Intracerebral Hemorrhage (ICH)

s. spontaneous ICH (sICH), intraparenchymal hematoma (IPH)

Last updated: August 8, 2020

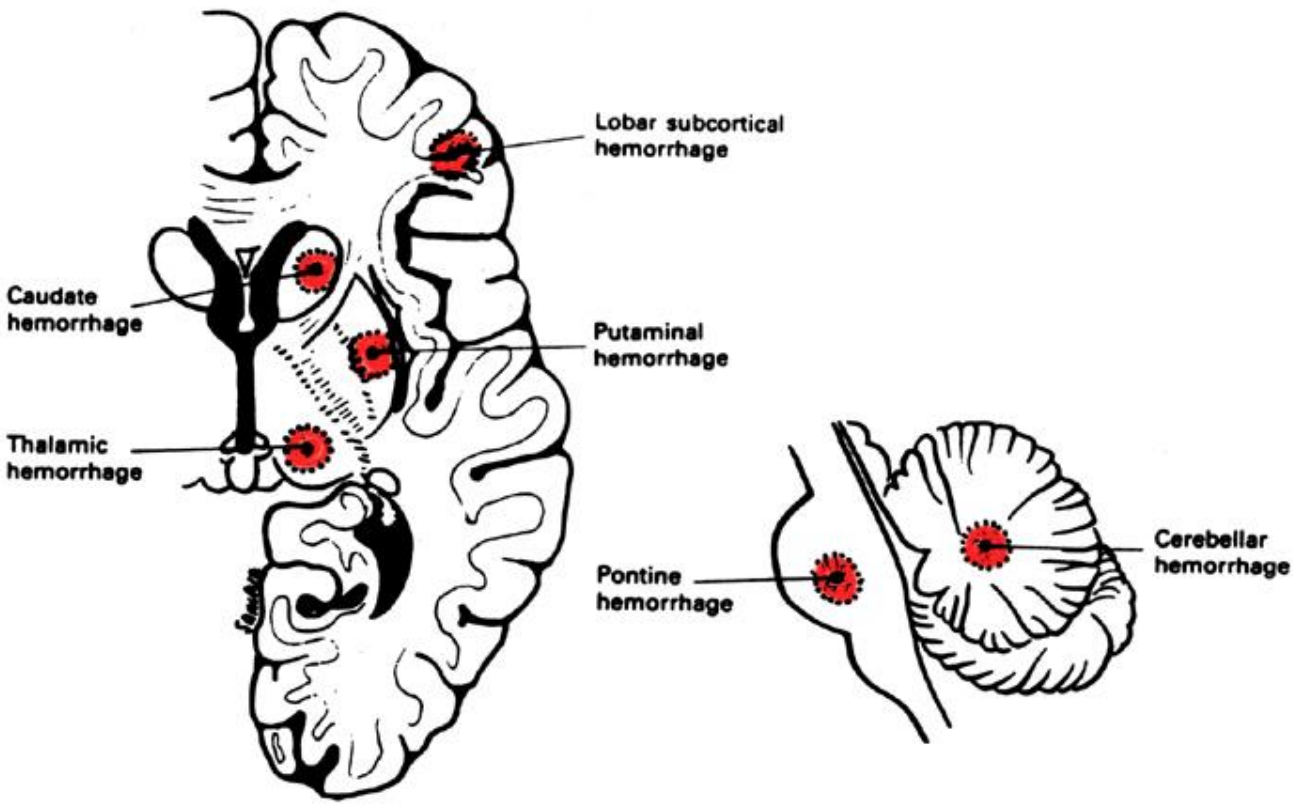
ICH - blood clot in brain parenchyma (usually from rupture of small penetrating artery)

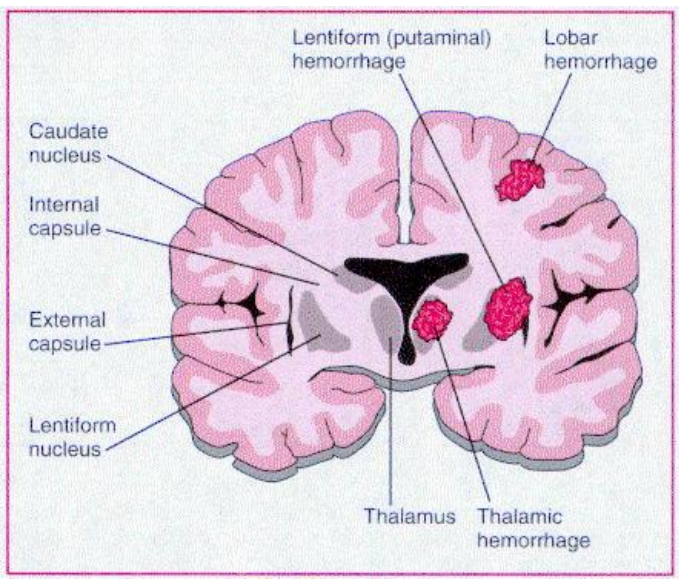
- **spontaneous ICH** - no immediately preceding trauma.
- **spontaneous ICH** - most common type of nontraumatic INTRACRANIAL hemorrhage.

Commonest sites of ICH:
Putamen (40-44%)
Thalamus (10-15%)
Cerebellum (5-10%)
Pons (5-15%)
Caudate (4-7%)
Lobar subcortical (10-25%)

i.e. 60% basal nuclei, 20% posterior fossa, 20% thalamus & subcortical white matter

- in whites, most of the initial and recurrent ICHs tend to be ***lobar***, whereas ***deep*** hemorrhages (both initial and recurrent) are more common in Asians.





Source of picture: Anthony S. Fauci, Eugene Braunwald "Harrison's Principles of Internal Medicine" (1998); McGraw-Hill (Tx); ISBN-13: 978-0070202917 >>

ETIOLOGY

Multiple microbleeds:
Elderly – chronic *hypertension* or *amyloid* angiopathy.
vs.
Children – *cavernomas* or *hematologic abnormalities*

Any age - acute disseminated encephalomyelitis (s. acute hemorrhagic leukoencephalopathy, Weston-Hurst disease).

1. **Arterial hypertension** – most common cause of ICH (called hypertensive ICH).

ICH accounts for ≈ 15% deaths in chronic hypertension

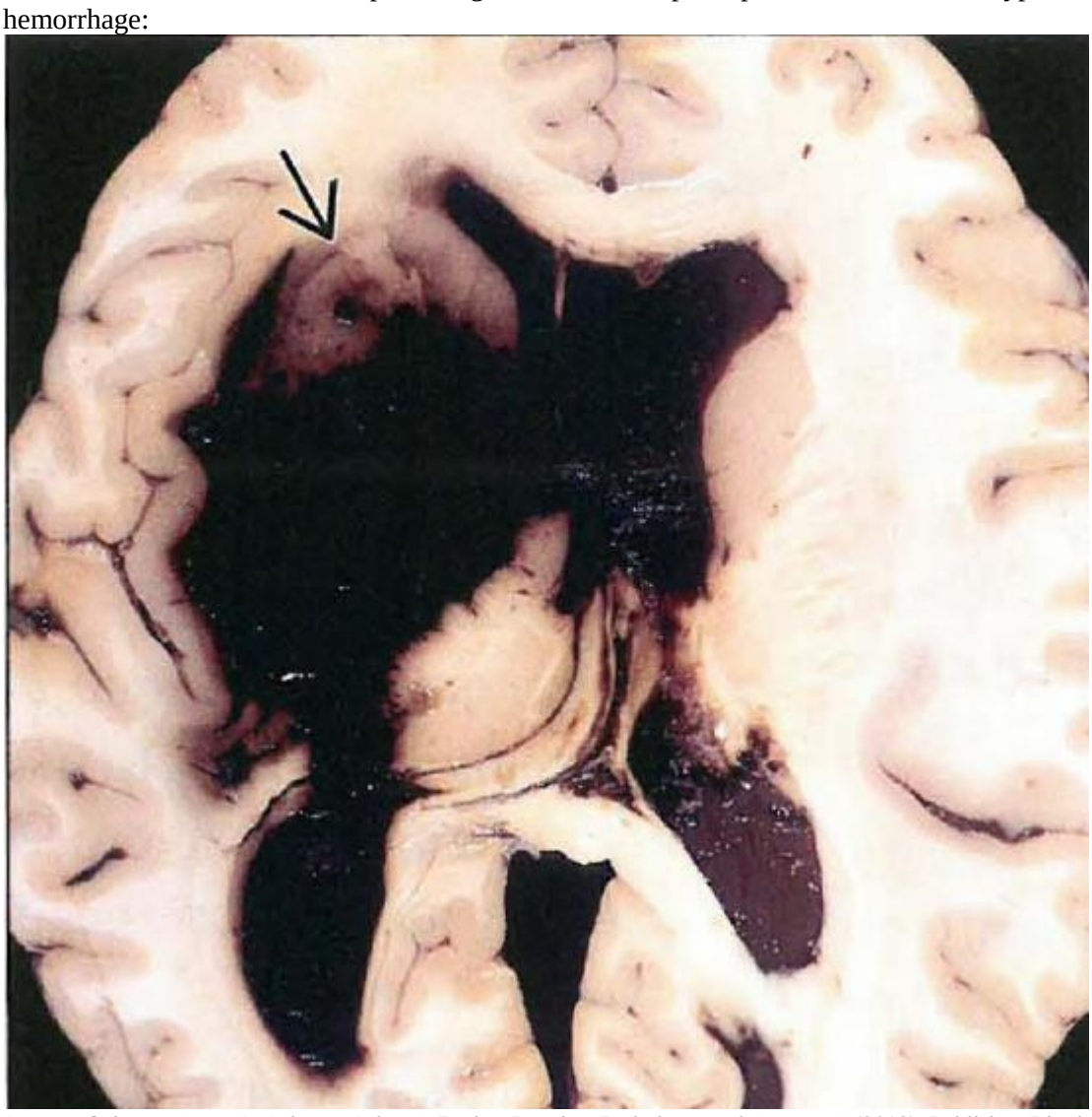
- **acute hypertension** can be caused by sympathomimetic drugs.
- **chronic hypertension** causes ***hyaline arteriolosclerosis (lipohyalinosis)*** ÷ ***fibrinoid necrosis*** and **CHARCOT-BOUCHARD microaneurysms**.
- mostly affected are ***deep penetrating arteries**** (of circle of Willis and of basilar artery) - feed directly off medium-sized arteries and are not protected by usual step-down in vessel size that protects more distal end arteries of cortical vessels from high intraluminal pressure; *subcortical arteries* are less frequently affected.

*occlusion of these arteries causes LACUNAR INFARCTIONS

- commonest sites for hypertensive ICH (in order of frequency):
  1) **putamen / external capsule** – classic!
  2) thalamus
  3) cerebellum
  4) pons
  5) caudate

N.B. lobar subcortical white matter is not usual site for hypertensive ICH! (because of improved hypertension control, percentage of lobar ICH has increased)

Hematoma centered in striatocapsular region - external capsule/putamen - classic for hypertensive hemorrhage:



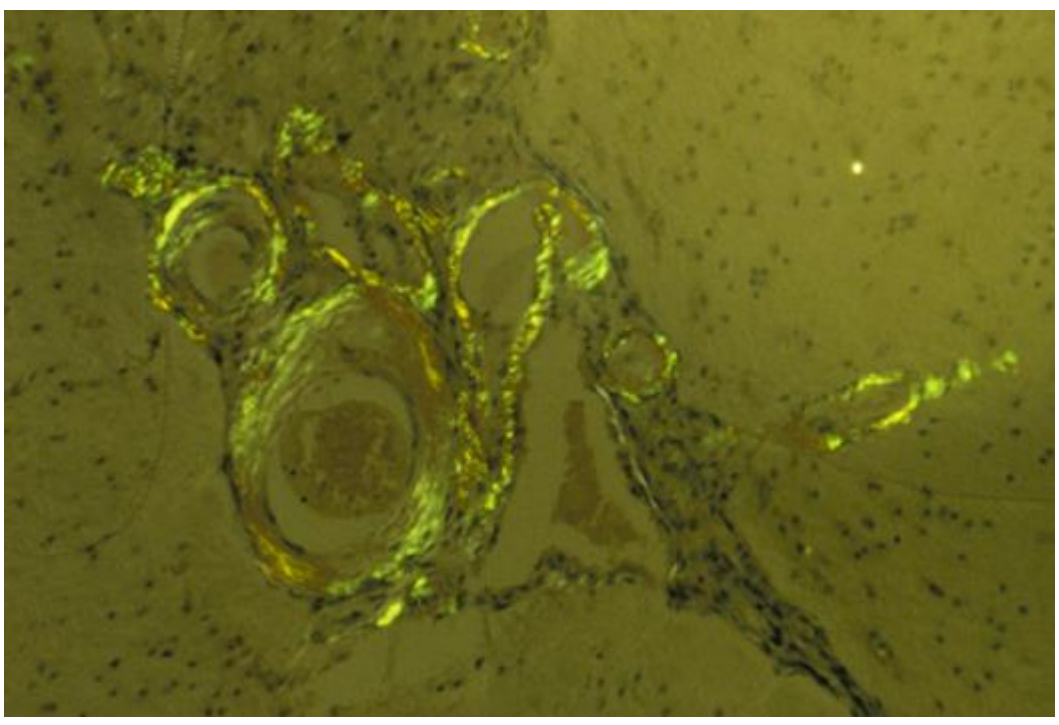
Source of picture: Anne G. Osborn "Osborn's Brain - Imaging, Pathology, and Anatomy" (2012); Publisher: Lippincott Williams & Wilkins; ISBN-13: 978-1931884211 >>

2. **Cerebral amyloid angiopathy (s. congophilic angiopathy)**
   - appears in Alzheimer's disease (rare in patients < 55, except in Down syndrome) – look for dementia when collecting PMH / ROS.
   - amyloid deposits (chemically related to Alzheimer plaques) in **media** of *smaller cerebral arteries* (but not elsewhere in body – no systemic amyloidosis!).
   - probably amyloid potentiates PLASMINOGEN.
   - multiple small nonhypertensive ***lobar hemorrhages***.
   - diagnosed only postmortem by Congo red staining ("congophilic angiopathy").
   - clinical diagnosis - **modified Boston criteria** (sensitivity 94.7%, specificity 81.2%).

