

Colors and Contact Dermatitis

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The diagnosis of skin diseases relies on several clinical signs, among which color is of paramount importance. In this review, we consider certain clinical presentations of both eczematous and noneczematous contact dermatitis in which color plays a peculiar role orientating toward the right diagnosis. The conditions that will be discussed include specific clinical-morphologic subtypes of eczematous contact dermatitis, primary melanocytic, and nonmelanocytic contact hyperchromia, black dermographism, contact chemical leukoderma, and others. Based on the physical, chemical, and biologic factors underlying a healthy skin color, the various skin shades drawing a disease picture are thoroughly debated, stressing their etiopathogenic origins and histopathologic aspects.

The diagnosis of skin diseases is based, to some degree, on a visual analysis process, which interprets the type, shape, distribution, and color of skin lesions. On a perceptive level, the first information to be taken in when examining skin lesions is color, and this is sometimes sufficient in itself to formulate a correct diagnosis. No dermatology textbook has ever failed to consider color as a characteristic, sometimes pathognomonic, feature of skin conditions and their clinical evolution. Therefore, color has a decisive importance in clinical dermatology.

After a brief introduction considering biologic and physical factors determining a normal skin color, in the present work, we analyze various clinical pictures pertaining to eczematous and noneczematous contact dermatitis, in which color has a peculiar role in the diagnostic process (Table 1).

NORMAL SKIN COLOR

Climbing the evolutionary ladder, skin colors constantly decline and lose their importance. In comparison with their vertebrate relatives (amphibian, fish, reptiles, and birds) and many invertebrates, mammals are lightly and less variably colored. Man, the least colorful creature, only shows variety in the genetically transmitted "continuum melaninic," clinically expressed as phototypes I to VI.¹⁻⁵ The base skin color varies among humans depending on their ethnic origin and hence different genetics and geographic distribution. Individual variability also affects skin color, depending on the quantity and quality of chromophores and their localization.

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The authors have no funding or conflicts of interest to declare.

DOI: 10.1097/DER.0000000000000046

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Mechanisms responsible for a normal skin color are both of physical and chemobiologic type. The epidermis behaves as an optical filter; incident white visible light can either be transmitted, absorbed (and transformed into energy forms such as heat), refracted in its 7 primary and secondary colors, or reflected. Skin color derives from a combination of reflected and refracted light, whose wavelengths mainly depend on 4 biochromes, 2 of which are intraepidermal (melanin and carotenoid) and 2 are intradermal (oxyhemoglobin and reduced hemoglobin). Various other chromophores contribute to human skin color in pathologic conditions, such as porphyrins and bilichromes.²⁻⁵ The main skin color determinant is melanin, with its broad absorption in the visible and UV range, conferring a variable brownish shade to the skin. In the absence of melanin, the skin exhibits a bright red color because oxyhemoglobin in superficial vessels is no longer concealed by the brownish biochrome. By contrast, when skin contains large amounts of melanin, it is difficult to appreciate its vascularity. A reddish or bluish red skin tone is the result of the relative quantities of oxyhemoglobin and methemoglobin in skin capillaries (70% oxyhemoglobin), arterioles (95% oxyhemoglobin), and venules (50% oxyhemoglobin). Carotenoids are yellow to orange-red exogenous pigments, usually ingested in fruits and vegetables, which localize in the epidermal stratum corneum and in subcutaneous fat. They play a marginal role in determining a normal skin color but give a yellowish hue when deposited in vast excess.

SKIN COLORS IN CONTACT DERMATITIS

Red and its Nuances

The first place in the chromatic scale of contact dermatitis goes to red.

Bright Red Tone

Most haptens, particularly nonsteroidal anti-inflammatory drugs and plants (Fig. 1), exert a strong inflammatory action. The

TABLE 1. Most Common Colors and Respective Causative Substances in Eczematous and Noneczematous Contact Dermatitis

Color	Tone	Causative Substances	Dermatitis
Red	Bright	Most allergens	Common eczematous contact dermatitis
	Pinkish	Nickel	Nickel contact dermatitis
	Purpuric	Paraphenylenediamine, isopropyl- <i>N</i> -paraphenylenediamine, textile azoic dyes, <i>A. americana</i> L., Peru balsam	Purpuric contact dermatitis
	Lilac	Color film–developing agents, methacrylic acid esters, nickel, epoxy resin, aminoglycoside antibiotics	Lichenoid contact dermatitis
	Violet	Promethazine and other phenothiazines	Phenothiazines contact dermatitis
Brown		Psoralens, <i>J. regia</i> , <i>L. inermis</i> , Tinopal CH 3566, azoic dyes, paraphenylenediamine, cutting oils, fragrances, anthralin, permanganates, phenothiazines, coal tar	Berloque dermatitis
			<i>Juglans regia</i> hyperchromia
			<i>Lawsonia inermis</i> hyperchromia
			<i>Cynara scolymus</i> L. hyperchromia
			Pigmented contact dermatitis
			Riehl melanosis
			Anthralin discoloration
			Permanganates discoloration
			Photocontact dermatitis (postinflammatory hyperchromia)
			Phytophotocontact dermatitis (postinflammatory hyperchromia)
			Contact chemical leukoderma
			Contact dermatitis (postinflammatory hypochromia)
White		Phenol and catechol derivatives, sulfhydryls, mercurials, cinnamic aldehyde	Black dermatographism
Black		Metal particles (nickel, iron, platinum, silver, gold, copper), <i>Toxicodendron</i>	Black-spot poison ivy dermatitis
Silver		Silver	Contact with silver salts
Gray-brown		Mercury, dioxins	Contact with mercury and dioxins
Miscellaneous		Dyes	Contact with dyes

dermatitis they induce is thus typically a bright red color because of intense hyperemia with a consequent rise in oxyhemoglobin levels.

