and are more expensive than the traditional Giemsa blood smear. Some investigators suggest such immunologic based tests be confirmed with a Giemsa blood smear.

- **Treatment**

Drug treatment of malaria is not always easy. Chloroquine phosphate is the drug of choice for all malarial parasites except for chloroquine-resistant *Plasmodium* strains. Although almost all strains of *P. malariae* are susceptible to chloroquine, *P. falciparum*, *P. vivax*, and even some *P. ovale* strains have been reported as resistant to chloroquine. multiple drug-treatment protocols for treatment of drug-resistant *Plasmodium* strains (for example, quinine sulfate plus doxycycline or tetracycline, or clindamycin, or atovaquone-proguanil. The WHO's treatment policy, recently established in 2006, is to treat all cases of uncomplicated *P. falciparum* malaria with artemisinin-derived combination therapy (ACTs). ACTs are drug combinations (for example, artesunate-amodiaquine, artesunate-mefloquine, artesunate-pyronaridine, dihydroartemisinin-piperaquine, and chlorproguanil-dapsoneartesunate) used to treat drug-resistant *P. falciparum*.

- **Prevention**

i. Methods used in order to prevent the spread of disease, or to protect individuals in areas where malaria is endemic, include prophylactic drugs, mosquito eradication and the prevention of mosquito bites.
ii. **Vector control:** use of the pesticide DDT and other means

iii. Mosquito nets and bedclothes

iv. A completely effective vaccine is not yet available for malaria,

v. Several potential vaccines targeting the pre-erythrocytic stage are being developed, with RTS,S showing the most promising results so far

vi. Education in recognizing the symptoms of malaria has reduced the number of cases

vii. Recognizing the disease in the early stages can also stop the disease from becoming a killer. Education can also inform people to cover over areas of stagnant, still water e.g. Water Tanks which are ideal breeding grounds for the parasite and mosquito, thus cutting down the risk of the transmission between people.

==========

ii) Candidiasis (Fungal disease)

Candidiasis or **thrush** is a fungal infection (mycosis) of any of the *Candida* species (all yeasts), of which *Candida albicans* is the most common. Also commonly referred to as a **yeast infection**.

- **Morphology**

Candida albicans is a diploid fungus that grows both as yeast and filamentous cells. The morphology of *Candida albicans* cells was determined from their maximum length, maximum diameter and septal diameter in a mathematical ratio, the morphology index (Mi), which usually ranged from approximately 1 for spherical yeast cells to approximately 4 for true hyphae, with elongated yeast cells and pseudohyphae giving intermediate values.

Mi could be determined with high reproducibility for *C. albicans* grown in a variety of environments. The highest mean Mi was seen with cells grown in serum and Eagle's medium at 37°C, the lowest with cells grown in Sabouraud glucose broth at 26°C. Variant strains of *C. albicans* gave Mi values that remained constant in a variety of growth environments. The Mi facilitated detection of two variants that grew exclusively in the yeast form, one that grew as elongated yeasts but could be induced to form pseudohyphae in serum, and one consistently pseudohyphal variant.

- **Pathogenecity**

A yeast infection results from an overgrowth of yeast (a type of fungus) anywhere in the body. Candidiasis is by far the most common type of yeast infection. There are more than 20 species of *Candida*, the most common being *Candida albicans*. These fungi live on all surfaces of our bodies. Under certain conditions, they can become so numerous they cause infections, particularly in warm and moist areas. Examples of such infections are vaginal yeast infections, thrush (infection of tissues of the oral cavity), skin and diaper rash, and nailbed infections.

Candidal infections commonly occur in warm moist body areas, such as underarms. Usually your skin effectively blocks yeast, but any breakdown or cuts in the skin may allow this organism to penetrate. Typical affected areas in babies include the mouth and diaper areas.

Vaginal yeast infection, which is the most common form of vaginitis is often referred to as vaginal Candidiasis. In women, yeast infections are the second most common reason for vaginal burning, itching, and discharge. Yeasts are found in the vagina of 20% to 50% of healthy women and can overgrow if the environment in the vagina changes. Yeast infections are more common after menopause

In adults, oral yeast infections become more common with increased age. Adults also can have yeast infections around dentures, in skin folds under the breast and lower abdomen, nailbeds, and beneath other skin folds. Most of these candidal infections are superficial and clear up easily with treatment. Infections of the nailbeds often require prolonged therapy.

Rarely, the yeast infection may spread throughout the body. In systemic candidal disease (in which the fungus enters the bloodstream and spreads throughout the body), up to 45% of people may die. Even common mouth and vaginal yeast infections can cause critical illness and can be more resistant to normal treatment.

Yeast infections that return may be a sign of more serious diseases such as diabetes, leukemia, or AIDS.

In people who have a weakened immune system because of cancer treatments, steroids, or diseases such as AIDS, candidal infections can occur throughout the entire body and can be life-threatening. The blood, brain, eye, kidney, and heart are most frequently affected, but *Candida* also can grow in

the lungs, liver, and spleen. *Candida* is a leading cause of esophagitis (inflammation in the swallowing tube) in people with AIDS.

