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FACULTY OF MEDICINE
MAKERERE UNIVERSITY

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INFECTIOUS DISEASES INSTITUTE

Quarterly Newsletter of the AIDS Treatment Information Centre, Infectious Diseases Institute, Makerere University, Kampala

Soil Transmitted Helminths

By Dr. Natalie Prevatt

Soil transmitted helminths (intestinal worms) are the most common infections worldwide [1]. They are so called because part of their life cycle is outside the human host in soil. Patients become infected by ingesting eggs (whipworm & roundworm) or by penetration of the skin (hookworm). As such, the prevalence of soil-transmitted helminthiasis is modified by lifestyle; the greatest burden being in children and in places where poverty is rife and hygiene is poor due to a lack of latrines and walking barefoot. Many Ugandans are infected with more than one species at a time.

Whipworm (Trichuris trichiura)

Whipworm eggs passed out in stool contaminate soil and vegetables. If swallowed, the eggs travel to the caecum to liberate larvae. Adult worms, known for their whip like shape, bury their thin anterior body in the mucosa of the caecum, colon, or rectum and feed on tissue juices rather than blood. Heavier infestations are thought to progress lower down the bowel with rectal infestation being associated with heavy worm burden.

Infections are mostly asymptomatic but they may cause vague abdominal discomfort. Heavy infestations occasionally cause dysentery and thus anaemia. There are no extra-gastrointestinal symptoms. Severe infestation often leads to rectal prolapse. Small worms (<0.5cm) will be seen on the prolapsed rectal wall.

Diagnosis

Rectal prolapse, with worms seen on bowel wall, is indicative of T. trichurius. Otherwise stool examination can be diagnostic. Patients often have a mild eosinophilia but this is common in many helminth infections.

Management

Mebendazole is more effective than albedazole for Whipworm. Whipworm is also capable of direct infection from anus to mouth and so hand hygiene should be encouraged.

Management strategy	Drug and dose	Common side effects
Treat the worms	Mebendazole 100mg PO BD 3 days OR Albendazole single dose 400mg PO (child 10mg/kg)	Mebendazole treatment may cause diarrhoaea and abdominal pain with expulsion of worms Albendazole treatment may cause headache, dizziness, nausea and vomiting Albendazole is contraindicated in pregnancy but pregnant women should be dewormed. In Uganda, we use mebendazole
Treat the prolapse	Reduction of prolapse: patient in knee to chest position, gentle pressure with soft wet cloth	

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INSIDE THIS ISSUE :

EDITORIAL

Last year five institutions came together to run a pilot for a new kind of postgraduate medical course. 24 doctors from Uganda, Tanzania, North America, Europe and the UK joined a six week programme focussing on the evidence-based management of common and neglected tropical diseases (NTDs). The course was made possible by a unique funding mechanism whereby overseas doctors paid international fees to generate income for local doctors to attend at low cost.

The first half of the course was based in Moshi, Tanzania, after which the class moved en masse to the Infectious Diseases Institute at Makerere University. A dozen teaching faculty from the London School of Tropical Medicine and Hygiene joined local colleagues to deliver over 80 seminars and 50 small group practical classes. An important principle of the course was building an esprit de corps and so students also spent weekends relaxing together at the Tanzanian coast and Murchison Falls.

ATIC has invited the students to write this issue focussing on Neglected Tropical Diseases. Over a billion people suffer from one or more NTD and these diseases are increasingly attracting political attention. Though rarely fatal, NTDs cause severe morbidity including physical and mental disability, disfigurement and blindness. Children account for three quarters of the total Disability Adjusted Life Years.
NTDs are neglected at an international level since they don't travel easily or pose threats to the Western World, but they are also neglected at national level as they rarely kill and mostly affect poor populations with little political voice. The students hope that in writing this edition these Neglected Tropical Diseases might be less neglected in your personal clinical practice.

And what of the pilot study? It was a success and as a result this year's course will be expanded to run for three months from September 2011. Partner institutions Johns Hopkins and the University of Washington will join LSHTM, KCMC and Makerere University in founding the first East African Diploma in Tropical Medicine. Successful participants will be awarded a DTM&H from the London School. Local places are limited and enquiries about Ugandan scholarships should be addressed to Professor Moses Joloba at the Faculty of Biomedical Sciences, Makerere University.

By Dr. Natalie Prevatt

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REVIEWERS

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Roundworm (Ascaris Lumbricoides)

Ascaris eggs can only become infectious after a period in soil and so direct anus to mouth transmission is not possible.

Eggs contaminate soil and vegetables. If swallowed their larvae are released in the stomach. These larvae penetrate mucosa of the small intestine and enter blood and lymphatic systems. In two weeks they reach the alveoli of the lung and migrate up the respiratory tract and down the oesophagus where they develop in to adults. Adults are 15-40cm long; they live in the small intestine and gain nourishment from food that is eaten – ***they do not suck blood.***

What are the clinical signs?

Prevalence peaks in children age 3-8 years and ***Ascaris worms are rarely noticed unless seen in stools.*** They are however a source of nutrient deficiency and can precipitate protein energy malnutrition. Wandering worms may enter diverticula, cause appendicitis, cholangitis, pancreatitis or liver abscess. They occasionally enter the nasal cavity. Rarely, ascaris worms may tangle into a bolus and cause intestinal obstruction.

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Ascaris pneumonitis is the most common clinical problem and one you should recognize. When larvae pass through the lung they cause a fever, with wheeze, shortness of breath and an urticarial rash. If this is accompanied by eosinophillia it is classed as Loffler's syndrome. Occasionally the symptoms of ascaris pneumonitis are more serious and the patient presents with haemoptysis, chest pain and cyanosis.

