**Introduction**

Vascular anomalies are abnormal formations or growths within the vascular system. They are heterogeneous childhood conditions associated with confusing terminologies and occasional significant morbidity and mortality in infants and children. These vascular “birthmarks” are common diseases. The morbidity is about 2.5%; most of the lesions occur in oral and maxillofacial regions, which account for 40–60% of the total lesions. There are many types of vascular anomalies that require different treatment approaches. In 1996, the International Society for the Study of Vascular Anomalies (ISSVA) approved a classification system modified from the schema originally proposed by Mulliken and Glowacki. The classification was based on differences in the cellular kinetics and natural history of these lesions. Vascular tumors demonstrate endothelial cell hyperplasia, which spontaneously involutes. In contrast, the vascular malformations have flattened endothelial cells with normal endothelial cell turnover and do not involute spontaneously. The classification was further amended. This summary outlines the classifications, treatments, and complications of these lesions. Using keywords search of “vascular anomalies”, “hemangioma”, and “vascular malformation” and with limits set to exclude animal and bench studies, this overview aims to summarize the therapeutics efficacies of medical and surgical interventions for these lesions. Case reports are generally excluded unless they add unusual information on treatment modalities. Many new and exciting areas of discovery occur almost daily in the field of vascular anomalies. Owing to the breadth of this topic, it is certain that not all articles can be reviewed. Only the most recent and clinically relevant breakthroughs in the field are presented.

**Classification**

Vascular anomalies are defined as localized defects of the vasculature in a restricted area of the body. These defects are secondary to errors in vascular morphogenesis. Hemangiomas are vascular tumors characterized by rapid growth, increased endothelial turnover, and increased numbers of mast cells. Vascular malformations grow commensurately with the patient or expand secondary to hemodynamic alteration and
are characterized by a normal endothelial cell cycle and normal numbers of mast cells. Based on ISSVA, broadly, vascular anomalies are divided into two categories, vascular tumors and vascular malformations. Each of these can be further divided into multiple entities. Vascular tumors can be congenital or acquired, and are characterized by a proliferative phase of tumor growth, which may occur in utero or postnatally (eg strawberry hemangiomas). Vascular malformations are congenital, non-proliferative, and static, and composed of dysplastic developmental aberrations of blood or lymphatic vessels.

Vascular tumors are divided into hemangiomas and miscellaneous vascular tumors. The hemangiomas are divided into proliferative hemangiomas (infantile hemangioma) and non-proliferative hemangiomas (proliferation occurs in utero but not postnatally). Non-proliferative hemangiomas are further subdivided into non-involuting congenital hemangiomas (NICH) and rapidly involuting congenital hemangiomas (RICH). NICH and RICH are confusing entities that can only be differentiated retrospectively after the proliferation stage. Other vascular tumors include spina bifida, pyogenic granuloma, glomus tumor, angiosarcoma, myofibromatosis, hemangiopericytoma, kaposiform hemangioendothelioma, and tufted angioma (Table 1). Vascular malformations include malformations of the capillary, veins, lymphatic vessels, arteries, and any combination of the above. They are classified into “low flow,” “high flow,” and “complex combined” (Table 1).

### Imaging

The use of imaging could help in the differentiation between hemangiomas, vascular malformations, and other soft tissue tumors. MRI, MRA, and ultrasound are all useful in providing information as to the extent of the lesion. Table 2 summarizes features of MRI imaging in these lesions.

### Hemangiomas

#### Proliferative hemangiomas

Hemangiomas can be proliferative or non-proliferative. Infantile hemangiomas are characterized by a proliferative phase followed by an involutional phase. 60% of these lesions are superficial, 10% are deep (ie subcutaneous), and 30% have components of both. Most are distributed in a localized manner, but some may be segmented within a single anatomical unit or present with multiple localized lesions. 10% of all children are affected by these benign vascular tumors, majority of which begin to appear in the neonatal period, while others present themselves at birth. This condition is more common in females, with a female-to-male ratio of 3:1, and appears more frequently in the head and neck region. The reason for the gender difference in prevalence remains unknown.

