

Cutaneous allergic reactions to tattoo ink

Ravneet Ruby Kaur, BSN, MD,¹ William Kirby, DO, FAOCD,² & Howard Maibach, MD³

¹UCLA-Olive View, Sylmar, CA, USA

²Kirby Dermatology, Beverly Hills, CA, USA

³University of California, San Francisco, CA, USA

Summary

Tattoo artists use many compounds to create tattoo pigment and several allergic reactions can occur as a result of these additives. The compositions of many inks have been identified; however, as new mixtures are created it becomes difficult to identify the specific ingredients in a particular ink. Allergic reactions to a particular pigment can manifest in several ways including allergic contact dermatitis and photoallergic dermatitis. Subsequently, tattoo ink or pigment allergy reactions can be classified as acute inflammatory reactions, allergic hypersensitivities, and granulomatous, lichenoid, and pseudolymphomatous types of reactions. This paper will review the clinical manifestations and the most common compounds associated with cutaneous reactions to tattoo ink.

Keywords: tattoo, allergic contact dermatitis, urticaria, ink allergy, laser

Background

When tattoo ink is injected in the dermis, the ink pigment granules are engulfed by keratinocytes, fibroblasts, and phagocytic macrophages lying under the dermal layers. The ink pigments become encapsulated in fibrous tissue and become less reactive histologically,¹ thus, allergic reactions to tattoo pigments are uncommon. That stated, the introduction of foreign substances into the skin can result in an immunologic reaction. In the case of tattoos, this sensitivity is due to the constituents of the ink pigments or ink as both terms are used interchangeably in the literature.

When ink allergies occur they manifest clinically with pruritis, localized edema, an eczematous eruption with serous drainage, or rarely an exfoliative dermatitis. They may also appear lichenoid (Fig. 1). Verrucous papules or plaques may be seen rarely (Fig. 2).

Sensitivity to a particular pigment can manifest in several ways including allergic contact dermatitis and photoallergic dermatitis. Furthermore, tattoo ink reactions can be classified as acute inflammatory reactions, allergic hypersensitivities, and granulomatous, lichenoid, and pseudolymphomatous types of reactions. Histology shows acanthosis, spongiosis, and a lymphocytic perivascular infiltrate.

Components of ink

Tattoo artists use numerous compounds to create pigment. The exact chemistry of some formulations has been identified; however, as new mixtures are created it remains difficult to identify the specific ingredients in a particular ink.² One study used light and transmission electron microscopy with x-ray microanalysis to examine the pigment and found several metallic elements including aluminum, iron, calcium, titanium, silicon, mercury, and cadmium in the red dyes, which could cause allergic reactions.^{3,4}

Professional and amateur tattoos differ in their physical and chemical composition of ink: Amateur tattoos

Correspondence: Ravneet Ruby Kaur, BSN, MD, 14445 Olive View Dr, Department of Medicine #2B182, Sylmar, CA, USA. E-mail: rubyk@ucla.edu

Accepted for publication August 16, 2009



Figure 1 Lichenoid reaction to red ink in a black and red tattoo.



Figure 2 Ink allergy—reaction to blue ink with a palpable plaque, erosions and localized edema.

tend to use elemental carbon particles compiled from cigarette ash, pencil particles, graphite, or inks, such as India ink. Professional artists often incorporate organic dyes mixed with insoluble metallic elements. They have a propensity to mix pigments to achieve a desired color^{5,6} (see Table 1).

Granulomatous and lichenoid reactions

Granulomatous and lichenoid hypersensitivity reactions may also occur but both are less common than eczematous reactions.⁷ Granulomatous reactions are

most commonly associated with mercury (red pigment)⁸ and consist of a collection of epithelioid cells, lymphocytes, and a few giant cells. Unlike eczematous hypersensitivity tattoo reactions which have patch tests that may be positive, granulomatous and lichenoid tattoo reactions are more commonly associated with negative patch test results. A granulomatous reaction seen in violet areas of a tattoo contained aluminum particles⁹ and permanent eyeliner tattoos are also reported to cause granulomatous reactions.^{10,11}

Lichenoid reaction is thought to be a T-cell mediated reaction and the lymphocytic T-cell infiltrate may simulate a graft-versus-host response.^{12,13} Clinically, verrucous papules or plaques characteristic of hyperkeratotic lichen planus are usually seen but are limited to the red portion of the tattoo. However, one patient reportedly developed a generalized lichen planus reaction.