Diagnosis

Diagnosis is by demonstrating eggs in stool. This can be done in level two and three health centres. Abdominal ultrasound Scan can be used to demonstrate obstruction by ascaris in a level 4 facility. The blood count may show an hypochromic microcytic anaemia and eosinophilia.

Ascaris pneumonitis is diagnosed clinically. The presence or absence of eggs in stool is not useful, for example if the worms are all male there may be no eggs produced. Larvae and eosinophils can be found in sputum but this is rarely analysed. Worms might be seen on endoscopy. CXR is non-specific – it may show diffuse interstitial shadowing or other opacities. Treatment is therefore usually presumptive.

Management strategy	Drug and dose	side effects
Treat the worms	Albendazole single dose 400mg PO (child 10mg/kg) (heavy infection may need repeat on day 2 and/or 3) OR Mebendazole 100mg PO BD 3 days	Larval death may aggravate symptoms- and thus treatment at the time of severe pneumonitis is questionable Migration of ascaris has been reported after mebendazole and so albendazole is first line (*Other side effects as above)
Treat the wheeze/cough/ rash/dyspnoea	Bronchodilator (Salbutamol) & steroid (prednisolone)	Same as when used in asthmatics
Treatment of intestinal obstruction	Usually managed conservatively with IV fluid, antispasmodic and Albendazole +/- nasogastric aspiration of worms	If the patient becomes increasingly sick; laparotomy will be required

Hookworm (Ancylostoma duodenale or Necator americanus)

Hookworm larvae live in surface soil and enter humans by penetrating intact skin. From here they enter the blood and lymphatic systems and travel to the lung. They enter the alveoli and migrate via the pharynx to the small intestine where they mature into adults which are about 1cm long. Hookworm use their mouthparts to pierce the intestinal wall and suction on to the mucosal surface. They feed on blood but each one can only consume 0.25ml per day. After three to five weeks they start to produce eggs.

Symptoms

Pneumonitis is possible with hookworm but the most common complaint is that of 'ground itch' at the site where larvae have entered the skin.

In heavy infestations patients may have a pot-belly with abdominal discomfort, flatulence, nausea, intermittent vomiting and diarrhoea. These abdominal symptoms, along with general malaise, are known to affect learning capacity in school children.

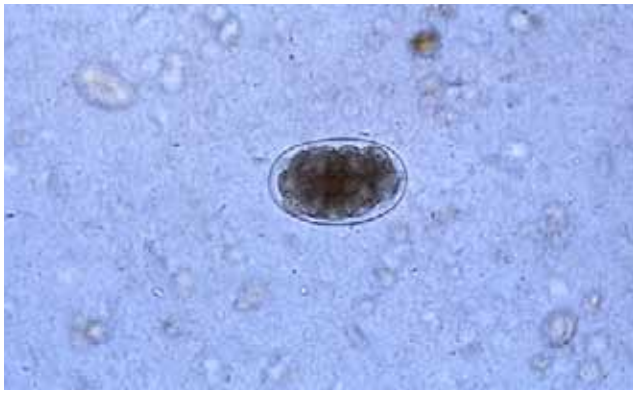
Is hookworm infestation dangerous?

Hookworm adults consume very little blood and only a little extra blood is lost from bleeding at the site of attachment. Where dietary intake is poor hookworm infestation can gradually contribute to multifactorial iron deficiency anaemia, and this may occasionally be associated with oedema due to hypoalbuminaemia. Children are most at risk of anaemia, which is associated with growth stunting and cognitive impairment.

Acute bloody diarrhoea has occasionally been reported in children with very heavy infestations.

Diagnosis

Hookworm eggs, with their characteristic ellipsoidal shape, can be seen on faecal microscopy. This should be possible in level two or three health centres. The blood count may show an hypochromic microcytic anaemia.



Light micrograph of a hookworm egg. Courtesy of Science photo library (http://www.sciencephoto.com/images/download)

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Management

Management strategy	Drug and dose	side effects
Treat the worms	Albendazole single dose 400mg PO (child 10mg/kg) OR Mebendazole 100mg PO BD 3 days (more commonly prescribed but less effective)	Larval death may aggravate symptoms and thus treatment at the time of severe pneumonitis is questionable
Treat iron deficiency anaemia	Child with Hb<9.3 requires iron/folate tablets OD for 3 months (WHO guidance) Child with Hb< 4 requires blood transfusion (Hb<5 + other features of severity requires transfusion) (WHO guidance)	Do not give oral iron to severely malnourished children There are always serious risks associated with blood transfusion

Despite the fact that deworming is only seen to increase Hb by a mean of 1.7g/l [2], this is enough to reduce the burden of anaemia as classified by WHO cut offs, and so deworming of school-aged children is stated by WHO to be '…probably the most economically efficient public health activity … in sub-Saharan Africa' [1]. The cost of treatment is only 50 Ugandan shillings per patient [4]. WHO recommends children above 12 months be dewormed three times per year in high prevalence areas [3], and school health programmes also include hygiene education. There has been a national control programme in Uganda since 2003. A longitudinal study of eight districts where the programme was implemented found the intensity of hookworm infection decreased by 75% after one year and 93% after two years. [5]

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Leprosy (Hansen's disease)

By Dr. Maryirene Ibeto

Leprosy is a chronic inflammatory disease caused by Mycobacterium leprae; also known as Hansen's disease after G. A. Hansen who identified the bacillus in 1873.

