Vascular Lasers

1

Laser Dermatology: Pearls and Problems. David J. Goldberg. Published 2008 by Blackwell Publishing, ISBN: 978-1-4051-3420-0.

Vascular Lasers

1

KEY POINTS

- The pulsed dye laser, originally only used in a purpuric mode, is now highly successful without the induction of purpura for the treatment of most vascular lesions
- Pulsed dye lasers used for the treatment of port-wine stains lead to the best results when the clinical endpoint is purpura
- Facial erythema can be treated equally well with both pulsed dye laser and intense pulsed light treatment
- Twenty years after pulsed dye laser treatment of port-wine stains was initiated, the exact number of treatments remains an enigma
- Some leg spider veins can be treated with laser treatment; sclerotherapy remains the gold standard

Introduction

Cutaneous vascular lesions, especially those occurring on visible sites, such as the face, may cause significant psychological distress. This is true not only of port-wine stains (PWS), whose detrimental effect on patient is well recognized [1,2], but also of other vascular malformations, proliferations, and ectasias. Frequently, however, the latter conditions tend to be underdiagnosed and undertreated. The introduction of compact and more affordable lasers, being used in an outpatient setting, allowed for easier patient access with more reliable and cosmetically pleasing results.

The treatment of vascular lesions is one of the most commonly requested cutaneous laser procedures. Since the introduction of the argon laser, a variety of lasers and light sources have been used in the treatment of vascular lesions. These include visible and infrared lasers, as well as broadband light sources. Despite some limitations, lasers and light source devices remain the modality of choice for a variety of vascular lesions.

Essential Concepts

Vascular Laser Biology, Chromophores, and Tissue Targets

A large variety of vascular-specific lasers and light-based devices have been developed over the years. All of the systems currently in use are based on the principles of selective photothermolysis introduced by Anderson and Parrish [3]. Photons of light produced by lasers are absorbed by tissue chromophores within a specific target of interest, producing heat. The heat is dissipated through conduction; therefore, if sufficient energy is delivered faster than the rate of cooling, heat accumulates within the target and selectively destroys it.

Tissue absorption and scattering determine penetration of laser light into the skin. Collagen is the major cause of scattering, which decreases as the wavelength of light increases. Therefore, longer wavelengths can penetrate deeper into the skin and, subsequently, the choice of a specific laser will depend on the depth of the desired tissue target. As the wavelength is increased into the far-infrared region, light begins to be heavily absorbed by water, which limits its penetration.

Oxyhemoglobin and, to a lesser extent, deoxyhemoglobin are the main chromophores for vascular lasers. The major absorption peaks of oxyhemoglobin are 418 nm (blue), 542 nm (green), and 577 nm (yellow) [4]. The largest peak is at 418 nm; however, this wavelength does not allow adequate penetration into the skin. The other two peaks, as well as a broad absorption band between 800 and 1100 nm form the basis for vascular lasers in use today.

The patient's Fitzpatrick skin type is important when considering a vascular laser, as melanin may compete with oxyhemoglobin for light absorption, potentially resulting in dyschromia. Melanin absorbs mainly in the ultraviolet and the visible light spectrum, with decreasing absorption in the near-infrared region of the spectrum. Therefore, longer wavelengths are better used in patients with Fitzpatrick types IV toV to minimize the risk of dyspigmentation.

Laser Settings: Pulse Duration, Spot Size, Fluence, and Cooling Methods

Heat is transferred from erythrocytes containing the hemoglobin to the surrounding endothelial cells, causing damage to the blood vessel wall. If light is pulsed with exposure time less than or equal to the thermal relaxation time (TRT), heat is

maximally confined to the target – in this case, the blood vessel wall.

TRT is directly proportional to the square of the size of the object and inversely proportional to thermal diffusivity, an intrinsic property of a material to diffuse heat [3]. Thus, as the blood vessel diameter is doubled, the cooling time increases fourfold. A useful quick approximation of TRT, in seconds, is the square of the target size in millimeters [5]. Additional considerations in determination of TRT for larger targets, such as large-caliber vessels of the legs, will be discussed in a later section.

Once the TRT is determined, an appropriate pulse duration, also known as the pulse width, is selected to match the target blood vessel diameter. As an example, the TRT of capillaries is in the order of tens of microseconds, that of venules is in the hundreds of microseconds, whereas in adult PWS, the TRT is between 1 and 10 ms [6]. As the delivered pulse duration surpasses the TRT of smaller blood vessels, sufficient heat diffusion is afforded, allowing for the preferential treatment of larger-caliber vessels [3]. It is thus crucial to know the specific structure and composition of the vascular lesion to be treated [7].

The theory of selective photothermolysis requires sufficient fluence, also known as energy density, to reach a damaging temperature within the target – approximately 70ºC for blood vessels [3]. Precise choice of fluence is important, as excessive fluences may result in increased incidence of adverse effects, such as scarring and dyspigmentation.

Laser beam diameter, or spot size, also influences the choice of fluence. Compared to a smaller spot size, a larger spot size results in a smaller percentage of light being scattered outside the actual delivery of light, with subsequent delivery of greater amount of energy and greater damage to the deeper dermal target. Consequently, with all other factors being equal, lower fluences can be used with larger spot sizes [8]. In addition to the depth of the target, the choice of spot sizes is also influenced by the overall size of treated lesion. The largest spot size accommodated by the treatment area is typically selected, with small spot sizes usually reserved for isolated small superficial blood vessels.

Absorption of light energy, by competing epidermal melanin, and retrograde conducted heat from the actual treated dermal target may result in undesired epidermal damage. This may eventuate in blistering, dyspigmentation, and scarring. Epidermal cooling is employed to minimize the risk of such undesired damage. Cooling allows for higher fluences to be used, thus enhancing treatment efficacy [9]. Localized cooling

also has an additional benefit of providing local anesthesia and reducing swelling, making the treatment more tolerable to the patient. Epidermal cooling can be achieved through contact, including ice packs, cold gel, and sapphire window; cold air convection; or automated liquid cryogen spraying immediately prior to laser pulse, a process known as dynamic cooling [9].

Classification of Vascular Lesions

The composition and structure of the vascular lesion, as well as its natural history, need to be ascertained prior to treatment. Such assessment will allow the proper selection of the appropriate vascular laser and laser settings. In some instances, varying composition within the same lesion will require changes in laser parameters or a decision to use multiple separate lasers. In other instances, such as some hemangiomas of infancy, laser therapy may not always be appropriate and may be reserved for very early or for complicated cases.

With continuing expansion of clinical indications for vascular lasers, a proper classification system is important. The most useful classification system is based on endothelial characteristics. Thus, congenital vascular lesions can be subdivided into (1) hemangiomas, with endothelial cell hyperplasia, and (2) vascular malformations, with normal endothelial cell turnover and variable degree of vessel ectasia [10]. Most acquired vascular lesions, such as telangiectasias, spider and cherry angiomas, venous lakes, pyogenic granulomas, and leg vein abnormalities, are characterized by vessel ectasia.

PWS are the most common type of congenital vascular malformation. They represent low-flow capillary malformations, are present at birth, and most commonly occur on the face and neck. They may also be part of several rare conditions, such as Sturge–Weber and Klippel–Trenaunay syndromes. PWS increase in size, proportionally to the growth of the child, and never involute. As the degree of vascular ectasia increases over time, the lesion becomes darker and frequently develops hypertrophy and nodularity in adulthood. Histologically, an abnormal papillary dermal plexus of ectatic vessels varying in size between 10 and 300 μm underlies a normal epidermis at the depth of 0.1 to 1 mm [11]. Such variability, within the same lesion, may make laser treatment that much more difficult.

Hemangiomas of infancy most often appear after the first few weeks of life, although a white or pink macule may sometimes be discerned prior to the onset of actual hemangiomas growth. Following the initial presentation, hemangiomas grow at a much faster rates when compared to the rest of the body

[10]. Depending on the location of the lesion, such rapid growth may at times impinge on the larynx, trachea, or eyes, endangering breathing or vision. Ulceration may also occur and may result in bleeding, pain, infection, and scarring. Hemangiomas may be subdivided based on the depth in tissue into three categories: superficial, appearing as bright red plaques; deep, appearing as bluish subcutaneous nodules; and combined or mixed [12]. Multiple or extensive hemangiomas also occur and may be segmental or diffuse, sometimes with visceral involvement. Most hemangiomas begin to involute after 12 to 15 months of growth, a process that may take up to 10 years. Following involution, residual epidermal atrophy with telangiectasias and fibro-fatty tissue may persist [13]. It is also important to recognize a recently described rare hemangioma variants, such as the non-involuting congenital hemangioma (NICH) and the rapidly involuting congenital hemangioma (RICH). The prognosis for these lesions is different from the conventional hemangioma of infancy [14].

Pearls and Problems

PWS: Pulsed Dye Laser

The pulsed dye laser (PDL) is generally considered to be the gold standard in the treatment of PWS (Figure 1.1). This laser has undergone several modifications since its original inception in an attempt to allow the laser to penetrate deeper into the dermis, to target deeper and larger vessels, and to better protect the epidermis, especially in darker skin.

