

# **BRAIN-EATING AMOEBAE**

## **Biology and Pathogenesis of *Naegleria fowleri***

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**Dedication**

*To our beloved children, Salahuddin Ahmed Khan, Mohammad Hafeez Khan and Imaan Asadi Khan, who bring so much joy to our lives.*

**Ruqaiyyah Siddiqui and Naveed Ahmed Khan**

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## Preface

The purpose of this book is to provide a reference for *Naegleria fowleri* as a quick guide for clinical colleagues, health professionals, researchers, and students. It is purposefully kept brief, and is divided into easy to follow sections, covering all aspects of *N. fowleri*. This compilation will serve as an essential reference for microbiologists, immunologists, physicians, and public health officials, in the field of basic and medical microbiology, as well as an invaluable reference for new and experienced researchers who wish to understand this organism better. This book is the definitive guide to the current knowledge and ongoing research in this medically and ecologically important organism. We are indebted to Drs. Jennifer R. Cope and Ibne Karim M. Ali (Waterborne Disease Prevention Branch in the National Center for Emerging and Zoonotic Infectious Diseases), for superbly composing the chapters on current practices and advances in diagnostics and therapeutics against *N. fowleri* infection.

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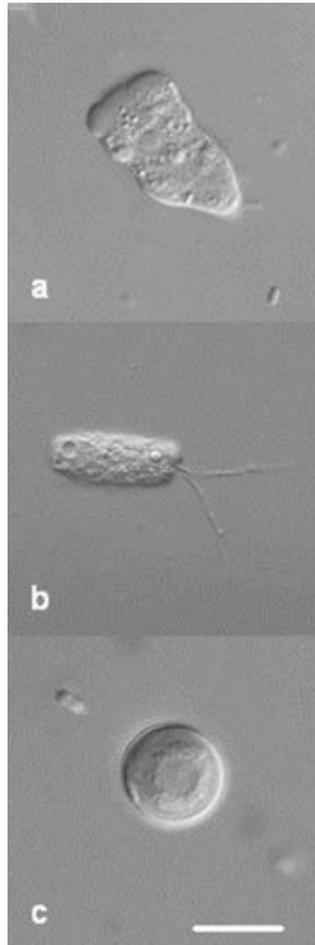
## Synopsis

*Naegleria fowleri* is a eukaryotic protist pathogen that causes primary amoebic meningoencephalitis. It enters the brain via the nasal route and kills the host within days. The most distressing aspect is that the disease almost always results in death with more than 90% mortality rate. Despite our advances in antimicrobial chemotherapy and supportive care, it is considered as one of the world's deadliest known parasites. This is, in part due to our incomplete understanding of the biology, ecology, pathogenesis, pathophysiology, and lack of available effective drugs. A complete knowledge of this parasite, how it lives in the environment, and produces disease is crucial for the rational development of preventative and therapeutic strategies against this fatal, albeit rare disease.

## Introduction to *Naegleria*

The genus *Naegleria* is a group of protist organisms that are widely distributed in the environment. Among the different species, *N. fowleri* is the only species that is known to infect people by entering the body through the nose via contaminated water, and produces primary amoebic meningoencephalitis, which is almost always fatal. *N. fowleri* has a three stage life cycle, consisting of a trophozoite stage, a flagellate form, and a cyst stage (Figure 1). It is widely accepted that the trophozoite stage is the only infective stage of the amoeba. *N. fowleri* reproduces asexually by binary fission during the trophozoite stage. In the absence of food but presence of water, *N. fowleri* trophozoites transform into the flagellate form to travel long distance in search of nutrients. The flagellate form is a transient stage that can neither encyst, nor reproduce. Under harsh conditions, trophozoites transform into the cyst form. The cyst is a dormant stage during which they remain inactive with little metabolic activity, but remain viable, for years. Both the flagellate and the cyst are non-feeding, and non-reproductive forms. Only the trophozoite form is able to feed, divide, and encyst. Cysts will excyst to yield trophozoites under favourable environmental conditions. When studying biology and pathogenesis, *N. fowleri* has often been compared against the well-studied non-pathogenic *N. gruberi*, however it is considered more appropriate to compare *N. fowleri* against closely related non-pathogenic *N. lovaniensis*. Given the opportunity and access, *N. fowleri* infect humans via the nose during swimming, nasal cleansing, bathing etc. and enter the brain via the olfactory neuroepithelial route to produce brain infection. The true burden of primary amoebic meningoencephalitis due to *N. fowleri* on human health is not known, as the majority of infections in less developed countries go unnoticed and in many developing countries the public has limited access to clean water. Furthermore, the

pathogenesis and pathophysiology associated with *N. fowleri* infection, as well as the molecular identification of virulence traits of *N. fowleri*, which will be potential targets for therapeutic interventions, and/or the development of preventative strategies remain incompletely understood.



**Figure 1.** *N. fowleri* (a) trophozoite form, (b) flagellate form, and (c) cyst form (courtesy: B. S. Robinson, Australian Water Quality Centre, South Australian Water Corporation). Bar is 10 $\mu$ m.