

DRUGS AND CHEMICALS ASSOCIATED WITH HYPERPIGMENTATION OR DISCOLORATION

Drug or chemical	Clinical features	Histopathology/comment
HEAVY METALS		
Arsenic	<ul style="list-style-type: none"> • Areas of bronze hyperpigmentation ± superimposed “raindrops” of lightly pigmented skin; favors axillae, groin, palms, soles, nipples and pressure points • Dyspigmentation appears 1–20 years after arsenic exposure, with a strong dose-response relationship • Palmoplantar keratoses and squamous cell carcinoma typically develop after dyspigmentation (see Chs 58 & 88) 	<ul style="list-style-type: none"> • Dermal and epidermal deposition of arsenic • Increased epidermal melanin synthesis
Bismuth	<ul style="list-style-type: none"> • Generalized blue–gray discoloration of the face, neck and dorsal hands • Oral mucosa and gingivae may be involved 	<ul style="list-style-type: none"> • Bismuth granules in the papillary and reticular dermis
Gold (chrysiasis)	<ul style="list-style-type: none"> • Permanent blue–gray discoloration in sun-exposed areas, mostly around the eyes 	<ul style="list-style-type: none"> • Gold particles within lysosomes in dermal macrophages, especially in perivascular and perieccrine areas
Iron	<ul style="list-style-type: none"> • Permanent brown pigment at injection sites or in areas of application of ferric subsulfate (Monsel's) solution as a hemostatic agent • Dermal hemosiderin deposits (due to lysis of extravasated red blood cells and release of their iron stores) are commonly observed in the setting of venous hypertension, in pigmented purpuric dermatoses and as a side effect of sclerotherapy of superficial veins 	<ul style="list-style-type: none"> • Pigment coats collagen fibers and is deposited in dermal macrophages
Lead	<ul style="list-style-type: none"> • “Lead line” in gingival margin • Nail discoloration 	<ul style="list-style-type: none"> • Lead line is due to subepithelial deposition of lead granules
Mercury	<ul style="list-style-type: none"> • Slate-gray discoloration, particularly in skin folds 	<ul style="list-style-type: none"> • Brown–black granules free in dermis, in association with elastic fibers and within macrophages
Silver (argyria)	<ul style="list-style-type: none"> • Diffuse slate-gray discoloration (Fig. 67.5A), increased in sun-exposed areas; occurs in settings of occupational exposure, alternative medications or systemic absorption from use of silver sulfadiazine on extensive burns/wounds • The nail unit (diffuse or localized to the lunulae) and sclerae may also be affected • Sites of topical application (e.g. of silver sulfadiazine to burns or ulcers) 	<ul style="list-style-type: none"> • Silver granules in the basement membrane and the membrana propria of eccrine glands; highlighted by darkfield illumination (Fig. 67.5B)

