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ZOONOTIC HELMINTHIC NEMATODES INFECT HUMAN EYES CAUSING FROM ASYMPTOMATIC TO BLINDNESS WITH REFERENCE TO EGYPT

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Abstract

Blindness and ocular diseases represent one of the most traumatic events for humans as they have the potential to severely impair both their quality of life and their psychological equilibrium. Although it is highly unusual, blindness has always been of great interest in human medicine. Apart from AIDS, chronic obstructive pulmonary disease, cardiac disorders, leukemia, and others, many causes of blindness induced by parasites (Protozoa, Helminthes and Diptera) are of major public health concern worldwide. This review focused on zoonotic nematodes that affect the human eye.

Key words: Egypt, Ascariasis, Dirofilariasis, Loiasis, Onchocerciasis, Thelaziasis, Toxocariasis, Trichinellosis, Overview.

Introduction

Nowadays, zoonotic helminths that affect human eyes (HIE) may cause blindness with severe socio-economic consequences to human communities. Infections include nematodes, cestodes and trematodes, which may be transmitted by vectors, food consumption, congenial and those acquired indirectly from the environment. Adults and/or larvae of HIE may localize into human ocular tissues externally (lachrymal glands, eyelids, conjunctival sacs) or into ocular globe (intra-vitreous retina, anterior andlor posterior chamber) causing symptoms due to parasitic localization in the eyes or to immune reaction elicited in the host (Morsy *et al,* 2021). But, data on HIE are scant and mostly limited to case reports from different countries

Review and General Discussion

1- Ascariasis: (F. Ascarididae), causes *Ascaris lumbricoides*, is the large Nematoda of humans, growing t o a length of up to 35 cm. Also, *Ascaris suum* infects pigs, and *Parascaris equorum* infects equine, is commonly called an ascarid (Leles *et al,* 2012). *A. lumbricoides* is the commonest helminth infected humans worldwide. Infection can cause morbidity by compromising nutritional status, affecting cognitive processes, inducing tissue reactions such as granuloma to larval stages, and by causing fatal intestinal obstruction (Andrew *et al,* 2012). It secretes inhibitors to target digestive and immune-related host proteases that include pepsin, trypsin, chymotrypsin/elastase, cathepsins, & metallocarboxypeptidases (Grasberger *et al,* 1994). The worm causes subconjunctival mass, granulomatous iridocyclitis, choroiditis, recurrent vitreous hemorrhage, chronic dacryocystitis and invasion into the sub-retinal space (Mirjana *et al,* 2014).

Besides, Klotz *et al.* (2000) in USA reported that the human eye as well as exposure of the eye directly to the environment renders it vulnerable to a number of uncommon infectious diseases caused by fungi and parasites, (more than gram-positive or gram-negative bacteria) either by direct introduction via trauma or surgery, by extension from infected adjacent tissues, or by hematogenous dissemination to eye. Liesegang and Forster (1980) in USA reported that the yeast *Candida albicans* is the commonest cause of endogenous endophthalmitis, and filamentous fungi, such as *Fusarium solani* and *Aspergillus flavus*, may constitute up to one-third of all cases of traumatic infectious keratitis. Petrovic Janicijevic *et al.* (2014) in Serbia reported that *A. lumbricoides* causes subconjunctival mass, granulomatous iridocyclitis, choroiditis, recurrent vitreous hemorrhage, chronic dacryocystitis and invasion into a subretinal space caused by *A. lumbricoides* as ocular pathology. The old woman was treated by local antibiotics, corticosteroids, and Mebendazole tablets (100mg in morning for 2 weeks).

In Egypt, A. *lumbricoides* was reported in nearly all governorates by many authors after the first one by Nagaty *et al.* (1959) with a rate of 0.1% (El Shazly *et al,* 2006) in Dakahlia Governorate to 27.31% in a village in Menoufia Governorate (Bakr *et al,* 2009).

