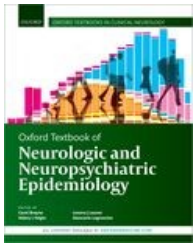

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CHAPTER

36 Epidemiology of bacterial and parasitic infections of the central nervous system

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Abstract

This chapter looks at the epidemiology of bacterial and parasitic infections of the central nervous system (CNS). Bacteria and parasites are important infections of the CNS, but the epidemiology has changed significantly over the last few decades with the introduction of vaccines; appearance of organisms resistant to antimicrobial and anti-parasitic drugs; increase in number of immunocompromised people from human immunodeficiency virus (HIV) and oncological conditions; and increased movement of people throughout the world. The CNS infections present with a multitude of symptoms and signs, which often overlap, making case definitions for epidemiological studies difficult. The main syndromes of CNS infections are meningitis, encephalitis, epilepsy, and paralysis. Most bacteria gain access to the CNS via blood, although scalp, ear, and oropharyngeal infections are possible routes of infection. The chapter then discusses acute bacterial meningitis, brain abscesses, ventriculitis, tuberculosis meningitis, malaria, cysticercosis, onchocerciasis, sparganosis, and paragonimiasis.

Keywords: bacterial infections, parasitic infections, vaccines, HIV, CNS infections, meningitis, encephalitis, epilepsy, paralysis

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Introduction

Bacteria and parasites are important infections of the CNS, but the epidemiology has changed significantly over the last few decades with the introduction of vaccines, appearance of organisms resistant to antimicrobial and anti-parasitic drugs, increase in number of immunocompromised people from human immunodeficiency virus (HIV) and oncological conditions, and increased movement of people throughout the world.

The CNS infections present with a multitude of symptoms and signs, which often overlap, making case definitions for epidemiological studies difficult. The main syndromes of CNS infections are outlined in Table 36.1.

Table 36.1 Clinical syndromes associated with bacterial and parasitic infections on the central nervous system

Syndrome	Pathology	Clinical manifestations	Aetiological agents
Meningitis	Inflammation of meninges of the brain	Headache, photophobia, neck stiffness, fever	Bacteria, virus, parasites
Encephalitis	Inflammation of the brain and spinal cord parenchyma	Impaired consciousness, fever	Virus
Epilepsy	Focal lesions	Generalized, focal, and/or focal becoming generalized seizures	Parasites, bacteria
Paralysis	Myelitis	Weakness of limbs	Bacteria, virus

Bacteria

Most bacteria gain access to the CNS via blood, although scalp, ear, and oropharyngeal infections are possible routes of infection. The bacteria usually produce meningitis, with direct invasion of the brain parenchyma causing brain abscesses and bacterial infection of the ventricular system as ventriculitis.

Acute Bacterial Meningitis

The introduction of vaccines has had a major impact on the epidemiology of acute bacterial meningitis (ABM), particularly in children.[1] Most epidemiological studies rely on confirmation of the diagnosis in health facilities, since the diagnosis depends upon detection of bacteria in the CSF. The clinical features lack sensitivity (particularly in neonates and infants) and specificity. Thus, the reported incidences generally under-report the incidence, as the diagnosis of ABM is not made since a lumbar puncture is not performed or people may die before diagnosis is made.

The diagnosis, and thus case definition depends upon obtaining a CSF sample. The appearance, cell count, and protein concentration are suggestive of ABM, but it is the detection of the bacteria which confirms the diagnosis for the case definition. Detection of the bacteria can be obtained by microscopy (Gram stains), culture or detection of bacterial antigens, or more recently nucleic acids. The sensitivity and specificity of these methods varies considerably, not only between the methods, but also with the laboratories, immune status of the patient, and organism (Table 36.2).