TOXIC AND HEAVY METALS AND THEIR CUTANEOUS IMPACT					
Metal	Form	Cutaneous health hazards	Treatment and protection	IDLH*	Cancer risk
Aluminum	Alum, sulfates	Irritant contact dermatitis	Wash off	–	–
Antimony	Metal	Irritant contact dermatitis	Soap wash immediately	50 mg/m ³	–
Arsenic	Inorganic	(see Table 88.11)	Avoidance, chelation	–	Lung, bladder and skin cancer
Barium	Chloride, nitrate	Irritant contact dermatitis, burns	Water flush immediately	50 mg/m ³	–
Beryllium	Metal	Dermatitis, granulomas	–	–	Lung cancer
Bismuth	Telluride	Irritant contact dermatitis	Soap wash immediately	–	–
Boron	Borates, oxide	Erythema, irritant contact dermatitis	Soap wash, water flush	–	–
Cesium	Hydrate, hydroxide	Irritant contact dermatitis, burns	Water flush immediately	–	–
Chromium	Hexavalent	Allergic and irritant contact dermatitis, skin ulceration, burns; systemic absorption can lead to renal failure, hepatic failure, anemia, coagulopathy	Water flush promptly	–	Lung cancer
Cobalt	Metal dust	Dermatitis, diffuse nodular fibrosis	Soap wash	20 mg/m ³	–
Copper	Metal dust	Dermatitis	Soap wash promptly	100 mg/m ³	–
Gold	Elemental salts	Most common: lichen planus, lichenoid drug eruption, allergic contact dermatitis, eczematous dermatitis, PR-like eruption, pruritus, flushing, erosive stomatitis Less common: chrysiasis, erythema nodosum, erythema multiforme, toxic epidermal necrolysis, exfoliative dermatitis	Avoid gold-laden liquor	–	–
Indium	Metal	Irritant contact dermatitis	Soap wash	–	–
Iron	Salts	Irritant contact dermatitis, mucosal irritation	Soap wash	–	–
Lead	Metal	Irritant contact dermatitis, gingival lead line	Soap wash promptly	100 mg/m ³	–
Lithium	Hydride	Irritant contact dermatitis, burns	Brush off gently, DO NOT WASH	0.5 mg/m ³	–
Magnesium	Carbonate	Irritant contact dermatitis	–	–	–
Manganese	Cyclopentadienyl tricarbonyl	Irritant contact dermatitis	Soap wash	–	–
Mercury	Elemental, inorganic, organic	Acrodynia, tattoo reaction (cinnabar), granulomas, exanthem, cutaneous hyperpigmentation, allergic and irritant contact dermatitis, baboon syndrome	Soap wash promptly	10 mg/m ³ (elemental) 2 mg/m ³ (organic)	–
Nickel	Elemental	Allergic contact dermatitis	Water wash immediately	10 mg/m ³	Lung and nasal cancer
Osmium	Tetroxide	Irritant contact dermatitis	Soap wash immediately	1 mg/m ³	–
Platinum	Metal	Irritant contact dermatitis	Soap wash	–	–
Polonium	²¹⁰ Po radionuclide	Erythema, alopecia; ulceration in higher doses	Avoid ingestion; wash off	0.1–0.3 GBq (fatal in 3–4 weeks)	–
Selenium	Elemental, alloy	Irritant contact dermatitis, skin burns	Soap wash immediately	1 mg/m ³	–
Silver	Metal	Argyria, irritant contact dermatitis, skin ulceration	Water flush	10 mg/m ³	–
Tellurium		Dermatitis, garlic smell of sweat	Soap wash promptly	25 mg/m ³	–
Thallium	Soluble	Alopecia, acneiform papules, keratotic plaques on hands and feet, Mees' lines	Water wash promptly	15 mg/m ³	–
Tin	Metal, organic	Irritant contact dermatitis, skin burns, pruritus	Water flush immediately	100 mg/m ³ (metal) 25 mg/m ³ (organic)	–
Tungsten		Irritant contact dermatitis	Soap/water wash immediately	–	–
Uranium		Irritant contact dermatitis, skin burns	Soap/water wash immediately	10 mg/m ³	Lung cancer
Vanadium	Dust, fume	Irritant contact dermatitis, green tongue	Soap wash promptly	–	–
Zinc	Chloride	Irritant contact dermatitis, skin burns (fixes tissue <i>in situ</i>), mucocutaneous hyperpigmentation	–	–	–

*Concentration posing immediate danger to life and health (IDLH). Since 1979, the National Institute for Occupational Safety and Health (NIOSH) has not allowed detectable levels of known carcinogens. Therefore there are no values in the IDLH column for carcinogens.

Table 88.12 Toxic and heavy metals and their cutaneous impact^{49–61}. GBq, gigabecquerel; PR, pityriasis rosea.

Exogenous pigmentation

A wide variety of chemicals, either from occupational or medicinal exposure, can produce discoloration of the skin. Some of these may not only produce an alteration of pigmentation by being deposited in the dermis but may also result in an increase in the amount of melanin in the skin. Of importance are the metals silver, gold, mercury and bismuth, which are cumulatively deposited in the dermis and can produce permanent disfiguring pigmentation. A number of drugs can discolour the skin. These include the antimalarials, the phenothiazines, clofazimine and minocycline. Of less importance is the transient staining of the skin produced by picric acid, dinitrophenol and chemical dyes.

