

An Overview of the Effect and Epidemiology of Viral Central Nervous System Infections in African Children

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Viral infections in Africa are common. Polio still persists in the continent despite vaccination campaigns. Many of the common viral infections, such as by the nonpolio enteroviruses, lack effective therapies and leave devastating sequelae to infected neonates and infants. Rarer conditions, such as by West Nile virus, have generated a fascinating conundrum as to how the virus spread to other parts of the world, such as the United States of America. This infection illustrates that these conditions should not be considered isolated to Africa alone but that they represent examples of potentially lethal infections which, although predominantly found in Africa, have the capacity to spread wider afield.

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Introduction

The burden of disease related to the sequelae of infections of the central nervous system (CNS) is significant, but the true prevalence is unknown in Africa. Conditions such as polio persist in specific regions of Africa. Nonpolio enteroviruses result in frequent infections, especially in the neonatal and infantile age groups. Many of the viral infections lack effective therapies and leave irreversible neurologic deficits. Rabies virus infection represents a public health tragedy where the lack of capacity to contain infected domestic pets results in the death of many children in Africa. The following sections focus on a group of key viral infections of particular relevance to Africa. The other major viral infection that is endemic in Africa is due to the human immunodeficiency virus; this has been addressed in another article in this edition.

Polio

Poliovirus is a highly infectious enterovirus of antigenic types 1, 2, and 3. The global effort to eradicate polio is the largest public health initiative in history. With widespread immunization, poliomyelitis has become extremely rare, and the 3 remaining countries of the world in which it is

endemic are Nigeria, Pakistan, and Afghanistan, with sporadic cases reported elsewhere.¹ Man is the only natural host for polioviruses, and it most commonly infects younger children. Crowded and poor living conditions encourage the spread of poliovirus. Vaccine-associated cases also occur. The Global Polio Eradication Initiative provides technical assistance and guidance to countries in Africa to ensure polio eradication in the region within a set timeline, and total eradication of the disease worldwide remains a priority of the World Health Organization.²

Natural History and Clinical Features

In children, most cases are subclinical or present as simple febrile illness. However, in a minority of infections by the wild virus, it proceeds to invade the CNS, causing aseptic meningitis (nonparalytic polio) or, more rarely, paralytic polio because of the virus attacking the motor cells in the spinal cord.

Initial symptoms consist of headache, vomiting, and fever, followed by meningeal irritation. Symptoms of upper respiratory tract infection are common in children. Spinal poliomyelitis is characterized by asymmetric flaccid paralysis involving the legs and arms with absent deep tendon reflexes. Involvement of the brainstem results in respiratory problems and bulbar impairment. Paralysis of the intercostal muscles and diaphragm is also seen.

There is no specific treatment for polio, and therapy remains symptomatic and supportive.

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The challenges in African countries that still report polio infections include the following: (1) children are based in remote areas where immunization programs are lacking and (2) maintaining high-quality and effective surveillance programs. Nigeria is still a potential source of the virus in the continent, and other countries need to conduct annual vaccination exercises to guard against resurgence of the infection. On the continent, the World Health Organization, UNICEF, and Rotary International have spearheaded efforts to eradicate the disease. The role of the traditional and religious leaders in a country such as Nigeria as key stakeholders for vaccination programs cannot be overemphasized.² They are the mobilizers, sensitizers, and creators of awareness.

Nonpolio Enteroviruses

Nonpolio enteroviruses circulate in all populations. Some 68 enterovirus serotypes are recognized, with most being nonpolio enteroviruses.³ The main virus types, that is, Coxsackie viruses, echoviruses, enteroviruses, and heparnaviruses, have a wide range of presentations ranging from asymptomatic to brainstem encephalitis, as well as meningitis and acute flaccid paralysis resembling polio.⁴ Enteroviruses are the most common cause of aseptic meningitis and can cause serious disease in infants and the immunocompromised.³

The Global Polio Eradication Initiative has succeeded in reducing the circulation of wild poliovirus, but nonpolio enteroviruses implicated in acute flaccid paralysis remain prevalent.

