

# We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

4,800

Open access books available

122,000

International authors and editors

135M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index  
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?  
Contact [book.department@intechopen.com](mailto:book.department@intechopen.com)

Numbers displayed above are based on latest data collected.  
For more information visit [www.intechopen.com](http://www.intechopen.com)



## Epilepsy Secondary to Parasitic Zoonoses of the Brain

Humberto Foyaca-Sibat

*Walter Sisulu University, Nelson Mandela Academic Hospital,  
Division of Neurology Mthatha,  
South Africa*

### 1. Introduction

In spite of natural disaster like the one we are seeing today in Japan (March 20, 2011) where thousand of peoples died due to earthquake and tsunami and some food are contaminated by radioactivity , and other disasters caused by human beings by different modalities of war like the one we are seeing today at the North of Africa plus different modalities of terrorism, destruction of their environment and so forth; world population continues to grow and there has been ever increasing need to develop and maintain food products with a high protein content (particularly livestock and fish) under intensive farming situations, which is inevitably leading to a greater spread of animal diseases and their transmission to humans (McCarthy & Moore 2000; Keiser & Utzinger 2005).

Improved diagnosis and/or recognition of neglected human infections can account for some diseases apparently emerging or re-emerging in recent times (e.g. Human fascioliasis). Climate change has also been suggested as a cause for disease spread and is a concern for the future (McCarthy & Moore 2000); thousand of wild or domestic animals are becoming sick and birds that usually migrate from one continent to another one they don't do it today. It will bring serious consequences to humans being by the increment of the number of infectious disease is transmitted from animals to humans (known by zoonotic diseases). Zoonotic infectious agents are among the most prevalent on earth and are thought to be responsible for more than 60 per cent of all human infections and 75 per cent of emerging human infectious diseases (Cunningham 2005). The success and widespread epidemiology of these infections can be attributed to a range of human factors including social and dietary changes as well as an increased mobility of the human population (McCarthy & Moore 2000; Vorou *et al.* 2007).

Some zoonotic diseases are grouped as neglected tropical diseases (NTD) which are uncommonly recognized or diagnosed in developed countries; are less well understood than more common infections due to a of lack of research interest and/or insufficient funding; and, lastly, remain mysterious or unknown to health care providers because of minimal or no instruction regarding the diseases during medical students training. However, certain food-borne trematode infections in particular remain "neglected" NTD, according to the World Health Organization. These include clonorchiasis (Chinese liver fluke disease), fascioliasis (sheep liver fluke disease), opisthorchiasis (fish liver fluke disease), and paragonimiasis (lung fluke disease). These diseases most often significantly

affect large numbers of poverty-stricken individuals, generally in resource-limited regions, and receive very little interest from funding or government agencies. As these diseases have complex life cycles and are rarely encountered in the developed world, they receive little attention in the education of physicians, which furthers their enigmatic status. (Tolan, 2011)

For human, domestic animal and wildlife health, key effects of directional climate change include the risk of the altered occurrence of infectious diseases. Many parasite zoonoses have high potential for vulnerability to the new climate, in part because their free-living life-cycle stages and ectothermic hosts are directly exposed to climatic conditions. For these zoonoses, climate change can shift boundaries for ecosystem components and processes integral to parasite transmission and persistence, and these shifts can impact host health. The vulnerable boundaries include those for spatial distributions, host-parasite assemblages, demographic rates, life-cycle phenologies, associations within ecosystems, virulence, and patterns of infection and disease (Polley & Thomson, 2009)

Zoonotic infections of humans are caused by a wide variety of agents including viruses (e.g. avian influenza and rabies), bacteria (e.g. brucellosis and salmonellosis), parasites (e.g. leishmaniasis, schistosomiasis, neurocysticercosis and toxocariasis) and others 'unconventional' agents such as prions (e.g. Bovine spongiform encephalopathy and its variant: Creutzfeldt-Jakob disease). As we previously reported (Foyaca-Sibat et al., 2010), the infectious agent may be transmitted in a variety of ways, as can be seen in Table 1

Direct contact with animal flesh (Tularemia)
Drinking of cows or goats milk ((TB and Brucellosis)
Inhalation of dust particles contaminated by animal excreta or products (Q Fever & Anthrax)
Eating of insufficiently cooked infected flesh (Anthrax, Trichinosis, Taeniosis- <i>T solium</i> )
A bite by insect vectors (Plague, Scrub Typhus and Equine Encephalomyelitis) or a bite from a diseased animal (Rabies)
Others ways

Table 1. Some zoonotic infections and its way of transmission

A seizure complication of zoonotic infections can consist of a single seizure or can go on to become chronic epilepsy. Seizures can arise as an acute, sub-acute, or long-term consequence of an infectious states. Seizures are temporary abnormal electro-physiologic phenomena of the brain, resulting in abnormal synchronization of electrical neuronal activity. They can manifest as an alteration in mental state, tonic, clonic or tonic-clonic movements, and various other psychic symptoms (such as déjà vu, jamais vu, etc.).

A seizure can last from a few seconds to more than 20 minutes like: status epilepticus, a continuous seizure that will not stop without intervention and patients does not regain their normal level of consciousness between the attacks.

Sometimes, a seizure can also be as subtle as marching numbness of a part of the body, a brief loss of memory, sparkling of flashes, sensing an unpleasant odour, a strange epigastric sensation, a sensation of fear, levitation, laryngeal constriction, peribuccal paresthesiae and dysphagia (last four seen in insular seizures). Therefore seizures are typically classified as motor, sensory, autonomic, emotional or cognitive. The type of epileptic complication and

when it arises from an infection depend on the nature of the infectious illness, its duration, and the type and extent of damage to the brain but in general antiseizures and antiepileptic treatment follow the same pattern describe for epilepsy secondary to neurocysticercosis(NC). We recommend to readers to consult our book about “ Treatment approach to epilepsy”

Human infections caused by parasitic helminths are of particular importance given the relatively recent acknowledgement of a number of species as important human pathogens (McCarthy & Moore 2000; Mas-Coma et al. 2005; Garcia et al. 2007). The main aim of this chapter is to review all information related to parasitic zoonoses of the brain causing epilepsy based on our personal experience and the medical literature and the way forward of toxocariasis (Robinson, 2009).

### **1.1 Zoonotic diseases**

Around the world the three major components of climate change already evident and escalating in magnitude and significance are; 1) warming; 2) altered patterns of precipitation; and 3) an increased incidence of extreme climatic events. For the structure and function of ecosystems, the impacts of climate change vary with place and with time, and among the key outcomes are shifting boundaries for many components and processes within the systems. Among these components are pathogens and infectious diseases, including those caused by helminth, arthropod and protozoan parasites in people, domestic animals, and wildlife (Polley, 2010)

#### **1.1.1 Rabies**

From viral zoonotic infections, rabies keeps the leadership in mortality rate. The word “rabies” is derived from a Latin word which means “madness” or “rage” – the very characteristic of people with this disease. A person with this illness usually dies of fatal encephalitis. This disease is caused by the bullet shaped rhabdovirus which is commonly called the rabies virus. The virus is transmitted to a human being when he or she is bitten by an infected animal, usually with dogs. There are reports which claim that even the saliva of those infected animals could cause rabies. Rabies virus from saliva could enter skin scratches and the eyelids. In fact, aerosols of bat secretions in caves have caused rabies to some researchers. Workers who have macerated infected tissues in the laboratory for analysis have acquired the virus and developed the disease; probably aerosols from the macerated tissue entered the workers' mouth, nose, or eye linings. (Sace, 2009) Rabies presents about 30 days after contact with a rabid animal. A nonspecific prodrome of fever, headache, sore throat, and abdominal pain progresses to an agitated, hallucinatory delirium followed by coma and death. Seizures occur in about 10% of cases (Goldstein & Harden, 2002) and rabies vaccine therapy has been excluded as antiseizures treatment many years ago (Inkeman et al., 1938)

#### **1.1.2 Avian influenza**

Avian influenza viruses do not typically replicate efficiently in humans, indicating direct transmission of avian influenza virus to humans is unlikely. However, since 1997, several cases of human infections with different subtypes (H5N1, H7N7, and H9N2) of avian influenza viruses have been identified and raised the pandemic potential of avian influenza virus in humans. A better understanding of the biological and genetic basis of host restriction of influenza viruses is a critical factor in determining whether the introduction of

a novel influenza virus into the human population will result in a pandemic. (Lee & Saif, 2009) Epilepsy is not a known complication in this group and its presence suggests reviewing the clinical diagnosis.

### 1.1.3 Slow virus infections

Slow virus infections are also known as prion diseases. Prions are proteinaceous infectious particles (PrPs). The brain pathology of prion diseases consists of a vacuolar (spongiform) degeneration of the neuropil, cortical neurons, and subcortical gray matter with neuronal loss and gliosis. Early diagnosis is difficult, in part because prions do not have nucleic acids, making conventional nucleic acid-based viral detection systems ineffective. PrPs also elude detection by not producing a humoral immune response (Johnson & Gibbs, 1998) As part of this group is: bovine spongiform encephalopathy (BSE) which is thought to have originated in Great Britain where it was first observed (April 1985) and was officially diagnosed. Control measures have since reduced incidence of the disease, and currently fewer than 100 new cases are reported per week. It occurs in cattle between two and eight years old and is always fatal.

A transmissible spongiform encephalopathy of adult cattle, transmitted by feed containing protein in the form of meat and bone meal derived from infected animals. Affected adults may have seizures as part of the serious neurological illness. Renkawek et al (1992), hypothesized that a defect of Na<sup>+</sup>/K<sup>+</sup> -ATPase of the astrocytes could be the most common pathogenetic factor for the congenital convulsive status and for the spongy state.

Cellular prion protein (PrP<sup>c</sup>) plays an essential role in maintaining neurotransmitter homeostasis in the central nervous system. This discovery has been made possible by the observation that both a deficiency and an excess of the protein have a considerable effect on this homeostasis. Surprisingly, in both cases, the central nervous excitability threshold is altered to such an extent that an epileptic seizure may result. Thanks to this discovery, we now have more tools at our disposal that can help us to deepen our basic understanding of epilepsy. (IBEC, 2009)

As under normal conditions the protein is found in adequate concentrations, it was expected that greater amounts of PrP<sup>c</sup> would provide greater protection against seizures. Surprisingly, however, the study showed that this is not the case. With an excessive amount of the protein, the level of excitability of the central nervous system is increased even more than in the absence of PrP<sup>c</sup>, due to the fact that both the excitatory and inhibitory mechanisms are altered. Such alterations further increase the possibility of suffering severe epileptic seizures. The protein, when present at adequate concentrations, is essential for maintaining neurotransmitter homeostasis or equilibrium in the central nervous system. The researchers of IBEC who participated in the study are currently involved in developing a description of the possible differences in the expression and modification of the cellular prion protein in epileptic patients. (IBEC, 2009)

### 1.1.4 Neurobrucellosis

Brucellosis is a major ubiquitous zoonosis transmitted from livestock to humans. It is a public health problem in developing countries. The estimated mean incidence of neurobrucellosis is 4% with clinical manifestations that are variable and often multi-focal in the same patient. (Guenifi et al., 2010)

Neurobrucellosis is a rare form of systemic brucellosis, a disease acquired through ingestion of unpasteurized dairy products, it can affect any part of the nervous system and can mimic any neurological disease which may manifest as stroke, encephalitis, meningitis, or

psychiatric disorders and should be suspected in individuals with pyrexia of unknown origin so that early detection and treatment could prevent long-term sequelae such as focal neurologic deficits, hydrocephalus, transient ischemic attack, intracerebral vasculopathy, granulomas, seizures, paralysis of sixth and seventh cranial nerves and psychiatric illness and seizures responding well to first AED, doxycycline, rifampin, and ceftriaxone (Obiako et al., 2010; Asuman et al., 2010; Türel et al., 2010).

Early detection and treatment is the only predictor of a favourable outcome of neurobrucellosis, but there is no standardized treatment protocol. Neurobrucellosis may be difficult to diagnose especially in patients with atypical syndromes. Therefore, it should be suspected in patients who experience inexplicable neurological and psychiatric problems and the CSF must be adequately analysed. It should be kept in mind and to be included in differential diagnosis for any patient presenting central or peripheral neurological manifestations especially in the endemic zones. (Guenifi et al., 2010 Tekin-Koruk et al., 2010)

### 1.1.5 Neurosalmonellosis

*Salmonella* serotypes *typhi*, *typhimurium*, and *enteritidis* occurred most frequently. The precipitating factors of these infections included meningitis, trauma, and intracranial hematoma. Focal intracranial infections are unusual manifestations of salmonellosis. In one hundred years only 43 such infections have been reported in the world literature. Brain abscess occurred more often in adults; in contrast, subdural empyema presented more often in children and fever, signs and symptoms of increased intracranial pressure, change in mental status, seizures, and focal neurologic deficits were the commonest clinical features. (Rodriguez et al., 1986)

## 2. Zoonotic parasites

Zoonotic parasites are separated into four categories, such as direct-zoonotic, meta-zoonotic, cyclo-zoonotic, and sapro-zoonotic parasites. Direct-zoonotic parasites, such as, *C. parvum*, *T. gondii*, and *P. carinii* have been prevalent in endemic areas and places where the prevalence of HIV/AIDS is increasing. Meta-zoonotic parasites can infect humans from invertebrate intermediate hosts, such as, *Babesia bovis*, *Babesia divergens*, *Plasmodium schweizeri*, *Clonorchis sinensis*, *Fasciola hepatica*, *Paragonimus westermani*, *Diphyllobothrium latum*, *Dipylidium caninum*, *Dirofilaria immitis*, *Brugia malayi*, *Onchocerca gibsoni*, and *Polymorphus boschadisi* and some of them like *C. sinensis*, *H. nocens*, *M. yokogawai*, *P. westermanii*, and sparganum (*Spirometra* spp.), remain prevalent among people who consume raw freshwater fish or crabs in endemic areas. Cyclo-zoonotic parasites have vertebrate intermediate hosts, such as, *Taenia multiceps*, *Echinococcus granulosus*, *Taenia saginata*, *Taenia solium*, sparganum (*Spirometra* spp.), *Porrocaecum crassum*, *Contraeaecum osculatum*, *Capillaria hepatica*, and *Gnathostoma spinigerum*. Cyclo-zoonotic parasites, such as, *T. saginata*, *T. solium*, and *T. asiatica*, are still prevalent in peoples who consumed raw cattle or pig meat and there is a tendency to increase and spread all over the world due to globalization. Sapro-zoonotic parasites mean that parasites can infect humans from soil or water, such as, *Ancylostoma caninum*, *Ascaris suum*, *Capillaria hepatica*, *Strongyloides stercoralis*, *Trichuris vulpis*, and *Hypoderma bovis*.

