

Review Article

Parasitic Infestations of the Central Nervous System - A Review Article

Kelechi Michael Azode^{1,*} , Ese Enaorho Ewoye² , Chigozie Chidozie Okongwu² 

¹Neurosurgery Unit, Department of Surgery, Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Nigeria

²Department of Morbid Anatomy and Forensic Medicine, Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Nigeria

Abstract

Despite being associated with tropical regions of the world, parasitic infestations of the central nervous system have rapidly evolved over the years to involve previously non-endemic countries. This has been aided by transmigration of populations and ecological drifts, thereby creating health problems of immense socioeconomic implications. Pathophysiologic processes that accompany these infections involve the elaboration of leucocytes, macrophages and inflammatory cytokines leading to the denudation of the blood brain barrier with consequent vasogenic edema with increased intracranial pressure. These infestations manifest with various symptoms of neurologic importance which may include headaches, altered sensorium, and progressive neurologic deficits attributable to the mass effect of tissue necrosis caused by neuroinflammatory reaction to the presence of the parasites. This article attempts to survey the predisposing factors, clinical outcomes and complications of these infestations, while exploring the complex interplay between the clinical presentation, diagnostic modalities and interactions between humans and their environment which aid the proliferation of these parasites. It is imperative to highlight the importance of optimal clinical scrutiny and judgment in diagnosing these conditions while advocating for public health intervention strategies and collaborative research efforts to ameliorate the potential complications of these infestations which exert an extreme impact in the prognosis of affected patients with attendant neurologic sequelae.

Keywords

Parasitic Infestation, Neuroinflammation, Clinical Presentation

1. Introduction

Parasitic infestations have been an age-long health problem of mankind with a worldwide distribution and rising prevalence in developing countries of the world with their associated poor health seeking behaviors, increased poverty indices, reduced level of sanitation with deficient knowledge and disposition to healthy living practices.

Developing countries are recording an increasing preva-

lence of these conditions and this has been attributed to the increasing immigration of infected individuals, rising incidence of immunosuppression due to HIV/AIDS, post transplantation immunomodulation therapies and diabetic mellitus [1].

These infestations could be broadly classified into those caused by unicellular protozoan organisms and multicellular

*Corresponding author: kelechiazode@yahoo.com (Kelechi Michael Azode)

Received: 13 March 2025; **Accepted:** 24 March 2025; **Published:** 19 April 2025



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helminths with life cycles involving definitive and intermediate hosts of which humans comprise a majority of the latter. They vary from neurocysticercosis, cerebral plasmodiasis, toxoplasmosis, echinococcosis, schistosomiasis to the relatively rare cerebral amoebiasis, paragonimiasis, toxocariasis, sparganosis and trypanosomiasis with an American and African variant of the latter [2].

Neurologic manifestation of these spectrum of diseases may result in meningitis, intracranial space occupying lesions, ischemic stroke, encephalitis and symptoms of myeloradiculopathy.

Given the non-specificity of the neurological and clinical features of these diseases, diagnosis is often multimodal, imploring a combination of neuroimaging, immunologic and serology test modalities [3].

2. Helminthic Infestations

2.1. Neurocysticercosis

Neurocysticercosis is a parasitic infestation of the Central nervous system, the aetiologic agent of which is the larva of the helminth *Taenia solium*. It is a significant cause of both adult onset and juvenile epilepsy³ accounting for 30% of cases of epilepsy in endemic areas [4].

The life cycle of *T. solium* is an interplay involving humans who serve as the definitive host and pigs who are the intermediate host. Pigs consume the eggs of the parasite contained in inappropriately disposed human fecal matter and these eggs are harbored in the muscles of pigs. Humans become infected by consumption of poorly prepared pork meat containing the larva of the parasite [5]. Following ingestion, the larva invades the systemic circulation and seed into the vascular grey white matter junction of the brain, thalamus and basal ganglia [6]. In the process, eosinophils, macrophages and lymphocytes are recruited which in turn cause the release of pro-inflammatory cytokines interleukin- β and TNF- α resulting in granuloma formation around the cysticerci.

The vesicular stage of the disease on magnetic resonance image appears as a well circumscribed hypointense lesion with a mural nodule which may be indicative of the scolex of the parasite with no perilesional edema, this clear cystic fluid becomes turbid in the colloidal vesicular stage which is the most symptomatic stage. This develops to a hyperintense nodular lesion with some perilesional edema characteristic of the granular stage. The cyst becomes mineralized and calcified with little or no perilesional edema in the nodular calcified stage [1].

Documented areas of involvement are intraparenchymal [7], subarachnoid [8], intraventricular [9], spinal [10].

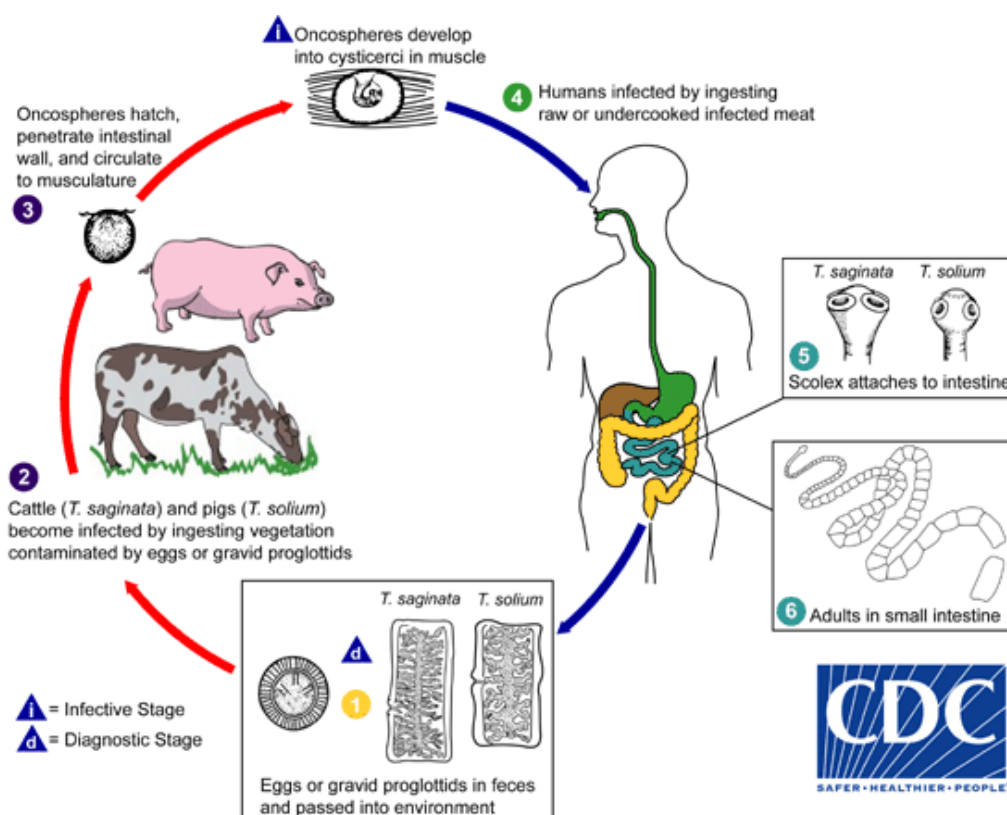


Figure 1. Life Cycle of Taeniasis showing Pigs as intermediate host who consume eggs of the parasite in contaminated vegetation. Humans as the definitive hosts of the parasite get infected from consuming poorly prepared pork meat [5].

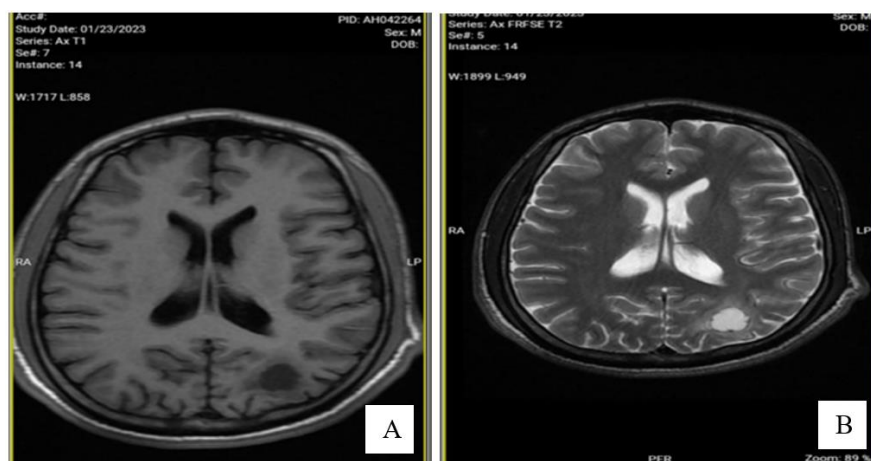


Figure 2. Axial magnetic resonance images of a 23 year old male managed for neurocysticercosis (A) T1 Image showing isointensity of the lesion. (B) T2 image showing hyperintensity.

Clinical manifestation varies depending on the size and location of the lesion as well as the host immune response and range from epilepsy due to degeneration of the walls of the cyst to headache, altered sensorium and features of meningeal irritation [1].

Histologic description though may vary depending on which stage of the parasite development that the biopsy was obtained, however may reveal lateral projections from the walls of the proglottids of the taeniids called the genital pore with a thick radially striated shell containing hooked embryo.

Diagnosis is multimodal embodied in a revised diagnostic criterion comprising of a combination of clinical history,

immunodiagnostic tests, neuroimaging and histopathology analysis.

Treatment is multidisciplinary, the goals of which are to control symptoms, eradication of parasite and relief of raised intracranial pressure. Anti-epileptic medications taken together with corticosteroids have proven beneficial in reducing morbidity and mortality that may emanate from the pathology [11]. Praziquantel and albendazole has also demonstrated efficacy in reducing intraparenchymal parasite load with surgical procedures such as intraventricular catheter placement, decompressive craniotomies and cyst resection reserved for indicated cases [12].

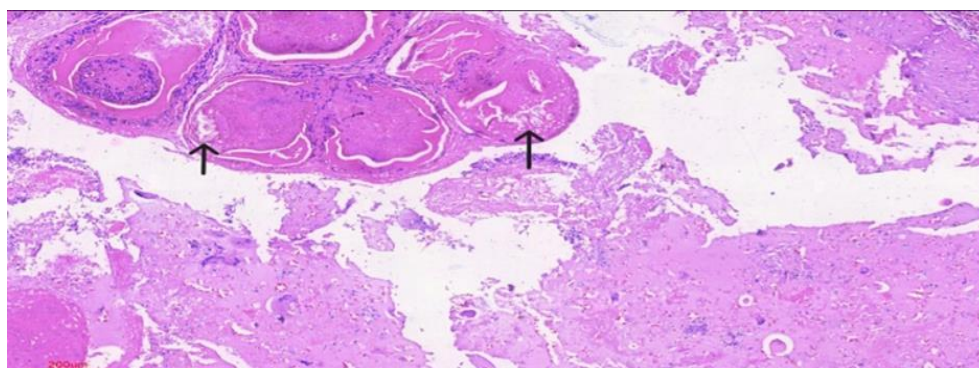


Figure 3. Histology slides of a patient with neurocysticercosis showing cyst walls encircling the parasite and surrounded by foamy macrophages and giant cells.

2.2. Echinococcosis

This is a prevalent condition in the pediatric and adolescent age groups accounting for 50-70% of CNS hydatid cases [13, 14]. Two variants of the disease are the alveolar echinococcus and the cystic echinococcus caused by *Echinococcus multilocularis* and *Echinococcus granulosus* respectively with the alveolar variant having an infiltrative pattern of spread,

comprising of multiple irregular shaped cysts which are not properly delineated from surrounding brain tissue [1]. A prevalence of 2.7% and 25.6% have been observed in Eastern and Northern Africa respectively [15].

Humans get infected by ingesting eggs of the parasite which release oncospheres that invade the walls of the intestine and spread to various organs in which the oncosphere develops into a hydatid cyst.

