**Infective Causes of Stroke in Tropical Regions**

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**Abstract**

Vascular diseases of the brain are the second reason of the death and the first cause of morbidity and disability worldwide. In tropical areas stroke has some particular features related to the nature of torrid zones. There are some special causes of the stroke, mainly infectious, although some of them are non-infectious. The most important etiologies are malaria, tuberculosis, cysticercosis, syphilis, and Chagas’ disease. The mean age of the patients with stroke in tropical areas seems to be less than that in developed countries, and the disease is more prevalent in younger adults. Prevention and/or treatment of the classic risk factors as well as factors related to tropical zones are the mainstays of controlling the disease. It has to be mentioned that lack of human as well as financial resources makes it difficult to control and treat the disease properly. Herein, the etiologies and risk factors of the cerebrovascular diseases in tropical regions will be reviewed.

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**Introduction**

The tropics or torrid zones are the areas between two parallels of latitudes on the earth. The latitudes are located 23° north and south of the equator. This region receives sun light more directly causing higher temperature in this area.¹ Direct sun shine, warm weather, distance from oceans, and different climate characters of those regions cause some special diseases more than other regions. Latin and Central America, sub-Saharan Africa, Middle East, India, and south-eastern countries in Asia are the major countries located in the torrid zones. Non-communicable diseases are an important threat to the health of adults in Africa and other tropical countries. Worldwide, cerebrovascular diseases (CVA) are second to ischemic heart disease as a cause of death leading to 4.4 million death each year with about 3 million death in developing countries.² Stroke is a vascular brain injury and a medical emergency caused by sudden interruption of blood flow. The WHO definition of stroke is a syndrome characterized by rapidly developing clinical signs of focal neurologic deficit, lasting 24 hours or longer and/or leading to death with no apparent cause other that of vascular origin.³ The objective of this study is to review the risk factors of stroke, and highlight some special topics related to stroke in tropical regions and principals of their management.

**Epidemiology**

There are several types of CVA, and each type has different causes. The three main types of CVA are cerebral infarction, which consists of more than 85% of stroke cases in developed countries. Ten percent of causes are intracerebral hemorrhage, and the remaining 5% are
subarachnoid hemorrhage. Data on the current epidemiology of stroke in tropical areas are sparse. The prevalence of stroke was not verified in sub-Saharan countries, although the mortality of stroke in adults was reported to be 5.5% of all deaths in Tanzania. The prevalence of stroke survivors in Sub-Saharan Africa was 300/100,000 (95% CI: 250-357) in the population aged over 15 years. This was about half the number that one would expect in a high-income country. In a study in one of the largest city in Ghana, stroke, heart failure, and renal diseases were accounted for 23% of acute medical admissions and 29% of deaths. In some countries the leading cause of stroke was infective bacterial or tuberculous meningitis.

### Risk Factors in Tropical Regions

Stroke is more common in people over 60 years of age, with no major difference between males and females. Mean age of stroke patients in Africa is less than 60 years. Females as many as half of the males are represented in hospital studies in Africa, because women are less interested in admission to the hospitals. In urban Nigeria the crude prevalence rate of stroke was 1.14/1,000 (males: 1.51; females: 0.69). Age adjusted mortality is higher than that in developed countries like Britain, especially in younger patients. Stroke prevalence rates in this study were lower than those in most developed countries. The lower rates might be related to lower incidence and higher stroke mortality in developing countries.

Hypertension is a major risk factor in developed countries, but it is difficult to confirm it because patients die before admission to the hospital. Abnormal autoregulatory system may induce hypertension in the first post-stroke days. The incidence of stroke is increasing in sub-Saharan Africa, and stroke prevention is an essential way for successful management of stroke. Hypertension was the commonest risk factor in all population groups (55%), but was higher in black patients (59%). It is estimated that if the 10-20 million people who had hypertension in sub-Saharan Africa were treated, about 250,000 deaths would be prevented annually.

In Sierra Leone and Mauritania 60% and 56% of the patients were admitted to the hospital due to cerebrovascular accidents had hypertension, respectively. In a study from February 2000 over a period of a year in Gambia, hypertension and smoking were the most prevalent risk factors of stroke. Uncontrolled hypertension is one of the major causes of stroke in Latin America, but other risk factors such as heavy alcohol consumption and smoking also play a role.

Diabetes, as a major risk factor of stroke, has been reported in 2-10% of the population in tropical areas. The prevalence of diabetes in South Africans older than 30 years is 5.5%. Ten percent of stroke patients in adult males and females over 30 years were attributable to diabetes. In one study in sub-Saharan Africa, stroke was accounted for approximately 30% of all diabetic deaths.

