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**DR. RAPPLEY REPLIES:** Dr. Selman's comments confirm the importance of thorough history taking whenever symptoms of attention deficit–hyperactivity disorder (ADHD) are present. An inadequate amount of sleep can result in irritability, inattention, and daytime sleepiness[1]; disordered sleep (which may include snoring, sleep apnea, and periodic limb movements of sleep) may result in similar symptoms.[2] Although such symptoms are common in children with sleep problems, sleep disorders appear to occur in a small subgroup of children with ADHD.[3] Absence seizures are associated with periods in which the child appears inattentive to his or her surroundings; ADHD, primarily the inattentive type, is distinguished by pervasive difficulty with attention.[4] Disorders of sleep, seizure disorders, and behavioral problems, including symptoms of ADHD, may be especially prominent in children with genetic syndromes and children with mental retardation of unknown cause.[5]

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## Prophylaxis against Rabies

**TO THE EDITOR:** As noted by Rupprecht and Gibbons (Dec. 16 issue),[1] delay before postexposure prophylaxis against rabies is initiated may result in treatment failure and death.[2] The incubation period for rabies in dogs could be much longer than 10 days. Furthermore, in previous studies, the rabies virus was isolated from the saliva and cerebrospinal fluid of many dogs before they had any signs of rabies,[3] and up to 18 percent of the infected dogs died without having shown any signs of illness beforehand.[4] Therefore, management by 10-day observation in many areas where rabies is still prevalent might put patients' lives at risk. According to World Health Organization (WHO) recommendations, all patients with a category 3 exposure (i.e., a transdermal bite or contamination of the mucous membranes with saliva) should receive immune globulin and vaccine immediately, and treatment should be stopped only if the animal remains healthy throughout the 10-day period of observation or is euthanized and found to be negative for rabies by appropriate laboratory tests.[5]

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**TO THE EDITOR:** In their review, Rupprecht and Gibbons recognize that rabies immune globulins are in short supply and note that "multisite intradermal vaccination is another possible strategy to accelerate the immune response." However, the risks associated with not using immune globulins in cases of severe rabies exposure should be emphasized. A similar statement, since withdrawn, from the Thai Health Ministry led to one tragic death. The eight-site method was used without immune globulin in a Thai child with facial dog bites, and the child died of rabies 15 days later.[1] Recent studies have shown that the multisite accelerated method will result in increased antibody titers by day 14

but not in significantly earlier ones.[2,3] This topic was discussed at a 2004 WHO meeting, at which the need for immune globulin in the optimal treatment of severe rabies exposure was reaffirmed.

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**TO THE EDITOR:** In their review of rabies prophylaxis, Rupprecht and Gibbons mention that multiple intradermal vaccination is an alternative strategy for accelerating the immune response. Because of the high cost of rabies vaccine, the intradermal route is often used in tropical countries. However, in these countries, chloroquine is used regularly. In our view, it is important to mention that weekly oral chloroquine prophylaxis against malaria has been associated with an impaired antibody response to intradermal rabies vaccination.[1,2] If chloroquine is being used concurrently, intramuscular injections are preferable.[3] If the intradermal route is chosen, chloroquine should not be used.

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**THE AUTHORS REPLY:** In response to Dr. Kurathong: As we discuss in our review, postexposure prophylaxis against rabies should begin when rabies is considered seriously. In developed countries, where rabies is controlled among domestic animals, suspect dogs are observed and postexposure prophylaxis administered only when there is a significant suspicion of rabies.

It is important to differentiate between the incubation period (i.e., the time between exposure and onset) and the period when transmission is likely. Incubation periods are quite variable, lasting from days to years (average duration, approximately one to three months). In contrast, animals excrete rabies virus for only a few days before obvious illness. The 10-day observation period refers to the suspect biting dog. Postexposure prophylaxis is unnecessary unless the animals sickens, after which euthanasia and laboratory diagnosis should be performed. No documented human cases have occurred when the dog remains normal during this period.[1] If there is an increased prevalence of rabies, as there is in developing countries, postexposure prophylaxis begins after a bite and is discontinued if the animal remains normal or test results are negative.

The comments of Drs. Wilde and Hemachudha and of Dr. Van den Enden highlight potential difficulties in postexposure prophylaxis in countries where rabies is endemic. Rabies vaccines are potent, but many factors affect immunity, including genetic characteristics, nutrition, concomitant diseases, and concomitant use of other drugs. Serologic analyses of vaccine recipients, such as Peace Corps volunteers, showed substantial differences in responses after vaccination.[2] Antimalarial drugs, such as chloroquine, may interfere with optimal responses after primary vaccination with intradermal vaccine. If antimalarial drugs are administered, vaccination should ideally be given by the intramuscular route. Nevertheless, there have been no documented instances of failure of postexposure prophylaxis as a result of the use of antimalarial drugs. Unfortunately, malaria is endemic in most regions where canine rabies persists: the costs of intramuscular vaccination make it impractical for routine use in these regions, as opposed to occasional use in travelers. The high costs and lack of availability of rabies immune globulin, which we agree is routinely indicated for high-risk exposures, also remain a problem in these areas.

Clearly, elimination of canine rabies is the ultimate solution to problematic postexposure prophylaxis.[3] Scarce and costly biologic agents for use in humans are not a practical approach to the ef-

fective management of rabies in areas where it is endemic.

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# Case 38-2004: A Large Tumor of the Skull

**TO THE EDITOR:** In Case 38-2004 (Dec. 16 issue),[1] Richardson et al. provide an excellent discussion of the treatment options available for patients with multiple myeloma. In my opinion, the diagnostic workup for the patient is missing two important tests that should be done routinely, especially in the setting of oligosecretory and extramedullary myeloma. The first is functional imaging with whole-body positron-emission tomography (PET) scanning.[2] In this patient, a PET scan would have helped identify occult sites of plasmacytoma, thus providing an accurate assessment of his tumor burden. The second test is the measurement of monoclonal free light chains in the serum, which is an easily available measure of tumor activity, even in oligosecretory settings.[3] It would have been helpful to know the level of measurable free light chains in this patient before and after radiation treatment and during relapse. Measurement of free light chains is quite sensitive and specific for monitoring the response and for detecting an early relapse. An accurate assessment of the tumor burden early in the course of disease could improve patient outcomes by prompting the implementation of definitive therapy, rather than palliation of symptoms.

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**THE AUTHORS REPLY:** Dr. Badros suggests that whole-body PET scanning and measurement of free light chains in the serum should be done routinely. We agree that in the setting of nonsecretory myeloma, PET scanning and measurement of free light chains can be helpful in establishing the extent of disease, particularly if protocol participation or intensive therapy is planned. However, the routine use of these tests is not supported by the clinical practice guidelines of the National Comprehensive Cancer Centers Network.[1]

We agree that studies have suggested that measurement of free light chains is sensitive and specific in monitoring the response and detection of early relapse, and if used in conjunction with PET scanning, provides an additional tool for the assessment of tumor burden.[2] This patient chose a more conservative approach to therapy, and therefore, because more intensive treatment was deferred, the use of these additional tests would have been of less value in this particular setting.

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