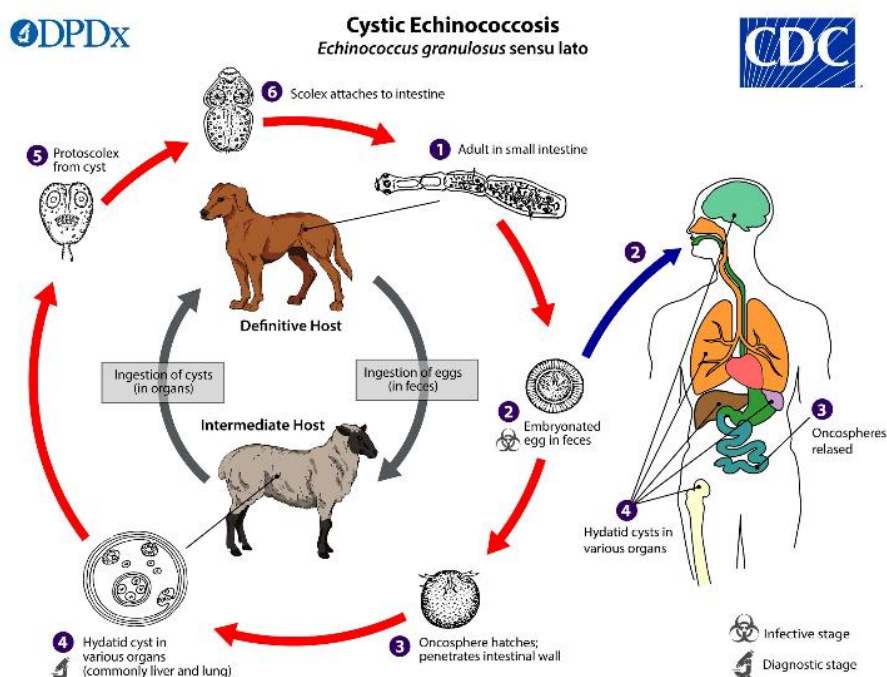


Figure 4. Life Cycle of Echinococcosis showing that humans get infected by ingesting food or water containing eggs of the parasite passed on by infected dogs or sheep [16].

Three layers have been described for brain parenchymal lesions comprising of an outer dense and fibrous pericyst layer, a middle acellular lamellated ectocyst membrane and an inner germinal layer which generates daughter vesicles. These parasites access the CNS through hematogenous route or

spread from contiguous structures, stimulating host immune response that results in neuroinflammation and granuloma formation. The lesions are usually located in the middle cerebral arterial territory and clinical manifestations include headache, seizures and focal neurological deficits [1].

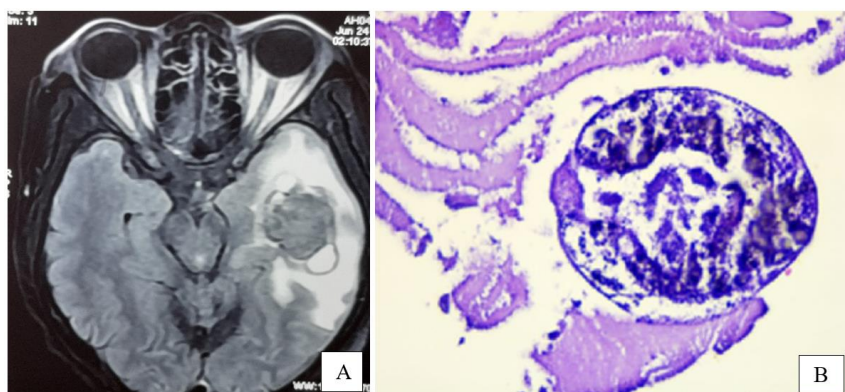


Figure 5. (A) Axial T2 FLAIR image showing multiple sac like echinococci daughter cysts in the left temporal lobe surrounding a central necrotic core with perilesional edema (B) Histology slide of a cerebral hydatid cyst showing a calcified scolex of *Echinococcus granulosus* [17].

Diagnosis is usually by detection of hydatid antigens by Enzyme Linked Immunosorbent Assay (ELISA) and immunoelectrophoresis with antigen assay having a higher specificity and lower sensitivity than antibody assay.

Treatment is by the use of anthelmintic therapy using mebendazole or albendazole.

2.3. Neuroschistosomiasis

This is a problem of public health importance with an endemic prevalence across 74 countries and over 230 million infected individuals and 120 million symptomatic cases [18, 19]. The variants are *Schistosoma haematobium* and *Schistosoma mansoni* which has a predilection for the spine and

Schistosoma japonicum which causes brain parenchymal lesions [1].

Humans get infected percutaneously by the cercariae of the parasite released by fresh water snail. Embolization of the

cercariae and maturation into schistosomulae occurs during transition through the cerebral arteries which provides a medium for spread to the CNS with an alternative retrograde spread through the basilar plexus of veins [1].

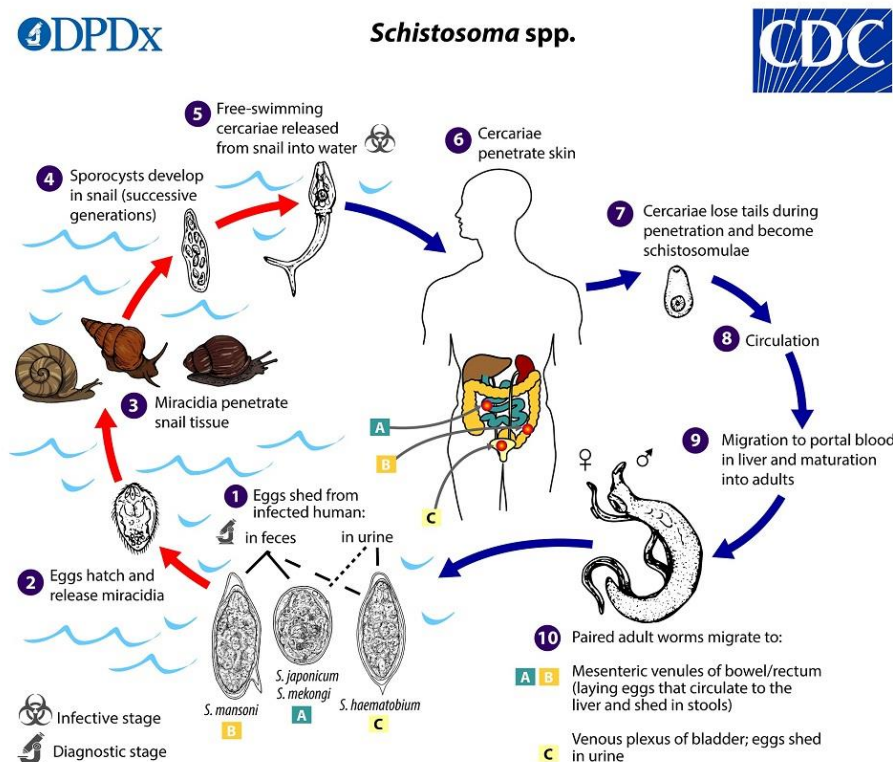


Figure 6. Life cycle of *Schistosoma* spp showing the bulinus snail as the intermediate host which releases cercariae that infects man, the definitive host of the parasite [20].

Cerebral parenchymal lesions may be located in the choroid plexus, leptomeninges, cerebellum, brainstem and cerebral hemispheres while spinal lesions are localized at the lower spinal cord and conus medullaris area where there exists an anastomosis between the pelvic veins and the valveless vertebral venous plexus [1].

Clinical features may include headache, seizures, focal

neurologic deficit and myeloradiculopathy. Diagnostic modalities involve an isolation of the eggs of the parasite in stool or urine samples in combination with serologic assay for antibodies to parasite specific antigens. Neuroimaging is useful for visualization of contrast enhancing nodular granulomatous lesions within the CNS [21].

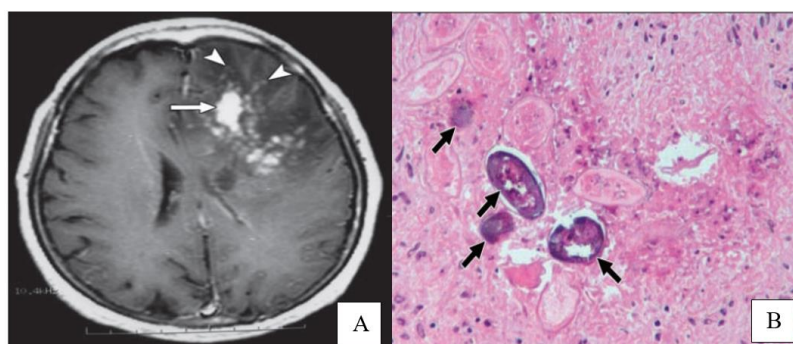


Figure 7. (A) Axial T1 image with contrast showing an aggregate of nodular lesions which are contrast enhancing in the left frontal lobe with marked perilesional edema and effacement of the left lateral ventricle. (B) Histopathologic slide with arrows showing multiple ova of *Schistosoma japonicum* and granuloma formation around them [22].

Praziquantel as a schistosomicidal agent has been proven effective, however a synchronous administration of steroids is crucial in order to ameliorate the inflammatory response that may follow treatment [21].

2.4. Toxocariasis

Toxocariasis is a parasitic zoonotic infestation caused by

the larvae of roundworms of dogs (*Toxocara canis*) and cats (*Toxocara cati*) [21]. While seroprevalence rates has been reported as 2.4% and 7% in some European countries [23], an adult and pediatric seropositive rates of 30.4%, 29.6% respectively have been documented in Jos Plateau state Nigeria with gender distribution of 34% and 25.9% for females and males respectively [24].

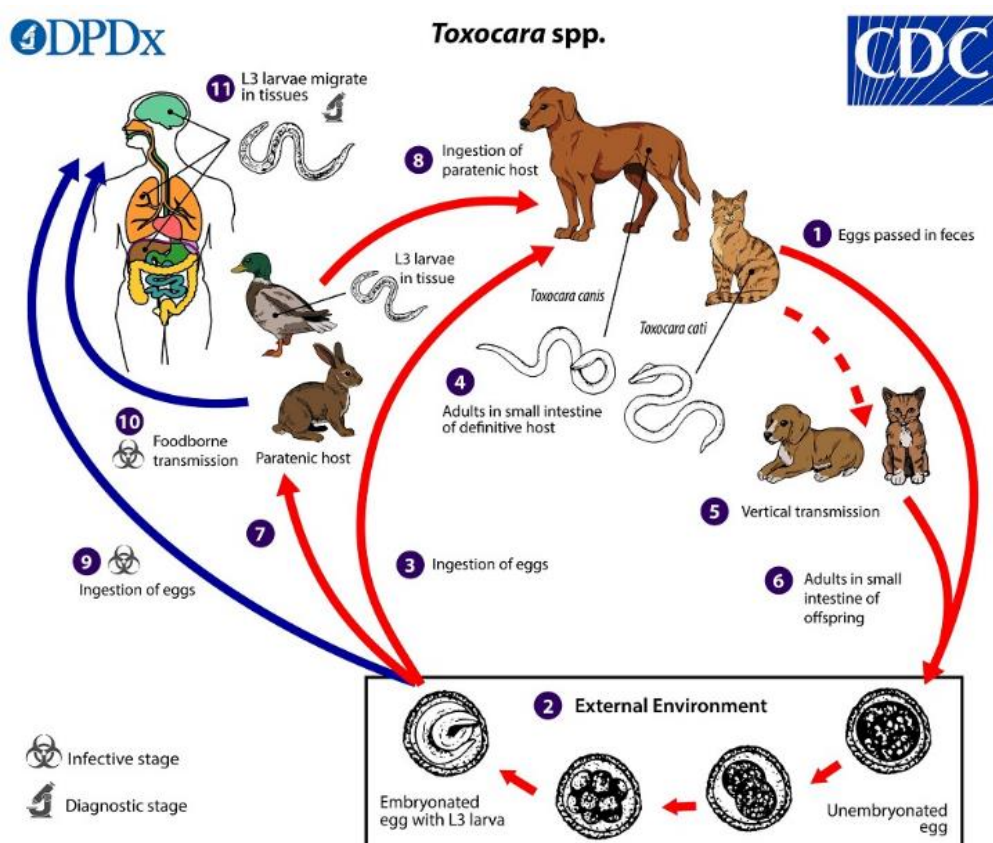


Figure 8. Life cycle of toxocariasis showing a complex interplay between multiple intermediate hosts and humans as the definitive host who get infected from consumption of poorly prepared animal food [25].