Table 36.2 The major causes of ABM vary with age

Age group	Most common organisms
Newborns	Group B *Streptococcus, Strepyococcus pneumoniae, Listeria monocytogenes, Escherichia coli*
Infants and children	*Streptococcus pneumoniae, Neisseria meningitidis, Haemophilus influenzae* type b (Hib), group B *Streptococcus*
Adolescents and young adults	*Neisseria meningitidis, Streptococcus pneumoniae*
Older adults	*Streptococcus pneumoniae, Neisseria meningitidis, Haemophilus influenzae* type b (Hib), group B *Streptococcus, Listeria monocytogenes*

Prior to the advent of the vaccines against the major causes of ABM, the annual incidence of ABM was reported up to 11 per 100,000. The best epidemiological data comes from the USA, where the reported annual incidence during 1964–1971 varied from 6.7 to 10.6 per 100,000.[2,3,4,5] Haemophilius meningitis was the most common, with an annual incidence of 2.8 to 4.3 per 100,000, followed by pneumococcal meningitis 1.1 to 2.6 per 100,000.

The epidemiology of ABM has changed significantly with the introduction of vaccines. In the USA, there was significant reduction in the annual incidence from 1986 to 1995 of bacterial meningitis cause by *H. influenzae* from 2.9 to 0.2 per 100.000 (94% reduction) and *N. meningitidis* 0.9 to 0.6 (33% reduction) with the introduction of the haemophilus and meningococcal vaccines.[6] The incidence of group B Streptococcus meningitis also decreased from 0.4 to 0.3 (25%) and suggesting more widespread use of antibiotics. The median age of patients with ABM increased from 15 months in 1986 to 25 years in 1995, driven by the reduction in haemophilius meningitis.[6]

The introduction of the PCV-7 and MCV4 vaccines were associated with significant declines in the pneumococcal and meningococcal meningitis respectively, although the annual incidences appeared to be decreasing prior to the introduction of these vaccines, and the meningitis caused by serogroups not covered by the vaccines also decreased (Fig. 36.1).

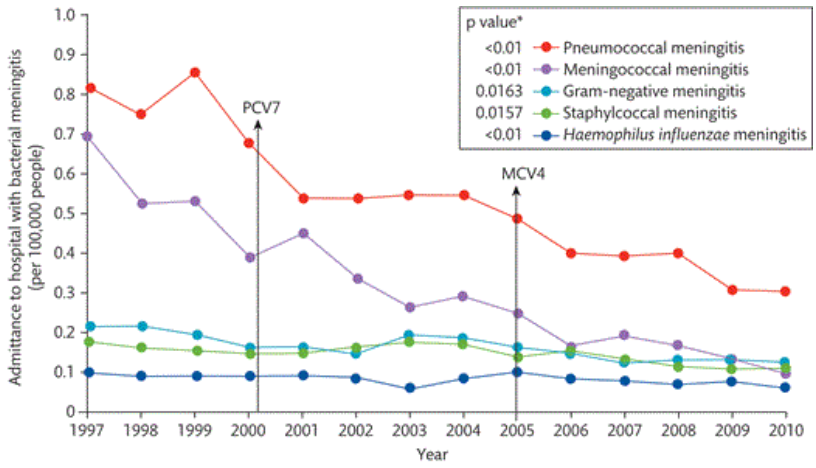

Fig. 36.1 Meningitis trends for different bacteria, 1997–2010.

Case estimation based on total number of cases per 100,000 people by international Classification of Diseases code (320 0, 320 1, 320 3, 320 82, and 036) from hospital discharges across the USA with the nationwide inpatient sample Healthcare Cost and Utilization Project net database. * p values calculated on the basis of the comparison between 1997 and 2010.Reproduced with permission from Castelblanco R.L. et al.Epidemiology of bacterial meningitis in the USA from 1997 to 2010: a population-based observational study. *The Lancet: Infectious Diseases*, 14(9):813–819. Copyright © 2014 Elsevier Ltd. All rights reserved. DOI:https://doi.org/10.1016/S1473-3099(14)70805-9.