Many of carnivorous parasites are zoonotic parasites because dogs and cats have lived with humans for a long period of time. On the other hand, anthroponotic parasites mean that the

parasites can be transmitted from humans to animals. Some examples of these are *E. histolytica*, *C. sinensis*, *D. latum*, and *Trichuris trichiura*. (Youn H, 2009). On the other hand, along with social, epidemiological and environmental changes, together with improvements in our ability to diagnose helminth infections, several neglected parasite species are now fast-becoming recognized as important zoonotic diseases of humans, e.g. anasakiasis, several fish-borne trematodiasis and fasciolosis. Direct zoonotic parasites infect humans directly from animals, such as:

### 2.1.1 Neuroamebiasis

There is about 65,000 species of protozoan parasites worldwide. Unicellular organisms, almost all protozoa, live by holozoic nutrition. Protozoa are divided into 5 phyla, Sarcomastigophora, Apicomplexa, Microspora, Myxozoa, and Ciliophora. Sarcomastigophora have flagella or pseudopodia for locomotive organs, reproduce by binary fission, and include *Trichomonas* spp., *Giardia* spp., and amoeba (including *Endolimax nana*, *Entamoeba coli*, *E. histolytica*, and *Iodamoeba bu\_tschlii*). Amebae can invade the central nervous system, causing rare but fatal infections and seizures can complicate any of the amoeba-caused clinical syndromes.

Although, epidemiologic data are inadequate to comment on the seizure incidence and prevalence is well-known that intracranial infection by *Entamoeba histolytica* can cause brain abscess (Shah et al., 1994) with an associated focal neurological signs, and other signs due to raised intracranial pressure such as: abducens palsy which can be identified ipsilateral or contralateral of the infective mass. Some micro abscess located near to the cerebral cortex can cause partial, partial with secondary generalization or generalized motor seizures but not only *E histolytica* cause neurological manifestation as can be seen in the Table 2.

Zoonotic protozoa	Neurological complications	Clinical features
<i>Entamoeba histolytica</i>	Amebic brain abscess (resembles brain abscess, tumours, chronic meningitis, or a combination of these)	Meningeal sings Focal signs Seizures
<i>Naegleria fowleri</i>	Primary amebic meningoencephalitis (acute meningoencephalitis)	Meningeal signs Seizures Stupor/coma
<i>Acanthamoeba</i> or <i>Hartmannella</i>	Granulomatous amebic encephalitis (resembles brain abscess, tumour, chronic meningitis, or a combination of these)	Meningeal signs Seizures Focal deficits Stupor/coma
<i>Plasmodium falciparum</i> . ( <i>P. malariae</i> and <i>P. vivax</i> are infrequent causes of CNS malaria.)????	Cerebral malaria*	Epileptic seizures Coma

\*There are concerns that endemic infections and infestations, such as malaria and neurocysticercosis, could be responsible for the increased incidence of epilepsy in the developing world. (Sander & Perucca, 2003)

Table 2. Some protozoans than can infect cerebral hemispheres

### 2.1.2 Cryptosporidiasis

Cryptosporidial infection can thus be transmitted from fecally contaminated food and water, from animal-person contact, and via person-person contact. The probability of transmission from just a small amount of contamination is fairly high, (DuPont, *et al.*, 1995). Infection is by ingestion of infective oocysts (*Cryptosporidium*) from the environment or from contaminated food or water.

Climate change has the potential to alter survival rates for the cysts and oocysts (which are infective when voided by the hosts) and, because both parasites are found in surface water, shifts in local and regional hydrology may alter parasite distributions and the risks of human and animal exposure. In human settlements altered patterns of precipitation and extreme climatic events may disrupt the integrity of the infrastructure, particularly water supplies and sewage disposal, increasing the risk of human infection. Risk for epilepsy is not certain in most of the cases. In addition, these elements of the climate change may result in increased run-off and contamination of water with animal feces, and increased risk of zoonotic transmission. (Polley, 2010).

### 2.1.3 Neurotoxoplasmosis

The most important zoonotic protozoa recently are *T. gondii*, *C. parvum*, and *Pneumocystis carinii* (Hong, 1991; Chai *et al.*, 1996; Choi *et al.*, 1997). The first one affects the nervous system more than others. Before AIDS, reactivation of neurotoxoplasmosis occurred most often in patients with hematologic malignancies. Because many of these patients receive immunosuppressive therapy, the relative contribution of immune dysfunction from malignancy versus immune suppression from drugs is difficult to define. (Dukes, 1997). neurotoxoplasmosis can also occur in patients receiving immunosuppressive chemotherapy after organ transplantation or for collagen vascular disorders. *Toxoplasma gondii* is a causal agent. *T.gondii* is an intracellular protozoan parasite. Most human infections with *T. gondii* are asymptomatic, but it can potentially cause four syndromes as can be seen in Table 3:

Meningoencephalitis during primary infection of an immunocompetent host
Epilepsy, intracerebral mass lesions or encephalitis in immunocompromised hosts
Retinochoroiditis associated with primary infection or reactivation of an earlier infection
Congenital toxoplasmosis, encephalitis, and retinochoroiditis as a result of transplacental fetal infection. (McCabe <i>et al.</i> , 1987)

Table 3. Clinical presentation of neurotoxoplasmosis

The only definitive host for *T. gondii* is domestic cats. Transmission of *T. gondii* to humans occurs commonly, usually by eating undercooked meat or by inadvertent ingestion of oocysts from cat feces. Systemic parasitemia occurs after the invasion of the gut lining by toxoplasma and it is certainly associated with seizures and it is one of the most common opportunistic infections in advanced stage of HIV infections, so cases of neurotoxoplasmosis have increased dramatically since 1981. Neurotoxoplasmosis is responsible for over one-



third of neurologic symptoms in AIDS patients. (Dukes, 1997). (In contrast, both primary CNS and metastatic lymphoma account for approximately 5% each.) More than 95% of toxoplasmic encephalitis in patients with AIDS is due to reactivation of chronic latent infection. For most HIV-infected patients, toxoplasmic encephalitis develop after the CD4 count falls below 100. (Dukes, 1997). In the United States, 10–40% of AIDS patients are latently infected, and 30–50% of these will develop toxoplasmic encephalitis. (Dukes, 1997)

Clinical manifestations are variable, ranging from an insidious process to an acute confusional state. Reported seizure rates range from 18% to 29% and may include partial, complex partial, and generalized seizures (Porte & Sande, 1992; Ragnaud et al., 1993). Detection of antibodies to *Toxoplasma* in sera from patients suffering from recurrent unprovoked seizures were performed using "in-house" indirect hemagglutination assay and by commercially available anti-*Toxoplasma* immunoglobulin G and immunoglobulin M enzyme-linked immunosorbent assays. Serum antibody to toxoplasmosis were detected in 12.3% and 15.3% by indirect hemagglutination assay and enzyme-linked immunosorbent assays and respectively. Controls showed seropositivity of 5.7% for antibodies to *Toxoplasma* using the same methods. Seropositivity was higher in children compared to adults. Individuals with rural background (living in relatively unhygienic conditions) were more commonly affected compared to people living in urban areas. (Mirdha, 2003)

The presence of positive antibody titers to *Toxoplasma* and *Toxocara* in an adult epileptic population has been examined in relation to other observations of aetiological importance. With *Toxoplasma*, and more particularly with *Toxocara*, a higher incidence of positive antibody titers were recorded than in non-epileptic populations. Comparison with previous studies in childhood epilepsy indicate that the incidence of positive titres increased with age throughout adult life. Reported seizure rates range from 18% to 29% and may include partial, complex partial, and generalized seizures. ([http://professionals.epilepsy.com/page/infectious\\_toxoplas.html](http://professionals.epilepsy.com/page/infectious_toxoplas.html))

Despite attention to the age of onset of epilepsy, presumed etiological factors, and electroencephalographic and clinical observations, no causal relationship between parasitic infection and the etiology of epilepsy was established (Critchley et al., 1982). However, Stommel et al. (2001) found a statistically significant correlation between chronic *T. gondii* infection and cryptogenic epilepsy in a group of patients with cryptogenic epilepsy and they proposed that the dormant *T. gondii* cysts containing bradyzoites are responsible for some cases of cryptogenic epilepsy, although other explanations for this finding exist: (a) The cryptogenic subpopulation could be more susceptible to the parasitic infection for reasons unrelated to epilepsy; or (b) The cryptogenic epilepsy patients could be more susceptible to *T. gondii* infection and have intrinsic immunologic differences that predispose them to epilepsy, implying an immune basis to the epilepsy. Because there are certainly multiple etiologies for cryptogenic epilepsy, any statistical analysis may only partially reflect an etiology. In any case, antiparasitic and antiepileptic treatment is mandatory. For more detailed information about antiepileptic and antiseizures medicine please consult our book: "Treatment approach of epilepsy" ISBN 978-953-307-678-2

Therapy for toxoplasmic encephalitis is the combination of pyrimethamine and sulfadiazine. Clindamycin can be used as an alternative to sulfadiazine. Serial neuroimaging provides the best follow-up to assess treatment progress. Maintenance anticonvulsant therapy is usually required. Newborns of women contracting toxoplasmosis during pregnancy should be treated with clindamycin to reduce the likelihood of developing late neurologic sequelae, including seizures. (Georgiev, 1994)

#### 2.1.4 Neurohymenolepiasis

*Hymenolepis nana* is also known as the Dwarf Tapeworm and it is the cestode that most commonly infects humans, especially school-aged children when they ingest infective eggs from accidental ingestion of insects (immature fleas, flour beetles, meal worms, cockroaches) that carry the parasite in their body cavities, most commonly by direct fecal-oral exposure. Infective eggs are ingested by insects and hatch in their guts. After hatching, they invade into the body cavity and become cysticercoid larvae, which are infectious for humans. After the insects are consumed and digested, the larvae are released in the small intestine and mature within 25 days into 50-cm adults. When the adult tapeworm begins to pass eggs, insect hosts can become infected again.

Most infections produce no symptoms (Craip, 2007). *Hymenolepis nana* infestations are prevalent in highly populated areas where hygiene and sanitary conditions are poor. The symptom frequency seems to correlate with increasing worm burden and in order of decreasing frequency includes restlessness, irritability, diarrhea, abdominal pain, restless sleep, anal pruritus, and nasal pruritus. Rare symptoms include anorexia, increased appetite, vomiting, nausea, bloody diarrhea, hives, extremity pain, headache, dizziness, behavioural disturbances, and seizures. (Tolan, 2011; Chero et al., 2007).

#### 2.1.5 Neurobaylisascariasis

Baylisascariasis is a rare parasitic infection caused by intestinal nematodes *Baylisascaris procyonis*, the raccoon roundworm (family Ascarididae) in the genus *Baylisascaris*. The three most pathogenic species are *Baylisascaris procyonis*, a parasite of raccoons (*Procyon lotor*), *B. melis*, which occurs in European badgers (*Meles meles*), and *B. columnaris*, which is found in skunks and was, at one time, thought to be the same species as *B. procyonis*. While fewer than 30 cases have been reported in the literature; the disease is likely under recognized. Raccoons have a high prevalence of infection and each worm is estimated to lay up to 179,000 eggs per day, and raccoons carry an average of 43-52 worms. Human infection occurs upon ingestion of viable eggs. The larvae of these three species can cause extensive damage in their intermediate/paratenic hosts: they migrate extensively, continue to grow considerably within these hosts, and sometimes invade the brain (most often fatal) or the eye including permanent blindness when the worms migrate into the retina.

Neural larva migrans occurs when the parasites migrate through the brain. The initial signs may be mild, with subtle behavioral changes, lethargy, somnolence or irritability, weakness, speech defects and/or mild changes in vision, but they can rapidly become severe. A variety of symptoms including ataxia, seizures, paresis or paralysis, developmental regression, tremors, torticollis, nystagmus and coma have been reported. Epileptic seizures are quite common and partial, secondarily generalized or generalized from the beginning can be seen. The antiepileptic medication of choice is oral carbamazepine from 200mg three times a day.

The diagnosis of baylisascariasis is difficult in live patients; there is no available, non-invasive definitive test. Unless a brain biopsy is done and a larva is found, antemortem diagnosis usually depends on serology, with supporting evidence from other tests. In neural larva migrans, antibodies to *Baylisascaris* can be found in serum and cerebrospinal fluid (CSF); a rising titer is usually seen. An enzyme linked immunosorbent assay (ELISA), indirect immunofluorescence and immunoblotting (Western blotting) have been developed to detect anti-*Baylisascaris* antibodies. (Institute for International Cooperation in Animal Biologics, 2009). We have not experience in diagnosis based on CT/MRI images. Although

the potential for long-term sequelae is unknown, short-term recovery has been reported in anecdotal cases. (Pai et al., 2007).

List of parasitic zoonoses infecting the brain is increasing gradually by emergent and re-emergent infection as can be seen in Table 4

AGENT	DEFINITE HOST(S)	INTERMEDIATE HOST(S)	NEUROLOGICAL PROBLEMS
<i>Taenia solium</i>	Human	Pig	Epilepsy and other symptoms and signs due to neurocysticercosis
<i>Toxocara canis</i> (cati?)	Dogs, cats	NA	Epilepsy and manifestation due to neurotoxocariasis
<i>Taenia (multiceps) serialis</i>	Dogs, foxes and jackals	Sheep, goats	Epilepsy and other clinical manifestations of neurocoenurosis
<i>Schistosoma japonicum</i>	Mammals	Snails	Neuroschistosomiasis and seizures.
<i>Gnathostoma spinigerum</i>	Dogs, mammals	Crustacean copepod, freshwater fish, frogs	Epilepsy, and other manifestations of neurognathostomiasis.
<i>Echinococcus granulosus</i>	Dogs, other canidae	Domestic ungulates	Neuroechinococcosis included seizures
<i>Cryptosporidium spp.</i>	Cattle, dogs, cats, humans	NA	
<i>Paragonimus spp.</i>	Mammals, including humans	Snails (1 <sup>ary</sup> ), crabs & crayfish (2 <sup>ndary</sup> )	Epilepsy and other signs of neuroparagonimiasis.
<i>Spirometra spp</i> (Sparganum)*	Dogs and cats	Fish, reptiles, amphibians,	Epilepsy and other clinical manifestations of neurosparganosis
<i>Baylisascaris procyonis</i>	Raccoons, dogs	Small mammals and birds	Epilepsy, meningoencephalitis, cranial nerve disorders
<i>Paragonimus</i>		Snail and crayfish	Epilepsy, blindness due to neuroparagonimiasis
<i>Angiostrongylus cantonensis</i>	Rats, Dogs	African giant land snails	Epilepsy and eosinophilic meningoencephalitis

\*Spargana can live up to 20 years in the human host

Table 4. Some parasitic zoonoses reported as affecting the brain

Cerebral malaria is caused by the protozoan parasite Plasmodium, transmitted to humans via the Anopheles mosquito. The disease is endemic to large parts of Africa, South America, and Southeast Asia. Cerebral malaria is an encephalopathy occurring in approximately 2% of outpatients and 10% of inpatients infected with Plasmodium. The World Health Organization definition of cerebral malaria requires some feature that can be seen in Table 5.