2- Dirofilariasis: The *Dirofilaria* genus includes more than 27 species, belongs to family *Onchocercidae* (Michalski *et al,* 2010). The widespread zoonosis nematodes with *D. repens* and *D. immiti* the commonest species considered to be endemic in the Mediterranean countries & Europe (Capelli *et al,* 2018). Both are transmitted by different species of mosquitoes to dogs and other wild animals. Dirofilariasis is transmitted neither person-to-person nor person-to-mosquito-to-person. The transmission of dirofilariasis requires mosquitoes as the intermediate host as well as the production of microfilariae, which does not take place in humans. Microfilariae circulate in the blood of both wild and domestic animals, and after about 15 days, larvae reach the infective stage of L3 and introduced into a new host (Simón *et al,* 2005). *D. immitis* (Heartworm) causes severe heart disease by locating in the pulmonary artery of dogs, cats and other carnivores, but less common in humans (McCall *et al,* 2008). *Dirofilaria repens* was a major cause of non-pathogenic subcutaneous infections in dogs, more rarely in other carnivores, but the major cause of human dirofilariasis in Europe (Masseron *et al,* 1995). In final the host, adult parasites were most commonly located in the skin or subcutaneous tissue, and microfilariae circulate in bloodstream of dogs, the major reservoir, spread by vectors as a zoonotic worm (Simón *et al,* 2012). The dirofilariasis increasing trend worldwide is the warming climate and the faster larval development in mosquitoes. Many human cases were reported worldwide directly related to sanitation, environmental conditions, and habits of patient (Tavakolizadeh and Mobedi, 2009). Human cases for examples, there were 2 young women in Tunisia (Sassi *et al,* 2006), an old man in Greece (Gorezis *et al,* 2006), one old woman in Croatica (Janjetović *et al,* 2010), a child in Iran (Mirahmadi *et al,* 2017), an old man in Italy (Montesel *et al,* 2019), seven cases (6 females & 1 male) in Bulgaria (Valeri, 2020), and Aykur*et al.* (2021) in Turkey reported an old man suffered from subconjunctival *D. immitis* with giant episcleral granuloma mimicking scleritis.

Diagnosis: The ocular dirofilariasis can be diagnosed in humans using the clinical signs and parasitological, serological, histopathological, ultrasound (sonography), and molecular methods (Tse *et al,* 2010). CDC (2020) reported that dirofilariasis was diagnosed most frequently by the examination of tissue of inflammation in lung obtained as part of the diagnostic investigation (small, round abnormalities) on chest x-rays or from the examination of tissue in nodules under the skin.

Clinically: Reports of ocular dirofilariasis (OD) due to *D. immitis* were rare, but *D. repens* is a typical agent found in humans. Orbital, subconjunctival, and intraocular infections were clinical forms of ocular dirofilariasis in humans (Younes *et al,* 2021).

3- *Loa loa* filariasis (Loiasis) is a skin and eye disease caused by a nematode worm *Loa loa*. Humans acquired infection via bite of the insect-vector deer or mango fly (*Chrysops* spp.), the major species *C. silacea and* and *C. dimidiata* (Duke, 1955). Adult *L. loa* worm migrates via the subcutaneous tissues of humans, occasionally crossing into the subconjunctival tissues of the eye where it can be easily seen. *Loa loa* does not normally affect man's vision, but can be painful when moving about the eyeball or across the nose bridge causing red itchy swellings below the skin called Calabar swellings (John and William, 2006). It is endemic to 11 countries, all in western or central Africa, with an estimated of 12-13million patients. The highest incidence was in Cameroon, Democratic Republic of Congo, Central African Republic, Nigeria, Gabon, Sudan and Equatorial Guinea, also with lower rate in Angola, Benin, Chad and Uganda, particularly the tropical equatorial rainforests. People at highest loiasis risk were those living in the rainforests of West or Central Africa and vectors are also attracted to smoke from wood fires, but they are attracted to houses and congregate outside (CDC, 2015). Travelers can be infected in less than 30 days after arriving in an affected area, although they are more likely infected whilst being bitten by multiple deerflies over the course of many months (Zierhut *et al,* 2014). The disease affects millions of people in in West and Central Africa and hence the name African eye-worm, but is rarely found in other continents, generally in African immigrants or travelers, which were asymptomatic for several years (Jain *et al,* 2008). However, there were sporadic cases in India (Barua *et al,* 2005), Korea (Cho *et al,* 2008), Italy, Norway, Spain (Varhaug, 2009), Australia, England, Germany (Bowler *et al,* 2011), and USA.

The first of *L. loa* case was noted in the Caribbean (Santo Domingo) in 1770. A French surgeon named Mongin tried but failed to remove a worm passing across a woman's eye. A few years later, the surgeon Francois Guyot (1778) noted worms in West African slaves eyes on a French ship to America; he successfully removed a worm from one patient's eye (Cox, 2002). The association between *L. loa* and Calabar swellings was realized by Patrick Manson (1910), and the insect-vector, *Chrysops* spp. was identified 1912 by the British parasitologist Robert Thompson Leiper (Garnham, 1970).

