Parasitic Diseases
The following information was excerpted from Duane's Clinical Ophthalmology, Volume 5, Chapter 33, Systemic Infectious and Inflammatory Disease, pages 28 to 37. Revised 1990.

Malaria

Endemic throughout the tropics, subtropics and temperate zones of the world.

*Plasmodium vivax* and *Plasmodium falciparum* account for 95% of infections and have the widest distribution. The remainder of infections are caused by *Plasmodium malariae* and *Plasmodium ovale*.

The vector for malaria is the female anopheline mosquito, which transmits the infective sporozoites (protozoa) while taking a blood meal. During the incubation period of 1 to 2 weeks, the patient is usually asymptomatic as the protozoa mature and multiply in the liver. In the second phase of the life-cycle, merozoites infect red blood cells and establish a synchronous cycle of hemolysys and reinfection that corresponds to the periodic febrile paroxysms experienced by the patient.

Other common clinical features of malaria are anemia and splenomegaly. Lethargy, anorexia, jaundice, hepatomegaly, nausea, vomiting, diarrhea, leukopenia, eosinophilia, and thrombocytopenia may also occur.

Untreated malarial infection usually resolve in 12 to 18 months; however, *P. vivax*, *P. ovale*, and *P. malariae* infections may be chronic. *P. falciparum* infections are the most dangerous and life threatening.

The most common ocular complication of malaria are conjunctival hyperemia, subconjunctival hemorrhage and yellow pigmentation of the conjunctiva due to erythrocyte breakdown products. Retinal hemorrhages and edema may result from vaso-occlusive events and the presence of anemia. Widespread thrombosis, diffuse retinitis and proliferative retinopathy may develop. Papilledema, optic neuritis, paralytic strabismus and pupillary abnormalities are also possible complications.

Malaria is diagnosed by demonstrating the parasite in the blood of infected patients.

Leishmaniasis

Leishmaniasis is a tropical disease caused by protozoa of the genus Leishmania. The disease may primarily affect the reticuloendothelial system as visceral leishmaniasis (kala-azar) of the skin (cutaneous leishmaniasis). The disease has worldwide distribution in the tropics and subtropics, including the Mediterranean, India, Central Asia, China, the Middle East, Africa, and South and Central America. Transmission occurs through the bite of the sandfly.

Clinically, patients rapidly develop anemia, pancytopenia, and hypersplenism. In cutaneous leishmaniasis, the manifestations are varied and include single or multiple nodules, ulcers, and lepromatous lesions.

The most common ocular abnormality seen in visceral leishmaniasis is intraretinal hemorrhages. Although these may be due to hematogenous spread of the parasites to the eye, they more likely are a response to the hematologic abnormalities present in this condition. Cutaneous leishmaniasis may produce scarring and mutilation of the face and eyelids. Lesions close to the eyes may cause an accompanying papillary conjunctivitis or keratitis.
The diagnosis of leishmaniasis can be made by identifying the parasite in a biopsy of skin, lymph glands, liver, spleen, or bone marrow. ELISA serology and immunofluorescent antibody tests are also available.

Toxoplasmosis

Toxoplasmosis is a parasitic infection caused by the obligate intracellular protozoan *Toxoplasma gondii*. All infections are ultimately related to cats, the definitive host for this organism. Toxoplasmosis occurs worldwide.

*T. gondii* reproduces in the small intestines of cats, and oocysts are shed in cat feces. Children can ingest the infectious oocytes while playing in contaminated soil or sand. Adults usually become infected by consuming raw or undercooked meat from infected sheep, goats, pigs, or cattle that have acquired the infection from the soil.

In the active phase of infection, actively proliferating tachyzoites destroy the cells they parasitize and invade adjacent cells, producing progressively enlarging focal lesions. Eventually, the replicating process is arrested by the immune response of the host and quiescent tissue cysts are formed. The cysts can remain latent for years.

