Aneurysms, Subarachnoidal Hemorrhage

Last updated: August 8, 2020

ANEURYSM

- pathologic focal blood vessel dilatation (Lat. *aneurysma* - dilatation).
  - aneurysm is prone to rupture.
  - some lie entirely within subarachnoid space; others are buried in brain substance.

ETIOPATHOPHYSIOLOGY, PATHOLOGY

FALSE aneurysms (s. pseudoaneurysms) – **encapsulation of perivascular hematoma** – cavities that lack any components of vessel wall, but communicate with vessel lumen; cavity is lined by blood clot (periadventitial hematoma is seen on imaging).

- caused by ***penetrating vessel injuries*** (most commonly; pseudoaneurysm grows in hours), ***periadventitial infections*** or ***malignant process*** (rare).

  N.B. intracerebral hematoma may harbor and simultaneously obscure traumatic aneurysm - angiography is diagnostic procedure of choice (esp. indicated for penetrating head injuries!; absolutely indicated in all stab wounds to head)

TRUE aneurysms – dilatations of vascular lumen caused by **weakness of vessel wall** (at least adventitia is present in aneurysm wall).

1. **Saccular ("berry") aneurysms** (> 90%) – ***rounded outpouchings*** (i.e. neck with dome)
   - why intracranial arteries are susceptible to aneurysm development:
     1) walls lack external elastic lamina
     2) very thin adventitia
     3) lie unsupported in subarachnoid space
   - sac is composed of only **intima** and **adventitia**;
     - *media* ends at junction of aneurysm neck with parent vessel.
     - *intima* is typically normal or thickened hyalinized (subintimal cellular proliferation is common).
     - *internal elastic membrane* is reduced or absent (normal internal elastic membrane can withstand pressures over 600 mmHg without bulging - as long as membrane remains intact, defects in media are inconsequential).
     - hemosiderin-laden leukocytes may infiltrate *adventitia*.
   - sac lumen often contains thrombotic debris.
   - atherosclerotic changes in parent vessel are common.
   - etiology:

     1) **developmental (congenital)** - focal defects in media (present at birth); over period of years arterial pressure balloons out vessel wall (i.e. aneurysm is "congenital" in sense that defect in arterial wall is present from birth, but actual aneurysm develops over years after birth).

        Familial inheritance pattern has been noted in < 2% of intracranial aneurysms

        - congenital media defects in vessels of circle of Willis are found in 80% normal vessels at autopsy.
        - *congenital abnormalities* (e.g. fenestrations of vertebrobasilar junction, persistent trigeminal arteries, vessel asymmetry / hypoplasia, coarctation of aorta) increase incidence of saccular aneurysms.
        - AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD) - most common genetic abnormality associated with multiple intracranial aneurysms (present in 5-40% ADPKD patients; prevalence of aneurysms is 7-fold vs. in general population) - all patients should undergo screening MRA.
        - **chromosomal loci** associated with intracranial aneurysm:

          8q - likely acts via SOX17 (formation and maintenance of endothelial cell)
          9p - likely acts via CDKN2A (may have similar role to SOX17).

     2) **hemodynamically induced degenerative vascular injury** - hemodynamic shear stresses (esp. at bifurcation points) cause occurrence, growth, thrombosis, and rupture of aneurysms.

        N.B. apex of vessel bifurcation is site of maximum hemodynamic stress!

     3) **high flow-related** (caused by high-flow states) – aneurysms occur along PROXIMAL* and DISTAL** vessels feeding ***AVM***.

        *do not increase risk of hemorrhage
        **thin-walled intranidal aneurysms exposed to arterial pressure - likely site for AVM hemorrhage (i.e. AVMs that bleed often have intra-nidal aneurysms)

     4) **traumatic** (< 1% all aneurysms) - caused by ***blunt vessel injuries***. see p. TrH1 >>

     5) **oncotic** - direct ***tumor invasion*** (e.g. meningioma) or implantation of ***metastatic emboli**** (e.g. left atrial myxoma, choriocarcinoma) → vessel wall infiltration → disruption.

        *metastatic implants often involve peripheral cerebral vessels at gray-white junction

     6) **vasculopathy / vasculitis-related** - fibromuscular dysplasia, connective tissue disorders (SLE*, Marfan, Ehlers-Danlos, Osler-Weber-Rendu syndromes, pseudoxanthoma elasticum, Takayasu arteritis).

        *aneurysms can be saccular, fusiform, or bizarre-looking mixture of both.

     7) **drug-related**: *COCAINE*, *HEROIN*, *EPHEDRINE*, *METHAMPHETAMINE* – can induce cerebral vasculitis - ***necrotizing angiitis*** (histologically similar to periarteritis nodosa) with focal arterial ectasias.

2. **Fusiform (s. dolichoectatic) aneurysms** (no identifiable neck):

   1) **atherosclerotic** (7% all aneurysms) - unusual form of atherosclerosis damages media → arterial stretching and elongation that may extend over considerable length (may have serpentine, giant, bizarre shapes).
      - occur in older patients.
      - affect PROXIMAL arteries (*vertebrobasilar system* is commonly affected).
      - perforating branches often arise from entire length of aneurysm.
      - intraluminal clots are common (→ occlusion of small ostia of perforating vessels → infarcts).
      - bleed rarely (mass effects are much more common).

   2) **mycotic (infectious)** (0.5-3% all aneurysms) - any aneurysm resulting from ***infectious process*** ***that involves (destroys) arterial wall***:

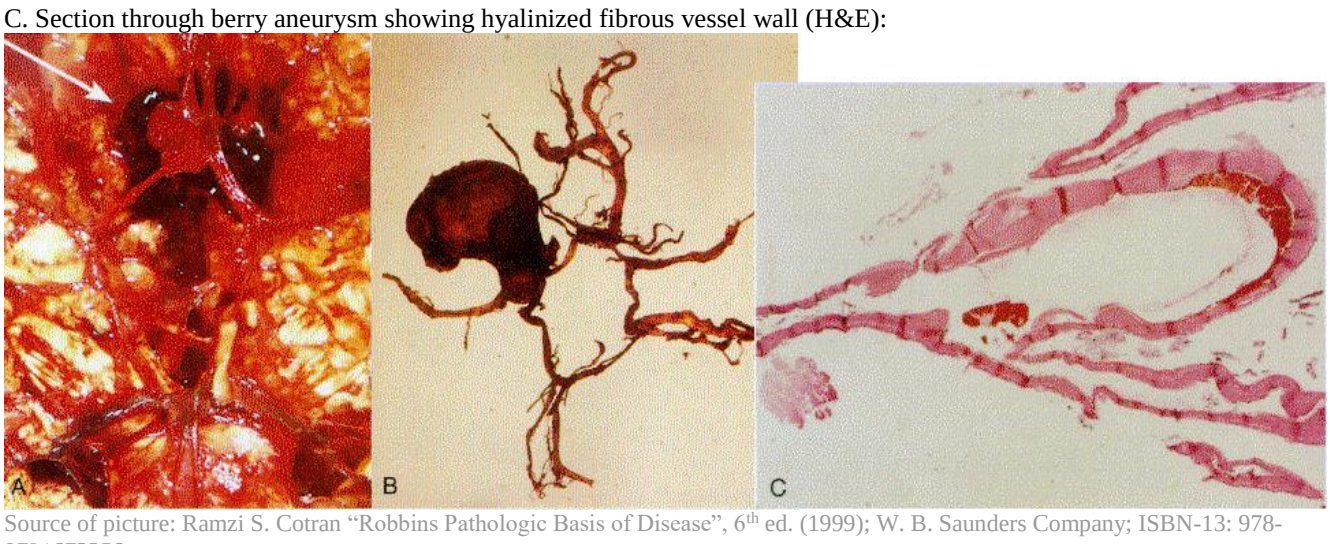
      a) septic embolus (e.g. IV drug abuse, bacterial endocarditis) → extension from lumen to adventitia; most common on DISTAL vessels (due to embolic nature).
      b) meningitis → extension from periphery to lumen (e.g. aneurysms of basal circulation associated with fungal infections).

      - frequently multiple (20%), very friable - greater propensity to bleed! (rupture is fatal in 80% patients!)

3. **Dissecting aneurysms** – when intramural hematoma extends into subadventitial plane (e.g. in fibromuscular dysplasia, trauma).
   - elongated, ovoid, or saccular.
   - most affect extracranial segments of ICA, VA.

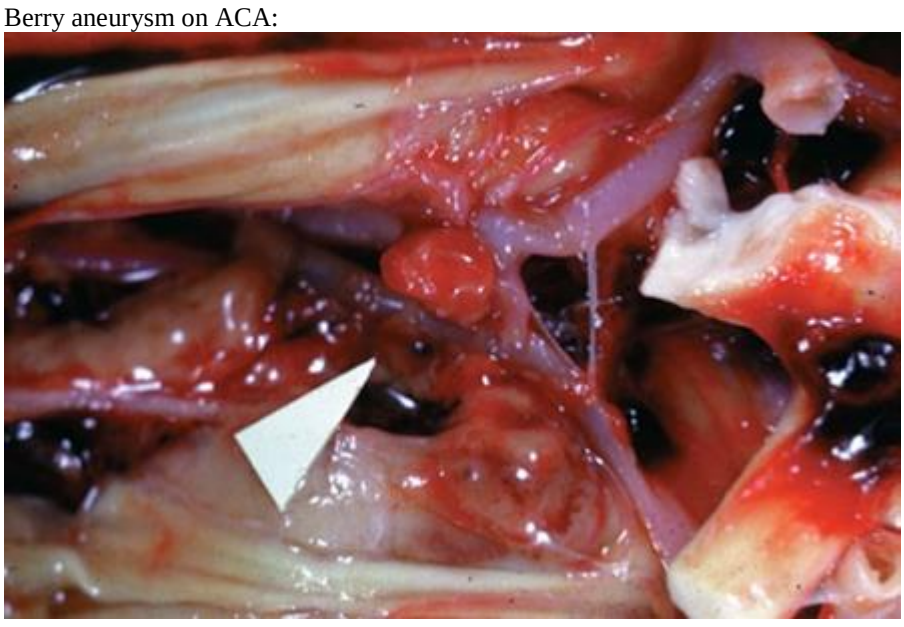
A. Dissected base of brain - aneurysm of ACA (*arrow*).
B. Dissected circle of Willis - large aneurysm.

C. Section through berry aneurysm showing hyalinized fibrous vessel wall (H&E):



Source of picture: Ramzi S. Cotran "Robbins Pathologic Basis of Disease", 6th ed. (1999); W. B. Saunders Company; ISBN-13: 978-0721673356 >>

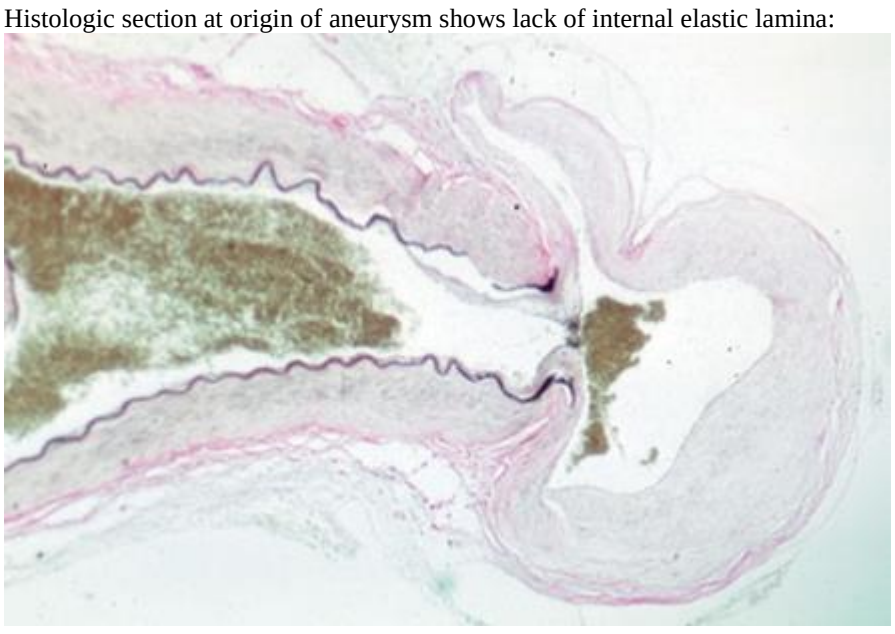
Berry aneurysm on ACA:



Three berry aneurysms:

Source of picture: "WebPath - The Internet Pathology Laboratory for Medical Education" (by Edward C. Klatt, MD) >>

Histologic section at origin of aneurysm shows lack of internal elastic lamina:



ANEURYSM GROWTH

- due to ***wall shear stress*** caused by rapid changes of blood flow direction (result of systole and diastole) - "water hammer effect".

- hemodynamic stresses continually damage intima at aneurysm cavity neck → progression of most saccular aneurysms.
- thrombosis and rupture are also explained by intra-aneurysmal hemodynamic stresses.
- ***arterial hypertension*** may contribute to, but is not only cause of, aneurysm formation and rupture; normal blood pressure in hemorrhagic stroke favors diagnosis of saccular aneurysm!

Geometric relationship between aneurysm and its parent artery:

Lateral aneurysms (e.g. arise directly from ICA) - blood moves into aneurysm at distal aspect of its ostium and exits at its proximal aspect, producing slow-flow vortex in aneurysm center; lumen opacification proceeds in cranial-to-caudal fashion; pronounced contrast stagnation!

Aneurysms that arise at origin of branching vessels or terminal bifurcation - rapid intra-aneurysmal circulation; no vortex formation, no contrast stasis.

N.B. these patterns of intra-aneurysmal flow influence use of endovascular treatment devices.

GIANT SACCULAR ANEURYSMS

- diameter > 2.5 cm.
- 3-5% of all intracranial aneurysms (3 times more common in women).
- slow growth occurs by ***recurrent intra-aneurysmal hemorrhages*** from highly vascularized membranous wall of aneurysm.
  - giant sacs commonly contain multilayered laminated clots of varying ages and consistency, which occasionally are calcified.
- outer wall is fibrous and thick (seldom rupture into subarachnoid space) - giant aneurysms typically produce ***symptoms related to mass effect*** and ***distal thromboembolism***.

MULTIPLICITY

Intracranial aneurysms are multiple in 10-30% cases (females : males = 5 : 1); of these:

75% have 2 aneurysms
15% have 3 aneurysms
10% have > 3 aneurysms (females : males = 11 : 1)

- multiple aneurysms are common with vasculopathies (e.g. FMD).
- many are at mirror sites bilaterally.

LOCATION

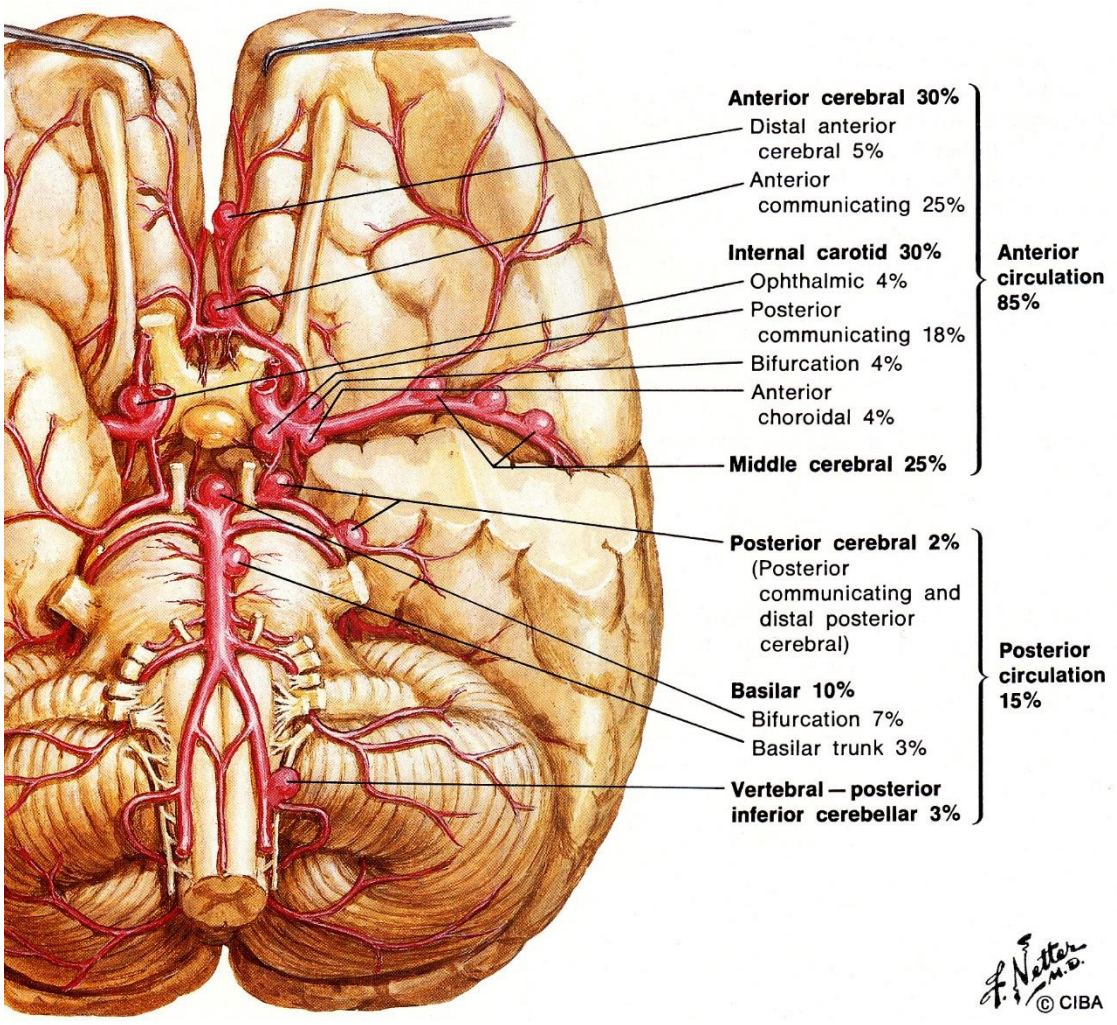
Traumatic, mycotic aneurysms – **distal sites** in intracranial circulation.

Saccular aneurysms (developmental / degenerative) – **proximal sites** (bifurcations of major arteries → rupture into basal cisterns):

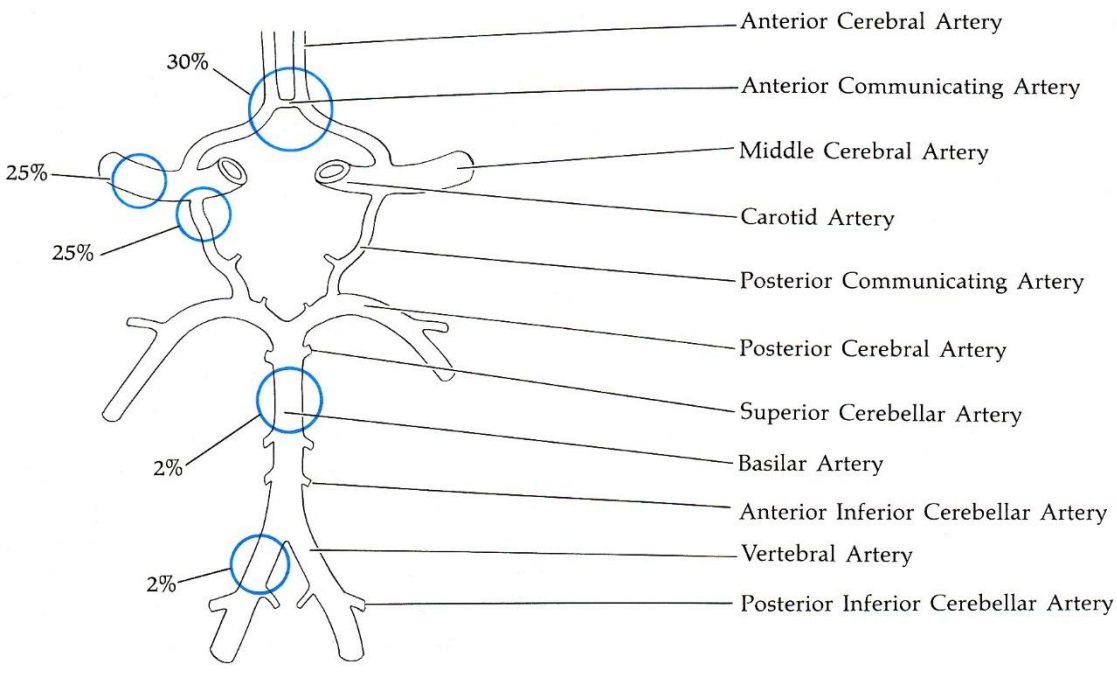
1. **Anterior (carotid) circulation** (86.5%)
   - AComA (25%)
   - PComA (25%)
   - MCA (20%)
   - ICA bifurcation (7.5%)
   - ACA (5%)
   - pericallosal/callosomarginal artery bifurcation (4%).
2. **Posterior (vertebrobasilar) circulation** (13.5%):
   - BA bifurcation (7%)
   - BA trunk (AICA origin, SCA origin) (3.5%)
   - PICA origin (3%)

N.B. **atherosclerotic aneurysms** affect predominantly **posterior circulation**.

- carotid artery is affected most commonly in individuals < 18 yrs.



Source of picture: Frank H. Netter "Clinical Symposia"; Ciba Pharmaceutical Company; Saunders >>



Ophthalmic complex aneurysms:

1. **Dorsal ophthalmic** – on ICA above ophthalmic branch
2. **Ophthalmic artery**
3. **Superior hypophyseal artery**

PEDIATRIC ANEURYSMS

- account for < 2% cases.
- most commonly **traumatic** and **mycotic**.
- posterior circulation aneurysms are more common.
- diameter ≈ 17 mm - larger than in adults!

EPIDEMIOLOGY

PREVALENCE: ≈ 1-2% (0.3-6%) population.

- female : male ratio = 1.6 : 1

RISK FACTORS

1. **Hypertension**
2. **Smoking**

Exposure to **exogenous estrogens** in women - associated with a lower frequency of cerebral aneurysms, based on a retrospective case-control study.

CLINICAL FEATURES

Aneurysm rupture:

a) **minor aneurysmal hemorrhage** (WARNING LEAK, s. SENTINEL BLEED) - may be clinically silent (or headache with meningeal irritation); may precede rupture with wide variation in latency.
b) **SAH** (significant morbidity and mortality) - most common presentation of intracranial aneurysm! *see below*
c) **intraparenchymal** hematoma (more common with distal aneurysms) ← direct rupture of aneurysm into brain, secondary rupture of subarachnoid hematoma into brain parenchyma.
d) **intraventricular** hemorrhage (13-28%) - sources are ACA-AComA (40%), ICA (25%), MCA (21%), VBA (14%).
e) **subdural** hematoma (2-5%) ← tearing of arachnoid by jet of blood.

- most aneurysms do not cause symptoms until they rupture.
- aneurysms typically become symptomatic in 40-60 years; peak incidence of SAH is 55-60 yrs.
- risk of rupture ≈ up to 1% per year;
  aneurysms < 7 mm or aneurysms in anterior circulation ≈ 0.05% per year
  aneurysms at other locations, aneurysms > 10 mm, aneurysms in patients who had bled from prior aneurysm ≈ 0.5% per year.
- risk factors for aneurysm growth and rupture:
  1) cigarette smoking
  2) female sex
  3) younger age
  4) hypertension
  5) aneurysm size (La Place law states that tension is determined by radius of aneurysm and pressure gradient across wall of aneurysm) - rupture rate is directly related to aneurysm size (≤ 5 mm - 2% risk of rupture; 6-10 mm - 40% have already ruptured upon diagnosis).
- traumatic aneurysms occasionally cause *epistaxis*.

Nonhemorrhagic symptoms (relatively uncommon):

More common with giant aneurysms (diameter > 2.5 cm)

1. **Mass effect**:
   1) **cranial neuropathies** (e.g. CN3 palsy due to PComA aneurysm - requires urgent treatment!!!).
   2) **visual loss** (ophthalmic artery aneurysm compresses CN2)
   3) **pituitary dysfunction** (intrasellar aneurysms)
   4) **seizures**
   5) subacute, unilateral, periorbital **headaches** (aneurysmal expansion, thrombosis, intramural hemorrhage)
   6) **brain stem compression** (respiratory dysfunction, cardiovascular instability)

2. **Emboli** → **TIAs / cerebral infarction** (esp. with large partially thrombosed MCA aneurysms)
   H: anticoagulation.
   N.B. it might be sign of ***sentinel bleeds*** when thrombi start forming and shedding!!! – pay close attention to such patients (anticoagulation might be dangerous?)

