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Rabies

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Rabies

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relevant to this
article.

Objectives After completing this article, the reader should be able to:

1. Explain the pathogenesis and epidemiology of rabies virus.
2. Describe the clinical manifestations of rabies.
3. Identify the most appropriate tests available to diagnose rabies infection.
4. Outline the specific measures to be taken after exposure to rabies.
5. Appreciate the strategies used to eradicate reservoirs of rabies virus in terrestrial wildlife.

Case Study

A previously healthy 13-year-old boy is admitted to the hospital with the chief complaints of altered mental status and unsteady gait. Five days prior to this admission, he developed low-grade fever, generalized body pain, dry cough, and listlessness. Over the course of the next few days, he developed abdominal pain and nausea. Two days prior to this admission, he was noted to be confused, have an unsteady gait, and have difficulty swallowing. He has no history of trauma, ingestion, or bites. His mother mentioned that he had fed a raccoon in his backyard 2 to 3 months ago. The raccoon later was found dead. On examination, the boy's temperature is 100°F (37.8°C). He has fluctuating consciousness, hypersalivation, and hydrophobia. He has an ataxic gait and appears disoriented. The results of his cerebrospinal fluid (CSF) examination are: clear fluid with no red blood cells, 50 white blood cells/mm³, 70% lymphocytes, 20% monocytes, glucose of 41 mg/dL (2.3 mmol/L) (serum glucose of 90 mg/dL [5 mmol/L]), protein of 155 mg/dL, and no organisms on Gram stain. CSF bacterial culture exhibits no growth at 72 hours.

Introduction

The word “rabies” is derived from a Sanskrit word “rabhas” meaning “to do violence.” In Greek, “Lyssa” means “mad rage”; therefore, the genus of the virus that causes rabies is named Lyssavirus. The word hydrophobia means “fear of water” and is derived from two Greek words: hydor (water) and phobos (fear).

Rabies, an acute, progressive encephalitis usually resulting in death, is a major public health problem in most parts of the world. However, some locations are considered rabies-free, including Antarctica, Hawaii, many islands in the Pacific, and a few islands in the Caribbean. Rabies is a zoonotic disease because most humans acquire the disease after having been exposed to an infected animal. The incidence of rabies has decreased significantly in developed countries, such as the United States, because of mandatory vaccination of all domestic animals. On the other hand, the incidence of rabies remains high in developing nations of Asia and Africa because of a lack of immunization of domestic animals, resulting in significant health concerns for both the local population and tourists.

History

Rabies was described as early as 2300 BC. Wound cauterization to prevent rabies was practiced in the 1st century AD. Its mode of transmission, via saliva, was recognized initially in the early 19th century. The pathogenesis and clinical signs of rabies were described by Lord Louis Pasteur in 1880, who later developed the first rabies vaccine. In 1903, Adelchi Negri in Milan identified the pathognomonic Negri bodies, associated with

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rabies virus, in brain tissue. Direct fluorescent antibody testing, enabling detection of rabies antigen in tissues, was developed in 1958.

Virology

Rabies is a neurotropic virus belonging to the Rhabdoviridae family in the genus *Lyssavirus*. It has a bullet-shaped nucleocapsid with a single, negatively stranded, nonsegmented RNA core surrounded by a lipoprotein envelope. According to the World Health Organization, at least seven different serotypes of the *Lyssavirus* genus infect humans and animals. Most cases of human rabies are caused by *Lyssavirus* serotype-1, commonly known as “rabies virus.” This viral serotype is found worldwide. The other serotypes have limited geographic distribution and cause infection primarily in insectivorous bats, rarely causing human disease.

Pathogenesis

The virus usually is transmitted via saliva inoculated into a bite or cut on the skin or mucosa. Nonbite exposures, such as licking, scratching, or through inhalation, occasionally transmit the virus. Human-to-human transmission is rare and has been described mostly after corneal or other organ transplants. Studies in baby hamsters and adult skunks have shown that the virus replicates in the muscle tissue, at or near the site of entry, for most of the incubation period. Thereafter, it proceeds rapidly to the peripheral nerves via the neuromuscular connections. Once within the nerves, the virus may travel as rapidly as 12 to 24 mm/d. In experimental animals, mortality was reduced by amputating the inoculated limb before the virus began replicating in the peripheral nerves, indicating that maximum benefit of postexposure treatment occurs only when it is instituted as soon as possible after the exposure. After replication in the peripheral nerves, the virus reaches the central nervous system (CNS) via the dorsal root ganglia and sensory neurons. Occasionally, the virus may enter the CNS without replicating in the peripheral muscles. Upon reaching the CNS, the virus multiplies further, infecting virtually every neuron.

