Vascular malformations:

1. **Venous malformations**: congenital venous anomalies pathologically characterised by **anomalous veins** (thickened and hyalinised walls) separated by normal brain. These anatomically abnormal veins **drain normal brain tissue**. It is thought that they result from intrauterine ischemic event occurring during the formation of medullary veins resulting in collateral venous drainage. This is the most common vascular malformation accounting **for 65% of all cases**. The prevalence in autopsy series up to **2.5%.** Most commonly located adjacent to the cortex or in periventricular region. Infratentorial lesions are always in the cerebellum. Most commonly solitary and commonly associated with other vascular malformations particularly cavernomas. The majority are asymptomatic. The risk of haemorrhage if any is minimal (prospective risk in 1 study **was 0, 3% per year**) and one should always look for another cause of haemorrhage (associated cavernoma). The association with seizures is controversial and rarely do they can thrombose causing infarction. This malformation gives the appearance of caput medusae on angiograms (radially arranged anomalous veins that converge into large draining vein). Surgery is not indicated for these benign lesions and injury to these veins can cause venous infarction.
2. **Capillary telangiectasia:** The second most common vascular malformation characterised by **a tuft of dilated capillaries** with normal intervening brain (no gliosis or hemosiderin). The capillaries are normal except for dilatation. They are solitary in 78% of cases and most commonly located in the pons (71%). Grossly look like a small area of petechial haemorrhage. Microscopically there are small tufts of capillaries which are structurally normal. Normal parenchyma is present in between the capillaries. These are **angiographically occult** lesions not detected on CT or angiogram. MRI-small homogeneously enhancing lesions with loss of signal on gradient echo sequences. These are benign and asymptomatic lesions and usually discovered incidentally at autopsy or on MRI scan and only extremely rarely are associated with haemorrhage and in that case one should look for other cause and treat the ICH as usual.
3. **Cavernous angiomas (cavernomas):**

- 5-13% of the four classically described vascular malformations, the others being AVM, venous angioma (malformation) and capillary telangiectasia. The incidence in autopsy and MRI studies is about **0.5%.** 80% supratentorial, 20% infratemporal, **10-20% multiple**. The size ranges from 1 mm to few cm. There are two forms of cavernomas

1. Sporadic: the majority are of cases. Usually single
2. Familial cases have been described mostly in Hispanic population. The gene has been mapped to **q7 with autosome dominant inheritance and**

incomplete penetrance. Multiple lesions and strong family history of epilepsy are pathognomonic. The disease results from mutations of KRIT1gene that codes for Krev-1/rap1a binding protein and is divided into 10 exons. 19 distinct mutations of the gene have been reported.

- **Pathology**: lobulated, mulberry like lesions composed of sinusoidal spaces lined with endothelium, **lacking the tight junctions** (hence the ooze like pattern of haemorrhage) the wall of these vessels **lacks smooth muscle** and **internal elastic membrane**. These spaces are separated by fibrous tissue without intervening brain tissue. The lesion is surrounded by hemosiderin rim and area of gliotic brain (hence the increased incidence of seizures).They grow through red cell diapedesis. According **to Spetzler all cavernomas are associated with venous malformation at surgery**

- **Presentations:**
    1. The most common presentations are **seizures** (40-80%). There is 2.4% /year cumulative risk of seizures and 75-88% of patients become seizure free after surgical resection of the lesion. Medically controlled seizures are not indication for surgery. Patients with intractable seizures should be assessed by (EEG, MRI, PET and neuropsychological assessment).Functional MRI may be helpful to delineate the eloquent areas. Surgical options include lesionectomy alone or with resection of adjacent tissue depending on the location
    2. Haemorrhage.
    3. Less commonly neurological deficit from the mass effect and from haemorrhage.
    4. The sudden onset of neurological deficit is the most common presentation of infratentorial lesions (97%).
- Diagnosis is made by 1. MRI scan (very sensitive and specific) but not pathognomonic, lesions that can resemble cavernoma are melanoma mets, some GBMs with calcification, oligodendrogliomas with haemorrhage. On MRI these lesions are well **demarcated, lobulated, heterogenous** lesions (blood products of variable age**), minimal enhancement with hemosiderin low intensity rim**. There are three bleeding patterns (oozing, intralesional haemorrhage leading to lesion expansion and extralesional haemorrhage). On 2. CT scan cavernomas are hyperdense, occasionally calcified with faint enhancement. These are angiographically occult lesions
- **Natural history** as above.
- Management: Three treatment options