Humans become infected by ingesting raw vegetables or undercooked vegetables or animal gizzard harboring the larvae of the parasite [1]. The occult, visceral larva migrans and ocular forms of the disease have been described [26]. CNS involvement may manifest as epilepsy, optic neuritis, eosinophilic meningitis, meningomyelitis and meningoradiculitis [27]. Migration of the larvae to the eyes may predispose affected individuals to having ocular larva migrans which could manifest as inflammation of the eyes and consequent visual disturbances. Medical treatment involves the use of anthelmintics albendazole and mebendazole and multidisciplinary care is implicated in management of complications of the disease [21].

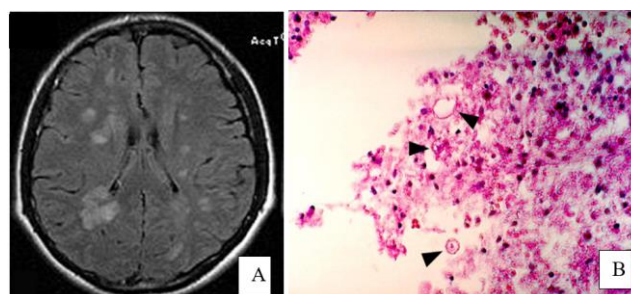


Figure 9. (A) Brain CT scan image of a patient with toxocariasis showing multiple bilateral hyperdense lesions in the periventricular and subcortical regions with biventricular effacement [28]. (B) Histology slide with arrows showing larva of *Toxocara spp.* in the brain with surrounding layer of inflammatory cells [21].

2.5. Strongyloidiasis

Strongyloidiasis is a helminthic parasitic infestation predominant in humid tropical areas. It is caused by *Strongyloides stercoralis*. It is estimated that 30-100 million individuals worldwide are infected with the parasite [29] with a prevalence of 0-3.8% in the United States of America [30] and 19.72% noted in Africa according to molecular surveys. [31].

The complex life cycle of the parasite involves an interplay between free living and parasitic forms. Humans get infected through skin contact with contaminated soil harboring the

filariform larvae of the parasite which penetrate the skin and migrate to the lungs of the affected individual. Autoinfection occurs when the parasite is coughed up and eventually swallowed. Systemic spread through the enterohepatic circulation creates a potential pathway for CNS involvement [32]. The parasite triggers the innate and active immune response with activation of T-regulatory cells which modulate the immune response by elaboration of inhibitory cytokines through cell to cell contact thereby ameliorating tissue damage from neuroinflammation induced by the parasite [33].

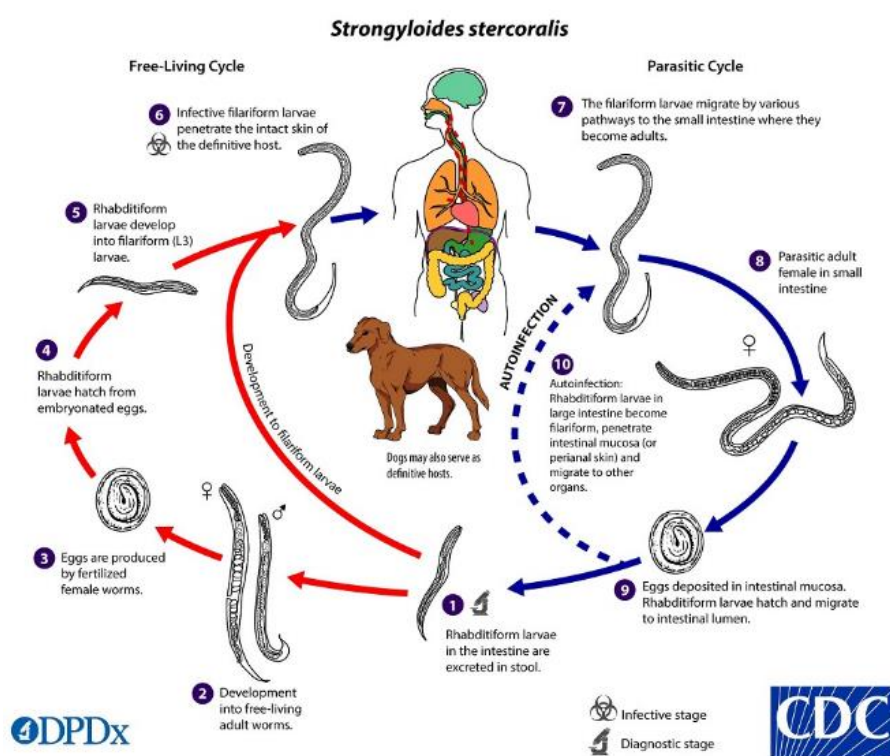


Figure 10. Life cycle of *Strongyloides stercoralis* showing an interconnection between the parasitic and free living forms of the parasite [34].

Dissemination to the CNS clinically manifests with features of aseptic meningitis with CSF spinal tap analysis yielding gram negative organisms [35]. It has been associated with factors that may compromise host immunity such as

chemotherapy, corticosteroid administration and malignant conditions. This portends a poor prognosis with attendant significant morbidity and mortality [21].

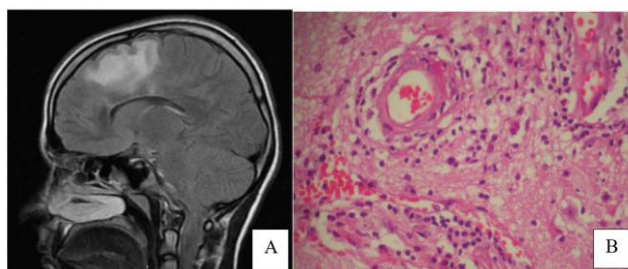


Figure 11. (A) MRI FLAIR image of a 13 year old female patient showing a hyperintense lesion in the frontal lobe anterior to the Rolandic sulcus with an irregular hyperintense rim of perilesional edema (B) Histopathology slide of a resected specimen from the lesion showing vasculitis with surrounding eosinophilic cells and macrophages [36].

Diagnosis of strongyloidiasis is made by isolation of the larvae of the parasite in stool samples or resected tissue specimen. Serologic tests are widely available however, sensitivity have been observed to be reduced in cases of hematologic malignant conditions and HTLV-1 infection [37].

Varying dosage regimen of ivermectin therapy has been the drug treatment of choice. It has been shown to have a tolerable side effect profile, good patient compliance outcome and better parasite clearance rate when compared to albendazole [38].

2.6. Neurotrichinellosis

The aetiopathologic agent of this zoonotic infestation which affects individuals who consume poorly cooked infected livestock is *Trichinella* spp. Humans contract the disease by ingesting undercooked pork or animal meat with the muscles of such animals harboring the encysted larvae of the parasite [39]. Variants of the parasite noted to cause human infection include *T. pseudospiralis*, *T. papuae*, *T. murelli*, *T. nativa*, *T. britovi*, *T. nelsoni*, *T. spiralis* [39], with the latter being implicated in Neurotrichinellosis [40].

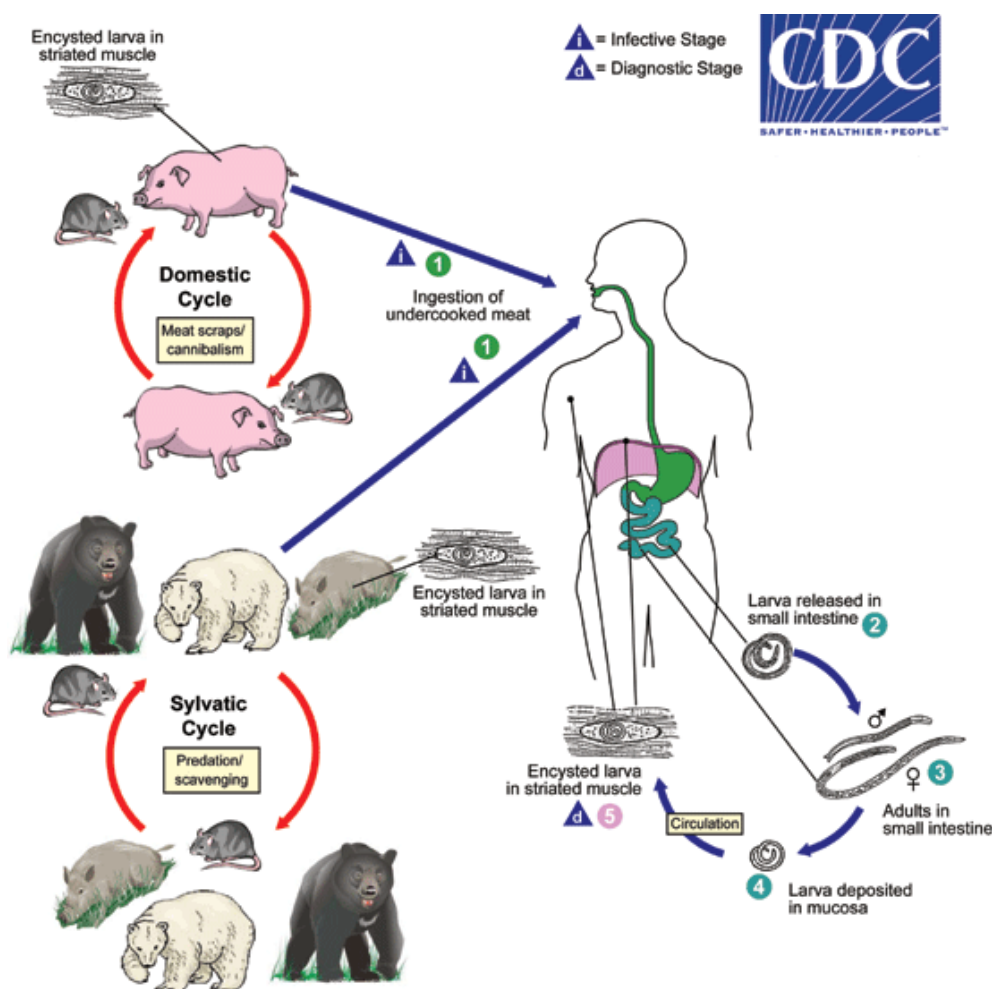


Figure 12. Life cycle of *Trichinella* spp. Humans contract the disease by consumption of undercooked animals [39].

CNS involvement which occurs in 10-15% of reported cases [41] arises as a result of elaboration of cytokines and pro-inflammatory mediators inducing macrophage and eosinophil migration to help wall off the larvae of the parasite [40, 41] and affected individuals present with symptoms such as headache, somnolence, disorientation, cranial neuropathies, myelitis, encephalitis and meningitis [40]. The pathogenesis of neural invasion includes occlusion of cerebral arteries by

cysts, larvae and granuloma with consequent vasculitis and thrombotic obliteration of the vessels, reactive granuloma formation and atopy. [40, 41].

Affected individuals often demonstrate laboratory evidence of hyper eosinophilia with serological tests such as western blot and Enzyme Linked Immunosorbent Assay (ELISA) being useful in detecting antibodies to the parasite antigen [42].

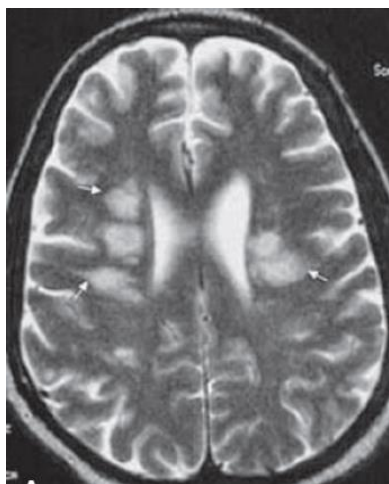


Figure 13. Axial T2 weighted image of a patient with neurotriinellosis showing multiple bilateral subcortical hyperintense lesions with minimal rim of perilesional edema [43].