Acquired toxoplasmosis infections are usually asymptomatic. The most common clinical manifestation is lymphadenopathy (89%), accompanied by fever, headache, and at times hepatosplenomegaly and a rash. Less common features include central nervous system involvement, myocarditis, and pericarditis, and atypical pneumonia.

Toxoplasmosis is transmitted to the fetus when the mother becomes acutely infected during her pregnancy. Most cases are asymptomatic. However, fetal infections in the first trimester are likely to be severe, resulting in prematurity, fetal death, or neonatal infection. Children born with congenital toxoplasmosis commonly have hepatosplenomegaly, jaundice, fever, anemia, lymphadenopathy, and chorioretinitis. Other complications include pneumonia, rash, convulsions, intracranial calcifications, microcephaly, hypothermia, eosinophilia, and abnormal bleeding time. Affected infants have a 12% mortality rate, and the survivors frequently have permanent and severe neurologic damage, including mental retardation, convulsion, spasticity and palsy, severely reduced vision (63%), hydrocephalus or microcephaly, and deafness.

In cases of congenital toxoplasmosis, the chorioretinitis usually involves the macula bilaterally. The active lesions appear as large (3 to 4 disc diameters), ill-defined yellow areas underlying a dense vitritis. The choroid may become necrotic, revealing white sclera beneath the lesion. When the lesion heals, it leaves behind large, atrophic chorioretinal scars with hyperpigmented borders.

Almost all cases of *Toxoplasma* chorioretinitis in adults are reactivations of congenital infection. Repeat attacks often develop in the same eye at the edge of old atrophic lesions and are believed to be caused by the breakdown of *Toxoplasma* cysts in the retina with renewed proliferation of the tachyzoite form. The acute lesions are elevated with indistinct borders and most often are located in the posterior pole. Ophthalmoscopy is frequently obscured by a dense vitreous exudate, giving the classic "headlight-in-a-fog" appearance. Vision may be lost by nonclearing vitreous debris, tractional retinal distortion or detachment, epiretinal membrane formation, or direct scarring of the macula.

Diagnosis of toxoplasmosis is made by serology. A variety of specific IgG and IgM tests are available. Treatment of toxoplasmosis is indicated in patients with clinically active systemic disease, congenital toxoplasmosis, symptomatic immunocompromise, and vision threatening lesions.
Trichinosis

Trichinosis is a myositis (muscle inflammation) caused by larvae of the nematode Trichinella spiralis. Periorbital edema occurs in about 90% of patients, and the extraocular muscles are commonly involved.

The disease occurs nearly worldwide, except in Australia. Prevalence of infection in the United States has been estimated at 2%, infestation of less than ten parasites per gram muscle tissue usually being asymptomatic.

Trichinosis is associated with ingestion of undercooked pork and occasionally of wild game meats. After ingestion of cysts by humans, reproduction takes place in the intestines and larval offspring migrate through mesenteric vessels to disseminate. The larvae survive and encyst only in skeletal muscle fibers, and the cysts later calcify. Extramuscular larvae die and may stimulate granulomatous inflammation.

The patient usually first experiences nausea, abdominal pain, and diarrhea lasting 1 to 2 days. A maculopapular rash, fever, and prostration may occur. Myositis ensues over the next few weeks, presenting with muscle pain, tenderness, and weakness. The most active, best perfused muscle are particularly affected, including the diaphragm, intercostals, tongue, extraocular muscles, deltoids, and gastrocnemius. Widespread nervous system disease may occur, presenting variably as polyneuritis, focal or diffuse paresis, meningitis, or encephalitis. Myocarditis and pulmonary involvement has been reported.

Periorbital edema occurs during the myositic phase. Pain on eye movements is due to extraocular muscle involvement. Conjunctivitis and subconjunctival hemorrhage are common.

Diagnosis is made by muscle biopsy and/or serologic tests.

