Intracerebral Hemorrhage (ICH)

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

Last updated: October 3, 2024

TRAUMATIC ICH (TICH) → see p. TrH1 >>

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.

GUIDELINES

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2022) >>

Steven M Greenberg et al. 2022 Guideline for the Management of Patients With Spontaneous Intracerebral Hemorrhage: A Guideline From the American Heart Association/American Stroke Association. Stroke. 2022 Jul;53(7):e282-e361.

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

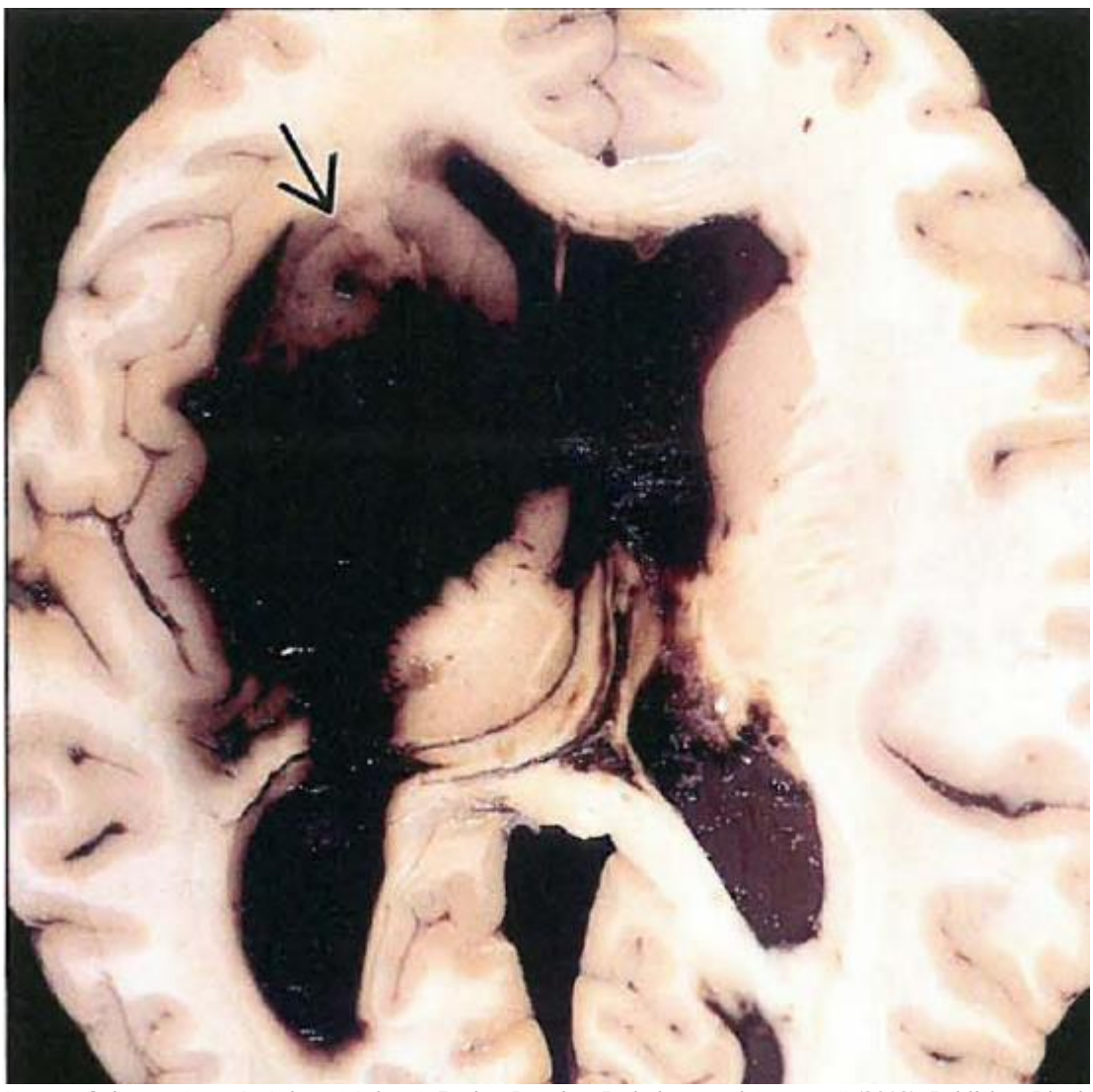
- **acute hypertension** can be caused by sympathomimetic drugs.
- **chronic hypertension** causes ***hyaline arteriolosclerosis (lipohyalinosis)*** ÷ ***fibrinoid necrosis*** and **CHARCOT-BOUCHARD microaneurysms**.
- mostly affected are ***deep penetrating arteries**** (of circle of Willis and of basilar 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:

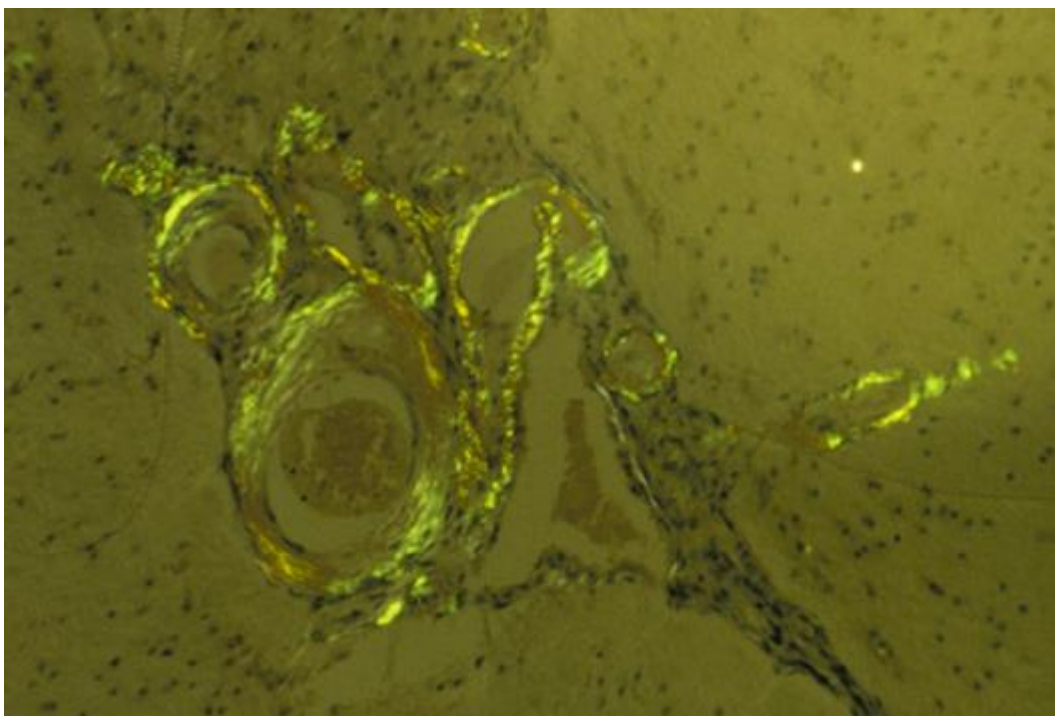


Source of picture: Anne G. Osborn "Osborn's Brain - Imaging, Pathology, and Anatomy" (2012); Publisher: Lippincott Williams & Wilkins; ISBN-13: 978-1931884211 >>

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

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

YOUNG PERSONS (spontaneous ICH or extra-axial bleed):
1. Vascular causes - AVM, aneurysm, cavernoma, venous thrombosis (judicious anticoagulation + hydration + observation), vasculitis
2. Bleeding disorders
3. ADEM

4. Tumor
5. Illicit drug (amphetamines, cocaine)

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

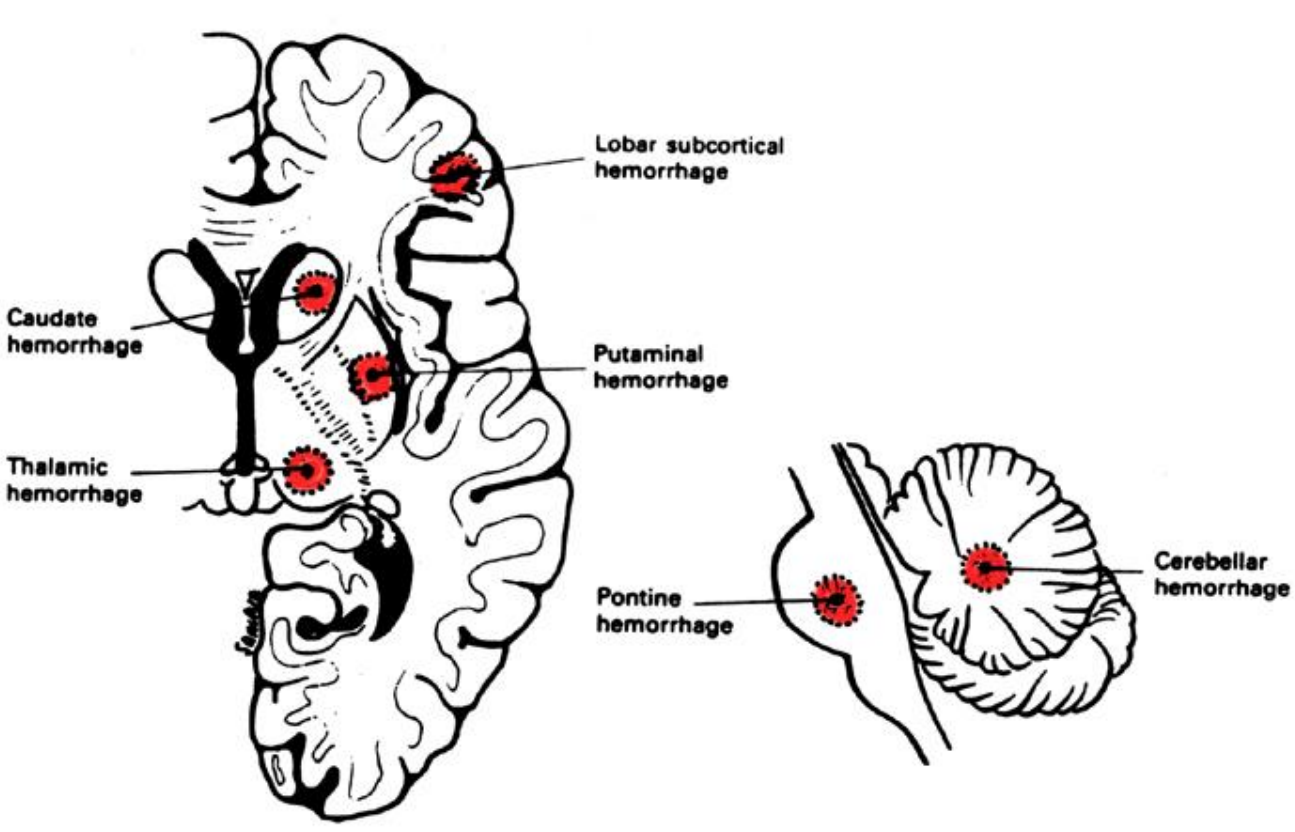
LOCATION

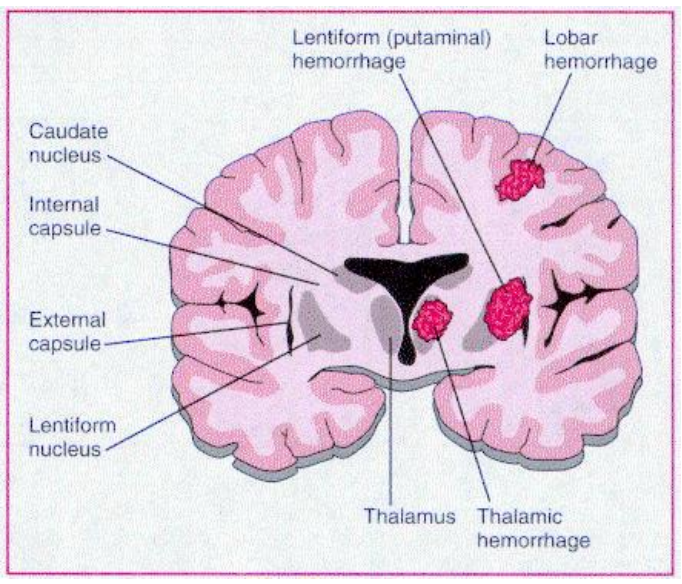
Commonest sites of ICH:

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.