The relationship between stroke and high serum levels of low density lipoprotein (LDL) has been shown in several studies. Overall, about 29% of ischemic stroke burden in adult males and females more than 30 years were attributable to hypercholesterolemia with marked variation by population group. High cholesterol was estimated to cause 4.6% of all deaths in South Africa in year 2000. Dyslipidemia was commonest in whites (37%), but least common in blacks (5%). Obesity was present in 44% of stroke patients in Burkina Faso.

Smoking is an increasing problem in the population at risk. It has an additive effect on the other risk factors. The prevalence of current smoking and ever smoking were 3.0% and 15.6%, respectively in Malawi. The prevalence of smoking in 33 countries of Western Pacific and South East Asian regions ranged 26-82% in males and 1-65% in females. The percentage of haemorrhagic stroke attributable to smoking ranged 4-12% in males and 1-9% in females. Risk factors other than smoking increased with age in a study done in Sub-Saharan Africa.

Pregnancy and oral contraceptives (OCP) consumption are important risk factors for venous infarction, especially in early postpartum period. There is not any published data about the effect of OCP in Sub-Saharan Africa. Positive past history of stroke, cardiac diseases, obesity, and lack of physical exercises are other important risk factors. Between 4-10% of patients had a positive past history of stroke and up to 11% had a history of transient ischemic attack (TIA). In only 22% of patients an atherosclerotic plaque in major extracranial vessels is shown. Cardiac emboli in young adults due to rheumatic heart disease are more prevalent than coronary artery diseases in African patients. It was reported that 22% of strokes were attributed to physical inactivity. Forty-five percent of ischemic strokes were attributed to excess body weight.

The main mechanisms for the cerebrovascular diseases in tropical countries are the same as those in other areas, but it is estimated that between 6 to 12% of the vascular accidents had other unusual etiologies. Those are mainly cerebral malaria, tuberculosis, neurosyphilis, cysticercosis, Chagas’ disease, and brucellosis. To the best of our knowledge there is a little
reliable information related to the CVDs and tropical infections. Recently, increasing population and travelling from tropical low-income areas to high-income industrialized countries has led to increased presentation of the above mentioned disorders in the developed countries.26,27

**Malaria**

There are about 400 to 500 million cases of malaria around the world with 30% are located in Asia and the major remainder in Africa.28 Malaria itself causes 0.5 to 2.5 million deaths each year. Cerebral malaria (CM) which is the most severe complication of malaria is an acute and diffuse encephalopathy associated with *Plasmodium falciparum* infection. Cerebral malaria could be responsible for up to 10% of strokes in endemic regions.29 Neurological focal signs due to vascular injuries are rare, but may produce severe outcome. Early and adequate treatment is effective way of preventing permanent sequel. The precise mechanism is not known, but the histopathologic hallmark of cerebral malaria is vascular engorgement with infected and non-infected red blood cells with parasites, metabolic disturbances, and host immune responses.30 Quinine is the mainstay of treatment, and has to be prescribed with adequate loading dose (20 mg/kg of the dihydrochloride salt infused over 4 hours) to ensure that a parasiticidal concentration is reached in the blood.31 Artemisinin derivatives are also good alternatives. Arteether is used intramuscularly, and artesunate is used intravenously, which may decrease the mortality secondary to CM.32,33 Fluid, electrolyte balance and acid-base correction are important cornerstones of treatment. Dexamethasone may prolong coma in the survivors and should not be used in CM.34

**Tuberculosis**

Central nervous system tuberculosis (TB) is a serious type of extra-pulmonary TB, and continues to be an important public health problem in developing countries. World Health Organization estimates that one-third of the world’s population is infected with *Mycobacterium tuberculosis* (MTB), with the highest prevalence of tuberculosis in Southeast Asia.35 Different forms of CNS tuberculosis may cause motor deficit. These are tuberculous myelopathiy,36 intramedullary tuberculoma,37 syringomyelia,36 radiculomyelitis,38 and tuberculous meningitis (TBM),39 however, the main cause of stroke is TBM. Stroke occurs in 15-75% of patients with TBM occurs, especially in advance stage of the disease with severe illness. The majority of strokes may be asymptomatic, because of being in a silent area or the patient is in deep coma.40