Metals

Introduction and general description

Argyria

This may develop as a result of systemic absorption or from external contact with silver [1,2]. The silver may be deposited in the skin either as a result of medication containing silver salts [3,4,5] or from industrial exposure [2]. Localized argyria is most commonly caused by mechanical impregnation related to occupational exposure [2].

Most reported cases of generalized argyria occur following ingestion of colloidal silver, which is widely marketed as a folk remedy for various conditions, including diabetes, AIDS, cancers

and infections: a cumulative dose of 4–5 g is required to produce clinical signs [6]. Light and electron microscopy studies [1,2,7–9] show silver granules in the dermis that are most numerous in relation to the basal lamina of the eccrine sweat glands, and in the dermal elastic fibres. Furthermore, silver particles may be seen lying free within the cell cytoplasm of epithelial cells of the secretory segment of eccrine sweat glands and in mast cells [9,10]. Silver granules are readily visible with dark-field illumination. X-ray-dispersive microanalysis confirms that the granules contain silver [2,10]. Silver is widely deposited in the tissues as well as in the skin. The diagnosis of argyria is established by skin biopsy.

The pigmentation is usually a slate-grey colour and may be clinically apparent after a few months, but usually takes many years to develop and depends on the degree of exposure. The hyperpigmentation is most apparent in sun-exposed areas of the skin, especially the forehead, nose and hands (Figure 88.57). In some patients, the entire skin has a slate blue-grey colour. The sclerae, nails and mucous membranes may additionally become hyperpigmented.

Blue macules have appeared at the sites of acupuncture needles [6]. Cases have followed the use of silver salts for the irrigation of nasal, oral and urethral mucous membranes and the excessive use of an oral smoking remedy containing silver acetate [1,10]. ‘Food supplements’ may also contain colloidal silver [8].

The pigmentation is usually permanent: treatment with depigmenting agents is not effective. Sun protection can limit further pigmentary changes [9].

Arsenic

Prolonged ingestion of inorganic arsenic may result in diffuse pigmentation, most intense on the trunk. The hyperpigmentation is characterized by macular areas of depigmentation within areas of hyperpigmentation produce the distinctive ‘raindrop’ appearance, diffuse dark brown spots or diffuse darkening of the skin on the

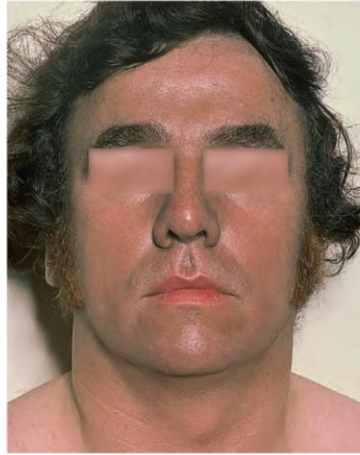


Figure 88.57 Occupational argyria.

limbs and trunk [1,2]. Many cases also show arsenical keratoses, usually appearing as bilateral thickening of the palms and soles. Nodular keratosis may also occur as multiple raised keratotic lesions in the palm and soles [2].

Bismuth

The administration of bismuth at regular intervals over a period of years has often been practised, yet generalized pigmentation is extremely rare. The diffuse grey pigmentation resembles that of argyria and involves also the sclera and the oral and sometimes the vaginal mucous membrane [1]. A distinctive blue-black line occurs at the gingival margin. This is due to deposition of bismuth that reacts with hydrogen sulphide formed by bacteria in the mouth [2].

Chrysiasis and chrysoderma

These are terms used to describe permanent pigmentation of the skin due to parenteral administration of gold salts.

