

Update on Biotin Therapy in Dermatology: Time for a Change

Shari R. Lipner MD PhD

Weill Cornell Medicine, Department of Dermatology, New York, NY

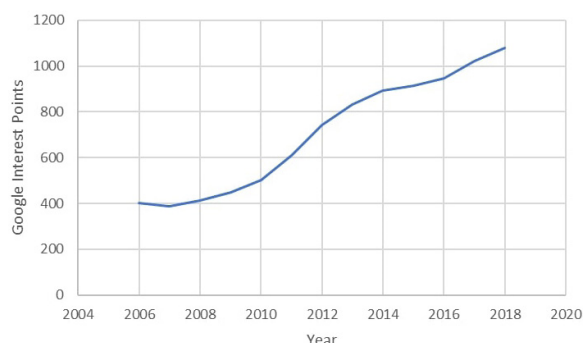
INTRODUCTION

Biotin (vitamin B7 or H) is found in milk, nuts, egg yolks, cereals, supplements, synthesized by intestinal bacteria, and is required for gluconeogenesis, fatty acid synthesis and amino acid catabolism.¹⁻³ Biotin deficiency results in neuromuscular dysfunction, alopecia, and dermatitis in animals and humans.^{4,5,6} Biotin deficiency is rare, but may occur with inborn errors of metabolism (holocarboxylase synthetase and biotinidase deficiencies), parenteral nutrition, malnutrition, antiepileptic therapy, and consumption of large quantities of egg whites, due to avidin binding to biotin and blocking its absorption.⁷ Established daily allowances for biotin are lacking,⁸ but 30 micrograms/day for adults is recommended,⁹ which is easily obtained from diet alone.¹⁰

Several studies have utilized biotin to treat dermatologic conditions, but they are small and without adequate controls.¹¹⁻¹⁷ Biotin, 2.5 mg daily, had a beneficial effect for brittle nails in firmness, thickness, and fragility.¹⁸⁻²¹ Biotin may be helpful for select hair disorders, but only in patients with inherited or acquired biotin deficiencies.^{22,23} Furthermore, in an analysis of 16 biotin products on amazon.com, only 27.2%, 15.03%, and 2.8% of consumers reported benefit for hair, nails, and skin, respectively.²⁴ Biotin has been suggested to alleviate xerosis with isotretinoin treatment for acne, and to modify the lipid profile in seborrheic dermatitis, but has not been formally studied.²¹

Despite its limited benefit, worldwide interest in biotin for treatment of skin, hair and nails has been rising and physician prescribing is prevalent.²⁵⁻²⁸ Between 2006 and 2018, there was a 167% increase in google searches for “biotin” (Figure 1).

FIGURE 1. Plot of Google Trends search term “biotin” by year (2006 to 2018). Google Trends Interest Points are defined by how frequently a given search term is entered into Google’s search engine relative to the site’s total search volume over a given period of time.



In survey-based studies, 66% of 300 United States (US) dermatologists recommended supplements,²⁷ and 60% of Saudi Arabian dermatologists treated hair loss with supplements, including biotin.²⁸

On November 28, 2017, the Food and Drug Administration (FDA) issued a warning that biotin may interfere with laboratory tests, including troponins, thyroid-stimulating and parathyroid hormones.²⁹ These immunoassays rely on biotin-streptavidin technology,^{30,31} with biotin in the blood causing falsely elevated or reduced levels.^{32,33,34-36} This FDA warning was prompted by a report of a myocardial infarction and death due to falsely low troponin levels. The FDA had recommended that physicians ask patients about supplement usage,²⁹ and discontinue biotin for 8 hours for patients taking 10 mg/day,³⁷ 3 days for 100 – 300 mg/day,^{38,39} 7 days for children taking 2 and 15 mg/kg/daily,^{35,40} and informing the laboratory if a diagnostic test was performed while taking biotin.²⁹

