CHAPTER I

INTRODUCTION
Rabies has a long and interesting history. It has been mentioned in ancient literature and in holy books like "Talmud".

The Greeks called rabies "lyssa" which means madness. The Romans used the word "rabare" indicating rage. The Latin word "rabies" comes from a Sanskrit word "rabhas" which translated means violence. The German word "tolwutt" originates from Indogermanic "Dhvar", to damage and "wutt" from middle German "wuot" which is rage. The French word for rage is derived from the noun "robere", to be mad. In all the languages the word has a meaning of madness, rage and violence indicating the nature of disease.

Aristotle in fourth century B.C. wrote that dog suffer from madness, become irritable and all the animals they bite become diseased. He believed that mankind was exempt from the disease, even though hydrophobia was already known as a disease of human beings at that time. Hippocrates is supposed to have mentioned rabies.

Roman writers described the infectivity of saliva of rabid dogs and the infectious material was termed "virus" a Latin for poison. Celsus in first century studied rabies and concluded that bite of all the animals were dangerous to man and animals. Writers in early Christian era have described rabies in dogs as well as man.
The earliest well documented evidence of rabies is found in Great Britain in the Laws of Howel the Good, of Wales, which were revived in 1025. In them, an outbreak is alluded to, as a most noteworthy event and that during that year there was a madness among the dogs.

From this period literature on rabies gradually expanded but little progress was made to understand the disease. Superstitious practices were followed till fifteenth century for prevention of disease. Until the middle ages the epizootics were rare, but by seventeenth century rabies was widespread in entire Europe.

The cases of bites of dogs, foxes, wolves and badgers were recorded. Various theories were put forward by many workers regarding the cause of disease until Pasteur demonstrated the cause of rabies beyond doubt.

The identity of human and canine disease was established in 1821 by transmitting rabies to the dog from a saliva of a case of hydrophobia, by Magendi (Jhala, 1971). This established the importance of rabies as zoonoses. However, earlier reports indicated dog to dog transmission of rabies by inoculation of saliva of rabid animal. By the turn of eighteenth century rabies was endemic throughout the world, occasionally taking a form of epizootic.

Rabies was known as disease in India long ago, and is mentioned in ancient literature. Rabies is endemic in India.
The susceptibility of various animals to natural or artificial infection with the rabies virus varies from species to species. Skunks, opposums, and fowls are highly resistant, whereas foxes, cats, jackals, wolves, kangaroo rats, cotton rats are highly susceptible. Dogs and human beings fall in between. The species which fall in between these groups are responsible for maintaining reservoir of infection in nature.

The systematic studies in India on rabies started at the beginning of this century. The Haffkine Institute of Bombay, and the Pasteur Institute at Coonoor in South India and Central Research Institute at Kasauli carried out considerable work on rabies.

In India systematic studies on epidemiology of rabies have been reported in dogs and that too are few in number. Rabies like viruses have not been reported so far nor identified. In India more than 90 per cent rabid bites are from dogs only. Therefore dogs play very important role in epidemiology of rabies.

The stray dog population is uncontrolled. In metropolitan cities of India dogs are being caught and destroyed, but the gap is always filled by migration of dogs from rural areas since rural areas does not have such programmes. The reasons are mainly financial, though social and religious beliefs play an important role.

Nanavati (1980) reported an example of city of Bombay to understand the magnitude of dog destruction programme.
About 4000 dogs are caught every year and destroyed, and almost equal number are detained, sold or given to research institutions. About 17,000 licences are issued every year and against that only 3,000 dogs are immunised every year against rabies. It costs about 1.2 million rupees annually and about 100 persons are employed for this work alone.

Rabies is almost always fatal. The official figures of human deaths from rabies in India are 1,000 to 1,500 deaths per year. Jhala (1971) estimated about 10,000 deaths from rabies alone. Schawabe in a seminar on Veterinary Public Health by WHO suggested annual number of human deaths from rabies about 15,000.

Kaplan (1977) states that in Shri Lanka there are, on an average 200 human deaths a year from rabies in a population of 12.5 million. By using the figure on India suggested by Schawabe, and extrapolating the figure of Shri Lanka, the figure is fifty per cent more, but still it is too low.