Neuroimaging modality and CSF analysis are useful in depicting multiple focal ischemic lesions and elevated protein levels with pleocytosis respectively. The anti-inflammatory property of steroids is valuable in addition to the antihelminthic drugs albendazole and mebendazole in the treatment of the condition [40].

3. Filariasis

This is a compound group of parasitic infestations caused by *Wuchereria bancrofti*, *Brugia malayi*, *Brugia timori* transmitted by the bites of mosquitoes. The blackfly is the principal vector for *Onchocerca volvulus* [21]. About 120 million are infected with the disease with an endemicity in about 80 countries [44]. Another literature has documented that 37 million people are hosts to *Onchocerca volvulus* of which 99% of this population resident in Africa [45].

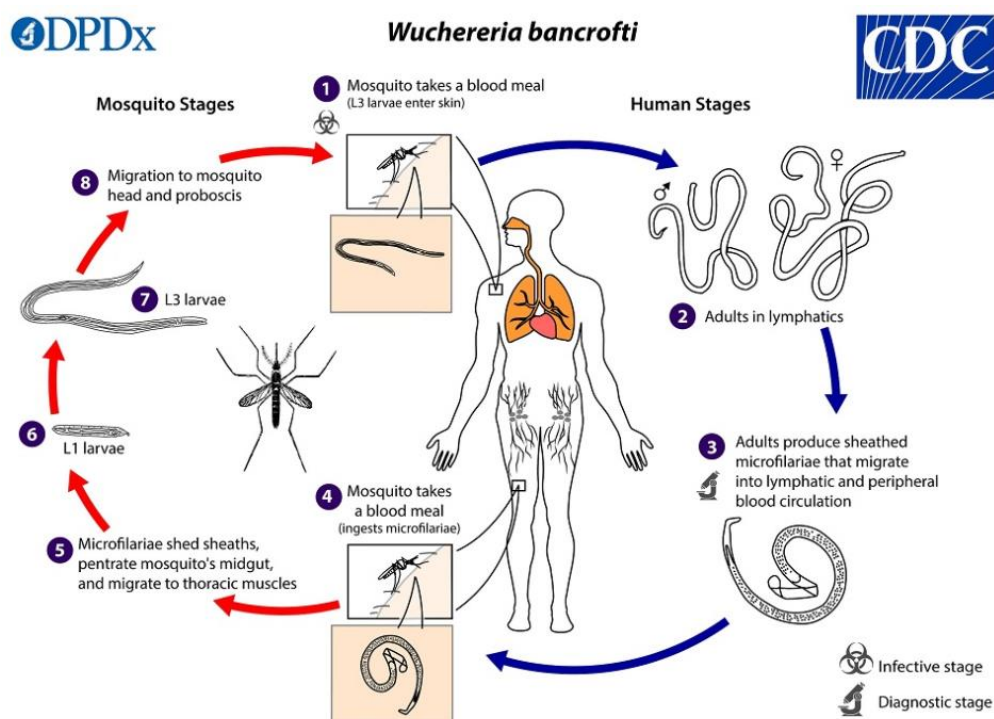


Figure 14. Life Cycle of the filarial infestation, *Wuchereria bancrofti* [46].

Factors that determine neurological manifestations include host immune response, virulence invasion factors and size of the parasite [44]. Histopathological findings include leptomeningeal congestion, thrombosis, cerebral edema, intracerebral hemorrhage, necrosis, neovascularity, perivascular inflammatory cells infiltrate, gliosis and granuloma formation [47].

Nodding syndrome, a juvenile onset epileptic disorder characterised by repetitive 5-20 head nods per minute as a

result of transient recurrent episodes of loss tone in the neck extensor muscles, has shown association with onchocerciasis; the latter having a potential for propagating similar neuroinflammatory mechanisms implicated in the pathogenesis of the syndrome [48].

Diagnosis involves isolation of the parasite microfilaria in blood samples. Diethylcarbamazine and Ivermectin are drugs of choice in treating the pathology [49].

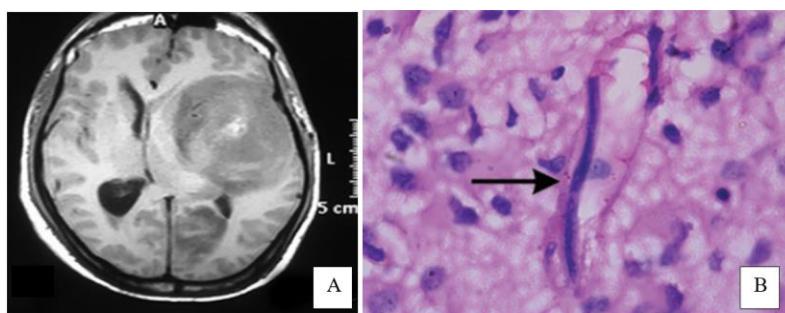


Figure 15. (A) Axial T1 MRI of a 27 year old male with neurofilariasis showing a concentric shaped mixed intensity lesion in the left cerebral hemisphere abutting on the basal ganglia, obliterating the left ventricle with periventricular hyperintense lesions (B) Histopathology slide with arrow showing microfilariae within a cerebral capillary in a background of reactive gemistocyte and inflammatory cells with widening of the Virchow Robin spaces [44].

4. Protozoan Infestations

4.1. Toxoplasmosis

This is an infestation that has a high rate of morbidity and mortality in immunocompromised individuals. It is a zoonotic infestation, found in 10-34% of all AIDS autopsies [1] and transmitted by toxoplasma gondii which cats are the definitive

host of the parasite [50]. It is reported that worldwide about 6 billion people have contracted the disease [50], with a 23.9% seroprevalence rate documented in Nigeria [51], 46% and 12.3% in Tanzania and China respectively [52, 53]. A 66-year retrospective review in Nigeria documented a human seroprevalence rate of 32% with subgroup analysis indicating that the southwest and northwest parts of the country had the highest rates of 37% and 32% respectively [54].

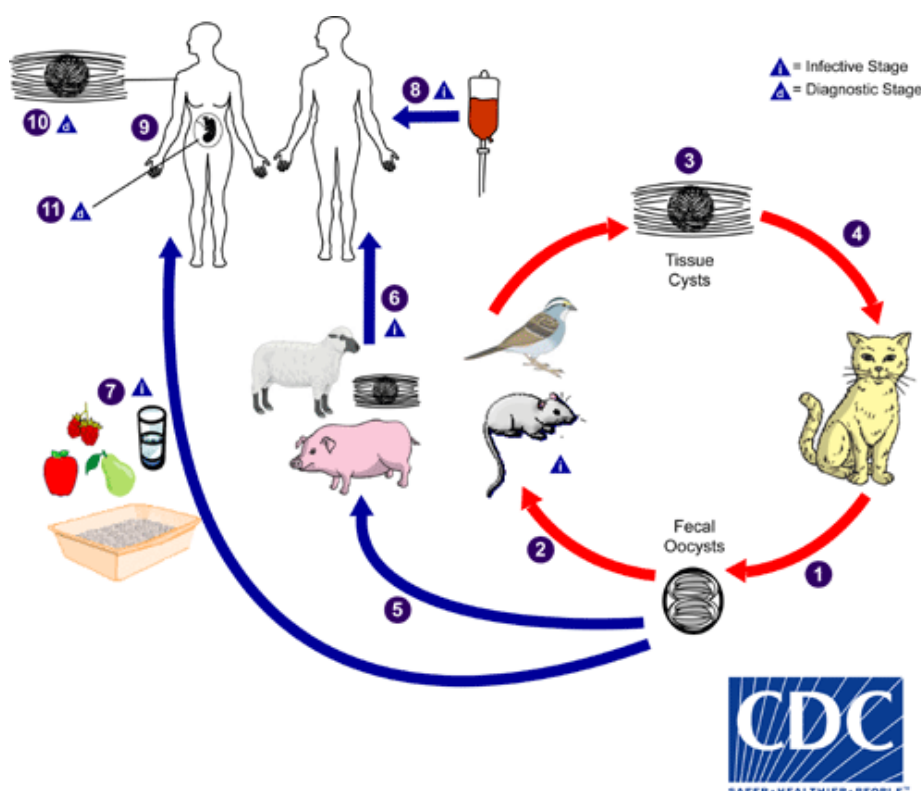


Figure 16. Life Cycle of *Toxoplasma gondii*. [55].

Variety of ways in which human infestation could occur includes consumption of poorly cooked meat of animals with

the cysts of the parasite or foods and water contaminated with feline feces including disposing contents of pet cat litter box.

Organ transplantation, blood transfusion and vertical transmission from an infected mother to her fetus are other ways the parasite infects humans [55].

Pathogenic mechanism of CNS invasion includes elaboration of pro-inflammatory cytokines, denudation of blood brain barrier through which migration of tachyzoites occurs culminating in cyst formation in the brain parenchyma [1, 56]. Reactive of latent infection in AIDS patient usually occurs when CD4 cells count is < 100 cells/ μ L [1]. Regions of

predilection in cerebral spread include the thalamus, basal ganglia, corpus callosum, corticomedullary junction and brainstem. The acapsular lesions usually has a central zone of coagulative necrosis, a peripheral rim of encysted parasites with a hypervascular granulomatous inflammatory layer of cells interposed between them. These parenchymal involvement may exist either as solitary or multiple lesions with 15% and 85% incidence respectively [57-59].

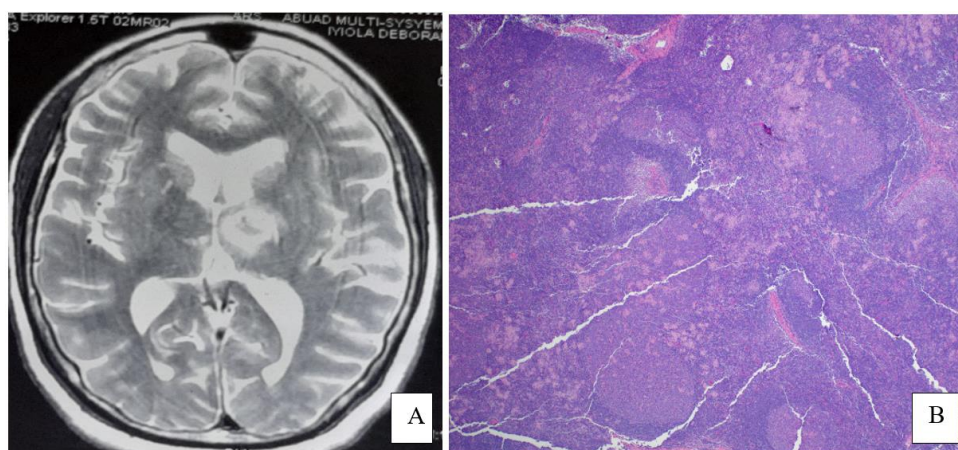


Figure 17. (A) Axial contrast MRI of a patient with Cerebral toxoplasmosis showing bi-thalamic concentric shaped lesions abutting on the wall of the 3rd ventricle. The left lesion is contrast enhancing. (B) Histopathology slides of cerebral toxoplasmosis showing the classic triad of interfollicular and perfollicular epithelioid histocytes with patches of B-lymphocytes in a background of reactive germinal regions.

Clinical manifestation includes headaches, focal neurological deficits, seizures or cranial neuropathies. MRI T2 FLAIR sequence may reveal a target sign with a central necrotic area, an intermediate hypointense rim of inflammatory cells and a peripheral hyperintense zone of vasogenic edema [58, 59].

Diagnosis of the condition includes immunologic measurement of IgM and IgG response to the parasite antigen. IgM which appears first transiently following an acute infection has a variable specificity. IgG usually peaks within 30-60 days and consequently has a lifelong persistence. Isolation of the parasite DNA using polymerase chain reaction from resected brain specimen or cerebrospinal fluid. Histopathology analysis of such samples is also a viable diagnostic tool [60].

Primary preventive measures such as regular hand washing after gardening or handling cats, hygienic storage and preparation of fruits and vegetable, avoidance of consumption of undercooked livestock meals are valid [61].

Sulfadiazine and pyrimethamine supplemented with folinic acid are treatment options. It has been advocated that prophylaxis using trimethoprim sulfamethoxazole should be commenced in patients with CD4 counts < 100 cells/ μ L to prevent recurrence of latent infection [62].