Almost 15% of people with weakened immune systems develop a systemic illness caused by *Candida*. These infections enter into the bloodstream through breakdowns or cuts in the skin or mucous membranes. Candidal organisms may build up in an area because of frequent use of antibiotics, which kill the bacteria that normally keep them under control.

Use of devices implanted in the skin such as urinary catheters and IV ports also provide access for the yeast to enter the body. IV drug users utilizing dirty needles may inject the yeast directly into their bloodstream or deep tissues.

- **Diagnosis**

The only definitive way to diagnose a vaginal yeast infection is to complete a full gynecologic exam. In healthy children and adults, a quick exam in the mouth or of the skin usually confirms the diagnosis of candidiasis. If there is any confusion about the diagnosis, the health care practitioner may obtain a small scraping of the area, which will be placed on a slide with potassium hydroxide and examined for a branching pattern consistent with yeast.

Diagnosis of a yeast infection is done either via microscopic examination or culturing. For identification by light microscopy, a scraping or swab of the affected area is placed on a microscope slide. A single drop of 10% potassium hydroxide (KOH) solution is then added to the specimen. The KOH dissolves the skin cells but leaves the *Candida* cells intact, permitting visualization of pseudohyphae and budding yeast cells typical of many *Candida* species.

For the culturing method, a sterile swab is rubbed on the infected skin surface. The swab is then streaked on a culture medium. The culture is incubated at 37 °C for several days, to allow development of yeast or bacterial colonies. The characteristics (such as morphology and colour) of the colonies may allow initial diagnosis of the organism that is causing disease symptoms

- **Treatment**

In clinical settings, candidiasis is commonly treated with antimycotics—the antifungal drugs commonly used to treat candidiasis are topical clotrimazole, topical nystatin, fluconazole, and topical ketoconazole.

iii) Typhus fever (Rickettsial disease)

Typhus is a bacterial (Rickettsial) disease spread by lice or fleas.Typhus is caused by one of two types of bacteria: *Rickettsia typhi* or *Rickettsia prowazekii*. The form of typus depends on which type of bacteria causes the infection.

Rickettsia typhi causes murine or endemic typhus. Endemic typhus is uncommon in the United States. It is usually seen in areas where hygiene is poor and the temperature is cold. Endemic typhus is sometimes called "jail fever."

Murine typhus occurs in the southeastern and southern United States, often during the summer and fall. It is rarely deadly. Risk factors for murine typhus include:

- Exposure to rat fleas or rat feces
- Exposure to other animals (such as cats, opossums, raccoons, skunks, and rats)

Rickettsia prowazekii causes epidemic typhus and Brill-Zinsser disease. Brill-Zinsser disease is a mild form of epidemic typhus. It occurs when the disease re-activates in a person who was previously infected. It is more common in the elderly. Lice and fleas of flying squirrels spread the bacteria.

- **Symptoms**

Symptoms of murine or endemic typhus may include:

- Abdominal pain
- Backache
- Diarrhea
- Dull red rash that begins on the middle of the body and spreads
- Extremely high fever (105 - 106 degrees Fahrenheit), which may last up to 2 weeks
- Hacking, dry cough
- Headache
- Joint and muscle pain
- Nausea
- Vomiting

Symptoms of epidemic typhus may include:

- Chills
- Cough
- Delirium
- High fever (104 degrees Fahrenheit)
- Joint pain (arthralgia)
- Lights that appear very bright; light may hurt the eyes
- Low blood pressure
- Rash that begins on the chest and spreads to the rest of the body (except the palms of the hands and soles of the feet)
- Severe headache
- Severe muscle pain (myalgia)
- Stupor

The early rash is a light rose color and fades when you press on it. Later, the rash becomes dull and red and does not fade. People with severe typhus may also develop small areas of bleeding into the skin (petechiae).

- **Diagnosis**

A complete blood count (CBC) may show anemia and low platelets. Other blood tests for typhus may show:

- High level of typhus antibodies
- Low level of albumin
- Low sodium level
- Mild kidney failure
- Mildly high liver enzymes

- **Treatment**

Treatment includes antibiotics such as:

- Doxycycline
- Tetracycline
- Chloramphenicol (less common)

Tetracycline taken by mouth can permanently stain teeth that are still forming. It is usually not prescribed for children until after all of their permanent teeth have grown in.

Patients with epidemic typhus may need intravenous fluids and oxygen.

- **Outlook (Prognosis)**

Without treatment, death may occur in 10 - 60% of patients with epidemic typhus. Patients over age 60 have the highest risk of death. Patients who receive treatment quickly should completely recover.

Less than 2% of untreated patients with murine typhus may die. Prompt antibiotic treatment will cure nearly all patients.

Possible Complications: -

Renal insufficiency, Pneumonia, Central nervous system damage

- **Prevention**

Avoid areas where you might encounter rat fleas or lice. Good sanitation and public health measures reduce the rat population.Measures to get rid of lice when an infection has been found include: Bathing, Boiling clothes or avoiding infested clothing for at least 5 days (lice will die without feeding on blood), Using insecticides (10% DDT, 1% malathion, or 1% permethrin).

Alternative Names Murine typhus; Epidemic typhus; Endemic typhus; Brill-Zinsser disease; Jail fever.

==========