From the CNS, the virus spreads to the rest of the body, especially the salivary glands, via the peripheral nerves. The virus can be transmitted via saliva because of active replication within the salivary glands. The pathologic changes of rabies are minimal and disproportionate to the clinical symptoms. These changes are most evident in neuronal tissues. On gross examination, the brain in furious rabies (see definition in Clinical Phases section) may appear to have meningeal congestion; paralytic rabies (see definition in Clinical Phases section) primarily

causes significant inflammation and necrosis of the spinal cord, resulting in acute inflammatory polyneuropathy (Guillain-Barré syndrome). Encephalitic changes may be seen microscopically, as evidenced by perivascular cuffing, neuronophagia, and limited necrosis. Occasionally, there may be evidence only of meningitis.

Eosinophilic, intracytoplasmic viral inclusions, called Negri bodies, frequently are concentrated within the hippocampal pyramidal cells and less frequently in the cortical neurons and cerebellar Purkinje cells. The Negri bodies also may be seen in the tissues of the skin, cornea, adrenal glands, and other organs. The sensitivity of demonstrating Negri bodies, however, varies. Until the development of the fluorescent antibody technique, histologic detection of Negri bodies was considered the only pathognomonic test. The most remarkable systemic abnormality is myocarditis that resembles the cardiac involvement seen with tetanus or pheochromocytoma. Microscopic evidence of atrial-ganglioneuritis suggests that the virus probably reaches the heart via myocardial nerves. However, the presence of Negri bodies in the myocardium indicates direct viral invasion of the cardiac tissue.

Natural rabies infection causes significant immunosuppression, resulting in an inadequate immune response. Patients who develop a rapid cellular immune response usually progress more rapidly to fatal encephalitic rabies than do those who do not develop this response. The virus may persist within macrophages for a long time before emerging to cause disease. This persistence could explain the long incubation period seen in some cases.

Epidemiology

Rabies primarily is a disease affecting many animals. The virus tends to be maintained in the wild animal population for many years despite high mortality from the infection, making eradication very difficult. Even though any mammal can be infected, certain ones appear to be reservoirs for human infections because they have a higher viral inoculum in their saliva and shed the virus for a longer period, making them more infectious. These mammals include dogs, cats, striped skunks, raccoons, bats, foxes, wolves, and jackals. Human transmission from small rodents such as squirrels and hamsters is rare, even though they are susceptible to the virus, because these animals succumb to the illness soon after acquiring the infection. However, large rodents such as woodchucks and beavers are capable of transmitting rabies to humans.

The epidemiology of human rabies reflects that of local animal rabies. Over the last 50 years, the incidence of human rabies has decreased significantly worldwide, especially in developed countries. Of the 47 cases of

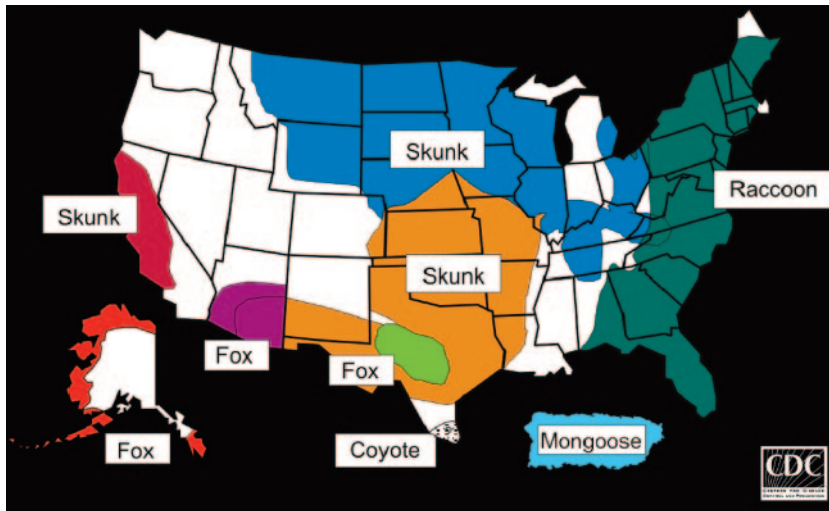


Figure. Centers for Disease Control and Prevention data from 2001 regarding terrestrial animal reservoirs of rabies virus.

