
Vascular anomalies are common problems in infancy and childhood. GPs need to have a good understanding about these conditions in order to be able to decide whether urgent referral for investigation or treatment is needed, and to consider possible associated problems. Most are uncomplicated and require no active management. In recent years these conditions have been re-classified and new standardised terminology introduced. There have been considerable advances in the identification of underlying genetic causes and changes in approach to treatment. This two part article will discuss the most common or important vascular anomalies GPs may encounter in children. Part one will discuss vascular malformations, and part two will deal with vascular tumours. Discussion about primary lymphedema or malignant vascular tumours is beyond the scope of this article.

Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>CM</td>
<td>Capillary malformation</td>
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<tr>
<td>VM</td>
<td>Venous malformation</td>
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<tr>
<td>LM</td>
<td>Lymphatic malformation</td>
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<tr>
<td>AVM</td>
<td>Arteriovenous malformation</td>
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<tr>
<td>CVM, CLM, VLM, CVLM</td>
<td>Combinations of capillary + venous + lymphatic malformation</td>
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<td>GVM</td>
<td>Glomuvenous malformation</td>
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<td>CMTC</td>
<td>Cutis marmorata telangiectatica congenita</td>
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<td>IH</td>
<td>Infantile haemangioma</td>
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<tr>
<td>RICH</td>
<td>Rapidly involuting congenital haemangioma</td>
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<tr>
<td>NICH</td>
<td>Non involuting congenital haemangioma</td>
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<td>KHE</td>
<td>Kaposiform haemangioendothelioma</td>
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<td>LIC</td>
<td>Localized intravascular coagulopathy</td>
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<td>KMP</td>
<td>Kasabach Merritt phenomenon</td>
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<td>SWS</td>
<td>Sturge-Weber syndrome</td>
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<td>KTS</td>
<td>Klippel- Trenauney syndrome</td>
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<td>HHT</td>
<td>Hereditary haemorrhagic telangiectasia</td>
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<td>PWS</td>
<td>Parkes- Weber syndrome</td>
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<tr>
<td>PDL</td>
<td>Pulsed dye laser</td>
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<tr>
<td>ISSVA</td>
<td>International Society for the Study of Vascular Anomalies</td>
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Vascular anomalies were broadly classified into tumours and malformations by Mullikan and Glowacki in 1982. This was updated by a consensus meeting of the International Society for the Study of Vascular Anomalies (ISSVA) in 2014 (Table 1), standardising terminology. Older terms are provided for reference but it is encouraged that the new terminology be used now to aid understanding, communication and research about these disorders.

Table 1 Classification of vascular anomalies
issva.org/classification
(conditions discussed in the body of the text in bold type)
VASCULAR TUMOURS

BENIGN
Infantile haemangioma
(outdated term: strawberry naevus)
Congenital haemangioma
Rapidly involuting
Non involuting
Partially involuting

Pyogenic granuloma
Spindle cell haemangioma
Epithelioid haemangioma

VASCULAR MALFORMATIONS

SLOW FLOW
Capillary malformation
(outdated term: port wine stain)
Lympatic malformation
(outdated term: cystic hygroma)
Venous malformation
(outdated term: cavernous haemangioma)

FAST FLOW
Arteriovenous malformations/
Arteriovenous fistulae

LOCALLY AGGRESSIVE/BORDERLINE
Tufted angioma
Kaposiform haemangioendothelioma
Kaposi’s sarcoma
Retiform haemangioendothelioma
Papillary intralymphatic angioendothelioma (Dabska tumour)

Combinations
CM/LM/VM/AVM

Malformations may include any combination of vessels.

