SMGroup

# Ocular Parasitic Infections

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**Published Date:** July 26, 2017

## TOXOPLASMOSIS

One of the main parasitic causes of the ocular involvement is Toxoplasma gondii which is an obligate intracellular parasite. Nearly one-third of the world's population is thought to be infected by T. gondii. Toxoplasma is more prevalent in areas with hot and humid climates such as: Central America, Asia, and Caribbean. On the other hand, Europe also reports numerous cases, with higher prevalence in Albania and France. Risk factors such as geographic region, meat consumption patterns, animal reservoirs and climatic conditions play an important role in transmitting the disease. In the recent years, there has been a decrease in the number of cases of toxoplasmosis in developed countries due to improvement in hygiene and sanitary conditions and also keeping livestock on farms. Nevertheless immigration of the population may be a factor that can change the map of the disease in the coming years, and this may be more predominant for the European continent. However, in developing countries, the number of new cases with toxoplasmosis has increased as a consequence of increasing population, urbanization, and the consumption of uncontrolled meat and water. Toxoplasma gondii completes its life cycle in two phases: the intestinal phase (cat and other animals) and the extra-intestinal phase (mice, human and animals). The toxoplasmosis life cycle includes three stages: oocysts, tachyzoites and bradyzoites. Humans are a casual host of the parasitic life cycle chain.

After swallowing, oocysts release sporozoites, which penetrate the intestinal mucosa and reach into other organs such as the brain, eyes, liver, spleen, lymph nodes, etc. Ocular involvement is not common, but is one of the major symptoms that force the patient to seek medical care. One of the worst complications is congenital toxoplasmosis, which is associated with multiple fetal injuries. In congenital toxoplasmosis ocular involvement is generally bilateral, whereas the acquired form is usually unilateral. In immunocompromised patients is a commonly encountered pathology. The diagnosis of the ocular congenital toxoplasmosis in children is made by the clinic manifestations such as the presence of focal necrotizing retinitis, vitritis, anterior uveitis and cataracts or the use of advanced techniques such as the presence of specific antibodies or the parasite DNA diagnosed with PCR technique. The presence of antibody in the serum is a widely used method in establishing the toxoplasmosis diagnosis but has a limited role in establishing the diagnosis of ocular toxoplasmosis. A high titer of IgG for a period of 3 weeks helps to diagnose. The presence of specific IgM indicates an acute systemic or ocular infection. The most specific test for ocular toxoplasmosis is the detection of antibodies via ELISA method in the intraocular liquid. The Goldmann-Witmer **(GW)** coefficient is a test that compares the levels of intraocular antibody production to that of serum, as measured by enzyme-linked immunosorbent assay **(ELISA)** or radioimmunoassay. The coefficient is defined as GW = X/Y; where GW = Goldmann-Witmer coefficient; X = specific antibody in aqueous or vitreous divided by total IgG in aqueous or vitreous; and Y = specific antibody in serum divided by total IgG in serum. A GW ratio > 4 is diagnostic of local antibody production to a specific microbial pathogen. Specific IgG are the result of the immune response to tachyzoites located at the site of the infection. Ocular toxoplasmosis is considered to be reactivated in patients with typical toxoplasma lesions in retina and choroid, when there is specific IgG, specific IgM and that responds to anti-toxoplasma medication. In the immunosuppressed chorioretinitis from toxoplasma needs 2-3 months to resolve. The necessary treatment for fovea lesions includes a combination of three drugs: Pyrimethamine, Sulfadiazine and systemic corticosteroids. In addition to this first therapeutic line, other preparations such as trimethoprim-sulfamethoxazole, clindamycin, azithromycin and atovaquone are also used. Trimethoprim-sulfamethoxazole **(Bactrim)** appears to be a good alternative in pregnant women. Progressive and recurrent necrotizing retinitis can cause several vision-impairing complications if not treated in time such as: retinal detachment, glaucoma, and choroidal neovascularization.