Excessive administration of gold leads to its deposition in connective tissue. The diagnosis is confirmed histologically on microscopy with dark-field illumination and on electron microscopy with electron probe microanalysis [1]. The granules of gold are larger and more irregular than those of silver.

Chrysiasis has not been observed in any patient who has received less than 50 mg/kg of gold thiosulphate, and appears to be inevitable in any patient receiving more than 150 mg/kg. It may develop after a few months or after a longer latent period. The pigmentation is blue-grey or may show a purplish hue, and is limited to light-exposed skin and to the sclerae (Figure 88.58) [2]. The oral mucous membrane is not affected. The discoloration is permanent.

Mercury

Repeated applications of mercury-containing compounds can produce localized hyperpigmentation of the treated areas [1,2,3]. The pigment is observed in the upper dermis around capillaries and associated with collagen and elastic fibres. Electron microscopy



Figure 88.58 Chrysiasis: mild lilac discoloration on the forehead and eyelids contrasting with the yellow of the elastotic skin on the bridge of the nose and eyebrows in 64-year-old woman with rheumatoid arthritis who 8 years earlier had been treated with parenteral gold for over 2 years.

shows an increase in melanin pigmentation and the metal is present as granules in dermal macrophages [1,3].

Systemic administration of mercury results in gingival hyperpigmentation. A case report of homicidal subcutaneous injection of metallic mercury resulted in widespread skin lesions, remote from the radiologically visible mercury; these appeared at 40 days and began to clear at 6 months [4].

Differential diagnosis

See Box 88.3a.

Medication

See Drug-induced hyperpigmentation.

Tattoos

Accidental tattoos

Pigmented particles may be accidentally introduced as contaminants of wounds or may, at high velocity, penetrate previously intact skin.

Superficial abrasions contaminated with chemically inert particles may be followed by disfiguring tattoos. Such irregularly spattered pigmentation is quite commonly seen after road accidents and blast injuries. Some particles may eventually be extruded, but the disfigurement is often permanent. These tattoos often respond well to the Q-switched Nd : YAG laser (Figure 88.59) [1]. Small lesions may also be excised.

Colliers' stripes

These are a very distinctive occupational mark in coalminers [2]. The bluish grey, linear or angular stripes develop at the sites of abrasions. The commonest sites are the forehead, bridge of the nose, wrists and elbows. Histologically, particles of coal dust up to 100 μm in diameter are seen at all levels in the dermis. They tend to be grouped around blood vessels.

Therapeutic agents

Iron salts. The use of solutions of ferric sulphate and ferric chloride in the treatment of dermatitis has been followed by a reddish-brown tattoo [3,4]. The pigmentation may disappear after a few months or may persist indefinitely [5].

Occupational contact with iron salts [6] produced red-brown punctate perifollicular pigmentation of the forearms in a man employed in pickling metal in hydrochloric acid.

Crystal violet (gentian violet; hexamethyl pararosaniline chloride). This has, exceptionally, given rise to a tattoo when applied to a wound of the face [7].

Decorative tattoos (see also Chapters 23 and 123)

History and prevalence

From ancient times, the practice of tattooing has developed along more or less parallel lines in most cultures. Tattoos have traditionally been based on aesthetic considerations, i.e. to accentuate beauty, or as a permanent adornment in a more sociological or



(a)



(b)



(c)



(d)

Figure 88.59 (a–d) Traumatic tattoo: accidental tattoo following explosion during school chemistry experiment; excellent response to Nd : YAG laser.

cultural context to make a statement. Occasionally, when used in a sociocultural context, tattoos serve to accentuate aggression or ugliness in order to make the wearer more intimidating. Tattoos with words or a name as a symbol of dedication or devotion have always been popular. Tattoos have also been used for more sinister motives. Tattoos were used as a means of identification by the Nazis in the Second World War for members of concentration and labour camps as well as for members of the SS. Formerly associated with religious ceremonies, fertility and marriage rites, tattooing in contemporary westernized civilizations thus fulfils a number of diverse functions and in so doing it survives and flourishes.