human rabies reported in the United States between 1990 and 2004, 38 cases were acquired in the United States from contact with animals that had rabies virus infections; the remaining cases were acquired in developing countries outside the United States. Four of the cases occurred in transplant recipients from an undetected single-organ donor; death occurred in most of these cases. In Asia, Africa, and other areas where animal control programs are not developed extensively, humans acquire rabies primarily from infected dogs or cats (canine rabies). In countries that have stringent rabies immunization and quarantine policies, human cases often occur after exposure to wild terrestrial animals and bats. The current incidence of canine rabies in the United States from local dogs and cats is low, despite numerous reports of canine bites, especially in children. Until recently, most of the human rabies cases in the United States had been in travelers returning from areas at risk for canine rabies. However, with the steady increase of animal rabies over the last 2 decades, bats, raccoons, skunks, foxes, and coyotes increasingly are becoming the major reservoir of human rabies in North America. The Figure shows a 2001 map of animal reservoirs for rabies virus in the United States. Two small-bodied bats, the eastern pipistrella bat (*Pipistrellus subflavus*) and the silver-haired bat (*Lasiurus noctivagans*), are especially important reservoirs for rabies throughout the continental United States and Alaska. In recent years, when the source of exposure has been unknown, molecular techniques frequently have determined the cause of rabies infection to be from bats. Human rabies is more common in males

younger than 15 years of age, reflecting their greater likelihood of exposure.

Clinical Manifestations

Three possible outcomes follow a definite rabies exposure: no infection, asymptomatic infection demonstrable by serologic immune response, or symptomatic rabies.

The initial signs of rabies in animals are a change in disposition, restlessness, and fear. Wild animals may demonstrate an unusual lack of fear of humans. Over the next few days, most infected animals develop the furious syndrome that is characterized by increased restlessness, snapping, and drooling. By contrast, a few infected animals may

become lethargic (dumb syndrome). Most affected canines die within 10 days of becoming symptomatic. Rarely, a few might survive for as long as 1 month before succumbing to the disease.

Clinical Phases

Human rabies infection evolves through five clinical phases: incubation, prodrome, acute neurologic phase, coma, and death or recovery.

Incubation

The incubation period varies in length, with the patient usually being asymptomatic. The incubation period may be as short as a few days or as long as several years after exposure. The mean duration in most patients (>75%) is 30 to 90 days. The length of the incubation period depends on the innervation of the site of bite, the number and severity of bite(s), the proximity of the bite's location to the CNS, the quantity of virus inoculated, and the age and immunity of the host. Incubation periods typically are shorter in children, in persons who have extensive bites to the face or head, and in those receiving corticosteroids.

Prodrome

A typical prodrome lasts 2 to 10 days and correlates with the viral invasion of the CNS, especially into the limbic system, brainstem, and spinal cord. During this phase, the patient presents with mild and nonspecific respiratory or gastrointestinal symptoms, frequently leading to the misdiagnosis of a bacterial or viral infection. These manifestations may include fever, headache, chills, malaise,

fatigue, sore throat, cough, nausea, vomiting, diarrhea, dysphagia, vertigo, irritability, anxiety, and apprehension. As the disease progresses, the patient develops alteration in personality, photophobia, and insomnia. A specific symptom often seen in most patients during this time is paresthesia at the site of the bite, described as burning pain, numbness, tingling, or itching.

Acute Neurologic Phase

This phase correlates with widespread invasion of the CNS by the virus. It begins with the patient developing obvious signs of neurologic dysfunction. Patients may present as having either furious rabies or paralytic rabies. Both presentations involve the development of fever, nuchal rigidity, muscle fasciculation, convulsions, hyperventilation, or hypersalivation.

