NEUROLOGY CONFERENCE 2
CNS INFECTIONS IN SSA

PROF E BADOE  MRCP(UK)  FRCPCH FGCP
HEAD OF NEUROLOGY SERVICES, DEPT OF CHILD HEALTH,
5TH SEPTEMBER, 2019
EAN REGIONAL TEACHING COURSE, SUB SAHARAN AFRICA
This monument was erected by

Colonel I. K. Acheampong,

Deputy High Commissioner of

National Health Commission

On the 1st Day of November, 1976

TO THE GLORY OF GOD

By His Grace and Grace of

Sir Frederick Gordon Guinness

Founded in 1875

from the Mission Church of

The Catholic Church in the

City of Accra on the

20th Anniversary of the Opening of the

Christian Mission Field in the City on October 6, 1975.
DEPT OF CHILD HEALTH
Infections of the CNS are devastating with a high mortality and morbidity in SSA.
IMPACT AND EPIDEMIOLOGY OF VIRAL, PARASITIC AND BACTERIAL INFECTIONS IN SSA

• Neglected tropical disease (NTDs) affect the poorer countries in SSA.

• Polio remains active and the non polio enteroviruses. Adenovirus are rife.

• Rarer conditions like the West Nile virus, chinkungunya, zika and ebola predominantly found in SSA
POLIO

• Recent headlines in Ghana – endgame in sight?
POLIO

• Nigeria- hopes to declare a polio free status next year after 3 years without a case

• Highly infectious enterovirus of antigenic types 1, 2, and 3.
POLIO

• In children wild virus may invade CNS causing an aseptic meningitis (non paralytic polio)

• Pathological lesions involve the anterior horn cells, motor and sensory nuclei of the medulla, reticular formation, cerebellar vermis

• Common spinal poliomyelitis characterized by asymmetrical flaccid paralysis involving the legs, arms or trunk with absent tendon reflexes

• Urinary retention is present in 20-30% of cases
ENTERO VIRUSES

• Important potential cause of neurologic disease in African children.

• Enter host via gastrointestinal tract, replicate and can lead to an infection of the CNS

• Infections typically occur during tropical rainy season. Lowest during harmattan. Risk of infection linked to poor hygiene, poor sanitation and overcrowding
ENTEROVIRUSES

• Signs:
  • Diarrhea
  • abdominal discomfort
  • maculo-papular rash

• Children present with acute encephalitic features
ENTEROVIRUSES

• Enterovirus 71 causes acute flaccid paralysis resembling Guillain barre syndrome

• Recent studies suggest it can now be detected in blood using PCR techniques. Lafolie J et al. Lancet infect dis 2018.
  • Currently RT-PCR on CSF samples for detection.
ENTEROVIRUSES

• Management:
  • Supportive care.
  • Pleocornil prevents virus from attaching to cellular receptors and releasing viral DNA. Benefit in certain cases.
RABIES

- Prevalence in SSA second globally to Asia with around 24,000 deaths each year

- Virus in infected mammals like dogs, cats.

- In Africa, mainly through dog bites. Lyssa virus after Greek spirit of madness and frenzy
RABIES

• Incubation period of 20 to 60 days

• Signs:
  • Chills
  • Fever
  • Headache
  • Sore throat
  • Abdominal pain

• Pain or itching at the site of inoculation common
RABIES

- Virus replicates in skin and reaches CNS by retrograde axonal transport via peripheral nerves

- Furious "rabies:
  - Hydrophobia
  - violent episodes of hyperexcitability and lucidity followed by coma and death
RABIES

• Copious flushing of wound with saline solution or cetrimide plus chlorhexidine solution

• Infiltrate wound with rabies immunoglobulin 10 IU/kg.

• Update tetanus immunization.