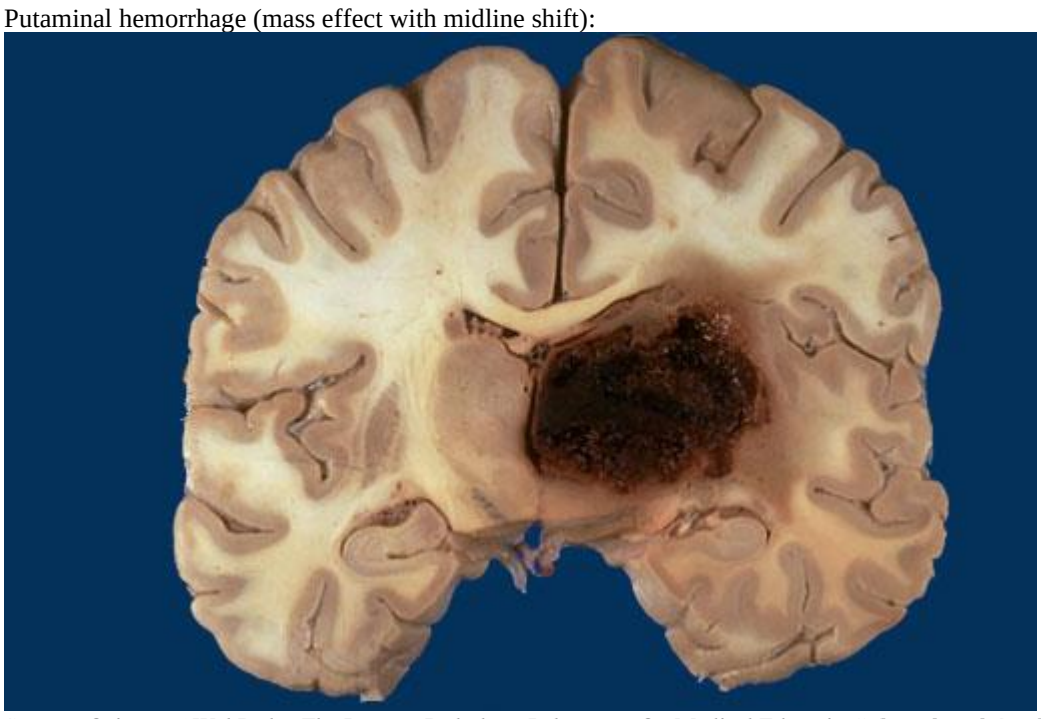
Source of picture: Anthony S. Fauci, Eugene Braunwald "Harrison's Principles of Internal Medicine" (1998); McGraw-Hill (Tx); ISBN-13: 978-0070202917 >>

MACROSCOPICALLY

- 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.

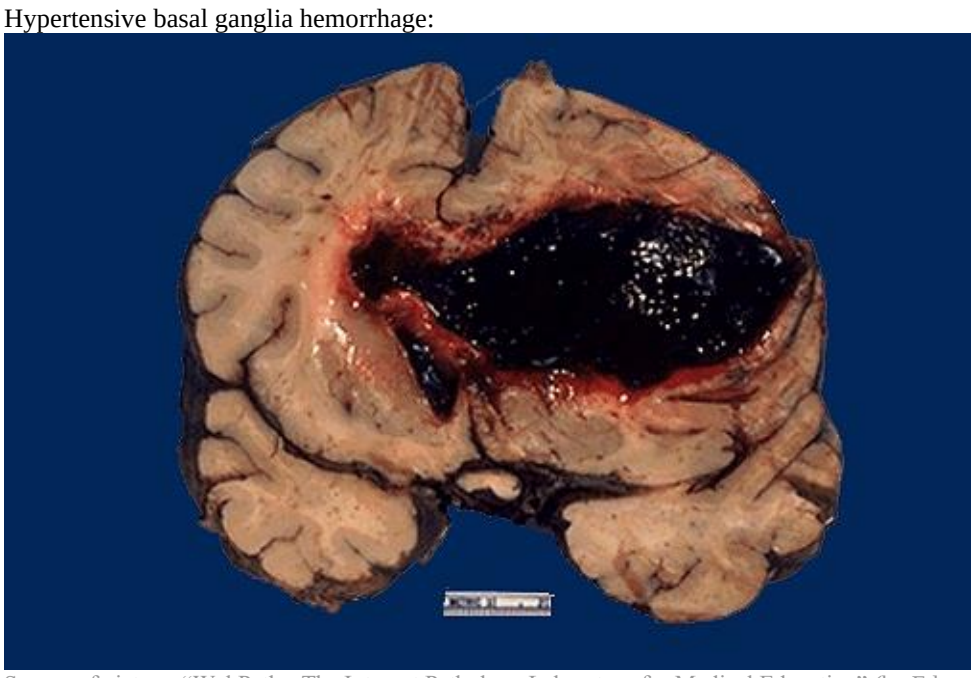
- if patient survives initial ICP changes, blood is absorbed over weeks ÷ months → **cavity or cleft** (lined by glial scar and hemosiderin-containing macrophages) that may disconnect brain pathways.
  – *less frequently*, blood clot is treated as FOREIGN BODY - **calcifies** and is surrounded by thick 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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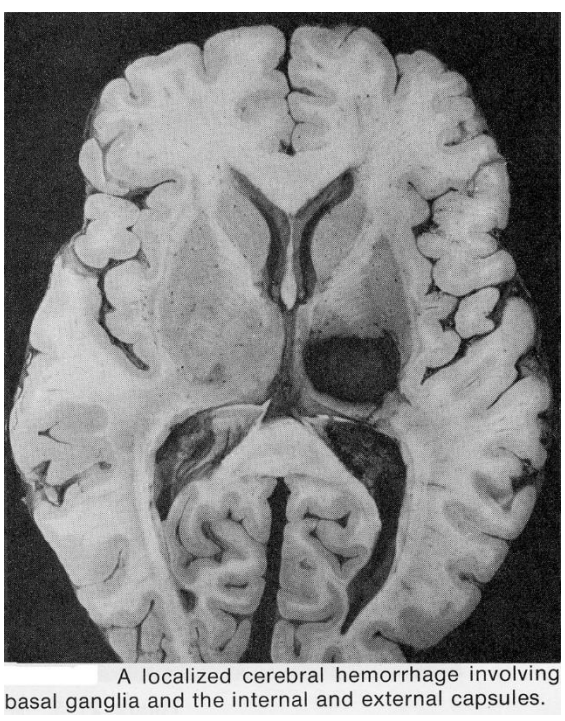
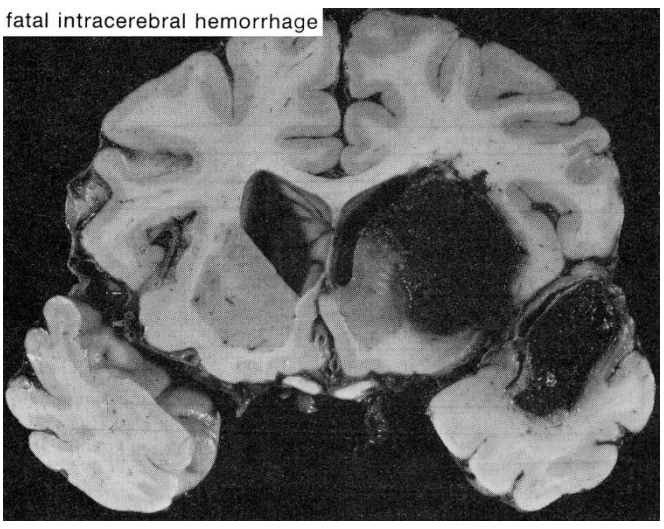
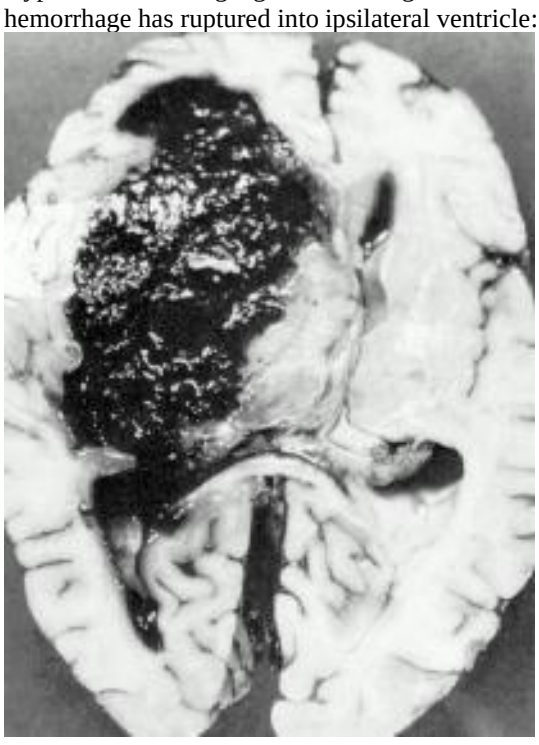


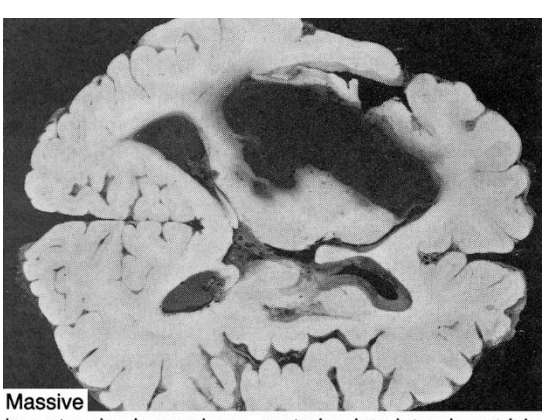
A localized cerebral hemorrhage involving basal ganglia and the internal and external capsules.