Malignant
Angiosarcoma
Epitheloid haemangioendothelioma

Anomalies of major named vessels
Lymphatics, veins, arteries

Isolated malformations
Syndromic malformations: associated with other anomalies

VASCULAR TUMOURS

VASCULAR MALFORMATIONS

Key points
• Vascular malformations are structural anomalies of blood vessels.
• They are broadly classified into slow flow and fast flow anomalies.
• Slow flow malformations involve capillaries, lymphatics and veins.
• Fast flow malformations are arteriovenous malformations and fistulae.
• Malformations may include any combination of vessels.
• They are always congenital but may not be apparent at birth.
• They may be isolated anomalies or part of a syndrome.
• Syndromal malformations may be associated with visceral involvement, neurological and ocular abnormalities or soft tissue overgrowth.

Vascular malformations are structural anomalies of blood vessels, caused by development errors occurring early in intrauterine life. They are always congenital but may not be present until the child is older. They grow in proportion with the patient and do not regress, often thickening with time.

Vascular malformations are classified according to type of blood vessel involved and broadly divided into slow flow and fast flow types. They may involve only one single vessel type or a combination of any and multiple vessel types (Table 2).

Vascular malformations may be sporadic or inherited. They may be isolated abnormalities or one part of a syndrome, and associated with defects in other systems.

Some vascular malformations (venous and lymphatic) may be associated with a coagulopathy.
TABLE 2: Vascular malformations
Simplified (see issva.org/classification)
Combinations of each and all of malformations listed below can occur – two or more vascular malformations can be found in one lesion

<table>
<thead>
<tr>
<th>Capillary (CM)</th>
<th>Lymphatic (LM)</th>
<th>Venous (VM)</th>
<th>Arteriovenous malformation or fistula (AVM/AVF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naevus simplexTelangiectasia (benign, essential) Hereditary haemorrhagic telangiectasia Cutis marmorata telangiectatica congenita</td>
<td>Common LM Macrocystic Microcystic Mixed</td>
<td>Common VM</td>
<td>Sporadic</td>
</tr>
<tr>
<td>Cutaneous or mucosal CM</td>
<td>Generalized lymphatic anomaly</td>
<td>Familial VM cutaneo-mucosal (VMCM)</td>
<td>In HHT</td>
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<tr>
<td>Sturge-Weber syndrome: facial CM, leptomeningeal and ocular involvement</td>
<td>Primary lymphedemas</td>
<td>Blue rubber bleb naevus (Bean) syndrome</td>
<td>In CM-AVM</td>
</tr>
<tr>
<td>CM –AVM syndrome</td>
<td>Others: LM in Gorham Stout syndrome</td>
<td>Glomuvenous malformation</td>
<td>Others</td>
</tr>
<tr>
<td>CM + bone /soft tissue overgrowth</td>
<td></td>
<td>Maffucci syndrome</td>
<td></td>
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<tr>
<td>CM + micro or macrocephaly</td>
<td></td>
<td>Klippel-Trenauney syndrome : CLVM +limb overgrowth</td>
<td>Parkes -Weber syndrome: CM+AVM+ limb overgrowth</td>
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</tbody>
</table>

Naevus Simplex
This is also known as macular stain, ‘salmon patch’, ‘angel kiss’, ‘stork bite’. This is the most common vascular anomaly, found in 40-60% newborns. It is usually located on the face especially glabella, eyelids, nasolabial folds and philtrum but also on midline nuchal skin. It is less common on the scalp, nose, lip and back. There may be multiple lesions. Facial lesions tend to fade with time but nuchal stains persist into adult life. Naevus simplex is harmless and of no medical consequence, except in very rare case where a large complex lesion is located over the spine. Investigation is only warranted if the vascular stain is associated with another anomaly located over the spine such as a dermal sinus or pit, lipoma or hypertrichosis, or deviated gluteal cleft ( if the lesion is located over the lumbosacral spine). In these cases imaging is indicated to exclude spinal dysraphism.
Capillary malformations

Capillary malformations (CMs) are common lesions found in less than 0.3% of newborns. Equal numbers of males and females are affected. It has been recently discovered that some CMs are due to a somatic mosaic activating mutation in the GNAQ gene in vascular endothelial cells. In isolated CMs this mutation occurs later in intrauterine life than in the syndromal variety.