• Commence antirabies vaccine and immunoglobulin depending on condition of animal at time after attack.
Rabies

- Ethiopia has one of the highest rates in Africa
- Global strategic plan to eliminate rabies by 2030
- Africa lacks an effective rabies control program
- Lacks information about actual cases of rabies
- Unwillingness to bring dogs for vaccination
- Many dogs are ownerless

- Lack of surveillance and diagnostic capacity for rabies detection and cost of dog vaccination campaigns. *Lembo T plos negl trop dis 2010*
WEST NILE VIRUS (ARTHROPOD –BORNE ENCEPHALITIS)

- Mosquito born RNA virus (flavivirus and broadly arboviruses)

- Endemic throughout Africa

WEST NILE VIRUS (WNV)

• WNV maintained in nature in a cycle between birds and mosquitoes and culex species plays largest role in transmission

• Humans and horses are incidental hosts

• Approximately 5% of patients with symptomatic infection develop neurologic disease
WNV

• Diagnosis:
  • Diagnosis is by detecting IGM antibody in CSF, serum
  • Detecting virus in nucleic acid in CSF blood

• Treatment:
  • It is supportive

• Prevention:
  • focus on surveillance, elimination of mosquito breeding sites and adult mosquito management using pesticides.
WNV

• Treatment:
  • It is supportive

• Prevention:
  • focus on surveillance, elimination of mosquito breeding sites and adult mosquito management using pesticides.
COMMONEST VIRUS IN SSA?


- Most commonly detected virus in the CNS was adenovirus followed by mumps, human herpes virus 6, and rabies virus.
HERPES SIMPLEX ENCEPHALITIS (HSE)

- Presents with encephalopathy (altered mental state), deteriorating level of consciousness, focal seizures, focal neurological abnormalities

- Neonatal HSE commoner. Skin lesions may be present
HERPES SIMPLEX ENCEPHALITIS (HSE)

Diagnosis:

• Best neuroimaging is MRI

• EEG required?

Management:

• High dose iv aciclovir is most effective when started early
TEMPORAL LOBE AFFECTED IN HERPES
PARASITIC CNS INFECTIONS

• Cerebral malaria (CM)
  • 90% of deaths occur in Africa (WHO 2008)

• Cases falling in Africa.
  • Prevention strategies appear to be working
CM

- Vascular level occlusion leads to microhemorrhages and reduced perfusion

- Altered transmembrane transport, hypoxia, cell swelling, anaerobic glycolysis, lactic acidosis and cell death

- Changes lead to endothelial damage with increased blood brain barrier permeability

- Changes lead to brain swelling and raised ICP reducing cerebral blood flow
CM

• Diagnosis based on unrousable coma in the presence of P. falciparum parasitaemia in the peripheral blood

• Recently important to include an assessment for malaria retinopathy in the diagnosis of CM Beare NA, Lewallen S, Taylor T. Redefining cerebral malaria by including malaria retinopathy. Future microbiol mar; 6(3):349-55

• Primary treatment is with parenteral quinine or artemisinin derivatives. Artemisinin have a better safety profile, fewer serious side effects
NEUROCYSTICERCOSIS

• Very common parasite in the CNS in SSA

• Important cause of seizures in children in endemic countries

• Pig production widespread in Cote Ivoire and Togo

• Nigeria has 5 million pigs (biggest in West Africa)
NEUROCYSTICERCOSIS

• Infection by Taenia solium

• Neurocysticercosis reflects the death of larvae within the brain and spinal cord

• Presents with headache, seizures, focal deficits, visual dysfunction, behavioural changes and papilledema
NEUROCYSTICERCOSIS

**Diagnosis**
- MRI and CT show circular or ring enhancing lesions typically with adjacent oedema.
- CSF - eosinophilic lymphocytosis and elevated protein.
- Enzyme linked immunoelectrotransfer blot (ELISA) assay. Sensitivity 98% specificity 100%.

**Treatment** with albendazole for 7 days. Dexamethasone or prednisolone given before or concurrently to minimize symptoms associated with parasite death.
HUMAN AFRICAN TRYPANOSOMIASIS

Trypanosoma brucei gambiense – West African trypanosomiasis

Trypanosoma brucei rhodesiense – East African disease (Tanzania, Uganda, Malawi and Zambia 95% of cases)

Currently 50,000-70,000 cases in Africa

10,000 new cases annually (WHO 2016)

Transmitted by bite of tse tse fly
TRYPANOSOMIASIS

- Initial multiplication of parasites at infection site followed by hemolymphatic stage
- Waves of parasitemia
- Invasion of nervous system next causing leukoencephalitis (meningoencephalitic stage)
- West African disease indolent
- East African disease more acute progression
TRYPANOSOMIASIS