In all cases caused by MTB, the bacterium settled in the lungs and disseminated to the nervous system through the hematogenous system. Rupture of rich nodules into the subarachnoid space is the beginning phase of meningitis. It induces lymphocytic infiltration around the meningeal blood vessels, and finally causes arteritis in almost all cases and cerebral infarction.41 The pathophysiologic mechanism involved consists of chronic basal meningitis followed by tension hydrocephalus and raised intracranial pressure.42 Neurological involvement accounts for up to 5% of extrapulmonary TB, especially in children and/or immunodeficient patients.43 There are different reports about the incidence of stroke in neutrotuberculosis. Dastur et al.44 reported cerebral infarction in 41% of 100 autopsied brain. In post-computer tomography era the reported incidence is between 28 to 38% without any prominent sex dominance.45,46 The highest rate of vascular infarction during TBM, diagnosed by MRI, is reported more than two thirds of the patients.47 Ninety-two percent of the involved arteries were in the anterior cerebral circulation (carotid system).43,46 Lenticulostriate arteries of both middle and anterior cerebral arteries are mostly involved. Large infarctions are mainly due to middle cerebral artery involvement, and brainstem infarction is due to occlusion of penetrating branches of basilar artery.46,48 A recent report showed that the hazard ratio of ischemic stroke for tuberculosis patients (not meningeal or CNS tuberculosis) was 1.52-times (95% CI, 1.21-1.91; P<0.001) higher than that for control group.49 The current guidelines for treatment are based on the advances of the recent chemotherapeutic achievement of anti-TB drugs,50 and medical or surgical management for ischemic strokes. Early treatment is mandatory, and delayed treatment is associated with a higher rate of mortality and morbidity. Dexamethasone appears useful as an adjunctive treatment, especially in patients with severe tuberculous meningitis.

**Syphilis**

Syphilis is the great masquerader. Two types of symptomatic neurosyphilis, paranchymatous and meningovascular have been described.42,51 About 5% of untreated syphilitic patients will develop neurosyphilis,52 especially in young adults. Two different types of vascular pathology have been described in meningovascular syphilis. Hübner arteritis, which had been described since long times ago, is the most common type and involves the large and medium sized vessels. The other pathology is Nissl’s endarteritis characterized by intimal and adventitial proliferation, mainly on small
Cardiovascular disease is one of the main causes of stroke, and low socioeconomic status are important factors for disease expansion in endemic areas.64 It seems to be that chagasic cardiomyopathy is a more common cause of stroke in areas where Chagas' disease is prevalent.65 The diagnosis of chagasic cardiomyopathy is established 10-30 years after the initial infection, and affects 30% of patients.66 The main risk factors for stroke secondary to Chagas' disease are a family member with Chagas' disease (OR=10.1) and past history of living in a mud-brick house during childhood (OR=8.9).67 Trypanocidae drugs such as nifurtrinom and benznidazole are the drugs of choice. Monitored administration of warfarin in stroke due to chagasic cardiomyopathy is recommended.68

**Brucellosis**

Brucellosis is a zoonotic disease with different neurological manifestations and still a common health problem in many parts of the world, especially Middle East,70 Latin America and the Mediterranean Sea.1 The involvement of CNS occurs in less than 3-5% of patients, mainly in the form of meningitis or meningoencephalitis,71 and diabetes insipidus,72 but the other forms such as vasculitis, transient ischemic attacks, ischemic strokes and venous thrombosis occurs rarely.73,74 Recently, in a local population in Egypt, it was reported that CNS involvement (vascular stroke, meningoencephalitis, and dementia) was recorded in nine patients out of 27 patients (33.3%) with brucellosis.75 Treatment is a special problem, and there are different protocols. A combination of doxycycline with rifampin and/or co-trimazole for six weeks or more has been recommended.71,73 Other infectious and non-infectious diseases associated with stroke are summarized in table 1.

| Infectious causes of stroke in tropical regions |
|------------------------------------------------|
| Infectious Causes                          | Non-infectious Causes |
| Cerebral Malaria                          | Sickle Cell Disease  |
| Tuberculous Meningitis                    | Takayasu Disease     |
| Neurosyphilis                             | Behçet Disease       |
| Cysticercosis                             | Moyamoya             |
| Chagas' Disease                           |                        |
| Brucellosis                               |                        |
| Viral Hemorrhagic Fever                   |                        |

**Crimean-Congo Hemorrhagic Fever**

Crimean-Congo Hemorrhagic Fever (CCHF) is thought to be an old disease first described in the former Soviet Union. Since 1999 Iranian Ministry of Health reported a cluster of viral hemorrhagic fever in Sistan-Balochestan, Isfahan and Golestan provinces in Iran. Fever, myalgia, petechia, purpura, bleeding, thrombocytopenia, anemia and
leukopenia are the main signs, symptoms and laboratory findings.\textsuperscript{36} Intracerebral hemorrhage due to severe thrombocytopenia may cause hemiparesis or hemiplegia.\textsuperscript{36} Hemorrhage in the arm compress median or ulnar nerves, and present itself as motor deficit.\textsuperscript{36}