Echinococcosis

Uniocular echinococcosis (hydatid disease) is caused by the larval stage of the canine tapeworm Echinococcus granulosa, which produces characteristic tissue cysts throughout the body. In the natural life-cycle of the parasite, the dog is the most common definitive host and acquires the infection by eating the flesh of infected sheep, cattle, or pigs. At one time, the disease was endemic in areas where sheep and cattle were raised. Although the incidence has decreased as the result of education and control measures, there are still foci of concern in South America, and sporadic cases still occur in the United States, Europe, the Middle East and Asia.

Most infections occur in children who ingest the eggs while playing in contaminated soil, or by contact with infected dogs. The eggs hatch in the small intestine. Emerging oncospheres (larvae) penetrate the intestinal wall and are carried by the bloodstream to various organs, where they develop into hydatid cysts. Liver lesions are the most common (60 - 70%), followed by lesions of the lung (20%), kidney, spleen, brain, and other tissues. The cysts typically grow slowly and do not produce symptoms for many years unless they are located in the eye or the central nervous system. Damage is caused primarily by the mechanical effect of the growing cyst and may result in portal hypertension, pneumothorax, bone fractures, focal neurologic deficits, and increased intracranial pressure. Spontaneous rupture of a cyst can produce serious allergic sequelae, including fatal anaphylactic reactions.
**Echinococcosis, cont.**
The overall incidence of ocular involvement in hydatid disease is small. The cysts rarely appear in the lids or under the conjunctiva. Within the globe, they tend to develop in the vitreous or between the choroid and retina and may produce retinal detachment. Intraorbital cysts may produce proptosis, and enlarging intracranial cysts may lead to the development of papilledema.

Echinococcosis is definitely diagnosed by microscopic examination of cyst fluid, which is best obtained at the time of surgery. The lesions can be identified in roentgenograms, computed tomograms, and sonograms. The eosinophil count is elevated in approximately 25% of patients. Serologic assays for *E. Granulosa* are both sensitive and specific.

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**Cysticercosis**

Cysticercosis is a parasite infection caused by human infestation with the larval stage of *Taenia solium*, the pork tapeworm. Central nervous system and ocular involvement are common and produce most of the significant clinical complication is cysticercosis.

Cysticercosis is endemic to all continents except Australia and is prevalent wherever raw or inadequately cooked pork is eaten. It is commonly found in Mexico, Central America, and South America as well as Africa, China, Pakistan, and India. In recent decades, infection in North America and Europe has become uncommon.

Ordinarily, the human is the definitive host and the pig is the intermediate host in the life-cycle of *Taenia solium*. Tapeworm infection is acquired by ingestion of cysticercus larvae in raw or inadequately cooked pork. The adult tapeworm may reside harmlessly in the small intestine of a human for years and grow to attain a length of 2 to 7 meters. By ingesting the eggs of the parasite, the human may also become the intermediate host of *Taenia solium*, leading to the clinical condition of cysticercosis. Once inside the small intestine, the eggs hatch and the emerging oncospheres penetrate the intestinal wall and are disseminated throughout the body by the circulation, where they develop into mature larvae (cysticerci cellulosae) after 60 to 70 days. The most frequent location of involvement by the larvae is subcutaneous and intermuscular tissue, followed by that of the eye and brain. Lesions in the heart, liver, lungs, and abdominal cavity have also been reported.

Patients with cysticercosis may be totally asymptomatic or only notice the appearance of small, painless subcutaneous nodules. Symptoms related to cerebral cysticercosis usually do not appear until after a latent period averaging 4 to 5 years and most commonly manifest as a seizure disorder. Focal or diffuse neurologic deficits, increased intracranial pressure, hydrocephalus, meningitis, and transeverse myelitis may result from meningeal, parenchymal, ventricular, or spinal cysts.

