

# Paradoxical Hypertrichosis After Laser Therapy: A Review

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**BACKGROUND** Laser hair removal is a safe and effective procedure for the treatment of unwanted body hair but is not exempt from side effects. A rare but significant adverse effect with this treatment modality is paradoxical hypertrichosis.

**OBJECTIVE** To evaluate the potential etiologies, risk factors, related laser types, and treatment options for the development of excess hair after laser therapy.

**MATERIALS AND METHODS** An analysis of previously published case studies and review articles along with our own experience was used to gather information regarding this phenomenon.

**RESULTS** Paradoxical hypertrichosis has a low incidence, ranging from 0.6% to 10%, and most commonly occurs on the face and neck. All laser and light sources have the potential to cause hair induction, especially in individuals with darker skin types (III–VI); with dark, thick hair; and with underlying hormonal conditions. Possible causes include the effect of inflammatory mediators and subtherapeutic thermal injury causing induction of the hair cycle. Treatment for paradoxical hypertrichosis is laser therapy of the affected area.

**CONCLUSIONS** Paradoxical hypertrichosis is a rare side effect of laser hair removal; the pathogenesis of this event remains widely unknown. We recommend further large-scale studies to investigate this effect.

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Unwanted body hair can be emotionally and socially devastating, resulting in the search for various treatment modalities. With the recent advances in technology and favorable results, lasers have become a common method of hair removal. Nevertheless, outcomes can be variable and distressing at times. A rare but notable adverse effect of laser treatment is the appearance of excess hair around the previously treated area, known as paradoxical hypertrichosis (Figure 1). Here we discuss the possible etiologies, associated laser types, and treatment plans for this event.

## History and Prevalence

Hypertrichosis is the widespread or localized growth of unwanted hair in a non-male pattern.<sup>1,2</sup> Hairs are usually darker, longer, and more abundant than is

normal with regard to race, sex, and age. Hypertrichosis results when telogen or resting follicles are stimulated into anagen (active growth) or when nonpigmented vellus hair follicles are converted into longer, darker terminal hair follicles. Hypertrichosis can be congenital (hypertrichosis lanuginosa) or acquired (iatrogenic) from medications such as cyclosporine, steroids, penicillin, and streptomycin.<sup>3–5</sup> It can also occur as sequelae from underlying medical conditions, such as thyroid disease and porphyria.<sup>2</sup> Hypertrichosis has also been seen arising within a surgical scar and tattoo and surrounding a wart associated with human papilloma virus-1.<sup>6–8</sup> Sunlight has also been identified as having the tendency to induce hypertrichosis, and agents such as psoralens and porphyrins can potentiate it. Although the mechanism for this effect is not clear, ultraviolet irradiation, which is a potent inducer of the

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**Figure 1.** Photographs of a 22-year-old woman (skin type IV) (A) before and (B) after two treatments with a long-pulse 755-nm alexandrite laser of the chin and beard area with the GentleLASE (Candela Corp, Wayland, MA): 18-mm spot size, energy level of 20 J/cm<sup>2</sup>, and 3-ms pulse.

cyclooxygenase 2 enzyme and causes the production of high levels of prostaglandin E2 in the skin, has been suggested as the source.<sup>9</sup> Prostaglandins have recently been noted to stimulate excess eyelash growth when used in the treatment of glaucoma. Topical formulations of prostaglandins have similarly resulted in body hair growth, especially in animal models. No matter what the cause, because excess hair growth can be physically and emotionally unappealing, several treatment modalities have been employed: tweezing, waxing, threading, and the use of depilatories, electrolysis, intense pulsed light (IPL), and laser epilation.<sup>10–12</sup> Of these, the most readily used is laser hair removal. Kuriloff and colleagues first described the use of lasers for hair removal in 1988 for pharyngoesophageal hair growth.<sup>13</sup> Accordingly, several researchers studied various lasers and how they affected pigmented hair follicles.<sup>14</sup> Dover and colleagues and Grossman and colleagues individually determined that the ruby laser selectively injured pigmented hair follicles, and