M. leprae multiplies very slowly and the incubation period is at least five years. Only approximately 5% of people who are infected go on to develop clinical features. Transmission is via droplets from the nose and mouth of untreated patients with severe disease. Household contacts are most at risk of contracting the disease but M leprae is not very infectious and studies have demonstrated this transmission is sufficiently low not to give secondary prophylaxis.

Many countries claim to have eliminated Leprosy en route to the WHO year 2000 target but this is a controversial area where diagnosis and reporting may distort the true picture. In Uganda there is a leprosy reporting and referral system largely based on NGO facilities. Leprosy is still regularly reported across multiple districts, with 346 cases reported in Uganda in 2009. However there is a gradual downward trend of new case detection rates.

Clinical features include:

Skin lesions

- Asymmetrical
- Usually macules or plaques (scaly and dry in tuberculoid leprosy, shiny and smooth in lepromatous leprosy)
- Lighter than normal skin colour
- Decreased sensation to touch, heat or pain

Signs of peripheral nerve damage:

- Numbness or absent sensation in the hands, arms, feet, and legs
- Associated muscle weakness
- Reduced autonomic nerve function (decreased sweating, dry cracked feet, eyebrows lost)
- Palpable thickened nerves (not diagnostic without other clinical features)
- Large nerve palsies (wrist drop/claw hand/ foot drop)

Signs of eye damage

- Decreased corneal sensation (leading to ulcers and regular conjunctivitis)
- Lid lag leading to cataract
- Chronic iritis
- Acute iritis (acute red photophobic eye) occurs in patients with facial patches, and in treatment reactions.

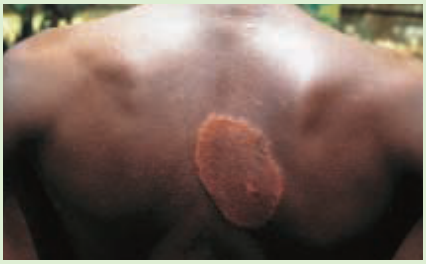
Differential Diagnosis

For pale lesions the differential diagnosis includes vitiligo, post inflammatory skin changes, tinea infection and pityriasis vesicolor. Papules on the other hand may be mistaken for early Buruli ulcer, sarcoid or Kaposi's sarcoma. For nerve palsies differentials include trauma, compression or entrapment of the affected nerve, causes of a mononeuritis multiplex and diabetic neuropathy.

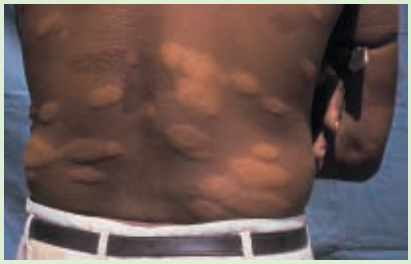
Diagnosis

WHO classifies leprosy in to two forms based on clinical manifestations and the results of slit skin smears. In the classification based on ZN staining of slit skin smears, patients showing negative smears at all sites are grouped as paucibacillary leprosy (PB), while those showing positive smears at any site are grouped as having multibacillary leprosy (MB). In the absence of slit skin smear services, clinical criteria alone can be used for classifying and deciding the appropriate treatment regimen for patients.

In the classification based on clinical criteria alone, patient presenting with 1-5 skin lesions are grouped into PB leprosy and those with >5 skin lesions are MB leprosy



PB 1-5 lesions



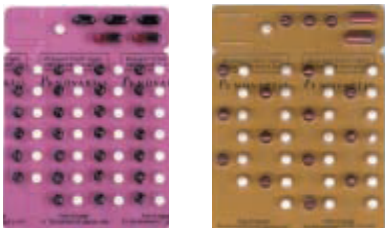
MB >5 lesions

All forms of the disease may eventually cause nerve damage, with sensory loss in the skin and muscle weakness. In the long-term patients often lose the use of their hands or feet due to repeated injuries resulting from lack of sensation and poor protection.

Treatment of Leprosy

Multidrug therapy (MDT) is crucial, and has been made available by WHO free of charge since 1995. Drugs come in ready-made blister packs. Treatment regimes at regional level depend on classification as PB or MB. PB is treated for 6 months, whereas MB is treated for 12 months. It is particularly important to ensure that patients with MB disease are not treated with the PB regimen.

PB blister packs



MB blister packs

Table of WHO recommended MDT regimes for leprosy:

Leprosy type	Standard regimen for adult	Standard regimen for child aged 10-14
Multibacillary (MB) leprosy	Rifampicin: 600 mg once a month + Dapsone: 100 mg daily + Clofazimine: 300 mg once a month and 50 mg daily Duration= 12 months	Rifampicin: 450 mg once a month + Dapsone: 50 mg daily + Clofazimine: 150 mg once a month and 50 mg every other day Duration= 12 months
Paucibacillary (PB) leprosy	Rifampicin: 600 mg once a month + Dapsone: 100 mg daily Duration= 6 months	Rifampicin: 450 mg once a month + Dapsone: 50 mg daily Duration= 6 months

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For children below 10 years of age, the dose must be adjusted according to body weight. Leprosy in younger children is rare due to the long incubation of the disease.

Patients with anaesthesia must be trained to inspect and ***clean wounds and to moisturise their feet daily.*** They may need lifestyle changes and protective shoes.

Common problems with MDT

Reversal reactions – type 1 and type 2:

Type 1 is a delayed hypersensitivity reaction that usually begins during the first months of treatment. It is characterised by erythematous skin lesions, tenderness in the peripheral nerves and new or worsening motor loss. A reducing regime of oral corticosteriods for 12 weeks (eg. Prednisolone 40mg/day reducing by 5mg each month)(0.5mg/kg/day for child) should be added to MDT.