4.2. Amoebiasis

This is a spectrum of diseases caused by *Entamoeba histolytica* responsible for amoebic liver abscess and brain abscess, *Naegleria fowleri* and *Acanthamoeba spp* which are aetiological agents for primary amoebic meningoencephalitis and granulomatous amoebic encephalitis respectively [1].

Epidemiologic studies on *Entamoeba histolytica* have indicated an overall prevalence of 11.2% in southwest Nigeria [63], 4.8% prevalence for males and 4.1% for females in south eastern Nigeria [64].

Granulomatous amoebic encephalitis occurs commonly in immunocompromised and debilitated patients who present with a long course of neurologic deficits and meningeal irritation. Neuroimaging features include solitary or multiple parenchymal lesions in the diencephalon, thalamus and posterior fossa with inflammation of the meninges, underlying cerebral cortex and associated cerebral edema [65]. *Acanthamoeba castellanii*, *Acanthamoeba polyphaga* and *Balamuthia mandrillaris* have been implicated in the aetiopathogenesis of this condition [47].

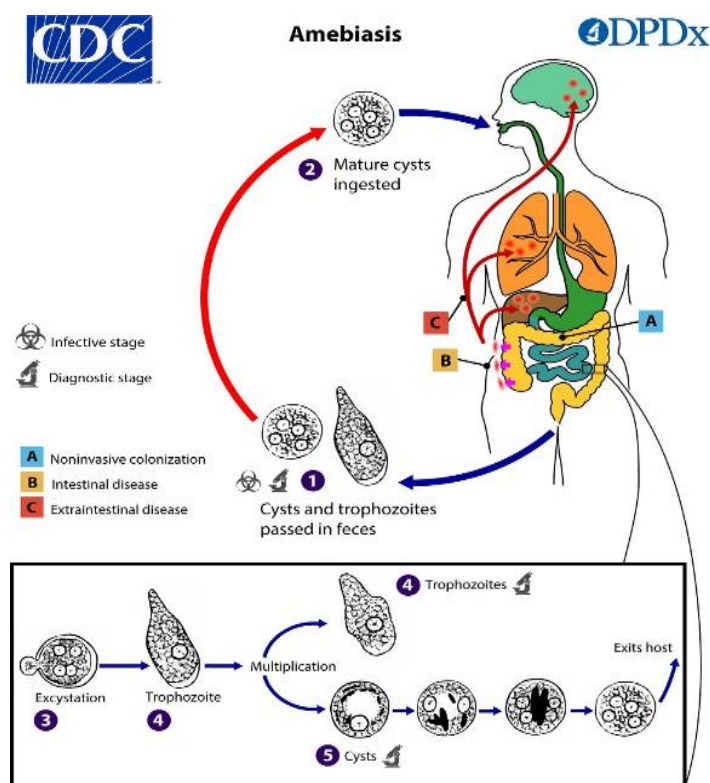


Figure 18. Life cycle of amebiasis depicting human transmission occurs from ingestion of mature cyst through various media including contaminated water and food [66].

Primary amoebic meningoencephalitis caused by *Naegleria fowleri* usually affects young adults and children who present with acute onset of symptoms. The pathogen gains entry into the cranial cavity through the olfactory tract when individuals come into contact with contaminated water or dust particles harboring the parasite. Neuroimaging may reveal meningeal vessel congestion, basilar exudates and obliteration with cerebral edema [65].

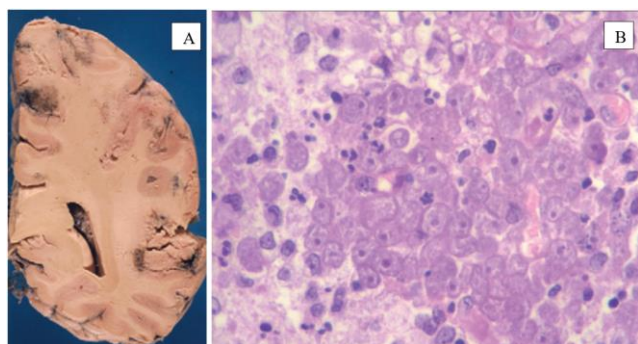


Figure 19. (A) Gross specimen showing the left half of the coronal section of a brain with granulomatous amebic encephalitis showing multiple petechial hemorrhagic nodules with adjacent areas of tissue necrosis in the subcortical white matter and cerebral cortex (B) Histopathologic slide showing granulomatous amebic encephalitis caused by *Balamuthia mandrillaris*. There is marked eosinophilia around the trophozoites of the parasite with a prominent large lymphocyte in the background. [47].

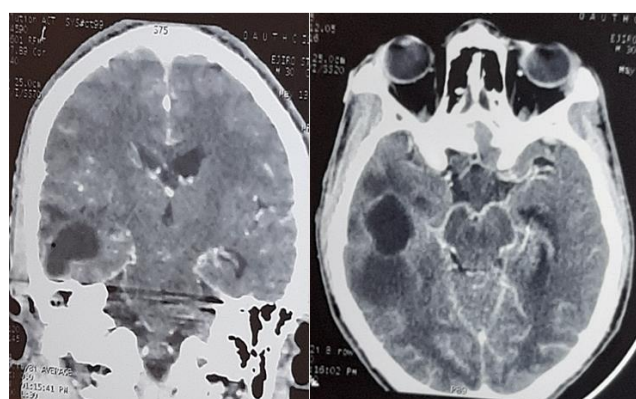


Figure 20. Contrast enhanced coronal and axial CT scan images of a patient with right temporal lobe amebic brain abscess showing an irregular shaped hypointense lesion with mild perilesional edema and encephalomalacia of surrounding brain tissue.

Entamoeba histolytica is the causative agent responsible for amoebic brain abscess which has been noted to occur concomitantly in 0.66-4.7% of patients with amoebic liver abscess. Affected individuals manifest clinical signs of meningeal irritation, motor paralysis, seizure and cranial nerve palsy [67].

Hematogenous spread of trophozoites from the intestine through the enterohepatic circulation to the brain, adherence to endothelial cells and subsequent infiltration through the blood brain barrier provides an access for the trophozoites into the brain [68]. Reactive tissue inflammation and necrosis usually accompany such pathogenic process culminating in clinical manifesta-

tions such as fever, neurologic deficits, seizures and severe headache [69].

Diagnosis of the condition implores the use of a multimodal approach comprising of detailed clinical evaluation with a high index of suspicion, neuroimaging modalities and isolation of the parasite trophozoites in surgically drained abscess or biopsied tissue specimen [68].

4.3. Cerebral Malaria

This is a severe clinical manifestation of *Plasmodium falciparum* infestation transmitted to humans by the bite of the female *Anopheles* mosquito in which parasitized red blood cells in the cerebral micro vessels induce endothelial injury with consequent inflammation and blood brain barrier disruption [70].

It accounted for 19.7% of complications of severe malaria [71] and 45.5% of mortality in a 4-year retrospective autopsy review with the age group 1-5 years recording the highest mortality rates. Notable risk factors among others included pediatric age group, immigrant status and pregnancy [72].

The pathophysiologic mechanism of the disease involves a sequestration of red blood cells containing ring trophozoites of the parasite within the microvasculature of the brain which triggers the activation of endothelial cells and release of chemokines, cell adhesion molecules and pro-inflammatory cytokines, these elaborate the recruitment of T-cells and giant cells to the affected brain tissue thereby accentuating the host immune response with consequent endothelial disruption. These compromises the integrity of the blood brain barrier leading to cerebral edema and attendant raised intracranial pressure [73, 74].

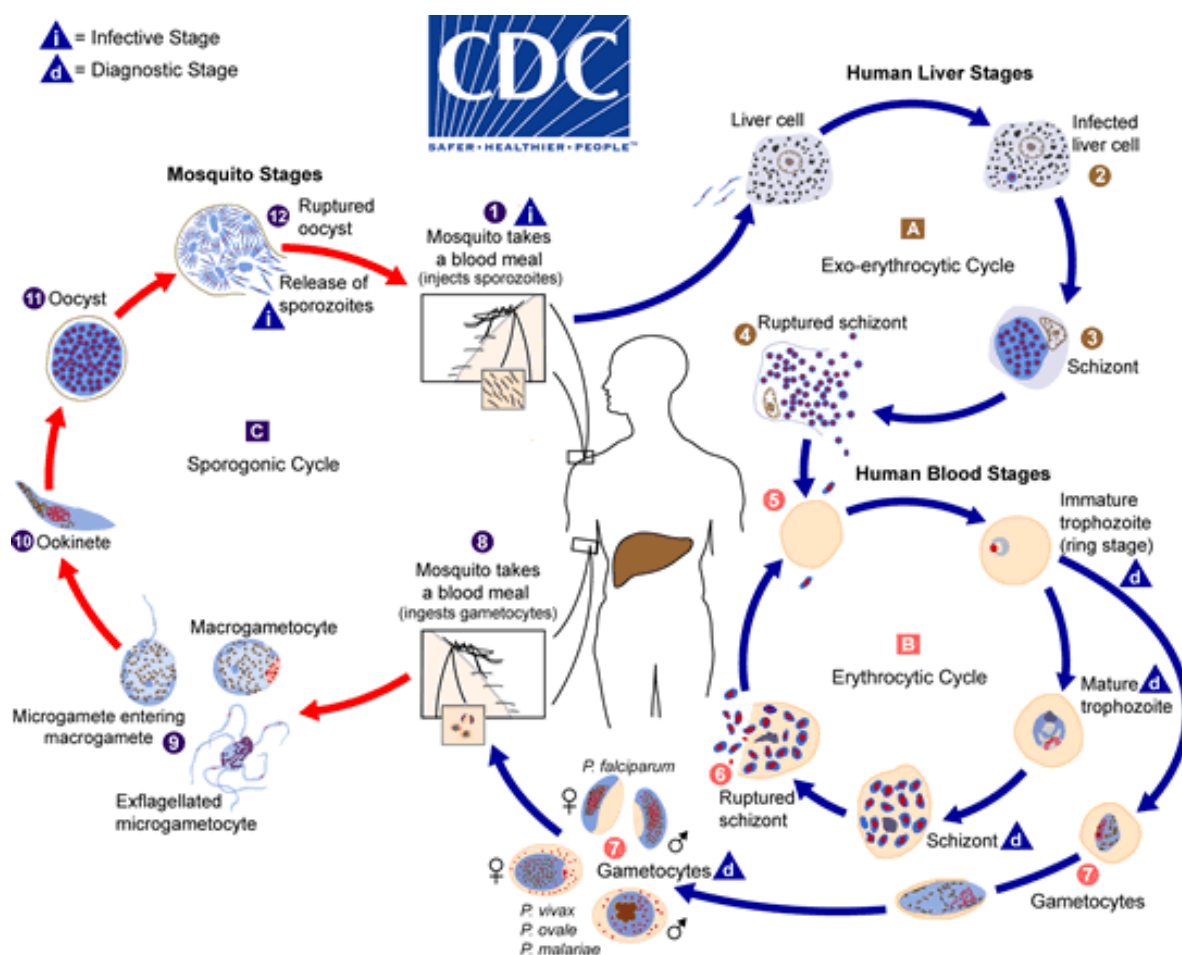


Figure 21. Life cycle of Plasmodiosis [75].

Susceptibility weighted sequence of MRI, done in the acute stage may reveal areas of petechial hemorrhages

which are a result of microthrombi formation in the cerebral microvasculature [76].