Signs of moderate / severe CAA (vs. absent / mild CAA) in patients with lobar ICH:
1) SAH (89% vs 42%; P=.014)
2) intracerebral hemorrhage with finger-like projections (39% vs 0%; P=.043)
3) presence of APOE ε4 (genotyping from peripheral blood samples) (50% vs 8%; P=.002).

- SAH + either APOE ε4 or finger-like projections is 96% sensitive to rule in CAA-associated lobar ICH.

   - prognosis – see below >>



3. **Structural lesions** – most common etiology in ***lobar hemorrhages*** (vs. only rarely affect basal ganglia, thalamus, pons)

Child with ICH – AVM until proven otherwise!

1) ruptured **vascular malformations & aneurysms*** - second most common cause of ICH!
   e.g. young normotensive patients with lobar and intraventricular hemorrhages
   ***aneurysms** rarely bleed only into brain, causing local hematoma near brain surface (e.g. when surrounding subarachnoid space has been 'sealed off' by preceding SAH)
2) hemorrhages within **tumors** (esp. glioblastoma multiforme, metastases of melanoma, renal carcinoma, choriocarcinoma).

4. **Hemorrhagic transformation of ischemic stroke** (esp. venous thrombosis, embolic stroke).

5. **Hyperperfusion after carotid stenting / endarterectomy.**

6. **Venous sinus thrombosis.**

7. **Bollinger's Spät-apoplexie** - delayed ICH post TBI.

ETIOLOGY ACCORDING TO PATIENT'S AGE

YOUNG PERSONS – vascular disorders (AVM, aneurysm, vasculitis), drug abuse (amphetamines, cocaine), hematologic abnormalities

ELDERLY PERSONS – hypertension, amyloid angiopathy, tumors, coagulopathies (incl. anticoagulants).

PRECIPITATING conditions

1. **Pregnancy** (esp. with eclampsia)
   - eclampsia causes > 40% ICHs in pregnancy.
   - ICH is common cause of death from eclampsia.
2. **Acute BP rises** (can cause ICH even in absence of preexisting severe hypertension!), e.g. sympatheticomimetic drugs (esp. cocaine, amphetamines).
3. **Bleeding diatheses** (esp. iatrogenic anticoagulation and thrombolysis, liver dysfunction) - hemorrhages can occur at any site, tend to evolve slowly and be multiple.
4. **Trauma** (4-23% head injury cases) - multifocal inhomogeneous hemorrhages (most common in frontal and temporal lobes). see p. TrH1 >>
5. Heavy **alcohol** consumption (acute or chronic).
6. **Drug** abuse (amphetamines, cocaine)

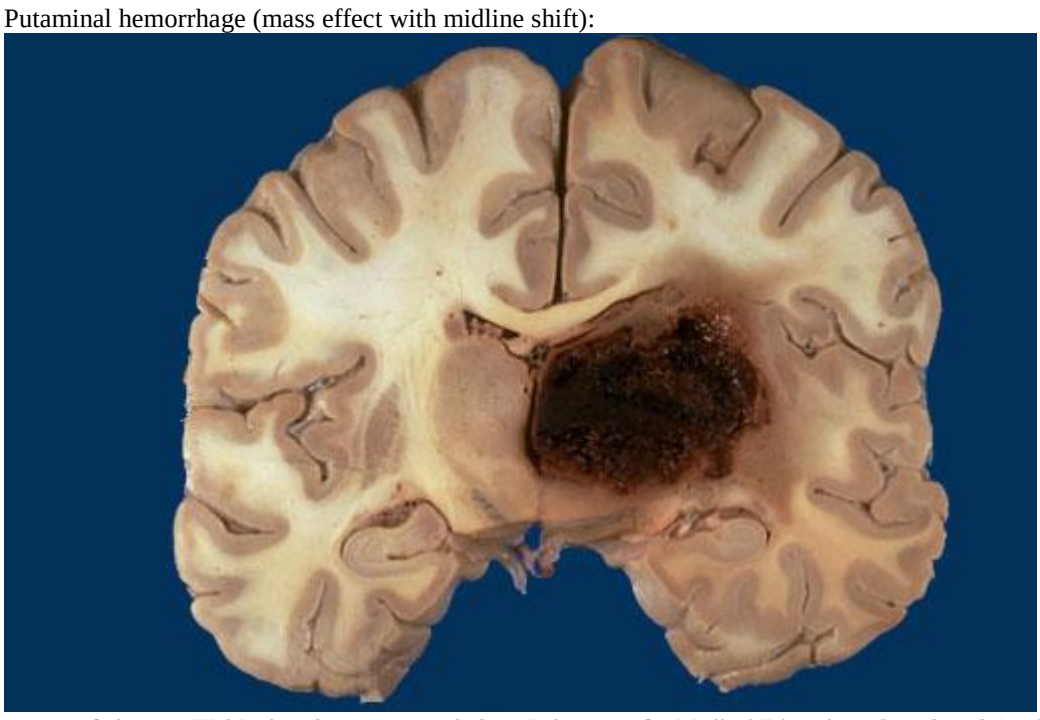
RISK FACTORS

1. **Age > 70** (increases ICH risk 7x) – amyloid angiopathy, use of anticoagulants
2. **Male** sex
3. **Non-Caucasian** race
4. **Previous** CVA (23x)
5. **NSAID use** – only DICLOFENAC and MELOXICAM (RR 1.27; 95% CI, 1.02– 1.59 and RR 1.27; 95% CI, 1.08–1.50, respectively).
6. **Statin use**; however, the ischemic stroke benefit greatly outweighs the risk.

PATHOLOGY, PATHOPHYSIOLOGY

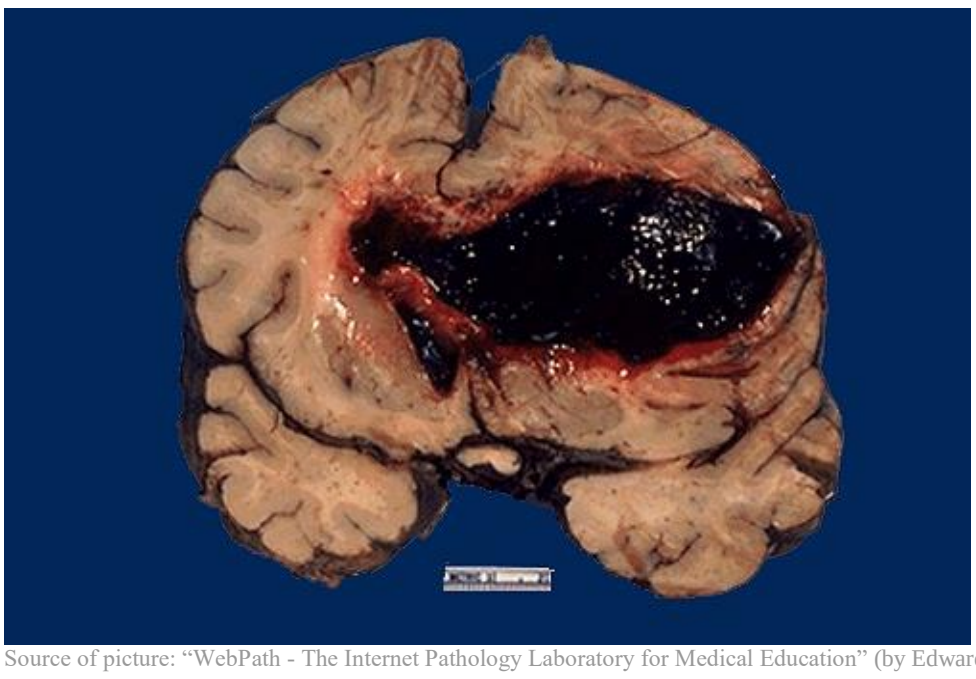
- hematomas are at first soft and dissect along white matter fiber tracts (rather than destroying brain tissue locally).
- hematoma may spread (lobar and cerebellar hemorrhages tend to remain confined within parenchyma):
  a) **intraparenchymal** extensions
  b) **intraventricular** extension (primary intraventricular hemorrhage is rare!) → acute hydrocephalus
  c) **SAH**
- *bleeding is spontaneously limited* by resistance of surrounding tissue pressure (usually within 30 minutes);
  – once bleeding stops, it generally does not start again.
  – in severe cases, bleeding continues until death.
- large hematoma causes ***mass effect*** → distorts structures (with ischemic pressure damage), increases ICP → herniation.
- if patient survives initial ICP changes, blood is absorbed over weeks ÷ months → **cavity or cleft** (lined by glial scar and hemosiderin-containing macrophages) that may disconnect brain pathways.
  – *less frequently*, blood clot is treated as FOREIGN BODY - **calcifies** and is surrounded by thick glial membrane.

Putaminal hemorrhage (mass effect with midline shift):



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

Hypertensive basal ganglia hemorrhage:



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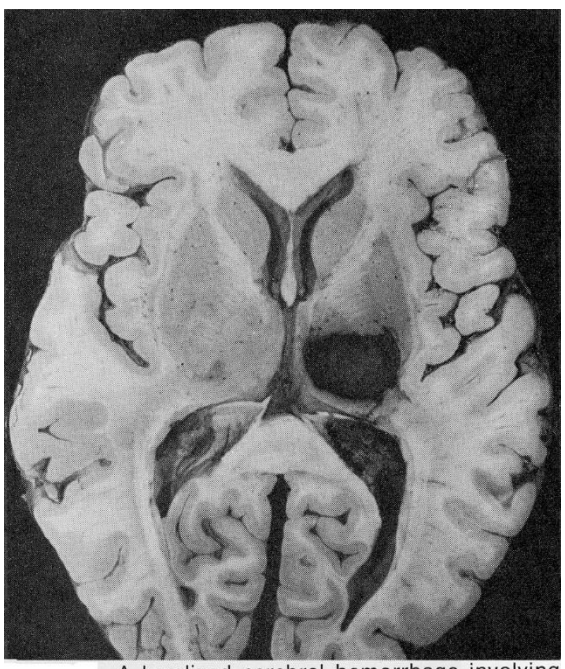
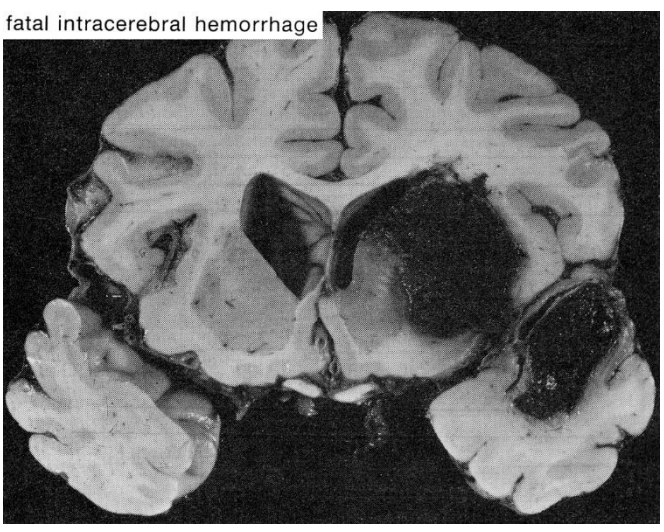
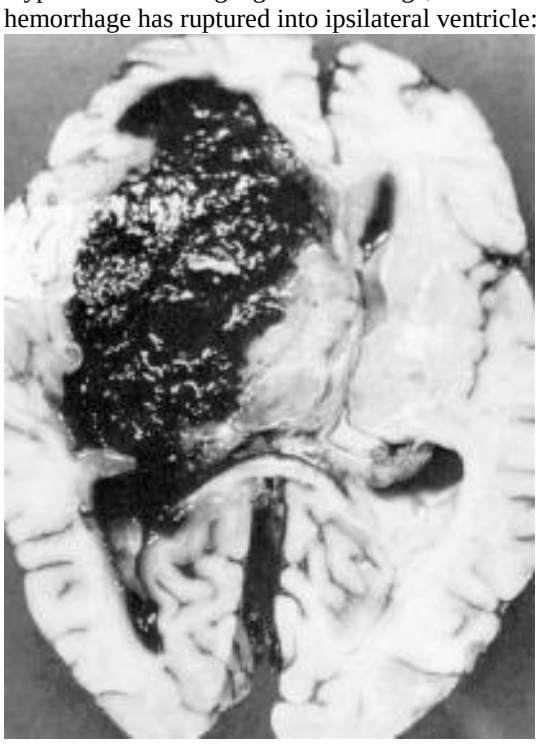
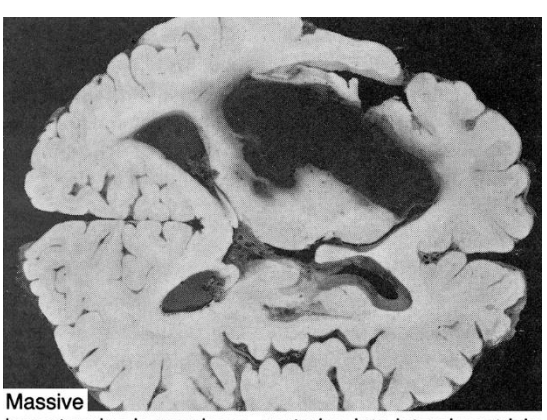


A localized cerebral hemorrhage involving basal ganglia and the internal and external capsules.

