

# **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**

# Contents

<b>Preface</b> .....	<b>9</b>
<b>Synopsis</b> .....	<b>11</b>
<b>Introduction to <i>Naegleria</i></b> .....	<b>13</b>
<b>Chapter 1: Primary amoebic meningoencephalitis</b> .....	<b>15</b>
1.1. The disease	
1.2. Pathology	
1.3. Risk factors	
<b>Chapter 2: Clinical and laboratory diagnosis</b> .....	<b>27</b>
2.1. Computed tomographic (CT) appearance	
2.2. Clinical specimens	
2.3. Microscopic identification of amoebae	
2.3.1. Cerebrospinal fluid	
2.3.2. Brain tissue	
2.3.3. Amoebic culture	
2.3.4. Enflagellation experiment	
2.4. Serologic tests	
2.5. Antigen detection tests	
2.6. Molecular Detection	
2.7. Conclusions and future work	
<b>Chapter 3: Chemotherapeutic and disinfection strategies</b> .....	<b>45</b>
3.1. Current Treatment Recommendations	
3.1.1. Amphotericin B	
3.1.2. The Azoles	
3.1.3. Macrolides	
3.1.4. Rifamycins	
3.1.5. Rokitamycin	
3.1.6. Tetracyclines	
3.1.7. Miltefosine	
3.2. Strategies to reduce elevated intracranial pressure	
3.3. Other drugs	
3.4. Amoebicidal activity of animal serum	
3.5. Other agents as disinfectants	
3.5.1. Chlorine	
3.5.2. Peracetic acid and monochloramine	
3.5.3. Simulated solar disinfection	
3.5.4. Pulsed electric fields	
3.5.5. Inhibition of <i>Naegleria fowleri</i> by microbial iron-chelating agents	
3.5.6. Delta 9-tetrahydrocannabinol	
3.6. Resistance of pathogenic <i>Naegleria</i> to some common physical and chemical agents	
3.7. Future Drug targets	
3.8. Future prospects: Strategies to deliver antiamoebic drugs	

<b>Chapter 4: Pathogenesis .....</b>	<b>63</b>
4.1. Axenic growth and pathogenic potential of <i>N. fowleri</i>	
4.2. <i>In vivo</i> models	
4.3. <i>In vitro</i> models	
4.3.1. Organotypic slice cultures from rat brain tissue to study <i>N. fowleri</i> infection	
4.4. Ultrastructural features: amoebae from brain tissue <i>versus</i> culture medium	
4.5. Light and electron microscopic observations on the pathogenesis of <i>N. fowleri</i> in mouse brain and tissue culture	
4.6. Routes of entry into the central nervous system	
4.7. Contact-dependent mechanisms	
4.7.1. Adhesion	
4.7.2. Phagocytosis and amoebastomes	
4.8. Membrane-associated cytolytic protein	
4.9. Contact-independent mechanisms	
4.9.1. Pore-forming polypeptides	
4.9.2. Cytolytic activity of <i>N. fowleri</i> cell-free extract	
4.9.3. Hydrolases	
4.9.4. Nitric oxide	
4.9.5. Haemolytic activity	
4.10. Additional potential pathogenicity factor	
<b>Chapter 5: The host-damage response to <i>N. fowleri</i> .....</b>	<b>83</b>
5.1. Role of immune response	
5.2. Cell-mediated immunity	
5.3. Neutrophils	
5.4. Activated macrophages destruct <i>N. fowleri</i>	
5.5. T-lymphocytes	
5.6. Antibodies	
5.7. Activation of complement	
5.8. Natural killer cell	
5.9. Immune evasion	
5.10. Immunization using whole parasites	
5.10.1. Immunization using cell supernatants	
5.10.2. Passive immunity	
5.10.3. Immunization with the rNfa1 protein	
<b>Chapter 6: Cell Biology and Speciation .....</b>	<b>101</b>
6.1. Discovery of <i>N. fowleri</i>	
6.2. Different life forms of <i>N. fowleri</i>	
6.3. Ultrastructural analysis	
6.3.1. Centrin, centrioles and microtubule-organizing centers (MTOCs)	
6.3.2. Nucleolar protein BN46/51	
6.3.3. Flagellar rootlet of <i>Naegleria</i>	
6.3.4. Flagellar tubulin	
6.3.5. Microfilaments	
6.3.6. Actomyosin complex	
6.4. Motility	
6.5. Biochemical composition	

- 6.5.1. Membrane carbohydrate moieties
- 6.5.2. Trypanothione/trypanothione reductase and glutathione/glutathione reductase systems
- 6.5.3. Selenocysteine biosynthesis
- 6.5.4. Expression of CD45-like glycoprotein
- 6.5.5. Adenylyl cyclases
- 6.5.6. Beta-glucosidase and beta-galactosidase
- 6.5.7. Acid phosphatase and heme proteins
- 6.5.8. Pyrophosphate-dependent phosphofructokinase
- 6.5.9. Cytosolic heat shock protein 70
- 6.5.10. Low-molecular-mass thiol compounds
- 6.5.11. Membrane-bound black bodies
- 6.5.12. Tet-like dioxygenase
- 6.5.13. Sterol biosynthesis
- 6.5.14. Other enzymes
- 6.6. Genome of the genus *Naegleria*
  - 6.6.1. The mitochondrial genome and a 60-kb nuclear DNA segment
- 6.7. Mitochondrial RNA editing
- 6.8. RNA polymerase
- 6.9. Ribosomal DNA (rDNA)
  - 6.9.1. Large subunit ribosomal DNA
  - 6.9.2. Small subunit ribosomal DNA
  - 6.9.3. Kinetic and secondary structure analysis of group I ribozyme
- 6.10. Classification

