cate that use of indoor tanning, which exposes users to intense levels of UV radiation, and the prevalence of sunburn, a biological indicator of overexposure to UV radiation, have decreased in recent years, particularly among adolescents and young adults. Decreases in indoor tanning and sunburn would be expected to result in decreases in melanoma incidence rates over time. Although primary skin cancer prevention efforts have often focused on children, adolescents, and young adults, the steady increase in melanoma incidence rates among older adults indicates a need for efforts that promote skin cancer preventive behaviors throughout adulthood. Such efforts could focus on groups at high risk, such as outdoor workers and intentional tanners. Ongoing surveillance of melanoma incidence is warranted to monitor progress toward national skin cancer prevention goals and guide prevention strategies.

Dawn M. Holman, MPH
MaryBeth B. Freeman, MPH
Meredith L. Shoemaker, MPH

Author Affiliations: Division of Cancer Prevention and Control, Centers for Disease Control and Prevention, Atlanta, Georgia.

Corresponding Author: Dawn M. Holman, MPH, Division of Cancer Prevention and Control, Centers for Disease Control and Prevention, 4770 Buford Hwy NE, MS F76, Chamblee, GA 30341-3717 (dholman@cdc.gov).

Accepted for Publication: November 14, 2017.

Published Online: January 31, 2018. doi:10.1001/jamadermatol.2017.5541

Author Contributions: Ms Holman had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: All authors.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Holman, Freeman.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: All authors.

Administrative, technical, or material support: Shoemaker.

Study supervision: Holman.

Conflict of Interest Disclosure: None reported.

Funding/Support: This research was supported in part by appointments (Ms Shoemaker and Ms Freeman) to the Research Participation Program at Centers for Disease Control and Prevention administered by the Oak Ridge Institute for Science and Education through an interagency agreement between the US Department of Energy and the Centers for Disease Control and Prevention. Ms Holman is a federal employee, and her work on this article was performed as part of her official duties.

Role of the Funder/Sponsor: The funders/sponsors had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention or the National Institutes of Health.


Variable Response to Naltrexone in Patients With Hailey-Hailey Disease

Hailey-Hailey disease (HHD) is a genetic intraepidermal blistering disorder characterized by chronic macerated erosions in intertriginous areas. The recent report of 2 case series demonstrating the efficacy of low-dose naltrexone in the treatment of HHD represents exciting progress in the management of a disease with limited therapeutic options. Herein we present 3 additional cases of HHD demonstrating varying responses to naltrexone.

Methods | Three patients with biopsy-proven HHD were started on naltrexone based on patient request and followed every 4 to 6 weeks or as needed for physician assessment of clinical response, subjective quality of life, and incidence of adverse effects. This case-report study was granted exemption by the Partners Healthcare institutional review board.

Results | Case 1. A woman in her 30s presented with a 10-year history of HHD. Past treatments included topical steroids and oral antibiotics. The patient was started on naltrexone 4.5 mg nightly, topical clobetasol for flares, and topical tacrolimus for maintenance therapy. After 18 months she experienced 95% clearance of her erosions and ulcerations with relief in pruritus and pain, requiring only minimal amounts of clobetasol.

Case 2. A woman in her 30s with a 15-year history of HHD poorly responsive to topical antibiotics, antifungals, and steroids, was started on naltrexone 12.5 mg nightly, given the ability to quarter the commercially available 50-mg tablets covered by her insurance. The patient demonstrated complete resolution of erosions and ulcerations within 2 months (Figure). However, she stopped treatment owing to concerns that 12.5 mg was higher than dosages discussed on HHD online forums. Three weeks later she experienced a flare in the inframammary and inguinal areas and restarted naltrexone at 4.5 mg. After 1 month, she reported that her erosions were improving but at a slower rate than on the 12.5-mg dose.

Case 3. A woman in her 60s with a 17-year history of HHD resistant to topical, intralesional, intramuscular, and systemic steroids, topical antifungals, and oral antibiotics, was started on naltrexone 50 mg nightly, as she also had brachioradialis pruritus. After 1 month, her HHD had neither improved nor worsened, and she was started on acitretin 10 mg daily to improve disease control. The patient experienced 30% clearance in the extent of disease within 1 month. However, she discontinued naltrexone owing to cost, resulting in a flare 2 weeks later. Naltrexone 4.5 mg was started and acitretin increased to 25 mg daily, but her flare progressed over the next 10 days, requiring methylprednisolone, an oral prednisone taper, and...
intralesional triamcinolone to achieve control. Since then, she has initiated glycopyrrolate 1 mg 3 times per day and naltrexone 4.5 mg and achieved 30% clearance of HHD over the last 3 months. The patient is pleased because no lesions are exudative, eroded, or symptomatic.

Discussion | Online testimonials and recent publications have documented dramatic responses of HHD to naltrexone.\(^2,3\) However, we demonstrate response variability and the possible use of adjunctive agents to achieve a desired effect. Clinicians should carefully manage patient expectations and explain the potential use of naltrexone in a multipronged approach to treatment. When used with topical steroids or acitretin, positive results can be observed with low frequency and dosages of these adjunctive agents, allowing for simplified regimens.

Our cases suggest that the previously published 4.5-mg dose may not be sufficient, and that 12.5-mg to 50-mg doses can be safely attempted for an adequate response. Caution should be taken with immediate cessation of 12.5-mg to 50-mg doses, given evidence of flares following discontinuation. While no adverse effects were noted, we suggest monitoring patients on 12.5-mg to 50-mg doses for adverse effects such as depression, increased pain, and elevated liver function tests. Additional studies are needed to fully characterize optimal dosing regimens of naltrexone for HHD given the variability of response.

Severine Cao, BA
Evelyn Lilly, MD
Steven T. Chen, MD, MPH

Author Affiliations: Harvard Medical School, Boston Massachusetts (Cao, Lilly, Chen); Department of Dermatology, Massachusetts General Hospital, Boston (Lilly, Chen); Department of Internal Medicine, Massachusetts General Hospital, Boston (Chen).

Corresponding Author: Steven T. Chen, MD, MPH, Department of Dermatology, Massachusetts General Hospital, 50 Staniford St, Boston, MA 02114 (stchen@partners.org).

Accepted for Publication: October 18, 2017.

Published Online: January 17, 2018. doi:10.1001/jamadermatol.2017.5463

Author Contributions: Drs Chen and Lilly had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Chen.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Cao.

Critical revision of the manuscript for important intellectual content: Lilly, Chen.

Administrative, technical, or material support: Cao.

Study supervision: Lilly, Chen.

Conflict of Interest Disclosures: None reported.

Additional Contributions: We thank the patients with Hailey-Hailey disease for granting permission to publish this information.


Rituximab as Single Long-term Maintenance Therapy in Patients With Difficult-to-Treat Pemphigus

Pemphigus is a rare, chronic, relapsing, and potentially life-threatening autoimmune bullous dermatosis. European guidelines recommend administration of systemic corticosteroids as a first-line therapy.\(^1\) According to its previously published efficacy as a corticosteroid-sparing agent in refractory disease, rituximab, an anti-CD20 monoclonal antibody, is recommended as a second- or third-line therapy.\(^1,3\) A French randomized clinical trial demonstrated that rituximab is effective and well tolerated as a first-line therapy, enabling a marked decrease in cumulative dose and duration of co-administered corticosteroid.\(^5\)