

RABIES

Edited by Alan C. Jackson and William H. Wunner
2002. Pp. 493. London: Academic press:
An Elsevier Science Imprint.
Price £69.50. ISBN 0-12-379077-8

Rabies is a major health problem in developing countries and has emerged again in the USA due to bat rabies virus variants. There have been major advances in the last decade, especially in the field of molecular biology, which have led to a better understanding of its epidemiology, pathogenesis and diagnosis and to the development of effective control programmes in wildlife. This is a comprehensive book, dealing with the history of rabies from antiquity to the modern era and the molecular virology, epidemiology, pathology, clinical manifestations and diagnosis of the disease, as well as preventive measures in humans and animals.

The opening chapter, on the history of the disease, depicts ancient facts and recent developments. The portraits of Louis Pasteur (Wellcome Library, London) are a befitting tribute to the man whose work on rabies remains a legend. The structure of the rabies virus is discussed in detail, with an account of its molecular composition, chemical architecture and genome organization. There is further description of the molecular biology of rabies virus proteins. The application of molecular methods has added a new dimension to the epidemiology of rabies. The genetic analysis of a virus population can identify the topographical features that partition animal populations and serve as barriers for rabies transmission, but this information is yet to be employed to predict epidemic spread. The chapter on epidemiology deals predominantly with rabies in wildlife, including racoons, foxes, skunks and bats, with a limited account of canine rabies which is prevalent in developing countries. There is a good description of clinical rabies in animals and humans and the differential diagnosis is well discussed.

Considerable progress has been made in understanding the pathogenesis of rabies. The highly neurotropic virus binds to nicotinic acetylcholine receptors at the neuromuscular junction and it spreads by axonal transport via peripheral nerves to the CNS. Recent research has thrown light on the pathophysiology of brain dysfunction in rabies. Various mechanisms, such as defective neurotransmission, electrophysiological alteration, ion channels and apoptosis, are responsible for this dysfunction. The main pathological features of rabies were well known around the turn of the nineteenth century. The chapter on pathology includes the recent electron microscopic and immunohistochemical techniques that have made it possible to achieve significant

progress in understanding the pathology and pathogenesis of rabies. Electron microscopy has confirmed the viral nature of Negri bodies and elucidated the mode of maturation and spread of rabies virus within the nervous system.

The coverage of diagnostic evaluation deals with animal as well as human rabies. There is a good account of the procedures involved in public health laboratories for animal testing. Virus isolation by culture has been in use for a long time. It is now supplemented by detection of viral RNA by molecular methods. The methods of rabies diagnosis rely on the demonstration of virus, viral antigen or viral RNA in peripheral nerves and tissues or the detection of antibodies in the serum or CSF. Serological tests for *Lyssavirus*-specific antibody can also provide an estimate of vaccine efficacy and an indication of disease prevalence in areas of enzootic rabies. The different methods used to measure *Lyssavirus*-specific antibody are discussed, such as antigen-antibody assays, antibody-function assays and antigen-function assays.

The section on immunology gives a fair description of the molecular components of specific immune responses during rabies virus infection. The rabies virus becomes invisible to the immune system after it enters the CNS because apoptosis of the infected neurons is not induced. Rabies virus antigens cannot be captured by professional antigen-presenting cells or trigger a primary immune response. There is further immunosubversion by peripheral immunosuppression, mediated by infection of the brain. Despite these well-adapted viral strategies, infection can be limited by humoral immunity. The immunological basis for the efficiency of post-exposure vaccination includes the role of CD4 and CD8 lymphocytes as well as the protective role of antibodies and B lymphocytes. There are three types of rabies vaccine available: nerve tissue-derived vaccines, high-quality cell-culture vaccines produced under stringent control, and lower-quality cell-culture vaccines. The next generation of rabies vaccines is dealt with in detail. Oral rabies vaccines for wildlife include the SAG-1 and SAG-2 modified live rabies vaccines and live recombinant vectored vaccines. Nucleic acid (DNA)-based vaccines are being developed as a rather simple (they consist of a basic plasmid preparation) yet versatile approach to the induction of immune responses when injected directly into the host, compared with the use of conventional vaccines.

The section on public health management deals with pre- and postexposure vaccination, advice about vaccination in pregnancy, travel to developing countries, large-scale human exposure and postexposure treatment in immunosuppressed patients. The largest number of human rabies cases occurs in developing countries, and most patients receive nerve tissue

vaccine. This vaccine is notorious for neurological complications but description of this aspect is conspicuous by its absence.

Unlike most of the monographs on human rabies, this book depicts the control of canine and wildlife rabies. Restriction of the movement of dogs, the killing of rabid and bitten dogs, the separation and observation of possibly exposed dogs and the widespread vaccination of dogs have led to the elimination of canine rabies in Europe. The policy of mass destruction of freely roaming unsupervised dogs has been found to be ineffective and has been replaced by more emphasis on canine vaccination. There is an excellent description of oral rabies vaccination for the control of rabies in wildlife. It covers the development of the vaccine and of vaccine bait, and the large-scale distribution of vaccine bait. The role of mathematical models in the success of this programme is discussed.

Rabies continues to be a major public health problem, as it was in antiquity. Though canine rabies has been controlled in the developing countries, it is responsible for more than 30 000 deaths per year in developing countries. The book ends with a commentary on future developments and challenges. The strength of the book lies in the multi-disciplinary contributions of experts in medicine, pathology, virology, immunology, epidemiology and veterinary medicine. It will be a useful collection for medical and veterinary clinicians, public health workers and research scientists involved in the diagnosis and prevention of rabies.

I. M. S. Sawhney
Department of Neurology,
Morrison Hospital,
Swansea, UK

DOI: 10.1093/brain/awh018