Data from other parts of the world is less robust, since many countries do not have the facilities for the diagnosis or the epidemiological framework (accurate denominators and case ascertainment) to provide accurate measures. Areas such as those in Africa have high incidences, with reported annual incidences of 46 (31–52) per 100,000 for haemophilius and 38 (11–48) for pneumococcal meningitis, compared to Europe 16 (12–22) and 6 (5–9) per 100,000.[1] The incidence of menininggococcal meningitis is estimated to be 1–2, increasing to 2–10 during epidemics in Europe. Epidemics of meningococcal meningitis occur in a region stretching across Africa from Ethiopia to Senegal. The annual incidence reaches over 1000 per 100,000 during epidemics, usually caused by serogroup A.[1] In 2012, a vaccination programme in Chad reduced the incidence in by 94% with the incidence in three regions of 2.48 per 100 000 compared to 43.8 per 100 000.[7]

The risk factors for the development of ABM varies according to the organism, the age, and immune competency of the patient. For neonatal meningitis the risk factors are premature rupture of membranes, prolonged rupture of membranes (>18 h), maternal colonization with group B Streptococcus (GBS), maternal chorioamnionitis, low socioeconomic status, low birth weight, and prematurity.[8] The common risk factors for community acquired pneumococcal, meningococcal, and haemophilius meningitis in older children and adults include living in crowded conditions, smoking, splenectomy (including splenic atrophy as in sickle cell disease), and HIV infection.[9] Specific risk factors for pneumococcal meningitis include B-cell dysfunction, complement deficiencies, haematological cancer and cochlear implants, and older patients (>65 years). For meningococcal meningitis risk factors are late complement deficiency and complement inhibitor treatment, and for haemophilius meningitis risk factors are diminished humoral immunity.

The outcome of ABM is determined by the aetiological organism, age of the patient, and their immune competency. In neonates ABM is associated with a poor outcome. In areas of low incidence the mortality is about 4 per 100,000 per year from haemophilius and pneumococcal meningitis, compared to about 30 per 100,000 per year in Africa.[1] The proportion of those with long-term sequelae for meningitis caused by haemophilius is 9.5% (95% CI: 7.1–15.3), pneumococcus is 24.7% (16.2–35.3) and meningococcus is 7.2% (4.3–11.2).[1]

Brain Abscesses

Brain abscesses are focal infections of the brain parenchyma, caused by a variety of organisms, mainly bacteria. The clinical features depend upon the location, size, growth rate of abscess, aetiological agent and number of abscesses, and the immunocompetency of the host. Thus, the case definition is not well defined, and epidemiology is not well described. The classical triad of headache, fever, and focal neurological deficits is not sufficiently sensitive or specific for epidemiological studies.

The few recent population based studies provide annual incidence estimates per 100,000 of 1.3 in Minnesota (USA) in 1981,[10] 0.3 in Helsinki (Finland) between 1970 and 2012,[11] and 0.4 in Copenhagen (Denmark) between 1994 and 2007.[11] These studies demonstrated a decline in the annual incidence, for example from 2.7/100,000 in 1935 to 0.9/100,000 in 1984 the Minnesota study.[10] All these studies reported a male predominance.[12] However, there have been no studies reported from LMIC nor in immunocompromised individuals, in whom the incidence would be higher.

Overall an aetiological agent could be identified in 68% of cases, with 23% having multiple organisms.[13] The most common pathogens identified are *Streptococcus sp.* and *Staphylococcus sp.* However, most studies were conducted on bacteria, and thus other organisms may have been under-reported.