Management of Stroke

Management consists of drug therapy, physical rehabilitation, control of risk factors and good nursing care. Antiplatelet drugs are the mainstay of drug treatment.\textsuperscript{76} They consist of aspirin, dipyridamole, ticlopidine and clopidogrel. The two last drugs are platelet surface glycoprotein inhibitors.\textsuperscript{77} For patients with embolic diseases due to cardiac problems or vascular atherothrombotic plaques anticoagulant drugs such as heparin or warfarin could be used. Aspirin is the most frequently used drug in all countries for acute therapy and secondary prevention. Main benefits of aspirin consist of low price and known adverse effects. The most important adverse effect is peptic ulcer and GI bleeding. In those cases ticlopidine and clopidogrel could be useful, but both are expensive. Dipyridamole has an additive pharmacologic effect when used with aspirin. Thrombolyis, carotid endarterctomy and vascular stenting are new procedures which are not available in most countries located in tropical regions. Nursing care include early rehydration, prevention of bedsores, protecting from aspiration pneumonia and rehabilitation. The latter is a combination of physical, occupational and speech therapy. It should be mentioned that in some situations such as intracranial hemorrhage secondary to CCHF or cerebral malaria antiplatelet drugs and heparin are contraindicated. Treatment of the risk factors such as hypertension, diabetes mellitus, and hypercholesterolemia, and smoking cessation are important features of the stroke management. Decreasing salt intake as well as weight and increase in physical activity also are the other important aspects of stroke management.\textsuperscript{3,78,79} Effective stroke prevention calls for comprehensive risk reduction including blood pressure control. Population-based health education programs and appropriate public health policy associated with high-risk strategies for hypertensive persons and stroke patients should be developed.\textsuperscript{90} The common problems to secondary prevention in Sub-Saharan Africa include high cost of treatment, difficulties in accessing care and lack of blood pressure control in clinics.\textsuperscript{5}

Conclusion

The major mechanisms for CVDs and their risk factors in tropical countries are the same as that for other areas. A number of vascular accidents had other unusual etiologies. The main problems of stroke in tropical countries are not the same as industrialized countries. The first one is financial limitations, which leads to inappropriate medical care in the hospitals, and the lack of sophisticated imaging facilities that are used for stroke. The other important factor is the lack of secondary prevention success like control of hypertension, hyperlipidemia and tropical infections. The third reason is the lack of human resources experienced in the field of tropical medicine and neurology. The last one which has the equal importance is the lack of definite certificate for death and lack of post-mortem autopsy. The diagnosis is based on clinical, laboratory and radiological findings. It seems that there are many challenges facing physicians and health directors in tropical-low income countries.

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Conflict of interest: Nothing to declare

References

1 Gomes J, Chalela JA. Stroke in the tropics. Semin Neurol. 2005;25:290-9. doi: 10.1055/s-2005-917665. PubMed PMID: 16170741.
2 Yikona J. Prevention of hypertension and stroke in Africa. Lancet. 2000;356:678-9. doi: 10.1016/S0140-6736(05)73822-8. PubMed PMID: 10968457.
3 Walker R. Stroke. In: Parry E, Godfrey R, Maybey D, Gill G, eds. Principles of medicine in Africa. London: Cambridge University Press; 2004. p. 798-809.
4 Walker RW, McLarty DG, Kitange HM, Whiting D, Masuki G, Mtasiwa DM, et al. Stroke mortality in urban and rural Tanzania. Adult Morbidity and Mortality Project. Lancet. 2000;355:1684-7. PubMed PMID: 10905244.
5 Connor MD, Thorogood M, Modi G, Warlow CP. The burden of stroke in Sub-Saharan Africa. Am J Prev Med. 2007;33:172-3. doi: 10.1016/j.amepre.2007.04.006. PubMed PMID: 17673107.
6 Samiullah S, Humaira M, Hanif G, Ghouri AA, Shaikh K. Etiological patterns of stroke in young patients at a tertiary care hospital. J Pak Med Assoc. 2010;60:201-4. PubMed PMID: 20225778.
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7 Owolabi LF, Shehu MY, Shehu MN, Fadare J. Pattern of neurological admissions in the tropics: Experience at Kano, Northwestern Nigeria. Ann Indian Acad Neurol. 2010;13:167-70. doi: 10.4103/0972-2327.70875. PubMed PMID: 21085525.

8 Danesi M, Okubadejo N, Ojini F. Prevalence of stroke in an urban, mixed-income community in Lagos, Nigeria. Neuroepidemiology. 2007;28:216-23. doi: 10.1159/000108114. PubMed PMID: 17851261.

9 Connor M, Rheeder P, Bryer A, Meredith M, Beukes M, Dubb A, et al. The South African stroke risk in general practice study. S Afr Med J. 2005;95:334-9. PubMed PMID: 15931448.

