* Results from abnormal cellular proliferation or architectures (malformations affecting the vascular endothelium)
* May affect any organ and they may traverse any tissue plane.
* The assessment is based on the clinical features and special investigations such as doppler US, histology and gadolinium enhanced MRI.
  + angiography may be needed mainly for embolization rather than diagnosis
* Complex lesions should by managed by:
  - Surgeons - dermatologist - radiologist
  - pedetrician - histopathologists
  - specialist nurses
  - groups that provide vital reassurance.
* Lesions vary in size from small to complex with secondary effect that may cause significant morbidities and mortalities.
* Difficulties in the tx means that much management are supportive with the emphysis of the disease controlled rather than cured.

Edited by:
Dana Almanzalji ~

اذكرونا بدعوة طيبة ... ☺
وإذا في أي خطأ خبروني حتى أحذه.

INTRODUCTION

- Vascular lesions, including vascular neoplasms and vascular malformations, are common in newborns .
- Although the majority of these lesions are benign and self-limited conditions, some may be part of complex syndromes or systemic disorders or may be associated with complications.

CLASSIFICATION OF VASCULAR ANOMALIES

- Vascular anomalies were classified by Mulliken and Glowacki in 1982 into infantile haemangiomas and vascular malformations, based on clinical and histological characteristics.

- The International Society for the Study of Vascular Anomalies (ISSVA) modified the terms to tumours and malformations in 1996, and this simple structure is applicable to in excess of 90% of lesions

ISSVA 2014

The 2014 ISSVA classification for vascular anomalies

Vascular anomalies

Vascular tumours

Benign
Infantile haemangioma
Congenital haemangioma
- Rapidly involuting (RICH)
- Non-involuting (NICH)
- Partially involuting (PICH)

Tufted angioma
Others
Locally aggressive or borderline
Kaposiform haemangioendothelioma
Kaposi sarcoma
Others
Malignant
Angiosarcoma
Others
Associated with other lesions
PHACES syndrome[a]

Vascular malformations

Simple
Slow Flow
Capillary malformations (CM)
Venous malformations (VM)
Lymphatic malformations (LM)
High Flow
Arteriovenous malformations (AVM)
Arteriovenous fistula (AVF)

Combined
Combined channel malformations e.g. CVM, CLM, LVM, CAVM
Others

Associated with other anomalies (<5% of cases)

Klippel-Trenaunay syndrome: CM + VM +/- LM + limb overgrowth
Parkes Weber syndrome: CM + AVF + limb overgrowth G
Servelle-Martorell syndrome: limb VM + bone undergrowth
Sturge-Weber syndrome: facial + leptomeningeal CM + eye anomalies +/- bone and/or soft tissue overgrowth G
Limb CM + congenital non-progressive limb hypertrophy
Maffucci syndrome: VM +/- spindle-cell hemangioma + enchondroma
Macrocephaly - CM (M-CM / MCAP) G
Microcephaly - CM (MICCAP) G
CLOVES syndrome: LM + VM + CM +/- AVM + lipomatous overgrowth G
Proteus syndrome: CM, VM and/or LM + asymmetrical somatic overgrowth G
Bannayan-Riley-Ruvalcaba sd: AVM + VM +macrocephaly, lipomatous overgrowth G

Of major named vessels
Affect lymphatics, veins, arteries
Anomalies of origin [course, number, length, diameter (aplasia, hypoplasia, stenosis, ectasia / aneurysm), valves]
Communication (AVF) persistence (of embryonal vessel)

[a] Posterior fossa malformations, Haemangioma, Arterial anomalies, Cardiovascular anomalies, Eye anomalies, Sternal clefting and/or Supraumbilical raphe.

Modified from Dasgupta & Fishman, 2014[2]

ISSVA 2014

ISSVA Classification for vascular anomalies

Vascular anomalies				
Vascular tumors	Vascular malformations			
	Simple	Combined *	of major named vessels	associated with other anomalies
Benign Locally aggressive or borderline Malignant	Capillary malformations Lymphatic malformations Venous malformations Arteriovenous malformations* Arteriovenous fistula*	CVM, CLM LVM, CLVM CAVM* CLAVM* others	See details	See list

* defined as two or more vascular malformations found in one lesion

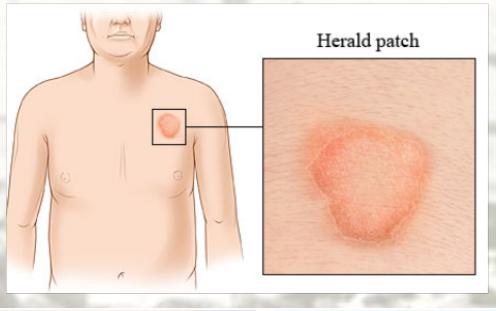
* high-flow lesions

Vascular tumours

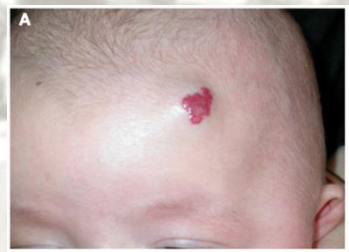
- The majority of vascular tumours are benign and 95% are infantile haemangiomas.

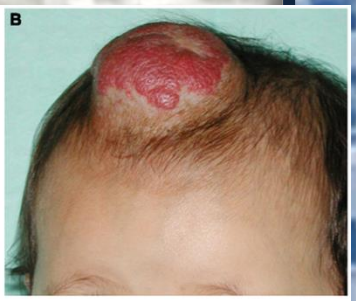
Infantile haemangiomas

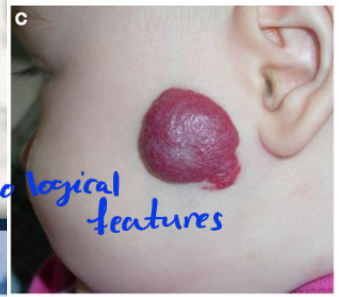
- Benign (strawberry naevae) , self limiting vascular tumors.
- 10% of full term vs 20% of premature babies

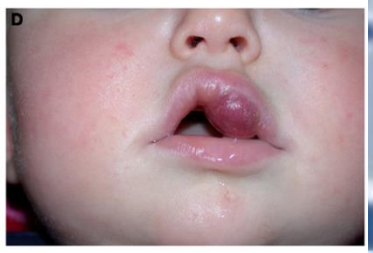


- F:M 2:1
- Predilection for the head and neck









- Presentation → not present at birth usually, although small groups present with herald patch (بتعطينا فكرة انه المرض محكم haemangioma يصير منه)
  + First noticed at 2 week of age
  + to undergo at 3 stages cycle with a characteristic histopatho

Infantile haemangiomas

- Stage 1:
  - A rapid proliferating phase during the first 5-8 months of life is characterized by rapid, distressing and potentially disfiguring growth of the haemangioma.
  - These are soft and warm, with a prominent Doppler signal. (high flow)
  - When situated on the skin surface they appear bright red (hence the term 'strawberry naevus')

and in their color in the subcutaneous is bluish or no color

- There may be ulceration with bleeding or obstruction of the adjucent structures

Stadies shows ↓ cellular tumor turnover + presence of blump endothelial cells with a multi laminated basal membrane

- Active angiogenesis with upregulation of the angiogenic factors, vascular endothelial growth factors and basic fibroplast growth factor => all matched with the process of tumors with uncontrolled, rapidly deviding cells.