Some patients developed lymphatic dysfunction causing lymphedema, episodic angioedema (Calabar swellings) in arms and legs caused by immune reactions. The swelling measures 3-10cm in surface area; with or without pitting erythematous. In chronic cases they formed cyst-like enlargements of connective tissue around the muscle tendons sheaths, becoming very painful when moved. The swellings may last for one to three days and may be accompanied by localized urticaria and pruritus. They reappear at referent locations at irregular time intervals. Subconjunctival migration of an adult worm to eyes also occur frequently, and this is the reason *L. loa* is known as African eye worm (Padgett and Jacobsen, 2008). Passage over the eyeball can be sensed, but it usually took less than 15 minutes. Eye-worms affect men and women equally, which was risky in advanced ages. Eosinophilia is often prominent in filarial infections. Dead worms may cause chronic abscesses that lead to granulomatous reactions and fibrosis formation.

Vector: Deer flies (also known in some parts of the mid-Atlantic United States as sheep flies) are bloodsucking insects considered pests to man and cattle (Townsend, 2018). They are large flies with large clear wings with dark bands and large brightly-colored compound eyes of 250 species of genus *Chrysops* of worldwide distributed. During a blood meal, an infected fly (genus *Chrysops*, day-biting flies) introduces third-stage filarial larvae onto the skin of human, where they penetrate into the bite wound. Larvae develop into adults that commonly stay in subcutaneous tissue. Female measures 40-70x0.5 mm, males measure 30-34x0.35-0.43mm. Adults produce microfilariae measuring 250 -300x6-8μm, sheathed and with diurnal periodicity. Microfilariae were recovered from spinal fluids, urine, and sputum. During the day they are found in peripheral blood, but during the noncirculation phase, they were found in the lungs. Fly ingested microfilariae during a blood meal; microfilariae lose their sheaths and migrate from midgut via hemocoel to *Chrysops* thoracic muscles develop into first-stage larvae and finally third-stage infective larvae, which migrate to the fly's proboscis to infect another man when the fly takes a blood meal (CDC, 2015).

Al-Talafha *et al.* (2005) in Jordan Valley reported *C. flavipes*. Al Dhafer *et al.* (2009) in Saudi Arabia found *C. flavipes* among 31 species. Müller *et al.* (2012) in Sinai reported *C. flavipes* among 22 tabanids species. El Haouari *et al.* (2014) reported *C. mauritanicus* an endemic species to Al Maghrib countries; Algeria, Morocco, and Tunisia. Dörge *et al.* (2020) in German found *C. relictus*, & *C. caecutiens* among 170 tabanids known in Europe, which horse flies list was not yet completely identified.

Diagnosis: Microscopic examination of *L. loa* microfilariae is a practical test. Blood collection must be diurnal between10:00a.m. and 2:00 p.m. But, diagnosis can be difficult, especially in light infections where there are very few microfilariae in the blood.

Treatment: Loiasis is treated by chemotherapy (Diethylcarbamazine® (DEC) as 6mg/ kg/3 times daily for 12 days for adults and children, or by Ivermectin®, which was suitable, but Albendazole® proved helpful, and superior to ivermctin**.** In some urgent instances surgery is involved, though the surgical worm removal must be in very short time. However, loiasis was a major obstacle to ivermectin treatment for onchocerciasis control and lymphatic filariasis elimination in central Africa (Chippaux *et al,* 1996). Nam *et al.* (2008) in USA used proparacaine & povidone-iodine drops, a wire eyelid speculum, and 0.5ml 2% lidocaine with epinephrine 1:100,000, injected superiorly. A 2mm incision was made and the forceps removed the immobile worm. Gatifloxacin drops and an eye-patch over ointment were utilized post-surgery, without complications. They added that unfortunately, patient did not return for DEC therapy to manage additional worms and microfilariae in his body. Loiasis is a major impediment for onchocerciasis and lymphatic filariasis (LF) elimination programmes implementing mass drug administration (MDA) with ivermectin, due to risk of severe adverse events (SAEs) in individuals with high *L. loa* microfilariae (mf) levels (Boussinesq, 2006).

In Egypt, Müller *et al.* (2012) reported *C. flavipes* in Sinai, which was not the main vector species of loasis.

