Contact Dermatitis is an inflammatory skin reaction involving the epidermis and dermis that is caused by exposure to allergenic or irritating substances in the environment. The acute form is characterized by erythema, edema, vesiculation, and pruritus, while the chronic form may exhibit xerosis, lichenification, and hyperkeratosis. Josef Jadassohn, the German dermatologist who initially described contact dermatitis due to mercury in 1895 is considered the “father” of contact dermatitis.1

There are two main types of contact dermatitis: irritant and allergic. Irritant contact dermatitis is the more common of the two. Any agent that disrupts the epidermal skin barrier can provoke an irritant contact dermati-
tis, which can arise from continuous exposure to moisture (eg, frequent hand washing), drainage onto peristomal or periwound skin, or in the diaper area from incontinence. Other causes are chemicals, including soaps, detergents, acids, alkalis, coal tar and other industrial solvents, and some plants. Acute irritant reactions are caused by direct cytotoxic damage to keratinocytes, while chronic reactions usually result from repeated exposure to agents that cause slow damage to cell membranes, disrupting the skin barrier. No one is immune from the risk of developing an irritant contact dermatitis, but each individual’s ability to withstand irritants will vary.2–4

Allergic contact dermatitis is a classic Type IV hypersensitivity reaction. It is characterized by an inflammatory reaction following the skin’s absorption of an antigen, and recruitment of previously sensitized antigen-specific T cells into the skin. Contact antigens are primarily small molecules with a molecular weight less than 500 Daltons. Their small size allows them to penetrate the stratum corneum of the epidermis. Following skin entry, the antigens are taken up and processed by Langerhans cells in the skin. The Langerhans cells then migrate to regional lymph nodes where they present the processed antigen to T lymphocytes. T cells that recognize the antigen then undergo clonal expansion and then migrate back to the epidermis—the sensitization phase.2–4 When sensitized patients are later re-exposed to the same antigen, the antigen bearing Langerhans cells interact with antigen-specific T cells already present in the skin. These T cells then become activated and release inflammatory mediators, which causes an allergic contact dermatitis within 24 hours.2–5 The array of contact allergens is diverse; among the most common are nickel sulfate, neomycin sulfate, balsam of Peru, fragrances, thimerosal, sodium gold thiosulfate, formaldehyde, quaternium-15, neomycin sulfate, balsam of Peru, fragrances, thimerosal, and cancermedicaments, and fragrances.8 Furthermore, wounds are often covered with occlusive dressings, which can further exacerbate these reactions on compromised skin.9 It is essential to consider contact dermatitis in any patient with a wound that fails to respond to therapy or in patients who have physical exam findings suggestive of contact dermatitis.

Silver
Silver is a naturally occurring mineral that has been used extensively throughout history. Some of its favorable properties include a bright metallic luster, ductility, and easy malleability. Silver has had a wide variety of uses in healthcare settings. Metallic silver has been used in surgical prosthesis, surgical splints, and fungicides, while soluble silver compounds have been used in treating mental illness, epilepsy, nicotine addiction, gastroenteritis, and infectious diseases such as gonorrhea and syphilis. Due to its broad spectrum of uses, there are many situations where people may be exposed to silver (eg, ingestion, inhalation of dust or fumes, acupuncture needles, catheters, dental amalgams, or skin contact via topical medicaments or jewelry).10

Silver in Wound Care
Silver compounds are widely used in wound care for their antimicrobial properties. Silver ions are bactericidal, acting on the cell membranes of bacteria. Silver ions are released from silver dressings in a controlled, slow manner. Silver dressings help to facilitate control of bacteria in the wound bed; they prevent bacterial contamination and may control antibiotic resistant bacteria.11 However, laboratory studies have shown that silver can be cytotoxic to keratinocytes and fibroblasts in cell culture.12 Currently, a plethora of agents that contain silver are available. Examples of silver salts include silver nitrate, silver sulfadiazine, silver sodium carboxymethylcellulose dressing (Aquadress® Ag, Convatec, Skillman, NJ), silver coated foam (Contreet Foam® , Coloplast, Humlebaek, Denmark), and silver combined with hydrocolloid (Contreet-HC®, Coloplast). Adsorbed silver comes in the form of silver charcoal (Actisorb™, Systagenix,
Adverse Cutaneous Effects of Silver

Silver products are generally well tolerated, but there are some known side effects. One well-described complication of silver products is argyria. Argyria is a blue to slate gray discoloration of the skin that results from the deposition of silver granules in the basement membrane and the membrana propria of eccrine glands. These findings are highlighted by dark-field microscopy. Argyria may occur in both systemic and localized forms. Systemic argyria may occur when there are elevated serum silver levels with subsequent deposition of silver, primarily in the tissues of sun-exposed skin. Localized cutaneous argyria can result from direct skin absorption of topical silver. Fisher et al. described a case of argyria localized to a scar following the use of silver sulfadiazine cream. Although there is no effective treatment for argyria, the discoloration may fade somewhat over time.

