tant preliminary data that can be used to power a larger and longer trial to confirm these hypotheses.

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PRACTICE GAPS

Failure to Maximize Patient Adherence Strategies in Clinical Practice

Patient adherence to topical medications averages only 25% to 35%. Sagransky et al found that an additional office visit 1 week after the initial consultation was associated with higher medication adherence in patients with atopic dermatitis. While this difference did not reach statistical significance, and trials with larger sample sizes are necessary to examine the precise impact of this intervention, the pilot study presents an opportunity to deliberate on the failure to maximize adherence strategies in clinical practice and the role of dermatologists and their medical staff in implementing these strategies.

Although increasing evidence suggests that nonadherence is a major contributor to perceived treatment failure, few studies have evaluated whether dermatologists are using methods to increase adherence in real-world practice.[1] Interventions by dermatologists to improve patient adherence can be categorized into nonpharmacologic and pharmacologic approaches. Nonpharmacologic approaches include patient education, reminders, frequent follow-ups, and encouragement of self-monitoring. Pharmacologic interventions include simplification of medication regimens and consideration of patient preferences in choosing formulations for more individualized therapy.

Patient education has been the primary nonpharmacologic approach studied to increase adherence. Patient education will be more effective if it begins with identification of patients' perceptions and misperceptions regarding medications. This type of tailored counseling may help patients overcome misconceptions that contribute to nonadherence. While most dermatologists would agree that good clinical practice includes giving patients clear and detailed instructions on the proper use of medications and their associated adverse effects, short encounter times in most practices make such face-to-face counseling challenging. Therefore, innovative methods for disseminating patient educational materials need to be considered. For example, educational materials for commonly recommended topical agents may be posted on a practice's Web site as either static text-based Web pages or instructional videos. The nonvideo online materials could also be printed and handed to patients during the visit. As a systems solution, electronic medical record systems may be configured to create automated and customizable patient educational materials that are linked to prescription orders and delivered to patients with their prescription. For practices that are primarily paper based, hard-copy handouts are still a time-honored means of con-

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veying educational information, which should be written at an appropriate literacy level to ensure maximum comprehension.

Other nonpharmacologic adherence strategies include empowering support staff to provide face-to-face patient counseling, which will likely lead to increased adherence and save physicians' time. Another strategy is encouraging patients to self-monitor medication adherence. Asking patients to keep a medication diary and bring back medication tubes at each visit may also promote greater adherence.

Strong evidence exists in adherence literature that a complicated medication regimen is associated with lower adherence. To increase adherence, dermatologists need to consider designing regimens with the fewest possible number of medications and the lowest dosing frequency.[2] While medications with combined formulations are often more costly, this increased cost may be justified for selected patients if it significantly improves adherence and prevents unnecessary office visits resulting from nonadherence.

To close this practice gap, dermatologists need to address the issue of medication adherence explicitly with their patients, their medical staff, and themselves. While changes in existing practices may be difficult to implement, increasing patient adherence is a worthwhile effort at the heart of effective therapeutics.

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RESEARCH LETTER

Phase 1 Clinical Trial of Intralesional Injection of *Candida* Antigen for the Treatment of Warts

Warts are benign epidermal tumors caused by human papillomaviruses (HPVs). There are more than 100 distinct HPV types that have been isolated from cutaneous and mucosal lesions, of which the closely related HPV types 2, 27, and 57 predominantly cause common warts.[1]

It is well established that cell-mediated immune response plays a major role in controlling HPV infections.[2] Therefore, treatment techniques such as immunotherapy have been used to activate the immunologic response to HPV. One method of immunotherapy is the intralesional injection of skin test antigens such as *Candida*, mumps, and/or *Trichophyton*. Studies have shown that such therapies resolve not only the treated warts but also distant, untreated warts.[3]

To our knowledge, little work has been done to elucidate the immunologic mechanisms behind skin test antigens immunotherapy. Herein, we report immunologic response data from patients undergoing *Candida* injection immunotherapy for the treatment of warts, measured by an ex vivo interferon γ–enzyme-linked immunospot (IFN-γ ELISPOT) assay.

Methods. The study protocol was approved by the institutional review board of the University of Arkansas for Medical Sciences (UAMS), and the clinicaltrials.gov identifier is NCT00569231. Patients were recruited during the period between February 2007 and May 2009 from the outpatient Dermatology Clinic at UAMS. Informed consent was obtained from all participants.

Eighteen patients, each with at least 2 cutaneous, nongenital, nonfacial warts and no previous *Candida* antigens treatment for warts were enrolled into the study. Each patient received an intralesional injection of 0.3 mL of *Candida* antigen (Candin; Allermed Laboratories, San Diego, California) into their largest wart at the baseline visit and then at each visit every 3 weeks thereafter. The clinical responses and adverse events were assessed.

The sequences of antigens used in the ex vivo IFN-γ ELISPOT assay were chosen from HPV-57 since HPV-2a, -27, and -57 were the most common HPV types detected in the warts of patients previously recruited in our clinics.[3] The peptide sequences that contained HLA class I A2 hot spots and HLA class II DR hot spots and that were similar among HPV-2a, -27, and -57 were chosen using the predictive engines of MULTIPRED[4]: HPV-57 E1-peptide-(231-260 and 251-286), E2-peptide-(188-208), E4-peptide-(10-30), E6-peptide-(17-55), and L1-peptide-(380-412). The IFN-γ ELISPOT assay protocol was performed as previously described,[5] except 300 000 peripheral blood mononuclear cells were presented with 10 μM of each of the HPV-57 peptides, and the incubation period was extended to 40 hours.

Results. Eighteen patients were enrolled, and 11 completed the study (**Table**). Of the 11 patients who completed the study, 9 had complete resolution of their treated warts (82%), 1 had partial resolution (9%), and 1 had no response (9%). Complete resolution of the first distant untreated warts was observed in 6 of 8 patients (75%), while that of the second distant warts were observed in 6 of 6 patients (100%). The median number of injections required for complete resolution was 4. None of the 18 patients experienced vaccine-related adverse events higher than grade 2 (moderate). Typical adverse events were injection site pain and mild erythema.

The IFN-γ ELISPOT assay was performed on only 10 of the 11 patients who completed the study (Table) be-

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