Laser treatment of pediatric vascular lesions: Port wine stains and hemangiomas

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Pediatric vascular lesions can be medically threatening and psychologically distressing to patients. This article reviews literature on the laser treatment of two common pediatric vascular lesions, port wine stains and hemangiomas. The purpose of this report was to distinguish the lesions from one another and to present the advantages, disadvantages, complications, and limitations of laser treatment for each lesion type. This review is not a comprehensive inventory but instead highlights the studies that best show promising results or the limitations of laser treatment for the lesions. Overall, port wine stain laser treatment promoted notable clearing with low side effects, whereas hemangioma laser treatment provided inconsistent benefits and severe side effects occasionally. Laser treatment of port wine stains is safe and effective, but laser treatment of hemangiomas remains controversial and is best for lesions without deeper components. (J Am Acad Dermatol 2008;58:261-85.)

VASCULAR LESION LASER TREATMENT HISTORY

Lasers were first used to treat cutaneous pathologies in 1963 by Dr Leon Goldman. Although Goldman originally used a ruby laser for skin treatment, argon and carbon-dioxide continuous wave (CW) lasers soon became the main treatment modalities for the first generation of dermatologic lasers. Emitting in the blue-green section of the electromagnetic spectrum with peak emissions at 488 and 514 nm, the argon laser successfully lightened port wine stain (PWS) and hemangioma but carried a high risk of hypertrophic scarring. The CW carbon-dioxide laser emitted at 10,600 nm and ablated epidermal and dermal lesions but also had high rates of hypertrophic scarring and pigmentation problems. CW lasers (eg, argon and CW neodymium:yttrium-aluminum-garnet [Nd:YAG]) are not used to treat PWSs and are only of historical importance. Dermatologic laser treatment was revolutionized in the 1980s as a result of the theory of selective photothermolysis by Anderson and Parrish. The pulsed dye laser (PDL) was the first laser developed with selective photothermolysis in mind. It avoided the nonspecific thermal damage caused by previous lasers by matching the laser wavelength to the wavelengths absorbed by target chromophores. This enabled the PDL to specifically target particular tissues. Today, the PDL is the gold standard for the treatment of PWSs, but an optimal laser treatment for hemangiomas has yet to be discovered.

LASER SKIN INTERACTIONS

Lasers designed around the principles of selective photothermolysis deliver energy precisely into the target with minimal damage to surrounding tissue. This energy targeted at and absorbed by chromophores is converted to heat, which creates a thermal effect within the tissue. The buildup of denatured material increases exponentially with temperature, and proportionally with time. Near a certain critical temperature, coagulation results. This critical temperature is specific to particular targets. Between 60°C and 70°C, collagen and other structural proteins are denatured. Between 70°C and 80°C, nucleic acids

Abbreviations used:
CM: capillary malformation
CW: continuous wave
EMLA: eutectic mixture of local anesthetics
GLUT1: glucose transporter 1
LPDL: long pulsed dye laser
Nd:YAG: neodymium:yttrium-aluminum-garnet
PDL: pulsed dye laser
PWS: port wine stain
TRT: thermal relaxation time

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Funding sources: None.
Conflicts of interest: None declared.
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Published online December 10, 2007.
0190-9622/534.00
© 2008 by the American Academy of Dermatology, Inc.
doi:10.1016/j.jaad.2007.10.492

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Temperatures above 100°C bring intracellular water to its boiling point. The vaporizing steam produced in tissue leads to a sudden increase in pressure and injury to most of the cell structures and blood vessels. Rapid vaporization is especially valuable in separating or ablating tissues, although if heating at these high temperatures continues, charring results.2,3

The longer the tissue is exposed to the laser, the more thermal energy diffuses into surrounding tissues by conduction. Thermal relaxation time (TRT), measured in seconds, is the amount of time for a particular type of tissue to lose half the heat gained from the laser. To keep the laser from causing widespread damage to other tissues, the laser ablation must occur faster than heat is conducted into outside tissue. Effective heating occurs using a pulse duration approximately equal to the target’s TRT. Different blood vessels have different TRTs: capillaries have a TRT of tens of microseconds, PWS venules have a TRT of tens of milliseconds, and leg veins have a TRT of hundreds of milliseconds. Small targets (eg, nevus of Ota) are treated with submicrosecond pulses, whereas bigger targets (eg, hair follicles) are treated with longer pulses. TRT also depends on the shape of the tissue. All other things equal, spheres will cool faster than cylinders, and cylinders will cool faster than planes.4

To effectively target specific tissues, these factors of pulse duration, spot size, and TRT, in addition to selecting a particular wavelength, must be taken into account.

To limit damage and improve results, skin cooling is used during laser treatment. The 3 main types of skin cooling are precooling, parallel cooling, and postcooling with the nomenclature relating to the temporal application of the coolant. Precooling lowers skin temperature before the arrival of the laser pulse on the skin. For very short pulses (<5 milliseconds), less time is needed to extract heat, and the precooling provides any necessary epidermal protection. Dynamic cooling devices such as the cryogen cooling spray allow the most vigorous epidermal precooling. Parallel cooling chills the skin during the laser pulse and is best for pulses longer than 5 to 10 milliseconds. Postcooling helps alleviate pain and erythema.4

LASER TREATMENT OF PEDIATRIC VASCULAR LESIONS

For the treatment of vascular lesions, laser wavelengths are matched with hemoglobin absorption peaks. These absorption peaks are located at 418, 542, and 577 nm, all within the visible spectrum. Specifically targeting hemoglobin thermally damages blood vessels, which yields a spectrum of damage. The primary mechanism is thermal coagulation of the vessel wall and surrounding dermis. An optimal wavelength to target oxygenated hemoglobin is 577 nm. At 577 nm, light penetrates skin easily, has limited melanin absorption, and is well absorbed by blood vessels. According to early data of Anderson and Parrish,3 a 577-nm wavelength pulse on the forearms of pale-skinned volunteers caused considerable vascular changes with almost no damage to the epidermis or structures between vessels, although some purpura was observed. Targeting hemoglobin in hamster cheek pouches, researchers observed an immediate brown discoloring of the blood, followed by a sudden decrease in blood flow, and permanent hemostasis ensued. Since those early studies, technology has been further refined, and today, a 595-nm wavelength is generally standard for microvascular areas, to achieve precise absorption with slightly deeper penetration.3

To target tissues below the pigmented tissue, such as microvessels, it is best to choose a wavelength poorly absorbed by the competing pigment (eg, melanin), and better absorbed by the vascular targets. Since the discovery of selective photothermolysis, PDLs have come to the forefront of vascular lesion treatment, and because they can selectively target hemoglobin, they are particularly effective for PWSs.

The PDL emits yellow light in adjacent nonoverlapping pulses of around 450 µs, which is the lower end of the TRT for skin vasculature.2 Fluences range from 5 to 10 J/cm² and spot sizes range from 2 to 10 mm.5

In 1981, Greenwald et al6 studied the histologic changes occurring from the use of a 577-nm PDL on normal-appearing human skin. The immediate result of the PDL was erythrocyte aggregation, vessel rupture, and hemorrhage. Primary changes were almost entirely related to vascular structures and essentially involved the superficial vascular plexus. The vasculitic change took place in roughly the upper 0.5 mm of the dermis, whereas deeper in the dermis (0.5-1.1 mm) a scattered, mostly perivascular polymorphonuclear leukocytic infiltrate was intermittently associated with lymphocytes.6 The threshold fluence to trigger significant vascular injury was roughly 3 J/cm², although minimal hemorrhage and erythrocyte agglutination have been observed at 1 J/cm². A fluence of 5 J/cm² caused the most severe vascular injury, as full-thickness epidermal necrosis and subepithelial blister formation occurred.6

Tan et al7 subsequently reported that a week after PDL treatment of PWSs, damaged vessels were replaced by fine granulation tissue, and blood
vessels in the papillary dermis had smaller luminal diameters than controls. One month after PDL treatment, no abnormally dilated PWS blood vessels remained, and all treated vessels had a small luminal diameter, thicker walls, and more conspicuous endothelial cells and pericytes than controls. No significant changes were seen in the epidermis at 30 days. Researchers concluded that PWSs could be treated with the PDL without damage to the epidermis, pigment cells, or adnexal structures.

CONSIDERATIONS FOR PEDIATRIC LASER TREATMENT

Anesthesia is an important concern when using laser treatment on infants and children. Topical anesthetics include 4% to 5% liposomal lidocaine, a eutectic mixture of local anesthetics (EMLA) (2.5% prilocaine and 2.5% lidocaine), and many other compounded topical anesthetic preparations. However, it is important to note that EMLA may blanch pale lesions, making them more difficult to treat. Use of EMLA in infants younger than 3 months is associated with an increased risk of methemoglobinemia as a result of immaturity of erythrocyte methemoglobin reductase, the enzyme that converts methemoglobin to hemoglobin. Children with glucose-6-phosphate dehydrogenase deficiency or hemoglobinopathies may also be at increased risk. Alternatives include injectable lidocaine for small areas of the face and neck, or general anesthesia for larger areas.

A 1997 study by Grevelink et al found no increased risk of procedural complications using general anesthesia during pediatric PWS laser treatment. In addition, treatment without risk of unexpected movement was faster and covered a larger area. Although noting that the long-term side effects of general anesthesia on the developing brain were unknown, researchers advocated general anesthesia for PWS laser treatment in younger children with larger lesions, and topical or local anesthesia for children with smaller lesions.

Laser safety is a significant concern for the patient, physician, and clinic personnel. Adults may use standard goggles for eye protection, but these shields may be inadequate for infants and small children. In such cases, patches of overlapping white gauze may be used to cover the periorbital area, as these will nonspecifically absorb and reflect laser light. Metal corneal shields may be used if the laser surgery occurs close to the eye.

Patient and parental anxiety are also important issues for the physician to address. Often, simple reassurances from the physician are inadequate under such circumstances. It is useful to outline potential treatment options (including no treatment) and the advantages and disadvantages of each treatment type. Patients and parents may also want to view before-and-after photographs and make contact with other parents and pediatric patients in similar circumstances. Parents must be adequately informed of aftercare procedures, including follow-up appointments, and expected side effects.