• East african disease can present with
  • Headache
  • personality changes
  • psychiatric disorders

• Characteristic sleep disturbance
TRYPANOSOMIASIS

Diagnosis:

• direct observation of intracellular trypomastigotes in serum or CSF.
• Neuroimaging typically show more than one ring enhancing lesions involving both grey and white matter
• Stage 1 drugs- suramin and pentamidine
• Stage 2 (encephalitic stage) arsenic compounds (melarsoprol.) Or dl-a – difluoromethylornithine(dfmo)
TOXOPLASMOSIS

- Widely distributed causing infection in all warm blooded animals including humans
- Parasitic infection caused the protozoan toxoplasma gondii
- In Africa childhood toxoplasmosis through congenital infections
- A study suggests T gondii widespread in Mali and elsewhere in West Africa in both urban and rural areas. Ouologuem DT djimde AA et al. Toxoplasma gondii seroprevalence in mali. J parasito apr;99(2): 371-4
TOXOPLASMOsis

- Children with HIV-toxoplasmosis due to reactivation of latent infection

TOXOPLASMOSIS

- Incidence of toxoplasma encephalitis reduced among HIV infected people receiving trimethoprim-sulphamethoxazole or dapsone/pyrimethamine therapy as prophylaxis against pneumocytis carinii pneumonia

- Congenital toxoplasmosis occurs when maternal infection occurs late in pregnancy

- Leads to ocular disease (chorioretinitis or congenital neurologic deficits or learning disabilities)
TOXOPLASMOSIS

• Learning difficulties do occur. Advancing age of child due to recrudescence of bradyzoite cysts established in infant holland GN. Ocular toxoplasmosis. The influence of patients age. Mem inst oswaldo cruz 2009 mar;104(2):351-7

• In immunocompromised children/adults clinical manifestations of CNS toxoplasmosis include headache, altered mental status, focal neurologic deficits, ataxia, cranial nerve palsies Patchell RA. Neurological complications of organ transplantation ann neurol 1994 nov;36(5):688-703
TOXOPLASMOSIS

Diagnosis:

- Anti-
  toxoplasma antibodies by ELISA both sensitive and specific

- Multiple ring enhancing lesions in the basal ganglia or cerebrum on CT or MRI in the presence of anti-toxoplasma IgG antibodies suggest presence of CNS toxoplasmosis

- Drug treatment of CNS toxoplasmosis includes pyrimethamine, sulfadiazine and folinic acid
IMAGE OF TOXOPLASMOSIS
SCHISTOSOMIASIS (BILHARZIAS)

• Second only to malaria as the most devastating parasitic disease.

• Tourists at risk from eco tourism

• Ghana an endemic area especially after construction of the big Akosombo dam in 1965.
  • First disease prevalence study in Ghana surveys in 1963 estimated 15-20% of people in Ghana were infected with schistosomiasis in their lifetime!
SCHISTOSOMIASIS

• Neuroschistosomiasis is the most severe clinical form of the infection.
• In Ghana S mansoni and S haematobium predominate.
• Neurological complications from egg deposition and follows migration of adult worms to the brain or spinal cord
• Followed by granuloma formation surrounding thousands of eggs deposited and the hallmark of neuroschistosomiasis. Neurological complications of schistosoma infection. Trans R soc trop med hyg 2008
SCHISTOSOMIASIS

- Neuro signs- RICP, myelopathy, radiculopathy
- Headache, visual disturbance, delirium, seizures, ataxia and encephalopathy
- Spinal cord involvement - back pain, limb pain, muscle weakness, sensory loss, bladder dysfunction
- Acute transverse myelitis and sub acute myeloradiculopathy of lumbar sacral region probably most commonly reported neurological manifestation of S mansoni and S haematobium
SCHISTOSOMIASIS

• Cortex involvement, subcortical white matter/basal ganglia or internal capsule leads to acute encephalitis in *S japonicum* carod-artal FJ. Neurological complications of schistosoma infection. *Trans R Soc trop Med Hyg.* 2008

• Diagnosis:
  • Positive diagnostic finding of eggs in stool plus neuroimaging and above listed presentation makes neuroschistosomiasis likely
  • Definitive diagnosis by biopsy and histopathological study when granulomas exist
SCHISTOSOMIASIS

Management:

• Praziquantel effective for all species and curative in 60-90% of cases. If not effective oxamniquine can be used.

