Vascular anomalies are a common finding in children. Although most of these lesions are benign, they can be a severe cosmetic problem and cause structural and functional damage to nearby tissues. As a result, physicians are tasked with developing effective treatment options with superior safety profiles. Vascular anomalies may be divided into tumors and malformations. Vascular tumors, such as infantile hemangiomas, typically appear a few weeks after birth, whereas the majority of vascular malformations, such as port-wine stains, are present at birth. Although these lesions vary in appearance, etiology, and disease course, many are treated in a similar fashion. In this review, we focus on treatment modalities for some of the more-prevalent childhood vascular lesions, including port-wine stains, primary telangiectasias, infantile hemangiomas, pyogenic granulomas, and angiomas.

The authors have indicated no significant interest with commercial supporters.

Vascular Malformations

Port-Wine Stains

Characteristics

PWS, also known as nevus flammeus, are the most common childhood vascular malformation, occurring in 0.3% of newborns. A PWS is a slow-flowing capillary malformation, described as a cluster of pink to purple, sharply demarcated patches. They are typically located in a unilateral distribution on the head and neck and may involve the mucous membranes. Like most vascular malformations, PWS are present at birth and do not involute spontaneously. Over time, these lesions darken, with 11% thickening and 24% developing nodules. PWS can be isolated malformations, or they may be associated with conditions that have systemic involvement. When PWS are located in a trigeminal distribution, Sturge-Weber syndrome, characterized by glaucoma, leptomeningeal venous angiomas, seizures, hemiparesis contralateral to the facial lesion, and intracranial calcifications, must be considered. PWS may also be associated with other syndromes such as Proteus (with an overgrowth of the skeleton; skin, adipose, and central nervous system tissue; severe disfigurement; tumors; pulmonary complications; deep vein thrombosis; and pulmonary embolism), Beckwith–Wiedemann (with exomphalos, macroglossia, and gigantism), and Bonnet–Dechume–Blanc (with unilateral arteriovenous malformations involving the retinas, brain, and skin of the face). For this reason, children

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© 2013 by the American Society for Dermatologic Surgery, Inc. ● Published by Wiley Periodicals, Inc. ● ISSN: 1076-0512 ● Dermatol Surg 2013;1–10 ● DOI: 10.1111/dsu.12129
born with PWS should receive a complete diagnostic evaluation.

**Treatment**

Treatment is usually recommended for PWS even when they are not associated with an underlying systemic condition. These lesions can cause significant morbidity, bleeding, and psychological and cosmetic concerns. The most effective treatment is vascular-specific laser therapy, most notably pulsed dye laser (PDL).\(^7\) Despite significant technologic advances, many PWS cannot be completely eliminated with PDL treatment alone. As a result, physicians have become interested in combining existing therapies to maximize results.

**Laser**

PDLs emit wavelengths that specifically target oxyhemoglobin, treating the vascular abnormality with minimal damage to the surrounding tissue. Effective treatment protocols include wavelengths of 585 to 600 nm, fluences of 6 to 12 J/cm\(^2\), and pulse durations of 0.45 to 10 ms with concomitant epidermal cooling. Sequential treatment sessions every 4 to 8 weeks are recommended.\(^8\) Common side effects include transient erythema, edema, and mild purpura that spontaneously resolve in a few days. Progressive lesional fading is seen after each treatment, with multiple (≥9) treatments typically necessary to achieve >75% improvement (Figure 1A,B).\(^9\)

Studies have suggested that laser treatment is most effective when initiated in the first year of life, in part because infant skin is thinner, thus enhancing laser penetration.\(^10,11\) As mentioned above, PWS become thick and nodular with advancing age, so treating early allows the malformation to be treated at its smallest.