4- Onchocerciasis, also known as river blindness, or Robles' disease is a disease caused by parasitic nematode *Onchocerca volvulus* with symptoms include severe itching, bumps under the skin, and blindness (WHO, 2024). It is the second commonest cause of blindness after trachoma (CDC, 2013). The parasite originated in Africa and was exported to the Americas by the slave trade, as part of the Columbian exchange that introduced other old world diseases such as yellow fever into the New World. Microfilariae cause loiasis was first identified by an Irish Naval Surgeon, John O'Neill (1874) who was seeking to identify the cause of a common skin disease along the west coast of Africa, known as craw-craw (O'Neill, 1875). Rudolf Leuckart, a German parasitologist, later examined specimens of the same filarial worm sent from Africa by a German missionary doctor (1890) and named the organism *Filaria volvulus* (Robles, 1917). Then, Robles sent specimens to Émile Brumpt, a French Parasitologist, who named it *O. caecutiens* in 1919, indicated that the parasite caused blindness or Latin "*caecus*" meaning blind (Strong, 1942).

Walker and Barnett (2007) reported that transmission occurred within limited areas of Africa, Central and South America, and the Arabian Peninsula. Goldman and Schafer (2012) reported that in Africa, the major vectors are members of the *S. damnosum* complex, while numerous species serve as vectors of the parasite in Latin America. They added that onchocerciasis was endemic in 34 countries, predominantly in equatorial 27 Africa, with small foci in six Latin American countries (Guatemala, southern Mexico, Venezuela, Brazil, Colombia, and Ecuador) and one in Yemen, with about 90 million people were at risk, with 37 million people infected. About 270 000 individuals developed blindness from onchocerciasis and another 500 000 have severe visual disability.

Pathogenesis: Adult worms encapsulated

by fibrous tissue and form subcutaneous nodules, often overlying bony prominences. Microfilariae move through subcutaneous, dermal and ocular tissues, and lymph system, provoking a minimal immune response while alive; when they die, they incite a clinical inflammatory response (Brattig, 2004).

Adults and microfilariae harbor endosymbiotic *Wolbachia* bacteria essential for the filarial worm's fertility and survival. Released *Wolbachia*-derived antigens from dying parasites activated innate immune responses and played an essential role in the development of anterior segment onchocercal eye disease in an experimental murine model. *Wolbachia* bacteria mediate corneal pathology by activating Toll-like receptors on mammalian cells, which stimulate recruitment and activation of neutrophils and macrophages (Saint André *et al,* 2002). N.B.: In areas where both onchocerciasis and loasis are endemic, blood must be obtained to evaluate for evidence of *L. loa* microfilariae prior to give ivermectin. In areas of coinfection, onchocerciasis treatment with ivermectin facilitate entry of loasis microfilariae into CNS, leading to encephalopathy, and potentially fatal neurologic sequelae (Klion *et al,* 1999).

Clinical pictures: Abdel Fattah *et al.* (1986) in Sudan was reported the following; 1- Punctate keratitis, and sclerosing keratitis. 2- Uveitis typically presented with flare in the absence of an accompanying cell infiltrate. 3- Optic atrophy as a relatively chronic finding after an episode of optic neuritis. & 4-Onchochorioretinitis a common chronic finding, damaging retinal pigment epithelium, frequently just temporal to the macula. Thus, more extensive loss of the retinal pigment epithelium occurs with retinal death and atrophy and loss of the underlying choroid. Fluorescein angiography clarified chorioretinal lesions.

Symptoms: Pham *et al.* (2020) reported that skin symptoms occurred years before eye problems. Skin changes can included: a- bumps under skin measures over an inch in size, b- skin irritation, c- intense itching, d- swelling, e- thinning, & f- patches where normal skin lost color. Eye symptoms included: a- decreased vision, b- eye redness, c- eye pain, d- light sensitivity, & e- clouding of normally clear front surface of the eye (the cornea). They added that other disease conditions can cause many of these symptoms, and thus a careful examination by an ophthalmologist is needed to make the correct diagnosis.

Diagnosis: Mazzotti test consisted of a 50 mg oral diethylcarbamazine (DEC) that killed microfilariae and associated symptoms of worsening pruritus about 20 to 90 minutes later; an acute papular rash with edema, fever, cough as well as musculoskeletal symptoms. Symptoms generally reach a peak at about 24hrs and then subside over the next 48 to 72hrs (Ozoh *et al,* 2007).

