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Diagnosis and Management of Human Rabies

Recently two patients died of rabies in London hospitals. Though both patients were infected abroad, this tragic coincidence has concentrated public attention on a problem which seems to threaten Britain now more than at any other time since the last important outbreak in 1918-22. The adequacy of quarantine regulations has been questioned.[1] An epizootic of fox rabies is spreading across France, animals are being smuggled into Britain, and our membership of the Common Market is likely to increase cross-Channel traffic of all kinds. So medical practitioners in this country may be increasingly concerned in the management of people bitten by potentially rabid animals while abroad and even in the early diagnosis of rabies encephalitis.

In a timely article in this issue of the *B.M.J.* (p. 740) Dr. L. Klenerman and colleagues rightly emphasize the risks of bites by imported laboratory animals and the need for a well-defined plan of action for dealing with such accidents. Proper treatment started soon after the bite can reduce the risk of developing rabies,[2 3] but once the virus has reached the central nervous system and produced symptoms of the disease the outlook is virtually hopeless. The incubation period varies from 10 days to many years, but is usually one or two months. The illness starts gradually with a few days of non-specific prodromal symptoms including fever, headache, myalgia, chills, sore throat, respiratory and gastrointestinal upsets, insomnia, and anxiety and other psychological disturbances. Pain and paraesthesiae of the bitten area, recorded in 30-80% of reported series of cases, are the earliest symptoms which may suggest the diagnosis of rabies. After the prodrome the disease may progress in two different ways, its course depending on the pattern of infection of the central nervous system.[4 5]

The commoner form, known as "furious rabies," is characterized by hydrophobia and episodes of generalized arousal. Hydrophobia is an overwhelming and indescribable terror of water associated with violent contractions of inspiratory muscles, including those inserted into the larynx. Initially it occurs in response to attempts to drink water and subsequently to the sight, sound, or even mention of water. The inspiratory spasms may result from a variety of other stimuli including a draught of air on the skin (aerophobia). A diagnostic response is usually produced if the patient is asked to swallow accumulated saliva or if a current of air is directed on to the face. Inspiratory spasms may be complicated by retching, vomiting, coughing, aspiration into the trachea, grimacing, opisthotonos, asphyxiation with cardiac arrest, and convulsions. Also typical of this form of rabies is cyclical arousal, in which brief periods of confusion, shouting, aggression, and agitation, sometimes of maniacal intensity, are interspersed with spells of mental lucidity and calm. Other abnormalities include paralysis of palatal and pharyngeal muscles causing inability to swallow, cranial nerve lesions, drooling and spitting saliva, cardiac arrhythmias (especially supraventricular tachycardia), high fever, and a wide range of behavioural disturbances. Within a few days patients lose consciousness and pass into the encephalitic phase of the disease, in which various patterns of periodic, apneustic, and ataxic breathing are vestiges of the hydrophobic inspiratory spasms. Unless the airway is kept open by cuffed endotracheal tube or tracheostomy, and ventilation supported artificially, these patients are unlikely to survive more than a few days.

A rarer presentation is the paralytic form, "dumb rabies," which develops particularly after infection by vampire bats[6] and in patients given antirabies vaccination.[7] Motor and sensory disturbances usually start in the bitten limb and progress as an acute ascending paralysis accompanied by pain and paraesthesiae with flaccid paraplegia, sphincter disturbance, and respiratory and bulbar paralysis. Even without intensive care patients may survive as long as two to three weeks. Signs of furious rabies, including hydrophobia, may develop before the terminal encephalitic coma supervenes.

The diagnosis of rabies may be suspected at the prodromal stage if the patient mentions an animal bite or if there is paraesthesia of the bitten area. Hydrophobia, which occurs in at least half the cases, is pathognomonic of rabies but may be simulated by hysterical patients who fear that they have the disease. In the absence of hydrophobia furious rabies must be distinguished from other causes of muscle spasm, particularly tetanus, which can also result from bites. Trismus, muscle rigidity between spasms, and a shorter incubation period (usually less than two weeks, but occasionally up to three months) suggest tetanus. In rabies lymphocyte pleocytosis and increased protein are found in about 25% of cases, whereas in tetanus the cerebrospinal fluid (C.S.F.) is normal.[8] Patients with rabies have been referred to otolaryngologists because of laryngopharyngeal symptoms and to psychiatrists because of their bizarre behaviour. Paralytic rabies may be confused with other causes of acute ascending (Landry's) paralysis. Absence of sensory disturbances and remission of fever before paralysis

has developed suggest poliomyelitis.[7] Rabies postvaccinal myelitis usually appears within two weeks of the start of vaccination.[9] The acute ascending paralytic form has a 30% mortality from respiratory paralysis, but patients with the paraplegic and neuritic types almost always recover rapidly.[10] Abnormal C.S.F. is the rule in poliomyelitis, acute infective polyneuritis, and postvaccinal and viral encephalomyelitides.

