More than 17 million Americans suffer from acne vulgaris.\textsuperscript{1} Approximately 80-90\% of all adolescents experience some degree of acne.\textsuperscript{2} Adults are also affected. Acne has been associated with other clinically relevant issues, including depression.\textsuperscript{3} While studies have demonstrated patients’ perceptions about a link between diet and acne,\textsuperscript{3-7} reviews published in or prior to 2005 have not shown a conclusive correlation.\textsuperscript{8-10} In addition, methodological issues have limited conclusions that could be drawn from the literature before 2005. A 2009 review evaluated the published literature on the association between diet and acne risk and severity. Authors showed that dairy products and high-glycemic-index foods increased the risk for acne, whereas the studies did not conclusively demonstrate an association between acne and other foods, such as chocolate or salt.\textsuperscript{11}

**Pathophysiology**

Acne forms as a result of obstruction and inflammation of hair follicles and their accompanying sebaceous glands (pilosebaceous units). Acne can be inflammatory or noninflammatory and may involve colonization of the follicle with bacteria (most commonly *Propionibacterium acnes*). With increased hormonal activity, sebum production and blocking of follicles also increase; the latter leading to closed comedones (whiteheads) or open comedones (blackheads).

**Dairy Products**

Migration studies have demonstrated that as populations shifted toward a more Westernized diet, either through relocation or a local cultural change, the prevalence of acne increased. This trend was observed in Canadian Inuit\textsuperscript{12} who increased their consumption of soda, beef, dairy products, and processed foods, as well as among Okinawan Japanese\textsuperscript{13} who decreased their starch intake and increased their total animal product intake.

Authors of a large case-control study\textsuperscript{14} evaluated the association between milk and acne in the adolescent diets of more than 47,000 nurses. Among participants who had been diagnosed with severe acne as teenagers, those with the highest level of total milk intake (>3 servings per day) reported having acne more frequently, when compared with individuals with the lowest level of intake (≤1 serving per week). This association was strongest (a 44\% increase) for skim milk intake, suggesting fat content was not the determining factor for acne risk. Researchers hypothesized that the hormones found in milk played a role in acne risk.

Two large prospective cohort studies examined the association between diet and acne among 9-15 year-old children, including 6094 girls\textsuperscript{15} and 4273 boys.\textsuperscript{16} For girls, there was a significant association with acne severity for all categories of cow’s milk (total, whole, low-fat, skimmed, and chocolate). For boys, the association was significant for total and skimmed milk. Girls were approximately 20\% more likely to experience severe acne if they consumed ≥2 servings of milk per day, when compared with girls who consumed ≤1 serving of milk per week. Boys were approximately 16\% more likely to experience severe acne if they consumed ≥2 servings of milk per week.
milk per day, when compared with boys who consumed ≤1 serving of milk per week.

A study from 2005 showed that components of milk, other than lipids, have insulin-stimulating abilities. Insulin drives insulin-like growth factor 1 (IGF-1), which in turn increases testosterone and decreases the production of sex hormone-binding globulin (SHBG). Another study observed a positive correlation between levels of IGF-1 and acne.18

**High-Glycemic-Index Foods**

Authors of 2 large cross-sectional studies19 in Papua New Guinea (n=1200) and Paraguay (n=115) found no cases of acne in either population. Researchers speculated that the rural populations’ low-fat and low-glycemic-index diets could be the reason for the absence of acne in these groups.

Authors of a randomized controlled trial20 examined the effect of low-glycemic-load diets on acne risk and insulin sensitivity. Individuals assigned to the low-glycemic-load diet experienced improvement in the mean number of acne lesions, when compared with the control group. In addition, the low-glycemic-load diet group’s mean weight decreased, and insulin sensitivity and SHBG levels increased.21 Increases in SHBG levels correlated with decreased lesion counts. As SHBG levels increase, free androgen levels would be expected to decrease accordingly. These investigative findings support the role of low-glycemic-load diets in influencing hormonal levels, as well as improving insulin sensitivity and acne.20-22

**Fat and Fatty Acid Intake**

Although there have been no published, large, well-controlled studies that examine the effect of fat or fatty acid intake on acne risk, omega-6 fatty acids are pro-inflammatory and their pro-inflammatory mediators have been associated with acne.23 By contrast, omega-3 fatty acids have anti-inflammatory properties24 and may be associated with decreased risk of acne by decreasing IGF-1 levels and follicle inflammation. Typically, Western diets have a low ratio of omega-3 to omega-6 fatty acids, as compared with diets observed in non-industrialized nations.25

Additionally, diets high in saturated fats have been associated with increased IGF-1 levels, while diets that are low-fat and high in fiber have been linked with decreased IGF-1 levels.26

**Chocolate**

In a crossover trial examining the effect of chocolate intake on acne, 65 participants consumed 112g of dairy-free cocoa-enriched bars of chocolate each day for 4 months. Researchers compared the results to the same group’s consumption of chocolate bars without the cocoa enrichment and found no significant difference between the groups.27 Similarly, other intervention trials showed no effect of chocolate on acne.28,29 However, these trials had no control groups and the results were not quantified.