10 Lisk DR. Hypertension in Sierra Leone stroke population. East Afr Med J. 1993;70:284-7. PubMed PMID: 8306904.

11 Diagana M, Traore H, Bassima A, Druet-Cabanan M, Preux PM, Dumas M. [Contribution of computerized tomography in the diagnosis of cerebrovascular accidents in Nouakchott, Mauritania]. Med Trop (Mars). 2002;62:145-9. PubMed PMID: 12192710.

12 Garbusinski JM, van der Sande MA, Bartholome EJ, Damaix M, Gaye A, Coleman R, et al. Stroke presentation and outcome in developing countries: a prospective study in the Gambia. Stroke. 2005;36:1388-93. doi: 10.1161/01.STR.0000170717.91591.7d. PubMed PMID: 15947255.

13 Camargo EC, Bacheschi LA, Massaro AR. Stroke in Latin America. Neuroimaging Clin N Am. 2005;15:283-96. doi: 10.1016/j.nic.2005.07.002. PubMed PMID: 16198941.

14 Diagana M, Millogo A, Bouteille B, Preux PM. Affections neurologiques en milieu tropical. EMC-Neurologie. 2005;2:232-56. doi: 10.1016/j.emcn.2004.08.001.

15 Bradshaw D, Norman R, Pieterse D, Levitt NS, South African Comparative Risk Assessment Collaborating Group. Estimating the burden of disease attributable to diabetes in South Africa in 2000. S Afr Med J. 2007;97:708-15. PubMed PMID: 17952227.

16 McLarty DG, Unwin N, Kitange HM, Alberti KG. Diabetes mellitus as a cause of death in sub-Saharan Africa: results of a community-based study in Tanzania. The Adult Morbidity and Mortality Project. Diabet Med. 1996;13:990-4. PubMed PMID: 8946159.

17 Norman R, Bradshaw D, Steyn K, Gaziano T, South African Comparative Risk Assessment Collaborating Group. Estimating the burden of disease attributable to high cholesterol in South Africa in 2000. S Afr Med J. 2007;97:708-15. PubMed PMID: 17952228.

18 Zabsonre P, Yameogo A, Millogo A, Dyemkouma FX, Durand G. [Risk and severity factors in cerebrovascular accidents in west african Blacks of Burkina Faso]. Med Trop (Mars). 1997;57:147-52. PubMed PMID: 9304007.

19 Muula AS. Prevalence and determinants of cigarette smoking among adolescents in Blantyre City, Malawi. Tanzan Health Res Bull. 2007;9:48-51. doi: 10.4314/thrb.v9i1.14292. PubMed PMID: 17547101.

20 Martiniuk AL, Lee CM, Lam TH, Huxley R, Suh I, Jamrozik K, et al. The fraction of ischaemic heart disease and stroke attributable to smoking in the WHO Western Pacific and South-East Asian regions. Tob Control. 2006;15:181-8. doi: 10.1136/tc.2005.013284. PubMed PMID: 16728748; PubMed Central PMCID: PMC2564655.

21 Goldzieher JW. Perspectives in evaluating the safety and effectiveness of steroidal contraceptives in different parts of the world. Int J Gynaecol Obstet. 1977;15:63-8. PubMed PMID: 923897.

22 Drife J. Benefits and risks of oral contraceptives. Adv Contracept. 1990;6:15-25. PubMed PMID: 2291444.

23 Joubert J, Norman R, Lambert EV, Groenewald P, Schneider M, Bull F, et al. Estimating the burden of disease attributable to physical inactivity in South Africa in 2000. S Afr Med J. 2007;97:725-31. PubMed PMID: 17952230.

24 Joubert J, Norman R, Bradshaw D, Goedecke JH, Steyn NP, Puoane T. Estimating the burden of disease attributable to excess body weight in South Africa in 2000. S Afr Med J. 2007;97:683-90. PubMed PMID: 17952225.

25 Hornabrook RW. Cerebral malaria. In: Marsden PD, Bruce-Chewatt LJ, eds. Topics in tropical neurology. 1st ed. Philadelphia: F A Davis; 1975. p. 29-44.

26 Ryan ET, Wilson ME, Kain KC. Illness after international travel. N Engl J Med. 2002;347:505-16. doi: 10.1056/NEJMra020118. PubMed PMID: 12181406.

27 Yonekawa Y, Ogata N, Kaku Y, Taub E, Imhof HG. Moyamoya disease in Europe, past and present status. Clin Neurol Neurosurg. 1997;99:S58-60. doi: 10.1016/S0303-8467(97)00042-5. PubMed PMID: 9409407.

