DIFFERENTIAL DIAGNOSIS

The diagnosis of rabies may be difficult without a history of animal exposure, and no exposure to an animal (e.g., a bat) may be recalled. The presentation of rabies is usually quite different from that of acute viral encephalitis due to most other causes, including herpes simplex encephalitis and arboviral (e.g., West Nile) encephalitis. Early neurologic symptoms may occur at the site of the bite, and there may be early features of brainstem involvement with preservation of consciousness. Anti-*N*-methyl-D-aspartate receptor (anti-NMDA) encephalitis occurs in young patients (especially females) and is characterized by behavioral changes, autonomic instability, hypoventilation, and seizures. Postinfectious (immune-mediated) encephalomyelitis may follow influenza, measles, mumps, and other infections; it may also occur as a sequela of immunization with rabies vaccine derived from neural tissues, which are used only in resource-limited and resource-poor countries. Rabies may present with unusual neuropsychiatric symptoms and may be misdiagnosed as a psychiatric disorder. Rabies hysteria may occur as a psychological response to the fear of rabies and is often characterized by a shorter incubation period than rabies, aggressive behavior, inability to communicate, and a long course with recovery.

As previously mentioned, paralytic rabies may mimic Guillain-Barré syndrome. In these cases, fever, bladder dysfunction, a normal sensory examination, and CSF pleocytosis favor a diagnosis of rabies. Conversely, Guillain-Barré syndrome may occur as a complication of rabies vaccination with a neural tissue–derived product (e.g., suckling mouse brain vaccine) and may be mistaken for paralytic rabies (i.e., vaccine failure).

TREATMENT RABIES

There is no established treatment for rabies. There have been many recent treatment failures with the combination of antiviral drugs, ketamine, and therapeutic (induced) coma—measures that were used in a healthy survivor in whom antibodies to rabies virus were detected at presentation. Expert opinion should be sought before a course of experimental therapy is embarked upon. A palliative approach may be appropriate for some patients.

PROGNOSIS

Rabies is an almost uniformly fatal disease but is nearly always preventable with appropriate postexposure therapy during the early incubation period (see below). There are seven well-documented cases of survival from rabies. All but one of these patients had received rabies vaccine before disease onset. The single survivor who had not received vaccine had neutralizing antibodies to rabies virus in serum and CSF at clinical presentation. Most patients with rabies die within several days of the onset of illness, despite aggressive care in a critical care unit.

PREVENTION

Postexposure Prophylaxis Since there is no effective therapy for rabies, it is extremely important to prevent the disease after an animal exposure. Figure 232-5 shows the steps involved in making decisions about PEP. On the basis of the history of the exposure and local epidemiologic information, the physician must decide whether initiation of PEP is warranted. Healthy dogs, cats, or ferrets may be confined and observed for 10 days. PEP is not necessary if the animal remains healthy. If the animal develops signs of rabies during the observation period, it should be euthanized immediately; the head should be transported to the laboratory under refrigeration, rabies virus should be sought by DFA testing, and viral isolation should be attempted by cell culture and/or mouse inoculation. Any animal other than a dog, cat, or ferret should be euthanized immediately and the head submitted for laboratory examination. In high-risk exposures and in areas where canine rabies is endemic, rabies prophylaxis should be initiated without waiting for laboratory results. If the laboratory results prove to be negative, it may safely be concluded that the animal's saliva did not

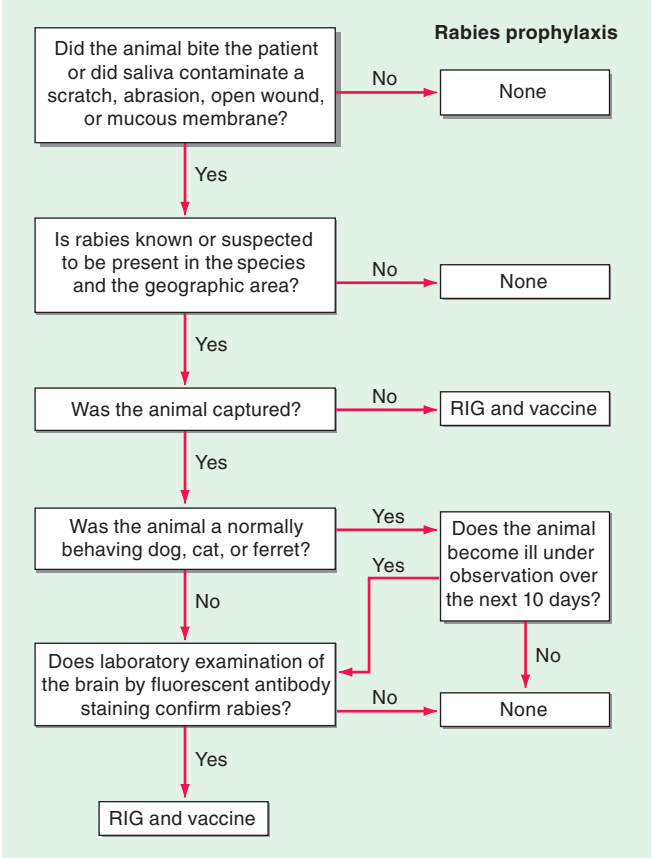

FIGURE 232-5 Algorithm for rabies postexposure prophylaxis. RIG, rabies immune globulin. (*From L Corey, in Harrison's Principles of Internal Medicine, 15th ed. E Braunwald et al [eds]: New York, McGraw-Hill, 2001; adapted with permission.*)

contain rabies virus, and immunization should be discontinued. If an animal escapes after an exposure, it must be considered rabid, and PEP must be initiated unless information from public health officials indicates otherwise (i.e., there is no endemic rabies in the area). Although controversial, the use of PEP may be warranted when a person (e.g., a small child or a sleeping adult) has been present in the same space as a bat and an unrecognized bite cannot be reliably excluded.

PEP includes local wound care and both active and passive immunization. Local wound care is essential and may greatly decrease the risk of rabies virus infection. Wound care should not be delayed, even if the initiation of immunization is postponed pending the results of the 10-day observation period. All bite wounds and scratches should be washed thoroughly with soap and water. Devitalized tissues should be debrided, tetanus prophylaxis given, and antibiotic treatment initiated whenever indicated.

All previously unvaccinated persons (but not those who have previously been immunized) should be passively immunized with rabies immune globulin (RIG). If RIG is not immediately available, it should be administered no later than 7 days after the first vaccine dose. After day 7, endogenous antibodies are being produced, and passive immunization may actually be counterproductive. If anatomically feasible, the entire dose of RIG (20 IU/kg) should be infiltrated at the site of the bite; otherwise, any RIG remaining after infiltration of the bite site should be administered IM at a distant site. With multiple or large wounds, the RIG preparation may need to be diluted in order to obtain a sufficient volume for adequate infiltration of all wound sites. If the exposure involves a mucous membrane, the entire dose should be administered IM. Rabies vaccine and RIG should never be administered at the same site or with the same syringe. Commercially available RIG in the United States is purified from the serum of hyperimmunized human donors. These human RIG preparations are much better tolerated than are the equine-derived preparations still in use in