Unarousable coma
Evidence of acute infection with <i>P. falciparum</i>
No other identifiable cause of coma

Table 5. Some clinical features of cerebral malaria

Clinical manifestations of cerebral malaria are diverse. Fever is nearly universal, as is comorbidity with clinical features of *P. falciparum* systemic infection. Clinicians working in tropical and subtropical regions regard any new CNS-attributable sign developing within the context of *P. falciparum* parasitemia as evidence of possible cerebral malaria. The cardinal feature is a disturbed level of consciousness, usually ranging from lethargy to stupor to coma, although an agitated delirium can also occur. To conform to the strict diagnosis of cerebral malaria, the patient must remain comatose for more than 6 hours after the seizure to distinguish the coma from postictal consciousness suppression. Generalized tonic-clonic seizures occur in more than 40% of adult patients. Partial seizures are uncommon. Seizures are associated with prolonged coma and increased risk of neurologic sequelae and death (Labar & Harden, 1997). Apart from brain edema other possible seizure causes are included in Table 6.

Cerebral hypoxia
Fever
Hypoglycemia
Lactic acidosis
Drugs (including antimalarials)

Table 6. Other possible causes of epileptic seizures due to malaria

Antimalarial medicine include: chloroquine and mefloquine. Other metabolic disturbances secondary to malarial systemic effects should be considered as a cause of seizures (Labar & Harden, 1997). Neurologic sequelae of cerebral malaria, including epilepsy, affect approximately 10% of survivors; for unclear reasons, children tend to be more frequently affected than adults (Marsden, 1975). Cerebral malaria is a medical emergency and treatment is tripartite:

Specific antimalarial therapy (quinine, quinidine, etc.)
Management of coexistent seizures
Treatment of associated superinfections.

Generalized seizures can be followed by rapid neurologic deterioration, so prompt treatment is required. Subclinical or nonconvulsive seizures should be suspected in patients with persistent coma.

## 2.2 Some major zoonotic trematodes (flukes)

There are 3 kinds of trematodes, such as monogenean, aspidogastreaean, and digenean trematodes, with digenean being the only zoonotic trematodes. The characteristics of digenean trematodes are dorsoventrally flattened, unsegmented, and leaf-like worms and have 1 or 2 suckers (oral and ventral suckers), rarely armed with hooks or clamps. All digenean trematodes have 1 or 2 intermediate hosts and first intermediate hosts are molluscs. Almost all zoonotic trematodes have the 2nd intermediate hosts, such as cyprinoid freshwater fish or crustacean (Young, 2009)

### 2.2.1 Neuroparagonimiasis

Paragonimiasis is a parasitic disease caused by *Paragonimus* trematodes, commonly known as lung flukes. Humans become infected by eating raw or undercooked crayfish (also known as crawfish and crawdads) or freshwater crabs that harbor the parasites. Paragonimiasis most frequently involves the lungs, but can affect other organs, including the brain and skin. In North America, *Paragonimus kellicotti* causes infections among dogs, cats, and wild carnivores, but rarely infects humans. After humans eat raw or undercooked crayfish that harbor *P. kellicotti*, the parasite penetrates through the intestinal wall into the peritoneal cavity, then through the diaphragm into the pleural space and lungs, and can migrate to other organs, including the brain (Chronic headache, epilepsy, etc.) and skin. Eggs laid in the lungs are excreted in the sputum, or swallowed and passed with stool. *Paragonimus* species are endemic in Africa, the Americas, and Asia, but the distribution of *P. kellicotti* is still being determined (Procop, 2009) Migration of the parasite to the brain can cause severe complications, including permanent blindness.

Liver and intestinal infections caused by fish-borne zoonotic trematodes (FZTs) are increasingly being recognized as serious public health problems and are especially widespread in Southeast Asia, including Vietnam, Lao People's Democratic Republic, Thailand, Cambodia, People's Republic of China, and North and South Korea. Liver flukes are associated with high incidence of bile duct cancer (WHO, 1995, 2002), and cause serious pathologic changes in the heart, brain, and spinal cord (Chai, 2005). The epidemiology of FZTs is complex because humans and reservoir hosts, such as dogs, cats, pigs, and fish-eating birds, harbor egg-shedding adult stages. (Thien et al., 2007; Chi et al., 2008; Phan et al., 2010)

### 2.2.2 Neuroschistosomiasis

Schistosomiasis is an important parasitic disease, occurring in more than 200 million people worldwide. Neuroschistosomiasis causes focal and generalized seizures; headache; and myeloradiculopathy with lower limb and back pain, bladder dysfunction, paresthesia, and weakness. Dizziness, nausea, and increased intracranial pressure can also occur in cerebellar schistosomiasis. (Wan et al., 2009). Visual scintillation from occipital mass has been described. (Fowler et al., 1999)

Schistosomiasis is endemic throughout much of the tropics. Three different schistosomal species (*S haematobium*, *S japonicum*, and *S mansoni*) can cause infection that involves the brain and spinal cord. Brain involvement is found in about 4% of all patients infected by *S mansoni*. The life cycle starts with cercariae, which penetrate the human skin and transform into schistosomulae. From there they migrate to the lungs and the liver. The organisms then mature into mating pairs of male and female worms, which settle in the mesenteric veins the

adult worm laid eggs that are excreted with stool or urine. Different mechanisms of invasion of the brain have been discussed: the eggs may reach the brain through the valveless venous plexus of Batson, which joins the deep iliac veins and inferior vena cava with veins of the spinal cord and brain, or eggs may migrate to the brain via pulmonary arteriovenous shunts, or portalpulmonary arteriovenous shunts. Finally, the worms themselves may enter the cerebral veins and place their eggs directly at the ectopic site, which could be the cerebrum, cerebellum, leptomeninges, brainstem, or choroid plexus (Wan et al., 2009)

Neuroschistosomiasis usually follows the egg migration into the brain or spinal cord vasculature, leading to microinfarction or granuloma formation. Neurologic manifestations are rare, occurring in only 1- 2% of cases, but they can include a wide range of focal and nonfocal CNS symptoms, including seizures. . Neurologic disease during Katayama fever responds to steroids with or without antischistosomal therapy. Cerebral schistosomiasis may require surgical resection of the granuloma like masses. Praziquantel is the primary antischistosomal agent. Antiepileptic drugs are used as needed (Schachter, 2004).

### 2.2.3 Neurofascioliasis

Fascioliasis is a well-known parasite of herbivorous animals; it has a worldwide distribution on the animal reservoir host. A large variety of animals such as sheep, goat, cattle, buffalo, horses and rabbits show infection an rate that varies from 70% to 90% in some areas. Infection of the human host was very sporadic until the last two decades. However, it has now become an important trematode-borne infection of emerging concern until today. The estimated number of people infected is being estimated 2.4 million in 61 countries. An estimated number of populations at risk are considered more than 180 million throughout the world. Until today, largest number of infected people have been reported from Bolivia, China, Ecuador, Egypt, France Iran, Peru and Portugal. In Nepal's context, sporadic cases had been reported from human hospital since last decade,-while screening of human population has yet not been done. Same way in Iraq, Lebanon, Morocco, and Tunisia. (Karki, 2011).

Ectopic spinal localization of *Fasciola* may occur during the transmigrating path of the parasite through the peritoneum or from the liver through the portal venous system and affect spinal cord causing paraplegia (Devendra et al., 2006). Park & Sohn (2010) reported the first case presenting cerebral lesions secondary to hepatic fascioliasis. Therefore seizures disorders does not represent a problem for this parasitism. CNS involvement can be associated with the hepatic stage of fascioliasis.

### 2.3 Some major zoonotic cestodes (tapeworms)

There are 2 kinds of cestodes, such as *Eucestoda* and *Cotyloda*. Cestodes are hermaphroditic and endoparasitic worms with an elongated flat body without a body cavity or alimentary canal. Their bodies are comprised of 3 parts, such as, scolex, neck, and strobila. *Eucestoda* have 1 intermediate host, but *Cotyloda* have 2 or more intermediate hosts. In Cheju (South Korea) many years ago, the pigsty was located below the toilet, so that pigs were raised to eat the stool and infected with the eggs of *Taenia* spp. Humans were habituated to eat raw pork products, especially the liver, so they became infected with the metacestodes of *Taenia* spp., *T. solium* and *Taenia asiatica*.

Min (1990) reported a review paper on cestode infections such as: the Pseudophyllidea, i.e., *D. latum*, *Diphyllobothrium yonagoense*, sparganum of *Spirometra erinacei*, and the

Cyclophyllidea, i.e., *H. diminuta*, *H. nana*, *Mesocestoides lineatus*, *T. saginata*, *T. solium*, and *E. granulosus*. He reported that the plerocercoid larva of *Spirometra* spp. (sparganum) infects humans through 16 kinds of animal hosts, such as, snakes, frogs, and so on.

Sparganosis first reported in swine in 1911 in Indochina. It is a disease found in snakes, reptiles, and mammals, including swine and man. It is caused by migration of the second larval stage (spargana) of the cestode *Spirometra*. (Mueller, 1974). Human sparganosis occurs worldwide. The majority of cases has been reported from China, Korea, Japan, and Southeast Asia. Approximately 70 cases of human sparganosis have been reported from the United States, most from the Southeast region of the country. Transmission to humans has occurred through intact mucous membranes, by the ingestion /handling of frogs and snakes, poultry, and pork, and by ingestion of contaminated water. Disease in man can produce subcutaneous, cerebral, ocular, visceral, and metastatic forms depending upon the migration of the parasite. (Pullar &McLenan 1949; Gordon, 1954; Gray et al., 1999).

### 2.3.1 Neuroechinococcosis

Echinococcosis is caused by tapeworms of the genus *Echinococcus*, common parasites of dogs and cats, who are the definitive hosts; humans can be intermediate hosts. The disease is endemic in countries around the Mediterranean: Greece, Turkey, and Lebanon have the highest prevalences. The small adult worms live in the definitive host's gut and discharge eggs into feces. If inadvertently ingested by a human, the eggs hatch in the human's gut, enabling the organism to penetrate the human's gut wall and spread hematogenously. Once located in a final tissue site, the organism forms a slowly enlarging cyst, a hydatid. When in the CNS, cysts usually locate in brain parenchyma. Clinical manifestations are secondary to this mass lesion, raised intracranial pressure, or both. Although praziquantel has activity against these organisms, the primary treatment of CNS hydatids is surgical. Antiepileptic management is a crucial adjunctive treatment. (Schachter, 2004)

### 2.3.2 Neurocoenurosis

Another parasitic zoonosis which shows similar symptoms to NC is coenuriasis, due to invasion of the brain by the larval stage known by *Coenuruses cerebralis* (CC) of the tapeworm *Multiceps multiceps*. Watson and Lurie (1956) from Edendale Hospital in Pietermaritzburg, South Africa reported five cases from 1951 to 1956 and described their anatomic-pathological finding on post-mortem examinations. One year later also in South Africa, Plumber et al (1957) reported some cases and reviewed the medical literature. At the time that they reviewed the available English-language medical literature a total 14 case from South Africa were found. From his anatomopathological report we could not find gross different from racemose NCC and other descriptions about CC. At the veterinary side, two rare clinical manifestations of coenuriasis in sheep we reported in two lambs of 6-7 weeks old. In humans, symptoms include headaches, seizures, vomiting, paraplegia, hemiplegia, dysphasias, and epilepsy.

## 2.4 Some major zoonotic nematodes (roundworms)

Nematodes are characterized as free-living or parasitic, unsegmented, cylindrical, and elongated round worms with a body cavity and alimentary canal. Almost all nematodes are sex-separated and their life cycles are direct or indirect. The major intestinal nematodes are *Ascaris lumbricoides* (roundworm), *Enterobius vermicularis* (pinworm), hookworms, *Trichuris*

*trichiura* (whipworm), *Trichostrongylus orientalis*, and *Strongyloides stercoralis*. As imported zoonotic nematode infections, loiasis cases due to the *Loa loa*. As indigenous infections, there have been several human *Thelazia callipaeda* infections. *Dirofilaria immitis* infections are very popular among dogs but very scanty medical information about this parasite in human beings is found.

#### 2.4.1 Neuroangiostrongyliasis

Angiostrongyliasis is caused by the rat lungworm. *Angiostrongylus cantonensis* is endemic through Southeast Asia and the Pacific Islands. The infection in humans, an accidental host, is associated with eosinophilic meningitis. The dog tapeworm, *Echinococcus granulosus*, can infect humans with up to 2% of clinical cases presenting with brain cysts. The infection has a cosmopolitan distribution. Humans get infected with dog feces and CNS infection is usually associated with signs of increased intracranial pressure (Hughes & Biggs, 2002, 2002a) and epileptic seizures. There is no established antiparasitic treatment. Comorbid seizures are managed under the similar protocol for other parasitic zoonoses infecting the brain (Schachter, 2004).