Pseudolymphomatous reactions

Another form of delayed reaction to tattoo pigment may lead to a pseudolymphomatous reaction. First published by Ullmann in 1903,¹⁴ the mechanism remains unknown. In the few published cases, the infiltrate is localized to the red area of the tattoo. Lymphadenosis benigna cutis (pseudolymphoma) can develop after injection of an antigen, persistent nodular arthropod bites, wearing of earrings, and in association with tattoo pigments.^{15,16} Likely, chronic antigen stimulation caused by the red exogenous pigment is the cause as the dye acts as an antigen leading to a proliferation of lymphoid cells. The incubation period varies from a few weeks to 12 years.¹⁷

Pseudolymphoma is characterized by red to violet indurated nodules and plaques which are clinically similar to cutaneous B-cell lymphoma. Knowledge of this type of reaction to tattoo pigment may prevent a mistaken diagnosis of lymphoma. Histology can be used to differentiate pseudolymphoma from cutaneous lymphoma. Important features of a pseudolymphoma include germinal centers, a mixed cell infiltrate, prominent vasculature, and predominant involvement of the upper dermis compared with the lower dermis. Immunohistochemistry reveals that lymphocytes in pseudolymphoma are primarily polyclonal.¹⁸

Hypersensitivity reactions

In addition, contact urticaria is another reaction thought to be triggered by tattoo placement. In one

Table 1 Composition of tattoo pigments⁴¹

Tattoo ink/ pigment color	Ingredient	Comments and relevant information
Black	Iron Oxide Carbon Logwood	Natural black pigment is made from magnetite crystals, powdered jet, wustite, bone black, and carbon. Black pigment from carbon is commonly made into India ink. Logwood is extracted from <i>Haematoxylon campechisnum</i> in Central America and the West Indies. Black tattoo pigments are extremely rarely associated with allergic reaction; however, there have been a handful of cases reported. ²⁶ Most amateur tattoos are black accounting for the low frequency of allergic reactions seen with amateur tattoos.
Brown	Ochre (Ferric oxide)	Ochre is composed of ferric oxides mixed with clay. When heated ochre changes from yellow to a reddish color.
Red	Cinnabar/Mercuric sulfide Cadmium Red Iron Oxide/Common Rust Naphthol-AS pigment	Reactions most commonly occur to red pigments which may be caused by a variety of components, particularly mercury sulfide (cinnabar). ^{12,19,27} Cinnabar and cadmium pigments are toxic. Naphthol red is least reported to cause reactions. Mercury in red pigment causes most lichenoid tattoo reactions. ²⁸ In 1976, the Food and Drug Administration limited mercury in tattoo dyes to 3 ppm. Despite this restriction, allergic reactions to the red pigments still occur. ²⁹ Patch testing for mercuric chloride may show a positive reaction but is not reliable for cinnabar.
Yellow	Cadmium Yellow Ochres Curcuma Yellow Chrome Yellow (PbCrO ₄ , often mixed with PbS)	Yellow pigments rarely cause allergic reactions but when they occur, they are more often photo-aggravated/toxic reactions due to cadmium sulfide (a light-sensitive material). ³⁰ Thus, upon exposure to sunlight, the area with yellow pigments may develop edema and erythema. ^{31,32} Red tattoos have also been associated with photo-aggravated reaction, but it is likely related to a cadmium additive used to brighten the red pigment. ³² Curcuma is derived from tumeric or curcumin.
Green	Chromic Oxide (Casalis Green or Anadomis Green) Lead chromate Phthalocyanine dyes Ferrocyanides and Ferricyanides	Greens pigments may be mixtures, such as potassium ferrocyanide (yellow or red) and ferric ferrocyanide (Prussian Blue). Allergies to green and light-blue pigments are less common but when they do occur they are often related to chromium, aluminum or chloride cobalt additives. ^{19–21,30,33,34} Chromium has been associated with local eczematous reactions, hand eczema and generalized eczematous eruptions. ³³ Patch testing may be positive for 0.5% potassium dichromate.
Blue	Azure Blue Cobalt Blue Copper phthalocyanine Cobalt aluminate	Blue pigments from minerals include copper carbonate, sodium aluminum silicate (lapis lazuli), calcium copper silicate (Egyptian Blue), other cobalt aluminum oxides and chromium oxides. The blues and greens least likely to cause allergic reaction are copper phthalocyanine pigments which are more stable than cobalt or ultramarine pigments. Copper phthalocyanine pigments have FDA approval for use in contact lenses and infant toys and furniture.
Violet (purple)	Manganese ammonium pyrophosphate Various aluminum salts Dioxazine/carbazole	Some purple pigments, especially bright magentas, are photoreactive and lose their color after prolonged exposure to light. Dioxazine and carbazole result in the most stable purple pigments. It is not confirmed, but manganese may cause granulomatous allergic reactions in some purple tattoos. ^{9,35}
White	Lead carbonate Titanium dioxide Barium sulfate Zinc Oxide	Titanium oxides are one of the least reactive white pigments with no described allergic reactions. ³⁶ White pigment may be used alone or to dilute the intensity of other pigments.
Henna	Henna dye and paraphenylene-diamine (PPD)	Temporary henna tattoos involve painting henna dye onto the skin to obtain a brownish stain. Henna itself is safe. PPD, a textile dye and common industrial allergen, is often mixed into temporary henna tattoos and can cause a contact dermatitis. ^{37–40}