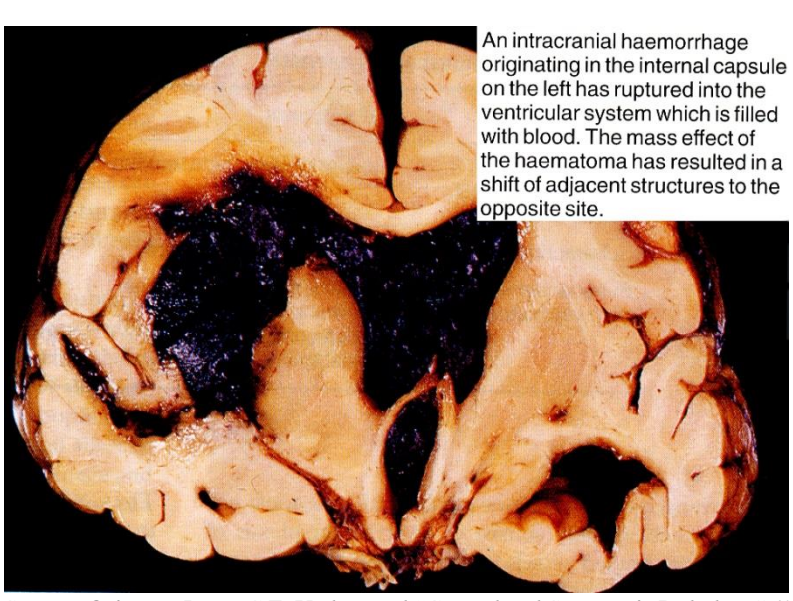
fatal intracerebral hemorrhage

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



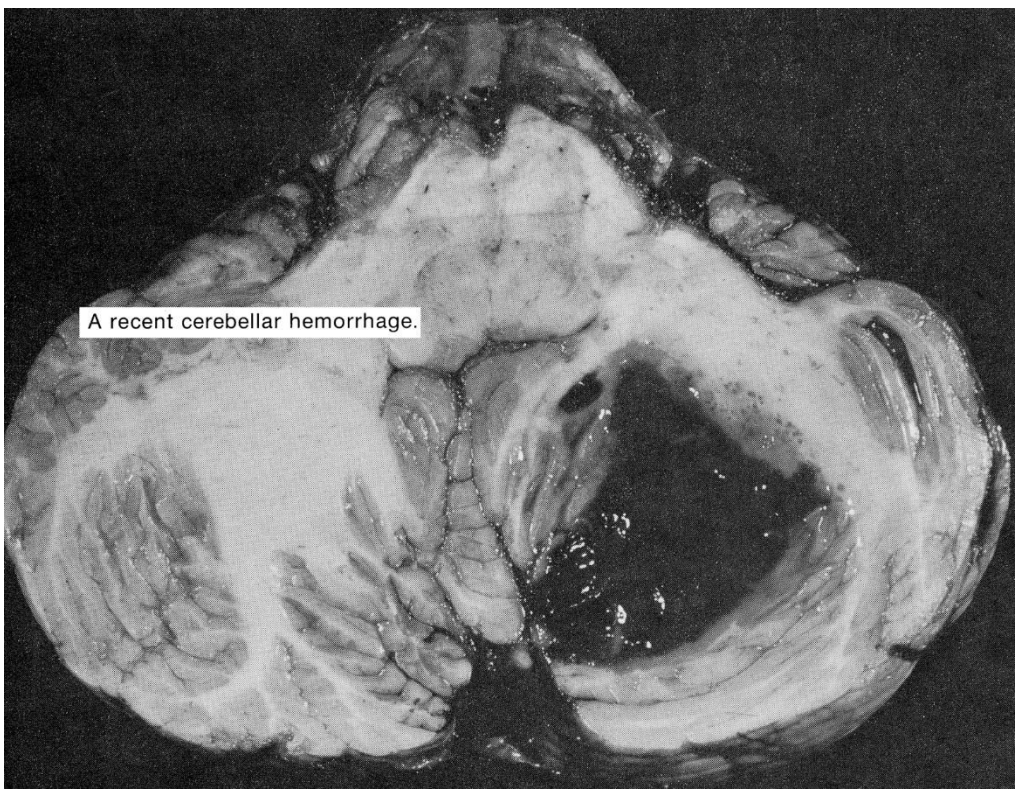


Massive hypertensive hemorrhage, rupturing into lateral ventricle



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.

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 (ROTEM vs. prothrombin time, aPTT, 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.

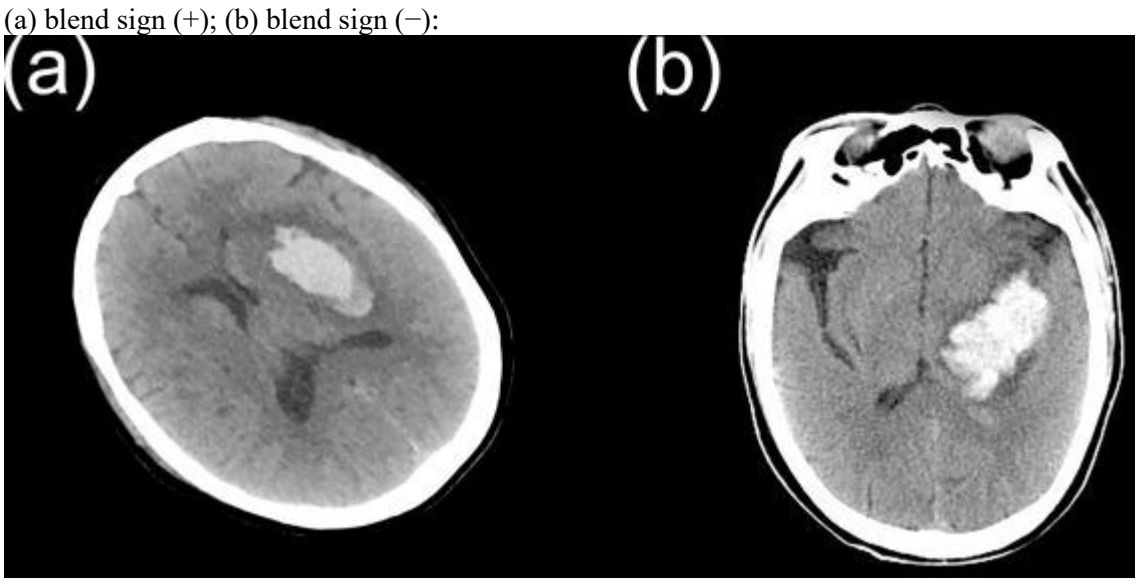
- performed immediately in suspected acute ICH!
- follow-up CT is frequently requested (changes in lesion size, ventricular system).
  1/3 of patients have ICH size growth on repeat imaging!
- fresh hematoma - homogeneous rounded area of increased density (≈ 30-80 HU) + mass effect (vs. hemorrhagic infarctions - 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!

- 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.
- 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 hematoma - *predicts hematoma expansion*:

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



Yu et al. 2017

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2022)

2b	B-NR	5. In patients with spontaneous ICH, using non-contrast computed tomography (NCCT) markers of HE to identify patients at risk for HE may be reasonable.[106]

Serial imaging

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2022)
Serial CT is recommended within first 24 hours:

2a	B-NR	2. In patients with spontaneous ICH and/or IVH, serial head CT can be useful within the first 24 hours after symptom onset to evaluate for hemorrhage expansion.[97–99]

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2022)
Serial CT is recommended if low GCS:

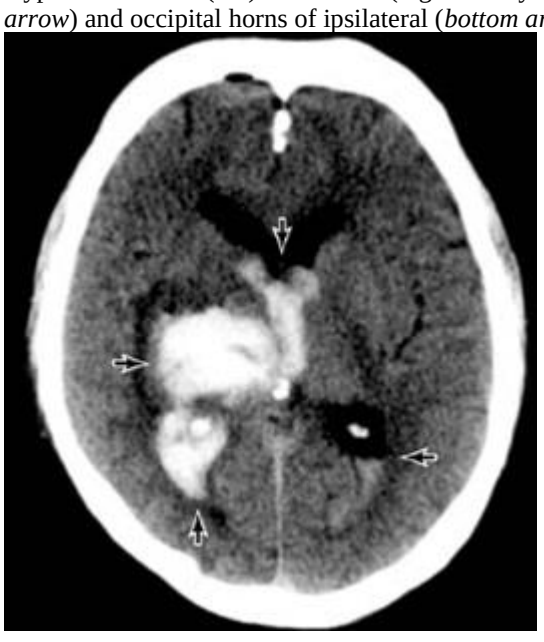
2a	C-LD	3. In patients with spontaneous ICH and/or IVH and with low GCS score or ND, serial head CT can be useful to evaluate for hemorrhage expansion, development of hydrocephalus, brain swelling, or herniation.[100–102]

- 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***).

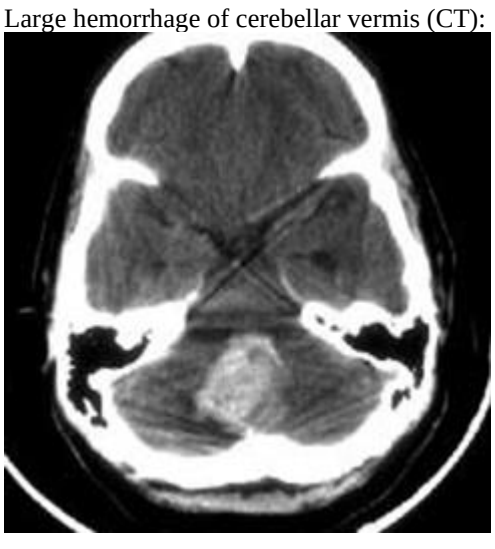
*vs. **gyral enhancement** typical of infarction

- 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.