#### 2.4.2 Neurognathostomiasis

Gnathostomiasis is a parasitic infection caused by the third-stage larvae of the helminths *Gnathostoma spp.*, which are seen mostly in tropical and subtropical regions. The genus *Gnathostoma* belongs to the order *Spirurida*, one of the largest groups of nematodes. The genus has 12 species. These groups are characterized biologically by requiring one or more intermediate hosts in their life cycles. It is a food-borne zoonosis endemic in areas where people are accidental hosts in which the parasite fails to reach sexual maturity after eating raw freshwater fish or shellfish, especially Thailand and other parts of Southeast Asia, Japan, and increasingly Latin America, particularly Mexico. (Daengsvang, 1981; Nawa, 1991)

Visceral disease is more serious than the cutaneous manifestations and, in the case of central nervous system disease, may be fatal. (Herman & Chiodina, 2009). The main features of CNS involvement can cause radiculomyelitis, radiculomyeloencephalitis, eosinophilic meningitis, and subarachnoid hemorrhage. The hallmark symptoms are an acute onset of excruciating radicular pain and/or headache (subarachnoid hemorrhage or eosinophilic meningitis), with subsequent paralysis of the extremities and/or cranial nerve palsies. The typical clinical picture can be explained by the migratory pathway of the parasite, which gains entry to the spinal cord along nerve roots (cranial, cervical, thoracic, or lumbar), causing intense radicular pain (or headache in the case of cranial nerve or cervical root involvement) which usually lasts from 1 to 5 days. Cranial nerve palsies tend to occur after the onset of paralysis, and if multiple they signify a poor prognosis. Cerebral involvement is usually indicated by a depressed consciousness level or coma, but interestingly, mental confusion does not tend to occur (Herman & Chiodini, 2009).

The main differential diagnosis of neurognathostomiasis is with *Angiostrongylus cantonensis*, another highly prevalent parasite in Southeast Asia. This may produce a similar eosinophilic meningoencephalitis, but the acute nerve root pain, signs of spinal cord compression, and hemorrhagic or xanthochromic spinal fluid seen in gnathostomiasis are absent with *Angiostrongylus* infection (Herman & Chiodini, 2009). The *Gnathostoma* larva is more invasive than that of *Angiostrongylus* and therefore produces more frequent focal neurological signs.



In contrast, the *Angiostrongylus* larva, which is considerably smaller (120  $\mu\text{m}$  wide and 12 mm long) and usually multiple, more commonly causes a meningoencephalitis, and although neurotropic, it is rarely fatal (Herman & Chiodini, 2009).

The triad of eosinophilia, migratory lesions, and obvious exposure risk are highly suggestive of the diagnosis of gnathostomiasis. Eosinophilia of the cerebrospinal fluid (CSF) is also highly supportive of neurognathostomiasis, with reported levels of 5 to 94% and a total CSF white cell count of up to 500/ $\text{mm}^3$  (range, 20 to 1420/ $\text{mm}^3$ ), but may also be found with several other parasites, e.g., *Angiostrongylus cantonensis*, *Toxocara canis*, *Strongyloides stercoralis*, *Ascaris lumbricoides*, *Paragonimus westermani*, *Fasciola hepatica*, and *Trichinella spiralis* and with schistosomiasis, cystercercosis, and other infections such as coccidiomycosis and aspergillus infection. Because no single area of the nervous system is inaccessible to the highly invasive gnathostome larva and multiplicity and/or rapid progression of lesions beyond the degree of cerebral edema explained by further migration of the parasite. Therefore epileptic seizures and epilepsy can be expected and treated accordingly. Multiple cranial nerve palsies are signs of poor prognosis. (Boongird et al., 1977)

### 2.4.3 Neurotrichinellosis

Trichinellosis also called trichinosis, trichinellosis or trichiniasis (Trich from Greek *thrix* meaning hair) is an infection due to nematodes of the genus *Trichinella*, most commonly *T spiralis*. Infection is initiated by ingestion of viable larvae in raw or undercooked meat. Digestive action liberates the larvae. The liberated larvae develop into adults in the duodenum and jejunum, where they mate and bear offspring. The adult worms are expelled in the stool. Eosinophilia develops in response to the presence of the worm. Patients who develop neurologic and cardiac dysfunctions have marked eosinophilia associated with arteriolar microthrombi, often simply from the numbers of larvae, leading to areas of cerebral and myocardial infarction.

Neurological involvement may occur in 0.2%–52% of cases with trichinellosis spirallis, generally in the most severely affected patients. However, another author refers that involvement of the central nervous system occurs in 10-20% and mortality rates may then approach 50% (Clausen, 1996). Apart from *Trichinella spiralis* other parasitic infections that may cause abnormal mental status and eosinophilia include toxocariasis (Despommier, 2003), angiostrongyloidiasis, and baylisascariasis (Gavin et al., 2005). Clinical signs and symptoms are meningitis, encephalitis, cranial nerve deficits, paresis, aphasia, convulsions and coma (Fourestie et al., 1993; Gay et al., 1982) Small hypodense areas in the white matter and in the cortex have been reported long time ago (Ellrodt et al., 1987). Absence of pets at home or contact with raccoons, the lack of eosinophils in the CSF, and the lack of ocular larva migrans on examination argue against trichinellosis. (Madariaga, 2007) Treatment of choice is thiabendazole and steroids. Epileptic seizures and epilepsy are managed following same protocol used routinely. For more details please consult the book : "Treatment approach for epilepsy" ISBN 978-953-307-678-2.

### May dogs cause epilepsy?

Of course no, I always remember my parents when they said: "El perro es el mejor amigo del hombre" (The dog is the best man's friend) and they were right, I had a very good one

because I also had a very good veterinarian friend. Without any doubt dogs are the most common pet animals worldwide and they perform a range of cultural, social, and economic functions at home and in our society. Dogs were domesticated from wolves as recently as 15000 years ago (Morey, 2006), or perhaps as early as 100000 years ago based on recent genetic fossil and DNA evidence (Savolainen *et al.*, 2002, Lindbald-Toh, 2005). Evidence suggests that dogs were first domesticated in East Asia, possibly China, and the first people to enter North America took dogs with them (Savolainen *et al.*, 2002).

Dogs are kept as pets and companions, for hunting, as guards, draught animals, for food, or for commercial purposes (Swai E *et al.*, 2010). Some studies also suggest that keeping pets be associated with a higher level of self-esteem in children (Paul and Serpell, 1996; Knobel *et al.*, 2008). It is fairly common for a dog to become infected with an internal or external parasite at some point in their lifetime. Parasites can infect your pet any time of year and there is a long list of them. (See figure 1)

External parasites, such as fleas and ticks may be less prevalent outside during certain times of the year however they often survive in the house during the winter months, creating an uninterrupted life cycle. Other internal parasites such as worms may affect your pet all year long. Nevertheless, dogs have been living with humans since early civilization, studies of dog's parasitic zoonoses affecting the human brain in sub-Saharan Africa are scanty and very limited information is available in the medical literature. Dogs can carry over a dozen forms of zoonotic diseases mainly to their owners if they do not practice appropriate hygiene and disease-control measures. And to some peoples are at a higher risk of contracting zoonotic diseases such as: peoples with malignancies, young children, immunocompromised patients, and over expose persons. Some zoonotic diseases are fairly common in dogs, while others are exceedingly rare.

Apart from the tapeworm, other parasites can spread from dogs to humans (See figure 1). Hookworm and roundworm are both zoonotic infections that can be spread through the improper handling of contaminated dog feces. Several species of these parasites can thrive in the colons of both humans and dogs. Hookworm and roundworm can both be spread through the accidental ingestion of dog feces that is contaminated with parasite eggs or larvae. This can occur through improper handling of waste, and people may become infected by walking barefoot on soil that has been contaminated with infected dog feces. Nowadays, veterinary practices have the important responsibility of educating pet owners about the potential risk of zoonotic parasites and the different measures that can be taken for their control and prevention (CDC, 2004).

Another parasitic zoonosis associated with dogs and epilepsy is toxocariasis. The definitive hosts of *T. canis* and *T. cati* are dogs and cats, respectively. Infection in dogs is usually acquired in the uterus or through nursing. In the United States, it has been reported that up to 80% of puppies less than 6 weeks old are infected with *T. canis*. Hence, puppies are the most important sources of contamination of the environment. Cats of any age can contaminate the environment with *T. cati*. However, human infection with *T. cati* has been less often reported (Little, 2003).. Humans acquire the infection through ingestion of the eggs of the parasite that have been present in the environment for at least two weeks but that may have survived for several years. This make young children at a particularly high risk of infection due to their normal geophagy behavior. In the developing world, the environment is likely to be heavily contaminated with eggs that are infectious to humans.

The fact that most communities are largely agricultural, that most pet animals freely roam everywhere and that there is a lack of sanitation could lead to a high risk of infection in persons of all ages. Dogs without veterinarian care are not our best friend. The choice is yours advise is mine.

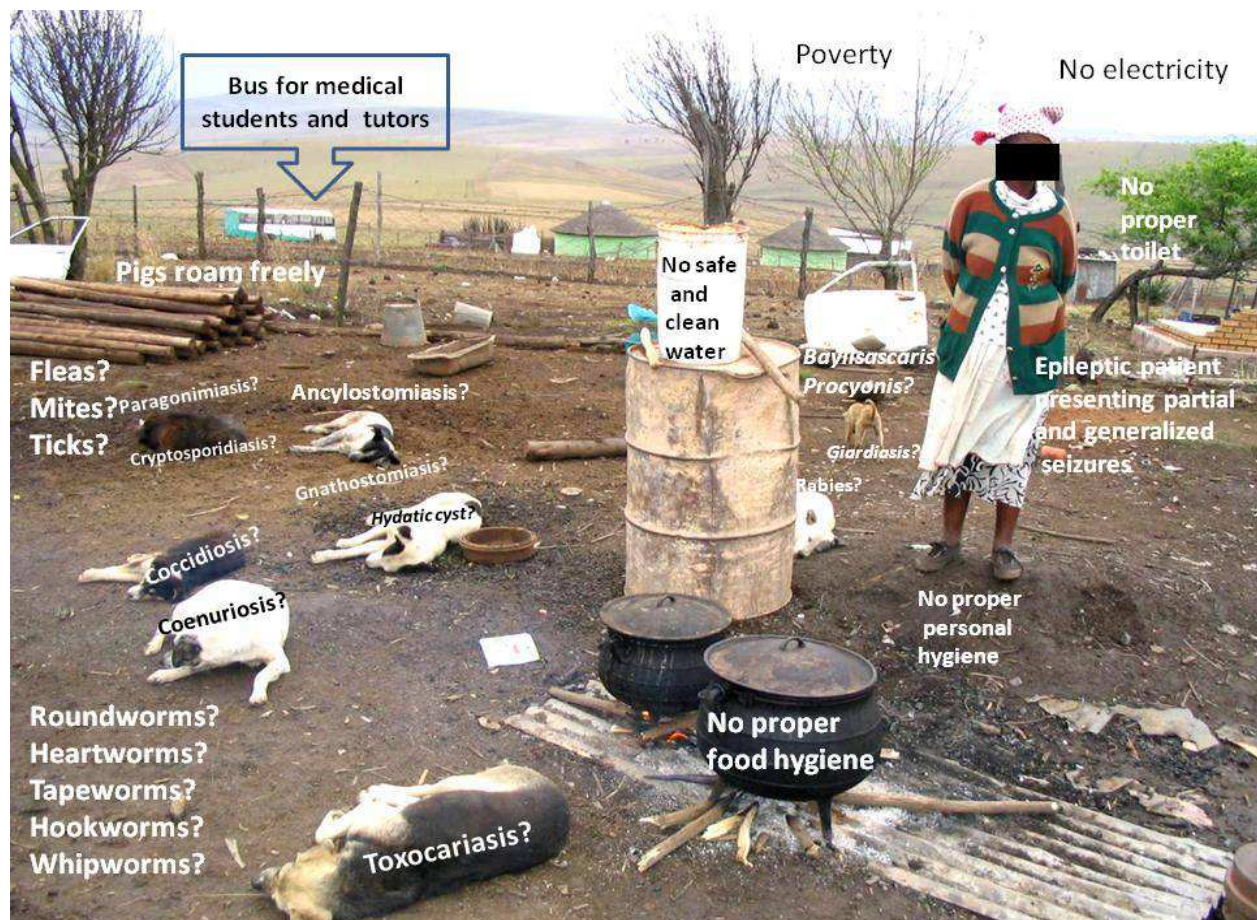


Fig. 1. Rural community at the former Transkei in South Africa.

## 2.5 Neuroborreliosis

Within days to weeks, *Borrelia burgdorferi* the causative agent of Lyme disease, spreads hematogenously and it probably enters the CNS at this time. One to two months postinfection, *B. burgdorferi* localizes and becomes sequestered in certain tissues. The nervous system is involved in up to 20% of untreated North American patients. Meningitis (typically lymphocytic) is the most common neuropathology abnormality in early disseminated of Lyme disease.

Neurologic deficits, including seizure, can be the initial clinical manifestation. Neurologic abnormalities that have been reported to be associated with early CNS Lyme disease include: acute aseptic meningitis, acute purulent meningitis chronic lymphocytic meningitis, recurrent meningitis, acute meningoencephalitis, acute focal encephalitis, encephalomyelitis, leukoencephalitis, acute cerebellar ataxia, acute parkinsonian syndrome, acute transverse myelitis, subacute myelitis, cognitive deficits affective disturbance, and

epileptic seizures. Lyme disease should be suspected in any patient with chronic lymphocytic meningitis or mild meningoencephalitis with associated cranial neuritis or radiculitis. Lab tests include serologic assays like immunofluorescent assay and enzyme-linked immunoassay tests for anti-*B. burgdorferi* antibodies. Specific anti-*B. burgdorferi* antibody also appears in CSF, where it can be detected even when serum antibody tests are negative. (To establish whether these antibodies are synthesized intrathecally, serum and CSF antibody levels should be measured simultaneously. Treatment for epilepsy did not differ from other parasitic zoonoses although epilepsy seems to be a minor problem in this condition even in HIV-positive patients (van Burgel et al., 2010; Henningson et al., 2010).

### 2.6 Neurococcidiosis

*Coccidiosis* is an intestinal disease that affects several different animal species including canines and humans. *Coccidia* is one of the most prevalent protozoal infections in North American animals, second only to giardia. *Eimeria* and *Isospora* are the two genera that are often referred to as "coccidia." These two genera contain a large number of species that infect a variety of animals throughout the world. The diseases caused by these microscopic protozoal parasites are referred to collectively as coccidiosis, and they vary tremendously in virulence. Some species cause diseases that result in mild symptoms that might go unnoticed (i.e., Mild diarrhea) and eventually disappear, while other species cause highly virulent infections that are rapidly fatal. The causative agent is a protozoan that has the ability to multiply rapidly. The major damage is due to the rapid multiplication of the parasite in the intestinal wall, and the subsequent rupture of the cells of the intestinal lining. Several stages of multiplication occur before the final stage, the oocyst, is passed in the feces. Oocysts are extremely resistant to environmental stress and are difficult to completely remove from the environment. Oocysts are frequent contaminants of feed and water and when the sporulated oocysts are ingested by other animals they start the life cycle over in the new host. Neurococcidiosis is characterized by epileptic seizures among other signs but it has been reported in calves and cows (Oliveira et al., 2009)

### 2.7 African trypanosomiasis

African trypanosomiasis, or sleeping sickness, is caused by *Trypanosoma brucei*. The tsetse fly is the arthropod vector. CNS involvement is the principal clinical consequence. An inflammatory nodule, a chancre, appears within several days at the site of parasite inoculations by the biting tsetse fly. Parasite replication and local tissue invasion are followed by lymphatic and bloodstream entry, causing a diffuse lymphadenopathy and parasitemia with high fever.