FURIOUS RABIES. This phase develops in 80% of cases and is characterized by anxiety, marked agitation, hallucinations, and other bizarre behavior. Signs of hydrophobia or aerophobia (fear of breeze) may occur, in which patients develop painful spasms of the pharynx, initially triggered by an attempt to drink water or by air blowing on the face. However, as the illness progresses, these signs may be triggered by a variety of tactile, audio, visual, or olfactory stimuli. Such reactions are due to violent diaphragmatic contractions from an exaggerated respiratory protective reflex. The patient's mental status initially fluctuates among periods of agitation, relative normalcy, and severe depression. Neurologic signs include hyperreflexia and excess cholinergic signs such as hypersalivation, lacrimation, mydriasis, and hyperpyrexia. Unless the patient dies abruptly, paralysis soon occurs, and the mental status rapidly deteriorates from disorientation to stupor and finally, coma. The clinical picture at this time may mimic that of meningitis, encephalitis, drug toxicity, tetanus, or polyneuropathy.

PARALYTIC RABIES. This phase is seen less often (about 20% of cases). It is more frequent after exposure to bats or in persons who have received improperly inactivated rabies vaccines that contain fixed virus strains. Hydrophobia and hyperactivity are characteristically absent. The patient may develop any one of the following four clinical patterns of paralytic rabies: 1) the most common presentation is paresthesia and weakness (prominent at the site of the bite) that rapidly progresses to paraplegia, triplegia, or quadriplegia; 2) less often, quadriplegia at the onset of illness; 3) occasionally, presentation as transverse myelitis with combined motor and sensory involvement; or 4) rarely, clinical findings

that may mimic Landry-Guillain-Barré syndrome, presenting with fever and symmetric ascending paralysis but with intact sensory function. Eventually, the patient progresses into complete respiratory paralysis. Most patients who have paralytic rabies develop myoedema (swelling of muscles). Some patients may develop hydrophobia and signs of furious rabies just before they become terminally ill.

Coma

During the transition from the acute neurologic phase to coma, a patient may develop periods of rapid, irregular, jerky (apneustic) breathing followed by generalized paralysis and coma. The patient usually dies from respiratory failure unless mechanically ventilated at this time. Ultimately, patients succumb to the complications of prolonged ventilation.

Non-neurologic signs involving the following organs also may develop:

- Cardiac: tachycardia, arrhythmia, hypotension, or congestive cardiac failure
- Respiratory: hypoxia, hyperventilation, atelectasis, pneumothorax, or pneumomediastinum
- Diabetes insipidus, hypothermia, hyperthermia, autonomic dysfunction, or the syndrome of inappropriate antidiuretic hormone secretion involving the CNS
- Gastrointestinal: vomiting, diarrhea, ileus, severe gastrointestinal pain, or bleeding

Differential Diagnosis

Infection with rabies virus may mimic some of the following conditions:

- Infectious: herpes simplex virus, arboviruses, poliomyelitis, herpes B virus, cerebral malaria, tetanus, botulism, and typhoid and rickettsial diseases
- Noninfectious: Guillain-Barré syndrome; intoxication with poisons, drugs, or alcohol; allergic postvaccinal encephalomyelitis; and acute porphyria
- Rabies hysteria: a rare psychological condition that occurs in exposed adults who believe that they have developed rabies. Many of these adults have some knowledge about the clinical manifestations of rabies, and they may present with symptoms and signs indistinguishable from those of rabies.

Diagnosis

Human rabies frequently is misdiagnosed, especially in countries such as the United States, where the incidence is rare. Some 20% of cases may have no documented history of exposure. No useful diagnostic tests recognize

the infection during the incubation period. During the symptomatic phase, a peripheral hematologic profile and urinalysis usually are nonspecific. In one third of patients, initial results of the CSF analysis, electroencephalography (EEG), and computed tomography (CT) scan of the head may be normal. Later in the illness, CSF may show pleocytosis (30 to 300 white blood cells/mm³), a normal glucose concentration, and a moderately elevated protein level (100 to 200 mg/dL). Nonspecific abnormal changes also may be noted on an EEG or a CT scan of the head. A thorough history that includes the patient's place of residence, possible exposure, and travel to rabies-endemic areas is very important for early diagnosis. Specific tests for rabies usually are not available in most hospitals and may have to be requested from a state health department laboratory.

