ORIGINAL ARTICLE

Rising Concern over Cosmetic Tattoos

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BACKGROUND A rise in popularity of cosmetic tattoos has led to an increase in adverse reactions. Due to more pressing concerns, the Food and Drug Administration (FDA) has not traditionally enforced its authority over tattoo inks.

OBJECTIVE To raise awareness of the dangers of cosmetic tattoos.

MATERIALS AND METHODS We reviewed FDA policies regarding tattoo ink, different ink components, adverse reactions, and various treatment options for cosmetic tattoo removal.

RESULTS AND CONCLUSION An increase in consumer complaints has prompted FDA investigation into tattoo inks and their safety. It is important that further complications be reported to the FDA to promote regulation of cosmetic tattoo inks.

The authors have indicated no significant interest with commercial supporters.

Cosmetic tattoos, often referred to as permanent makeup, have become increasingly popular since the late 1970s. Permanent makeup is generally used to replace traditional temporary eye liner, lip liner, blush, or eyebrow pencil. Individuals may choose to undergo cosmetic tattooing to save time or as an adjunct to reconstructive surgery, commonly after breast surgery. Cosmetic tattoos may also be applied to camouflage conditions such as vitiligo or alopecia. Although cosmetic tattoos are intended to enhance facial features, they ironically do not age well. For example, a lip liner tattoo that once traced a youthful full lip will become displaced outside the lip's border as the lip thins with age.

The process by which tattoo inks are injected into the dermis to give the appearance of temporary makeup is called micropigmentation. Currently, a variety of professionals and nonprofessionals, including physicians, nurses, cosmetologists, estheticians, and makeup artists, perform micropigmentation. There is also variability in the setting in which these procedures are performed, the methods of anesthesia, sterility, and artistic ability. With the gain in popularity of micropigmentation, societies such as the American Academy of Micropigmentation have been established to improve the quality of practice through a certification process in this technique.

Tattoo Regulation

The pigments in tattoo inks contain color additives, which are defined as any material that can impart color to a food, a drug, a cosmetic, a medical device, or the human body. The color additives used in inks require premarket approval under the federal Food, Drug, and Cosmetic Act to ensure that they are used safely and appropriately. Approved color additives are listed in the U.S. Code of Federal Regulations (21 CFR Parts 73, 74, 82), but this approval does not extend to injected use. No color additives are Food and Drug Administration (FDA)

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approved for injection into the skin (21 CFR 70.5b) (www.fda.gov). Therefore, no tattoo pigments are approved for use. The majority of tattoo ink is industrial-grade color intended for use as printer ink or automobile paint. Although tattoo ink is subject to regulation by the FDA, state and local health authorities regulate the practice of tattooing, including those performed in salons and tattoo parlors. These departments mainly regulate sanitation requirements and prohibit tattooing minors.

In the past, tattoo ink regulation has not been a priority because of other, more-pressing public health concerns. The FDA has not traditionally enforced its authority over tattoo inks or the pigments found within them, but in recent years, there has been increasing concern regarding adverse reactions to tattoo ink pigment.

Tattoo Pigment Components

Tattoo pigments are composed of inorganic and synthetic organic pigments (Table 1).[1] Inorganic tattoo pigments come from mineral sources such as metal oxides, salts, and minerals. Magnetite ($FeO{\cdot}Fe_2O_3$) and charcoal (C) are often found in black tattoo ink; hematite (Fe_2O_3) and cinnabar (HgS) are used in red ink; limonite ($FeO{\cdot}OH{\cdot}nH_2O$) is used for yellow pigment; corundum (Al_2O_3), rutile (TiO_2), and zincite (ZnO) are used for white pigment, and blue pigment can be achieved with ferric ferrocyanide ($Fe_4[Fe(CN)_6]_3$) and cobaltous aluminate ($CoAl_2O_4$). These compounds are naturally occurring, but they may fade or change color over time. Mercury and cadmium salts are no longer found in tattoo inks because of their toxicity. Synthetic organic pigments, such as anthraquinone (yellow), phthalocyanine (blue, green), azo (mostly yellow, orange, red, magenta, purple), and indigoid (violet–blue), are synthesized chemical compounds that create brighter, more-diverse colors. Newer fluorescent inks may even glow under black light. In addition to pigment, tattoo inks contain diluents and preservatives, such as glycerin or ethanol, which facilitate the dyeing process in the skin.