Recurrent cycles of hemo-lymphatic parasitemia follow, with corresponding bouts of fever alternating with periods of well-being. (African trypanosomiasis and malaria are two of the few causes of true intermittent fever. Trypanosomes eventually enter the CNS to cause meningoencephalitis, with a full range of neuropsychiatric signs and symptoms, including sleep-wake cycle abnormalities (e.g., Daytime drowsiness and nocturnal insomnia), from which the disease derived its name. Frequent episodes of awakening during sleep, blurring of sleep stages, and irregular bursts of rapid EEG activity during stage 4 sleep occur.

Generalized convulsions become common as the disease progresses to later stages. If untreated, mortality approaches 100%. Of the three drugs usually used for treatment

(suramin, pentamidine, and melarsoprol), only melarsoprol penetrates the blood-brain barrier to be effective in CNS disease. Its use is complicated by an up to 18% incidence of severe, reactive arsenic encephalopathy, which can result in permanent neurologic damage or death. Consequently, melarsoprol should be used only in patients with CNS involvement. In a study of melarsoprol effects on patients with *T. gambiense* in the meningoencephalitic stage, EEG tracings before treatment showed marked abnormalities in the form of periodic delta outbursts. (Hamon & Camara, 1991)

### **2.8 American trypanosomiasis**

American trypanosomiasis, also known as Chagas' disease, is an acute or chronic infection caused by *Trypanosoma cruzi* and occurs only in the western hemisphere. Chagas disease is the third most common parasitic infection worldwide after malaria and schistosomiasis. (WHO 2005). Seizures sometimes occur at stroke onset, and epilepsy is quite a frequent complication after chagasic stroke. Chronic vascular epilepsy, characterized by secondary generalised seizures, have been reported in around 20% of patients surviving chagasic stroke, whereas around 10% of stroke patients without the Chagas disease have seizures (Carod-Artal et al., 2005). The effect of uncontrolled seizures on cognition and disability in Chagas disease is unknown. No prospective epidemiological studies have addressed the risk of acute seizures and their recurrence in acute chagasic stroke (Carod-Artal & Gascon, 2010)

## **3. Other helminth parasitic infections to be considered**

The capacity of climatic conditions to modulate the extent and intensity of parasitism is well known since long ago. Concerning helminths, among the numerous environmental modifications giving rise to changes in infections, climate variables appear as those showing a greater influence, so that climate change may be expected to have an important impact on the diseases they cause. However, the confirmation of the impact of climate change on helminthiasis has been reached very recently. Only shortly before, helminthiasis were still noted as infectious diseases scarcely affected by climate change, when compared to diseases caused by microorganisms in general: viruses, bacteria, and protozoans (Mas-Coma et al., 2009). In this group we have: neurocysticercosis as a leading cause of epilepsy in developing countries and some developed places. (Foyaca-Sibat, 2011), and also sparganosis and toxocariasis among others.

### **3.1 Neurosparganosis**

Sparganosis is a rare parasitic infection caused by the larval cestode of *Spirometra* that results from ingesting the plerocercoid harbored in frogs, snakes, and chickens. Reported worldwide, sparganosis is most prevalent in Southeast and Eastern Asia. The diagnosis is suggested by a wandering lesion, especially in endemic areas; the tunnel sign on a post contrast MRI is characteristic. The preferred treatment is the surgical removal of live worm. (Shirakawa et al., 2010) In the endemic area of sparganosis, where other neurological parasitic infestations (e.g. cysticercosis and gnathostomiasis) are also common, the clinical usefulness of MR imaging is very limited in providing a definitive diagnosis of cerebral sparganosis. A history of risky behaviour (e.g. drinking impure water, eating frog or snake

meat, or using frog or snake meat as a poultice) might be a clue and offers supporting evidence for a presumptive diagnosis in cases of abnormal brain MR imaging results ( Song et al., 2007; Chiu et al., 2010; Wiwanitkit, 2010). 4 cases had a history of eating raw frogs or snakes. 5 showed eosinophilia in peripheral blood, all with positive anti-Sparganum mansoni antibody in serum and cerebrospinal fluid. Cerebral MRI showed placeholder in all patients. Diagnosis was confirmed by pathological examination of operations and species identification. All patients were cured by operation removal and praziquantel treatment. (Chen & Shi, 2010).

### 3.2 Neurofilariasis

Filariasis and onchocerciasis are parasitic helminth diseases that constitute a serious public health issue in tropical regions. The filarial nematodes that cause these diseases are transmitted by blood-feeding insects and produce chronic and long-term infection through suppression of host immunity. Disease pathogenesis is linked to host inflammation invoked by the death of the parasite, causing hydrocoele, lymphoedema, and elephantiasis in lymphatic filariasis, and skin disease and blindness in onchocerciasis. (Taylor et al., 2011) As far we know, epilepsy secondary to filariasis has not been reported.

This capability, coupled with an integrated, multidisciplinary and ecological approach, makes possible the identification of parasitic infections and diseases likely to be particularly susceptible to climate change and, with adjustments for regional variations, the exploration of some of the possible consequences of accelerating climate change of the occurrence of these diseases and for animal and human health. This is a very urgent need, and without such an attempt to anticipate the possible, society is likely to be a more or less impotent spectator to the certainty of continual ecological calamities. (Polley, 2010).

### 3.3 Neurocysticercosis

Neurocysticercosis (NC) is a parasitic infection of central nervous system (CNS) caused by the larval stage (*Cysticercus cellulosae*) of the pig tapeworm *Taenia solium*. This is the most common helminth to produce CNS infection in human being. The occurrence of acquired epilepsy or the syndrome of raised intracranial pressure in a person living in or visiting a region where taeniasis is endemic or even in one living in close contact with people who have taeniasis should suggest a diagnosis of cysticercosis; the NC may remain asymptomatic for months to years and sometimes its diagnosis is made incidentally when neuroimaging is performed. Symptoms and signs are related both to the parasite which can show a different biological behavior from one place to another, and to the inflammatory-immunological response of the host. NC is the most common cause of acquired epilepsy worldwide and most of the patients taking phenytoin or carbamazepine for a proper control of their seizures, respond very well NC is also an important cause of ischemic stroke secondary to infectious vasculitis (Foyaca-Sibat & Ibañez-Valdés, 2003). The most common cause of epilepsy due to NC is calcified lesion with or without evidence of perilesional edema. The prognosis of this situation is worse when there is an associated intraventricular cyst (Figure 2) that usually does not respond well to praziquantel and albendazole should be prescribe (Foyaca-Sibat & Ibañez-Valdés, 2003). More information about NC can be found in this book.

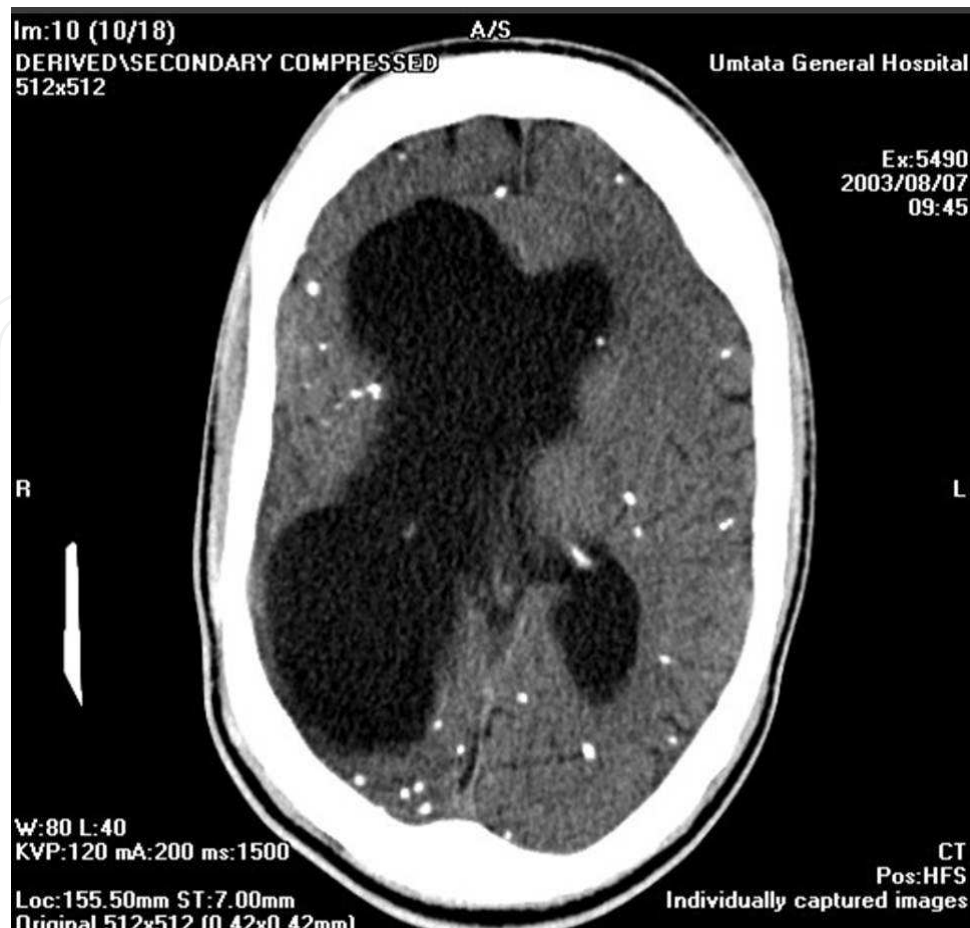


Fig. 2. Shows multiple intraparenchymal calcified NC with and without perilesional edema and hydrocephalus secondary to intraventricular NC.

#### 4. Neurotoxocariasis and effect modification of HIV

##### 4.1 Introduction

Human toxocariasis is usually contracted by exposure to contaminated soil. This disease is rarely transmitted by raw meat or giblets of paratenic animals, such as chickens, lambs, or cows. Hoffmeister et al, (2007) reported a case of isolated cerebral toxocariasis presumably caused by the consumption of the raw duck liver. Their patient, a 55-year-old woman had sudden-onset hemiparesis of the right leg, eosinophilia of 30%, and markedly elevated total serum IgE levels. Magnetic resonance imaging demonstrated multiple cerebral hyperintense lesions on T2-weighted images.

Tests for antibodies to *Toxocara* in serum and cerebrospinal fluid yielded highly positive results and repeated courses of albendazole and corticosteroids led to significant clinical improvement. Previously, Kim et al., (2003) reported a case of cerebral infarction which was caused by toxocariasis in adults, who had headache, abdominal pain and a right side weakness. He had only a history of ingestion of raw liver of deer. Although the seriousness of infection of *Toxocara canis* depends on the site of parasite migration, the aberrant larvae occasionally invade the CNS. Neurological problems, such as epilepsy, neuropsychological deficits, and ataxia have been observed clinically in humans and in the case of ocular larval migrans, vision loss and permanent blindness may result (Akao et al., 2003; Nithiuthai et al., 2004).

Three recent case-control studies conducted in rural Bolivia, Burundi and Italy (Nicoletti et al., 2002, 2007, 2008) reported a significant association between seropositivity to *T. canis* and epilepsy. The adjusted odds ratios (OR) in these three studies were 2.70 (95%CI=1.41-5.19), 2.13 (95%CI: 1.18-3.83) and 3.90 (95%CI: 1.91-7.98), in Bolivia, Burundi and Italy, respectively. Of particular interest, in 2 of the 3 studies, the OR of epilepsy associated with seropositivity to *Toxocara* spp. was higher among persons with partial seizures (OR=4.70, 95%CI=1.47-15.1 and OR=4.69, 95%CI: 2.24-9.80, respectively). The opposite was true in Burundi where the association was stronger among persons with generalized seizures (OR=2.52; 95%:1.01-6.26). Toxocariasis has also been associated with epilepsy in a study of children in Italy (Alpino et al., 1990). In this study, prevalence of antibody to *T. canis* was compared in 91 children with epilepsy younger than 18 years and 214 controls. The OR for seropositivity was estimated to 2.0 (95% CI=1.0-4.0). The association was present primarily in children less than 5 years of age. Whether exposure precedes the onset of seizures or is a result of behaviors such as geophagy in children with epilepsy is uncertain. However, there was no association between pica and seropositivity in the study by Alpino et al. (1990) and Nicoletti et al. (2002), the association between seropositivity and epilepsy was stronger for adults than for children and for those with partial seizures than for those with generalized seizures. These findings argue against exposure being a consequence of seizures rather than an antecedent. Pica had a protective effect in the most recent study of Nicoletti et al. conducted in Sicily (2008).

Recall bias is unlikely since an overestimation of the association rather than an underestimation was observed. Persons with early onset seizures (<15 years old) showed a stronger association between toxocariasis and epilepsy, which tends to support the hypothesis that young children are at higher risk of infection. The prevalence of infection with *Toxocara* spp. was 50.8% among the control group in Burundi, suggesting that the exposure to this zoonotic parasite in SSA is very high (Nicoletti et al., 2002).