Direct fluorescent antibody staining (DFA) that detects rabies-specific antigen is a reliable, rapid test. Acceptable specimens for DFA are saliva, brain tissue, and other neural tissues. Because the virus localizes to the nerve plexus surrounding the hair follicles, a good specimen that becomes positive early during the illness is a full-thickness biopsy of the skin taken from the nape of the neck at the hairline. It is important to remember that prior rabies immunization does not induce CSF antibodies to the virus. Thus, the presence of high CSF rabies antibody titers supports the diagnosis of clinical rabies.

Virus can be isolated in culture from saliva, CSF, urine, and respiratory secretions, usually during the second or third week of symptoms. The virus may not grow if the culture is performed too early in the course of the illness because the virus replicates slowly. Likewise, the virus may not be isolated on culture, if obtained late in the infection, because of neutralization by virus-specific antibodies.

The current diagnostic test of choice is reverse transcriptase-polymerase chain reaction (RT-PCR) because this type of testing is specific and is the most sensitive and earliest to yield results. The best specimens for this test are saliva or brain tissue. Unlike other diagnostic techniques, RT-PCR also can be performed successfully on decomposing brain tissue. This test has the added advantage of determining the geographic and host species origin of a particular rabies virus, especially when the exposure is unknown.

Treatment

No specific antirabies agent is available to treat the disease once the patient becomes symptomatic; most of the management is supportive. Supplemental oxygen and mechanical ventilation are essential for most patients during the period of agitation and hyperventilation.

Tranquilizers are useful in controlling hyperactivity and agitation. Focal or generalized seizures may require anticonvulsant therapy. Adequate fluid administration and vasopressors may correct hypotension. Cardiac arrhythmia may require antiarrhythmic agents. Treatment with diuretics, fluid restriction, and digoxin may be necessary to treat congestive cardiac failure. Use of rabies-specific immunoglobulin (RIG) or rabies vaccine after the onset of disease has not been shown to be protective or to increase the survival rate.

In a recent case report, a patient who had developed rabies after sustaining a bite from a bat was managed empirically with an "intense antiexcitotoxic strategy" until the patient's natural immune response matured. This regimen consisted of placing the patient in a deep, drug-induced coma by using benzodiazepines, barbiturates, ketamine, and amantadine. The latter two agents also have been reported to be effective against rabies virus. Ribavirin was used initially in conjunction with the previously noted therapy but later was discontinued due to drug-related toxicities. The patient survived the illness with neurologic impairment. Further studies are required to determine if such a treatment protocol is truly effective in increasing survival from rabies infection.

Prognosis

The prognosis in most cases of rabies infection is grave. Death usually results from severe neurotransmitter imbalance. However, five to six survivors have been documented in the medical literature, which has provided hope for a possible cure in the future. Most survivors have been reported to suffer neurologic sequelae, usually involving the cerebellum.

Hospital Isolation

Rabies virus can be identified from saliva, CSF, impressions from the cornea, and urine. Because the shedding and infectivity between humans is not clearly understood, direct contact with infected secretions or tissues must be avoided. The patient suspected of having rabies infection must be placed in contact and droplet isolation, which requires caregivers to wear gowns, gloves, masks, and goggles when in direct contact with the patient. Contacts who are exposed prior to diagnosis may be at risk of developing rabies and should be offered postexposure prophylaxis.

Prevention

Because most human cases of rabies are fatal and no specific therapy is available, the emphasis is placed on prevention. Fortunately, effective vaccines are available. Nerve tissue vaccines were developed more than 70 years

ago from animal brain and spinal cord tissues (Semple-type). These vaccines now are used predominantly in developing countries because they are relatively inexpensive. However, these vaccines frequently are associated with increased central and peripheral neurologic complications. Antibody titers should be monitored in all recipients of the nerve tissue vaccines because their immunogenicity may vary. Avian vaccines derived from duck embryos were the next vaccines to be introduced, but they are less immunogenic than the brain tissue vaccines.

Finally, cell culture vaccines, which include human diploid cell vaccine (HDCV), rhesus monkey diploid cell vaccine (rabies vaccine, adsorbed), and purified chick embryo cell vaccine, among others, are available primarily in developed countries such as the United States. These vaccines are more expensive but are safe and immunogenic. In addition, antibody titers need not be monitored in recipients of cell culture vaccines unless there is reason to suspect poor antibody response. Use of steroids during vaccination may blunt the immune response.