TABLE 1. Tattoo Pigment Components

Color	*Pigment*
Red	Mercury sulfide (cinnabar), cadmium selenide (cadmium red), sienna (red ochre, ferric hydrate and ferric sulfate), azo dyes, hematite
Yellow	Cadmium sulfide (cadmium yellow), ochre, curcumin yellow, azo dyes, limonite, anthraquinone
Green	Chromium oxide (casalis green), hydrated chromium sesquioxide (guignet green), malachite green, lead chromate, ferro-ferric cyanide, curcumin green, phthalocyanine dyes (copper salts with yellow coal tar dyes)
Blue	Cobalt aluminate (azure blue), phthalocyanine, ferric ferrocyanide, indigoid
Violet	Manganese violet, indigoid
White	Titanium dioxide, zinc oxide, corundum
Tan	Iron oxides
Brown	Ochre
Black	India ink, carbon, iron oxide, logwood extract, magnetite

Adverse Reactions

Between 1988 and 2003, only five cases of adverse reactions were reported to the FDA. More recently, there has been a tremendous increase in consumer complaints, with more than 150 adverse reactions to permanent makeup procedures reported to the FDA in 2003 and 2004. The FDA and Centers for Disease Control and Prevention (CDC) identified 101 of these patients as having adverse reactions at their tattoo sites. The most commonly reported reactions were tenderness and itching associated with allergic reactions and bumps secondary to granulomatous reactions.[2] After investigation by the FDA and CDC, it was found that most of these reactions were due to tattoo ink manufactured by a single company (Premier Products, Arlington, TX). The company voluntarily recalled the associated ink pigments in September 2004. This has prompted FDA investigation of tattoo ink safety at the National Center for Toxicological Research. This laboratory is currently investigating the chemical composition of tattoo inks, how the body metabolizes them, short- and long-term safety, and interactions with light and lasers. It has been found that azo pigments, such as pigment red (PR) 9, PR 22, and pigment yellow 74, decompose into known carcinogens with exposure to light and laser irradiation.[3,4]

Safety risks of unsterilized needles in tattoos have been well established, but studies are lacking on the safety of the tattoo ink itself. Several histologic reactions to tattoo ink have been described, including pseudolymphomatous,[5] lichenoid,[6] granulomatous,[5,7,8] mild acanthosis,[9] scleroderma-like,[10] pseudoepitheliomatous hyperplasia,[11,12] and allergic contact dermatitis.[13] The lichenoid pattern is the most common and is thought to represent a delayed hypersensitivity reaction.[14] Coincidental lesions such as sarcoidosis,[15,16] B-cell lymphoma,[17] pseudolymphoma,[18,19] melanoma,[20–22] basal cell carcinoma,[23] non-Hodgkin's lymphoma,[24] and squamous cell carcinoma[25,26] have also been reported to occur. Magnetic resonance imaging (MRI) may interact with tattoo ink, causing irritation.[27] Nevertheless, MRI is still recommended when indicated regardless of the presence of a cosmetic tattoo. Tattoo pigment may complicate evaluation of metastatic disease in people with malignant melanoma by migrating into regional lymph nodes, mimicking metastases.[28,29]

Red pigment is most commonly implicated in adverse reactions, but the safety of tattoo pigment components for injection into the skin is not well established because no tattoo ink or additive is FDA approved. Mercury contained in red mercuric sulphide (cinnabar) is well known to be the causative agent of allergy in red tattoos.[9,30,31] Mercury-free dyes such as cadmium red (cadmium selenide), sienna and red ochre (ferric hydrate), and organic vegetable dyes (e.g., Brazilwood) have largely replaced mercury-containing dyes, but inflammatory responses to mercury-free pigments still occur.[11,31–33]

Some manufacturers promote alcohol- and preservative-free tattoo inks, but these inks run the risk of microbial contaminants. In 2004, Starbrite Colors tattoo inks were taken off the market in Belgium because of microbial contamination with *Pseudomonas aeruginosa* and Acremonium mold (www.fda.gov/downloads/AboutFDA/Transparency/Basics/UCM246800.pdf).

Treatment of Tattoos

The removal of cosmetic tattoos, similar to treatment of other decorative tattoos, is often more costly and complicated than their original acquisition. Laser treatment requires multiple painful sessions that are expensive and sometimes incompletely successful. With an increase in the number of ink colors, tattoo removal is becoming increasingly difficult.

Historically, removal of undesired tattoos included tissue-destructive techniques such as dermabrasion and salabrasion,[34–37] cryosurgery,[38] electrosurgery,[39,40] and surgical excision.[41,42] Although effective at removing the tattoo ink, these treatments often led to scarring and unwanted skin pigmentation changes. Thus, more-specific (laser) technologies that minimize untoward side effects have replaced them. Early laser systems (e.g., ruby,[43] carbon dioxide [CO_2],[44] argon[45]) were initially used to vaporize tattooed skin, but they also resulted in significant scarring and hypopigmentation. Intense pulsed light devices also lead to scarring and are not appropriate for tattoo removal.[46] The concept of selective photothermolysis revolutionized the treatment of tattoos by preferentially targeting the tattoo pigment with specific wavelengths and pulse durations of laser light that the tattoo ink particles selectively absorb while adjacent structures are left essentially unharmed.[47] Tattoo ink particles are small and therefore require Q-switched (QS) laser systems with brief