N.B. symptomatic aneurysms have significantly higher risk of rupture (6% per year).

SITE SPECIFIC CLINICAL FEATURES

- **AComA aneurysms** (usually silent until rupture) – suprachiasmatic pressure may cause altitudinal visual field deficits, abulia / akinetic mutism, amnestic syndromes, hypothalamic dysfunction, leg paraparesis (!)
- **ACA aneurysms** (usually silent until rupture) – frontal lobe syndromes, anosmia, motor deficits.
- **MCA aneurysms** – hemiparesis (face & hand), hemisensory loss, aphasia / visual hemineglect, visual field defects, pain in or behind eye and in low temple.
- **PComA aneurysms** – CN3 palsy (if acute – due to rapid aneurysm growth or sentinel bleed – both need urgent treatment!!!), hemiparesis, progressive retro-orbital headaches.
  30% of acute CN3 palsies are due to PComA aneurysms
- **ICA aneurysms**:
  SUPRACLINOID aneurysms – ophthalmoplegia (CN3), variable visual defects and optic atrophy (CN2), chiasmal compression (bilateral temporal hemianopsia), hypopituitarism, anosmia.
  INTRACAVERNOUS aneurysms (extradural - do not cause SAH) – ophthalmoplegia (CN3, 4, 6), facial sensory loss / facial pain mimicking trigeminal neuralgia (CN5), retroorbital pain.
- **basilar tip aneurysms** – bitemporal hemianopsia, oculomotor palsy, vertical gaze paresis, coma.
- **VA**, **PICA aneurysms** – vertigo, lateral medullary syndrome, ataxia, bulbar dysfunction, spinal involvement, occipital and posterior cervical pain.

DIAGNOSIS

Angiography – criterion standard; preferred in patients with SAH.
CTA – preferred for unruptured intracranial aneurysms.
MRA – alternative to CTA (esp. in screening for aneurysm or following after coiling*).
*CTA would have lots of metal artefacts and difficult visualization of any recurrences

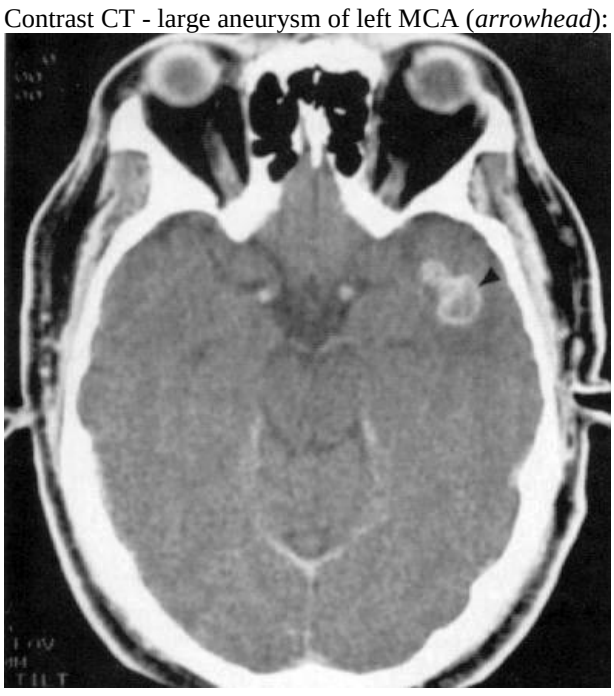
CT

Noncontrast CT can visualize *large aneurysms* (≥ 10 mm) or that *contain calcium* (mural calcification is uncommon, but both punctate and curvilinear types have been identified).

Accuracy of high-resolution axial CT in diagnosis of aneurysms ≥ 3 mm is ≈ 97%

- *bone erosion* in long-standing lesions near skull base.
- patent aneurysms - well-delineated, isodense ÷ slightly hyperdense mass in suprasellar subarachnoid space or sylvian fissure; IV contrast → enhance intensely and uniformly.
- partially thrombosed aneurysm - patent lumen inside thickened (often partially calcified) wall that is lined with laminated clot.
  – residual lumen and outer rim of aneurysm may enhance strongly with IV contrast.
  – atherosclerotic debris in aneurysm wall appears hypodense on CT.

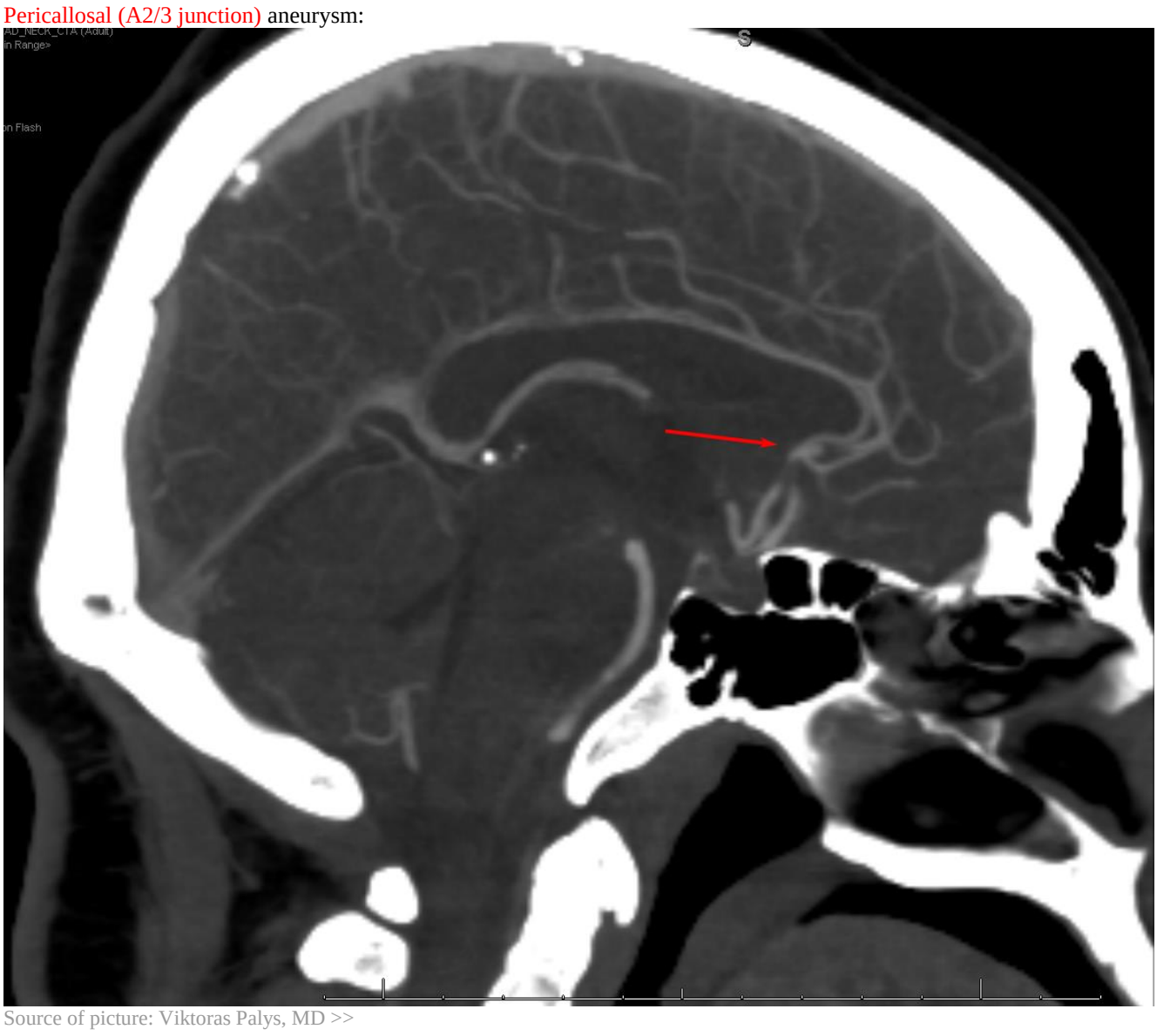
Contrast CT - large aneurysm of left MCA (*arrowhead*):



CTA

- sensitivity 97% in detecting aneurysms.
- important in detection of vasospasm.

Pericallosal (A2/3 junction) aneurysm:



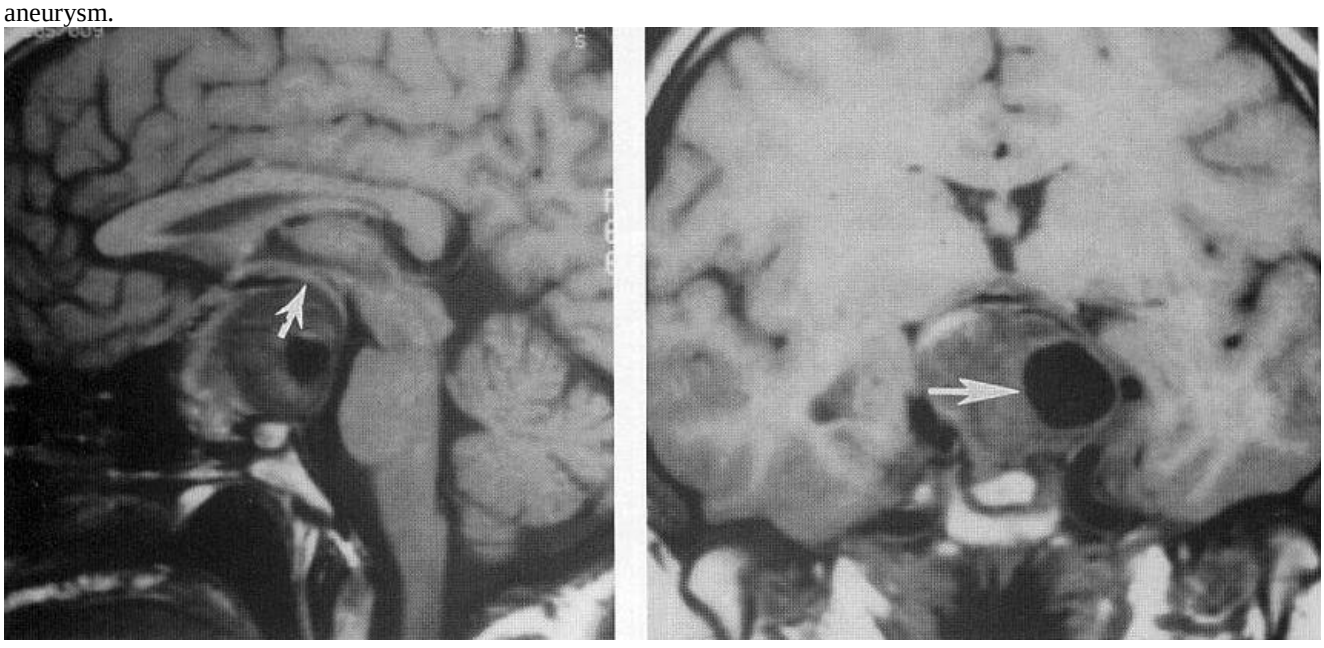
Source of picture: Viktoras Palys, MD >>

MRI

- aneurysm appearance is highly variable and complex!

- patent aneurysms - hyperintense or hypointense signals; well-delineated mass with high-velocity signal loss (flow void) on T1- and T2-weighted images; turbulent flow in aneurysm gives some signal heterogeneity (helps to differentiate aneurysms from other mass lesions).
  - IV contrast typically does not enhance patent aneurysms with high flow rates, but wall enhancement may occur.
- partially thrombosed aneurysms - complex MRI signal - area of high-velocity signal loss in patent lumen with surrounding concentric layers of multilaminated clot.
  - larger aneurysms may have thick signal void rim (hemosiderin-containing mural thrombus and hemosiderin-laden fibrous capsule).
  - if intraluminal flow is slow / turbulent, residual lumen may be isointense with remainder of aneurysm.
- completely thrombosed aneurysms - variable MRI findings;
  - *recently thrombosed* aneurysm may be isointense with brain parenchyma.
  - *subacute thrombus* is hyperintense on T1 and T2.
  - *repeated episodes of intramural hemorrhage* leave multilayered clots.

Giant aneurysm extending into suprasellar region:
A) sagittal T1-MRI - heterogeneous mass resulting in upward compression of 3rd ventricle floor (*arrow*).
B) coronal T1-MRI - large flow void (*arrow*) within lesion, indicating partially thrombosed giant suprasellar aneurysm.



MRA

- reliable 3D imaging of aneurysms ≥ 3 mm (sensitivity is 87% and specificity is 92%); most useful as screening tool.

- for **head** – MRA without contrast (time-of-flight TOF protocol).
- for **neck** – with gadolinium.

ANGIOGRAPHY

- criterion standard for revealing and delineating features of intracranial aneurysm.

- aneurysms may be multiple - visualizing entire intracranial circulation (incl. AComA, PComA, both PICAs) is important.
- **3D rotational angiography** is preferable.
- 6-vessel cerebral angiogram = both vertebral and internal carotid arteries + external carotid arteries (for dural AV fistula as cause of hemorrhage.)
- patent aneurysm - contrast-filled outpouching that arises from arterial wall or bifurcation.
- thrombosed aneurysm - occasionally appears normal; large thrombosed aneurysm can cause *avascular mass effect*.
- not indicated for benign perimesencephalic bleeds.

Aneurysms must be distinguished from:

1. **Infundibulum** (incomplete regression of fetal vessel);
   - most common location is at origin of PComA from ICA (less commonly - origin of anterior choroidal artery).

- smooth funnel-shaped triangular dilatations ≤ 3 mm in diameter, regular in shape, distal vessel exits from apex.
- found in 7-13% of otherwise normal arteriograms
- rarely may bleed
- 13 reported cases of progression to aneurysm.
- treat only if accessible during surgery for another reason – wrapping, or placing in encircling clip, or sacrificing artery if it can be done safely (infundibula lack true neck)

2. **Vascular loop** (overlapping projection of 3-dimensional vessel onto 2-dimensional image); H: 3D-angiography.

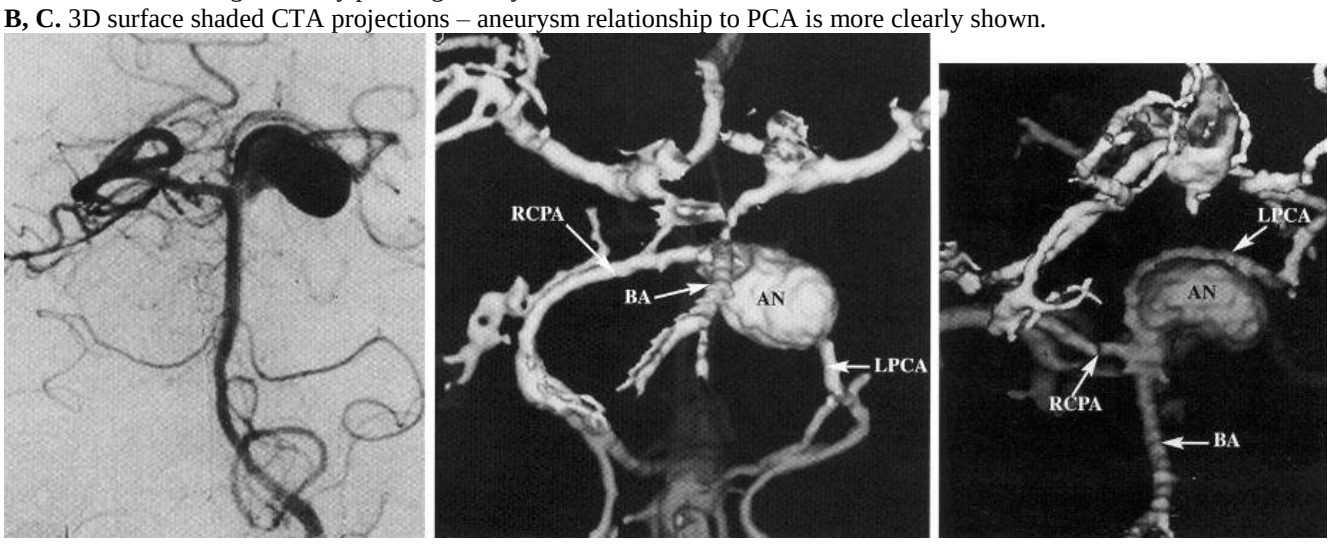
Features to take note of when analyzing angiogram:

1. **Dome size**:
   - aneurysm may be *partially thrombosed* and filling part may be much smaller than overall size (MRI or CT helps with this)
   - *large aneurysms* (≥ 15 mm diameter) are associated with lower rates of complete occlusion by coiling.
2. **Neck size**:
   - narrow necks < 5 mm are ideal for coiling (vs. *broad necks** ≥ 5 mm are associated with incomplete occlusion and recanalization with coiling)

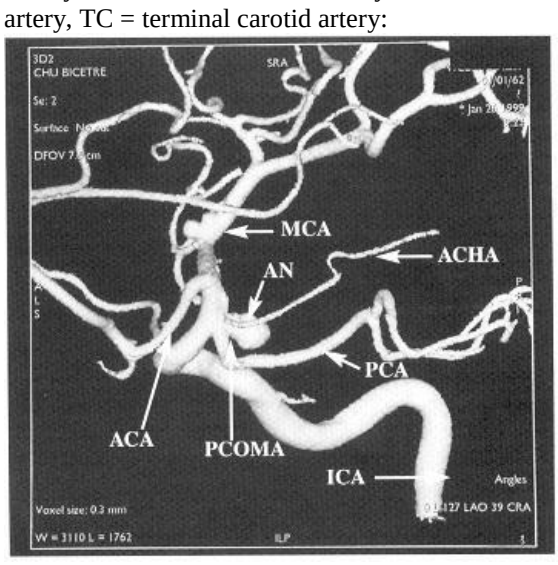
*stent or balloon-assisted coiling may be needed

3. **Dome : neck ratio** ≥ 2 is associated with higher rate of coil occlusion

Giant basilar tip aneurysm (AN = aneurysm, BA = basilar artery, LPCA = left posterior cerebral artery, RPCA = right posterior cerebral artery):
A. Townes view - large laterally pointing aneurysm.
B, C. 3D surface shaded CTA projections – aneurysm relationship to PCA is more clearly shown.



PComA aneurysm (3D rotational angiogram); origin of anterior choroidal artery lies close to, but is clearly separate from aneurysm sac; smaller MCA aneurysm. AN = aneurysm, ACHA =anterior choroidal artery, LACA = left anterior carotid artery, TC = terminal carotid artery:



Source of picture: Ronald G. Grainger, David J. Allison "Grainger & Allison's Diagnostic Radiology: A Textbook of Medical Imaging", 4th ed. (2001); Churchill Livingstone, Inc.; ISBN-13: 978-0443064326 >>

SCREENING

- with **MRA**.

Indications:

1) ≥ 2 immediate **relatives** with intracranial aneurysms
2) AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD)

Other: family history of SAH, sudden death, stroke and migraine.

Target population – all adults > 30 years within one generation from index case.

Recommendations in literature (for ADPKD patients)

Torres VE, Harris PC, Pirson Y. Autosomal dominant polycystic kidney disease. Lancet. 2007;369: 1287–1301.
Chapman AB, Devuyst O, Eckardt K-U, Gansevoort RT, Harris T, Horie S, et al. Autosomal-dominant polycystic kidney disease (ADPKD): executive summary from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Kidney Int. 2015

(i) no systematic screening of intracranial aneurysms in ADPKD patients
(ii) targeted screening in patients with a good life expectancy who present with a family history of intracranial aneurysms or SAH, patients with previous intracranial aneurysm rupture, those with high risk professions and anxious patients despite adequate information
(iii) the use of TOF MRI without gadolinium enhancement as the screening method of choice
(iv) rescreening at 5–10-year intervals in at-risk patients

Different opinions have also been published, advocating systematic screening for all patients with ADPKD as well as screening before major elective surgery or renal transplantation.

Jynarque (TOLVAPTAN) - selective vasopressin V2-receptor antagonist - first medicine to slow kidney function decline in adults at risk of rapidly progressing autosomal dominant polycystic kidney disease (ADPKD); due to possible liver injury Jynarque is available only through a restricted distribution program called the Jynarque REMS.

TREATMENT

Treatment of **ruptured** aneurysms differ significantly from **unruptured** aneurysms!

RUPTURED ANEURYSMS

- treated ***urgently*** (within 72 h of hemorrhage) - to prevent rebleeding and to permit aggressive management of vasospasm (with HHH). *see below (SAH) >>*

UNRUPTURED (INCIDENTAL) ANEURYSMS

- managed ***electively***:

a) **close OBSERVATION** (e.g. annual CTA) – possible indications:

< 7 mm incidental aneurysms in anterior circulation have very low rupture risk in patients with no history of SAH

1) patient's life expectancy < 5 years – any type of treatment carries 5% risk of complications; aneurysm rupture risk is 1%/year – to outweigh risks, patient must live > 5 years after treatment!
2) no previous SAH
3) aneurysm diameter < 5-10 mm (esp. if patient's age > 50 yrs)
4) mycotic aneurysms – first treat with a/b (observe shrinkage with angiography q7-10 days; if aneurysm enlarges, it should be attacked surgically).
5) small AVM-related aneurysms (may disappear or shrink after successful treatment of AVM)

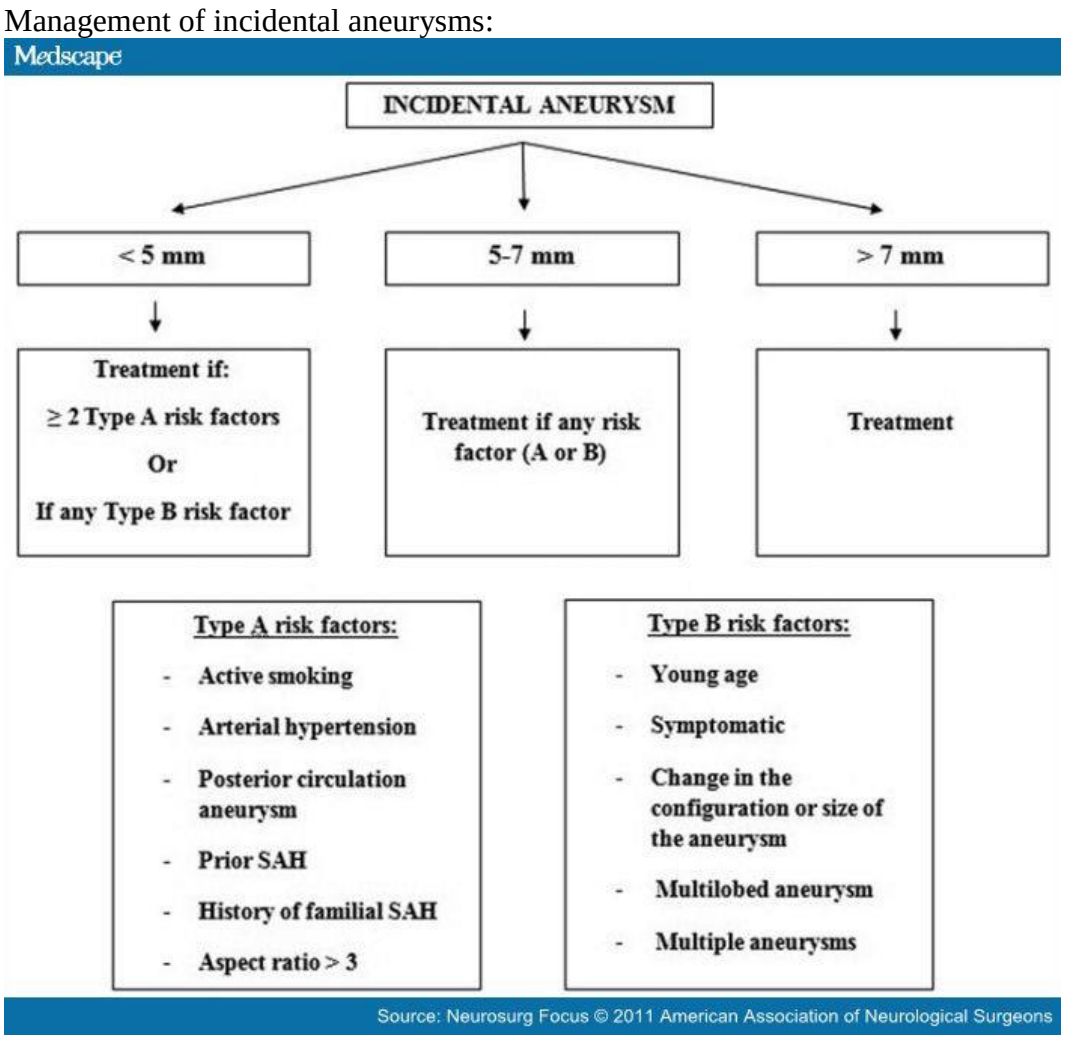
- **educate** such patients about:
  - warning signs and symptoms of SAH!
  - the only lifestyle modification that is necessary – to stop smoking!

b) **TREATMENT** (**clipping** or **coiling***) – possible indications: *see below (SAH) >>*

1) young patients regardless of aneurysm size
2) symptomatic aneurysm (symptoms must be pathophysiologically related to aneurysm)
3) aneurysm growth (increase in diameter ≥ 1 mm) / change of configuration (e.g. development of bleb)
4) previous ruptured aneurysm

*endovascular approach is first line treatment

Management of incidental aneurysms:



N.B. posterior circulation aneurysms have higher risk of rupture!