Case Reports of Contact Dermatitis Secondary to Silver

The literature reveals that silver has also been implicated as the causative agent in contact dermatitis, although it is generally thought to be a rare occurrence.

In 1948, Gaul and Underwood reported the case of a 26-year-old man who presented for the evaluation of dermatitis involving his feet. The patient underwent patch testing and the sites were circled with 10% silver nitrate. Within one day, the patient developed erythema, edema, and vesiculation at the site of silver nitrate application. Confirmatory patch testing with silver compounds resulted in positive reactions to 2-week-old 10% silver nitrate, silver foil, and argyrols (silver protein antimicrobial). However, there was no reaction to freshly prepared 10% silver nitrate. It was thought that this patient reacted to ionizable silver, considering that he only reacted to the aged solution, which would have had a chance to decompose into small amounts of colloidal silver, silver nitrate, and nitric acid following exposure to light and air. Further history revealed that this patient had sensitized himself to silver by applying silver nitrate solution to his foot dermatitis prior to presentation, which had caused the dermatitis to worsen.

Another report by Bjornberg described how a patch test skin marker containing fuchsin-silver nitrate could cause irritant contact dermatitis. Bjornberg observed that this reaction only occurred when older bottles of the solution were used and attributed this finding to concentration of the solution over time by evaporation. Patch testing with the individual components of the solution did not produce any skin reactions.

Ozkaya recently reported another case of contact dermatitis from silver nitrate in a patch test marker. The patient was a 42-year-old man who underwent patch testing to evaluate his hand eczema. The test sites were marked using the Chemotechnique skin marker (Chemotechnique Diagnostics, Vellinge, Sweden). The following day erythema, infiltration, and papules developed along the marked lines. The Chemotechnique skin marker ink is composed of 1% methyrosanilin, 10% silver nitrate, and denatured ethanol/aqua in equal parts to 100%. Three months later, a second patch test was placed with the individual components of the skin marker. Results showed a (+++) reaction to silver nitrate. Interestingly, the patient had a history of a generalized dermatitis that developed after application of topical 1% silver sulfadiazine cream (Silverdin®, Deva, Istanbul, Turkey) 5 years previously when he used it to treat a thermal burn injury. A repeat application of the Silverdin cream was positive for a contact reaction, but they were unable to test the individual ingredients to confirm that the allergy was to the silver component.

Gaul later performed a study to determine the incidence of sensitivity to metals. In this study, 100 patients underwent patch testing with metal disks and 1% metal salt solutions. One case of silver sensitivity was identified in a 55-year-old man who was a postmaster and had chronic hand dermatitis. The patient reacted to pure silver, developing an erythematous rash that later became dry and scaly. He also reacted to silver nitrate with the formation of vesicles that evolved into a scaly dermatitis. The patient’s job required him to handle coins. The distribution of his dermatitis corresponded to contact with these coins, which likely contained silver alloys.

Another case report by Marks described a 33-year-old woman who developed a papular eruption under her wristwatch strap. The woman worked as a radiographer processing x-ray films. The localized rash was present under the wristwatch strap, but not under the watch portion, although both parts were composed of gold. Patch testing resulted in a 3+ reaction to 1% silver chloride complexed with sodium thiosulphate, a 1+ reaction to 1% silver nitrate, and a 2+ reaction to used fixing fluid that was taken from the tank. However, it is important to note that the patch testing results from wristwatch filings and fix-
ing fluid components were negative. This indicates that the patient had an allergic contact dermatitis to ionic silver, secondary to her watchstrap being contaminated with silver particles from her x-ray processing.

Catsakis et al reported the case of a 52-year-old woman with a multiple year history of chronic periodontitis. The patient had multiple old silver amalgam restorations present. Once the silver amalgams were replaced with gold castings, her periodontitis resolved. A patch test with 2% silver nitrate resulted in substantial inflammation with blister formation and subsequent postinflammatory hyperpigmentation and scarring. Further inquiry revealed that the patient had a history of developing a rash and swelling after wearing silver jewelry.