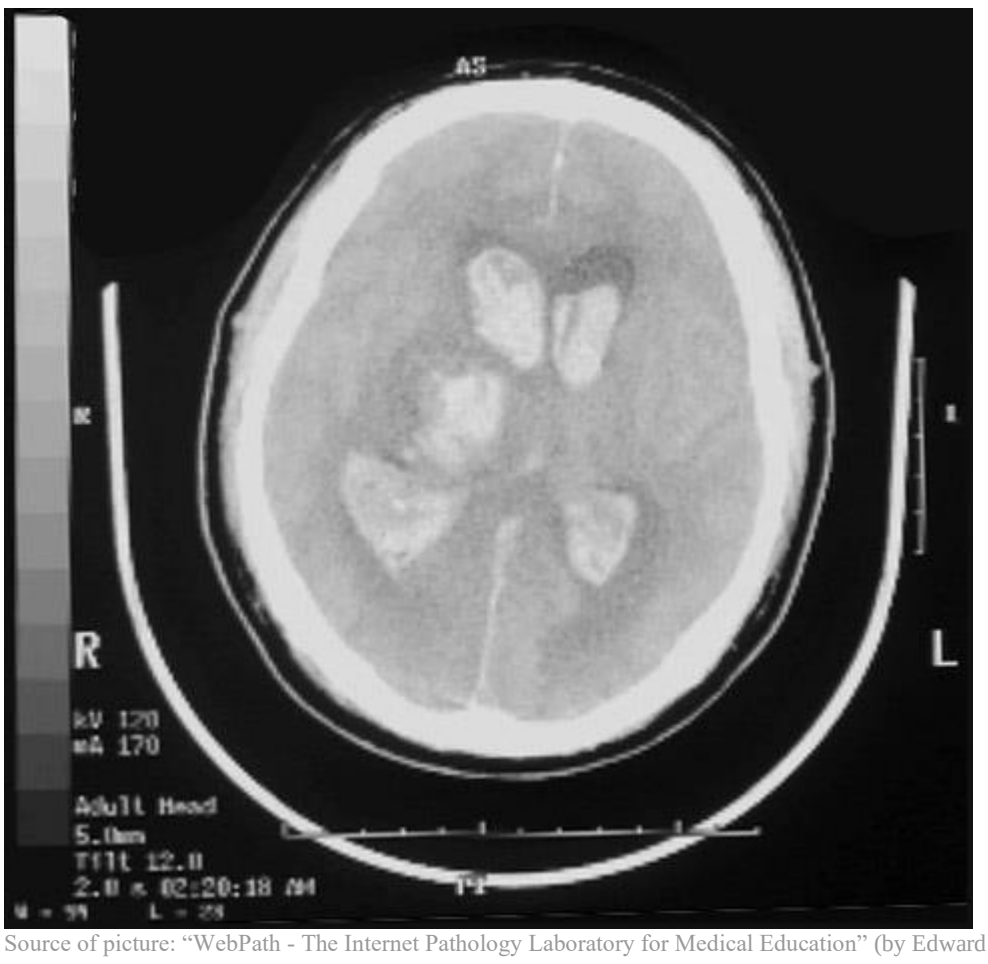
Hypertensive ICH (CT): hematoma (high-density signal) in thalamus (*left arrow*) with extension into 3rd ventricle (*top arrow*) and occipital horns of ipsilateral (*bottom arrow*) and contralateral (*right arrow*) lateral ventricles:



Large hemorrhage of cerebellar vermis (CT):



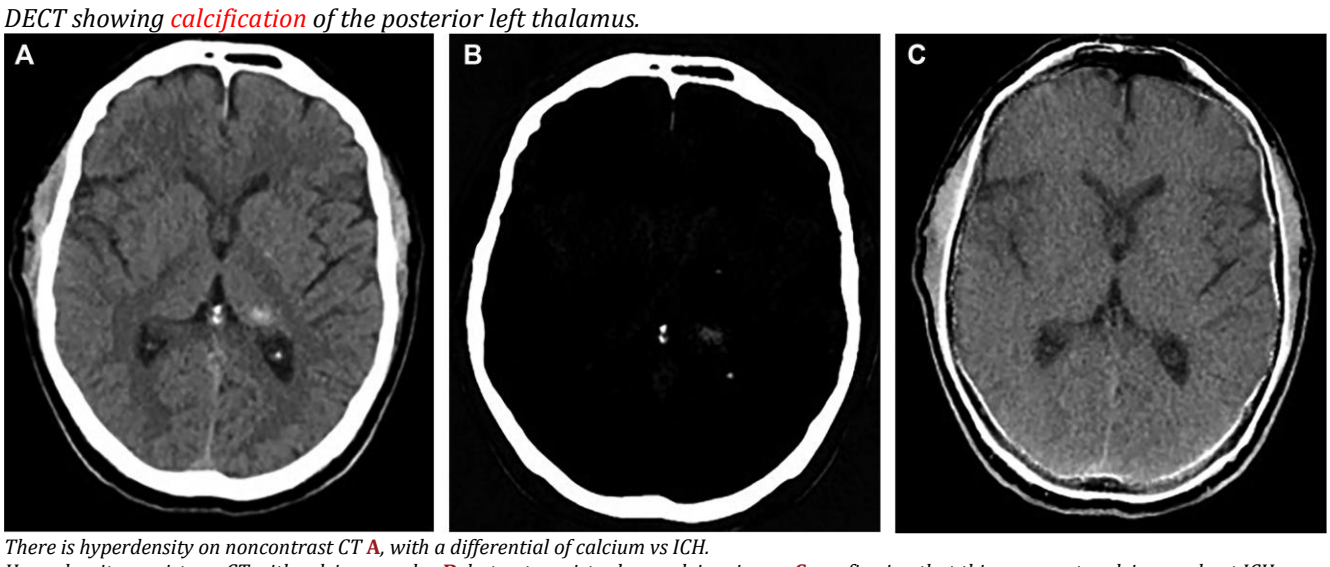
Thalamic hemorrhage that has extended into ventricular system:



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

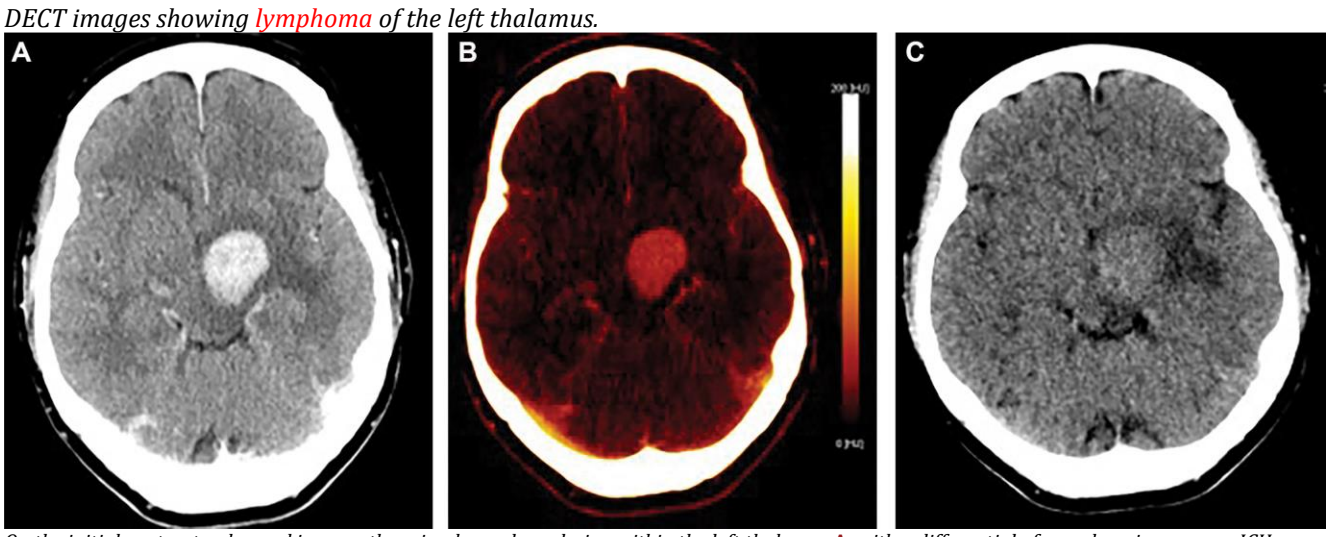
Dual-energy CT (DECT) allows differentiation between blood and calcium and other hyperdense etiologies:

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.



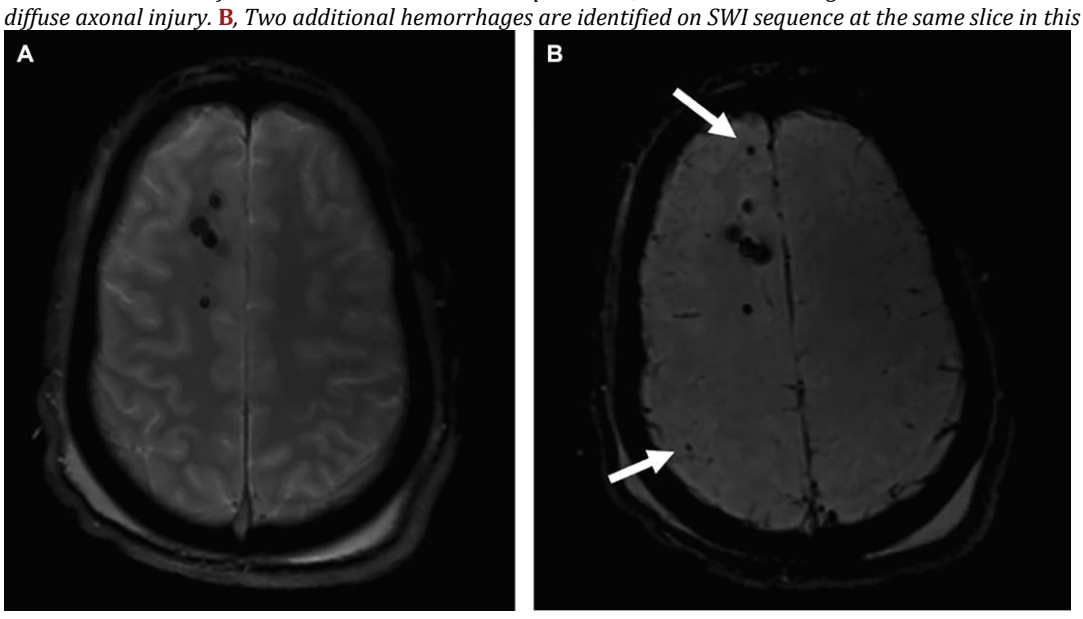
*On the initial contrast-enhanced images, there is a hyperdense lesion within the left thalamus **A**, with a differential of an enhancing mass vs ICH. There is persistent hyperdensity on the iodine overlay image **B** and only mild hyperdensity on the virtual noncontrast image **C** indicating that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

MRI

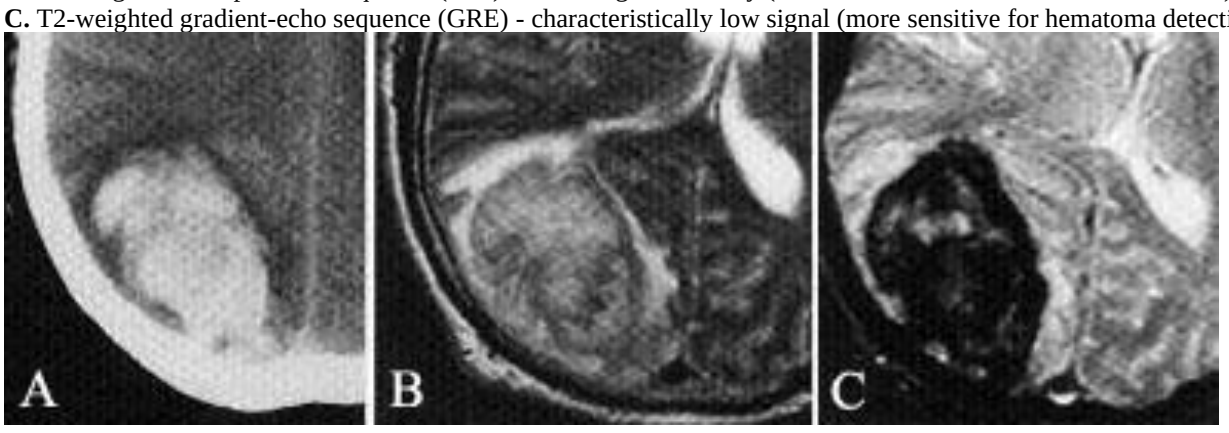
- picture depends on precise sequence used and ***age of hemorrhage*** (hemoglobin degradation products [different paramagnetic properties] play important role) – further see p. D51 >>