Most patients (86%) with brain abscesses have readily identifiable risk factors,[13] which are associated with specific pathogens. These risk factors include: immunodeficiency, penetration of the blood brain barrier, or haematogenous spread from distant infections.[12] More recently, genetic susceptibility was suggested, with increased risk of developing brain abscesses in subjects with specific polymorphisms of the intercellular adhesion molecule-1 (ICAM-1, K469E/E) and monocyte chemoattractant protein-1 (MCP-1, -2518 ANG/G).[14] The abscesses in HIV infected patients are most often caused by *Toxoplasmosis gondii, Mycobacterium sp.*, and *Nocardia sp*. The abscesses that occur in patients with solid-organ or haematopoietic cancers, stem-cell transplantation, or neutropaenia following chemotherapy are caused usually by fungi such as *Aspergillus, Candida sp., Mucorales*, and *Scedosporium* species, or bacteria such as *Escherichia coli, Enterobacter, Klebsiella, Proteus*, and *Salmonella species*. The organisms identified following penetrating trauma, neurosurgery, or infections of the ear and paranasal sinuses are *Staphylococcus aureus*, anaerobic and aerobic Streptococcus species, but also enterobacteria, Klebsiella, Proteus, and Salmonella species. Haematogenous spread can occur from endocarditis, congenital heart disease, pulmonary or dental infections, endocarditis, congenital heart disease, lung infections, or dental infections. *S. aureus* and *Streptococcus spp.* are the organisms most commonly found with endocarditis, whilst a mixture of organisms including *Fusobacterium, Prevotella, Actinomyces, Bacteroides*, and *Haemophilus* species are found following dental infections.

Ventriculitis

Ventriculitis occurs most commonly after invasive procedures such external ventricular drainage or ventriculo-shunts for hydrocephalus. There is little data on the incidence of this infection, although it is reported that 8% of people who have external ventricular drainage[15] develop ventriculitis.[16] The most common organisms are *Staphlycoccus aureus* or *S. epidermis*, but other organisms such as enterobacteriaceae and *Pseudomonas spp*., *Acinetobacter spp*. and *Candidia spp*. are also isolated.

Tuberculosis Meningitis

It was estimated that in 2015, 10.2 million (95% UI, 9.2–11.5 million) tuberculosis incident cases occurred, with 10.1 million (9.2–11.1 million) prevalent cases and 1.3 million (1.1–1.6 million) deaths.[15] The age-standardized tuberculosis incidence rate (per 100000 people) was 154.4 (140.0–172.2) in men and 86.3 (78.0–97.4) in women. Mortality was double in men (21.9 (16.5–29.5)) versus women (10.8 (8.5–13.1)). Since 1990, the incidence has decreased by about 2%, with more rapid decreases in the last ten years.[15] The changes in the epidemiology are influenced by the rolling out of the BCG vaccine and introduction of isonazid prophylaxis (both of which are particularly effective in preventing tuberculosis meningitis) and the advent of HIV and multi-drug resistant organisms.

The major CNS manifestations of *Mycobacterium tuberculosis* infection are meningitis and tuberculoma. Tuberculosis meningitis (TBM) occurs in about 1% of the tuberculosis cases, accounts for 94% of the CNS manifestations,[17] and is associated with significant mortality and morbidity. It occurs most commonly in children, who have the highest mortality and most severe morbidity. Diagnosis of TBM is often difficult since it has an insidious course and is often diagnosed late. The clinical features are not specific, and the diagnosis from the CSF are hampered by poor sensitivity of the tests or slow growth of the organism. Attempts are being made to improve the consistency of the definitions used.[18] The definitive diagnosis is made by identifying *M. tuberculosis* from the CSF either by microscopy or culture. Thus, the sensitivity of microscopy of the CSF stained with Ziehl-Neelson stain and conventional PCR is about 60%. Real time PCR increased the sensitivity to about 80%, but interferon release assays still only have a sensitivity of 50–70%. In a recent multi-centre study, of 506 TBM patients the sensitivities of interferon-c release assay (Quantiferon) was 90%, automated culture systems 82%, Lowenstein Jensen medium 73%, and Ziehl-Neelson stain 27%.[19]

The risk factors for developing TBM include young age (particularly under five years), HIV infection, immune suppression, and diabetes. In a study of children with CNS tuberculosis in the USA,[20] risk factors identified in multivariate analysis were age <5 years (adjusted odds ratio (aOR): 3.3 (95% CI: 2.0–5.4)), birth in the USA (aOR: 1.8 (1.2–2.7)), and Hispanic origin (aOR: 1.5 (1.1–2.1)). There is little recent comparable data from adults. There are differences in the propensity of the *M. tuberculosis* strains to cause TBM, with those of the Indo-Oceanic or East Asian Beijing lineages more likely to cause meningitis than the Euro-American strains.

