# EFFECTS OF INTERNET QUACKERY

# ARGYRIA IN THE SILVER STATE

Laura E. Cohen, MD, Richard Spurlock, BSBA, Anthony Salem, MD, and Eduardo Mercado, PAC-MPAS

Within a two-week period, two patients presented to this Nevada VA medical center with what has been considered a rare disorder.

Is this the start of a dangerous trend?

rgyria, from the Greek word argyos meaning silver, is a rare, generalized, blue-gray discoloration of the skin, hair, nails, and mucous membranes caused by local or systemic absorption of silver compounds. Argyria was much more common in the early 20th century than it is today due to medications containing silver and silver in the workplace. Unfortunately, its incidence appears to be on the rise, a phenomenon that may be attributable to internet advertising.

In this article, we report on two patients who, within two weeks of

**Dr. Cohen** is the chief of the dermatology section at the VA Southern Nevada Healthcare System (VASNHS), Las Vegas, NV. **Mr. Spurlock** is a fourth year medical student at the University of Miami School of Medicine, Miami, FL. At the time of this writing, **Dr. Salem** was the chief of staff and **Mr. Mercado** was a physician assistant in the dermatology section, both at the VASNHS. Currently, Dr. Salem is the chief of hospital at Mike O'Callaghan Federal Hospital, Nellis Air Force Base, NV, and Mr. Mercado is a physician assistant in private practice in New Port Richey, FL.

each other, presented to the VA Southern Nevada Healthcare System in Las Vegas, NV with argyria. Both were elderly men whose internet searches had prompted them to ingest silver as a colloidal solution in hopes of obtaining antibiotic benefit. These cases are remarkable for several reasons: the unusual histories, the harmful toxin involved, and the role of the internet in promoting dangerous anecdotal information.

## TWO UNUSUAL REFERRALS

A 63-year-old man was referred to our facility's dermatology section by his primary care physician to be evaluated for facial discoloration of unknown duration. The patient had a history of hypertension, coronary artery disease, gout, hyperlipidemia, and thrombocytopenia. Upon specific questioning, the patient recounted that, for at least one year on a daily basis, he had been ingesting a solution made of colloidal silver, which he believed

would act as a "natural antibiotic." He indicated that he had found the information about colloidal silver in an internet advertisement, and he had made his own solution by immersing silver electric probes in water.

Less than two weeks later, a 76-year-old man was referred to our dermatology section by his primary care physician to be evaluated for a "silvery tan" on his face. He had a history of tremors treated with primidone. He too acknowledged using a colloidal silver solution for antibiotic benefit on an intermittent basis for about one year. This patient, like the previous one, had learned about the remedy through internet marketing.

The differential diagnosis for argyria includes: exposure to particular heavy metals (mercury, bismuth, arsenic, gold, and lead), adverse effects of certain medications (phenothiazines, antimalarials, amiodarone, minocycline), ochronosis, hemochromatosis,

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polycythemia vera, Addison's disease, diffuse metastatic melanoma, and cyanosis.<sup>2,3</sup> Nevertheless, since both of these patients presented with the classic silver-violet discoloration of the face, neck, lower lip, and nail bed (including the lunula), and with a silvery sheen to the hair, we suspected argyria immediately in both cases and confirmed this by histopathologic examination.

### **CHARACTERISTIC FINDINGS**

We observed microscopic fine silver granules in the basement membrane zone surrounding the sweat glands (Figure 1), in the arrectores pilorum and connective tissue sheath surrounding the hair follicles (Figure 2), and in sebaceous glands. Dark field microscopy also revealed fine silver granules in the dermis of both patients (Figures 3 and 4). In previous reports of argyria, silver deposits were not found in the epidermis.<sup>4</sup> Our cases were consistent with these findings.