Contemporary life finds tattooing more popular than ever [8], even among the elite [9]. Tattoos are no longer the exclusive preserve of street gangs, prisoners and members of the armed forces [8,9]. Tattooing is viewed by many as an acceptable fashion accessory like any other, and is increasingly popular in Western societies with the young and with women, as well as the more traditional male stereotypes [8,9]. Tattooing and body piercing are now so common that health care workers are advised to maintain a non-judgemental attitude to tattoos [8], even in the face of the unexpected [10]. The decision to have a tattoo may be taken when an individual is in no position to make such a lifelong commitment, for example when intoxicated, under peer pressure or when mentally unwell [11,12]. Tattoos may also be a manifestation of deliberate self-harm [11,12].

Another contemporary trend is the use of temporary black henna 'tattoos' [13,14]. These are not true tattoos but represent application of a black dye to produce a tattoo-like appearance that lasts for a few days. Unfortunately, a high concentration of the well-known contact sensitizer *para*-phenylenediamine is usually present in these 'tattoos', which results in a risk of contact allergy [13,14].

Techniques and materials

The professional tattooist uses an electric needle to introduce particles of pigment into the dermis (see Chapter 23). The amateur, often a

child, pricks particles of soot or Indian ink into skin with any pointed object. The pigments commonly employed include the following:

- Blue-black (carbon).
- Red (cinnabar and vegetable dyes).
- Light blue (cobaltous aluminate).
- Green (chromic oxide or chromium sesquioxide).
- Yellow (cadmium sulphide).
- Brown (ochre, iron oxides).

Complications of tattoos

Infection, allergy to tattoo pigments (Figure 88.60) and koebnerization of other disorders, particularly sarcoidosis, to tattoos represent



Figure 88.60 Lichenoid reaction in the red areas of a tattoo.



Figure 88.61 Keloid reaction to decorative tattoo: flattened areas have responded to the injection of triamcinolone.

the most common complications of tattoos. A sarcoidal granuloma in a tattoo may be the presenting manifestation of generalized sarcoidosis [15]. Foreign-body granulomas of sarcoid type are, however, extremely unusual after decorative tattoos, but have been reported in ochre tattoos, which have a high silica content [16]. Tattooing may also be complicated by keloids (Figure 88.61). Complications of tattoos are discussed in further detail in Chapter 123.

Removal of tattoos

Although most people who choose to have tattoos are satisfied with them, there are many who wish to have them removed [17]. In a recent study of 154 attendees with tattoos at a sexual health clinic in Denmark, 21 (13.6%) expressed regret about one or more of their tattoos [18]. Fortunately, the technology for removing them has improved greatly in recent years. Small tattoos may be amenable to removal by simple surgical techniques. Lasers are also widely used for tattoo removal. Their use is discussed in detail in Chapter 23.

Reactions to gold

Gold (Au)

- Atomic number: 79
- Atomic weight: 196.96 Da
- Normal concentrations: whole blood = 0.055 ng/mL

Synonyms and inclusions

- Gold poisoning
- Chrysiasis

Introduction and general description

Elemental gold is inert, however mono- and trivalent forms combine with electron donors. These ions bind strongly with sulfhydryl groups [1].

Gold is an inert substance present throughout the world and exposure is predominantly through the mining industry and as a therapeutic agent. Introduction of gold into the skin can also occur from tattoos, piercings, dental restorations and prolonged wearing of gold jewellery [2]. Gold has been used to treat rheumatoid arthritis, pemphigus and psoriatic arthritis. As an isotope ^{198}Au has been used to treat cancers. Edible gold leaf is used in liqueurs and as a flavourless wrap in expensive foods [3].

Pathophysiology

A wide variety of immune reactions to gold are recognized; most typical is a type 4 cell-mediated hypersensitivity, resulting in a lichenoid eruption. Type 1 (immediate) and type 3 (immune complex) reactions also occur.

