ocular parasitology

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This book discussed about serious problem which affect thousands of people around the world leading to severe symptoms and incase of ignorance to this complains or absence of professional health care personnel it may lead to loss of vision and when one loss the power of vision which is the main sense which enable people to feel with the beautiful things in nature and around them. reader will find useful information about the anatomy and physiology of the eye and they also know many parasites that cause vision disorders and may lead to blindness in their last stage of the disease caused by that ocular parasites.

Mosab Nouraldein Mohammed Hamad: Head of Parasitology and Medical Entomology Department, Medical Laboratory Department, Faculty of Health Sciences, Elsheikh Abdallah Elbadri University, Sudan. Member in African Society of Laboratory Medicine; Member in International Society of Infectious Diseases.

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Ocular parasitology

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Contents

Dedication:

To my mother (Medina Abdelrahman).

Acknowledgement:

To my colleagues at soba university hospital especially those in Microbiology and parasitology department.

Introduction:

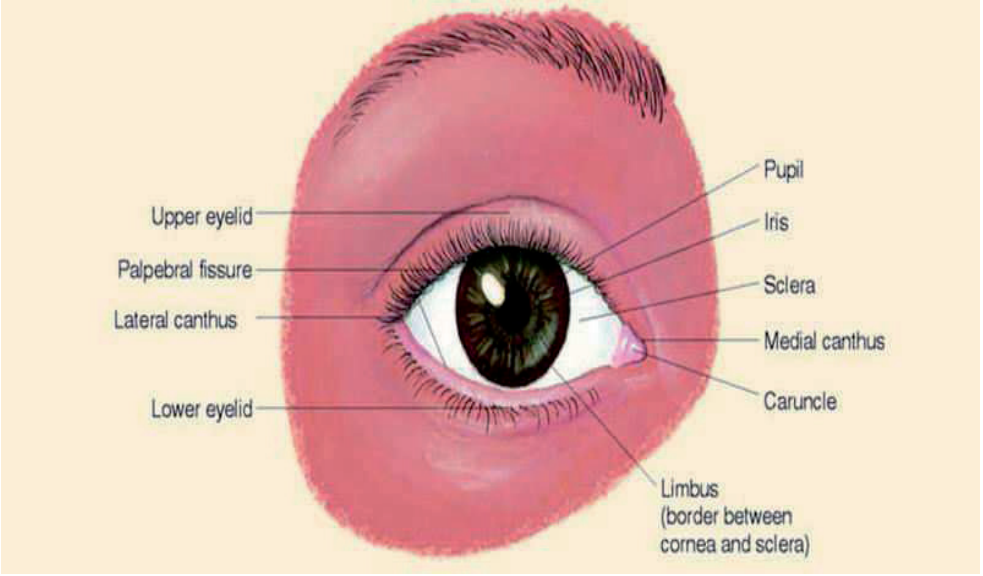
The human ey**e** is an organ which reacts to light and pressure. As a sense organ, the mammalian eye allows vision. Human eyes help provide a three dimensional, moving image, normally colored in daylight. Rod and cone cells in the retina allow conscious light perception and vision including color differentiation and the perception of depth. The human eye can differentiate between about 10 million colors and is possibly capable of detecting a single photon.

Similar to the eyes of other mammals, the human eye's non-image-forming photosensitive ganglion cells in the retina receive light signals which affect adjustment of the size of the pupil, regulation and suppression of the hormone melatonin and entrainment of the body clock. [1]

Structure and function of the eye:

The eye is one of the major sensory organs in the human body. It is responsible for vision, color differentiation (the human eye can differentiate between approximately 10 million colors) and maintaining the biological clock of the human body. To understand how the eye does everything that it does, we need look into the structure of human eye.

The eye is arguably the most complicated organ in the human body, with a number of parts fitted together in a near-spherical structure. Each part in the system is responsible for a certain action which is a part of the function of the eyes. The eye structure can be broadly classified as External structure and internal structure.



The parts of the eye that are visible externally comprise of the external structure of the eye-

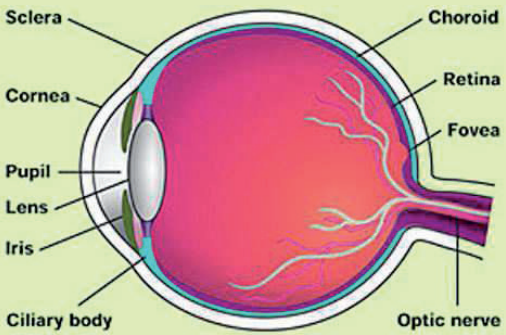
Sclera: It is a tough and thick white sheath that protects the inner parts of the eye. We know it as the 'White of the eye'.

Conjunctiva: It is a thin transparent membrane that is spread across the sclera. It keeps the eyes moist and clear by secreting small amounts of mucus and tears.

Cornea: It is the transparent layer of skin that is spread over the pupil and the iris. The job of the cornea is to refract the light that enters the eyes.

Iris: It is a pigmented layer of tissue that makes up the colored portion of the eye. Its primary function is to control the size of the pupil, depending on the amount of light entering it.

Pupil: It is the small opening located at the middle of the Iris. It allows light to come in.



The internal structure of the eye includes the following parts:

Retina: It is the screen at the end of the eye, where all the images are formed. It is extremely sensitive to light because of the presence of Photoreceptors, which are photosensitive cells that detect dim and colored lights.

Lens: It is a biconvex, transparent and adjustable structure that focuses light to the retina, hence forming images on it.

Aqueous humor: It is a watery fluid that is present in the area between the lens and the cornea. It is responsible for the nourishment of both the lens and the cornea.

Vitreous Humor: it is a transparent semi-solid, jelly-like substance that fills the interior of the eyes. Its role is that it maintains the shape of the eye and also causes refraction of light before it reaches the retina.

Optic nerve: Located at the end of the eyes, behind the retina, the optic nerve is responsible for carrying all the nerve impulses from the photoreceptors to the brain, without which vision would not be possible. [2]

How the eye work:

In a number of ways, the human eye works much like a digital camera:

1. Light is focused primarily by the cornea — the clear front surface of the eye, which acts like a camera lens.
2. The iris of the eye functions like the diaphragm of a camera, controlling the amount of light reaching the back of the eye by automatically adjusting the size of the pupil (aperture).
3. The eye's crystalline lens is located directly behind the pupil and further focuses light. Through a process called accommodation this lens helps the eye automatically focus on near and approaching objects, like an autofocus camera lens.
4. Light focused by the cornea and crystalline lens (and limited by the iris and pupil) then reaches the retina — the light-sensitive inner lining of the back of the eye. The retina acts like an electronic image sensor of a digital camera, converting optical images into electronic signals. The optic nerve then transmits these signals to the visual cortex — the part of the brain that controls our sense of sight. [3]

Acanthamoeba Infection

Background:

The free-living amoebae that cause human infections include Acanthamoeba, Naegleria, Balamuthia mandrillaris, and, rarely, Sappinia. All 4 genera cause serious CNS or ocular infections. Distinct from enteric pathogenic protozoa, they all are usually soil/water commensals, have no human carrier state, involve no insect vector, and cause sporadic disease associated with specific behaviors and exposures.

Acanthamoeba are among the most prevalent environmental protozoa and have been classified by 18s rDNA sequencing into at least 20 genotypes, designated T1-T20. The most common environmental and human pathogens belong to the T4 genotype. The following species of *Acanthamoeba* have been associated with human disease:

- *Acanthamoeba castellanii* (T4)
- *Acanthamoeba polyphaga* (T4)
- *Acanthamoeba culbertsoni* (T10)
- *Acanthamoeba palestinensis* (T2)
- *Acanthamoeba astronyxis* (T7)
- *Acanthamoeba hatchetti* (T11)
- *Acanthamoeba rhysodes* (T4)
- *Acanthamoeba byersi* (T18)
- *Acanthamoeba divionensis* (T4)
- *Acanthamoeba heady* (T12)
- *Acanthamoeba lenticulata* (T5)
- *Acanthamoeba triangularis* (T4)
- *Acanthamoeba griffini* (T3)

The life cycle consists of 2 stages: a trophozoite (which is 14-40 µm in diameter) and a cyst (which has a double-layered wall with a diameter of 12-16 µm). Cysts are quite resistant to environmental and chemical insults.

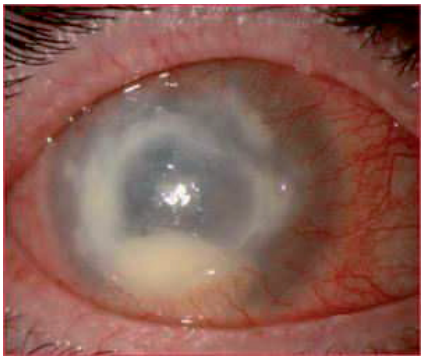
Acanthamoeba was first established as a cause of human disease in the 1970s and might be considered an emerging infection. This genus causes 3 clinical syndromes: granulomatous amebic encephalitis (GAE), disseminated granulomatous amebic disease (e.g., skin, sinus, and pulmonary infections), and, most commonly, amebic ocular keratitis. Individuals who develop GAE or disseminated disease are usually immunocompromised, whereas those with keratitis are usually immunocompetent. Disseminated disease and GAE carry a poor prognosis, and treatment strategies are not well defined; *Acanthamoeba* keratitis is a sight-threatening infection that carries a favorable prognosis when diagnosed and treated early.

Clinicians must be aware of the risk of ocular keratitis secondary to contamination of contact lenses so as to advise patients on preventive measures. Patients with contact lenses should be warned of exposure to water containing ubiquitous *Acanthamoeba* cysts, especially by swimming, showering, and using homemade lens-cleaning solutions.

Early recognition of the signs of keratitis (discomfort, blurred vision) are nonspecific but warrant prompt review of lens hygiene and aggressive diagnostic intervention. Therapies are most effective at the earliest stages of infection.

Severely immunosuppressed patients with subacute onset of headache, cognitive impairment, and focal neurologic signs should be considered at risk for granulomatous amebic encephalitis (GAE). While multiple ring enhancing lesions more commonly suggest toxoplasmosis, nocardia, and tuberculosis, exclusion of GAE requires biopsy. [(4)]

Acanthamoeba Keratitis



Acanthamoeba keratitis, first recognized in 1973, is a rare, vision threatening, parasitic infection seen most often in contact lens wearers. It is often characterized by pain out of proportion to findings and the late clinical appearance of a stromal ring shaped infiltrate. It is both difficult to diagnose and difficult to treat.

Two of the eight known species of Acanthamoeba, *A. castellanii* and *a polyphaga*, are responsible for most infections. Acanthamoeba are commonly found, free-living amoeba that have been located in various environments including pools, hot tubs, tap water, shower water, and contact lens solution. In May, 2007, the FDA announced an outbreak of Acanthamoeba keratitis that was associated with Complete Moisture plus Multi-Purpose Solution manufactured by Advanced Medical Optics.