The mortality from TBM occurs in up to 88%.[21] In a recent review of children with TBM, the mortality was 19.3% (95% CI 14.0–26.1), with neurological sequelae found in 53.9% (95% CI 42.6–64.9) of the survivors.[22] Corticosteroids reduce mortality by about 25%, with a pooled analysis finding a relative risk of 0.75 (95% CI 0.65–0.87); based upon 1337 participants.[23] The median mortality in those without corticosteroids was 41% in this meta-analysis. This review did not find a significant effect on neurological sequelae.

Malaria

Malaria is caused by *Plasmodium* species transmitted by *Anopheles sp*. mosquitos. There are five species of *Plasmodium* known to infect humans: *P. falciparum, P. vivax, P. ovale, P. malariae*, and *P. knowlesi*. Most of these parasites cause an acute infection, characterized by fever, headaches, and gastrointestinal symptoms. *P. falciparum* is responsible for the most deaths and it is associated with most of the neurological complications. It can cause seizures, psychosis, and an encephalopathy (cerebral malaria), as well as post-malaria syndromes. *P. vivax* was not thought to be associated with neurological complications, but there have been recent reports of severe vivax malaria with encephalopathy and seizures, although the most common manifestations are severe anaemia, thrombocytopenia, and hepatic dysfunction.[24] *P. ovale* and *P. malariae* do not appear to have neurological complications. *P. knowlesi* is a relatively recently described infection of humans (2004) restricted to South East Asia, but is not usually associated with neurological complications.[25]

There are significant problems in studying the epidemiology of malaria infections. First, in malaria endemic areas, a significant proportion of the population may be infected with the parasites but not have any clinical symptoms. Thus, when a person develops symptoms such as headache, seizures, or coma, there may be causes other than the malaria infection. Exclusion of these causes is important, but rarely possible in malaria endemic areas because of lack of laboratory and neuroimaging facilities. Thus, models are developed to determine the malarial attributable fraction. So for example, Kariuki et al. used logistic regression to model malaria-attributable fractions for seizures (the proportion of seizures caused by malaria) in a malaria endemic area.[26] Second, a person may be infected with more than one species of *Plasmodium*, and thus it is difficult to attribute the infection to one particular species of malaria. Third, the surveillance systems in many LMICs do not capture all malaria cases, since there is inconsistent reporting, with under-reporting or reporting cases which have not been confirmed by diagnostic tests, the cases treated by private health institutions are not captured. Methods such as the Malaria Atlas Project (https://map.ox.ac.uk/) model the parasite prevalence measured in cross-sectional surveys and the incidence to determine the burden of malaria. Despite these reservations the burden of malaria has been reported and tracked over the last few decades.

In 2016, the WHO estimated that there were 216 million cases of malaria in the world.[27] Over 90% of the cases were in sub-Saharan Africa, where children in malaria endemic areas bear the brunt of infections, and 7% in South East Asia. *P. vivax* was estimated to cause 4% of the infections, mainly in South East Asia, Eastern Mediterranean, and South American regions. The number of cases has dropped from 237 million in 2010, possibly due improved preventative measures such as insecticide spraying, insecticide treated bed nets, and more effective treatment. However, the estimated number of cases has increased from a nadir in 2013 and 2014, when there were an estimated 210 million cases.