Several factors, including the patient's age and Fitzpatrick skin type, anatomical location, size, composition, and color,

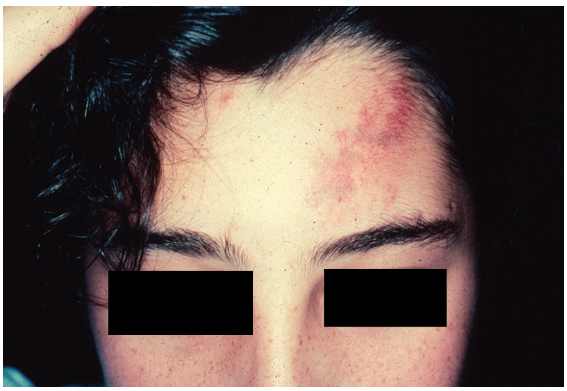


Figure 1.1 PWS ideally treated with the PDL.

influence the response of the PWS to the PDL. Of the head and neck lesions, those that are centrofacial, or dermatomal in the V2 distribution, are slower to respond to laser treatment [15]. PWS located on the extremities, and especially on distal extremities, respond more slowly than those on the trunk [16]. Smaller lesions respond better, with a 67% decrease in post-laser treatment size for those under 20 cm^2 compared to a 23% decrease in those over 40 cm^2 [17]. Ectasia, within ring-like vessels in the superficial horizontal plexus, as demonstrated by videomicroscopy, respond better to laser treatment, than those within capillary loops [18]. While application of this finding is difficult in clinical practice, it may explain some of the cases of differential response to treatment using identical laser parameters. Red color indicates more superficially located vessels and portends a better treatment prognosis. Purple color is attained by deeper-located larger-caliber vessels, whose response to treatment is intermediate, while that of pink lesions, with deep smaller-caliber vessels, is poor [19,20]. Early treatment of PWS has been shown to have better outcome [21,22], although this point remains somewhat controversial [23]. In general, fewer treatments are required, and better clearance can be achieved, in children less than 10 years old. Those PWS patients in whom therapy is started before 2 years of age potentially getting the best results [24,25].

After the above factors are analyzed through physical examination, realistic expectations have to be discussed with the patient or the parents. Such a discussion includes the number of required treatments, potential adverse effects, and the possibility of lightening rather than complete clearance of the PWS. Digital photographs prior to, and following treatments, are important to document gradual improvement.

Anesthetic requirements should also be considered prior to treatment. Cooling techniques, especially cryogen spraying, have made laser treatments tolerable for most adults. Topical anesthetics may be used, but may also cause vasoconstriction and render treatments less effective. Children may require conscious sedation or general anesthesia, especially when large lesions are being treated. Such techniques should be performed by a trained anesthesiologist and care must be taken to avoid any oxygen escape following intubation, as laser ignition of the oxygen may occur.

Generally, when using a 585-nm PDL, treatment of a PWS in a child, treatment is initiated at 6 to 8 J/cm^2, which may then be increased by 0.5 to 1 J/cm^2 at subsequent visits, if tolerated without adverse effects. Alternatively, several test spots using incremental fluences can be performed in the least obvious

portion of the PWS lesion 4 weeks prior to the actual treatment to determine the minimal purpuric dose. Lower fluences may be used for the eyelids, upper lip, neck, and over bony prominences. Fluences should also be lowered if moderate to extensive tanning is present, due to increased absorption of laser energy by the epidermal melanin with subsequent higher risk of scarring.

Laser emitted pulse duration is adjusted to the size of the vessels to be treated, and usually varies between 0.45 and 3 ms on the 585-nm PDL. As discussed previously, the largest spot size, usually 7 or 10 mm, is used to decrease scattering at the periphery of the laser beam and to deliver more of the original energy to the target. As a result, a 10-mm spot size requires only about half to two-thirds of the fluence of the 5-mm spot size [5]. If cryogen spray cooling is utilized, spray duration of 30 to 50 ms is used with a delay of 30 to 50 ms before the laser pulse. Spray duration may be lowered on darker skin tones to prevent cryogen-induced blistering and dyspigmentation.

Increasing the wavelength of the PDL to 595 or 600 nm allows for deeper penetration of the laser beam. This currently popular 595-nm wavelength is farther away from the oxyhemoglobin absorption peak at 577 nm; thus, higher fluences – 1.5 to 2 times those used with the 585 nm laser – may be used. This wavelength modification, with fluences of up to 16 J/cm^2, has been shown to be safe and efficacious when a longer pulse duration, 1.5 ms, and appropriate cooling are used [26–28]. In addition, PWS previously resistant to the 585-nm, 0.45-ms PDL may significantly lighten with increased wavelengths, pulse durations, and fluence [29].

Because significant and prolonged purpura may be a complication of treatment with the PDL, attempts have been made to use subpurpuric doses in combination with multiple passes to achieve clearance of PWS (Figure 1.2). This may be achieved by lowering the fluence or by increasing the pulse duration, usually to 10 ms. Results have been mixed, with most studies documenting some improvement, but not equivalent to that achieved with a purpuric dose [30,31]. Thus, patients should be warned that considerably more treatments would be required if such a technique were to be undertaken.

During treatment, pulses are overlapped by approximately 10% to avoid skip areas. Direct overlapping, or pulse stacking, at vessel-rupturing doses should be avoided to prevent non-specific collateral damage from extravasated hemoglobin from the first pulse. Although controversial, multiple passes may at times be done if fluences are carefully chosen to only produce intravascular purpura, rather than vessel rupture [32].

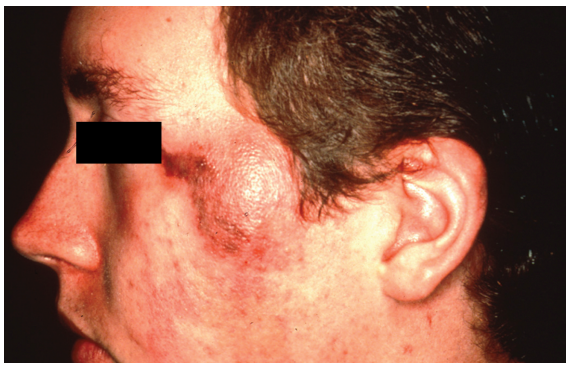


Figure 1.2 Typical purpura ideally seen after PDL of PWS.

As larger-caliber vessels generally respond better to PDL treatment, several in-treatment maneuvers may be undertaken to increase vessel clearance. Dependent position of the treated area, increased ambient temperature, and increased central venous pressure, through positive end-expiratory pressure during intubation, may all achieve dilation of the blood vessel with possible better laser-induced results [33,34].

The immediate clinical endpoint of treatment is transient intravascular purpura, also known as coagulum. Whitening of the treatment area should be avoided, as it indicates impending blistering, which may potentially result in scarring. Following treatment, local edema and pain may be experienced and may be alleviated with the use of ice packs or mild analgesics. If blistering or crusting occurs, topical antibiotics should be applied. Sun protection following laser treatment is important to decrease the risk of hyperpigmentation. Treatments are usually repeated at 4- to 8-week intervals.

On the average, a lightening of around 12% may be expected after each treatment and 4 to 15 or more treatments are needed for sufficient, though not necessarily complete, clearance [35]. Continued improvement may be observed with additional treatments.

The incidence of long-term adverse effects associated with PDL is low. As described above, purpura is the most common side effect of treatment, but usually only lasts 5 to 14 days. Even with the use of test spots, post-treatment crusting may be observed in 25% of patients [36]. Transient spongiotic dermatitis has been reported in 3.7% of patients with a personal or family history of atopic dermatitis. Among possible long-term laser-induced complications, the most common is hypopigmentation of at least 6 months with an incidence of 3.7%. Atrophic scarring

has been noted in 1.3% of patients, but may be more commonly related to the use of older laser systems. Hypertrophic scarring, and the development of pyogenic granuloma following treatment, is rare [37,38]. Patients on oral isotretinoin therapy may have to wait for at least 6 months following discontinuation of medication before PDL treatments can be undertaken due. This issue is controversial and relates to a possible increased incidence of post-treatment keloid formation and hypertrophic scarring. It must be kept in mind that the incidence of these and, potentially, other adverse effects is likely to change with the introduction of the newer, even safer, systems.

PWS: Other Lasers and Light-Based Devices

The development and recent advances in the PDL technology have improved, but not perfected, the treatment of capillary malformations. Deeper-seated and nodular PWS in adults still remain problematic for PDL treatment. In response to this problem, various additional lasers and light-based devices with vascular specificity have been tried with some success. Although generally not as well studied as PDL, such devices offer promise for improved future treatment options in the future.

Potassium-titanyl-phosphate (KTP) lasers produce a green light with a wavelength of 532 nm, near the 542-nm absorption peak of oxyhemoglobin. Although this laser's penetration into the skin is more superficial when compared to the PDL, it has been used on PDL-resistant PWS with resultant further lightening. Fluences between 18 and 24 J/cm^2, with pulse widths between 9 and 14 ms, produce the best results [39]. The KTP laser is more operator dependent than is the PDL. The handpiece has to be moved continuously during treatment, with care being taken not to stack pulses. The clinical endpoint of treatment with the KTP laser is transient vessel clearance without epidermal blanching. Because of this laser's more superficial penetration into the dermis, higher fluences must be used with this laser as compared to the PDL. In addition, a higher proportion of KTP laser energy is absorbed by the epidermis. This may lead to increased rates of adverse effects, which include blistering, erosions, and crusting (eventuating in scarring) and hyperpigmentation in 10% and 7% of treated patients, respectively [39,40]. Recently, however, significant improvement in KTP laser treated PWS was noted with lower fluences, 9.5 to 20 J/cm^2, and longer pulse widths, 15 to 50 ms. Such treatment parameters may also be associated with a much lower risk of adverse effects [41]. Thus, optimal treatment parameters, while using the KTP laser for PWS, may still have to be determined.

At 1064 nm, the long-pulsed neodymium:yttrium–aluminum–garnet (Nd:YAG) laser allows for much deeper penetration into the dermis with vascular specificity due to the broad absorption peak of oxyhemoglobin above 800 nm. Coagulation of blood vessels, as deep as 2 to 3 mm from the dermo-epidermal junction, can be achieved [42]. This allows targeting of some of the deeper vasculature that the PDL may not be able to reach. These deeper, larger-caliber blood vessels typically require pulse durations between 3 and 15 ms. Since the absolute absorption of hemoglobin at 1064 nm is lower than that at 585 nm, substantially higher fluences need to be used with this longer wavelength. Because of this, proper cooling is paramount with this laser. Such cooling can be achieved through pre- and post-pulse contact cooling using a cooling handpiece, frozen gel, or ice packs. The choice of proper delivered treatment fluence can be somewhat complicated with the Nd:YAG laser, as even minimally slightly higher than required fluences may result in epidermal damage and potential scarring. It is recommended that a minimum purpura dose – defined as the minimum fluence causing subtle darkening or purpura lasting longer than 15 minutes – be determined and used in subsequent treatments. Generally, the purple color within a PWS requires Nd:YAG laser fluences between 40 and 60 J/cm^2, red requires between 50 and 130 J/cm^2, and pink requires 90 and 250 J/cm^2 [42,43]. During treatment, non-overlapping pulses are delivered following contact cooling. The immediate clinical endpoint is subtle dusky purpura without signs of epidermal damage, such as grayish discoloration. Such purpura typically resolves in 3 days. Following treatment, patients may also develop moderate urticaria-like edema, which may be improved with the use of mid-potency topical steroids [43]. Additional short-term effects may include erythema, transient post-inflammatory hyperpigmentation, and, rarely, erosions. Focal thrombosis, presenting as darkening and hardening of portions of the PWS may sometimes occur days to months following treatment [43]. Treatments are usually performed every 4 to 6 weeks.