In addition to determining optimal laser parameters and appropriate patient treatment age, varying laser techniques have been investigated. A double-pass technique using a PDL produces better blanching than the typical single pass technique.\(^12\) Treated areas are generally lighter, without evidence of scarring after a series of laser treatments, but residual PWS can darken over time because of progressive vessel ectasia.\(^13\) Longer wavelengths and pulse durations (along with more epidermal cooling to prevent excess tissue damage) can be applied to lesions that initially respond to PDL treatment but reach a treatment plateau.\(^14\) The long-pulse alexandrite (755 nm),\(^15\) long-pulse 1,064-nm neodymium-doped yttrium aluminum garnet (Nd:YAG),\(^16\) and dual 595-nm PDL and 1,064-nm Nd:YAG\(^17\) lasers have proven useful in these latter cases, particularly when lesions have developed nodularity, because of the ability of these systems to achieve deeper dermal penetration.\(^18\)
**Laser and Topical Therapy**

Although lasers continue to be used as the primary treatment for PWS, preliminary studies have evaluated the use of adjunctive anti-angiogenic therapy. Daily or three times weekly application of topical imiquimod 5% between laser treatment sessions has been shown to reduce PWS color reduction more than PDL treatment alone. Side effects of imiquimod treatment include minor skin irritation in a minority of patients. Other investigators have demonstrated in rodents that PDL treatment followed by a 14 day course of rapamycin prevented reformation and reperfusion of blood vessels more than PDL alone.

**Other**

Intense pulsed light (IPL) has also been advocated for PWS treatment. Although vascular-specific lasers remain a more-effective treatment option, IPL should be considered in PDL-resistant patients. A randomized side-by-side study showed that PDL was generally more effective in inducing clearance, but in PDL-resistant lesions, six of 15 patients had more than 75% clearance with IPL.

**Primary Telangiectasias**

**Characteristics**

Telangiectasias appear as dilated blood vessels on the skin and mucus membranes. Primary (or essential) telangiectasias have no causative or coexisting cutaneous or systemic diseases. Although primary telangiectasias are usually a sporadic finding, a benign hereditary form has also been described. This condition, known as generalized essential telangiectasia, consists of patchy reticular telangiectasias that may progress to involve large body surface areas. Generalized essential telangiectasia can present at any age and has no known etiology, although familial cases have been described with an autosomal-dominant inheritance pattern. Children with telangiectasias should be fully evaluated to exclude causes of secondary telangiectasias such as connective tissue diseases, xeroderma pigmentosum, poikiloderma, and ataxia-telangiectasia.

**Treatment 3**

As with PWS, PDL is the most commonly applied treatment for primary telangiectasias. Complete resolution of linear and spider facial telangiectasias is typically achieved after two to three sequential 595-nm PDL treatments using a 7- to 10-mm spot and fluences from 6 to 10 J/cm². Post-treatment purpura can be avoided using longer pulse durations (>6 ms), but lack of purpura after treatment generally yields less-favorable clinical results. Pulse stacking and use of multiple sequential passes have also been cited as techniques that may yield better clinical responses. Lasers with longer wavelengths, such as the long-pulse alexandrite (755 nm) and long-pulse Nd:YAG (1,064 nm) systems may be used for deeper lesions but may increase the risk of scarring and ulceration.

**Vascular Tumors**

**Infantile Hemangiomas**

**Characteristics**

Hemangiomas are the most common tumor in infancy (1–2% incidence of all live births and ≥10% at 1 year of age), with a greater incidence in premature infants. These vascular tumors characteristically increase in size, stabilize, and then spontaneously involute over several months. Frieden and colleagues recently discovered that the most rapid hemangioma growth occurs before 8 weeks of age, especially between 5.5 and 7.5 weeks. In addition to prematurity, other risk factors include Caucasian race, female sex, chorionic villous sampling, and multiple-gestation pregnancy. Hemangiomas are typically classified as superficial, deep, or mixed. Superficial hemangiomas are the most common (50–60% of cases), appearing bright red and sometimes protuberant. In contrast, deep hemangiomas are rare (15% of cases), less well defined, firm, cystic, or compressible and may exhibit a bluish hue underneath normal-appearing skin. Mixed hemangiomas combine characteristics of superficial and deep lesions and account for 25% to 30% of cases. Hemangiomas can also be
classified as focal or segmental. Focal hemangiomas tend to grow in a tumor-like fashion, whereas segmental hemangiomas are larger and plaque-like. Segmental hemangiomas are more aggressive, with greater ulceration and local destruction.\textsuperscript{30} Left untreated, 60\% of infantile hemangiomas will involute by 5 years, and 90\% to 95\% will maximally involute by 9 years. It was established in 2000 that glucose transporter-1 stains positive in hemangiomas, making this marker useful in distinguishing hemangiomas from other vascular tumors.\textsuperscript{31} Location does not appear to affect resolution in most situations, although lip lesions are the most persistent. Size does not appear to affect involution.\textsuperscript{1}

