Editorial

The Status of Immunotherapy in the United States, 2002

Nanette B. Silverberg, MD

Immunotherapies are agents that modulate the immune response to enhance or positively alter general or local immunity. Alterations in the local immune milieu can be administered in a variety of manners. Immunotherapy is a daily event in childhood. Vaccination is the most common form of human intervention in the immune system. When a vaccination is administered, a component of a pathogen or a closely related agent is administered in an immunogenic vehicle. The intended outcome is the production of a specific immune response that will stem the course of infection with the designated pathogen. Vaccination for noninfectious pathogens is a new area of development. Currently vaccines are being developed to reduce immune attack of the pancreas in diabetes, to promote malignant cell destruction (eg, melanoma), and to generate anti-B amyloid protein for Alzheimers.[1]

Immunotherapies can be divided into those that produce specific immunity versus those that provide nonspecific alterations in the immune response. The specific immunotherapies include vaccinations and antigenic injection of mumps or *Candida* antigen. Nonspecific immunotherapy agents include oral cimetidine,[2] which has been successfully used in children and adults as a therapy for warts, and topical immunotherapies, such as squaric acid dibutylester (SADBE).[3] SADBE, diphenylcyclopropenone (DCP), and dinitrochlorobenzene (DNCB) are potent allergens used to modulate cutaneous immune response. DNCB is mutagenic and is not used in children.

Vaccinations have proven helpful in both bacterial and viral illnesses. Those useful in dermatology include pneumococcal and varicella vaccination. In the future, 2 vaccinations will tremendously benefit dermatology—herpes and human papillomavirus vaccination. The former vaccine has already been proven to prevent disease acquisition in women, though it has not proven beneficial to men.

In this issue, Dr. Signore reviews data from his personal experience treating patients with *Candida* antigen injections.[4] Immunotherapy use against pathogenic organisms is not a new concept. Tuberculin jelly has been used in the past as a topical wart immunotherapy. However, because children are not given the BCG vaccine in the United States and the rate of tuberculosis infection is low in the population, the utility of this substance in the United States would be limited.[5] Two previous articles looked at the issue of mumps and *Candida* antigen injections.[6,7] These articles indicated a highly favorable response to therapy. The utility of this type of immunotherapy is that it harnesses the immune system to promote generalized wart immunity. Response rates to mumps antigen tend to be high because it has been the recommendation of the American Academy of Pediatrics to vaccinate against mumps in early childhood. Furthermore, *Candida* exposure is ubiquitous. Although there are rare patients with innate inability to respond to *Candida* antigens through the production of cell-mediated immunity, *Candida* antigen is a potent immunogen. Thus, all the studies that have looked at the topic have shown regression of warts at sites distant to the originally injected warts.[6,7]

As was previously suggested by Dr. Signore in 2001, double-blind placebo controlled trials are necessary to confirm the role of this agent in wart therapy.[8] However, it appears that this is a highly effective option for patients who can tolerate injections. Furthermore, there appear to be fewer local side effects (although there is a high incidence of flulike symptoms that are short-lived) and thus greater tolerability as compared with topical immunotherapy using SADBE[3,9] or DCP.[9] Despite the side effects, SADBE and DCP are easier to administer to children because of the lack of needles. In addition, side effects are generally well tolerated and usually do not require discontinuation of therapy. In addition, these therapies produce a measurable increase in antiviral antibodies and improved nonspecific immunity, making them attractive and scientifically sound.

Candida antigen extends our range of wart therapeutic options. Given that no wart therapy has exceeded 80% clearance rates in clinical trials (even cryotherapy is only 76% effective[10]), the need for multiple alternatives is required. Immune harnessing is an important option for wart therapy. Until we have a vaccine for all human papillomaviruses, immunotherapy is the closest we can get to a cure.

REFERENCES

1. Poland GA, Murray D, Bonilla-Guerrero R. New vaccine development. *Br Med J*. 2002;324:1315-1319.
2. Orlow SJ, Paller AS. Cimetidine therapy for multiple viral warts in children. *J Am Acad Dermatol*. 1993;28:794-796.
3. Silverberg NB, Lim JK, Paller AS, et al. Squaric acid immunotherapy for warts in children. *J Am Acad Dermatol*. 2000;42:803-808.
4. Signore RJ. *Candida albicans* intralesional injection immunotherapy of warts. *Cutis*. 2002;70:185-192.
5. Lahti A, Hannuksela M. Topical immunotherapy with tuberculin jelly for common warts. *Arch Dermatol Res*. 1982;273:153-154.
6. Phillips RC, Ruhl TS, Pfenniger JL, et al. Treatment of warts with *Candida* antigen injection. *Arch Dermatol*. 2000;136:1274-1275.
7. Johnson SM, Roberson PK, Horn TD. Intralesional injection of mumps or *Candida* skin test antigens: a novel immunotherapy for warts. *Arch Dermatol*. 2001;137:451-455.
8. Signore RJ. *Candida* immunotherapy of warts. *Arch Dermatol*. 2001;137:1250-1251.
9. Buckley DA, Du Vivier AWP. The therapeutic use of topical contact sensitizers in benign dermatoses. *Br J Dermatol*. 2001;145:385-405.
10. Bunney MH, Molan MW, Williams DA. An assessment of methods of treating viral warts by comparative treatment trials based on standard design. *Br J Dermatol*. 1976;94:667-679.