Infantile haemangiomas

- Stage 2.
  - A prolonged involuting phase lasts until the age of 7-9 years.
  - During this phase the lesions initially become darker with a grey hue, slowly lose their color and have fine capillary telangiectasia.

- Increase in the flow of mast cells, fibroplast, gradual substitution of endothelial cells by a fibrofatty tissues, angiogenesis suppression factors, tissue inhibition metaloproteases

Infantile haemangiomas

- Stage 3.
  - A final involution phase is characterized by the presence of a soft lump that is visible in the case of superficial lesions and less so in deeper lesions.
  - The lesion regresses by the age of 7 years in 70% of cases, and by 9 years in 90%.
  - Histologically, the cellular parenchyma has been substituted almost completely with a fibro-fatty residue.

Infantile haemangiomas

- Features:
  - Localized / diffused
  - Histologically share features of placental tissue
  - Expression of glucose transporter protein GLUT-1
  - PHACE association
  - Associated with other abnormalities or syndromes like PHACE Syndrome. P→ posterior fossal transformations, H→ haemangiomas A→ arterial anomalies, C→ Coarctation of the aorta / cardiac effect E→ eye abnormalities

Management

- Treatment is mostly expectant + Clarrifications to the parients about the natural history anel the probability to deal with any complication in case anything happened. Usually after the proliferative phase, the patient is seen yearly or every few years. Every child in the family accept the final appearance of the lesion they are usually discharge.
- Rarely biopsy
  - GLOT-1 newly staining
- CBC → to roll out any complication such as thrompocytopenia.
- MRI/ US → to see internal lesions, if there is ≥8 skin haemangioma to predict the likelyhood of cardiac failure.

Management

- ***Active intervention is necessary in the presence of complications such as***:
  - large size or disfigurement causing a significant deformaties of the face or wherever the lesion locates..
  - multiple lesions causing high-output cardiac failure
  - obstruction of vital structures (vision, airway)
  - persistent ulceration. → causing bleeding or predisposing to infections

↳ if the haemangioma is located in the subglottic space

Treatment

- Propranolol :
  - 1st line
  - Cause vasoconstriction
  - 1-2mg/kg/day

For superficial or periocular regions : topical timolol can be used for treatment.

- ↓ the expression of proangiogenic factors of the haemangioma growth phase causing apoptosis of the capillary endothelial cells
- Absence of any contraindications such as sensitivity to β-blockers, bronchospasm, hypotension or bradycardia and following a routine haematological-biochemical investigations.
- Monitoring and adequate follow up are mandatory to exclude and manage complications of this tx

- Propranolol has replaced the use of systemic steroids

Steroids

- Second line
- Intra-lesional injection of localized lesions may be used
  - 2mg/kg every 4-6 weeks → in the use of triamcinolone acetonide.
  - pts response to the medication
    - good response
    - moderate
    - don't respond
- Systemic therapy
  - Rebound growth!!

to to avoid this, tapering of the dose should be done

Embolization

- Is useful in high-output cardiac failure and for treating troublesome, bleeding lesions.

4 Late excision of the fibro-fatty residue or loose skin of the involuted lesions may be planned, usually after the age of 4, but some lesions are still involuting and the best is to wait until the process of involution is complete.

Surgery

- Excision

not considered as a major indication → between age 2-4 there are occasions when surgery is appropiate to minimize the deformity from attenuation of the vital structure such as the eyelid, the nasal margins and the lips

Lo lesions on the nose, the eyelid and the lips cause a significant deformity interfering even with the feeding of the baby and breathing

- Tracheostomy → is sometimes needed in the neonatal period, for lesions causing obstruction in upper airways.

major indication → During infancy if the vision is affected → excesion of the periorbital lesion may be indicated, if the lesion is obstructing the vision we go into a condition called a lazy eye → the brain will ignore the eye without a vision and this will cause permanent vision loss which is called amblyopia.

Pulsed-dye laser

- There is no evidence that laser treatment alters the natural history of haemangioma.
- It is useful for surface residual telangiectasia (after the age of 10 years).
- It was used to help coagulate the surface of ulcerated lesions, but dressings are the principal form of wound care.

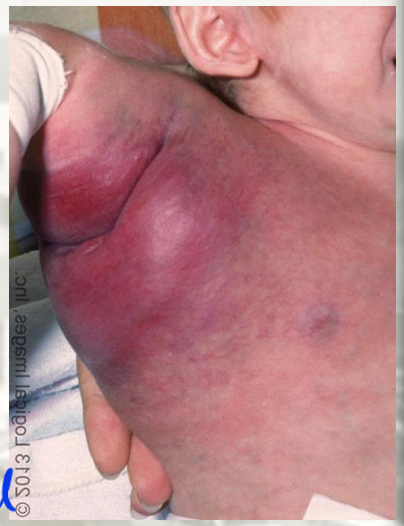
Kaposiform haemangioendotheliomas

KHE

- Locally aggressive vascular tumor, characterized by rapid growth and extension before the final regression
- Appear early infancy, although later appearance is possible

* Purpile or pink in color pulging masses, sometimes are painful, ulcerating, infiltrative, hard with a diffuse edges

- Presentation
  - Kasabach-Merritt phenomenon KMP
    - related to tufted haemangioma that are a localized form of KHE.