## ACANTHAMOEBA KERATITIS

Acanthamoeba keratitis is caused by Acanthamoeba spp., which is a free living parasite. It is found throughout the environment in two forms: trophozoites and cysts. A person can be infected through the eye, nose, or damaged skin. Eye infection can cause keratitis with visual impairment and granulomatous encephalitis. Low hygienic conditions, wearing contact lenses for a long time, rinsing lenses with contaminated water are among the key factors that serve to inflict infection. Keratitis from Acanthamoeba is very common in people who use lenses. The incidence in developed countries varies from 1 to 33 cases per million inhabitants using lenses.

While in developing countries, where people using lenses are limited in number the risk factors are: trauma, exposure to contaminated water, the use of folk medicines in the eyes, poor socio-economic conditions, etc. Acanthamoeba pathogenesis has several stages such as: epithelial adhesion, amoeba stromal invasion, keratocyte separation, and induction of inflammatory response, photophobia, and stromal necrosis that leads to blindness. The diagnosis of keratitis from Acanthamoeba is difficult to establish. Common symptoms are massive pain, photophobia and tearing. The presence of contact lenses with the above complaints indicates an acanthamoeba infection. Confocal microscopy, as a non-invasive procedure, can be used for in vivo diagnosis. Cysts of acanthamoeba will appear as spherical, hyper-reflective structures that are distinctly distinguished from their double wall. Laboratory confirmation is performed after parasite isolation in culture or immuno-fluorescence detection. The gold standard for Acanthamoeba detection is still the plate culture technique but it requires a long time. PCR is used to detect free parasites of acanthamoeba and to differentiate genotypes. New techniques such as MALDI-TOF and H-NMR spectroscopy are being tested for rapid identification of acanthamoeba. The healing chances are good if the pathogen is found in the cornea but can cause blindness if the stroma is invaded. There are currently no methods or a single drug that can eliminate both cystic and trophozoite forms, while the trophozoite form is much more readily eliminated. If treatment is started early, clinical improvement is observed within 2-3 weeks. Biguanides such as PHMB and chlorhexidine have been reported to be the most effective drugs for treatment of infection. The main preventive measure is good lenses disinfection. It is recommended to remove lenses if contact with water occurred such as showering, swimming, etc.

## LEISHMANIA

Leishmaniosis is caused by a protozoal parasite of Leishmania type. Humans are infected by the bite of infected female phlebotomine sandflies. Worldwide, 1.3 million new cases are reported every year. Ocular involvement from Leishmania has been reported in countries such as India, Sudan, Iran, Turkey and Italy. Anterior uveitis is the most common clinical manifestation of the infection that may progress to glaucoma. Focal retinal whitening, 'cotton' woolspots, hemorrhage and increased tortuosity of blood vessels are seen in fundus oculi. In severe cases lesions are observed in the form of flames caused by hemorrhages of the anterior capillaries of the optic fibers. Optic nerve neuropathy is observed in mucosal leishmaniasis. Severe forms can progress to ptosis and secondary ectropion in cutaneous leishmaniasis that can eventually cause eye problems. Rarely the palpebra can be involved in the cutaneous form of Leishmania. The most frequent lesions are chalazion like but can also be seen in form of ulcers, cutaneous carcinoma, or chronic unilateral granulomatous blepharitis. Chronic dacryocystitis has been reported in patients with cutaneous leishmaniasis, which affects tear formation resulting in eye dryness. Endo-ocular lesions have been observed in patients with disseminated mucocutaneous leishmaniasis. Leishmania diagnosis can be established by direct isolation of the parasite from tissues with biopsy, culture, detection of antigens or antibodies. Amastigotes can be easily isolated in cutaneous or mucocutaneous lesions

but is difficult to isolate them from the eye. Molecular methods like PCR can identify the parasitic genome with 100% sensitivity and specificity. Leishmaniasis treatment depends on clinical forms. Anti- leishmanial medications include: lipophilic amphotericin B, antimony pentavalent, sodium stibogluconate, miltefosine and paromomycin.