Although not a laser, the intense pulsed light (IPL) device is a non-coherent light source that delivers multiple wavelengths of visible and near-infrared light simultaneously. The IPL may also be used in the treatment of vascular lesions, including PWS. The high-intensity flashlamps used in IPL typically emit wavelengths between 500 and 1200 nm. Various filters may be used to (1) adjust emitted wavelengths to the depth and size of treated target structure, as well as (2) to decrease melanin absorption to allow for treatment of darker skin types. Emitted

pulse durations can be highly variable and can be set to values between 0.5 and 88.5 ms, depending on the TRT of the target. Fluence must be carefully chosen, as the large spot size (120 to 600 mm^2) and multiple IPL delivered simultaneous wavelengths may result in epidermal heating and potential adverse effects. If higher fluences need to be delivered, this can be accomplished with multiple pulses, or pulse splitting. Delay between pulses may be set between 1 and 300 ms – usually 20 to 30 ms – to allow for sufficient cooling of the epidermis and smaller blood vessels. The heating achieved with such a technique is not additive, but follows a complex curve. Red and pink PWS can be treated with pulse durations of 2.5 to 5 ms, whereas purple PWS may require longer pulse duration and possibly multiple pulses. Chilled gel is used to cool the epidermis and/or contact cooling, plus topical anesthetics are used to reduce pain associated treatment. Treatments are usually repeated every 3 to 6 weeks. Clearance, even in patients with skin type IV, may be achieved in previously untreated lesions with fluences ranging from 24 to 75 J/cm^2, with the best improvement achieved in pink and red PWS [44,45]. Adverse effects following IPL treatment are mostly transient and may include immediate erythema and purpura in up to 75% of patients, lasting for up to 7 days, blistering in up to 8%, and swelling for several hours to a week in up to 27% of patients [44,45]. A rare complication of terminal hair development within a treated PWS has also been reported [46]. Scarring, although rare, may always occur [44,45]. Most authors do report a steep IPL treatment learning curve. Extensive experience with this device may be necessary prior to the successful treatment of PWS.

Hemangiomas

PDL laser treatment of uncomplicated hemangiomas represents one of the major controversies in laser surgery today (Figure 1.3) [47]. The scarcity of published prospective, randomized controlled studies and the use of multiple laser wavelengths and widely varying treatment parameters further complicates the matter of laser hemangioma treatments. In addition, there is a lack of a standard goal in the laser treatment of uncomplicated hemangiomas. Some studies report on such characteristics as lightening or clearance, whereas others assess clinical involution.

While the involution of hemangiomas likely involves induction of cellular immunity, the precise mechanism underlying this process is very poorly studied. It has been argued that low-fluence, shorter pulse durations may induce limited

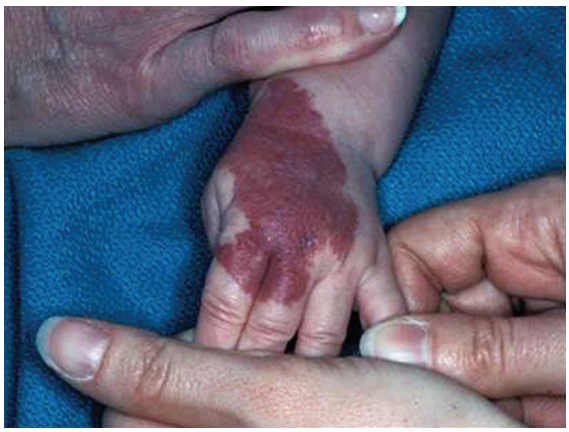


Figure 1.3 Ideal flat red hemangioma for treatment response to PDL.

vascular endothelial damage with thrombus formation, complement activation, and Vasculitis [47]. However, since the precise pathophysiology of the hemangioma involutionary process has yet to be worked out, the development of targeted laser treatments based on this mechanism cannot realistically proceed at this time.

The current goal of laser therapy for hemangiomas is complete or partial clearance of the lesion. Laser parameters are selected based on the depth and size of blood vessels comprising the lesion. The choice of parameters may, at times, be elusive, as the lesion represents an active rapidly growing tumor.

Since the PDL has very limited penetration into the dermis, only the treatment of flat matured or early, pre-proliferative red hemangiomas less than 2 mm in thickness is realistic with this laser. There is no laser-induced effect on deep hemangiomas, while only the superficial component of mixed hemangiomas may improve with this treatment. Compression of mixed hemangioma with a glass slide to reduce the thickness has not been found to increase the effectiveness of treatments. Multiple studies have documented reduction in the thickness of hemangiomas treated at an early stage [48–50], although some have also noted increased incidence of adverse effects, especially with older laser equipment that may have been used without effective cooling [51]. Complete clearance in early flat hemangiomas is achievable with the PDL at a much higher rate than would be expected with natural resolution. It has also been noted that good clearance can be achieved with the use of subpurpuric doses, while scarring is more common when confluent purpura is reached. Thus, lower fluences, between 6 and 7 J/cm^2 using a

585-nm PDL and between 9 and 12 J/cm^2, or using a 595-nm PDL, and longer pulse durations of 1.5 to 20 ms in combination with cryogen cooling, may result in clinical efficacy with lower risks of complications [52]. Treatments can usually be tolerated without anesthesia. During treatment, spot overlap should not exceed 10% to 20%. Confluent purpura should be avoided, as vessel rupture may lead to non-specific heating of the dermis from extravasated erythrocytes. Laser therapy may be performed every 3 to 4 weeks, with very superficial early hemangiomas requiring 2 to 4 treatments on the average. In addition to purpura lasting up to 2 weeks, adverse effects associated with treatment of superficial hemangiomas may include short-term swelling, blister formation, and crusting, transient dyschromia in 4% to 7% of patients, and atrophic scars in approximately 2% to 4% of treated patients. Rarely, ulceration may be induced by PDL within 1 to 2 days of treatment [53].

During the proliferative or early involuting phases, PDL is typically reserved for treatment of ulcerations. Lower fluences, 5 to 7 J/cm^2, are used with cryogen cooling to induce superficial vessel closure without further ulceration of the lesion. Treatments can be undertaken at 2-week intervals, with most hemangiomas requiring 1 to 2 treatments for complete re-epithelialization. In addition, pain is reported to be decreased within the first 3 days following PDL treatment [54,55].

As previously mentioned, residual changes are common following complete involution of hemangiomas and may include telangiectasias, atrophic or redundant skin, and underlying fibro-fatty tissue. These changes present several different targets for laser surgery. Telangiectasias associated with resolution of hemangiomas are effectively treated using the PDL with protocols similar to those described below for other types of telangiectasias [56]. Atrophic or redundant skin may be treated with surgical excision. Alternatively, either ablative or non-ablative laser remodeling may be attempted to induce dermal collagen deposition.

The KTP laser has also been evaluated for treatment of small superficial hemangiomas. Using a 5-mm spot size, fluence of 20 J/cm^2, and pulse duration of 50 ms, improvement, in terms of cessation of growth, regression, and complete resolution were found to be slightly less likely than those results achieved with a short-pulsed (0.3 to 0.45 ms) 585-nm PDL. However, purpura, crusting, blistering, and transient hyperpigmentation are also less prevalent compared to the PDL laser. Swelling is more pronounced and longer lasting with the KTP laser. The incidence of atrophic scarring following KTP laser treatment is similar to that seen with the PDL [57].

Owing to its deeper penetration into the dermis, the long-pulsed 1064-nm Nd:YAG laser can be used percutaneously or intralesionally to induce involution in deeper or rapidly proliferating hemangiomas. The intralesional technique involves the use of a flexible fiberoptic wand introduced through a cutaneous puncture. Percutaneous Nd:YAG laser irradiation using fluences of 80 to 90 J/cm^2 can be effective in reducing lesion size or inducing complete resolution in deep or mixed-type hemangiomas. Pre-cooling with ice water, ice cubes, or cryogen spraying is used to prevent epidermal damage and is especially important in darker skin tones [58]. Local anesthesia may be required to reduce patient discomfort. The immediate clinical endpoint of treatment is blanching of the lesion. Pulses should not overlap and may be delivered 2 mm apart to decrease the risk of scarring. Following treatment, transient erythema and swelling occur in most patients and may last several days, while crusting may be present for as long as 2 weeks. The incidence of atrophic scarring may be slightly higher as compared to what is seen with the PDL. Treatments are usually repeated every 6 to 8 weeks.

Treating hemangiomas with IPL represents a new application of this device. In the few studies to date, promising results have been obtained in centrofacial hemangiomas using an IPL with a 590-nm filter, fluences of 36 to 45 J/cm^2, and triple pulses with pulse durations of 2.5 to 6 ms and pulse delay of 20 to 30 ms [59]. The large IPL spot size allows for greater penetration into the dermis and for shorter overall treatment time. During treatment, pre-cooling is achieved with a chilled gel, followed by ice packs immediately after therapy. Burning and erythema lasting up to 2 days are common. Also of note, the number of sessions required to clear a hemangioma is usually larger than that with the PDL. Additional studies are needed before the efficacy of this treatment modality can be properly assessed.