Patch test DEC was given as a topical preparation to a small area of the skin to assess for local skin reaction. Toè *et al.* (2000) in Cameroon, Gabon, and Central African Republic found that children who tested positive with a 10% DEC solution ranged from 25 to 77%, which significantly correlated with nodules prevalence and reflection of the endemicity level. Patch test was an alternative to skin snipping in low prevalence areas, as being non-invasive, cheap, and more sensitive than skin snipping.

Diagnosis of *O. volvulus* in endemic areas became increasingly unpopular with skin snip (Boatin *et al*, 1988). But, when skin snips are negative and clinical suspicion of infection was high, the biochemical methods, including skin-snip PCR, ELISAs, EIAs, & antigen surveys to exclude infection (Harnett, 2002). CDC (2021) declared that the gold standard test for of onchocerciasis remains the skin snip biopsy. The biopsy is performed using a sclerocorneal biopsy punch or by elevating a small cone of skin (3 mm in diameter) with a needle and shaving it off with a scalpel, which resulted in removal of around 2mg of tissue. Tissue is incubated in normal saline at room temperature for 24hrs to allow the microfilariae (larvae) to emerge, which can then be identified microscopically. The sites for the skin snip are usually over the iliac crest, the scapula, and the lower extremities. CDC added that Skin snip sensitivity may be limited in the pre-patent stage of infection, which can last approximately 12-18 months, and in low intensity infections. If a patient has skin nodules caused by *Onchocerca* infection, nodulectomy allows for the identification of adultsin the tissue. Slit lamp eye exam can be used to visualize microfilariae, or lesions they caused, in patients with eye disease.

The differential diagnosis of the diffuse papular dermatitis seen in acute onchocerciasis is extensive and may include food allergies, leprosy, pinta, syphilis, vitamin A deficiency, and yaws (Smith *et al,* 2018).

Treatment: Patients in endemic areas with ongoing high levels of transmission with Ivermectin® (150mcg/kg) single oral dose and repeated every 3 to 6 months until asymptomatic. Doxycycline® (200mg daily for six weeks) was an alternative treatment; followed by one ivermectin dose (150mcg/kg) given four to six months after completion of doxycycline therapy. Doxycycline should be given prior to ivermectin to optimize *Wolbachia* depletion, thereby reducing inflammatory reactions caused by ivermectin. Patients not in endemic areas or areas with low transmission levels were treated by ivermectin every three to six months (150mcg/kg) until asymptomatic. Doxycycline (200mg daily for six weeks) was an alternative treatment, followed by a single ivermectin (150mcg/kg) dose given four to six months after completion of doxycycline (Duke, 2005). But, in areas where onchocerciasis and loiasis were endemic, assessment for loiasis must be done before ivermectin mass treatment (Twum-Danso and Meredith, 2003).

Also, other *Onchocerca* species infect cattle as *O. armillata*, *O. gibsoni*, *O. gutturosa*, *O. lienalis*, & *O. ochengi* (Ishizawa *et al,* 2015), deer (*O. cervipedis*, *O. flexuosa* & *O. jakutensis* (Bosch *et al,* 2016), horses as *O. cervicalis* (Marques *et al,* 2004), wild boars as *O. dewittei japonica* (Uni *et al*, 2010), as well as dogs and wolves as *O. lupi* (Colella *et al,* 2018).

In Egypt, Rubtsov (1962) reported one species of F. Simuliidae. Belqat *et al.* (2018) reported that published records were provided for 52 *Simulium* nominal species, one undescribed morphospecies, and two cytospecies of black flies known from North Africa, with relevant literature, selected synonyms, and taxonomic comments. They added that Morocco has the greatest simuliid diversity (44 nominal species), followed by Algeria (34 species), Tunisia (18 species), Libya (5 species), and Egypt (2 species). A new site for *S. ruficorne* Macquart is recorded for simuliid-poor Egypt.