28 Idro R, Jenkins NE, Newton CR. Pathogenesis, clinical features, and neurological outcome of cerebral malaria. Lancet Neurol. 2005;4:827-40. doi: 10.1016/S1474-4422(05)70247-7. PubMed PMID: 16297841.

29 Carod-Artal FJ. [Strokes caused by infection
in the tropics]. Rev Neurol. 2007;44:755-63. PubMed PMID: 17583870.
30 Wassmer SC, Combes V, Grau GE. Pathophysiology of cerebral malaria: role of host cells in the modulation of cytoadhesion. Ann N Y Acad Sci. 2003;992:30-8. PubMed PMID: 12794044.
31 Newton CR, Hien TT, White N. Cerebral malaria. J Neurol Neurosurg Psychiatry. 2000;69:433-41. doi:10.1136/jnnp.69.4.433. PubMed PMID: 12794044.
32 Huda SN, Shahab T, Ali SM, Afzal K, Khan HM. A comparative clinical trial of artemether and quinine in children with severe malaria. Indian Pediatr. 2003;40:939-45. PubMed PMID: 14581730.
33 Newton CR. Interaction between Plasmodium falciparum and human immunodeficiency virus type 1 on the central nervous system of African children. J Neurovirol. 2005;11:45-51. doi: 10.1080/13550280500511881. PubMed PMID: 16540455.
34 Hoffman SL, Rustama D, Punjabi NH, Surampaet B, Sanjaya B, Dimpudus AJ, et al. High-dose dexamethasone in quinine-treated patients with cerebral malaria: a double-blind, placebo-controlled trial. J Infect Dis. 1988;158:325-31. doi: 10.1093/infdis/158.2.325. PubMed PMID: 3042874.
35 Raviglione MC, Snider DE Jr, Kochi A. Global epidemiology of tuberculosis. Morbidity and mortality of a worldwide epidemic. JAMA. 1995;273:220-6. doi: 10.1001/jama.273.3.220. PubMed PMID: 7807661.
36 Alavi-Naini R, Moghtaderi A, Koohpayeh HR, Sharifi-Mood B, Dimpudus AJ, et al. A comparative clinical trial of artemether and quinine in children with severe malaria. Indian Pediatr. 2003;40:939-45. PubMed PMID: 14581730.
37 Misra UK, Kalita J, Maurya PK. Stroke in tuberculous meningitis. J Neurol Sci. 2011;303:22-30. doi: 10.1016/j.jns.2010.12.015. PubMed PMID: 21272895.
38 Del Brutto OH. Infections and stroke. Handb Clin Neurol. 2009;93:851-72. PubMed PMID:18804684.
39 Misra UK, Kalita J, Maurya PK. Stroke in tuberculous meningitis. J Neurol Sci. 2011;303:22-30. doi: 10.1016/j.jns.2010.12.015. PubMed PMID: 21272895.
40 Del Brutto OH. Infections and stroke. Handb Clin Neurol. 2009;93:851-72. PubMed PMID:18804684.
41 Misra UK, Kalita J, Maurya PK. Stroke in tuberculous meningitis. J Neurol Sci. 2011;303:22-30. doi: 10.1016/j.jns.2010.12.015. PubMed PMID: 21272895.
42 Bayindir C, Mete O, Bilic B. Retrospective study of 23 pathologically proven cases of central nervous system tuberculomas. Clin Neurol Neurosurg. 2006;108:353-7. doi: 10.1016/j.clineuro.2005.03.001. PubMed PMID: 16644403.
43 van der Weert EM, Hartgers NM, Schaaf HS, Eley BS, Pitcher RD, Wieselthaler NA, et al. Comparison of diagnostic criteria of tuberculous meningitis in human immunodeficiency virus-infected and uninfected children. Pediatr Infect Dis J. 2006;25:65-9. doi: 10.1097/01.inf.0000183751.75880.f8. PubMed PMID: 16395106.
44 Dastur DK, Lalitha VS, Udani PM, Parekh U. The brain and meninges in tuberculous meningitis-gross pathology in 100 cases and pathogenesis. Neurol India. 1970;18:86-100. PubMed PMID: 5459296.
45 Dharmasa S, Gupta AK, Tandon PN. Tuberculous meningitis--a CT study. Br J Radiol. 1982;55:189-96. doi: 10.1259/0007-1285-55-651-189. PubMed PMID: 7066619.
46 Leiguarda R, Berthier M, Starkstein S, Nogués M, Lylyk P. Ischemic infarction in 25 children with tuberculous meningitis. Stroke. 1988;19:200-4. doi: 10.1161/01.STR.19.2.200. PubMed PMID: 3344536.
47 Rojas-Echeverri LA, Soto-Hernández JL, Garza S, Martínez-Zubieta R, Miranda LI, García-Ramos G, et al. Predictive value of digital subtraction angiography in patients with tuberculous meningitis. Neuroradiology. 1996;38:20-4. doi: 10.1007/BF00593210. PubMed PMID: 8773269.
48 Lan SH, Chang WN, Lu CH, Lui CC, Chang HW. Cerebral infarction in chronic meningitis: a comparison of tuberculous meningitis and cryptococcal meningitis. QJM. 2001;94:247-53. doi: 10.1093/qjmed/94.5.247. PubMed PMID: 11353098.
49 Shu JJ, Chiu HY, Kang JH, Chen YH, Lin HC. Tuberculosis and the risk of ischemic stroke: a 3-year follow-up study. Stroke. 2010;41:244-9. doi: 10.1161/STROKEAHA.109.567735. PubMed PMID: 20035070.
50 Thwaites G, Chau TT, Mai NT, Dobrzenski F, McAdam K, Farrar J. Tuberculous meningitis. J Neurol Neurosurg Psychiatry. 2000;68:289-99. doi: 10.1136/jnnp.68.3.289.
Infective causes of stroke in tropical regions

