CME CREDIT

ONE MINUTE CONSULT

BRIEF QUESTIONS AND ANSWERS ON CURRENT CLINICAL CONTROVERSIES

# Q: Should speculations about immune-mediated adverse effects of Lyme disease vaccine deter us from giving it?

**LEONARD SIGAL, MD***
University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School, New Brunswick, New Jersey

A: I USUALLY TRY TO DISSUADE people from receiving Lyme disease vaccine if their risk of exposure to the vector *Ixodes* tick is low—but not because of any risk of arthritis from the vaccine itself. Rather, I do this because vaccination breeds complacency about taking personal precautions.

## SIMPLE PRECAUTIONS ARE EFFECTIVE

Most cases of Lyme disease are acquired near the home, so personal precautions are of paramount importance. These precautions are highly effective in preventing Lyme disease:

- Clear areas of brush and high grass at the edge of wooded areas, where the rodent hosts of ticks reside.
- Do a "tick check" and take a shower using a wash cloth after each day spent in areas infested with the vector.
- Apply a one-yard edge of wood chips at the forest edge.
- Apply acaricide to this wood chip border. (Acaricides are not needed on the lawn, as ticks do not reside there.)

## VACCINE SAFE, EFFECTIVE

The vaccine currently available was developed on the basis of animal and human trials. First, animal studies showed that passive transfer of antibodies to *Borrelia burgdorferi* (the causative organism of Lyme disease) prevents infection. Later, antibodies against a protein in the outer coating of the organism (outer surface protein A—OspA) were found to be protective, and active inoculation with OspA prevented *B burgdorferi* infection.

Recombinant OspA vaccines were developed by Connaught and by SmithKline Beecham laboratories and underwent large trials in the United States. (I was involved with the field testing of the Connaught vaccine.) The SmithKline Beecham vaccine was licensed and is marketed as LymeRix; the Connaught vaccine was never licensed. Both vaccines were very efficient in preventing Lyme disease. Side effects were very mild and self-limited; by 3 days after inoculation the adverse event profiles were essentially identical in people who received the active vaccine and people who received placebo. (In addition, other molecules are being evaluated for use as vaccines against Lyme disease.)

## SPECULATION ABOUT POSSIBLE IMMUNE-MEDIATED EFFECTS

However, some findings have raised speculation that the currently available vaccine may cause potentially serious immune-mediated effects.

Steere et al[1] found that patients who developed refractory Lyme arthritis (arthritis that does not respond to antibiotic therapy and is therefore termed "noninfectious" arthritis) often had the genetic marker HLA-DR4, also seen in rheumatoid arthritis, and that seroreactivity with OspA appeared at the same time as the onset of arthritis. Some experts then speculated that immune reactivity with OspA might be involved in the immunopathogenesis of refractory synovitis. It was thought that this might be an autoimmune process in which the synovial inflammation was brought on by the infection but

**No reason to avoid vaccination for people who need it**

*The author has acted as a consultant for SmithKline Beecham Inc, which manufactures Lyme disease vaccine.

continued in the absence of active infection. Subsequent studies showed that a sequence within OspA resembled an amino acid sequence within the human integrin lymphocyte function-associated antigen-1 (hLFA-1), a protein expressed on many immune cells. This led to concern that molecular mimicry between OspA and hLFA-1 might cause noninfectious arthritis.

Despite the speculations, the vaccine has not been found to cause immune-mediated articular or other damage, nor has the molecular mimicry been found to be of clinical significance. Further, since the HLA-DR4 phenomenon is not clearly related to the pathogenesis of arthritis, there is no reason to test people for HLA-DR4 to determine if they can safely receive the vaccine, and there is no reason to test for HLA-DR4 in those already vaccinated to see if they are likely to develop arthritis. Although the pathogenesis of refractory or chronic Lyme disease-related arthritis remains unclear, it seems to depend on prior infection with *B burgdorferi*.

## WHO SHOULD RECEIVE THE VACCINE?

Thus, there is no reason to avoid the vaccine if the patient needs it, ie, if he or she lives or works in an area infested with *Ixodes* ticks. Yet, patients should also receive education about the importance of simple personal precautions that are highly effective in preventing Lyme disease. The vaccine is part of a program of personal protection, but it should not be the primary prevention strategy.

On the other hand, people at minimal risk (ie, residing in nonendemic areas) or transient risk (ie, making a brief sojourn in an endemic region) do not need to be vaccinated against Lyme disease, and I try to dissuade them from it. Personal precautions and knowledge of the disease provide much better protection. In addition, *Ixodes* ticks can spread other diseases, including ehrlichiosis and babesiosis. When people become complacent about personal precautions, they increase their risk of being bitten by ticks and acquiring other dangerous infections.

## VACCINATION SCHEDULE

The original studies used a "0-1-12" protocol, meaning that the second dose was given 1 month after the first dose, and the third dose 12 months after the first dose. There is now evidence that the vaccine can be effective if given according to a 0-1-6 or even a 0-1-2 protocol.

**Lyme disease vaccination should not be the primary prevention strategy**

## REFERENCES


1. **Kalish R, Leong JM, Steere AC.** Association of treatment-resistant chronic lyme arthritis with HLA-DR4 and antibody reactivity to ospA and ospB of *Borrelia burgdorferi*. Infect Immun 1993; 61:2774–2779.



***ADDRESS:*** *Leonard Sigal, MD, University of Medicine and Dentistry of New Jersey, MEB 484, Robert Wood Johnson Medical School, 1 Robert Wood Johnson Place, New Brunswick, NJ 08903-0019.*