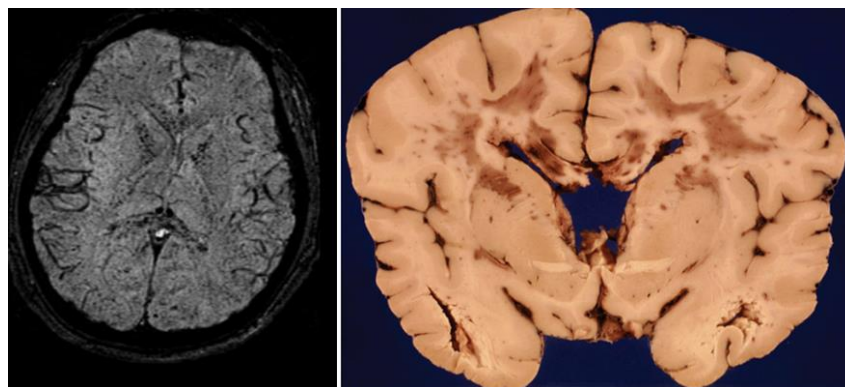


Figure 22. Cerebral malaria (A) Axial view of susceptibility weighted MRI sequence showing multiple areas of petechial hemorrhages noted at the corpus callosum, internal capsule and grey white matter junction.⁷⁶ (B) Coronal view of gross brain specimen with cerebral malaria showing areas of multiple petechial hemorrhages involving the cerebral white matter, internal capsule and corpus callosum with flattening of the gyri [47].

Macroscopic evaluation of gross brain specimen usually reveals leptomeningeal congestion, flattening of the gyri, obliteration of the ventricles and increased brain weight from cerebral edema; other findings include petechial hemorrhage in the brain stem, cerebellum, cerebral white matter and corpus callosum [47].

Common microscopic findings include congestion of the capillaries with sequestration of parasitized red blood cells within them leading to necrosis of the blood vessels surrounded by a rim of gliosis, infected red blood cells and hemozoin pigmentation [47].

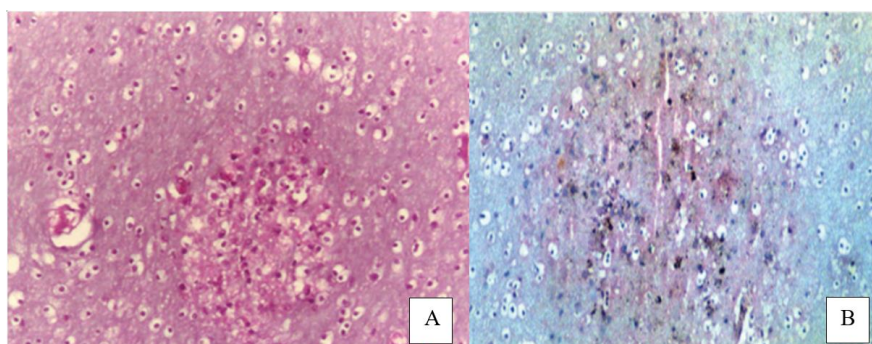


Figure 23. Histopathology slides in cerebral malaria. (A) Durck granuloma which is a collection of brain microglial cells around a capillary containing parasitized red blood cells. (B) Hemozoin pigment, a crystalline brownish discoloration due to iron-porphyrin complex derived from anaerobic metabolism of glucose and hemoglobin breakdown by plasmodium parasites in the red blood cells. [47].

The case definition for post malaria neurologic syndrome have been documented which comprises of acute confusional state, generalized tonic clonic seizures and tremors have been documented in 22 patients following treatment for malaria with a median symptom free interval of 96hrs, associated with mefloquine treatment with a median onset interval of 84hrs and affected patients having negative blood smears for malaria parasite as at the time of symptom manifestation [77]. It has also been reported in patients treated with quinine and artemisinin derivatives with laboratory findings of elevated CSF protein and lymphocytic meningitis [78].

4.4. Trypanosomiasis

This is a compound protozoan infestation made up of the American trypanosomiasis (Chagas disease) caused by *Trypanosoma cruzi* and Human African trypanosomiasis (sleeping sickness) caused by *Trypanosoma brucei rhodesiense* and *Trypanosoma brucei gambiense* [47]. Chagas disease is endemic in about 21 countries of Latin America with a global prevalence of 6-7 million individuals with a decreased global prevalence and Disability Adjusted Life-years of 11.3% and 23.7% respectively [79].

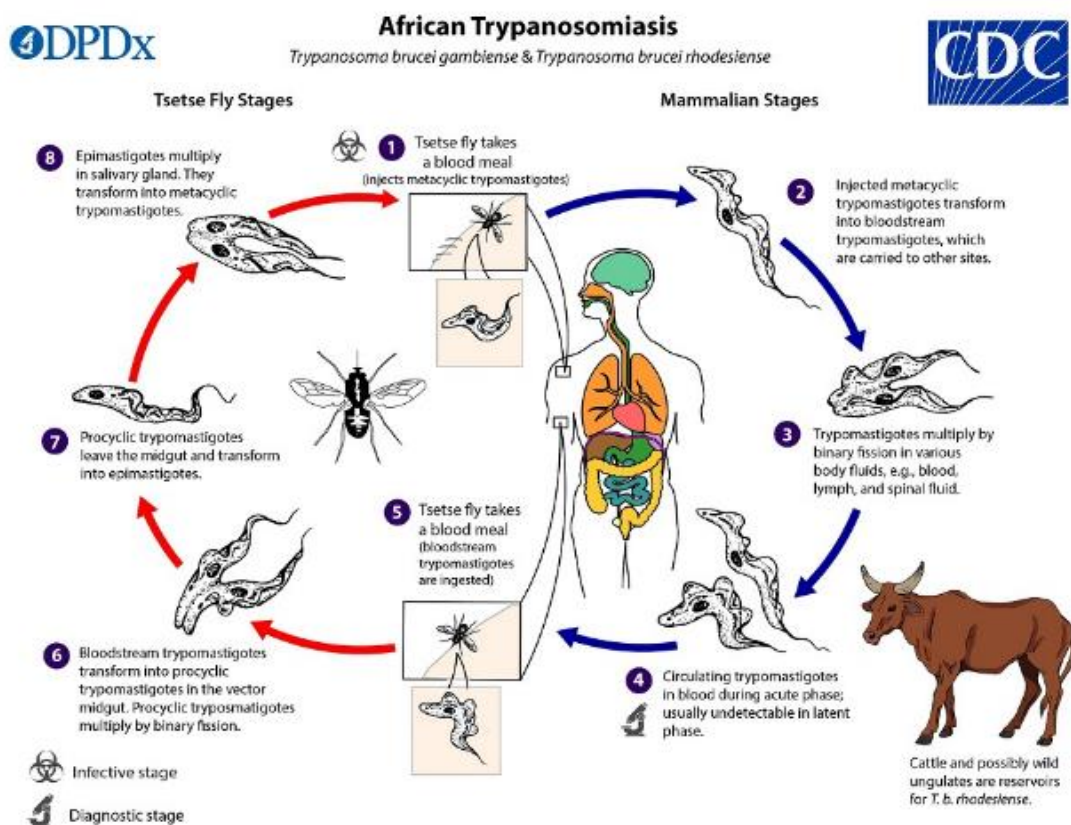


Figure 24. Life cycle of African trypanosomiasis [80].

Humans contract *T. cruzi* when bitten by the triatomine bugs; other means of transmission include mother to child, organ transplantation and consumption of food containing the parasite ova [79]. Following invasion into the body, they rupture blood cells containing them thereby producing a local zone of inflammation which elicits the release of inflammatory mediators, interleukins, CD4 T-cells and CD8 T-cells. Gross pathologic findings on the cerebral cortex of affected patients include capillary congestion, multiple petechial hemorrhages and cerebral edema [81]. Histopathologic microscopic analysis may reveal areas of necrosis and hemorrhage with clumps of microglia, macrophages, neutrophils and astrocytes arranged in a poorly differentiated nodular pattern with perivascular infiltrate of lymphocytic cells usually located in the cerebral cortical white matter, cerebellum and brainstem. Vascular infarcts are usually located in the middle cerebral artery territory and the amastigote form of the parasite may be delineated by in situ hybridization, polymerase chain reaction and immunohistochemistry [81-83].

The parasites responsible for African trypanosomiasis gain entry into the brain parenchyma by spread either through the cerebral capillary architecture or through the choroid plexus with subsequent leptomeningeal involvement [85]. Histopathologically, the disease manifest macroscopically as engorged meninges and cerebral edema, microscopically features of meningoencephalitis in the hypothalamus, thalamus, brainstem, cerebellum, basal ganglia and cerebral

subcortical white matter may be seen [81, 86]. Peculiar features on histopathology include presence of mudberry like cells or mott cells with eosinophilic cytoplasmic inclusions called Russell body which are representative of residual IgM type immunoglobulins; other features that may be seen are consistent with astrocyte proliferation, microglial nodules formation and hyperplasia of microglial cells [47].

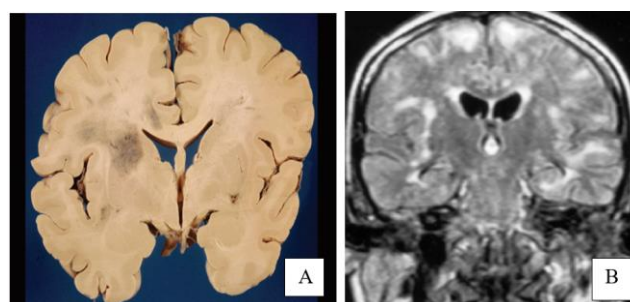


Figure 25. (A) Coronal section of a gross brain specimen of a patient who had Chagas disease showing necrotic hemorrhagic area involving the right cerebral white cortical matter and the basal ganglia with anterior limb and genu of the right internal capsule [47]. (B) Coronal section of T2 FLAIR image of a 52 year old female patient with cerebral Chagas disease showing multiple areas of hyperintense lesions along the sylvian fissures, parafalcine regions and cerebral convexities. [84].

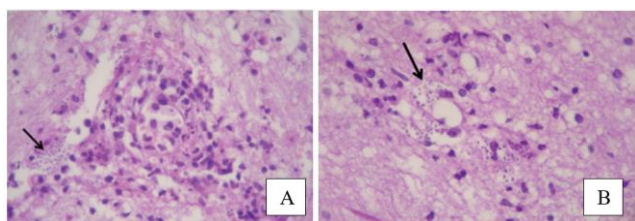


Figure 26. Hematoxylin-eosin staining of a resected brain specimen of a patient with Chagas encephalitis in low power (A) and high power (B) magnification with an arrow showing amastigote nest in a background of perivascular aggregate of eosinophils and lymphocytes. [47].

5. Discussion

Parasitic infestations of the central nervous system is a problem of public health concern associated with significant morbidity and mortality. These conditions often present with non specific symptoms thereby creating a diagnostic dilemma [49]. Irrespective of having a high index of clinical suspicion, the paucity of specific diagnostic tools leads to missed diagnosis and presents an impediment to diagnosis and intervention [41]. Immunocompromised patients are at risk of developing these conditions; other favourable risk factors being mass migration from endemic to non endemic regions thereby triggering new outbreaks and climate change that may help the vectors thrive better thereby promoting the spread of these infestations [56, 60, 62]. The zoonotic transmission of most of these diseases implies for a collaborative effort between medical and veterinary personnel to adopt a holistic approach that takes into cognizance human-animal interactions with an understanding of the life cycles and routes of transmission of these parasites so as to effectively mitigate the incidence of infestation [51-53].

Strategies to curb the incidence of these infestations include active surveillance to determine clusters and favourable risk factors for spread, public enlightenment on preventive measures, health education to both the public and clinicians to enable them promptly recognise pertinent clinical features and adopt a timely intervention. Government policies aimed at poverty alleviation programs, providing accurate diagnostic instruments, human and capital development in the health sector in terms of personnel training can help control the prevalence of these conditions [87-89].

To improve the prognosis of patients with these conditions and its overall impact in the society involves adoption of measures such as developing accurate diagnostic tools which are user friendly, introduction of vaccines and optimal preventive strategies, augmenting methods for detecting of cognitive, psychiatric and neurologic sequelae, advanced research methods to broaden knowledge and understanding of the patho-mechanisms of these diseases with the potential of developing vaccines for their prevention, enhanced multidisciplinary approach with improved rehabilitation techniques for patients with neuro-cognitive sequelae. These measures can help resolve some of the myriad of problems

associated with these infestations and improve the prognosis of patients with neuroinfectious diseases [79, 81, 87, 88].