Gold, after being engulfed by macrophages, is stored in lysosomes (aureosomes). It inhibits lysosomal enzyme activity, histamine release from mast cells, phagocytosis and the inflammatory effects of prostaglandins [4]. Gold also reduces the production of proinflammatory cytokines including tumour necrosis factor α (TNF- α), interleukin-1 (IL-1) and IL-6 [4]. There has been an association between human leukocyte antigen (HLA) types and cutaneous gold reactions, particularly with HLA-DRW3, HLA-DR5, HLA-B7, HLA-B8 and HLA-B27 [5–8]. A study has shown that gold dermatitis in patients with rheumatoid arthritis is associated with both HLA-B35 and disease duration [9]. Antibodies to the Ro 52-kDa antigen are associated with skin eruptions in rheumatoid arthritis patients treated with gold [10].

Pathology

The histology of a gold-induced eczematous and lichenoid eruption is characterized by a sparse dermal perivascular infiltrate, predominantly of CD4+ HLA-DR-positive helper T lymphocytes, an increase in the number of dermal Langerhans cells and epidermal macrophage-like cells, and Langerhans cell apposition to mononuclear cells [11]. Metallic gold particles can be demonstrated in dermal macrophages and around blood vessels [12].

Clinical features

The use of gold in rheumatoid arthritis is associated with a 23–30% incidence of reactions [3,13,14]; most of these are minor, but about 15% may be severe or even fatal [15]. Rashes and mouth ulcers are

common [2,3,16–21], representing about 50% of all complications with parenteral gold and 35% of those with oral gold. Localized or generalized pruritus is an important warning sign of potential toxicity. Gold reactions may simulate exanthematic eruptions [22], erythema annulare centrifugum [23], seborrhoeic dermatitis or lichen planus [24,25]. A mixture of these patterns, sometimes with discoid eczematoid lesions, is characteristic. Lichen planus is often of the hypertrophic variety especially on the scalp, and severe and irreversible alopecia may follow [26]. There may be striking and persistent postinflammatory hyperpigmentation. Permanent nail dystrophy has followed onycholysis [27]. Yellow nails have been described [28].

In one study, eczematous or lichenoid rashes persisted for up to 11 months after cessation of therapy [21]. A patient with a lichenoid and seborrhoeic dermatitis-like rash on gold sodium thiomalate therapy had a positive intradermal test to gold thiomalate; patch tests were positive to thiomalate (the thiol carrier of gold thiomalate) but negative to gold itself [29]. Interestingly, the same patient subsequently developed a seborrhoeic dermatitis-like eruption, but not a lichenoid eruption, while on auranofin. This time, patch tests were positive to both auranofin and gold.

A previous contact dermatitis from gold jewellery may be reactivated [30]. Other reactions documented include erythema nodosum [31], severe hypersensitivity reactions [32], vasculitis [33], polyarteritis, an SLE-like syndrome, generalized exfoliative dermatitis and toxic epidermal necrolysis. Psoriasis was reported to be exacerbated in a patient with arthritis treated with gold [34]. Prolonged administration of gold may cause a distinct grey, blue or purple pigmentation of exposed skin (chrysiasis), which is a dose-dependent reaction that occurs above a threshold of 20 mg/kg; gold granules are seen within dermal endothelial cells and macrophages [35–39]. Even in the absence of pigmentation, gold can be detected histochemically in the skin up to 20 years after therapy. Localized argyria with chrysiasis has been caused by acupuncture needles [40]. An unusual late cutaneous reaction involved the appearance of widespread keloid-like angiofibromatoid lesions [41]. Oral lesions due to gold include erythematous eroded areas and lichenoid reactions. Stomatitis may be seen as a result of gold reactions [42]. Gold cyanidation process used in the gold industry causes irritant reactions on the skin with discoloration of fingernails [43].

A benign vasodilatory 'nitritoid' reaction, consisting of flushing, light-headedness and transient hypotension, may occur immediately after the first injection of gold [2,44]. It occurs in roughly 5% of patients taking gold sodium thiomalate. Non-vasomotor effects including arthralgia, myalgia and constitutional symptoms within the first 24 h are recognized. Mucous membrane symptoms include loss of taste, metallic taste, stomatitis, glossitis and diarrhoea. Punctate stomatitis may occur with or without skin lesions. Gold is also deposited in the cornea and may cause keratitis with ulceration.