CMs are usually sporadic but are occasionally inherited in an autosomal dominant pattern. They are present at birth, grow in proportion to body growth and do not regress. CMs are flat pink or red macules of various sizes with a geographic contour. They sometimes thicken and darken with age, developing papules or nodules as adults. They can involve any part of the skin but are about half of CMs are on the face. CMs can also occur on mucosal surfaces. CMs do not bleed spontaneously. They may be complicated by the development of pyogenic granulomas within the lesion, and by soft tissue hypertrophy particularly with mucosal lesions. This may lead to gingival thickening and dental anomalies with facial lesions.

CMs are mostly a cosmetic issue. However as the face is the most commonly involved site this may lead to significant disfigurement and psychological distress. The aim of active treatment is to reduce erythema. There is no good evidence that treatment reduces thickening of the lesion. No active management maybe indicated, or requested by the parents. If treatment is considered the most effective modality is vascular laser. The gold standard is the pulsed dye laser (585nm or 595nm). The mode of action is by selective photothermolysis, with haemoglobin as the target chromophore. Multiple treatment sessions are needed for lightening of the lesion and recurrence is common. Treatment is more effective for lesions on the lateral face and neck than mid face, trunk and limbs. Infants usually require a general anaesthetic, which means delaying commencement of treatment for the first 2-3 years to avoid any effect on brain development. Some centres are now treating very young infants early without general anaesthetic as it is known that multiple episodes of general anaesthetic for very young children are risky. It has been considered that earlier treatment for CMs might result in better response but to date the evidence supporting this is contentious.

However early referral of an infant with a facial CM is suggested to allow for discussion of these issues with the parents. Although not usually requested for children, cosmetic camouflage can be effective and helpful. There is early evidence that topical rapamycin ointment might be effective alone for small lesions, or in combination with vascular laser for larger or more significant lesions.

Most capillary malformations are isolated anomalies, but they may be associated with other developmental defects.

Syndromal capillary malformations

Sturge-Weber syndrome

This is a neurocutaneous disorder where a CM involving the forehead and eyelids is associated with central nervous system and ocular anomalies. These include leptomeningeal homolateral CVM which may cause epilepsy, hemiparesis and intellectual disability; and choroidal CVM with resulting bullphthalmos, glaucoma, retinal detachment and visual field defects. There may be heterochromia of iris, with the more deeply pigmented iris ipsilateral to the CM. Growth hormone deficiency (without pituitary or hypothalamic abnormality detected on imaging) may also be associated with this syndrome.
CMs suspicious for associated CNS and ocular anomalies include any lesions involving the forehead segment (a line from lateral canthus of the eye to the auricle, and extending to the midline). A CM is especially suspicious if it involves more than one facial segment, involves both forehead and eyelids, is bilateral, or involves the midline segment. Please note that the distribution is now NOT considered to be dermatomal with respect to the branches of the trigeminal nerve.

Sturge-Weber syndrome occurs in approximately 10% of patients with facial CMs. It has now been shown that SWS is due to a GNAQ mutation occurring earlier in embryogenesis than the mutation causing isolated CMs.

If SWS is suspected referral to a paediatric dermatologist or paediatrician is advised, especially if the CM is bilateral, involves the central forehead or more than one segment. Eye assessment should be arranged expeditiously. It is important that even if this is normal, review should continue on a regular basis to monitor for development of vision threatening glaucoma.

MRI should be arranged if a facial CM suspicious of SWS is present or a neurological abnormality is detected. It should be noted that there may be false negative MRIs in infants under 9-12 months, so this may need to be repeated if imaging is negative but neurological abnormalities are subsequently detected. There is evidence that early treatment with low dose aspirin may prevent CNS sequelae. The rationale for this approach is that thrombosis may occur within leptomeningeal CVMs. It is also apparent that they are not static and neurological features may be progressive. Antithrombotic therapy may prevent the progression of impaired cerebral blood flow and hypoxic-ischaemic neuronal injury. However consideration needs to be balanced against the increased risk of intracranial haemorrhage in patients with SWS.