The proportion of neurological and psychiatric conditions that can be attributed to malaria infections is difficult to determine for the reasons outlined above. In malaria endemic areas of sub-Saharan Africa, where children have most symptomatic malaria infections, nearly 48% of children admitted to hospital have neurological features such as seizures, prostration, coma, and agitation.[28] With the decrease in malaria between 2002 and 2008, the incidence of all acute symptomatic seizures decreased by 69%, with 93% of this decrease in malaria-associated seizures.[26] The adjusted malaria-attributable fractions for seizures with falciparum parasitaemia were 93% (95% CI 90–95%) for all acute symptomatic seizures, 92.9% (95% CI 89–96%) for convulsive status epilepticus, 94% (95% CI 91–96%) for repetitive seizures, and 92% (95% CI 86–96%) for focal seizures.[26]

The mortality in patients with cerebral malaria is determined by the age of the patient, affected organ systems, and antimalarial and supportive treatment used. In the large SEAQUAMAT trial in Asian adults

with severe malaria, overall mortality of cerebral malaria was 34%, whereas mortality was 17% in comatose patients without other organ involvement. In comatose patients with concomitant metabolic acidosis and renal impairment, mortality increased to 70%.[29] Using similar definitions in the large AQUAMAT trial in African children with severe malaria, overall mortality of cerebral malaria was 6% without other organ involvement, increasing to 43% with concomitant metabolic acidosis and renal impairment.[30] The reported case fatality of cerebral malaria in the USA is 18%[31] and France of 25%.[32]

Neurological sequelae are rare in adults (<3%) and include psychiatric sequelae, persisting problems with balance, and hemiparesis.[30] Sequelae are more common in children following cerebral malaria, with up to 11% of African children with persistent deficits and up to 25% with neurocognitive deficits.[33]

Cysticercosis

Taenia solium is an intestinal tapeworm that is ubiquitous.[34] The infection of the intestine is known as taeniasis, but it is the larval forms that cause cysticercosis, which involves the CNS and the eye. Humans can be definitive or intermediate hosts of *T. solium*, with pigs acting as intermediate hosts. Eating raw or undercooked pork containing cysticeri leads to adult *T. solium* worms in the small intestine (definitive host), which is usually asymptomatic. If eggs from the adult worm, found in food or water contaminated by human faeces, are ingested (including self-infection), the eggs will develop into oncospheres which penetrate that intestinal wall, enter the circulation and lodge as cysticerci in tissues such as the muscles, brain, eye, and lung (intermediate host). It is the cysticerci that give rise to the neurological complications of *T. solium*, that is, neurocysticercosis.

Neurocysticercosis can be asymptomatic (cysticerci found on CT scans or at post-mortem) or classified as one or more of the following clinical syndromes: parenchymal, subarachnoid, intraventricular, spinal, or ocular. Single enhancing nodules are more frequent in younger people (<30 years) and subarachnoid neurocysticercosis in older age groups. The main presenting symptoms are headache (23–98%), seizures (37–92%), papilloedema (48–94%), meningism (29–33%), nausea and vomiting (74–80%).[35] Other less common presentations include dementia, psychosis, focal neurological deficits, cranial nerve palsies, visual disturbances, ataxia, and rarely spinal cord compression. The clinical syndromes are determined by the burden and location of cysts, whether the organisms are alive, dying, or dead, and host response to the cysts. The peak incidence of cysticercosis is 20–50 years, although the clinical manifestations are different between children and adults.

The diagnosis of neurocysticercosis is based upon clinical examination, neuroimaging, and serology, since the manifestations are protean, and few patients have pathognomonic features. Criteria have been developed to aid the diagnosis (Box 36.1):

Box 36.1 Diagnostic criteria for neurocysticercosis

Absolute

- Histological proof (biopsy of a brain or spinal cord lesion)
- Cystic lesions with scolex on neuroimaging
- Retinal cysticercosis visible on fundoscopic examination

Major

- Lesions highly suggestive of neurocysticercosis on neuroimaging
- Positive serum antibodies on enzyme-linked immunoelectrotransfer blot (EITB)
- Cyst resolution after antiparasitic treatment
- Single brain enhancing lesion spontaneously resolved

Minor

- Suggestive lesions on neuroimaging
- Suggestive clinical manifestations
- Positive CSF antigen or antibodies on ELISA
- Extraneural cysticercosis