PubMed PMID: 10675209; PubMed Central PMCID: PMC1736815.
51 Joosten AA, Prevo RL, de Vos RA, Hendrix MG, Boomstra S, Jansen Steur EN. Pachymeningitis luetica: a case report. Clin Neurol Neurosurg. 2000;102:176-9. doi: 10.1016/S0303-8467(00)00092-5. PubMed PMID: 10996719.
52 Danielsen AG, Weismann K, Jørgensen BB, Heidenheim M, Fugleholm AM. Incidence, clinical presentation and treatment of neurosyphilis in Denmark 1980-1997. Acta Derm Venereol. 2004;84:459-62. doi: 10.1080/00015550410017308. PubMed PMID: 15846637.
53 Landi G, Villani F, Anzalone N. Variable angiographic findings in patients with stroke and neurosyphilis. Stroke. 1990;21:333-8. doi: 10.1161/01.STR.21.2.333. PubMed PMID: 21743160.
54 Kayal AK, Goswami M, Das M, Paul B. Clinical spectrum of neurosyphilis in North East India. Neurol India. 2011;59:344-50. doi: 10.4103/0028-3886.82719. PubMed PMID: 21743160.
55 Chahine LM, Khoriaty RN, Tomford WJ, Hussain MS. The changing face of neurosyphilis. Int J Stroke. 2011;6:136-43. doi: 10.1111/j.1747-4949.2010.00568.x. PubMed PMID: 21371276.
56 Jay CA. Treatment of neurosyphilis. Curr Treat Options Neurol. 2006;8:185-92. doi: 10.1007/s11940-006-0009-7. PubMed PMID: 16569377.
57 Alarcón F, Hidalgo F, Moncayo J, Viñán I, Dueñas G. Cerebral cysticercosis and stroke. Stroke. 1992;23:224-8. doi: 10.1161/01.STR.23.2.224. PubMed PMID: 1561652.
58 Barinagarrementeria F, Cantú C. Frequency of cerebral arteritis in subarachnoid cysticercosis: an angiographic study. Stroke. 1998;29:123-5. doi: 10.1161/01.STR.29.1.123. PubMed PMID: 9445339.
59 Alarcón F, Vanormelingen K, Moncayo J, Viñán I. Cerebral cysticercosis as a risk factor for stroke in young and middle-aged people. Stroke. 1992;23:1563-5. doi: 10.1161/01.STR.23.11.1563. PubMed PMID: 1440703.
60 Bustos JA, Pretell EJ, Llanos-Zavalaga F, Gilman RH, Del Brutto OH, Garcia HH, et al. Efficacy of a 3-day course of albendazole treatment in patients with a single neurocysticercosis cyst. Clin Neurol Neurosurg. 2006;108:193-4. doi: 10.1016/j.clineuro.2004.12.013. PubMed PMID: 16412842.
61 Alarcón F, Maldonado JC. Short course of albendazole therapy for neurocysticercosis. Clin Neurol Neurosurg. 2006;108:810-1. doi: 10.1016/j.clineuro.2006.03.008. PubMed PMID: 16647198.
62 Py MO. Neurologic manifestations of Chagas disease. Curr Neurol Neurosci Rep. 2011;11:536-42. doi: 10.1007/s11910-011-0225-8. PubMed PMID: 21904918.
63 Dias JC, Silveira AC, Schofield CJ. The impact of Chagas disease control in Latin America: a review. Mem Inst Oswaldo Cruz. 2002;97:603-12. doi: 10.1590/S0074-02762002000500002. PubMed PMID: 12219120.
64 Cruz-Reyes A, Pickering-López JM. Chagas disease in Mexico: an analysis of geographical distribution during the past 76 years--a review. Mem Inst Oswaldo Cruz. 2006;101:345-54. doi: 10.1590/S0074-02762006000400001. PubMed PMID: 16951802.
65 Mancuso FJ, Almeida DR, Moisés VA, Oliveira WA, Mello ES, Poyares D, et al. Left atrial dysfunction in chagas cardiomyopathy is more severe than in idiopathic dilated cardiomyopathy: a study with real-time three-dimensional echocardiography. J Am Soc Echocardiogr. 2011;24:526-32. doi: 10.1016/j.echo.2011.01.013. PubMed PMID: 21353762.
66 Carod-Artal FJ. Stroke: a neglected complication of American trypanosomiasis (Chagas' disease). Trans R Soc Trop Med Hyg. 2007;101:1075-80. doi: 10.1016/j.trstmh.2007.06.007. PubMed PMID: 17663015.
67 Carod-Artal FJ, Vargas AP, Horan TA, Nunes LG. Chagasic cardiomyopathy is independently associated with ischemic stroke in Chagas disease. Stroke. 2005;36:965-70. doi: 10.1161/01.STR.0000163104.92943.50. PubMed PMID: 15845889.
68 Oliveira-Filho J, Viana LC, Vieira-de-Melo RM, Faïçal F, Torreão JA, Villar FA, et al. Chagas disease is an independent risk factor for stroke: baseline characteristics of a Chagas Disease cohort. Stroke. 2005;36:2015-7. doi: 10.1161/01.STR.0000177866.13451.e4. PubMed PMID: 16081855.
69 Carod-Artal FJ, Ribeiro Lda S, Vargas AP. Awareness of stroke risk in chagasic stroke patients. J Neurol Sci. 2007;263:35-9. doi: 10.1016/j.jns.2007.05.022. PubMed PMID: 17574599.
70 Ranjarb M, Rezaiee AA, Hashemi SH, Mehdipour S. Neurobrucellosis: report of a rare disease in 20 Iranian patients referred to a tertiary hospital. East Mediterr Health J. 2009;15:143-8. PubMed PMID: 19469437.
Yetkin MA, Bulut C, Erdinc FS, Oral B, Tulek N. Evaluation of the clinical presentations in neurobrucellosis. Int J Infect Dis. 2006;10:446-52. doi: 10.1016/j.ijid.2006.05.007. PubMed PMID: 16914346.