Pinkish Red Tone

Nickel allergic contact dermatitis is characterized by peculiar features; the primary focus at the contact site consists of small papulovesicular elements, sparsely distributed or sometimes confluent in patches. Secondary lesions, often symmetrical, consist of scattered papules and papulovesicles.^{6,7} The latter lesions, which are generally follicular, are only slightly infiltrated and exudative and tend to look like small, pinkish red lichenoid papules (Fig. 2).⁸ Nickel, therefore, although it is a strong sensitizer, seems to be a weak inflammatory agent.

Purpuric Red Tone

The purpuric red of purpuric contact dermatitis is the result of extravasation of red blood cells, a sign of vessel involvement.⁹ Substances frequently triggering a purpuric allergic contact dermatitis include paraphenylenediamine and isopropyl-*N*-phenyl-*p*-phenylenediamine in rubber products, and textile azoic dyes.^{9–20} Various authors^{13,15} have shown that azoic compounds show an elective affinity to the endothelium. As we have also reported,^{20,21} *Agave americana* L. of the Agavaceae family can induce a purpuric irritant contact dermatitis. Histologic analysis of the peculiar lesions showed features suggestive of leukocytoclastic vasculitis, such as fibrinoid degeneration of skin capillaries and venules, a

neutrophilic infiltrate, and karyorrhexis.²¹ Open test with a fragment of agave leaf induced purpuric folliculitis after 10 minutes, whereas biopsy 24 hours after open testing revealed the histologic findings described previously.²¹ Cases of purpuric vasculitis–like eruptions caused by Peru balsam have also been reported (Fig. 3).^{22,23}

Lilac-Red Tone

Lichenoid allergic contact dermatitis (or lichen planus–like contact dermatitis) has been reported after exposure to some substitutes



Figure 1. Bright red erythemato-vesico-bullous lesions due to plants (*Ficus carica*).



Figure 2. Secondary slightly infiltrated scattered pinkish red papules and papulovesicles due to nickel involving the décolleté.

of paraphenylenediamine, such as color film–developing agents.^{24–31} Other substances that are reported as causes, even if exceptional, are methacrylic acid esters used in the car industry,³² nickel,³³ epoxy resin,³⁴ and aminoglycoside antibiotics.³⁵ Clinically, this form is characterized by eczematous lesions that evolve to or are associated with papular lesions with peculiar lilac-red tones. Positive patch test reactions are eczematous in nature but might turn lichenoid.³¹ In most cases, histopathologic findings are compatible with lichen planus.^{24–26,28,35,36} In 5 unpublished cases that we observed, 3 were due to color film–developing agents (2-amino-5-diethylaminotoluenehydrochloride, *N-N*-diethyl-paraphenylenediamine, hydroxylamino hydrochloride, respectively; Fig. 4) and 2 were due to paraphenylenediamine; the histologic features were comparable, displaying a patchy mononuclear infiltrate in the upper dermis but no hypergranulosis,



Figure 3. Purpuric contact dermatitis due to Peru balsam.

along with foci showing moderate spongiosis and focal basal stratum vacuolization. The latter is a cause of incontinentia pigmenti, which could explain the peculiar color of the skin lesions, deriving from the combination of inflammatory red and dermal melanin blue.

Violet-Red Tone

Promethazine hydrochloride [10-(2-dimethylaminopropyl)-phenothiazine hydrochloride] has been extensively used topically for decades, given its antihistaminic and antipruritic activities.^{37–40} Up until the 1990s, especially during summertime, we observed hundreds of promethazine photosensitization cases. In Italy, this dermatitis was colloquially named *farganite*, from the commercial name of the promethazine cream that was most widely used at that time (Fargan[®]). Similar products based on the same molecule are still available in Italy; however, it has been more than a decade since we observed a case of this dermatitis, likely thanks to a vigorous preventive campaign. Clinically, the dermatitis used to present with intensely erythematous-edematous lesions, scarcely exudative, smooth, and glossy, which tended to acquire a peculiar violet nuance as the days went by (Fig. 5).⁴⁰ A range of factors comes into play in determining the violet-red tinge. Phenothiazines, as pigments, distribute widely in human tissues (kidney, skeletal muscle, heart, eye, brain, and reticuloendothelial system), when used either topically or systemically.^{41,42} In sensitized subjects, topical promethazine application and contemporary or subsequent sun exposure lead to intense inflammation and melanogenesis stimulation, with an increase in melanosome transfer from melanocytes to both keratinocytes and dermal macrophages.^{43,44} The intense erythema of the inflammatory process



Figure 4. Lilac-red lichenoid allergic contact dermatitis due to color film–developing agents.