Both patients demonstrated diffuse hyperpigmentation of the skin manifested primarily in sunexposed areas of the body—a phenomenon that is characteristic of argyria and has been described as an "intradermal photograph." The silver is deposited systemically throughout the patient's visceral and mucosal tissues as well.6 The reason for the marked photodistribution is believed to be twofold. First, proteins in the skin complex with silver particles, which are reduced by light in a process similar to that of photo imaging. Second, the exposure of the silver particles to light stimulates melanogenesis, giving the skin a blue-gray appearance.<sup>7</sup> This can be a very significant, cosmetic, adverse effect—especially since the discoloration tends to be irreversible.

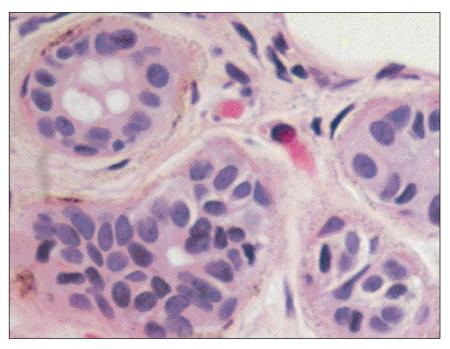


Figure 1. Photomicrograph demonstrating fine silver granules in the basement membrane zone surrounding the sweat glands of our first patient.

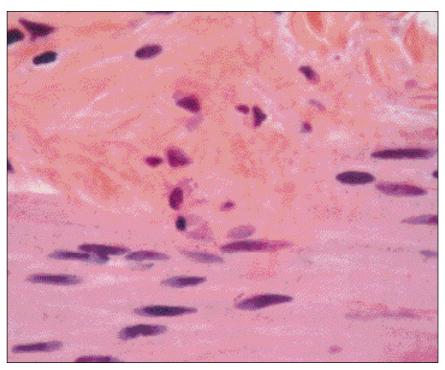


Figure 2. Photomicrograph demonstrating fine silver granules in the arrectores pilorum and connective tissue sheath around the hair follicles of our first patient.

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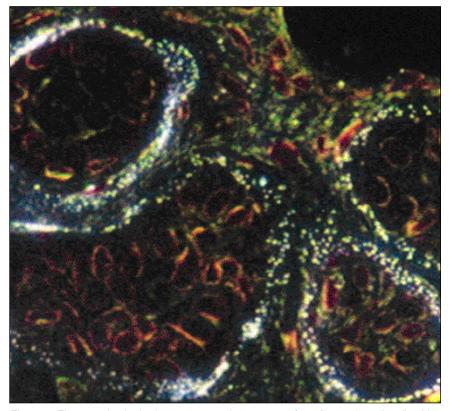


Figure 3. The granules in the basement membrane zone of our first patient visualized by dark field microscopy.

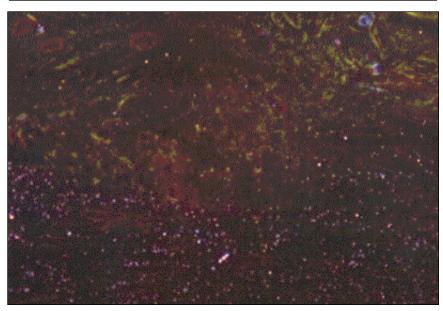


Figure 4. The granules in the arrectores pilorum and connective tissue sheath around the hair follicles of our first patient visualized by dark field microscopy.

#### **SNAKE OIL ON THE WEB**

Our first patient brought in the device that he purchased through the internet to make his colloidal silver (Figure 5). This machine works by generating an electric current through 99.9% silver electrodes to create a suspension of silver in water. The length of time the current flows through the solution determines the concentration of silver.

There are a great number of internet sites that sell colloidal generators and promote the use of colloidal silver as a treatment for a variety of diseases. Many such web sites make outrageous claims about colloidal silver (Table). Some of these web sites acknowledge that ingesting silver can cause argyria, but also maintain that "this condition has never been known to occur from silver in the colloidal state." Unfortunately, as our patients and others have demonstrated, this isn't the case.