Cysticerci may be found anywhere in the eye or orbital adnexa. Intraocular lesion caused by cysticercosis most commonly occur in the vitreous or subretinal space, but subchoroidal, subhyaloid, anterior chamber, and subconjunctival cysticerci have also been reported. Symptoms may initially be referable to the shadows cast by the moving larvae in front of the retina, or the patient may present with severe loss of vision, marked uveitis, retinal detachment, or leukocoria. The lesion appears as a whitish or grayish vesicle up to 20 mm in diameter. At times, a protruding scolex or the characteristic undulations and contractions of the vesicle may be seen. Bilateral and multifocal involvement are rare. Ultrasonography may identify the cystic structure of the larva.
Definitive diagnosis of cysticercosis is usually based on excision of larvae and their examination under the microscope. Computed tomography may be diagnostic in some cases of cerebral cysticercosis. Plain roentgenograms may locate calcified lesion in muscles and subcutaneous tissue, which can then be biopsied. At the present time, serologic testing is unreliable.

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Toxocariasis

Toxocariasis is a nematodal infection that has two clinical manifestation; visceral larval migrans and ocular toxocariasis (ocular larva migrans). Visceral larva migrans is caused by systemic dissemination of *Toxocara* larvae. In ocular toxocariasis the organisms are typically limited to the posterior segment of the eye.

*Toxocara canis* is found worldwide. Infection rates vary geographically. Positive serologies have been reported in 14.3% of English schoolchildren, 5% of children in New York, and 86% of children on the Caribbean island of St. Lucia.

The causative organism, *T. canis*, normally parasitizes the small intestine of dogs and is capable of only limited development in the human host. Transplacental infection occurs in the dog. As many as 50% of puppies and 20% of adult dogs harbor the parasite. Puppies born with patent infections shed numerous ova from birth. Children are most frequently infected by ingesting eggs present in contaminated soil or by direct contact with puppies. In humans, ingested ova mature in the small intestine and the larvae migrate to other sites in the body where they elicit a granulomatous reaction. Lesions are most frequently found in the liver by also occur in the lungs, heart, striated muscle, brain and eyes.

The clinical features of visceral larva migrans are abdominal pain, nausea, vomiting, hepatomegaly, lethargy, sleep and behavior disturbances, pharyngitis, cervical adenitis, cough, wheezing, pneumonia, headache, limb pain, and fever.

Ocular toxocariasis may present with decreased vision, strabismus, leukocoria, or uveitis. Most commonly a subretinal granuloma is present in the posterior pole in an otherwise quiet eye. In the early stages, it is elevated above the retina and may resemble a neoplasm. Later, a well-defined chorioretinal scar with a central granuloma develops. Peripheral lesions caused by Toxocara have also been described. Less frequently an exudative endophthalmitis with retinal detachment is seen that must be distinguished from retinoblastoma, Coat's disease, and other causes of posterior uveitis.

Both visceral larva migrans and ocular toxocariasis are clinical diagnoses based on signs and symptoms together with a history of exposure to ascarid-infected pets or pica. The demonstration of larvae in biopsied material is difficult and rarely achieved. *Toxocara* ELISA serology and eosinophil count are probably the only useful laboratory tests in establishing the diagnosis of toxocariasis. The *Toxocara* ELISA test is both sensitive and specific in active cases of visceral larva migrans but may not be as reliable in cases of occult toxocariasis or long-standing visceral larva migrans. The ELISA assay should be performed on undiluted sera in suspected cases of ocular toxocariasis. The eosinophil count is also typically elevated, but a normal eosinophil count does not exclude the diagnosis of toxocariasis.

Both forms of toxocariasis are usually self-limited, and expectant observation is advisable unless the patient is severely symptomatic or has active ocular inflammation.

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Ophthalmomyiasis refers to the invasion of the human eye by the larval form (maggots) of flies of the order Diptera. Other forms of myiasis produce lesions of the skin, nasal cavity, ear, anus, vagina, intestine, and bladder. Myiasis has a worldwide distribution. The flies that infect humans are also responsible for diseases seen in cattle, deer, and horses.