Venous Malformations

Venous malformations are low-flow vascular lesions characterized by ectasia of venous blood vessels lined by normal endothelium. They are most commonly present at birth and continue to grow proportionally with the rest of the body. Occasional acquired cases can be seen, frequently occurring on the lips (Figure 1.4). Clinically, venous malformations present as faint blue macules, doughy, easily compressible bluish masses, or, less commonly, complex deep-infiltrating structures. Additional studies, such as magnetic resonance imaging or Doppler ultrasonography, can be obtained to confirm the

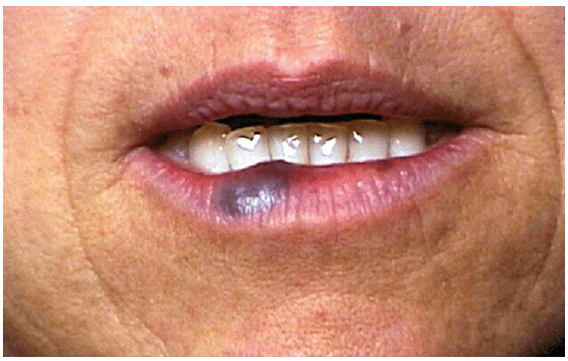


Figure 1.4 Venous lake uniquely responsive to millisecond-domain Nd:YAG laser.

diagnosis. Histologically, phleboliths and organizing thrombi can be seen within dilated vascular channels. Complications, including pain, bleeding, or intravascular coagulopathy, may occur. Treatment options for venous malformations include surgical excision, sclerotherapy, and lasers.

The choice of lasers is limited by the relative depth of vessels within the lesion. Due to their very superficial penetration into the dermis, KTP and dye lasers are typically not effective in the treatment of these lesions.

In contrast, the long-pulsed 1064-nm Nd:YAG laser has been used successfully for venous malformations. Topical or general anesthesia, depending on the location and size of lesion, is usually required to decrease patient discomfort. Fluence of 250 J/cm^2 and pulse duration of 10 ms would be appropriate for the deep, highly ectatic variety of this malformation [60]. The concomitant use of a cooling device reduces the risk of scarring.

Adverse effects associated with the use of the Nd:YAG laser for treatment of venous malformations include reports of pyogenic granuloma formation, scarring [60], superficial burns, and herpes labialis [61]. Of note, venous malformations are very prone to recanalization and subsequent recurrence as late as 6 months following treatment, so patients should be properly advised and followed [61].

Recently, IPL devices have also been used in the treatment of venous malformations. Small lesions under 100 cm^2 respond best, sometimes after 2 to 3 treatments, with clearance of 70% to 100%. Typical parameters include an IPL with a 590-nm filter, long-pulse mode, triple pulses, and fluences around 80 J/cm^2. Adverse effects may include prolonged erythema for up to 5 days, swelling, blistering, and crusting for up to 2 weeks, prolonged pain, and, rarely, bleeding, dyschromia, and scarring

in less than 1% of treated patients [62]. However, since IPL treatment of this lesion is not well described in the literature, optimal treatment parameters and clearance rates need to be confirmed through larger studies.

Arterial and Arteriovenous Malformations

These high-flow malformations are present at birth and most frequently occur on the extremities or trunk as macular erythema. Nodular proliferation typically starts at puberty or following trauma and results in an erythematous to violaceous subcutaneous pulsatile mass, in which a palpable thrill may frequently be discerned [33]. Angiography, Doppler ultrasonography, or magnetic resonance imaging may be used to confirm the diagnosis. Because of their high-flow rates, selective photothermolysis is not feasible and laser therapy for these conditions is disappointing.

Facial Telangiectasias

Facial telangiectasias are a common acquired condition, affecting around 15% of adults with Fitzpatrick skin types I to III. Diffuse telangiectasias may be associated with a variety of conditions, including rosacea, chronic steroid use, actinic damage, and connective tissue diseases, such as CREST syndrome. The lesions are characterized by ectatic post-capillary venules, ranging from 0.1 to 1 mm in diameter, located in the superficial dermis at the average depth of 0.2 to 0.25 mm [33]. Because of their relatively superficial location within the dermis, facial telangiectasias are very amenable to laser and light-based therapy, with PDL, KTP, Nd:YAG lasers, and IPL devices used most frequently (Figure 1.5).

Both the 585-nm, 0.45-ms and the 595-nm, 1.5-ms dye lasers have been used extensively for facial ectasias. Traditionally, fluences of 4 to 10 J/cm^2 were used, depending on the spot size, with 1 to 3 treatments needed for good cosmetic clearance. During treatment, pulses should not overlap by more than 30%. Because of the circular spot size, a reticulated or meshwork-like pattern may be created following a single treatment. The immediate endpoint is similar to that in treatment of PWS, namely vessel coagulation with blanching, followed by purpura. Although makeup may be worn in the absence of blistering or crusting, long-lasting purpura of up to 2 weeks is cosmetically unacceptable to many patients. Additionally, post-treatment edema may be extensive, occasionally obscuring vision when the PDL is used near the eyelids [63]. As a result,

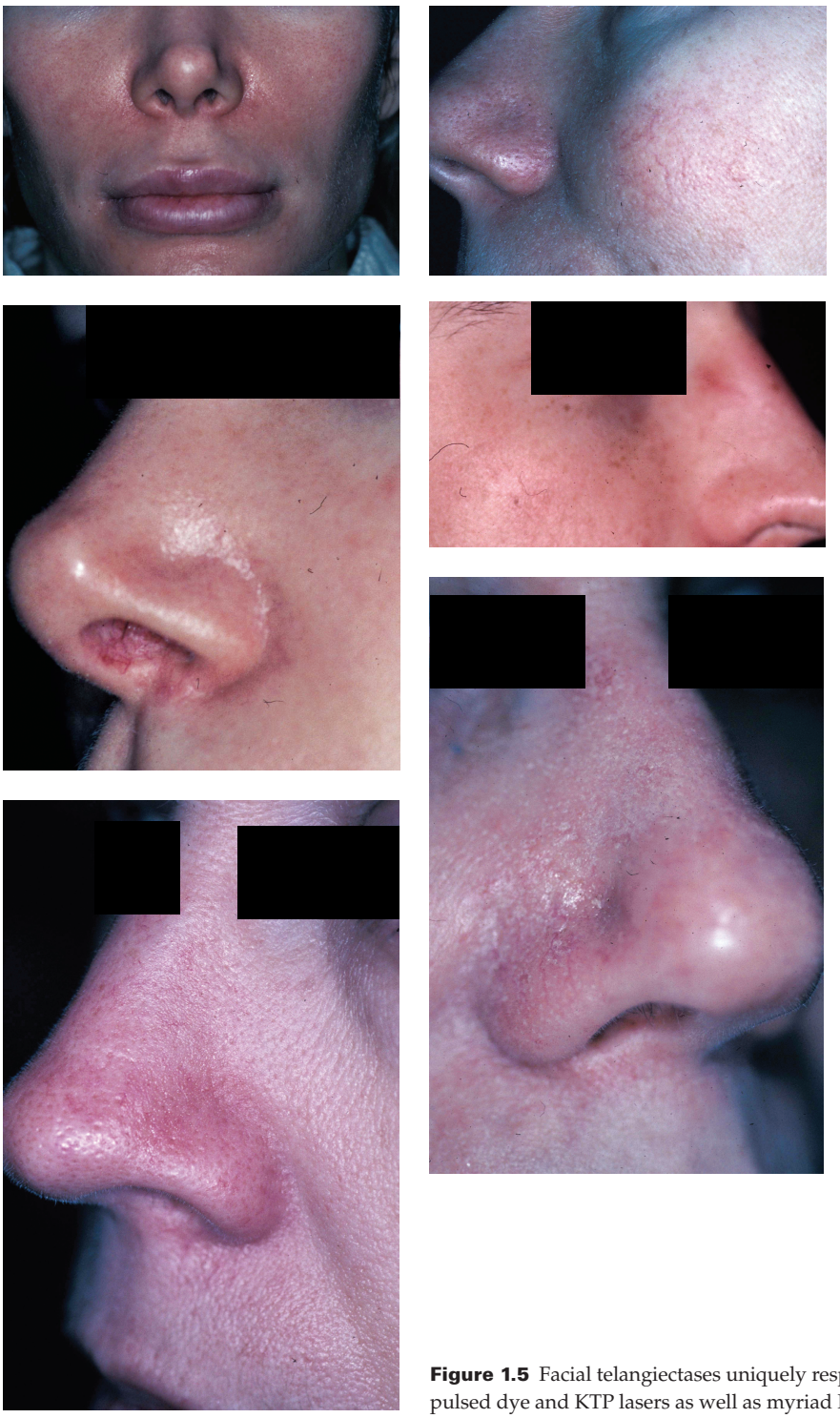


Figure 1.5 Facial telangiectases uniquely responsive to pulsed dye and KTP lasers as well as myriad IPL sources.

subpurpuric doses – achieved by using longer pulse durations of 6 to 10 ms and lowering fluences to just below the purpuric threshold – have been utilized in this region, frequently in combination with pulse stacking or multiple passes. Although somewhat less efficacious, especially in the treatment of larger-caliber, blue telangiectasias, subpurpuric doses are considerably more cosmetically elegant [63–65]. Adverse effects associated with the long PDL may include erythema, swelling, crusting, and transient hyperpigmentation [66]. Patients should also be instructed to avoid sun exposure following treatment to lesson the incidence of post-inflammatory hyperpigmentation.

The 532-nm KTP lasers are ideally suited for tracing small isolated linear telangiectasias less than 1 mm in diameter, as their small spot sizes – between 0.25 and 4 mm – may be difficult to use on larger areas. When used with pulse duration in the millisecond range and fluences between 9 and 25 J/cm^2, depending on spot size, good cosmetic clearance may be achieved after a single treatment [67]. During treatment, the handpiece is moved in a continuous manner to prevent pulse overlap that may result in scarring. The immediate clinical endpoint is blood vessel graying and clearance. The addition of a cooling device and chilled gel reduces the incidence of pain and other potential adverse effects, which may include erythema, edema, blistering, and crusting [68]. Despite slightly lower clearance rates with the KTP laser, the lack of purpura leads to higher patient satisfaction and tolerability compared to the traditional PDL therapy. High-flow vessels, such as those seen on the sides of the nose, will invariably require multiple KTP laser treatments.