- *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:

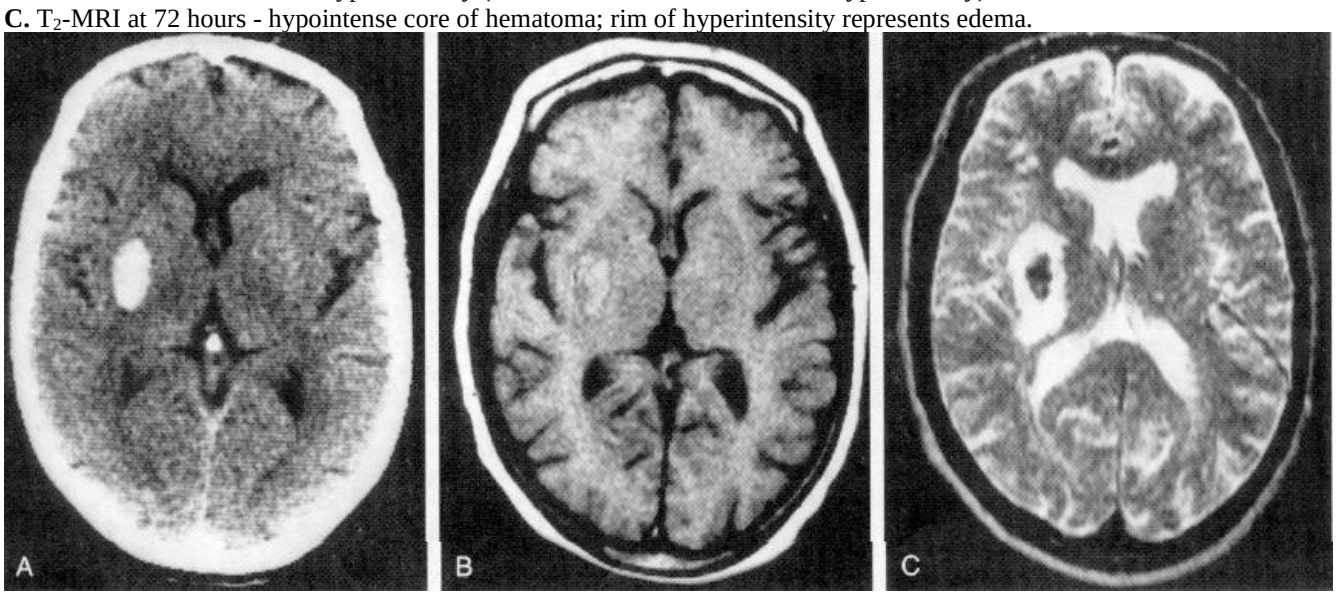
*SWI is more sensitive for ICH than traditional GRE sequences. **A**, Standard GRE image shows several small ICH in a patient with diffuse axonal injury. **B**, Two additional hemorrhages are identified on SWI sequence at the same slice in this patient (arrows).*



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)

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2015)
CTA and contrast-enhanced CT may be considered to help identify patients at **risk for hematoma expansion** (Class IIb; Level of Evidence B).
CTA, CTV, contrast-enhanced CT, contrast-enhanced MRI, MRA, MRV, catheter angiography can be useful to evaluate for underlying **structural lesions** (incl. vascular malformations and tumors) when there is clinical or radiological suspicion (Class IIa; Level of Evidence B)

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2022)
CTA within the first few hours of ICH onset may be reasonable to identify patients at risk for subsequent **hematoma expansion**.

2b	B-NR	4. In patients with spontaneous ICH, CT angiography (CTA) within the first few hours of ICH onset may be reasonable to identify patients at risk for subsequent HE.[103–108]

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2022)
In **spontaneous IVH and no detectable parenchymal hemorrhage**, DSA is recommended to exclude a **macrovascular cause** (yield of DSA is up to 58%, esp. in younger patients).

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2022)
Acute CTA plus consideration of venography is recommended (to exclude macrovascular causes or cerebral venous thrombosis):
a) **lobar** spontaneous ICH + age < 70 years
b) **deep/posterior fossa** spontaneous ICH + age < 45 years
c) **deep/ posterior fossa** spontaneous ICH + age 45-70 years + no history of hypertension*

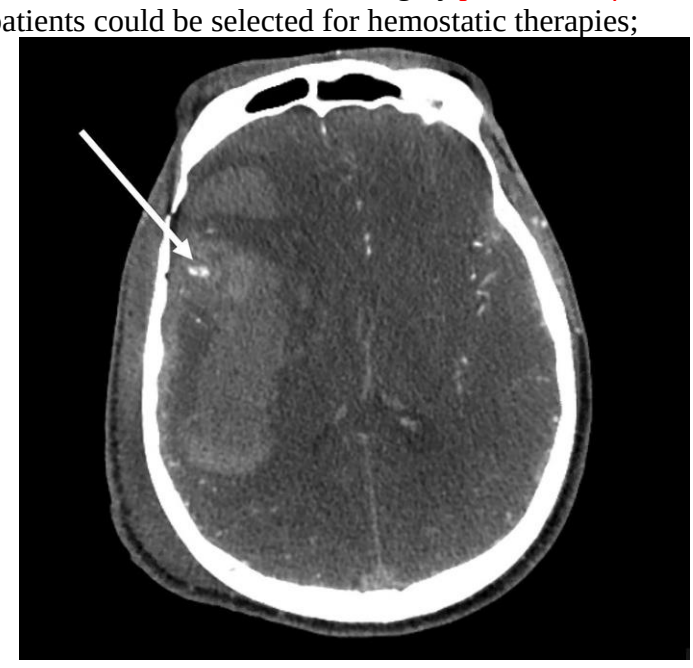
*history of hypertension, use of antihypertensive drugs before ICH, or evidence of left ventricular hypertrophy on admission ECG

- 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*, *IV drug* use - high likelihood of vascular malformations, mycotic aneurysms, venous sinus thrombosis (from dehydration).

  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

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!

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 ventricles)
b) **secondary** (extension of ICH) - most of IVHs - hypertensive hemorrhages involving 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). see ICH score >>
- 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, trapped ventricle, thrombotoxicity and inflammation (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 1/3 (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.

CONSERVATIVE MEASURES

GENERAL MEASURES

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2015)
Initial monitoring and management should take place in ICU / dedicated stroke unit with physician and nursing neuroscience acute care expertise (Class I; Level of Evidence B).

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2022)
Early aggressive mobilization within the first 24 hours after ICH appears to worsen 14-day mortality.

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2015, 2022)
Both hyperglycemia (> 180-200) and hypoglycemia (< 40-60) should be treated (Class I; Level of Evidence C).

COR	LOE	Recommendations
1	C-LD	1. In patients with spontaneous ICH, monitoring serum glucose is recommended to reduce the risk of hyperglycemia and hypoglycemia.[256,299]
1	C-LD	2. In patients with spontaneous ICH, treating hypoglycemia (<40–60 mg/d, <2.2–3.3 mmol/L) is recommended to reduce mortality.[299–301]
2a	C-LD	3. In patients with spontaneous ICH, treating moderate to severe hyperglycemia (>180–200 mg/dL, >10.0–11.1 mmol/L) is reasonable to improve outcomes.[78,302–307]

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2015)
A formal screening for dysphagia should be performed in all patients **before the initiation of oral intake** to reduce the risk of pneumonia (Class I; Level of Evidence B).

- dysphagia is the most common medical sequelae seen in this patient population; if failed → early enteral feeding.

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2015)
Treatment of fever may be reasonable (Class IIb; Level of Evidence C).

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2015)
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

Target SBP 130-150 mmHg (newer data < 160) – achieve acutely but smoothly with careful titration!
N.B. acute lowering of SBP to < 130 is potentially harmful!

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2022)

2a	B-NR	1. In patients with spontaneous ICH requiring acute BP lowering, careful titration to ensure continuous smooth and sustained control of BP, avoiding peaks and large variability in SBP, can be beneficial for improving functional outcomes.[138]
2a	C-LD	2. In patients with spontaneous ICH in whom acute BP lowering is considered, initiating treatment within 2 hours of ICH onset and reaching target within 1 hour can be beneficial to reduce the risk of HE and improve functional outcome.[139,140]
2b	B-R	3. In patients with spontaneous ICH of mild to moderate severity presenting with SBP between 150 and 220 mm Hg, acute lowering of SBP to a target of 140 mm Hg with the goal of maintaining in the range of 130 to 150 mm Hg is safe and may be reasonable for improving functional outcomes.[138,141–147]
2b	C-LD	4. In patients with spontaneous ICH presenting with large or severe ICH or those requiring surgical decompression, the safety and efficacy of intensive BP lowering are not well established.[148]
3: Harm	B-R	5. In patients with spontaneous ICH of mild to moderate severity presenting with SBP >150 mm Hg, acute lowering of SBP to <130 mm Hg is potentially harmful.[146,149,150]

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2015)
Measures to control BP should begin in **all patients immediately** after ICH onset (Class I; Level of Evidence A).
For patients presenting with **SBP 150-220 mmHg** 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).
For patients presenting with **SBP > 220 mmHg**, it may be reasonable to consider aggressive reduction of BP with a continuous intravenous infusion and frequent BP monitoring (Class IIb; Level of Evidence C).
A long-term goal of BP <130/80 mmHg is reasonable (Class IIa; Level of Evidence B).

see INTERACT2 >>

- ***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) (2010) - 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 (2013) – patients with small-moderate ICH and presenting with SBP 150-220 within 6 hours → 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 BP reduction resulted in non-significantly lower poor outcome rate*!
- 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.

Next trial was designed to determine even earlier BP reduction:

Antihypertensive Treatment of Cerebral Hemorrhage (ATACH) 2 trial (2016) - randomizing ICH (< 60 mL with GCS ≥ 5) patients to goal **SBP of 110-140 mmHg** (intensive group) vs. **140-180 mmHg** (standard group) within 4.5 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).

- *enrollment was stopped because of futility* after a prespecified interim analysis:

	Intensive group	Standard group
death or disability	38.7%*	37.7%
serious adverse events within 72 hours	1.6%	1.2%
renal adverse events within 7 days	9.0%	4.0%, P=0.002

*relative risk, 1.04; 95% confidence interval, 0.85-1.27

CONCLUSION: treatment of ICH to achieve a target SBP of 110-140 mmHg *did not result in a lower rate of death or disability* than standard target of 140-180 mmHg.

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)

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2022)
In patients with spontaneous ICH or IVH and **hydrocephalus**, ventricular drainage should be performed to reduce mortality. see EVD in ICH >>
In **reduced level of consciousness**, ICP monitoring and treatment might be considered to reduce mortality and improve outcomes.
Bolus hyperosmolar therapy may be considered for transiently reducing ICP.