## CHAGAS DISEASE

Chagas disease is caused by Trypanosoma cruzi. It is a chronic systemic disease. The parasitic life cycle has two phases: trypomastigote and amastigote and is found in two hosts: humans who serve as a reservoir and insects serving as transmitters. Humans are infected by insect bites. If the insect bite is near the orbit edema and erythema of palpebral and periorbital tissue will be present associated with constitutional signs such as temperature, general weakness and anorexia. During the acute phase, the role of serology is limited. The diagnosis of the acute form of the disease is established by growing the trypomastigote in blood agar or by direct isolation in culture. The clinical manifestations play a very important role in establishing the diagnosis. Injuries of the pigmented retinal epithelium have been observed in the intermediate and chronic forms of the disease in southern America. Acute forms are treated with nifurtimox and benznidazole. Benznidazole is given in doses of 5-7.5 mg / kg, 2 times daily for 60 days. Nifurtimox is given in doses up to 8-10 mg/kg, 3-4 times a day for 90 days. Within few weeks of treatment, the symptoms disappear but the infection persists. On average, 30% of chronic infections have residual complications.

## MALARIA

Malaria is caused by the parasite of Plasmodium type, transmitted by the bite of Anopheles female mosquito. The parasite life cycle takes place in both humans and mosquitoes. In the human body plasmodium goes into the extra-erythrocytic and intra-erythrocytic phases. After the erythrocytic phase some of the merozoites form the gametes that are picked up by the female mosquito while sucking human blood. A 2014 report stated that 3.3 million people are at risk of being affected by malaria. The severe complications observed after P. falciparum infection are caused by the occlusion of the blood vessels from the parasite which subsequently causes hypoxia. Uncomplicated malaria rarely can affect the eye mostly causing eyelid edema, conjunctival chemosis or hemorrhage and anterior uveitis. On the other hand, severe ocular complications can be observed from cerebral malaria caused by P. falciparum leading to vision defects, papilledema, optic neuritis, cortical visual loss or optic nerve atrophy. Often cerebral infarcts from cerebral malaria may affect pupillary reflexes and eye movements. Patients with cerebellar lesions may present with nystagmus. White focal or generalized areas can be observed in the retina. Changes in color of peripheral blood vessels can be observed in fundus oculi, while the white retinal hemorrhage is observed at the center of malaric retinopathy. The diagnosis of malaria is established either by direct microscopy or antigen detection. Direct light microscopy, where peripheral blood is Giemsa stained is the gold standard in diagnosis. In some cases typical ocular lesions can lead to malaria diagnosis. Treatment depends on the Plasmodium species that

cause the disease. Artemisin is recommended in cases caused by P. falciparum. Chloroquine and primaquine in cases of P. vivax. Overdose with quinine results in decreased vision, macular and retinal degeneration, scotoma, color disorders. If not treated, malaric retinopathy can cause coma and death.

## GIARDIASIS

Giardiasis is caused by Giardia duodenalis. Infection is transmitted by ingestion of the parasite through contaminated water, foods, or fecal-oral route. It is seen in both developed and developing countries. In most cases the clinical manifestation is diarrhea and malabsorption, but one-third of the patients develop extra-intestinal manifestations. Retinal "salt and pepper" degeneration lesions have been reported in 20% of children infected with G.lamblia. This appearance is caused by the damage of retinal cells and the release of the granular pigments in the retina which give black spots images on the light pink background of the retina. The diagnosis is established by isolating the parasite in feces with direct microscopy. Concentration techniques have a higher sensitivity. The selected treatment is metronidazole for 5-7 days or ornidazole/tinidazole as a single dose. If present intestinal infection should be treated, there is no specific treatment required for retina involvement.

## ONCHOCERCIASIS

Onchocerciasis, also known as "river blindness" is caused by a nematode called Onchocerca volvulus. It is transmitted from person to person through bites of infected black flies of Simulium species. They live along rivers so people living in the surrounding villages are at increased risk of infection. The parasitic life cycle goes through black flies and humans. During the bite, the black fly recovers the larvae from blood and injects theminto the next person. In the subcutaneous tissue, larvae grow into filaria. Grown filarias produce hundreds of larvae that are deposited and remain in the human body for 3-5 years. The larvae migrate to the skin, eyes and other organs. Onchocerciasis is predominantly found in tropical areas, 99% of cases are reported in sub-Saharan Africa. Cases of Onchocerciasis have also been reported from countries such as the Middle East, Latin America, Brazil, Guatemala, Mexico and Venezuela. The inflammatory response elicited by dead larvae can cause visual loss due to sclerosing keratitis. In addition to keratitis other manifestations are iridocyclitis, chorioretinitisand atrophy of the optic nerve. Autoimmune response is also known to cause inflammation of the posterior part of the eye. There is a symbiosis between this parasite and the Wolbachia bacteria, so if the bacteria is killed by antibiotic therapy there will be a reduction of the parasite survival. Wolbachia is an intracellular bacterium that lives in symbiosis with all stages of development of Onchocerca volvulus. As such, disruption of the symbiosis with antibiotics slows down the development of the parasite. Wolbachia contributes directly to the parasite metabolism. Eye infection can be diagnosed either by slit lamp examination or sclero- corneal punch biopsy. New techniques such as skin PCRs are important in the diagnosis when the larvae cannot be visualized. This technique has 84-91%