Trifiletti RR, Restivo DA, Pavone P, Giuffrida S, Parano E. Diabetes insipidus in neurobrucellosis. Clin Neurol Neurosurg. 2000;102:163-5. doi: 10.1016/S0303-8467(00)00089-5. PubMed PMID: 10996715.

Bingöl A, Togay-Işikay C. Neurobrucellosis as an exceptional cause of transient ischemic attacks. Eur J Neurol. 2006;13:544-8. doi: 10.1111/j.1468-1331.2006.01286.x. PubMed PMID: 16722984.

Zaidan R, Al Tahan AR. Cerebral venous thrombosis: a new manifestation of neurobrucellosis. Clin Infect Dis. 1999;28:399-400. doi: 10.1086/515097. PubMed PMID: 10064259.

Shehata GA, Abdel-Baky L, Rashed H, Elamin H. Neuropsychiatric evaluation of patients with brucellosis. J Neurovirol. 2010;16:48-55. doi: 10.3109/13550280903586386. PubMed PMID: 20151851.

Misra UK, Kalita J, Nair PP. Role of aspirin in tuberculous meningitis: a randomized open label placebo controlled trial. J Neurol Sci. 2010;293:12-7. doi: 10.1016/j.jns.2010.03.025. PubMed PMID: 20421121.

Bednar MM. Stroke: antithrombin versus antiplatelet therapy. Expert Opin Investig Drugs. 2000;9:355-69. doi: 10.1517/13543784.9.2.355. PubMed PMID: 11060682.

Gill GV. Diabetes and diet. Trop Doct. 2002;32:57. PubMed PMID: 11991041.

Gill G, Ala L, Gurgel R, Cuevas L. Accuracy of aneroid sphygmomanometer blood pressure recording compared with digital and mercury measurements in Brazil. Trop Doct. 2004;34:26-7. PubMed PMID: 14959969.

Lemogoum D, Degoute JP, Bovet P. Stroke prevention, treatment, and rehabilitation in sub-saharan Africa. Am J Prev Med. 2005;29:95-101. doi: 10.1016/j.amepre.2005.07.025. PubMed PMID: 16389133.