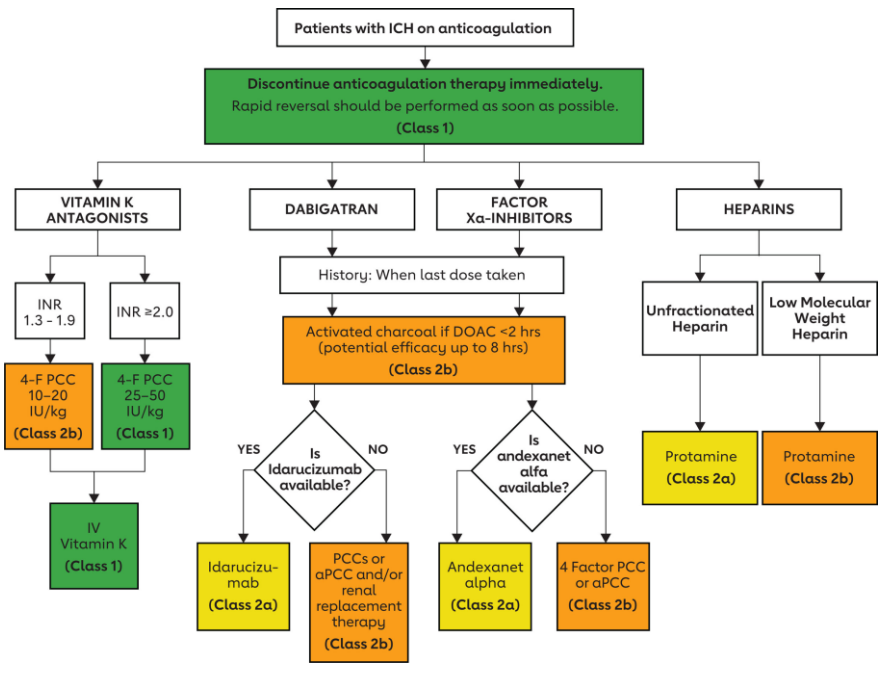
Causes of elevated ICP in ICH:

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 - risk of further deterioration from ***secondary damage*** (including herniation) for up to a week - monitor for ICP↑ (esp. with cerebellar hemorrhages).

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2015)
Corticosteroids should not be administered for treatment of elevated ICP in ICH (Class III; Level of Evidence B) - not effective and increase complications!
AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2022)
Prophylactic corticosteroids or early continuous hyperosmolar therapy appears to have no benefit for outcome.

REVERSAL OF BLEEDING DIATHESIS (COAGULATION)

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2022)



AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2022)
Role of RECOMBINANT FACTOR VIIA (RFVIIA), TXA to improve functional outcome is unclear

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; currently, *use of rFVIIa is not recommended*! (exceptions may be patients taking DABIGATRAN, RIVAROXABAN, or APIXABAN)

Noncoagulopathic patients

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2015)
Although rFVIIa can limit the extent of hematoma expansion in **noncoagulopathic** ICH patients, there is an increase in thromboembolic risk with rFVIIa and no clear clinical benefit in unselected patients. Thus, rFVIIa is not recommended (Class III; Level of Evidence A).

Patients on new oral anticoagulants (DOAC) DABIGATRAN / RIVAROXABAN or APIXABAN

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2015, 2022)

1) idarucizumab / andexanet alpha
2) PCCs for factor Xa inhibitors (for DABIGATRAN only if idarucizumab is not available)
3) FEIBA (not in 2022 guideline)
4) rFVIIa (not in 2022 guideline)
5) activated charcoal if the most recent dose of anticoagulant was taken < 2 hours earlier.
6) hemodialysis might be considered for DABIGATRAN if idarucizumab is not available (Class IIb; Level of Evidence C).

Patients on warfarin (VKA) → 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!

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2015, 2022)

Stop VKA + replace vitamin K–dependent factors + IV vitamin K (Class I; Level of Evidence C).

4-factor PCCs may have fewer complications and correct the INR more rapidly than FFP and might be considered over FFP (Class IIb; Level of Evidence B).

rFVIIa does not replace all clotting factors, and although the INR may be lowered, clotting may not be restored in vivo; therefore, rFVIIa is not recommended for VKA reversal in ICH (Class III; Level of Evidence C).

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.

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2015, 2022)

Protamine sulfate may be considered to reverse HEPARIN (Class IIb; Level of Evidence C).

Patients on LMWH → PROTAMINE but reversal is incomplete.

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2022)

Protamine sulfate may be considered to partially reverse LMWH (Class IIb; Level of Evidence C).

Hemophilia → FACTOR VIII (to achieve level of 80-100% of normal).

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)

REVERSAL OF BLEEDING DIATHESIS (PLATELETS)

N.B. if not going to OR - platelet transfusion is not recommended!

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2022)

Platelet transfusions outside the setting of emergency surgery or severe thrombocytopenia appears to worsen outcome.

- **thrombocytopenia** → PLATELET TRANSFUSION.

Patients on antiplatelet agents

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2022)

Platelet transfusions, desmopressin, TXA - no convincing benefit (exception is emergency craniotomy for hematoma removal - reversal of ASPIRIN with platelet transfusions might reduce postoperative hemorrhage volume*).

*it is not known whether this effect also pertains to EVD and minimally invasive surgery

PATCH (Platelet transfusion versus standard care for spontaneous ICH associated with antiplatelet therapy

M Irem Baharoglu et al. Platelet transfusion versus standard care after acute stroke due to spontaneous cerebral haemorrhage associated with antiplatelet therapy (PATCH): a randomised, open-label, phase 3 trial. Lancet, Volume 387, Issue 10038p2605-2613June 25, 2016

- multicentre, open-label, masked-endpoint, randomised trial at 60 hospitals in the Netherlands, UK, and France.
- 190 adults within 6 h of supratentorial ICH if they had used antiplatelet therapy for at least 7 days beforehand GCS at least 8.
- standard care vs. standard care with platelet transfusion within 90 min of diagnostic brain imaging.
- results - platelet transfusion seems inferior to standard care:
  - 24% participants assigned to platelet transfusion died during hospital stay (vs. 17% assigned to standard care).
  - odds of death or dependence at 3 months were higher in the platelet transfusion group (adjusted common odds ratio 2·05, 95% CI 1·18–3·56; p=0·0114).
  - 42% participants who received platelet transfusion had a serious adverse event during their hospital stay, vs 29% who received standard care.

- **patients on antiplatelet** → PLATELET TRANSFUSION 2 doses (3 doses if on dual antiplatelet; 1 dose for aspirin only and only if goes to surgery, otherwise - DDAVP)

COR	LOE	Recommendations
2b	C-LD	1. For patients with spontaneous ICH being treated with aspirin and who require emergency neurosurgery, platelet transfusion might be considered to reduce postoperative bleeding and mortality.[206]
2b	C-LD	2. For patients with spontaneous ICH being treated with antiplatelet agents, the effectiveness of desmopressin with or without platelet transfusions to reduce the expansion of the hematoma is uncertain.[207–209]
3: Harm	B-R	3. For patients with spontaneous ICH being treated with aspirin and not scheduled for emergency surgery, platelet transfusions are potentially harmful and should not be administered.[210]

VENOUS THROMBOEMBOLISM

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2015)
Intermittent pneumatic compression for DVT / PE prevention should begin the day of admission (Class I; Level of Evidence A)
Graduated compression stockings are not beneficial to reduce DVT or improve outcome (Class III; Level of Evidence A).
After **documentation of bleeding cessation**, low-dose subcutaneous low-molecular-weight or unfractionated heparin may be considered for DVT / PE prevention in patients with lack of mobility after 1 to 4 days from onset (Class IIb; Level of Evidence B).
Symptomatic DVT or PE: systemic anticoagulation or IVC filter placement is probably indicated (Class IIa; Level of Evidence C). The decision between these 2 options should take into account several factors, including time from hemorrhage onset, hematoma stability, cause of hemorrhage, and overall patient condition (Class IIa; Level of Evidence C).

- 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)

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2022)
Proximal DVT, PE – delay therapeutic anticoagulation for 1-2 weeks (use retrievable IVC filter meanwhile).

COR	LOE	Recommendations
Prophylaxis		
1	B-R	1. In nonambulatory patients with spontaneous ICH, intermittent pneumatic compression (IPC) starting on the day of diagnosis is recommended for VTE (DVT and pulmonary embolism [PE]) prophylaxis.[275,276]
2a	C-LD	2. In nonambulatory patients with spontaneous ICH, low-dose UFH or LMWH can be useful to reduce the risk for PE.[277–280]
2b	C-LD	3. In nonambulatory patients with spontaneous ICH, initiating low-dose UFH or LMWH prophylaxis at 24 to 48 hours from ICH onset may be reasonable to optimize the benefits of preventing thrombosis relative to the risk of HE.[277,281,282]
3: No Benefit	B-R	4. In nonambulatory patients with spontaneous ICH, graduated compression stockings of knee-high or thigh-high length alone are not beneficial for VTE prophylaxis.[276,278,283,284]
Treatment		
2a	C-LD	5. For patients with acute spontaneous ICH and proximal DVT who are not yet candidates for anticoagulation, the temporary use of a retrievable filter is reasonable as a bridge until anticoagulation can be initiated.[285]
2b	C-LD	6. For patients with acute spontaneous ICH and proximal DVT or PE, delaying treatment with UFH or LMWH for 1 to 2 weeks after the onset of ICH might be considered.[286,287]

ASM

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2022)
Prophylactic antiseizure medication is not is not beneficial to improve functional outcomes, long-term seizure control, or mortality (Class III; Level of Evidence B).

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2015)
Clinical seizures should be treated with antiseizure drugs (Class I; Level of Evidence A).
Patients with a **change in mental status** who are found to have **electrographic seizures on EEG** should be treated with antiseizure drugs (Class I; Level of Evidence C).
Continuous EEG is probably indicated in ICH patients with **depressed mental status that is out of proportion to the degree of brain injury** (Class IIa; Level of Evidence C).

- 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! – attempt to secure distal aneurysms endovascularly prior to OR

INDICATIONS

Surgery – mainly for life-threatening ICH

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

   N.B. in contrast to cerebellar hemorrhage, evacuation of brainstem hemorrhages may be harmful in many cases

   AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2022)
   Indications for immediate surgical evacuation (± EVD) of cerebellar hemorrhage (Class I; Level of Evidence B):
   a) **volume** (≥ 15 mL) ← new addition in 2022; 15 mL ≈ 3 cm diameter
   b) neurological **deterioration**
   c) **brainstem** compression
   d) **hydrocephalus**

   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.

   AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2015)
   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, i.e. lobar ICH).

   AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2022)
   For **supratentorial ICH > 20-30 mL with GCS 5–12**, minimally invasive hematoma evacuation with endoscopic or stereotactic aspiration with or without thrombolytic use can be useful to ***reduce mortality*** compared with medical management alone (grade 2a) but effectiveness to improve ***functional outcomes*** is uncertain (grade 2b).
   - it may be reasonable to select minimally invasive hematoma evacuation over conventional craniotomy to improve functional outcome (grade 2b).

   AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2015)
   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!

   AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2015)
   Early hematoma evacuation is not clearly beneficial compared with hematoma evacuation when patients **deteriorate** (Class IIb; Level of Evidence A).
   Supratentorial hematoma evacuation in ***deteriorating*** patients might be considered as a life-saving measure (Class IIb; Level of Evidence C).