At the onset of infantile hemangiomas, faint erythema, localized telangiectasia, or blanched macules may be observed. When mature, superficial hemangiomas are typically raised, bright red lobulated tumors with clearly defined borders. The lesions may develop small capillaries protruding from the surface. While infantile hemangiomas may occasionally look similar to capillary malformations, infantile hemangiomas follow the natural history that is typical of hemangiomas. Deep hemangiomas can be compressed, but feel firm to the touch. In terms of appearance, these lesions present with nodular swelling that is blue in color, with telangiectatic vessels. Mixed hemangiomas (both superficial and deep) may show characteristic features of both.

Infantile hemangiomas typically undergo rapid proliferation in the first 6 months of appearance, reaching the maximum size between 6 and 8 months for superficial, and 1 and 2 years for deep hemangiomas. On average, these lesions will resolve spontaneously at a rate of 10% per annum. The earlier the resolution phase begins, the more likely the lesion will be healed with good cosmetic results. Lesions situated on the face tend to heal less well and may result with redundant skin, telangiectasia, and skin atrophy after regression.

#### Non-proliferative hemangiomas

NICH and RICH are congenital conditions and are not as common as the infantile hemangiomas. Lesions are usually around the elbows and knees, as well as along the mandibular border. These rare hemangiomas have no obvious sex predilection. NICH and RICH are pink or violet. NICH have circumscribed edges and

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**Table 1. Classification of vascular anomalies.**

<table>
<thead>
<tr>
<th>VASCULAR TUMORS</th>
<th>VASCULAR MALFORMATIONS</th>
<th>LOW FLOW</th>
<th>HIGH FLOW</th>
<th>COMPLEX COMBINED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemangioma (infantile hemangioma, NICH, RICH)</td>
<td>Capillary malformation (PWS)</td>
<td>Arteriovenous malformation</td>
<td>Capillary VM</td>
<td></td>
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<tr>
<td>Kaposiform hemangioendothelioma</td>
<td>VM</td>
<td>Arteriovenous fistula</td>
<td>Capillary lymphatic VM</td>
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<tr>
<td>Tufted angioma</td>
<td>Lymphatic malformation</td>
<td>Arteriovenous fistula</td>
<td>Capillary VM</td>
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<tr>
<td>Pyogenic granuloma</td>
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<td>Capillary arteriovenous malformation</td>
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<tr>
<td>Hemangiopericytoma</td>
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<td>Capillary arteriovenous lymphatic malformation</td>
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<td>Myofibromatosis</td>
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<td>Angiosarcoma</td>
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appear slightly bossed. RICH are firm, raised hemangiomas. NICH do not change after birth, and may be excised if the patient suffers from psychological problems. Conversely, RICH will begin shrinking rapidly after birth and will typically disappear by 6–14 months of age. The obvious differences in behavior served to differentiate RICH, NICH, and common infantile hemangioma. NICH and RICH also have distinctive histopathologic and ultrasonographic features.

Associations and complications of hemangiomas. Hemangiomas can be associated with conditions involving internal organs such as heart or liver failure and spine problems. One group of abnormalities associated with facial lesions is known as the PHACE (posterior fossa malformations, hemangioma, arterial anomalies, cardiovascular defects, eye abnormalities and others such as supraumbilical raphe) syndrome. Hence, it is worthwhile to include imaging in the investigation of hemangiomas, which can be helpful in delineating the extent of the lesion as well as in differentiating the different classes of vascular anomalies. Ultrasound, MRI, and MRA can be used to show which cell types are within the hemangioma (Table 2). If the presence of malignant tissue is suspected, biopsies should be taken.

Many complications may arise with hemangiomas. Ulceration can occur during the proliferative phase and may cause severe pain, bleeding, and wound infection. Subglottic hemangiomas and hemangiomas near the eyes or around the ears can cause obstruction of the airway, amblyopia ex anopsia, or occasionally impaired hearing. Lesions surrounding the eyes may induce pressure on the cornea, causing astigmatism. Large systemic hemangiomas can cause death due to high cardiac output failure. Hepatic hemangiomas can cause heart failure, anemia, and hepatomegaly in only a few months of age. Hemorrhage, functional impairments (eg of the hands), digital gangrene, spinal dysraphism, and permanent scarring or disfigurement are possible, albeit rare complications. The patient may also suffer from psychological problems.

