Review

Oncocerciasis

Wani MG
MBchB, MMed (ophth), MSc. ClinEpi
Provincial ophthalmologist, Manicaland Province
15 Eighth Avenue/3rd Street
P O Box 2481
Mutare, Zimbabwe
Tel/Fax 263 20 6827
E-mail wanimena@mweb.co.zw

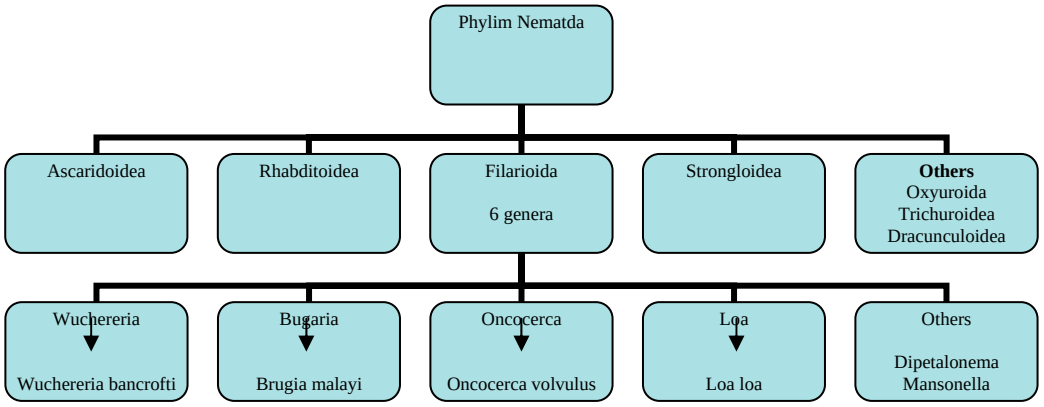
Abstract

Oncocerciasis is a parasitic disease that primarily affects economically disadvantaged communities in Africa and Latin America. It results from infection with filarial nematode *Oncocerca volvulus,* transmitted to man through the bite of infected black fly of *genius simulium.* It is the second commonest infectious cause of blindness responsible for an estimated 340,000 cases of blindness and one million cases of visual impairment. The disease is endemic in 30 countries in Africa, six countries in Latin American and in Yemen. More than 85% of the world population is at risk of infection while 18 million are already suffering from the disease. Infection intensity and ocular morbidity including blindness is highest along fast flowing rivers where the vector breeds. Oncocercal blindness has serious social and economic impact. It strikes mainly at economically active adults at the prime of their life thereby leading to reduction in productivity, death and abandonment of fertile agricultural lands. The systemic and ocular manifestations of Oncocerciasis are discussed in this review in order to bring awareness of the importance of this disease in the epidemiology of blindness and visual impairment in South Sudan where it is endemic

Introduction

Nematodes are unsegmented round worms. They have an elongated cylindrical bodies covered by tough cuticle and a cavity in which the organs lie. Phylum **Nematoda** includes a great number of species some of which are free leaving and others parasitic. There are seven super families, four of which are of clinical importance to man [fig 1].

Fig 1 taxonomic classification of nematodes



The super family Filarioidea is composed of parasites of subcutaneous or connective tissue, lymphatic system or serous cavities. These worms do not lay eggs but give birth to larvae. In order to complete their development the larvae require a second host (vector) in which development has to occur to produce infective form. Man cannot therefore acquire the parasite directly from an infected person. Transmission has to be trough the bite of an infected black fly in which the larvae has to developed. The four specicies of medical importance, their main vector and distribution are shown in [fig 2]

Fig 2 Specicies of filarial nematodes of medical importance

Specicies	Adult worm	Microfilariae	Vector	Distribution
Wuchereria bancrofti	Lymphatic	Blood	Culex species	Tropics
Bruglia malayi	Lymphatic	Blood	Mansonia	South East Asia, India Sri Lanca
Loa loa	Subcutenous	Bood	Chrysops species	West/Central Africa
Oncocerca Volvulus	Subcutenous	Skin/eyes	Simulium	Africa/South America

Oncocerca volvulus

Oncocerca volvulus is almost exclusively a parasite of man. The adult worm lives encysted in fibrous subcutaneous nodules (fig 3) although some nodules may be so deeply situated as to be impalpable [1]. Each nodule contains 1-2 males and 2-3 female worms lying in a twisted tangled mass. The male worms are shorter (3.5cm) while the females are much longer (50-70cm). Female adult worms can live for up to

9-10 years and can produce close to 1600 microfilariae/day, resulting in total microfilaria load of 150 million or more[2].