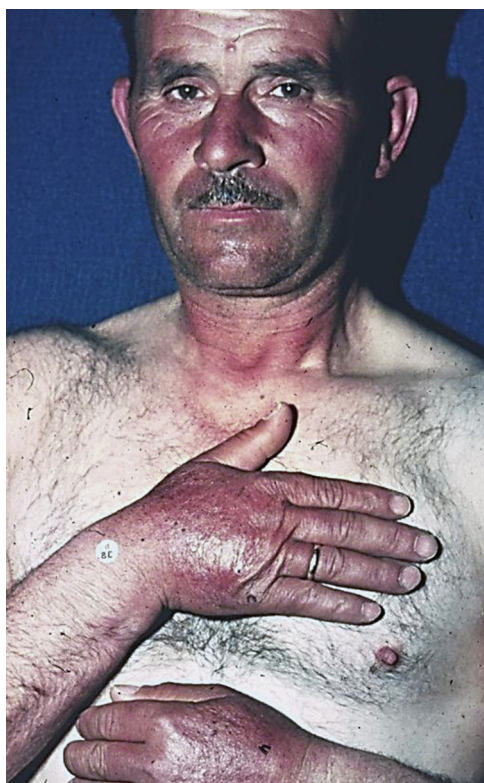


Figure 5. Violet-red promethazine photoallergic contact dermatitis.

combines with the brownish nuance caused by epidermal melanin and blue tones from dermal melanin.

Brown and its Nuances

Contact brown hyperchromia can be primary, melaninic and nonmelaninic, and secondary.^{45,46}

Primary Hyperchromia

Berloque dermatitis is a primary (the affection is rarely preceded by erythema) melaninic hyperchromia of variable intensity. It is an irritant contact phytophotodermatitis caused by furocoumarins, especially bergapten (5-MOP) contained in *Citrus bergamia*, the essence of which was commonly used in perfumes and tanning products. The typical pendantlike manifestations appeared if sun exposure occurred within 2 hours of applying perfume. The wavelengths involved were those higher than 320 nm. In the past years, we observed quite a few cases of berloque dermatitis with either localized (perfumes) or diffuse (tanning products) skin involvement. Nowadays, the European legislation bans the use of berloque essence in cosmetics, save for its coumarin-free detoxed version. Nevertheless, we occasionally observe brown hyperchromia cases in the perilabial area, particularly in children who have eaten unpeeled bergamotti fruits. As a matter of fact, *C. bergamia* is widespread in the south of Italy.⁴⁶

Juglans regia (walnut) induces a primary brown irritant contact hyperchromia, nonmelaninic in origin. In autumn, the time of

walnut hulling, hyperchromia of variable intensity can be observed on the hands, the color ranging from light brown to darker tones, depending on the intensity and duration of contact (Fig. 6).^{46,47} This dermatitis can also extend to the forearms and, in rare cases, presents with bullous lesions. Similarly, the nail plates go dark. The duration of the hyperchromia ranges from weeks to 2 to 3 months, according to the pigmentation intensity. The pathogenetic mechanism is as follows: juglone, the active ingredient of *J. regia*, is a naphthoquinone. The activated quinone C = O group shows an elective affinity for the –NH₂ group exposed by keratin amino acids. The reaction elicits C = N highly pigmenting chromophores, conjugated to mobile electrons. These groups absorb colors in the visible range, violet in particular, and reflect yellow and red, giving rise to a color spectrum ranging from yellowish red, through red, to dark brown.⁴⁷ The skin color induced by *Lawsonia inermis* (henna tree) is based on the same action mechanism; lawsone, the active principle, is also a naphthoquinone.

Contact brown hyperchromia from contact with artichoke (*Cynara scolymus* L.) is different altogether. *Cynara scolymus*, an imposing herbaceous plant with enormous flower heads surrounded by fleshy bracts, is cultivated in Mediterranean regions and other temperate areas. Cynarin, the active ingredient of artichoke, is a polyphenol ester [(1-carboxy-4, 5-dihydroxy-1, 3-cyclohexylenebis – (3, 4-dihydroxycinnamate)] that undergoes oxidation; it stains the fruit itself and the hands while cleaning/cutting artichokes.

As first described by Osmundsen⁴⁸ in 1970, pigmented contact dermatitis is a melaninic primary hyperpigmentation, usually observed in dark phototypes and mostly occupational. The author described an intense and bizarre skin hyperpigmentation due to contact with the optical whitener Tinopal CH 3566 used in washing powders. The sites involved were those of textile contact dermatitis, inducing a brownish blue to grayish hyperchromia. The same stain developed at patch tests application sites. Histologic finding demonstrated melanin deposits in and outside upper dermal melanophages. Pigmented contact dermatitis can also be caused by azoic dyes. An epidemic outbreak due to contact



Figure 6. Primary nonmelaninic hyperchromia after *Juglans regia* walnut hulling.

with naphthol AS was reported in a textile business.⁴⁹ Hyperpigmentation was noticeable in dark-skinned individuals, whereas fair-skinned ones showed signs of traditional eczema. Other reported culprit dyes include Sudan I, Vacanceine Red,⁵⁰ and Brilliant Lake Red R.⁵¹ Isolated occupational cases from insoluble cutting oils⁵² and paraphenylenediamine⁵³ have also been reported.