PORT WINE STAINS

The International Society for Study of Vascular Anomalies, based on the groundbreaking work of Mulliken and Glowacki, classified two types of vascular anomalies: vascular malformations and vascular tumors. PWSs are common pediatric lesions that are vascular capillary malformations (CM) composed of ectatic vessels in the papillary dermis. They usually begin as pink macules, becoming more red with time, and they can progress to develop nodules by adulthood.

Origin

Vascular malformations are localized defects of vascular morphogenesis, probably caused by disruptions in pathways monitoring embryogenesis and vasculogenesis. It is unclear whether true angiogenesis occurs in some of these lesions, which would explain their tendency to worsen, thicken, and expand. Although their exact cause has yet to be determined, PWSs evolve because of a progressive ectasia of the cutaneous superficial vascular plexus. One theory behind their development suggests this progression is caused by an abnormal neural regulation of blood flow. As cutaneous vascular flow is mostly regulated by neural mechanisms, nerve distribution could affect the development of these lesions. A 1986 study by Smoller and Rosen found that, compared with normal-appearing skin, PWSs had significantly less nerve density and a higher vessel-to-nerve ratio. As there were no sensory problems with PWSs, the researchers suggested that this high vessel-to-nerve ratio was caused by a deficiency of autonomic nerves. Decreased levels of autonomic nerves could result in significant shifts in blood flow regulation, which may then lead to the PWS’s characteristic progressive vascular ectasia. Hemangiomas had normal nerve density levels. Researchers suggested that the neural regulation of vascular flow could also affect the development of other cutaneous ectasia conditions, such as essential telangiectasia.

Although PWSs are congenital in almost all cases, in rare circumstances PWSs can be acquired, developing in adolescence or adulthood. In some patients, this can be attributed to trauma.
Prevalence

PWSs occur in 0.3% to 0.5% of newborns. They appear equally prevalent among male and female patients, and between premature and full-term infants. PWSs are also associated with disorders such as Sturge-Weber syndrome and Klippel-Trenaunay syndrome. Sturge-Weber syndrome is a sporadic neurologic disorder in which facial CMs, usually in the forehead or upper eyelid area, are linked to ipsilateral ocular and leptomeningeval anomalies. The characteristic intracranial vascular anomaly is leptomeningeval angiomatosis, which generally involves occipital and posterior parietal lobes but can impact other cortical regions and both cerebral hemispheres as well. Neurologic problems resulting from Sturge-Weber syndrome include epilepsy, mental retardation, attention-deficit hyperactivity disorder, migraines, and strokelike episodes. Ocular problems such as glaucoma may be present at birth or develop slowly over time. However, only patients with PWSs in ophthalmic (or V1 trigeminal) cutaneous regions carry this risk of related neuro-ocular symptoms.

Klippel-Trenaunay syndrome is the association of a superficial CM with progressive overgrowth of the affected extremity and varicosities. It can also include underlying lymphatic anomalies, lymphedema, and increased limb length or girth.

Diagnosis

PWSs are easy to recognize via physical examination, appearing as well-defined red macular stains, although some are diffuse and multifocal. The PWS is a slow-flow vascular CM with a quiescent endothelium and does not show the markers of proliferation seen in infant hemangiomias during their proliferative stage. In contrast, PWS growth is proportional to the child’s growth. Facial PWSs usually appear according to the sensory trigeminal nerve distribution within 3 key areas: V1, the ophthalmic region, including the forehead and upper eyelid; V2, the maxillary region; and V3, the mandibular region. Aging PWS skin usually thickens and develops nodularity and pyogenic granulomas, whereas most PWSs on the head and neck darken and thicken with age. PWSs do not follow the lines of Blaschko.

With age, the upper jaw may enlarge in all 3 planes, creating an asymmetric maxilla by overgrowth and an open bite deformity in adolescents. The gum and lips may also grow larger, and this can lead to macrocheilia with lip incompetence, and epulis with gingival bleeding. Histologically, there is an increase in dilated capillaries and ectasias that occupy a deeper part of the reticular dermis. PWSs on the trunk or limbs generally do not undergo hypertrophic skin changes.

Who requires treatment?

PWSs can cause significant psychologic and social problems, and in these circumstances, medical treatment becomes necessary. Children younger than 1 year seem to have the most effective lightening and require fewer treatments than older individuals, and so physicians advise treating the patient as early as physically possible to decrease the psychologic effect of the birthmark and avoid hypertrophy with age. However, contrary to other research, good PWS lightening in response to laser treatment can occur in all age groups: in a 1998 study, van der Horst et al treated patients with a PDL and found no significant difference in lesion clearing between age groups.

It is important to note that some PWSs can recur years after treatment, despite a promising response to initial laser treatments. However, most recurrences are far less visible than the original lesion and tend to develop gradually during several years.

A 1996 study by Orten et al suggested a trend between the amount of time elapsed since treatment cessation and the number of patients experiencing lesion recurrence. Up to 1 year after treatment, only 3% (2 of 64) of patients had PWS recurrences, whereas 21% (5 of 24) had recurrences 2 years after treatment, 40% (4 of 10) had recurrences 3 years after treatment, and 50% (2 of 4) had recurrences more than 3 years after treatment cessation.

In addition, a 2001 case study by Ozluer and Barlow documented a 49-year-old patient who had almost total clearing with PDL treatment only to experience a partial recurrence 2.5 years later. Evidence of such recurrences suggests that PDL treatment addresses the vascular aspects of PWSs but not the underlying neurologic cause. Physicians may do well to inform patients that, in some cases, laser treatment of PWSs can help manage the lesions but cannot stop their overall progression.

Treatment limitations

PDL treatment, discussed in the next section, remains the standard of care in the treatment of PWSs today. Lesions located on the periorbital area, lateral facial cheeks, chest, and proximal aspect of the arms respond best to treatment, whereas the malar areas of the face and distal limbs do not respond well, even with many treatment sessions. Patients with PWS and darker skin (type V) are at risk for hypopigmentation or hyperpigmentation but should still be considered for PDL, as it is possible to get a good response.

Certain lesion complications call for additional types of treatment. Facial and gingival PWSs with hyperplastic changes need special care. A cobblestone
appearance of the V2 skin or nose may necessitate excision after maximal laser treatment. Orthodontic management and orthognathic surgery may be advised when there is gaping between teeth and openbite anomalies. Macrostellia correction when the patient is an adolescent or adult will re-establish fully competent lips.12

LASER TREATMENT OF PWS

Currently, the PDL is the most accepted laser for PWS treatment. However, a lack of controlled studies with a single parameter difference has made it difficult to verify the best settings for pediatric PWS treatment.22 In general, however, PDL parameters are as follows: 585- to 600-nm wavelength, 4- to 12-J/cm² fluence, 1.5- to 10-ms pulse duration, and minimum 7-mm spot size. A larger spot size produces a better outcome, as the laser beam can penetrate deeper into the lesion. Larger spot sizes may require decreased peak fluences as a result of laser limitations.10

Histologic observations of PWSs after PDL treatment reveal an intact epidermis whereas papillary dermal blood vessels contain agglutinated erythrocytes, fibrin, and thrombi.13 Treated tissue should become dark purple, but not grayish, as this is an indication of possible overtreatment.22 One month after PDL PWS treatment, destroyed ectatic vessels are substituted by normal-looking vessels, without signs of dermal scarring.13 The treatment effect decreases as the number of treatments increases, although a slow improvement is generally apparent with prolonged treatment (Table I).10

Clinical recommendations

When treating PWSs, it is best to target the smaller, superficial capillaries first and the larger, deeper capillaries last, as these are more difficult to treat. For deeper, more resistant capillaries, a longer wavelength (maximum of 600 nm) can be used for greater tissue penetration and a longer pulse duration (maximum of 3 ms, although increased for nodular purple PWSs) can be used for destroying these larger vessels.10 The PWS has a nonuniform response to laser treatment,10 most likely because lesions are often made of different blood vessels with different depths of involvement.15 Different blood flow rates through vessels may also affect the efficacy of laser treatment. The important end point of the treatment is purpura.23

PWS edges, which typically respond best, should be treated first, to avoid accidentally treating unaffected skin. The lesion does not need to be outlined before treatment—an outline can simply be traced with initial laser pulses before reactive erythema develops over several minutes. When treating central areas, the laser is never aimed tangentially at the skin, as this will alter the fluence in unpredictable ways and may reduce effectiveness of the dynamic cooling device. To avoid reticulations, overlapping pulses are used with the gaussian beam profile (Candela, Candela Corp, Wayland, Mass), although less overlap is needed with the Cynosure laser (Cynosure Inc, Westford, Mass) as the beam profile is more flat topped. It is best to avoid using an anesthetic such as EMLA, as it may blanch pale lesions, making them more difficult to view during treatment.

It is also important for darker-skinned patients to wait as long as 3 to 6 months between sessions to allow postinflammatory hyperpigmentation, if it has occurred, to resolve.22 Although ice can be used for additional anesthesia, cooling devices such as the DCD (Candela Corp, Wayland, Mass) or SmartCool (Cynosure Inc, Westford, Mass) are necessary for epidermal protection and are now standard for both the Candela and Cynosure PDLs. These devices allow significantly higher fluences to be used safely, enhancing laser efficacy.