What was the impact of this 2017 FDA warning on patient self-prescribing and physician recommendation of biotin? Not much. Google searches from December 1, 2017 to November 30, 2019 increased by 64% and 50%, worldwide and in the US, respectively, compared to the period January 6, 2006 to November 30, 2017.⁴¹ Furthermore, in a survey-based study of dermatology 447 outpatients in June 2018, 34% reported past or current biotin supplementation. Of the patients still taking biotin, 40% were taking it following the 2017 biotin warning, and only 7% knew about the FDA warning. While 55% had self-prescribed, 29% reported the recommendation from a primary care physician or dermatologist.⁴² In a survey-based study of 113 dermatologists, 51% were still prescribing biotin 2 years after the FDA warning.⁴³ While 119 biotin articles were published in the 2 years following the 2017 FDA warning, only 21% cited biotin risks, and only 5% mentioned the FDA warning. Using Altmetric, which measures media attention on scientific research, these biotin articles were not published in high impact journals, and generally received low “media attention scores,” which makes it unlikely that biotin risks and the FDA warning were communicated to physicians and the public.⁴⁴

On November 5, 2019, the FDA updated their 2017 safety communication that biotin supplementation can interfere with laboratory tests, and reported that they continue to receive adverse event reports due to falsely low troponins.⁴⁵ While some lab developers have successfully mitigated the biotin interference in their assays, there are 17 troponin and

many other non-troponin assays that are still subject to this interference.⁴⁵

What can we do to protect our patients from missed diagnoses and subsequent consequences from biotin supplementation? Since the 2017 FDA warning clearly had no effect on patient behavior, it is equally unlikely that the 2019 update will be influential. One approach is to fine diagnostic companies heavily or prohibit use of immunoassays that use biotin-streptavidin technology. Another approach is to use more resources (CME activities, articles in high impact journals, live or online lectures) educating physicians about the lack of evidence for biotin as an effective therapy for medical and dermatologic conditions and laboratory interference. We have a duty to employ current and updated evidence based medicine in treating our patients to give them the most effective and safe therapies.

DISCLOSURES

The author has no relevant conflicts.