- most neurosurgeons would treat ant. circulation aneurysms if they are > 4-5 mm (esp. young patient with newly discovered aneurysm vs. you would leave alone stable 7 mm aneurysm that was discovered 10 years ago in 85 yo patient).

International Study of Unruptured Intracranial Aneurysms (ISUIA)

International Study of Unruptured Intracranial Aneurysms Investigators. Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment. Lancet 2003 ; 3 62 : 103 – 110.

- natural history of unruptured aneurysms + risks of treatment of unruptured aneurysms

- 4060 patients from 61 centers worldwide.
- ***risk of rupture*** for a particular aneurysm over the patient's remaining lifetime can be compared to the ***mortality/morbidity risk of treatment*** (7.1-12.6%).
- 5-year cumulative rupture rates (5 YRR):

(multivariate analysis showed that age was not a factor)

< 7 mm aneurysms:

	Cumulative 5 YRR	
	Group 1	Group 2
Cavernous carotid artery aneurysms	0	0
A.comm or ACA aneurysms	0	1–5%
Vertebrobasilar, PCA or P.comm aneurysms	2–5%	3–4%

Group 1 – no previous SAH. Group 2 – previous SAH from a separate aneurysm; no difference between groups in aneurysms ≥ 7 mm

7–12 mm aneurysms:

	Cumulative 5 YRR
Cavernous carotid artery aneurysms	0
A.comm or ACA aneurysms	2–6%
Vertebrobasilar, PCA or P.comm aneurysms	14.5%

> 12 mm aneurysms:

	Cumulative 5 YRR	
	13–24 mm	>25 mm
Cavernous carotid artery aneurysms	3.0%	6.4%
A.comm or ACA aneurysms	15.5%	40%
Vertebrobasilar, PCA or P.comm aneurysms	18.4%	50%

FOLLOW-UP

See below >>

SUBARACHNOID HEMORRHAGE (SAH)

- blood extravasation into subarachnoid space (between pia and arachnoid).

ETIOLOGY

1. **Traumatic SAHs** (most frequent SAHs!) see p. TrH1 >>
2. **Nontraumatic SAHs**:

In 15-20% of SAH patients, angiography fails to identify an etiology!

a) 75-90% - **aneurysm** rupture (tear is at dome and ≤ 0.5 mm long); peak age 55-60 yrs (only 20% cases occur at age 15-45 yrs).
a) 4-10% - bleeding from **AVM**; most patients 20-30 yrs.
b) 5-15% - **other**:
1) ***benign (nonaneurysmal) perimesencephalic SAH*** - bleeding immediately anterior to brainstem and adjacent areas (interpeduncular fossa, ambient cisterns) - rupture of *small pontine or perimesencephalic veins* (i.e. not arterial source - **prognosis is excellent – no rebleeds reported**!)
- imaging - center of hemorrhage is anterior to midbrain with or without extension of blood to the anterior part of the ambient cistern or the basal part of the sylvian fissure, incomplete filling of the anterior interhemispheric fissure and no extension of the lateral sylvian fissure or the ventricles.
- patients less commonly develop hydrocephalus, vasospasm, or other complications and have lower risk of recurrent bleeding - no need for repeat angiography.

2) ***occult aneurysm*** (initially compressed by hematoma or did not opacify because of vasospasm or clot); H: repeat angiography (1 wk later); indication for 3rd angiogram:
a) blood just in front of brainstem – benign perimesencephalic SAH – 3rd angio not indicated.
b) blood more widely distributed – 3rd angiogram 6 weeks later: 4-5% chance of detecting aneurysm.
3) intracranial artery ***dissection***
4) bleeding from ***tumor*** (such as pituitary adenoma).
5) ***spinal cord*** aneurysm or AVM.
6) ***dural malformation***
7) some ***drugs*** (e.g. cocaine)
– 50% patients who have drug abuse problem along with CNS symptoms have SAH (of these 50% have underlying abnormality such as aneurysm or vascular malformation; others are due to hypertensive response to drugs)
8) amyloid angiopathy, bleeding diatheses, sickle cell anemia, pituitary apoplexy

- relationship between **hypertension** and aneurysmal SAH is "uncertain".
hypertension per se is not significant risk factor, but aneurysms do rupture under conditions associated with sudden BP rise (coitus, athletic events, etc)
- evidence for association with **smoking** is indirect.

EPIDEMIOLOGY

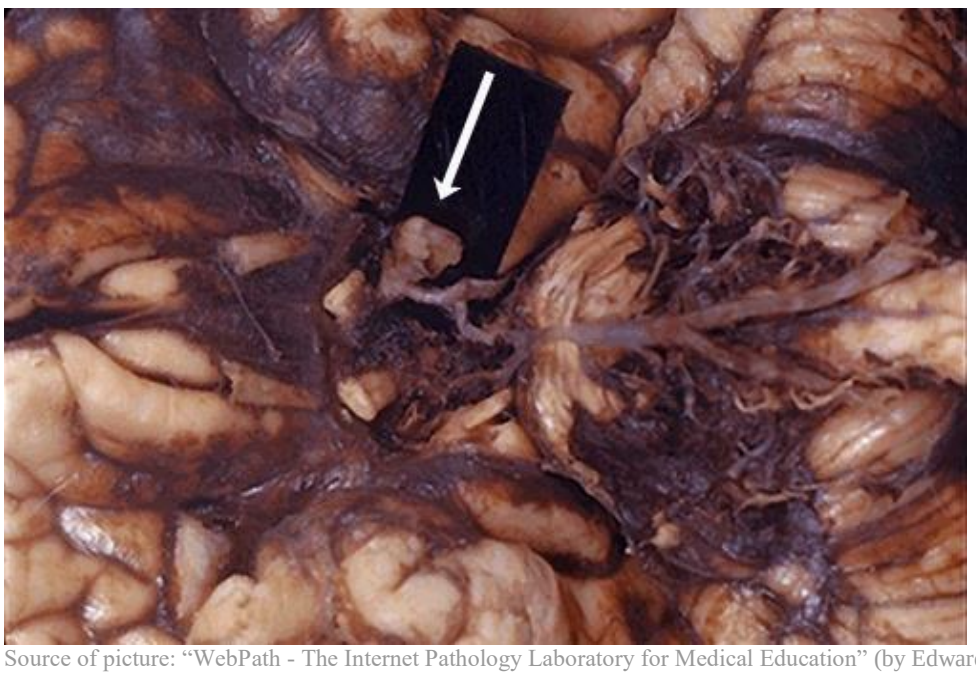
- INCIDENCE has not decreased over decades (unlike for other stroke categories), but survival improved;
– 10-fold variation in age-adjusted incidence: from 2.0 cases / 100 000 population / year in China to 22.5 cases / 100 000 / year in Finland (a little bit less in Japan)
– rate of aneurysmal SAH in western populations: 6-8 / 100,000 population / year
– *incidence increases with age* and peaks at 50 yrs.
80% SAHs occur in people aged > 40 years
15% in people aged 20-40 years
4.5% in people aged 10-20 years
0.5% in children < 10 years
- significant risk factors for aneurysmal SAH:
1) smoking (risk of SAH increased 3-6-fold; risk increased 6-fold if positive family history of aneurysmal SAH).
2) hypertension (conflicting data – *see above*)
3) North American blacks (2.1 times greater risk than in whites)
4) females (1.24 : 1)
5) 3rd trimester of pregnancy*- SAH is leading cause of maternal mortality (5-25% maternal deaths during pregnancy):
75% from aneurysms (esp. older multiparous women)
25% from AVMs (esp. younger nulliparous women)
*recent reviews have suggested that, contrary to conclusions from prior studies, risk of SAH is not increased during pregnancy.
6) hormone replacement therapy in postmenopausal women
7) heavy alcohol consumption (controversial)
8) reduced lung function (reduced FEV1, reduced FEV1/FVC) - significantly associated with increased incidence of SAH - comparable with effects of hypertension and smoking
"Our hypothesis is that matrix degradation of vessel walls, which is major reason for SAH, and degradation of lung tissue, which is major reason for reduced FEV1, share common mechanisms"
9) long-term (esp. > 3 years) low-dose **ASPIRIN** has protective effective against SAH and does not increase risk of intracerebral hemorrhage.

- aneurysm size matters; AComA aneurysm size correlates linearly with risk of rupture.
- oral contraceptives, hormone replacement therapy, hypercholesterolemia, physical activity are not significantly related!

PATHOLOGY

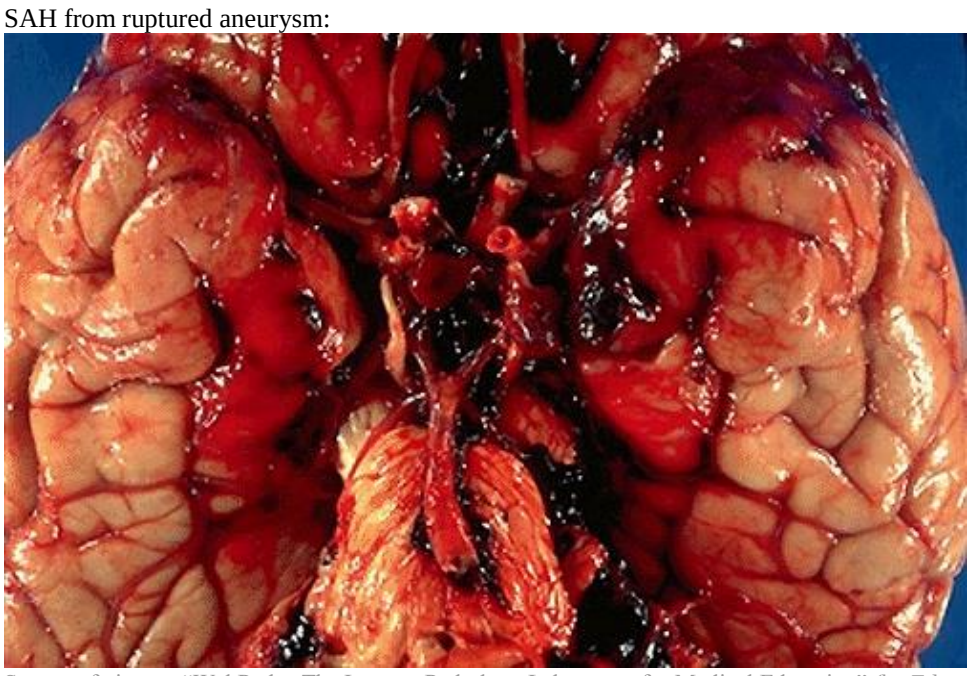
- surrounding brain parenchyma - **brownish pigmentation** and **fibrous adhesions**.
- aneurysm size may be diminished postmortem.
- ruptured fundus may be visualized with ***calcifications of aneurysm wall*** and ***intraluminal thrombus***.
- SAH may be complicated by:
intracerebral hemorrhage (20-40%)
intraventricular hemorrhage (13-28%)
subdural hematoma (2-5%) - over *convexity* (most commonly due to PComA aneurysm) or *interhemispheric* (distal ACA).

Ruptured berry aneurysm in circle of Willis:



Source of picture: "WebPath - The Internet Pathology Laboratory for Medical Education" (by Edward C. Klatt, MD) >>

SAH from ruptured aneurysm:



Source of picture: "WebPath - The Internet Pathology Laboratory for Medical Education" (by Edward C. Klatt, MD) >>

CLINICAL FEATURES

- 10-50% patients had **premonitory symptoms** 10-20 days (few hours ÷ few months) prior to rupture (due to sentinel leaks, aneurysm expansion, embolization) *see above*

  Sentinel SAH headache should be considered in differential diagnosis of all new headache!

- 30-40% patients are at rest at time of SAH (e.g. sleeping);
  remaining 60-70% are at physical / emotional strain (defecation, coitus, head trauma, etc).

1. Sudden excruciating **headache** ("thunderclap headache"* - "worst in patient's life") – localized (to side of aneurysm) or generalized.
- reaches maximum intensity within 1 minute.
- location of headache is variable - does not give clue as to site of hemorrhage.
- present in 97% cases; absence of headache represents amnesia for event.

*N.B. thunderclap headache is not limited to SAH and may be seen with cerebral venous thrombosis, reversible cerebral vasoconstriction syndromes, crash migraine, benign orgasmic cephalgia - lack of SAH evidence should prompt **MRV**, **CTA**; angiography no longer recommended

2. Arterial blood (pressure 100-150 mmHg) squirting into CSF space (pressure ≈ 10-15 mmHg) → sudden ICP elevation (± transient abrupt generalized vasospasm, seizures) → transient* **alteration in consciousness** (syncope in 33-50% cases at onset**).

*10% patients are comatose for several days

**massive SAH, in contrast to other kinds of stroke, may cause sudden death!

Deterioration of consciousness few days after hemorrhage:
a) rebleeding (sudden worsening)
b) vasospasm (gradual deterioration)
c) hydrocephalus (gradual deterioration)

3. Blood induces **STERILE MENINGITIS** → **meningeal irritation signs** (neck stiffness, photophobia, nausea & vomiting, low back pain*) - may take several hours to manifest; may become more severe during first week (blood breakdown in CSF).

*irritation oflumbar nerve roots by dependent blood

4. **Focal neurological findings**;
- CN3 palsy is most frequent (PComA aneurysm).
- CN6 palsy is due to ICP↑ (false localizing sign).
- clinical signs can localize ruptured aneurysm in only ≈ 30% patients.

5. Focal or generalized **seizures** (10-25%) - most occur within 24 hours (sudden ICP rise + direct cortical irritation by blood).

6. **Autonomic disturbances** (due to subarachnoid accumulation of blood degradation products – CHEMICAL HEMIC MENINGITIS) – fever (!), nausea & vomiting (!), sweating, cardiac arrhythmias / ischemia.

7. **Ocular hemorrhage** (20-40%) - elevated ICP causing venous hypertension and disruption of retinal veins.
1) **subhyaloid (preretinal) hemorrhage** - seen funduscopically in 11-33% cases as bright red blood near optic disc that obscures underlying retinal vessels.
2) **(intra)retinal hemorrhage**: may surround fovea
3) hemorrhage within vitreous humor (**Terson syndrome**);
   - funduscopy reveals vitreous opacity
   - usually bilateral.
   - complications: elevated intraocular pressure, retinal membrane formation → retinal detachment, retinal folds.
   - vitrectomy if vision fails to improve spontaneously in 6-12 mos
   - long-term prognosis for vision is good

GRADING CLINICAL SEVERITY

Hunt & Hess scale (on admission and pre-op):

Grade	Clinical Findings	Survival Rate	Vasospasm Rate
0	unruptured aneurysm		
1	asymptomatic (or minimal headache and slight nuchal rigidity)	70%	22%

1A	no acute meningeal or brain reaction but *fixed neurologic deficit*		
2	moderate ÷ severe headache and nuchal rigidity, no neurologic deficit other than CN palsy	60%	33%
3	lethargy, confusion, mild focal deficit	50%	52%
4	stupor, moderate ÷ severe hemiparesis, possible early decerebrate rigidity, and vegetative disturbances	20-40%	53%
5	deep coma, decerebrate rigidity, moribund appearance	10%	74%

Add one grade for **serious systemic disease** (HTN, DM, COPD, severe atherosclerosis) or **severe vasospasm** on angiography

International Cooperative Aneurysm Study:
Grades 1 and 2 were operated upon as soon as aneurysm was diagnosed; Grade 3 managed until condition improved to Grade 2 or 1 (exception: life threatening hematoma or multiple bleeds which were operated on regardless of grade).
Study results:
- with normal consciousness, H&H grades 1 and 2 had identical outcome; hemiparesis and/or aphasia had no effect on mortality.
- mortality:
  - admission H&H grade 1 or 2: 20%.
  - patient taken to OR (for any procedure) at H&H grade 1 or 2: 14%.
  - major cause of death in Grade 1 or 2 is rebleed.
  - signs of meningeal irritation increases surgical risk.

World Federation of Neurological Surgeons (WFNS) Scale:

Grade	Glasgow Coma Scale	Clinical Findings
I	15	No headache or focal signs
II	15	Headache, nuchal rigidity, no focal signs
III	13-14	
IV	7-12	Headache, nuchal rigidity, focal signs
V	3-6	

New version - **World Federation of Neurological Surgeons (WFNS) Scale**:

Grade	GCS	Major focal deficit*
I	15	-
II	13-14	-
III	13-14	+
IV	7-12	+/-
V	3-6	

*aphasia, hemiparesis / hemiplegia

DIAGNOSIS

Algorithm in suspected SAH:

CT without contrast
positive ↓ positive ← ↓ negative
angiography **LP**

NONCONTRAST CT

Acute SAH - areas of increased density in subarachnoid spaces.
- IV contrast may obscure SAH detection!

False-negative CT:
a) hemorrhage from lesion in *spinal cord*.
b) CT performed *too early* (only small amount of blood being present).
c) subarachnoid *blood disappeared* before imaging.

CT sensitivity 95-98% (maximum sensitivity is within 12-48 hours)

sensitivity decreases to 80% at 72 hours, 50% at 1 week

Negative CT does not preclude SAH!!!

For subtle SAH, look in occipital horns of lateral ventricles and dependent portions of sylvian fissures.

If CT is negative, but SAH is still suspected → lumbar puncture or repeat CT later or FLAIR MRI

In patients with minimal symptomatology (e.g. sentinel leaks), lumbar puncture is considerably more accurate than CT!

N.B. you have only one chance with LP – if you repeat it, it will be flase-positive from small amount of blood from first LP

Bleeding site localization:

N.B. blood may quickly spread diffusely throughout CSF spaces, providing little clue to its site of origin.
- *suprasellar cistern* blood is common from many bleeding sites.
- blood within *cistern of lamina terminalis, anterior interhemispheric fissure* – AComA.
- blood within *sylvian fissure* – MCA or PcomA.
- blood predominantly in *prepontine or peduncular cistern* – basilar apex or SCA.
- *lateral ventricle* blood – AComA
- *3rd ventricle* blood – basilar tip.
- *4th ventricle* blood – posterior fossa aneurysms (esp. at PICA takeoff) – almost pathognomonic for PICA!!!!
- surrounding edema and inflammation may be appreciated with IV contrast following noncontrast CT.

blood in basal cisterns, sylvian fissure, or intrahemispheric fissure - **saccular aneurysm** rupture;
blood over convexities or within superficial brain parenchyma - **AVM** or **mycotic aneurysm** rupture.

HIJDRA score - amount of cisternal and ventricular blood seen on CT.

FISHER grade - amount of blood seen on CT (predicts vasospasm):
Fisher 1 - no blood detected
Fisher 2 - diffuse thin (< 1 mm) layer, no clots
Fisher 3 - localized clot and/or vertical layer (≥ 1 mm) – high risk of vasospasm!
Fisher 4 - intracerebral or intraventricular clot with diffuse or no SAH.

Only Fisher 3 is associated with clinical vasospasm (amount of blood in cisterns and fissures is important prognosticator for vasospasm!)

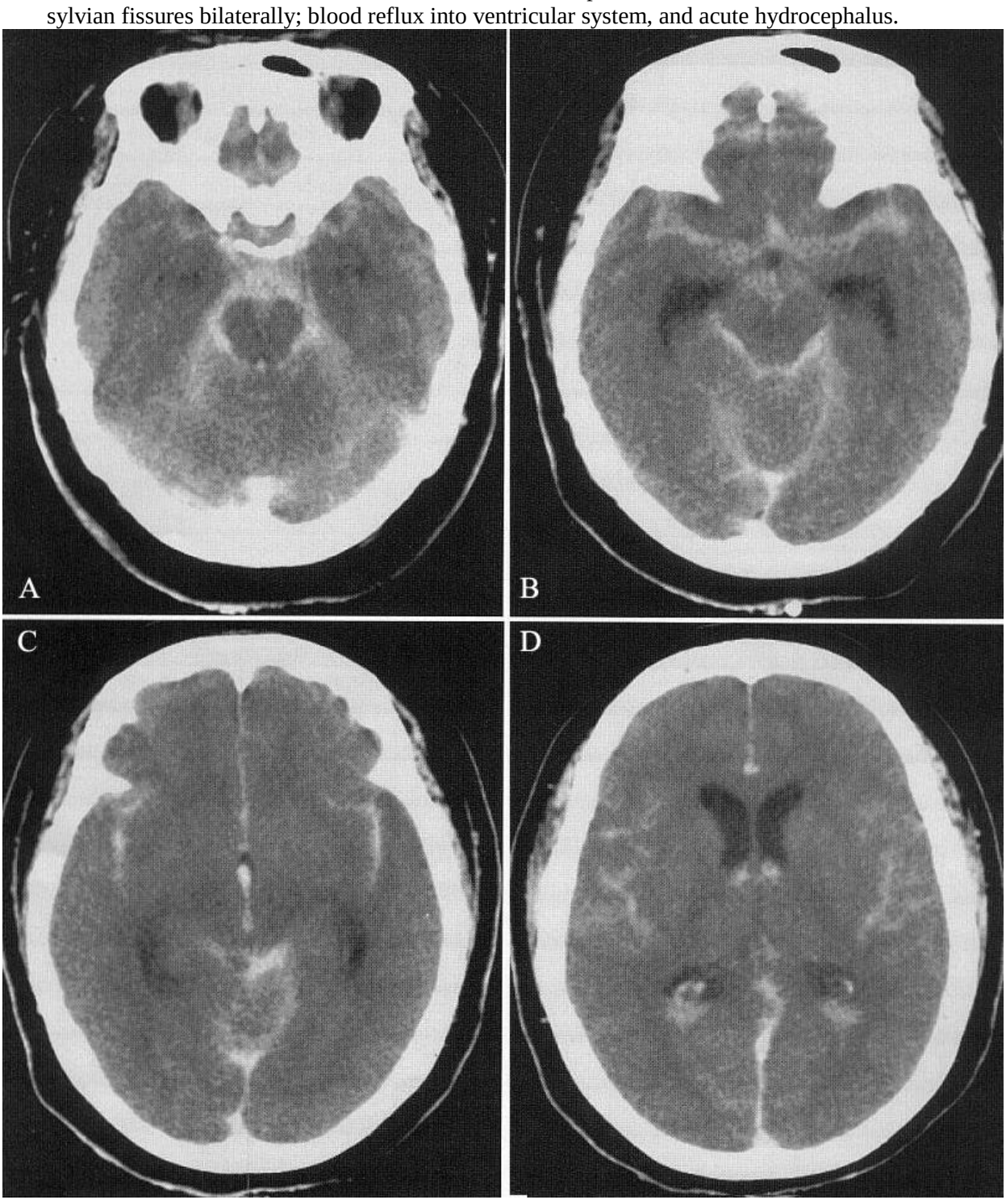
- "vertical layer" refers to blood within "vertical" subarachnoid spaces including interhemispheric fissure, insular cistern, ambient cistern

– reflux of blood into ventricles frequently indicates obstruction of CSF circulation, and is associated with high incidence of hydrocephalus

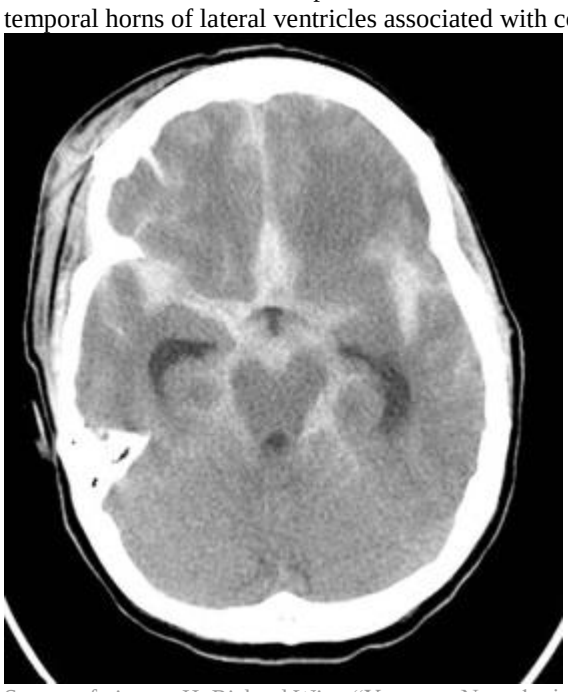
Things that can mimic SAH on CT:

1. Pus
2. Contrast (IV and especially intrathecal)
3. Pachymeningeal thickening seen in spontaneous intracranial hypotension

Nonenhanced CT - massive SAH in basal cisterns and supracerebellar cistern and lesser amounts in sylvian fissures bilaterally; blood reflux into ventricular system, and acute hydrocephalus.