case, a hypersensitivity to the cobalt chloride contained in blue ink was the cause. Patch testing was positive for only chloride cobalt and this was thought to be through a nonimmunological mechanism.¹⁹ A release of chemical mediators including histamine, prostaglandins, leukotrienes and others was observed without antibody involvement. The presence of eosinophilic cells in the infiltrate suggests an allergic response as well. Cobalt salts are frequently used as a color indicator in provocative sweat testing. Many patients will develop a non-immunologic contact urticaria (NICU) to cobalt salts and thus it is likely that cobalt will produce a transient NICU in most patients.²⁰ Bjornberg previously described a hypersensitivity allergic reaction to cobalt in light-blue pigment.²¹ It has been suggested that there is also the rare appearance of pure immunologic contact urticaria as evidenced by clearing of the urticaria when the tattoo is removed. The hypothesis was confirmed when surgical removal of the tattoo led to resolution of urticarial symptoms.¹⁹ This is important as some cases of "idiopathic" urticaria may actually be related to tattoo pigment hypersensitivity. Tattooed patients experiencing urticarial signs and symptoms may want to consider allergy testing, consisting of, open, prick, or possibly intradermal testing for an immediate type reaction and IgE hypersensitivity. Should another patient present with this same condition, Koch's postulates would be completed by a cobalt challenge test after clearing.

Localization of disease in tattoos

Localization of skin disease in tattoos has also been documented; there have been recent reports of keratoacanthomas, as well as melanomas, verrucas, and reticulosarcomas at the site of tattoos.^{3,22} In eight patients with 11 keratoacanthomas, the authors found that red tattoo ink was associated with 82% of the keratoacanthomas. They concluded that the association with red tattoo ink suggests a form of hypersensitivity associated with adnexal hyperplasia.²²

Hypersensitivity after laser treatment of tattoos

A patient with an allergic reaction to tattoo ink may present requesting removal via the gold standard of treatment for a tattoo, the Q-switched laser. Not only is Q-switched laser treatment not indicated for removing tattoos showing signs of allergic reactions but, ironically, in some cases, tattoos not displaying the signs of a cutaneous allergy may show signs of hypersensitivity

after Q-switched laser treatment as light from a Q-switched laser can stimulate an allergic response.²³ Before laser treatment, tattoo pigment is localized within perivascular fibroblasts, mast cells, and macrophages. After Q-switched laser treatment, rapid thermal expansion fragments the pigment-containing cells causing the pigment to become extracellular. This extracellular ink may be released into the vascular supply and thus recognized as foreign by the immune system causing a hypersensitivity response. Anaphylactic shock is thus also a rare possibility.