1. Observation and follow up: for asymptomatic lesions, for deep lesions with single minor haemorrhage. Patients are warned that anticoagulants may increase the sequelae of haemorrhage and **pregnancy is associated with increased risk of haemorrhage.**

2. Surgical; resection for lesions with recurrent haemorrhage, single life threatening haemorrhage, lesions enlarging on serial imaging and lesions causing intractable epilepsy. 75-88% of patients with seizures become seizure free with surgical resection of the lesion. For brain stem lesions with one or more haemorrhage, lesions causing progressive deficit **and coming to pial or ependymal surface.** One should resect the cavernoma and preserve the venous malformation which presents in 24% of patients with supratentorial cavernoma and the majority of patients with infratentorial cavernoma

(Spetzler et al). Thalamic and capsular lesions are removed only if they come to pial or ependymal surface (transcallosal, transcortical or interhemispheric approach if the lesion comes to the medial cortex" posterior thalamic lesions". Durally based cavernomas are rare, mostly found in the middle fossa and can be very vascular. Preoperative angiogram and embolisation may be useful.

3. **Stereotactic radiosurgery**: for surgically not-accessible symptomatic lesions (deep brain stem and basal ganglia lesions). In one study looking at 45 deep lesions there was significant reduction in the haemorrhage rate comparing with historic controls. Controversial (biopsy is needed to establish diagnosis, the effect of the therapy can't be assessed by neuroimaging and the effect on epilepsy is not known. Radiation of brain stem lesions is associated with high risk of neurological deficit.

- Treatment results: only complete excision or obliteration of the lesion can prevent recurrent haemorrhage. 70% of patients with epilepsy gain control with or without medications.
- Summary for posterior fossa (Brain stem lesions) lesions: surgery is indicated

1. In patients who present with haemorrhage or acute neurological deterioration from brain stem cavernoma that **extends to pial surface**. Symptomatic deep brain stem lesions may be treated with radiosurgery as part of prospective trial
2. For cerebellar lesions (deep or superficial), which are symptomatic with bleeding or progressive deficit.

- For surgical techniques look Yuman's 2325(important). The safest trajectory to the lesion can be designed using frameless stereotaxy and the two point method "one point is in the centre of the lesion, the second where the lesion most closely reaches the surface. Intraoperative neurophysiological monitoring (SSEP, BAER) is useful. False negative and false positive recording can occur and there is poor correlation with postoperative outcome. Always preserve the associated venous malformation. Postoperative MRI is mandatory and if there is residual lesion, early reoperation should be performed.

4. Arteriovenous malformations

- Vascular anomalies characterised by fistulous communications between the arteries and veins without intervening capillaries. It consists of feeding dilated thickened arteries, nidus of coiled abnormal vessels and dilated draining veins. It contains brain parenchyma which is gliotic (with hemosiderin). 25-30% is calcified. This is a high flow low resistance shunt resulting in ischemia of the surrounding tissue (steal phenomenon). The arteries are dilated with thickened walls due to muscular hyperplasia and fibrosis (fibromuscular cushions). These are congenital lesions, although acquired factors (hormones and venous outflow abnormalities) may play a role. AVM may be associated with hereditary conditions such as Rendu-Osler-Weber and Wyburn-Mason syndromes.
- **AVM hemodynamics**: these are high flow low resistance A-V shunts

1. Pressure within the arterial feeders is less than systemic pressure.
2. Pressure within the draining veins is higher than in systemic veins
3. Blood that would normally supply adjacent cortex will flow to the AVM (steal phenomenon)

4. The arteries within the adjacent cortex respond by vasodilatation (autoregulation), the prolonged vasodilatation results in loss of the ability to constrict in response to elevated blood pressure (loss of autoregulation).

- Prevalence in autopsy studies **0.1-.02%.** AVMs account for 40% of spontaneous ICH in patients < 40. The majority are supratentorial with few located in the cerebellum, brain stem and within the ventricles. Usually they are triangular in shape with the apex pointing towards the ventricles. **1-2**% are multiple
- **Clinical presentations**:

1. Asymptomatic: **40%** asymptomatic in population based study
2. Haemorrhage: the most common presentation **65%.** The bleeding can be ICH, SAH, IVH or combination of those. The annual risk of haemorrhage is **2-4**%. Each haemorrhage carries **10% mortality and 30%** permanent neurological morbidity. The risk in the first year after haemorrhage ranges **6-18%** in different studies. The life-time risk of haemorrhage can be estimated using the formula (105-age) or 1-(risk of no haemorrhage) $^{\text{years of life remaining}}$.