Type 2 is due to immune complex deposition which typically occurs years into or after treatment, and can be recurrent. It is characterised by fever, lymphadenopathy, iritis, neuritis, arthritis, erythema nodosum and raised white blood cell count. Patients may be systemically unwell and high dose oral corticosteriods (60-80mg/day) should be added to MDT.

Silent nerve damage on therapy:
Patients should be checked for sensory and motor function regularly. Any patient with a reduction in nerve function should also be started on oral corticosteroids.

Clofazimine side effects:
Skin discolouration (reverses after drug is stopped).

Rifampicin side effects:
Temporary red discolouration of the urine; occasional serious hypersensitivity reaction; induction of liver enzymes such as cytochrome P450 leading to drug interactions.

Dapsone syndrome:
Starts with rash, fever and eosinophilia. May progress to exfoliative dermatitis, hepatitis, psychosis and death. If suspected, dapsone should be discontinued immediately and the patient should be referred to hospital.
In the large majority of cases MDT is very safe and effective in curing leprosy.
The remaining challenge in the path of leprosy elimination lies in achieving early diagnosis and treatment. Patients living with the effects of leprosy need careful and supported care of anaesthetic hands and feet.

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Schistosomiasis

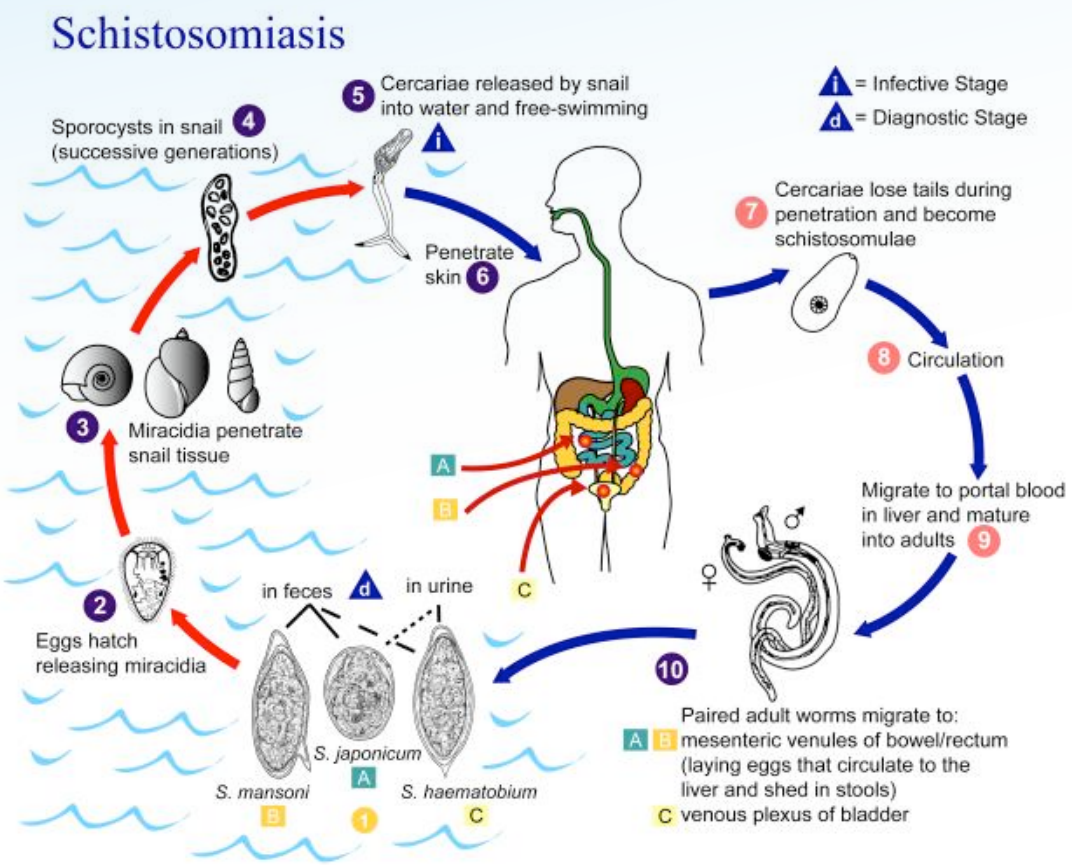
By Dr. Joao Pires

Schistosomiasis is a debilitating disease that remains one of the most prevalent parasitic infections in the tropics. Three species— Schistosoma haematobium, S. japonicum, and S. mansoni— cause the bulk of an estimated global burden of 4.5 million disability-adjusted life years.[1,2] Schistosomiasis is particularly common in Uganda where almost all cases are due to S. mansoni. Most patients live in villages near rivers and lakes but with increasingly mobile populations, doctors throughout Uganda will encounter cases suffering from the chronic effects of Schistosomiasis.

Human infection occurs when infective cercariae penetrate intact skin. These organisms, which are released from infected snails in freshwater, enter subcutaneous tissue and transform into schistosomes. These migrate via venous or lymphatic vessels, to reach the lungs, and finally liver parenchyma.

Sexually mature schistosomes then descend into veins at specific anatomic locations: intestinal veins (S. mansoni, S. japonicum, S. mekongi, and S. intercalatum) and vesicular veins around the bladder (S. haematobium).

After mating, the females deposit their ova intra-vascularly. Then, depending upon the location, ova reach the lumen of the bowel or bladder and are voided with stools or urine. About half of the ova remain in host tissues, causing the disease. The ova that reach fresh water, release miracidia that penetrate the snail.