Fig 3 Oncocerca nodule containing mass of worms

Tangled worms in a nodule whose wall has been digested. Note the twisted mass of male and female worms

Parasite life cycle

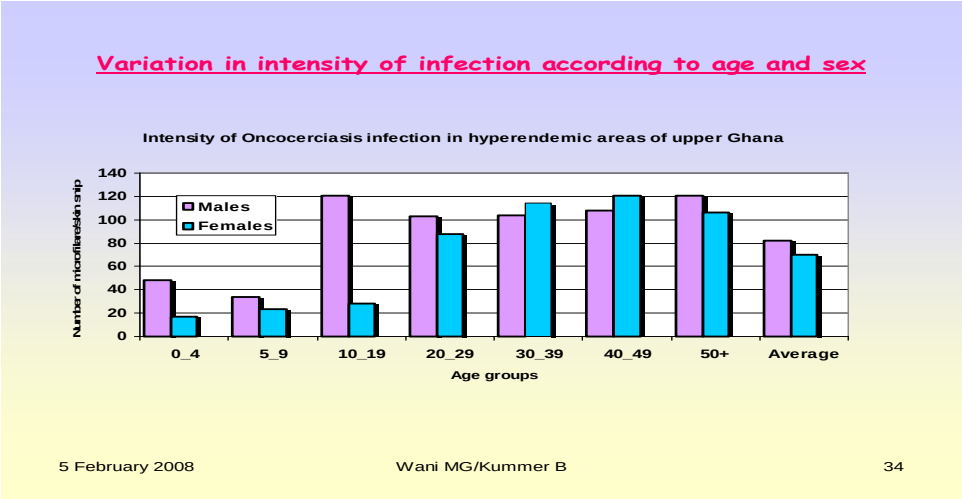
Microfilaria released by the female worm migrates to skin and subcutaneous tissue where they are picked up by the vector during a blood meal. In the vector they develop after 3 moulds into third stage infective larvae ready to be transmitted during the next blood meal and thereby completing their life cycle. After entering the new host, the infective form moulds twice to become immature adults. These become encysted in fibrous nodules were the male fertilizes the female which then begin producing millions of microfilarie

The Vector

The main African vector of *Oncocerca. Volvulus* is *Simulium Damnosum.* It is made of several cytospecieces. These dominate different environments and many do not feed on man and therefore do not transmit disease. The other important vector is *S neavei* which occurs mainly in East Africa. The larvae are always attached to bodies of crabs in contrast to s damnosum whose larvae live on rocks and vegetations. One other African specieces, S *Albivirgulatum* is found in the Republic of Congo

Simulium bites by day and can make long wind assisted flights covering several kilometers. Exposure to the bite of simulium depends on several factors including distance of the dwellings from the breeding site of the fly, the age and sex of the victim, occupation and habits of the individual. Boys are exposed to transmission 2

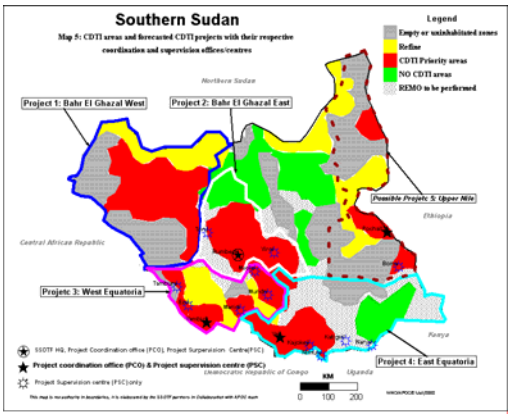
times more than girls while there is no sex difference in the exposure of men and women [fig 4]. Occupation is another factor that may expose a person to intense transmission and high risk of blindness. Fishing or farming activities associated with the river as well as Ferry men and those who have to dig sand along river banks have high chance of transmission. Levels of transmission among expatriate workers living in Tent hotels along the Nile is not currently known



Epidemiology of Oncocerciasis in South Sudan

Nearly all parts of south Sudan have oncocerciasis of varying intensity. High prevalence can be found along the Nile basin and its distributaries. The Bhar El Gazel States, Western and Eastern Equatoria States and some areas of Jongole State have high prevalence. These areas are currently targeted by the oncocerciasis control program (fig 4)

Map of S. Sudan showing CDTI priority areas [red] where there is high prevalence of oncocerciasis.



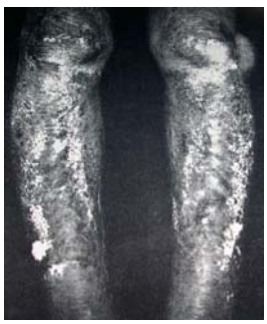
Clinical Features of Oncocerciasis

There is a wide spectrum of clinical manifestations and marked geographic variation in clinical picture which may be related to pathogen city of Oncocerca volvulus, vector biting habits and host immune response. Signs and symptoms of oncocerciasis can be classified into Dermal, lymphatic, ocular and systemic.