5- Thelaziasis: *Thelazia* is an emerging zoonotic nematode worm, which parasitize eyes and associated tissues of various birds, and mammal hosts, including humans (Beatriz *et al,* 2020). *Thelazia* species infestation is called eye-worms, or thelaziasis (thelaziosis). It is also known as oriental eye-worm due to its geographical distribution in Asia Pacific region (China, India, Thailand, Indonesia, Japan and Korea) and Russia (Prabhakar *et al,* 2015). Adults are usually found in the eyelids, tear glands, tear ducts, or the so-called third eyelid nictitating membrane (Otranto and Dutto, 2008). Occasionally, they were found in eyeball itself, either under the conjunctiva (membrane covers eye white part) or in the eyeball vitreous cavity (Xue *et al,* 2007). It affects all ages even a sever months old Indian baby (Handique *et al,* 2015) *T. callipaeda* (ocular thelaziosis) was reported as a causal agent in dogs, cats, and foxes and human (Otranto *et al,* 2013). *Thelazia* species are transmitted by many species of flies (*Diptera*, *Drosophilidae*, and/or *Steganinae*) that feeds on lachrymal secretions of mammals which do not bite, but feed on tears (Otranto and Dantas-Torres, 2015). Awareness of this emerging infection is critical for timely diagnosis among ophthalmologists and clinicians to prevent ocular pruritus, lacrimation, epiphora, exudative conjunctivitis, or corneal edema to keratitis and corneal ulceration in severe cases leading to blindness (Vieira *et al,* 2012). Marino *et al.* (2018) in Spain reported *T. callipaeda* circulated among dogs and *P. variegata*, where they caused zoonotic ocular thelaziasis, and added that in general, patients with thelaziasis are asymptomatic or present with excessive lacrimation, and that 2 species associated with disease in humans are *T. callipaeda* (Oriental eye worm) & *T. californiensis* (California eye worm). Sah *et al.* (2018) in Nepal reported ocular thelaziasis in a 6-month-old child presented with conjunctivitis, and his visual acuity and dilated fundal examination were normal. He acquired infection from his infected mother. Do Vale *et al.* (2019) in Portugal reported that *T. callipaeda* was first described at the beginning of the 20^{th} Century in Asia, but the eye-worm was frequently reported in Europe in the 21^{st} Century. They added that to date, thelaziosis was described in the European countries (in appearance order) Italy, France, Germany, Switzerland, Spain, Portugal, Belgium, Bosnia and Herzegovina, Croatia, Serbia, Romania, Greece, Bulgaria, Hungary, Slovakia, England, Turkey & Austria.

Diagnosis in man and animals was usually based on finding the adult and/or larval eyeworms mostly in conjunctival sac or medial or lateral canthus of the eye by a clinical and ophthalmological examination of infected patient (Shen *et al,* 2006).

Treatment Adults and larvae of *T. callipaeda* were mechanically removed by rinsing conjunctival sac with sterile physiological saline with or without local anesthesia with 1% dicaine (Zakir *et al,* 1999). For infested pet animals, topical instillation of organophosphates or moxidectin 1% was effective for *T. callipaeda* or ectoparasiticide products, such as imidacloprid (10%) and moxidectin (2.5%) spoton formula, was effective in treating dog thelaziosis win 5 to 9 (96%) days of treatment (Ferroglio *et al,* 2008).

In Egypt, all insect-vectors of ocular thelaziosis were encountered in Egypt (Morsy, 2012: El Bahnasawy *et al,* 2013). However, no human or animal cases were reported.

6- Toxocariasis: Human toxocariasis (visceral-and ocular larva migrans) is a widespread parasitic disease, with children were more frequently infected because of their closer contact with contaminated soil and relatively frequent geophagia (Rubinsky-Elefant *et al,* 2010). Macpherson (2013) in USA reported that human infection occurred by ingestion of embryonated eggs or larvae from a range of wild and domestic paratenic hosts mainly dogs, where most cases were asymptomatic, and clinically overt infections may go undiagnosed. El-Sayed and Ramadan (20170 in Egypt mentioned that due to larvae migrate-on via tissues, human infection was classified into visceral, cerebral, ocular, and covert toxocariasis. Rostami *et al.* (2019) in Iran reported that usually toxocariasis may be associated with complications as allergic and/or neurological disorders, possibly including cognitive or developmental delays in children, and chemotherapy depended on symptoms and location of larvae, included albendazole or mebendazole with anti-inflammatory corticosteroids. They added that infection increased, with adverse impact on human health worldwide, particularly underprivileged, tropical and subtropical communities.

