

PUBLIC HEALTH

Yellow fever vaccination: be sure the patient needs it

Epidemiology: Between 1996 and 2001 multiple organ system failure developed in 7 people within 2 to 5 days after yellow fever vaccination.¹ Six of them died, including 2 who were vaccinated even though they were planning to travel to countries where yellow fever has never been reported.

The vaccine is still recommended for travellers visiting areas that report yellow fever activity (www.cdc.gov/travel/yfever.htm), but physicians need to be clear about the indication and risks surrounding this vaccine, and they should report any adverse events following vaccination to Health Canada (www.hc-sc.gc.ca/hpb/lcdc/publicat/ccdr/00vol26/26s1/index.html) or to the US Centers for Disease Control and Prevention (CDC) (www.vaers.org).

Yellow fever is a mosquito-borne disease caused by an enveloped RNA virus in the flavivirus group.² It is found in tropical South America (Bolivia, Brazil, Colombia, Ecuador, French Guiana, Peru and Venezuela) and much of sub-Saharan Africa. Humans and primates are the principal animals infected by the vector, the biting mosquito. There are 2 main transmission cycles. Sylvatic (or jungle) yellow fever occurs in monkeys that are infected by wild mosquitoes; sporadic human cases arise when humans enter the forest and are also bitten by these mosquitoes. Urban yellow fever occurs when infected human migrants introduce the virus to domestic mosquitoes in areas with high human populations; these outbreaks tend to spread outward from a single source and affect a wide area and large number of people.^{3,4} The World Health Organization says the transmission of yellow fever is increasing, with about 200 000 cases occurring each year, mostly in Africa. Meanwhile, the number of people travelling from North America to South America and Africa has more than doubled since 1988.⁵

Clinical management: The virus replicates in local tissues and lymph nodes, then spreads to the liver, spleen, bone marrow and myocardium.² It lies silent

during an incubation phase that lasts 3 to 6 days and then presents with fever, myalgia, headache, anorexia and vomiting. Often the fever is accompanied by a paradoxically slow pulse. Most patients improve after 3 to 4 days. However, 15% enter a "toxic phase" within 24 hours, and their condition progresses to disseminated intravascular coagulation.² Fever reappears, and hemolytic and hepatic jaundice rapidly develop (hence, "yellow" fever), which is accompanied by abdominal pain and vomiting. Bleeding can occur from the nose, mouth, eyes or stomach, and kidney function deteriorates. Treatment is supportive, but half the patients in the toxic phase die within 2 weeks; the rest recover without significant organ damage.³

Yellow fever is easily confused with malaria, typhoid, rickettsial diseases, hemorrhagic viral fevers, arboviral infections such as dengue fever, leptospirosis, viral hepatitis and poisoning (e.g., carbon tetrachloride poisoning). Health Canada's Committee to Advise on Tropical Medicine and Travel has prepared initial assessment guidelines for fever in the international traveller.⁶ The range of diagnostic tests includes enzyme-linked immunosorbent assay to detect viral antigen in the blood, polymerase chain reaction to determine the viral genome, and serologic assays to determine specific antibodies. Yellow fever is one of 3 diseases — plague and cholera are the other 2 — that are subject to international quarantine regulations. Any suspected case should be reported to the medical officer of health.

Prevention: Recently the CDC's Advisory Committee for Immunization Practices reviewed the 7 cases of multiple organ system failure associated with the live, attenuated 17D-204 and 17DD yellow fever vaccine strains. Liver biopsies were collected in 4 cases, and 3 demonstrated histopathologic changes consistent with wild yellow fever virus.¹ This highlights the need for better surveillance of vaccine usage and improved understanding of how this virus is attenuated.

Despite the rare complications created by multiple organ system failure, the vaccine is still recommended for people planning to travel to areas reporting yellow fever activity or within the endemic zone, because the risk of death from yellow fever far outweighs the risk of multiple organ system failure. The live, attenuated 17D-204 and 17DD yellow fever vaccines are the most commonly used, with a single dose conferring immunity that lasts 10 years or more.

Yellow fever vaccines are still considered among the safest and most effective viral vaccines. Since 1965, about 8 million doses have been administered to US travellers, and about 300 million more to people in areas where yellow fever is endemic. Of those vaccinated, 2% to 5% reported headaches, myalgia and fever 5 to 10 days after being vaccinated.¹

The vaccine should never be given to infants less than 4 months old, to pregnant women or to people hypersensitive to eggs, and it should be administered judiciously to elderly people and to people with compromised immune systems.⁷ — *Erica Weir, CMAJ*

References

1. Notice to readers: fever, jaundice and multiple organ system failure associated with 17D-derived yellow fever vaccination, 1996–2001. *MMWR Morbid Mortal Wkly Rep* 2001;50:643–5. Available: www.cdc.gov/mmwr/previewmmwrhtml/mm5030a3.htm (accessed 2001 Sept 5).
2. Shoff W, Hinfey P, Behrman AJ, Shepherd S. Yellow fever. *Emed J* 2001;2(2). Available: www.emedicine.com/emerg/topic645.htm (accessed 2001 Sept 5).
3. World Health Organization. *Yellow fever* [fact sheet 100]. Geneva: WHO; 1999. Available: www.who.int/inf-fs/en/fact100.html (accessed 2001 Sept 5).
4. American Public Health Association. *Control of communicable diseases manual*. 17th ed. Washington: The Association; 2000. p. 553–8.
5. World Health Organization. Yellow fever, 1996–97. *Wkly Epidemiol Rec* 1998;73:354–9.
6. Fever in the international traveller. Initial assessment guidelines. An Advisory Committee Statement (ACS) / Committee to Advise on Tropical Medicine and Travel (CATMAT). *Can Commun Dis Rep* 1997;23(ACS-1). Available: www.hc-sc.gc.ca/hpb/lcdc/publicat/ccdr/97vol23/2307_sup/ccdr_e.html (accessed 2001 Sept 4).
7. *Comprehensive yellow fever vaccination requirements*. Atlanta: US Centers for Disease Control and Prevention; 2000. Available: www.cdc.gov/travel/yfever.htm (accessed 2001 Sept 4).