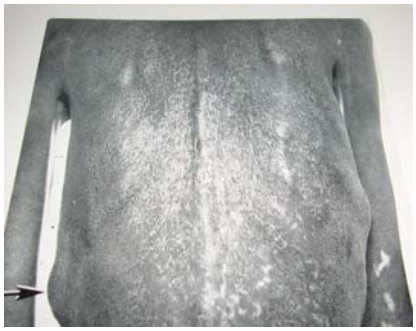
Dermal oncocerciasis

Pruritis is the most common early manifestation of oncocerciasis. It may affect upto 30% of the population in hyperendemic areas. Itching can be so intense as to render the patient sleepless, fatigued and depressed. Many patients suffer from low self esteem and may be socially ostracized as a result of social stigma. Patients may scratch the skin with objects such as sticks and stones leading excoriation and secondary infection. The first visible signs in the skin other than evidence of scratching are an alteration in pigmentation with areas of hyper or hypo pigmentation. After years of chronic infection atrophy of skin develops leading to an appearance called *Lizard skin.* This is characterized by thin epidermis with shiny fragile surface. The normal dermal structure is replaced by thin un-elastic scar tissue. Another characteristic aspect of oncocercal skin disease is leopard skin, a spotty de-pigmentation occurring in the anterior aspects of lower extremities. In Africa oncodermatitis is typically generalized, diffuse and maximal on the lower trunk, pelvic girdle, and thighs [fig 5]

Fig 5 Dermal changes in Oncocerciasis



Leopard Skin



Lizard skin

Skin nodules

Adult worms of oncocerca volvulus are found encapsulated in skin nodules which are usually subcutaneous but may also be found in deep layers, near to joint capsules, bones and fasciae and therefore often impalpable. A nodule contains on average 1-2 males and 2-3 females. A typical onco-sarcomata is easy to recognize and differentiate from *Lipoma, lymph node, Dermoid cyst*, *Ganglia or histoplasmosis*. They appear as firm round elongated non tender subcutaneous tumor. The size may vary from half a centimeter to 10 cm. Nodules are usually freely mobile but may be fixed to fascia or skin. Distribution of nodules may vary according to regions which may relate to frequency of bites to different parts of the body in different regions and availability of clothing to cover the body. In Africa for instance, people rarely cover their trunks or wear huts hence high frequency of bites occur on the trunk, buttocks, pelvis and legs where most nodules are found [fig 6]. In Central America nodules are found mainly on neck and head and in lower parts of the body in Yemen. Presence of nodules on or near the head has importance significance for ocular involvement and blindness rates. Microscopically a nodule has an outer scar tissue enclosing the adult worms. Soft tissue composed of granuloma, fibrin, macrophages and ploymorphonuclear neutrophils may surround the worms in some nodules where portions of the worm may lie free.

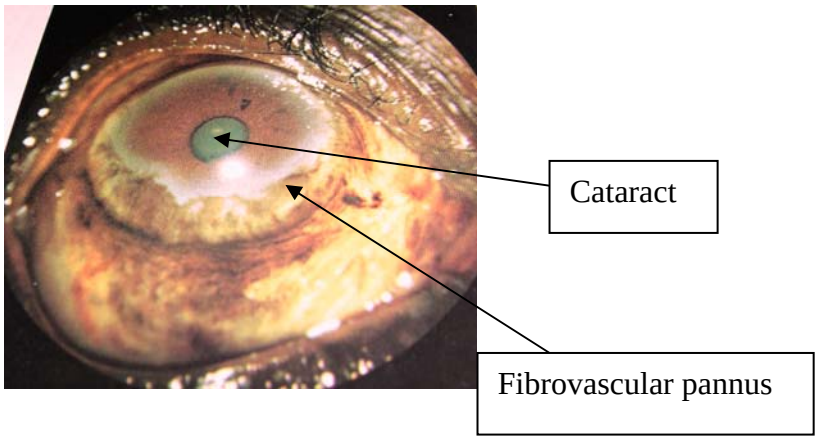
Skin nodules on trunk, pelvis and abdomen in scantly dressed African female

Ocular manifestations

Ocular manifestations due to oncocerciasis may involve any part of the eye from conjunctiva and cornea to uvea and posterior segment including retina and optic nerve. The first sign of ocular involvement is the inversion of the anterior segment where micorfilariae can be seen swimming freely in the anterior chamber. Conjunctiva reaction with inflammation and chemosis can be seen. The cornea is involved in punctuate Keratitis which appear as snowflake opacities of 0.5mm in diameter representing dead microfilaria surrounded by inflammatory infiltrate.