Transmission of these viruses is usually by the fecal-oral route or the respiratory route.⁵ Enterovirus infections typically occur during the tropical rainy season, and the risk of infection is directly correlated with poor hygiene, poor sanitation, and overcrowding. It is lowest during the Harmattan period (the dry and dusty West African northeasterly trade wind that blows from the Sahara into the Gulf of Guinea between the end of November and the middle of March).⁶

Signs of enteroviral disease may include diarrhea, abdominal discomfort, and a maculopapular rash.⁷ Children may present with acute encephalitic features, including seizures, fever, and coma, which may resemble those of herpes simplex encephalitis.⁸ Enterovirus 71 can cause flaccid paralysis resembling Guillain-Barré syndrome and can be a cause of diagnostic confusion, especially in settings with limited diagnostic resources.⁹

Treatment and Outcome

Most children with enteroviral CNS infections are managed with supportive care alone. Approved antiviral therapy is not commercially available.¹⁰ Pleconaril, an antiviral compound, which prevents the virus from attaching to cellular receptors and releasing viral RNA into the cell, may be of benefit in certain cases.^{11,12}

Conclusion

Enteroviruses remain an important potential cause of neurologic disease in African children because of their spread by the fecal-oral route and their emergence with the near elimination of polio from the continent. They present with a spectrum of neurologic disease associated with Guillain-Barré syndrome, aseptic meningitis, and polio-like paralysis. Active surveillance for this group of viruses remains important in the continent.

Rabies

Patients with rabies are reported across the African continent. This neglected enzootic disease has a prevalence in Africa that is second globally to Asia, with approximately 24,000 deaths estimated each year, despite the availability of effective vaccines.¹³ Rabies is rare in industrialized countries where both human and animal rabies have been eradicated as a result of quarantine and vaccination of domestic animals. This policy is not a high priority in the African continent.¹⁴

Rabies is a viral zoonosis caused by a negative-stranded RNA virus belonging to the *Lyssavirus* genus. Most human cases (90%) result from the bites of domestic dogs, who remain the principal maintenance host.¹⁵

The virus is in the saliva of infected mammals such as dogs, cats, foxes, and bats. It is transmitted to man through a bite or skin abrasion, but a history of an animal bite is absent in many cases.¹⁶ Clinical onset is nonspecific with “chills,” fever, headache, sore throat, malaise, nausea, or abdominal pain after a variable incubation period that averages 20-60 days.¹⁷ Pain or itching at the site of inoculation is common. The virus replicates in the skin and reaches the CNS by retrograde axonal transportation via the peripheral nerves. The overlap of symptoms with other infections prevalent in Africa such as cerebral malaria can lead to misdiagnosis, and as such, rabies should be included as a differential diagnosis especially where there is hypotonia and areflexia.¹⁸ The disease may develop as “furious rabies” with involvement of the CNS, characterized by hydrophobia, violent episodes of hyperexcitability, and lucidity, followed by coma and death. Hydrophobia, which is present in 20%-50% of patients, produces spasms of the laryngeal muscles, diaphragm, and accessory respiratory muscles, which can lead to respiratory arrest and death.¹⁹ More rarely, the disease develops as “dumb rabies” in which ascending paralysis, no hydrophobia, and more prolonged illness occurs.¹⁹

In Ghana, the Standard Treatment Guidelines for post-exposure management include the following: (1) Remove saliva from site of exposure by copiously flushing the wound with saline solution or cetrimide plus chlorhexidine solution.²⁰ (2) Infiltrate the wound with rabies immunoglobulin 10 IU/kg body weight. (3) Update tetanus immunization and commence antirabies vaccine and immunoglobulin, depending on the condition of the animal at the time of the attack and after 10 days observation of the animal. The experience in most African countries such as Ghana is that rabies tends to develop in seemingly normal animals, and therefore, any doubts about the

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