Treatment of hemangiomas. Most hemangiomas do not require any treatment, and only need close observation to ensure that complications do not arise. For small, simple hemangiomas, pressure occlusion, pulsed-dye laser, cryosurgery, and surgical excision may be considered to help reduce the appearance of the lesion.

The medical treatment for higher-risk hemangiomas includes systemic steroids. The use of systemic steroids, however, is only effective during the proliferative stage; hence, the treatment must begin early. The normal starting dose is between 2 and 5 mg/kg/day, depending on whether it is superficial (lower dose) or deep (higher dose). It is recommended to use a single dose in the morning to avoid adrenal suppression. Typically, changes can be seen after 7–10 days. The course of steroids usually lasts 6 weeks, and an additional few weeks to taper off. There are rarely severe long-term complications sustained from systemic steroids, but short-term side effects may occur. Regular echocardiograms should be performed to rule out myocardial hypertrophy as a result of prolonged use of steroids. A second course of steroids may be required if the hemangioma re-proliferates. Lesions on the tip of the nose tend not to respond well to steroid treatment. For at least 3 months after the treatment, live vaccines should be avoided. Different studies show that effectiveness can range from 30 to 90%.

An investigation into the use of β-blockers in the treatment of infantile hemangiomas was carried out using 8–10 mg/kg/day of acebutolol. Acebutolol is a selective β-adrenergic receptor-blocking agent. It most likely reduces the blood flow to the hemangioma by decreasing the heart rate or by stopping the vasodilator response to the β-adrenergic stimulation. Patients who had no response to steroids or had serious side-effects that required a change in the treatment were recruited. Rapid improvement was observed immediately after the introduction of acebutolol. The color intensity and size decreased. Acebutolol was continued until the hemangioma stabilized. Another β-blocker, propranolol, has been observed to cause rapid involution in severe infantile hemangiomas at a dose of 1 mg/kg three times daily. Propranolol is a relatively recent therapy of hemangiomas with fewer side effects, a different mechanism of action, and greater efficacy than the current first-line corticosteroid therapy. In the recent years, propranolol has been proposed as a first-line treatment for all problematic proliferative infantile hemangiomas. Many of these studies do not have the same patient population or duration/ regimen of treatment for hemangiomas; however, based on the available data in the literature, it appears that propranolol could be an emerging and effective treatment for infantile hemangiomas. Further randomized controlled trials are recommended. Propranolol is generally less effective in NICH and RICH.

If propranolol or corticosteroids are not effective, treatment using interferon alpha-2a should be used for life-threatening
Vascular Malformations

Vascular malformations are dysplastic changes that occur during the formation of blood or lymphatic vessel formation, which range from flat lesions to substantial, protruding growths. They are non-proliferative. Symptomatic slow-flow vascular malformations include venous malformations (VMs) and lymphatic malformations, as well as combined anomalies. An accurate diagnosis and multidisciplinary treatment strategy for management of congenital malformations can improve the overall treatment success with a reduced morbidity and recurrence compared to the conventional approaches.

Capillary malformations—port wine stain (PWS).

PWSs are the most common form of vascular malformations. They are usually present at birth and grow proportionately as the child grows. As the child ages, the lesions thicken and darken. They are distinct from hemangiomas in that they are non-proliferative, have ectatic vessels in the dermis, and have normal endothelial cell turnover.

PWSs are treated using pulsed-dye laser. Immediately after the treatment, the area has a characteristic blue-gray color and then purpuric within a few hours. The discoloration takes 1–2 weeks to resolve, after which the area lightens over the following weeks. This treatment produces a better response in younger children with thinner skin and fewer ectatic vessels.