REFERENCES

- Zempleni J, Kuroishi T. Biotin. *Adv Nutr*. 2012;3(2):213-4. doi: 10.3945/an.111.001305
- Said HM. Biotin: biochemical, physiological and clinical aspects. *Subcell Biochem*. 2012;56:1-19. doi: 10.1007/978-94-007-2199-9_1
- Mock DM. Biotin: From nutrition to therapeutics. *J Nutr*. 2017 doi: 10.3945/jn.116.238956
- Daft FS, Ashburn LL, Sebrell WH. Biotin deficiency and other changes in rats given sulfanilylguanidine or succinyl sulfathiazole in purified diets. *Science*. 1942;96(2492):321-2. doi: 10.1126/science.96.2492.321
- Bonjour JP. Biotin in man's nutrition and therapy – a review. *Int J Vitam Nutr Res*. 1977;47(2):107-18.
- Swick HM, Kien CL. Biotin deficiency with neurologic and cutaneous manifestations but without organic aciduria. *J Pediatr*. 1983;103(2):265-7.
- Nyhan WL. Inborn errors of biotin metabolism. *Arch Dermatol*. 1987;123(12):1696-98a.
- Higdon J, Drake VJ. An evidence-based approach to vitamins and minerals. In: books. Thieme, 2nd ed., 2012.
- Institute of Medicine (US) Standing Committee on the Scientific Evaluation of Dietary Reference Intakes and Its Panel on Folate OBV, and Choline. Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B6, Folate, Vitamin B12, Pantothenic Acid, Biotin, and Choline. Washington: National Academies Press (US) 1998.
- Zempleni J, Mock DM. Biotin biochemistry and human requirements. *J Nutr Biochem*. 1999;10(3):128-38.
- Likura Y, Odajima Y, Nagakura T, et al. Oral biotin treatment is effective for atopic dermatitis in children with low biotinidase activity. *Acta Paediatr Scand*. 1988;77(5):762-3.
- Lipner SR, Scher RK. Biotin for the treatment of nail disease: what is the evidence? *J Dermatolog Treat*. 2017;1-4. doi: 10.1080/09546634.2017.1395799
- Piraccini C. M. TS, Iorizzo M., Rech G., Tosti A. Triangular worn-down nails: report of 14 cases. *G Ital Dermatol Venereol*. 2005;140(2):161-64.
- Möhrenschlager M, Schmidt T, Ring J, et al. Recalcitrant trachyonychia of childhood – response to daily oral biotin supplementation: report of two cases. *J Dermatolog Treat*. 2000;11(2):113-15.
- Gloster H, Jr., Kindred C. Habit-tic-like and median nail-like dystrophies treated with multivitamins. *J Am Acad Dermatol*. 2005;53(3):543-4. doi: 10.1016/j.jaad.2005.03.045
- Shelley WB, Shelley ED. Uncombable hair syndrome: observations on response to biotin and occurrence in siblings with ectodermal dysplasia. *J Am Acad Dermatol*. 1985;13(1):97-102.
- Boccaletti V, Zendri E, Giordano G, et al. Familial uncombable hair syndrome: ultrastructural hair study and response to biotin. *Pediatr Dermatol*. 2007;24(3):E14-6. doi: 10.1111/j.1525-1470.2007.00385.x
- Colombo VE, Gerber F, Bronhofer M, et al. Treatment of brittle fingernails and onychoschizia with biotin: scanning electron microscopy. *J Am Acad Dermatol*. 1990;23(6 Pt 1):1127-32.
- Floersheim GL. [Treatment of brittle fingernails with biotin]. *Z Hautkr*. 1989;64(1):41-8.
- Hochman LG, Scher RK, Meyerson MS. Brittle nails: response to daily biotin supplementation. *Cutis*. 1993;51(4):303-5.
- Piraccini BM, Berardesca E, Fabbrocini G, et al. Biotin: overview of the treatment of diseases of cutaneous appendages and of hyperseborrhea. *G Ital Dermatol Venereol*. 2019;154(5):557-66. doi: 10.23736/S0392-0488.19.06434-4.
- Patel DP, Swink SM, Castelo-Soccio L. A review of the use of biotin for hair loss. *Skin Appendage Disord*. 2017;3(3):166-69. doi: 10.1159/000462981
- Trueb RM. Serum Biotin Levels in Women Complaining of Hair Loss. *Int J Trichology*. 2016;8(2):73-7. doi: 10.4103/0974-7753.188040
- John JJ, Lipner SR. Consumer perception of biotin supplementation. *JCMS*. 2019;23(6):613-16. doi: 10.1177/1203475419871046
- Soleymani T, Lo Sicco K, Shapiro J. The infatuation with biotin supplementation: is there truth behind its rising popularity? a comparative analysis of clinical efficacy versus social popularity. *J Drugs Dermatol*. 2017;16(5):496-500.