**Conclusion**

Population-based and migration studies have suggested a correlation between diet and acne. Large, well-controlled, observational studies have demonstrated that diets high in dairy products are associated with an increase in the risk for and severity of acne. Researchers have found significant associations between all varieties of cow’s milk and acne. The relationship between milk and acne severity may be explained by the presence in dairy of normal reproductive steroid hormones or the enhanced production of polypeptide hormones such as IGF-1, which can increase androgen exposure, and thus, acne risk. Recent findings also describe an association between a high-glycemic-index diet and longer acne duration. In addition, randomized clinical trials have demonstrated that a low-glycemic-load diet can influence hormonal levels and improve insulin sensitivity and acne. No study has established a positive association between acne and chocolate, saturated fat, or salt intake.

**References**


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**Current Concepts in Laser Tattoo Removal**

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**ABSTRACT**

Today, more than 10% of the Western population has at least 1 tattoo, with prevalence of up to one-fourth in the cohort younger than 30 years of age. Many of these individuals come to regret their decision within months due to several reasons, often socially-related, and seek medical treatment. The discovery of selective photothermolysis has enabled the targeted destruction of tattoo pigments with only minimal damage to the surrounding tissue and limited risk of adverse effects, which contrasts previously used nonspecific methods. This treatment modality requires laser pulses of short durations (nanoseconds) and high intensities. However, the inappropriate use of laser parameters, such as inadequate pulse duration, can unnecessarily increase the incidence of permanent adverse effects. This article provides an overview of applicable laser systems and therapeutic strategies for optimized tattoo removal.

**Key words:** adverse reactions, intense pulsed light source, IPL, laser, Q-switched, quality-switched, tattoo removal

Tattooing as a means of body art dates back to the early beginnings of modern civilization. In recent years, there has been a remarkable increase in the number of individuals seeking this permanent form of skin embellishment, especially in the population under 30 years of age. A study in 2004 reported a prevalence of 24% among college students in the US. The proliferating popularity of tattoos has correspondingly given rise to an increase in requests for their removal. The various motivating reasons behind tattoo regret include social stigmatization, familial pressure, a desire to improve career opportunities, and maturity-related factors. On average, tattoo removal is initiated after 14 years of remorse, but it can occur within months.

Tattoos consist of small particles of pigment situated in the dermis of the skin. These pigments are mainly found intracellularly, but small extracellular aggregates are also present, ranging in size from about 0.1-10 µm in interstitial space.

Not all tattoos are decorative. Certain events can lead to unintentional exogenous pigmentation (e.g., embedded gunpowder or dirt particles from the road following an accident) that can result in esthetically displeasing skin discolorations.

**Mechanisms of Laser Tattoo Removal**

With laser removal, tattoo pigment particles can be selectively destroyed without harming the surrounding tissue by means of selective photothermolysis. This requires the correct choice of laser parameters, including wavelength, radiant exposure, and pulse duration of the laser applied. Three main laser-induced mechanisms are involved in the targeted destruction of inoculated tattoo pigments. Firstly, the ink molecules must absorb the laser light in order to convert a sufficient amount of light energy to heat within the pigment particle. Usually, the type of tattoo pigment in the skin and its absorption spectrum is unknown to both the patient and physician. Transient skin whitening after laser treatment (lasting up to 30 minutes) can serve as an indicator of proper light absorption by the pigments. Secondly, the radiant exposure of the applied laser pulses must be high enough (approximately $10^7$ W/cm²) in order to generate a sufficiently high temperature increase in the color pigment particle. If treated properly, particles will reach very high absolute temperatures of several hundred degrees Celsius. Thirdly, the pulse duration must be in the range of nanoseconds (ns) due to the size of the tattoo pigment particles (a few microns).

**Q-switched Lasers**

High intensity, ultra-short pulse durations are provided only by a special laser technique known as “Q-switching”. At present, there are 4 different types of Q-switched (Qs) lasers that are employed successfully in tattoo removal (Table 1): 532 nm and 1064 nm Nd:YAG, alexandrite, and ruby. With appropriate use, the risk of scarring is less than 4.5% for all treatments. During the laser treatment of tattoos, energy impulses should be placed without considerable overlap in order to avoid additional thermal damage.