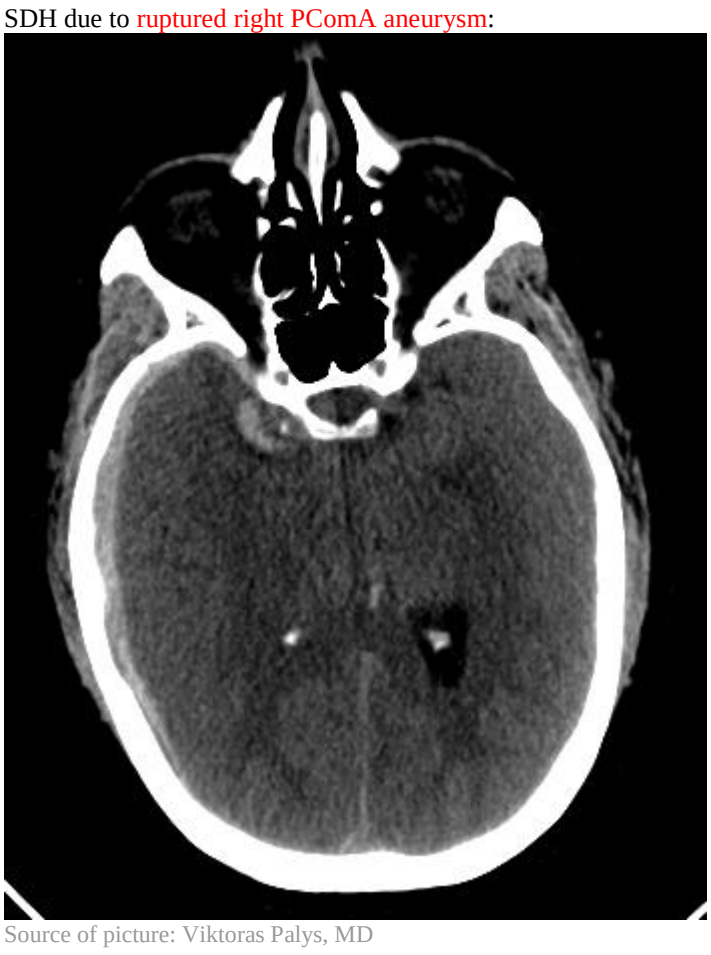


Acute diffuse SAH within suprasellar cistern, ambient cistern, and frontal and temporal sulci. There is dilation of both temporal horns of lateral ventricles associated with communicating hydrocephalus:



Source of picture: H. Richard Winn "Youmans Neurological Surgery", 6th ed. (2011); Saunders; ISBN-13: 978-1416053163 >>

SDH due to ruptured right PComA aneurysm:



Source of picture: Viktoras Palys, MD

LUMBAR PUNCTURE

- most sensitive test for SAH - indicated if CT is negative - ***nonclotting hemorrhagic*** CSF with ***xanthochromic*** supernatant (may be absent within first few hours!; 100% present after ≥ 12 hours).

Parameter	"Traumatic Tap"	SAH
Xanthochromia	Absent	Onset: 4-6 hr Still present in 40% at 4 wks
RBC count (serial tubes)	Decreasing	Constant
Blood clot formation	Rapid	Slower

- opening pressure↑ (remains for many days), proteins↑
- proportion of WBCs to RBCs is that of peripheral blood (≈ 1:1000) → WBC count increases after 24 hours (chemical meningitis); also [glucose] decreases.
- LP should not be performed if CT demonstrates SAH.
  N.B. if aneurysm is unsecured, excessive lowering of CSF pressure increases transmural pressure across wall of aneurysm → rebleed (remove only minimum volume of CSF needed for diagnostic studies).
- you have *only one chance*; repeat LP may be xantochromic from previous LP.
- differential of xanthochromia: jaundice, high protein levels in CSF.

ANGIOGRAPHY

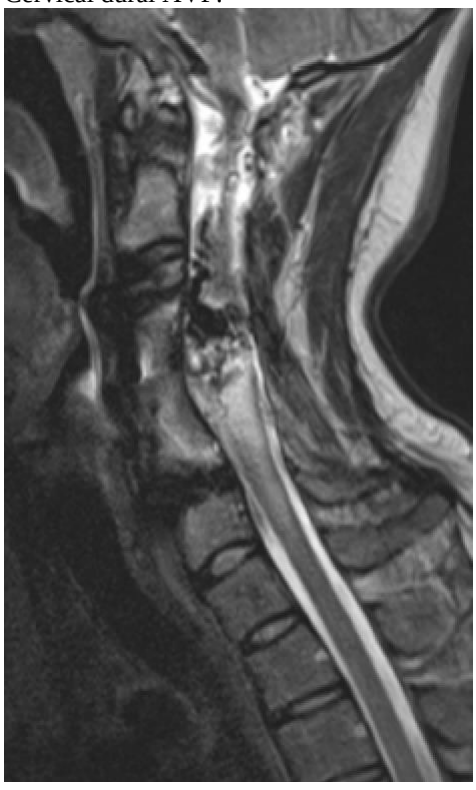
- indicated in all patients after SAH diagnosis!

- explore all 4 vessels.
- signs of ruptured aneurysm (if ≥ 1 aneurysm is found - which aneurysm needs to be treated acutely):
  1) **contrast extravasation** (pathognomonic but extremely rare)
  2) **larger aneurysm** will be site of rupture more frequently than smaller one – most important (practically) criterion! (all others below – only soft signs)
  3) **mass effect** adjacent to aneurysm (focal parenchymal or cisternal hematoma)
  4) **focal vasospasm** (but subarachnoid blood quickly spreads along basal cisterns)
  5) **irregularly shaped** aneurysm (lobulation, smaller daughter dome)
     Murphey's "teat," "tit," or "excrescence" - Dr. Francis Murphey (the Semmes-Murphey Clinic in Memphis, Dr. Murphey did not formally publish this important work) recognized that a ***focal sacculation on the dome of an aneurysm*** may be angiographic evidence of a culpable aneurysm in the setting of SAH with multiple intracranial aneurysms present.

N.B. acute angiography occasionally yields negative results (e.g. due to thrombosis or vasospasm) → repeat angiography 1 and 4* weeks later.
*3 angiograms still give 4% false-negatives; 4-week angio is not indicated if SAH blood pattern is compatible with benign perimesencephalic bleed

Before calling angiogram negative, one must:
1) visualize **both PICA origins** (via one VA injection if there is enough reflux down contralateral VA).
2) visualize **AComA***; if both ACAs fill from one side, this is satisfactory.
   * perform ***cross compression*** AP study with carotid injection (first, rule-out plaque in carotid to be compressed), or use a ***higher injection rate*** to facilitate flow
3) see no **infundibulum** (see above) co-localized to SAH.

- after first negative angiogram, order **cervical MRI** to rule out cervical AVM / AVF as source of SAH.
  Cervical dural AVF:



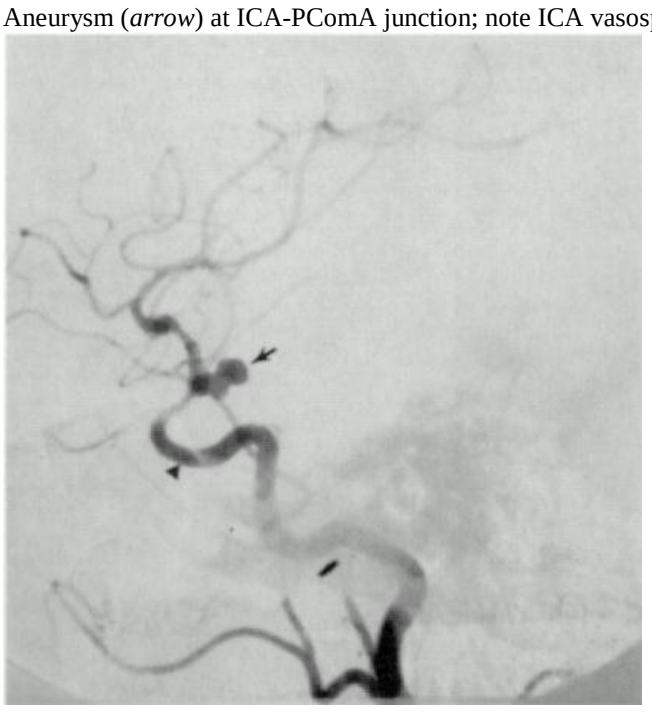
- ***trial balloon occlusion of parent artery*** - for giant and fusiform aneurysms that may need to be surgically "trapped" because they lack defined neck for surgical clipping.

Diagnostic yield in angiographically negative SAH:
Sadigh G et al. Radiological Management of Angiographically Negative, Spontaneous Intracranial Subarachnoid Hemorrhage: A Multicenter Study of Utilization and Diagnostic Yield. Neurosurgery 85:126–133, 2019

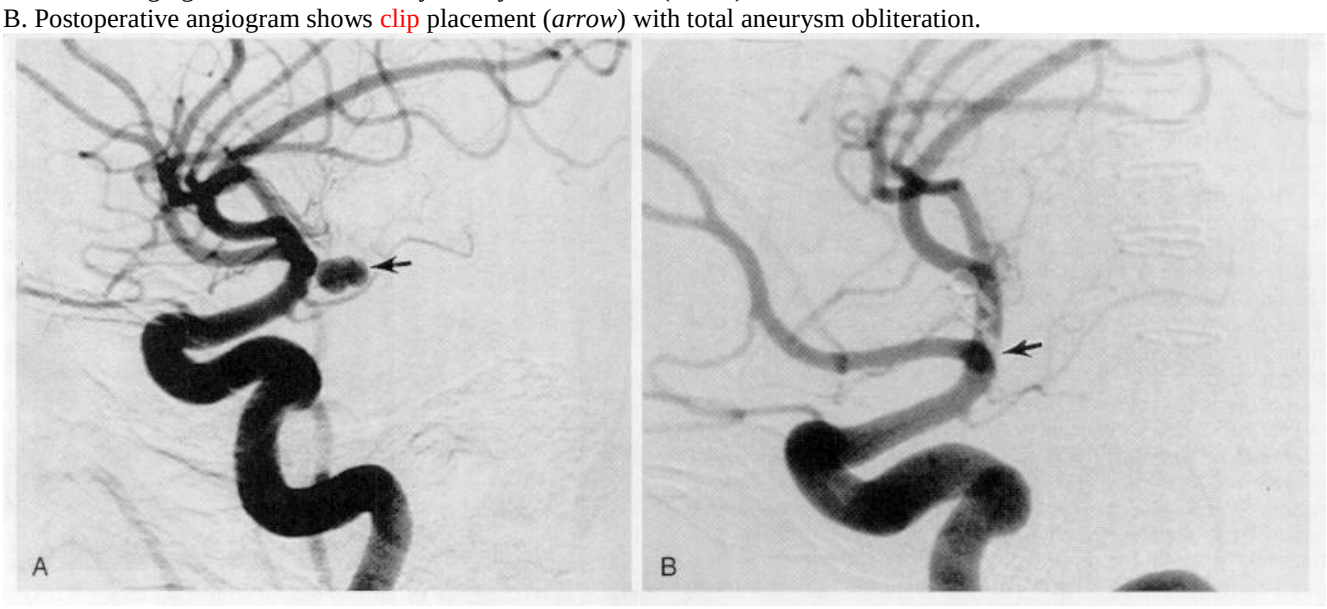
brain MRI – positive in 0.7% (1.2% in nonperimesencephalic pattern)
cervical spine MRI – positive in 0.2% (0.3%)
same-admission **follow-up DSA** – positive in 3.3% (7.4%)
same-admission **follow-up CTA** – positive in 1% (1.7%)
after discharge **follow-up DSA** – positive in 2%
after discharge **follow-up CTA** – positive in 3.7%

In patients with perimesencephalic hemorrhage, none of the follow-up imaging was positive for any etiology to explain SAH!

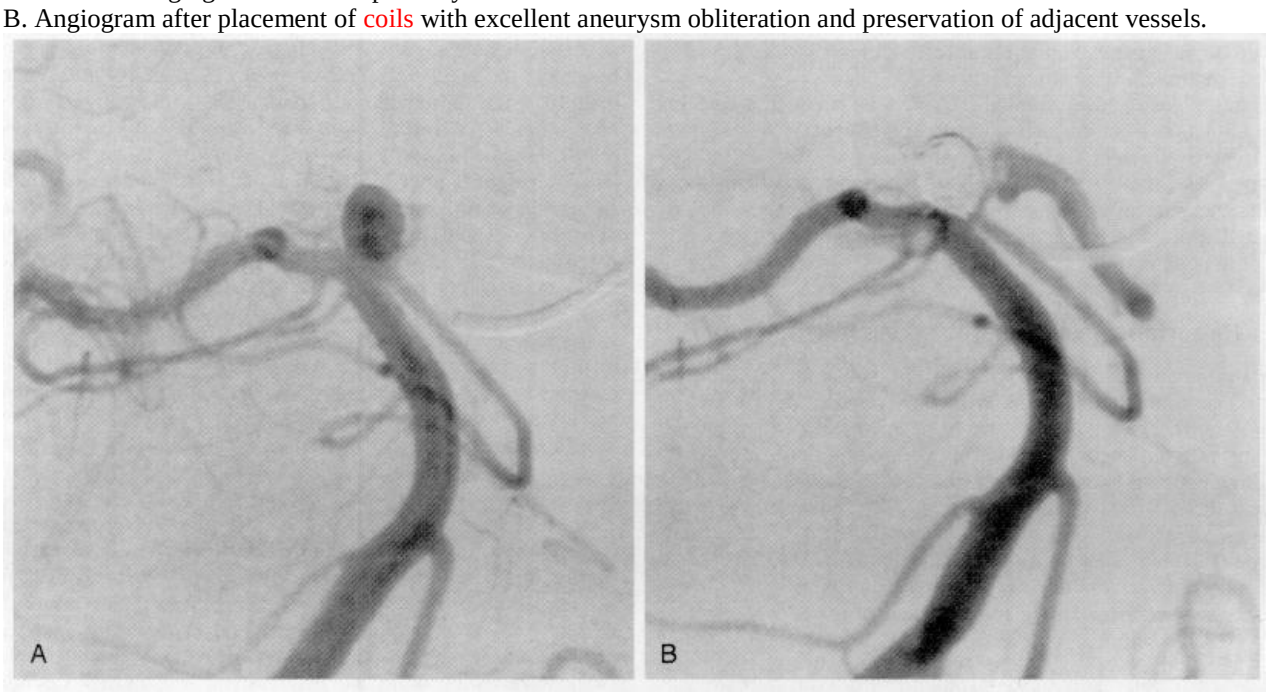
Aneurysm (*arrow*) at ICA-PComA junction; note ICA vasospasm adjacent to aneurysm:



A. Carotid angiogram - distal ICA berry aneurysm 4 × 6-mm (*arrow*)
B. Postoperative angiogram shows clip placement (*arrow*) with total aneurysm obliteration.



A. Vertebral angiogram - basilar tip aneurysm.
B. Angiogram after placement of coils with excellent aneurysm obliteration and preservation of adjacent vessels.



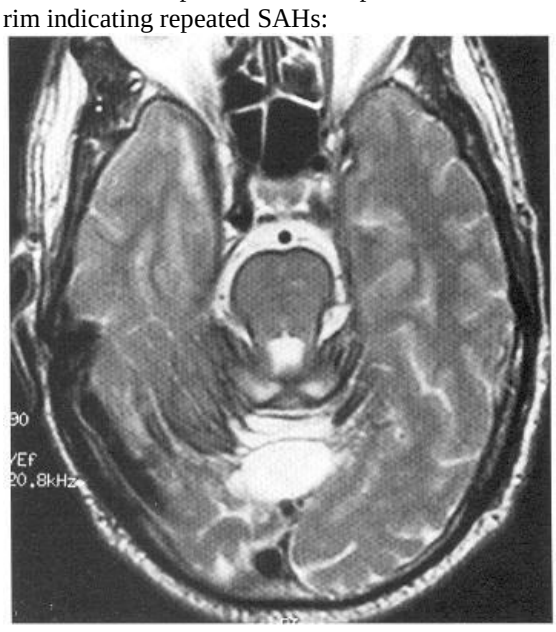
MRI

- not sensitive for SAH within first 48 hours further see p. D51 >>

N.B. fast fluid-attenuated inversion recovery (FLAIR) sequences detect SAH with *sensitivity that is equal to or greater than that of CT*! (subarachnoid hemorrhage produces dramatic hyperintensity in normally hypointense CSF).

- useful to diagnose AVMs.
- useful for diagnosing and monitoring unruptured aneurysms.
- ***MRI with gadolinium IV bolus*** better than CTA visualizes previously coiled / clipped aneurysms (lots of metal artifacts on CT).
- cases of repeated bleeding show areas of **SUPERFICIAL HEMOSIDEROSIS** (i.e. subpial black T2 hemosiderin):

Axial T2-MRI - pons, mesial temporal lobes and cerebellar folia are outlined by low signal intensity hemosiderin rim indicating repeated SAHs:



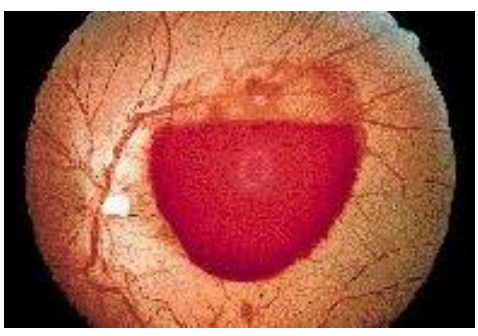
TRANSCRANIAL DOPPLER

- to assess for **vasospasm**; done routinely every day until risk of vasospasm decreases (patient "beyond window" of vasospasm).

- disadvanatge – monitors only major branches of Willis circle.
- index of Lindegaard may be more specific.

FUNDUSCOPY

1) papilledema
2) **TERSON syndrome** - pathognomonic of SAH - **subhyaloid hemorrhages** (25%; often bilateral) between retina and vitreous membrane – due to ***blood dissection*** along optic nerve sheath + subarachnoid blood around optic nerve ***compresses central retinal vein*** at its exit from nerve:



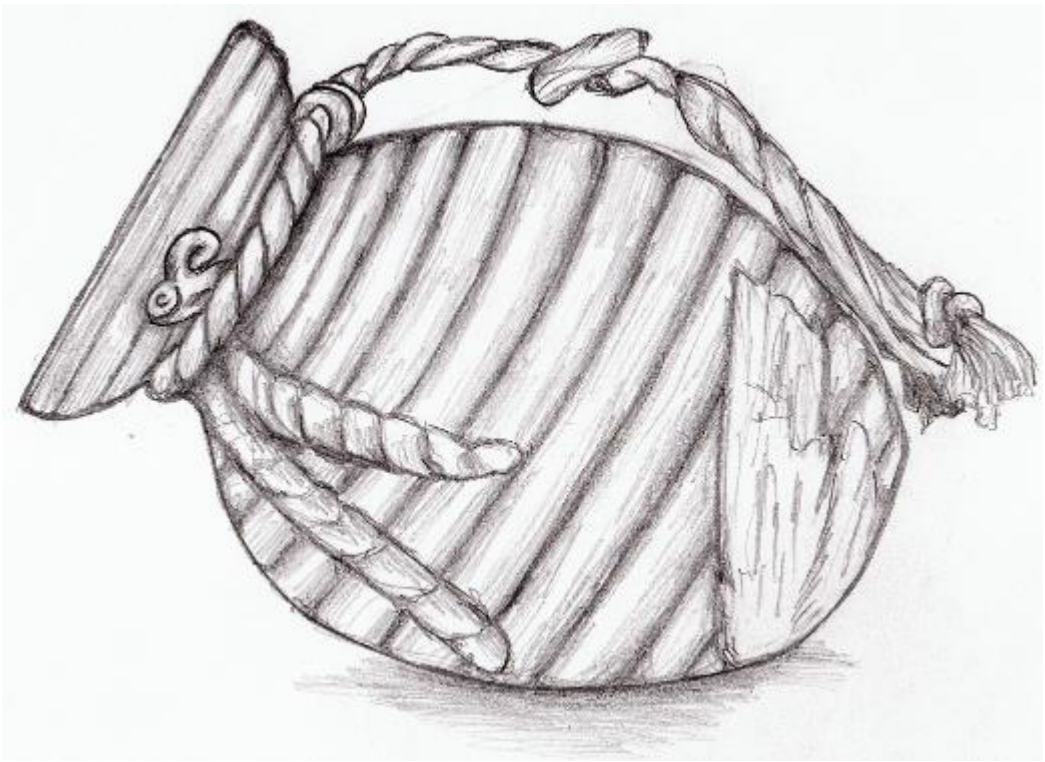
CARDIAC MANIFESTATIONS

- SAH causes circulating catecholamines↑ and autonomic stimulation:
  1) subendocardial myocardial ischemia
  2) peaked P waves, prolonged QT, tall or inverted T waves, U waves
  3) arrhythmias (tachy-, brady-)

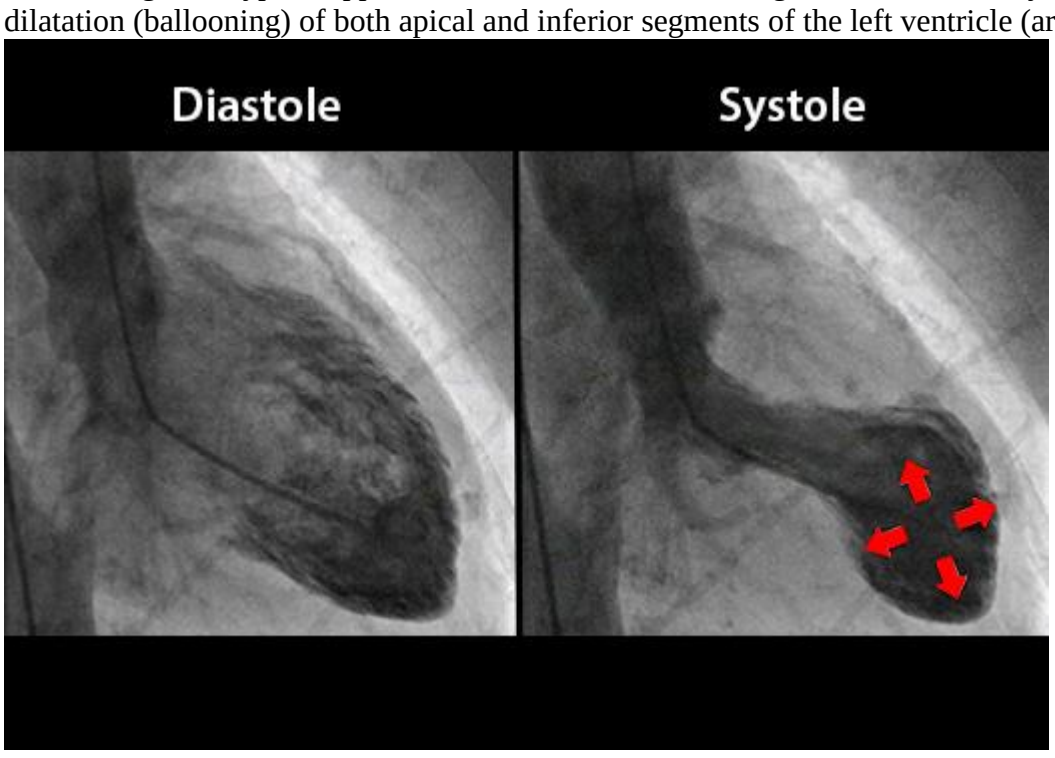
TAKOTSUBO CARDIOMYOPATHY - transient stress cardiac syndrome (due to circulating catecholamines↑) that involves left ventricular apical akinesis and mimics acute coronary syndrome.