- Callender VD, Belpulsi D. Biotin Alone or a science-driven nutraceutical multi-targeted approach? *J Drugs Dermatol*. 2019;18(9):952-53.
- Dickinson A, Shao A, Boyon N, et al. Use of dietary supplements by cardiologists, dermatologists and orthopedists: report of a survey. *Nutr J*. 2011;10:20. doi: 10.1186/1475-2891-10-20
- Mubki T. Use of vitamins and minerals in the treatment of hair loss: a cross-sectional survey among dermatologists in Saudi Arabia. *JCMS*. 2014;18(6):405-12. doi: 10.2310/7750.2014.14008
- US FDA. Biotin (Vitamin B7): Safety Communication - May Interfere with Lab Tests. 11/28/2017
- Diamandis EP, Christopoulos TK. The biotin-(strept)avidin system: principles and applications in biotechnology. *Clin Chem*. 1991;37(5):625-36.
- Wilchek M, Bayer EA. The avidin-biotin complex in bioanalytical applications. *Anal Biochem*. 1988;171(1):1-32.
- Piketty ML, Polak M, Flechtner I, et al. False biochemical diagnosis of hyperthyroidism in streptavidin-biotin-based immunoassays: the problem of biotin intake and related interferences. *Clin Chem Lab Med*. 2017;55(6):780-88. doi: 10.1515/ccclm-2016-0606
- Li D, Radulescu A, Shrestha RT, et al. Association of biotin ingestion with performance of hormone and nonhormone assays in healthy adults. *JAMA*. 2017;318(12):1150-60. doi: 10.1001/jama.2017.13705
- Sharma A, Baumann NA, Shah P. Biotin-induced biochemical Graves' Disease: A teachable moment. *JAMA Intern Med*. 2017;177(4):571-72. doi: 10.1001/jamainternmed.2016.9295
- Kummer S, Hermesen D, Distelmaier F. Biotin treatment mimicking Graves' disease. *N Engl J Med*. 2016;375(7):704-6. doi: 10.1056/NEJMc1602096
- Elston MS, Sehgal S, Du Toit S, et al. Factitious Graves' disease due to biotin immunoassay interference—a case and review of the literature. *J Clin Endocrinol Metab*. 2016;101(9):3251-5. doi: 10.1210/jc.2016-1971
- Grimsey P, Frey N, Bendig G, Zitzler J, Lorenz O, Kasapic, D, Zaugg CE. Population pharmacokinetics of exogenous biotin and the relationship between biotin serum levels and in vitro immunoassay interference. *Int J of Pharmacokinetics*. 2017;2(4):247-56.
- Minkovsky A, Lee MN, Dowlatshahi M, et al. High-dose biotin treatment for secondary progressive multiple sclerosis may interfere with thyroid assays. *AACE Clin Case Rep*. 2016;2(4):e370-e73. doi: 10.4158/EP161261.CR
- Batista MC, Ferreira CES, Faulhaber ACL, et al. Biotin interference in immunoassays mimicking subclinical Graves' disease and hyperestrogenism: a case series. *Clin Chem Lab Med*. 2017;55(6):e99-e103. doi: 10.1515/ccclm-2016-0628
- Henry JG, Sobki S, Arafat N. Interference by biotin therapy on measurement of TSH and FT4 by enzyme immunoassay on Boehringer Mannheim ES700 analyser. *Ann Clin Biochem*. 1996;33 (Pt 2):162-3. doi: 10.1177/000456329603300214
- Wang Y, Lipner SR. Google trends analysis of public interest in biotin for dermatological conditions following the FDA warning. *Dermatol Ther*. 2020 Jun 26:e13904. doi: 10.1111/dth.13904. Online ahead of print.
- John JJ, Cooley V, Lipner SR. Assessment of biotin supplementation among patients in an outpatient dermatology clinic. *J Am Acad Dermatol*. 2019;81(2):620-21. doi: 10.1016/j.jaad.2018.12.045
- Waqas B, Wu A, Yim E, Lipner SR. A survey-based study of physician practices regarding biotin supplementation. *J Dermatolog Treat*. 2020 May 25:1-2. doi: 10.1080/09546634.2020.1770178. Online ahead of print.
- Chang MJ, Lipner SR. Altmeter analysis of biotin in scholarly outputs following the biotin FDA warning. *J Am Acad Dermatol*. 2019 doi: 10.1016/j.jaad.2019.11.035
- US FDA UPDATE: The FDA Warns that Biotin May Interfere with Lab Tests: FDA Safety Communication. 11/5/2019

AUTHOR CORRESPONDENCE

Shari R. Lipner MD PhD

E-mail:..... shl9032@med.cornell.edu