<table>
<thead>
<tr>
<th>Q-switched Lasers</th>
<th>Wavelength</th>
<th>Radiant Exposure</th>
<th>Pulse Duration</th>
<th>Spot Sizes</th>
<th>Tattoo Colors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alexandrite</td>
<td>755 nm</td>
<td>8 J/cm²</td>
<td>50-100 ns</td>
<td>≤7 mm</td>
<td>Black, blue, green</td>
</tr>
<tr>
<td>Nd:YAG</td>
<td>532 nm</td>
<td>≤12 J/cm²</td>
<td>≤10 ns</td>
<td>≤8 mm</td>
<td>Red</td>
</tr>
<tr>
<td></td>
<td>1064 nm</td>
<td>≤12 J/cm²</td>
<td>≤10 ns</td>
<td>≤8 mm</td>
<td>Black, blue</td>
</tr>
<tr>
<td>Ruby</td>
<td>694 nm</td>
<td>8-10 J/cm²</td>
<td>≤40 ns</td>
<td>≤6 mm</td>
<td>Black, blue, green</td>
</tr>
</tbody>
</table>

Table 1: Suitable Q-switched lasers used for tattoo removal and for various ink colors
**Intense Pulsed Light Sources**

Intense pulsed light (IPL) sources (lasers with millisecond pulses and low light intensities) are not suitable for tattoo removal. These devices normally have light intensities that are not sufficiently high enough to destroy the pigment particles, but rather simply heat the ink granules. This results in unspecific thermal damage to the adjacent tissue, which can cause significant scarring and pigmentary changes.\(^\text{9}\)

**Tattoo Ink Colors and Skin Color**

Black tattoo ink is most suitable for removal with any type of the aforementioned Qs lasers due to the color's broadband absorption, whereas laser destruction of other color pigments are met with varying degrees of efficacy owing to their light absorption occurring at different wavelengths. In general, bluish-black tattoos are more responsive than other colors to laser therapy and lighter inks tend to be resistant. In particular, purple, yellow, and green tones can be therapeutically challenging. Consequently, multicolor tattoos may require the use of 2 or more types of Qs devices in order to cover the spectrum of colors. Table 1 shows a list of suitable Qs lasers recommended for different tattoo colors.

In patients with darker skin types (Fitzpatrick IV-VI) the Qs 1064 nm Nd:YAG-laser should be favored due to deeper penetration and less melanin absorption, and hence, reduced risk of potential side-effects, such as depigmentation and scarring.\(^\text{10,11}\)

Nonetheless, test treatments should always be performed because of the possibility of permanent unwanted pigmentary changes from light to dark colors in multicolored tattoos and skin areas with permanent makeup (e.g., laser-induced allergic reactions from red ink, brown tones turn to black, and flesh tones or white turn to black or dark green). This effect is caused by the reduction of iron-containing pigments (used in certain cosmetic applications, such as permanent makeup) to iron-oxide. Titanium dioxide, a white pigment that is widely used to lighten or brighten two-thirds of all tattoo colors,\(^\text{12}\) can also darken following irradiation with Qs laser energy.

**Treatment Effects**

Frequently, lightening of the tattoo can be immediately noticeable after laser treatment. This effect has also been demonstrated in experimental studies. Dozier et al. showed that there is no considerable difference in the level of lightening, irrespective of whether the treatment was performed in vivo (tattoos on animals) or ex vivo (harvested human skin).\(^\text{13}\)

Elaborate publications using histopathologic and electron-microscopic examinations of laser treated tattooed skin showed that after absorption into the intracellular pigment molecule, the energy of the ultrashort laser pulse is converted to heat, leading to a reduction in both pigment size and density, as well as triggering molecular structural changes.\(^\text{14,15}\) This rapid localized heating causes gas and plasma formation and subsequent dermal vacuolization, leading to the visible transient whitening of the skin after therapy.

The delayed onset of tattoo color fading (often weeks after treatment) is the result of cellular mechanisms (phagocytation by macrophages), which transport and dispose the ink particles via the lymphatic system and reorganize the remaining pigment granules. About 4 weeks after laser-assisted treatment the remaining particles can again be encapsulated intracellularly within dermal phagocytic cells (macrophages), contributing to further lightening.\(^\text{4,13}\)

Due to the described mechanisms of delayed tattoo lightening, retreatment should not be performed at intervals shorter than 1 month. Based on the author's experience, spacing treatment sessions at intervals between 6 weeks to 2 months apart have generated optimal outcomes.

In general, professional tattoos require more treatment sessions than amateur tattoos, which is attributable to the higher density of ink pigments used and deeper skin placement. Normally, irrespective of the chosen Qs laser system, several (up to 10 or more) treatment sessions are needed for complete tattoo removal.

**Patient Expectations**

It is advisable to counsel patients on expected treatment outcomes, and that often times a complete clearance of the tattoo color pigments cannot be achieved by laser therapy. Side-effects are generally few, but they commonly include transient hypopigmentation both during and after treatment, and patients must be informed prior to commencing treatment.