- Treatment → The lesions are steroid resistant and in severe cases chemotherapeutic agents or embolization are required for tx.
  - MTOR +ve : Sirolimus

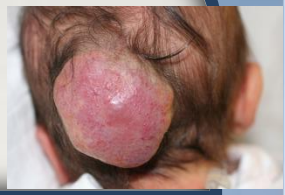
- complicated by a dangerous thrombocytopenia and the risk of systemic bleeding
  ⇒ called kasabach-marrit phenomenon
- The rate of systemic complications is high with high mortality rate

Diagnosis is confirmed by histology and by looking to some gene sequence that prove the diagnosis

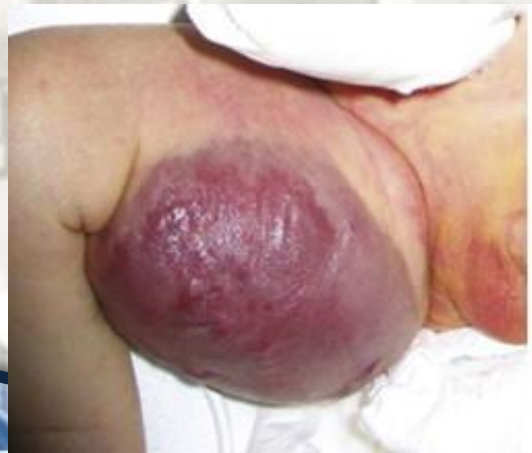
Congenital haemangioma

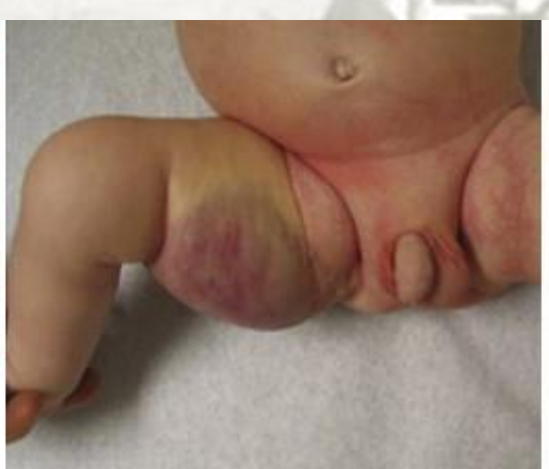
- As the name suggests these are fully developed at birth and three subtypes have been recognized so far.
- They are negative for GLUT-1.

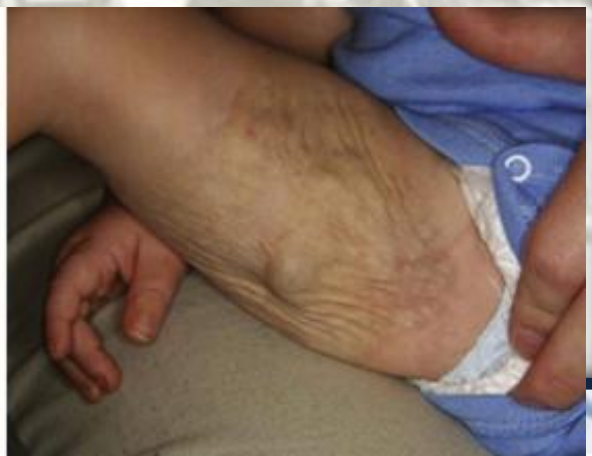
Rapidly involuting congenital haemangiomas



- These are un- common entities that, unlike infantile haemangiomas exhibit a much faster involution with full regression by 1 year of age.
- They present as large masses, often on the legs. They are firmer than infantile haemangiomas, with or without telangiectatic changes. They leave a plaque-like residuum, which may regress further to leave an atrophic patch of skin







RICH

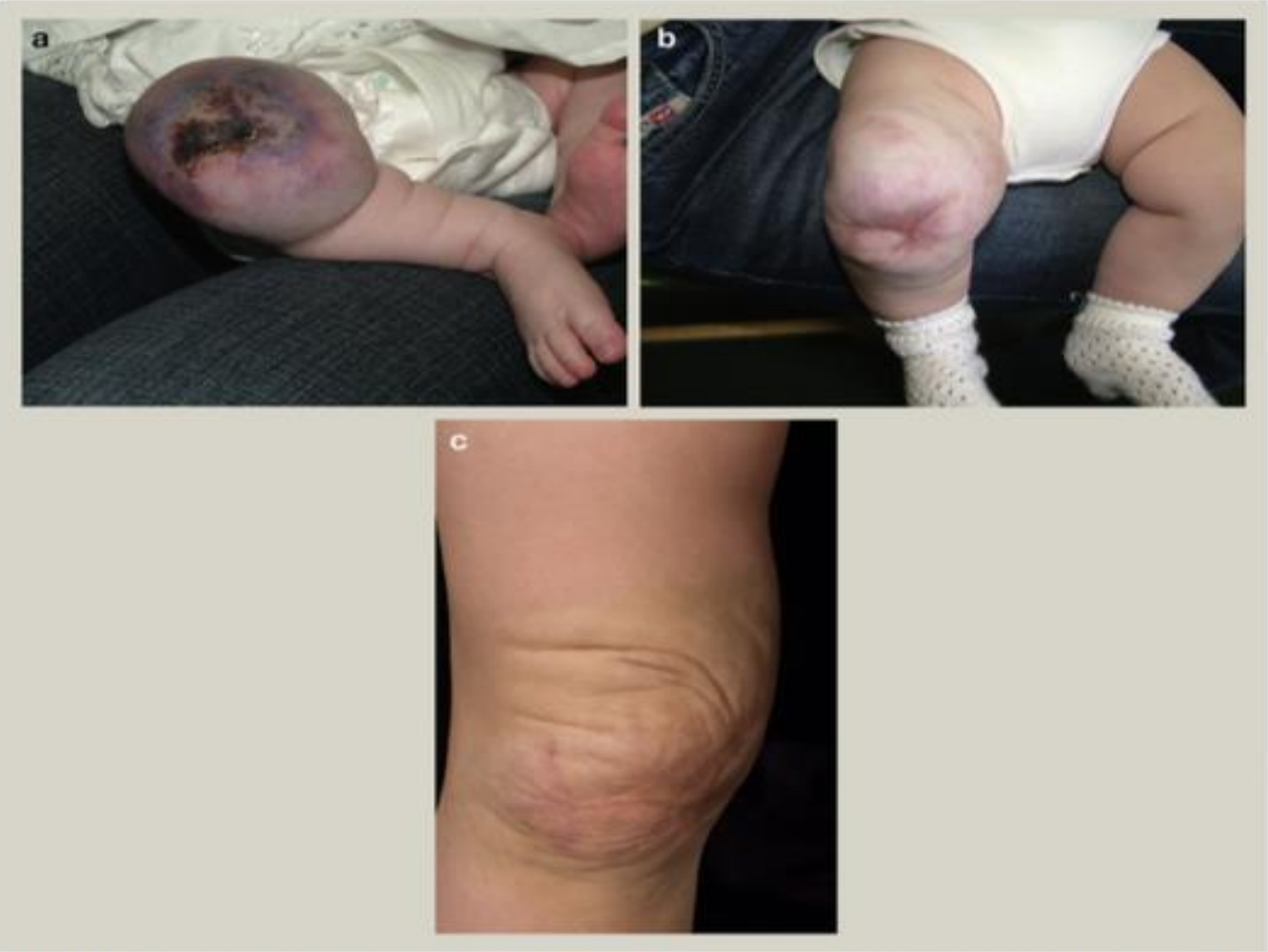
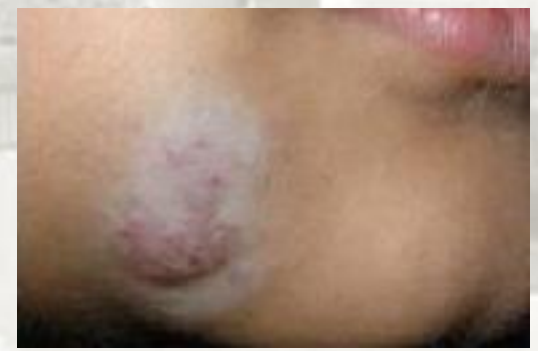
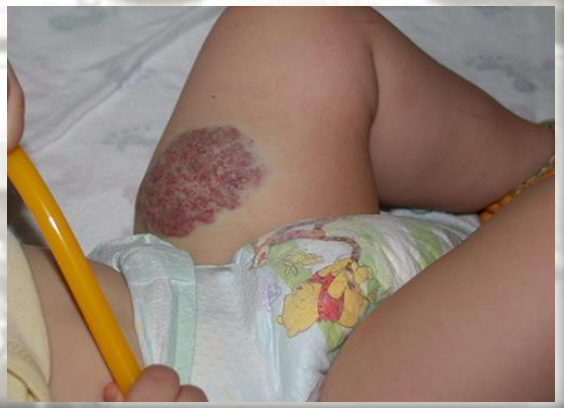