One of the greatest benefits of using pulsed yellow light is the capability to treat small children effectively with the relatively small risk of scarring or permanent pigmentation problems.10 Pediatric PWSs have a better response to PDL treatment than adult PWSs.12 Treatment at such an early age is most likely successful because of the thinner skin of infants and their smaller, more superficial vessels.22 However, no laser treatment is completely risk free. There still exists a very low chance (<1%) of hypertrophic and atrophic scarring when treating pediatric PWSs.23,24 Cutaneous atrophy is a rare result 1 to 2 months post-PDL treatment but generally resolves at between 3 to 18 months. Clearance is strongly influenced by the location of the lesion, as the head and neck (specifically the periorbital area and lateral facial cheeks) respond much better than the trunk and lower extremities. In addition, darker-skinned patients can have epidermal sloughing after treatment, necessitating wound care and causing pigmentary changes.15,22 Finally, the best results require multiple treatments. Very rarely does a lesion clear after only one or two sessions.24

More resistant PWSs, nodular or hypertrophic, may not respond to PDL treatment and are often better suited to long PDL (LPDL) (595-600 nm, 1.5-40 ms), pulsed Nd:YAG laser, a PDL/pulsed Nd:YAG laser combination, pulsed alexandrite laser, or potentially intense pulsed light.15 Of these options, intense pulsed light is the least effective.
<table>
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<tr>
<th>Study</th>
<th>No. of patients</th>
<th>Age range</th>
<th>Laser parameters</th>
<th>No. of treatments</th>
<th>Results</th>
<th>Side effects</th>
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<tbody>
<tr>
<td>Reyes et al (1990)</td>
<td>73</td>
<td>13 mo-14 y</td>
<td>PDL: 557 or 585 nm, 360 or 450 µs, 5 mm 5.50-7.0 J/cm² depending on age</td>
<td>Average of 2</td>
<td>Lightening increased in proportion to No. of treatments. Younger patients responded better than older patients.</td>
<td>Cutaneous depressions, hypopigmentation, hyperpigmentation</td>
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<td>Ashinoff et al (1991)</td>
<td>12</td>
<td>6-30 wk</td>
<td>PDL: 585 nm, average 6.20 ± 0.16 J/cm², 450 µs, 5 mm</td>
<td>Average of 2.8 ± 1.4</td>
<td>Overall, 10 of 12 (83%) patients showed ≥ 50% lightening after a mean of 2.8 ± 1.4 treatments; 5 of 12 (42%) patients had ≥ 75% lightening; 5 of 12 (42%) patients had 50%-74% lightening; two of 12 (16%) patients displayed 26%-49% lightening. Younger patients needed fewer treatments to achieve positive result.</td>
<td>Not noted</td>
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<td>Renfro et al (1993)</td>
<td>259 (137 adults, 122 children)</td>
<td>Adults: 18-70 y (mean age 33.1 y) Children: 6 wk-17 y (mean age 5.9 y)</td>
<td>PDL: 577 or 585 nm, 5.75-8.5 J/cm², 450 µs, 5 mm</td>
<td>Adults: 1-8 (mean 3.7) Children: 1-7 (mean 3.9)</td>
<td>Retrospective study analyzed PWS results by subdivision of head and neck, dermatomal distribution, and midline regions. PWSs in centrofacial and V2 regions did not lighten as much as other regions of head and neck. Midline lesions had excellent response to PDL.</td>
<td>Transient cutaneous depressions, hypopigmentation, and hyperpigmentation; all side effects resolved spontaneously within 8 mo</td>
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<td>Study</td>
<td>Total</td>
<td>Age Range</td>
<td>Treatments</td>
<td>Lesion Clearing</td>
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<td>Kauvar et al (1995)</td>
<td>69</td>
<td>10 d-64 y</td>
<td>PDL: 577/585 nm, 5.75-8.0 J/cm², 450 µs, 5 mm</td>
<td>Pediatric and adult study for persistent PWSs showed significant lightening occurred in patients who had 10-25 repetitive treatments. Repetitive treatments could improve PWS lightening without increased risk of side effects. One patient of 69 (1%) experienced atrophy and hypopigmentation, 3 of 69 (4%) patients experienced hyperpigmentation.</td>
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<td>Morelli et al (1995)</td>
<td>83</td>
<td>2 wk-17 y</td>
<td>PDL: 577 or 585 nm, 6.0-7.5 J/cm², 450 µs, spot size not noted</td>
<td>Approximately 5-14</td>
<td>Lesion clearing was inversely proportional to age and size. Differences in lesion clearing were not related to number of treatments. Researchers indicated lesion size and patient age must be considered before treatment. PDL treatment for PWSs recommended as early as possible. Not noted</td>
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<tr>
<td>Nguyen et al (1998)</td>
<td>91</td>
<td>2 wk-17 y</td>
<td>PDL: 577 nm, 585 nm, 6.0-7.5 J/cm², 450 µs, 5 mm Cooling: ice used in a few cases</td>
<td>5-10</td>
<td>Location was the most important factor in lesion clearing, followed by size, then age. Bony areas of the face, such as central forehead, cleared best. Lesion clearing was inversely proportional to age and size. Not noted</td>
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<tr>
<th>Study</th>
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<th>Results</th>
<th>Side effects</th>
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<tr>
<td>van der Horst et al</td>
<td>89</td>
<td>0-31 y</td>
<td>PDL: 585 nm, 6-8 J/cm², 450 μs, 5 mm</td>
<td>Average of 5</td>
<td>No significant difference in lesion lightening across age groups. Researchers could not confirm efficacy of earlier PWS treatment.</td>
<td>Small blisters, crusting, headaches</td>
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<td>et al (1998)¹⁹</td>
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<td>Cooling: gauze dressing soaked in ice water used during treatment</td>
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<td>Geronemus et al (2000)</td>
<td>16</td>
<td>Mean age 3.4 mo</td>
<td>PDL: 595 nm, 11-12 J/cm², 1.5 ms, 7 mm</td>
<td>Average of 3.2</td>
<td>In all, 10 of 16 (63%) patients had &gt;75% lesion clearing after a mean of 4 treatments. Researchers concluded that increasing PDL parameters helped lighten PWSs with minimal risk or side effects.</td>
<td>In all, 3 of 16 (19%) patients developed dermatitis</td>
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<td>Ahcán et al (2004)³⁶</td>
<td>10</td>
<td>Mean age 16.2 y</td>
<td>Standard KTP (Dualis KTP, Fotona d.d. (Ljubljana, Slovenia)): 532 nm, 10-14 J/cm², 25 ms, 3 mm</td>
<td>1</td>
<td>Hybrid laser achieved same results as KTP laser and used lower fluence. Hybrid laser deemed more effective than standard KTP laser in PWS treatment.</td>
<td>Isolated beam-sized atrophic scars appeared in two test areas where both lasers were used; no other side effects</td>
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<td>Hybrid Nd:YAG/KTP (Dualis KTP+, Fotona d.d.): Nd:YAG: 1064 nm, 10.8-18 J/cm², 25 ms, 3 mm</td>
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<td>KTP: 532 nm, 6-10 J/cm², 25 ms, 3 mm</td>
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<td>Cooling: tetrafluoroethane spray used with both lasers</td>
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<td>Study</td>
<td>Age (Range)</td>
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<td>Tanghetti et al (2005)</td>
<td>Not noted</td>
<td>10</td>
<td>Sequential PDL/Nd:YAG treatment PDL: 595 nm, 7-15 J/cm², 10-40 ms Nd:YAG: 1064 nm, 50-100 J/cm², 10-40 ms Different time delays used between lasers. Sequential lasers showed significant improvement to resistant vessels. Lower than average fluences used for both lasers.</td>
<td>Not noted</td>
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<td>Huikeshoven et al (2007)</td>
<td>12-42 y (mean 23 y)</td>
<td>51</td>
<td>Original study PDL: 585 nm, 6-8 J/cm², 450 μs, 5 mm Cooling: gauze dressing soaked in ice water used during treatment Average of 5 during van der Horst (1998) study, median of 7 treatments before follow-up study.</td>
<td>Follow-up study of van der Horst et al (1998). Median 9.5 y since participation in original study. Overall, PWSs were significantly darker at follow-up than at end of previous study. However, PWSs were still significantly lighter than before receiving any treatment. Significant PWS darkening had occurred since original study.</td>
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</table>

Nd:YAG, Neodymium:yttrium-aluminum-garnet; PDL, pulsed dye laser; PWS, port wine stain.
It is important to note that PWS treatment with the long-pulsed 1064-nm Nd:YAG laser is generally only recommended for the most skilled laser surgeons. Even when cooling is used, the long-pulsed Nd:YAG laser can cause scarring.25 Fluence levels can greatly affect treatment efficacy, and only the minimal purpuric threshold fluence should be used. Using fluences higher than the minimal purpuric threshold can produce methemoglobin, which has a much higher absorption than hemoglobin or oxyhemoglobin and can lead to increased scattering.26 If the long-pulsed 1064-nm Nd:YAG laser is used for PWS treatment, it is best to find the minimal purpuric threshold with test spots or to treat the PWS sequentially, using a PDL first and the Nd:YAG laser second. This allows for reduced fluences when using the Nd:YAG laser.25

A study by Tanghetti et al27 in 2005 also reported successful use of sequential PDL/Nd:YAG laser treatment for PWSs, showing significant improvement to resistant lesions while using fluences lower than those used for either laser alone.

In 1990, Reyes and Geronemus23 observed the effects of the PDL on PWSs in 73 children between the ages of 3 months and 14 years. The amount of lightening increased as the number of treatments increased. After an average of 2.5 treatments, 33 of the 73 (45%) patients had lesions that lightened more than 75%, 31 of 73 (43%) patients had 50% to 75% lightening after an average 1.7 treatments, 5 of 73 (7%) patients had 26% to 59% lightening after an average of 2.0 treatments, and 4 of 73 (5%) patients had less than 25% lightening after an average of 1.0 treatment. Overall, lesions lightened 53% after one treatment.

In terms of the effect of age on PWS lightening, younger patients responded significantly better than older patients. The 44 of 73 (60%) patients between 3 months and 6 years old showed 55% lightening after one treatment, whereas the 29 of 73 (40%) older patients had 48% lightening after one treatment.23

A 1991 study by Ashinoff and Geronemus28 treated 12 children, aged 6 to 30 weeks, who had PWSs located on the head and neck. The goal was to determine whether the earliest possible PDL treatment was efficient and safe versus later treatment. Overall, the mean number of PDL treatments was 2.8 ± 1.4. The mean percent lightening was 70.2 ± 2.6. In all, 5 of 12 (42%) patients displayed more than 75% lightening with a mean of 3.8 ± 1.6 treatments, 5 of 12 (42%) patients displayed 50% to 74% lightening after a mean of 2.0 ± 0.7 treatments, and two of 12 (16%) patients displayed 26% to 49% lightening after a mean of 2.5 ± 0.7 treatments. No patients had less than 25% lightening. In general, 10 of the 12 patients showed 50% or more lightening after a mean of 2.8 ± 1.4 treatments. No patients exhibited scarring, atrophy, hyperpigmentation, or hypopigmentation. PWSs on the cheek or upper lip needed more treatments than those on the neck or periocular regions to achieve equivalent lightening.

Researchers concluded that, although their sample size was small, results were consistent with previous studies indicating younger patients needed fewer treatment sessions to achieve a positive result.29,30 Researchers supported the PDL as a safe treatment option for infants with PWSs and counseled patients to have PWS treatment as early as possible to prevent physical and psychologic distress.28

A 1993 retrospective study by Renfro and Geronemus31 analyzed whether PWSs located on different anatomic regions of the head and neck had different responses to PDL treatment. Researchers evaluated photographs of 259 adults and children before and after treatment by anatomic subdivision of the head and neck, dermatomal distribution, and midline lesion response. Lightening was assessed on a scale of 0% to 100% in increments of 5%. A response scale was also used to evaluate lightening: poor indicated 0% to 25% lightening, fair indicated 26% to 50% lightening, good indicated 51% to 75% lightening, and excellent indicated 76% to 100% lightening.