In later stages *Sclerosing Keratitis* may develop usually as a result of large number of micorfilariae in the cornea. This is a fibrovascular tissue growing initially in the inter palperbral fissure and inferiorly and progressing to reach central cornea, causing blindness. Anterior Uveitis can lead to posterior synechie especially occurring at 6 o'clock position causing the characteristic pear shaped pupil also called *Onco pupil.* Uveitis may cause cataract and glaucoma which can contribute to visual loss in oncocerciasis [fig 7]

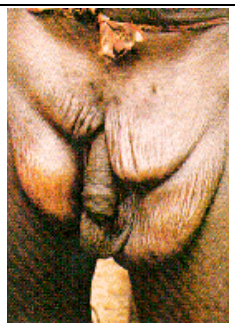
A wide spectrum of retinal changes may exist. In the early stages of retinal involvement *cotton wool sports* (soft exudates) may be observed. In advanced cases chorioretinal atrophy may occur associated with retinal pigment clumping. Optic atrophy is usually associated with peripheral visual field loss, key hole vision and total loss of sight. Blindness results from sclerosing Keratitis, iridocyclitis, chorioretinitis or optic atrophy



Lymphatic Oncocerciasis

In heavy microfilarial infestation some of the parasites pass to lymph nodes draining areas of oncocercal dermatitis. Any superficial nodes including cervical, axillary, epitrochlear, inguinal and femoral may be involved. These nodes contain varying number of microfilariae most frequently in the capsule and subcapsular sinusoids. Enlargement of inguinal nodes in combination with wrinkled skin, may gives rise to hanging groin. Elephantiasis of the scrotum may also occur[3]

Fig 8: Hanging groin and elephantiasis of the scrotum in lymphatic Oncocerciasis



Hanging groin

Elephantiasis of the scrotum

Systemic Oncocerciasis

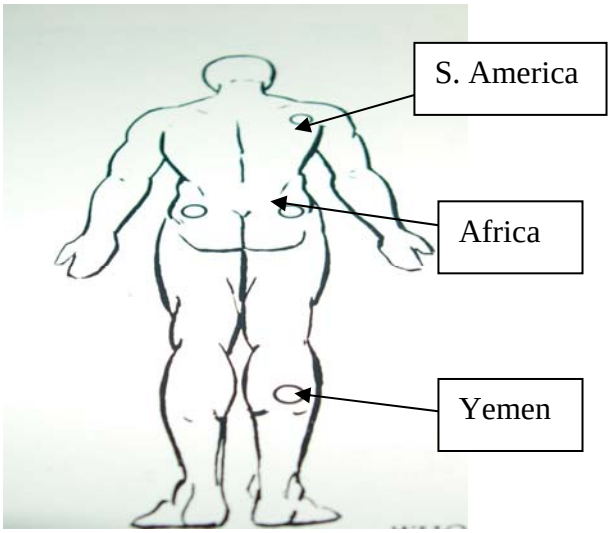
Oncocerciasis can be considered a systemic disease. Small number of microfilariae can be found not only in skin, eyes and lymph nodes, but also in deeper organs including liver, kidney, spleen, pancreas, lung, peripheral nerves and arteries. Body fluids like blood urine, tears CSF and peritoneal fluid as well as vaginal fluid may contain micorfilariae. In hyper-endemic areas patients with heavy parasite load may loose weigh and suffer from lethargy. Systemic effects of oncocerciasis may lessen productivity and increase mortality

Diagnosis

Skin snips

The best method for parasitological diagnosis of oncocerciasis is the skin snip. The snip should be taken from sites where maximum yield is expected as shown in the picture. The main areas in Africa include the iliac crest. Skin snips can be taken with a razor blade or with forceps or curved scissors. After taking the snip is transferred immediately to a drop of normal saline or distilled water on a microscope slide and examined with x10 objective. The number emerging from the snip is counted in 30 minutes. Afterwards the snip is allowed to dry and fixed and stained for identification of infective species in areas where *D. Streptocerca* is suspected

Sites where skin snip biopsy will yield maximum number of microfilariae in different regions



Mazzotti Test

In 1948 mazzotti described an allergic reaction following the administration of 50 mg of Diethyl Carbamazine (DEC). Reaction usually starts 15-30 minutes after taking the tablets although it may be delayed for 24 hours. Itching is usually the first symptom of this reaction followed by erythema and papular eruption. Papules are usually discrete but may coalese to form generalized brawny induration. Severe reactions can cause fever, pulmonary oedema or even shock. DEC also causes migration of O. Volvulus

into the cornea, urine and sputum of patients who react with respiratory distress and productive cough. Because of these severe reactions Mazzotti test is not recommended as a routine diagnostic test.