- patients often present with **chest pain**, **ST elevation**, and **↑ cardiac enzymes**
- on cardiac angiography, left ventricular apical ballooning is present and there is no significant coronary artery stenosis.

Japanese word *takotsubo* translates to "octopus pot" resembling shape of left ventricle during systole on imaging studies:



Ventriculogram - typical appearance of - left ventricle during diastole and end-systole - aneurysmal dilatation (ballooning) of both apical and inferior segments of the left ventricle (arrows):



COMPLICATIONS

VASOSPASM

- due to irritation by blood - delayed narrowing of large capacitance arteries at base of brain (radiographic vasospasm) that can lead to *delayed ischemic neurologic deficit (DIND)* (clinical s. symptomatic vasospasm)

Most significant cause of disability and death! (causes death in 7% SAH patients) - must be aggressively treated. *see below >>*

- most commonly seen following aneurysmal SAH (but may also follow other intracranial hemorrhages and SAH of unknown etiology).
- occurs at days 3 ÷ 21 (never before day 3; rarely starts after day 17) with **peak incidence days 4-14**.
  - clinical vasospasm resolves by day 12 → gradual radiographic resolution over 3-4 weeks
  - vasospasm develops earlier in patients with previous SAH.
- angiographic incidence 30-70% (on bleed day 7); of these, only 20-50% patients become symptomatic.
- more blood is surrounding arteries, more likely there will be vasospasm; vasospasm risk correlates with:
  1. Amount of blood in SA space:
     - if CT fails to demonstrate blood or shows only thin layer, vasospasm is unlikely.
     - if CT shows clot ≥ 5 x 3 mm, severe spasm follows in nearly all cases.
  2. Speed of blood clearance
     - one of reasons to have EVD
- pathogenesis: arterial blood at high pressure contacts vessels at base of brain (vasospasm is rare in SAH with distribution limited to *cerebral convexity*).
- putative responsible agent – ENDOTHELIN (other candidates – OXYHEMOGLOBIN, SEROTONIN, CATECHOLAMINES, PROSTAGLANDINS, SUBSTANCE P, CALCITONIN GENE PEPTIDE, PLATELET-DERIVED GROWTH FACTOR).
- risk factors: higher HH grade, more blood on CT (clots are especially spasmogenic when in direct contact with proximal 9 cm of ACA and MCA) and thus antifibrinolytic therapy, age↑, preexisting hypertension, history of active cigarette smoking, hypovolemia.
- angiographic dye can exacerbate spasm.
- most common sites – terminal ICA, proximal ACA > proximal MCA; more distal arteries become involved later.

  N.B. involved territory is not related to location of ruptured aneurysm!???? (Greenberg says there is good but not perfect correlation)
- vasospastic vessels show ***medial necrosis*** and ***inflammation*** within first few weeks, and later ***medial atrophy***, ***subendothelial fibrosis***, ***intimal thickening***.

  Vasospasm is chronic condition with ***definite long-term changes*** in morphology of involved vessels!

CLINICAL FEATURES

(may develop over few days and fluctuate; 10% present abruptly) – DIND (delayed ischemic neurologic deficit): headache, deterioration in mental status, new-onset focal neurologic deficits.

Lethargy (with or without focal neurological deficit) is vasospasm, until proven otherwise! → emergency CT to rule out other pathology (vasospasm may be clinically indistinguishable from rebleeding!)

MONITORING

1) routine serial **neuro exams**
2) routine daily **TCD** (normal velocities are < 100); alternative – **continuous EEG** (look for assymetry)
3) baseline and follow-up **perfusion CT, CTA**

DIAGNOSIS

- arterial narrowing with slowing of contrast filling:

1) **CTA** (with **pCT**) – first test to do if SAH patient develops any neuro deficit*; some neurosurgeons do it routinely (e.g. at SAH bleed day 10 or if TCDs↑↑↑)

*at the same time put NPO order as patient potentially may go to OR

2) **MRI-DWI and PWI** - may detect early ischemia.
3) **angiography** – can confirm diagnosis and afford treatment (e.g. intra-arterial VERAPAMIL)
4) **EEG** – ↓ percent of α activity (6-14 Hz) called "relative alpha" (RA) from mean 0.45 to 0.17 predicted onset of vasospasm earlier than TCD or angiography; ↓total EEG power (amplitude) - 91% sensitive for predicting vasospasm
5) **TCD**:

ACA: > 100

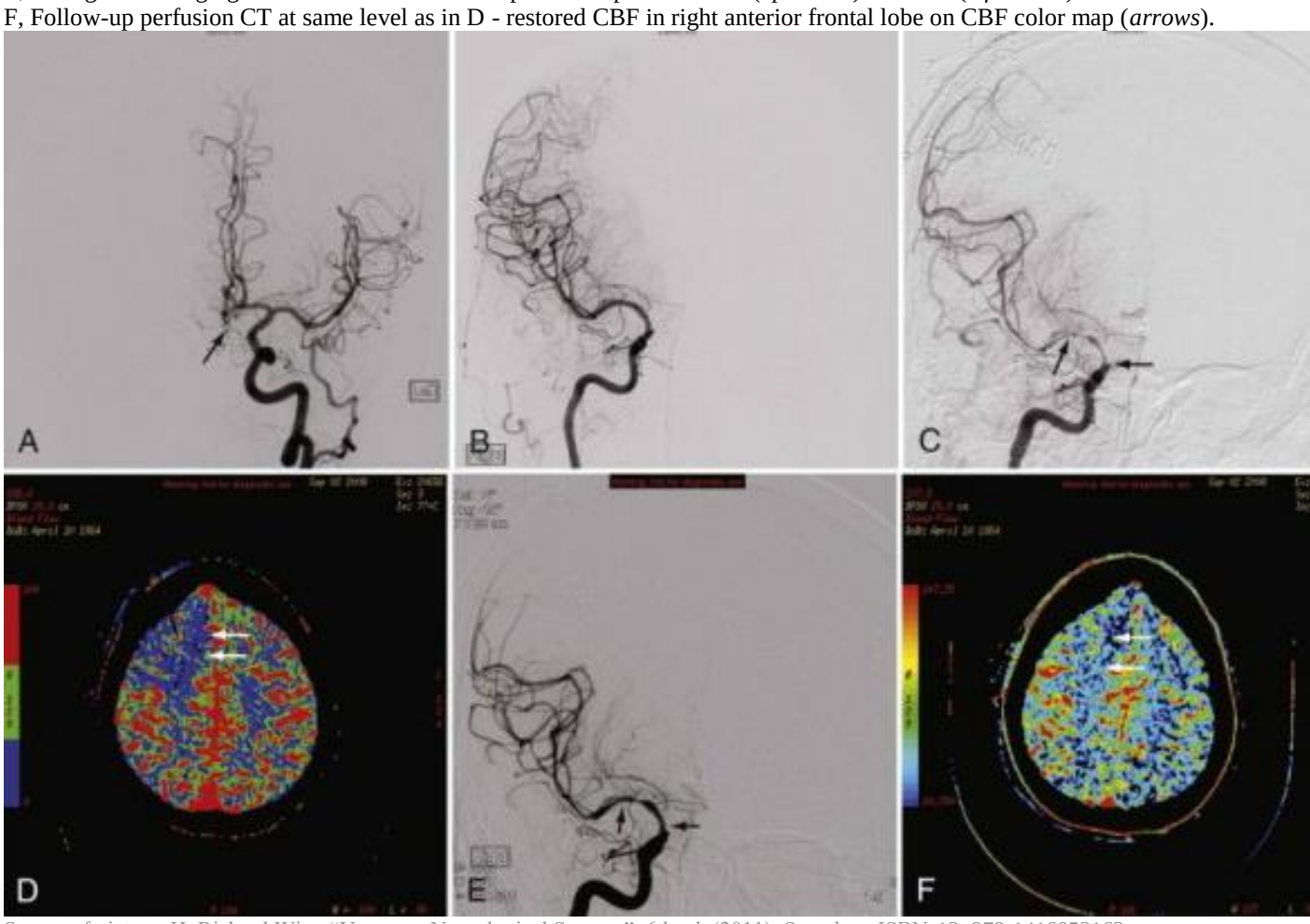
Mean **MCA** velocity	MCA:ICA (Lindegaard) ratio**	Interpretation
< 120	< 3	Normal
120-200*	3-6	120-160 Mild spasm 160-200 Moderate spasm
> 200	> 6	Severe vasospasm

*velocities in this range are specific for vasospasm but are only 60% sensitive

**differentiates vasospasm from hyperemia

- TCD changes may precede clinical symptoms by up to 24-48 hrs.
- findings are often more helpful when baseline studies performed before vasospasm are available (e.g. increases of > 50 cm/sec/d may suggest vasospasm)

A, AP left ICA angiogram - ruptured anterior communicating artery aneurysm (*arrow*).
B, AP right ICA angiogram - absent A1 segment of right anterior cerebral artery and no vasospasm.
C, AP right ICA angiogram 7 days after admission - severe vasospasm of M1 segment of right middle cerebral artery (MCA) (*up arrow*) and supraclinoid right ICA (*left arrow*).
D, Perfusion CT cerebral blood flow (CBF) map - vasospasm-induced decreased CBF (blue areas) within right frontal lobe (*arrows*).
E, AP right ICA angiogram after intra-arterial verapamil - improved MCA (*up arrow*) and ICA (*left arrow*) vessel caliber.
F, Follow-up perfusion CT at same level as in D - restored CBF in right anterior frontal lobe on CBF color map (*arrows*).



Source of picture: H. Richard Winn "Youmans Neurological Surgery", 6th ed. (2011); Saunders; ISBN-13: 978-1416053163 >>

PREVENTION

- see below >>

TREATMENT

- see below >>

REBLEEDING (RERUPTURE)

- from aneurysm rerupture.

- clinically - new headache, sudden neurologic worsening, sudden ICP↑, bright blood in EVD.
- diagnosis - **CT** show presence of new blood in subarachnoid space.
- EVD increases risk of rebleeding of unsecured aneurysms

N.B. rebleeding carries mortality ≈ 51-85% !!!

Rebleeding risk of untreated aneurysms:
1st day – 4%*
each next day during first 2 weeks – 1.5%** (2 wks cumulative – 20%, 6 mos cumulative – 50%)
after 6 months – bleeding risk returns to baseline (1-3%/yr)

*"blow out" hemorrhages – due to unstable thrombus
**lysis of clot sitting over rupture site

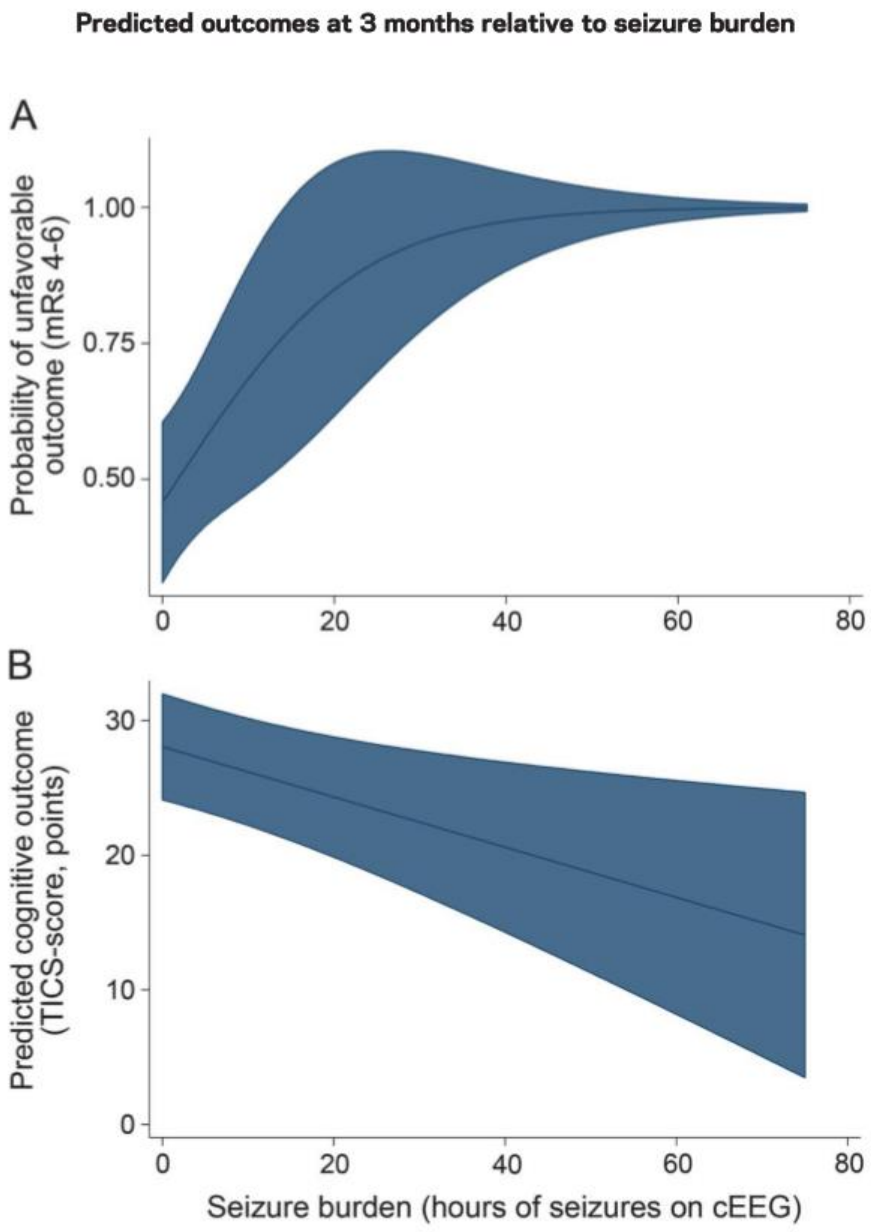
N.B. risk of rebleeding in SAH of unknown etiology, SAH with AVMs, SAH with incidental multiple unruptured aneurysms, are all similar at 1-3 %/yr

- prevention: N.B. bed rest does not prevent rebleeding!
  1) control HTN
  2) do not drain EVD below 10
  3) TRANEXAMIC ACID (Cyklokapron®)1 g q6h IV (e.g. if patient needs to be transferred before securing aneurysm)
  4) EPSILON-AMINOCAPROIC ACID (Amicar®) 10 g IV loading dose → IVI 48 g/d; incidence of hydrocephalus and stroke is increased with prolonged use!

SEIZURES

- seizure INCIDENCE (excluding seizures at time of hemorrhage): 3-12% of SAH patients have seizures during acute illness
- majority of seizures are ***nonconvulsive*** (cannot be detected without EEG)

  N.B. seizure burden (number of hours of seizures) is associated with unfavorable functional (mRS 4-6) and cognitive outcome - every hour of seizure on cEEG is associated with odds ratio of 1.10 (95% CI 1.01–1.21, p = 0.04) to 3-month disability and mortality!!!



De Marchis et al. (Neurology 86 January 19, 2016)

- 10.5% incidence of seizures in 5 years follow-up (20% for MCA, 9% for PCA, 2,5% for ACA aneurysms)

ACUTE OBSTRUCTIVE HYDROCEPHALUS

- blood within **ventricles** blocks *foramen of Monroe*, *sylvian aqueduct*, blood within **basal cisterns** blocks *4th ventricular outlet*.

- develops in 15-20% cases acutely
- most present within first 24 hours (or within first 7 days).
- most reliable clinical measure is **level of consciousness***; any change in level of consciousness → emergent CT (dilated ventricles** → immediate ***ventriculostomy***).

*30-60% cases show no impairment of consciousness
**earliest finding is ballooning of frontal horns

N.B. ventriculostomy increases risk of rebleeding (if aneurysm is unprotected!); therefore:

  - keep EVD drainage at least at 10 (when aneurysm is secured – may drop to 0)
  - patients with dilated ventricles (but no compromise of level of consciousness) should be treated conservatively.

- blood may obstruct ventriculostomy catheter (H: intraventricular injection of tPA or urokinase 10,000-12,000 U followed by clamping drain for 1 h and then opening tube).
- *hydrocephalus resolution* is assessed periodically by clamping EVD while monitoring ICP/neuro status.

DELAYED COMMUNICATING HYDROCEPHALUS

- blood in **subarachnoid space** obliterates *arachnoidal villi*;

- develops in 8-45% cases
- develops ≥ 10 days after SAH - incontinence, gait instability, cognitive deterioration (abulia).
- prophylaxis: **EVD** (clears blood from CSF).
- treatment: ***ventriculoperitoneal shunt***.

N.B. usually it is temporary condition and prolonged EVD/LD helps to avoid shunt in some patients; some experts would even use intermittent LP with multiple passes to create CSF leak in spine as temporary "safety valve" until condition resolves.

NON-NEUROLOGICAL

SAH-INDUCED HYPONATREMIA

- develops in 10-34% cases
- majority of cases are due to ***cerebral salt wasting*** (atrial natriuretic peptide*↑?); the rest – due to ***SIADH***

*not brain natriuretic peptide

- may be first sign of vasospasm!
- treatment: see p. 2514 >>
  SIADH – ***fluid restriction***
  CSW – fluid repletion with ***normal saline*** or ***slightly hypertonic (1.5-3%) NaCl*** at rates above maintenance requirements, ***hydrocortisone*** / ***fludrocortisone***, ***salt tabs***.
- hyponatremic patients have ***3 times incidence of delayed cerebral infarction*** than normonatremic patients!

ACUTE NEUROGENIC PULMONARY EDEMA

- unrelated to HHH therapy.
- almost universal in severe SAH.
- H: gentle ***diuresis***, ***dobutamine***, ***PEEP***.

Patients undergoing triple-H therapy can develop **cardiogenic pulmonary edema** as they "fall off' Starling curve with volume expansion!

NEUROGENIC STUNNED MYOCARDIUM (S. TAKOTSUBO CARDIOMYOPATHY)

- myocardial hypokinesis (↓ ejection fraction) not attributable to coronary artery disease or myocardial abnormalities.

- putative mechanism: hypothalamic ischemia → local (myocardial) catecholamine surge (peak 2 days to 2 weeks post SAH).
- clinically: hypotension (may be compensated by ↑SVR), CHF, arrhythmias.
- reverses completely in most cases within about 5 days; 10% progress to MI.

- diagnosis: as MI on echocardiography and EKG but cardiac enzymes tend to be lower than expected for degree of myocardial impairment.
- treatment: DOBUTAMINE (for SBP < 90 and low SVR), MILRINONE (for SBP > 90 and normal or increased SVR, esp. if patient is on chronic β-blockers).

OTHER

Neurogenic sympathetic hyperactivity → **arrhythmias** (90% patients), **myocardial ischemia** (cardiac myonecrosis)

- most prevalent in first 48 hours.
- HHH therapy to prevent cerebral ischemia may exacerbate ***myocardial*** ischemia; therapy for myocardial ischemia (nitrates) may increase ICP and exacerbate ***cerebral*** ischemia.
- **2D echocardiography** is more sensitive in detecting myocardial ischemia than is ECG.

CAVERNOUS-CAROTID aneurysm rupture typically produces **carotid-cavernous fistula** (rather than SAH).

Heparin-induced thrombocytopenia, DVT - occur infrequently but not uncommonly.

TREATMENT

Three factors that improve outcome:

1) **early referral** to hospital that has physicians experienced in treating aneurysms.
2) **urgent** aneurysm treatment
3) **aggressive** treatment of **vasospasm**.

SAH per se treatment

Vasospasm prevention (nimodipine, pravastatin, Mg sulfate) see below >>

REGIMEN

– dark quiet environment in ICU; visitors are limited to immediate family;

- **strict bed rest** (no out of bed for any reason, limit number of daily visitors) for 2 weeks → gradually return to normal activities over 3rd week.
  Bed rest does not prevent rebleeding!
- elevate head of bed at 30°
- avoid straining during defecation
- midazolam IV prior to procedures that may increase ICP.
- frequent turning and calf compressions.

EVD

If GCS < 14 (esp. if blood in ventricles) – insert EVD (drain continuously at 10 cmH_2O*; when aneurysm is secured – drain at 0 cmH_2O) *Greenberg recommends 15-25 mmHg

- elevated ICPs require mannitol, etc.
- don't start challenging EVD until day 6-7.
- don't start challenging EVD if on vasopressors.
- don't start challenging EVD until CSF output becomes < 100 mL/8 hr.

Speed of EVD weaning

Ramazan Jabbarliet al. Gradual External Ventricular Drainage Weaning Reduces The Risk of Shunt Dependency After Aneurysmal Subarachnoid Hemorrhage: A Pooled Analysis. Operative Neurosurgery, opy009, https://doi.org/10.1093/ons/opy009 Published: 26 February 2018

- chronic posthemorrhagic hydrocephalus necessitating shunt placement is a common complication of SAH.
- two German university hospitals with different EVD management regimes (rapid weaning [RW] vs gradual weaning [GW]) - 455 and 510 SAH survivor patients.
- patients with GW were less likely to develop shunt dependency (27.5% vs 34.7%, P = .018); multivariate analysis confirmed independent association between RW regime and shunt dependency (P = .026).
- shunt-dependent SAH patients undergoing GW required significantly longer time until shunting (mean 29.8 vs 21.7 d, P < .001) and hospital stay (mean 39 vs 34.4 d, P = .03).
- patients with GW were at higher risk for secondary shunt placement after successful initial weaning (P = .001).
- risk of CSF infection was not associated with the weaning regime (15.3% vs 12.9%, P = .307).
- at the expense of longer treatment, GW may decrease the risk of shunt dependency after SAH without an additional risk for infections; due to the risk of secondary shunt dependency, SAH patients with GW require proper posthospital neurological care.

LD

- there are centers that place LD along with EVD to improve outcomes.
- lumbar drainage was associated with lower rates of symptomatic vasospasm or delayed cerebral ischemia (20% vs. 45%, P < 0.001) and higher rates of favorable outcome (79.4% vs. 60.4% P < 0.001).

Panni P et al. Lumbar drainage and delayed cerebral ischemia in aneurysmal subarachnoid hemorrhage: a systematic review. J Neurosurg Sci. 2017 Dec;61(6):665-672. doi: 10.23736/S0390-5616.16.03151-9. Epub 2015 Feb 4.

DIET

No nicotine patch for smokers!

- antacids (e.g. RANITIDINE)
- antiemetics (e.g. PROMETHAZINE, ONDANSETRON)
  Avoid phenothiazines - lower seizure threshold!
- stool softeners (e.g. DOCUSATE); bedside commode requires less straining than bed pan and is preferred for patients who are able to get out of bed.

IV FLUIDS

– use only isotonic solutions (to minimize cerebral edema).

- early aggressive fluid therapy to head off cerebral salt wasting: NS + 20 mEq KC/L at 2 ml/kg/hr (typically 140-150 ml/hr)
- if Hct < 40%, give 500 ml of 5% albumin over 4 hrs upon admission.

HEADACHE

– the best is Fioricet® (Dr. Rivet avoids it due to caffeine – risk of vasospasm)

- in general, medications are not helpful with headache.
- avoid NSAIDs (bleeding risk; however, if aneurysm is secured, IBUPROFEN is OK), avoid sedatives and opioids (unless patient is with clear sensorium)

- in acute crisis, FENTANYL is OK – short acting and does not release histamine (does not elevate ICP)!