Eosinophilia is common, and serum IgE may be raised [45]. Other immunological reactions are rare, although pulmonary fibrosis is recorded [46]. Blood dyscrasias, especially thrombocytopenic purpura, and occasionally fatal neutropenia or aplastic anaemia occur in a small proportion of cases and usually present within the first 6 months of therapy. Jaundice occurs in about 3% of cases, and may result from idiosyncratic intrahepatic cholestasis [47]. Proteinuria and renal damage are well recognized.

Management

Generally, there are no effective treatments for chrysiasis – localized or generalized. Recently, a case of localized chrysiasis was successfully treated with a long-pulsed ruby laser [48].

Dimercaprol has been used with varied success. Acetyl cysteine and granulocyte colony-stimulating factor have been used mainly to reduce the haemopoietic side effects [3].

Chrysiasis is a rare adverse effect among individuals who have received long-term gold salt therapy. Chrysiasis typically begins with mauve discoloration of the periorbital region, which deepens gradually into a blue to slate-gray color and extends to other sun-exposed areas.¹ Laser-induced localized chrysiasis has also been reported²⁻⁴ to occur immediately after administration of Q-switched ruby laser, alexandrite laser, and Nd:YAG laser.

Gold salts were used widely as a disease-modifying antirheumatic drug for treatment of rheumatoid arthritis in the 20th century, but the use declined with the approval of new drugs. The common cutaneous adverse effects of gold salt therapy include general pruritus, nonspecific maculopapular eruption, lichen planus-like dermatitis, pityriasis rosea-like dermatitis, and oral ulcers.⁵ Chrysiasis seems to be a rare cutaneous discoloration, mainly in sun-exposed areas, that may occur with cumulative gold salt doses as low as 1.05 g.¹ In addition to skin, gold salt concentrates in the lens, cornea, and reticuloendothelial system.

The pathomechanism of chrysiasis is not fully understood; however, the cumulative doses of gold salts and UV light have been suggested to play important roles. Trotter et al² proposed that Q-switched laser can produce high peak power generated by a short pulse duration and development of an extremely high temperature that directly alters physiochemical properties in dermal gold deposits from crystalline to elemental gold, resembling colloid gold. The color of the colloid gold in solutions is blue-purple, which is similar to the pigmentation associated with chrysiasis. Yun et al³ observed that laser-induced chrysiasis in patients who receive therapy with gold salts is primarily an irradiance-dependent rather than a fluence-dependent phenomenon.

The diagnosis of chrysiasis can be made primarily on clinical grounds in most cases in the setting of a history of gold salt use and characteristic facial lesions. In suspicious cases, we suggest that a rechallenge test with Q-switched laser may be considered in an unobvious site (as in [Figure 1B](#)) if a skin biopsy specimen cannot be obtained.