Nowadays, Riehl melanosis, which mainly affects the face of middle-aged women ("female facial melanosis") and is caused by sensitizing fragrances and chemicals in cosmetics, is also considered a pigmented contact dermatitis.⁵⁴ Histopathologic studies have shown both increased and decreased epidermal melanin in the involved skin, as well as large amounts of melanin in numerically increased dermal macrophages, because of pigment incontinence due to degenerating keratinocytes.⁴⁵

Finally, topical anthralin (dithranol) and permanganates can cause exogenous nonmelanotic dark brown discoloration, of both an occupational (pharmacists, nurses) and a nonoccupational nature.

Postinflammatory Hyperpigmentation

Brown secondary hyperchromia are postinflammatory and melanic in nature. They often follow phytophotocontact dermatitis (plants containing psoralens), especially if toxic in nature. Hyperpigmentation may persist up to several months.^{46,54,55} Hyperpigmentation also arises after the application of many photosensitizing chemicals, such as drugs (phenothiazines, sulfonamides, nonsteroidal anti-inflammatory drugs). Coal tar derivatives, which are some of the most commonly encountered occupational photosensitizers in the form of dust, vapor, or fumes, induce secondary pigmentation on exposed skin, partly due to melanin deposits and partly to the dyeing effect of coal tar itself.⁵⁶

White and its Nuances

Primary Leukoderma

Primary contact chemical leukoderma (also known as contact leukoderma, contact vitiligo, and chemical vitiligo) presents with white vitiligo-like lesions and is induced by a series of substances that can induce depigmentation with a specific direct melanocytotoxic effect ("primary melanocytopenic leukoderma").^{57–60} Among the causative compounds, phenol and catechol derivatives have been most studied. Hydroxylation of the 4-(*para*) position in phenols and catechols and substitution of a non-polar alkyl side group (in 1- position for hydroquinone) exacerbate the depigmentation. Hydroquinone, although no longer used in cosmetics in Europe, monobenzyl ether of hydroquinone, *p*-tertiary butylphenol, and *p*-tert-butylcatechol are the most common causative molecules in this chemical group. Alkylphenols are used as antioxidant and anticorrosion agents in the industrial sector and are also contained in many commercially available products such as varnishes, adhesives, pesticides, resins, industrial oils, disinfectants, rubber items, and printing inks.⁵⁷

Contact chemical leukoderma is mainly limited to occupational contexts (occupational chemical leukoderma, occupational vitiligo), although a number of nonoccupational cases have been reported. In occupational cases, although the hands and forearms are typically affected because of the use of rubber gloves, depigmentation can extend to distant sites, sometimes symmetrically. The clinical onset occurs weeks to months after the contact; indeed, for depigmentation to occur, the preexisting melanin reservoir must be exhausted and metabolized. Likewise, depigmentation can also affect patch tests site after approximately 4 to 8 weeks.^{61–64} Morphologically, chemical leukoderma usually manifests with "confettillike" macules showing well-defined margins, with a subsequent tendency to coalesce. In most cases, withdrawal of the eliciting factor allows spontaneous progressive repigmentation.^{54,65}

Besides those mentioned previously, in both human and animal *in vivo* studies, many other substances have been reported to cause chemical leukoderma, including sulfhydryls, mercurials, and cinnamic aldehyde.^{54,66,67} The pathogenic mechanism of contact chemical leukoderma is fairly complex, far from completely understood, and shares many features with idiopathic vitiligo. Phenols and catechols are structurally similar to tyrosine, the substrate of tyrosinase that triggers the biochemical pathway for melanin synthesis. Derivatives of these chemical compounds compete with tyrosine for hydroxylation by tyrosinase and therefore interfere with melanin synthesis. It is not yet clear how this leads to further melanocyte apoptosis. A role of tyrosinase in mediating the cytotoxic effect of phenols and catechols has been hypothesized but later has been proved to be incorrect.^{66–69} Recently, another melanocyte-specific enzyme, that is, tyrosinase-related protein 1 (Typr1), has been shown to mediate the action of phenol and catechol derivatives.⁷⁰ Supporting this concept, Typr1 overexpression has been demonstrated in a line of cultured vitiligo melanocytes.⁷¹ Typr1 might act through the conversion of phenols and catechols and contemporary reactive oxygen species generation, the latter exerting oxidative stress on melanocytes.⁶⁶

Differential diagnosis of contact chemical leukoderma encompasses idiopathic vitiligo. However, vitiligo can be associated with ocular disturbances as well as systemic disorders (thyroid disease, diabetes mellitus, alopecia areata, pernicious anemia) and may be familial.^{72,73} Histologic examination is not useful because in these diseases, melanocytes are either depleted or absent.