  Avoid Demerol® - lowers seizure threshold!
- **glucocorticoids** may help reduce head & neck ache (irritative effect of subarachnoid blood); no good evidence that they are neuroprotective - routine use is controversial.

BP GOALS

- **SBP goal**: unsecured aneurysm < 140; secured (clipped / coiled) 100-160; up to 180-220 (if secured and in vasospasm)
- maintain **BP** in range that allows for sufficient ***cerebral perfusion**** yet limits risk of ***rebleeding***;
  - β-blockers (labetalol) / Ca-antagonists (nicardipine) IV are agents of choice → start long-acting ACEI.
  - most clinicians avoid nitrates (NITROPRUSSIDE, NITROGLYCERIN) which elevate ICP;

    *state of consciousness may be used as guide to level of cerebral perfusion - administer hypotensive medications up to level that patient begins to experience drowsiness.

Always avoid HYPOVOLEMIA!

Arterial-line indications: hemodynamically unstable, stuporous or comatose, difficult to control hypertension, requiring frequent labs (e.g. ventilator patients).

- pulmonary-artery catheter (aka Swann-Ganz catheter) is out of favor.

OXYGENATION

- must be adequate.

- some experts target for early moderate hyperoxemia in intubated patients; studies show no benefit on outcomes.

ANTIEPILEPTICS

- controversial

- generalized seizure may be devastating in presence of tenuous aneurysm – seizures increase risk of rebleeding!
- AEDs are given by many authorities at least for 1 week post-op
- Keppra® (LEVETIRACETAM): start with 500 mg PO or IV q 12 hours
- alternative - PHENYTOIN (load with 17 mg/kg, maintenance of 100 mg TID)
- some prophylaxis is provided by barbiturates (e.g. PHENOBARBITAL) when given for sedation or burst suppression.

FEVER CONTROL

- normothermia, particularly in immediate post event period (14 days), is crucial, and lack of maintenance may negatively affect outcomes.
- very aggressive fever control (beyond Tylenol and external cooling measures) may improve outcomes without causing significant harm (maybe pneumonia↑).

NOT TO USE

- **antifibrinolytics** (e.g. tranexamic acid) reduce rebleeding from 19-24% to 9-11%, but do not improve or even worsen outcome:
  1) delay clot lysis → vasospasm, hydrocephalus → cerebral ischemia↑
  2) all sort of ischemic complications

  Vermeulen M et al. Antifibrinolytic treatment in subarachnoid hemorrhage. N Engl J Med 1984 Aug 16; 311: 432-7

  A randomised, placebo-controlled, double-blind study in 479 patients with subarachnoid hemorrhage showed a significant ($p < 0.001$) reduction in the rate of rebleeding (from 24% in placebo-treated patients to 9% in those who received intravenous tranexamic acid 6 g/day for the first week and 4 g/day thereafter for up to 4 weeks, with some patients receiving oral therapy at a dosage of 6 g/day for the third and fourth weeks). Treatment was started within 72 hours of hemorrhage in all patients. Overall outcome was not improved after 3 months, however, because of an increase in the incidence of cerebral ischemia (15% in the placebo treated group vs 24% in patients who received active treatment).

  Kassell NF, Torner JC, Adams Jr HP. Antifibrinolytic therapy in the acute period following aneurysmal subarachnoid hemorrhage: preliminary observations from the Cooperative Aneurysm Study. J Neurosurg 1984; 61: 225-30

  In an analysis of 672 patients participating in the International Cooperative Study on the Timing of Aneurysm Surgery, in which patients who received antifibrinolytic therapy (tranexamic acid or EACA) and those who did not were compared, inhibition of fibrinolysis was associated with a significant reduction in the rate of rebleeding (11.7 vs 19.4%; $p = 0.01$). However, significant increases in rates of ischaemic deficit (32.4 vs 22.7%; $p = 0.01$) and hydrocephalus (13.5 vs 6.8%; $p = 0.02$) were also reported.

  Findings of other studies published during the 1970s and early 1980s have been inconsistent in terms of clinical benefit of tranexamic acid in these patients.

- **anticoagulants** and **antiplatelets** are contraindicated; exceptions:
  1) heparin in prophylactic doses
  2) antiplatelets after stent-assisted coiling (but usually it is not used in case patient will need second surgery – shunt placement); some experts start ASPIRIN after all coilings (even if patient has EVD or may need EVD in near future), especially if there is some coil protrusion into vessel lumen.

  Aspirin may be associated with reduced DCI risk

  Post-treatment Antiplatelet Therapy Reduces Risk for Delayed Cerebral Ischemia due to Aneurysmal Subarachnoid Hemorrhage. Marvin Darkwah Oppong et al. Neurosurgery, Volume 85, Issue 6, December 2019, Pages 827–833

  - aspirin use after aneurysm treatment was independently associated with reduced DCI risk ($P < .001$, adjusted odds ratio = 0.41, 95% confidence interval 0.24-0.65) and favorable outcome ($P = .02$, adjusted odds ratio = 1.78, 95% confidence interval 1.06-2.98).
  - aspirin was associated only with minor bleeding events ($P = .02$ vs $P = .51$ for major bleeding events).

- **caffeine** (e.g. Fioricet), **nicotine** patch, **vasopressin** – vasoconstrictor properties.

VASOSPASM prophylaxis

For all SAH patients!!!

NIMODIPINE - Ca^{2+} channel blocker

- 60 mg PO q4h or 30 mg PO q2hr (to avoid periodic dips in BP)
- start within 96 h of SAH; no effect on reversing chronic vasospasm once that has started.

N.B. does not alter radiographic vasospasm, and there is no statistically significant difference in mortality, however, *risk of strokes and outcome are improved*!

- for 21 d or until patient is discharged home in good neurological condition, whichever occurs first.
- early impressions that NIMODIPINE prevents vasospasm have not been confirmed (i.e. actual mechanism of action unknown but may involve ***brain protection against ischemia*** - blocking Ca^{2+} influx into damaged neurons).
- *if capsule cannot be swallowed*, hole can be made at both ends of capsule with 18-G needle, and contents extracted into syringe → empty contents into nasogastric tube in situ and wash down tube with 30 mL isotonic saline.
- contraindications: systolic BP < 90 mmHg; sick sinus syndrome; 2-3° AV block (except when using pacemaker).
- dosage is halved for liver failure.
- drug interactions:
  β-blockers - increased depressant effects on myocardium and AV conduction;
  FENTANYL - may cause severe hypotension;
  CIMETIDINE - may increase blood [nimodipine].

British Aneurysm Nimodipine Trial

Pickard JD et al. Effect of oral nimodipine on cerebral infarction and outcome after subarachnoid haemorrhage: British aneurysm nimodipine trial. BMJ 1989 ; 298 : 636 – 642

- class I evidence.
- at 3 months nimodipine reduced the incidence of:
  cerebral infarction by 1/3 (22% with nimodipine vs 33% with placebo, p = 0.014);
  poor outcomes by 40% (20% vs 33%, p < 0.001).
- no significant effect on mortality between the groups.

NEWTON (Nimodipine microparticles to Enhance recovery While reducing TOxicity after subarachNoid hemorrhage) study

- EG-1962 (Edge Therapeutics, Inc.) - polymer-based microparticle containing nimodipine.
- delivered as single dose, delivers high and sustained concentrations of nimodipine over 21-day period.

Although other calcium antagonists, such as NICARDIPINE, have been investigated, a Cochrane review of 27 RCTs concluded that there was only evidence to support the prophylactic use of nimodipine.

Dorhout Mees SM et al. Calcium antagonists for subarachnoid haemorrhage. Cochrane database of systematic reviews 2007 , Issue 3. Art no.: CD000277. DOI: 10.1002/14651858.CD000277.pub3

PRAVASTATIN 40 mg/d for 21 day

Pravastatin in the prevention of vasospasm

Tseng MY et al. Effects of acute treatment with pravastatin on cerebral vasospasm, autoregulation, and delayed ischemic deficits after aneurysmal subarachnoid hemorrhage: a phase II randomized placebo-controlled trial. Stroke 2005; 36 : 1627 – 1632

	Placebo	Pravastatin group	Degree of change	Statistical significance
Vasospasm on TCD	25%	17%	−32%	$p = 0.006$
Severe vasospasm	12%	7%	−42%	$p = 0.044$
Duration of severe vasospasm	1.2 days	0.5 days	−0.8 days	$p = 0.068$
Period of impaired ipsilateral cerebral autoregulation	5.3 days	3 days	−2.4 days	$p = 0.011$

- trend for more post-operative deficits in the pravastatin group (p = 0.115) but a trend for more deaths in the placebo group (again, not significant).
- pravastatin reduced vasospasm-related DIDs by 83 % (p < 0.001) and mortality by 75 % (p = 0.037).
- beneficial effects were still present at 6 months (Tseng et al. 2007).

Simvastatin in Aneurysmal Subarachnoid Hemorrhage (STASH)

http://www.medscape.com/viewarticle/824943

Peter Kirkpatrick: "There is no place for the generalized treatment of SAH patients with simvastatin during the acute stages."

↓

High Dose Simvastatin in Subarachnoid Hemorrhage (HDS-SAH)

40 mg vs. 80 mg of simvastatin.
G Wong, MD: no difference between the 2 doses:

Endpoint	Simvastatin, 40 mg (n = 124) (%)	Simvastatin, 80 mg (n = 131) (%)	Odds Ratio (95% CI)
Delayed ischemic deficit	24	27	1.2 (0.7 - 2.0)
Clinical vasospasm	12	15	1.2 (0.6 - 2.5)
Delayed cerebral infarction	17	16	1.0 (0.5 - 1.8)
Favorable mRS score (0 - 2)	72	73	1.1 (0.6 - 1.9)

MAGNESIUM SULFATE 64 mmol/d IVI for 14 days – neuroprotective agent; beneficial for treatment of eclampsia, which shares pathophysiological mechanisms with delayed cerebral ischemia after aneurysmal SAH.

Magnesium for Aneurysmal Subarachnoid Hemorrhage trial (MASH-2)

- safe but no benefit compared with placebo (and no subgroup of patients who might benefit from magnesium).

IV Magnesium May Do More Harm Than Good in Subarachnoid Hemorrhage: http://www.medscape.com/viewarticle/723797?src=mpnews&spon=26&uac=121060BZ

Prophylactic intravenous magnesium sulfate for treatment of aneurysmal subarachnoid hemorrhage: a randomized, placebo-controlled, clinical study.: http://www.medscape.com/medline/abstract/20228677?cid=med&src=nlbest

Intravenous Magnesium Sulphate for Aneurysmal Subarachnoid Hemorrhage (IMASH): a randomized, double-blinded, placebo-controlled, multicenter phase III trial.: http://www.medscape.com/medline/abstract/20378868?cid=med&src=nlbest

CLAZOSENTAN (PIVLAZ®) - intravenous *endothelin receptor antagonist*.

- currently, in pivotal Phase III study.

CONSCIOUS-2: *No Benefit of Clazosentan on Vasospasm After SAH: http://www.medscape.com/viewarticle/737674?src=mpnews&spon=26*

FASUDIL - *Rho kinase (ROCK) inhibitor* - approved in Japan for treatment of cerebral vasospasm after aneurysm rupture.

- may reduce lesion burden in patients with cerebral cavernous malformation (CCM), study in mice suggests.

Clot removal during ***surgery*** or via ***EVD drainage*** (up to subarachnoid irrigation with thrombolytic agents)

Triple H therapy – not recommended (as prophylaxis)!

IMPROVES (Intensive Management of Blood Pressure or Volume Expansion in Subarachnoid Hemorrhage) - **volume expansion** or **blood pressure augmentation** for prevention of delayed cerebral ischemia; did not result in significant differences in neuropsychological outcomes at 6 months vs. patients with normovolemia and normotension;

- **blood pressure augmentation** was associated with worse neurobehavioral outcome;
- **hypervolemia** caused 4-fold increase in risk of adverse event.

VASOSPASM treatment

1. Drop **EVD drainage to 0**.

2. Aggressive **HHH s. hyperdynamic therapy** (aims to maintain cerebral perfusion pressure in setting of impaired cerebrovascular autoregulation):
   1) **hypertension** (DOPAMINE, NOREPINEPHRINE) – keep MAP 70-130 mmHg, systolic BP high (e.g. 180-240 mmHg; 160 mmHg if aneurysm is unsecured);
      - if tachycardia> 140-150 add PHENYLEPHRINE.
      - if SBP still low (esp. if SVR > 800 and PCWP 12-14 mmHg*), add DOBUTAMINE.

      *in severe vasospasm may increase to 18-21 mmHg (risk of pulmonary edema!)
   2) **hypervolemia** (target CVP ≥ 10 mmHg) – NS* > 200 mL/hr (plus, boluses of colloid, e.g. ALBUMIN**); if UO > 200 mL/hr Greenberg recommends DDAVP; some add FLUDROCORTISONE.

      *change to ½NS if [Na] > 150

      ****ALISAH study**: ALBUMIN in doses up to 1.25 g/kg/d ×7 days is tolerated and may be neuroprotective in SAH.

      DEXTRAN and HETASTARCH are not used - may induce coagulopathy!
   3) **hemodilution** (optimal hematocrit is 30-33%); for Hct < 25% give packed RBCs; MANNITOL 20% at 0.25 gm/kg/hr may improve rheological properties.

      N.B. use of pRBC transfusion to treat anemia is reasonable, although optimal hemoglobin goal is still undetermined (maintain Hct ≈ 30%)

- **central venous pressure (CVP)** should be maintained at 10-12 mmHg.
- ***Swan-Ganz catheterization*** is indicated - target **pulmonary capillary wedge pressure (PCWP)** to 14-20 mmHg (in normovolemia ≈ 10-12 mmHg).
- risks of HHH therapy
  1) rebleeding (if aneurysm is still not treated!)
  2) pulmonary edema
  3) myocardial ischemia
  4) dilutional hyponatremia

Hypertension/hypervolemia for symptomatic vasospasm

Kassell NF et al. Treatment of ischaemic deficits from vasospasm with intravascular volume expansion and induced arterial hypertension. Neurosurgery 1982 ; 11 : 337 – 343

Permanent improvement in neurological deficit	74%
No change in deficits	16%
Deterioration	10%
Most common complications	Aneurysmal re-bleed (19%) Pulmonary oedema (17%)
Most common cause of treatment failure	Established infarction (17%)

- reversal of deficits was seen within 1 h in 81%.
- HH is most effective for patients with mild deficits.

REFRACTORY VASOSPASM

→ **endovascular methods**:

a) **transluminal balloon angioplasty** – method of choice! (contraindicated if stroke already happened)

b) **intra-arterial medications** (for vasospasm in *distal vasculature*, where balloons may not access)

VERAPAMIL – 8 mg injected over 2 min; takes 30 min for full effect; effect lasts 24 hrs.
NICARDIPINE – 10-40 mg per procedure.
PAPAVERINE 200-300 mg infused over 30 mins – effect short-lived, more adverse side effects than angioplasty; largely abandoned because of limited success.

PROTOCOL

TCD↑ (close to 200) → triple H; if symptomatic – maximum therapy for 1 hour; if still symptomatic → angiography

ANEURYSM treatment

Unruptured (incidental) aneurysms – see above >>

All **ruptured** aneurysms are treated to avoid disastrous rebleeding (rare exceptions - hemodynamic instability, extreme old age, clinical condition approaching brain death).

TIMING OF TREATMENT

- ruptured aneurysm is treated ASAP (ideally within 24 h of SAH) (to prevent rebleeding* and to allow HHH therapy for vasospasm) even in patients with grade 5.
  - in absence of compressing hematoma, it is *not necessary to operate during nighttime*.

  *e.g. pregnant patients - risk of rebleeding during delivery when aneurysms are unclipped
- formerly, surgery was delayed until 2-3rd week after SAH; arguments against early surgery:
  1) inflammation and brain edema are most severe immediately following SAH.
  2) presence of solid clot complicates surgery.
  3) risk of intraoperative rupture of fragile aneurysm.
  4) risk of vasospasm due to mechanotrauma to vessels.

Although operative mortality (of early surgery) is higher,
overall patient mortality rate is lower (than of delayed surgery)

- do not delay treatment, if patient presents **≤ 10 days** after SAH.
- treatment **after 10 days** is associated with worse outcome (regardless of treatment modality)
  - if there is ***delay in aneurysm treatment*** plus significant risk for rebleeding (and no compelling medical contraindications) → short-term (< 72 hours) TRANEXAMIC ACID or AMINOCAPROIC ACID (Class IIa, Level B)
  - patient presents **≤ 7 days** after SAH – coiling has better results (after day 9, coiling = clipping).

International Cooperative Study on the Timing of Aneurysm Surgery

Kassell NF et al. The International Cooperative Study on the Timing of Aneurysm Surgery. Part 1: overall management results. J Neurosurg 1990 ; 73 : 18 – 36 .
Kassell NF et al. The International Cooperative Study on the Timing of Aneurysm Surgery. Part 2: surgical results. J Neurosurg 1990 ; 7 3 : 37 – 47 .

- 3521 SAH patients admitted within 3 days since bleed (83%, ie. 2922 had aneurysm surgery).
- 68 centers in 14 countries (24 in USA).
- only 6 months of follow up.
- conclusions:

good grade → early surgery by day 3.
poor grade, older age, pre-existing medical conditions = very poor prognosis ← should not be operated on before day 10.

  - main difference today is that we now have the option of endovascular treatment (often performed on poorer grade patients within the vasospastic period, largely because it is less risky to do so).
  - early surgery decreases risk of rebleeding but does not prevent vasospasm (however, vasospasm can be treated aggressively)
  - risk of waiting for delayed surgery: 12% rebleeding, 30% vasospasm with DIND.

METHODS

N.B. whereas coiling is somewhat safer than clipping for both ruptured and unruptured aneurysms (at least in acute perioperative period), clipping is slightly more durable.
  - coiling (vs. clipping) is associated with less risk of vasospasm.

Advantages
Coiling (vs. clipping) carries lower risk of vasospasm (due to endothelial damage during angiographic manipulation → less endothelin release?)

Complications (5% after coiling, 10% after clipping)
Seizures:
8.3% - after coiling
13.6% - after clipping

- MCA aneurysm location increased risk of seizures in both groups.

Morbidity and mortality (strongly correlates with patient's age):
clipping *of unruptured aneurysms* – morbidity 4-10.9%, mortality 1-3% (higher for *ruptured aneurysms*, but still < 5%).
coiling *of aneurysms* – morbidity 3.7-5.3%, mortality 1.1-1.5%.

Long term outcomes ar similar - decision to ***clip*** or ***coil***
should be made on individual basis

  - long-term rebleed rates might be slightly higher in ***coiling*** patients; thus, in patients < 40 yo ***clipping*** might be better.

International Subarachnoid Aneurysm trial (ISAT)

1-yr disability or death:
30.9% - clipping
23.5% - coiling

International Study of Unruptured Intracranial Aneurysms (ISUIA)

in patients with no prior history of subarachnoid hemorrhage, the overall 1-yr morbidity and mortality:
12.6% - clipping
9.8% - coiling.

ISAT (International Subarachnoid Aneurysm Trial)

Molyneux A , Kerr R , Stratton I , Sandercock P , Clarke M , Shrimpton J , Holman R ; International Subarachnoid Aneurysm Trial (ISAT) Collaborative Group . International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised trial. Lancet 2002 ; 3 60 : 1267 – 1274.

- class 1 evidence that has a greater impact on treatment of ruptured aneurysms than any other study; trial has led to a huge shift from surgery to endovascular treatment in some centers.
- 2143 patients (1073 coiled, 1070 clipped).
- inclusions: SAH within 28 days, good enough clinical state to justify treatment, aneurysms judged to be suitable for either technique (opinion of both surgeon and neuroradiologist) with equipoise regarding which method would be best.
- rates of rebleeding are higher after ***coiling*** (no statistical significance at 1 yr) but poor outcomes (mortality, dependence) are more common after ***clipping*** (coiling gives 22.6% relative risk reduction for poor outcome):

Outcome		Endovascular	Surgical	
Incidence of death or dependence (mRS 3–6)		23.5%	30.9%	at 1 yr; p < 0.002
Mortality at 1 year		85	105	
Incidence of re-bleeding (fatality in brackets)	Before treatment	17(7)	28(19)	
	Re-bleed <1 year	45(22)	39(24)	
	Re-bleed >1 year	7(2)	2(2)	
Re-treatment rate	<1 year	121	32	
	>1 year	15	1	
Complete occlusion at first follow-up angiography		66%	82%	

- critique:
  1) trial is biased towards ***small anterior circulation aneurysms*** (97.5%).
  2) it is not a trial of 'the best possible surgery vs the best possible endovascular treatment' but a trial of what ***the best option is for an 'average patient'*** (i.e. trial compares good interventional neuroradiologists to 'average' neurosurgeons rather than neurosurgeons who 'concentrate' on neurovascular surgery)
  3) primary endpoints were measured ***at 1 year***:
     - surgical group may just be slower to recover

- late re-bleed rate in the endovascular group is 0.21 % per patient-year vs. 0.063 % in the surgical group
- ISAT investigators suggest that surgery may be better in < 40 yrs age group (poor outcome at 1 year is much less in the surgical group)

SURGICAL CLIPPING

- clip across neck of aneurysm - to exclude aneurysm from circulation (without occluding normal vessels).

- Dandy performed first successful clipping in 1937, using clip designed by Harvey Cushing.
- all clips after 2000 are made of titanium – ***MRI compatible***.

Indications:

1) wide aneurysm neck (as is often in MCA bifurcation aneurysms); alternative – pCONus device
2) vessel branching off from dome

– better eliminates symptomatic mass effect created by aneurysm!
– if aneurysm contacts cranial nerve (causing neuropathy) it is more important to eliminate pulsations that mass itself.

Approach:
ANTERIOR CIRCULATION aneurysms:

a) pterional (fronto-temporal) approach.
   - opening of Sylvian fissure damages small veins → "brain retraction" ischemic changes in postoperative CT
b) minimally invasive approach – performed in Day Surgery unit.

POSTERIOR CIRCULATION aneurysms:

- head of BA (BA bifurcation above dorsum sellae) - modified pterional approach.
- head of BA (BA bifurcation below dorsum sellae) - subtemporal approach.
- BA trunk - posterior subtemporal approach.
- lower BA trunk and midline VA - far lateral inferior approach.
- VA where it pierces dura - midline suboccipital approach.

Prep and drape neck for rapid carotid proximal control – absolutely for ophthalmic aneurysms, strongly recommended for PComA aneurysms.

- for PComA aneurysms, check CTA preop – if fetal circulation, cannot sacrifice PComA!

Details: also see p. Op350 >>

- first identify parent artery (for possible temporary clipping in event of aneurysmal rupture).
- use ***operative microscope*** to dissect aneurysm neck free from feeding vessels without rupturing aneurysm.
- if lots of blood clots around – irrigate with saline.
- ***aneurysmal sac volume can be decreased*** (to soften aneurysm and facilitate manipulation):
  a) temporary clips (with low closing force) on parent artery ± aspiration of aneurysm sac (suction device placed over cotton pad)
  b) systemic hypotension
- incise arachnoid overlying aneurysm with tip of #11 blade.
- with small aneurysm dissector or spatula aneurysm walls are dissected away from perforating vessels.
- ***mobilize aneurysm in all directions*** - for visualization of any perforating vessels (that might inadvertently be incorporated by clip misplacement).
- **clips** are in various types, shapes, sizes, and lengths and currently are MRI compatible titanium.
  – giant aneurysms or aneurysms with calcified neck require specialized clips with added strength (tandem or booster clips - add force to closing of original clip).
- use clip as small as possible.
- *jaws of clip applier* are of same metal as clip, so as to avoid transfer of different metal type to clip.
- avoid placing clip too close to parent artery (may cause tear in aneurysmal sac).
  – if tear does occur → repair with clip graft (risk of damage to perforating vessels).
  – suturing in close proximity to aneurysm can result in damage to parent artery.
- if aneurysm is located at vessel bifurcation making T (like MCA bifurcation or ICA terminus) – apply clip parallel (not perpendicular) to T top – to minimize constriction.
- for *left PComA aneurysms*, use **pistol-grip aneurysm applier**.
- *INTRAOPERATIVE FLUORESCEIN ANGIOGRAPHY* is used (confirms aneurysm occlusion and patency of nearby vessels); alternative - immediate *POSTOPERATIVE ANGIOGRAPHY*.
- gently open basal cisterns → ***carefully remove as much of subarachnoid blood as possible*** (suction, lavage, ± cisternal infusion of rt-PA).
  advantages - reducing likelihood of vasospasm & hydrocephalus;
  disadvantages - clot aspiration is usually suboptimal + risk of iatrogenic trauma to pial surfaces and small vessels.
- after successful obliteration of ruptured aneurysm, patient remains at significant risk for vasospasm, hydrocephalus, and medical complications – must remain in ICU for at least 7-10 days.