## **Chapter 7: Cellular differentiation in *N. fowleri* ..... 127**

- 7.1. Cellular differentiation
- 7.2. Proteins in flagellates and growing amoebae of *N. fowleri*
- 7.3. Encystation and excystation: Amoeba to cyst and *vice versa*
- 7.4. Ultrastructural study of the encystation and excystation processes
  - 7.4.1. Effect of CO<sub>2</sub> on excystation
  - 7.4.2. Effect of steroid
  - 7.4.3. Enolase is expressed during cyst differentiation
- 7.5. Flagellation: Amoebae to Flagellates
  - 7.5.1. Effects of oxidative phosphorylation, protein synthesis, RNA synthesis, DNA synthesis
  - 7.5.2. *De novo* formation of cytoplasmic cytoskeleton
  - 7.5.3. Synthesis and assembly of the cytoskeleton of flagellates
  - 7.5.4. Flagellar rootlet during flagellate differentiation
  - 7.5.5. Synthesis of centriole and flagella proteins
- 7.6. Differentiation-specific mRNAs
  - 7.6.1. A calcineurin-B-encoding gene expressed during differentiation
  - 7.6.2. Two calmodulins in *Naegleria* flagellates
  - 7.6.3. CLP and CLB proteins
  - 7.6.4. Nucleolar protein BN46/51
  - 7.6.5. NgUNC-119, *Naegleria* homologue of UNC-119, localizes to the flagellar rootlet.
  - 7.6.6. Thymidine kinase
  - 7.6.7. Heat shock
  - 7.6.8. Effect of high hydrostatic pressure on transformation

7.6.9. Effect of ions	
7.6.10. Effect of bacterial suspensions	
7.6.11. Effect of $\beta$ -mercaptoethanol	
7.7. Flagellate to amoebae	
<b>Chapter 8: Growth and life cycle</b> .....	<b>153</b>
8.1. Food selection and ingestion	
8.2. Cultivation of <i>N. fowleri</i>	
8.3. Chemically defined medium	
8.4. Cell density within the biofilm	
8.5. Effect of pH, viscosity on <i>N. fowleri</i> growth	
8.6. Effect of porphyrin on <i>N. fowleri</i> growth	
8.7. Cell cycle	
8.8. Respiration in <i>N. fowleri</i>	
8.9. Storage	
8.9.1. Cryopreservation	
<b>Chapter 9: Ecology</b> .....	<b>161</b>
9.1. Free-living amoebae	
9.2. Isolation from the atmosphere	
9.3. Isolation from freshwater lakes	
9.4. Prevalence of <i>Naegleria</i> and wild animals	
9.5. Distribution of <i>Naegleria</i> from clinical samples and clinical settings	
9.6. Nasopharyngeal and oral regions of dental patients	
9.7. Serology of <i>Naegleria</i> spp.	
9.8. Effect of thermal pollution on the distribution of <i>N. fowleri</i>	
9.9. <i>N. fowleri</i> isolation from swimming pools	
9.10. <i>Naegleria fowleri</i> in the thermal recreational waters	
9.11. Assays for the identification of <i>N. fowleri</i> in environmental water samples	
<b>Chapter 10: War of the microbial worlds</b> .....	<b>173</b>
10.1. A host for virus-like particles	
10.2. <i>N. fowleri</i> and bacteria interactions	
10.3. Bacterial evasion of predation by <i>Naegleria</i> spp.	
<b>Chapter 11: Conclusions and Future Studies</b> .....	<b>183</b>
11.1. Rapid and non-invasive diagnosis	
11.2. Antiamoebic anesthetic agents	
11.3. Drug delivery	
11.4. Drug repurposing	
11.5. Biomarkers	
11.6. Drug targets	
11.7. A model organism with pathogenic potential	
<b>References</b> .....	<b>193</b>

## 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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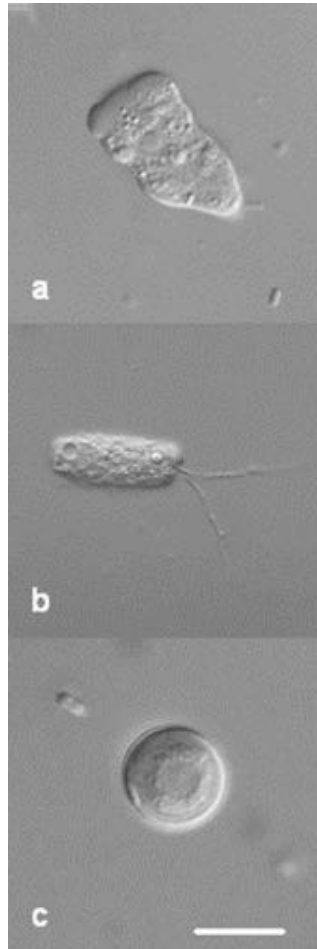
## Synopsis

*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.