Figure 5 Rapidly involuting congenital haemangioma (RICH) that was fully grown at birth and regressed spontaneously, shown at (**a**) 2 weeks; (**b**) 2 months; and (**c**) 2½ years of age.

Non-involuting congenital haemangiomas

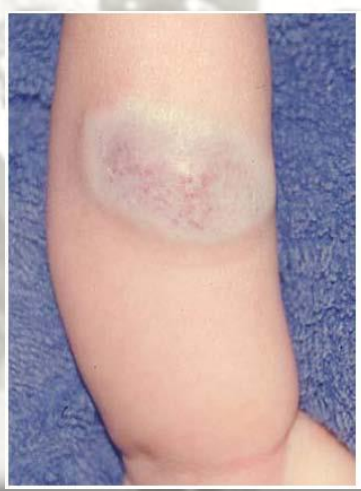
- These are rare tumours that mimic infantile haemangiomas and are of similar texture.
- They are present as round or oval masses, with flat shape or moderately bossed and accompanying telangiectasia, and may have a halo. → characteristic mark)
- They do not exhibit further growth and do not regress.
- Treatment is by surgical excision.

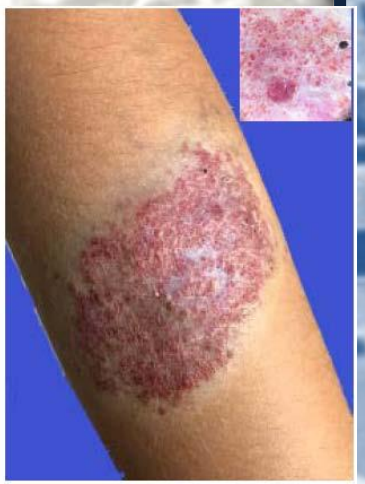




Partially involuting congenital haemangioma:

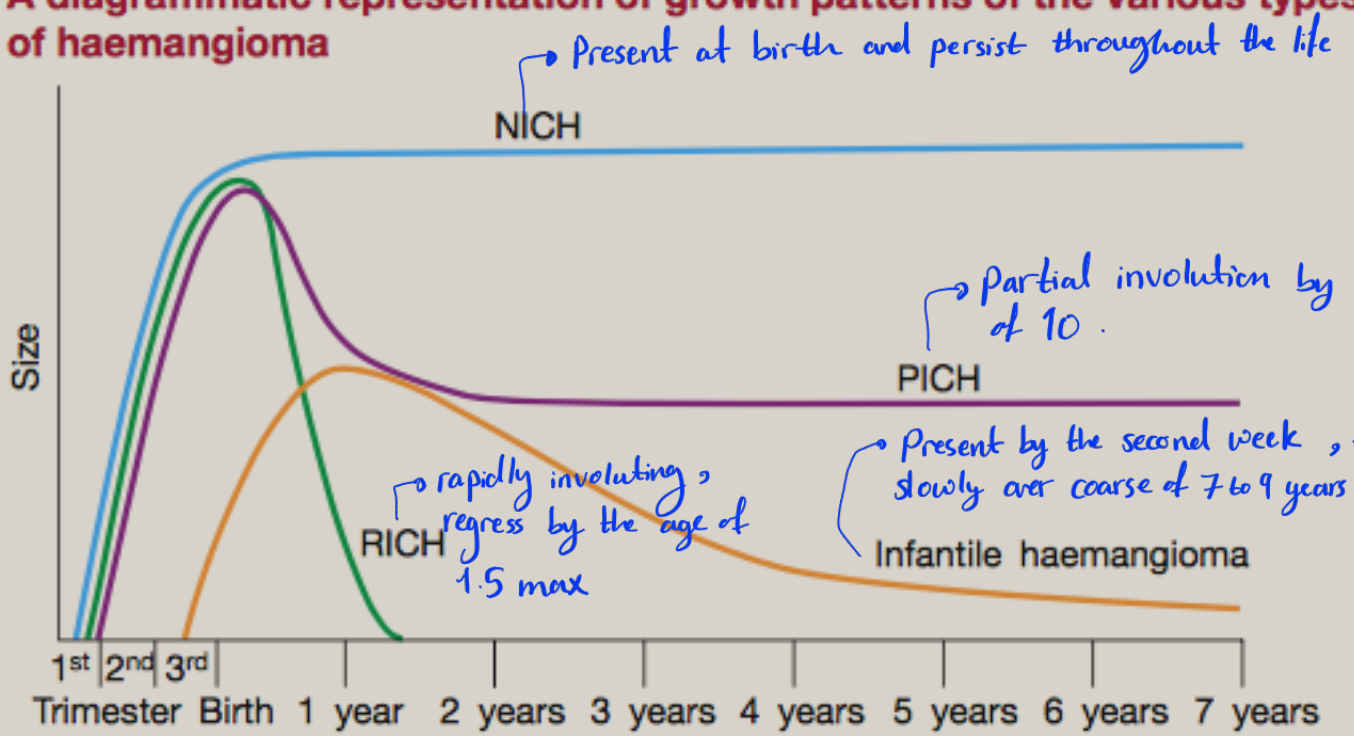
- This is a recently described variant which looks like a NICH but slowly regresses by age 10