Capillary malformation-arteriovenous malformation syndrome (CM-AVM syndrome)

In this disorder cutaneous CMs may be a marker for AVMs involving internal organs, particularly the brain and spinal cord. It is due to an inactivating mutation in the RASA-1 gene, and inherited in an autosomal dominant manner.

CMs are multiple and atypical. They are characterised by their small size and geometrical shape, usually surrounded by a halo of pallor. They can be located on the trunk, face or limbs. They develop in the first few years of life, and new lesions continue to appear throughout childhood. The vascular lesions may actually be or overlie AVMs. Large AVMs are usually present at birth.

If suspected, referral is required for assessment and consideration of imaging to look for brain and spinal AVMs. Referral to a genetics unit should also be arranged for mutation testing and assessment of other family members.

CM- macrocephaly syndrome

This is a sporadic disorder due to a mutation in the PI3KCA gene and presents with a patchy reticular CM associated with macrocephaly due to megalencephaly and hydrocephalus. Other features include asymmetry or overgrowth of limbs, developmental delay, hypotonia, syndactyly or polydactyly and connective tissue abnormalities.

CM- microcephaly syndrome

This is due to a mutation in the STAMBBP gene. Clinical features include diffuse, small CM and progressive microcephaly, global developmental delay, epilepsy and spastic quadripareisis.

Phakomatosis pigmentovascularis

This is a rare disorder where vascular malformations, usually a facial CM, are associated with melanocytic naevi or dermal melanocytosis. It is thought to be due to an anomaly of
vasomotor nerves and melanocytes, which are both derived from the neural crest. There may be systemic involvement with neurological, ocular or skeletal abnormalities.

Hereditary haemorrhagic telangiectasia (Osler-Weber-Rendu disease)
This disorder is characterised by multiple cutaneous, mucosal and visceral AVMs. It is inherited in an autosomal dominant manner. Mutations identified are in the endoglin gene (HHT1) and activin receptor like kinase type 1 /ALK-1 gene (HHT2) which cause defects in the development of blood vessels resulting in vessel wall weakness. Further mutations have been identified recently. Presentation is in later childhood, but may be even later in life. Clinical features are variable even within families. Patients develop multiple telangiectases on skin of fingers, hands, forearms, face and on the mucosa of the conjunctiva, nasopharynx and gastrointestinal tract. In about 30% of cases visceral AVMs may be present in the brain, lung, liver, retina and other organs. Epistaxis, frequent and especially nocturnal, is a common symptom. Complications include anaemia, life-threatening bleeding from GIT and lungs, cerebrovascular stroke and brain abscess, portal hypertension and oesophageal varices, and high output cardiac failure. Pregnancy can be complicated by pulmonary haemorrhage. Prognosis depends on severity and degree of systemic involvement. If the diagnosis is suspected referral should be made for assessment and genetic testing. Initial investigations should include FBC, urinalysis for haematuria and stool assessment for occult blood. Consideration should be given to organising MRI of the brain, chest X-ray and pulse oximetry, and liver ultrasound. Family members should be examined for cutaneous telangiectases, and chest X-ray and pulse oximetry arranged if the diagnosis is suspected. Management is directed towards prevention and management of bleeding and complications. Active management of AVMs can be undertaken with embolisation and surgery. Antibiotic prophylaxis prior to surgical or dental procedures may be required especially in presence of pulmonary AVMs.