sensitivity and 100% specificity. Other methods are ELISA and EIA that determine the presence of antibodies but do not differentiate an existing infection from a past one. The treatment of choice is ivermectin, 150-200 μg/kg every 6 months to prevent skin and eye injuries. Doxycycline can be used. A 6-week regime with doxycycline kills more than 60% of the parasite, while the percentage goes to 90%, 20 months after the treatment. Under these conditions it is suggested that treatment with ivermectin should begin one week before starting doxycycline. The best protective measure is prevention by using insect repellents.

## LOIASIS

Loiasis, called African eye worm by most people, is caused by the parasitic worm Loa loa. It is transmitted through bites of deerflies of the Chrysops genus. It affects almost 3 million people who live mainly in the forested areas of central and western Africa. There may be more than 29 million people who are at risk of getting loaisis in affected areas of Central and West Africa. These deerflies are mostly found in rubber plantations and are attracted by lit houses, bites occur mainly during the day and rainy seasons. After transmissionthe larvae develop into adult parasites over a year in the human body and migrate through cutaneous and subcutaneous tissue. The migration of adult parasites is not painful but is associated with a tickling sensation. Nose, conjunctive and palpebral areas can be affected. Ocular involvement can happen both in the larvae or adult phase. Adult parasites can survive for 15 years and have been found in conjunctiva, vitreous body and palpebra. Calabar edema of subcutaneous tissue during migration can result in angioedema due to a strong atopic reaction. Retinal aneurysms can lead to retinal haemorrhagefrom larval deposition in the blood vessels of the retina and choroid. Perivascular inflammation can be seen on ophthalmoscope and helps in establishing the diagnosis. Diagnosis is confirmed by larval isolation under direct microscopy after Giemsa stain. Larvae can also be seen in hemoculture. In patients with conjunctival involvement excision of the worm will determine the diagnosis. Serologic methods can help diagnose but won`t differentiate between a previous or present infection. If not treated it can cause eye complications. Surgical excision is the treatment of choice in eye involvement, while drugs are used to treat loiasis. Diethylcarbamazine **(DEC)** is the drug of choice for killing both larvae and adult parasites. Albendazole is sometimes used in patients who are not cured with multiple DEC treatments.

## DIROFILARIASIS

Dirofilariasis is caused by nematodes of the genus Dirofilaria. It is a worldwide parasitic infection. In the recent years there has been an increase in the number of cases reported by the Mediterranean countries. The parasite life cycle is in canines which also serve as the ultimate host. It can infect dogs and other mammals, including cats, foxes, sea lions, wolves, and others. Mosquitoes are an intermediate host of the parasite and a vector for transmission of the parasite from canines to humans when biting the later. The larvae migrate from the subcutaneous tissue to the right chambers of the heart and further to different parts of the body, where they mature.

Ocular manifestations depend on the location of the parasite. Palpebral involvement causes edema, pain, pruritis and conjuctival congestion. While the intraocular parasite will cause the sensation of a foreign body, diplopia, photophobia. Diagnosis of dirofilariasis in humans remains difficult. Diagnosis is made through the isolation of adult parasite. The intraocular presence is seen on ophthalmoscope examination. PCR has 100% sensitivity. If not treated the parasite causes ocular damage.