The shining accolades bestowed on colloidal silver are tarnished by the cosmetic consequences faced by its victims. Newman and Kolecki reported on a patient who presented with grayish discoloration of her skin after ingesting one fourth of a cup of colloidal silver three times a day for eight months. The patient learned about colloidal silver from web sites that touted it "as a natural alternative to antibiotics." <sup>10</sup>

And there's little evidence of its benefit. Spratt and colleagues tested the antimicrobial efficacy of four irrigants on five species of bacteria (Provetella intermedia, Peptostreptococcus micros, Streptococcus intermedius, Fusobacterium nucleatum, and Enterococcus faecalis). 11 One of the agents tested was colloidal silver

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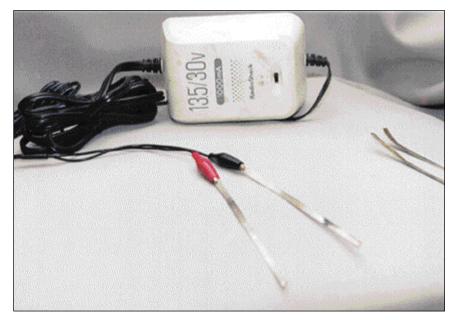


Figure 5. The device purchased over the internet by our first patient to make colloidal silver at home.

Table. Unsubstantiated, misleading claims commonly made about colloidal silver<sup>8</sup>

- "Can kill all disease causing bacteria, viruses, and fungi within six minutes of contact"
- "Has no harmful side effects"
- "Can be used as an antibiotic for all the acquired diseases of active AIDS"
- "Is effective with more than 650 different bacteria and virus types"
- "Has been used successfully against diseases including AIDS, cholera, diabetes, leprosy, leukemia, lupus, skin cancer, syphilis, and whooping cough"

5 ppm. The authors concluded that colloidal silver was largely ineffective as an antimicrobial agent.

# ADVERSE EFFECTS: NOT JUST COSMETIC

The risks of silver ingestion have been well documented—and they're not all cosmetic. Fung and Bowen reported that the average amount of elemental silver required to cause argyria was 3.8 g. 12 Argyria is by far the most common adverse effect of chronic silver ingestion, but there are others. Silver accumulates in tissues throughout the body, including in the central nervous system. It was once thought that silver did not cross the blood-brain barrier, but according to Rungby, it does. 13

Rungby's experiments with mice showed that the red nucleus, the brain stem motor nuclei, and the deep cerebellar nuclei are the areas in which silver accumulation is greatest, though smaller amounts of silver are deposited throughout the brain. This is consistent with a report by Westhofen and Schafer in which a 55-year-old woman with generalized argyria developed progressive taste and smell disorders, vertigo, and hypesthesia. <sup>14</sup> It was estimated that she had ingested 124 g of silver over a period of nine years. The peripheral and central nervous system disturbances she experienced were attributed to the deposition of silver in the corresponding histologic structures.

### **REGULATION AND LACK THEREOF**

The well documented adverse effects of colloidal silver far outweigh any alleged benefits derived from the product. In September 1999, the FDA recognized the hazards of colloidal silver, and made a final ruling on over-the-counter (OTC) drug products containing colloidal silver or silver salts, stating that such products generally are not recognized as safe and effective for internal or external use and are misbranded. The FDA issued this rule in response to the numerous silver-based products being marketed as treatment for serious diseases with no credible. supportive scientific basis. 15 Although this ruling stopped the sale of colloidal silver in the form of OTC drug products, colloidal silver preparations continue to be sold legally under the Dietary Supplement Health and Education Act (DSHEA), provided that product labeling includes the following statement: "This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease."<sup>15</sup>

The internet appears to be a venue of choice for colloidal silver manufacturers. There they prey upon uninformed people, who are

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desperate to find cures for a number of diseases.