However this disease should not be considered as an element in a statistical comparison, eventhough the figure is small as compared to other diseases like gastroentritis or tetanus, but in terms of human suffering. When a dog bites a human being a full treatment of fourteen injections in stomach has to be taken. About half a million people undergo antirabtic treatment every year, and almost equal number might not be taking treatment because of the distance and travel to be undertaken for a fortnight for the treatment, at times non-availability of vaccine and loss of wages.
Not all bites of infected or apparently healthy dog results in disease in humans. Dogs might show virus in saliva before the development of symptoms. Therefore, biting animal must be kept under observation for at least eleven days. Even if the animal survives this period, it does not necessarily mean that the bite is not infectious.

Before the findings of Negri bodies in 1903, the diagnosis of rabies was clinical only. After the death of an animal, the brain, specially the hippocampus is examined for the presence of Negri bodies. When they are found, are indicative of rabies infection. The brain material is inoculated intracranially in laboratory mice or rabbits. The presence of Negri bodies in brains of test mice or rabbits is regarded as evidence of infection.

Various staining techniques were used to identify Negri bodies in brain. Sellers (1927) first described a simple method to stain Negri bodies, which bears his name. Various other staining techniques were used, but with the introduction of immunofluorescence and development of a stable fluorochrome, its usefulness in the diagnosis of rabies was seen. Today it largely has replaced older staining methods for the direct microscopic examination of rabies. Recently an alternative method is beginning to be used for labelling antibodies by making use of an enzyme horseradish peroxidase and it has an advantage that it is possible to use ordinary light microscope in this case.
The immunoprotective mechanisms of the body give rise to antibodies as a response to an antigen. Thus when an infection occurs in an animal, specific antibodies are formed, which are found in the bloodstream. The serum containing antibodies when examined against a homologous or specific antigen, it reacts by combination which can be seen by various serological tests.

Serologic tests for detection of rabies antibody provide valuable tools for epidemiological studies including the determination of immune status of man and animals and the diagnosis of rabies infection by detection of presence of antibodies in specimens from live or dead animals. The usual tests are, the complement fixation test, neutralization test, haemagglutination and haemagglutination inhibition test. The other tests which employ specific antibodies are indirect fluorescent antibody test, inhibition of cytopathogenic effect in cell cultures and its modifications. Gel diffusion precipitation test is also an antigen-antibody reaction showing precipitation lines.

The peripheral movement of virus from the central nervous system carries the virus to all parts of the body. Therefore various staining techniques are being used to confirm diagnosis of rabies by detecting antigen in living subjects. Corneal impression smears from a clinical case of rabies are examined for the presence of antigen. Similarly a small piece of skin from suspected case of rabies is examined by cutting frozen
sections by adopting various staining techniques. Both these methods have certain limitations and their efficiency is yet to be proved beyond doubt.

The search for a really efficient and quick diagnostic test in rabies is not yet complete even in advanced countries. Rabies is endemic in most parts of the world. But the eradication of rabies is not difficult. The measures necessary have been known and successfully applied in different countries. Destructions of all stray dogs and liscencing of all pet dogs by law will reduce the incidence, provided the law is enforced strictly.

Rabies in Malaysia has been eradicated by simple measures, and the country is free from rabies since 1952. Australia is free from rabies. This is due to strict enforcement of quarantine and other such laws and geographical situation of being an island where it is possible to check and regulate entry points. United Kingdom, United States of America, New Zealand and Scandinavian countries have controlled rabies by simple measures of controlling stray dog population, vaccination of pet dogs, quarantine laws etc.

India is a large country and in the process of development. Rabies is a major public health problem. World Health Organisation has placed rabies first in the list of zoonoses. Dogs are the main source of infection and the population of stray dogs is on increase.

The Rabies Task Force of Indian Council of Medical Research observed in its proceedings of 1980 that no
epidemiological studies worth noting have been carried out except in case of dogs. The epidemiological studies in dogs are also not conclusive. The studies are made at various isolated places. The Task Force also stressed the need for evaluation of newer diagnostic techniques in rabies.

In a developing country like India where rabies is a problem, not every laboratory can be equipped with costly equipments. Therefore alternative methods which are quick, reliable and easy without depending upon costly and sophisticated instruments have to be developed.

With this view the present studies were undertaken. The epidemiological studies were carried out in stray dogs with particular reference to carrier state of rabies and the available diagnostic methods particularly the staining techniques are evaluated. A newly introduced staining technique, known as immunoperoxidase technique is studied and compared with other staining methods including fluorescent antibody technique. A simple diagnostic technique of passive cutaneous Anaphylaxis reaction in case of rabies reported by Mathew (1971) was studied for its practical applicability.