During the last decade, we have observed 21 cases of contact chemical leukoderma, 18 of which were occupational (unpublished data). In 17 cases, the hands and wrists were involved because of using rubber gloves (Fig. 7), whereas the perilabial region was affected in another case because of contact with a rubber mouthpiece. Among the 3 nonoccupational cases, 2 showed linear horizontal lesions at the upper third of the legs because of contact with the rubber band holding up socks. Our last case featured a single rounded achromic patch in the periumbilical region at the contact point with the jeans' metal button; the patient denied having primary contact dermatitis in the area and a nickel sulfate patch test resulted negative at 48 to 96 hours, with no sign of



Figure 7. Occupational contact chemical leukoderma due to rubber gloves use.

depigmentation 1 month later. In none of these patients was there a personal or family history of vitiligo, and the clinical lesions resolved spontaneously after withdrawal of the causative agents. The patients who developed hypochromia from contact with rubber refused patch tests with phenol and catechol derivatives. In 2 occupational cases that presented lesions of the wrists, an important histologic finding emerged, namely, absence of melanocytes, with mild, noticeable intraepidermal spongiosis. This characteristic could help to orientate a difficult differential diagnosis toward contact chemical leukoderma rather than idiopathic vitiligo.

Postinflammatory Leukoderma

Irritant and allergic contact dermatitis may leave whitish hypochromic lesions; this is the result of the increased keratinocyte mitotic index in the active phase of the dermatitis, which is accompanied by a reduced melanocyte to keratinocyte melanosome transfer (“secondary melanopenic leukoderma”). Nevertheless, a coexistence of hyperchromic and hypochromic outcomes is entirely possible.^{46,74}

Black

Black dermographism, first described by Urbach and Pillsbury⁷⁵ in 1943, is a common phenomenon, although often overlooked. It can be observed at contact sites between skin and metal jewelry (rings, bracelets, necklaces) and is caused by abrasion of the metal by “hard” dusts that are occasionally present on the skin. As a matter of fact, these powders (zinc oxide, pumice, coal), also contained in cosmetics and medicaments, are harder than the metals used in jewelry, such as nickel, iron, platinum, silver, gold, copper, and tin. Coal, also traceable in the environment, is the hardest powder and induces a particularly evident black dermographism because of strong abrasion and its intrinsic staining effect. By contrast, chromium and stainless steel are harder than these abrasive powders, so jewels made of these metals

do not produce this phenomenon. The black color results from free metal particles, so minute that they do not reflect light.^{46,76–79} The term *dermographism* is used improperly because it is not exclusive to the skin, being a physical effect rather than a biologic one, and thus reproducible on paper or tissue. Black dermographism can be easily verified by putting zinc oxide or titanium dioxide powders on the skin and then by rubbing with a gold or silver ring; black lines are immediately evident (Fig. 8).

After exposure to poison ivy, poison oak, and poison sumac, members of the *Toxicodendron* genus (formerly classed as *Rhus*, a benign genus), black spots can occasionally be found in contact dermatitis areas (“black-spot poison ivy dermatitis”). Histologically, the deposited material can be identified in the stratum corneum.⁸⁰ The same black deposit, resembling black enamel paint, can be observed at the injured sites on the plant. The sap tendency to turn black can thus help to identify the plants (black spot test).^{81–83} The black color derives from urushiol (3-pentadecylcatechol), the oleoresin component of poison ivy, a biphenolic compound, which undergoes oxidation and binds to cutaneous proteins, forming black molecules.

Other Colors

Exposure to topical silver salts from occupational or medical sources can induce localized argyria-forming silver speck deposits in the skin that provoke a blue to slate gray stain.⁸⁴

Recurrent contact with mercury, either from medical preparations or after industrial exposure, can cause a gray-brown skin pigmentation.^{85,86} A similar staining can follow exposure to several halogen derivatives of aromatic hydrocarbons, such as dioxin (2,3,7,8-tetrachlorodibenzodioxin) and polychlorinated biphenyls. Clinical manifestations involve the face, neck, and dorsal aspect of the hands. The underlying mechanism has yet to be fully understood; halogenated aromatic hydrocarbons could alter melanocytes through a direct action on tyrosinase, even in the absence of UV exposure.⁸⁷

The staff working in dye factories, particularly those handling finished chemical dyes, can present skin staining, generally superficial and with a variable persistence.⁸⁸

COMMENTARY

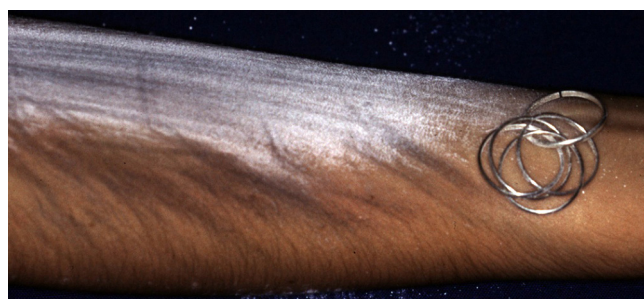


Figure 8. Immediate black dermographism induced by zinc oxide powder application and silver ring rubbing.