Risk factors include contact lens wear, exposure to organism (often through contaminated water), and corneal trauma. Low levels of anti-Acanthamoeba IgA in tears has also been shown to be a risk factor. It is thought that over 80% of Acanthamoeba keratitis appears in contact lens wearers. In one study, 75% of the patients were contact lens wearers; 40% wore daily soft lenses, 22% wore rigid gas permeable lenses, and 38% wore extended wear or other lenses.

Acanthamoeba is ubiquitous. Corneal trauma, followed by exposure to the parasite (often through a water supply or contact lens solution) in a patient with low tear levels of anti-Acanthamoeba IgA leads to infection. Acanthamoeba exist in two forms: trophozoites and cysts. The trophozoites are mobile and consume bacteria (which allows for the diagnosis on E. coli plates). The trophozoites form double walled cysts which are incredibly resistant to methods of eradication (including freezing, heating, and irradiation).

Since treatment is toxic, lengthy, and not necessarily effective, prevention is essential. Contact lens wearers should be taught how to clean their contact lenses properly. They should be instructed never to use tap water or even saline to clean their lenses. They should also be instructed to visit an ophthalmologist at the earliest sign of problems.

Diagnosis of Acanthamoeba keratitis is difficult and often delayed. If clinical suspicion exists, the involved area of cornea can be scraped with a sterile instrument (blade, spatula, needle, calcium alginate swab, or cotton tip applicator) under topical anesthesia at the slit lamp. The culture specimen can then be inoculated into a dish of E. coli plated over non-nutrient agar. Acanthamoeba trophozoites and cysts can also be identified with the help of Gram, Giemsa-Wright, hematoxylin and eosin, periodic acid-Schiff, calcoflour white, or other stains. Confocal microscopy has also been used to diagnose Acanthamoeba cysts with some success.

Patients should be asked about contact lens wear and hygiene, contact lens solutions, recent corneal trauma, and recent exposure to water sources.

A comprehensive eye exam should be performed with careful attention to the signs and symptoms described below.

Early signs may be mild and non-specific. Possible findings include epithelial irregularities, epithelial or subepithelial infiltrates, and pseudodendrites. Later signs include stromal infiltrates (ring-shaped, disc form, or nummular), satellite lesions, epithelial defects, radial keratoneuritis, scleritis, and anterior uveitis (with possible hypopyon). Advanced signs include stromal thinning and corneal perforation.

Acanthamoeba keratitis is characterized by pain out of proportion to findings. In one study, 95% of patients complained of pain. Patients may also complain of decreased vision, redness, foreign body sensation, photophobia, tearing, and discharge. Symptoms may wax and wane; they may be quite severe at times.

Because the currently available treatments for Acanthamoeba are both toxic and lengthy, accurate diagnosis is essential. Diagnostic procedures usually begin with culture. Since the clinical picture is often non-specific, cultures should be taken for possible bacterial, fungal, and perhaps even viral infections as well. If available, confocal microscopy may be performed. If culture results are negative or if the infection appears to be more stromal than epithelial, a small corneal biopsy may be considered.

The differential diagnosis for Acanthamoeba in its early clinical stages includes dry eye, herpes simplex virus keratitis, recurrent corneal erosion, staph marginal keratitis, and contact lens associated keratitis. The differential diagnosis of later clinical stages includes viral, bacterial, fungal, and sterile (such as from topical anesthetic abuse) keratitis.

Medical treatment for Acanthamoeba keratitis is still evolving. Success has been reported with various combinations of antibiotic, antiviral, antifungal, and antiparasitic drugs. Many of these topical treatments are not commercially available in the United States and need to be specially ordered. Different regimens include topical preparations of Brolene, Neomycin-Polymyxin B-Gramicidin, polyhexamethylene biguanide (PHMB), chlorhexadine, and voriconazole. Some practitioners recommend oral ketoconazole.

Patients should be followed very closely (daily or almost daily) initially, until clinical response is seen. Since recurrences can occur and Acanthamoeba cysts are so resistant to treatment, medical treatments should be tapered very slowly and, if necessary, continued for many months. Steroids are controversial and may worsen the condition by inhibiting the host immune response. Pain should be addressed.

Cases of corneal perforation may need to be managed with surgical interventions. If possible, penetrating keratoplasty should be reserved for cases of visually significant corneal scarring in quiet eyes. If there are still signs of active infection or even if there are cysts lingering in the cornea, then infection may recur in the graft.

Post-operative complications after penetrating keratoplasty include recurrence of Acanthamoeba infection as well as all of the other possible post-operative complications (such as infection, glaucoma, cataract, wound leak, astigmatism).

The prognosis for Acanthamoeba is worse than for many other types of infectious keratitis and prevention is therefore very important. However, especially if caught early, satisfactory outcomes can certainly be achieved. [5]

Biology of Acanthamoeba

The term acanth (Greek "acanth" means "spikes") was added to "amoeba" to indicate the presence of spine-like structures (now known as acanthopodia) on its surface. It contains one or more prominent contractile vacuoles, whose function is to expel water for osmotic regulation. Other types of vacuoles in the cytoplasm include lysosomes, digestive vacuoles and a large number of glycogen-containing vacuoles. The plasma membrane consists of proteins (33%), phospholipids (25%), sterols (13%), and lipophosphonoglycan (29%). The major phospholipids in *Acanthamoeba* are phosphatidylcholine (45%), phosphatidylethanolamine (33%), phosphatidylserine (10%), phosphoinositide (6%), and diphosphatidylglycerol (4%). The main fatty acids chains in *Acanthamoeba* are oleic acids (40-50%), and longer polyunsaturated fatty acids (20-30%) . *Acanthamoeba* contains low levels of glycolipids. Glucose accounts for about 60% of the sugars of the glycolipids of the whole cells and of the plasma membranes. Among sterols, the non-saponifiable fraction of the total lipids extracted from the trophozoites of pathogenic *Acanthamoeba* possesses ergosterol and 7-dehydrostigmasterol. *Acanthamoeba* has been shown to produce prostaglandins.

Acanthamoeba has long been studied as a model eukaryotic cell with special emphasis on the actin cytoskeleton-based motility .*Acanthamoeba* moves relatively fast compared to other cells, with a locomotory rate of approximately 0.8 µm/second. The movement involves the formation of a hyaline pseudopodium. The manner of *Acanthamoeba* movement is similar both at solid substrata and water-air interface. Adhesion forces developed between *Acanthamoeba* and the water-air interface are greater than gravity, and thus amoebae are also transported passively without detachment from the water surface. Actin microfilaments are most concentrated just beneath the plasma membrane, and are responsible for resisting tension and forming cytoplasmic protrusions.

Life cycle of *Acanthamoeba*

Acanthamoeba has two stages in its life cycle, a vegetative trophozoite stage with a diameter of 13-23 µm and dormant cyst stage of 13-23 µm .During the trophozoite stage (Greek "tropho" means "to nourish"), *Acanthamoeba* feeds on organic particles as well as other microbes and divides mitotically under optimal conditions (food supply, neutral pH, ~30°C) and 50-80mOsmol.

Exposure to harsh conditions result in cellular differentiation into a double-walled cyst form.

The outer walls consists of proteins and polysaccharides, while the inner wall possesses cellulose Both walls are normally separated by a space, except at certain points where they form opercula in the centre of ostioles (exit points for excysting trophozoite). The cyst wall composition for *A. castellanii* belonging to T4 genotype has been shown to contain 33% protein, 4 - 6% lipid, 35% carbohydrates (mostly cellulose), 8% ash, and 20% unidentified materials.

Using gas chromatography combined with mass spectrometry, the carbohydrate composition of cyst walls revealed a high percentage of galactose and glucose and small amounts of mannose and xylose. Linkage analysis revealed several types of glycosidic linkages including the 1, 4-linked glucosyl conformation indicative of cellulose. [6]

Distribution in the environment and clinical settings

Acanthamoeba has been isolated from diverse natural environments including sea water, ocean sediments, beaches, pond water, soil, fresh water lakes, hot spring resorts, salt water lakes, Antarctica, water-air interface, and even from the air. They have been isolated from bottled mineral water, distilled water bottles, thermally-polluted factory discharges, cooling towers of the electric and nuclear power plants, Jacuzzi tubs, ventilation ducts, humidifiers, air-conditioning units, shower heads, kitchen sprayers, sewage, compost, vegetables, surgical instruments, contact lenses and their cases, pigeon droppings, fresh water fish, as well as other healthy, diseased, and dead animals. They have been recovered from hospitals, physiotherapeutical swimming pools, dialysis units, portable and stationary eye wash stations, human nasal cavities, throat, pharyngeal swabs, lung tissues, skin lesions, human faeces, corneal biopsies, maxillary sinus, mandibular autografts, stool samples, urine of critically ill patients, cerebrospinal fluids and the brain necropsies. Based on the above, it is accepted that *Acanthamoeba* is ubiquitously present in the environment and that we commonly encounter this organism in our routine lives as evidenced by the presence of anti-*Acanthamoeba* antibodies in up to 100% healthy populations in New Zealand and more than 85% in individuals of London that came from different countries. [6]

Role in the Ecosystem

In soil, protists such as amoebae, flagellates and ciliates have two major ecological roles: (i) influencing the structure of the microbial community, and (ii) enhancing nutrient recycling. Both of these activities are associated with soil protists feeding on bacteria thus regulating bacterial populations in the soil. Among protists, free-living amoebae are the dominant bacterial consumers and are responsible for up to 60% of the total reduction in bacterial population. The primary decomposers (bacteria) directly decompose organic materials but are inefficient in releasing minerals from their own mass. The secondary decomposers, such as free-living amoebae, consume the primary decomposers and release mineral nutrients as waste products that are tied up in the primary decomposer's biomass. In this way, protists such as *Acanthamoeba* (as well as other grazers) make nutrients available that would otherwise remain inaccessible for much longer. The soil containing *Acanthamoeba* and bacteria showed significantly greater mineralization of carbon, nitrogen, and phosphorous compared with the soil containing bacteria but without *Acanthamoeba*. As well as bacterial consumption, amoebae promote bacterial populations in the soil. The mineral regeneration by the secondary decomposers (protists such as amoebae), relieved nutrient limitation for the primary decomposers. This was demonstrated with the findings that when nitrogen was limiting (but carbon present), nitrogen mineralization by *Acanthamoeba* permitted continued growth of bacteria (*Pseudomonas paucimobilis*) resulting in a greater bacterial biomass. And when carbon was limiting, *Acanthamoeba* was almost entirely responsible for nitrogen mineralization, with bacteria (*Pseudomonas paucimobilis*) contributing little. Using an experimental model system, the effects of grazing by *Acanthamoeba* on the composition of bacterial communities in the rhizosphere of *Arabidopsis thaliana* demonstrated reduction in bacterial populations leading to positive effect on plant growth. Overall, *Acanthamoeba* appears to play an important role in the regulation of bacterial populations in the environment and the nutrient cycling, thus contributing to the functioning of the ecosystems. [6]

Pathogenesis

Parasite adhesion to the host cell is a primary step and is mediated by a 130 kDa mannose-binding protein (MBP) expressed on the surface of *Acanthamoeba*. *Acanthamoeba mbp* consists of 6 exons and 5 introns that spans 3.6 kbp. The 2.5 kbp cDNA codes for an 833 amino acids precursor protein with a signal sequence (residues 1-21aa), an *N*-terminal extracellular domain (residues 22-733aa) with five *N*- and three *O*-glycosylation sites, a transmembrane domain (residues 734-755aa), and a *C*-terminal intracellular domain (residues 756-833aa). Other adhesins include a laminin-binding protein with a predicted molecular mass of a 28.2 kDa, a 55 kDa laminin-binding protein and a > 207 kDa adhesin.