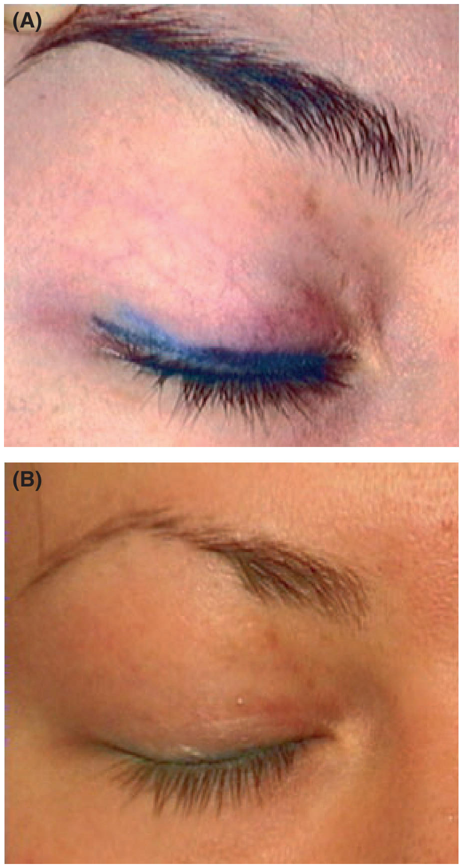

Figure 1. (A) Eye liner cosmetic tattoo before treatment. (B) Resolution of tattoo after Q-switched alexandrite laser treatment.

(nanosecond) pulse durations. The high energy delivered over an ultrashort time period results in shattering of the ink particles, which are then engulfed by tissue macrophages and cleared by the lymphatic system or through transepidermal elimination.

The QS 694-nm ruby laser was the first laser to selectively destroy tattoo ink without peripheral tissue damage. Other QS lasers such as the 532- and 1,064-nm neodymium-doped yttrium aluminum garnet (Nd:YAG) and 755-nm alexandrite lasers allow for removal of a variety of tattoo ink colors (Figure 1). Red ink absorbs the 532-nm Nd:YAG laser, and the red and infrared wavelengths of the 755-nm alexandrite and 1,064-nm Nd:YAG lasers are each effective for the treatment of black, blue, and green inks.[48,49]

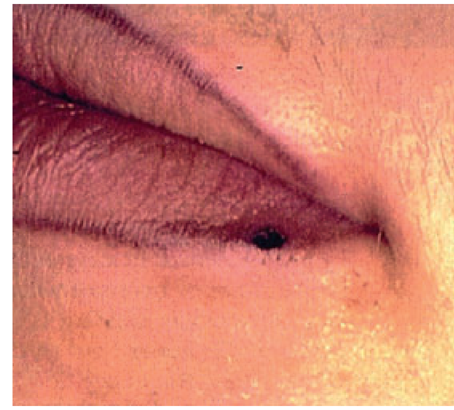

Figure 2. Tattoo ink darkening in permanent lip liner after Q-switched laser irradiation.

Cosmetic tattoos can be more difficult to treat because they generally contain red, brown, flesh-colored, and white inks containing iron oxides and titanium dioxide, which may turn irreversibly black after QS laser irradiation (Figure 2).[50] Chemical reduction of ferric oxide to ferrous oxide is thought to be responsible for the potentially permanent darkening of tattoos. It is impossible to predict which pigments will darken upon QS laser irradiation or if the darkened pigment will respond to further laser treatment. Therefore, one must proceed with caution when using QS lasers to treat pale-colored tattoo pigments containing metallic oxides and properly educate patients of their risks. Nevertheless, it is possible to treat the paradoxical darkening with continued QS laser treatments.[51] To preclude paradoxical darkening, alternative treatments may include pulsed CO_2[52] and erbium-doped YAG lasers,[53] which have been shown to be effective in vaporizing red, pink, and flesh-colored cosmetic tattoos. Newer techniques for tattoo removal involve combinations of QS pigment-specific (red and infrared) lasers with ablative fractional laser resurfacing, which have been reported to enhance the rate of pigment clearance and decrease risk of vesiculation.[54] Other novel technologies include the picosecond laser, which has been shown to be better in tattoo pigment clearance than the nanosecond lasers in Yorkshire pigs.[55]

Conclusions

A rise in the number of cosmetic tattoo procedures being performed has prompted further FDA investigation of tattoo ink safety. Adverse reactions to tattoo inks are becoming more common, and the number of complaints is likely greatly underreported. Consumers and medical professionals should be encouraged to report adverse reactions from permanent makeup to the FDA to promote FDA regulation of cosmetic tattoo inks (http://www.fda.gov/ora/fed_state/Small_business/sb_guide/regions.htm).

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