Environmental exposure to various chemicals in the occupational and nonoccupational settings can induce skin color alterations. The causal mechanisms vary; in most cases, the physiologic skin chromophores are involved (melanin, oxyhemoglobin, deoxygenated hemoglobin), at times with concurrent UV radiation, whereas in other cases, exogenous pigments are deposited in the skin.

As discussed previously regarding the different clinical presentations, 2 fundamental considerations emerge; first, skin colors can at times indicate the etiology of contact dermatitis. Second, besides numerous morphologic variants, assorted skin colors contribute to the stunning clinical-morphologic polymorphism of contact dermatitis, be it eczematous or noneczematous, which has no equal in the entire dermatological spectrum.

REFERENCES

1. Fitzpatrick TB. The validity and practicality of sun-reactive skin types I through VI. *Arch Dermatol* 1988;124:869–871.
2. Fitzpatrick TB, Bernhard JD, Cropley TG. The structure of skin lesions and fundamentals of diagnosis. In: Freedberg IM, Eisen AZ, Wolff K, et al, eds. *Dermatology in General Medicine*. 5th ed. New York, NY: McGraw-Hill; 1999:13–41.
3. Ortonne JP. La couleur de la peau humaine: de la recherche à l'esthétique. *Ann Dermatol Venereol* 2009;136(Suppl 6):5252–5256.
4. Cox NH, Coulson IH. Diagnosis of skin disease. In: Burns T, Breathnach S, Cox N, et al eds. *Rook's Textbook of Dermatology*. 8th ed. Oxford, United Kingdom: Wiley-Blackwell; 2010:5.1–5.26.
5. Anstey AV. Disorders of skin colour. In: Burns T, Breathnach S, Cox N, et al eds. *Rook's Textbook of Dermatology*. 8th ed. Oxford, United Kingdom: Wiley-Blackwell; 2010:58.1–58.59.
6. Calnan CD. Nickel dermatitis. *Br J Dermatol* 1956;68:229–236.
7. Calnan CD, Wells GC. Suspender dermatitis and nickel sensitivity. *Br Med J* 1956;2:1265–1268.
8. Meneghini CL, Angelini G. *Le Dermatiti da Contatto*. Rome, Italy: Lombardo Ed; 1982.
9. Foti C, Elia G, Filotico R, et al. Purpuric clothing dermatitis due to Disperse Yellow 27. *Contact Dermatitis* 1998;39:273.
10. Hellier FF. Dermatitis purpurica after contact with textiles. *Hautarzt* 1960;11:173–174.
11. Batschvarov B, Minkov DM. Dermatitis and purpura from rubber in clothing. *Trans St Johns Hosp Dermatol Soc* 1968;54:73–78.
12. Calnan CD, Peachey RDG. Allergic contact purpura. *Clin Allergy* 1971;1:287–290.
13. Fisher AA. Allergic petechial and purpuric rubber dermatitis. The PPPP syndrome. *Cutis* 1974;14:25–27.
14. Romaguera C, Grimalt F. PPPP syndrome. *Contact Dermatitis* 1977;3:102–103.
15. Shimunes E. Purpuric allergic contact dermatitis to paraphenylenediamine. *Contact Dermatitis* 1978;4:225–229.
16. Fisher AA. Purpuric contact dermatitis. *Cutis* 1984;33:346, 349, 351.
17. van der Veen JB, Neering H, de Haan P, et al. Pigmented purpuric clothing dermatitis due to Disperse Blue 85. *Contact Dermatitis* 1988;19:222–223.
18. Roed-Petersen J, Clemmensen OJ, Menné T, et al. Purpuric contact dermatitis from black rubber chemicals. *Contact Dermatitis* 1988;18:166–168.
19. Romaguera C, Grimalt F, Vilaplana J. Eczematous and purpuric allergic contact dermatitis from boots. *Contact Dermatitis* 1989;21:269.
20. Bonamonte D, Angelini G. Dermite da contatto purpurica. *Ann Ital Dermatol Allergol* 2001;55:53–61.