The initial binding leads to secondary events such as phagocytosis and toxin production resulting in the host cell death in a phosphotidylinositol 3-kinasedependent (PI3K) manner. The downstream effectors of PI3K involves activation of proapoptotic molecules, Bak and Bax, loss of mitochondrial membrane potential and release of cytochrome *c* as well as caspase activation, all well-known mediators of the apoptosis . Among host cell receptors, Toll-like receptor 4 (TLR4) showed involvement in *Acanthamoeba* recognition and exerting an effect through adaptor protein, Myeloid differentiation primary response 88 that led to the activation of transcription factors, nuclear factor-kappa B signalling through extracellular signal-regulated kinases (ERKs) inducing the secretion of cytokines including interleukin-8, tumor necrosis factor-alpha and interferon-beta in human corneal cells.

Using human brain microvascular endothelial cells (HBMEC), which constitute the blood-brain barrier, it is shown that *Acanthamoeba* abolished the HBMEC transendothelial electrical resistance by degrading occludin and zonula occludens-1 tight junction proteins in a Rho kinase-dependent manner leading to increased permeability.

Other factors that may contribute to *Acanthamoeba* pathogenesis include ecto-ATPases of approximate molecular weights of 62, 100, 218, 272, > 300 kDa and these are involved in caspase-3 activation .The neuraminidase activities of *Acanthamoeba* could be relevant in the colonization of the parasite, and also important in producing damage of the sialic acid-rich corneal epithelium and in the alterations of glycolipids associated with meningoencephalitis. Interestingly, the neuraminidases of *Trypanosoma cruzi* and *Acanthamoeba* are immunologically related as demonstrated by antibodies against neuraminidase of *Trypanosoma cruzi*, which reacted with *Acanthamoeba*. Two superoxide dismutases have been identified in *Acanthamoeba*: an iron superoxide dismutase (~50 kDa) and a copper-zinc superoxide dismutase (~38 kDa). The superoxide dismutase catalyzes the dismutation of the superoxide into oxygen and hydrogen peroxide and play a role in antioxidant defence. These enzymes may provide additional targets for chemotherapy and immuno-diagnosis of *Acanthamoeba* infections. *Acanthamoeba* has been shown to display plasminogen activator activity by catalyzing the cleavage of host plasminogen to form plasmin, which can activate host matrix metalloproteinases leading to degradation of the basement membranes.

Of contact-independent factors, *Acanthamoeba* possess hydrolytic enzymes including elastases, phospholipases, glycosidases and a variety of serine, cysteine and metalloproteases.

However, their precise mechanisms of action at the molecular-level are only beginning to emerge. That some of the above proteases are secreted only by the clinical isolates may indicate their role as potent virulence factors and/or diagnostic targets.

Future studies in the role of proteases as vaccine targets, search for novel inhibitors by screening of chemical libraries, or rational development of drugs based on structural studies will enhance our ability to target this pathogen. Overall, the mechanism by which *Acanthamoeba* breaches biological barriers is complex and is likely to involve both parasite (Adhesins, proteases, phospholipases) as well as host determinants [interleukin-beta, interleukin-alpha, tumor necrosis factor- alpha, interferon-gamma, host cell apoptosis]. In addition to aforementioned potential virulence factors, the ability of *Acanthamoeba* to survive harsh environmental conditions and its resistance to chemotherapeutic drugs by differentiating into cysts contributes to its pathogenicity[(6)].

Immune response to *Acanthamoeba* infections

The recurrence of AK infections is common, suggesting that the corneal infection alone does not induce protective immunity against the parasite antigens. Experimental animals immunized orally with *Acanthamoeba* antigens mixed with the cholera toxin showed significantly lower infection rates compared with the control groups (21.4% *versus* 72.6% respectively) and protection was associated with higher levels of parasite-specific sIgA. More specifically, oral immunization using recombinant MBP improved AK and protection was associated with the presence of elevated levels of anti-MBP sIgA in tears of the immunized animals. Similarly, oral immunization with a serine protease (~133 kDa) reduced the severity of the corneal infection by modulating MMP-2 and MMP-3 expression.

Overall, it is suggested that AK patients show decreased overall levels of sIgA as well as specific anti-*Acanthamoeba* sIgA, however the role of sIgA was questioned in a recent study in which neither normal tears nor AK tears had any protective effects on *Acanthamoeba*-mediated corneal epithelial cell cytotoxicity. Tear factors, in addition to sIgA such as lysozyme, lactoferrin, beta-lysins, prostoglandins, and other compounds with antimicrobial and immunological properties were also shown to have no significant effects on *Acanthamoeba*-mediated binding to and cytotoxicity of human corneal epithelial cells. Tears also contain complement that is composed of serum-borne molecules in a cascade-like manner. *Acanthamoeba* directly activates the complement system via the alternative pathway, however pathogenic amoebae are resistant to complement-mediated lysis due to expression of complement regulatory proteins including decay accelerating factor. The presence of macrophages in corneas exposed to the parasite-laden contact lenses prevented the development of full-blown AK *in vivo* by inducing an inflammatory response, in particular secretion of macrophage inflammatory protein-2.

For AGE, immunization with *Acanthamoeba* antigens using intranasal, intraperitoneal, intravenous or oral routes of administration had a protective effect validating that AGE is limited to individuals with a weakened immune response. The complement pathway and antibodies in the presence of phagocytes show potent lytic activity against *Acanthamoeba* in a contact-dependent manner. These interactions also stimulate secretion of pro-inflammatory cytokines including interleukin-1-beta, interleukin-6 and tumor necrosis factor-alpha.

Other studies in mice have shown significant increased natural killer cell activities in *Acanthamoeba*-infected animals suggesting that natural killer cells may also play a role in the protective immunity. Overall, a debilitated immune status of the host is a pre-requisite in AGE but the underlying mechanisms together with the role of the host ethnic origin (i.e., genetic predisposition) remain incompletely understood. Pathogenic *Acanthamoeba* are shown to degrade chemokines and cytokines, antibodies, complement pathway, and macrophages. [6]

Sappinia diploidea infection

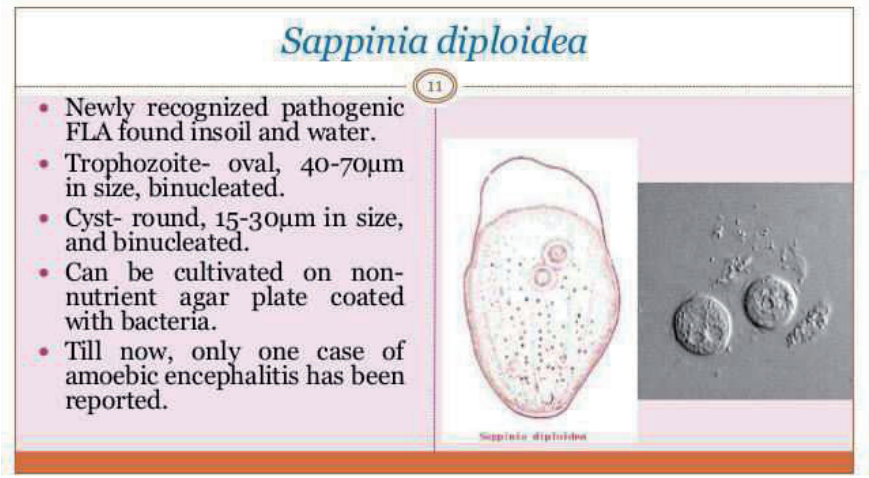
Sappinia can be found around the world. It's usually found in elk and buffalo feces, places where farm animals are known to eat, soil containing rotting plants, fresh water sources.

It is capable of causing infectious disease in humans.

Symptoms of a Sappinia infection include: Headache, Sensitivity to light, Nausea or upset stomach, Vomiting, Blurry vision, Loss of consciousness. A scan of the one, infected patient's brain also revealed a 2-centimeter tumor-like mass on the back left section of his brain.

Treatment for the one identified case of Sappinia infection included the removal of a tumor in the brain and a series of drugs given to the patient after surgery. This treatment lead to the patient's full recovery.

Specifically, it can cause amebic encephalitis. [7]



Toxoplasmosis

The most common finding in congenital toxoplasmosis is the ophthalmologic manifestation retinochoroiditis, which has a predilection for the posterior pole. It is seen in 75-80% of cases and is bilateral in 85% of cases. In acquired toxoplasmosis, the ocular form of the disease occurs much less frequently. Previously, only 1-3% of patients with acquired infection were believed to develop ocular toxoplasmosis. However, serologic studies suggest that ocular toxoplasmosis is more commonly associated with acquired infection than was previously believed.

Consultations with internal medicine or infectious disease specialists are always recommended in the treatment of ocular toxoplasmosis. (8)

Ocular toxoplasmosis occurs as a consequence of *Toxoplasma gondii* infection. *T. gondii*, an obligate intracellular parasite, is estimated to infect at least one billion people worldwide.

At least 25% of individuals who have *T. gondii* present with associated ocular manifestations.[1] Ocular inflammation secondary to *T. gondii* infection is the most frequent cause of posterior uveitis.

Classic findings include a white fundus lesion with overlying, intense vitreous cells that frequently is described as “headlights in a fog.” The presentation of ocular toxoplasmosis can include a wide range of clinical signs, which poses a diagnostic challenge. (9)

Toxoplasmosis is one of the most frequently identifiable causes of uveitis worldwide. In fact, *Toxoplasma gondii* infection is the most common cause of infectious posterior uveitis in non-immunocompromised individuals, and second only to cytomegalovirus retinitis in patients with HIV/AIDS.

Toxoplasma gondii is an obligatory intracellular parasite. While systemic signs and symptoms of infection are less common in healthy adults, such findings may be present in newborns and immunocompromised patients. Sexual reproduction of the parasite occurs in small intestinal epithelial cells of the cat, with subsequent fecal elimination of oocysts. Once ingested by other animals, which serve as intermediate hosts, the oocysts rupture to release tachyzoites, which ultimately travel to target tissues to become tissue cysts or bradyzoites.

Clinical Manifestation, Diagnosis

Traditionally, it was thought that most active ocular toxoplasmosis represented reactivation of congenital toxoplasmosis acquired transplacentally from the mother. Recently, however, it has been shown that acquired infections occur more frequently than previously suspected.

