MEDICAL PROTOZOOLOGY

(A Review of Some Medically Important Protozoa)

Phylum Diplomonadida (Diplomonads) – Formerly Archaezoa
Organisms in this group are sometimes categorized as **Phylum Sarcomastigophora**, Class Zoomastigophora, Order Diplomonadida.

Organisms categorized as diplomonads were formerly considered ancient forms (Archaezoa) because they lack mitochondria, golgi bodies and peroxisomes and were thought to have evolved before the **endosymbiotic** event giving rise to mitochondria took place. Currently taxonomists believe these organisms descended from typical eukaryotic cells, and that they lost their mitochondria during more recent times.

***Giardia lamblia* – Causative agent of Giardiasis**

Giardia lamblia is a type of flagellated protozoan that infects the small intestine and occasionally the bile ducts of humans and other animals. The active cells (**trophozoites**) are shaped like flattened teardrops, have two large nuclei and multiple flagella. Infection typically occurs when dormant stage cells (**cysts**) are ingested along with contaminated water or vegetable materials (though direct transmission can also occur). Each cyst contains two trophozoites, and these are released when the cysts reach the intestine. The trophozoites attach to the intestinal mucosa and feed on mucus and other epithelial secretions. If they are numerous (covering much of the mucosal surface) they interfere with digestion and the absorption of nutrients, especially fats. Symptoms include diarrhea, abdominal cramping and nausea (often intermittent). The diarrhea is often accompanied by large amounts of yellowish fatty mucus. *Giardia* are more commonly pathogenic in children than in adults (adults are often asymptomatic carriers), and species of *Giardia* other than *lamblia* can also be human pathogens.

Phylum Parabasala (Parabasalids) – Formerly Archaezoa
Organisms in this group are sometimes categorized as Phylum Metamonada, Class Parabasalia.

Organisms categorized as Parabasala also lack mitochondria and were formerly thought to be ancient forms. Each organism has only one nucleus, but also has a **parabasal body**, a structure similar to the Golgi. Parabasalids often live symbiotically within other types of organisms, but are not necessarily parasites. Examples include the heavily ciliated *Trichonympha* that inhabit the guts of termites, and the *Trichomonas* organisms that live within the human vagina.

***Trichomonas vaginalis* – Causative agent of trichomoniasis**

Various species of *Trichomonas* may live within human hosts, but only *Trichomonas vaginalis* is pathogenic. These organisms live primarily within the vagina, but can travel to the cervix or vulva, and can infect the urethra and prostate in males. Infection causes inflammation accompanied by a creamy white discharge, with severe itching and chaffing. *Trichomonas* are transmitted directly through sexual intercourse or may be transferred from mother to infant during childbirth. Trichomoniasis is considered the most common curable STD, and in the United States infects an estimated 3.7 million people. Infection is more common in women than in men, and more common in older women than in younger ones.

Phylum Amoebozoa (Amoebas)
Organisms in this group were formerly categorized within the Phylum Sarcomastigophora and Subphylum sarcodina. They remain difficult to accurately classify.

***Entamoeba histolytica* – Causitive agent of amoebiasis or amoebic dysentery**

Although most amoebas are free-living inhabitants of fresh and salt water, many are parasitic, and some are pathogens. ***Entamoeba histolytica*** is one type of amoeba than lives in the large intestines of humans and other animals. These amoebas enter their hosts in the **cyst** form, usually with contaminated water or vegetable material. The cyst walls are digested away in the stomach and duodenum, allowing the **trophozoites** (four per cyst) to be released. The trophozoites live in the caecum and reproduce by means of binary fission. In most cases they cause no or little damage, living on bacteria and nutrients supplied by the host; however, the name *histolytica* (meaning tissue lysing or splitting) indicates that these organisms can invade tissue.

In about 10% of infections, the amoebas invade the intestinal mucosa causing tissue lysis and ulceration. In severe infections they may penetrate the submucosa, muscularis and serous membrane to enter the peritoneal cavity (typically resulting in secondary bacterial infection). Symptoms vary depending on the severity and location of the infection, but typically include nausea, cramps and diarrhea. More severe infections result in abdominal tenderness, dysentery, dehydration and general incapacitation. Symptoms may develop within days of exposure or as much as a year later depending on host condition. Rarely the amoebas travel via the portal system to the liver, causing amoebic hepatitis.