Renfro and Geronemus31 discovered mean lightening in the centrofacial regions had a good response (70.7%) to the PDL, whereas the remaining grouped regions had an excellent response (82.3%) to the laser. The V2 dermatomal region revealed a good response to treatment (73.8%), but this region lightened significantly less than the V1, V3, and C2/C3 regions, which had an excellent response (82.4%) when combined. Midline lesions also had an excellent response to treatment (92.4%). It is important to note that differences in anatomic regions, dermatomal distributions, and midline lesion responses were similar between adults and children, so these data were pooled.

Researchers concluded that PWSs do indeed show a differential response to PDL treatment based on anatomic location, and noted that the initial lesion color may also influence treatment response.31

In 1995, Kauvar and Geronemus32 examined whether persistent PWSs would respond to repetitive PDL treatments. A total of 69 patients whose lesions had failed to lighten more than 75% within 9 treatments participated. The persistent PWSs were hypertrophic or nodular, extremely large (>50 cm²), located on the limbs, and/or had a centrofacial distribution that medically affected areas of the cheek, upper lip, and nose. They found that...
significant improvements in lightening occurred in patients who had 10 to 25 repetitive treatments and concluded that repetitive treatments could improve lightening in difficult PWSs without an increased risk of side effects.\textsuperscript{32}

A 1995 study by Morelli et al\textsuperscript{33} evaluated the importance of age and lesion size regarding the effect of PDL treatment on facial PWSs in children. Children younger than 1 year showed the highest percentage of clearing (mean 65.41%). Children aged 1 to 2 years had a mean clearing of 61.67%, children older than 2 years to 6 years had a mean clearing of 54.06%, children older than 6 years to 12 years had a mean clearing of 49.29%, and children older than 12 years to 18 years had a mean clearing of 58.02%. The rate of clearing decreased as age increased. Most patients with lesions clearing 75% or 100% were younger than 1 year. Differences in clearing rates between groups were not caused by number of treatments.

In terms of size, 15 of the 47 patients with PWSs under 20 cm\textsuperscript{2} had 100% clearing, whereas 3 of the 36 patients with PWSs more than 20 cm\textsuperscript{2} had lesions that totally cleared. Lesions under 20 cm\textsuperscript{2} showed a mean clearing of 60.52%, lesions between 20 and 40 cm\textsuperscript{2} showed a mean clearing of 61.5%, and lesions more than 40 cm\textsuperscript{2} showed a mean clearing of 41.41%. Overall, 18 patients had 100% clearing of their lesions. Smaller lesions cleared better than larger lesions at all ages. Researchers acknowledged size and patient age must be considered before starting PWS treatment. As in the 1991 study of Ashinoff and Geronemus,\textsuperscript{28} researchers recommended PDL treatment for PWSs as early as possible.\textsuperscript{33}

In 1998, Nguyen et al\textsuperscript{34} examined how quickly facial PWSs decreased in size as a function of treatment number, lesion size, lesion location, and patient age. In terms of location, the face was divided into 4 categories: central forehead (13 patients), peripheral face (39 patients), central face (27 patients), and mixed (12 patients), which was a combination of central and peripheral face regions. The central forehead showed the greatest mean improvement with the first treatment (100% decrease after first 5 treatments, 0% after second 5 treatments), followed by the peripheral face (58%, 28%), central face (48%, 14%), and a combination of peripheral and central face (21%, 9%). All of the central forehead PWSs cleared totally by 5 treatments, but none of the mixed PWSs cleared fully, even with an average of 14 treatments.

Regarding response as a result of size, the average decrease in size was best for smaller PWSs.Lesions under 20 cm\textsuperscript{2} had the best result after treatment and cleared 67% after the first 5 treatments, then 21% after the second 5 treatments, followed by lesions 20 to under 40 cm\textsuperscript{2} (45%, 8%), and lesions more than 40 cm\textsuperscript{2} (23%, 29%). The lesions more than 40 cm\textsuperscript{2} had a small decrease in size initially but steadily responded with more treatments.

In terms of age, the average decrease in size was greatest for the youngest patients. Patients younger than 1 year improved 63% after the first 5 treatments, and 33% after the second 5 treatments, followed by patients aged 1 to 6 years (48%, 15%), and patients older than 6 years (54%, 10%).

Location was determined as the most important factor in lesion clearing, followed by size, then age. Nguyen et al\textsuperscript{34} concluded the best results could be seen in patients younger than 1 year who had small PWSs under 20 cm\textsuperscript{2} located on bony areas of the face, such as the central forehead. Maximal improvements were seen in the first 5 treatments regardless of size, age, or lesion location. These factors may help improvement predictions and patient expectations in PDL treatment of PWSs.\textsuperscript{34}

A 1998 study by van der Horst et al\textsuperscript{19} seemed to contradict previous studies with regard to the effect of treatment age on lesion clearing. The goal of the study was to assess whether PWS treatment at a very early age, when skin is thinner and the lesion is smaller, would yield better results than treatment at an older age. Researchers discovered there were no significant differences in lesion lightening across age groups, and the average reduction in color across age groups was 40%. Researchers concluded they could not confirm early PWS treatment was more effective than later PWS treatment, although they suggested that further treatments would likely lead to a higher average rate of clearance. Because past literature did not use standard parameters for patient age or original PWS color, van der Horst et al\textsuperscript{19} found it difficult to compare their findings with previous studies.

A study by Geronemus et al\textsuperscript{35} in 2000 aimed to modify traditional PDL parameters for treating PWSs (585 nm, fluences 4-8 J/cm\textsuperscript{2}, pulse duration 450 μs, spot size 5-10 mm) to include a longer wavelength, longer pulse duration, and higher energy fluences by using dynamic cooling spray. Approximately 10 of the infants had more than 75% clearing after an average of about 4 treatments. Two infants had less than 25% clearing and 14 infants had partial regions of total clearing. An average of 3.2 treatments was administered. There were no signs of atrophic or hypertrophic scarring, hypopigmentation, or hyperpigmentation. Three patients developed dermatitis after the third treatment, and this was treated with low-level topical corticosteroids.
Geronemus et al\textsuperscript{35} concluded that modifying PDL parameters to include dynamic cooling spray, a longer wavelength and pulse duration, and higher-energy fluences would lighten PWSs with minimal risk or side effects. Researchers also noted study findings were a significant improvement over the results of van der Horst et al,\textsuperscript{19} as this study only achieved a 40\% improvement in infants and children after 5 treatments. It is important to note that van der Horst et al\textsuperscript{19} did not use dynamic cooling spray, but gauze dressings soaked in ice water, and this may have affected lesion clearing.\textsuperscript{35}

In 2004, Ahcin et al\textsuperscript{36} compared the effects of a hybrid laser, the Nd:YAG/KTP, with the effects of a standard KTP laser on PWSs. This novel laser system emitted two wavelengths of 1064 and 532 nm simultaneously, with the hypothesis that the 1064-nm wavelength would induce bulk dermal heating, reducing the light dosage at 532 nm necessary to cause irreversible thermal damage to the PWS vessels. A hybrid laser may then be preferable to a standard KTP laser as the lower energy dosage might potentially reduce skin damage and healing times. As melanin absorption lowers quickly with the irradiation wavelength, it was predicted the two-wavelength setup should lead to less heat deposited in the epidermis while causing the therapeutic effect in the underlying vessels and improving the safety of the procedure.

Each tested lesion section received a blanching score on a scale of 1 to 4, with 1 indicating poor (<25\% clearance), 2 indicating fair (26\%-50\% clearance), 3 indicating good (51\%-75\% clearance), and 4 indicating very good (76\%-100\% clearance). Overall, the dual-wavelength laser was able to achieve the same results 8 weeks after one treatment as the KTP laser while using a lower fluence. Test regions from both areas scored a mean 2.6 ± 0.7 on the blanching scale. However, the mean fluence used for the Nd:YAG/KTP laser was 8.2 ± 1.9 J/cm\textsuperscript{2}, whereas the mean fluence for the standard KTP laser was 12.4 ± 2.1 J/cm\textsuperscript{2}. At 8 weeks, isolated beam-sized atrophic scars appeared in two test areas where both lasers were used, but no other side effects resulted from either treatment.

Researchers asserted that the additional 1064-nm radiation in the Nd:YAG/KTP laser significantly increased the efficacy of the laser treatment of PWSs when compared with the standard 532-nm KTP laser. The addition permitted a 30\% lower fluence for the 532-nm wavelength in the dual-wavelength laser while achieving an identical clinical result. Ahi\textsuperscript{26} also expressed that future research must be done to assess how much this additional change improves safety from epidermal injury and how much more efficacy this new system can provide over current dermatomic laser systems. Although the PDL is currently the main laser treatment used for PWSs, other studies have confirmed the efficacy of the KTP laser used in an intralernal bare fiber delivery on hemangiomas of infancy.\textsuperscript{37}

A 2005 study by Tanghetti et al\textsuperscript{27} revealed that PWSs may benefit from sequential PDL/Nd:YAG laser treatment. Ten patients with PWSs and 10 patients with telangiectatic leg veins were treated with the 595-nm PDL, followed by the 1064-nm Nd:YAG laser, with varying time delays used between the lasers. Researchers found that not only did resistant vessels significantly improve, the fluences used for both lasers were lower than the effective fluences used for either laser alone.

In 2007, Huikeshoven et al\textsuperscript{38} conducted a follow-up study of van der Horst et al\textsuperscript{19} (1998) to determine the long-term efficacy of PDL PWS treatment. A total of 51 patients from the original study participated, and the median time between participation of the original study and the follow-up study was 9.5 years. Researchers discovered that, in general, the PWSs were significantly darker since the original 5 treatments. However, they also noted that the median darkening was still significantly lighter than the median color before the original treatments. Overall, Huikeshoven et al\textsuperscript{38} acknowledged that, although the PDL remained the gold standard for the treatment of PWSs, it was important to inform patients before treatment about possible PWS redarkening.