Reproduced with permission from CDC (authors: Alexander J. da Silva, PhD and Melanie Moser)3

Schistosomal infection differs between the early stages and the later chronic disease.

Early/Acute manifestations:

- Cercarial dermatitis (swimmer's itch): Self-limiting itchy maculopapular rash due to cercarial penetration of the skin.

- Katayama Fever: lethargy, fever, and myalgia mimicking a viral or malarial illness develop 1-2 months after exposure. Generalised lymphadenopathy and hepatosplenomegaly are common at this time. A complete blood count will show eosinophilia and is a useful tool in differential diagnosis. Symptoms usually resolve over several weeks, however, intense infection can result in death.

Chronic manifestations are much more common in endemic areas like Uganda. There is a granulomatous response to the parasite ova, resulting in fibro-obstructive disease in the veins. The onset is insidious and the clinical picture depends on the species, severity of infection, and immune response to the eggs.

- Intestinal schistosomiasis (mesenteric veins): colicky abdominal pain and bloody diarrhoea. Chronic bleeding can lead to severe iron-deficiency anaemia.

- Hepatic shistosomiasis (portal veins): dyspepsia, flatulence, and pain in the left hypochondrium (due to spleen enlargement) are common early symptoms. Presinusoidal blockage of blood flow leads to portal hypertension. Oesophageal varices occur and variceal bleeding might be the first presentation. In late-stage disease, typical fibrotic changes occur along with deteriorating liver function, ascites, hypoalbuminaemia, and defects in coagulation.

- Urinary shistosomiasis (vesicular veins): major manifestations occur in children and young adults. Dysuria, urinary frequency, and terminal haematuria occur. Schistosoma. heamatobium infestations create a setting for repeated bacterial infection, compromised kidney function, and finally renal failure. It is also epidemiologically associated with squamous cell bladder carcinoma.

- Ectopic adult worms are infrequent but important causes of disease such as Schistosomal myelopathy which may present as paraplegia.

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Schistosoma mansoni, revealing the egg's characteristic lateral spine. Reproduced with permission from CDC.

Diagnosis

The "gold standard" for identifying schistosomal infection is to demonstrate parasite eggs in stool (S. mansoni, S. japonicum, S. mekongi, and S. intercalatum) or urine (S. haematobium). Determining the intensity of infection is important in endemic areas, as many of the complications are related to heavy parasite burden. It is performed by sampling 20-50 g of stool (using Kato-Katz technique). This is very important in patients with chronic liver/intestinal disease.

Simple stool examination has very low sensitivity. Serology, using antibody test cannot differentiate active and past illness, and therefore is not recommended in endemic regions.

Treatment

Praziquantel is the treatment of choice for all forms of schistosomiasis. It is widely available in Uganda, being recommended in the national guidelines as a stat dose of 40 mg/kg4 for children and adults. There is some evidence that Artemesinins kill cercariae and the increasing use of ACT for treating malaria may have an effect on Schistosomal carriage.

Prevention

Ugandan's Health Sector Strategic Plan 2010-2015 follows WHO guidelines for prevention and control. These are based on mass preventive treatment, snail control, and improved sanitation and health education[5]. One key strategy is to implement periodic mass chemotherapy in endemic areas. As part of the national vector control program, the Ministry of Health has begun 3 monthly Prazinquantel administration for schoolchildren in Masindi District. This program undertakes frequent surveys to determine effectiveness, and data is expected in the near future.

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Human African Trypanosomiasis (Sleeping Sickness)

By Dr. Shamzah Araf

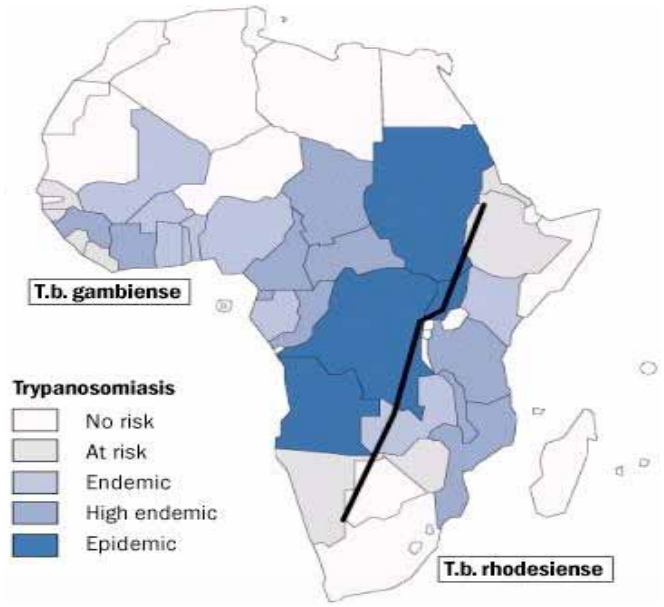

Figure 1: Distribution of gambiense and rhodesiense sleeping sickness (separated by the black line) in sub-Saharan Africa, 1999. (Reproduced with permission from WHO)

Human African Trypanosomiasis is caused by Trypanosoma brucei rhodesiense (East and Southern Africa, East and South East Uganda) and Trypanosoma brucei gambiense (West and central Africa, North West Uganda). It is transmitted by the Tsetse fly. Uganda is unique in having both forms of the disease and, whilst there is currently no overlap in transmission, the distance between the two forms is reducing. This geographical separation is important in identifying the type of infection as both types have differing modes of diagnosis and treatment. Tb gambiense is predominantly a chronic neurological condition whereas Tb rhodesiense is an acute illness with its reservoir in cattle. Worldwide, approximately 40 000 cases are reported to the WHO each year.