Arteriovenous malformations. Arteriovenous malformations are localized, extensive high-flow malformations. They are high flow congenital vascular malformations that may occur in any part of the body. The clinical presentation depends on the extent and size of the lesion and can range from an asymptomatic birthmark to congestive heart failure. At birth, these lesions appear very similar to hemangiomas and PWSs. Hormonal changes (for example during puberty) cause enlargement and thickening of the lesions. Multiple ulcerations and skin atrophy usually follow as a result of arterial steal. Ultrasound scans may reveal multiple arteriovenous shunts (which are absent in hemangiomas), while MRIs can differentiate arteriovenous from VMs and hemangiomas. These lesions are often painful due to the presence of phleboliths and ulceration. Local bleeding and ischemia are possible complications.

The treatment for arteriovenous malformations is primarily supportive, including analgesics for painful episodes, physiotherapy, and elastic stockings for malformations on the limbs. Surgical resection may be performed to prevent re-expansion. To prevent tissue ischemia and collateral perfusion, ligation or embolization of the feeding arteries must be avoided. Anticoagulants may be required during pregnancy to prevent clotting in the arteriovenous malformation. Superficial malformed vessels can be treated using foam sclerotherapy, whereas ethanol sclerotherapy can improve deep arteriovenous malformations. Detailed investigations including duplex ultrasound, MRI/MRA, and CT/CTA are required to develop an appropriate treatment plan (Table 2). Appropriate management is best achieved via a multi-disciplinary approach, and interventions should be undertaken by appropriately trained physicians.

VMs. VMs are congenital lesions that can cause pain, decreased range of movement, compression on adjacent structures, bleeding, consumptive coagulopathy, and cosmetic deformity. They are slow-flow lesions that are usually present at birth but may occasionally only be visible later in life. They can be localized to skin, subcutaneous tissues, muscle, mucosa, or a combination, on any part of the body. They may appear as discolored, prominent veins or blue colored swelling of the soft tissue. If muscles or joints are involved, bleeding or pain may occur.

Extensive VM of limbs may cause severe functional impairment, with characteristic blue skin. The limb may be shortened, and pathological fractures may occur during
infancy. The involvement of muscles is very common. Localized intravascular coagulation may lead to chronic consumptive coagulopathy with a resultant tendency to bleed.

The use of compressive, elastic garments is the main treatment. Aspirin may be taken to reduce thrombosis. Superficial lesions are often injected with sclerosant, or the veins involved are removed. Deep lesions may require surgical intervention as well, depending on the extent of the VM.

Elastic stockings play an extremely important role in the treatment of extensive VMs, and it is suggested that they be worn from infancy onward. Other treatment options include embolization and sclerotherapy, excision of VM and surrounding skin and muscle, and synovectomy (if the knee joint is involved). Treatment of congenital VMs poses a major clinical challenge. Ethanol sclerotherapy alone or combined with surgical excision is the accepted treatment in symptomatic malformations after failed treatment attempts with the tailored compression garments. Endovascular therapy, mainly consisting of intralesional sclerosant injection, is now accepted as the primary treatment for most of these lesions. Magnetic resonance imaging and ultrasonography supplement physical examination for diagnosis and assessment of the extent of malformation. Although most vascular malformations are not cured, the majority of patients benefit from endovascular treatment. Endovascular treatment is usually carried out under general anesthesia. Sclerosants for VMs include ethanol, 3% sodium tetradecyl sulfate, and bleomycin. Complications of sclerotherapy include tissue necrosis, peripheral nerve injury, hemoglobinuria, deep vein thrombosis, and pulmonary embolism. Successes have been achieved with ethanol sclerotherapy in most lesions; however, severe complications are more likely to occur when more ethanol is used. Percutaneous sclerotherapy of VMs using absolute ethanol and bleomycin A5 is safe and effective, which may be the technique and the choice for treatment of VMs.

A simple and descriptive classification system for VMs may serve as a basis for interventional therapy. Puig and colleagues developed a classification system as follows: type I, isolated malformation without peripheral drainage; type II, malformation that drains into normal veins; type III, malformation that drains into dilated veins; and type IV, malformation that represents dysplastic venous ectasia. They tested the hypothesis if the type of VM would determine whether low-risk sclerotherapy was indicated, and concluded that sclerotherapeutic intervention in patients with type-III and type-IV VMs must be carefully considered, whereas it can be safely performed in low-risk patients with type-I and type-II lesions.