**HEMANGIOMAS**

Unlike PWSs, hemangiomas are benign proliferations of endothelial tissue. These vascular tumors are the most common tumors occurring in the neonatal stage. Histopathologic findings include endothelial cell hyperplasia, lobule formation, mast cells, and a prominent basement membrane, with fibrofatty tissue replacement and decreased mast cells during the involution phase (Table II).\textsuperscript{16}

**Origin**

It has been suggested that some hemangiomas originate from a first-trimester developmental error, most likely between 6 to 10 weeks of gestation.\textsuperscript{59} Clues to the lesion’s origin are revealed in a more recent understanding of vasculogenesis and angiogenesis.\textsuperscript{40} Regarding vasculogenesis, irregular arteries in some patients with hemangioma have been linked to developmental-field defects appearing at about 8 to 10 weeks of gestational age. In addition, chorionic villus sampling, which carries 10 times the risk for hemangiomas, infrequently disturbs vascular
structures, creating the possibility of vasculogenic errors that may generate a better environment for hemangioma growth. The increased incidence of hemangiomas in children born to women postchorionic villus sampling suggests hemangiomas are of placental origin. In this sampling procedure, a fetal trophoblast sample is surgically removed from the placenta, leading to placental embolization and maternofetal transfusion. There is an argument that hemangiomas may originate from this embolization of placental cells: compared with other benign vascular tumors, proliferations, or malformations, hemangiomas uniquely express high levels of the placenta-associated vascular antigen glucose transporter 1 (GLUT1). Similar placenta-linked antigens, such as the Lewis Y antigen, have also been observed in hemangiomas.

Table II. Comparison between port wine stains and hemangiomas

<table>
<thead>
<tr>
<th>Pediatric vascular lesion</th>
<th>Port wine stains</th>
<th>Hemangiomas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Origin</td>
<td>Present at birth. Grow in proportion to child’s growth. Unclear origin: possibly a result of vascular channel developmental defects or segmental deficiency of autonomic innervation of postcapillary venules.</td>
<td>Absent or small at birth. Grow rapidly in early infancy. Unclear origin: possibly a first-trimester developmental error regarding vasculogenesis and/or angiogenesis or a result of embolized placental cells. Possible autosomal dominant inheritance.</td>
</tr>
<tr>
<td>Prevalence</td>
<td>Affect 0.3%-0.5% of newborns. Equal prevalence in male and female patients. No significance between premature and full-term infants. Associated with Sturge-Weber and Klippel-Trénaunay syndromes. Very rare late onset in adolescents and adults, usually caused by trauma.</td>
<td>Affect 1.1%-2.6% of newborns. Usually develop after birth. Affect 10% of Caucasian children within first year. Three times more common in female than male patients. More common in premature infants. Higher prevalence in infants of mothers postchorionic villus sampling.</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Vascular malformation. Usually well-defined red macular stains. Histology shows flattened endothelium. Slow growth throughout lifetime. No regression or ulceration. GLUT1 negative.</td>
<td>Superficial, deep, or mixed vascular tumors. Histology shows plump endothelial cells. Specific growth and involution phases. Many hemangiomas spontaneously disappear, others grow to disfiguring sizes. Ulceration is possible. GLUT1 positive.</td>
</tr>
<tr>
<td>Who requires treatment</td>
<td>All patients require treatment, because of the expansive nature of PWSs, and their tendency to cause psychologic problems.</td>
<td>Treatment is controversial because of unpredictable growth of hemangiomas. Life- or function-threatening lesions, lesions in locations that will permanently scar and ulcerated lesions are high priorities for treatment.</td>
</tr>
<tr>
<td>Treatment types</td>
<td>Laser treatment, plus surgery for individual nodules and soft-tissue hypertrophy, and orthodontic management for complications.</td>
<td>Systemic and direct corticosteroids, vincristine, recombinant interferon alfa-2a and -2b, imiquimod, surgery, laser treatment, cryotherapy, active nonintervention.</td>
</tr>
<tr>
<td>Laser treatment</td>
<td>PDL treatment, 585-600 nm, with fluences 4-12 J/cm², 1.5- to 10-ms pulse duration, minimum 7-mm spot size.</td>
<td>PDL treatment, for superficial, ulcerating, and residual telangiectasia of involuted hemangiomas only. Occasionally CW or KTP intrallesional bare fiber treatment. Currently, no optimal laser treatment for hemangiomas.</td>
</tr>
</tbody>
</table>

CW, Continuous wave; GLUT1, glucose transporter 1; PDL, pulsed dye laser; PWS, port wine stain.
displaced during development) that proliferate faster after birth than normal blood vessels. Although this suggestion is speculative, it would explain the larger incidence of hemangiomas in premature infants, as the probability of immature autonomous rests would be higher in premature infants than in full-term infants.40

Changes in fetal vascular development and angiogenesis at the molecular or chromosomal level could also explain the unregulated growth of hemangioma blood vessels. Rapid tumor growth in the postnatal phase is possibly a result of the loss of angiogenic inhibitors from the placenta or mother.39 Vascular endothelial and basic fibroblast growth factors are critical to angiogenesis, especially regarding embryonic development, growth, differentiation, wound healing, and placentation. Notably, messenger RNA for these growth factors are up-regulated in proliferative hemangiomas, whereas the tissue inhibitor of metalloproteinase-1, an angiogenesis inhibitor, is not expressed in proliferating hemangiomas.41 Further clues in angiogenesis include higher levels of basic fibroblast growth factor in the urine of infants with hemangiomas. This also suggests a potential way to monitor treatment efficacy.40

Prevalence

Hemangiomas are usually not present at birth.16 Hemangiomas of infancy or their precursors are seen in 1.1% to 2.6% of term neonates8 but can occur in as many as 10% of Caucasian children within their first year of life.43 Hemangiomas occur in all races, but are more common in Caucasian infants than infants of African or Asian descent.39 The incidence of hemangiomas is 3 times higher in female infants than male infants.40 There is also an increased occurrence in premature infants, and this higher prevalence has been linked to both decreasing gestational age and lower birth weights.39 Hemangiomas are more common in infants of mothers who underwent chorionic villus sampling (a reported 21% incidence in infants exposed at 9-12 weeks’ gestation).39 In rare instances, these vascular tumors have reportedly been inherited and this has been linked to an autosomal dominant pattern of inheritance.39

Diagnosis

In 1982, a biologic classification system of vascular birthmarks was put forward by Mulliken and Glowacki11 based on clinical manifestations, histopathologic features, and natural history. Hemangiomas were classified as vascular tumors with a growth phase characterized by endothelial proliferation and hypercellularity and an involution phase.40 More than 90% of vascular anomalies can be categorized as hemangiomas by history and physical examination alone.39 A minority is confused with other lesions such as tufted angiomas, Kaposiform hemangioendothelioma, and hemangiopericytoma.39

Most hemangiomas are focal, tumorlike lesions that usually appear near embryonic fusion lines. Less common are hemangiomas that are more segmental and involve an area of skin linked to derivation from the embryologic mesenchymal prominences. These are more plaquelike and often tied to lesion complications and anomalies.39

The first sign of a hemangioma is usually an erythematous patch, a hypopigmented macule, or a circumscribed region of telangiectasia.44 Hemangiomas can be superficial, deep, or a combination of the two.10 Superficial lesions are raised and bright red and were historically called strawberry or capillary hemangiomas. Deeper hemangiomas are slightly raised and bluish.44 Superficial hemangiomas are the most common, representing 50% to 60% of cases. Mixed lesions combining superficial and deep hemangiomas represent 25% to 35% of cases. Deep hemangiomas are the least common and represent approximately 15% of cases.16 Of hemangiomas, 60% occur on the head and neck, 25% occur on the trunk, and 15% occur on the extremities.39 In terms of size, isolated lesions can range from a few millimeters to several centimeters in diameter. Around 20% of infants with hemangiomas have multiple lesions.40

The hemangioma life cycle differs from vascular malformations and most tumors because the lesion grows rapidly before spontaneously involuting.40 Their typical growth pattern has 3 stages: proliferation, plateau, and involution.16 Hemangiomas are by nature heterogeneous and the length of a particular lesion’s life cycle stages is difficult to predict. The proliferation phase dominates in approximately the first 6 to 8 months of life, although deeper lesions can grow from 12 to 24 months.40 During proliferation, the lesion can develop a tense surface and have a firmer texture (especially during crying or activity).16 Blood flow can cause them to warm to touch during this time. The proliferating hemangioma is made of masses of plump, quickly dividing endothelial cells, both with and without lumens, and multilamination of the basement membrane is apparent.39

It is difficult to predict the onset of involution, but it may occur within the first year of life and can continue for several years. It is indicated by a lesion color change from bright red to gray or purple, surface flattening, and the separation of the superficial plaque into smaller segments before clearing. The lesion texture changes to a softer, fattier-feeling
tissue, and there is less surface change with crying or activity. Histologically, the vascular lumens dilate, the endothelial cells flatten, and the fibrous tissue is deposited in a lobular shape. Although it is unclear how the involution change is initiated, it correlates with a 5-fold increase in apoptotic cells. It is suggested mast cells may synthesize apoptotic markers and induce lesion regression. The fully involuted hemangioma is not always resolved to look like normal-appearing skin. The literature reveals approximately 50% of patients have no trace of the lesion at resolution. Mild changes can involve telangiectasias, atrophic wrinkling, or yellow discoloration. Significant changes can involve redundant skin with underlying fibrofatty residua or scarring (especially if the lesion had ulcerated). Alopecia is also a possibility, as a result of potentially destroyed hair follicles. The involuted hemangioma has a few capillary-like feeding vessels and draining veins with flattened endothelium in a stroma of fibrofatty tissue, collagen, and reticulin fibers. Pericytes, fibroblasts, interstitial cells, and mast cells are also present. Hemangiomas that resolve before the patient is 6 years old are less likely to leave residual scars, extra skin, or telangiectasias than those involuting after 6 years of age.

Hemangiomas show a strong immunoreactivity for the placenta-associated vascular antigens Fcy receptor II, merosin, and Lewis Y antigen. In addition, GLUT1, usually found in the microvascular endothelia of blood-tissue barriers but not normal-appearing skin, was discovered to be a specific marker for hemangiomas in all development phases. It is helpful in distinguishing hemangiomas because GLUT1 is robustly expressed in the complete endothelial lining of hemangioma vessels but absent in other vascular lesions. GLUT1 staining also identifies hemangiomas as having a distinctive vascular phenotype, as opposed to being an overgrowth of cutaneous vasculature.