Presentation

Tetse fly bites are painful but the patient may not remember. A chancre may appear at the site of the bite, typically increasing in size for 2-3 weeks before regressing.

There are two stages of the disease, an early haemo-lymphatic stage and the later meningo-encephalitic stage, which is due to infection of CSF (cerebrospinal fluid) and the brain.
The early stage is characterised by fevers, headache, pruritis, lymphadenopathy, arthralgia and hepatosplenomegaly. The meningo-encephalitic stage includes motor signs (tremors, muscle fasciculation, weakness, cerebellar signs, athetoid movements), sensory signs (hyperaesthesia), and mental changes (personality change, psychiatric symptoms) including the classic sleep disturbance.

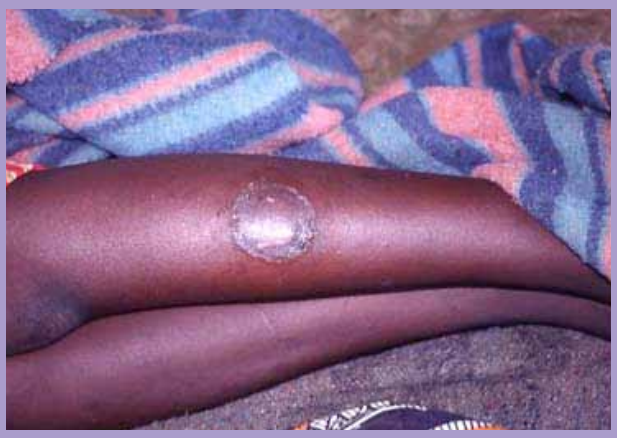

Figure 2: Chancre on leg at the site of the tsetse fly bite.

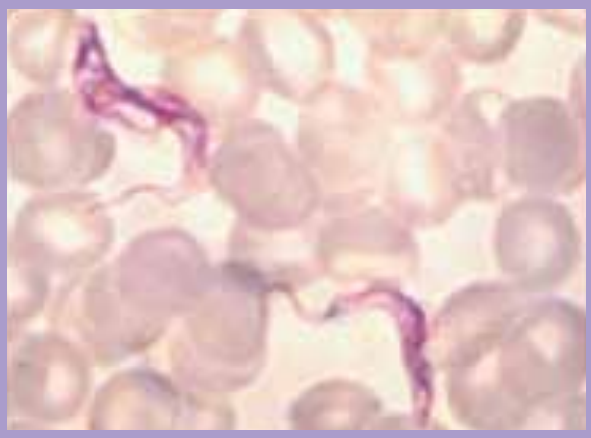

Figure 3: Blood film showing trypanosomes. (Reproduced with permission from WHO)

Tb rhodesiense infection is much more rapidly progressive and death occurs within a few months if left untreated. Tb gambiense infection can run a chronic course, for an average of 3 years. Patients tend to present at a more advanced stage, and may be misdiagnosed as having a psychiatric illness.

Diagnosis

Patients with Tb rhodesiense are identified based on their presenting symptoms and signs. Identification of trypanosomes is much easier in Tb rhodesiense disease because of a higher density of parasites in the bloodstream. Diagnosis is made by examination of thick and thin blood films from either whole blood or buffy coat preparations.

For Tb gambiense infection (less acute symptoms) the Card Agglutination Test for Trypanosomiasis (CATT) is a screening test that can be performed on blood. However, because of the low positive predictive value, microscopic parasitological confirmation is still required.

Identification of Tb gambiense is more challenging because circulating numbers of the parasite are much less, and this is particularly so in the later stages of disease when most patients present. Lymph node, bone marrow and chancre aspirates can be microscopically examined for parasites. Concentration techniques such as quantitative Buffy coat analysis use centrifugation to concentrate trypanosomes at the level of the white blood cells. Multiple capillary tubes may be examined from the same patient to increase the sensitivity.

A lumbar puncture is performed to stage the disease as the haemo-lymphatic or meningo-encephalitic form. The WHO criteria for second stage disease following CSF examination is >5 WBC/mm3, or the presence of trypanosomes, or an increased protein count (>370mg/L). In field conditions a CSF WBC count of >20 cell/mm3 may be used as the cut-off and this difference is an area of debate.

Management

Not all of the useful drugs penetrate CSF and so treatments vary depending on the stage of the disease. The overall health of the patient should be optimised with treatment of any co existent infections, and of anaemia.

Table 1: Treatment of Tb gambiense based on WHO guidelines

Stage of disease	Treatment
Stage 1 disease	IM pentamidine 4mg/kg per day for 7 days (Peadiatric dose: IM pentamidine 4mg/kg per day for 7 days)
Stage 2 disease (1st line)	IV eflornithine 400mg/kg per day every 12 hrs for 7 days plus oral nifurtimox 15mg/kg per day, every 8hrs for 10 days.
Stage 2 disease (2nd line)	IV eflornithine 400mg/kg per day every 6 hours for 14 days.
Stage 2 disease (3rd line)	IV melarsoprol 2.2mg/kg per day for 10 days

Melarsoprol can cause encephalopathy in 5-10% of patients, with up to a 50% fatality rate3. To reduce the risk and severity of adverse reactions in second stage disease, steroids (prednisolone 1mg/kg up to a maximum of 40mg per day) can be given a day before the first melarsoprol injection and then daily throughout treatment.

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Table 2: Treatment of Tb rhodesiense based on WHO guidelines.