Absolute ethanol sclerotherapy alone can deliver excellent results in complex forms of VMs with considerable but acceptable morbidity and may be able to reduce the morbidity involved with the conventional surgical therapy alone on complex forms of VM. No recurrence or deterioration in the therapy results was observed during the follow-up period (average, 10.2 months) after the completion of multi-staged therapy.

Lymphatic malformation. Lymphatic malformations usually affect the axilla or neck regions and are present at birth or very soon after. They can be divided into macrocystic and microcystic types; the former is more responsive to injectable sclerosants. Imaging studies are mostly useful for confirming the clinical diagnosis, estimating the extent of the lesion, and determining the feasibility of surgical resection. These lesions can be treated by sclerotherapy using doxycycline, bleomycin, OK-432, or other sclerosants; CO₂ laser ablation; or surgical excision.

Major Vascular Malformation Syndromes

Sturge–Weber syndrome (encephalotrigeminal angiomatosis). Vascular malformations on three of the anatomical sites of neuroectodermal origin (cutaneous PWS on trigeminal nerve dermatome, vascular malformation on the ipsilateral pia mater, and ipsilateral ocular vascular anomalies) are collectively known as Sturge–Weber syndrome. The associations include leptomeningeal malformations, causing ischemia and possible mental retardation, epilepsy, and glaucoma. MRI scans and single photon emission computed tomography (SPECT) may allow earlier diagnosis and show the extent of the malformation.

A multidisciplinary approach involving neurologists, dermatologists, and ophthalmologists is required in the management of patients with this condition. Pulsed-dye laser may be used for cosmetic treatment.

Klippel–Trénaunay syndrome (KTS). Klippel–Trénaunay syndrome is a complex congenital anomaly, characterized by VMs of the limbs, port-wine stains, and hypertrophy of the soft tissue and bone. Venous drainage is often abnormal because of embryonic veins, agenesis, hypoplasia, valvular incompetence, or aneurysms of deep veins. This rare syndrome appears mostly in the lower limbs. KTS commonly presents itself as capillary malformation on the limbs in the neonatal period, followed by other features that develop when the child becomes ambulatory. For most patients, a nonoperative treatment approach is sufficient. Pulsed-dye laser can be used for the capillary malformations, elastic stockings for VMs, prophylactic antibiotics for recurrent cellulitis, anticoagulants for deep-vein thrombosis and intermittent pneumatic compression, and aspirin or ibuprofen for recurrent thrombophlebitis. Camouflage and psychological support may be considered. Surgical procedures may be necessary for severe cases, for example, epiphysiodesis for limb length discrepancies, vein stripping, or sclerotherapy. Although removal is often incomplete, and vascular malformations recur in 50% of patients, the patients note an overall improvement after avulsion or excision of varicosities and vascular malformations. The management of patients with KTS is primarily nonoperative. These patients with patent deep veins can be considered for excision of symptomatic varicose veins and VMs. Although the recurrence rate is high, clinical improvement is significant, and reoperations can be performed if needed. Occasionally, deep vein reconstruction, excision of persistent sciatic veins,
or subfascial endoscopic perforator surgery is indicated. The patients should receive multidisciplinary care in qualified vascular centers experienced in managing these rare lesions.  

Angiokeratomas (hyperkeratonic capillary malformations). Angiokeratomas are benign, mixed anomalies of the blood vessels and the epidermis. They appear as asymptomatic dark red to black nodules with verrucous surfaces. Angiokeratomas may be misdiagnosed due to their rarity. A biopsy of the lesion can produce a more accurate diagnosis. Surgical excision or laser is required to remove the lesions.  

Other Vascular Anomalies

Spider nevus (nevus araneus). Spider nevus is a common childhood angioma that occurs in 15% of children. It is characterized by a central vascular punctum with fine vessels that radiate outwards. It can be treated by electrodesiccation, cryotherapy, or pulsed-dye laser.  