To diagnose a particularly questionable lesion, imaging studies are often used. These include Doppler ultrasound, computed tomography, and magnetic resonance imaging. If the diagnosis has not been determined through the use of imaging studies, a biopsy should be considered. Ulceration during the proliferative phase is the most common complication of hemangiomas, occurring in 5% to 13% of all infantile hemangiomas. Ulceration most commonly occurs in segmental superficial plaque-type or nodular lesions. It can present at any location but is most frequently seen on the lip, perineum, or intertriginous areas. Ulcerations are painful, increase the risk of infection, and cause scarring and textural changes. However, most bleeding episodes are small and can be stopped with firm pressure.

Hemangiomas can also be associated with PHACES syndrome (posterior fossa malformations, hemangiomas of the cervicofacial region, arterial anomalies, cardiac anomalies, eye anomalies, and sphenocleal clefting or ectopia cordis) and thyroid disease. In addition, about 20% to 40% of patients have lasting skin alterations: the tip of the nose, the lip, and the parotid areas can have very slow involution periods; and large superficial hemangiomas often resolve with disfiguring scars.

Who requires treatment?

Treatment of hemangiomas remains extremely controversial because there are a wide range of outcomes for hemangiomas, from fully resolved to disfiguring scars to life-threatening obstructions, and it is extremely difficult to predict whether a given single lesion is benign or whether it will impair the patient. Because there is the possibility of rapid change in early infancy, it is important to decide quickly whether treatment is required, an extremely difficult choice given the heterogeneity of hemangiomas. One argument dictates an aggressive approach, using early intervention to lessen the impact of a potentially threatening lesion, whereas the contrasting argument advises a wait-and-see approach, in the belief that most hemangiomas resolve with a more cosmetically adequate outcome without treatment. According to the 1997 “Guidelines of care for hemangiomas of infancy” in the Journal of the American Academy of Dermatology, the major goals of hemangioma management are: (1) preventing or reversing life-threatening or function-threatening complications; (2) preventing permanent disfigurement after involution; (3) decreasing psychosocial stress for the patient and family; (4) avoiding aggressive and possibly scarring treatments for those lesions likely to have an excellent prognosis without therapy; and (5) preventing or treating ulceration to lower scarring, infection, and pain. Although there is no controversy surrounding the necessity of treating life-threatening or function-impairing lesions, deciding whether to treat less threatening lesions is a more difficult decision. However, the Journal of the American Academy of Dermatology advises the following as general indications of treatment: (1) life-threatening and function-threatening hemangiomas (ie, liver, vision, airway involvement); (2) hemangiomas in locations likely to permanently scar (nose, ear, lip, glabellar area); (3) large facial hemangiomas, especially those with a major dermal component (which carry a greater chance of scarring); (4) smaller
hemangiomas in exposed areas (face and hands) using treatment unlikely to scar or cause significant side effects; (5) ulceration; and (6) pedunculated hemangiomas, which have a greater chance of leaving considerable fibrofatty tissue after involution. For minor lesions, a re-evaluation when the patient is 4 to 5 years old is recommended, to assess whether treatment is necessary before kindergarten.

**Treatment types and limitations**

According to the 1997 *Journal of American Academy of Dermatology* guidelines, the type of treatment advised for a hemangioma depends on: (1) anatomic location of the lesion; (2) depth of involvement (superficial, deep, or mixed); (3) size and extent of the hemangioma; (4) lesion’s current phase (proliferation, plateau, or involution); (5) presence of functional impairment; (6) whether the physician has experience with certain treatments (ie, lasers); (7) availability of certain treatments (ie, lasers); and (8) amount of parental concern. Early treatments using irradiation or excisional surgery often lead to more negative results than an untreated lesion. Today, the following treatments are used for hemangiomas: corticosteroids, intralesional interferon alfa, imiquimod, vincristine, a variety of lasers, debulking surgery, systemic and intralesional steroids, interferon, and PDL therapy. According to the 1997 *Journal of American Academy of Dermatology* guidelines, the type of treatment advised for a hemangioma depends on: (1) anatomic location of the lesion; (2) depth of involvement (superficial, deep, or mixed); (3) size and extent of the hemangioma; (4) lesion’s current phase (proliferation, plateau, or involution); (5) presence of functional impairment; (6) whether the physician has experience with certain treatments (ie, lasers); (7) availability of certain treatments (ie, lasers); and (8) amount of parental concern.

**LASER TREATMENT OF HEMANGIOMAS**

PDL treatment of hemangiomas is still somewhat controversial because of the natural characteristics of hemangiomas in addition to the potential side effects of the PDL on the lesions. Although it is noncontroversial for the treatment of involuting and ulcerating hemangiomas, researchers are still divided over its use for superficial hemangiomas in the proliferating stage, especially segmental lesions. Ideally, parents consider treatment options while the lesion is a precursor, which presents as an early macular stain. Precursor lesions may be treated with the PDL at 595 nm, at fluences of 6 to 7 J/cm², with epidermal cooling. This low-dose treatment may cause early involution of superficial components and prevent development of deep components. However, it is rare for the lesions to be seen at such an early stage—by the time they are presented to a physician, most lesions have already entered the proliferative stage.

For lesions at the proliferative stage, pediatric dermatologists often prefer a conservative approach, waiting and watching the lesion for several months during early proliferation, sometimes through early involution, to determine whether the lesion will develop a deeper component or segmental morphology. However, if treatment is delayed, researchers question whether the efficacy of uncomplicated superficial hemangioma treatment is compromised. A 2002 study by Batta et al showed no significant benefit to early PDL treatment of uncomplicated hemangiomas, although treated lesions had a higher risk of atrophy and hypopigmentation. Generally, the hemangiomas that respond best to PDL treatment may often be the lesions that are most likely to involute with nice cosmetic results spontaneously, ultimately without treatment. These are likely the same types of lesions that would respond well to topical corticosteroids or imiquimod.

In terms of more complicated lesions, when PDL is used on diffuse or segmental proliferating hemangiomas, there is an increased risk of ulceration. A chart review by Witman et al in 2006 revealed complications from PDL treatment of hemangiomas could include atrophic scarring, ulceration, and in one instance, life-threatening hemorrhaging, pain, and residual scarring. However, it is important to note that the PDL was not originally intended for hemangioma treatment, but for PWS treatment. Therefore, it is possible that biological differences between the two lesions may account for the different treatment responses. Although PWSs are fixed, slow-flow vascular malformations, hemangiomas are high-flow tumors packed with tiny blood vessels, with little dermis between the vessels. High fluences are extremely effective on PWSs, but these parameters cannot be used on hemangiomas as the target vessels are much closer.

The benefits of the PDL treatment are also limited by the depth of laser penetration, as the PDL can only injure to a depth of around 1.2 mm. For this reason, it is not very effective in treating deeper components of hemangiomas, which may continue to grow even if the superficial component recedes. Lesions raised 3 mm or less are more likely to completely resolve than lesions thicker than 3 mm, which may pose greater challenges when attempting to stop progression and achieve total resolution.

PDL treatment is an accepted therapy for ulcerating hemangiomas, which are complications of hemangiomas with an unknown origin. These complications can sometimes occur after an infection or...
trauma. PDL therapy decreases pain in the ulcerated region, although unfortunately the laser treatment can infrequently cause ulceration as well.10

The deeper parts of the lesion are more likely to respond to nonselective CW Nd:YAG lasers or the newer long-pulsed Nd:YAG lasers,13 although there is also the risk of scarring, blistering, crusting, pigmentation problems, and textural abnormalities regarding these lasers13,25,37. Such complications are a result of deep thermal injury from using intensely penetrating, near infrared wavelengths. Because of the Nd:YAG laser’s narrow band of safety and efficacy, only the lowest effective fluence should be used. However, Nd:YAG laser treatment of hemangiomas is generally only recommended for the most experienced laser surgeons.

KTP lasers are also an option, especially for deeper, thicker lesions. The KTP laser is actually a type of Nd:YAG laser (1064 nm) that is modified when the 1064-nm light is passed through a KTP crystal. The absorption of the now 532-nm wavelength by hemoglobin is extremely strong compared with the 1064-nm Nd:YAG light.37 This pulsed laser has pulse durations ranging from 1 to 100 milliseconds administered to tissue via a fiberoptic hand piece. Advantages include the high absorbance of the 532-nm wavelength by hemoglobin and a lack of posttreatment purpura. However, KTP lasers have a limited penetration depth caused by the short 532-nm wavelength, and because this wavelength competes with melanin more than longer wavelengths, this can cause dyschromias.13 However, when the KTP laser is used with an intralesional bare fiber, the laser light is sent directly into the deep component of the hemangioma, delivering the maximum amount of laser energy to this section while limiting cutaneous damage.37 This allows for better lesion penetration than a PDL laser but carries less risk of scarring than an Nd:YAG laser.37

Clinical recommendations

Overall, laser treatment of hemangiomas is still controversial and a recent study by Batta et al38 showed PDL treatment of uncomplicated hemangiomas did not achieve better results than a wait-and-see approach.10 Laser treatment is currently used for thin, superficial lesions; ulcerated hemangiomas; and residual erythema and telangiectases.39,40 Recommended treatment for superficial or ulcerating hemangiomas is the PDL, 585 to 595 nm, with fluences of 5 to 7.5 J/cm², pulse durations between 300 and 450 μs, spot sizes of 5 to 7 mm, and a concomitant cooling device.

The PDL is not a good choice for deep or mixed hemangiomas,39 as it cannot penetrate deeper than 1.2 mm. In addition, the risk of scarring is greater for PDL treatment of hemangiomas than PDL treatment of PWSs.39 However, the intralesional bare fiber KTP laser may be considered for deep hemangiomas, although this treatment is operator dependent, does not rely on the principles of photothermolysis, and carries the risk of ulceration. Suggested parameters include a wavelength of 513 nm, power of 2 to 5 W, and a 600-μm bare fiber.

CW lasers are rarely used for hemangioma treatment anymore and are considered historical treatment modalities.

Currently, there are no optimal laser systems for hemangioma treatment.40 Patients and parents should consider options very carefully, remembering that treatment, especially of deep or complicated hemangiomas, may not lead to improvements and that many pediatric dermatologists prefer watchful waiting to aggressive treatments (Table III).