21. Ricks MR, Vogel PS, Elston DM, et al. Purpuric agave dermatitis. *J Am Acad Dermatol* 1999;40:356–358.
22. Meneghini CL, Angelini G. Secondary polymorphic eruptions in allergic contact dermatitis. *Dermatologica* 1981;163:63–70.
23. Bruynzeel DP, van den Hoogenband HM, Koedijk F. Purpuric vasculitis-like eruption in a patient sensitive to balsam of Peru. *Contact Dermatitis* 1984;11:207–209.
24. Buckley WR. Lichenoid eruptions following contact dermatitis. *AMA Arch Derm* 1958;78:454–457.
25. Canizares O. Lichen planus-like eruption caused by color developer. *AMA Arch Derm* 1959;80:81–86.
26. Hyman AB, Berger RA. Lichenoid eruption due to colour developer. *Arch Dermatol* 1959;80:243–244.
27. Mandel EH. Lichen planus-like eruptions caused by a color-film developer. *Arch Dermatol* 1960;81:68–71.
28. Fry L. Skin disease from colour developers. *Br J Dermatol* 1965;77:456–461.
29. Meneghini CL. Lichenoid contact dermatitis. *Contact Dermatitis Newsletter* 1971;9:194.
30. Goh CL, Kwok SF, Rajan VS. Cross sensitivity in colour developers. *Contact Dermatitis* 1984;10:280–285.
31. Lidén C. Lichen planus in relation to occupational and non-occupational exposure to chemicals. *Br J Dermatol* 1986;115:23–31.
32. Kawamura T, Fukuda S, Ohtake N, et al. Lichen planus-like contact dermatitis due to methacrylic acid esters. *Br J Dermatol* 1996;134:358–360.
33. Lombardi P, Campolmi P, Sertoli A. Lichenoid dermatitis caused by nickel salts? *Contact Dermatitis* 1983;9:520–521.
34. Lichter M, Drury D, Remlinger K. Lichenoid dermatitis caused by epoxy resin. *Contact Dermatitis* 1992;26:275.
35. Lembo G, Balato N, Patruno C, et al. Lichenoid contact dermatitis due to aminoglycoside antibiotics. *Contact Dermatitis* 1987;17:122–123.
36. Brancaccio RR, Cockerell CJ, Belsito D, et al. Allergic contact dermatitis from color film developers: clinical and histologic features. *J Am Acad Dermatol* 1993;28:827–830.
37. Sidi E, Hincly M, Gervais A. Allergic sensitization and photosensitization to phenergen cream. *J Invest Dermatol* 1955;24:345–352.
38. Epstein S. Allergic photocontact dermatitis from promethazine (phenergen). *Arch Dermatol* 1960;81:175–180.
39. Soto JM. Promethazine photosensitivity. *Contact Dermatitis Newsletter* 1968;3:53.
40. Angelini G. Topical drugs. In: Rycroft RJG, Menné T, Frosch PJ, eds. *Textbook of Contact Dermatitis*. 2nd ed. Berlin, Germany: Springer-Verlag; 1995:477–503.
41. Satanove A. Pigmentation due to phenothiazines in high and prolonged dosage. *JAMA* 1965;191:263–268.
42. Haddad RI. Blue skin pigmentation and chlorpromazine. *J Ky Med Assoc* 1977;75:124–126.
43. Zelikson AS. Skin pigmentation and chlorpromazine. *JAMA* 1965;194:670–672.
44. Hashimoto K, Wiener W, Albert J, et al. An electron microscopic study of chlorpromazine pigmentation. *J Invest Dermatol* 1966;47:296–306.
45. Mosher DB, Fitzpatrick TB, Ortonne JP, et al. Hypomelanoses and hypermelanoses. In: Freedberg IM, Eisen AZ, Wolff K, et al eds. *Dermatology in General Medicine*. 5th ed. New York, NY: McGraw-Hill; 1999:945–1017.
46. Bonamonte D, Angelini G. Disordini pigmentari da contatto. *Ann Ital Dermatol Allergol* 2001;55:1–15.
47. Bonamonte D, Foti C, Angelini G. Hyperpigmentation and contact dermatitis due to *Juglans regia*. *Contact Dermatitis* 2001;44:101–102.