Factors associated with increased risk of haemorrhage are:

A. History of previous haemorrhage
B. Presence of aneurysms (7% per year for feeding vessel aneurysms and 9.5% for intranidal aneurysms)
C. Size (higher risk of haemorrhage for AVMs with small nidus (higher arterial pressure within the nidus of small AVMs.
D. Impaired venous drainage (deep venous drainage and single draining vein)
E. Age (2% in the first 10 years, 4% second 10 years, 7%per year > 60years)-controversial
F. Male sex-controversial
G. Pregnancy (controversial)
H. HTN-controversial.

Angiographic features associated with high risk of haemorrhage include deep venous drainage, periventricular location, single draining vein, stenotic venous drainage.

3. Seizures **15-35%** present with seizures: either from mass effect on the cortex, ischemia or gliosis. More with large lesions in frontal and temporal regions. Surgical excision of the AVM results in cure **in 56**% and excision of the AVM +cortical excision **75%**. Seizures can develop after surgery in **10-15%** of patients.
4. Neurological deficit: **10%** present with transient, permanent or progressive deficit. This may be the result of recurrent small haemorrhages, steal phenomenon and mass effect from the AVM. There is **1.5% annual** neurological decline with untreated **large AVMs**.
5. Headaches: 15%

- **Classifications**: Martin-Spetzler's classification based on size (<3cm, 3-6 cm and >6cm), eloquence (primary motor, sensory, language, visual cortex, thalamus, hypothalamus, brainstem and cerebellar peduncle) and deep venous drainage. When applied prospectively there is no difference in the outcome between grade 1 and 2 and grade 4 and 5. The outcome of grade 3 depends on the presence or absence of deep perforators and can behave as grade 1, 2 or 4, 5.

- Investigations: CT scan –**serpiginous** isointense or hyperintense vessels that strongly enhance following contrast administration, 25-30% calcifications. MRI-**honeycomb of flow voids**. Cerebral angiogram with **superselective** injections demonstrates the angioarchitecture of the AVM.
- AVMs may increase in size remain stable, decrease in size and 2-3% spontaneously disappear (thrombosis of single draining vein due to kinking from mass effect, atherosclerosis and thrombosis of the feeding arteries.
- **Treatment options**: for more detail look table pp 2200.

1. Observation: for grade 6 (panhemispheric) and some grade 4 and 5 with deep perforators. The major morbidity from surgery 44-57% and 11-20% mortality or major disability. Each case should be considered individually and weighted against the natural history taking into consideration the patients age and neurological status.
2. **Microsurgical resection**: is the treatment of first choice for **grade 1 and 2** and associated with **zero mortality** <1% permanent deficit and angiographic obliteration rate of **99%** in most recent series. For grade 3 without deep perforators (similar results). For young patients with grade 4 and 5 with out deep perforators (preceded by embolisation) and as part of multimodality treatment for grade 4 and 5 lesions.
3. Focused radiosurgery: **Grade 3 with deep perforators**, deep AVM (thalamic, hypothalamic, brain stem)<3 cm and as a second choice in grade 1 and 2 and as part of multimodality treatment for some grade4 and 5 lesions .**Obliteration rate for lesions< 3cm in diameter at 2-3 years is 70-90%**. The most important factor affecting the obliteration rate is the peripheral (marginal) dose that can be given safely which is inversely proportional to the diameter of the nidus (at marginal dose of 6 Gy obliteration rate is 23%, at 28 Gy-77%.). **Permanent radiation necrosis** can develop in **3%.**Other potential complications include vasculitis, delayed malignancy.
4. Embolisation: A. as the only treatment **cure rate is < 5%, morbidity 8%** B. As adjunct to microsurgery for grade 4 and 5 lesions. The risk is higher than the benefit for grade 1 and 2.
5. Combinations of 2,3 and 4: for complex grade 4 and 5 lesions

- **Complications of surgery**:

1. Neurological deficit from resection of functional brain tissue caused by intraoperative haemorrhage or the attempt to control it (large size, deep perforators, deep venous drainage and eloquent brain increase the risk). **Of complications leading to permanent neurological deficit 83% are present on emergence from GA and 13% develop in the first 9 days after surgery.**
2. Intraoperative aneurysm rupture: In the presence associated aneurysm one should deal with the aneurysm first.
3. Normal pressure break through bleeding or arterial-capillary-venous hypertension syndrome(described by Spetzler in 1978 as a cause of postoperative haemorrhage and brain swelling. See below
4. Vasospasm: occurs in only 2%
5. New seizure disorder 10%
6. General complications (infection, PE-21%)