6. Conclusion

CNS parasitic infestations bears a global burden of impact with significant morbidity and mortality for affected patients. Factors that have perpetuated its prevalence includes limitations to diagnostic modalities, paucity of their knowledge, practice and application of preventive measures, as well as transmigration of population demographics across zones of endemicity. It is pertinent to emphasize that a multidisciplinary and multimodal approach with involvement of health, veterinary and environmental personnel is imperative to improve surveillance and create public awareness on these conditions. Favorable government policies are also advocated to boost efforts aimed at ameliorating the noxious effects of these conditions on public health.

Abbreviations

TNF	Tumor Necrosis Factor
CNS	Central Nervous System
FLAIR	Fluid-Attenuated Inversion Recovery
ELISA	Enzyme Linked Immunosorbent Assay
AIDS	Acquired Immune Deficiency Syndrome
HTLV-1	Human T-Lymphotropic Virus Type 1
MRI	Magnetic Resonance Image

Author Contributions

Kelechi Michael Azode: Conceptualization, Data curation, Formal Analysis, Supervision, Validation, Writing – original draft, Writing – review & editing

Ese Enaorho Ewoye: Formal Analysis, Investigation, Resources

Chigozie Chidozie Okongwu: Formal Analysis, Investigation, Resources

Conflicts of Interest

The authors declare no conflicts of interest.

References

- [1] Abdel Razek AA, Watcharakorn A, Castillo M. Parasitic diseases of the central nervous system. *Neuroimaging Clin N Am*. 2011 Nov; 21(4): 815-41, viii. <https://doi.org/10.1016/j.nic.2011.07.005> Epub 2011 Sep 3.
- [2] Idro R, Ogwang R, Barragan A, Raimondo JV, Masocha W. Neuroimmunology of Common Parasitic Infections in Africa. *Front Immunol*. 2022 Feb 10; 13: 791488. <https://doi.org/10.3389/fimmu.2022.791488>

- [3] Winkler AS. Neurocysticercosis in sub-Saharan Africa: a review of prevalence, clinical characteristics, diagnosis, and management. *Pathog Glob Health*. 2012 Sep; 106(5): 261-74. <https://doi.org/10.1179/204773212Y.0000000047>
- [4] Ndimubanzi PC, Carabin H, Budke CM, et al. A systematic review of the frequency of neurocysticercosis with a focus on people with epilepsy. *PLoS Negl Trop Dis* 2010; 4(11): e870. <https://doi.org/10.1371/journal.pntd.0000870>
- [5] Center for Disease Control. DPDx Laboratory Identification of Parasites of Public Health Concern. Taeniasis: <https://www.cdc.gov/dpdx/taeniasis/index.html>
- [6] Coyle CM. Neurocysticercosis: an update. *Curr Infect Dis Rep*. 2014 Nov; 16(11): 437. <https://doi.org/10.1007/s11908-014-0437-6>
- [7] Montano SM, Villaran MV, Ylquimiche L, et al. Neurocysticercosis: association between seizures, serology, and brain CT in rural Peru. *Neurol*. 2005; 65: 229-33.
- [8] Fleury A, Carrillo-Mezo R, Flisser A, Sciotto E, Corona T. Subarachnoid basal neurocysticercosis: a focus on the most severe form of the disease. *Expert Rev Anti-Infect Ther*. 2011; 9: 123-33.
- [9] Cuether AC, Andrews RJ. Intraventricular neurocysticercosis: 18 consecutive patients and review of the literature. *Neurosurg Focus*. 2002; 12: e5.
- [10] Alsina GA, Johnson JP, McBride DQ, Rhoten PR, Mehringer CM, Stokes JK. Spinal neurocysticercosis. *Neurosurg Focus*. 2002; 12: e8.
- [11] Del Brutto OH. Neurocysticercosis. *Handb Clin Neurol*. 2014; 121: 1445-59. <https://doi.org/10.1016/B978-0-7020-4088-7.00097-3>.
- [12] Del Brutto OH. Human Neurocysticercosis: An Overview. *Pathogens*. 2022 Oct 20; 11(10): 1212. <https://doi.org/10.3390/pathogens11101212>
- [13] Siyadatpanah A, Brunetti E, Emami Zeydi A, Moghadam YD, Agudelo Higuera NI. Cerebral Cystic Echinococcosis. *Case Rep Infect Dis*. 2020 Feb 29; 2020: 1754231. <https://doi.org/10.1155/2020/1754231>.
- [14] El Saqui A, Aggouri M, Benzagmout M, Chakour K, El Faiz Chaoui M. Cerebral hydatid cysts in children: about 15 cases. *Pan Afr Med J*. 2017 Apr 13; 26: 205. French. <https://doi.org/10.11604/pamj.2017.26.205.8398>
- [15] Karshima, S. N., Ahmed, M. I., Adamu, N. B. et al. Africa-wide meta-analysis on the prevalence and distribution of human cystic echinococcosis and canine *Echinococcus granulosus* infections. *Parasites Vectors* 15, 357 (2022). <https://doi.org/10.1186/s13071-022>
- [16] Center for Disease Control. DPDx Laboratory Identification of Parasites of Public Health Concern. Echinococcosis : <https://www.cdc.gov/dpdx/echinococcosis/index.html#>
- [17] Demir MK, Yapıcıer Ö, Jameel MA, Bozbuğa M. Cerebral hydatid disease with serpent sign, calcifications, and peripheral enhancement. *Acta Neurol Belg*. 2020 Oct; 120(5): 1173-1175. <https://doi.org/10.1007/s13760-019-01104-8> Epub 2019 Feb 28.
- [18] Carod Artal, F. J. Cerebral and spinal schistosomiasis. *Curr. Neurol. Neurosci. Rep*. 2012, 12, 666-674.
- [19] John, C. C.; Carabin, H.; Montano, S. M.; Bangirana, P.; Zunt, J. R.; Peterson, P. K. Global research priorities for infections that affect the nervous system. *Nature* 2015, 527, S178-S186.
- [20] Center for Disease Control. DPDx Laboratory Identification of Parasites of Public Health Concern. Schistosomiasis. <https://www.cdc.gov/dpdx/schistosomiasis/index.html>
- [21] Tunali V, Korkmaz M. Emerging and Re-Emerging Parasitic Infections of the Central Nervous System (CNS) in Europe. *Infect Dis Rep*. 2023 Oct 25; 15(6): 679-699. <https://doi.org/10.3390/idr15060062>
- [22] Liu H, Lim CC, Feng X, Yao Z, Chen Y, Sun H, Chen X. MRI in cerebral schistosomiasis: characteristic nodular enhancement in 33 patients. *AJR Am J Roentgenol*. 2008 Aug; 191(2): 582-8. <https://doi.org/10.2214/AJR.07.3139>
- [23] Ma, G.; Holland, C. V.; Wang, T.; Hofmann, A.; Fan, C. K.; Maizels, R. M.; Hotez, P. J.; Gasser, R. B. Human toxocariasis. *Lancet Infect. Dis*. 2018, 18, e14-e24.
- [24] Ajayi OO, Duhlińska DD, Agwale SM, Njoku M. Frequency of human toxocariasis in Jos, Plateau State, Nigeria. *Mem Inst Oswaldo Cruz*. 2000 Mar-Apr; 95(2): 147-9. <https://doi.org/10.1590/S0074-02762000000200002>
- [25] Center for Disease Control. DPDx Laboratory Identification of Parasites of Public Health Concern. Toxocariasis. <https://www.cdc.gov/dpdx/toxocariasis/index.html>
- [26] Xinou E, Lefkopoulou A, Gelagoti M, Drevelegas A, Diakou A, Milonas I, Dimitriadis AS. CT and MR imaging findings in cerebral toxocaral disease. *AJNR Am J Neuroradiol*. 2003 Apr; 24(4): 714-8.
- [27] Duprez TP, Bigaignon G, Delgrange E, Desfontaines P, Hermans M, Vervoort T, Sindic CJ, Buysschaert M. MRI of cervical cord lesions and their resolution in *Toxocara canis* myelopathy. *Neuroradiology*. 1996 Nov; 38(8): 792-5. <https://doi.org/10.1007/s002340050350>
- [28] Dietrich CF, Cretu C, Dong Y. Imaging of toxocariasis. *Adv Parasitol*. 2020; 109: 165-187. <https://doi.org/10.1016/bs.apar.2020.03.001> Epub 2020 Apr 25.
- [29] Centers for Disease Control and Prevention, 2014. Parasites—Strongyloides. Available at: <https://www.cdc.gov/parasites/strongyloides/>
- [30] Lynn MK, Morrissey JA, Conserve DF. Soil-Transmitted Helminths in the USA: a Review of Five Common Parasites and Future Directions for Avenues of Enhanced Epidemiologic Inquiry. *Curr Trop Med Rep*. 2021; 8(1): 32-42. <https://doi.org/10.1007/s40475-020-00221-2> Epub 202.
- [31] Eslahi AV, Badri M, Nahavandi KH, Houshmand E, Dalvand S, Riahi SM, Johkool MG, Asadi N, Hoseini Ahangari SA, Taghipour A, Zibaei M, Khademvatan S. Prevalence of strongyloidiasis in the general population of the world: a systematic review and meta-analysis.