Toxoplasma infection is asymptomatic in most immunocompetent patients and, when it occurs, is usually benign and self-limited. The infection may be much more severe, however, in the fetus and immunocompromised patients.

The clinical presentation of ocular toxoplasmosis depends on patient age, and the location, size and severity of retinochoroiditis. Ocular manifestations include floaters and blurred vision. Decreased visual acuity may occur as a result of macular involvement or severe vitreous inflammation. In immunocompromised patients, the clinical presentation may be rather atypical.

Toxoplasmic retinochoroiditis is a recurrent disease in two-thirds of patients.

Active toxoplasmic retinochoroiditis is whitish and moderately exudative with ill-defined borders and involves the macula in a majority of patients.[12] Mild to moderate anterior segment inflammation may or may not be a presenting feature, vitreous inflammation is virtually always present. Retinal vasculitis in the vicinity of an active lesion or in the distant retina may also be seen.

Retinochoroiditis in patients with HIV/AIDS may show atypical features, such as large confluent areas of retinochoroidal necrosis and/or active bilateral lesions.

Optic neuritis, punctate outer retinitis, neuroretinitis, papillitis and pseudoretinitis are other atypical manifestations of this disorder. During the healing process, retinochoroidal shunt and even choroidal neovascularization, gliosis and vitreous tractional bands may develop.

The diagnosis of ocular toxoplasmosis is made mainly by clinical observation of a focal necrotizing retinochoroiditis.

In atypical cases, serologic tests such as serum anti-Toxoplasma titers of IgM and IgG may be helpful to support the diagnosis. Negative results are of importance to exclude atypical ocular toxoplasmosis. In cases where the diagnosis is uncertain, demonstration of anti-Toxoplasma antibody titers in the aqueous humor or vitreous can be helpful. Polymerase chain reaction (PCR) of aqueous and vitreous samples is another tool with high sensitivity and specificity.

Fluorescein angiography and indo-cyanine green angiography findings in toxoplasmic retinochoroiditis are nonspecific.

Two recent non-invasive photography techniques, i.e., infrared and autofluorescence, may further enhance our ability to determine the extent of retinochoroiditis. Autofluorescence imaging of toxoplasmic retinochoroidal scars demonstrates a dark area (hypo-autofluorescence) due to lack of functional retinal pigment epithelium. Acute, active lesions may also show hypo-autofluorescence due to the presence of overlying retinal edema. In fact, autofluorescence imaging can be used to monitor the effect of medical therapy, since it better demonstrates resolution of active retinal edema.

Differential Diagnosis

Recurrent toxoplasmic retinochoroiditis adjacent to a scar area may be confused with serpiginous choroiditis. Necrotizing retinitis due to CMV, herpes simplex virus, herpes zoster virus, fungal retinitis (candidiasis, blastomycosis), septic retinitis, ocular toxocariasis, sarcoidosis, syphilis and tuberculosis are other diagnoses to exclude when considering toxoplasmosis. Punctate outer

retinal toxoplasmosis is an atypical form of ocular toxoplasmosis that may be confused with other white dot syndromes.

Prevention

Transmission can occur by ingesting oocysts, tachyzoites, tissue cysts or bradyzoites. In addition to contaminated food, water source contamination is increasingly recognized as a source of infection. The disease can also be acquired by transfusion of whole blood or leukocytes, by organ transplant, or accidentally in laboratory workers.

Prevention of the initial infection is the most effective way of reducing Toxoplasma-related morbidity. Raw meat, raw eggs, unwashed vegetables and unpasteurized milk should not be consumed.

Preventive strategies include cooking and freezing meat, washing fruits and vegetables, hand washing[8] and avoiding the use of contaminated water. Blood transfusions and organ transplants from sero-positive donors should be avoided. Prevention of disease transmission is also crucial for immunocompromised individuals and sero-negative pregnant women. Cat vaccination may interrupt the parasite life cycle.

Treatment

The goal of treatment is to arrest the multiplication of the parasite during the active period of retinochoroiditis and to minimize damage to the retina and optic nerve. Despite being a self-limiting disease in most instances, Toxoplasma infection may cause decreased vision secondary to optic nerve or macular involvement, and severe vitreous inflammation. Patients with the following characteristics are considered by most to be appropriate treatment candidates:

- optic nerve involvement—either direct or within two disc diameters;
- a lesion within the temporal arcades or threatening the arcade vessels;
- a large lesion with subretinal hemorrhage and/or serous retinal detachment regardless of location;
- severe vitreous inflammation;
- loss of more than two lines in visual acuity;
- persistent retinochoroidal inflammation for more than one month;
- toxoplasmic retinochoroiditis in the first year of life;
- a newborn diagnosed with con-genital toxoplasmosis regardless of the presence or absence of ocular lesions; and
- Any lesion in an immunocompromised host.

Since active lesions, even far from the macula, may be associated with loss of visual acuity due to macular edema, intense Vitritis, macular tractions or detachment, treating any active lesions may be indicated, particularly given the emergence of safer treatment regimens. Furthermore, tachyzoites released from reactivated tissue cysts may spread to other sites in the retina. For this reason, some believe that treatment of any active lesion may be associated with a decreased overall tachyzoite burden, hence diminishing the risk of recurrences.

That said, an evidence-based systematic review of the literature disclosed a lack of evidence to support routine antibiotic treatment for acute toxoplasmic retinochoroiditis. [10]

Philophthalmus gralli

Philophthalmus gralli, commonly known as oriental avian eye fluke, is found in conjunctiva sac of eyes of many species of birds. The oriental eye fluke is described to parasitize the conjunctiva sac of various galliforms and anseriforms (Nollen and Murray 1978). In Brazil this parasite was reported in native anseriforms species (Muniz-Pereira and Amato 1993). It was first discovered by Mathis and Leger in 1910 in domestic chickens from Hanoi, Vietnam. Birds are definitive hosts and freshwater snail species are intermediate hosts (e.g. *Tarebia granifera* and *Melanoides tuberculata*.). Human cases of philophthalmosis are rare, but have been previously reported in Europe, Asia, and America (i.e., Yugoslavia, Sri Lanka, Japan, Israel, Mexico, and the United States).

Life cycle

Philophthalmus gralli reaches sexual maturity in a bird and produces eggs. Fully Embryonated eggs are shed into the water from the definitive host's eyes. Miracidium is induced to hatch when ripe eggs are released from the worm into water. Upon contact with a snail, the miracidium perforates the host epidermis with the aid of secretions and the anterior cilia. It penetrates the snail far enough to release a single rediae. The mother redia localizes in the heart and produces daughter rediae, which migrate to digestive glands to continue its development and produce megalurous cercariae. Cercariae are released from the snail and encyst on aquatic vegetation or other solid objects in the water. The definitive host, which is usually an aquatic bird, becomes infected upon ingestion of metacercariae. Excystment of the metacercariae occurs immediately upon reaching the mouth or crop of the bird and not in the stomach or intestine as in many other digenetic trematodes. Within 3 to 5 hours after ingestion, immature worms may be found in the esophagus, nasal passages, the orbit and the lobes of the lacrimal gland. Humans rarely serve as incidental hosts, but may do so when they ingest metacercariae on aquatic vegetation.

Morphology

P. gralli egg is non operculate and oval. The shell is thin and elastic and has an internal thickening at the small end.

The miracidia is composed of twenty epidermal plates arranged in 4 tiers: 6, 8, 4, 2 cells on each respective tier. It consists of two excretory pores and two pairs of lateral sensory papillae.

The morphology of a redia is elongated and cylindrical. It has a well-developed anterior pharynx and a long intestinal tract. Birth pore is found between first and second quarter of body. Lateral processes are near posterior tip of body.

The cercaria has two suckers: a ventral sucker and rounded subterminal sucker. Intestinal ceca bifurcate posterior to pharynx. Excretory bladders are located at posterior end of the cercarial body.

The metacercarial cyst is elongated and oval-shaped with sensory papillae. The excysted metacercarial is oval-shaped with a subterminal sucker and a ventral sucker.

The adult form of *P. gralli* is fusiform shaped. Body surface is covered by small spines at acetabular region. The two suckers are orally and subterminally located. Pharynx is located immediately posterior to oral sucker. Acetabulum is located at anterior third level of body. Both female and male organs are found within the body.

Treatment

The most common way to rid of Philophthalmus gralli is removal with forceps or flushing the worms out. Doramectin may also be used.

Symptoms

Clinical symptoms are a result of flukes attaching to the conjunctiva. It has different effect depending on the host. Infection may cause congestion and erosion of the conjunctivae, conjunctivitis with persistent lacrimation, and semilunar fold swelling in chickens, ostriches, and humans, respectively.

The birds had swollen eyes and severe conjunctivitis and constant lacrimation accompanied by a purulent exudates. A fraction of the birds became semi-blind from the infection. [11]

Toxocariasis

Despite being one of the most common zoonotic infections worldwide, human toxocariasis has been one of the neglected tropical diseases. Although most human infections are asymptomatic, two main syndromes of human toxocariasis are classically recognized: systemic toxocariasis, which encompasses diseases in major organs; and ocular toxocariasis (OT), disease in the eye or optic nerve, caused by the migration of Toxocara larvae into the eye. OT is usually a unilateral disease, which typically presents as retinal granuloma, a yellowish or whitish inflammatory mass, in the posterior pole or peripheral retina. Granuloma itself or other comorbid conditions such as epiretinal membrane, macular edema, and retinal detachment can lead to permanent retinal damage and visual loss in eyes with OT. OT is diagnosed clinically by identification of clinical signs on ophthalmologic examination. Serological tests, such as enzyme-linked immunosorbent assay (ELISA) for detection of serum antibody against the Toxocara larvae, can confirm the diagnosis. In addition, serum immunoglobulin E and detection of ocular fluid antitoxocara antibody by ELISA may give additional aid to the diagnosis. Standard treatment of OT is corticosteroid in patients with active intraocular inflammation. Although the role of anthelmintic therapy is unclear, favorable outcome has been reported by combined corticosteroid and albendazole therapy in eyes with active inflammation. Prevention, by increasing public awareness and reducing the risk of infection, is also important. Recently, the association between ingestion of uncooked meat or liver and toxocariasis was reported, especially in adult patients.[12]

Ocular toxocariasis is a rare infection caused by roundworms, Toxocara canis and Toxocara cati. It was first recognized to be associated with dogs in the 1940s. It typically affects children and can lead to profound monocular loss of vision despite known medical and surgical therapies. Its prevalence has been estimated in certain populations and found to be rare. Presentations typically include posterior uvietis with symptoms and signs such as reduced vision, photophobia, floaters, leukocoria, and retinal granulomatous disease. Management includes quieting inflammation, eliminating the offending organism, and repairing vitreoretinal Sequelae. Prognosis is often correlated to presentation and the degree to which Sequelae are present. Vision typically ranges from 20/40 to 20/400 depending on these factors.