We were unable to find a well-designed studies from countries where parasitic zoonoses are endemic that assessed the association between HIV infection, NC and cerebral toxocariasis. While it is possible that HIV infection may modify the association between known risk factors and parasitic zoonotic infections of the brain, to our knowledge, this has never been addressed (personal communication by Carabin H, 2010). More information about parasitic zoonoses of the brain and epilepsy can be found in our book entitled *Epilepsy. Clinical manifestations*. ISBN 978-953-307-1341-2

In 2004 and 2005, we conducted a pilot study at the St-Elisabeth hospital in Lusikisiki (ECP) which included 296 consecutive patients consulting the medical clinic for suspected new-onset seizures or existing epilepsy cases. Each week, four (4) randomly selected, consenting patients with confirmed seizure disorder were transported to Mthatha for CT scan of the brain. The prevalence of seropositivity to antigens of *T. solium* was 8% (95%CI: 4.5%-13%). A total of 92 patients with recurrent seizures and who also completed a questionnaire were referred to Mthatha for a CT-scan. Of these, 34 (37.0%, 95%CI: 27.1%-47.7%) had a definite diagnosis of neurocysticercosis (NCC), 14 of whom had active lesions visible on CT, 39 (42%) had no CT abnormality, and 19 (21%) had other, undefined non-NCC calcifications. Our results showed that serology alone cannot be used to diagnose NCC in this population (Foyaca-Sibat et al., 2009)

HIV status was available from 50 patients with confirmed seizures or epilepsy. Among the 47 patients with antibody ELISA results available, the antibody seroprevalence of *T. solium*



was 30.0% among HIV positive patients and 48.1% among HIV negative patients. Interestingly, among the 33 patients with antigen ELISA results, the antigen seroprevalence of *T. solium* was 16.7% among the HIV positive patients but only 9.5% among the HIV negative patients. These preliminary results suggest that HIV patients may be less able to mount a detectable antibody response to cysticercosis and might be more likely to be infected with active cysts. A total of 22 of these patients (13 HIV negative and 9 HIV positive) were referred for a CT-scan. Of these, 5 HIV negative and 7 HIV positive patients had CT evidence of NC with 2 HIV negative and 5 HIV positive patients harboring active cysts. These very preliminary and imprecise results do suggest that there may be an association between NC and HIV infection. (Foyaca-Sibat et al., 2009)

#### 4.1.1 The specific research aims of the current pilot study are

1. Conduct a pilot study to compare the cross-sectional seroprevalence of toxocariasis and cysticercosis in six groups: patients in the advanced stage of HIV, those who are HIV positive but not in the advanced stages, and HIV negative patients, each group being further subdivided into those with and without selected neurological disorders. Our research hypothesis was: the prevalence of parasitic zoonoses is higher among people with advanced HIV but CNS manifestations are more common among people in the early stages for HIV as compared to HIV negative people living in the Eastern Cape Province (ECP) of South Africa.
2. Conduct a pilot study to estimate the interaction between HIV and cysticercosis or toxocariasis in the occurrence of neurological complications in adolescents and adults with HIV infection. To estimate the interaction between HIV and cysticercosis and toxocariasis on the prevalence of neurological disorders and generate new, testable hypotheses about the biological mechanisms for such interactions.

The long-term goal of this project is to develop a multidisciplinary-based interventions to more effectively control preventable parasitic zoonotic infections that are associated with epileptic disorders and that may disproportionately affect people living with HIV/AIDS.

We did a pilot cross-sectional study comparing six groups of patients defined by HIV infection status (advanced HIV, HIV positive not in the advanced stages, and HIV negative) and the presence of clinical manifestations of selected CNS disorders (yes/no).

Advanced-stage HIV patients (groups 1 and 2) are individuals who have met the WHO definition of stage 3 HIV/AIDS in the past 12 months (WHO, 2005). Patients who have ever been diagnosed with stage 4 HIV/AIDS are excluded. Only stage 3 patients not yet on HAART at the time of the study were included. (See figure 3)

Newly (< 12 months) diagnosed HIV patients not in the advanced stage (Groups 3 and 4) are defined as persons living with HIV/AIDS (PLWH/A) under care who have CD4 counts >350 cells/mm<sup>3</sup> and who are not HIV stages 3 or 4 as defined by the WHO (WHO 2005) when the study starts or at the time of diagnosis of a neurological disorder. We needed to invite some of these patients to participate in the study during their first visit to the HIV clinic in order to recruit a sufficient number of these early stage patients.

Groups 1-4 were sampled from the Mthatha Hospital Complex's HIV/AIDS clinic which is likely to represent the largest source of PLWH/A under care in the ECP, Nelson Mandela Academic Hospital (NMAH) is included. Patients in Groups 1 and 3 have been diagnosed with epilepsy at any time following their diagnosis of advanced HIV (group 1) or HIV

positivity (group 3) respectively. We used this inclusion criteria due to the possibility that co-infection with the study helminths may accelerate the progression of HIV infection to advanced stages.

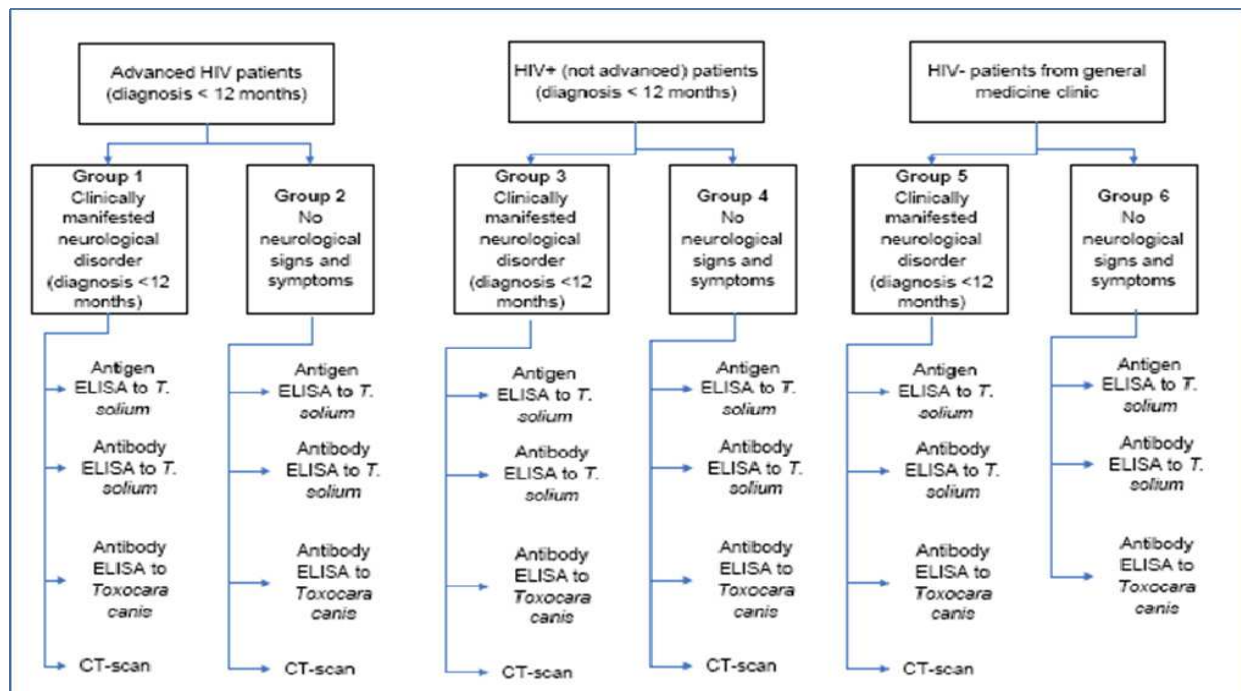


Fig. 3. Shows graphical composition of each group (Made by Prof. H Carabin from University of Oklahoma, USA)

Group 5 was sampled from the neurology/epilepsy/neurocysticercosis clinic at the NMAH. We took a random sample of clinic patients newly diagnosed with epilepsy within the previous 12 months and who tested negative for HIV at that time or anytime following the initial visit. Group 6 consisted of HIV negative patients referred to the general medicine clinic of the NMAH and who have no history of any neurological disorders. Group 6 had a negative HIV diagnostic test resulted in the past month. For Groups 5 and 6, if the patients had never been tested for HIV, we offered the test. Only those HIV seronegative was included in these groups. If tested participants do not wish to be informed about their HIV status (very common situation), we respected their choice. If they test positive and want to be informed, we do so and then refer them to the HIV/AIDS clinic for their care.

The sampling strategy depended on the expected number of patients available on each group, but we were aiming at sampling 50 patients in each group.

#### 4.2 Statistical method

Data is analyzed to estimate the cross-sectional associations between HIV and infections with *T. solium* and *Toxocara spp.* and their potential interactions in clinically apparent neurological complications. The 6 groups, which are fixed by design, will be modeled as an interaction term between HIV status and the presence or absence of neurological disorders. Either the serological results or the presence of parasitic brain lesions on CT-scan (i.e., NC or neurological toxocariasis) are the “outcomes” in the statistical analyses since they are the random variables

in this design. This approach allows us to test if there is indeed such interaction and if not, to assess the independent cross-sectional association between serological results (dependent variable) and HIV status and neurological disorders (independent variables).

We used three Bayesian multivariate logistic regressions with the presence/absence of antigen to cysticercosis, antibodies to cysticercosis and antibodies to *Toxocara* as outcomes. To estimate the association between the presence of NC and neurological toxocariasis (dependent variable) and HIV status among those with or without neurological disorders (independent variables), we used the same approach except that only groups 1-5 are represented. In all instances, we also run models adjusting for potential confounding variables such as age, gender, family history of epilepsy, area of residence, etc.

We want to emphasize that these analyses are also meant to direct our thinking in generating new hypotheses on the interaction between HIV and brain infection with parasitic zoonoses on neurological disorders in the developing world. We did not identify any causal relationships with data from a pilot cross-sectional study. Because of space limitation, power calculations cannot be presented here

### 4.3 Study design and methods

All patients meeting the inclusion criteria based on HIV stage and epilepsy have the opportunity to be included in this study. Thus, women and minorities meeting the eligibility criteria had the possibility of being included. For the CT-scan of the brain, pregnant women were excluded due to the risk to the fetus, but invited to come back to the exam after delivery.

#### 4.3.1 Selection criteria

Fifty patients diagnosed with epilepsy in the past 12 months and receiving care at the neurology/epilepsy/neurocysticercosis clinic of the NMAH and who tested negative to HIV at that time or any time following the initial visit were invited to participate. Fifty HIV negative patients without neurological disorders, sampled from patients regularly attending a dermatology/general medicine clinic at the WSU hospital complex, were invited to participate by their physician who was informed of their eligibility by a member of the research team. Subjects included in the study were selected at random, and there are no selection criteria based on sex/gender or racial/ethnic groups.

The study is conducted in the former Transkei in South Africa where all population living in rural areas are black. Knowledge gained from this pilot study will assist in developing more definitive, prospective studies of the interaction between infections with parasitic zoonoses and HIV infection on the occurrence and clinical presentation of epilepsy at ECP of South Africa where HIV and cysticercosis are known as endemic.

A blood 10mL sample is collected on all participating subjects for the detection of antibodies to the larval stages of *T. solium* and of *Toxocara* spp and for the detection of the antigens to the larval stages of *T. solium*. Sera will be identified by their research identification numbers and stored in the NMAH laboratory. For HIV negative participants who have not been tested for HIV in the past 12 months, part of the sera will be used to test for HIV.

Each participant is assigned a research identification number. Data retained on participants will only be identified by their research ID. Information linking participants to their research ID will be stored in secured files in the research office. All of the biological specimens and the interview assessments listed above will be collected specifically for the purposes of the proposed research project.

Informed consent is obtained for all participants. All consent forms included a section in which the objectives of the study are clearly stated. This is followed by a description of what participation in the study involves for the subject. Because we know that a certain proportion of the population is illiterate, the explanation was read to the potential participants. Subjects that know how to sign asked to do it on a form that clearly explains, in simple words of either English or isi-Xhosa (local language in Mthatha), the objectives of the study. The culturally acceptable age at which individuals can be asked for either their assent or consent to participate is discussed with our local colleagues. The consent will clearly state that individuals may terminate participation at any time.

Persons who consent to participate in the study were identified by name and with an alphanumeric code. Only one coding sheet linking the names to the codes is created and it has a password protected. Every effort was made to keep the subject's personal data confidential. Until the end of the study, all data were entered into a password-protected database. All consent forms and the coding sheet were maintained in a locked file cabinet. Any data sent for data analysis was anonymous and with alphanumeric codes for the subjects names.

All investigators and collaborators completed the CITI training-course on the Protection of Human Research. All are sworn to the Hippocratic Oath and committed to respecting the norms of good clinical practice, as well as the requirements of the Helsinki Declaration.

The research protocol was evaluated and approved by Mthatha Umtata General Hospital, University of Transkei, and Walter Sisulu University IRB and the respective Ethical Committees (UGH:0001/99, UNITRA:0018/05, and WSU:0068/009).

Subjects who may require sedation for the CT-scan of the brain were excluded from this part of the study. Patients who do not know their HIV status or are HIV negative (groups 5 and 6) are offered an HIV test if they have not been tested in the past month. A diagnosis of HIV can be very upsetting and may lead to psychological distress. In order to assist newly diagnosed HIV positive participants, they were referred for counseling and treatment to the HIV clinic of the Mthatha Hospital Complex.

The benefits of the information gained from the study outweigh the minimal risk involved. All subjects either have already received or we offer a neurological examination and a CT-scan to determine the cause of their epilepsy, other neurological symptoms or the presence of silent CNS lesions. Individuals who have either never been tested or have not been recently tested for HIV it was given the opportunity to be tested.

#### 4.4 Preliminary results

A brief summary about our preliminary findings can be seen in Table 6

Total = 48 participants enrolled with neurological disorders
46% Female, Median Age=29 Mean Age=33
98% Rural or semi-rural residence
Approx 60% HIV Positive
Of those with CT completed,
High proportion calcified lesions on CT
8 excluded due to CD4 counts>200

Table 6. Some preliminary results

#### **4.5 Discussion, challenges to date, and conclusions**

Our preliminary results were presented and discussed as: "Effect modification of HIV-associated central nervous system diseases by parasitic zoonoses in the Eastern Cape Province, South Africa" at 138th APHA Meeting, in Denver, Colorado, United States of America on November 9, 2010. (Abstract #222895).

Longer-term benefits of this study included a better understanding of the interaction between HIV and parasitic zoonoses on the development of seizure disorders. If the effects of parasitic zoonoses are more severe in HIV infected patients, future studies could be conducted to assess whether the risk factors for infection are the same in HIV positive and HIV negative patients, and control interventions to reduce the burden of these preventable causes of brain infection could be tested. Given that a very large proportion of HIV patients develops some neurological disorder in the course of their infection, being able to reduce the prevalence of some causes of these disorders would benefit patients themselves and the society as a whole by a reduction of medical costs and potential increase in productivity of these patients, especially in a region in which both HIV infection and parasitic zoonoses are highly prevalent.

Poor research capacity often means that there is a misunderstanding of the goals of the research and its ability to be combined with clinical and teaching services. A national political action strikes on campuses across South Africa escalated to violence, forcing the closure of WSU campus among others on four separate occasions. Though the majority of learners expressed their discontent peacefully, a small minority responded with violence. Campus activities were paralyzed on four occasions during the first phase of our study. The majority of the population speaks Isi-Xhosa (95% in ECP). Translations of study materials from English proved difficult as few references exist containing vocabulary for scientific purposes.