- **Causes of postoperative haemorrhage are** :

1. Residual AVM: obtain angiogram if possible before taking patient back to theatre (intraoperative angiogram is useful particularly in giant AVMs, in 2 studies residual AVMs were found in 10-18%)

2. Inadequate haemostasis: meticulous haemostasis is of paramount importance (Ask the anaesthetist to raise the B/P to normal at the end of haemostasis then ask to lower B/P before closing)
3. NPPB syndrome: can be reduced by multistage treatment including multistage embolisation and maintaining the B/P 10% below normal during the first 2 days after surgery.

- **Normal perfusion breakthrough bleeding (arterial-capillary-venous hypertension syndrome)**

1. AVMs are high flow low resistance arteriovenous shunts. This shunt results in ischemia of the normal brain supplied by distal branches of the feeding arteries (steal phenomenon). These arteries become maximally dilated as part of autoregulation to compensate for the low pressure within their lumen. Prolonged local hypotension and vasodilatation leads to thinning of their walls and loss of autoregulation.
2. Excision of the AVM removes the low-resistance circulation that exists in parallel with normal circulation of the brain. The feeding artery pressure suddenly increases towards systemic arterial pressure. Also the pulasatility within these arteries increases. This increase in pressure and pulasatility can lead to rupture of the maximally dilated, thin –walled arterioles particularly at sites of aneurysmal weakness.
3. The brain swelling can be explained by either increase in the blood flow through these dilated arterioles (loss of autoregulation) or by propagated venous thrombosis of the major draining system.
4. Angiographic features that may be associated with NPPB syndrome are large size, high flow, and large calibre feeding arteries, diminished perfusion in surrounding brain (angiographic steal).
5. NPPB syndrome can be avoided by staged occlusion of the AVM (embolisation followed by surgery in few weeks time) and by maintaining the patients blood pressure 10% below his normal pressure in the few days after surgery

- **Arteriovenous malformations and Aneurysms**: About 10% of patients with AVMs have aneurysms as well. The presence of associated aneurysm increases the annual risk of haemorrhage. These aneurysms can be classified as :

1. Flow related 85%: **proxima**l on circle of Willis artery that gives origin to feeders, **distal** of a feeding artery and **intranidal**.
2. Non flow related 15% on arteries distant from the AVM.

- Treatment options for patients with haemorrhage include (clipping the aneurysm and excision of the AVM through the same craniotomy if possible (**this is the ideal treatment**), coiling the aneurysm followed by elective excision of the AVM.
- For elective cases there are 2 schools. The argument for excision of the AVM without treating the aneurysm is that many flow related aneurysms can involute after removing the AVM. The argument against that is the small risk of aneurysm enlargement and rupture due to increased resistance in the arterial system after excluding the low resistance shunt.

- **AVMs and pregnancy**: ICH is the third cause of maternal mortality. It can be due to eclampsia, ruptured AVM, aneurysm, HTN and choriocarcinoma. Controversy exists whether pregnancy increases the risk of AVM rupture (Horton et al reported the risk of haemorrhage to be 3.5% while Robinson reported the risk to be as high as 87%).
- **AVMs in CHILDREN**: ruptured AVM is the most common cause of ICH in children and 15-33% of patients with AVMs are younger than 20 years of age. Neonates can present with congestive heart failure due to high left to right shunting. AVMs can grow in size and can reoccur after negative angiogram. Most series report **higher mortality** from ruptured AVM in children (**6.5-35%)** and **higher rebleeding rate 22%-29% in the first year**. Despite the high mortality rate children are more likely than adults to improve after ICH.