Toxocariasis is a zoonosis, which results from infection with common roundworms Toxocara canis and Toxocara cati. It exists as two major categorizations, visceral larva migrans (VLM) and ocular larva migrans (OLM). Although seroprevalence as measured by Toxocara antibody levels in the United States has been estimated at 13.9%, symptomatic infection is significantly less common, especially OLM.

The prevalence of this disease has been measured in certain subpopulations as well as the general population. In a North Californian uveitic population, 1% of patients were found to have ocular toxocariasis. According to Morbidity and Mortality Weekly Report released by the CDC, from September 2009 until September 2010 there were 68 new cases of ocular toxocariasis in the country with an emphasis of new cases from the South (57%). There is a concern of underreporting and misdiagnosis. One study performed at a large academic institution found that 26% of misdiagnosed retinoblastomas were later identified as toxocariasis.

Typically, this disease manifests in children and early adolescents but 23 case studies found afflicted patients ranging from 8 to 45 years of age. In 2010 the CDC reported an average age in the United States of 8.1 years with a range from 1 to 60 years of age.

Infection by roundworms, Toxocara canis or Toxocara cati. These nematodes live and mature in dog or cat intestine, respectively. As a mature adult the organism releases eggs which are passed in the stool. Contact with infected materials leads to human infection.

Geophagia, exposure to and ownership of puppies and kittens (specifically young dogs and cats). In puppies 2 to 6 months old the prevalence of Toxocara canis has been reported to be over 80%. In dogs older than one year this number drops to 20%.

In humans, after contact with infected fecal material, the roundworm migrates throughout various organs but is unable to sexually mature. Reactive inflammatory processes lead to the organism's encapsulation. Ocular larva migrans is a result of the ingested egg developing and migrating to the eye causing local disease.

The majority of patients will either own or have exposure to a dog or cat. Patients without this history likely were unknowingly in contact with contaminated surfaces or are reported as geophagic by their parents. The vast majority of patients report unilateral reduced vision as well as other symptoms typical of uveitis, such as photophobia.

OLM is unilateral in 90% of cases. Ocular toxocariasis typically presents as posterior uvietis, namely, granulomatous disease of the peripheral (up to 50%) or central (up to 25%) retina. Other common presentations include endophthalmitis (up to 25%) and intermediate uveitis. It is also rarely associated with granulomas of the optic disc.

The most common sign associated with ocular toxocariasis is Vitritis as it is identified in over 90% of patient. Other presenting signs include leukocoria, ocular injection, and strabismus.

Symptoms:

Decreased vision, pain, photophobia, and floaters.

Clinical diagnosis:

OLM is largely a clinical diagnosis based on history.

Laboratory diagnosis:

Unlike in VLM, OLM patients do not typically have marked eosinophilia. The most useful test for ocular toxocariasis is an ELISA.

ELISA for Toxocara excretory secretory (TES) antigen has a 90% sensitivity and specificity of VLM. OLM is not as easily detectable in peripheral blood tests and so this test is supportive but not the gold standard of diagnosis in ocular presentations. Specificity is lowered due to cross reaction with other helminthic infections. In addition, the value of this test is compromised secondary to the high prevalence of seropositivity to Toxocara without symptomatic infection in the general population. In one study this ELISA was found positive in 50% of patients while negative in 36.4% of patients and unknown in 13.6% of patients (N=22). In particular, one patient in this study with a negative serum ELISA was later found to have a positive aqueous ELISA.

Differential diagnosis:

- Retinoblastoma (in this case B scans typically find calcifications which are extremely uncommon in OLM. Non inflamed eyes without cataract are also suggestive of Retinoblastoma.)
- Coats Disease
- Persistent Fetal Vasculature
- Retinopathy of Prematurity
- Familial Exudative Vitreoretinopathy
- Idiopathic Peripheral Uveoretinitis
- Toxoplasmosis
- Histoplasmosis
- Optic Neuritis

Management

Management of this disease focuses on three main points:

- Minimizing inflammation
- Eliminating the offending organism
- Addressing vitreal and retinal complications secondary to infection

Treatment:

Anti-inflammatory therapy:

Topical steroids are typically used to limit inflammation in order to prevent the development of tractional membranes and resulting retinal detachments. Other options include periocular injections and oral medication. In the case of anterior segment inflammation, cylcoplegics are also used to prevent the formation of synechiae.

Anti-parasitic therapy:

The use of these drugs is unproven in the case of ocular toxocariasis. There is some support for the use of albendazole or thiabendazole to eradicate the organism. Albendazole is the preference of some physicians as it has increased blood brain barrier penetration.

Surgery:

The CDC reports that 25% of patients presenting with new cases of ocular toxocariasis require surgery. Vitrectomy is the most common surgical therapy for ocular toxocariasis. The most common indications for surgical intervention are persistent vitreous opacification, hemorrhage, tractional retinal detachment, and epiretinal membranes. Other indications for retinal surgery include rhegmatogenous retinal detachments. Tractional retinal detachments are more common in cases that include granulomas located in the peripheral retina.

Sequelae:

A list of Sequelae of this disease more commonly includes cystoid macular edema, traction retinal detachment, epiretinal membranes, and cataract. With more infrequency OLM has also

been associated with retro lenticular membrane, rhegmatogenous retinal detachment, anterior lens capsule membrane, and macular holes.

Prognosis:

Prognosis is typically excellent for those patients without Sequelae. These cases are mostly self-limited or controlled with medical management. It has been identified that median visual acuity depends on presentation. A median visual acuity of 20/50 has been associated with patient presentations with posterior pole granulomas. Patients with peripheral granulomas had a median visual acuity of 20/70 and presentations with endophalmitis were associated with a median visual acuity between 20/200 and 20/400.

Those that require surgical intervention typically have a poorer prognosis and visual acuity. In very rare cases ocular Toxocara has been associated with no light perception. [13]

Onchocerciasis

- Onchocerciasis, commonly known as “river blindness”, is caused by the parasitic worm Onchocerca volvulus.

- It is transmitted to humans through exposure to repeated bites of infected blackflies of the genus Simulium.
- Symptoms include severe itching, disfiguring skin conditions, and visual impairment, including permanent blindness.
- More than 99% of infected people live in 31 African countries. The disease also exists in some foci in Latin America and Yemen.
- Community-directed treatment with ivermectin is the core strategy to eliminate onchocerciasis in Africa. In the Americas the strategy is biannual large-scale treatment with ivermectin.
- In July 2016, Guatemala became the fourth country in the world after Colombia (2013), Ecuador (2014), and Mexico (2015) to be verified free of onchocerciasis after successfully implementing elimination activities for decades. [14]

Onchocerciasis is an eye and skin disease caused by a worm (filaria) known scientifically as Onchocerca volvulus. It is transmitted to humans through the bite of a blackfly (simulium species). These flies breed in fast-flowing streams and rivers, increasing the risk of blindness to individuals living nearby, hence the commonly known name of "river blindness". Within the human body, the adult female worm (macrofilaria) produces thousands of baby or larval worms (microfilariae) which migrate in the skin and the eye.

Consequences of the disease:

The death of microfilariae is very toxic to the skin and the eye, producing terrible itching and various eye manifestations (lesions). After repeated years of exposure, these lesions may lead to irreversible blindness and disfigurative skin diseases sometimes named "leopard" skin and "lizard" skin.

In some West African communities, about 50% of men over the age of 40 years had been blinded by the disease. Finally, people fled the fertile river valleys to settle in less productive upland country. Hence the annual economic losses were estimated, in the 1970s, at US$ 30 million.

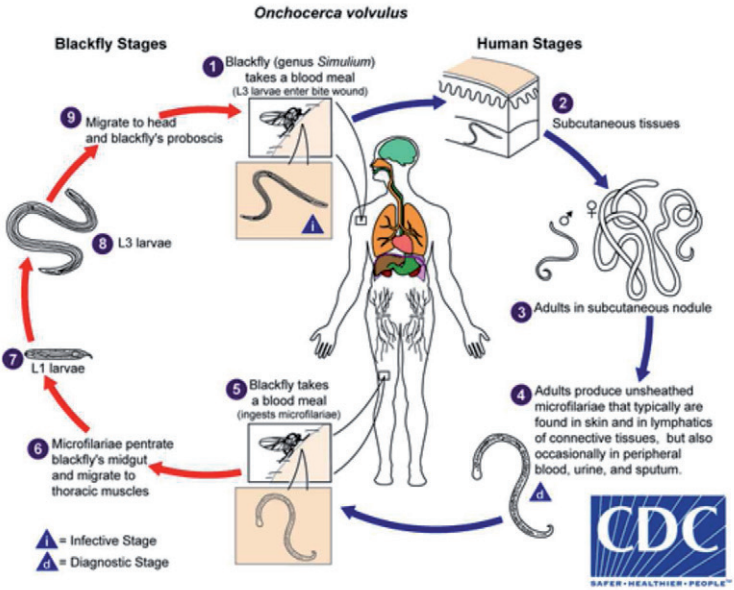
Distribution:

The distribution of onchocerciasis is linked to the location of blackflies which are naturally found close to the fast-running streams and rivers in the inter-tropical zones. Therefore, about 90% of the disease occurs in Africa. Onchocerciasis is also found in six countries in Latin America and in Yemen in the Arabian Peninsula, where the disease is believed to be exported by the slave trade. [15]

Onchocercal infections are found in tropical climates. The main burden is in 30 countries in sub-Saharan Africa, though the parasite is found in limited areas in the Americas and in Yemen in the Middle East. In the Americas, transmission of onchocerciasis has been interrupted in 11 of the 13 foci. Interventions to limit transmission stopped in Colombia in 2008, in Ecuador in 2010, in Mexico in 2012, and in Guatemala in 2012. Transmission and interventions to limit transmission continue in one area in Venezuela and one area in Brazil. The World Health Organization (WHO) estimates that at least 25 million people are infected with *O. volvulus* worldwide; of these people 300,000 are blind and 800,000 have some sort of visual impairment. Some 123 million people are at risk for becoming infected with the parasite.