Cutis marmorata telangiectatica congenita
This is a rare, sporadic, mosaic condition which presents at birth or in the first few months of life with a reticulated CM usually involving one limb (usually lower limb) and an adjacent segment of the trunk. There may be atrophy and ulceration of the skin and soft tissue, with asymmetry of the affected limb (either hypertrophy or atrophy). It may be associated with glaucoma, and occasionally other congenital malformations. Diagnosis is clinical. Physiological mottling (cutis marmorata) of the skin is common in neonates but disappears on warming. In CMTC the cutaneous abnormalities do not resolve with warming. They usually fade or resolve spontaneously with in the first few years of life.

Venous malformations
Venous malformations consist of ectatic venous channels which may involve any site or structure (skin, mucosa, muscle, bones, nerves or viscera). These are always present at birth but may not become present until puberty or later in life due to progressive dilatation of the vessels. They are skin coloured or bluish, and compressible. Skin temperature overlying the lesion is normal and there is no thrill or bruit. VMs are often associated with soft tissue hypertrophy. They can be complicated by pain due to the development of phleboliths. They may be more extensive than clinically apparent. VMs may be associated with coagulopathy. Most venous malformations are sporadic but some are inherited. Recently mutations in TIE2 gene have been identified as the cause of inherited VMs.
Glomulovenous malformations (GVM) are a variant of VM. These are inherited in an autosomal dominant fashion and are due to mutations in the *glomerulin* gene. GVMs usually present as multiple, painful, non-compressible lesions on the limbs. They can be distinguished from standard VMs histopathologically by the presence of aberrant smooth muscle cells (glomus cells) around the ectatic venous channels. They are not associated with coagulopathy.

VMs can be isolated or associated with other anomalies.

**Syndromal VMs**

**Klippel-Trenauney syndrome (KTS)**
This is an uncommon disorder, usually sporadic with extensive capillary, venous and lymphatic malformation of a limb associated with soft tissue and bony hypertrophy. Lower limbs are affected in 95% of cases, upper limbs in 5%, and both in 15%. It is usually unilateral.

Atypical persistent embryological veins (lateral vein and persistent sciatic veins) are present in most cases.

KTS presents at birth with an extensive vascular malformation. With time, there is development of varicose veins and lymphedema, and enlargement of the affected limb. It can be complicated by pain, ulceration, infection, localised intravascular coagulopathy, thrombosis (superficial and deep) and pulmonary embolus. Discrepancies in leg length can be noted. Leg lengths needs to be monitored clinically and radiologically. Orthopaedic review is recommended.

If a child presents with an extensive vascular malformation of a limb, referral is indicated for assessment, and imaging (Doppler ultrasound and MRI) to evaluate the extent of the malformation and any associated soft tissue or bony hypertrophy.

**Blue rubber bleb naevus syndrome (Bean syndrome)**
This is characterised by multiple small rubbery VMs, which are commonly located on palms and soles. There may be associated visceral VMs, most commonly involving the gastrointestinal tract.

**Mafucci syndrome**
This condition is characterized by enchondromas and vascular malformations, usually venous (sometimes lymphatic or arteriovenous).

It is sporadic. Males and females are affected equally. VMs can involve the skin and viscera. The enchondromas may be solitary or multiple, and are most commonly located on the hands and feet, resulting in deformity. There is a significant risk of malignant transformation to chondrosarcoma.

**Investigation of VMs**

**Coagulopathy**
VMs, especially if large or multiple, may be associated with localised intravascular coagulopathy in up to 40% of cases. This can evolve to become generalized (disseminated intravascular coagulation). This may be triggered by surgery, sclerotherapy, pregnancy or puberty.

LIC is due to bleeding from consumption of clotting factors triggered by abnormal flow characteristics of blood within the ectatic vessels.

D-Dimer and fibrin degradation products are both increased, and fibrinogen reduced. These should be measured in patients with VMs. Platelet count and function are normal.
**Imaging**
Doppler ultrasound is useful as initial investigation. This shows a slow flow compressible vascular malformation which may contain phleboliths. MRI more precisely identifies the exact location and extension of the lesion. It is needed prior to active treatment.