A 1993 study by Ashinoff and Geronemus44 assessed whether the PDL, which had produced great improvements in PWSs, could prevent deeper growth of hemangiomas. The report involved 4 case studies of patients aged 4 to 7 weeks, treated with a 585-nm PDL with fluences from 5.5 to 7.75 J/cm² and varying pulse durations, spot sizes, and number of treatments. Although most of the superficial components of the lesions resolved after PDL treatment, the laser had no effect on deeper parts of the hemangiomas, which continued to grow after PDL treatment in all 4 patients. However, it is important to note the extremely small sample size of the report.44

Achauer et al37 used a less familiar technique in 1998, when they treated infant hemangiomas using intralesional bare fiber technique with a KTP laser. Intralesional laser photocoagulation requires directly penetrating the hemangioma with an Nd:YAG laser (600-μm bare fiber). It allows the light to be delivered directly into the deep hemangioma via a bare fiber delivery system, lowering cutaneous damage by bypassing direct contact with the skin surface. The goal was to expressly target the deepest sections of the lesion.

The exact mechanism by which this technique works is still unclear, but it is suggested that the laser likely produces thrombogenesis in many regions of the hemangioma. The laser can produce a maximum of 15 to 20 J of CW energy. Previous studies32 have shown photocoagulation resulting between 60°C and 100°C, causing coagulation necrosis, homogeneous coagulation, good hemostasis, and closing of the lymphatic vessels and alveoli, without transient temperature fluctuation in patients.
### Table III. Hemangioma laser studies

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of patients</th>
<th>Age range</th>
<th>Laser parameters</th>
<th>No. of treatments</th>
<th>Results</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ashinoff et al (1993)</td>
<td>4</td>
<td>4-7 wk</td>
<td>PDL: 585 nm, 5.5-7.5 J/cm², varying pulse durations and spot sizes</td>
<td>1-9</td>
<td>Superficial components resolved, but no effect noted on deeper components of hemangiomas. Deeper sections continued to grow after treatment.</td>
<td>Not noted</td>
</tr>
<tr>
<td>Achauer et al (1998)</td>
<td>12</td>
<td>1 mo-3.5 y</td>
<td>Intralesional bare fiber KTP: 532 nm, 15 J, 0.6 mm bare fiber</td>
<td>1-3</td>
<td>All patients had &gt;50% hemangioma reduction at 6 mo. Intralesional steroids used in parallel with laser therapy in 6 cases. Researchers deemed the KTP intralesional photocoagulation technique effective for the treatment of bulkier hemangiomas.</td>
<td>In all, 3 of 12 patients ulcerated (a 25% risk); no other side effects noted</td>
</tr>
<tr>
<td>Poetke et al (2000)</td>
<td>165</td>
<td>2 d-7 y</td>
<td>PDL: 585 nm, 5-7 J/cm², 300 μs, 5 mm</td>
<td>Administered during 2.5 y until lesions cleared or were unresponsive</td>
<td>52/153 (34%) Superficial proliferating hemangiomas and 12/18 (67%) superficial involuting hemangiomas cleared. Superficial involuting lesions showed the most progress. Researchers believed the PDL to be an effective choice for superficial hemangiomas but not a good choice for deeper components of hemangiomas.</td>
<td>Small scars, hyperpigmentation, hypopigmentation; normal-appearing skin color reappeared within 8 wk for all patients, no permanent damage</td>
</tr>
<tr>
<td>Raulin et al (2001)</td>
<td>50</td>
<td>Infants (no age range given)</td>
<td>PDL: 585 nm, 5.3-6.8 J/cm², 0.3-0.45 ms, 7 mm Long-pulsed frequency-doubled Nd:YAG: 532 nm, 20 J/cm², 1-50 ms, 5 mm</td>
<td>PDL: average of 3 Nd:YAG: average of 2.6</td>
<td>In PDL group, 27/29 (93%) lesions regressed or stopped growing. In Nd:YAG group, 23/33 (70%) lesions regressed or stopped growing. The PDL was judged to be slightly more effective treatment for lesion regression.</td>
<td>Swelling in all lesions, more pronounced in Nd:YAG-treated hemangiomas; Nd:YAG lesions showed more crusting and blisters; PDL lesions showed more purpura, hypopigmentation, and hyperpigmentation; atrophic scarring occurred in one lesion in each group</td>
</tr>
<tr>
<td>Authors</td>
<td>Study Size</td>
<td>Duration</td>
<td>PDL Settings</td>
<td>Lesion Response</td>
<td>Side Effects</td>
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<tr>
<td>Hohenleutner et al (2001)</td>
<td>548</td>
<td>3-36 mo</td>
<td>PDL: 585 nm, 5-10 J/cm², 450 μs, 5 or 7 mm</td>
<td>85/617 (14%) Lesions resolved completely, 92/617 (15%) seriously regressed, 419/617 (68%) stopped growing, and 21/617 (3%) progressed. Researchers did not find any age-related differences in treatment results. PDL was able to stop further progression or induce regression in most cases. No lesions with deep, fast-progressing components were included in the study.</td>
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<td>Batta et al (2002)</td>
<td>121</td>
<td>1-14 wk</td>
<td>PDL: 585 nm, 6.0-7.5 J/cm², 450 μs, 3-5 mm</td>
<td>Lesion clearing between PDL-treated group and observation group was not significant. No benefit of early PDL treatment was found. PDL-treated lesions had a higher risk of side effects. PDL treatment of hemangiomas was not significantly better than a wait-and-see approach. Skin atrophy, and hypopigmentation were more likely to occur in PDL-treated children; complications such as ulceration, bleeding, infection, and conditions requiring steroids were not significantly different between groups.</td>
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<tr>
<td>David et al (2003)</td>
<td>78</td>
<td>Mean age 5.5 mo</td>
<td>PDL: 585 nm, 5.0-6.8 J/cm², 300-500 μs, 5 or 7 ± 0.5 mm</td>
<td>All patients had ulcerated hemangiomas. In all, 71 of 78 (91%) patients reacted to laser therapy alone after an average of two treatments. Results supported the use of the PDL for ulcerating hemangiomas. In all, 6 of 78 (8%) patients needed concomitant oral prednisone for 6 wk; no significant complications</td>
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<tr>
<td>Study</td>
<td>No. of patients</td>
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<tr>
<td>Kono et al (2006)&lt;sup&gt;46&lt;/sup&gt;</td>
<td>52</td>
<td>1-3 mo</td>
<td>PDL: 585 nm, 5.5-7.0 J/cm&lt;sup&gt;2&lt;/sup&gt;, 450 µs, 7 mm</td>
<td>Treatments repeated at 4-wk intervals until hemangiomas cleared, stopped growing or responding, or parents discontinued treatment</td>
<td>Only superficial hemangiomas in preproliferative or early proliferative stage were included. Patients with LPDL showed slightly more improvement than those with PDL and had a significantly shorter average interval of maximal proliferation. Patients with PDL had more complications. Researchers determined that the LPDL with cryogen cooling spray was safer and more efficient.</td>
<td>Hypopigmentation, hyperpigmentation, textural changes</td>
</tr>
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<td>Burstein et al (2006)&lt;sup&gt;55&lt;/sup&gt;</td>
<td>400</td>
<td>Not noted</td>
<td>Intralesional bare fiber KTP: 513 nm, 2-5 W, 600-µm bare fiber; PDL: 585 μm, 6-15 J/cm&lt;sup&gt;2&lt;/sup&gt;</td>
<td>3-9</td>
<td>The deep component of hemangiomas was injected with 0.125% mepivacaine, 5% Kenalog solution at the end of the laser treatment. If superficial component existed, it was treated with PDL. All patients had at least a 75% reduction in lesion size. Researchers concluded the KTP delivered via intralesional bare fiber was an efficient treatment of deep hemangiomas.</td>
<td>In all, 8 of 400 (2%) patients experienced ulceration</td>
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</table>

LPDL, Long pulsed dye laser; Nd:YAG, neodymium:yttrium-aluminum-garnet; PDL, pulsed dye laser.
or changes in hemoglobin levels. Bulkier vascular tissue reduces without serious side effects, and after inflammation reactions lasting 7 to 10 days, 25% to 50% reduction often occurs between 4 and 6 weeks.52

Achauer et al37 chose the KTP laser over the Nd:YAG laser because it was less likely to cause scarring and was more hemoglobin specific. Researchers treated 12 patients aged 1 month to 3.5 years. Approximately 11 of 12 (92%) patients had more than 50% reduction at 3 months, with approximately 1 of 12 (8%) patients achieving a more than 50% reduction at 6 months. Five of 12 (42%) patients required only one treatment, 6 of 12 (50%) required two treatments, and one of 12 (8%) required 3 treatments. Three patients ulcerated after laser treatment, indicating a high risk of ulceration (25%), but no other side effects were observed. Functioning in obstructed areas improved markedly during follow-up, as measured by observation and photodocumentation. Researchers concluded the KTP intraleisional photococagulation technique was effective in treating bulkier hemangiomas that obstruct function.37

In 2000, Poetke et al47 studied the effect of the PDL on superficial versus mixed hemangiomas in children. In all, 165 children with 225 distinct hemangiomas participated. Children were aged 2 days to 7 years. Patients were divided into 3 groups: flat cutaneous hemangiomas (100 patients with 153 lesions), mixed cutaneous-subcutaneous hemangiomas (47 patients with 54 lesions), and superficial hemangiomas in the involution stage (18 patients with 18 lesions).

Results were described as excellent if the hemangioma totally cleared, good when the lesion involuted slower or did not lighten completely, and a failure if the lesion changed little or grew further. Patients with failed lesions received further treatment with a continuous mode 1064-nm Nd:YAG laser at 25 to 46 W and a spot size of 5 mm.

Overall, an excellent response was seen in 52/153 (34%) superficial proliferating hemangiomas and 12/18 (67%) superficial involuting hemangiomas. Good results were seen in 80/153 (52%) superficial proliferating hemangiomas, 21/54 (39%) mixed hemangiomas, and 6/18 (33%) superficial involuting hemangiomas. The superficial involuting lesions showed the greatest progress.

Of 225 lesions, 206 (92%) did not develop textural changes after therapy, whereas 8 of 225 (4%) patients had small scars in regions that had ulcerated before treatment. Hyperpigmentation occurred in 2/225 (1%) lesions and hypopigmentation occurred in 9/225 (4%) lesions. Normal-appearing skin color reappeared within 8 weeks for all patients, with no permanent effects. Each patient received an average of 2.0 ± 1.1 treatments.