\textbf{Treatment 3}

The majority of hemangiomas are treated with simple observation, because 70\% resolve spontaneously without severe complications. The other 30\% of hemangiomas may result in hemorrhage, ulceration, and disfigurement of the underlying tissue.\textsuperscript{1} Depending on location, a hemangioma may cause airway or orbital obstruction, hearing loss, or spinal abnormalities. Early treatment is advised for hemangiomas that interfere with the function of a vital organ, involve large portions of the face or inguinal area, risk ulceration, or cause psychological suffering.\textsuperscript{32} Hemangiomas requiring treatment are most effectively managed early to affect the proliferation phase directly.\textsuperscript{33} A variety of treatments are available, including topical, intralesional, oral, and laser therapies.

\textbf{Oral 2}

Oral corticosteroids have been the first-line treatment for hemangiomas since the 1960s. A course of prednisone is generally effective in decreasing the size and severity of hemangiomas but can cause numerous side effects, including impaired immunity, hypertension, and hyperglycemia.\textsuperscript{34–36} An effective dosing regimen consists of 1.5 to 2 mg/kg per day of prednisone for 4 to 8 weeks.\textsuperscript{32} One meta-analysis showed that 3 mg/kg might be a more effective dose, stabilizing growth in 90\% of patients.\textsuperscript{34} Although corticosteroids may still be prescribed, other therapies are currently advocated because of the risk of side effects associated with corticosteroid use.

Recent studies favor the use of propranolol, a nonselective beta-adrenergic blocker, as first-line treatment for infantile hemangiomas. Leaute-Labreze and colleagues\textsuperscript{37} first discussed its use at a dose of 2 mg/kg per day. Other beta-blockers, such as acebutolol, have also been found to be effective, but propranolol use is generally favored.\textsuperscript{38} Price and colleagues\textsuperscript{39} found that propranolol therapy was more cost effective and had fewer surgical complications than oral steroids. Koay and colleagues\textsuperscript{40} reported that propranolol and oral steroids could be combined at lower doses, reducing the adverse side effects of both drugs. Young infants are commonly started on a course of propranolol while hospitalized to monitor for any adverse reactions, most commonly hypotension. Older children often start treatment as outpatients, with appropriate counseling and monitoring. Hypoglycemia has been cited as a rare and dangerous side effect of propranolol.\textsuperscript{41} Diarrhea and hyperkalemia have also been described.\textsuperscript{42,43} The appropriate course of propranolol has not been standardized, but physicians should be aware that hemangiomas can have rebound growth if treatment is not continued through the growth phase—generally 1 year.

Recombinant interferon-alpha (3 million U/m\textsuperscript{2} per day) and vincristine, a vinca alkaloid chemotherapy agent (0.05 mg/kg per day), have been used successfully to treat proliferative hemangiomas.\textsuperscript{1} These treatments are reserved as third-line therapy because of the risk of immunosuppressive side effects with vincristine and irreversible spastic diplegia with interferon-alpha.\textsuperscript{44}

\textbf{Intralesional and Topical Agents 2}

Ophthalmologists first used intralesional and topical steroids to treat periorbital hemangiomas.\textsuperscript{45} Because of concerns regarding ocular damage, intralesional therapies are more commonly applied on the lip and
nose. Triamcinolone acetonide (10 mg/mL) injections are administered every 4 weeks at doses not exceeding 3 to 5 mg/kg per treatment.\textsuperscript{28} Class 1 topical corticosteroids are applied twice daily with monitoring every 2 weeks.\textsuperscript{46,47} Topical beta-blockers, specifically timolol maleate 0.5\% gel, have also been shown to be effective in treating superficial hemangiomas.\textsuperscript{48} Lastly, the use of 5\% imiquimod, an immune modulator and upregulator of interferon-alpha, has been used as successful therapy alone or in combination with laser.\textsuperscript{49}