Stage of disease	Treatment
Stage 1 disease	IV suramin test dose 4-5mg/kg on day 1. On day 3, 10, 17, 24, 31, 20mg/kg max dose per injection 1g (Peadiatric dose: 2mg/kg test dose on day 1. Then 20mg/kg on day 3, 10, 17, 24 and 31)
Stage 2 disease	IV Melarsoprol 3.6mg/kg, 3.6mg/kg, 3.6mg/kg as a series of 3 injections spaced by an interval of 7 days. Max dose 180mg per day

There is a significant relapse rate and patients should be followed up with 6 monthly lumbar punctures for 2 years. It may take up to 6 months for the CSF parameters to return to normal. Treatment of any disease relapse is difficult. For Tb rhodesiense infection another course of melarsoprol can be given and for Tb gambiense infection that was only treated with stage 1 drugs; melarsoprol or eflornithine should be tried.

Prevention

Controlling the Tb gambiense relies on population screening programs and tsetse fly traps. In Tb rhodesiense disease, cattle are the main reservoir and so cattle treatment and spraying with insecticides is central to control programs. This proved very successful in the first half of the 20th century when total cases fell to a few thousand per year. However political unrest and dismantling of control programmes has led to a marked rise in recent years.

Table 3: Differences between Tb rhodesiense and Tb gambiense

	Tb Rhodesiense	Tb Gambiense
Geographical location	East and Southern Africa (East and South-East Uganda)	Central and West Africa (north-West Uganda)
Reservoir	Predominantly animal/cattle	Predominantly animal/cattle
Presentation	Acute illness, rapidly progressing. Chancre more common	Chronic illness, usually presents in 2nd stage. Posterior triangle lymphadenopathy classically seen (Winterbottom's sign)
Diagnosis	Blood film examination for trypanosomes	CATT serological screening followed by parasitological confirmation using concentration techniques.
Prevention	Tsetse fly traps, cattle treatment. Population screening.	Tsetse fly traps. Population screening

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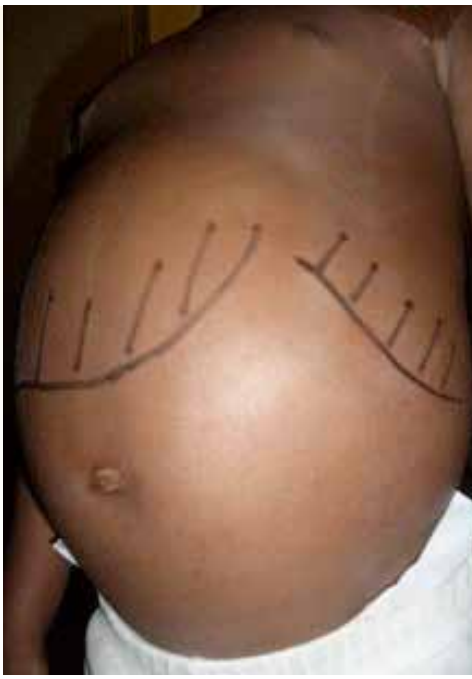
VISCERAL LEISHMANIASIS

By Dr. Alexandra Vasconcelos

Visceral leishmaniasis (VL), also known as kala-azar, is a disease caused by intra-macrophage protozoa, transmitted through the bites of phlebotomine sandflies[1,2,3]. It is still one of the most neglected diseases, with around two million new cases per year.[1,2,3]

VL is caused by two different Leishmania species (L. donovani and L. infantum), depending on geography: L. donovani in East Africa and India, and L. infantum in Europe/ North Africa/ Latin America.[1,2,3]

Leishmaniasis (by L. donovani) is endemic in East Africa, causing at least 4000 deaths annually in Sudan[4]. VL was rarely described in Uganda until 1997, when Médecins Sans Frontières began to provide assistance to Amudat Health Centre in Pokot County. The disease in Uganda appears to be restricted to this semi-arid area in Nakapiripirit District, as an extension of the larger focus in the West Pokot District in Kenya[5]. Most of the local population has heard of VL but it is known locally as termes which means 'a very enlarged spleen'.[6] The number of patients treated in Uganda more than tripled between 2000 and 2005, from 175 to 690 cases per year. [6] The highest incidence is in children and young adults.



HOW IS VL TRANSMITTED?

VL is transmitted from one mammal to the next by bites of infected sandflies. Sandflies are noiseless fliers; typically most active in evening hours. They inoculate flagellated forms of the parasite known as promastigotes into skin.

The parasites secrete factors which attract macrophages and allow them to enter and multiply within. Eventually the macrophages rupture, releasing many amastigotes in to the liver, spleen and bone marrow. [7]

HOW DOES VL PRESENT?

The incubation period after a bite ranges from ten days to more than a year. Patients present with symptoms of a persistent systemic infection including fever, fatigue, loss of appetite and weight loss. There are also signs of parasitic invasion of the blood and reticulo-endothelial system. These include lymphadenopathy, which may be the only manifestation, and non-tender splenomegaly or hepatosplenomegaly.

Fatigue is gradually worsened by anaemia. There is usually pancytopenia (low WBC, RBC and platelets). Signs of malnutrition including oedema, skin and hair changes develop as the disease progresses. Inter-current infections are common. Darkening of the skin of the face, hands, feet and abdomen is typically found in India. In the Sudan, and rarely in Uganda, a cutaneous nodule or ulcer or mucosal lesion containing Leishmania may be present.

WHAT IS POST-KALA-AZAR-DERMAL LEISHMANIASIS (PKDL)?

PKDL is a complication of VL; it is a hypopigmented, maculopapular or nodular rash which is usually full of parasites. It is seen in patients who have recovered from VL. It usually appears 6 months to years after apparent cure of the disease but may occur earlier or even concurrently with VL. PKDL heals spontaneously in the majority of African cases. [1,2,3]

WHAT IS THE DIFFERENTIAL DIAGNOSIS?