There is a lack of knowledge regarding the interactions of HIV and helminthic infections, how their effects on immunological response affect risk of co-infection, and the role of altered immune responses that result from these infections.

Our pilot study is well underway and will lead to the development of new hypotheses on the interaction between HIV and parasitic infections of the brain.

#### **5. Acknowledgment**

We like to express our gratitude to those veterinarian doctors working in this field particularly: Professors Rosina "Tammi" Krecek, Albert Lee Willingham III, Linda Cowan, Samson Mukaratiwua and other members of our Cysticercosis Working Group for Eastern and Southern Africa (CWGESA) for their dedications and commitment.

Special thanks to Professor Helen Carabin from Department of Biostatistics and Epidemiology College of Public Health University of Oklahoma Health Sciences Center for her invaluable enthusiasm, persistence, and leadership in our research team.

We want to thank to all radiologists and radiographers from Nelson Mandela Academic Hospital and Inkhosi Albert Luthuli Central Hospital in South Africa for their contribution to this study.

Many thanks are due to The Cuban Ministry of Health, The Institute of Tropical Medicine "Pedro Kouri", authorities of Faculty of Health Sciences, Directorate: Research Development from the Walter Sisulu University and some of mine colleagues from Nelson Mandela Academic Hospital for their unconditional support.

Special mention is made of Mrs Noluntu Funani. Research Coordinator at the Office of President. South Africa Medical Research Council, who gave me a valuable help.

We also acknowledge financial support from, Directorate of Research Development from Walter Sisulu University in South Africa, University of Oklahoma, and South African Medical Research Council. The founder had no role in study design, data collection and analysis, decision to publish, or preparation of this chapter.

I sincerely thank to INTECH open access publisher for supporting this chapter and to my beautiful friends Ms Dragana Manestar and Natalia Reinic for their kind attention and nice support.

My sweet wife Lourdes de Fátima was so patient with my late nights, and I want to thank her for her faithful support in writing this book. Words cannot express my gratitude to Lourdes for her advices, encouragement, and assistance in polishing this chapter.

Finally, I wish to declare my eternal, deepest love and gratitude to Lorna María Foyaca García, Thabo Humberto Jorge Foyaca Ibañez and Fátima Susana Adolfinia Foyaca Ibañez, because without their love and unconditional support this chapter would not have been written.

## 6. References

- Akao, N., M. Tomoda, E. Hayashi, R. Suzuki, M. Shimizu-Suganuma, K. Schichionohe and K. Cerebellar ataxia due to *Toxocara* infection in Mongolian gerbils, *Meriones unguiculatus*. *Vet. Parasit.*, 113: 229-237, 2003.
- Asuman I, Nurgul C, Ilknur E, Derya E, Seniha S, Seyfi O, Pasa G. Neurobrucellosis with transient ischemic attack, vasculopathic changes, intracerebral granulomas and basal ganglia infarction: a case report. *Journal of Medical Case Reports* 2010;4(1):340.
- Bartolini A. Epilepsy and toxocariasis: a case-control study in Italy. *Epilepsia* 2008;49:594-599.
- Bayliascariasis. Institute for International Cooperation in Animal Biologics. Iowa State University College of Veterinary Medicine. Full article available at the URL: [www.cfsph.iastate.edu/IICAB/](http://www.cfsph.iastate.edu/IICAB/).
- Boongird, P., P. Phuapradit, N. Siridej, T. Chirachariyavej, S. Chuahirun, and A. Vejajiva. 1977. Neurological manifestations of gnathostomiasis. *J. Neurol. Sci.* 1977;31:279-291.
- Carod-Artal FJ, Vargas AP, Horan TA, Nunes LG. Chagasic cardiomyopathy is independently associated with ischemic stroke in Chagas disease. *Stroke* 2005; 36: 965-70.
- Carod-Artal FJ, Gascon J. Chagas disease and stroke. *Lancet Neurol* 2010; 9: 533-542
- Chero JC, Saito M, Bustos JA, Blanco EM, Gonzalvez G, Garcia HH. Hymenolepis nana infection: symptoms and response to nitazoxanide in field conditions. *Trans R Soc Trop Med Hyg.* Feb 2007;101(2):203-205.
- Centers for Disease Control and Prevention [homepage on the Internet] c-2005 Guidelines for veterinarians: prevention of zoonotic transmission of ascarids and hookworms of dogs and cats. National Center for Infectious Diseases, Division of Parasitic Diseases [updated 2011 March 22]. Available at the URL: [http://www.cdc.gov/ncidod/dpd/parasites/ascaris/prevention.htm#pet\\_owners](http://www.cdc.gov/ncidod/dpd/parasites/ascaris/prevention.htm#pet_owners) Last accessed 03/20/2011.
- Clausen MR, Meyer CN, Krantz, Moseril C, Gommeg G, Kayser L, et al. *Trichinella* infection and clinical disease. *QJ Med* 1996; 89:631-636

- Chai JY, Lee SH, Guk SM, Lee SH. An epidemiological survey of *Cryptosporidium parvum* infection in randomly selected inhabitants of Seoul and Chollanam-do. *Korean J Parasitol* 1996; 34:113-119.
- Chai JY, Murrell KD, Lymbery AJ. Fish-borne parasitic zoonoses: status and issues. *Int J Parasitol*. 2005;35:1233-1254.
- Chen XH, Shi GF. Clinical analysis of 6 cases with cerebral sparganosis mansoni. *Zhongguo Ji Sheng Chong Xue Yu Ji Sheng Chong Bing Za Zhi*. 2010 Oct 30;28(5):397-398
- Chiu CH, Chiou TL, Hsu YH, Yen PS. MR spectroscopy and MR perfusion character of cerebral sparganosis: a case report. *Br J Radiol* 2010;83:e31-4
- Choi WY, Nam HW, Kwak NH, Huh W, Kim YR, Kang MW, Cho SY, Dubey JP. Foodborne outbreaks of human toxoplasmosis. *J Infect Dis* 1997; 175: 1280-1282.
- Craig P, Ito A. Intestinal cestodes. *Curr Opin Infect Dis*. Oct 2007;20(5):524-32 Critchley EMR, Vakil SD, Hutchinson DN, Taylor P. *Toxoplasma*, *Toxocara*, and Epilepsy *Epilepsy* 982;23(3):315-321.
- Daengsvang, S. Gnathostomiasis in Southeast Asia. *Southeast Asian J. Trop. Med. Public Health*.1981;12:319-332.
- Devendra V, Shalini K, Vimala V, Priti V, Nuzhat H. Ectopic Fascioliasis in the Dorsal Spine: Case Report. *Neurosurgery* 2006;59(3):706-707.
- Dukes CS, Luft BJ, Durack DT. Toxoplasmosis. In WM Scheld, RJ Whitley, DT Durack (eds), *Infections of the Central Nervous System*. Philadelphia: Lippincott-Raven, 1997;785-806
- Fujita, 2003. Cerebellar ataxia due to *Toxocara* infection in Mongolian gerbils, *Meriones unguiculatus*. *Vet. Parasitol.*, 113: 229-237. Despommier D, 2003. Toxocariasis: clinical aspects, epidemiology, medical ecology, and molecular aspects. *Clin Microbiol Rev* 16: 265-272.
- Ellrodt A, Halfon P, Le Bras P, Halimi P, Bouree P, Desi M, Caquet R. Multifocal central nervous system lesions in three patients with trichinosis. *Arch Neurol* 1987; 44:432-4.
- Foyaca-Sibat H, Ibañez-Valdés LdeF "Intraventricular neurocysticercosis in HIV patients" *The Internet Journal of Neurology* 2003;2(1):23-31  
[http://www.ispub.com/journal/the\\_internet\\_journal\\_of\\_neurology/volume\\_2\\_number\\_1\\_37/article/intraventricular\\_neurocysticercosis\\_in\\_hiv\\_positive\\_patients.html](http://www.ispub.com/journal/the_internet_journal_of_neurology/volume_2_number_1_37/article/intraventricular_neurocysticercosis_in_hiv_positive_patients.html)
- Foyaca-Sibat H, Ibañez-Valdés LdeF."Pseudoseizures and Epilepsy in neurocysticercosis" *Electron J Biomed* 2003;2(2):20-29 Full free article available at the URL: <http://www.uninet.edu/reb/2003/n2/2foyaca.html>
- Foyaca Sibat H, Ibañez-Valdés LdeF. Vascular dementia due to a Binswanger Disease in patients with active neurocysticercosis. *Rev Electron Biomed / Electron J Biomed* 2003;1(1):32-42. Full article available at the URL: <http://biomed.uninet.edu/2003/n1/foyaca.html>
- Foyaca-Sibat H, Cowan LD, Carabin H, Serrano-Ocaña G, Krecek RC, Willingham A. "Accuracy of the serological exam for the diagnosis of neurocysticercosis in outpatients with epilepsy, Eastern Cape Province, South Africa" *PLOS Neglected Trop.Dis*.Dec.2009;3(3):1-7
- Foyaca-Sibat H, Ibañez-Valdés LdeF & J. Moré-Rodríguez : Parasitic Zoonoses Of The Brain: Another Challenger?. *The Internet Journal of Neurology*. 2010 Volume 12 Number 2 [http://www.ispub.com/journal/the\\_internet\\_journal\\_of\\_neurology/volume\\_12\\_number\\_2\\_4/article/parasitic-zoonoses-of-the-brain-another-challenger.html](http://www.ispub.com/journal/the_internet_journal_of_neurology/volume_12_number_2_4/article/parasitic-zoonoses-of-the-brain-another-challenger.html)

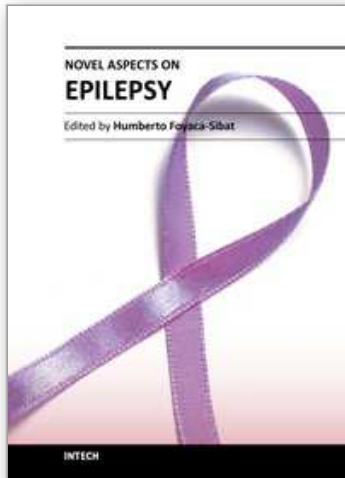
- Fourestie V, Douceron H, Brugieres P, Ancelle T, Lejonc JL, Gherardi RK. Neurotrichinosis. A cerebrovascular disease associated with myocardial injury and hypereosinophilia. *Brain*. Jun 1993;116 (Pt 3):603-616.
- Fowler R, Lee C, Keystone JS. The role of corticosteroids in the treatment of cerebral schistosomiasis caused by *Schistosoma mansoni*: Case report and discussion. *Am J Trop Med Hyg*. 1999;6(1):47-50
- Gavin PJ, Kazacos KR, Shulman ST, 2005. Baylisascariasis. *Clin Microbiol Rev*. 2005;18:703-718
- Garcia H. H., Moro P. L., Schantz P. M. Zoonotic helminth infections of humans: echinococcosis, cysticercosis and fascioliasis. *Curr. Opin. Infect. Dis*. 2007;20, 489-494.
- Gay T, Pankey GA, Beckman EN, Washington P, Bell KA. Fatal CNS trichinosis. *JAMA* 1982; 247:1024-1025.
- Georgiev V. Management of toxoplasmosis. *Drugs* 1994;48:79-88.
- Chi TTK, Dalsgaard A, Turnbull JF, Tuan PA, Murrell KD. Prevalence of zoonotic trematodes in fish from a Vietnamese fish-farming community. *J Parasitol*. 2008;94:423-428
- Gordon HM, Forsyth BA. Sparganosis in feral pigs in New South Wales. *Aust Vet J* 1954;30:135-138.
- Goldstein MA and Harden CL. Infectious states. In: Ettinger AB and Devinsky O, eds. *Managing epilepsy and co-existing disorders*. Boston: Butterworth-Heinemann; 2002;83-133.
- Gray ML, Rogers F, Little S, et al. Sparganosis in feral hogs (*Sus scrofa*) from Florida. *J Am Vet Med Assoc* 1999;215(2):204-208.
- Guenifi W, Rais M, Gasmi A, Ouyahia A, Boukhrissa H, Mechakra S, Houari M, Nouasria B, Lacheheb A Neurobrucellosis: description of 5 cases in Setif Hospital, Algeria. *Med Trop (Mars)*. 2010;70(3):309-10.
- Cunningham A. A. A walk on the wild side—emerging wildlife diseases. *Br. Med. J*. 2005;331: 1214-1215.
- Hamon JF, Camara P. Electroencephalographic study of meningoencephalitis from *Trypanosoma gambiense* before and after treatment with melarsoprol. *Neurophysiol Clin* 1991;21:173-181.
- Henningsson AJ, Malmvall BE, Ernerudh J, Matussek A, Forsberg P. Neuroborreliosis—an epidemiological, clinical and healthcare cost study from an endemic area of the south-east of Sweden *Clinical Microbiology and Infection*. 2010;16(8):1245-1251.
- Herman JS, Chiodini PL. Gnathostomiasis, Another Emerging Imported Disease. *Clinical Microbiology Reviews*, 2009;22(3):484-492.
- Hoffmeister B; Glaeser S; Flick H; Pornschlegel S; Suttorp N; Bergmann F. Cerebral toxocariasis after consumption of raw duck liver. *The Amer J Trop Med Hyg*. 2007;76(3):600-602.
- Hong ST. Serologic response to *Pneumocystis carinii* of Seoul National University Hospital patients. *Korean J Parasitol* 1991; 29: 355-361.
- Hughes AJ, Biggs BA. First report of human angiostrongyliasis acquired in Sydney. *N Engl J Med* 2002; 346: 668-675. Hughes A, Biggs B. Parasitic worms of the central nervous system: an Australian perspective. *Intern Med J* 2002; 32:541-553-539.
- IBEC- Institute for Bioengineering of Catalonia. "Discovery of a new function of prion protein improves understanding of epilepsy." *ScienceDaily* 31 December 2009. Full article is available at the URL:  
<http://www.sciencedaily.com/releases/2009/11/091127175422.htm> (Last review on 20 March, 2011)