The variable-pulse 1064-nm Nd:YAG laser can also be used for facial telangiectasias (Figure 1.6). With deeper penetration and decreased absorption by melanin compared to the PDL, laser light emitted by this device is a good treatment option for larger, bluish telangiectasias, such as the ones found around the nasal alae, as well as for lesions in darker-pigmented individuals. A small spot size – between 1.5 and 3 mm – in combination with long pulse durations of 20 to 40 ms and pre- and post-treatment cooling is recommended in order to avoid overheating of the surrounding dermis with subsequent risk of scarring. Fluences may range between 120 and 170 J/cm^2 for a 3-mm spot size and 220 to 420 J/cm^2 for a 1.5-mm spot size [69,70]. Shorter pulse durations with higher fluences are typically required for the treatment of smaller, red vessels. Longer pulse durations with lower fluences should be used in darker skin types to decrease the risk of dyschromia. The actual selection of treatment parameters depends on observation of the clinical endpoint of vessel blanching. By using small spot sizes

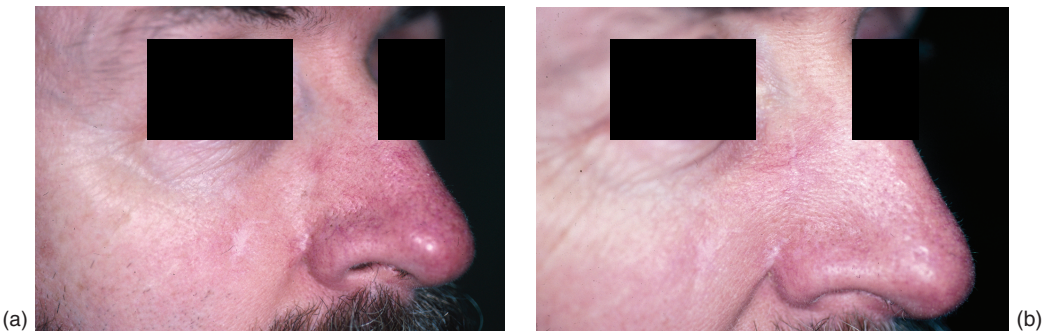


Figure 1.6 (a) Facial telangiectasia before treatment with a millisecond Nd:YAG laser and **(b)** improvement in facial telangiectasia after treatment with a millisecond Nd:YAG laser.

and avoiding high fluences, the rates of complications are relatively low, with adverse effects including mild pain during the procedure, mild blistering, and crusting [69,70]. While very effective for treating individual vessels of various diameters, the small spot sizes used for treatment of telangiectasias preclude the use on more extensive surface areas.

As previously mentioned, IPL devices have a large spot size, making it one of the most convenient treatment options for diffuse facial erythema, such as that associated with rosacea (Figure 1.7). Both small and large vessels can be safely and effectively cleared after an average of 2 to 4 treatments in patients with skin types I to IV. Most frequently, larger telangiectasias require a 590-nm cutoff filter with long pulse durations of around 10 ms delivered as triple pulses, with average fluence of 50 J/cm^2. Fine telangiectasias may be treated with a 560- or 570-nm filter in double-pulse mode with pulse duration of 6 to 7 ms and average fluence of 40 J/cm^2. The clinical endpoint is vessel blanching with perilesional erythema. Adverse effects may include erythema, edema that may last over 1 week, purpura for over 3 days, blisters, and transient hypo- or hyperpigmentation [71,72]. However, the effective treatment of telangiectasias and rosacea using an IPL device with low incidence of adverse effects requires experience and prolonged learning time of up to 18 months [71].

Telangiectatic Leg Veins

Ambulatory phlebectomy and sclerotherapy remain the gold standards for treatment of telangiectatic leg veins. However, sclerotherapy may not be feasible in patients with needle phobia,

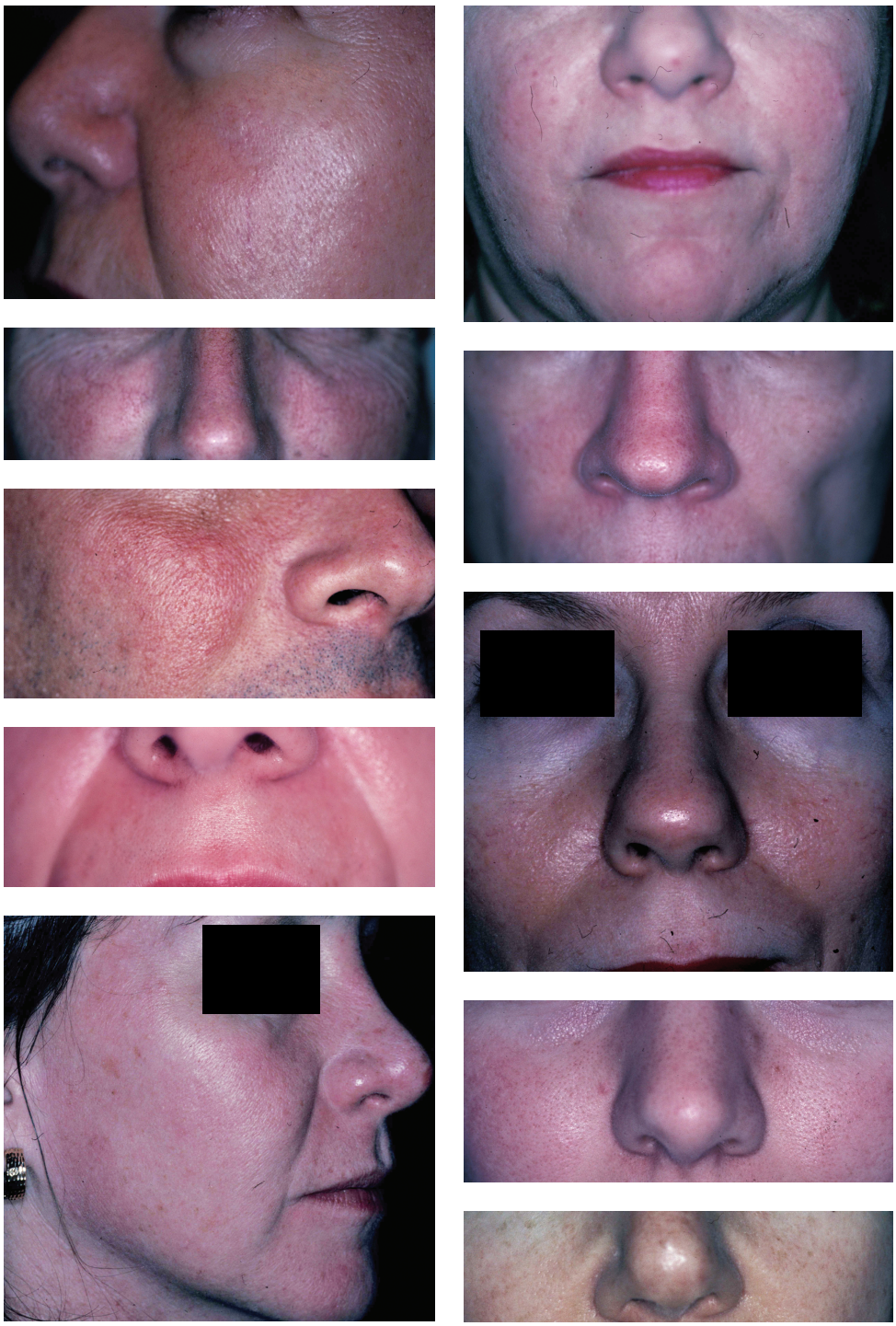
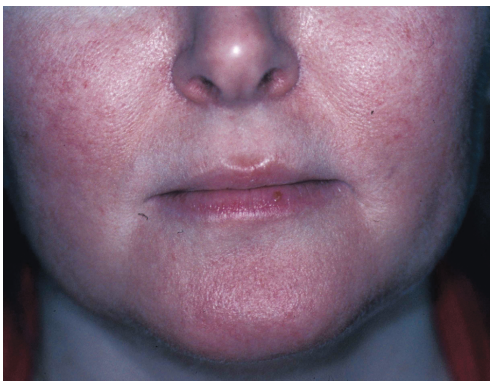


Figure 1.7 Facial erythema can be successfully treated with either the PDL or IPL source.



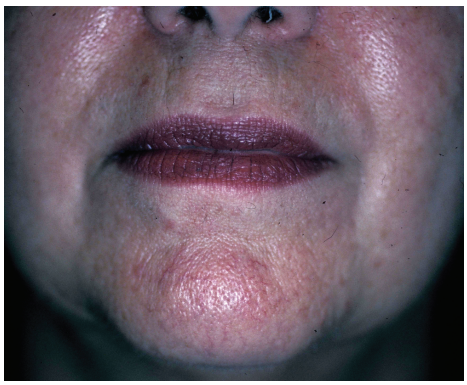


Figure 1.7 (Continued)

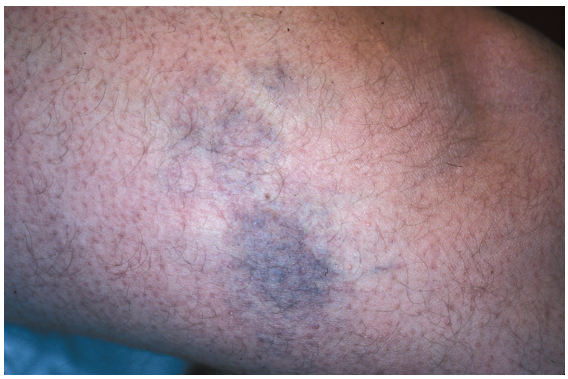


Figure 1.8 Leg spider veins that may be amenable to Nd:YAG laser treatment.

allergies to components of sclerosants, popliteal fossa or ankle telangiectasias, and telangiectatic matting. Recent advances in laser technology, as well as better understanding of leg vein pathology and laser physics, hold a promise for improved treatment options with fewer complications (Figure 1.8).