Congenital Haemangioma

A diagrammatic representation of growth patterns of the various types of haemangioma



NICH, non-involuting congenital haemangioma;
PICH, partially involuting congenital heamangioma;
RICH, rapidly involuting congenital haemangioma

Adapted from Mulliken & Enjolras 2004

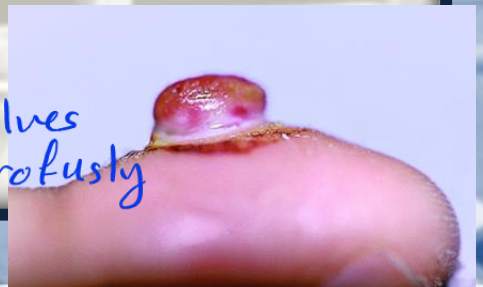
- Present more in childrens and young adults, but can be present at any age.

Pyogenic granuloma (PG)

- although the name indicates infection the cause is unknown.

- lobular capillary hemangioma
  - benign vascular tumor of the skin or mucous membranes characterized by rapid growth and friable surface.
  - starts as a small red papule that grows rapidly over weeks to months and then stabilizes
  - bleeds profusely after minor trauma and may become ulcerated. Bleeding is difficult to control and often recurrent.

- Surgical treatment is required because PG resolves spontaneously and often bleeds repeatedly and profusly



Vascular malformations

- Presentation → Present at birth and may present later on in life.
- Regression → do not regress
- Endothelial cell mitotic rate → normal mitotic rate with abnormal vascular morphology → unlike the haemangioma

Vascular malformations

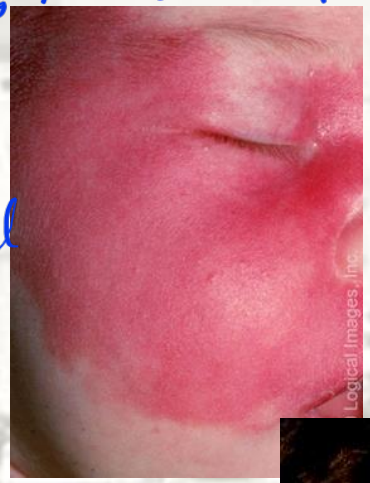
- Types:
  - Flow characteristics
  - Vessel type:
    - capillary, venous, lymphatic and arterial components, or a combination

- Symptoms → they are a space occuping lesions so they may causes
  - soft tissue and skeletal muscles hypertrophy.
  - infection
  - bleeding
  - blood dyscrasia