Flies may directly deposit their eggs directly on the lid margins, or they may be transmitted by the patient's hand or a secondary vector such as a tick or mosquito. The eggs hatch, and the larvae burrow beneath the conjunctiva of the upper and lower fornices, producing small undulating nodules with concomitant conjunctival irritation. Less commonly, the larvae penetrate the sclera and may be found in the anterior chamber, vitreous, or subretinal space associated with variable amounts of inflammation. When confirmed to the uveal tissue, the larvae leave rather typical subretinal migratory tracts that are hypopigmented and hyperfluoresce on angiography. Vision is usually not disturbed unless the organism crosses through the maculae. Rarely, the larvae invade the orbit and cause massive destruction of its contents. The potential for bony erosion with fatal intracranial extension should not be overlooked.

Mechanical debridement of the organisms is the only treatment available for this condition and may include orbital exenteration in advanced cases of orbital myiasis.

**Glossary of Terms:**

- **Atrophy**: wasting away of a body tissue
- **Choroid**: the blood vessel layer underneath the retina
- **Chorioretinitis**: inflammation of the choroid and retina, with it’s origin in the choroid
- **Conjunctiva**: the transparent tissue lining of the front of the eye and the inside of the eyelids
- **Conjunctivitis**: inflammation of the conjunctiva
- **Cornea**: the transparent dome of tissue which is the initial optical component of the eye
- **Endophthalmitis**: inflammation of the eye, resulting in loss of function, blindness
- **Eosinophil**: one type of white blood cell, which mediates the body’s allergic response to an allergan
- **Eosinophilia**: manifesting a type of allergic reaction
- **Granuloma**: an accumulation of white blood cells, resembling a mass or tumor
- **Hepatomegaly**: an enlargement of the liver
- **Hepatosplenomegaly**: enlargement of the liver and spleen
- **Hydrocephalus**: an abnormal increase in the amount of fluid in the cranium, causing an enlargement of the head, and wasting of the brain
- **Hyperemia**: localized increase in blood vessel diameter - rendering the involved tissue more red in appearance
- **Hypersplenism**: overactivity of the spleen
- **Keratitis**: inflammation of the cornea
- **Leukopenia**: decreased white blood cell count
- **Leukocoria**: a condition rendering the pupil white - usually a cataract, can also be tumourous or a retinal detachment
- **Lymphadenopathy**: tenderness/irritation of the lymph glands
- **Macula**: the region of the eye responsible for central, fine-detailed, vision
- **Microcephaly**: condition where the cranium is smaller than normal
- **Myocarditis**: inflammation of the heart muscle
- **Neoplasm**: new growth different from surrounding tissue, a tumor
- **Oocysts**: immature egg
Optic Neuritis: an inflammation of the optic nerve.
Papilledema: a swelling of the optic nerve at its entry point into the eye.
Pericarditis: an inflammation of the tissue around the heart.
Pharyngitis: an inflammation of the pharynx (sore throat).
Platelets: small blood cells playing a principal role in blood coagulation.
Proptosis: a forward protrusion of the eye.
Reticuloendothelial: refers to the tissue system responsible for removing worn out blood cells from the blood (lymph nodes, etc.).
Retina: the nervous tissue lining of the eye.
Retinitis: an inflammation of the retina.
Retinoblastoma: a malignant tumor of the retina.
Retinopathy: disease or damage to the retina.
Roentgenograms: an imaging technique using x-rays.
Sclera: the white outer shell of the eye.
Splenomegaly: enlargement of the spleen.
Strabismus: non-alignment of the eyes (cross-eyed, wall-eyed, etc.).
Sub-conjunctival hemorrhage: hemorrhage lying underneath the conjunctiva.
Sub-retinal granuloma: granuloma lying underneath the retina.
Thrombocytopenia: disorder of platelets, causes destruction of platelets and decreased production of platelets.
Vaso-occlusion: blockage of a blood vessel.
Vitreous: the viscous fluid compartment of the eye.
Vitritis: an inflammation of the vitreous.