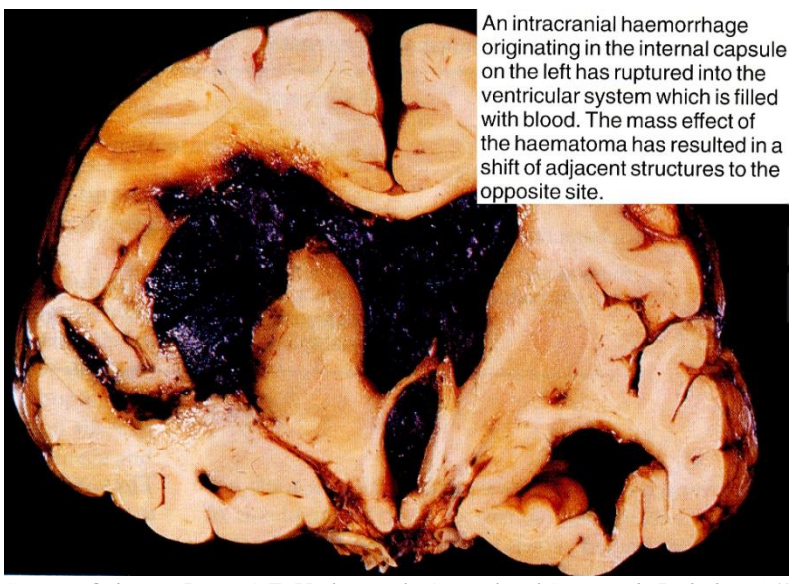


Hypertensive basal ganglia hemorrhage;
hemorrhage has ruptured into ipsilateral ventricle:



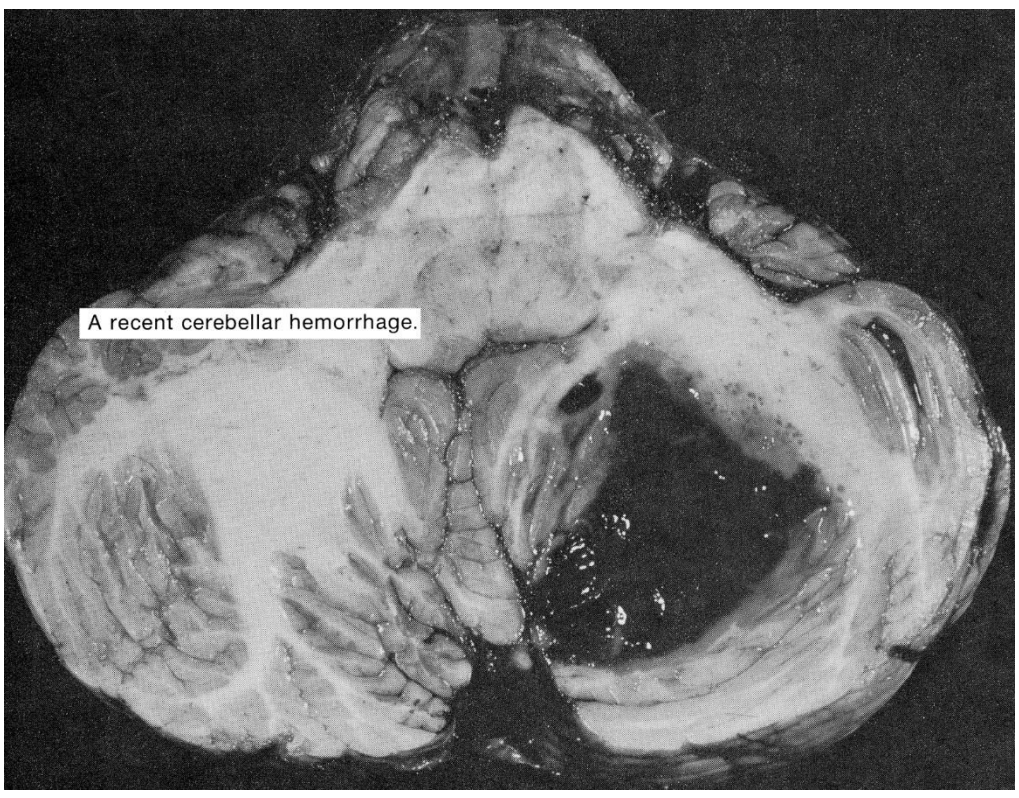


Massive hypertensive hemorrhage, rupturing into lateral ventricle



An intracranial haemorrhage originating in the internal capsule on the left has ruptured into the ventricular system which is filled with blood. The mass effect of the haematoma has resulted in a shift of adjacent structures to the opposite site.

Source of picture: James C.E. Underwood "General and Systematic Pathology" (1992); Churchill Livingstone; ISBN-13: 978-0443037122 >>



EPIDEMIOLOGY

- ≈ 10-15% of all strokes (up to 30% in blacks and Asians).
- men ≥ women.
- peak INCIDENCE (for spontaneous ICH) ≈ 60 yrs (incidence in individuals > 55 yrs doubles with each decade until age 80 years).

CLINICAL FEATURES

Most clinically destructive ICH are located near basal ganglia, internal capsule, thalamus, cerebellum, or brain stem!

- often *history of arterial hypertension*.
- usually ***no prodromal attacks***.
- most hemorrhages occur *during activity* (e.g. sexual intercourse, Valsalva's maneuvers, parturition labor).
- presentation:
  a) MAXIMUM AT ONSET (33%)
  b) SMOOTH PROGRESSION over several hours (66%) - because hemorrhages arise from tiny vessels; further clinical evolution is due to brain swelling.
     – 20% of patients experience a decrease in the GCS of ≥ 2 points between the prehospital EMS assessment and the initial evaluation in the ED.
     – another 15-23% of patients demonstrate continued deterioration within the first hours after hospital arrival.

Abrupt & increasing focal signs → mass effect (ICP↑) → herniation → death

1. **Focal signs** – depend on site of hemorrhage (as hematoma enlarges, focal symptoms increase);
   – if hematoma remains small, the only symptoms relate to focal blood collection. *see below*

2. **Signs of mass effect** (develop after hematoma becomes large enough to raise ICP):
   1) headache (40-50%).
   2) nausea & vomiting (40-50%).
   3) normal ÷ decreased level of consciousness (50%); may progress to coma in 24-48 hrs (consciousness is sometimes impaired at start – esp. pontine or thalamic hemorrhage).

3. **Seizures** (clinical 6-16%, electrographic 28-31%, status 0.4% within first 7 days*)
   *much more common with lobar hemorrhage (≈ 25% patients) - cortical irritation by blood.

   CAVE score for seizure risk:
   1. **C**ortical involvement
   2. **A**ge > 65 y
   3. **V**olume > 10 mL
   4. **E**arly seizures

   ≥ 2 present – epilepsy risk↑

4. **Meningeal irritation** – if bleeding extends to subarachnoid space.

CLINICAL	SITE OF HEMORRHAGE			
	Putaminal	**Thalamic**	**Pontine**	**Cerebellar**
Unconsciousness	Later	Later	Early	Late
Hemiparesis	Yes	Yes	Quadriparesis	Late
Sensory change	Yes	Yes	Yes	Late
Hemianopia	Yes	Yes	–	–
Pupils (Size / Reaction)	Normal / +	Small / ±	Very small / +	Normal / +
Gaze paresis	Contralateral (*eyes look to ICH*)	Upward (*eyes look to nose tip*)	Bilateral (*centrally positioned eyes*)	Ipsilateral (*eyes look away from ICH*)
Response to calorics	Yes	Yes	–	±
Ocular bobbing	–	–	Sometimes	Sometimes
Gait lost	–	–	Yes	Yes
Vomiting	Occasional	Occasional	Often	Severe

Ocular signs are rapid method of localizing hemorrhages!

DIAGNOSIS

Lumbar puncture is contraindicated! – may cause herniation;
CSF does not provide definitive diagnostic information

– CSF is usually bloody several hours after hemorrhage, but sometimes it is normal initially.

Either CT or MRI may be used for initial neuroimaging (but MRI may be more difficult to perform because of impaired consciousness, vomiting, or agitation)

BLOOD

CBC, chemistries, coagulation studies (prothrombin time, PTT, bleeding time, platelet count), arterial blood gas analysis (in patients with reduced alertness), toxicology screen.

EEG

- polymorphic slow waves over region.

IMAGING

NONCONTRAST CT

- very reliable! - accurately documents hematoma, mass effect, intraventricular hemorrhage, hydrocephalus.

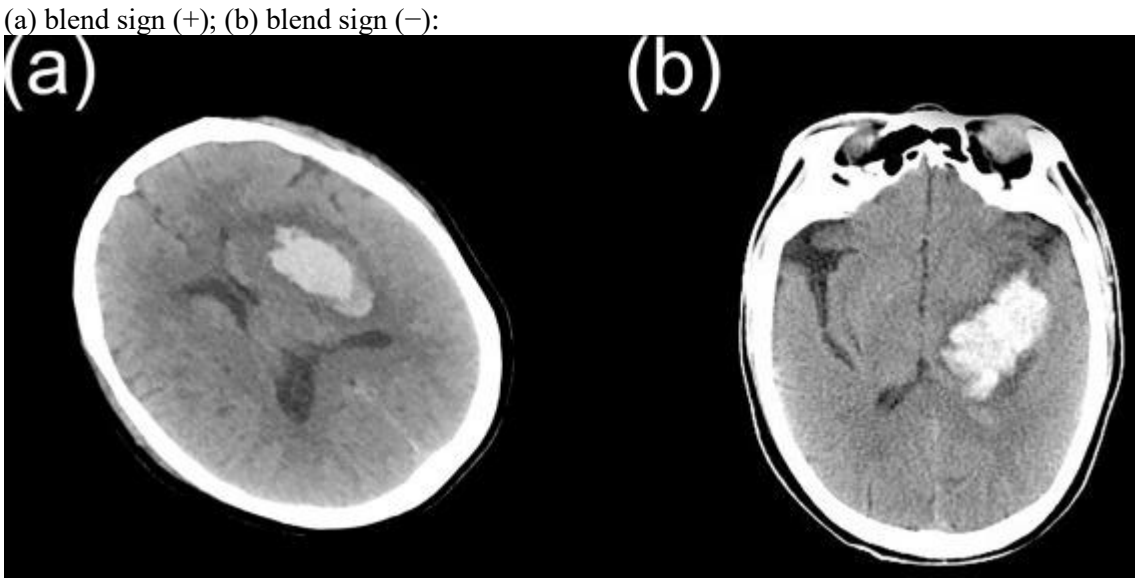
- performed immediately in suspected acute ICH!
- follow-up CT is frequently requested (changes in lesion size, ventricular system).
  1/3 of patients have ICH size growth on repeat imaging!
- fresh hematoma - homogeneous rounded area of increased density (≈ 30-80 HU) + mass effect (vs. hemorrhagic infarctions - areas of increased density [blood] interspersed with areas of decreased density [infarction]).
  – acute hematoma **volume ≥ 80 cm^3** is usually fatal.
  – no edema around ***fresh clot*** (!!!); but ***clot retraction*** → fine rim of low density.
  – in severely anaemic patients (Hct ≤ 20%), hematomas can be isointense to surrounding brain.
  – multifocal hemorrhages at poles (frontal, temporal, or occipital) suggest TRAUMATIC etiology.
  – TUMORS can acquire similar density in contrast CT!

  CT is always performed *without* contrast medium if hemorrhage is possible!

- layering in clot (as if fluid-blood layer) or mixed iso-hyperdense picture:
  a) hyperacute / ongoing bleeding
  b) coagulopathic patient

- **blend sign** - blending regions of high and low density with clear boundary within the hematoma - *predicts hematoma expansion*:

(a) blend sign (+); (b) blend sign (−):



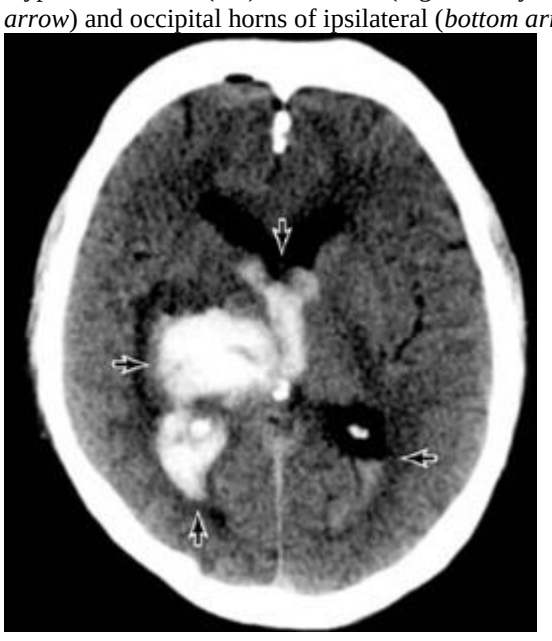
Yu et al. 2017

- blood *may leak into ventricles*:
  a) adheres to ependyma or choroid plexus;
  b) sinks to most dependent part of ventricular system (usually occipital horns) → fluid level within ventricular fluid.
- after several days, hematoma becomes less radiodense (density decreases by ≈ 2 HU/d) from periphery towards centre (therefore appears smaller); vasogenic edema develops in surrounding white matter (IV contrast → **ring enhancement***).

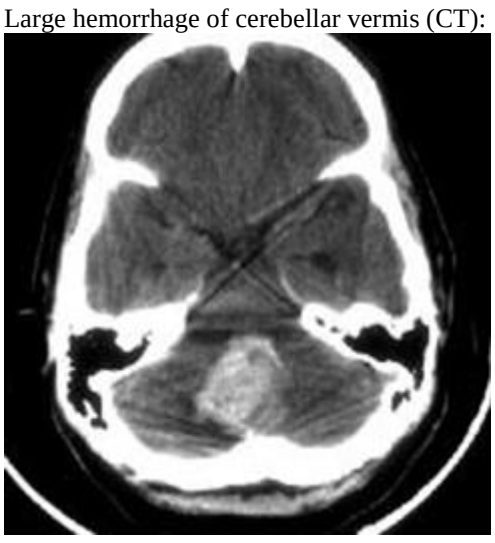
*vs. **gyral enhancement** typical of infarction

- after 2 weeks, CT density becomes similar to that of brain or CSF (i.e. isointense); surrounding rim of contrast enhancement may persist for months.
- in chronic stage, lesion becomes hypodense slit-like cavity (many disappear into isodense tissue) - resembles infarct; H: MRI.