Treatment of Oncocerciasis

Oncocerciasis is the second commonest cause of infectious blindness and causes immense suffering and debility from non ocular symptoms like itching and skin changes. Treatment of oncocerciasis has immense social and economic benefit for the individual and community at large. Reduction in microfilarial load can limit ocular manifestation of disease there by preventing loss of sight, limit transmission and reduce disabling symptoms of itching and excoriation of skin.

The two drugs for treating oncocerciasis (Diethylcarbamazepine DEC and Suramin sodium) have largely been abandoned to due to presence of serious and long lasting side effects. DEC does not kill the adult worm so that the skin is usually repopulated by new microfilariae 6-12 months after treatment. Optic neuritis, chorioretinitis and protenuria do occur and can be very severe

New drugs have now been synthesized and old compounds are been re-examined in an effort to find improved chemotherapeutic regimens that are safe and affordable.

Ivermectin, a macrocyclic lactone produced by the *Actinomycete streptomyces avermitilis* is a broad spectrum anti-parasitic, displaying efficacy against Nematodes and arthropods. It was first used in veterinary medicine until 1982 when the first application in humans was reported. Since then subsequent studies have determined its efficacy and safety. Ivermectin was shown to improve both eye and skin lesions and the number of microfilare in the anterior chamber reduced considerably.

A single dose of 150µg/kg (0.15-0.2mg/kg) body weight given every 6 months suppresses microfilarial load as shown by marked decrease in skin snip counts. Incidence of side effect which are related to death of micorfilariae also decreased with subsequent treatment. Dosing schedule is shown in the table. Dosage is determined by height and/or weight. Children under the age of two years, weighing less than 15kg or height less than 90cm, pregnant or women in the first two weeks of lactation as well as those who are very ill should be excluded. Mass distribution of Ivermectin is the only way to ensure reduction in transmission by keeping the

parasite load low in those who are infected. This can be carried out once every 6 months in highly endemic communities

Drug	Height (cm)	Weight (kg)	Dose (tablets)	Duration	Comment
Ivermectin 6mg	90 - 119	15 - 20	1/2	Once	Repeat after six months
	120 - 140	21 - 44	1		
	141 - 158	45 - 64	$1^{1/2}$		
	159+	65 - 84	2		

Ivermectin is considered a safe drug although some side effects requiring treatment have been reported. Approximately 10% of patients will develop severe side effects which include intense itching, skin oedema, artralgia and bone pain, severe headache and fever. These side effects can be treated with antihistamines and Acetylsalicylic acid

Concomitant infection with intestinal parasites

Oncocerciasis patients leaving in hyper- endemic areas are often co-infected with intestinal parasites. In one study done in Sierra Leone West Africa[4], more than 88% of patients were found to be co infected with *Trichuris Trichura, Ascaris Lumbricoides, schistosoma mansoni* and *hookworm*. 64% were found to have protozoan cysts in their stools, most of which were *Entamoeba coli.* Treatment with ivermectin was found to reduce significantly egg counts of

Ascaris lumbricoides, No effect on hookworm eggs has been demonstrated so far. Treatment of oncocerciasis with ivermectin may therefore have a positive effect on other intestinal nematodes and may even clear cysts of *entamoeba coli*

Nodulectomy

Excision of Oncocerca nodules (nodulectomy) is one of the earliest methods of treating oncocerciasis. Nodulectomy does not reduce microfilarial skin counts possibly because some nodules are so deeply located that they may not be palpable. Excisions of nodules close to head may help protect the eye from heavy infestation with micorfilariae and may thus delay or even prevent blindness.

References

1. Oncocerciasis, *symptomatology, pathology and diagnosis*, Edited by AA Buck, division of malaria and other parasitic diseases, WHO Geneva 1974: 9-80
2. Gordon JJ, Darwin CM, Robert AW; The epidemiology of eye disease , 2nd Edition, Arold, 338 Euston road, London NW1 3BH
3. World Health organization expert committee on Oncocerciasis, Third Report. Technical report series 752. World Health organization, Geneva 1987: 1-167
4. Njoo FL, Belling GA, Oosting J, Vetter JCM, Stilma JS, Kijlstra A; Concurrent parasitic infections in oncocercisasis and the occurrence of adverse reactions after Ivermectin treatment. *Am J of Tropical Medicine and Hygiene 1993;48:652-657*