## THELAZIASIS

Thelaziasis is an Arthropod-born disease of the eye and adnexa. *Thelazia callipaeda* **(TC)** and *Thelazia californiensis* are parasite of *Thelazia callipaeda* genus and are transmitted to humans through the drosophilus genus flies. It is also known as the Oriental worm. TC and *Thelazia californiensis* have been found in the human eye. The life cycle consists of flies that serve as intermediate hosts and cattle, horses and dogs as the ultimate host. In the first phase the larvae are found in lacrimal glands of the definitive host. The vector while feeding ingests larvae in the first stage and accidentally releases larvae of the third stage. About five to six weeks later these larvae turn into adult worms in the eye of the infected person. The parasite causes damage primarily to anterior part of the eye. This pathology is favored by poor sanitation. The treatment involves excision of the parasite and the local use of thiabendazole. Prevention of Thelaziasis is by protective measures like using bed nets at night, keeping the eyes, face and nose clean while sleeping to prevent the vectors, maintaining personal hygiene, keeping the surroundings clean, and creating public awareness about the disease.

## CYSTICERCOSIS

Cysticercosis is caused by larvae of Taenia solium. Factors facilitating the spread of T solium infection include inadequate sanitation, breeding pigs in unsanitary conditions, and eating uncooked pork. After ingestion tapeworm eggs reside in the intestine where they eliminate eggs along with the human stools. The incubation period may vary from months to years. Autoinoculation has been observed in people suffering from taenia and cause neurocystercosis. Consumption of raw or undercooked swine meat is the main source of infection. Ocular cysticercosis is endemic in tropical areas, such as sub-Saharan Africa, India, East Asia, Mexico and Latin America. due to poor sanitation and hygiene conditions. The ocular involvement is documented in some case reports. Ocular cysticercosis may be extraocular (in the subconjunctival or orbital tissues) or intraocular (in the vitreous, subretinal space, or anterior). The free cyst can be seen in the vitreous body. Involvement of orbital muscles or cranial nerves can cause paralysis. Diagnosis is determined by ophthalmoscope examination and imaging studies such as ultrasound, CT or MRI. The use of laboratory techniques such as PCR real time and LAMP can aid in the diagnosis of cysticercosis. If not treated, ocular complications will persist. Treatment includes both surgical and drug management. Surgical removal is mandatory in individuals with intraocular cysts. Albendazole combined with corticosteroids is the treatment of choice. Steroids are used to

reduce inflammation around the lesion. In individuals with uveitis, perioperative corticosteroid administration is recommended.

## ECHINOCOCCOSIS

Echinococcosis is caused by infection with the larvae of Echinococcus spp. The overall prevelance of echinococcal infection is not clear. It is endemic in the Middle East as well as other parts of the world, including India, Africa, South America, New Zealand, Australia, Turkey and Southern Europe. Ocular involvement are reported in 1% of cases. It is caused by ingestion of the echinococcus eggs through contaminated water and food. The eggs are released in the stool of meat-eating animals that are infected by the parasite and eliminated in the environment. In humans they pass through the intestinal wall in the systemic circulation. Most common ocular involvement cause proptosis from placement of the cyst within the orbit, space occupying lesions, which may be further complicated with keratitis or corneal ulcerations. Other complications may include erosion of orbit wall, optic nerve atrophy, and neuritis. Echinococcus cysts are also reported in the retina. Diagnosis is determined by clinical manifestations suggesting the presence of the cyst and radiological studies such as ultrasound, CT and/or MRI. The "Double Wall" sign is a characteristic of the cyst seen on ultrasound. Positive serology also helps diagnose even though a positive ELISA Ig G has a sensitivity of 64.8 to 100%, and specificity of 87.5 to 100%. PCR has a high specificity and sensitivity and can be used to establish the diagnosis. Aspiratory cytology can also be used. Hydatid disease can be treated medically and or surgically. Medical therapy is mostly with antihelminthic mebendazole or albendazole which is the gold standard and found to be useful in the prevention of recurrence specially when cyst ruptures during excision and contents contaminate the surgical site. Surgical excision may be required for isolated ocular lesions when they are growing and causing symptoms and visual loss. Surgical excision of the cyst is the treatment of choice.