The unique pathophysiology of leg vein ectasias lies in their relatively large diameter, increased depth in the skin, increased deoxyhemoglobin content, greater hydrostatic pressure, and vessel wall thickening as part of stasis changes. The underlying pathology is clearly complex. Part of the problem appears to be incompetent valves in the communications between the superficial and deep venous channels. Since valves are absent in the superficial venous system, increase in hydrostatic pressure as a result of unobstructed communication with the deep system results in back pressure, vascular dilation, and thickening of

the blood vessel wall. This communication further complicates treatment, as recurrences are common unless the underlying vascular pathology is corrected. Small ectatic leg veins may be subdivided into telangiectasias, venulectasias, and reticular veins, measuring 0.03 to 0.3 mm, 0.4 to 2.0 mm, and 2.0 to 4.0 mm, respectively. These vessels course through the dermis at various depths between 0.15 and 1 mm, with those smaller than 1 mm in diameter typically lying more superficially [73]. The red vessels have a higher concentration of oxygen and oxyhemoglobin compared to the blue ones, which have higher deoxyhemoglobin levels [74].

Several additional laser concepts become important when treating large-caliber vessels. An extended theory of selective photothermolysis relates to the selective destruction of non-uniformly absorbing targets, such as blood vessels. Since the highly absorbing target – in this case, hemoglobin – has to transfer energy through diffusion to the blood vessel to cause sufficient heating of the vessel wall, the pulse duration needs to be considerably longer than the calculated TRT. This duration is known as the thermal damage time [75]. In addition, the TRT of a cylindrical object, such as leg vessels, is higher than that of a sphere. Thus, much longer pulse durations, up to 50 or 70 ms, may at times be used for leg vein laser treatments.

For effective vessel damage to occur, the entire wall has to be heated sufficiently. With vessel diameters of over 1 mm, it is important to select wavelengths and fluences that will not only penetrate the dermis to the depth of the vessel, but will also deliver sufficient energy to the distal wall.

Finally, methemoglobin, an oxidized form of hemoglobin, is formed when blood is heated [76]. Methemoglobin has an absorbance that is 4.75 times higher than that of oxyhemoglobin in the near-infrared range [77]. For larger-caliber vessels, higher energies are used to heat larger volumes; thus, changes in the optical properties of blood with heating become more important and may influence the response of the vessel wall to multiple laser pulses. Higher energies may also result in epidermal damage unless adequate cooling is employed.

Shorter wavelengths, such as those emitted by the pulsed dye and KTP lasers, are generally reserved for treatment of small superficial telangiectasias, especially matted telangiectasias – a frequent complication of sclerotherapy or laser treatment of leg veins. While effective for this indication, as discussed previously, the PDL causes prolonged purpura. In addition, transient or even permanent dyschromia is frequently noted following treatment on the legs with both lasers [78,79]. Although the

clearance rates are improved with the long-pulsed longer-wavelength PDL, the rates of hyperpigmentation are still very high, around 40% [79].

Several near-infrared lasers have been evaluated for treatment of leg telangiectasias. These include the long-pulsed alexandrite laser, diode lasers, and the long-pulsed Nd:YAG laser. These lasers take advantage of the broad oxyhemoglobin absorption peak from 800 to 1200 nm.

Light emitted by the alexandrite laser at 755 nm penetrates tissue for up to 3 mm. An additional advantage of this laser is a relatively high absorption of laser light by deoxyhemoglobin at this wavelength. However, melanin absorption is also significant and the laser can only be used in skin types I to III without a suntan. When a 3 ms pulse duration is used, higher fluences, up to 90 J/cm^2, are required to clear leg telangiectasias. Even with cooling, the incidence of purpura, dyschromia, and matting is high, limiting the usefulness of this laser [80]. Vessels smaller than 0.4 mm, or larger than 1.0 mm, in diameter respond poorly to alexandrite laser therapy [81].

Diode lasers have wavelengths of 800, 810, 910, or 940 nm. Although lower wavelengths, such as 810 nm, give relatively low rates of clearance [80], the newer 940 nm diode lasers equipped with a cooling device hold promise for successful treatment of vessels between 0.8 and 1.4 mm in diameter. The immediate clinical endpoint of treatment is vessel clearance. This longer-wavelength laser also allows for safe treatment of patient with skin types I to IV, with adverse effects limited to pain, mild short-lasting erythema, transient crusting, telangiectatic matting, and transient hypopigmentation [73].

Millisecond-domain Nd:YAG lasers currently offer the best results of all lasers for ectatic leg veins of up to 3 mm in diameter. Small spot sizes of 1.5 mm are used for smaller red telangiectasias with pulse durations of 30 to 50 ms and fluences of up to 600 J/cm^2, whereas larger blue veins require larger spot sizes, such as 3 mm, longer pulse durations of 50 to 60 ms and lower fluences of up to 370 J/cm^2 [82]. With proper parameters and cooling, this laser can be safely used in patients with skin types I to V. If contact or cryogen spray cooling is used, the adverse effects may include bruising, transient hyperpigmentation, and pain. However, treatment of larger-caliber veins may be associated with considerable discomfort, and patients may prefer sclerotherapy for such vessels [83]. An additional consideration in the treatment of leg veins using an Nd:YAG laser is the use of non-uniform pulse sequences. This concept is based on the increased laser energy absorption by methemoglobin

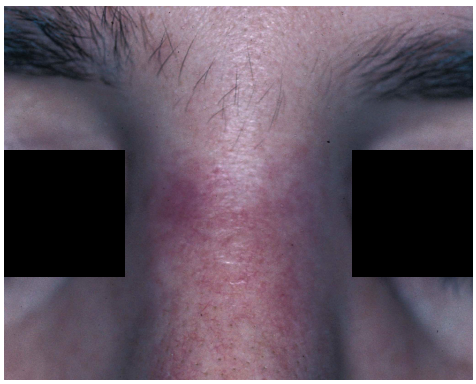
produced during heating of blood, as described above. If long exposure is achieved through a sequence of shorter pulses, the later pulses require considerably less energy than the first. Taking advantage of this concept, similar clinical improvement in leg veins can be achieved using less overall fluence. The result is decreased pain, lower incidence of adverse effects, and successful use in patients with skin type VI [84].

Miscellaneous Vascular Lesions

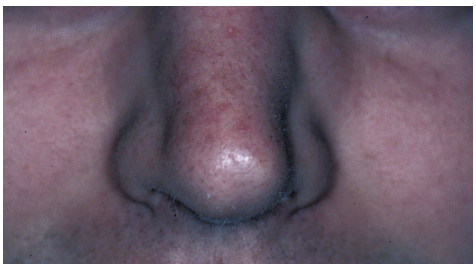
Spider Angiomas

Also known as spider nevi, spider angiomas consist of a central feeder arteriole 0.1 to 0.5 mm in diameter connected to superficial ectatic capillaries at the depth of 0.3 mm [33]. Multiple spider angiomas may be present in hyperestrogenic states, such as liver cirrhosis, and hereditary hemorrhagic telangiectasia, or Osler–Weber–Rendu, syndrome. Because of the superficial nature of these lesions, KTP and PDL are very effective at clearing spider angiomas (Figure 1.9).

The feeding arteriole is usually treated first. A helpful technique used to isolate and to decrease blood flow within the central arteriole is diascopy. Laser pulses are then delivered directly to the vessel, followed by release of diascopy and treatment of surrounding telangiectasias [33]. Good results can be achieved using a KTP laser with pulse duration of 10 to 14 ms and fluences between 10 and 12 J/cm^2 [85]. If using a PDL, a spot size of 5 or 7 mm and fluences between 8 and 10 J/cm^2 are usually effective [86]. One to two treatments administered 4 to 6 weeks apart may be needed for complete clearance. Aside from purpura seen with the PDL



(a)



(b)

Figure 1.9 **(a)** Spider angioma before laser treatment and **(b)** resolved angioma after laser treatment.

therapy, the incidence of adverse effects is low when treating these lesions.

Cherry Angiomas

Cherry angiomas are common acquired vascular tumors, most commonly found on the trunk. They present as bright red well-circumscribed papules and tend to increase in number with age. Histologically, large interconnected vascular dilations, ranging from 10 to 50 μm in diameter, are closely packed within the papillary dermis [87].

A variety of lasers and light sources can be used in the treatment of this benign vascular lesion, including argon, KTP, PDL, and Nd:YAG lasers and IPL devices [88,89]. All modalities of treatment work well.

Pyogenic Granulomas

Pyogenic granulomas, also known as lobular capillary hemangiomas, are eruptive vascular lesions frequently arising at sites of trauma. They are most commonly seen in children and are prone to bleeding. Multiple lesions may appear in association with isotretinoin or anti-retroviral therapy. Histologically, lobules of dilated capillaries are separated by myxoid stroma. A central feeding arteriole is always present and resembles that of a spider angioma [33].

Thin pyogenic granulomas are very amenable to laser treatment. PDL is most commonly used for these lesions (Figure 1.10). Standard purpuric doses with cooling are typically used with good clearance after 1 to 2 treatment sessions [90,91]. Alternatively, tissue vaporization using CO_2 laser may be performed, but may be associated with scarring [92].

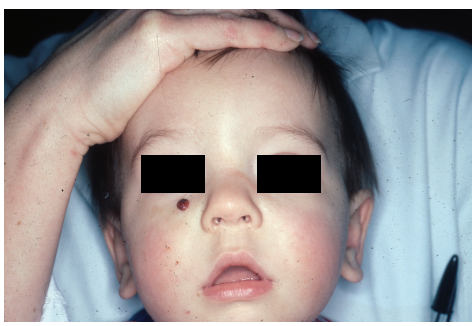
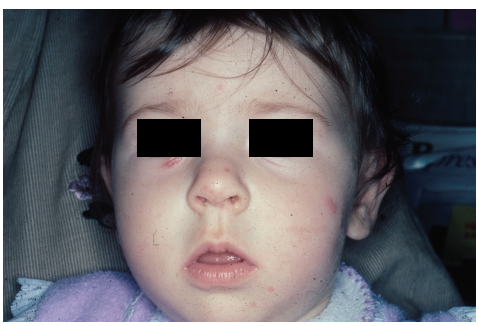
(a)   (b)

Figure 1.10 (a) Pyogenic granuloma before laser treatment and **(b)** improvement in pyogenic granuloma after PDL treatment.