Kong and Peng (2020) in China reported that seroprevalence ranged from 12.14% to 44.83%, with an overall in children of 12.14%(1993) and elevated to 19.3%(2015), among the 103 cases reported during 1983-2019, ocular larva migrans (OLM), visceral larva migrans (VLM), and neural larva migrans (NLM) were 92.23%, 6.80%, & 0.97% respectively. They concluded that the true number of cases and toxocariasis prevalence in China seemed to be underestimated and neglected

In Egypt, high prevalence of human toxocariasis by anti-*Toxocara* antibodies IgG was 6.2% among suspected children, 18% among adults (Antonios *et al,* 2008), and 7.7% in general populations (El Shazly *et al,* 2009a). Youssef and Uga (2014) in Egypt reported that patients with bronchial asthma, hepatomegaly or hepto-splenomega- ly, lymphadenopathy, neurological disorder, gastrointestinal troubles and dermatitis were thought to be prone to toxocariasis.

In Egypt, as to ocular toxocariasis, Khalil *et al.* (1989) among 25 suspected cases of visceral toxocariasis & 25 healthy controls, four serological tests were used precipitin absorption test (PAT), counter immunoelectrophoresis (CIEP), indirect fluorescent antibody test (IFAT), and enzyme linked immunosorbent assay (ELISA), the EE antigen proved to be more sensitive than adult worm antigen, in IFAT & ELISA gave the highest positivity and highest titer (1/256 & 1/4096 respectively). Safar *et al.* (1990) showed ocular cases positivity of 36% by PAT, 0% by CIEP, 32% and 28% by IFAT with embryonated egg (EE) and frozen section antigens (FS) respectively and 40% by ELISA.

As to dogs Oteifa and Moustafa (1997) in Cairo examined 600 soil samples from three sports clubs and three public parks in Heliopolis district, and reported *Toxocara* eggs in 182 samples (30.30%). El-Beshbishi *et al.* (2005) recorded eggs in 9.1% of soil samples in 4 rural villages (Dakahlia) with high intensity in outdoors than in fields or indoors (12-15, 1-4, &1-2 eggs/10gm respectively). El-Tras *et al.* (2008) in Kafrelsheikh Governorate found that dogs 14/25(56%) were infected with *T. canis* and 2/25 (8%) with *T. leonine*, and non-embryonated and embryonated *T. canis* eggs were on hair of pet dogs El Shazly *et al.* (2009b) reported *Toxoc-ara* eggs contaminated soil in periphery of streets, crop fields and fruit gardens, indoors and 13-19 eggs/10gm soil at canal banks in Dakahlia and El-Minia Governorates. Haridy *et al.* (2009) in Cairo reported that among 299 (9.83%) pet dogs passed *Toxocara* eggs in stools. Khalafalla (2011) in Northern Nile Delta reported *T. cati* (9%) and *T. sleonine* (5%) in stray cats.

El-Sayed and Masoud (2019) reported that in spite of > 84% prevalence of among toxocariasis patients, incidence of ocular toxocariasis was underestimated. They added that ocular toxocariasis diagnosis can be done by ophthalmic examination and immunodiagnostic methods to show specific antibodies in sera and ocular fluids. They concluded that proper diagnosis and either medical or surgical treatment can minimize ocular posterior pole granuloma, peripheral granuloma, or chronic endophthalmitis morbidity. Morsy (2020) reported that toxocariasis being a neglected socioeconomically risky zoonotic nematode that afflicted millions of the pediatric and adolescents worldwide, especially in impoverished communities, but more or less reported from all Egyptian Governorates. He added that human toxocariasis was not often fatal, but inflammatory response to larvae migrating associated with increased leukocytosis, including generalized lymphadenopathy, endophthalmitis, granulomatous hepatitis, asthma, endomyocarditis, and high eosinophilia (>30%) as well as malignancy. He concluded that tuberculosis, toxocariasis and toxoplasmosis must be among the common infectious lymphadenitis causes in children., and that when dealing with suspected OLM both *Toxoplasma gondii* and /or tuberculosis must be in mind.

7- Trichinellosis: Trichinosis is a parasitic infection caused by nematodes of the genus *Trichinella*. Pigs are the most important source of human infection, although a number of other animals are also epidemiologically important hosts. Consumption of raw or undercooked meat is the principal mode of transmission. Trichinellosis was reported worldwide, with highest human prevalence in China, Thailand, Mexico, Argentina, Bolivia, the former Soviet Union, Romania, and other parts of Central Europe (Marincu *et al,* 2012). Infection was reported in few Arab Countries as Lebanon (Haim *et al,* 1997) and Egypt (Siam *et al,* 1979), as well as among wild rodents (Loutfy *et al,* 1999).