The people most at risk for acquiring onchocerciasis are those who live near streams or rivers where there are *Simulium* blackflies. Most of the areas where the blackflies are found are rural agricultural areas in sub-Saharan Africa. Usually, many bites are needed before being infected, so people who travel for short periods of time (generally less than 3 months) to areas where the parasite is found have a low chance of becoming infected with *O. volvulus*. Those travelers to at-risk areas most likely to become infected are long-term missionaries, Peace Corps and other long-term volunteers, and field researchers. [16]

Life cycle:



During a blood meal, an infected blackfly (genus *Simulium*) introduces third-stage filarial larvae onto the skin of the human host, where they penetrate into the bite wound ❶. In subcutaneous tissues the larvae ❷develop into adult filariae, which commonly reside in nodules in subcutaneous connective tissues ❸. Adults can live in the nodules for approximately 15 years. Some nodules may contain numerous male and female worms. Females measure 33 to 50 cm in length and 270 to 400 µm in diameter, while males measure 19 to 42 mm by 130 to 210 µm. In the subcutaneous nodules, the female worms are capable of producing microfilariae for approximately 9 years. The microfilariae, measuring 220 to 360 µm by 5 to 9 µm and unsheathed, have a life span that may reach 2 years. They are occasionally found in peripheral blood, urine, and sputum but are typically found in the skin and in the lymphatics of connective tissues❹. A blackfly ingests the microfilariae during a blood meal❺. After ingestion, the microfilariae migrate from the blackfly's midgut through the hemocoel to the thoracic muscles❻. There the microfilariae develop into first-stage larvae ❼and subsequently into third-stage

infective larvae❽. The third-stage infective larvae migrate to the blackfly's proboscis ❾and can infect another human when the fly takes a blood meal❶. [17]

Pathology:

The blackflies that transmit the parasite bite during the day. Female blackflies need to ingest blood for ovulation, so they feed on humans. If a blackfly bites an infected person, onchocerciasis larvae can be ingested by the blackfly after which they migrate to the flight muscles. The larvae develop inside the blackfly and become infective for humans in about 10 to 12 days. They migrate to the biting parts of the fly where they can be transmitted back to humans when it bites again.

Humans become infected when blackflies deposit *Onchocerca* infective larvae into the skin when biting to extract blood. Once inside the human body, the larvae mature into adults in around 3 months to 1 year. Most adult female worms live in fibrous nodules under the skin and sometimes near muscles and joints. Adult male worms are usually found near the female worms. Nodules form around the worms as part of the interaction between the parasite and its human host. Inside the nodules the worms are relatively safe from the human immune response. As adults, female worms produce thousands of new larvae daily. The larvae become detectable in the skin 10 to 20 months after the initial infection. The adult worms can live up to 15 years inside the human body, and their larvae have a lifespan up to 2 years.

Some people do not experience symptoms while infected with *O. volvulus*, as the larvae can migrate through the human body without provoking a response from the immune system. But many people do have symptoms, which include itchy skin rashes, nodules under the skin, and vision changes. There can be non-painful swelling of lymph glands, but this is not common. Most symptoms of onchocerciasis are caused by the body's response to dead or dying larvae. The inflammation caused in the skin, in addition to causing itching, can result in long-term damage to the skin. This can cause changes in the color of the skin that result in a "leopard skin" appearance, and can cause thinning of the skin with loss of elastic tissue that gives the skin a "cigarette-paper" appearance and can contribute to conditions such as "hanging groin.". The inflammation caused by larvae that die in the eye results initially in reversible lesions on the cornea that without treatment progress to permanent clouding of the cornea, resulting in blindness. There can also be inflammation of the optic nerve resulting in vision loss, particularly peripheral vision, and eventually blindness. [18]

Diagnosis:

The diagnosis of onchocerciasis can be difficult in light infections, which are more common in persons who have travelled to but are not residents of affected areas. There are multiple ways that the diagnosis can be made:

- The most common method of diagnosis is the skin snip. A 1- to 2- mg shaving or biopsy of the skin is done to identify larvae, which emerge from the skin when it is put in physiologic solutions (e.g. normal saline). Typically 6 snips are taken from different areas of the body. Polymerase chain reaction (PCR) of the skin can allow for diagnosis if the larvae are not visualized.
- In patients with nodules in the skin, the nodule can be surgically removed and examined for adult worms.
- Infections in the eye can be diagnosed with a slit-lamp examination of the anterior part of the eye where the larvae or the lesions they cause are visible.

- Antibody tests have been developed to test for infection, though they are not widely available in the United States. These tests cannot distinguish between past and current infections, so they are not as useful in people who lived in areas where the parasite exists, but they are useful in visitors to these areas. Some of the tests are general tests for infection with any filarial parasite and some are more specific to onchocerciasis. [19]

Treatment:

People who are found to be infected with *O. volvulus* should be treated in order to prevent the long-term skin damage and blindness. The recommended treatment is ivermectin, which will need to be given every 6 months for the life span of the adult worms or for as long as the infected person has evidence of skin or eye infection. Ivermectin kills the larvae and prevents them from causing damage but it does not kill the adults. There is a promising new treatment using doxycycline that kills the adult worms by killing the *Wolbachia* bacteria on which the adult worms depend in order to survive. If you are infected, it is possible that your doctor will want to treat you both with the ivermectin and the new treatment. Before any treatment is begun, however, you need to make sure that you are not also infected with *Loa loa*, another filarial parasite found in central Africa that is sometimes found in the same areas where *O. volvulus* is found, because *Loa loa* can be responsible for severe side effects to the medications used to treat onchocerciasis. [20]

Prevention and control:

There are no vaccines or medications available to prevent becoming infected with *O. volvulus*. The best prevention efforts include personal protection measures against biting insects. This includes wearing insect repellant such as N, N-Diethyl-meta-toluamide (DEET) on exposed skin, wearing long sleeves and long pants during the day when blackflies bite, and wearing permethrin- treated clothing. [21]

Loiasis

Loiasis, called African eye worm by most people, is caused by the parasitic worm *Loa loa*. It is passed on to humans through the repeated bites of deerflies (also known as mango flies or mangrove flies) of the genus *Chrysops*. The flies that pass on the parasite breed in certain rain forests of West and Central Africa. Infection with the parasite can also cause repeated episodes of itchy swellings of the body known as Calabar swellings. [22]

Epidemiology and Risk Factors:

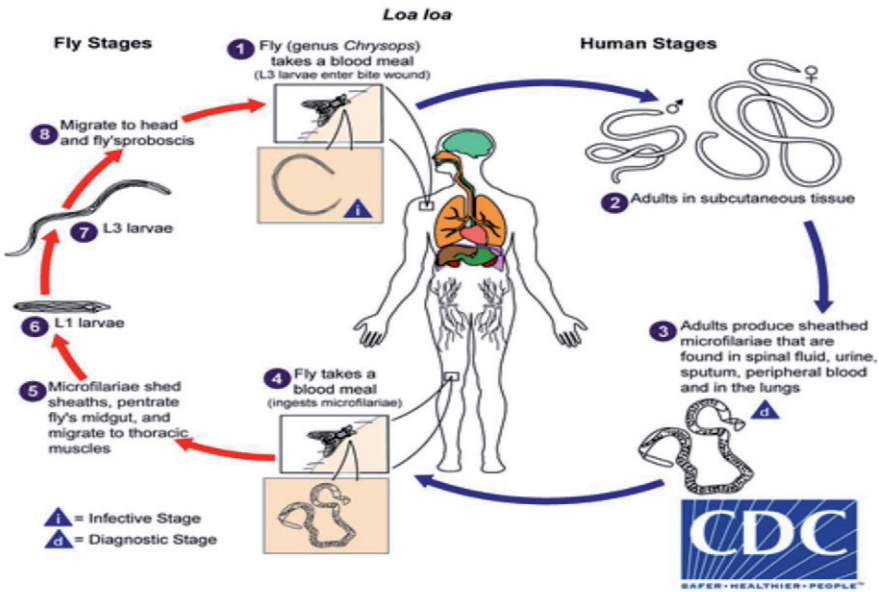
Loa loa parasites are found in West and Central Africa. Ten countries have areas where there are high rates of infection (i.e., where more than 40% of the people who live in that area report that they have had eye worm in the past). An estimated 14.4 million people live in these areas of high rates of infection. Another 15.2 live in areas where 20–40% of people report that they have had eye worm in the past.

The people most at risk for Loiasis are those who live in the certain rain forests in West and Central Africa. The deerflies that pass the parasite to humans usually bite during the day and are more common during the rainy season. They are attracted by the movement of people and by smoke from wood fires. Rubber plantations are areas where more deerflies may be found. The flies do not typically enter homes, but they might be attracted to homes that are well lit.

Travelers are more likely to become infected if they are in areas where they are bitten by deerflies for many months, though occasionally they get infected even if they are in an affected area for less than 30 days.

Your risk of infection depends on the number of bites received, the number of infected deerflies in the area you visit, and the length of your stay in the area. [23]

Life cycle



The vector for *Loa loa* filariasis are flies from two species of the genus *Chrysops*, *C. silacea* and *C. dimidiata*. During a blood meal, an infected fly (genus *Chrysops*, day-biting flies) introduces third-stage filarial larvae onto the skin of the human host, where they penetrate into the bite wound❶. The larvae develop into adults that commonly reside in subcutaneous tissue❷. The female worms measure 40 to 70 mm in length and 0.5 mm in diameter, while the males measure 30 to 34 mm in length and 0.35 to 0.43 mm in diameter. Adults produce microfilariae measuring 250 to 300 µm by 6 to 8 µm, which are sheathed and have diurnal periodicity. Microfilariae have been recovered from spinal fluids, urine, and sputum. During the day they are found in peripheral blood, but during the non-circulation phase, they are found in the lungs❸. The fly ingests microfilariae during a blood meal❹. After ingestion, the microfilariae lose their sheaths and migrate from the fly's midgut through the hemocoel to the thoracic muscles of the arthropod❺.

There the microfilariae develop into first-stage larvae ❻and subsequently into third-stage infective larvae❼. The third-stage infective larvae migrate to the fly's proboscis ❽and can infect another human when the fly takes a blood meal❶. [24].

Disease:

The deerflies (genus *Chrysops*) that pass *Loa loa* on to humans bite during the day. If a deerfly eats infected blood from an infected human, the larvae (non-adult parasites) will infect cells in its abdomen. After 7–12 days the larvae develop the ability to infect humans. Then the larvae move to the mouth parts of the fly. When the deerfly breaks a human's skin to eat blood, the larvae enter the wound and begin moving through the person's body.

It takes about five months for larvae to become adult worms inside the human body. Larvae can become adults only inside the human body. The adult worms live between layers of connective tissue (e.g., ligaments, tendons) under the skin and between the thin layers of tissue that cover muscles (fascia). Fertilized females can make thousands of microfilariae a day. The microfilaria then move into the lymph vessels of the body (the lymph vessels contain the blood cells that fight infection). Eventually they move into the lungs where they spend most of their time. These microfilariae enter the blood from time to time, usually around midday. It takes five or more months for microfilariae to be found in the blood after someone is infected with *Loa loa*. The microfilariae can live up to one year in the human body. If they are not consumed in a blood meal by a deerfly they will die. Adult worms may live up to 17 years in the human body and can continue to make new microfilariae for much of this time.