Conclusions

Vascular lasers were among the first to be developed in accordance with the principles of selective photothermolysis. Over the years, multiple modifications have taken place to better adjust to the specific characteristics of treating vascular lesions. Treatment options have further expanded with the introduction of IPL devices. As new therapies emerge, treatment of vascular lesions will likely continue to improve with higher clearance rates, faster resolution, and fewer adverse effects.

References

1. Kalick SM, Goldwyn RM, Noe JM. Social issues and body image concerns of port wine stain patients undergoing laser therapy. *Laser Surg Med* 1981;**1**:205–13.
2. Lanigan SW, Cotterill JA. Psychological disabilities amongst patients with port wine stains. *Br J Dermatol* 1989;**121**:209–15.
3. Anderson RR, Parish JA. Selective photothermolysis: precise microsurgery by selective absorption of pulsed radiation. *Science* 1983;**220**:524–7.
4. van Gemert MJ, Henning JP. A model approach to laser coagulation of dermal vascular lesions. *Arch Dermatol Res* 1981;**270**:429–39.
5. Kauvar ANB, Wang RS. Laser treatment of cutaneous vascular anomalies. *Lymphat Res Biol* 2004;**2**:38–50.
6. Dierickx C, Casparian JM, Venugopolan V, Farinelli WA, Anderson RR. Thermal relaxation of portwine stain vessels probed in vivo: the need for 1–10 msecs laser pulse treatment. *J Invest Dermatol* 1995;**105**:709–14.
7. van Gemert MJ, Smithies DJ, Verkruysse W, Milner TE, Nelson JS. Wavelengths for port wine stain laser treatment: influence of vessel radius and skin anatomy. *Phys Med Biol* 1997;**42**:41–50.
8. Keijzer M, Pickering JW, van Germert MJ. Laser beam diameter for port-wine stain treatment. *Laser Surg Med* 1991;**11**:601–5.
9. Chang CJ, Nelson JS. Cryogen spray cooling and higher fluence pulsed dye laser treatment improve port-wine stain clearance while minimizing epidermal damage. *Dermatol Surg* 1999;**25**:767–72.
10. Mulliken JB, Glowacki J. Hemangiomas and vascular malformations in infants and children: a classification based on endothelial characteristics. *Plast Reconstr Surg* 1982;**69**:412–20.
11. Barsky SH, Rosen S, Geer DE, Noe JM. The nature and evolution of port-wine stains: a computer-assisted study. *J Invest Dermatol* 1980;**74**:154–7.
12. Waner M, Suen JY. A classification of congenital vascular lesions. In: *Hemangiomas and Vascular Malformations of the Head and Neck*. Waner M, Suen JY, eds. John Wiley & Sons, New York, NY, 1999.
13. Fishman SJ, Mulliken JB. Hemangiomas and vascular malformations of infancy and childhood. *Pediatr Clin North Am* 1993;**40**:1177–200.

14. Mulliken JB, Enjolras O. Congenital hemangiomas and infantile hemangioma: missing links. *J Am Acad Dermatol* 2004;**50**:875–82.
15. Renfro L, Geronemus RG. Anatomical differences of port-wine stains in response to treatment with the pulsed dye laser. *Arch Dermatol* 1993;**129**:182–8.
16. Kauvar ANB, Renfro LR, Geronemus RG. Anatomical differences of PWS located in the trunk and extremities in response to treatment with the pulsed dye laser. *Laser Surg Med* 1994;**14**:47.
17. Nguyen CM, Yohn JJ, Huff C, Weston WL, Morelli JG. Facial port wine stains in childhood: prediction of the rate of improvement as a function of the age of the patient, size and location of the port wine stain and the number of treatments with the pulsed dye (585 nm) laser. *Br J Dermatol* 1998;**138**:821–5.
18. Motley RJ, Lanigan SW, Katugampola GA. Videomicroscopy predicts outcome in treatment of port-wine stains. *Arch Dermatol* 1992;**133**:921–2.
19. Fiskerstrand EJ, Svaasand LO, Kopstad G, Dalaker M, Norvang LT, Volden G. Laser treatment of port-wine stains: therapeutic outcome in relation to morphological parameters. *Br J Dermatol* 1996;**134**:1039–43.
20. Fiskerstrand EJ, Svaasand LO, Kopstad G, Ryggen K, Aase S. Photothermally induced vessel-wall necrosis after pulsed dye laser treatment: lack of responses in port-wine stains with small sized or deeply located vessels. *J Invest Dermatol* 1996;**107**:671–5.
21. Tan OT, Sherwood K, Gilcrest BA. Treatment of children with PWS using the flashlamp-pulsed tunable dye laser. *N Engl J Med* 1989;**320**:416–21.
22. Reyes BA, Geronemus R. Treatment of port-wine stains during childhood with the flashlamp-pumped pulsed dye laser. *J Am Acad Dermatol* 1990;**23**:1142–8.
23. van der Horst CM, Koster PH, de Borgie CA, Bossuyt PM, van Gemert MJ. Effect of the timing of treatment of port-wine stains with the flash-lamp-pumped pulsed-dye laser. *N Eng J Med* 1998;**338**:1028–33.
24. Alster TS, Wilson F. Treatment of port-wine stains with the flash-lamp-pumped pulsed dye laser: extended clinical experience in children and adults. *Ann Plast Surg* 1994;**32**:478–84.
25. Fitzpatrick RE, Lowe NJ, Goldman MP, Borden H, Behr KL, Ruiz-Esparza J. Flashlamp-pumped pulsed dye laser treatment of port-wine stains. *J Dermatol Surg Oncol* 1994;**20**:743–8.
26. Kauvar ANB. Long-pulse, high energy pulsed dye laser treatment of PWS and hemangiomas. *Laser Surg Med* 1997;Suppl 9:36.
27. Geronemus RG. High-radiant exposure modified pulsed dye laser photocoagulation with dynamic cooling of port-wine stains in infancy. *Arch Dermatol* 2000;**136**:942–3.
28. Kelly KM, Nanda VS, Nelson JS. Treatment of port-wine stain birthmarks using the 1.5-ms pulsed dye laser at high radiant exposures in combination with cryogen spray cooling. *Dermatol Surg* 2002;**28**:309–13.
29. Sivarajan V, Maclaren WM, Mackay IR. The effect of varying pulse duration, wavelength, spot size, and fluence on the response of

previously treated capillary vascular malformations to pulsed-dye laser treatment. *Ann Plast Surg* 2006;**57**:25–32.
30. Dierickx C, Farinelli W, Anderson R. Multiple pulse photocoagulation of port-wine stain blood vessels with a 585 nm pulsed dye laser. *Laser Surg Med Suppl* 1995;**7**:56.
31. Lou WW, Geronemus RG. Treatment of port-wine stains by variable pulsed width pulsed dye laser with cryogen spray: a preliminary study. *Dermatol Surg* 2001;**27**:963–5.
32. Tanghetti E, Sherr EA, Sierra R, Mirkov M. The effects of pulse dye laser double-pass treatment intervals on depth of vessel coagulation. *Laser Surg Med* 2006;**38**:16–21.
33. Astner S, Anderson RR. Treating vascular lesions. *Dermatol Ther* 2005;**18**:267–81.
34. McGill DJ, Mackay IR. The effect of ambient temperature on capillary vascular malformations. *Br J Dermatol* 2006;**154**:896–903.
35. Koster PH, van der Horst CM, Bossuyt PM, van Gemert MJ. Prediction of port wine stain clearance and required number of flashlamp pumped pulsed dye laser treatments. *Laser Surg Med* 2001;**29**:151–5.
36. Wlotzke U, Hohenleutner U, Abd-El-Raheem TA, Baumler W, Landthaler M. Side-effects and complications of flashlamp-pumped pulsed dye laser therapy of port-wine stains: a prospective study. *Br J Dermatol* 1996;**134**:475–80.
37. Levine VJ, Geronemus RG. Adverse effects associated with the 577- and 585-nanometer pulsed dye laser in the treatment of cutaneous vascular lesions: a study of 500 patients. *J Am Acad Dermatol* 1995;**32**:613–17.
38. Abd-el-Raheem TA, Hohenleutner U, Landthaler M. Granuloma pyogenicum as a complication of flashlamp-pumped pulsed dye laser. *Dermatology* 1994;**189**:283–5.
39. Chowdhury MM, Harris S, Lanigan SW. Potassium titanyl phosphate laser treatment of resistant port-wine stains. *Br J Dermatol* 2001;**144**:814–17.
40. Woo WK, Jasim ZF, Handley JM. Evaluating the efficacy of treatment of resistant port-wine stains with variable-pulse 595 nm pulsed dye and 532 nm Nd:YAG lasers. *Dermatol Surg* 2004;**30**:158–62.
41. Pence B, Aybey B, Ergenekon G. Outcomes of 532 nm frequency-doubled Nd:YAG laser use in the treatment of port-wine stains. *Dermatol Surg* 2005;**31**:509–17.
42. Yang MU, Yaroslavsky AN, Farinelli WA, Flotte TJ, Rius-Diaz F, Tsao SS, Anderson RR. Long-pulsed neodymium:yttrium–aluminum–garnet laser treatment for port-wine stains. *J Am Acad Dermatol* 2005;**52**:480–90.
43. Groot D, Rao J, Johnston P, Nakatsui T. Algorithm for using a long-pulsed Nd:YAG laser in the treatment of deep cutaneous vascular lesions. *Dermatol Surg* 2003;**29**:35–42.
44. Raulin C, Schroeter CA, Weiss RA, Keiner M, Werner S. Treatment of port-wine stains with a noncoherent pulsed light source: a retrospective study. *Arch Dermatol* 1999;**135**:679–83.