- ICH due to venous thrombosis – cerebral tissue is recoverable so ***only decompressive craniectomy*** if indicated due to mass effect → (venous thrombectomy) → heparin IVI postop

SURGICAL APPROACHES & TRIALS

No trials to date (STICH I-II, CLEAR up to III, MISTIE up to III) have demonstrated the benefit of surgery for ***non-life-threatening*** ICH

ENRICH, MIND results pending

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2022)
Craniotomy for hemorrhage evacuation: usefulness to improve ***functional outcomes*** or ***mortality*** is uncertain (grade 2b); if *patient is deteriorating*, craniotomy for hematoma evacuation might be considered as a lifesaving measure (grade 2b).
Coma with significant midline shift or refractory ICP - decompressive craniectomy with or without hematoma evacuation may be considered to reduce ***mortality*** (grade 2b) but effectiveness to improve ***functional outcomes*** is uncertain (grade 2b).

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

- 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 – **medical management alone vs. early surgery** (within 12 hours of randomization) for lobar ICH with clot ≤ 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 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).
  - subgroup analysis: patients with **poor prognosis (GCS 9-12)** are better off with early surgery!

N.B. patients with deep ICH esp. with IVH do worse with surgery!

Early hematoma evacuation has not been shown to be beneficial in the 2 largest randomized trials (STICH and STICH II), but *high crossover rates* to surgical intervention, *narrow patient-based inclusion criteria*, and the *focus on early surgery* leave unclarified whether surgery may benefit specific groups of patients with supratentorial ICH

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 lobar hematomas who are ***still awake*** (GCS ≥ 9) – with surgery done between 48 and 72 hrs with residual clot < 30 mL.

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

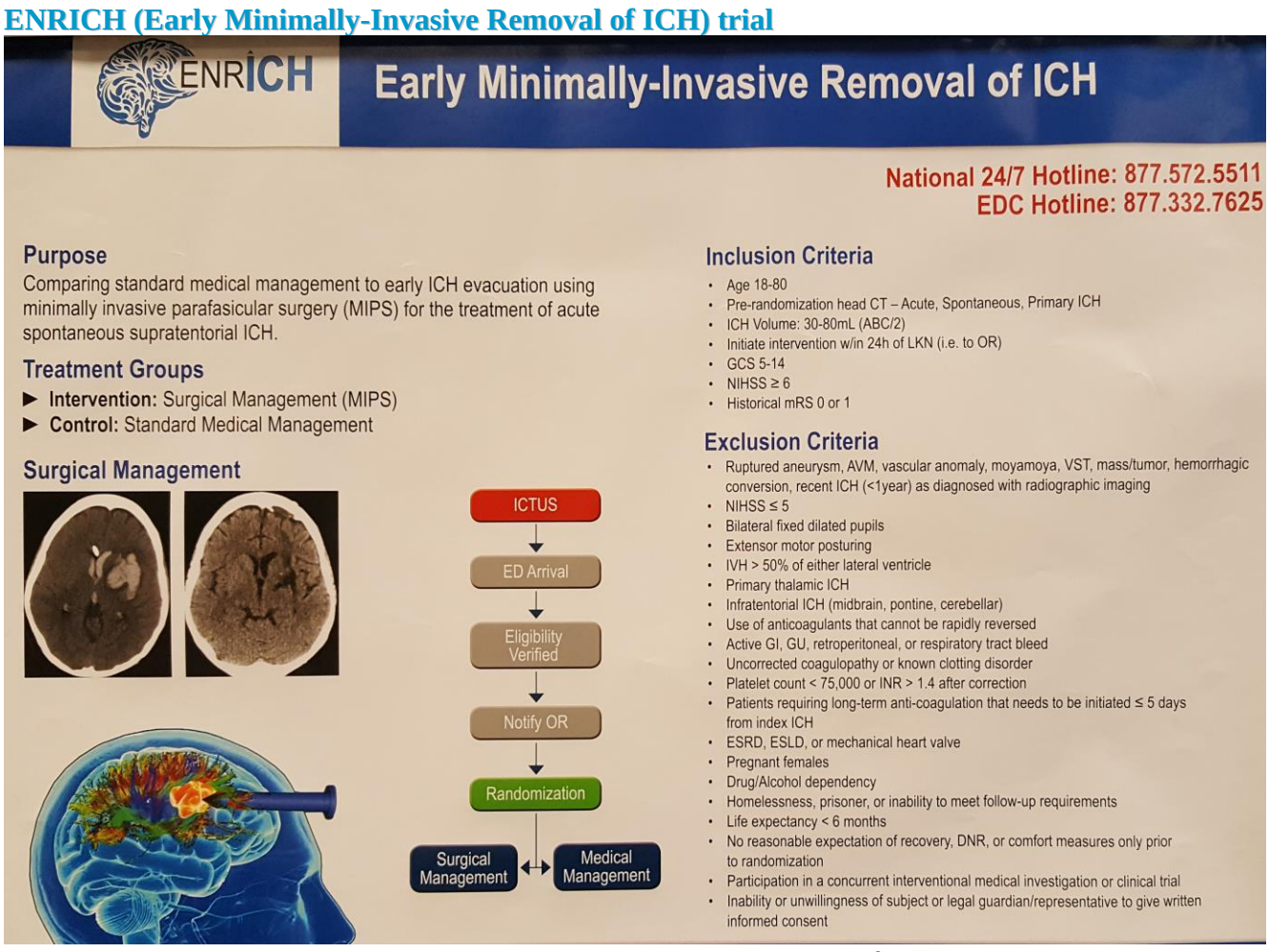
- **ultra-early craniotomy (within 4 hours from ictus)** was associated with an increased risk of rebleeding in a study that involved 24 patients.

Morgenstern LB et al. Rebleeding leads to poor outcome in ultra-early craniotomy for intracerebral hemorrhage. Neurology. 2001; 56:1294–1299.

B. Minimally invasive evacuation

Via transsulcal approach using **BrainPath**.

ENRICH (Early Minimally-Invasive Removal of ICH) trial



- 300 people with acute intracerebral hemorrhage from 37 centers in the United States.
- randomly assigned to receive either minimally invasive surgical removal of the hematoma using Nico Corporation's BrainPath and Myriad Technology (Indianapolis, IN) along with medical management (n=150) or medical management alone (n=150).
- both assigned groups had similar demographic and baseline characteristics.
- 30.7% had **anterior basal ganglia** hemorrhages and 69.3% had **lobar** hemorrhages.
- ***primary efficacy endpoint*** was mean score on utility-weighted modified Rankin scale (mRS) at 180 days:

posterior probability of superiority for surgical intervention + medical management versus medical management alone was .981, with participants showing a utility-weighted mRS mean score of:
.458 in the surgery and medical management group
.374 in the medical management group
mean between-group difference was:
.127 for people with lobar hemorrhage (95% Bayesian credible interval, .035 to .219)
.013 for people with anterior basal ganglia hemorrhage (95% Bayesian credible interval, -.147 to .116)

— ***secondary endpoints***: safety outcomes, including mortality at 30 days after intracerebral hemorrhage.
at 30 days, the percentage of participants who died was:
9.3% for those receiving surgery and medical management
18.0% for those receiving medical management only

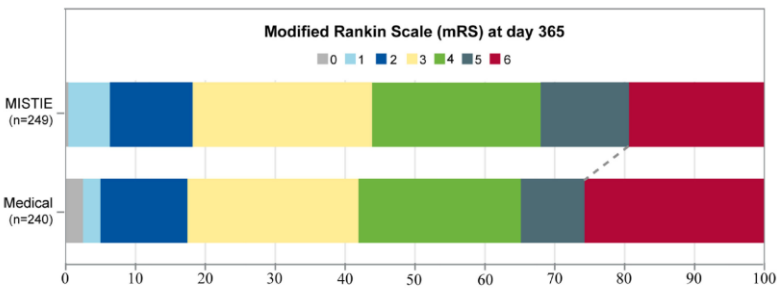
Stereotactic aspiration *via burr hole*; clot mobilization methods:
a) **mechanical** rotors.
b) **fibrinolytic** agent instillation.

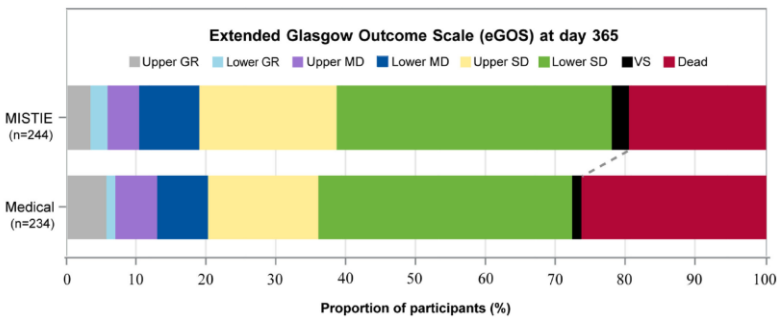
AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2015)
The **effectiveness** of minimally invasive clot evacuation with stereotactic or endoscopic aspiration ± thrombolytic usage is uncertain (Class IIb; Level of Evidence B).

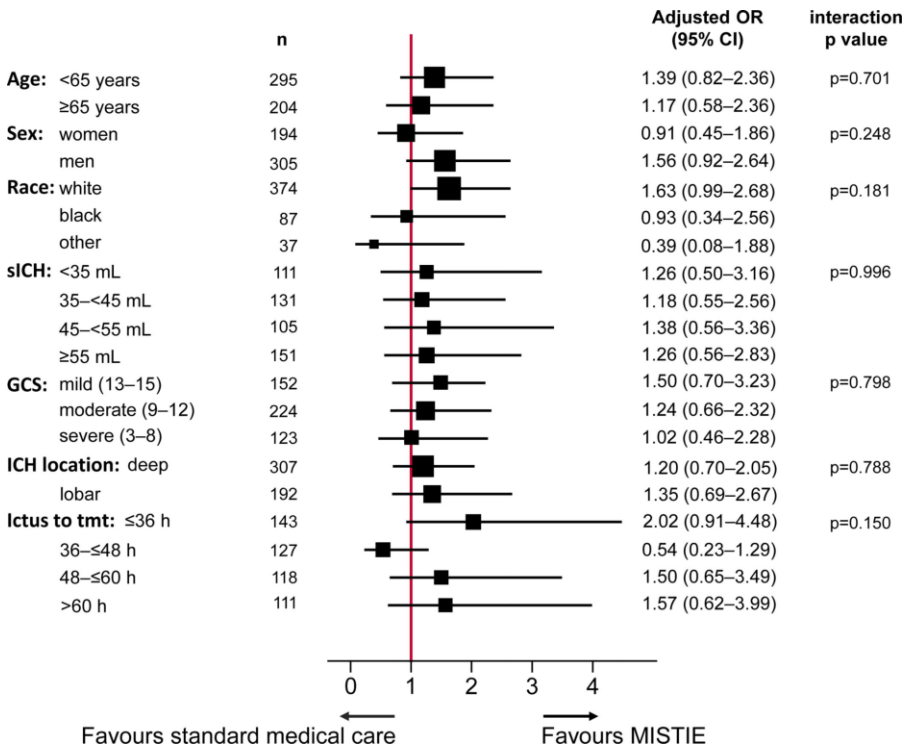
MISTIE (Minimally Invasive Surgery with Thrombolysis for ICH Evacuation) III - **minimally invasive surgery aspiration + 1 mg rt-PA through intraclot catheter q8hrs** (up to 9 doses total) vs. **medical therapy alone**

- 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) – ICH evacuation did not improve probability of achieving a good functional outcome

MISTIE cannot be pragmatically recommended!



