

# Emerging tropical neurological infections

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## ABSTRACT

A large majority of neurological infections remain undiagnosed worldwide. Emerging and re-emerging infections are likely to be responsible for a significant proportion of these. Over the last two decades, several new organisms producing neurological infection and the neurotropic potential of many other known pathogens have been identified. Large outbreaks caused by re-emerging pathogens such as Chikungunya virus, Zika virus and Ebola virus have led to better delineation of their neurological manifestations. Recognition of the pandemic potential of emerging pathogens and an improved understanding of their host–vector–environment interactions would help us be better prepared to meet these emerging threats.

## Introduction

The global landscape of neurological infections appears to be changing, and a key reason is the emergence and re-emergence of many neurotropic pathogens. This is especially true in tropical countries where the pattern of infectious diseases is different from temperate regions due to a multitude of geographical, socio-economic and socio-cultural factors. Aetiological agents traditionally taught in medical schools as common causes of neurological infections are seldom identified in outbreak investigations and surveillance studies from tropical countries.<sup>1,2</sup> This article will focus on some emerging neurological infections that have recently gained global attention.

## Dengue with neurological involvement

Dengue is the most important arboviral disease worldwide and is endemic in more than 100 countries, with half of the world population at risk.<sup>3</sup> Dengue virus (DENV, family Flaviviridae, genus Flavivirus, transmitted by *Aedes* mosquitoes) has four antigenically distinct serotypes (DENV-1 to DENV-4). Neurological involvement is seen in up to 21% of patients and is mainly associated with DENV-2 and DENV-3 serotypes.<sup>4,5</sup> DENV is identified in 4–47% of suspected encephalitis cases in endemic areas.<sup>6</sup> A high index of suspicion is required as many patients with neurological involvement do not exhibit features of the typical dengue fever syndrome.<sup>7</sup>

The spectrum of neurological manifestations in dengue is diverse. Dengue encephalitis and encephalopathy present with

altered consciousness, behavioural changes, headache, seizures and focal deficits. Encephalopathy is the commonest neurological abnormality reported, and results from several systemic disturbances (prolonged shock, hypoxia, metabolic derangements, intracerebral haemorrhage, brain oedema, acute liver failure or renal failure). Cerebrospinal fluid (CSF) analysis is usually normal. Neuroinvasive and neurotropic properties of DENV have been demonstrated over the recent years, confirming the existence of dengue encephalitis. Its diagnosis is supported by lymphocytic pleocytosis, detection of dengue-specific IgM, NS1 antigen or dengue-RNA (by RT-PCR), or virus isolation in CSF. Brain MRI may be normal or show cerebral oedema or non-specific changes. DENV antigen and RNA (by RT-PCR) have been detected from brain tissue in autopsy studies.<sup>4,5</sup>

Dengue-associated muscle dysfunction (myalgia, proximal weakness, elevated creatine kinase), while usually self-limiting, may occasionally lead to rhabdomyolysis. Typical myopathic changes are not usually seen on electromyography. Stroke following dengue is rare, and haemorrhagic strokes are commoner

## Key points

The global landscape of central nervous system infections is rapidly changing.

Neurological syndromes caused by many emerging pathogens, mainly viruses, have been defined in the last decade.

Emerging infections are likely to be responsible for a significant proportion of the burden of neurological infections, especially in tropical countries.

Outbreaks caused by emerging pathogens may result from the expansion of their geographical range, spread from animal reservoirs and development of new neurovirulence.

Diagnostic yields will improve if we start searching for emerging pathogens in observational studies, outbreak investigations and surveillance studies of neurological infections.

**KEYWORDS:** neurological infections, emerging infections, tropical infections

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## **Table of Contents Emerging Neurological Infections**

1. Understanding the eBook Emerging Neurological Infections
  - The Rise of Digital Reading Emerging Neurological Infections
  - Advantages of eBooks Over Traditional Books
2. Identifying Emerging Neurological Infections
  - Exploring Different Genres
  - Considering Fiction vs. Non-Fiction
  - Determining Your Reading Goals
3. Choosing the Right eBook Platform
  - Popular eBook Platforms
  - Features to Look for in an Emerging Neurological Infections
  - User-Friendly Interface
4. Exploring eBook Recommendations from Emerging Neurological Infections
  - Personalized Recommendations
  - Emerging Neurological Infections User Reviews and Ratings
  - Emerging Neurological Infections and Bestseller Lists
5. Accessing Emerging Neurological Infections Free and Paid eBooks
  - Emerging Neurological Infections Public Domain eBooks

- Emerging Neurological Infections eBook Subscription Services
- Emerging Neurological Infections Budget-Friendly Options
- 6. Navigating Emerging Neurological Infections eBook Formats
  - ePub, PDF, MOBI, and More
  - Emerging Neurological Infections Compatibility with Devices
  - Emerging Neurological Infections Enhanced eBook Features
- 7. Enhancing Your Reading Experience
  - Adjustable Fonts and Text Sizes of Emerging Neurological Infections
  - Highlighting and Note-Taking Emerging Neurological Infections
  - Interactive Elements Emerging Neurological Infections
- 8. Staying Engaged with Emerging Neurological Infections
  - Joining Online Reading Communities
  - Participating in Virtual Book Clubs
  - Following Authors and Publishers Emerging Neurological Infections
- 9. Balancing eBooks and Physical Books Emerging Neurological Infections
  - Benefits of a Digital Library
  - Creating a Diverse Reading Collection Emerging Neurological Infections
- 10. Overcoming Reading Challenges
  - Dealing with Digital Eye Strain
  - Minimizing Distractions
  - Managing Screen Time
- 11. Cultivating a Reading Routine Emerging Neurological Infections
  - Setting Reading Goals Emerging Neurological Infections
  - Carving Out Dedicated Reading Time
- 12. Sourcing Reliable Information of Emerging Neurological Infections
  - Fact-Checking eBook Content of Emerging Neurological Infections
  - Distinguishing Credible Sources
- 13. Promoting Lifelong Learning
  - Utilizing eBooks for Skill Development
  - Exploring Educational eBooks

#### 14. Embracing eBook Trends

- Integration of Multimedia Elements
- Interactive and Gamified eBooks

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