Heyl reported the case of a 23-year-old man who was a refinery clerk and had developed an erythematous papulovesicular rash on his forearms, face, and neck. The patient's job duties included weighing various powdered precious metal salts. Patch testing revealed a 3+ reaction to a 1% aqueous solution of “silver coat,” which is a powder with silver cyanide plus small amounts of sodium carbonate, sodium cyanide, and sodium nitrate. The patient's rash cleared while he was absent from work.

White and Rycroft investigated a series of cases of dermatitis affecting workers from a factory manufacturing silver fulminate explosive snaps. Over time, many employees developed a pruritic skin eruption involving the hands, arms, neck, and face. Stomatitis was also common. Interestingly, this reaction was often transient. In this study, ten employees who had been exposed to silver fulminate underwent patch testing, seven of which had a history of the rash. Four of 7 patients with a history of dermatitis had a positive reaction to 1% silver fulminate, as well as 1 of 3 patients without history of rash, and 12 of 34 controls. There were no reactions to silver nitrate. Therefore, in light of reactions to both sensitized employees and unsensitized controls, it was thought that silver fulminate likely induced both an irritant and allergic contact dermatitis.

Fraser-Moodie reported a case of a 43-year-old woman who was treated with silver sulphadiazine for a superficial burn wound. The burn wound progressively worsened with this regimen. Eventually, the medication was changed and she gradually improved. Patch testing revealed that the patient had a noticeably positive reaction to silver sulphadiazine. When the components of the cream were tested individually, she had a strongly positive reaction to both the cetyl alcohol base and silver nitrate, but not to the sulphacetamide sodium. Further history revealed that the patient developed skin erythema and pruritus following exposure to topical metals, including silver and gold. This patient practiced avoidance of these metals prior to reacting to silver sulphadiazine. For instance, she wore a plastic wedding ring and avoided wearing other metal jewelry, she wore gloves when touching metal handles, and she taped over the metal on her underwire bra.

Agarwal and Gawkrodger described a 66-year-old man with a 30-year history of dermatitis affecting his hands, forearms, and legs. Due to his profession as a jeweler, he was exposed to metal dust and semiprecious stones. Patch tests for silver nitrate (0.5% aqueous), colophonium (20% petrolatum), and fragrance mix were all positive. Patch testing for other metal salts were negative. His dermatitis resolved with the avoidance of silver and colophonium.

Finally, a study by Jankicevic et al showed that silver nitrate is a common contact allergen in patients with chronic venous leg ulcers in Serbia. This prospective study evaluated 75 patients with contact dermatitis and venous leg ulcers as well as 82 patients with contact dermatitis without ulcers. Subjects were patch tested with 43 substances. They found that 12% of patients with a leg ulcer had a positive reaction to 5% silver nitrate, whereas only 3.6% of patients without ulcers were allergic to 5% silver nitrate.

**Conclusion**

Contact dermatitis is a common skin reaction, and it is important to determine the causative agent. Silver dermatitis has been infrequently reported in the literature. In the handful of cases that have been reported, five of them were related to occupational exposure to silver compounds. Interestingly, several of the patients with proven contact dermatitis to silver had a history of skin reactions and even metal avoidance. This being said, it may not be possible to perform accurate patch testing for silver. Elemental silver is often combined with other elements to form an alloy, in order to enhance its durability and strength. A person's reaction to a silver compound may be due to other components of the alloy, rather than the elemental silver.

Although silver products are widely used in wound care for their antimicrobial properties, contact dermatitis due to silver in these agents has only been confirmed once thus far. It is possible that allergy to silver contained in wound care dressings and medicaments exists, but is simply missed because silver is not considered as a
potential allergen. The routine use of patch testing for silver allergy in patients with contact dermatitis would perhaps lead to an increase in the reported cases. Again, this can be difficult to confirm with patch testing. It is important to remember that silver wound products have many other ingredients in addition to the silver. The clinician must consider that a reaction to the silver-containing product may be due to one of the other ingredients, and not necessarily to the silver.

In any patient that has a wound that fails to respond to therapy, it is essential to consider the diagnosis of contact dermatitis. Each of the individual components of wound dressings and topical agents being used in the care of the patient needs to be considered as the potential causative factor. Although silver-containing products should be equally considered, the relative scarcity of reported cases of silver allergy make this a less likely causative allergen.

References