Fever may resemble malaria. The prolonged systemic response with reticulo-endothelial involvement may aso occur in typhoid, tuberculosis and brucellosis as well as leukaemia and lymphoma. In malarious areas, **VL should be suspected when irregular fever lasts for more than two weeks without response to antimalarial therapy.**

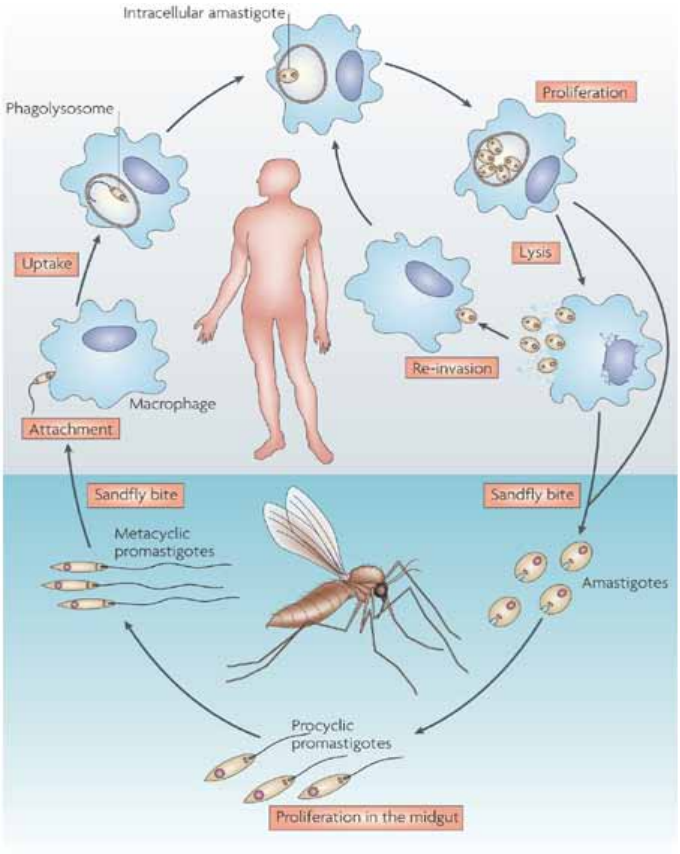
IS VL MORE COMMON IN HIV?

Malnutrition and HIV infection are important risk factors. In HIV positive patients the clinical features may be atypical.[8]

HOW DO YOU MAKE THE DIAGNOSIS OF VL?

As the presentation of VL lacks specificity, tests are required for confirmation.

Parasitological diagnosis: visualization of amastigotes by microscopic examination of tissue aspirates (spleen, bone marrow or lymph node) is the classical confirmatory test for VL. Detection of parasite DNA by PCR in blood or bone marrow aspirates is substantially more sensitive but its use is currently restricted to referral hospitals and research centres. A splenic aspirate carries significant risk or uncontrolled haemorrhage in the hands of the inexperienced.



Serological diagnosis: Two serological tests, the direct agglutination test and the rK39 antigen-based immune-chromatographic test were developed for field use and have shown diagnostic accuracy in most endemic areas. The rK39 test is fast, easier to perform and cheaper, and can therefore be used for early diagnosis of VL in rural areas.

WHAT IS THE WHO DIAGNOSTIC POLICY FOR HEALTH SERVICES IN ENDEMIC AREAS?

In rural district hospitals in highly endemic areas, the rK39 antigen-based immune-chromatographic test should be available. Patients with good clinical syndromes, no history of VL and a positive rK39 test should then be treated. In areas where the sensitivity of the rK39 test is below 90% and the patient's rK39 is negative, additional parasitological investigation may be necessary. Evidence of parasite persistence by direct microscopy of affected tissue should be used to diagnose relapses.

HOW DO YOU TREAT VL?

Since untreated VL has a high mortality rate there is some urgency to start treatment. However given the low specificity of clinical signs and the cost, complexity and side effects of drugs, **confirming the diagnosis first is important.**

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Treatment regimens recommended by WHO are:

Visceral leismaniasis caused by L. donovani in East Africa (Uganda, Ethiopia, Eritreia, Kenya, Somalia, Sudan)					
	Drug	**Dose**	**Administration**	**Duration**	*
1st line	Combination: Pentavalent Antimonals plus Paromomycin	20 mg Sb5+/kg per day + 15 mg/kg per day	intramuscularly or intravenously intramuscularly	17 days	(A)
2nd line	Pentavalent Antimonals	20 mg Sb5+/kg per day	intramuscularly or intravenously	30 days	(A)
3rd line	Liposomal amphotericin B	3-5 mg/kg per day	infusion	6-10 days (Up to a total dose of 30 mg/kg)	(B)
4rd line	Amphotericin B deoxycholate	0.75-1 mg/kg per day (daily or alternative days)	Infusion (infusion in 5% dextrose for 4h)	15-20 DOSES	(A)

**treatment regimens are qualified by grade of evidence adapted from Cochrane reviews as follows: (A) evidence obtained from at least one properly designed randomized controlled trial; (B) evidence obtained from well-designed trials without randomization; (C) opinions of respected authorities, based on clinical experience, descriptive studies or reports of expert committees; and (D) expert opinion without consistent or conclusive studies.*

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ATIC newsletter

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We hope this new development will make it easier for health workers to get the information they need to make good patient management decisions

We at ATIC remain committed to serving you