In general, the severity of infection in humans correlates with the number of ingested larvae. Mild infection (> 10 larvae/g of muscle) can be subclinical. The incubation period is generally 7 to 30 days; it varies with the number of ingested larvae (which correlates with how well meat has been cooked), host immune status, and species of Trichinella (Kociecka, 2000). The intestinal stage occurs from 2 to 7 day after ingestion, when encysted larvae liberated by gastric juices. Larvae mature into adult worms that burrow into the intestinal mucosa. Fertilized females release new larvae about a week after ingestion up to 5 weeks, depending upon the infection severity. This stage may be asymptomatic or accompanied by symptoms as abdominal pain, nausea, vomiting, and diarrhea. More prolonged diarrhea was attributed to repeated reinfection in previously infected and sensitized patients (MacLean *et al,* 1992). The muscle stage developed after the first week of ingestion; the period when adult-derived larvae in intestines disseminated hematogenously and enter skeletal muscle. For species other than *T. pseudospiralis* & *T. papuae*, each larva becomes encysted within a host muscle cell, but *T. pseudospiralis* & *T. papuae* larvae remain in the muscle without forming cysts. The encysted and free *Trichinella* larvae remain viable for years.

Trichinellosis cardinal clinical manifestations of occur during the muscle phase, as larvae enter skeletal muscles, muscle pain, tenderness, swelling, and weakness develop. Pain can be so extreme as to limit all movement, including breathing or tongue moving. High fever lasting a number of weeks may be observed. Physical findings include subungual splinter hemorrhages, conjunctival and retinal hemorrhages, periorbital edema and chemosis, visual disturbance, and ocular pain. Less common manifestations include macular or urticarial rash, headache, cough, dyspnea, and dysphagia, and occasionally hepatomegaly (Neghina and Neghina, 2011).

Meningitis or encephalitis developed in 10 to 24% of patients with severe cases (Mawhorter and Kazura, 1993). Neurologic manifestations developed early or late, and can be diffuse or focal in nature. Headache is common and often exacerbated by movement. Pathologic results can include edema, hemorrhage, emboli, infarctions, and perivascular infiltrates in fatal cases (Puljiz *et al,* 2005).

Diagnosis: Trichinosis is diagnosed based on clinical symptoms and confirmed by serology. Antibody levels are not detectable until after three or more weeks of infection so are not useful for early diagnosis. A definitive diagnosis was by identifying larvae on muscle biopsy, which was not generally required, but may be useful in the setting of diagnostic uncertainty. CT & MRI showed multifocal small lesions located in cerebral cortex and white matter (Kreel *et al,* 1988).

Treatment: *Trichinella* treatment was with systemic symptoms (including central nervous system manifestations, cardiac inflammation or pulmonary involvement) consists of antiparasitic therapy with corticosteroids (Watt *et al,* 2000). Anti-parasites; Albendazole® as 400mg orally twice daily for 10 to 14 days), or Mebendazole® as 200 to 400mg three times daily for 3 days, then 400 to 500 mg three times daily for 10 days (Murrell and Bruschi, 1994).

Recommendations

Several things one must do to reduce ocular nematodes infection.

1- Proper hand washing frequently, and teach children the importance of washing hands before eating, after using the bathroom, and after picking up animal waste.

2- Avoiding using other personal own items like clothes, towels, bed sheets…etc.

3- Avoiding pet animals or use repellent collars for pets at home and regular deworming.

4- Avoiding eating undercooked meat, fish, or sea-foods.

5- Proper washing of raw green vegetables and fruits.

5- Drink clean water, and avoid swallowing water from lakes, streams, or ponds.

6- Avoid the insect-borne disease, particularly mosquitoes indoors or outdoors.

7- Wash hands before handling or applying contact lenses.

8- Ocular parasitosis not always causes symptoms. But notice any unusual eye pain, inflammation or vision changes, and contract health care staff to treat with medication or surgically removal. Remember moving the worm from eye does not cure infection, as parasite may be found in other body parts.

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Explanation of figures

Fig. 1: *Dirofilaria repens* visible in human eye (Capelli *et al,* 2018).
Fig. 2: a- *Loa loa*, b- microfilaria.
Fig. 3: a- *Onchocerca volvulus*, b- microfilaria (Abdel Fattah *et al,* 1986)
Fig. 4: Thelaziasisin eye of dog (Wikipedia)
Fig. 5: *Toxocara canis* larvae (Khalil *et al,* 1989).
Fig. 6: *Trichinella spiralis* encysted larvae in human eyes (Wikipedia)