**Management of VMs**
Compression garments should be worn if the VM involves a limb. Appropriate footwear might be needed if the VM involves the lower limb. Sclerotherapy is often considered for active treatment. Various sclerosants may be used (such as 1% sodium tetradecyl sulphate). Several treatment sessions are usually required. If localised intravascular is present low molecular weight heparin is given around the time of surgery or sclerotherapy. Excision may be a reasonable treatment option if the lesion is confirmed by imaging to be small but recurrence is not uncommon.

**Lymphatic malformations**
Lymphatic malformations are congenital but may present later in life. They are usually sporadic. They can be broadly divided into macrocystic and microcystic lesions. They can occur in any tissue and in any location (cutaneous, mucosal or visceral). They usually present as a soft tissue mass, with overlying skin of normal colour. Bruising around the lump may occur. The superficial component, if present, may appear as confluent grouped vesicles likened to ‘frog spawn’. The vesicles are either clear or red if bleeding has occurred. LMs can enlarge with intercurrent fever and viral infection, which results in pain. The malformation itself can become infected manifesting as cellulitis. Compression of adjacent structures can occur with larger lesions. LMs undergo gradual dilatation and can be associated with bony overgrowth. If extensive and depending on location they can be complicated by chylothorax, chylous ascites, or elephantiasis of a limb. Biopsy of a lesion suspected to be a lymphatic malformation should be avoided as this can be complicated by infection and leakage. Appropriate referral should be made if a LM is suspected. Extensive lesions are best managed in a multidisciplinary clinic. Appropriate investigations include ultrasound to assess flow characteristics, and MRI to identify precise location and extent of the lesion. Antibiotics are indicated for treatment of infection. Compression garments are an important part of management of LM on a limb. Active management options include sclerotherapy with an ‘irritant’ sclerosant such as doxycycline. Excision can be undertaken for small lesions but recurrences are frequent.

**Arteriovenous malformations**
These are fast flow lesions that are congenital but may not manifest until later in life (at puberty or with trauma). They are usually sporadic but some forms are inherited, such as Capillary malformation-arteriovenous malformation (CM-AVM) syndrome or hereditary haemorrhagic telangiectasia. They are usually isolated anomalies but may be a feature of a syndrome. The AVM consists of a central nidus where there is direct communication between arteries and veins without normal intervening capillary bed. Surrounding veins have distorted muscular walls.
Any tissue (including muscle, bone or organ) or site may be involved, although 70% of AVMs involve the head and neck. Size varies considerably. At birth they usually present as a faint ill-defined lesion, which is red, and warm to palpation. The lesion becomes pulsatile, with a thrill and audible bruit towards the end of the first decade. The appearance of AVMs usually worsens with time, with hypertrophy of tissues and sometimes peripheral ischaemia.

AVMS are usually isolated but may be associated with other anomalies.

**Syndromal AVMs**

**Parkes-Weber syndrome**
This is characterized by a large cutaneous vascular malformation due to underlying arteriovenous anastomoses on limbs, associated with soft tissue and skeletal hypertrophy. It may be confused clinically with Klippel-Trenauney syndrome in young children, but the vascular lesions in each condition are distinctive.

**Cobb syndrome**
Cutaneous AVM (or AVM/VM) may be associated with spinal AVM resulting in neurological complications. This should be suspected if a large vascular malformation is located over the spine.

**Management of AVMs**
Complex AVMs are best managed by a multidisciplinary team in specialised clinics. They are often more extensive than clinically apparent. Investigations include ultrasound to identify the type of lesion and MRI/MRA to delineate the extent and exact location particularly before definitive therapy. Incomplete treatment can result in more pain and ulceration. Active management options include surgical excision and embolization.

**Combination lesions**
Vascular anomalies may comprise any combination of slow flow and fast flow vessels, including capillary, venous, lymphatic and arteriovenous malformations.