Because most human cases of rabies infection are related primarily to infection after animal exposure, especially to canines, vaccination of domestic animals substantially decreases the incidence of human rabies. Most developed nations have enforced strict rabies vaccination laws for pets and livestock. Recent programs to vaccinate wild terrestrial animals with oral rabies vaccine are becoming effective public health measures, especially in Europe and in the United States.

Pre-exposure prophylaxis is administered to persons at risk for exposure to rabies virus, including veterinarians, animal control officers, park officials, laboratory personnel working with rabies virus, and travelers to rabies-endemic countries. HDCV rabies vaccine is used preferentially in the United States because of its demonstrated safety and efficacy. The vaccine is not contraindicated for use in pregnant women. It is administered in a 1-mL dose intramuscularly three times, on days 0, 7, and 21. A booster dose is recommended every 2 to 3 years, especially for individuals frequently at risk of exposure. Immunization of all travelers for the prevention of rabies is controversial. However, selected immunization based on age and travel destination is appropriate. The Centers for Disease Control and Prevention currently recommends prophylactic rabies vaccination for individuals planning to stay for more than 30 days in remote areas of the world without access to medical facilities. Because chloroquine may decrease rabies antibody response, its concurrent use with rabies vaccine is not recommended.

Postexposure treatment (PET) that includes aggressive management of the bite or wound can reduce the

risk of acquiring rabies by 90%. Thorough washing with 20% soap solution and vigorous irrigation with a virucidal agent such as povidone-iodine is recommended. Mechanical scrubbing and adequate debridement are more effective than simple irrigation of the wound. Suturing or using occlusive dressings to cover the wound should be avoided when possible. Because acquiring a secondary bacterial or tetanus infection is common after an animal bite, tetanus vaccine and antibiotics should be administered when necessary.

The risk of developing rabies after exposure must be determined. Communication with local public health officials is useful in obtaining information about locally infected animal species and for the proper examination of the animals. In the United States, when an animal suspected of being infected with rabies is available, the local or state health department should be contacted about the management of such animals that bite humans. If the biting animal is a dog, cat, or ferret and is considered otherwise healthy, the animal should be confined and observed daily for 10 days. The animal should be evaluated by a veterinarian at the first sign of illness during the period of confinement. If the bite involves a stray or unvaccinated dog, cat, or ferret, the animal should be euthanized immediately and the head submitted for rabies examination. For animals other than dogs, cats, or ferrets, the management of the animal depends on many factors, including the biting incident and the animal's history (if available) and current health status. The animal's brain tissue should be examined for rabies only in a qualified laboratory as designated by the consulting local or state health department.

PET is recommended after a bite by a mammal that has not been vaccinated previously or whose vaccination status is unknown (undocumented) or when the animal is not available to monitor and the integrity of the skin or mucous membrane has been breached. Because bats have infected humans without a known bite, PET is recommended for adults or children sleeping in a room in which a bat is found or in those cases where it is difficult to exclude direct contact with bats. Because the risk of acquiring rabies is very low after a rodent bite, PET is not recommended routinely unless the rodent involved was a woodchuck or a beaver. PET should be offered to all individuals, including those who have received pre-exposure prophylaxis, if they become at risk for rabies. It is important to recognize that of the 30,000 to 40,000 individuals in the United States annually receiving PET, only a few actually are at risk for rabies infection.

PET includes the administration of RIG. Two types of RIG are available: human rabies immunoglobulin

(HRIG) and equine rabies immunoglobulin (ERIG). Only HRIG is available in the United States. Purified ERIG, available outside the United States, is as safe and as well tolerated as HRIG. RIG must be administered to the exposed individual as soon as possible and within 7 days of exposure. RIG always should be used in combination with rabies vaccine (active immunization) after primary exposure, but should not be used in individuals who have received prior rabies vaccination. The total dose of 20 IU/kg is infiltrated primarily around the bite site. Any remaining volume should be administered intramuscularly at a site distant from the wound. RIG is safe and usually free of adverse reactions.