**Laser Tattoo Removal Post-Treatment**

Under normal circumstances, specific post-operative care is not needed. As with other laser treatments, in order to reduce the risk of side-effects, some safety precautions should be taken, namely the avoidance of sun exposure before and 6 weeks after treatment, and the use of topical antimicrobial agents in case of blistering and crusting. Some authors recommend an immediate application of topical antibacterial ointment following the laser therapy session as part of routine post-operative care to reduce the risk of superinfection that can cause scarring.\(^\text{6}\)

Ho et al. conducted a study involving 120 Chinese patients with Fitzpatrick skin types III-V who received laser tattoo treatment.\(^\text{16}\) Patients experienced significantly lower scarring rates when applications of a heparin and allantoin based gel was used twice daily between laser treatments. Resultantly, study findings included a recommendation that this precautionary post-operative measure be considered for patients with darker skin types.

**Conclusion**

Tattoo removal should only be performed with Q-switched lasers (i.e., alexandrite, ruby, and 532 nm or 1064 nm Nd:YAG). In order to destroy the pigment particles while minimizing the risk of side-effects to the skin, strict
adherence to the rules of selective photothermolysis is strongly advisable. IPL sources; long pulse-duration pulsed-dye lasers; and Nd:YAG, alexandrite, or ruby devices without Q-switching that are also used in other indications of laser therapy (e.g. hair removal), are not suitable for tattoo pigment destruction. When considering their demonstrated safety and efficacy profiles, Q-switched lasers represent the favored therapeutic modality for successful tattoo removal.

References

**Update on Drugs**

<table>
<thead>
<tr>
<th>Name/Company</th>
<th>Approval Dates/Comments</th>
</tr>
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| **Hyaluronic acid dermal filler + 0.3% lidocaine**  
**JUVÉDERM® XC**  
Allergan, Inc. | The US FDA approved a new formulation of this hyaluronic acid dermal filler in February 2010 for the reduction of pain during treatment of moderate to severe facial wrinkles and folds (nasolabial folds). The addition of 0.3% preservative-free lidocaine may also shorten the treatment time by eliminating the need for an additional anesthetic. |

**Hyaluronic acid dermal filler + 0.3% lidocaine**  
**RESTYLANE®-L**  
**PERLANE®-L**  
**Medicis Aesthetics** | The US FDA approved additional formulations of these dermal fillers in February 2010 for the reduction of pain associated with the injectable correction of moderate to severe nasolabial folds. The approval provides the option of a single syringe containing a wrinkle filler with a local anesthetic. RESTYLANE®-L is approved for injection into the mid to deep dermis and PERLANE®-L is approved for implantation into the deep dermis to superficial subcutis. |

**Drug News**

In December 2009, labeling changes regarding possible hepatic effects of diclofenac sodium topical gel 1% (Voltaren® Gel) was issued by the US FDA and Endo Pharmaceuticals/Novartis Consumer Health. This non-steroidal anti-inflammatory topical agent is indicated for the relief of pain associated with osteoarthritis of the joints (i.e., involving the knees and hands). Healthcare professionals were notified of revisions to the Hepatic Effects section of the prescribing information, which included new warnings and precautions about the potential for elevation in liver function tests during treatment with any product containing diclofenac sodium. In the first month of treatment with diclofenac, or anytime during therapy, cases of drug-induced hepatotoxicity have surfaced in postmarketing surveillance reports. The severe hepatic reactions include liver necrosis, jaundice, fulminant hepatitis with and without jaundice, and liver failure, which in some cases have resulted in liver transplantation or even death. In patients receiving long-term therapy with diclofenac, treating physicians should measure transaminases periodically. Transaminases should be monitored within 4-8 weeks after initiating diclofenac treatment. The complete FDA warning, Dear Healthcare Professional Letter, and updated labeling can be found at: http://www.fda.gov/safety/medwatch/safetyinformation/safetyalertsforhumanmedicalproducts/ucm193047.htm

Latanoprost, a prostaglandin analog, can stimulate eyelash growth (number, thickness, and darkness) in patients using ocular preparations for the treatment of glaucoma. In addition, topical prostaglandin analog studies using animal models suggest their benefits in promoting body and scalp hair growth. A recent study by Faghihi et al.* explored the efficacy of latanoprost as a treatment for alopecia areata (AA) of the eyebrows and eyelashes. Over a 4 month period, 26 patients with symmetrical eyelash and eyebrow AA were treated with topical latanoprost on 1 side and the other side was not treated with any drug. Through photographic comparisons, the investigators found that only 1 of the latanoprost-treated patients showed partial hair regrowth on the treated side. The relationship between hair regrowth and latanoprost application was not statistically significant (p=1). Based on these findings, topical latanoprost is not a promising drug candidate for the treatment of AA. However, investigators suggest further studies be undertaken with larger sample populations, longer study duration, and higher drug dosages.