**Overgrowth syndromes**
Vascular malformations may be part of syndromes characterized by overgrowth of soft tissues. These are rare.

**CLOVE syndrome**
This eponymously named syndrome is caused by a somatic activating mutation in the PI3KCA gene. It is characterised by a fatty truncal (back or abdominal) mass of variable size which is noted at birth. This may extend into the chest, abdomen or into the spinal canal. There is a vascular malformation of the overlying skin (capillary, venous or lymphatic). In some patients an arteriovenous malformation can extend into the spinal cord. Other cutaneous features may include epidermal and melanocytic naevi. There may be associated skeletal, spinal and renal anomalies.

**Proteus syndrome**
In this disorder there is asymmetric, disproportionate and progressive overgrowth of body parts including bone, cartilage, muscle and connective tissue. It is due to mosaicism for a somatic activating mutation in the AKT-1 gene. It is associated with vascular malformations (CVLMs), epidermal naevi, connective tissue naevi, lipomas and café au lait macules.
PTEN Hamartoma syndrome (Bannayan-Riley-Ruvalcaba syndrome, Cowden syndrome)
This is a clinically heterogeneous syndrome due to a mutation in a tumour suppressor gene, and inherited in an autosomal dominant manner. Vascular malformations (AVM or CVLM) are associated with macrocephaly and lipomatous overgrowth. Patients develop multiple hamartomas of skin, oral mucosa and gastrointestinal tract, and are at risk for visceral malignancy.

Beckwith-Weidemann syndrome.
This is a congenital overgrowth syndrome where a centrofacial naevus simplex (involving upper eyelid, upper lip, nose) is associated with macroGLOSSIA, anterior abdominal wall defects and gigantism. There is a risk for development of certain tumours such as hepatoblastoma, Wilms tumour, neuroblastoma and rhabdomyosarcoma.

Tips for GPs
• Suspect Sturge Weber syndrome if a capillary malformation is located on the forehead, especially if it involves both forehead and eyelid, involves more than one segment, or is bilateral. In this case early referral is indicated to establish the diagnosis and to arrange an eye check and appropriate imaging.
• If a CM located over the spine is associated with another cutaneous anomaly suspect spinal dysraphism.
• Suspect hereditary haemorrhagic telangiectasia if multiple telangiectasia are noted on the fingers and oral mucosa, especially associated with epistaxis. Referral should be organised, and genetic testing and appropriate imaging considered.
• If atypical and multiple CMs are noted consider the possibility of CM-AVM syndrome due to RASA-1 mutation, and arrange appropriate referral.
• Venous malformations may be complicated by localised intravascular coagulopathy. Investigate with D-dimer, fibrin degradation products and fibrinogen especially before surgery as this may become disseminated.
• Lymphatic malformations may be more extensive than clinically apparent. They should be suspect if vesicles (sometimes haemorrhagic) are noted on the skin. Biopsy should be avoided.

Future directions
• Identification of genetic mutations and further understanding of the pathogenesis of vascular malformations.
• Clarification whether early intervention with aspirin alters neurological progression in Sturge-Weber syndrome.
• Further studies about effectiveness of topical rapamycin for CM and LM.
• Efficacy of oral sirolimus for extensive lymphatic malformations.

Further reading
1. ISSVA Classification of Vascular Anomalies ©2014 International Society for the Study of Vascular Anomalies
4. Classification of Vascular Anomalies and the Comprehensive Treatment of Hemangiomas
Burns, A Jay M.D.; Navarro, J Alberto M.D.; Cooner, Rebecca D. R.N., M.S., C.P.N.P
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5. Infantile hemangiomas: An update on pathogenesis and therapy Chen T et al


11. Genetics of hemangiomas, vascular malformations, and primary lymphedema Blatt J et al
J Pediatr Hematol Oncol 2014 36; 8: 587-593