Treatment of cutaneous reactions to tattoo ink

Treatment of cutaneous allergic reactions to tattoo ink clearly depends on the severity of the signs and symptoms. Conservative treatment options include topical, oral, and/or intralesional steroids, oral anti-histamines, and protection from UV light. NICU are not completely understood but are thought to be related to the degranulation of mast cells and basophils which occurs independently of IgE receptor activation. Leukotriene formation as well as histamine release may also be involved and thus oral anti-histamines may be helpful.²⁴ Destruction methods include cryotherapy, electrosurgery, surgical excision, dermabrasion, chemical destruction via acid, or ablation via a non-Q-switched laser such as carbon dioxide device. Additionally, a new technology consisting of encapsulating tattoo pigments in polymethyl methacrylate (PMMA) polymer beads, just a few microns in size, are being developed. These new micro-polymer pigments contain components like brown iron-oxide and orange beta-carotene which are easier to remove and cause less allergic reactions by minimizing the possibility of pigments leaking out into the dermis unlike standard tattoos.

Conclusion

Lastly, there are many presentations of cutaneous and allergic reactions to tattoo ink. It is very important for physicians to be aware of these reactions and the possibility of causing further reactions through treatment with laser or other modalities. Also, although unrealistic in practicality, it may be prudent for tattoo artists to perform a patch test for the more commonly reported allergens prior to placing a tattoo. Testing patients with a history of chemical intolerance might buoy a more realistically reached goal. However, in patients without a history of intolerance to metals there

is a risk of active sensitization through patch/intradermal testing. The dermatologist and allergist can help identify the chemical involved with patch and intradermal testing. Making such patch and intradermal antigens available from an "allergen bank", such as Klaus Andersen's in Odense, Denmark, would render an important public service.²⁵