45. Ho WS, Ying SY, Chan PC, Chan HH. Treatment of port wine stains with intense pulsed light: a prospective study. *Dermatol Surg* 2004;**30**:887–90.
46. Vlachos SP, Kontoes PP. Development of terminal hair following skin lesion treatments with an intense pulsed light source. *Aesthetic Plast Surg* 2002;**26**:303–7.
47. Anderson RR. Infant hemangiomas: a controversy worth solving. *Laser Surg Med* 2006;**38**:92–3.
48. Haywood RM, Monk BE, Mahaffey PJ. The treatment of early cutaneous capillary haemangiomata (strawberry naevi) with the tunable dye laser. *Br J Plast Surg* 2000;**53**:302–7.
49. Poetke M, Philipp C, Berlien HP. Flashlamp-pumped pulsed dye laser for hemangiomas in infancy: treatment of superficial vs mixed hemangiomas. *Arch Dermatol* 2000;**136**:628–32.
50. Hohenleutner S, Badur-Ganter E, Landthaler M, Hohenleutner U. Long-term results in the treatment of childhood hemangioma with the flashlamp-pumped pulsed dye laser: an evaluation of 617 cases. *Laser Surg Med* 2001;**28**:273–7.
51. Batta K, Goodyear HM, Moss C, Williams HC, Hiller L, Waters R. Randomised controlled study of early pulsed dye laser treatment of uncomplicated childhood haemangiomas: results of a 1-year analysis. *Lancet* 2002;**360**:521–7.
52. Kono T, Sakurai H, Groff WF, Chan HH, Takeuchi M, Yamaki T, et al. Comparison study of a traditional pulsed dye laser versus a long-pulsed dye laser in the treatment of early childhood hemangiomas. *Laser Surg Med* 2006;**38**:112–15.
53. Witman PM, Wagner AM, Scherer K, Waner M, Frieden IJ. Complications following pulsed dye laser treatment of superficial hemangiomas. *Laser Surg Med* 2006;**38**:116–23.
54. Morelli JG, Tan OT, Weston WL. Treatment of ulcerated hemangiomas with the pulsed tunable dye laser. *Am J Dis Child* 1991;**145**:1062–4.
55. David LR, Malek MM, Argenta LC. Efficacy of pulse dye laser therapy for the treatment of ulcerated haemangiomas: a review of 78 patients. *Br J Plast Surg* 2003;**56**:317–27.
56. Scheepers JH, Quaba AA. Does the pulsed tunable dye laser have a role in the management of infantile hemangiomas? Observations based on 3 years' experience. *Plast Reconstr Surg* 1995;**95**:305–12.
57. Raulin C, Greve B. Retrospective clinical comparison of hemangioma treatment by flashlamp-pumped (585 nm) and frequency-doubled Nd:YAG (532 nm) lasers. *Laser Surg Med* 2001;**28**:40–3.
58. Pham RT. Treatment of vascular lesions with combined dynamic precooling, postcooling thermal quenching, and Nd:YAG 1,064-nm laser. *Facial Plast Surg* 2001;**17**:203–8.
59. Angermeier MC. Treatment of facial vascular lesions with intense pulsed light. *J Cutan Laser Ther* 1999;**1**:95–100.
60. Sarig O, Kimel S, Orenstein A. Laser treatment of venous malformations. *Ann Plast Surg* 2006;**57**:20–4.
61. Derby LD, Low DW. Laser treatment of facial venous vascular malformations. *Ann Plast Surg* 1997;**38**:371–8.

62. Raulin C, Werner S. Treatment of venous malformations with an intense pulsed light source (IPLS) technology: a retrospective study. *Laser Surg Med* 1999;**25**:170–7.
63. Iyer S, Fitzpatrick RE. Long-pulsed dye laser treatment for facial telangiectasias and erythema: evaluation of a single purpuric pass versus multiple subpurpuric passes. *Dermatol Surg* 2005;**31**:898–902.
64. Alam M, Dover JS, Arndt KA. Treatment of facial telangiectasia with variable-pulse high-fluence pulsed-dye laser: comparison of efficacy with fluences immediately above and below the purpura threshold. *Dermatol Surg* 2003;**29**:681–5.
65. Goldberg DJ, Marmur ES, Amin S, Hussain M. Comparative treatment of small diameter (⩽400 micrometer) vascular lesions using extended pulse dye lasers. *Laser Surg Med* 2006;**38**:106–11.
66. Alam M, Omura NE, Dover JS, Arndt KA. Clinically significant facial edema after extensive treatment with purpura-free pulsed-dye laser. *Dermatol Surg* 2003;**29**:920–4.
67. Goldberg DJ, Meine JG. A comparison of four frequency-doubled Nd:YAG (532 nm) laser systems for treatment of facial telangiectases. *Dermatol Surg* 1999;**25**:463–7.
68. Kauvar AN, Frew KE, Friedman PM, Geronemus RG. Cooling gel improves pulsed KTP laser treatment of facial telangiectasia. *Laser Surg Med* 2002;**30**:149–53.
69. Sarradet DM, Hussain M, Goldberg DJ. Millisecond 1064 nm neodymium:YAG laser treatment of facial telangiectases. *Dermatol Surg* 2003;**29**:56–8.
70. Bevin AA, Parlette EC, Domankevitz Y, Ross EV. Variable-pulse Nd:YAG laser in the treatment of facial telangiectasias. *Dermatol Surg* 2006;**32**:7–12.
71. Clementoni MT, Gilardino P, Muti GF, Signorini M, Pistorale A, Morselli PG, et al. Intense pulsed light treatment of 1,000 consecutive patients with facial vascular marks. *Aesth Plast Surg* 2006;**30**:226–32.
72. Schroeter CA, Haaf-von Below S, Neumann HAM. Effective treatment of rosacea using intense pulsed light systems. *Dermatol Surg* 2005;**31**:1285–9.
73. Passeron T, Olivier V, Duteil L, Desruelles F, Fontas E, Ortonne JP. The new 940-nanometer diode laser: an effective treatment for leg venulectasia. *J Am Acad Dermatol* 2003;**48**:768–74.
74. Sommer A, Van Mierlo PL, Neumann HA, Kessels AG. Red and blue telangiectasias. Differences in oxygenation? *Dermatol Surg* 1997;**23**:55–9.
75. Altshuler GB, Anderson RR, Manstein D, Zenzie HH, Smirnov MZ. Extended theory of selective photothermolysis. *Laser Surg Med* 2001;**29**:416–32.
76. Alves OC, Wajnberg E. Heat denaturation of methemoglobin and oxyhemoglobin: evidence for the existence of a new hemochrome. *Int J Biol Macromol* 1993;**15**:273–9.
77. Kuenster JT, Norris KH. Spectrophotometry of human hemoglobin in the near infrared region from 1000 to 2500 nm. *J Near Infrared Spec* 1994;**2**:59–65.

78. Spendel S, Prandl EC, Schintler MV, Siegl A, Wittgruber G, Hellbom B, et al. Treatment of spider leg veins with the KTP (532 nm) laser – a prospective study. *Laser Surg Med* 2002;**31**:194–201.
79. Reichert D. Evaluation of the long-pulse dye laser for the treatment of leg telangiectasias. *Dermatol Surg* 1998;**24**:737–40.
80. Eremia S, Li C, Umar SH. A side-by-side comparative study of 1064 nm Nd:YAG, 810 nm diode and 755 nm alexandrite lasers for treatment of 0.3–3 mm leg veins. *Dermatol Surg* 2002;**28**:224–30.
81. McDaniel DH, Ash K, Lord J, Newman J, Adrian RM, Zukowski M. Laser therapy of spider leg veins: clinical evaluation of a new long pulsed alexandrite laser. *Dermatol Surg* 1999;**25**:52–8.
82. Sadick NS. Laser treatment with a 1064-nm laser for lower extremity class I–III veins employing variable spots and pulse width parameters. *Dermatol Surg* 2003;**29**:916–19.
83. Coles CM, Werner RS, Zelickson BD. Comparative pilot study evaluating the treatment of leg veins with a long pulsed Nd:YAG laser and sclerotherapy. *Laser Surg Med* 2002;**30**:154–9.
84. Mordon S, Brisot D, Fournier N. Using a "non uniform pulse sequence" can improve selective coagulation with a Nd:YAG laser (1.06 micron) thanks to met-hemoglobin absorption: a clinical study on blue leg veins. *Laser Surg Med* 2003;**32**:160–70.
85. Clark C, Cameron H, Moseley H, Ferguson J, Ibbotson SH. Treatment of superficial cutaneous vascular lesions: experience with the KTP 532 nm laser. *Laser Med Science* 2004;**19**:1–5.
86. Geronemus RG. Treatment of spider telangiectases in children using the flashlamp-pumped pulsed dye laser. *Pediatr Dermatol* 1991;**8**:61–3.
87. Aghassi D, Anderson RR, Gonzalez S. Time-sequence histologic imaging of laser-treated cherry angiomas with in vivo confocal microscopy. *J Am Acad Dermatol* 2000;**43**:37–41.
88. Dawn G, Gupta G. Comparison of potassium titanyl phosphate vascular laser and hyfrecator in the treatment of vascular spiders and cherry angiomas. *Clin Exp Dermatol* 2003;**28**:581–3.
89. Fodor L, Ramon Y, Fodor A, Carmi N, Peled IJ, Ullmann Y. A side-by-side prospective study of intense pulsed light and Nd:YAG laser treatment for vascular lesions. *Ann Plast Surg* 2006;**56**:164–70.
90. Tay YK, Weston WL, Morelli JG. Treatment of pyogenic granuloma in children with the flashlamp-pumped pulsed dye laser. *Pediatrics* 1997;**99**:368–70.
91. Goldberg DJ, Sciales CW. Pyogenic granuloma in children. Treatment with the flashlamp-pumped pulsed dye laser. *J Dermatol Surg Oncol* 1991;**17**:960–2.
92. Raulin C, Greve B, Hammes S. The combined continuous-wave/pulsed carbon dioxide laser for treatment of pyogenic granuloma. *Arch Dermatol* 2002;**138**:33–7.