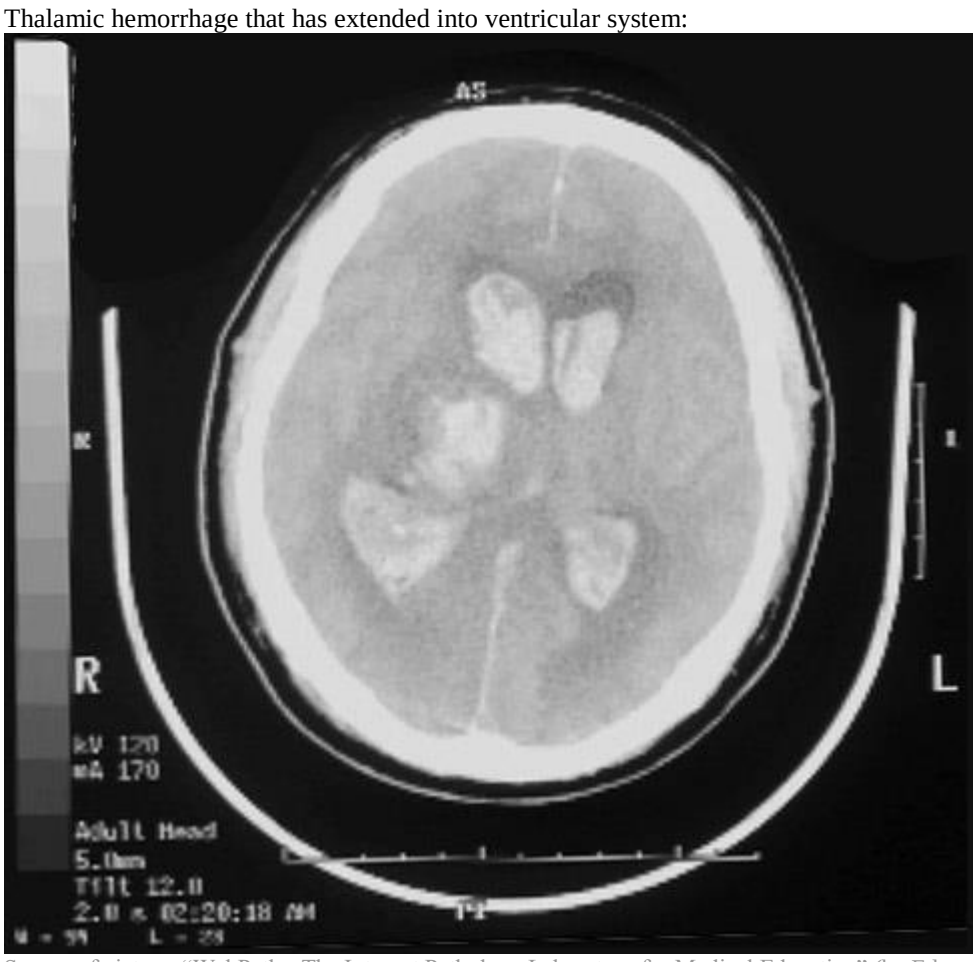
Hypertensive ICH (CT): hematoma (high-density signal) in thalamus (*left arrow*) with extension into 3rd ventricle (*top arrow*) and occipital horns of ipsilateral (*bottom arrow*) and contralateral (*right arrow*) lateral ventricles:



Large hemorrhage of cerebellar vermis (CT):



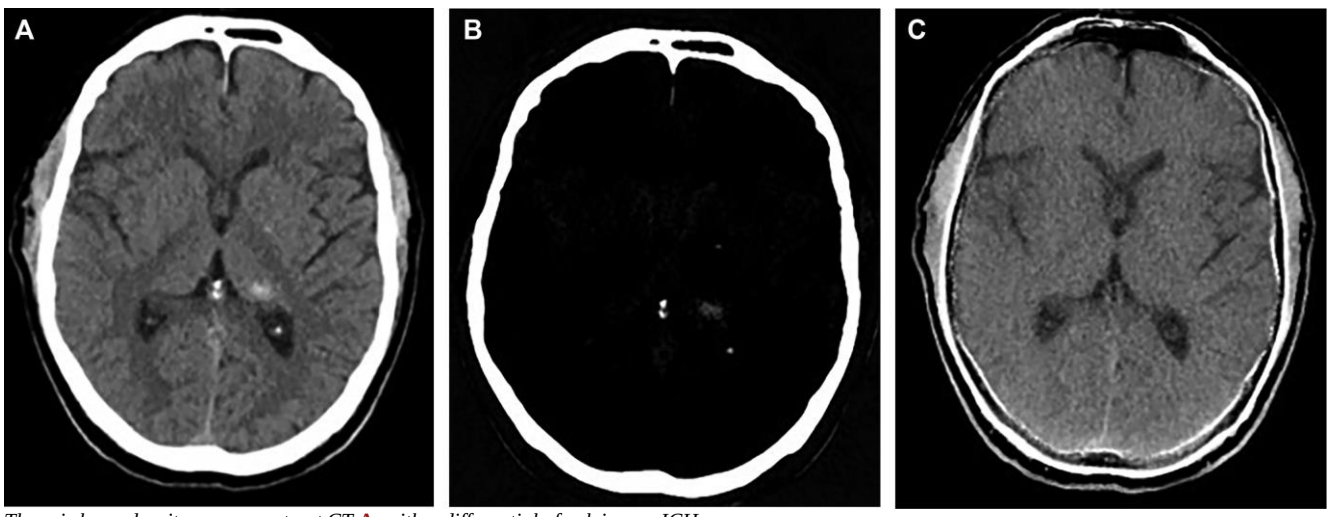
Thalamic hemorrhage that has extended into ventricular system:



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

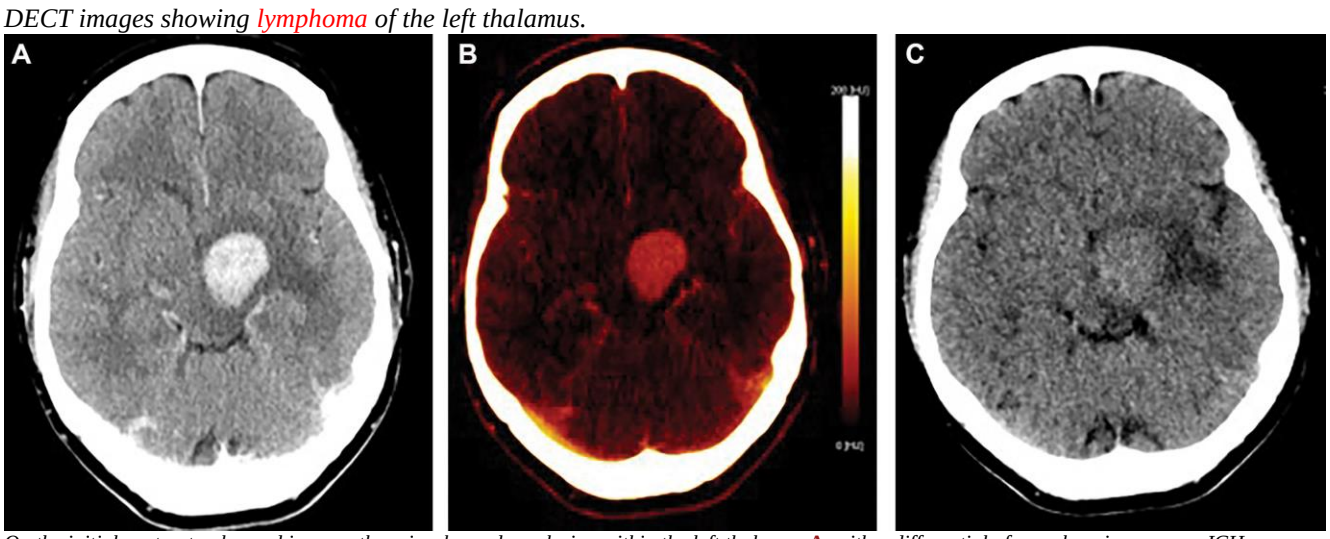
Dual-energy CT (DECT) allows differentiation between blood and calcium and other hyperdense etiologies:

DECT showing calcification of the posterior left thalamus.



There is hyperdensity on noncontrast CT **A**, *with a differential of calcium vs ICH.*
Hyperdensity persists on CT with calcium overlay **B**, *but not on virtual noncalcium image* **C**, *confirming that this represents calcium and not ICH.*

DECT images showing lymphoma of the left thalamus.



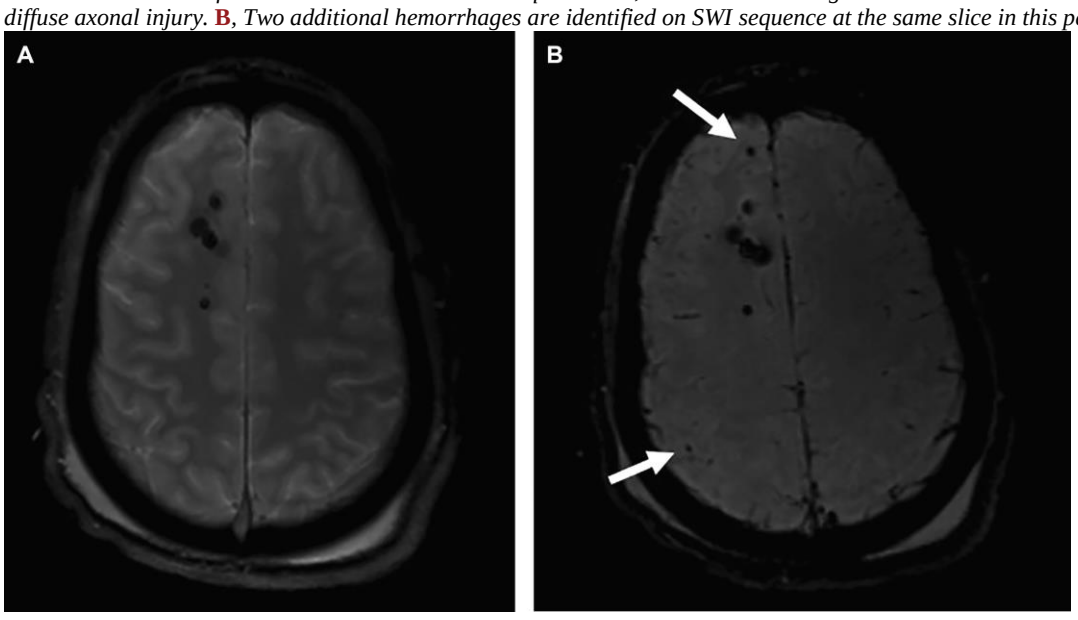
On the initial contrast-enhanced images, there is a hyperdense lesion within the left thalamus **A**, *with a differential of an enhancing mass vs ICH.*
There is persistent hyperdensity on the iodine overlay image **B** *and only mild hyperdensity on the virtual noncontrast image* **C** *indicating that this represents a hypercellular, enhancing tumor (lymphoma) and not ICH.*

MRI

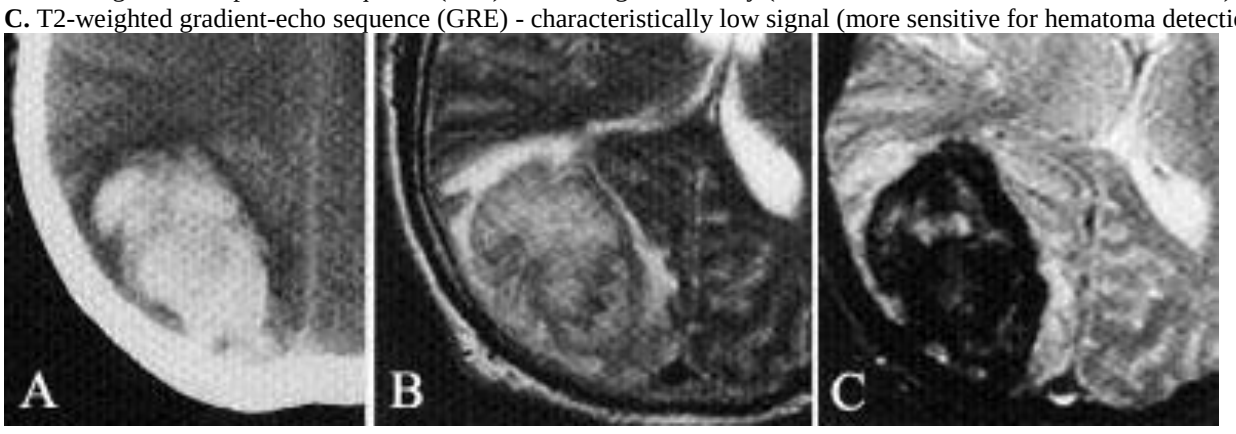
- picture depends on precise sequence used and ***age of hemorrhage*** (hemoglobin degradation products [different paramagnetic properties] play important role) – further see p. D51 >>

- *not highly sensitive in first few hours*!
- MRI is not necessary in most instances.
- one advantage of MRI - ability to detect small hemorrhages in brain stem (CT may not detect small pontine hemorrhages!).
- **T2* (either GRE or SWI)** is most sensitive sequence; SWI is more sensitive:

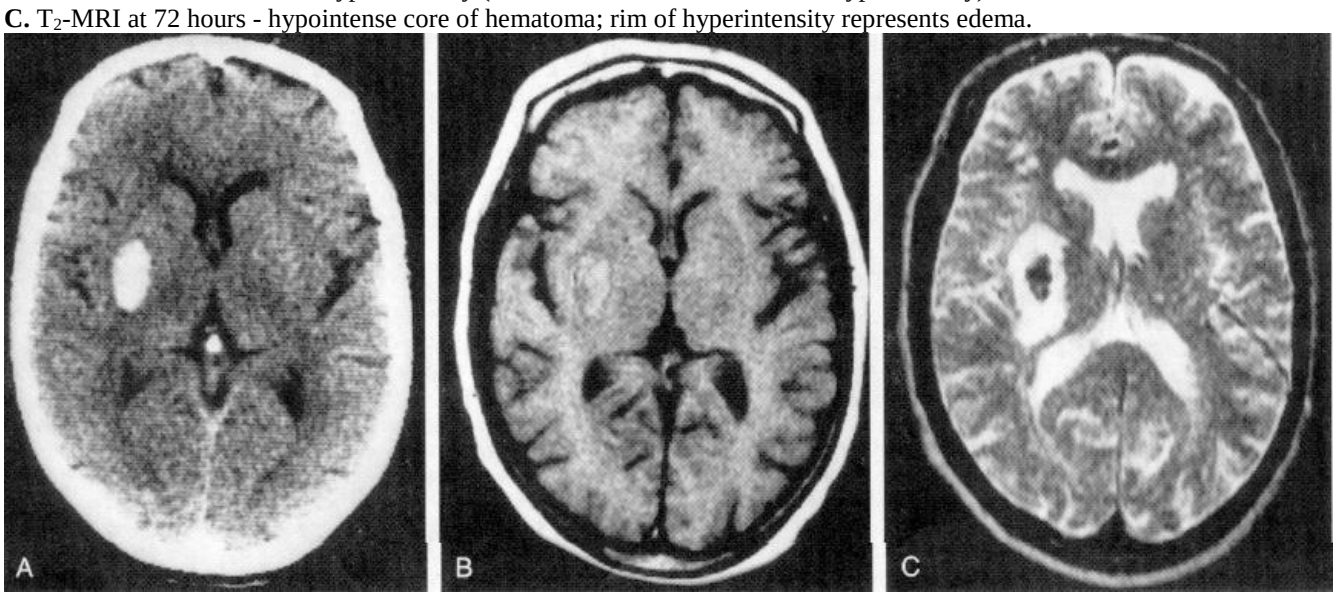
SWI is more sensitive for ICH than traditional GRE sequences. **A**, *Standard GRE image shows several small ICH in a patient with diffuse axonal injury.* **B**, *Two additional hemorrhages are identified on SWI sequence at the same slice in this patient (arrows).*



Occipito-parietal hematoma:
A. Unenhanced CT - high attenuation surrounded by low attenuation rim (clot retraction).
B. T2-weighted fast spin-echo sequence (FSE) - mixed signal intensity (could be mistaken for another mass lesion).
C. T2-weighted gradient-echo sequence (GRE) - characteristically low signal (more sensitive for hematoma detection).



Hypertensive putaminal hemorrhage:
A. CT at 24 hours - uniform hyperdensity.
B. T_1-MRI at 72 hours - mild hyperintensity (ischemic infarction would have hypointensity).
C. T_2-MRI at 72 hours - hypointense core of hematoma; rim of hyperintensity represents edema.



VASCULAR IMAGING (angiography / CTA / MRA)

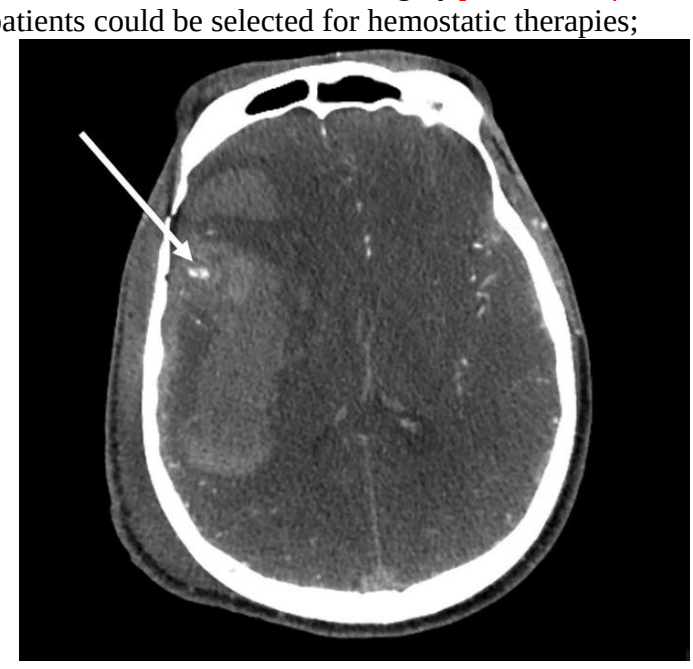
- indications (to exclude treatable causes - AVM, aneurysm, vasculitis, tumor):
  a) *any patient < 50-60 yrs (esp. children)* (i.e. amyloid angiopathy is unlikely)
  b) *no* history of *hypertension*
  c) hemorrhage in *location other than basal ganglia / thalamus* (e.g. lobar ICH).
  d) ICH after *cocaine* or *amphetamines* use (high likelihood of vascular malformations and aneurysms).

N.B. if *clinical syndrome* and *CT findings* are typical of hypertensive hemorrhage in basal ganglia, pons, or cerebellum, angiography is not necessary.

American Stroke Association (ASA) guidelines do not specify which patients may benefit from vascular imaging for evaluation of secondary causes.

- **CTA** is the first choice.
- if CTA is negative, **DSA** is considered (esp. patient < 45 yo without history of hypertension – diagnostic yield of DSA is 22%).
- timing of angiography – *delay** *until hematoma has resolved* (vascular lesions can be compressed by acute hematoma - not apparent angiographically).

  *if hematoma needs surgical evacuation → *immediate angiography*.
- **spot sign** - CTA marker of *contrast extravasation* (> 120 HU contrast spot) *within nonenhancing hematoma* and is not continuous with vessel - highly *predictive of hematoma expansion* and *poor outcome* – such patients could be selected for hemostatic therapies;



- **leakage sign** - defined as > 10% increase in Hounsfield units in hematoma in delayed phase of CTA - also a sensitive indicator for *predicting hematoma expansion*.
- if MRA is performed, phase-contrast MRA is preferable to TOF MRA.

SPECIFIC ANATOMIC LOCATIONS

Basal ganglia / thalamus

1. Hypertensive
2. Drug abuse (in young person)
3. Ruptured aneurysm – rare
4. Tumor – very rare

PUTAMINAL HEMORRHAGE

- most common form of ICH (putamen is most common site of *hypertensive ICH*) ≈ 33-50% of all ICHs.

Classic presentation of large hemorrhage (involves internal capsule, corona radiata, centrum semiovale, temporal lobe / insula, lateral ventricles):

1) rapidly progressing **contralateral hemiplegia** (incl. face) with less severe **hemisensory loss** (with small hematoma, there can be pure motor hemiparesis).
   - arm and leg gradually weaken until become flaccid or extend rigidly with Babinski sign.
   - *ALLESTHESIA* (with nondominant putaminal hemorrhage) - noxious stimulus on side of hemisensory disturbance is perceived on opposite normal side in corresponding area.
2) **homonymous hemianopia**
3) conjugate **horizontal gaze palsy** (eyes "look toward hematoma and away from hemiplegia").
4) global **aphasia** (dominant hemisphere) / **hemineglect** (nondominant hemisphere).

- ***massive*** putaminal hemorrhage → upper brainstem compression → lethargic ÷ comatose (within minutes to hours) with deep, irregular respirations.

THALAMIC HEMORRHAGE

- ≈ 10-20% of all ICHs.
- usual cause is *hypertension*.
- ICH may extend ***laterally*** to internal capsule, ***inferomedially*** to subthalamus and midbrain, or ***medially*** to 3rd ventricle.

Clinical presentation (resembles putaminal ICH):

1) contralateral **hemisensory deficit** of all modalities with later* & lesser degree **hemiparesis** (hemianesthesia precedes hemiparesis! – vs. putaminal ICH!)

   *dissection into internal capsule
2) **homonymous hemianopsia** (often clearing quickly)
3) **OCULAR SIGNS** (extension into upper midbrain): **impaired upward gaze** → downward-inward deviation of eyes (depression-convergence syndrome - eyes "look down at nose"), **skew deviation** (eye opposite hemorrhage displaced downward and medially), **small anisocoric and light-nonreactive pupils** (pupillary light-near dissociation), convergence-retraction nystagmus, pseudo-CN6 paresis (unilateral or bilateral), conjugate gaze palsy to side of lesion ("wrong-way eyes"), ipsilateral Horner's syndrome.

- some patients lose consciousness early in course (esp. with **medial thalamic** ICH), with subsequent abulia and difficulty making new memories.
- **dominant (left) thalamus** → aphasia, often with preserved verbal repetition.
- **nondominant thalamus** → neglect, apractagnosia or mutism.

LOBAR HEMORRHAGE

- bleeding within subcortical white matter (i.e. cerebral lobes outside basal ganglia).
- most patients are elderly!

Common causes:

1) *amyloid angiopathy* - most common cause in elderly
2) *tumor*
3) *vascular malformation, hematologic malignancy* – young person
4) *trauma*
5) extension of deep hemorrhage
6) hemorrhagic transformation of ischemic infarct
7) venous (sinus or cortical vein) thrombosis

Uncommon - acute disseminated encephalomyelitis (s. acute hemorrhagic leukoencephalopathy, Weston-Hurst disease).

Hemorrhages at gray-white matter interface – embolic phenomena: metastases, septic emboli, fungal infection.

Clinical presentation (resembles thromboembolic infarction!):

FRONTAL lobe - abulia, contralateral hemiparesis, conjugate gaze palsy toward side of hemorrhage.

PARIETAL lobe - contralateral hemisensory loss & mild hemiparesis, neglect of contralateral visual field, occasional hemianopia or anosognosia.

TEMPORAL lobe - visual field deficit, agitated delirium, Wernicke aphasia (extension into dominant parietal lobe → conduction or global aphasia).

OCCIPITAL lobe - contralateral homonymous hemianopia, ipsilateral orbital pain.

- normal pupils.
- headache, nausea & vomiting occur with same frequency but less intensity (as in deep, hypertensive hemorrhages).
- coma is less common (bulk of hemorrhage is comparatively small and located in subcortical white matter).
- **seizures** are common (frontal, temporal, or parietal lobes).

PONTINE HEMORRHAGE

- ≈ 10-15% of all ICHs.
- usually placed *symmetrically at junction of basis and tegmentum* (paramedian vessels from basilar artery).
- hematoma can extend rostrally into midbrain or rupture into 4th ventricle.

Clinical presentation (large pontine ICH):

1) abrupt **coma**; vomiting often occurs at onset
2) **quadriparesis**, decerebrate rigidity
3) **pinpoint** (1 mm) **reactive pupils** (check with magnifying glass)
4) grossly dysconjugate centrally positioned eyes (gaze paresis) with **absent oculocephalic & oculovestibular reflexes**
5) ± ocular bobbing.
6) ± ataxic Cheyne-Stokes respiration.

Death occurs within few hours (> 75%), but there are exceptional survivors!

- **lateral basis pontis** - pure motor hemiparesis.
- **lateral pontine tegmentum** - ipsilateral conjugate gaze paresis, ipsilateral internuclear ophthalmoplegia, "one-and-a-half" syndrome, ipsilateral miosis, ocular bobbing, ipsilateral hemiataxia with crossed hemisensory deficits.

CEREBELLAR HEMORRHAGE

- ≈ 8-10% of all ICHs.
- most common cause is long-standing *hypertension*.
- most common locations: dentate nucleus > vermis.
- clinical presentation: abrupt occipital **headache**, **nausea & vomiting** (may be severe and repetitive), severe **gait ataxia*** (astasia-abasia), **vertigo**, **dysarthria**, **nystagmus**.

*gait (truncal) ataxia may be only neurologic sign – test gait in all patients!!!

N.B. consciousness is preserved!

- clinical course is notoriously unpredictable (may deteriorate quickly – check patient very often) - may cause **brain stem** compression:
  1) ocular findings: caloric-resistant ipsilateral gaze palsy → *eye deviation toward opposite side*; small reactive pupils, skew deviation (**Magendie-Hertwig sign**), gaze-paretic nystagmus, ocular bobbing.
  2) cranial nerve findings (ipsilateral facial weakness, ipsilateral absence of corneal reflex)
  3) contralateral hemiparesis (late sign!)
  4) loss of consciousness (coma = too late for surgical evacuation!)

Neurosurgeon consultation is indicated for all patients!

More ***lateral (hemispheric)*** hemorrhage and ***smaller*** hematoma, more likely brainstem structures are spared (better prognosis)

- may obstruct CSF flow into or out of 4th ventricle → HYDROCEPHALUS (may cause reversible loss of consciousness; H: prompt ventricular drainage).
- further brain stem compression, cerebellar herniation → death (H: prompt clot evacuation!)

CAUDATE HEMORRHAGE

- ≈ 4% of all ICHs.
- may dissect posterolaterally into **internal capsule** and **putamen** (contralateral conjugate gaze paresis, contralateral hemiparesis).
- may dissect inferiorly into **thalamus** (upward gaze paresis, hemisensory deficits), **hypothalamus** (Horner's syndrome)

INTRAVENTRICULAR HEMORRHAGE (IVH)

a) **primary** (confined to the ventricles)
b) **secondary** (extension of ICH) - most of IVHs - hypertensive hemorrhages involving the basal ganglia and thalamus.

- occurs in ≈ 45% of patients with spontaneous ICH
- IVH is independent factor associated with poor outcome (risk of death increased from 20% without IVH to 51% with IVH).
- etiology - head trauma, vascular malformation, aneurysm, tumor, hypertension, and clotting disorders.
- clinical features: meningismus, headache, vomiting, mental status changes with few motor or sensory signs, "hormeotony" (periodic tonic spasms of limbs & atonic pauses).
- complications - obstructive hydrocephalus, delayed communicating hydrocephalus, thrombotoxicity and inflammation in reaction to ventricular blood.
- treatment – see below >>

TREATMENT

ICH is *the least treatable form* of stroke!

The two most pressing ICH investigational goals are: 1) **early BP control** and 2) **hematoma volume reduction**.