Zaias proposed the use of the pulsed laser for hair removal in 1991.<sup>15–17</sup> The Food and Drug Administration did not approve this cosmetic indication for hair removal until 1996. Since then, several lasers and IPL systems, with variable efficacies, light output parameters, and adverse effects, have become available for this purpose.<sup>18–20</sup> These devices target the chromophore melanin in hair follicles with millisecond pulse durations. Melanin absorbs the light energy in the hair shaft, which transforms to thermal energy, resulting in damage to the structure of the hair follicle.<sup>21–24</sup> Because of the short pulses of light energy, thermal damage is limited to the follicles, sparing the surrounding tissue. In most cases, laser hair removal is safe, and the results are long term,<sup>25–30</sup> but side effects may occur after this procedure. Adverse effects associated with laser hair removal are usually temporary and may include hypo- and hyperpigmentation, perifollicular edema, erythema, vesicle formation, and crusting.<sup>31,32</sup> Permanent side effects such as scarring and hypopigmentation are rare.<sup>33</sup> An uncommon but

striking adverse effect is an increase in hair density, color, or coarseness, or a combination of these at treated sites in the absence of any other known cause of hypertrichosis. This event has been called paradoxical hypertrichosis, terminalization, induction, and terminal hair growth. Moreno-Arias and colleagues first described paradoxical hypertrichosis in five of 49 females undergoing IPL treatment for facial hirsutism.<sup>34,35</sup> These women were all later diagnosed with polycystic ovarian syndrome. A second report came from Hirsch and colleagues, who noticed the paradoxical effect in 14 patients treated with the long-pulse 755-nm alexandrite laser.<sup>4</sup> All patients had darker skin types (III–IV), the majority were female, and most grew hair on the side of the face. Since then, more reports have been made about this, but prevalence is still widely unknown.<sup>36,37</sup> Its incidence has been reported to be from 0.6%<sup>3</sup> to 4.5%<sup>38</sup> to 10%.<sup>34</sup>

### Etiopathogenesis

Terminal hair has been observed to appear in various areas where it was not present before laser therapy, especially in areas of vellus hair growth. Marayiannis and colleagues showed that hair induction occurred several months after the onset of laser hair removal treatments and after at least three treatments had been performed.<sup>39</sup> This indicates that hair induction is a process that develops over time and that some type of local activation is necessary. It most often occurs with the treatment of vellus hair on the face and neck, and even though the overall hair count in the treated area is reduced, thicker, longer, and more pigmented hairs grow where the vellus hair previously existed. Moreno-Arias and colleagues also defined paradoxical hypertrichosis as the growth of hair in untreated areas in close proximity to treated areas.<sup>34</sup>

Several transient etiophysiological mechanisms such as inflammation, hyperemia, immobilization, and reflex sympathetic stimulation can explain the appearance of terminal hairs and its spontaneous regression after treatment or resolution of the

underlying condition. Reversible eyelid hypertrichosis in patients using prostaglandins for treatment of glaucoma suggested the relationship to inflammatory mediators.<sup>9</sup> The polypeptide thymosin b4, which promotes angiogenesis and wound healing, was also found to directly stimulate increased hair growth in normal rats and mice. This may also explain increased hair growth in humans.

In general, an increase in follicular vascularization that is accompanied by the upregulation of vascular endothelial growth factor in outer root sheath keratinocytes occurs during anagen, followed by a rapid regression in perifollicular vessels during catagen. Growing follicles have much higher perfusion requirements than resting follicles. These factors taken together raise the possibility that subtherapeutic thermal injury to the follicular vasculature may affect follicular cycling in such a way that terminal hair growth rather than miniaturization is induced. Alajlan and colleagues partially support this hypothesis, because the average fluence used on their patients (27.5 J/cm<sup>2</sup>) was at the lower effective standard range for an alexandrite wavelength in the literature.<sup>3</sup> The heat-induced inflammatory reaction that occurs in the follicular papilla, with an increase in the blood flow supply and growth factors for the follicle, might also play a role. Bouzari and Firooz hypothesized that heat produced by the laser is less than the temperature necessary for thermolysis of hair follicle.<sup>40</sup> However, the heat shock may induce follicular stem cell differentiation and growth by increasing the level of heat shock proteins (HSPs) such as HSP 27 in the tissue involved in the regulation of cell growth and differentiation. They believed that a better understanding of paradoxical hypertrichosis may also be useful in the treatment of alopecia.

Subtherapeutic injury to the follicle may also result in the release of factors that alter follicular angiogenesis and influence hair cycling.<sup>41,42</sup> Ultrastructural and light microscopy studies have demonstrated uniform induction of perifollicular inflammation associated with photoepilation that persists for up to 2 weeks. Although feasible, this

**TABLE 1. Contributing Factors to Paradoxical Hypertrichosis**

Thick hair
Dark hair color
Depth of treated hair—superficial
Presence of underlying untreated hormonal conditions (polycystic ovarian syndrome)
Use of hormone supplements or medications (corticosteroids)
Presence of post-treatment side effects (crusting, erythema, edema, hyperpigmentation)
Suboptimal treatment fluences—too low, yet enough energy to stimulate hair growth
Anatomic site (face and neck)
Sex (female; possibly because of sampling)
Darker skin types (III–VI)

idea does not explain why some follicles react in this way and others do not, because inflammation is not selective and thus is not limited to less thermally injured areas. Another hypothesis is that the process of laser epilation may serve to synchronize the cycling of hairs growing within the laser treatment sites.<sup>42</sup> For example, if all hairs within a given area are simultaneously in anagen, the overall hair density may appear to be greater than when hair cycling is asynchronous.