Capillary malformations

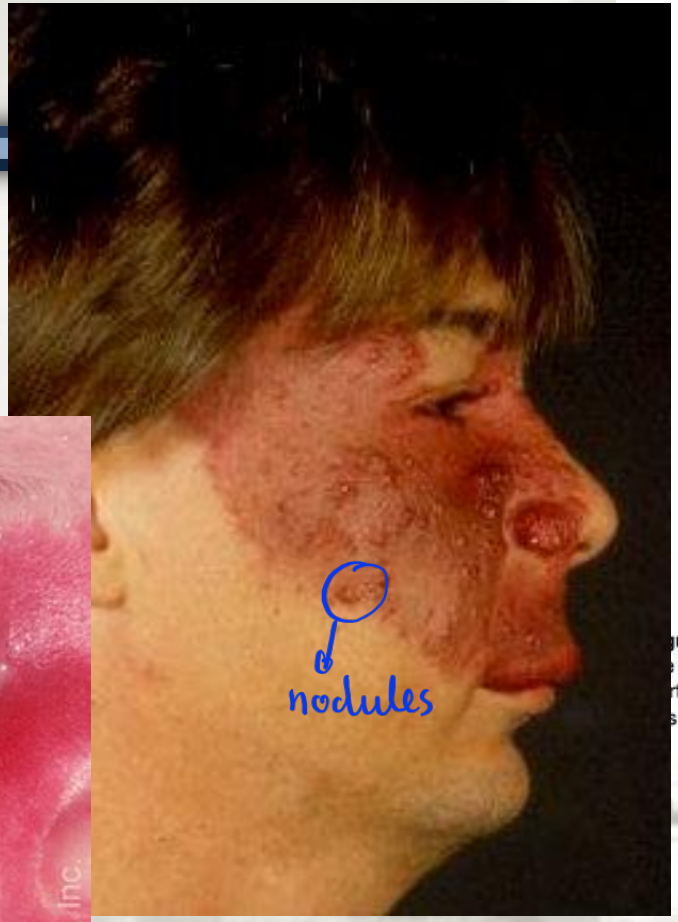
most common type

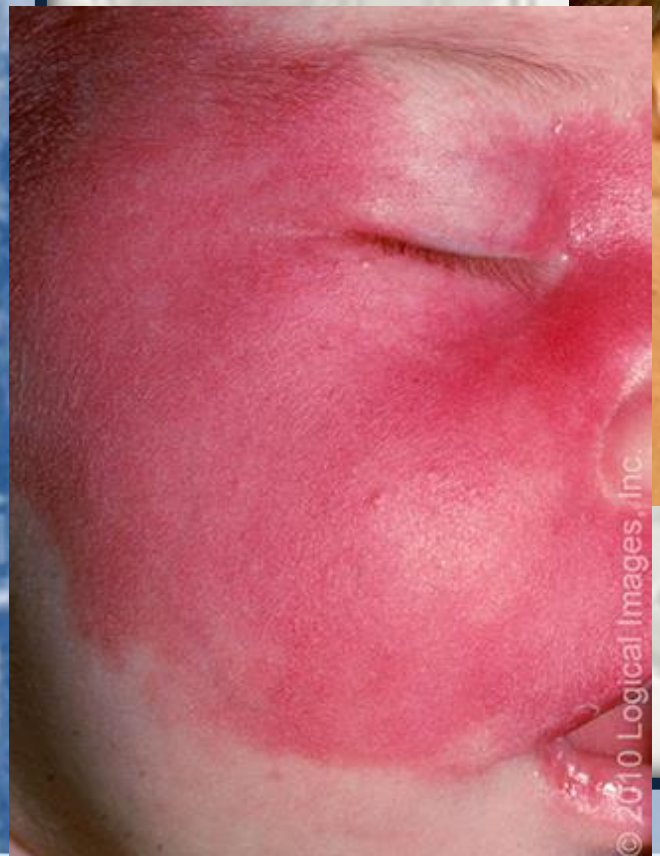
- Port wine stain
  - Secondary tissue hypertrophy, skin nodules, ↑ incidence of PG among those pts
  - It distributs on the face corresponding to the dermatome of the trigeminal nerve.
- 0.3% of newborns
  - Histology: ectatic (→ dilated) capillaries to venules sized dermal channels
- Presentation → macular patch, pink in infants and later become red and purple in adults.
- Associated syndromes → klippel-trenaunay syndrome, Sturge weber syndrome, parkes weber syndrome
  - Skin temperature and doppler signals are normal

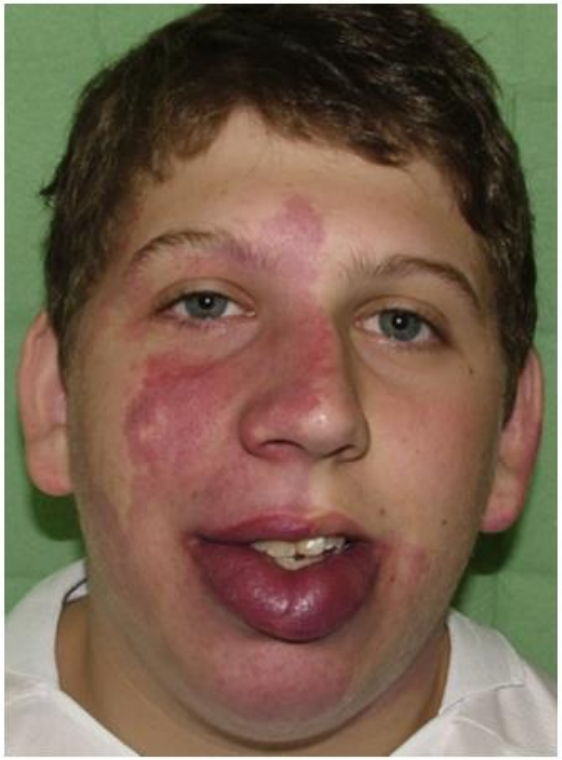


⇒ less common capillary malformations include :

- Cutis marmorata telangiectatica congenita (CMTC)







ure 6 A capillary malformation (port-wine stain) of the right side of face on a 19-year-old boy. Note the skeletal and soft tissue hypertrophy of the affected area. He had two operations to reduce the s in early teenage and a further procedure is planned.

↓

epsilateral facial hypertrophy on the affected site

Management:

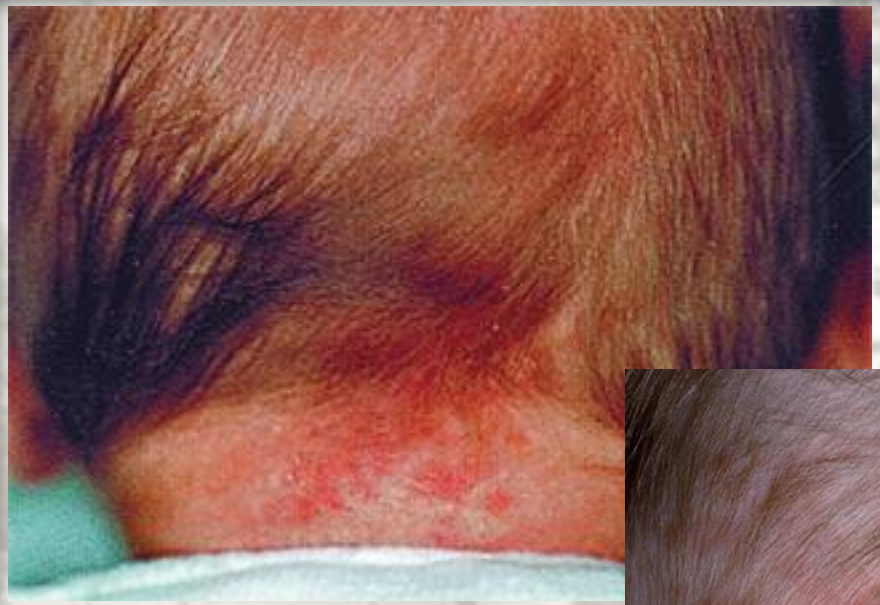
- the colour deformity may cause psychological concern and impair normal social interaction.
  - In teenager and adults tissue hypertrophy may cause further concern.

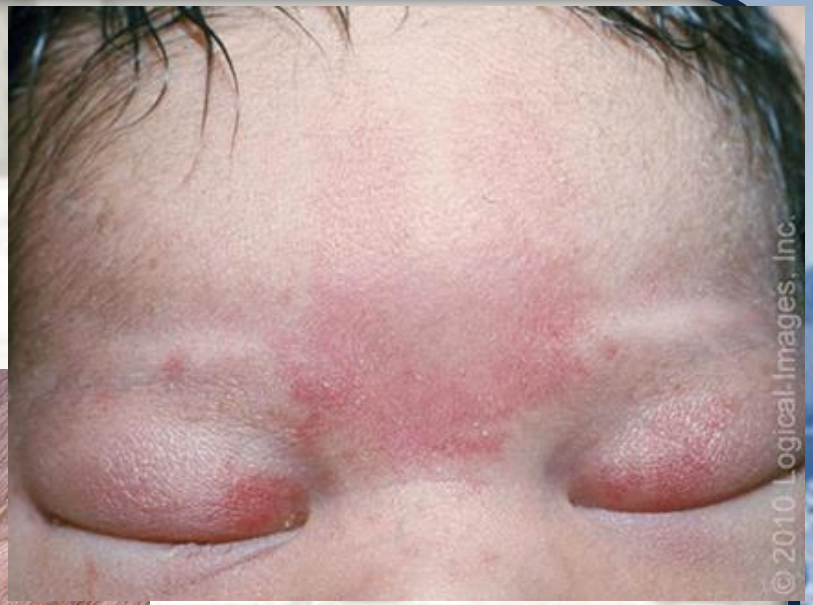
- Management is a combination of supportive with involvement of a clinical psychologist, with camouflage and the use of pulse dye laser therapy.
  - Which can lighten the colour for a number of years.
  - Surgery may be useful for reducing hypertrophied areas
    - the lower lip.