- hematoma expansion occurs in 16-40% patients (typically within first few hours); each 10% increase in hematoma size from baseline → 5% increase in mortality and 16% increase in chance of worse functional outcome.

Aggressive care early after ICH onset and postponement of new DNR orders until at least the ***second full day of hospitalization*** is probably recommended (Class IIa; Level of Evidence B). Patients with preexisting DNAR orders are not included in this recommendation. Current prognostic models for individual patients early after ICH are biased by failure to account for the influence of withdrawal of support and early DNR orders. DNR status should not limit appropriate medical and surgical interventions unless otherwise explicitly indicated (Class III; Level of Evidence C).

CONSERVATIVE MEASURES

GENERAL MEASURES

- bedrest during first 24 hours; clinically stable patients → progressive increase in activity (avoid strenuous exertion).
  N.B. all ICH patients with limited mobility need prophylaxis against DVT (*intermittent pneumatic compression stockings* same day; *low-molecular-weight heparin* next day following bleeding cessation)
- treatment of fever may be reasonable (Class IIb; Level of Evidence C).
- maintain normoglycemia (< 300 mg/dL); both hyperglycemia and hypoglycemia should be avoided (Class I; Level of Evidence C); target glucose level remains to be clarified.
- dysphagia screening for all ICH patients before they start oral intake - to reduce risk of pneumonia (Class I; Level of Evidence B) - most common medical sequelae seen in this patient population; if failed → early enteral feeding.
- systematic screening for myocardial ischemia or infarction (with ECG and cardiac enzymes) is reasonable (Class IIa; Level of Evidence C).

BP CONTROL

(wide BP swings are common in initial period): intra-arterial pressure monitoring + continuous ECG

Keep MAP 70-110 mmHg
Target SBP < 140 mmHg

- patients presenting with SBP 150-220 mm Hg and without contraindication to acute BP treatment, acute lowering of SBP to 140 mm Hg is safe (Class I; Level of Evidence A) and can be effective for improving functional outcome (Class IIa; Level of Evidence B). see INTERACT2 >>
  - for patients presenting with SBP > 220 mm Hg, it may be reasonable to consider aggressive reduction of BP (Class IIb; Level of Evidence C).
  - ***hypertension*** (systolic > 180, MAP > 130) increases bleeding and rises ICP.
  - ***hypotension*** (MAP < 70) lowers CPP.
- drugs: IV NICARDIPINE or LABETALOL or SODIUM NITROPRUSSIDE or TRIMETHAPHAN CAMSYLATE.

Table 3. Intravenous Medications That May Be Considered for Control of Elevated Blood Pressure in Patients With ICH

Drug	Intravenous Bolus Dose	Continuous Infusion Rate
Labetalol	5 to 20 mg every 15 min	2 mg/min (maximum 300 mg/d)
Nicardipine	NA	5 to 15 mg/h
Esmolol	250 μg/kg IVP loading dose	25 to 300 $\mu g \cdot kg^{-1} \cdot min^{-1}$
Enalapril	1.25 to 5 mg IVP every 6 h*	NA
Hydralazine	5 to 20 mg IVP every 30 min	1.5 to 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$
Nipride	NA	0.1 to 10 $\mu g \cdot kg^{-1} \cdot min^{-1}$
Nitroglycerin	NA	20 to 400 μg/min

IVP indicates intravenous push; NA, not applicable.
*Because of the risk of precipitous blood pressure lowering, the enalapril first test dose should be 0.625 mg.

Early intensive lowering of BP does not result in significant reduction of death or major disability, but improves functional outcomes.

Anderson CS et al. "Rapid blood-pressure lowering in patients with acute intracerebral hemorrhage." N Engl J Med. 2013 Jun 20;368(25):2355-65

BP lowering in acute ICH does not compromise perihematoma CBF on pCT (it was historically feared that lowering BP will worsen perihematoma penumbra perfusion).

Butcher KS et al. "The Intracerebral Hemorrhage Acutely Decreasing Arterial Pressure Trial". Stroke. 2013 Mar;44(3):620-6

INTERACT (Intensive Blood Pressure Reduction in Acute Cerebral Hemorrhage Trial) - rapid blood pressure reduction to SBP < 140 was found to be safe and caused reduced hematoma expansion (14% vs. 36%), but these results were not statistically significant.

INTERACT2 – patients with small-moderate ICH and presenting with SBP 150-220 → intensive treatment to **SBP < 140** vs. standard treatment to **SBP < 180** for 7 days:

- intensive treatment is safe.
- intensive treatment has no significant effect on *hematoma growth*.
- intensive treatment has favorable trend to reduce *poor outcome* (mRS ≥ 3): 52% vs. 55.6% with standard treatment (p = 0.06).
- intensive treatment led to modestly better *functional recovery* (OR for greater disability, 0.87; 95% CI, 0.77 to 1.00; P=0.04) and *quality of life* (mean health utility scores, intensive group 0.60±0.39 versus standard group 0.55±0.40; P=0.002).

N.B. study did not include patients with very high SBP on presentation (sustained > 220 mm Hg), large and more severe ICH, and those requiring surgical decompression.

Ongoing trial in phase III - **Antihypertensive Treatment of Cerebral Hemorrhage (ATACH) 2 trial** - randomizing ICH patients to goal SBP of < 140 mmHg vs. < 180 mmHg within 3.5 hours of symptom onset; BP targets are to be maintained for 24 hours after randomization using NICARDIPINE (LABETALOL may also be used if maximum amounts of nicardipine are used).

Perindopril Protection Against Recurrent Stroke Study (PROGRESS) - risk of ICH recurrence was lowest among patients with lower blood pressure levels on follow-up (median, 112 mmHg systolic and 72 mmHg diastolic) - Class I; Level of Evidence A.

ICP CONTROL

– elevating head of bed, analgesia, mild sedation, MANNITOL, etc. see p. S50 >>

Small hematomas and limited IVH usually do not need ICP treatment!
(there is evidence for ***differential pressure gradients*** in at least some cases of ICH, so that ICP may be elevated in and around the hematoma but not distant from it)

– GCS ≤ 8, transtentorial herniation, significant IVH or hydrocephalus - might consider ICP monitoring and treatment; CPP of 50-70 mmHg may be reasonable to maintain depending on the status of cerebral autoregulation (Class IIb; Level of Evidence C). see EVD in ICH >>

Causes of elevated ICP in ICH:
1) hydrocephalus from IVH
2) mass effect from the hematoma (or surrounding edema)

– initial insult from hemorrhage sets off cascade of various metabolic processes, which lead to perihematoma inflammation* and edema - patient is at risk of further deterioration from ***secondary damage*** (including herniation) for up to a week - monitor for ICP↑ (esp. with cerebellar hemorrhages).

*__corticosteroids__ should not be administered for treatment of elevated ICP in ICH (Class III; Level of Evidence B) - not effective and increase complications!

REVERSAL OF BLEEDING DIATHESIS

RECOMBINANT FACTOR VIIA (RFVIIA) (NovoSeven®, NiaStase®) 40-120 μg/kg q2h started within 3-4 hours limits hematoma growth, but slightly increases ischemic events (both cardiac and cerebral); *final result disappointing* – no effect on death and severe disability at 90 days; probable indication – ***spot sign*** (continuous bleeding) on CTA – ongoing trials to identify specific patient subpopulations that might benefit from VIIa; currently, *use of rFVIIa is not recommended*!

- **patient on warfarin** → four-factor (II, VII, IX, X) prothrombin complex concentrate PCC (Kcentra) is first line treatment; then vit. K (PHYTONADIONE 20-40 mg IV), FFP.
  N.B. PCC works faster and with less volume load than FFP!
- **patients on heparin** IVI → PROTAMINE - dose depends upon duration of time since heparin administration (do not exceed 50 mg IV over 10 min):
  immediately: 1-1.5 mg/100 U of heparin
  30-60 min: 0.5-0.75 mg/100 U of heparin
  > 2 h: 0.25-0.375 mg/100 U of heparin
  if heparin was administered by deep SC injection, 1-1.5 mg /100 U of heparin.
- **patients on LMWH** → PROTAMINE but reversal is incomplete.
- **hemophilia** → FACTOR VIII (to achieve level of 80-100% of normal).
- **thrombocytopenia** → PLATELET TRANSFUSION.
- **thrombolytic-associated bleeding** → CRYOPRECIPITATE 10 units IV, replacement of clotting factors*, AMINOCAPROIC ACID (5 g over 30-60 minutes → 1 g/h IV for continued bleeding).
  *Replacement of clotting factors:
  a) FRESH-FROZEN PLASMA 20 mL/kg – fluid overload!
  b) PCC (prothrombin complex concentrate), FACTOR IX COMPLEX concentrate, and RECOMBINANT ACTIVATED FACTOR VII – act very rapidly and with lower fluid volumes than fresh frozen plasma, but greater potential of thromboembolism.

N.B. anticoagulants (if indicated for other comorbid conditions, e.g. mechanical cardiac valves) can be restarted within 2-3 weeks after ICH (within 3-10 days if risk for thromboembolism is very high)

AED

N.B. according to AHA/ASA guidelines: prophylactic antiseizure medication is not recommended (Class III; Level of Evidence B).

- AEDs make no outcome difference.
- some studies suggest anticonvulsants may be linked to fever and poor outcomes; therefore, continuous EEG monitoring may provide rational way to direct therapy.
  – PHT is linked to worse outcomes.
  – LEV does not cause worse outcome overall but worse cognitive outcomes.
- secondary ICH has much higher seizure risk than primary ICH but still routine primary seizure prophylaxis is not recommended.
- short-term prophylactic anticonvulsants may be considered for ICH ***extending to cortex***.

NEUROPROTECTIVE STRATEGIES

Candidates:

1) MINOCYCLINE
2) DEFEROXAMINE
3) **Hypothermia**; more effective in combination with magnesium.

- FINGOLIMOD (sphingosine-1-phosphate receptor modulator approved for MS) may improve outcomes of ICH

Fu "Fingolimod for the Treatment of Intracerebral Hemorrhage: A 2-Arm Proof-of-Concept Study." JAMA Neurol. 2014 Jul 7.
Oral fingolimod 0.5 mg for 3 consecutive days for patients with primary supratentorial ICH and hematomal volume of 5-30 mL - safe and effective in reducing perihematoma edema and neurologic deficits, with enhanced recovery

SURGICAL TREATMENT

Pathophysiological cons for surgical evacuation – see p. TrH1 >>

Traditionally: ICH was considered a ***monophasic disease*** with little demonstrated benefit from support care or craniotomy and with medical management as the standard of care.

Modern thinking: ICH is a ***biphasic disease***, with the second phase of injury from perihematomal inflammation and edema accounting for the delayed neurological deterioration - time of intervention and volume control are critical

Preop CTA is a must!

INDICATIONS

1. **Cerebellar** hemorrhages compressing vital structures in medulla (suggested by *declining level of consciousness*, posturing, altered respiration, shifted or obliterated 4th ventricle, hydrocephalus).

Patients with cerebellar hemorrhage who are ***deteriorating*** neurologically or who have ***brainstem compression*** and/or ***hydrocephalus*** from ventricular obstruction should undergo surgical removal of the hemorrhage as soon as possible (Class I; Level of Evidence B).

Cerebellar hematomas > 2.5-3 cm require surgical evacuation within hours.

- surgery is not indicated - GCS score ≥ 14 (some investigators say ≥ 9) with small hemorrhage (< 3-4 cm) without hydrocephalus.
- contraindication (poor surgery results) - large midline hemorrhage with lost all brain stem functions and flaccid coma.

Small time margin between *alert state* (surgery still not indicated) and *irreversible coma* (surgery is too late)

- consider preoperative MANNITOL 1 g/kg.
- ***EVD*** has risk of upward herniation of cerebellum and does not relieve brainstem compression.

Initial treatment with ventricular drainage rather than surgical evacuation is not recommended (Class III; Level of Evidence C).

i.e. attempting to control ICP via means other than hematoma evacuation, such as EVD insertion alone, is considered insufficient and may actually be harmful, particularly in patients with compressed cisterns!

2. **Supratentorial** hemorrhages with signs of herniation, declining sensorium (esp. if clot is on nondominant side and ≤ 1 cm from cortical surface).

For **most supratentorial** ICHs, the usefulness of surgery is not well established (Class IIb; Level of Evidence A).

Routine evacuation of supratentorial ICH by standard craniotomy within 96 hours of ictus is not recommended!

Supratentorial hematoma evacuation in ***deteriorating*** patients might be considered as a life-saving measure (Class IIb; Level of Evidence C).

Early hematoma evacuation is not clearly beneficial compared with hematoma evacuation when patients **deteriorate** (Class IIb; Level of Evidence A).

SURGICAL APPROACHES & TRIALS

A. **Open** surgical evacuation via **craniotomy** (ultrasonography can confirm clot localization) – esp. for lobar clots within 1 cm of surface.

- surgery between 24-48 h is the best time - vessel has stopped leaking (either spontaneously, or after hemostatic therapy); if earlier - increased risk of rebleeding.
- aspirate, irrigate; most authors recommend leaving small bits of clot on vessels in order to avoid new hemorrhage.
- hemostasis: bipolar coagulation, cotton balls with peroxide, SurgiFoam / FloSeal; may finish by Surgicel on hematoma walls.

International Surgical Trial in Intracerebral Hemorrhage (STICH)

cf. STITCH trial – traumatic ICH – see p. TrH1 >>

Mendelow AD et al. STICH investigators. Early surgery versus initial conservative treatment in patients with spontaneous supratentorial intracerebral haematomas in the International Surgical Trial in Intracerebral Haemorrhage (STICH): a randomised trial. Lancet. 2005; 365:387–397

STICH I – early (within 24 hrs of randomization) surgery (craniotomy or CT-guided aspiration) vs. best medical management.

- class I evidence (1033 patients, 83 centers in 27 countries).
- craniotomy is as safe as medical treatment.
- no overall benefit from early surgery versus initial conservative treatment.