### Contributing Factors

In 2007, Willey and colleagues reported several important factors associated with failure to epilate and risk of hair stimulation.<sup>43</sup>

- **Hair thickness:** Thicker hair is easier to heat, whereas thinner hair, which contains less chromophore, absorbs light energy less efficiently and is more difficult to heat. This explains the failure to epilate fine hairs on the face, abdomen, linea alba, and back and shoulders in men.
- **Hair color:** Melanin is the chromophore absorbed during photoepilation. As a result, darker hair is more efficiently heated.
- **Depth of treated hair:** The optical penetration of light may be too superficial to adequately thermally injure deeply growing anagen hairs.<sup>43</sup>

Other factors associated with the paradoxical effect include underlying undiagnosed hormonal conditions (polycystic ovarian syndrome and associated ovarian hyperandrogenism), hormone supplements and medications inducing hypertrichosis (corticosteroids, finasteride), the incidence of vigorous laser and IPL post-treatment side effects (erythema, crusting, edema, hyperpigmentation), treatment with suboptimal fluences (when there is insufficient light energy to destroy melanocytes in the matrix of the follicle), anatomical site and sex (face and neck of women were most likely), and skin types III to VI (as a result of the greater likelihood of a shift between vellus and terminal hair in patients of darker skin types) (Table 1).

### Associated Lasers

Paradoxical hypertrichosis, first reported with IPL therapy, has now been seen after long-pulse alexandrite and diode laser treatment and is likely to be common to all current laser and light hair removal devices.<sup>44,45</sup> Radmanesh described terminal hair change that was detected after only a few sessions of IPL therapy in 51 of 991 patients.<sup>46</sup> Hirsch and colleagues described it in 14 patients who were treated with a long-pulse 755-nm alexandrite laser.<sup>4</sup> Willey and colleagues also observed that the 694-nm ruby, 755-nm alexandrite, and 810-nm diode lasers caused hair induction.<sup>43</sup> It is unclear whether hair removal with the 1,064-nm neodymium-doped yttrium aluminum garnet (Nd:YAG) laser is less likely to cause hair stimulation or if it is simply used less often, as is the case in their practice.

Paradoxical hair growth has also been reported when IPL systems are used for other indications. For instance, Kontoes and colleagues reported hair growth in two patients after IPL treatment of a tattoo and a port-wine stain, with hair growth occurring within the treated area.<sup>38</sup> Bernstein reported severe paradoxical hair growth from a single treatment using a conservative fluence with the 810-nm diode laser.<sup>47</sup> This paradoxical effect occurred 1 year after the initial treatment to this area

in a patient with Fitzpatrick skin type III, similar to the patients reported by Moreno-Arias and colleagues.<sup>34</sup> Additional treatments ( $n=3$ ) with the diode laser successfully removed this terminal hair. Unfortunately, the patient developed a ring of hair growth surrounding this second treatment area.

### Susceptible Population

In a recent review, Goldberg noted that induction tends to occur more frequently in patients with skin types III or higher and those with undiagnosed hormonal conditions, more commonly with IPL, and in an adjacent area of untreated skin.<sup>48</sup> The most frequent location of terminal hair growth, which has been observed in several studies, is on the lower face in women although reports on the backs of men have also been described. Therefore, women with vellus hair on the facial “beard area” should anticipate chronic treatment with multiple sessions. In a study of 14 patients who were treated using the long-pulse alexandrite laser performed by Hirsch and colleagues, all of the patients with hypertrichosis were of Mediterranean ancestry, with darker skin types (III–V), 93% were female, and 86% grew hair on the side of the face.<sup>4</sup> The overall incidence was 4.5% (30/750) and occurred most frequently on the face and neck (28/30 cases) of women. Only one patient reported having an underlying hormonal condition, polycystic ovarian syndrome, and another patient was receiving corticosteroid treatment for an underlying autoimmune condition. Hair induction was also strongly associated with any single episode of severe erythema, crusting, or hyperpigmentation. The new terminal hair became evident several months after the episode. This phenomenon may not be limited to the long-pulse alexandrite laser, so clinicians practicing photoepilation and their patients should be aware that hair induction may follow any severe episode of these three side effects at an undetermined time, which should be noted during the informed consent process.