## GNATHOSTOMIASIS

Gnathostomiasis is a food-borne zoonotic nematodiasis caused by the larval stage of Gnathostoma spp. Larvae ingestion during the third phase of their life cycle causes the disease. The final hosts that are pigs, cats and wild animals while intermediate hosts are some types of crustaces, fish, frogs and serpents. In the infected person the larvae migrate to the intestines, internal organs and the subcutaneous tissue. Depending on their localization, they may cause visceral, ocular or cerebral gnathostomiasis. Most of the cases have been reported from East Asia and Central and South America. However, sporadic cases have been reported worldwide. Ocular involvement is due to migration of the parasite and its metabolites causing an immune response. Involvement of the cornea and conjunctiva is manifested with conjunctival congestion and corneal ulcers respectively. Intraocular involvement causes glaucoma, uveitis, retinitis, and vitreous hemorrhage. It is a difficult disease to diagnose. Patients may have eosinophilia and raised IgE. If the parasite is not removed visual disturbances will persist, surgical excision is the treatment of choice.

## SCHISTOSOMIASIS

Schistosomiasis, or bilharziasis, is caused by the flat trematodes of Schistosoma genus. The adult parasite releases the larvae into water, the latter penetrates the human skin during swimming, fishing or hand washing clothes. Schistosomiasis transmission is highly dependent on environmental conditions, particularly those affecting the snail host. The larvae is matured in the human body into schistozom, the latter is deposited in the blood vessels. Eggs from the female parasite get eliminated through urine or stools. It is high prevalence pathology in countries such as central and southern Africa, China and southern Asia. Ocular involvement is not a typical clinical manifestation of schistosomiasis, but there have been reported cases of it. Although schistosomiasis is a widespread disease, ocular involvement remains rare. When it occurs it may cause uveitis or subretinal granuloma. Diagnosis is made by direct isolation of the eggs or larvae in the eye. Isolation of eggs in urine or stools can help in diagnoses. Specific and highly sensitive PCR based assays have been developed for the detection of schistosome DNA in faeces or sera and plasma. Antibody detection can be useful in a few specific circumstances, but its application is limited. If not treated, symptoms will persist. The treatment of choice for all forms of schistosomiasis is Praziquantel. Other drugs used to treat schistosomiasis are oxamniquine and metrifonate.

## FASCIOLOSIS

Fasciolosis is a foodborne parasitic infection that mainly affects the liver. This disease in humans shows an increasing importance, which relies on its recent widespread emergence related to climate and global changes. The major human health problems are known in Andean countries, the Caribbean, Northern Africa, Near East, Southeast Asia and Western Europe. It is caused by ingestion of the Fasciola hepatica cysts found on raw leaves. There are two important species of these trematodes F. hepatica and F. gigantica. Their life cycle begins with the release of eggs from adult parasites which further develop into free larvae, sporocysts, rediae and cercariae. The parasite life cycle has several hosts, humans, sheep and goats as a definitive host and Lymnaea snails as intermediary host. Eliminated eggs from the host stoolsmature in water. The motile larvae are formed by every egg about 2-3 weeks after it falls into freshwater. The larva gets into the body of the intermediate host preferring the lymph nodes where itundergoes all stages of the life cycle described above. When it reaches the phase of cercaries and metacercaries it is eliminated from the intermediate host in grass or water where it can be ingested from livestock or humans. As soon as it comes into contact with the gastric acid (metacercariae) it will migrate from the duodenum into the peritoneal cavity where they penetrate the liver capsule and parenchyma and end up in the bile ducts maturing in the adult form. The eggs are eliminated through bilewith stools. Direct larval migration to the eye is called Opthalmofascioliasis. Although ocular involvement is rare. Symptoms vary from conjunctival hyperemia, corneal edema, episcleritis, extra-ocular muscle paralysis, decreased perception of light, uveitis, etc. The diagnosis is either

by directly visualizing the larvae in the eye or by isolating it through excision of the parasite. The eosinophil count is nearly always greater than 5% of the total leucocytes and may be high. ELISA serology, presence of eggs in stools will help diagnoses. If not treated, complications may occur. Rapid surgical intervention to excise the larvae prevents ocular complications. Surgical excision is the treatment of choice in ocular involvement, although Triclabendazole is the drug of choice if needed.