Poetke et al47 stated that the PDL was effective and a top choice for superficial cutaneous hemangiomas on regions of possible functional impairment and on the face. Hemangiomas with deeper sections did not benefit from the PDL because of the limited depth of vascular injury the laser was capable of achieving. In addition, researchers admitted early treatment with the PDL may not inhibit proliferative growth of the deeper sections of the hemangioma, regardless of the early intervention.47

A 2001 study by Raulin and Greve53 compared the efficacy of the PDL versus the long-pulsed frequency-doubled Nd:YAG laser in treating superficial hemangiomas in infants. In the PDL group, regression resulted after an average of 3.0 treatments. Of the 29 hemangiomas, 27 (93%) regressed, with 11 lesions regressing 100%, 14 regressing between 70% to 90%, and two regressing less than 70%. The remaining two lesions showed growth regardless of therapy. In the frequency-doubled Nd:YAG group, hemangiomas needed an average of 2.6 treatments. Of the 33 lesions, 23 (70%) regressed, with 7 lesions regressing 100%, 13 regressing between 70% and 90%, and 3 regressing less than 70%. Six hemangiomas exhibited growth despite therapy, two did not change, and two did not have further treatments after the initial session.

In terms of side effects, temporary swelling was seen in all treated hemangiomas, although lesions treated with the Nd:YAG laser had swelling that was considerably more pronounced and longer lasting. The Nd:YAG laser lesions also showed more crusting and blisters (8 Nd:YAG vs one PDL), whereas PDL lesions revealed more purpura (25 PDL vs 5 Nd:YAG), hypopigmentation (3 PDL vs two Nd:YAG), and hyperpigmentation (6 PDL vs 0 Nd:YAG). One lesion in each group displayed atrophic scarring.

Researchers asserted the PDL was slightly more successful regarding lesion regression and was selected as the top choice for initial hemangioma treatment in infants. If parents wanted further treatment for cosmetic appearance while the lesion was in the regression stage, the Nd:YAG laser was recommended for its low levels of side effects and pain.53

A 2001 study by Hohenleutner et al54 examined the long-term results of the PDL treatment on childhood hemangiomas with the goal of inhibiting further growth or inducing regression. Lesions with a dominating or faster-growing subcutaneous region were not included in the study. Overall,
85/617 (14%) lesions achieved total resolution, 92/617 (15%) markedly regressed, 419/617 (68%) stopped growing, and 21/617 (3%) progressed. Researchers stated there was no difference in treatment results related to age and that the PDL treatment was able to stop further progression or induce regression in most of the hemangiomas. In addition, the PDL was quick, effective, and almost devoid of side effects. Researchers recommended early PDL treatment for superficial and small childhood hemangiomas. However, it is important to note that researchers did not include lesions with deep, fast-progressing components in this study.54

A 2002 randomized controlled study by Batta et al48 assessed the effect of PDLs on childhood hemangiomas versus a wait-and-see policy. In all, 121 infants aged 1 to 14 weeks were split into a PDL treatment group and an observation group. Batta et al47 found complete lesion clearing was not significant between the treatment and control groups, with 25 of 60 (42%) of the children treated with PDL exhibiting total clearing and 27 of 61 (44%) of the observation children showing complete clearing or minimal residual signs at 1 year old. Treatment did produce significantly better outcomes when a stricter definition of complete clearance was used that did not include residual signs, with 18 of 60 (30%) patients with PDL showing complete clearance versus 3 of 61 (5%) of the observation patients. Lesion heights were not significantly different between treatments, although PDL treatment did significantly improve hemangioma redness.

Children treated with PDL were more likely to have adverse reactions, such as skin atrophy (17 PDL vs 5 observation) and hypopigmentation (27 PDL vs 9 observation). Complications such as ulceration or painful ulceration, bleeding, infection, or conditions requiring steroids did not differ much between groups (12 PDL vs 13 observation).

The number of children whose parents believed the hemangioma problematic at 1 year of age did not significantly differ across the groups (11 PDL vs 9 observation). Problematic lesions assessed by the independent parent panel also did not differ significantly between groups. A total of 42 PDL lesions and 40 observed lesions were designated “not at all” problematic, 8 PDL lesions and 10 observed lesions were “a bit” problematic, 5 PDL lesions and 9 observed lesions were “quite a bit” problematic, one PDL lesion and one observed lesion were “a lot” problematic, and 4 PDL lesions and one observed lesion were “a big problem.” Researchers asserted that results did not reveal any useful benefit of early PDL treatment in uncomplicated hemangiomas but did indicate that treated lesions had a higher risk of skin atrophy and hypopigmentation. They concluded that for hemangioma treatment, PDL treatment did not outrank a wait-and-see policy.48

The significance of PDL treatment may increase when dealing with complicated lesions such as ulcerated hemangiomas. David et al50 conducted a large study in 2003 with 78 children who had ulcerated hemangiomas. In all, 71 of 78 (91%) patients reacted to laser therapy alone in a mean number of 2.0 treatments. Six of 78 (8%) patients with very large lesions needed concomitant oral prednisone (2-3 mg/kg/d) for 6 weeks. Four of these 6 patients stabilized or displayed involution, whereas two did not improve on the oral steroid/PDL combination therapy and required interferon in their treatment regimen to eventually stabilize. No patients required surgical excision to treat the ulceration. The mean follow-up time was 15 months with no apparent recurring ulceration or lesion regrowth in the study population.

Researchers concluded results supported treating ulcerated hemangiomas with the PDL. No significant long-term complications were seen, and the PDL was shown to be effective in treating pain, decreasing infection, and decreasing bleeding by assisting the epithelialization of the ulcer.50

In 2006, Kono et al56 examined the effects of the classic PDL versus a LPDL in treating children with hemangiomas. A total of 52 Asian infants, aged 1 to 3 months, with early hemangiomas were given either PDL or LPDL treatment. Only superficial hemangiomas in the preproliferative or early proliferative stage were included in the study. Children with mixed or deep hemangiomas, large facial lesions that could possibly cause vast cosmetic deformity, and lesions obstructing areas such as the ear, nose, or mouth were excluded.

Complete clearance, described as excellent with a percent improvement of 76% to 100% and minimal residual signs, was noted in 14 of 26 (54%) of the children treated with PDL and 17 of 26 (65%) of those treated with LPDL at 1 year old. Five patients with PDL and 7 with LPDL displayed moderate improvement (51%-75%), 4 with PDL and two with LPDL displayed mild improvement (26%-50%), and 3 with PDL and none with LPDL displayed no improvement or worse results (0%-25%). Children treated with PDL had more complications than those treated with LPDL, with hypopigmentation in 8 patients with PDL versus 3 with LPDL, hyperpigmentation in 4 patients with PDL versus two with LPDL, and textural changes in 6 patients with PDL versus one with LPDL. In addition, the average interval of maximum proliferation was significantly
shorter in the LPDL group (106 days) compared with the PDL group (177 days). Researchers concluded that the LPDL with cryogen spray cooling was a safer and more efficient treatment for childhood hemangiomas than the PDL.46

A 2006 study by Burstein et al55 updated the intrallesional bare fiber KTP treatment of hemangiomas. A total of 400 patients with deep hemangiomas were treated with a 513-µm KTP laser, delivered via a 600-µm bare fiber directly into the hemangioma. As most patients also had a superficial component, this layer was treated with a 585-µm PDL, with fluences from 6 to 15 J/cm². Patients with complications such as visceral hemangiomas or airway hemangiomas were also given systemic steroids, interferon, or both.

All patients exhibited a response to the KTP treatment. In all, 280 of 400 (70%) had 3 to 6 treatments, 80 of 400 (20%) had 6 to 9 treatments, and 40 of 400 (10%) had more than 9 treatments. All patients had at least a 75% reduction in the general size of their lesion, and this included diameter and thickness. Complications were minimal—no patients needed intraoperative transfusion during the laser treatments, and there were no incidences of nerve paresis or paralysis, or burns. Eight of 400 patients (2%) experienced ulceration.

Researchers concluded that the KTP laser was an efficient treatment of deep hemangiomas. Key changes from earlier trials included lowering the power from 15 to 20 W to 2 to 5 W (the ulceration rate decreased from 20% to 2%) and giving each patient a minimum of 3 treatments instead of one. Although researchers admit the precise mechanism and dosimetry curve of the KTP laser was not completely understood, they suggested the lower power dosage relies on selective absorption rather than a thermal effect that might predominate at higher power levels. Lowering the power not only seemed to lower the ulceration rate, but allowed both the superficial and deep components of the hemangioma to be treated at the same time. Overall, increasing the treatment sessions and decreasing the power allowed the skin more time to heal between treatments, prevented excessive thermal injury to the dermal/vascular plexus, and decreased the risk of necrosis.55

In addition, to achieve a higher level of scientific reproducibility, future research must avoid mistakes made in previous studies. Many studies suffered from a lack of clarification regarding statistics,23 treatment parameters,34,44,46,54 ages of patients,53,54 and parallel treatments.54 As van der Horst et al.19 noted, some PWS studies only included patients with light pink-red stains, which are known to have the best response to PDL treatment, as opposed to testing treatment on a range of light to dark stains.

As mentioned previously, there were no studies involving variation in only one parameter, so it was difficult to assess optimal treatment levels. It was also difficult to determine occasions for cooling and what cooling method should be used.19,35,46,48 A variety of cooling treatments were used, from gauze dressings soaked in ice water to dynamic cooling sprays, and this may have impacted the efficacy of the laser on lesion clearing. A few studies also had very short follow-up times, which did not allow for long-term assessment.47,48

Future research could involve clarifying standard parameters and cooling methods, extending follow-up periods, and identifying novel ways to treat deeper components of hemangiomas. More randomized controlled trials or strong evidence-based studies regarding hemangiomas have also been suggested.59 Future studies should also note the growth stage of the infantile hemangioma. It often correlates with patient age, although this is not always an exact correlation.

CONCLUSION

Overall, the literature reflects that laser treatment is safe and effective therapy for PWSs. However, laser treatment of hemangiomas remains controversial, as superficial involuting and ulcerating hemangiomas46,47,50,53,54 seem to benefit from laser treatment, but lesions involving deeper components do not.44,47

REFERENCES