Like Hirsch, Kontoes and colleagues also noted that the majority of patients developing hair induction

had dark skin types (III or IV). He believed that this indicated a greater tendency of hair follicle transformation from vellus to terminal in such individuals.<sup>38</sup> This may be why most reports on hair induction have been published from physicians working in Spain, Greece, and Iran, countries where the majority of the population has darker skin types. A study from the United Kingdom on the side effects of laser hair removal did not report any such cases. Half of the patients in this particular study had skin types I and II and another 25% had skin type III.<sup>14</sup> However, more research is needed to prove whether hair induction is truly a characteristic of dark skin types. In terms of sex, the percentage of hair induction was 7.7% (1 of 13) in men and 3.9% (29 of 737) in women.<sup>38</sup> It is not possible to draw valuable conclusions because of the small number of male patients undergoing laser hair removal. Furthermore, the areas usually treated in men (chest, back) are different from the ones treated in women (bikini, armpits, shanks, face), and because data suggest that hair induction is more common in the face and neck areas, it could be difficult to confirm whether hair induction affects both sexes equally.

### Treatment Protocols

Therapy for paradoxical hypertrichosis is based on two facets: treatment of the already present induced hair and the prevention of hair induction. Several researchers suggest the continuation of treatments and inclusion of the new hairy areas in the treatment areas, because induced hair responds to treatment in the same manner as other hair follicles. After a few treatments, all of the unwanted hair should be gone. Using a shorter-cut filter may also help in this matter, but to prevent the paradoxical effect, the use of higher laser fluences is widely emphasized.<sup>16,43,49</sup> In many studies, the explanation for increased hair growth is that suboptimal thermal energies delivered to nearby follicles result in induction of the hair follicle cycle.<sup>41,42</sup> As a result, higher fluences can be used to negate this effect. For the same reason, Willey and colleagues recommend the placement of

cold packs surrounding the treatment area during laser therapy.<sup>43</sup> The application of cold packs will prevent low energies from reaching peripheral follicles and thus limit hair growth. In addition to keeping the surrounding area cool, the researchers further recommend making two passes with the laser during treatments. Their practice employs the use of the long-pulse 755-nm Alexandrite laser using an 18-mm spot size with an energy setting of 12 to 14 J/cm<sup>2</sup> followed by a second pass using 8 to 10 J/cm<sup>2</sup>

1 minute later. Alternatively, a single treatment using one pass followed by a second single-pass treatment 1 week later may be tried. With this protocol in use, they have successfully treated all of their patients with hypertrichosis without paradoxical effect. Another suggestion is to decrease the amount of time between laser treatments. Willey and colleagues noted that terminal hair growth most often occurred between the third and fourth treatments but also occurred as late as after the tenth treatment.<sup>43</sup>

Schroeter and colleagues determined that most cases of terminal hair growth in their study occurred when treatment intervals were more than 8 weeks apart.<sup>50</sup>

As a result, they advise that the interval between treatments be between 4 and 6 weeks. We have experienced one case of paradoxical hypertrichosis in our practices. A 22-year-old Indian woman (skin type IV) was treated with a long-pulse alexandrite laser (GentleLASE, Candela Corp, Wayland, MA) for increased chin/beard area hair growth. She received a total of two sessions (one month apart) with the following parameters: 18-mm spot size, energy level of 20 J/cm<sup>2</sup>, and 3-ms pulse (Figure 1A, B).

Treatment for the paradoxical hair growth consisted of three sessions with the 1,064-nm Nd:YAG laser (CoolGlide, Cutera, Brisbane, CA), spot size of 10 mm, pulse duration of 30 ms, and energy fluence of 30 J/cm<sup>2</sup>, with complete ablation of the hair follicle bulbs. This resulted in full resolution of the excess hair growth.

## Conclusions

The mechanism of paradoxical hypertrichosis remains uncertain. Although much information has

been gleaned from various case reports and small studies with few patients about the possible etiology, risk factors, and prevalence, larger studies with relatively equal numbers of male and female subjects are imperative. Additionally, it would be beneficial to incorporate individuals from all Fitzpatrick skin types and to treat similar areas on the body to study the effects of photoepilation with various lasers. As a result, we recommend that further studies incorporate the following components:

- (1) Prospective study of a large group practice with a subsection of patients who have paradoxical hypertrichosis
- (2) Large sample size
- (3) Separation of patients into groups based on skin phototype (Group 1, Type I–II; Group 2, Type II–IV; and Group 3, Type V–VI)
- (4) Focus on high-risk areas such as the side of the face and shoulder
- (5) Long-term follow-up period ( $\geq 6$  months after laser treatment)
- (6) Standardization of measuring tools: digital photographs, hair counts, and physician and patient global counts

Only with data from these larger and more specific studies can we draw more precise conclusions regarding this phenomenon.

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