N.B. trial only looked at ICH for which the surgeon was uncertain regarding the benefits of surgery versus conservative management – trial confirms that surgeons are correct to be uncertain for these patients but the results cannot be extrapolated to all ICHs

Outcome	Early surgery group	Best medical management group	Statistical significance
Favourable outcome	26%	24%	None
Unfavourable outcome	74%	76%	None
Mortality	36%	37%	None

Mendelow AD et al. for the STICH investigators. Early surgery versus initial conservative treatment in patients with spontaneous supratentorial intracerebral haematomas in the International Surgical Trial in Intracerebral Haemorrhage (STICH): a randomised trial. Lancet 2005; 365 : 387 – 397

STICH II – early (within 12 hours of randomization) surgery for lobar ICH where the clot is within 1 cm of the cortical surface (STICH I subgroup analysis suggested that such patients might benefit from surgery).

- inclusion: conscious patients with superficial lobar hemorrhage (10-100 mL) within 1 cm of the cortical surface and without IVH and who were admitted within 48 hours of ictus.
- still no clear benefit from early surgery! (41% favorable outcome in surgery group vs. 38% in medical group, no statistical significance).

N.B. patients with deep ICH esp. with IVH do worse with surgery; but patients with poor prognosis (GCS 9-12) are better off with early surgery!

N.B. surgery is not beneficial for hemorrhages in **putamen**, **thalamus**, and **pons**.

In general, surgical evacuation is seldom justified

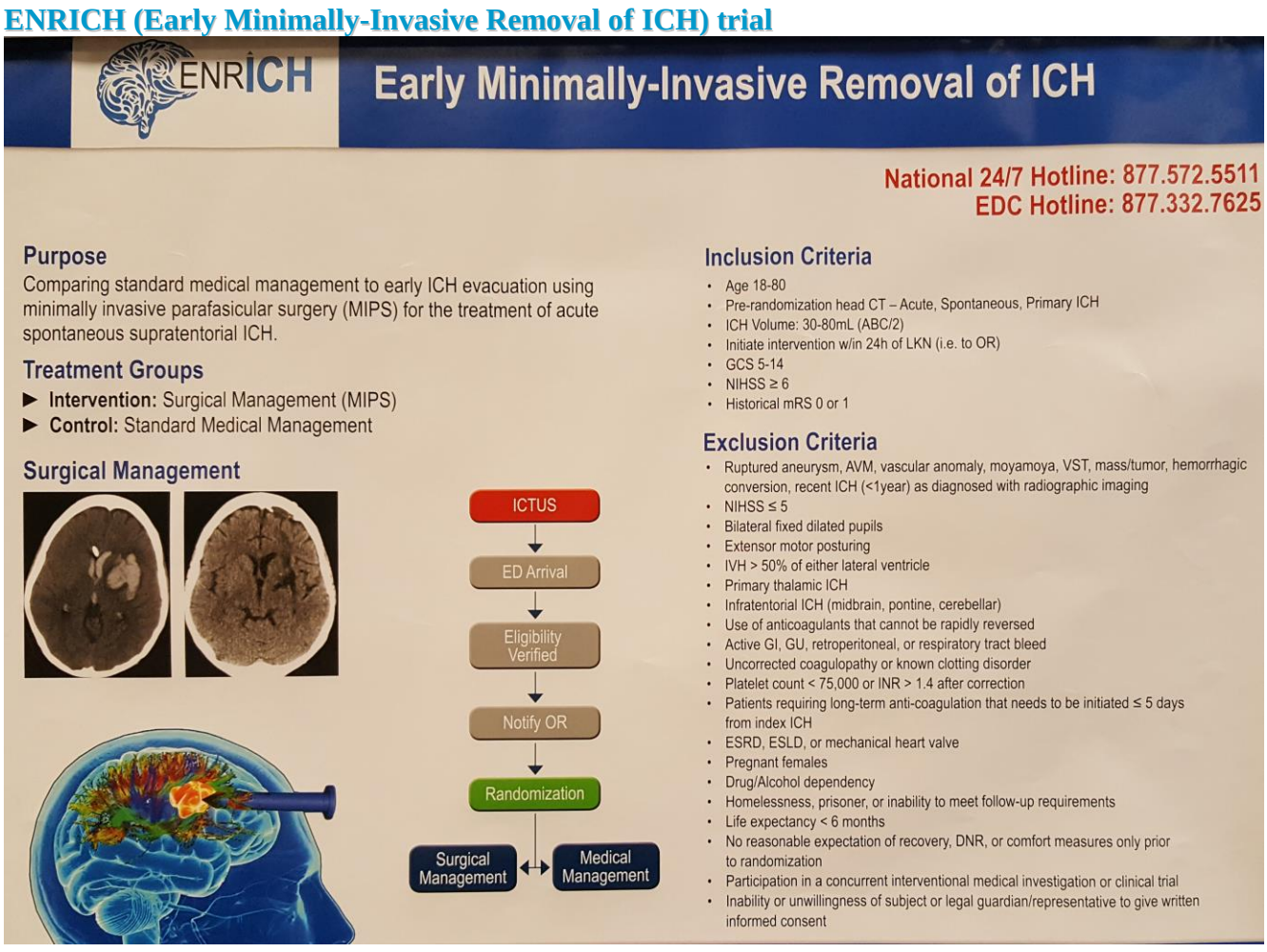
- does not substantially improve mortality + considerably increases risk of severe residual neurologic disability if patient survives.

- best candidates are patients with increasing moderate ÷ large hematomas who are ***still awake*** (GCS ≥ 9).

N.B. patients with massive hemorrhage who are in coma are not likely to benefit!

B. **Minimally invasive evacuation via transsulcal approach** using **BrainPath**.

ENRICH (Early Minimally-Invasive Removal of ICH) trial

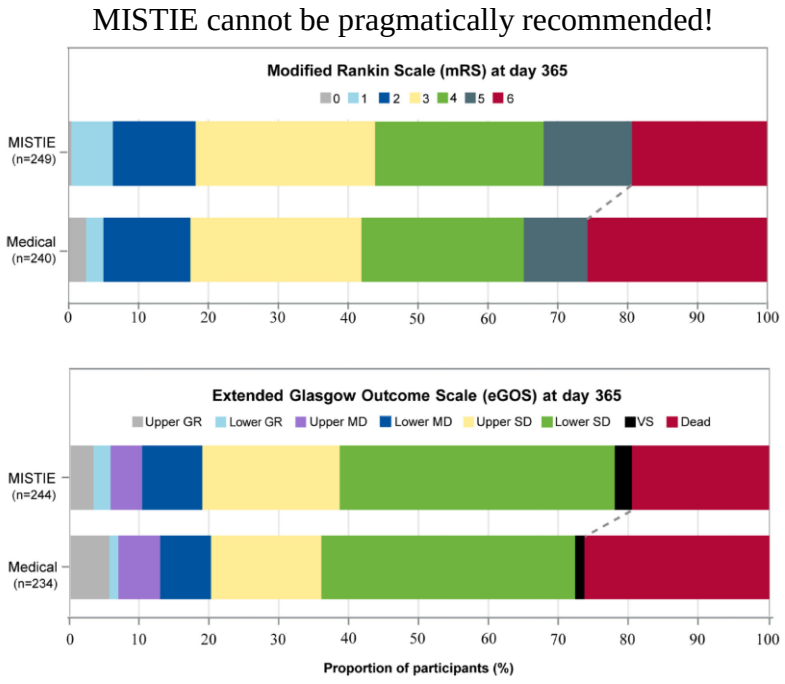


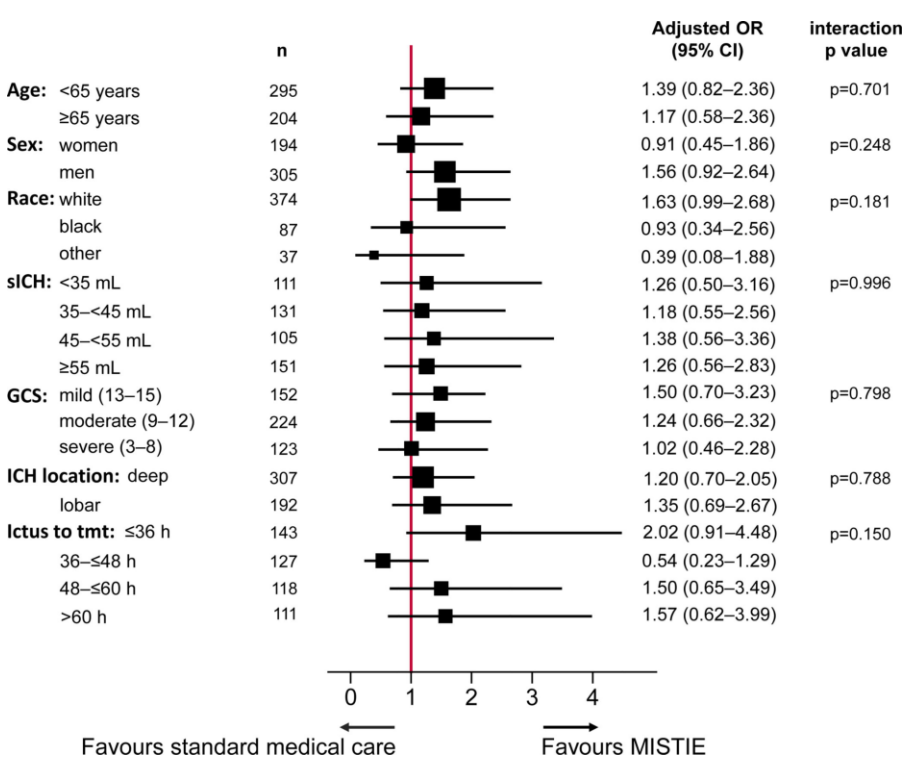
C. **Minimally invasive stereotactic aspiration** *via burr hole*; clot mobilization methods:
   a) **mechanical** rotors.
   b) **fibrinolytic** agent instillation.

MISTIE (Minimally Invasive Surgery with Thrombolysis for ICH Evacuation) III - **minimally invasive surgery aspiration + 1 mg rt-PA through intraclot catheter q8hrs** (up to 9 doses total) vs. **medical therapy alone**

- randomized, open-label, blinded endpoint, phase 3 trial done at 78 hospitals (USA, Canada, Europe, Australia, and Asia) – 499 patients.
- inclusion: spontaneous supratentorial ICH ≥ 30 mL with or without IVH not requiring EVD, with GCS ≤ 14 or NIHSS ≥ 6, in 18-80 yo patient with symptom onset within 24 hours of diagnostic CT, initiation of treatment from 12 to 72 hours of diagnostic CT, with first dose given within 76 hours of the diagnostic CT.
  N.B. no life-threatening mass effect requiring surgery.
- outcomes:
  - mean reduction in hematoma size: 69% in MISTIE group vs. 3% in standard group;
  - death at 7 days: 1% in MISTIE group vs. 4% in standard group (p=0.02);
  - death at 30 days: 9% in MISTIE group vs. 15% in standard group (p=0.07);
  - serious adverse event at 30 days: 30% in MISTIE group vs. 33% in standard group (p=0.012);
  - mRS score of 0–3 at 365 days: 45% in MISTIE group vs. 41% in standard group (adjusted risk difference 4% [95% CI –4 to 12]; p=0.33).

MISTIE cannot be pragmatically recommended!





Proponents of MISTIE argue:
- reduction of mortality is good enough
- should not included basal ganglia ICH (very poor prognosis)
- time to complete treatment on average was 5.1 days – way too long
- only 58% of patients on MISTIE group achieved surgical success (due to catheter malposition)

The effectiveness of minimally invasive clot evacuation with stereotactic or endoscopic aspiration ± thrombolytic usage is uncertain (Class IIb; Level of Evidence B).

Multicenter Study of Artemis, a Minimally Invasive Neuro Evacuation Device (MIND)

D. **Hemicraniectomy (DC)** - option for younger patients with rapidly declining conscious state and imminent herniation.

DC with or without hematoma evacuation might reduce mortality for patients with supratentorial ICH who are in a coma, have large hematomas with significant midline shift, or have elevated ICP refractory to medical management (Class IIb; Level of Evidence C).

E. **Ventricular drainage** for INTRAVENTRICULAR HEMORRHAGE with acute obstructive hydrocephalus (esp. in cerebellar hematomas, intraventricular hemorrhage), trapped ventricle:

Ventricular drainage as treatment for hydrocephalus is reasonable, especially if decreased level of consciousness (Class IIa; Level of Evidence B).

- ***endoscopic neurosurgical techniques*** for IVH evacuation may be advantageous compared with EVD

The efficacy of endoscopic treatment of IVH is uncertain (Class IIb; Level of Evidence B).

- **EVD** can be combined with **low-dose intraventricular fibrinolytics (catheter-based clot lysis)** to dissolve clot quicker (e.g. 1.0 mg tPA q 8-12 hrs) - dramatically reduced morbidity & mortality!!! (rationale: EVD alone is too slow in removal of intraventricular blood).
  - EVD must go into clot
  - clamp ventriculostomy for 30-60 minutes and monitor for increased ICP
  - monitor daily with CT.
  - clots dissolve on average within 3-4 days.

– ***clotted intraventricular catheter***: alteplase 0.5 mg IT once, reassess complications (tPA, frequent EVD access).

Although intraventricular rtPA in IVH appears to have a fairly low complication rate, the efficacy and safety of this treatment are uncertain (Class IIb; Level of Evidence B).

CLEAR (Clot Lysis Evaluating Accelerated Resolution of intraventricular hemorrhage) III trial – intraventricular tPA in patients with small ICH (< 30 mL) but with IVH (to test treatment for IVH and not to be obscured by large ICH):

– does not improve good functional outcome (mRS 0-3: 48% in alteplase group, 45% in saline group), but gives 10% reduction in mortality without increasing the number of patients left in a vegetative state or requiring nursing home care (best results in patients with > 20 mL or > 90% of blood removed; no benefit if IVH blood is < 20 mL to start).