Laboratory confirmation of rabies has been achieved early in the clinical course of the disease in man by finding specific fluorescence in corneal impression smears,[11] frozen skin biopsies,[12] and brain biopsy,[13] and by detecting fluorescent antibody in serum.[14] But none of these techniques is entirely satisfactory. The corneal test, though 100% specific, is falsely negative in 60% of cases.[15] Biopsy is unpleasant for the patient.[16] And antibody levels cannot be detected before about the eighth day of the illness[14] and are difficult to interpret in immunized people. The chances of finding Negri bodies in a brain biopsy specimen are small, and virus isolation from saliva, tears, or brain by mouse inoculation usually takes more than a week.[17]

The traditional view that rabies is inevitably fatal in man has recently been challenged by the prolonged survival of patients with proved disease[13 18] and the recovery of two with probable rabies.[19 20] These successes were attributed to intensive care, which protected the patients from respiratory and circulatory failure, raised intracranial pressure, and electrolyte disturbances.[4 5] Subsequent experience with patients in America and with the two recent patients in London has been disappointing, but intensive care remains the only known method of prolonging life. The use of human hyperimmune gammaglobulin or rabies antiserum seems logical in view of the evidence of viraemia,[21] but the value of these and other specific antiviral agents and corticosteroids is unproved. Patients must be heavily sedated to relieve their suffering. Though there is no adequately documented case of person-to-person transmission of rabies,[5 22] virus is present in secretions, so there is a risk of infection. Patients should therefore be barrier-nursed, and medical staff who are in close contact should be vaccinated against rabies and protected with adequate clothing, including face masks and goggles.

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Replantation of Severed Limbs

The development of microsurgery after the pioneer work of Jacobson and Suarez[1] in 1960 has made possible the replantation of severed limbs. The first successful operation was performed in China in 1963 and in America in 1964. Surgeons in China in particular have accumulated an extensive experience in experimental work and surgical operations.[2] Over 100 replantations were reported by the end of 1974.

According to the latest report[3] surgeons at the Chishueit'an Hospital, Peking, have operated on 40 patients for replantation of severed limbs between 1964 and 1972. Their success rate of 67% (27 cases) is remarkable because included in their series were 19 examples of ragged wounds, multiple fractures, and crushing. Among the most favourable cases, where the amputation was caused by saw or by sharp instrument, there were only 3 failures in 13 patients. An important factor was the time interval between injury and operation: the shorter the period of ischaemia the better the result. The 27 successes had an average of 9 hours' ischaemia, whereas the 13 failures averaged 12 hours'. But the time limit is not absolute. There was one replantation at wrist level which was successful after 33 hours' ischaemia. Another factor of importance was the level of amputation. When the amputation was through the wrist the success rate was high, 9 out of 10; through the palm, 8 out of 11; and the upper arm, 4 out of 6. The poorest results followed amputation in the forearm, and worst of all in the proximal part of the forearm, when none of the 5 operations was successful.

Other factors contributing to success were refrigeration of the severed limb, decompression procedures in deep fascia and skin, especially when postoperative swelling was obviously stopping venous flow. At least two veins should be anastomosed for every artery successfully joined, and vein transplant was often used. Selective excision of less important muscles—for example, superficial flexors of the fingers—allowed more room for the swelling. The many complications of replantation were mostly preventable or responded to treatment. Vasospasm and thrombosis occurred in 12 of the 40 cases. The vasospasm that followed refrigeration was temporary but that due to damage to a vessel required excision and grafting. Thrombosis was an indication for further operation without delay, and this could be time-consuming; in all, reoperation was required in one-quarter of the cases and was often rewarding. The only death in the series was attributed to poor general health.

The high success rate reported from Peking must in the main be attributed to the quality of the operating technique developed by practice in the replantation of severed rabbits' ears. The demand for this kind of surgery is due to the belief, commonly held among Eastern peoples, that reincarnation cannot be complete if a part of the body is missing. Further reports from China are to be expected in the near future. In the meantime surgeons in Great Britain should be encouraged to train and develop the technique of replantation so that a surgical team is ready to operate on a patient who comes to the accident service with his refrigerated severed hand, even if it means borrowing the ophthalmic surgeon's operating microscope to identify nerve topography as well as to repair the vascular channels.

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