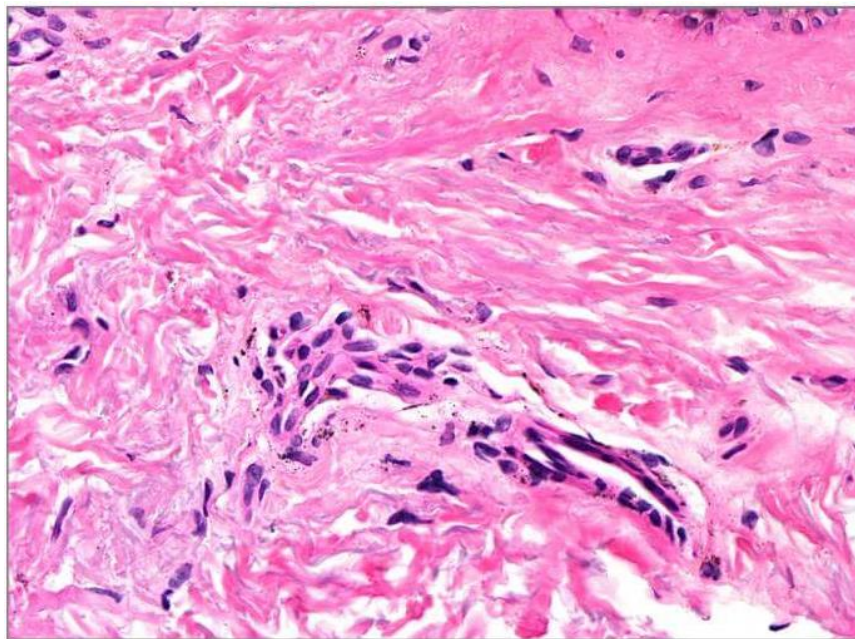
The discoloration associated with chrysiasis can be disfiguring. Treatment remains limited but may be attempted with long-pulsed laser, 595-nm pulsed dye laser, or surgical excision if there are few lesions.^{3,4,6} Patients receiving gold salts should be warned to avoid direct sunlight exposure to prevent progression of discoloration. We attempted treatments with pulsed dye laser and long-pulsed alexandrite laser, but the results were not satisfactory.

It is important for clinicians to routinely screen patients for previous use of gold salt therapy before laser treatment, especially those who are older than 40 years with a history of rheumatic disease, to avoid this possibly irreversible adverse effect.

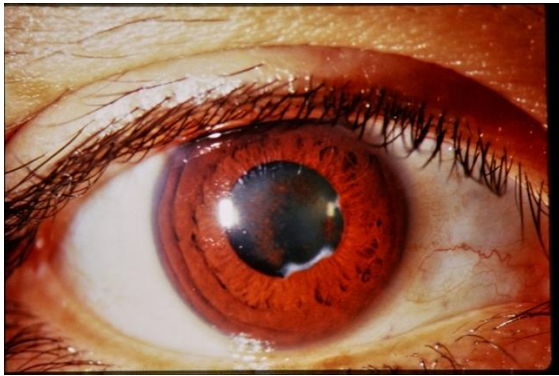
A Blue to slate-gray patches on the face



B Rechallenge test



Immediate pigmentation after laser treatment : Chrysiasis is an uncommon side effect that occurs in patients who are receiving prolonged treatment with either intravenous or intramuscular gold as a distinctive blue-gray pigmentation of light-exposed skin. Laser-induced chrysiasis is a rarely described phenomenon in individuals who have received systemic gold and are subsequently treated with a Q-switched laser.





Laser-induced chrysiasis: the shedding lentiginos on the left face are surrounded by blue “halos.” The dyschromia is most readily observed on the jaw and chin four days following treatment with a Q-switched alexandrite laser. Additional history revealed that the patient had received several years of intramuscular gold (sodium aurothio-glucose) to treat her rheumatoid arthritis.



Resolution of blue patches of laser-induced chrysiasis after a sequential series of laser sessions using a long-pulsed alexandrite laser, followed by a nonablative fractional laser and an ablative carbon dioxide laser.

Laser-induced chrysiasis has been observed following treatment with Q-switched lasers in patients who are receiving or have previously been treated with systemic gold. It is important to emphasize that this phenomenon can occur even decades after treatment with gold has been discontinued. The dyschromia secondary to chrysiasis persists. The facial discoloration in the authors' patient with laser-induced chrysiasis was successfully diminished by sequentially using three different lasers—a long-pulsed alexandrite laser, a nonablative Fraxel restore laser, and an ablative carbon dioxide laser. In summary, although gold is less commonly used today as a therapeutic agent in medicine, inquiry regarding a prior history of treatment with gold—particularly in older patients with rheumatoid arthritis—should be considered prior to treatment with a Q-switched laser. Also, treatment with a long-pulsed laser should be entertained in patients with either idiopathic or laser-induced chrysiasis.