Measures to avoid INTRAOPERATIVE ANEURYSMAL RUPTURE (principal surgical complication):

1) minimal brain retraction - paramount in aneurysm surgery! - use one blade only self-retaining retractor (e.g. Yasargil, Greenberg, Sugita)
2) induced systemic hypotension, diuretics
3) lumbar CSF drainage
4) hyperventilation
5) hypothermia (± circulatory arrest)

Key moment in aneurysm surgery – establishment of **proximal vascular control**!

Measures for CEREBRAL PROTECTION (surgery often requires temporary reduction / suspension of cerebral blood flow, either regionally or globally):

1) continuous **EEG monitoring**
2) **hyperosmolar agents**: 20% MANNITOL 1 g/kg IV 5 min prior to temporary clipping of parent artery - protects ischemic cerebral tissues from infarction for 30 min.
3) **anesthetic agents**: ISOFLURANE - preferred anesthetic agent for aneurysm surgery - effective in protecting against infarction during temporary ischemia.
4) **barbiturates** - better protective effects than other anesthetic agents - redistribute blood flow to ischemic regions ("reversed steal" phenomenon): THIOPENTAL (EEG burst suppression is dosage end point).
5) **hypothermia with cardiopulmonary bypass** - aneurysm can be opened and debulked in bloodless field; disadvantage – small perforating branches become transparent and blend unperceptively with aneurysm wall so that origin of perforator near neck cannot be visualized (safe dissection may be impossible); H: low perfusion rather than total circulatory arrest.
   – bypass can be achieved by ***open thoracotomy*** or ***cannulation of femoral artery and vein***.
   – *times of estimated safe circulatory arrest*: (1) 37°C = 3.5 min, (2) 19°C = 31 min, (3) 13°C = 65 min; therefore, as much dissection as possible is completed before arrest is instituted.

Perioperatively
AED (e.g. LEVETIRACETAM) for 7 days.

Outcomes, prognosis after clipping – see below >>

OPEN ALTERNATIVES TO SURGICAL CLIPPING

(if aneurysm cannot be clipped because of nature of aneurysm or poor medical condition):

a) **wrapping** (for *dissecting aneurysms*, *fusiform aneurysms*) with plastic ***resins*** (slightly better results) or ***muscle*** or ***fascia*** or ***gauze*** (cotton or muslin) – only modest benefits.
b) **trapping** (for *fusiform aneurysms*) - distal and proximal arterial interruption with direct surgery (ligation or occlusion with clip); *trial balloon occlusion* assesses which cases necessitate extracranial-intracranial (EC-IC) bypass to maintain flow distal to trapped segment.
c) **Hunterian principle (proximal ligation of parent artery)** (reduces intravascular pressure on aneurysm) - for *unclippable broad-based or giant aneurysms* (esp. ICA in cavernous sinus).
   – clamp is applied ≈ 2 cm below CCA bifurcation.
   – ***adjustable clamps*** (gradual occlusion) allow time for collateral circulation to increase.
   – if patient fails to tolerate CCA occlusion → *extracranial-intracranial bypass* can augment collateral flow.
d) **aneurysm excision** (for *giant MCA aneurysms*) → end-to-end or branch reconstruction of parent artery.

ENDOVASCULAR SURGERY

A. Balloon occlusion of feeding artery (e.g. for oncotic aneurysms) - pioneered in mid 1970s by Serbinenko at Moscow Institute of Neurosurgery.

B. Direct obliteration of aneurysmal lumen:

Systems
a) **detachable balloon** (silicon and latex)
b) **liquid embolic agents (glues)**
c) **GUGLIELMI detachable coil (GDC)** - primary treatment modality of aneurysms in many centers! - can be used to treat most aneurysms (initially used for aneurysms not amenable to surgical clipping).
   - FDA approved in 1995.
   - soft flexible* **platinum microcoils** are detached from stainless steel guide by passing very small direct current that causes electrolysis at solder junction - separation occurs within 2-10 minutes after satisfactory coil placement (some newer generation coils involve detachment strategies that do not involve electrolysis – takes only 20-30 seconds).
     *can be contoured to configuration of aneurysm
   - **coil sizes** range 2-20 mm in diameter and 2-30 cm in length.
   - coil induces ***electrothrombosis*** - positively charged electrode attracts negatively charged blood components (WBCs, RBCs, platelets, fibrinogen).
   - platinum is 3-4 times more thrombogenic than stainless steel.
   - technical limitations - aneurysms with wide necks* or complex morphologies.
     *coils can protrude into parent vessel and can compromise it
     (H: balloon-assisted and stent-assisted coil placements)
   - high rates of *recurrence secondary to coil compaction* – see below >>

d) **cPAX Aneurysm Treatment System** (NeuroVasx) - FDA approved; advantages:
   - can detach at any point chosen by clinician (platinum coils have fixed detachment zone)
   - continuous filling capability (decreases number of devices and amount of time required for treatment
   - polymeric material allows for noninvasive MRI and CT without metallic artifact.

e) **HydroCoil Embolic System** (HES; MicroVention, Inc) - platinum core with integrated hydrogel; *first generation* – exterior hydrogel coating – difficult handling; *second generation* – expandable hydrogel within the coil (once in contact with blood, expands to fill the lumen).
   - developed to reduce recurrence through enhancing packing density and healing within the aneurysm.
   - Hydrogel Endovascular Aneurysm Treatment Trial (HEAT) – testing 2nd generation HES; randomized 600 patients (28% with ruptured aneurysms):
     - assist devices (balloons and stents) were permitted at the discretion of the performing physician; flow diverters, however, were not permitted!
     - recurrence occurred in 4.4% subjects in the HES arm and 15.4% subjects in the bare platinum coil (BPC) arm (P = .002).
     - initial occlusion rate was higher with BPC (17.8% vs 28.3%, P = .003).
     - packing density and both major and minor recurrence rates were in favor of HES.
     - secondary endpoints (adverse events, retreatment, hemorrhage, mortality, and clinical outcome) did not differ between arms.

Indications for coiling:
a) poor clinical grade
b) medically unstable
c) increased surgical risk (e.g. cavernous sinus and many basilar tip aneurysms)
d) posterior circulation aneurysms
e) non-tortuous feeding vessels (i.e. endovascularly accessible aneurysm)
f) early vasospasm
g) aneurysm without defined surgical neck (although these are also difficult to "coil"); threshold for choosing coiling vs. clipping is 1 : 2 neck to corpus ratio.
h) basilar artery aneurysms (practically impossible to clip)

Coiling procedure
- ideally under general anesthesia.
- complete patient immobilization (and thus general anesthesia) is mandatory.
- arterial access via ***puncture of femoral artery***.
- HEPARIN bolus IV (100 U/kg) to achieve activated coagulation time > 250 seconds (in ruptured aneurysms, patients may not receive heparin until first coil is deployed).
- **6F guide catheter** is placed in cervical ICA or VA.
- find projection that allows optimal visualization of parent artery in relation to aneurysm.
- plastic microcatheter tip and Micro-Guide wire are shaped according to configuration of aneurysm.
- **microcatheters** are navigated into aneurysm cavity using *magnified road-mapping technique* (computer-generated technique that allows for real-time visualization of endovascular equipment superimposed over map of intracranial arteries).
- microcatheter should not touch walls of aneurysm.
- coils of decreasing sizes are delivered into aneurysm cavity and detached.
- first coil (framing coil) should be slightly smaller than diameter of aneurysm, and it should cross neck of aneurysm several times to form receptacle.
- *ANGIOGRAMS* are obtained before each coil is detached to ensure preservation of parent vessel.

- process is continued until **maximal angiographic obliteration** of aneurysm cavity is achieved.
  - check percentage at www.angiocalc.com
  - complete packing of aneurysmal sac and neck is possible with small aneurysms.
  - in larger aneurysms, neck cannot be occluded completely - higher risk of recurrence (H: balloon-assisted or stent-assisted technique).
- withdraw microcatheter cautiously from aneurysm → final angiogram.
- may reverse heparinization with PROTAMINE.
- patient is transferred to neurologic ICU.
- some experts start ASPIRIN immediately (was important with older generation more thrombogenic coils; now – only if coils are too close to normal vessel lumen)

Techniques for Stent Assisted Coil Embolization of Aneurysms
http://www.medscape.com/viewarticle/770793?src=mp

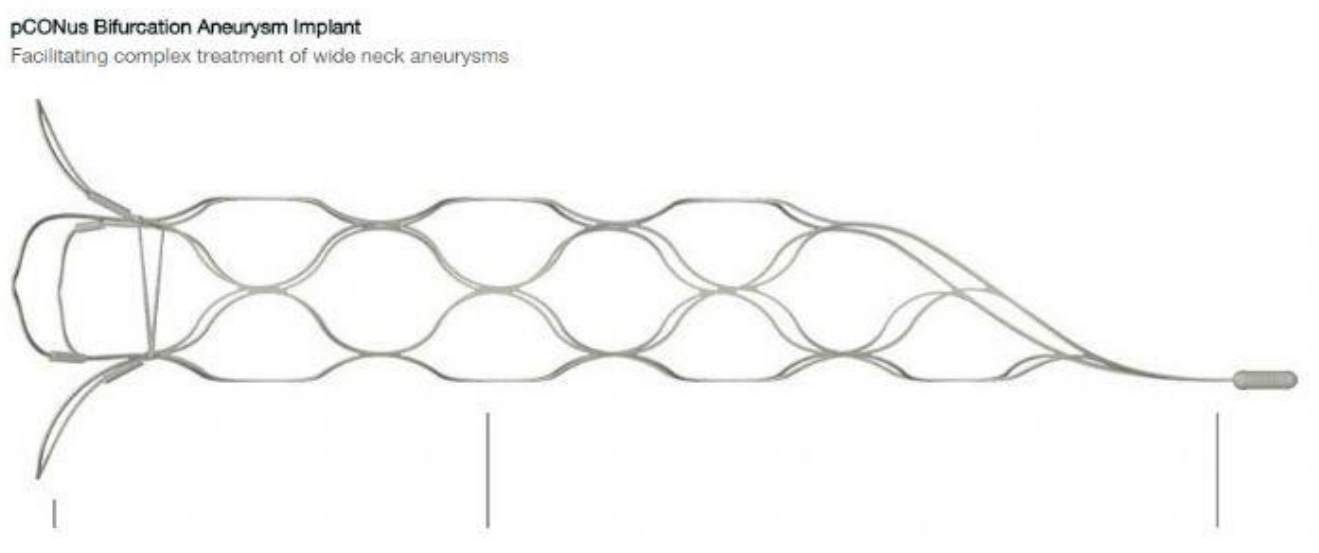
C. Stent-assisted coiling (SAC) - results in significantly lower rates of recanalization and rehemorrhage**!**

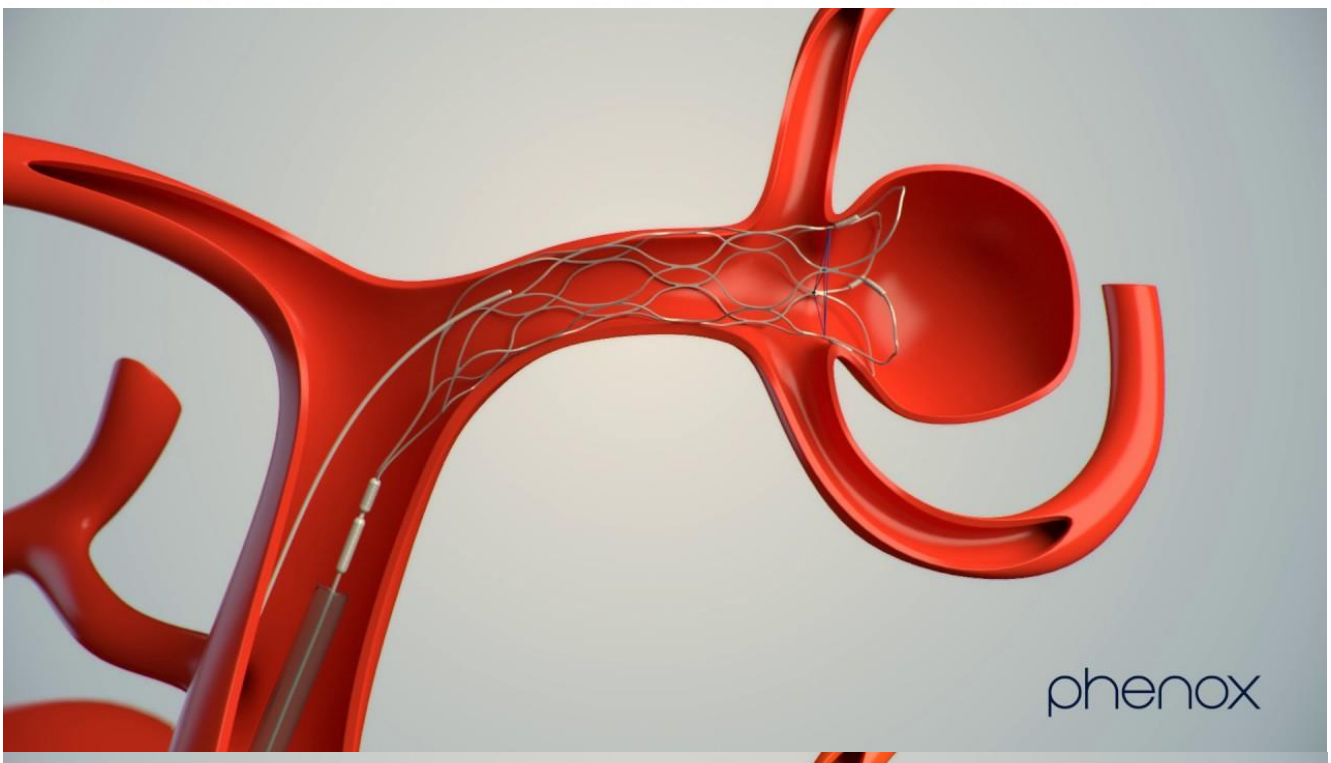
Indication - **"wide neck" aneurysm**:
a) neck width > 4 mm
b) dome-to-neck ratio < 2

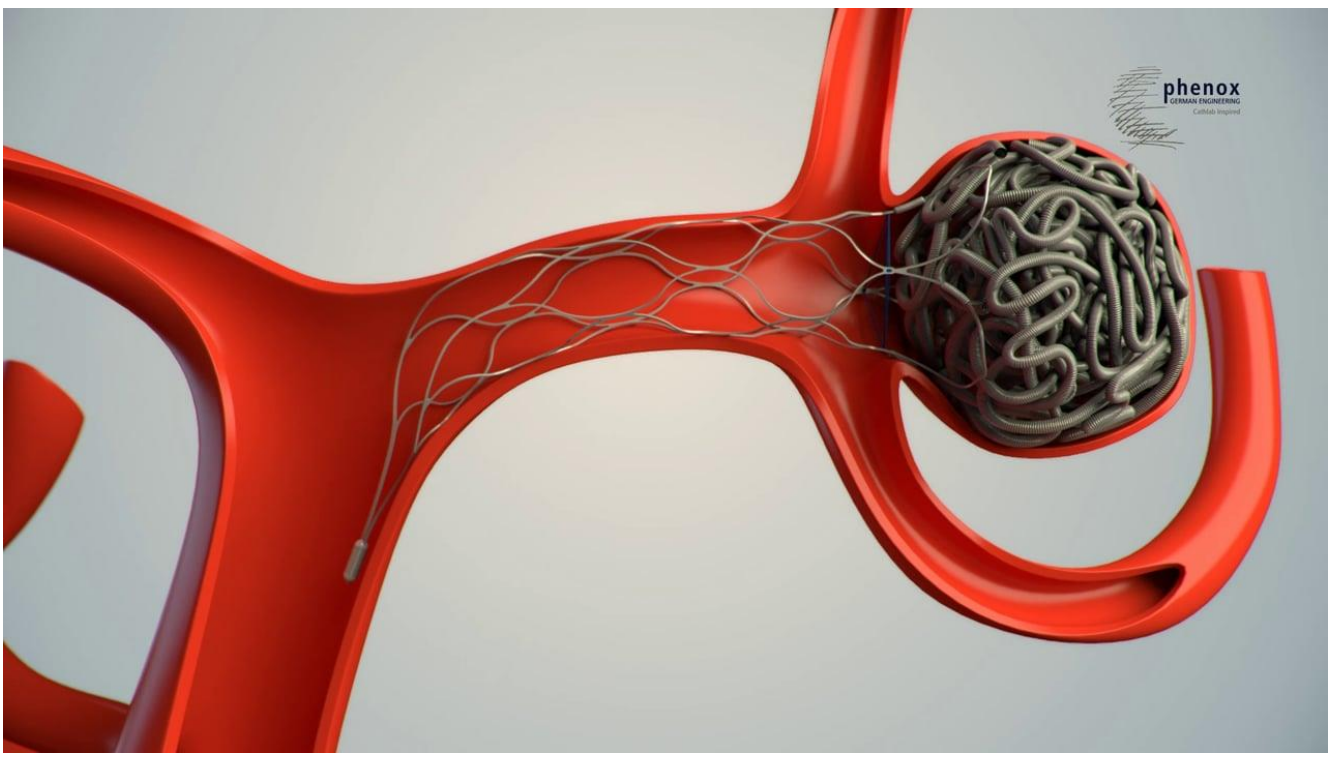
Generally, not used for *ruptured* aneurysms – because unable to use antiplatelets after procedure! (not due to rebleeding risk* but if patient will need EVD or shunting)
*aneurysmal bleeding is arterial and unaffected by platelet function

- stent ***prevents coil protrusion*** into parent vessel - allows for coil embolization of wide-necked aneurysms that might otherwise not be amenable to endovascular therapy.
- stent allows ***denser coil packing***.
- adds need for dual antiplatelet therapy - predisposes to delayed hemorrhagic complications; discontinuation of dual antiplatelet therapy → delayed thromboembolic complications.

pCONus device (Phenox) - stent acts as a device for aneurysm neck protection for wide-neck aneurysm coiling, e.g. at MCA bifurcation (traditionally, treated surgically):







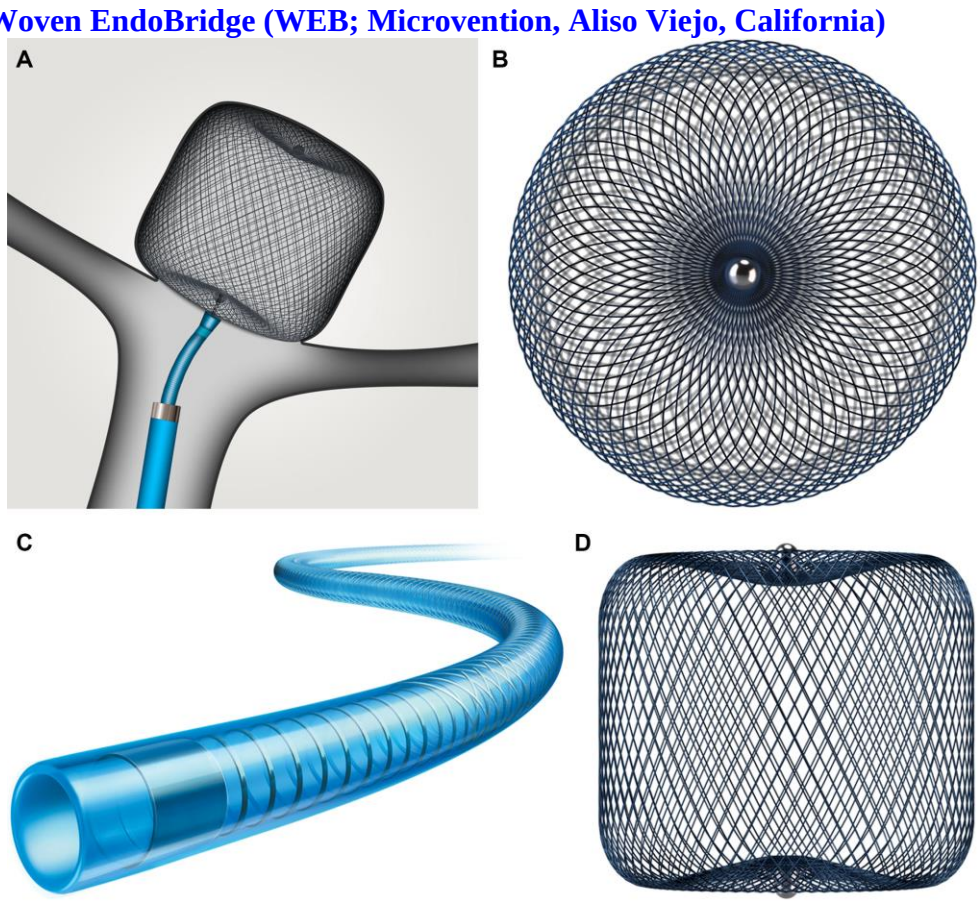
D. Balloon-assisted coiling (BAC)

- rates of hemorrhagic, thromboembolic, and overall procedural complications, plus rate of favorable outcomes are not significantly different between SAC and BAC.

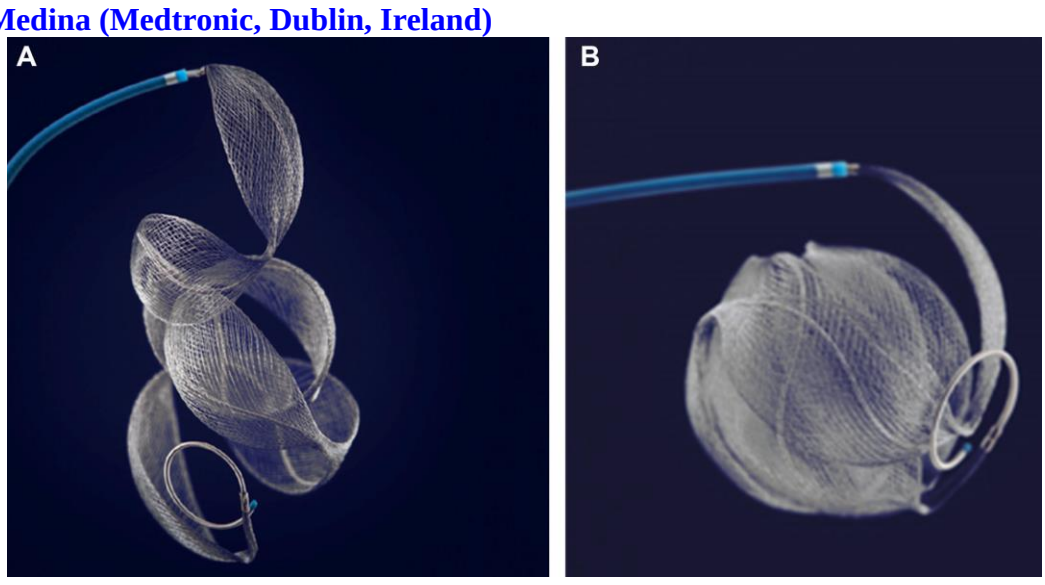
E. Endosaccular flow-disruptors - act from within the lesions.

- dual antiplatelet therapy is not required.