Clinical efficacy and safety of potassium titanyl phosphate (KTP) laser treatment and electrocoagulation (EC) for the treatment of spider nevi is comparable. KTP laser treatment is less painful and more favored.  

Pyogenic granuloma. Pyogenic granuloma is a common vascular tumor that appears either spontaneously or after trauma. It is usually found on exposed skin, but may also be found on PWSs or arteriovenous malformations. These lesions are red, pedunculated nodules that frequently bleed spontaneously. Curettage, cautery, or cryotherapy are treatment options. Recurrent pyogenic granuloma in a patient treated with diode laser without the use of anesthesia, sutures, anti-inflammatory drugs, or analgesics has been reported.  

Glomus tumor. An uncommon hamartoma of the glomus body, glomus tumors are painful, tender, and blue- or pink-colored nodules that occur mostly on the limbs, face, and genitalia. They are usually excised.  

Angioma serpiginosum. Angioma serpiginosum is a rare disorder of superficial blood vessels that is more common in females. They are minute pink or purple angiomatous puncta that are grouped together. They may be present with a livedoid pattern, and do not completely blanch. Laser treatment may be slightly helpful in reducing the appearance.  

Kasabach–Meritt syndrome. Kasabach–Meritt syndrome, which is quite rare, is composed of thrombocytopenia, microangiopathic hemolytic anemia, and localized consumption coagulopathy. There is no sex predilection. Lesions are often rapidly proliferating firm purpuric masses with irregular borders. The proliferation phase often lasts for 2–5 years. This syndrome carries a 20–30% mortality.  

The treatment for this syndrome may involve platelet transfusion when bleeding occurs, radiation therapy, chemotherapy, embolization, and surgical excision. Prednisolone may be helpful in suppressing coagulopathy and inducing regression of the tumor when given in 2–4 mg/kg/day doses. For life-threatening Kasabach–Meritt syndrome, interferon 2a may be used (3 mU/m²/day). This gives a variable response, which has mostly been successful. Complications such as fever, neutropenia, spastic diplegia, and deranged liver function are possible when using interferon 2a.  

Osler–Weber–Rendu (hereditary hemorrhagic telangiectasia). This is a rare, genetic, progressive cutaneous and mucosal telangiectasia of nostrils, digestive tract, and oral mucosa. It is transmitted in an autosomal dominant fashion, and occurs 1 in 5,000 people. Iron replacement, laser, electrodesiccation, antibiotic prophylaxis, transcatheter embolization, and surgical excision are the available treatment options for patients with this condition.  

Conclusions

Many medical and surgical modalities of treatment are available for various types of vascular anomalies. Accurate and timely diagnosis is important for optimal therapeutic efficacy. Therapeutic indications range from cosmetic and patient preference to life-saving interventions. Infantile hemangioma can be treated by beta-blockers, systemic corticosteroids, laser, and surgical excision. Vascular malformations are often mislabeled as hemangiomas, which do not usually respond to medical therapy. Physicians caring for children must understand the principles underlying the treatment for these anomalies.  

Author Contributions

Conceived and designed the experiments: KLH. Analyzed the data: KLH, PCS, JJL. Wrote the first draft of the manuscript: KLH. Agree with manuscript results and conclusions: KLH, PCS, JJL, CMC, DCL. Jointly developed the structure and arguments for the paper: KLH, PCS, JJL, CMC, DCL. Made critical revisions and approved final version: KLH. All authors reviewed and approved of the final manuscript.  

DISCLOSURES AND ETHICS

As a requirement of publication the authors have provided signed confirmation of their compliance with ethical and legal obligations including but not limited to compliance with ICMJE authorship and competing interests guidelines, that the article is neither under consideration for publication nor published elsewhere, of their compliance with legal and ethical guidelines concerning human and animal research participants (if applicable), and that permission has been obtained for reproduction of any copyrighted material. This article was subject to blind, independent, expert peer review. The reviewers reported no competing interests. Provenance: the authors were invited to submit this paper.  

REFERENCES

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