The internet is a very powerful tool for marketing dietary supplements, as has been observed by Drazen in a recent article regarding the marketing of human growth hormone.<sup>16</sup> In advertising this product, or so-called "human growth hormone releasers," readers are referred to an article on the web site of the New England Journal of Medicine, entitled "Effects of human growth hormone in men over 60 years old,"17 which was published in 1990. The fact that this article receives about 52 times the number of "hits" that other 1990 articles receive underscores the fact that consumers are being influenced by the marketing of human growth hormone manufacturers. Although the results of the study "were not sufficient to serve as a basis for treatment recommendations,"16 the promoters neglect to mention that fact. Unfairly presenting pieces of scientific information is a ploy commonly used in the marketing of dietary supplements.

#### A DANGEROUS TREND

It is clear that argyria is a major adverse effect of colloidal silver ingestion. The benefits, if any, have not been substantiated by scientific research despite claims made by unscrupulous internet merchants. Even if further investigation demonstrates that colloidal silver has beneficial effects, the public needs to be educated about the serious adverse effects of silver ingestion, and federal legislation may need to be enacted to stop the sale of products containing silver.

If the promotion and sale of silver products continues unchecked over the internet, argyria will no longer be a rare condition, but soon will become commonplace.

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#### REFERENCES

- Plack W, Bellizzi R. Generalized argyria secondary to chewing photographic film. Oral Surg Oral Med Oral Path. 1980;49:504–506.
- Rubegni P, de Aloe G, Maritati E, Mondillo S. Photo quiz. Blue-gray centrofacial hyperpigmentation. Am Fam Physician. 2001;63:1409–1410.
- Tanner LS, Gross DJ. Generalized argyria. Cutis. 1990;45:237–239.
- Sue YM, Lee JY, Wang MC, Lin TK, Sung JM, Huang JJ. Generalized argyria in two chronic hemodialysis patients. Am J Kidney Dis. 2001;37: 1048–1051.
- Shelley WB, Shelley ED, Burmeister V. Argyria: The intradermal "photograph," a manifestation of passive photosensitivity. J Am Acad Dermatol. 1987;16(1 pt 2):211–217.
- Gulbranson SH, Hud JA, Hansen RC. Argyria following the use of dietary supplements containing colloidal silver protein. Cutis. 2000;66:373–374.
- Padlewska KK, Schwartz RA. Argyria. eMedicine web site. October 29, 2003. Available at: www.emedicine.com/derm/topic595.htm. Accessed March 11, 2004.
- Barrett S. Colloidal silver: Risk without benefit. Quackwatch web site. February 20, 2004. Available at: www.quackwatch.org/01quackeryrelated topics/phonyads/silverad.html. Accessed March 11, 2004.
- Robey M. What is colloidal silver? Colloidal Silver Discovery Center web site. 1999. Available at: www.colloidal-silver.com/whatiscsinfo.htm. Accessed March 11, 2004.
- Newman M, Kolecki P. Argyria in the ED. Am J *Emerg Med.* 2001;19:525–526.
- Spratt DA, Pratten J, Wilson M, Gulabivala K. An in vitro evaluation of the antimicrobial efficacy of irrigants on biofilms of root canal isolates. *Int Endod J.* 2001;34:300–307.

- Fung MC, Bowen DL. Silver products for medical indications: Risk-benefit assessment. J Toxicol Clin Toxicol. 1996;34:119–126.
- Rungby J. An experimental study on silver in the nervous system and on aspects of its general cellular toxicity. Dan Med Bull. 1990;37:442–449.
- Westhofen M, Schafer H. Generalized argyrosis in man: Neurotological, ultrastructural and X-ray microanalytical findings. Arch Otorhinolaryngol. 1986;243:260–264.
- Dotzel MM. Food and Drug Administration final ruling on over-the-counter drug products containing colloidal silver ingredients or silver salts. 64 Federal Register 44653 (1999) (codified at 21 CFR §301).
- Drazen JM. Inappropriate advertising of dietary supplements. N Engl J Med. 2003;348:777–778.
- Rudman D, Feller AG, Nagraj HS, et al. Effects of human growth hormone in men over 60 years old. N Engl J Med. 1990;323:1–6.

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