48. Osmundsen PE. Pigmented contact dermatitis. *Br J Dermatol* 1970;83: 296–301.
49. Ancona-Alayón A, Escobar-Márques R, González-Mendoza A, et al. Occupational pigmented contact dermatitis from naphthol AS. *Contact Dermatitis* 1976;2:129–134.
50. Fujimoto K, Hashimoto S, Kozuka T, et al. Occupational pigmented contact dermatitis from azo-dyes. *Contact Dermatitis* 1985;12:15–17.
51. Kozuka T, Tashiro M, Sano S, et al. Brilliant Lake Red R as a cause of pigmented contact dermatitis. *Contact Dermatitis* 1979;5:297–304.
52. Fountain RB. Occupational melanoderma. *Br J Dermatol* 1967;79:59–60.
53. Hamada T, Horiguchi S. Chronic melanodermitis due to the rubber peephole of a ship radarscope. *Contact Dermatitis* 1978;4:245–246.
54. Wattanakrai P, Miyamoto L, Taylor JS. Occupational pigmentary disorders. In: Kanerva L, Elsner P, Wahlberg JE, et al eds. *Handbook of Occupational Dermatology*. Heidelberg, Germany: Springer-Verlag; 2000:280–294.
55. Bonamonte D, Foti C, Lionetti N, et al. Photoallergic contact dermatitis to 8-methoxypsoralen in *Ficus carica*. *Contact Dermatitis* 2010;62:343–348.
56. Emmet EA. Phototoxicity and photosensitivity reactions. In: Adams RH, ed. *Occupational Skin Disease*. 2nd ed. Philadelphia, PA: Saunders; 1990:184–193.
57. Gellin GA, Maibach HI. Chemically induced depigmentation. In: Maibach HI, Lowe E, eds. *Models in Dermatology*. Basel, Switzerland: Karger; 1985: 251–262.
58. Gellin GA, Maibach HI, Misiasek MH, et al. Detection of environmental depigmenting substances. *Contact Dermatitis* 1979;5:201–213.
59. Fisher AA. Differential diagnosis of contact leukoderma and idiopathic vitiligo. Part I. *Cutis* 1994;53:158.
60. Fisher AA. Differential diagnosis of contact leukoderma and idiopathic vitiligo. Part III: occupational leukoderma. *Cutis* 1994;53:278–280.
61. Malten KE, Seutter E, Hara I, et al. Occupational vitiligo due to paratertiary butylphenol and homologues. *Trans St Johns Hosp Dermatol Soc* 1971;57: 115–134.
62. Taylor JS, Maibach HI, Fisher A, et al. Contact leukoderma associated with the use of hair colors. *Cutis* 1993;52:273–280.
63. Kwok C, Wilkinson M, Sommer S. A rare case of acquired leukoderma following patch testing with an acrylate series. *Contact Dermatitis* 2011;64: 292–294.
64. Crépy MN, Bensefa-Colas L, Krief P, et al. Facial leukoderma following eczema: a new case induced by spectacle frames. *Contact Dermatitis* 2011;65: 243–245.
65. Ghosh S, Mukhopadhyay S. Chemical leukoderma: a clinico-aetiological study of 864 cases in the perspective of a developing country. *Br J Dermatol* 2009;160:40–47.
66. Boissy RE, Manga P. On the etiology of contact/occupational vitiligo. *Pigment Cell Res* 2004;17:208–214.
67. Yang F, Boissy RE. Effects of 4-tertiary butylphenol on the tyrosinase activity in human melanocytes. *Pigment Cell Res* 1999;12:237–245.
68. Yang F, Sarangarajan R, Le Poole IC, et al. The cytotoxicity and apoptosis induced by 4-tertiary butylphenol in human melanocytes are independent of tyrosinase activity. *J Invest Dermatol* 2000;114:157–164.
69. Picardo M, Passi S, Nazzaro-Porro M, et al. Mechanism of antitumoral activity of catechols in culture. *Biochem Pharmacol* 1987;36:417–425.
70. Manga P, Sarangarajan R, Ramnath E, et al. 4-(tert)butylphenol cytotoxicity is mediated by tyrosinase related protein-1. *Mol Biol Cell* 2002;13S:306a.
71. Le Poole IC, Yang F, Brown TL, et al. Altered gene expression in melanocytes exposed to 4-tertiary butyl phenol (4-TBP): upregulation of the A2b adenosine receptor 1. *J Invest Dermatol* 1999;113:725–731.
72. Cummings MP, Nordlund JJ. Chemical leukoderma: fact or fancy. *Am J Contact Dermatitis* 1996;6:126–127.
73. Gellin GA. Chemical leukoderma. *Am J Contact Dermatitis* 1996;6:126–127.
74. Meneghini CL, Angelini G. Hypopigmentation following acute contact dermatitis from a match-box. *Contact Dermatitis* 1975;1:55.
75. Urbach E, Pillsbury DM. The phenomenon of black dermographism. *JAMA* 1943;121:485.
76. Hurley HJ. Black dermographism. *Arch Dermatol* 1960;81:329–332.
77. Fisher AA. What causes gold smudge? *Jewelers Circular-Keystone* 1971;141:64.
78. Fisher AA. Black dermographism. A physical phenomenon. *Cutis* 1974;13: 187–189.
79. Rapson WS. Skin contact with gold and gold alloys. *Contact Dermatitis* 1985;15:56–65.
80. Mallory SB, Miller OF, Tyler WB. *Toxicodendron radicans* dermatitis with black lacquer deposit on the skin. *J Am Acad Dermatol* 1982;6:363–368.
81. Mallory SB, Hurwitz RM. Black-spot poison-ivy dermatitis. *Clin Dermatol* 1986;4:149–151.
82. Guin JD. Occupational contact dermatitis to plants. In: Kanerva L, Elsner P, Wahlberg JE, et al eds. *Handbook of Occupational Dermatology*. Berlin, Germany: Springer-Verlag; 2000:730–766.
83. Guin JD. The black spot test for recognizing poison ivy and related species. *J Am Acad Dermatol* 1980;2:332–333.
84. Buckley WR. Localized argyria. *Arch Dermatol* 1963;88:531–539.
85. Burge KM, Winkelmann RK. Mercury pigmentation. An electron microscopic study. *Arch Dermatol* 1970;102:51–61.
86. Kennedy C, Molland EA, Henderson WJ, et al. Mercury pigmentation from industrial exposure. An ultrastructural and analytical electron microscopic study. *Br J Dermatol* 1977;96:367–374.
87. Vierkötter A, Schikowski T, Ranft U, et al. Airborne particle exposure and extrinsic skin aging. *J Invest Dermatol* 2010;130:2719–2726.
88. Buckley WR, West W. Persistent dye staining of the skin. *Arch Dermatol* 1970;102:71–77.