References

- Kilmer SL. Laser treatment of tattoos. *Dermatol Clin* 1997; **15**: 409–17.
- Kuperman-Beade M, Levine V, Ashinoff R. Laser removal of tattoos. *Am J Clin Dermatol* 2001; **2**: 21–5.
- Sowden JM, Byrne JP, Smith AG, Hiley C, Suarez V, Wagner B, Slater DN. Red tattoo reactions: x-ray microanalysis and patch test studies. *Br J Dermatol* 1991; **124**: 576–80.
- Slater D, Durrant T. Tattoos: light and transmission electron microscopy studies with X-ray microanalysis. *Clin Exp Dermatol* 1984; **9**: 167–73.
- Sweeney S. Tattoos: a review of tattoo practices and potential treatment options for removal. *Curr Opin Pediatr* 2006; **19**: 391–5.
- Taylor C, Anderson R, Gange R, Michaud NA, Flotte TJ. Light and electron microscopic analysis of tattoos treated by Q-switched ruby laser. *J Invest Dermatol* 1991; **97**: 131–6.
- Wollina U, Gruner M, Schonlebe J. Granulomatous tattoo reaction and erythema nodosum in a young woman: common cause or coincidence? *J Cosmet Dermatol* 2008; **7**: 84–8.
- Ravits HG. Allergic tattoo granuloma. *Arch Dermatol* 1962; **86**: 287–9.
- McFadden N, Lyberg T, Hensten-Pettersen A. Aluminum-induced granulomas in a tattoo. *J Am Acad Dermatol* 1989; **20**: 903–8.
- Ro YS, Lee CW. Granulomatous tissue reaction following cosmetic eyebrow tattooing. *J Dermatol* 1991; **18**: 352–5.
- Vagefi MR, Dragan L, Hughes SM, Klippenstein KA, Seiff SR, Woog JJ. Adverse reactions to permanent eyeliner tattoo. *Ophthal Plast Reconstr Surg* 2006; **22**: 48–51.
- Winkelmann RK, Harris RB. Lichenoid delayed hypersensitivity reactions in tattoos. *J Cutan Pathol* 1979; **6**: 59–65.
- Clarke J, Back MM. Lichenoid tattoo reactions. *Br J Dermatol* 1979; **100**: 451–4.
- Ullmann J. Über eigentümliche Geschwulstbildung in einer Tätowierungsmarken. *Monatsch prakt Dermatol* 1903; **37**: 49–52.
- Blumental G, Okun MR, Ponitch JA. Pseudolymphomatous reaction to tattoos. Report of three cases. *J Am Acad Dermatol* 1982; **6**: 485–8.
- Zinberg M, Heilman E, Glickman F. Cutaneous pseudolymphoma resulting from a tattoo. *J Dermatol Surg Oncol* 1982; **8**: 955–8.
- Lubach D, Hinz E. Pseudolymphomatöse Reaktion in einer Tätowierung. *Hautarzt* 1986; **37**: 573–5.
- Rijlaarsdam JU, Bruynzeel DP, Vos W et al. Immunohistochemical studies of lymphadenosis benigna cutis occurring in a tattoo. *Am J Dermatopathol* 1988; **10**: 518–23.
- Bagnato GF, De Pasquale R, Glacobbè O, Chirico G, Ricciardi L, Gangemi S, Purello d'Ambrosio F. Urticaria in a tattooed patient. *Allergol et immunopathol* 1992; **27**: 32–3.
- Smith JD, Odom RB, Maibach HI. Contact urticaria from cobalt chloride. *Arch Dermatol* 1975; **111**: 1610–1.
- Bjornberg A. Allergic reaction to cobalt in light-blue tattoo markings. *Acta Derm Venereol* 1961; **41**: 259.
- Fraga GR, Prossick TA. Tattoo-associated keratoacanthomas: a series of 8 patients with 11 keratoacanthomas. *J Cutan Pathol* 2009. Mar 19. [Epub ahead of print] PMID: 19302572
- Ashinoff R, Levin VJ, Soter NA. Allergic reactions to tattoo pigment after laser treatment. *Dermatol Surg* 1995; **21**: 291–4.
- Grattan CE, Humphreys F; British Association of Dermatologists Therapy Guidelines and Audit Subcommittee. Guidelines for evaluation and management of urticaria in adults and children. *Br J Dermatol* 2007; **157**: 1116–23.
- Andersen KE, Paulsen E. Concordance of patch test results with four new TRUE test allergens compared with the same allergens from Chemotechnique. *Contact Derm* 2009; **60**: 59.
- Bhogal RH, Thomas SS. Necrotizing black tattoo reaction: what's in a name? *Am J Clin Dermatol* 2009; **10**: 131–3.
- Bendsoe N, Hansson C, Sterner O. Inflammatory reactions from organic pigments in red tattoos. *Acta Derm Venereol* 1991; **71**: 70–3.
- Taaffe A, Wyatt EH. The red tattoo and lichen planus. *Int J Dermatol* 1980; **19**: 394–6.
- Duke D, Urioste S, Dover J, Anderson RR. A reaction to a red lip cosmetic tattoo. *J Am Acad Dermatol* 1998; **39**: 488–90.
- Bjornberg A. Reactions to light in yellow tattoos from cadmium sulfide. *Arch Dermatol* 1963; **88**: 267.
- Kazandjieva J, Tsankov N. Tattoos: dermatological complications. *Clin Dermatol* 2007; **25**: 375–82.
- Nguyen LQ, Allen HB. Reactions to manganese and cadmium in tattoos. *Cutis* 1979; **23**: 71–2.
- Tazelaar DJ. Hypersensitivity to chromium in a light-blue tattoo. *Dermatologica* 1970; **141**: 282–7.
- Bjornberg A. Allergic reaction to chrome in green tattoo markings. *Acta Derm Venereol* 1959; **39**: 23–9.
- Schwartz RA, Mathias CG, Miller CH, Rojas-Corona R, Lambert WC. Granulomatous reaction to purple tattoo pigment. *Contact Derm* 1987; **16**: 198–202.
- Ross E, Yashar S, Michaud N. Tattoo darkening and non-response after laser treatment: a possible role for titanium dioxide. *Arch Dermatol* 2001; **137**: 33–7.

- 37 Gallo R, Parodi A, Cozzani E, Guarrera M. Allergic reaction to India ink in a black tattoo. *Contact Derm* 1998; **38**: 346–7.
- 38 Sonnen G. Type IV hypersensitivity reaction to a temporary tattoo. *Proc (Bayl Univ Med Cent)* 2007; **20**: 36–8.
- 39 Ramírez-Andreo A, Hernández-Gil A, Brufau C, Marín N, Jiménez N, Hernández-Gil J, Tercedor J, Soria C. Allergic contact dermatitis to temporary henna tattoos. *Acta Dermosifiliogr* 2007; **98**: 91–5.
- 40 Onder M. Temporary holiday “tattoos” may cause lifelong allergic contact dermatitis when henna is mixed with PPD. *J Cosmet Dermatol* 2003; **2**: 126–30.
- 41 About.com: Chemistry [Online]. 2009. [cited 2009 June 15]; Available from URL: <http://chemistry.about.com/library/weekly/aa121602a.htm>.