• Artemether can be effective against immature migrating larvae (schistosomula)
TUBERCULOSIS/DEVELOPMENTS

• TB responsible for more deaths than any other infection.

• Pan ACEA consortium identifying ways to accelerate TB drug development

• Platform for TB drug trials across Africa

• High dose rifampicin has shown great promise as part of regime to shorten the TB treatment regime
TUBERCULOSIS

• 4% of people with HIV in SSA are infected with TB.

• One in five such patients experience a severe inflammatory reaction known as TB-IRIS. Immune system as it recovers from treatment responds too vigorously to the TB infection.
TUBERCULOSIS

• New BCG vaccine engineered based on M tuberculosis to eliminate genes central to disease while maintaining those lost in BCG traditional vaccine that provoke a strong immune response.

• Currently we know BCG vaccine less effective in the older age group

TUBERCULOSIS

• Large scale trials going on in Senegal and Madagascar. Better protection for newborns on the horizon and prevention of TB meningitis?

• First live attenuated vaccine to reach clinical trials stage showing similar safety to BCG

• WHO recommends X pert MTB/RIF as the new molecular diagnostic test for TB. Both sensitive and specific.
TUBERCULOSIS

• New dipstick test on the horizon

• LAM –TB test detects lipoarabinomannan) a molecule derived from mycobacterium TB in the urine. LAM antigen a lipopolysaccharide derived from active TB cells or degenerating cells and occurs only in people with active TB

• Adding a dipstick test in trials shown to reduce risk of death by 17% at 8 weeks. Leads to better detection of TB than from sputum.

• A policy statement now from who on the use of LAM TB test for people living with HIV and active TB as a potential point of care test.
TUBERCULOSIS


• Sputum independent

• Developed in Tanzania at the national institute for medical research, Mbeya.

• Diagnoses active TB in children
TUBERCULOSIS

• First immunodiagnostic tool to detect active TB in children with sensitivity similar to culture

• Measures CD 27 phenotype of CD4 T cell.
HIV

• More than 3 million HIV infected children live in Africa

• One in five HIV related deaths in Africa attributed to opportunistic fungal infection.

• Cryptococcal meningitis responsible for 500,000 deaths in SSA. Molloy sf et al. Cryptococcal meningitis. a neglected tropical disease? Plos neg trop dis 2017;11;(6)

• Improving management of meningitis in HIV infected individuals new dipstick diagnostic test for cryptococcal infection developed
HIV

• Craglfa test - effective in resource limited setting like SSA. (Cryptococcal antigen lateral flow assay.

• Test provides an indication of the severity of infection and need for more treatment even when asymptomatic and revolutionizing cryptococcal antigen testing.

• A dipstick immunochromatographic assay

• Akin to home pregnancy test. No need for sophisticated lab to do tests lacking in SSA. Meets WHO standards
HIV

• New mosaic vaccine being developed by tomas hank at the university of oxford.

• Second generation vaccine
SUMMARY

• A not exhaustive but important CNS infections peculiar to SSA has been presented.

• Some are well known having existed since antiquity like rabies.

• Basic presentation of the diseases in ssa presented with short reviews of emerging viral infections in ssa like west nile virus.

• New developments in hiv, tb detection presented.
CONCLUSION

• Overview of the impact of CNS diseases shows that serious infections still exist on the continent.

• Immunization cover improving in SSA and polio, haemophilus type b meningitis, mumps meningoencephalitis, rubella embryopathy and subacute sclerosing encephalopathy are not routinely reported. A lot more not prevented by immunization as shown

• Virus infections in particular induce a wide spectrum of disease from benign to lethal situations,
REFERENCES/ACKNOWLEDGEMENTS


• Badoe E, Wilmshurst J. Overview of the effect and epidemiology of viral central nervous system infections in African children. Semin Pediatr Neurol 2014 21 (1) 26.9

• European Developing countries clinical trials partnership (EDCTP).9th forum website.