Epidemiological

- From or living in an endemic region
- Frequently travels to disease-endemic areas
- Household contact with taeniasis

Blood serological tests for neurocysticercosis are problematic since there is a high frequency of false positives, as the parasites may be present in sites outside the CNS, or low sensitivity in people with one lesion in the brain or calcified lesions. CSF serology is more sensitive and specific for neurocysticercosis. Antibody detection by enzyme-linked immunoelectrotransfer blot (EITB) is the most reliable, with a sensitivity of nearly 100% and specificity of 98% in blood for cysticercosis. It has low sensitivity in people with one lesion in the brain or calcified lesions.[36] The sensitivity is 80% and 100% specificity in CSF. Likewise, ELISA for IgG antibodies have sensitivities of >80% and specificity of nearly 100% in CSF.

Although *T. solium* is widely distributed through the world, most of the neurological complications occur in Latin America, Asia and Africa (Fig. 36.2).

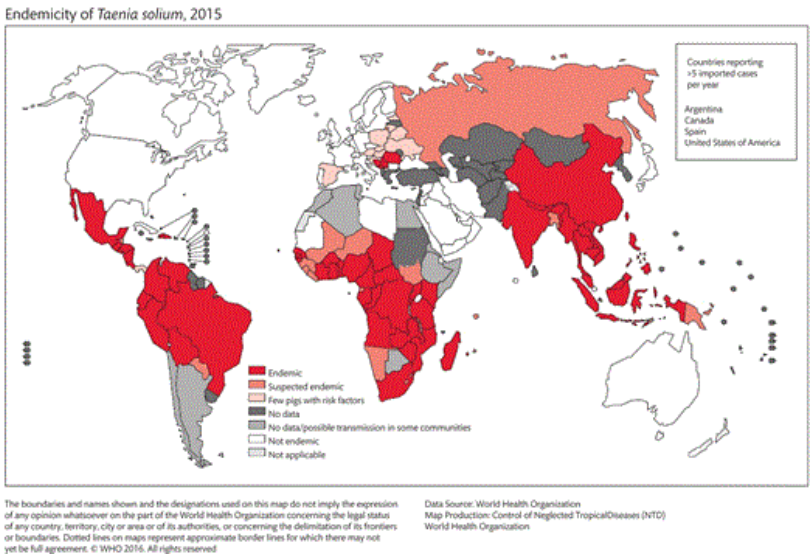

Fig. 36.2 Endemicity of Taenia solium 2015.

Reproduced with permission from World Health Organization. Taeniasis/cysticercosis. https://www.who.int/news-room/fact-sheets/detail/taeniasis-cysticercosis. Copyright © WHO 2016 (Accessed: 16 July 2019).

The prevalence of cysticercosis detected by various methods ranges up to 24% in endemic areas. Most of these studies have used serological diagnosis, which is not specific for active symptomatic disease.

Neurocysticercosis has many manifestations, but it is the seizures and epilepsy which is focus of most epidemiological research. Now there is compelling evidence from case control studies that cysticercosis is associated with epilepsy in South and Central America, Africa, and Asia. A recent meta-analysis found that the OR ranged from 0.2 to 25.4, with a common OR of 2.7 (95% CI 2.1–3.6) from a random effects model.[37] Three subgroup analyses performed gave OR of 2.2 (95% CI 1.6–3.0) for EITB-based studies, 3.2 95% CI 2.5–4.1) for CT-based studies and 1.9 (95% CI 1.2–3.0) for neurologist-confirmed epilepsy following a door-to-door survey. There did not appear to be any difference between the regions of the world, although there was considerable heterogeneity (I^2 78%, p<0.0001) between the studies. This meta-analysis was similar to another one where the OR calculated from a random effects model was 2.76 (95% CI: 2.19–3.48),[38] but also had considerable heterogeneity. In the same paper, the authors estimated that proportions of neurocysticercosis in people with epilepsy ranged from 10% (95% CI: 6–15) to 56% (45–67), with results from a random effects model estimating that 32% (95% CI: 27–36) of people with epilepsy had neurocysticercosis.