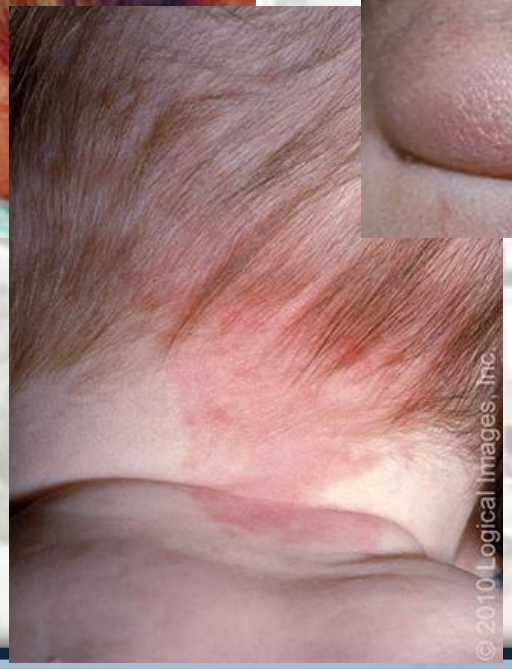
Capillary malformations

- **Nevus simplex (macular stain)** —
  - (macular stain, salmon patch, stork bite, or angel kiss) presents as single or multiple blanchable, pink-red patches in newborn infants.
  - These lesions occur in 40 to 60 % of infants, most commonly on the eyelid, glabella, and midline of the nape of the neck. Less common sites of involvement include the scalp, nose, lip, and back.
  - Nevus simplex generally fades within one to two years, although lesions on the back of the neck may persist unchanged with little consequence

Nevus simplex







Venous malformations

- These low-flow lesions are blue, compressible soft tissue masses that empty on elevation. They can affect most tissues
- Presentation
  - Disfigurement
  - Pain → due to the release of mediators from dissolution of clots
  - Coagulopathy → in large lesions
    - ↑ D-dimer/↓ fibrinogen

* Histology: composed of abnormal venous channels with flat endothelium. They have normal cellular turnover.

* Extensive lesions associated with ↑ mortality rate due to the formation of thrombi, emboli, internal bleeding and DIC.

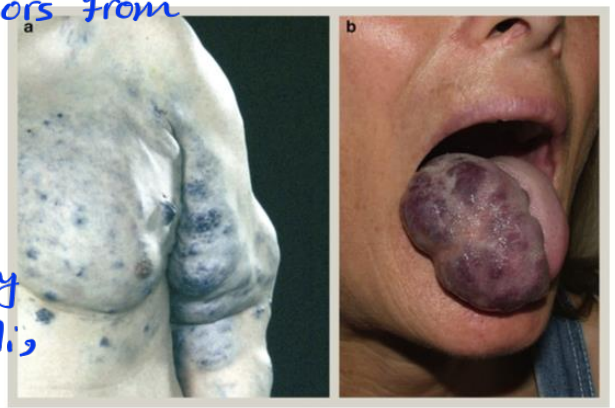
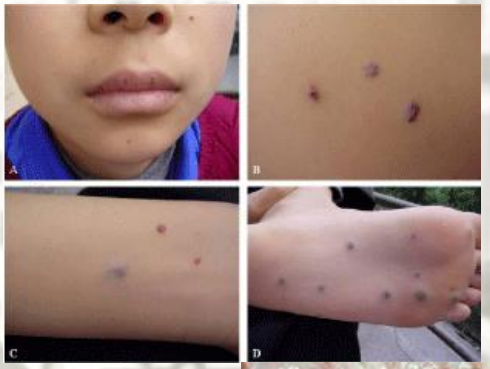


Figure 7 (a) In extensive venous malformations, as on the trunk of this man, there may be consumptive intravascular coagulopathy. (b) A woman with a venous malformation of the right side of the tongue, which had been treated once with sclerotherapy.

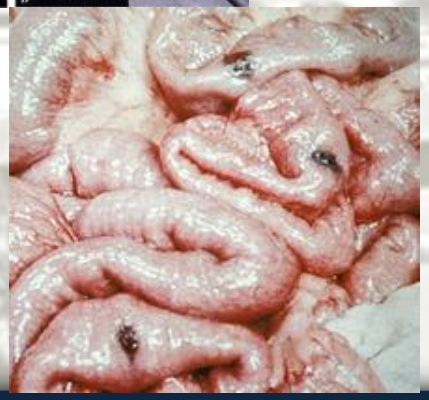
Venous malformations

- 5% genetic abnormalities
  - Krit-1, TIE-2 and Glomulin genes
  - Blue rubber bleb syndrome

+ Visceral lesions can cause melena and chronic anemia.



multiple lesions over the skin + the GI tract



Management

To control the symptoms

- Compression garments
- Non-steroidal anti- inflammatory drugs NSAIDS
  - ibuprofen.
  - to relieve the pain
- Sclerotherapy
  - Sodium tetradecyl sulfate, bleomycin, doxycyline
- Surgery (excision) → complicated by ↑ risk of hemorrhage due to the underlying coagulopathe + poor wound healing. So, it is used in minority of cases with ongoing functional issues, despite conservative measures as well as intralesional steroid therapy treatment.

+ Anticoagulation therapy + insertion of a filter in the IVC to ↓ the complications.