HDCV rabies vaccine (1 mL/dose) is administered intramuscularly on days 0, 3, 7, 14, and 28 in unvaccinated individuals. Previously immunized individuals require a booster dose of 1 mL/dose on days 0 and 3. The vaccine must be injected in the deltoid muscle because if the muscle is missed in gluteal injections, there may be vaccine failure. Booster doses may be given either intramuscularly or intradermally. In the United States, booster doses are given by intramuscular injection only. Intradermal vaccines currently are available outside the United States. The vaccine must never be administered at the same site as RIG because the antibodies in RIG might interfere with the immune uptake of the vaccine. The development of local reactions such as swelling, pain, or induration is common. Rarely, other symptoms such as fever, headache, malaise, nausea, abdominal pain, and adenopathy may develop.

The previous information is available in tabular form in the American Academy of Pediatrics *Red Book* (see Suggested Reading).

Future Prospects

Improved wildlife surveillance has begun to provide a better understanding of rabies disease in animals. More widespread wildlife vaccinations using oral rabies vaccine might provide a safe and effective method to control the disease in the wild, thereby eradicating the animal reservoir for rabies. Molecular technology has allowed better identification of viral strains, allowing determination of their geographic location and frequency of occurrence. Development of virus-specific monoclonal antibodies may provide effective passive immunotherapy. The availability of new antiviral therapy and specific immunomodulators might improve treatment and be curative. Finally, designing a subunit vaccine might provide a safer and more effective preventive tool.

Summary

Rabies is a zoonotic infection that results in progressive encephalitis and death. It is caused by a virus of the Lyssavirus genus. Rabies is a major public health problem all over the world. In the United States, most cases occur after exposure to wild terrestrial animals or bats. The virus usually replicates at the point of entry for a period of time before invading the CNS via peripheral nerves. Symptomatic rabies may present as the more common furious form or the less common paralytic type. Reliable and rapid diagnostic tests include DFA and RT-PCR. Currently, no therapeutic agents for treating disease caused by rabies virus are effective. However, there are effective and safe preventive measures, such as human diploid cell rabies vaccine and HRIG, which should be administered as soon as possible after exposure.

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PIR Quiz

Quiz also available online at www.pedsinreview.org.

5. The rabies virus affects both wild and domestic animals, with the added risk that certain mammals are more contagious with the rabies virus than others. The animal that is *less* likely to transmit rabies to humans is the:
 - A. Bat.
 - B. Dog.
 - C. Fox.
 - D. Raccoon.
 - E. Squirrel.

6. In African countries such as Ethiopia, in contrast to the United States, the *most* likely animal to transmit rabies to humans is the:
 - A. Bat.
 - B. Dog.
 - C. Fox.
 - D. Hyena.
 - E. Skunk.

7. The incubation period after exposure to a rabies-infected animal varies, but shorter incubation periods are more often seen in a(n):
 - A. Adult.
 - B. Bat aerosol exposure.
 - C. Face bite.
 - D. Finger bite.
 - E. Leg bite.

8. The *best* test to confirm a diagnosis of rabies earliest in a suspected human rabies case is a(n):
 - A. Cerebrospinal fluid rabies antibody test.
 - B. Computed tomography scan of the brain.
 - C. Direct fluorescent antibody test of the saliva for rabies-specific antigen.
 - D. Electroencephalogram.
 - E. Reverse transcriptase-polymerase chain reaction test of the saliva for rabies antigen.

9. A 5-year-old boy is playing in his backyard when he encounters a raccoon, which bites him on his hand. The animal escapes, and the child is brought to the emergency department for treatment. The wound is cleaned with 20% soap and povidone-iodine solution. The *best* next course of action is to:
 - A. Administer one dose of human diploid rabies vaccine (HDVC) as soon as possible.
 - B. Administer one dose of rabies immune globulin (RIG) and HDVC in the buttocks while awaiting the pathology report on the raccoon's brain.
 - C. Administer RIG immediately in the deltoid and start the HDCV, giving it on days 0, 3, 7, 14, and 28.
 - D. Contact animal control to capture the raccoon for rabies examination and administer RIG and HDVC to the boy as soon as it is determined that the raccoon has rabies.
 - E. Infiltrate the wound with RIG and immediately start HDCV vaccine, giving it on days 0, 3, 7, 14, and 28.

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