***Naegleria fowleri* – Causative agent of Primary Amoebic Meningoencephalitis**

Amoebas identified as *Naegleria fowleri* inhabit warm, stagnant bodies of freshwater and enter their hosts when water is inhaled deep into the nasal passages. The amoebas attach to olfactory nerves, travel through the cribriform plate (ethmoid bone) and enter the olfactory bulbs of the forebrain where they feed on nerve tissue and multiply. During this stage (approximately 3-7 days), the host loses olfactory function (cannot perceive odor) and sometimes the sense of taste. After the amoebas have multiplied and consumed the olfactory bulbs, they spread into the cerebrum causing frank symptoms of encephalitis (headache, nausea, rigidity of neck muscles, progressing to vomiting, delirium, seizures and eventually irreversible coma. Death usually occurs within 14 days due to respiratory failure when the infection has spread to the brain stem and the amoebas have destroyed the autonomic nerve cells of the medulla oblongata.

Phylum Apicomplexa, Class Sporozoea (Sporozoans)
Organisms in the phylum Apicomplexa are obligate intracellular parasites (**hypotrophs**) that are not motile in their mature forms. All are animal parasites and several are important human pathogens. Infective Apicomplexa cells carry specialized organelles forming a complex at their apical ends (hence the name). These organelles contain enzymes that help the protozoa penetrate host cells and gain access.

***Plasmodium vivax, malariae, ovale, falciparum* and *knowlesi* – Causative agents of Malaria**

The vectors involved in the transmission of malaria are mosquitoes in the genus ***Anopheles***. The protozoa enter their mammalian hosts along with saliva when the mosquitoes bite. The parasite stage entering the host is called a **sporozoite**, and these typically enter liver cells (exoerythrocytic stage) where they mature, reproduce and may persist indefinately. Eventually some parasites enter the bloodstream (erythrocytic stage) where they infect red blood cells (RBCs) and reproduce asexually by means of **schizogony**. When RBCs lyse, the parasites (now called **merozoites**) are released in large number. These can then enter new RBCs and repeat the process. The maturation of parasites within RBCs occurs at intervals of 24 hours (*P. knowlesi*), 48 hours (*P. vivax, ovale and falciparum*), or 72 hours (*P. malariae*). This accounts for the cyclic nature of malaria symptoms. When RBCs rupture, releasing a load of merozoites and hemoglobin into the bloodstream, fever develops. Symptoms include elevated temperature accompanied by severe chills (shivering, teeth chattering, etc.), followed by

headache and nausea – the fever may reach as high as 106^{o} F. This is followed by sweating and a drop in temperature (sometimes below normal), which lasts until the next cycle begins. Within the bloodstream some of the merozoites undergo differentiation to become **gametocytes**, and some of these are picked up by mosquitos as they feed. Inside the mosquito, gametocytes undergo **meiosis** forming **haploid gametes**, and these undergo **syngamy** (a type of sexual reproduction), resulting in the formation of new diploid cells.

The name malaria means "bad air' and was applied due to the association of disease with the air of swamps (before the mosquito connection was recognized). A complication of malaria called Blackwater fever involves hemolysis of RBCs and the dumping of hemoglobin into the bloodstream and into the urine (resulting in the production of dark urine due to hemoglobin breakdown). This can lead to kidney failure and is frequently fatal. Most cases of Blackwater fever involve malaria caused by *P. falciparum*.

***Toxoplasma gondii* – Causative agents of Toxoplasmosis**

Toxoplasma gondii is capable of infecting all types of warm-blooded animals (mammals and birds). It is one of the most common parasites of humans, infecting around one third of the total human population worldwide. In the 1970s it was estimated that between 17 and 35% of all Americans carry the organisms (which dogs and cats also carry). Although symptoms in normal adults may include fever, rash and enlarged lymph nodes, most infections are asymptomatic. In fetuses, infants born infected, and persons with severely compromised immune function (HIV/AIDS patients), nervous system damage is common, and fatal encephalitis is not unusual. These parasites can also damage the heart, liver, inner ears and eyes. Cats are the most common source of infection in humans, though contact with raw meat and direct fecal contamination can also result in infection.