Most people with Loiasis do not have any symptoms. People who get infected while visiting areas with Loiasis but do not come from areas where Loiasis is found (travelers) are more likely to have symptoms. The most common manifestations of the disease are Calabar swellings and eye worm. Calabar swellings are localized, non-tender swellings usually found on the arms and legs and near joints. Itching can occur around the area of swelling or can occur all over the body. Eye worm is the visible movement of the adult worm across the surface of the eye. Eye worm can cause eye congestion, itching, pain, and light sensitivity. Although eye worm can be scary, it lasts less than one week (often just hours) and usually causes very little damage to the eye. People with Loiasis can have itching all over the body (even when they do not have Calabar swellings), hives, muscle pains, joint pains, and tiredness. Sometimes adult worms can be seen moving under the skin. High numbers of blood cells called eosinophils are sometimes found on blood counts. Some people who are infected for many years may develop kidney damage though

development of permanent kidney damage is not common. Other rare manifestations include painful swellings of lymph glands, scrotal swellings, inflammation of parts of the lungs, fluid collections around the lung, and scarring of heart muscle. [25]

Diagnosis:

In people who have been bitten by the flies that carry *Loa loa* in areas where *Loa loa* is known to exist, the diagnosis can be made in the following ways:

- Identification of the adult worm by a microbiologist or pathologist after its removal from under the skin or eye
- Identification of an adult worm in the eye by a health care provider
- Identification of the microfilariae on a blood smear made from blood taken from the patient between 10AM and 2PM

Diagnosis of Loiasis can be difficult, especially in light infections where there are very few microfilariae in the blood. The specialized blood test is not widely available in the United States. A positive antibody blood test in someone with no symptoms means only that the person was infected sometime in his/her life. It does not mean that the person still has living parasites in his/her body. [26]

Treatment:

Decisions about treatment of loiasis can be difficult and often require advice from an expert in infectious diseases or tropical medicine. Although surgical removal of adult worms moving under the skin or across the eye can be done to relieve anxiety, loiasis is not cured by surgery alone. There are two medications that can be used to treat the infection and manage the symptoms. The treatment of choice is diethylcarbamazine (DEC), which kills the microfilariae and adult worms. Albendazole is sometimes used in patients who are not cured with multiple DEC treatments. It is thought to kill adult worms. Certain people with heavy infections are at risk of brain inflammation when treated with DEC. This can cause coma or sometimes death. People with heavy infections need to be treated by experienced specialists. Sometimes, other medical conditions need to be addressed first in order to make it safer to use DEC. Sometimes treatment is not recommended. [27]

Prevention and control:

There are no programs to control or eliminate loiasis in affected areas. Your risk of infection may be less in areas where communities receive regular treatment for onchocerciasis or lymphatic filariasis.

There are no vaccines that protect you from loiasis. If you are going to be in an area with loiasis for a long period of time, diethylcarbamazine (DEC)—300mg taken once a week—can reduce your risk of infection. Avoiding areas where the deerflies are found, such as muddy, shaded areas along rivers or around wood fires, may also reduce your risk of infection. You may reduce your risk of bites by using insect repellants that contain DEET (N,N-Diethyl-meta-toluamide) and wearing long sleeves and long pants during the day, which is when deerflies bite. Treating your clothes with permethrin may also help. [28]

Ocular Myiasis:

Myiasis is an infestation of the skin by developing larvae (maggots) of a variety of fly species (*myia* is Greek for fly) within the arthropod order Diptera. Worldwide, the most common flies that cause the human infestation are *Dermatobia hominis* (human botfly) and *Cordylobia anthropophaga* (tumbu fly). [29]

Myiasis of the human eye or ophthalmomyiasis can be caused by *Hypoderma tarandi*, a parasitic botfly of caribou. It is known to lead to uveitis, glaucoma, and retinal detachment.[1] Human ophthalmomyiasis, both external and internal, has been caused by the larvae of the botfly. [30]

The symptoms of external ocular Myiasis include acute ocular foreign body sensation, irritation, redness, lacrimation and photophobia and reduced visual acuity. Signs include eyelid edema with erythema, conjunctival edema, hemorrhages, chemosis and superficial punctuate keratitis. These clinical features may be mistaken for a periorbital cellulitis.

The treatment of external ophthalmomyiasis includes mechanical removal of larvae. The use of topical anesthetics or an anticholinesterase agent or both which paralyze the larvae has been recommended to facilitate their removal. Liquid paraffin has also been used. It cuts off the oxygen supply thereby killing the larvae. It is prudent to remove the larvae from conjunctiva promptly. Topical steroids and antibiotics relieve symptoms and prevent secondary bacterial infection respectively. Topical ivermectin has been shown to be effective in treating Myiasis. Follow-up examination is recommended to avoid the possible complication of internal ophthalmomyiasis. [31]

Ocular cysticercosis

Cysticercus cellulosae, the larval form of the pork tapeworm *Taenia solium,* is the causative organism of cysticercosis, in which humans are the intermediate hosts in the life cycle. Cysticercus cellulosae may become encysted in various bodily tissues, usually the eyes, central nervous system (CNS), and subcutaneous tissues. An immunologic reaction with fairly intense inflammatory signs and symptoms may be produced, and the surrounding structures may be compressed.

Ocular cysticercosis may be extra ocular (in the subconjunctival or orbital tissues) or intraocular (in the vitreous, subretinal space, or anterior chamber).

Pathophysiology:

Humans are the intermediate hosts for *T solium*, and pigs are the definitive hosts. A tapeworm larval cyst (cysticercus) is ingested with poorly-cooked infected pork; the larva escapes the cyst and passes to the small intestine, where it attaches to the mucosa with scolex suckers. Egg-containing proglottids develop as the worm matures in 3-4 months. The adult worm may live in the small intestine for as long as 25 years without symptoms (taeniasis) and pass gravid proglottids intermittently with the feces. Eggs extruded from the proglottid contaminate and persist on vegetation, where pigs consume them. *T solium* embryos penetrate the gastrointestinal mucosa of the animal host and are then hematogenously disseminated to peripheral tissues with the resultant formation of larval cysts (cysticerci).

Human cysticercosis occurs when *T solium* eggs are ingested via fecal-oral transmission from a tapeworm host. The human then becomes an accidental intermediate host. These oncospheres (primary larvae) penetrate the intestinal mucosa and enter the circulatory system. Hematogenous spread to neural, muscular, and ocular tissues occurs. Within these tissues, the oncospheres develop into secondary larvae (i.e., the cysticerci).

The incubation period may vary from months to years. The host inflammatory response to cysticerci depends on the parasite's ability to evade host immunity; therefore, inflammation is restricted to degenerating cysts whose ability to evade host defenses is faltering. Lack of inflammation occurs with both healthy cysticerci (active disease) and those that have involuted (inactive disease). Upon involution, cysts undergo granulomatous change and exhibit calcification.

Cysticercosis affects an estimated 50 million people worldwide. Ocular cysticercosis is endemic in tropical areas, such as sub-Saharan Africa, India, and East Asia. Other endemic areas include Mexico and Latin America. The reported incidence of ocular involvement varies from 10-30% in endemic areas. Some European studies report a higher incidence of ocular cysticercosis than neurocysticercosis. In Western countries, the most common site of involvement in ocular cysticercosis is subretinal. In India, both intraocular cysticercosis and extra ocular cysticercosis is observed with almost equal frequency.

Cysticercosis may cause significant visual loss, especially if the cyst is located intraocularly or is compressing the optic nerve.

The incidence is more common in the Asian and Latin American populations, in which cysticercosis is endemic. Orbital cysticercosis most frequently affects individuals aged 10-30 years. [32]

Cysticerci can lodge themselves in any part of the ocular and extra ocular tissue. Associated brain parenchyma involvement is quite rare. The clinical presentation, treatment and outcome mainly depends on the location of the cyst. [33]

Intraocular echinococcosis

A case report is given of a 2-year-old boy with a young subretinal hydatid cyst in his left eye. Without inflammation. Secondary convergent strabismus was present. The diagnosis was made by positive intra -cutaneous-test by Casoni. [34]

Chagas disease (American Trypanosomiasis)

Chagas disease is caused by the parasite *Trypanosoma cruzi*, which is transmitted to animals and people by insect vectors that are found only in the Americas (mainly, in rural areas of Latin America where poverty is widespread). Chagas disease (*T. cruzi* infection) is also referred to as American Trypanosomiasis.

It is estimated that as many as 8 million people in Mexico, Central America, and South America have Chagas disease, most of whom do not know they are infected. If untreated, infection is lifelong and can be life threatening.

The impact of Chagas disease is not limited to the rural areas in Latin America in which vector borne transmission occurs. Large-scale population movements from rural to urban areas of Latin America and to other regions of the world have increased the geographic distribution and changed the epidemiology of Chagas disease. In the United States and in other regions where Chagas disease is now found but is not endemic, control strategies should focus on preventing transmission from blood transfusion, organ transplantation, and mother-to-baby (congenital transmission).

Transmission

People can become infected in various ways. In Chagas disease-endemic areas, the main way is through vector borne transmission. The insect vectors are called triatomine bugs. These blood-sucking bugs get infected by biting an infected animal or person. Once infected, the bugs pass *T. cruzi* parasites in their feces. The bugs are found in houses made from materials such as mud, adobe, straw, and palm thatch. During the day, the bugs hide in crevices in the walls and roofs. During the night, when the inhabitants are sleeping, the bugs emerge. Because they tend to feed on people's faces, triatomine bugs are also known as "kissing bugs." After they bite and ingest blood, they defecate on the person. The person can become infected if *T. cruzi* parasites in the bug feces enter the body through mucous membranes or breaks in the skin. The unsuspecting, sleeping person may accidentally scratch or rub the feces into the bite wound, eyes, or mouth.

People also can become infected through:

- congenital transmission (from a pregnant woman to her baby);
- blood transfusion;

- organ transplantation;

- organ transplantation;
- consumption of uncooked food contaminated with feces from bug ; and

Accidental laboratory exposure. It is generally considered safe to breastfeed even if the mother has Chagas disease. However, if the mother has cracked nipples or blood in the breast milk, she should pump and discard the milk until the nipples heal and the bleeding resolves.

Chagas disease is not transmitted from person-to-person like a cold or the flu or through casual contact with infected people or animals. [35]

Epidemiology and risk factors:

Chagas disease, or American trypanosomiasis, is caused by the parasite *Trypanosoma cruzi*. Infection is most commonly acquired through contact with the feces of an infected triatomine bug (or "kissing bug"), a blood-sucking insect that feeds on humans and animals.

Chagas disease is endemic throughout much of Mexico, Central America, and South America where an estimated 8 million people are infected. The triatomine bug thrives under poor housing conditions (for example, mud walls, and thatched roofs), so in endemic countries, people living in rural areas are at greatest risk for acquiring infection. Public health efforts aimed at preventing transmission have decreased the number of newly infected people and completely halted vector borne transmission in some areas. Infection acquired from blood products, organ transplantation, or congenital transmission continues to pose a threat. [36]

Biology:

The protozoan parasite, *Trypanosoma cruzi*, causes Chagas disease, a zoonotic disease that can be transmitted to humans by blood-sucking triatomine bugs.