**Laser**

Vascular-specific PDL therapy is particularly useful in treating ulcerated hemangiomas, superficial hemangiomas, and postinvolution hemangiomas (Figure 2A,B). Laser treatment parameters are less aggressive (4–7 J/cm\(^2\), 0.45–1.5-ms pulse duration) than those used for other vascular abnormalities to reduce such side effects as ulceration, scarring, and hypopigmentation in these delicate lesions.\textsuperscript{50–52} Multiple treatments are needed at 4- to 6-week intervals during the proliferative phase.\textsuperscript{53} PDL is less effective in the treatment of mixed and deep hemangiomas than in ulcerated, superficial or postinvolution lesions because it has limited dermal penetration. A recent study by Admani and colleagues\textsuperscript{54} found that early PDL treatment is a safe and effective option for selected patients with infantile hemangiomas alone or in combination with systemic therapy. In addition, involuted hemangiomas that display a variable array of cosmetic defects can be treated later with PDL, fractional laser skin resurfacing,\textsuperscript{55} or plastic surgery. Brightman and colleagues\textsuperscript{56} reported five cases in which patients experienced 50\% to 75\% improvement in residual hemangioma textural skin irregularities with minimal side effects after ablative fractional laser skin resurfacing.

**Other**

Hemangiomas can be surgically excised, but the risk of postoperative scarring is high. Scarring is of particular concern when treating young children with lesions located in cosmetically sensitive areas such as the face and neck. Embolization is another treatment option for high-output lesions when there is the potential for cardiac failure.\textsuperscript{1}

**Pyogenic Granulomas**

**Characteristics**

PGs, also referred to as lobular capillary hemangiomas, occur at any age but are more common in children and pregnant women. In children, these lesions typically present between the ages of 6 to 10 years and appear most commonly on the face and upper extremities.\textsuperscript{57} Congenital PGs exist but are rare. These small, red, “glistening” papules grow rapidly and bleed easily with trauma. Glucose transporter (GLUT)-1 staining can be used to
distinguish them from infantile hemangiomas; PGs stain negative for GLUT-1, and infantile hemangiomas stain positive. PGs are thought to arise because of an unregulated angiogenic stimulus, but the exact pathogenesis is unknown. Trauma is commonly elicited as an inciting event, but other causes are being shown to contribute, including the use of certain systemic and topical drugs such as retinoids, 5-fluoracil, granulocyte colony-stimulating factor, and some human immunodeficiency virus protease inhibitors. PGs may also occur within a vascular malformation, such as a PWS, spontaneously or after laser treatment. If left untreated, these lesions will most likely persist and continue to cause bothersome bleeding.

Treatment
PGs, although benign, are often treated because they bleed easily and cause cosmetic concerns. They may mimic basal cell carcinomas and nodular melanoma, so it is essential to obtain biopsies for pathologic examination if malignancy is suspected. In children, skin cancer is a rare occurrence, so the prescribed treatment depends primarily on location, risk of scarring, and likelihood of recurrence.

Surgical
Surgical excision is the most common treatment prescribed because of the high recurrence rate of PGs. Full-thickness excision, shave excision, and curettage with or without cautery can effectively remove these lesions, but scarring, infection, and blood loss can occur. Full-thickness excision has been shown to result in a lower recurrence rate (2.9%) than other surgical methods such as curettage and electrocautery (7–15%).

Laser
Treatment with PDL or carbon dioxide (CO2) lasers is advocated in children with small PGs in cosmetically sensitive areas because of the low risk of scarring with lasers. Lee and colleagues reported recurrence rates of 0.43% after PDL treatment of PGs and 0.49% after CO2 laser vaporization.

Multiple (2–6) sequential PDL treatments are typically required for clearance, compared with a single CO2 laser vaporization procedure, but PDL treatments are easier for children to undergo because they are painless and have nominal postoperative recovery.

Cryotherapy
Although cryotherapy is an effective treatment with an acceptable side-effect profile and minimal scarring and dyspigmentation risk, it is not first-line therapy for PGs because of its high lesional recurrence rates and number of treatments necessary. Lee and colleagues found a recurrence rate of 1.6% after cryotherapy, including patients treated multiple times. In a study by Mirshams and colleagues, 18% of patients experienced resolution after one to four cryotherapy sessions.