- Inkelman I, Arieff AJ, Schiller M. Rabies vaccine in the treatment of epilepsy. *Am J Psychiatry*.1938; 94:1363-1368.
- Karki K. Human Fascioliasis an Emerging Zoonoses. The full article is available online at the URL: <http://www.scribd.com/doc/3608468/Human-Fascioliasis-3> (Last review on March 18, 2011)
- Keiser J., Utzinger J. Emerging foodborne trematodiasis. *Emerg. Infect. Dis.* 2005;11, 1507–1514
- Johnson RT, Gibbs CJ. Medical progress: Creutzfeldt-Jakob disease and related transmissible spongiform encephalopathies. *N Engl J Med* 1998;339:1994–2004
- Kim YB, Ko YC, Jeon SH, Park HM, Shin WC, Lee YB, Ha KS, Shin DJ, Lim YH, Ryu JS, Chung MS. Toxocariasis: An Unusual Cause of Cerebral Infarction. *J Korean Neurol Assoc.* 2003 Dec;21(6):651-654
- Lee CH, Saif YM. Avian influenza virus. *Comparative Immunology, Microbiology and Infectious Diseases.* 2009;32(4):301-310
- Lindbald-Toh, K. Genome sequence, comparative analysis and haplotype structure of the domestic dogs. *Nature.* 2005;38(7069): 803-819.
- Little SE. Parasitic zoonoses: parasites transmitted from cats and dogs to children. *Contemporary Pediatrics* 2003;5:1-21
- Labar DR, Harden C. Infection and Inflammatory Diseases. In J Engel Jr, TA Pedley (eds), *Epilepsy: a Comprehensive Textbook.* Philadelphia: Lippincott-Raven, 1997;2587–2596.
- Madariaga MG, Cachay ER, Zarlenga DS. Case Report: A Probable Case of Human Neurotrichinellosis in the United States. *Am. J. Trop. Med. Hyg.* 2007;77(2):347–349
- Marsden PD, Bruce-Chwatt LJ. Cerebral malaria. *Contemp Neurol Ser* 1975;12:29–44.
- Mas-Coma S., Bargues M. D., Valero M. A. Fascioliasis and other plant-borne trematode zoonoses. *Int. J. Parasitol.* 2005 35, 1255–1278.
- Mas-Coma S, Valero MA, Bargues MD. Climate change effects on trematodiasis, with emphasis on zoonotic fascioliasis and schistosomiasis. *Veterinary Parasitology.* 2009;163(4):264-280.
- McCarthy J., Moore T. A. Emerging helminth zoonoses. *Int. J. Parasitol.* 2000;30,1351–1360.
- McCabe RE, Brooks RG, Dorfman RF, et al. Clinical spectrum in 107 cases of toxoplasmic lymphadenopathy. *Rev Infect Dis* 1987;9:754–774
- Min DY. Cestode infections in Korea. *Korean J Parasitol* 1990; 28:123-144
- Mirdha BR. Status of *Toxoplasma gondii* infection in the etiology of epilepsy. *J Pediatr Neurol* 2003; 1(2): 95-98
- Morey, D., 2006. Burying key evidence: The social bond between dogs and people. *J. Archaeol. Sci.* 2006;33:158-175.
- Mueller JF. The biology of *Spirometra*. *J Parasitol* 1974;60:3-14.
- Neghina R, Neghina AM, Marincu L, Iacobiciu L. Reviews on Trichinellosis (II): Neurological Involvement. *Foodborne Pathogens and Disease* 2010;10: 1089
- Nawa Y. Historical review and current status of gnathostomiasis in Asia. *Southeast Asian J. Trop. Med. Public Health* 1991; 22(Suppl.):217-219.
- Nicoletti A, Bartoloini A, Reggio A, et al. Epilepsy, cyctercosis, and toxocariasis. A population-based case-control study in rural Bolivia. *Neurology* 2002;58:1256-1261.
- Nicoletti A, Bartolini A, Sofia V, Mantella A, Nsengiyumva G, Frescaline G, Preux P-M. Epilepsy and toxocariasis : a case-control study in Burundi. *Epilepsia* 2007;48:894-899.
- Nicoletti A, Sofia V, Mantella A, Vitale G, Contrafatto D, Sorbello V, Biondi R, Preux P-M, Garcia HH, Zappia M, Nikolic S, Vujosevic M, Sasic M, et al. [Neurologic manifestations in trichinosis]. *Srp Arh Celok Lek.* May-Jun 1998;126(5-6):209-13. [Medline].

- Nithiuthai, S., M.T. Anantaphrati, J. Waikagul and A. Gajadhar, 2004. Waterborne zoonotic helminthiasis. *Vet. Parasitol.*, 126: 167-193.
- Obiako OR, Ogoina D, Danbauchi SS, Kwaifa SI, Chom ND, Nwokorie E. Neurobrucellosis-- a case report and review of the literature. *Niger J Clin Pract.* 2010 Sep;13(3):347-50.
- Oliveira, P. C. L.; Sampaio, R. L.; Lacerda, M. S.; Alvarenga, R. R.; Espinoza, M. F. Neurological coccidiosis in an adult Gir cow - case report. *Ciência Animal Brasileira.* 2009;10(1):322-329. Full article is available at the URL: <http://www.revistas.ufg.br/index.php/vet/article/view/1145/4601> (Last review on March 20, 2011)
- Pai PJ, Blackburn BG, Kazacos KR, Warriar RP, Bégué RE. Full recovery from *Baylisascaris procyonis* eosinophilic meningitis. *Emerg Infect Dis.* 2007 Jun;13(6):928-30.
- Park SW, Sohn S. Cerebral Ischemia Caused by Hepatic Fascioliasis. *Korean J Stroke* 2010;12:33-35.
- Paul, E. and J. Serpell, 1996. Obtaining a new pet dog: Effects on middle childhood children and their families. *Appl. Anim. Behav. Sci.* 1996;47:17-29.
- Phan VT, Ersbøll KA, Nguyen VK, Madsen H, Dalsgaard A. Farm-level risk factors for fish-borne zoonotic trematode infection in integrated small-scale fish farms in northern Vietnam. *PLoS Negl Trop Dis.* 2010;4:742-746.
- Plummer J, Kleener H, Jobs K. Parasitic zoonoses in human brain. *SA Med J* 1957;10:78-87
- Polley L, Thompson RCA. Parasite zoonoses and climate change: molecular tools for tracking shifting boundaries. *Trends in Parasitology* 2009; 25(6):285-291.
- Polley L, Hoberg E, Kutz S. Climate change, parasites and shifting boundaries. *Acta Veterinaria Scandinavica* 2010; 52( 1):0147-0152. The electronic version of this article can be found online at: <http://www.actavetscand.com/content/52/S1/S1>
- Porter S, Sande M. Toxoplasmosis of the central nervous system in AIDS. *N Engl J Med* 1992;327:1643-1648
- Procop GW. North American paragonimiasis (caused by *Paragonimus kellicotti*) in the context of global paragonimiasis. *Clin Microbiol Rev* 2009;22:415--446.
- Pullar EM, McLenan GC. Sparganosis in a Victorian pig. *Aust Vet J* 1949;25:302-304.
- Ragnaud J, Morlat P, Dupon M, et al. Cerebral toxoplasmosis in AIDS. *Presse Med* 1993;22:903-908.
- Renkawek K, Renier WO, de Pont JHHM, Vogels OJM, Gabreëls FJM. Neonatal Status Convulsivus, Spongiform Encephalopathy, and Low Activity of Na<sup>+</sup>/K<sup>+</sup>-ATPase in the Brain. *Epilepsia* 1992;33(1):58-64
- Robinson MW, Dalton JP. Zoonotic helminth infections with particular emphasis on fasciolosis and other trematodiasis. *Phil. Trans. R. Soc. B* 2009;364(1530): 2763-2776.
- Rocha A, de Meneses AC, da Silva AM, et al. Pathology of patients with Chagas' disease and AIDS. *Am J Trop Med Hyg* 1994;50:261-268.
- Rodriguez RE, Valero V, Watanakunakorn CH. *Salmonella* Focal Intracranial Infections: Review of the World Literature (1884-1984) and Report of an Unusual Case. *Clin Infect Dis.* (1986) 8 (1): 31-41.
- Sace J. Rabies in Humans: Symptoms, Diagnosis, and Treatment. Edited & published by Leigh A. Zaykoski on Apr 10, 2009.
- Schachter S C. Helminthic parasitic infections. *Epilepsy.com* Editorial Board. Available at the URL: [http://professionals.epilepsy.com/wi/print\\_section.php?section=infectious\\_helminthic#helminthic\\_schistosom](http://professionals.epilepsy.com/wi/print_section.php?section=infectious_helminthic#helminthic_schistosom)

- Sander JW, Perucca E. Epilepsy and comorbidity: infections and antimicrobials usage in relation to epilepsy management. *Acta neurologica scandinavica* 2003;108(180):16-22.
- Savolainen, P., Y. Zang, J. Luo, J. Lundeborg and T. Leitner. Genetic evidence for an East Asian origin of domestic dogs. *Science*.2002; 298(5598):1610-1613.
- Shah AA, Shaikh H, Karim M. Amoebic brain abscess: a rare but serious complication of *Entamoeba histolytica* infection. *J. Neurol. Neurosurg. Psychiatr.*1994; 57 (2): 240-241.
- Shirakawa K, Yamasaki H, Ito A, Miyajima H, Hamamatsu D., Tokyo (H.Y.), and Asahikawa A.I., Cerebral sparganosis. The wandering lesion. *Neurology* 2010;74(2):
- Song T, Wang WS, Zhou BR, et al. CT and MR characteristics of cerebral sparganosis. *Am J Neuroradiol* 2007;28:1700-1705
- Stommel EW, Seguin R, Thadan VM, Schwartzman JD, Gilbert K, Ryan KA, Tosteson TD, Kasper LH. Cryptogenic Epilepsy: An Infectious Etiology? *Epilepsia* 2001;42(3):436-438.
- Swai ES, Kaaya EJ, Mshanga DA, Mbise EW. A Survey on Gastro-Intestinal Parasites of Non-Descript Dogs in and around Arusha Municipality, Tanzania. *Int. J. Anim. Veter. Adv.* 2010;2(3): 63-67.
- Thien PC, Dalsgaard AD, Thanh BN, Olsen A, Murrell KD. Prevalence of fishborne zoonotic parasites in important cultured fish species in the Mekong Delta, Vietnam. *Parasitol Res.* 2007;101:1277-84.
- Tolan RW. Hymenolepiasis. *eMedicine Specialties*. Jan 20, 2011. Full article available at the URL:<http://emedicine.medscape.com/article/998498-overview>
- Taylor MJ, Hoerauf A, Bockarie MD The Lancet Seminar: Lymphatic filariasis and onchocerciasis *The Lancet* 2011;376(9747):1175-1185
- Tolan RW Fascioliasis Due to *Fasciola hepatica* and *Fasciola gigantica* Infection: An Update on This 'Neglected' Neglected Tropical Disease. *Laboratory Medicine*. 2011;42(2):107-116
- Tekin-Koruk S, Duygu F, Gursoy B, Karaagac L, Bayraktar M. A rare case of seronegative neurobrucellosis. *Ann Saudi Med.* 2010; 30(5): 412-414.
- Türel Ö, Şanlı K, Hatipoğlu N, Aydoğmuş Ç, Hatipoğlu H, Şiraneci R. Acute meningoencephalitis due to Brucella: case report and review of neurobrucellosis in children. *The Turkish Journal of Pediatrics* 2010; 52: 426-429.
- van Burgel ND, Oosterloo M, Kroon FP, van Dam VP. Severe course of Lyme neuroborreliosis in an HIV-1 positive patient; case report and review of the literature. *BMC Neurology* 2010;10:110-117.
- Vorou R. M., Papavassiliou V. G., Tsiodras S. Emerging zoonoses and vector-borne infections affecting humans in Europe. *Epidemiol. Infect.* 2007;135:1231-1247.
- Youn H. Review of Zoonotic Parasites in Medical and Veterinary Fields in the Republic of Korea. *Korean J Parasitol* 2009;47:133-141.
- Wan H, Lei D, Mao Q. Cerebellar schistosomiasis: a case report with clinical analysis. *Korean J Parasitol.* Mar 2009;47(1):53-56.
- Watson KC, Laurie W. Cerebral Coenuriasis in the Bantu. *SA Med J.* 1956;9:23-30
- Wiwanitkit V. Cerebral sparganosis. *British Journal of Radiology* 2010;83:807
- World Health Organization. Control of food borne trematode infections. WHO technical report series no. 849. Geneva: The Organization; 1995. p. 1-157
- World Health Organization. Report: Joint WHO/FAO workshop on foodborne trematode infections in Asia: 2002 Nov 26-28 Ha Noi, Vietnam. Manila (Philippines): The Organization; 2004
- WHO. Chagas disease. Seventeenth programme report UNDP/TDR. Geneva, Switzerland: World Health Organization, 2005. Full available at the URL: [http://www.who.int/tdrold/publications/publications/pdf/swg\\_chagas.pdf](http://www.who.int/tdrold/publications/publications/pdf/swg_chagas.pdf) (Last acc



### **Novel Aspects on Epilepsy**

Edited by Prof. Humberto Foyaca-Sibat

ISBN 978-953-307-678-2

Hard cover, 338 pages

**Publisher** InTech

**Published online** 12, October, 2011

**Published in print edition** October, 2011

This book covers novel aspects of epilepsy without ignoring its foundation and therefore, apart from the classic issues that cannot be missing in any book about epilepsy, we introduced novel aspects related with epilepsy and neurocysticercosis as a leading cause of epilepsy in developing countries. We are looking forward with confidence and pride in the vital role that this book has to play for a new vision and mission. Therefore, we introduce novel aspects of epilepsy related to its impact on reproductive functions, oral health and epilepsy secondary to tuberous sclerosis, mitochondrial disorders and lisosomal storage disorders.

#### **How to reference**

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Humberto Foyaca-Sibat (2011). Epilepsy Secondary to Parasitic Zoonoses of the Brain, Novel Aspects on Epilepsy, Prof. Humberto Foyaca-Sibat (Ed.), ISBN: 978-953-307-678-2, InTech, Available from: <http://www.intechopen.com/books/novel-aspects-on-epilepsy/epilepsy-secondary-to-parasitic-zoonoses-of-the-brain>

**INTECH**  
open science | open minds

#### **InTech Europe**

University Campus STeP Ri  
Slavka Krautzeka 83/A  
51000 Rijeka, Croatia  
Phone: +385 (51) 770 447  
Fax: +385 (51) 686 166  
[www.intechopen.com](http://www.intechopen.com)

#### **InTech China**

Unit 405, Office Block, Hotel Equatorial Shanghai  
No.65, Yan An Road (West), Shanghai, 200040, China  
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元  
Phone: +86-21-62489820  
Fax: +86-21-62489821

© 2011 The Author(s). Licensee IntechOpen. This is an open access article distributed under the terms of the [Creative Commons Attribution 3.0 License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

IntechOpen

IntechOpen