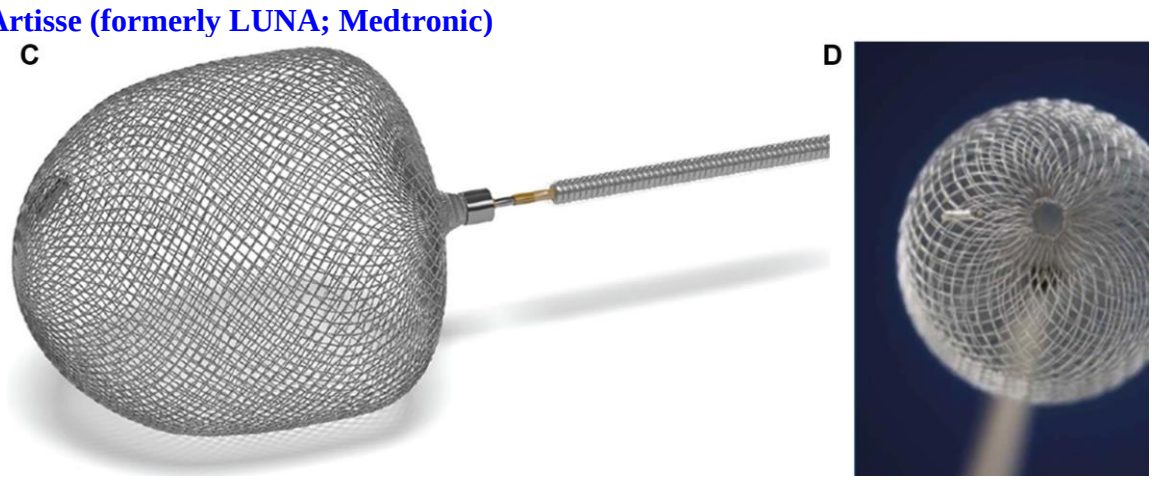
Woven EndoBridge (WEB; Microvention, Aliso Viejo, California)



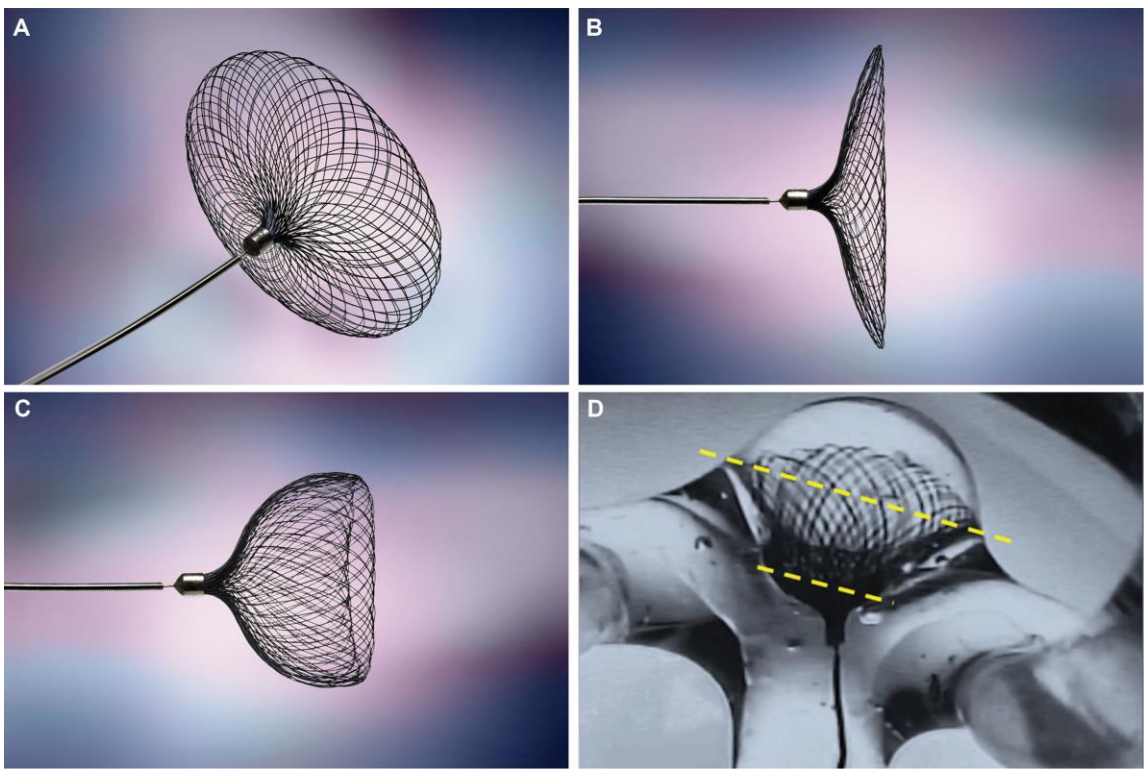
Medina (Medtronic, Dublin, Ireland)



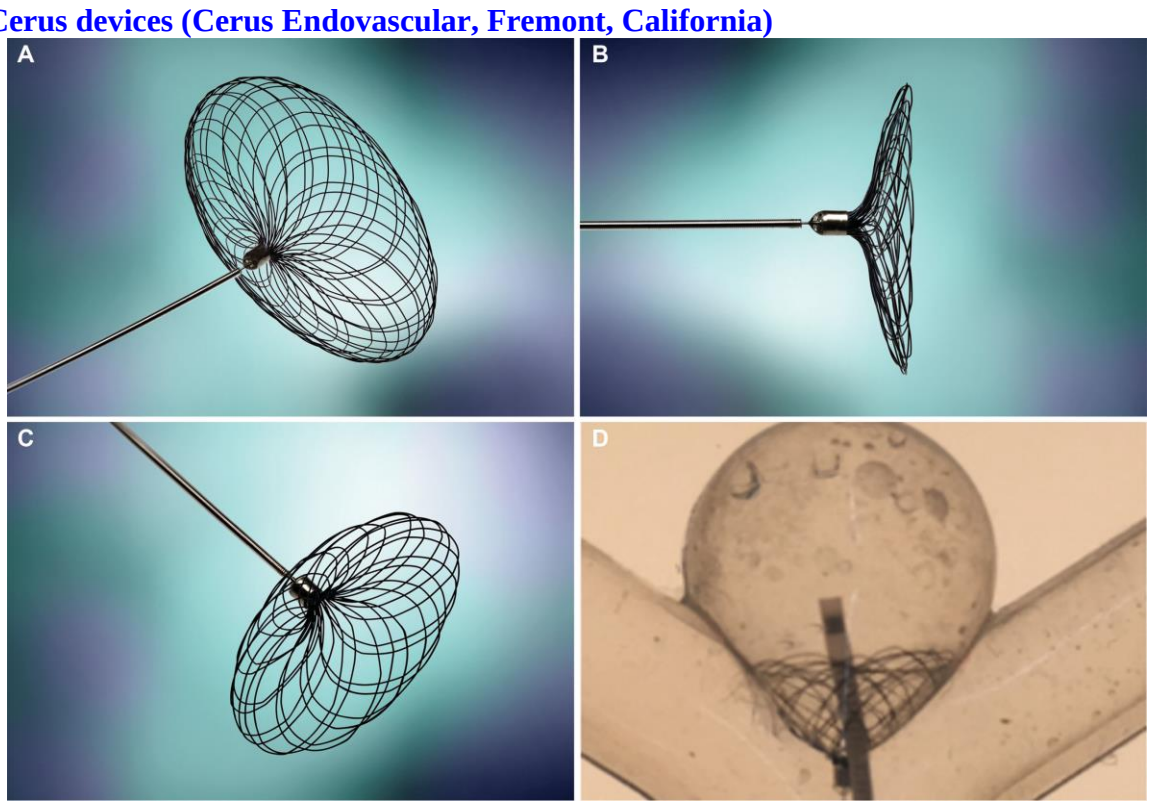
Artisse (formerly LUNA; Medtronic)



Contour (Cerus Endovascular, Fremont, California)



Cerus devices (Cerus Endovascular, Fremont, California)



F. Flow-diverting* endoluminal stents – operate from within the parent artery, i.e. do not catheterize aneurysm sac – reduced risk of rupture!

*term flow diverter, itself, may be a misnomer: though the flow diverter may contribute to the initial thrombus formation in the aneurysm, the final sequestration of the aneurysm from the parent vessel occurs only with endothelialization - this could be the reason why the devices may not work as well in the elderly, where the endothelium may not have the same regenerative capacity, or in thrombosed aneurysms, where inflammatory mediators and proteases secreted by the thrombus impede endothelialization.

- mechanism of action: provide a scaffold for endothelial cells growth at the aneurysmal neck while inducing intra-aneurysmal thrombosis - bimetallic microfabricate braid provides flexible yet supportive structure across aneurysm neck - scaffolding promotes ***endothelial re-pavement***, excluding aneurysm from circulation.

Silk flow diverter (SFD; Balt Extrusion)

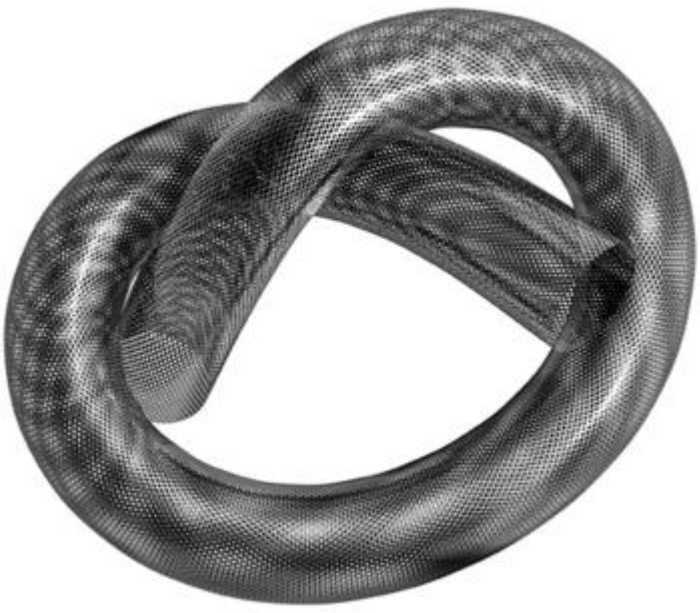
Flow Re-Direction Endoluminal Device (FRED; Microvention)

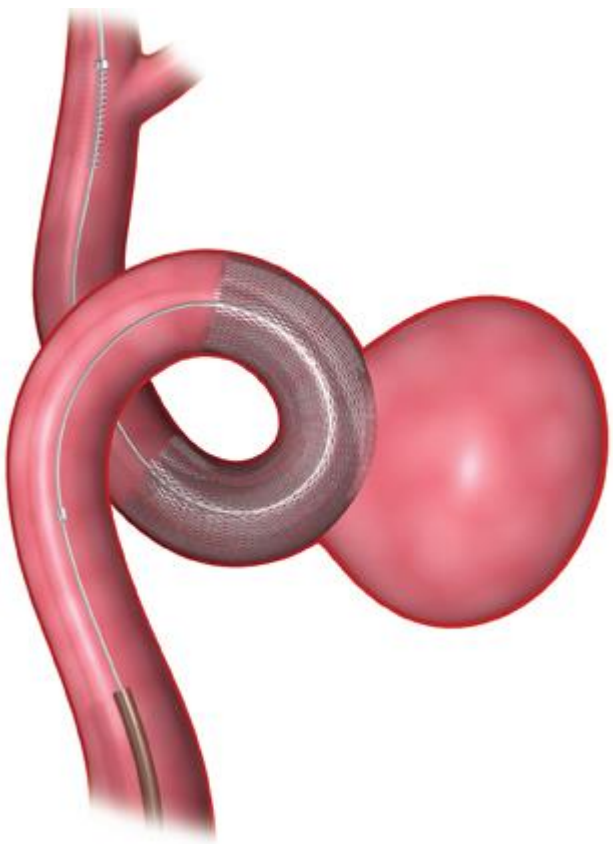
Surpass flow diverter (Stryker Neurovascular)

Pipeline™ Embolization Device (PED, Covidien/ev3) - moves therapy from mere endosaccular occlusion to true parent vessel remodeling.

Indications:
a) wide-necked aneurysms (neck > 4 mm) with unfavorable dome/neck ratios (< 1.5)
b) fusiform / dissecting aneurysms

- FDA approved for carotid artery - can block giant and wide-necked aneurysms.
  - aneurysm occlusion rates 84-94% (if aneurysm is going to occlude it happens within 6 months; still wait total 12 months – then coil)
  - jailed side branches preserve patency - incidence of major supraclinoid ICA *branch occlusion* after treatment is 0-7% and these events are not associated with new neurological deficits.
- can also use in basilar artery (preserves perforators) but not at the basilar tip.
  Safe in posterior circulation!
- flexible (allows it to be used in tortuous anatomy) mesh tube made of nickel-cobalt chromium alloy and platinum.
- may place *multiple devices, one inside another* (customized constructs with variable degrees of aneurysm coverage and flow disruption); but wait > 1 year for first stent effect (if see stagnant flow in aneurysm during angio, it is enough to thrombose aneurysm over time)
- 70% of aneurysms remain obstructed, without significant arterial stenosis 1 year after PED implantation.
- some experts use successfully also for ruptured aneurysms.
- patients should start ***dual antiplatelet therapy*** before implantation* → PLAVIX for 6 months + ASPIRIN indefinitely.
  *preferably 5 days of Plavix 75 mg/d; check assay on the day of surgery:
  if < 90 – do not proceed (if bleeding happens it will be catastrophic);
  if nontherapeutic, proceed with ReoPro intraop, then prasugrel (Effient) postop
  New stents are under development with laser-smoothed surfaces – will not need antiplatelet agents at all!
- contraindicated in active infection, inability to take antiplatelet therapy.





- adding coils to pipeline device increases rate and fastens aneurysm occlusion (rupture risk↓) and decrease risk of stent prolapse into wide-necked aneurysm cavity.

  N.B. do not pack coils densely (need only to promote thrombosis) – thrombotic mass effect on pipeline will cause stent stenosis (H: intrastent angioplasty)

SPECIAL SITUATIONS

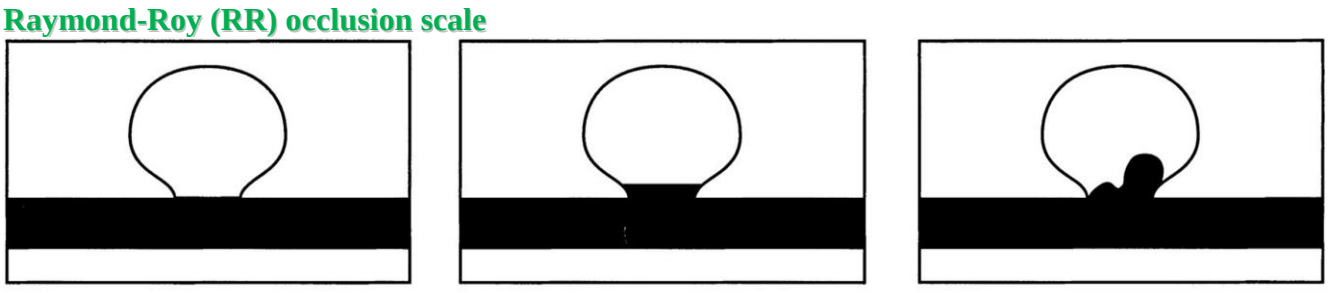
RECANALIZATION (OF PREVIOUSLY TREATED ANEURYSM)

Risk factors for recanalization:

1) large volume (> 600 mm^3) aneurysms
2) low volume (< 20%) packing.

- high rates (15-33% at 18 mos) of recurrence (recanalization).
- mechanisms: *coil compaction*, unorganized *unstable thrombus* formation, *absence of neointima* formation at the neck of coiled aneurysms.

Raymond-Roy (RR) occlusion scale

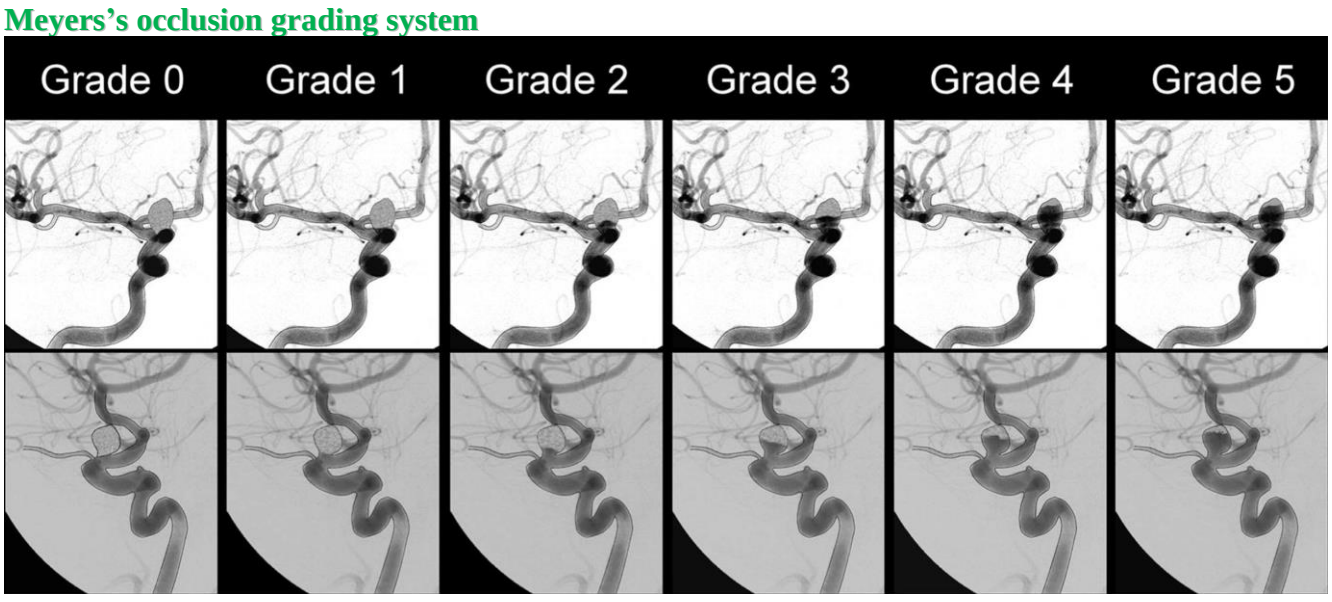


COMPLETE
Complete aneurysm occlusion

RESIDUAL NECK
Residual aneurysm neck

RESIDUAL ANEURYSM
Residual aneurysm dome

Meyers's occlusion grading system



Grade 0: complete and total aneurysm occlusion. Grade 1: ≥90% volumetric aneurysm occlusion. Grade 2: 70-89% volumetric aneurysm occlusion. Grade 3: 50-69% volumetric aneurysm occlusion. Grade 4: 25-49% volumetric aneurysm occlusion. Grade 5:< 25% volumetric aneurysm occlusion.

When to treat? If remnant ***keeps enlarging*** at each follow up (threshold to treat is lower for previously ruptured aneurysms).

- re-coiling is fairly safe technique
- additional techniques: complex shaped coils, balloon and stent technology, bioactive coils*

  *coated with various substances (swell within aneurysm, promote fibrous tissue formation) - enhanced thrombus permanency.

MULTIPLE ANEURYSMS

a) if incidental aneurysm is in field of surgical approach, it can be clipped along with ruptured aneurysm.
b) if incidental aneurysm is on contralateral side, then it can be clipped electively at another time (to prevent bilateral vascular injury at the same time).

WIDE-NECK ANEURYSMS

- now amenable to endovascular treatment with pCONus device – see above >>

ANEURYSM COEXISTING WITH AVM

(4-18% cases) – AVM excision may precipitate rupture of associated aneurysm (aneurysm subjected to increased flow resistance).

ANEURYSM CAUSING CN3 PALSY

– better results with clipping (than coiling).

CAROTID STENOSIS ASSOCIATED WITH ICA ANEURYSM

- stenosis may have "protective effect" on aneurysm - endarterectomy can expose aneurysm to increased hemodynamic stress and potentiate rupture;

H: elective aneurysm clipping → endarterectomy.

ANEURYSM PERFORATION WITH COIL

during endovascular coiling procedure; H: BP↓ and don't stop, continue coiling; place EVD.

CAROTID ANEURYSM WITHIN CAVERNOUS SINUS

– if ruptures, bleeding is contained but risk of CC fistula.

Differential from paraclinoid aneurysm (i.e. intradural) – CTA in coronal plane: look at **optic strut** (bony structure running transversely as floor of optic canal):

PARACLINOID aneurysm – above optic strut
CAVERNOUS aneurysm – below optic strut

Treatment indications:

1) **diameter** > 1 cm (risk of erosion through dura → SAH in case of rupture)
2) **symptomatic**:
   a) CC fistula
   b) CN palsies
   c) thrombemboli (from turbulent flow within aneurysm)

Treatment modalities:

a) stand-alone coil embolization or balloon remodeling technique
b) stent-assisted coil embolization
c) flow-diverter (pipeline)
d) clipping
e) bypass/trapping

RECANALIZATION IN PREVIOUS STENT-ASSIST COILED ANEURYSM

– attempt coiling again.

- if needs clipping, may need to open aneurysm sac to remove coils to allow neck clipping.

CERVICAL ICA ANEURYSMS

– treatment not indicated.

ICA TERMINUS ANEURYSMS

- high rate of recurrence after treatment.

ACHA ANEURYSMS

- AChA supplies posterior limb of internal capsule and optic radiation.
- treatment of AChA aneurysms poses particular challenges - complex anatomy of aneurysm + relatively small diameter of AChAs.
- limitation of vessel manipulation should be used to improve outcomes.

ACOMA ANEURYSMS

- aneurysms are known to rupture at nearly any size – risk proportional to size!

ANEURYSM WITH ATHEROMA

- even after clipping contrast may go in (neck is too stiff): H: place second reinforcing clip (piggyback on first clip).

FOLLOW UP

N.B. ***MRI with gadolinium IV bolus*** better than CTA or MRA visualizes previously coiled / clipped aneurysms (lots of metal artifacts on CT).
At some point perform ***simultaneous angiography and MRA*** so that in the future, aneurysm recurrence can be monitored using MRI.

After coiling

1. **1-vessel angiogram** - 6 months after coiling (if it was stent-assisted coil embolization, patient may discontinue PLAVIX, but will remain on ASPIRIN for life)
2. **4-vessel angiogram** - 18 months (1.5 yrs) + 42 months (3.5 yrs) after coiling.
3. Later – **MRA** / **CTA** every 4 years for life

After clipping (there is currently no standard protocol); recurrence risk is 0.26-0.053% / year

2 weeks – **clinical**
6 weeks – **clinical**
1 year – **angiography**
every 4-5 years – **CTA**

Risk for de novo aneurysm is 0.84-1.8% / year

PROGNOSIS

- risk and treatment of recanalization – see above >>

SAH

1/4 of patients with aSAH die, and roughly half of survivors are left with some persistent neurological deficit.

- overall MORTALITY is 45% (range: 32-67%):
  10-15% die before reaching medical attention
  20-25% die within 1 month
  50% deaths occur within 1 month
- prognosis is worse for:
  1) women
  2) blacks
  3) age > 70 yrs
  4) smokers – *smoking increases risk of aneurysm rupture 3-6 times*!
  5) posterior circulation aneurysms
  6) higher clinical grades
  7) aneurysms (vs. AVMs)
- causes of death:
  1) direct effect of aneurysm rupture (25%)
  2) rebleeding (17.6-25%) - mortality ≈ 51-85% !!!
     ≈ 15-20% aneurysmal SAHs rebleed in first 2 weeks – see above
  3) delayed ischemia due to vasospasm (7-32%)
  4) neurogenic pulmonary edema
  5) neurogenic stunned myocardium
- 25-50% survivors have moderate to severe neurological deficits.
- 66% of those who have successful aneurysm clipping never return to the same quality of life as before SAH.

Mortality after SAH has improved (Danish study):

Endpoint	1983 - 1987	2008 - 2012
30-day mortality (%)	38	25
1-year mortality (%)	43	31
5-year mortality (%)	51	37

UNRUPTURED ANEURYSMS

CLIPPING

- 10.1% of craniotomies result in a complication leading to a modified Rankin Scale score >1 at 12 months.
- significant risk factors for complications:
  1) age (odds ratio, 1.04; 95% CI, 1.02-1.06)
  2) size (odds ratio, 1.12; 95% CI, 1.09-1.15)
  3) posterior circulation location (odds ratio, 2.95; 95% CI, 1.82-4.78).
- cumulative 10-year risk of retreatment or rupture - 3.0% (95% CI, 1.3-7.0).

BIBLIOGRAPHY for ch. "Neurovascular Disorders" → follow this LINK >>