- **Endovascular management of AVMs**: Endovascular treatment most commonly used as adjunct to surgery and stereotactic radiosurgery; however it is occasionally used as the only treatment (curative or palliative). Embolisation carries the risk of ischemic infarction and alteration of the hemodynamics which may predispose to haemorrhage while waiting for surgery. Embolisation carries **1% risk of mortality and 8% risk of sustained morbidity.** The morbidity of surgery alone for grade 1-2 AVMs is less than that for embolisation and surgery, therefore **embolisation is indicated for grade 4, 5 AVMs and Grade 3 with deep perforators.**

1. As adjunct to surgery or radiosurgery : The goals of preoperative embolisation include **elimination of deep feeders**, occlusion of associated **aneurysms**, occlusion of intranidal **high flow fistula and reducing the size of the AVM**.In addition staged occlusion may **decrease the risk of NPPBB** syndromes. The goals of embolisation before radiosurgery include size reduction to a volume suitable for radiosurgery and targeted embolisation of angioarchitectural abnormalities believed to increase the risk of bleeding (to decrease the risk of haemorrhage during the 2 year latent period).The most commonly used materials nowadays are **GDC** and **NBCA** (n-butyl-cyanoacrylate).Surgical resection should be delayed for 1-3 weeks to allow progressive thrombosis and stabilisation of hemodynamics. Similarly RS should be delayed for few weeks after embolisation and angiogram should be obtained to delineate the final size of the AVM.
2. As the only treatment which may be curative for small AVMs and palliative for large inoperable AVMs. The **complete cure rate varies between 5-40%** (usually small AVMs with single feeder that can be treated with surgery or RS) For large inoperable AVMs embolisation may be used as a palliative treatment to target angioarchitecture features believed to increase the risk of haemorrhage (aneurysms, high flow intranidal fistulas). This can be repeated if these shunts reoccur.

Management of brain AVM by focussed radiation**:**

- many clinical series using heavy charged particles (protons and helium ions) or photons (gamma knife and LINAC) have shown that AVMs< 3cm in diameter treated with 20-25 Gy have a 3-year obliteration rate of 80-95%with a low complication rate 2.5-4.5% neurological deficit however the 3 year obliteration rate For AVMs > 4 cm using 15-20Gy was 33-50% with 20-30% complication rate (the larger the AVM the smaller the safe dose or radiation

that can be given).Stereotactic focused radiation works by causing endothelial injury which leads to thrombosis, proliferation of smooth muscle cells and myofibroblasts and the deposition of fibrous tissue leads to AVM obliteration.

- Limitations to focused radiation are : low obliteration rate for large AVMs, the latency period of 2-3 years for complete obliteration during which the risk of haemorrhage is similar to the natural history and serial angiogram are necessary to confirm complete obliteration
- Radiosurgical complications are divided into **early** within hours (nausea and vomiting develop in 10%) and **late** more than three months (neurological deficit depending on the size 2.5-30%), new seizures and radiation necrosis (2-20% generally occurring 6-9 months after the treatment and characterised by neuronal death, gliosis, endothelial proliferation and hyalinization. Clinically patients may develop new deficit or present with increased ICP symptoms due to associated oedema. Treatment includes steroids and occasionally surgery .The course is protracted and steroids may need to be given for long period).
- The **peripheral or marginal radiation dose is the most significant factor** determining obliteration rate. At 10 Gy marginal dose the obliteration rate was 43% comparing with 71% at 22Gy (Karlsson et at 1184 patients). The delay in cure (latent period) depends on the marginal dose and the total dose of radiation (average dose of 40Gy takes 22.5 month to cure while a dose of 20 Gy takes average 26 months).

Giant AVMs

- AVMs larger than 6 cm in diameter comprise **10%** of all AVMs. These lesions are associated with higher incidence of **neurological deficit** due to steal and higher incidence of **NPPBB** syndrome. Treatment is indicated for haemorrhage, intractable seizures, and progressive neurological deficit particularly in young patients. Contraindications to treatment include patient with severe neurological deficit, those with medical illness precluding surgery and in those with minimal or no symptoms. The decision to treat or not to treat should be on case by case basis.
- Treatment of these lesions is usually **multimodality** starting with **multistage embolisation** to obliterate deep perforators, associated aneurysms and high flow fistulas. Staged embolisation allows the AVM to adjust to changes in flow hemodynamics and decreases the risk of haemorrhage. The most commonly used agents are **PVA and NBCA**. Superselective catheterisation and the use of **amobarbital test** helps to reduce infarctions. This can be followed by either surgery or radiosurgery. Residual lesions after surgery can be treated by focused radiation and residual lesions after radiosurgery can be removed surgically(allowing 3 years for obliteration).The results of surgery can be improved by using neurophysiological monitoring (somatosensory potentials and ABSP for posterior fossa surgery. cortical mapping and corticography), frameless stereotaxy, intraoperative angiogram.
- **Spetzler** series of **32** patients 15 improved, 10 had neurological deficit 8 of them mild. **Heros** series 21 patients (12% morbidity and mortality for grade 4 and 39% for grade 5).