Lymphatic malformations

- Microcystic → seen in the superficial lesions usually described as lymphangioma circumscriptum.
  * Appear as small, raised, cutaneous vesicles usually filled with lymphatic fluids
- Macrocystic → classic neck lesions that usually called the cystic hygroma.
  * Appear as large, soft, subcutaneous swellings that easily transluminate

* Combination of micro + macro cystic lesion
* Complication: - infection - intralesional haemorrhage.
* Histology: abnormal dilated lymphatic channels without connection to the normal lymphatic system

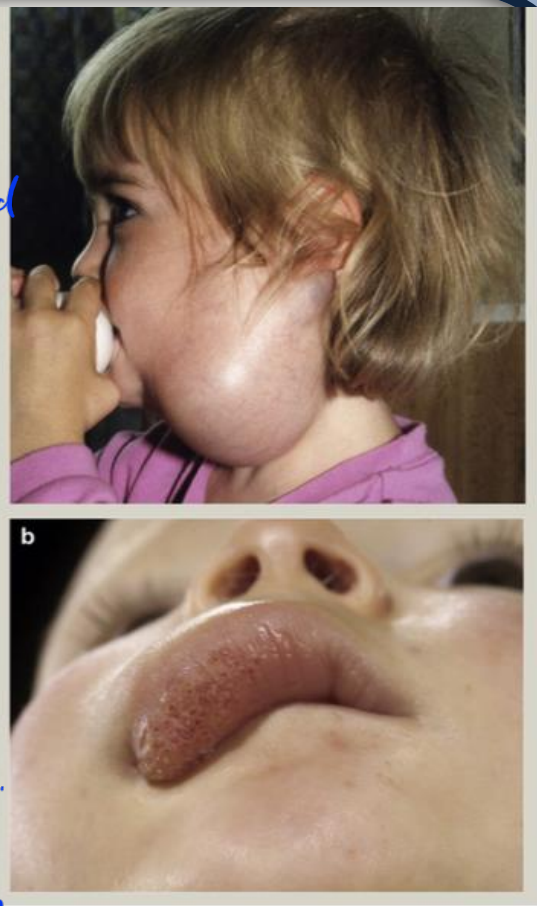


Figure 8 Lymphatic malformations: (**a**) macrocystic, of the neck that responded well to sclerotherapy; (**b**) microcystic lesions of the lip that bled and caused infection, leading to excision of the area.

+ Long term relieve of the symptoms can be achieved, unlike venous lesions

Management

- Sclerotherapy
  - OK-432

- Surgery has a role in microcystic lesions + in mixed lesions with a fibrofatty matrix (large lesions)
  - Seroma
  - Infection

  } Post op comlication

  ⇒ Suction drains + pressure garment can ↓ these problems.

+ Microcystic cutaneous lesions are prone to infection, so good skin care is essential + long term antibiotics.

Arteriovenous malformations (AVM)

Most aggressive vascular malformations causing a progressive deformity and causing a systemic risk

- They are high-flow malformations that have a characteristic nidus with arterial feeders, arteriovenous fistulas and enlarged veins

* They continue to recruit new vessels
* Rarely or seldom cured.

- presentation → present at birth, mimicks capillary malformations or haemangiomas of infancy, but their behavior is aggressive in later life.
  - sometimes triggered by pubertal changes, pregnancy or a trauma.

* Present with throbbing pain and ulceration with bleeding
* May cause cardiac failure.
* Warm lesions with a loud doppler signals
* Later stages may present with a pulsatile mass with bruit + purpule discoloration with engorged tortuous veins.

AVM Schobinger classification

Schobinger clinical classification for arteriovenous malformations

Stage	Description
I (Quiescence)	Pink/blue stain, warmth, and arteriovascular shunting
II (Expansion)	Stage I plus enlargement, pulsations, thrills and bruit
III (Destruction)	Stage II plus either dystrophic skin changes, ulceration, bleeding, pain or tissue necrosis
IV (Decompensation)	Stage III plus high-output cardiac failure

Adapted from Schobinger, Hansen, Probaz et al., 1998

Management:

- the symptomatic stages (III and IV) may warrant treatment with a combination of interventional radiology, excisional surgery and reconstruction. Some lesions can be controlled with repeated embolization.
- Embolic agents include
  - ethanol, cyanoacrylate (glue), coils, polyvinyl particles and onyx, a liquid ethylene vinyl alcohol copolymer.

Combined lesions

- There are several patients with vascular malformations where lesions have a mixed vessel type.
- These lesions occur either isolated or associated with overgrowth disorders such as Klippel- Trenaunay and Proteus syndrome.
- Patients often have significant morbidity with heavy, painful areas especially when involving a limb.
- They are also troubled by episodes of infection and wound breakdown. These patients require life-long care.

Molecular mechanisms

- The mammalian target of rapamin (MTOR) pathway22 is an intra- cellular signalling pathway which results in cell growth and survival

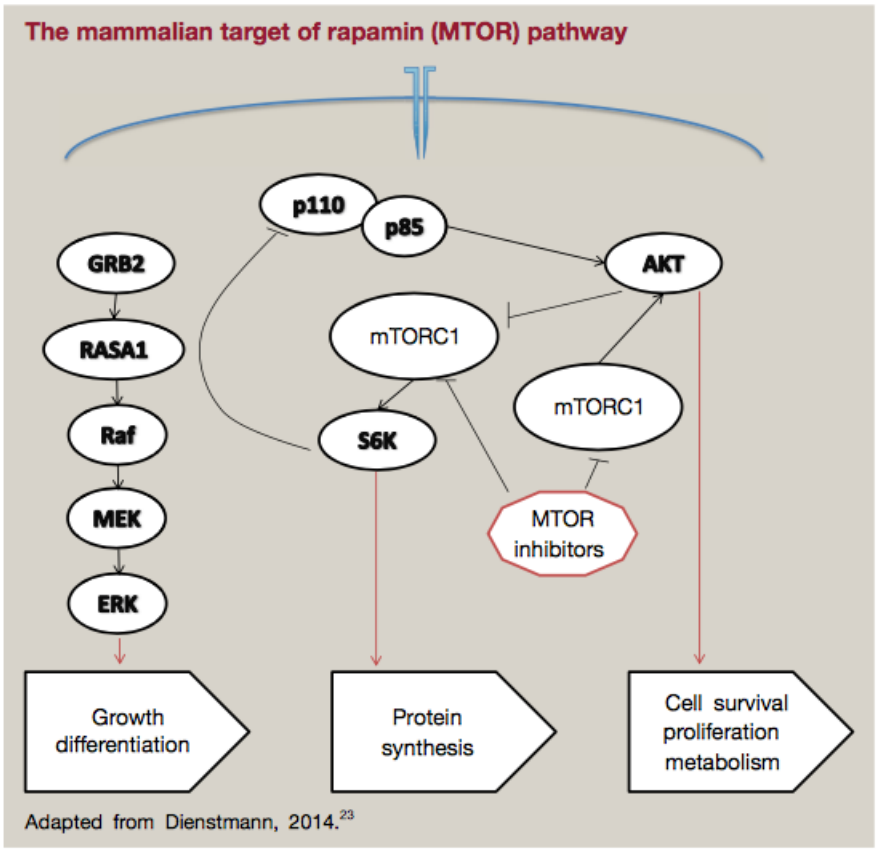


Figure 10 The mammalian target of rapamin (MTOR) pathway Adapted from Dienstmann, 2014.[22]

Conclusion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