Topical
Topical therapies are associated with high recurrence rates and are thus typically reserved for patients who refuse surgical and laser options. Silver nitrate cauterization can be used, but burning of unaffected skin is a common hazard. Use of topical phenol has also been reported, particularly in the treatment of periungual PGs, but multiple applications of a 98% solution are usually needed for clearance. A study reporting the use of imiquimod 5% cream demonstrated varied responses, including no lesional recurrence in some of the cases.

Intralesional
Sclerotherapy using intralesional injections of ethanolamine oleate, sodium tetradecyl sulfate, or polidocanol can lead to resolution of PGs but can cause cutaneous necrosis of the surrounding tissue.

Spider Angiomas
Characteristics
Spider angiomas, or nevus araneus, are commonly associated with high levels of estrogen, but they also appear in 15% of healthy preschool-aged children.
and 45% of school-aged children. Lesions are often seen on the dorsum of the hands, forearms, face, and ears, appearing as bright red papules or dilated vessels radiating from a central artery. Spider angiomas vary in size and often have surrounding erythema that can be blanched upon compression.

**Treatment**
Although spider angiomas are benign, they can be of cosmetic concern if they are present in a prominent location or are unusually large or numerous. Treatment with a PDL is the criterion standard, with only one or two laser sessions typically needed to remove them. (Figure 3A,B)

**Other Vascular Lesions**

**Venous Malformations**

**Characteristics**
Venous malformations are present at birth and, instead of regressing over time, often become more noticeable. They appear clinically as soft blue nodules containing a mass of venules or as large, widespread abnormalities. Venous malformations may be superficial, resembling varicose veins, or deep. Blue rubber bleb nevus syndrome is a rare condition in which a person will have numerous venous malformations, most commonly involving the skin and the gastrointestinal (GI) tract. Although cutaneous venous malformations pose a cosmetic concern, GI venous malformations can lead to death due to GI hemorrhage.

**Treatment**
Venous malformations have traditionally been treated using surgical resection, sclerotherapy, and compression, but Nd:YAG laser treatment is now commonly used. Multiple laser sessions at 8- to 12-week intervals have been shown to reduce lesional color and bulk while improving dermal contour with minimal side effects. Small lesions are typically eradicated, whereas large venous malformations are reduced in size after multiple treatments. In addition to laser therapy, larger malformations can be treated using percutaneous sclerotherapy with polidocanol microfoam and color Doppler ultrasonographic guidance. In blue rubber bleb nevus syndrome, cutaneous and mucocutaneous venous malformations have been similarly treated using Nd:YAG lasers. Yuksekaya and colleagues successfully used sirolimus to shrink venous malformations in patients with multiple, potentially life-threatening lesions.

**Angiokeratomas**

**Characteristics**
Angiokeratomas are characterized histologically by dilations of superficial dermal vessels and hyperkeratosis of the overlying epidermis. Angiokeratoma circumscription is a rare disorder, often presenting at
birth, consisting of solitary or multiple angiokeratomas, usually occurring unilaterally on the lower extremities. Angiokeratoma corporis diffusum, or Fabry disease, is an X-linked inherited disorder caused by a deficiency of the lysosomal enzyme alpha-galactosidase. This disease is characterized by angiokeratomas; irregularities in sweating; edema; scant body hair; painful sensations; and cardiovascular, gastrointestinal, renal, ophthalmologic, phlebologic, and respiratory involvement.

**Treatment**

Isolated angiokeratomas can be surgically excised, but this option may not be practical for conditions resulting in numerous lesions, such as angiokeratoma circumscriptum and Fabry disease. In these situations, laser therapy is commonly used. A variety of vascular-specific lasers have been used, including 532-nm Nd:YAG, 578-nm copper vapor, and 595-nm PDL.

**Conclusion**

Physicians who evaluate and treat childhood vascular lesions should be familiar with the risks and benefits associated with all available therapies. Treatment should be individualized for each patient based on known lesional response rates and available treatment options. The management of childhood vascular anomalies has advanced with the use of combination medical and surgical treatments, leading to greater clearance and minimal side effects. Additional studies are necessary to further enhance clinical outcomes.

**References**


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