



## Thoughtful vaccination

Few in mainstream medicine doubt the efficacy of vaccination and the net positive value of a thoughtful vaccination policy. We have witnessed within a professional lifetime the virtual eradication, at least regionally, of a number of previously devastating infectious diseases including polio, smallpox, pertussis, and measles. With growing understanding of disease mechanisms, the potential value of vaccination has expanded to include preventing sequelae of certain infections and malignancy—a holy grail in oncology, the true prevention of cancer. Sporadic local resistance to uniform vaccination against measles has resulted in geographic reappearance of the disease, providing further support for a uniform approach to vaccination against communicable diseases, with some potential to opt out, perhaps with associated societal repercussions for those who do so.

For most clinicians, certainly those of us dealing with chronically ill or immunosuppressed patients, the decision to recommend annual influenza vaccination and pneumococcal vaccinations per guidelines is an easy one. Vaccination against certain infections provides some protection for the individual patient and for the population, contributing to “herd immunity” and helping to protect against the occurrence of pandemics. But this is not the case for all vaccines. For some vaccines the issues of immunity and vaccination are more individual and complicated and warrant more education, reflection, and conversation.

The vaccine to protect against human papillomavirus is effective at reducing the incidence of cervical and anal cancers triggered by infection with certain strains of human papillomavirus. The viral infection itself is not immediately life-threatening. Thus, patients (and their parents) are asked to consider vaccination against a sexually transmitted virus (before sexual transmission of infection) to prevent a possible malignancy later in life. This decision can create social angst. Perhaps less socially challenging, but medically more complicated, is vaccination against the hepatitis B virus (HBV). HBV is also sexually transmissible, but the source in many patients infected with this virus is unclear. The HBV vaccine helps protect against clinically meaningful hepatitis and chronic liver disease from HBV and also will reduce the occurrence of HBV-associated hepatocellular carcinoma and progression of cirrhosis in patients coinfecting with hepatitis C virus.

More complex yet is vaccination against the varicella-zoster virus (VZV) to reduce the likelihood of shingles and its possible consequence, postherpetic neuralgia. Le, Sabella, and Rothberg, in this issue of the *Journal* (page 359), review clinical and public health challenges affecting the use of this vaccine.

We are almost all exposed to this virus as children, through natural infection (chickenpox) or vaccination; many infections are seemingly subclinical. My older son had the distinct misfortune of getting chickenpox in a quite memorable way, developing a concentrated collection of the pruritic vesicles underneath a newly placed arm cast. Whether we remember the initial infection or not, VZV sets up housekeeping and lies dormant for decades within sensory neurons. Decades later, it may erupt as shingles along the distribution of the infected nerves with characteristic painful

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vesicles, sometimes with persistent, extremely painful, and debilitating residua within the same dermatomal distribution: postherpetic neuralgia. The triggers for this fairly common scenario are only generically understood and include waning cellular immunity attributed to aging, malignancy, immunosuppressive medications, human immunodeficiency virus, and perhaps stress and depression.

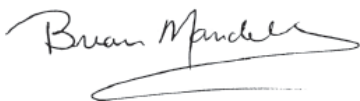
The zoster vaccine is unique in that it is given to bolster already present cellular immunity to prevent clinical recurrence of the earlier infection, decades after the virus has been dormant—not, as for the other vaccines noted above, to prevent primary infection. It doesn't matter if the patient has already experienced an episode of shingles. The currently available vaccine is a live-attenuated strain (Oka) of VZV. Another vaccine in clinical testing uses isolated viral components with adjuvant and thus eliminates current concerns of giving the live-attenuated vaccine to immunosuppressed and elderly patients, those who may benefit the most from it.

Fortunately, it seems that even significantly immunosuppressed and elderly patients tolerate the current vaccine, but at present it is suggested that these groups not receive the vaccine, and vaccination rates in these patients is low. Hopefully, additional data will accumulate regarding the safety of the vaccine and will permit its more widespread use within these patient groups, or a replacement “dead” vaccine will become available.

As Le et al nicely discuss, the current vaccine efficacy wanes over about 10 years, and then a booster vaccine should be considered, but there are few data to provide safety and efficacy outcome measures from patients who received a booster vaccination. The potential need to receive a booster injection after about a decade, the demonstrated greater efficacy against zoster when the initial vaccination is provided to patients ages 60 through 69 than in those over 70, and the lower absolute impact when given to patients ages 50 through 59 (baseline zoster incidence increases with age) should enter into the conversation with patients as to when they should receive the vaccine.

Additionally, there are the extremely provocative and as yet unanswered questions surrounding the implications of vaccination if VZV infection is a trigger of inflammatory vascular diseases such as giant cell arteritis in the elderly, as was proposed by the late Dr. Don Gilden.<sup>1</sup>

And yes, I did get the vaccine. I was 64 at the time.



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1. Gilden D, Nagel MA. Varicella zoster virus triggers the immunopathology of giant cell arteritis. *Curr Opin Rheumatol* 2016; 28:376–382.