- [32] Woll F, Gotuzzo E, Montes M. Strongyloides stercoralis infection complicating the central nervous system. *Handb Clin Neurol*. 2013; 114: 229-34.
<https://doi.org/10.1016/B978-0-444-53490-3.00017-0>
- [33] Montes M, Sanchez C, Verdonck K, Lake JE, Gonzalez E, Lopez G, Terashima A, Nolan T, Lewis DE, Gotuzzo E, White AC Jr. Regulatory T cell expansion in HTLV-1 and strongyloidiasis co-infection is associated with reduced IL-5 responses to Strongyloides sterc. *Handb Clin Neurol*. 2013; 114: 65-88.
<https://doi.org/10.1016/B978-0-444-53490-3.00005-4>
- [34] Center for Disease Control. DPDx Laboratory Identification of Parasites of Public Health Concern. Strongyloides stercoralis.
<https://www.cdc.gov/dpdx/strongyloidiasis/index.html>
- [35] Jain AK, Agarwal SK, el-Sadr W. Streptococcus bovis bacteremia and meningitis associated with Strongyloides stercoralis colitis in a patient infected with human immunodeficiency virus. *Clin Infect Dis*. 1994 Feb; 18(2): 253-4. <https://doi.org/10.1093/clinids/18.2.253>
- [36] Oktar N, Ozer HM, Demirtas E. Central Nervous System Strongyloides Stercoralis. A Case Report. *Turk Neurosurg*. 2020; 30(5): 776-779.
<https://doi.org/10.5137/1019-5149JTN.22886-18.2>
- [37] Keiser PB, Nutman TB. Strongyloides stercoralis in the Immunocompromised Population. *Clin Microbiol Rev*. 2004 Jan; 17(1): 208-17.
<https://doi.org/10.1128/CMR.17.1.208-217> 2004.
- [38] Datry A, Hilmarisdottir I, Mayorga-Sagastume R, Lyagoubi M, Gaxotte P, Biligui S, Chodakewitz J, Neu D, Danis M, Gentilini M. Treatment of Strongyloides stercoralis infection with ivermectin compared with albendazole: results of an open study of 60 cases.
- [39] Center for Disease Control. DPDx Laboratory Identification of Parasites of Public Health Concern. Trichinellosis.
<https://www.cdc.gov/dpdx/trichinellosis/index.html>
- [40] Bruschi F, Brunetti E, Pozio E. Neurotrichinellosis. *Handb Clin Neurol*. 2013; 114: 243-9.
<https://doi.org/10.1016/B978-0-444-53490-3.00019-4>
- [41] Rosca EC, Tudor R, Cornea A, Simu M. Central Nervous System Involvement in Trichinellosis: A Systematic Review. *Diagnostics (Basel)*. 2021 May 25; 11(6): 945.
<https://doi.org/10.3390/diagnostics11060945>
- [42] Neghina R, Iacobiciu I, Neghina AM, Marincu I. Trichinellosis, another helminthiasis affecting the central nervous system. *Parasitol Int*. 2011 Jun; 60(2): 230.
<https://doi.org/10.1016/j.parint.2011.01.007> Epub 2011 Feb 1.
- [43] Dupouy-Camet, Jean & Bruschi, Fabrizio. Management and diagnosis of human trichinellosis. *FAO/WHO/OIE Guidelines for the Surveillance, Management, Prevention and Control of Trichinellosis*. 2017 : 37-68.
- [44] Shrivastava A, Arora P, Khare A, Goel G, Kapoor N. Central nervous system filariasis masquerading as a glioma: case report. *J Neurosurg*. 2017 Sep; 127(3): 691-693.
<https://doi.org/10.3171/2016.9.JNS161092> Epub 2016 Dec 23.
- [45] Nyagang SM, Cumber SN, Cho JF, Keka EI, Nkfusai CN, Wepngong E, Tsoka-Gwegweni JM, Fokam EB. Prevalence of onchocerciasis, attitudes and practices and the treatment coverage after 15 years of mass drug administration with ivermectin in the Tombel Health D.
- [46] Center for Disease Control. DPDx Laboratory Identification of Parasites of Public Health Concern. Filariasis.
<https://www.cdc.gov/dpdx/lymphaticfilariasis/index.html>
- [47] Pittella JE. Pathology of CNS parasitic infections. *Handb Clin Neurol*. 2013; 114: 65-88.
<https://doi.org/10.1016/B978-0-444-53490-3.00005-4>
- [48] Arndts K, Kegele J, Massarani AS, Ritter M, Wagner T, Pfarr K, Lämmer C, Dörmann P, Peisker H, Menche D, Al-Bahra M, Prazeres da Costa C, Schmutzhard E, Matuja W, Hoerauf A, Layland-Heni LE, Winkler AS. Epilepsy and nodding syndrome in association with an.
- [49] Finsterer J, Auer H. Parasitoses of the human central nervous system. *J Helminthol*. 2013 Sep; 87(3): 257-70.
<https://doi.org/10.1017/S0022149X12000600> Epub 2012 Oct 10.
- [50] Klaren VN, Kijlstra A. Toxoplasmosis, an overview with emphasis on ocular involvement. *Ocul Immunol Inflamm*. 2002; 10: 1-26.
- [51] Kamani J, Mani AU, Egwu GO, Kumshe HA. Seroprevalence of human infection with Toxoplasma gondii and the associated risk factors, in Maiduguri, Borno state, Nigeria. *Ann Trop Med Parasitol*. 2009; 103: 317-21.
- [52] Swai ES, Schoonman L. Seroprevalence of Toxoplasma gondii infection amongst residents of Tanga district in north-east Tanzania. *Tanzan J Health Res*. 2009; 11: 205-9.
- [53] Xiao Y, Yin J, Jiang N, Xiang M, Hao L, Lu H, et al. Seroepidemiology of human Toxoplasma gondii infection in China. *BMC Infect Dis*. 2010; 10: 4.
- [54] Ohiole JA, Isaac C. Toxoplasmosis in Nigeria: the story so far (1950-2016): a review. *Folia Parasitol (Praha)*. 2016 Aug 22; 63: 2016.030. <https://doi.org/10.14411/fp.2016.030>
- [55] Center for Disease Control. DPDx Laboratory Identification of Parasites of Public Health Concern. Toxoplasmosis.
<https://www.cdc.gov/dpdx/toxoplasmosis/index.html>
- [56] Furtado JM, Smith JR, Belfort R Jr, Gattley D, Winthrop KL. Toxoplasmosis: a global threat. *J Glob Infect Dis*. 2011 Jul; 3(3): 281-4. <https://doi.org/10.4103/0974-777X.83536>
- [57] Batra A, Tripathi RP, Gorthi SP. Magnetic resonance evaluation of cerebral toxoplasmosis in patients with the acquired immunodeficiency syndrome. *Acta Radiol*. 2004 Apr; 45(2): 212-21. <https://doi.org/10.1080/02841850410003969>
- [58] Thurnher MM, Donovan Post MJ. Neuroimaging in the brain in HIV-1-infected patients. *Neuroimaging Clin N Am*. 2008 Feb; 18(1): 93-117; viii. <https://doi.org/10.1016/j.nic.2007.12.013>
- [59] Chang L, Cornford ME, Chiang FL, Ernst TM, Sun NC, Miller BL. Radiologic-pathologic correlation. Cerebral toxoplasmosis and lymphoma in AIDS. *AJNR Am J Neuroradiol*. 1995 Sep; 16(8): 1653-63.

- [60] Montoya JG. Laboratory diagnosis of *Toxoplasma gondii* infection and toxoplasmosis. *J Infect Dis.* 2002; 185: S73-82.
- [61] Lopez A, Dietz VJ, Wilson M, Navin TR, Jones JL. Preventing congenital toxoplasmosis. *MMWR Recomm Rep.* 2000; 49: 59-68.
- [62] Luft BJ, Chua A. Central nervous system toxoplasmosis in HIV pathogenesis, diagnosis, and therapy. *Curr Infect Dis Re.* 2000; 2: 358-62.
- [63] Oyerinde JP, Alonge AA, Adegbite-Hollist AF, Ogunbi O. The epidemiology of *Entamoeba histolytica* in a Nigerian urban population. *Int J Epidemiol.* 1979 Mar; 8(1): 55-9. <https://doi.org/10.1093/ije/8.1.55>
- [64] Umeche N. The incidence of amoebiasis among secondary school students in Calabar, Nigeria. *Folia Parasitol (Praha).* 1983; 30(3): 277-80.
- [65] Singh P, Kochhar R, Vashishta RK, Khandelwal N, Prabhakar S, Mohindra S, Singhi P. Amebic meningoencephalitis: spectrum of imaging findings. *AJNR Am J Neuroradiol.* 2006 Jun-Jul; 27(6): 1217-21.
- [66] Center for Disease Control. DPDx Laboratory Identification of Parasites of Public Health Concern. Amebiasis. <https://www.cdc.gov/dpdx/amebiasis/index.html>
- [67] Orbison JA, Reeves N, Leedham CL, Blumberg JM. Amebic brain abscess; review of the literature and report of five additional cases. *Medicine (Baltimore).* 1951 Sep; 30(3): 247-82.
- [68] Morán P, Serrano-Vázquez A, Rojas-Velázquez L, González E, Pérez-Juárez H, Hernández EG, Padilla MLA, Zaragoza ME, Portillo-Bobadilla T, Ramiro M, Ximénez C. Amoebiasis: Advances in Diagnosis, Treatment, Immunology Features and the Interaction with the In.
- [69] Haque R, Huston CD, Hughes M, Houghton E, Petri WA Jr. Amebiasis. *N Engl J Med.* 2003 Apr 17; 348(16): 1565-73. <https://doi.org/10.1056/NEJMra022710>.
- [70] Schiess N, Villabona-Rueda A, Cottier KE, Huether K, Chipeta J, Stins MF. Pathophysiology and neurologic sequelae of cerebral malaria. *Malar J.* 2020 Jul 23; 19(1): 266. <https://doi.org/10.1186/s12936-020-03336-z>
- [71] Orimadegun AE, Fawole O, Okereke JO, Akinbami FO, Sodeinde O. Increasing burden of childhood severe malaria in a Nigerian tertiary hospital: implication for control. *J Trop Pediatr.* 2007 Jun; 53(3): 185-9. <https://doi.org/10.1093/tropej/fmm002> Epub 2007 Feb 7
- [72] Elesha SO, Adepoju FB, Banjo AA. Rising incidence of cerebral malaria in Lagos, Nigeria: a postmortem study. *East Afr Med J.* 1993 May; 70(5): 302-6.
- [73] Hunt NH, Grau GE. Cytokines: accelerators and brakes in the pathogenesis of cerebral malaria. *Trends Immunol.* 2003 Sep; 24(9): 491-9. [https://doi.org/10.1016/s1471-4906\(03\)00229-1](https://doi.org/10.1016/s1471-4906(03)00229-1)
- [74] Dondorp AM, Ince C, Charunwatthana P, Hanson J, van Kuijen A, Faiz MA, Rahman MR, Hasan M, Bin Yunus E, Ghose A, Ruangveerayut R, Limmathurotsakul D, Mathura K, White NJ, Day NP. Direct in vivo assessment of microcirculatory dysfunction in severe falciparum.
- [75] Center for Disease Control. DPDx Laboratory Identification of Parasites of Public Health Concern. Plasmodiasis. <https://www.cdc.gov/dpdx/malaria/index.html>
- [76] Nickerson JP, Tong KA, Raghavan R. Imaging cerebral malaria with a susceptibility-weighted MR sequence. *AJNR Am J Neuroradiol.* 2009 Jun; 30(6): e85-6. <https://doi.org/10.3174/ajnr.A1568> Epub 2009 Mar 25
- [77] Nguyen TH, Day NP, Ly VC, Waller D, Mai NT, Bethell DB, Tran TH, White NJ. Post-malaria neurological syndrome. *Lancet.* 1996 Oct 5; 348(9032): 917-21. [https://doi.org/10.1016/s0140-6736\(96\)01409-2](https://doi.org/10.1016/s0140-6736(96)01409-2)
- [78] Tamzali Y, Demeret S, Haddad E, Guillot H, Caumes E, Jauréguiberry S. Post-malaria neurological syndrome: four cases, review of the literature and clarification of the nosological framework. *Malar J.* 2018 Oct 26; 17(1): 387. <https://doi.org/10.1186/s12936-018-2542-8>
- [79] World Health Organisation Newsroom fact sheets. Trypanosomiasis. [https://www.who.int/news-room/fact-sheets/detail/chagas-disease-\(american-trypanosomiasis\)](https://www.who.int/news-room/fact-sheets/detail/chagas-disease-(american-trypanosomiasis))
- [80] Center for Disease Control. DPDx Laboratory Identification of Parasites of Public Health Concern. African trypanosomiasis. <https://www.cdc.gov/dpdx/trypanosomiasisafrican/index.html>
- [81] Lucas S, Bell J, Chimelli L (2008). Parasitic and fungal infections. In: S Love, DN Louis, DW Ellison (Eds.), *Greenfield's Neuropathology*. Hodder Arnold, London, pp. 1447-1487.
- [82] Pittella JE. Central nervous system involvement in Chagas disease: a hundred-year-old history. *Trans R Soc Trop Med Hyg.* 2009 Oct; 103(10): 973-8. <https://doi.org/10.1016/j.trstmh.2009.04.012> Epub 2009 May 19
- [83] Carod-Artal FJ, Gascon J. Chagas disease and stroke. *Lancet Neurol.* 2010 May; 9(5): 533-42. [https://doi.org/10.1016/S1474-4422\(10\)70042-9](https://doi.org/10.1016/S1474-4422(10)70042-9)
- [84] Braakman HM, van de Molengraft FJ, Hubert WW, Boerman DH. Lethal African trypanosomiasis in a traveler: MRI and neuropathology. *Neurology.* 2006 Apr 11; 66(7): 1094-6. <https://doi.org/10.1212/01.wnl.0000209306.41647.13>
- [85] Gill D, Chatha D, Carpio-O'Donovan R. MR imaging findings in African trypanosomiasis. *AJNR Am J Neuroradiol* 2003; 24: 1383-5.
- [86] Chacko G. Parasitic diseases of the central nervous system. *Semin Diagn Pathol.* 2010 Aug; 27(3): 167-85. <https://doi.org/10.1053/j.semdp.2010.05.003>
- [87] Kenfak A, Eperon G, Schibler M, Lamoth F, Vargas MI, Stahl JP. Diagnostic approach to encephalitis and meningoencephalitis in adult returning travellers. *Clin Microbiol Infect.* 2019 Apr; 25(4): 415-421. <https://doi.org/10.1016/j.cmi.2019.01.008> Epub 2019 Jan 29.

- [88] Carpio A, Romo ML, Parkhouse RM, Short B, Dua T. Parasitic diseases of the central nervous system: lessons for clinicians and policy makers. *Expert Rev Neurother*. 2016; 16(4): 401-14. <https://doi.org/10.1586/14737175.2016.1155454> Epub 2016 Mar 4.
- [89] Semenza JC, Paz S. Climate change and infectious disease in Europe: Impact, projection and adaptation. *Lancet Reg Health Eur*. 2021 Oct; 9: 100230. <https://doi.org/10.1016/j.lanepe.2021.100230> Epub 2021 Oct 7.