Complication	CLEAR III trial patients	Literature meta-analysis
Hemorrhage*	16.8% (2.4% symptomatic hemorrhages) – both saline and alteplase groups	8.4% (0.7% symptomatic hemorrhage)
Infection**	4.4%	7.9%

*Intraventricular thrombolysis marginally increases the overall risk of symptomatic hemorrhagic complications after IVH, and only during the treatment phase.

Maged D Fam et al. Symptomatic Hemorrhagic Complications in Clot Lysis: Evaluation of Accelerated Resolution of Intraventricular Hemorrhage Phase III Clinical Trial (CLEAR III): A Posthoc Root-Cause Analysis. Neurosurgery, nyx587, Published: 23 December 2017

**Alteplase is associated with reduction in bacterial ventriculitis – 4% vs. 9% in placebo arm ($P = 0.05$).

CLEAR IV trial – patients with larger clots - awaiting a funding application.

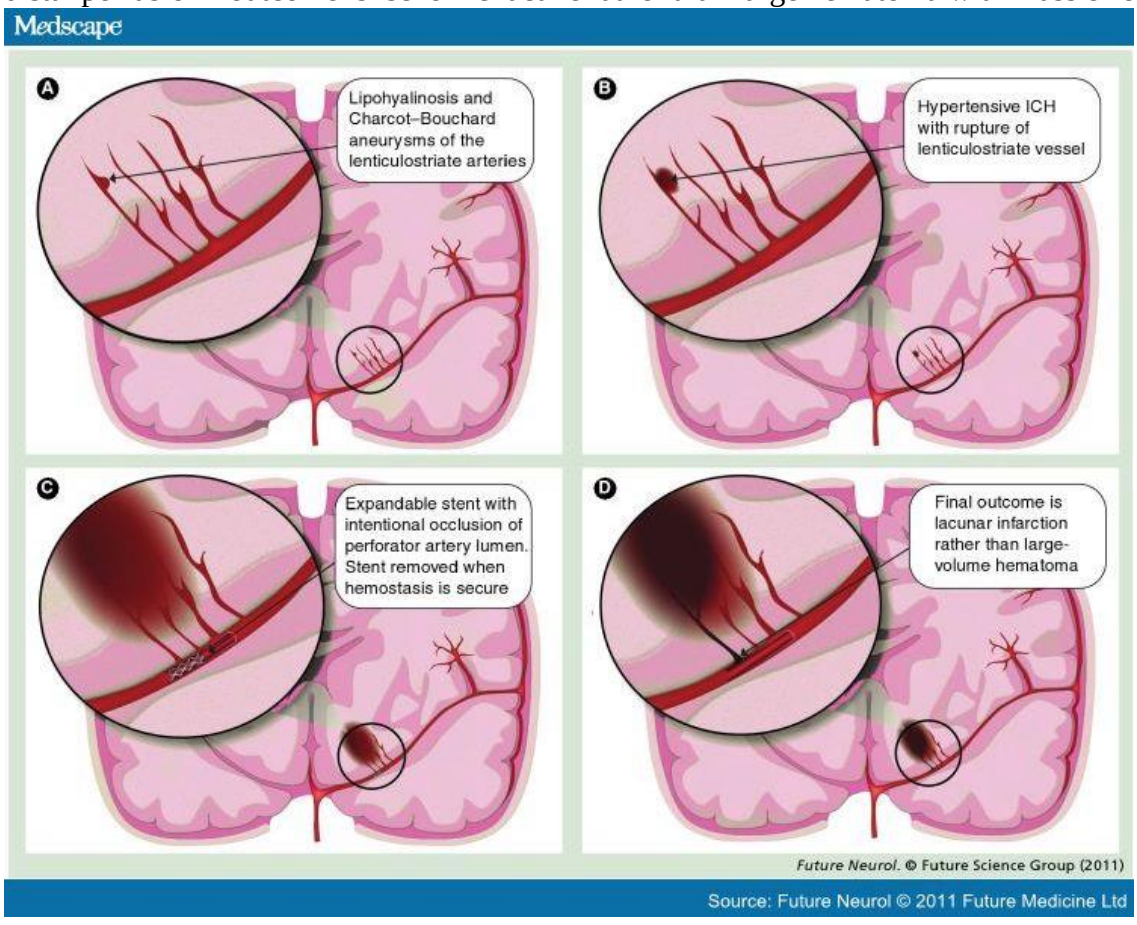
F. **Structural cause** (e.g. aneurysm repair, removal of bleeding AVM or tumor); i.e. bleeding structural / vascular lesion is also indication for surgery.

G. **Ventriculoperitoneal shunt** for chronic hydrocephalus.

– predictors of development of shunt-dependent hydrocephalus after ICH: thalamic ICH, persistently elevated ICP.

FUTURE APPROACHES

Hypertensive lipohyalinosis results in a Charcot–Bouchard aneurysm → vessel rupture → ICH (A–D) demonstrate inserting **temporary stent** to occlude origin of leaking vessel and maintaining distal perfusion - outcome is ischemic lacune rather than large hematoma with mass effect:



'Stereotactic extracranial cautery': imaging (MRI or CT) identifies bleeding vessel → stereotactic headframe technology 'aims' focused beam of electromagnetic energy (e.g. ultrasound or radiation) to target vessel and 'activates' intravenously injected microspheres, which have been labeled with hemostatic drug → localized thrombosis.

PROGNOSIS

- most patients who die of ICH do so during the ***initial acute hospitalization***, and these deaths usually occur ***in the setting of withdrawal of support*** because of presumed poor prognosis.
- 30-day MORTALITY is 40% (30-52% - higher than for ischemic stroke 10-30%):
  - brainstem ICH (60%)
  - deep ICH (44%)
  - lobar ICH (40%)
  - cerebellar ICH (34%)

ICH is most deadly form of stroke!
Half of deaths occur *within the first 24 hours*

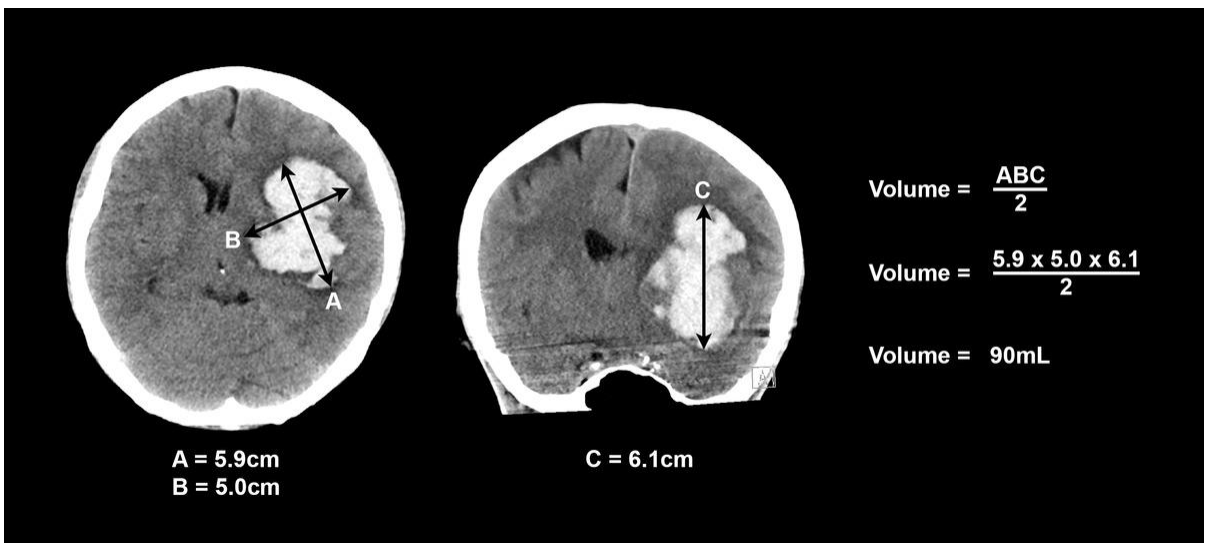
ICH

ICH score (Hemphill et al.) - Class I; Level of Evidence B guidelines emphasize obtaining as baseline severity score:

Feature	Finding	Points
GCS	3-4 5-12 13-15	2 1 0
Age	≥ 80 < 80	1 0
Location	infratentorial supratentorial	1 0
ICH volume	≥ 30 mL < 30 mL	1 0

Score	30-day mortality
0	0%
1	13%
2	26%
3	72%
4	97%
5	100%
6	100%

Intraventricular blood	yes no	1 0
	Total score	



- poor prognostic factors:
  1) age↑
  2) large hemorrhage size (supratentorial > 5 cm, posterior fossa > 3 cm)
     Death occurs due to **mass effect**; hematoma does not destroy, but displaces neural structures (may recover function when blood is resorbed)!
  3) brain stem hemorrhage (75% mortality at 24 hours!)
  4) intraventricular extension (89-90% morbidity, 58-78% mortality)

FUNCTIONAL RECOVERY

- there is no hard rule as to when recovery ends.
- prognosis is surprisingly good in patients who survive acute illness (½ deaths occur within first 2 days) - only 20% survivors require institutionalization (i.e. *most survivors achieve good status or complete recovery*).
- 10-25% patients with ICH can expect functional independence 6 months after ICH (≤ 10% when initial hematoma volumes are > 20-30 mL).
- growing evidence that ICH patients make slightly greater and faster gains in recovery than patients with ischemic stroke.

ICH RECURRENCE

Risk of recurrent hemorrhage is relatively low (1-15% annually); AVMs (can rebleed 2% annually); LVAD (risk of rebleed ↑ up to 5-fold);

– risk of ICH recurrence is highest in the first year; the ongoing risk extends for years, particularly in patients with lobar ICH.

Risk factors for ICH recurrence:

1) hypertension – the lower BP, the lower is risk; no established bottom BP where risk reduction would plateau or reverse (ICH patients should have their *BP lowered to or beyond the targets currently recommended in other high-risk groups*, i.e. <130/80 mm Hg in the presence of diabetes mellitus, heart failure, or chronic kidney disease).

   BP should be controlled in all ICH patients (Class I; Level of Evidence A). BP control should begin immediately after ICH onset (Class I; Level of Evidence A). A long-term goal of BP < 130 / 80 mmHg is reasonable (Class IIa; Level of Evidence B).

2) older age – higher prevalence of cerebral amyloid angiopathy.

3) location of the initial hemorrhage (1-year risk of ICH recurrence: 15% after lobar ICH vs. 2.1% for deep ICH).

4) anticoagulant use* - anticoagulation should be avoided after lobar ICH but can be considered in patients with deep ICH if the risk of thromboembolism is particularly high.
   Eckman MH et al. Can patients be anticoagulated after intracerebral hemorrhage? A decision analysis. Stroke. 2003;34:1710–1716
   – antiplatelet agents do not appear to dramatically increase the risk of hematoma expansion and therefore appear to be generally safe after ICH, including ICH caused by amyloid angiopathy

   Anticoagulation after nonlobar ICH and antiplatelet monotherapy after any ICH might be considered, particularly when there are strong indications for these agents (Class IIb; Level of Evidence B).
   The optimal timing to resume oral anticoagulation after anticoagulant-related ICH is uncertain. Avoidance of oral anticoagulation for ***at least 4 weeks***, in patients without mechanical heart valves, might decrease the risk of ICH recurrence (Class IIb; Level of Evidence B). Aspirin monotherapy can probably be restarted ***in the days*** after ICH, although the optimal timing is uncertain (Class IIa; Level of Evidence B).
   – there are reports that newer anticoagulants may have decreased risk of ICH.

   The usefulness of dabigatran, rivaroxaban, apixaban in patients with AFib and past ICH to decrease the risk of recurrence is uncertain (Class IIb; Level of Evidence C).

5) microbleeds (particularly lobar microbleeds) on gradient echo MRI

6) tobacco use

7) carriers of the apolipoprotein E ε2 or ε4 alleles

*only modifiable factors

   – there are some studies blaming **statins** for increased risk for ICH recurrence; however, meta-analysis (31 randomized controlled trials, 91 588 statin-treated patients) found no significant association between statin use and ICH (OR, 1.08; 95% CI, 0.88–1.32; P=0.47), whereas all strokes and all-cause mortality were significantly reduced with statin therapy.

   There are insufficient data to recommend restrictions on the use of statins in ICH patients (Class IIb; Level of Evidence C).

CEREBRAL AMYLOID ANGIOPATHY

- higher risk for recurrent ICH than ICH resulting from atherosclerosis - prognostic and therapeutic decisions about use of antithrombotic drugs.
- 7% annual risk of recurrence (vs. 1.1% risk with non-CAA-related ICH).
- there is no way to control risk of bleeding from amyloid angiopathy!!!

IVH

- no treatment - half die, 20% return home to live independently.
- EVD - 50% of patients live independently at home after 180 days; intraclot alteplase improves this number by 10% (CLEAR III trial).

SPECIAL SITUATIONS

LVAD (LEFT VENTRICULAR ASSIST DEVICE)

Two types of LVADs:
1) **pulsatile** flow
2) **nonpulsatile** flow (more and more popular) – cannot use BP cuff; use A-line – see MAP
   N.B. MAP > 90 mmHg is abnormal (risk of ICH↑)

– most important prognostic factor – GCS at presentation (no patients with GCS ≤ 11 did survive 30 days).
– patient is usually on Aspirin and warfarin; when to restart:
   [classic AFib with worst CHAD – annual stroke risk is only 18-20%]
– experts usually restart Aspirin in 7-14 days and warfarin in 14-21 days; no thrombotic complications reported from withholding so long.
– once restarted, risk of rebleed ↑ 5-fold in one Italian study but no increased risk in one Canadian study.

BIBLIOGRAPHY for ch. "Neurovascular Disorders" → follow this LINK >>
AHA/American Stroke Association 2015 "Guidelines for the Management of Spontaneous Intracerebral Hemorrhage". Stroke. 2015; 46:2032-2060