Sexual reproduction of *Toxoplasma gondii* occurs only within members of the cat family. Felids are therefore definitive hosts, and all other hosts are intermediate. Infection with *Toxoplasma* has been shown to influence host behavior in various ways. Rodents in particular display behavioral changes likely to increase their chances of being preyed upon by cats.

Phylum Ciliophora (Ciliates)
Most ciliated protozoa are free-living organisms, but a few types are parasites and some potential pathogens.

***Balantidium coli* – Causative agents of Balantidiasis**

Balantidium coli lives in the cecum and colon of humans, pigs, rats and other mammals. It is not readily transmissible from one host type to another due to differences in microbiota, but once it is adapted to a host species, it can become a serious pathogen. *Balanditium* enters the human host in cyst form along with contaminated food or water. Digestive enzymes dissolve the cyst walls and trophozoites are released in the colon. In most cases, *Balantidium* will feed on bacteria and fecal debris without causing disease symptoms, but rarely they invade the mucosa and submucosa of the gut wall causing abscesses and ulceration. Infection most likely occurs in people with malnutrition due to low stomach acidity and in immune compromised individuals. Disease symptoms typically include chronic diarrhea (with bouts occurring as often as every 20 minutes), alternating with constipation, but can result in severe dysentery. Fatal cases have occurred.

Phylum Euglenozoa (Hemoflagellates)
The Hemoflagellates include organisms in two genera, *Trypanosoma* and *Leishmania*. Species of *Trypanosoma* cause sleeping sickness and Chaga's disease, while *Leishmania* organisms cause a variety of diseases including Kala-azar and Oriental sore. All hemoflagellates live within the circulatory systems of their hosts, and are transmitted by insect vectors.

Trypanosoma cruzi – Causative agents of Chaga's Disease (American Trypanosomiasis)

Trypanosoma cruzi is usually transmitted by an insect vector (a true bug), often *Triatoma infestans* (sometimes called a kissing bug because they tend to bite people on the face during the night). The trypanosomes are not in the bug's saliva, but enter when infected excrement deposited by the bug is scratched into the bite wound (sometimes excrement is scraped into the eye). They then enter the bloodstream or lymphatic system and migrate to tissue cells. Infection can also occur through blood transfusions and organ transplants.
Acute symptoms include edema at the site of infection, with development of headache, fever, swollen lymph nodes and sometimes severe skin lesions at the infection site (especially in children). After 8-12 weeks, a chronic stage may develop (only in about 30-40% of those infected), with symptoms becoming evident 10-30 years later. These can result in enlargement of the liver spleen, lymphatic organs and heart ventricles (often resulting in heart failure). Treatment is effective only in the early stages of infection, though late stage treatment may delay end stage symptoms. Prevention involves elimination of the vectors.

Trypanosoma brucei – Causative agents of African Trypanosomiasis or Sleeping Sickness

African trypanosomiasis or sleeping sickness is caused by two sub-species of *Trypanosoma brucei*; *T. brucei gambiense* and *T. brucei rhodesiense*. Both are transmitted by an insect vector called the tsetse fly (genus *Glossina*), and can be passed to many alternate hosts (antelope, pigs, monkeys, dogs, etc.). The Trypanosomes live in the salivary glands of the flies, and so enter the host when the flies bite to feed. The bite itches and typically forms a lesion, but the trypanosomes quickly invade the circulatory and lymphatic systems. This causes severe swelling of the lymph nodes, accompanied by headache and fever at irregular intervals. In this form, the disease may persist for weeks or months making the victim susceptible to other diseases. If untreated, infection can lead to anemia, endocrine, cardiac and kidney dysfunction. Eventually, the trypanosomes may enter the cerebrospinal fluid (CSF), bringing on the true symptoms of sleeping sickness. Disruption of the normal Circadian rhythm causes victims to experience daytime sleep episodes and nighttime periods of wakefulness. Other neurological symptoms include confusion, tremor, general muscle weakness, semi-paralysis and speech disorders. If not treated, coma and death are inevitable. If the trypanosomes do not enter the CSF, symptoms disappear spontaneously and the host recovers. Prevention requires control of the tsetse flies or elimination of alternate hosts, the later of which is highly unlikely.