Life cycle:

An infected triatomine insect vector (or "kissing" bug) takes a blood meal and releases trypomastigotes in its feces near the site of the bite wound. Trypomastigotes enter the host through the wound or through intact mucosal membranes, such as the conjunctiva❶. Common triatomine vector species for trypanosomiasis belong to the genera *Triatoma*, *Rhodnius*, and *Panstrongylus*. Inside the host, the trypomastigotes invade cells near the site of inoculation, where they differentiate into intracellular amastigotes❷. The amastigotes multiply by binary

fission ❸and differentiate into trypomastigotes, and then are released into the circulation as bloodstream trypomastigotes❹. Trypomastigotes infect cells from a variety of tissues and transform into intracellular amastigotes in new infection sites. Clinical manifestations can result from this infective cycle. The bloodstream trypomastigotes do not replicate (different from the African trypanosomes). Replication resumes only when the parasites enter another cell or are ingested by another vector. The "kissing" bug becomes infected by feeding on human or animal blood that contains circulating parasites❺. The ingested trypomastigotes transform into epimastigotes in the vector's midgut❻. The parasites multiply and differentiate in the midgut ❼ and differentiate into infective metacyclic trypomastigotes in the hindgut❽.

Trypanosoma cruzi can also be transmitted through blood transfusions, organ transplantation, transplacentally, and in laboratory accidents. [37]

Disease:

Chagas disease has an acute and a chronic phase. If untreated, infection is lifelong.

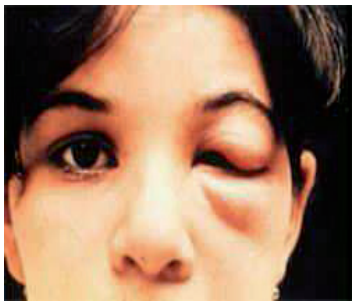
Acute Chagas disease occurs immediately after infection, May last up to a few weeks or months, and parasites may be found in the circulating blood. Infection may be mild or asymptomatic. There may be fever or swelling around the site of inoculation (where the parasite entered into the skin or mucous membrane). Rarely, acute infection may result in severe inflammation of the heart muscle or the brain and lining around the brain.

Following the acute phase, most infected people enter into a prolonged asymptomatic form of disease (called "chronic indeterminate") during which few or no parasites are found in the blood. During this time, most people are unaware of their infection. Many people may remain asymptomatic for life and never develop Chagas-related symptoms. However, an estimated 20 - 30% of infected people will develop debilitating and sometimes life-threatening medical problems over the course of their lives.

Complications of chronic Chagas disease may include:

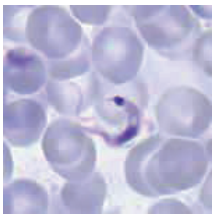
- heart rhythm abnormalities that can cause sudden death;
- a dilated heart that doesn't pump blood well;
- A dilated esophagus or colon, leading to difficulties with eating or passing stool.

In people who have suppressed immune systems (for example, due to AIDS or chemotherapy), Chagas disease can reactivate with parasites found in the circulating blood. This occurrence can potentially cause severe disease.



Romaña's sign, the swelling of the child's eyelid, is a marker of acute Chagas disease. The swelling is due to bug feces being accidentally rubbed into the eye, or because the bite wound was on the same side of the child's face as the swelling. Photo courtesy of WHO/TDR. [38]

Diagnosis:



Trypanosoma cruzi parasite in a thin blood smear. (CDC Photo)

The diagnosis of Chagas disease can be made by observation of the parasite in a blood smear by microscopic examination. A thick and thin blood smear are made and stained for visualization of parasites. However, a blood smear works well only in the acute phase of infection when parasites are seen circulating in blood.

Diagnosis of chronic Chagas disease is made after consideration of the patient's clinical findings, as well as by the likelihood of being infected, such as having lived in an endemic country. Diagnosis is generally made by testing with at least two different serologic tests. [39]

Treatment:

Treatment for Chagas disease is recommended for people diagnosed early in the course of infection (acute phase), congenital infection, and for those with suppressed immune systems. Many patients with chronic infection may also benefit from treatment.

Patients should consult with their primary health care provider. Some patients may be referred to a specialist, such as a cardiologist, gastroenterologist, or infectious disease specialist. [40]

Prevention and control:

In endemic areas of Mexico, Central America, and South America improved housing and spraying insecticide inside housing to eliminate triatomine bugs has significantly decreased the spread of Chagas disease. Further, screening of blood donations for Chagas is another important public health tool in helping to prevent transfusion-acquired disease. Early detection and treatment of new cases, including mother-to-baby (congenital) cases, will also help reduce the burden of disease.

In the United States and in other regions where Chagas disease is now found but is not endemic, control strategies are focused on preventing transmission from blood transfusion, organ transplantation, and mother-to-baby. [41]

Rarely Ophthalmic Parasites

Ocular parasitosis in human is more prevalent in geographical areas where environmental factors and poor sanitary conditions favor the parasitism between man and animals. Lesions in the eye can be due to damage directly caused by the infectious pathogen, indirect pathology caused by toxic products, or the immune response incited by infections or ectopic parasitism. The epidemiology of parasitic ocular diseases reflects the habitat of the causative parasites as well as the habits and health status of the patient. An ocular examination may provide clues to the underlying disease/infection, and an awareness of the possibilities of travel-related pathology may shed light on an ocular presentation.

Ocular parasitosis in human is more prevalent in geographical areas where environmental factors and poor sanitary conditions favor the parasitism between man and animals. In recent years, population shift and rapid transport have facilitated the spread of certain parasitic diseases from endemic to non -endemic areas. The routes of infection to man vary with species of the parasite and the animal hosts they infest. Lesions in the eye can be due to damage directly caused by the infectious pathogen, indirect pathology caused by toxic products, immune response incited by infections, or ectopic parasitism of the preadult or adult stages.

The epidemiology of parasitic ocular diseases reflects the habitat of the causative parasites as well as the habits and health status of the patient. Additional consideration must include local sanitation and the presence of a vector for transmission as well as the more complicated life cycles of the parasites and definitive hosts. Dietary history should be considered since most parasitic transmission is through food and water contamination. Travel history to endemic areas is important to determine the source of infection. An awareness of these is therefore important to the clinician evaluating this group of patients.

An ocular examination may provide clues to the underlying disease, and an awareness of the possibilities of travel-related pathology may shed light on an ocular presentation. The eye is involved both in a variety of systemic infections and may be the primary focus of other pathologies. The majorities of conditions affecting the eyes—other than injuries—are infectious.

In some occasions, the ophthalmic lesions occur as a result of antiparasitic treatment as it has been noticed in the prophylactic and therapeutic attempts to treat malaria [1, 2]. Drugs such as hydroxychloroquine and chloroquine can damage vision because of their toxic effects, which is due to slow accumulation of the drugs in the retinal epithelium that results in irreversible visual loss. Much debate and confusion have taken place over the type and frequency of ocular examination in patients taking these drugs.

Despite improved understanding of the clinical features of inflammatory eye diseases and advances in diagnostic testing, clinicians should maintain a high index of suspicion for infective parasitic diseases in patients thought to have inflammatory eye involvement.

Giardiasis

The protozoan disease giardiasis can cause ocular complications, including “salt and pepper” retinal changes. One study showed that asymptomatic, non -progressive retinal lesions are particularly common in younger children with giardiasis. This risk does not seem to be related to the severity of the infection, its duration, or the use of metronidazole but may reflect a genetic predisposition.

Diagnosis is confirmed by finding the cyst stage in the fecal smear. Treatment is the same as for intestinal infection, that is, metronidazole.

Leishmaniasis

Leishmania spp. is obligate intracellular protozoans which infect an estimated 12million persons. There are numerous species within the genus, and disease manifestation is, in part, species specific.

Once injected into humans during the sandfly blood meal, the promastigote develops into an amastigote after being engulfed by tissue macrophages. Within these cells, the amastigotes replicate and may spread either systemically or cutaneously.

Visceral leishmaniasis, or that which represents systemic disease, is known as kala-azar. The ocular manifestations of kala-azar are relatively uncommon and include chorioretinitis, central retinal vein thrombosis, iritis, papillitis, and keratitis. Additionally, flame-shaped retinal hemorrhages have been described. Glaucoma has been reported to develop after the successful treatment of kala-azar.

Ocular findings in cutaneous leishmaniasis represent a local phenomenon resulting from the initial site of infection near the eye with occasional spread to the lacrimal duct. Ptosis may be a presenting complaint. If the initial bite occurs on the conjunctival mucosa, the disease is termed Mucocutaneous leishmaniasis. This state may lead to severe ulceration and possible loss of the eye.

The diagnosis of leishmaniasis is made by direct demonstration of organisms on tissue smears or biopsy. Amastigotes are usually demonstrated fairly easily in the case of cutaneous or mucocutaneous ocular disease. However, amastigotes have not been directly identified in cases of ocular disease associated with kala-azar. When present, Leishmania spp. may be cultured on Novy, MacNeal, Nicolle’s medium (N.N.N.) as well as Schneider’s Drosophila medium supplemented with 30% fetal bovine serum. While available, serologic testing is not particularly useful for diagnosing cutaneous and mucocutaneous disease due to cross-reactivity with T. cruzi and Mycobacterium leprosum.

Treatment of choice is pentavalent antimony, sodium stibogluconate 15–20 mg per kg per day IM or IV for 15–20 days. A second or even a third treatment course with pentavalent antimonal can be given over 6–8 weeks if healing is not progressive.

Malaria

Caused by the Plasmodium species and transmitted via the bite of the female anopheles mosquito, this sometimes fatal infectious disease has characteristic findings in the eye. Signs of falciparum malaria in the eye include retinal whitening, retinal hemorrhage, papilloedema, and cotton wool spots. Much research done in endemic areas has shown a correlation between papilloedema or extramacular retinal oedema (retinopathy) and poor outcome in children with cerebral malaria. Studies show that retinopathy was associated with subsequent death, and the increasing severity of retinal signs was related to increasing risk of fatal outcome. Other studies have shown that retinal changes related to microvascular obstruction were common in adults with severe falciparum malaria and correlated with disease, severity and comma .It is important to emphasise that whilst these signs give a pointer to the severity of disease they do not alter the drug management of malaria. The outcome in terms of vision in patients with ophthalmological findings and severe malaria is usually good. Insights from retinal investigations have furthered the understanding of cerebral malaria.

Quinacrine and chloroquine are molecules with the same alkyl side chain but different nuclei. The photobiological effects of quinacrine and chloroquine are similar in model systems; thus, development of a bull's-eye maculopathy with quinacrine ingestion is an unsurprising potential side effect.

The definitive diagnosis of malaria is made by microscopic identification of the parasite in the blood smear. A thin blood film should be examined for at least 15 minutes, whereas a 5-minute search of a thick film should reveal parasites if present. The thick film is the most efficient method of detecting malarial parasites, but interpretation requires an experienced worker.

Antimalarial drugs may be classified as (1) suppressive, by acting upon asexual blood cell stages and preventing the development of clinical symptoms; (2) therapeutic, by also acting on asexual forms to treat the acute attack; (3) radical cure, for destruction of the EE forms; (4) gametocytocidal, for destroying gametes; (5) sporoniticidal, for drugs that render gametocytes noninfective in the mosquito. [42]

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