

What Is Your Diagnosis?



A 66-year-old woman presented to the emergency department with chest pain and dyspnea. Her skin was gray in color, particularly on the face and arms. The patient had a history of atrial fibrillation, but because of her aversion to Western medicine, she had not seen a physician in more than a year and had discontinued all medications, except for herbal and dietary supplements. She was taking more than 50 supplements daily including multiple vitamins, large quantities of carrot juice, *N*-acetylcysteine, and algae. She reported 1 year of intolerable abdominal pain that occurred 1 to 2 years prior to presentation, which she attempted to treat by consuming 1 qt of colloidal silver water daily; the abdominal pain had resolved by the time she presented to us and she had not consumed the colloidal silver water for at least 1 year prior to presentation. An electrocardiogram confirmed atrial fibrillation contributing to her presenting symptoms, which dissipated once appropriate medication was initiated.

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The authors report no conflict of interest.

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The Diagnosis: Argyria

The patient had consumed 1 qt of colloidal silver water daily for 1 year to treat abdominal pain because she was told by a homeopathic practitioner that it would cure any cancer. On clinical examination, her skin was gray in color, particularly on the face and arms (Figures 1 and 2). A skin biopsy revealed fine black granules in the lamina propria of the eccrine glands (Figure 3) and dark-field illumination also demonstrated reflective granules outlining the eccrine glands (Figure 4). These findings confirmed the suspected diagnosis of argyria.

Argyria is characterized by blue-gray or slate-colored pigmentation secondary to the presence of silver in the skin. The abnormal pigmentation can be localized or widespread, and it is most noticeable on sun-exposed skin, conjunctiva, sclera, mucous membranes, and nails, with sparing of the skin folds. The binding of silver to proteins is enhanced by exposure to light, and the presence of silver in cutaneous tissue is thought to stimulate melanin production, which explains the photoaccentuation.¹⁻³ The smallest amount of silver reported to produce generalized



Figure 1. Gray discoloration of the skin on the face of a 66-year-old woman who presented to the emergency department with chest pain and dyspnea.



Figure 2. The hand of an unaffected individual (left) compared to a patient with argyria (right).

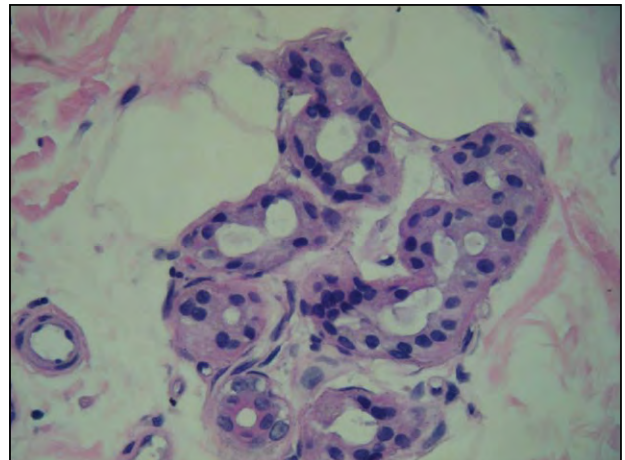


Figure 3. Histopathologic examination revealed fine black granules in the lamina propria of the eccrine glands (H&E, original magnification $\times 40$).

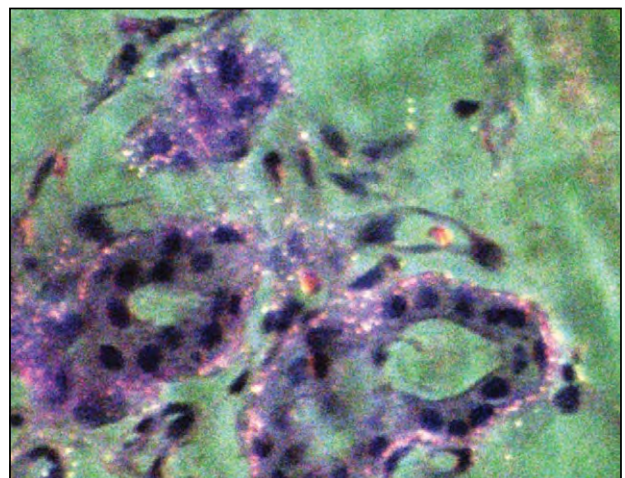


Figure 4. Dark-field illumination also demonstrated reflective granules outlining the eccrine glands (original magnification $\times 40$).

argyria is 4 to 5 g.⁴ Although argyria is a benign condition, high doses of silver can cause adverse effects, including death.⁵

Systemic argyria often is caused by application or ingestion of medications⁶ containing silver, such as nasal drops or eyedrops, topical medications, and oral tonics. Over-the-counter supplements are not regulated by the US Food and Drug Administration, and advertising can be misleading.⁷ Occupation-related exposure to silver is decreasing, though cases related to the increasing popularity of alternative medicine remain a concern.

The differential diagnosis for blue-gray or hyperpigmented skin includes hemochromatosis; alkaptonuria; Addison disease; melanoma; and exposure to heavy metals³ and medications such as amiodarone hydrochloride, bleomycin sulfate, chlorpromazine, imipramine hydrochloride, and minocycline.

Our case underscores the importance of obtaining a complete drug history for patients presenting with argyria, including over-the-counter medications and supplements. Medical history also is important, as the pigment changes may not appear for months to years after exposure.⁸ Our patient's medication history was especially important, as her gray skin color could easily have been mistaken from taking amiodarone for treatment of atrial fibrillation and cyanosis, which also could have caused her chest pain and dyspnea. Unlike cyanosis, argyria does not blanch with pressure.⁸

After argyria is diagnosed, it is important to immediately discontinue silver intake, as many patients experience extreme emotional distress from their pigmentation problems, and therapy for argyria is limited. Hydroquinone cream 5% may decrease the

number of silver granules in the upper dermis and sweat glands, but studies are limited. One report of treatment with a Q-switched Nd:YAG 1064-nm laser showed promising results.⁹ Sun protection also should be emphasized because of accentuation in sun-exposed areas.

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