Chapter 1

Introduction
INTRODUCTION

“In the last decade there has been an ever increasing awareness of Darwinian struggle with which the human species is engaged. Viral predators abound, in no less abundance than before, and present a constant threat to individual survival as well as to the success of population at large. These predators that cycle throughout their ecological niche and are encountering opportunities in our modern world to spread with a frightening vigour” (Alison, 1998).

The study of viral infections of the nervous system is a fascinating field of medical microbiology that has received considerable attention since the days of Louis Pasteur (Ravi, 2000).

New patterns of human movements leading to new contacts across what has been geographic boundaries, have given rise to a variety of viral infections. Many of these are infections of the nervous system, which accounts for significant mortality and morbidity worldwide especially among children.

Viral infections of the CNS are many which includes,

A. **Encephalitis:** An acute inflammatory disease of the brain due to direct viral invasion or to hypersensitivity initiated by a virus or other foreign protein.
B. **Aseptic meningitis:** A febrile meningeal inflammation characterized by CSF mononuclear pleocytosis, normal glucose, mild elevations in protein, and an absence of bacteria on examination and culture.

C. **Encephalomyelitis:** Inflammatory disease of the brain and spinal cord.

Encephalitis may be a primary manifestation or a secondary complication of a viral infection. Viruses causing primary encephalitis may be epidemic (arbovirus, poliovirus, echovirus, and coxsackievirus) or sporadic (herpes simplex, varicella-zoster, and mumps viruses).

Secondary encephalitis, usually a complication of viral infection, is considered to have an immunologic mechanism. Examples are encephalitides secondary to measles, chickenpox, rubella, smallpox vaccination, vaccinia, and many other less well-defined viral infections. These Para infectious or post infectious encephalitides (sometimes called acute disseminated encephalomyelitis) typically develop 5 to 10 days after onset of illness and are characterized by perivascular demyelination seen at autopsy; a virus is rarely isolated from the brain. In mumps, CNS involvement may be primary and post infectious.

Aseptic meningitis may be due to infections by viruses or other organisms or to noninfectious conditions.
Very rarely, encephalitis or other encephalopathies occur as a late consequence of viral infections. The best known is subacute sclerosing panencephalitis (SSPE) associated with the measles virus.

Measles is a highly contagious acute respiratory disease characterized by maculopapular rash with coryza, conjunctivitis and koplík’s spots so familiar to every mother. Until the advent of a live attenuated vaccine in the early 1960’s, measles was an epidemic disease worldwide. Today many countries have controlled measles, but the disease remains endemic in most countries, particularly in underdeveloped and developing countries like India. Before the availability of measles vaccine an estimated 130 million cases were reported each year globally. In 1998, WHO estimated approximately 30 million cases and 888,000 measles related deaths still occurring worldwide.

Though Measles virus infections normally cause an acute self-limiting disease, leading to virus specific immune response and establishment of life long immunity, on rare occasions it may also lead to complications involving the CNS.

Encephalitis is the least frequent of the rare complications of measles. Acute measles encephalitis (AME) also known as Post infection encephalitis (PIE), subacute sclerosing panencephalitis (SSPE) and subacute measles encephalitis (SME) or Measles inclusion body encephalitis (MIBE) are the three CNS syndromes associated with measles infection.

PIE: complicates 1 in 1000 cases mostly in individuals >2 years of age and usually within 2 weeks after the onset of rash. Characterised
clinically by the abrupt onset of fever and obtundation, frequently accompanied by seizures and multifocal neurological deficits.

**MIBE:** Occurs only in the immunocompromised persons at any age within months after measles. The Course is much more rapid and death occurs within months. Antibody is either absent or very low in CSF but measles virus, not cell free virus can be detected in brain.

**SSPE:** Subacute sclerosing panencephalitis (Alternate Names: Dawson’s Encephalitis, SSPE, Subacute Sclerosing Leukoencephalitis) is a late, progressive, slow neurological disease usually accompanied by high measles antibody titres in serum and CSF. SSPE occurs several years after a child contracts measles infection.

SSPE was first described by Dawson, in a 16-year-old boy with progressive neurological deterioration characterized by failing memory, slowing of movements and myoclonus. From India, the first case of SSPE was described by Desai and Iyer followed by a report by Mehta and co-workers.

Till date, there has been no specific therapy for SSPE, and the disease is invariably fatal. However, certain anti-viral drugs can slow the progression of the disease. A combination of oral isoprinosine and interferon alpha injected directly into the brain ventricles, appears to be the most effective treatment. Ribavirin and Amantadine are the other anti-viral medications and steroids that have been used with limited success. Patients responding to treatment need to receive it for the rest of their lives. Effective
immunization against measles to prevent development of this condition is the only solution presently available.

Although data on SSPE in India are scanty, the incidence may be as high as 21 cases per million populations. A comprehensive documentation on the epidemiological, serological features of the disease and its impact in India, are few and limited. Hence, the present study was planned and conducted to document such information and data, for a comprehensive understanding of the disease burden in India, and to help in better infection control and possibly eradication of the disease.

1.1 OUTLINE OF THE REMAINING CHAPTERS

The thesis has been presented in the following format. In chapter 1 an introduction to the topic is given, followed by review of literature in chapter 2. The aims and objectives of the study are outlined in chapter 3. The details of the materials and methods, is presented in chapter 4. The results are presented in chapter 5 and discussion in chapter 6. In chapter 7, the summary of the findings and the conclusions drawn from different aspects of the study are presented. Chapter 8 contains futurology.