However, people in endemic areas have cysticerci detected at post-mortem (up to 4% in subjects without pre-morbid neurological symptoms dying in endemic areas) or on neuroimaging, who are asymptomatic or do not develop epilepsy. Thus, determination of the casual pathway is problematic. One study in Honduras has shown that a reduction in transmission of *T. solium*,[39] and large-scale studies in Peru have demonstrated a reduction in transmission of *T. solium*,[40] but it is too early to assess the impact on epilepsy. However, there is a lack of longitudinal studies to examine the incidence of epilepsy following infection.

Onchocerciasis

Onchocerca volvulus causes onchocerciasis, which manifests river blindness and it is associated with epilepsy and cognitive impairment. It is transmitted by the black fly, *Simulium sp.*, which lives near fast-flowing streams and is endemic in some parts Africa and to a lesser extent in Latin America and the Arabian peninsula.

Onchocerciasis usually presents with eye or skin involvement. The eye involvement includes keratitis (which may lead to sclerosing keratitis and corneal scars), iritis, choroio-retinitis, and optic neuropathy. These are thought to be caused by the localized host inflammatory responses to dead or dying microfilariae.

Diagnosis is confirmed by finding onchocercial microfilaria from skin biopsies, although serology tests and PCR tests of parasite DNA and recombinant antigen-based enzyme-linked immunoassays have been developed.[41] The microfilaria are rarely found in the CSF.

The association onchocerciasis and epilepsy has been difficult to establish, partly because the putative mechanisms of epileptogenesis are unclear. Systematic reviews have demonstrated that prevalence of epilepsy increased on by 0.4% for each 10% increase in onchocerciasis prevalence.[42] A study of active convulsive epilepsy conducted in several countries of sub-Saharan Africa found an OR of 2.2 (CI 95%: 1.6–3.2) using serology.[43] A systematic review of 11 studies which used skin biopsies for diagnosis, found a pooled OR of 2.49 (95% CI: 1.61–3.86).[44] Presence of nodules for diagnosis of onchocerciasis analysed in four studies found an OR of 1.74; 95% CI: 0.94–3.20).

More recently *O. vulva* is being implicated in the pathogenesis of 'nodding syndrome' (NS) an epileptic encephalopathy found in isolated regions of Africa.[45] This syndrome usually presents in children and young adults, with myoclonic seizures, wasting, and cognitive impairment.

Sparganosis and Paragonimiasis

Sparganosis and paragonimiasis are caused by *Spirometra mansoni* and *Paragonimus sp.*, respectively. They are similar in that they have two intermediate hosts, with humans infected by drinking contaminated water, eating raw chicken or fish (sparganosis); or crabs (paragonimiasis), with the definitive hosts as cats and dogs. The CNS involvement is relatively uncommon. In both infections there may be an initial meningoencephalitis, followed by the development of the granulomata. In sparganosis the granulomas often become calcified (small punctuate calcification best seen on CT scan), whilst in paragonimiasis the granulomas evolve into encapsulated abscesses, developing into cystic lesions, which infrequently become calcified.[46] Seizures are common CNS manifestations of paragonimiasis, but they are usually acute symptomatic seizures, and epilepsy may develop in association with the chronic lesions.

Seizures are common CNS manifestations of paragonimiasis, but they are usually acute symptomatic seizures, and epilepsy may develop in association with the chronic lesions.

These are uncommon infections, mostly reported from South East Asia, China, Korea, and Japan, with sporadic cases reported from the rest of the world. Individual species vary across continents.

Conclusion

Infections of the CNS are a considerable burden in the world, with the epidemiology determined by the organisms, age, immune status, and geographical region. The incidence of CNS infections has decreased with the introduction of more effective antimicrobial and anti-parasitic agents, reduction in the transmission of vectors (e.g. malaria) and vaccines (meningitis). However, the development of antimicrobial resistance, HIV epidemic, and increase travel has increased the burden.

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