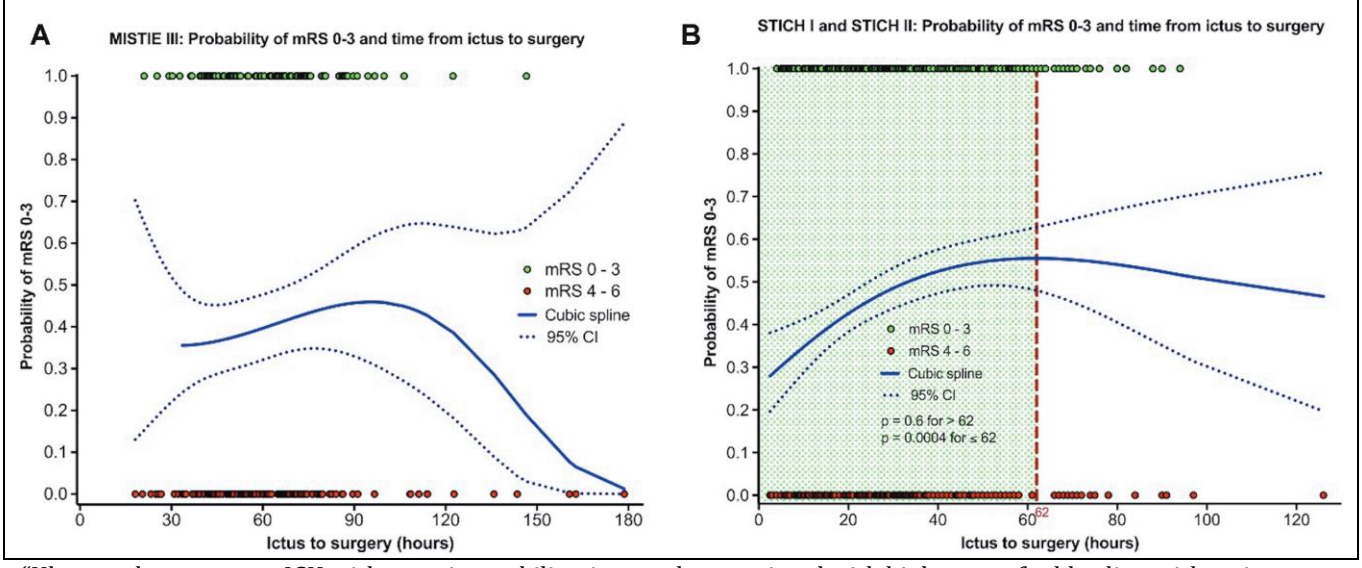




Proponents of MISTIE argue:
– reduction of mortality is good enough
– should not included basal ganglia ICH (very poor prognosis)
– time to complete treatment on average was 5.1 days – way too long!
– only 58% of patients on MISTIE group achieved surgical success (due to catheter malposition)

Both **MISTIE III** and **STICH II** showed that **end-of-treatment (EOT) clot volume** **< 28-30 mL** significantly increased the probability of good outcome (mRS of 0 to 3); further reduction beyond 28.8 mL increased the probability of good functional outcome by 8%/mL:

In regards to **surgery timing** to achieve best outcome:
MISTIE III showed best results if performed within 90-120 hrs after ictus
STICH I-II showed best results if performed at close to 62 hrs after ictus



"Ultra-early surgery on ICH without prior stabilization can be associated with high rates of rebleeding with serious clinical sequelae"

— it is an interesting question whether an **ideal surgical window** exists that is neither too early nor too late for optimal surgical intervention - allowing hemorrhagic stability but operating before brain parenchyma is irreversibly injured

It is reasonable to perform surgical evacuation in clinically stable medically optimized patients without significant co-morbidity and with spontaneous supratentorial ICH between 10 and 100 cc of volume without IVH prior to 62 h (i.e. between 48 and 72 hrs) from symptom onset with a goal EOT < 30 cc to best increase chances of good functional outcome.

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

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

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2015)
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).

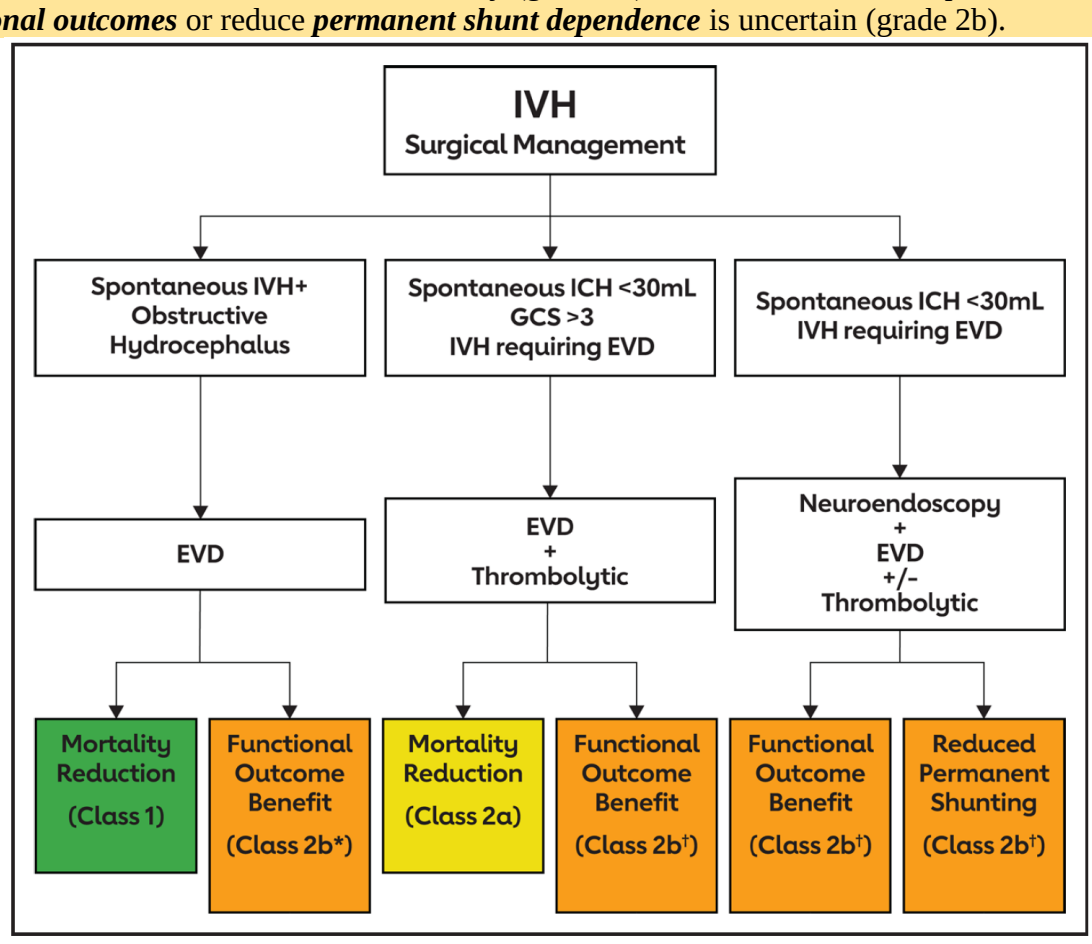
– systematic review of studies in which DC was performed in the setting of spontaneous ICH suggested that DC with hematoma evacuation might be safe and might improve outcome
*Takeuchi S, Wada K, Nagatani K, Otani N, Mori K. Decompressive hemicraniectomy for spontaneous intracerebral hemorrhage. **Neurosurg Focus**. 2013; 34:E5.*

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

INTRAVENTRICULAR HEMORRHAGE

A. **Ventricular drainage (EVD)** for INTRAVENTRICULAR HEMORRHAGE with acute obstructive hydrocephalus (esp. in cerebellar hematomas), trapped ventricle; also useful for clearing bloody CSF.

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2022)
Large IVH + impaired level of consciousness (GCS > 3), EVD is recommended in preference to medical management alone to ***reduce mortality*** (grade 1) but efficacy for improving ***functional outcomes*** is not well established (grade 2b).
– minimally invasive IVH evacuation with EVD plus thrombolytic is safe and is reasonable compared with EVD alone to ***reduce mortality*** (grade 2a) but effectiveness to improve ***functional outcomes*** or reduce ***permanent shunt dependence*** is uncertain (grade 2b).



– **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).

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 ($P = 0.05$).

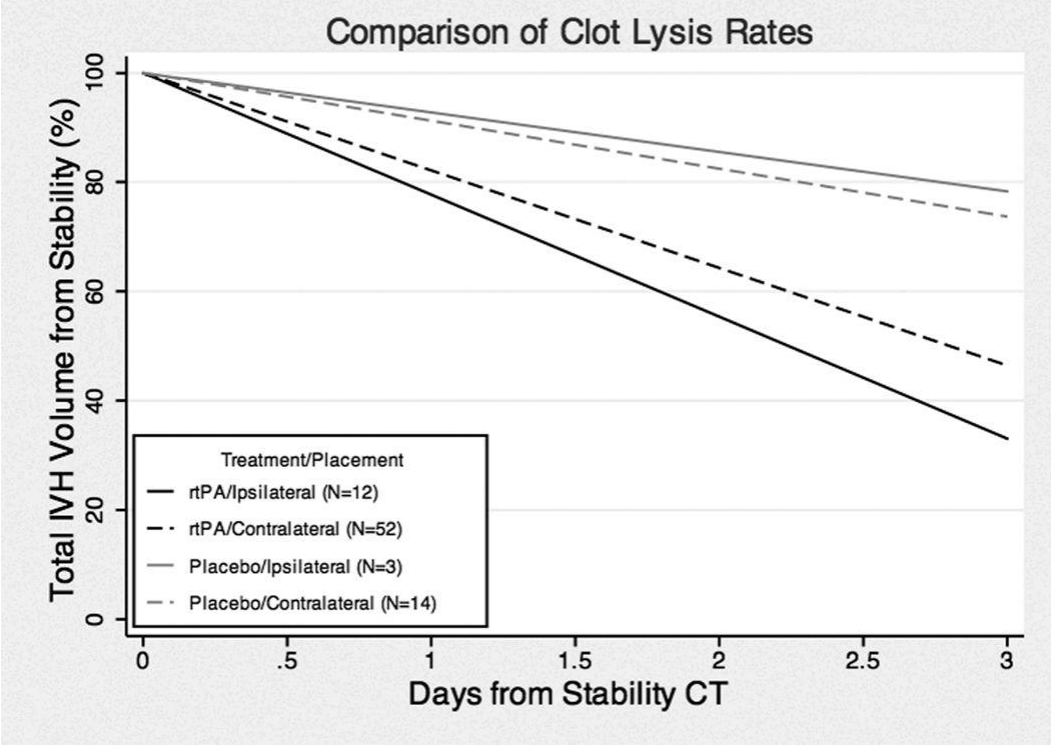
CLEAR IV trial – patients with larger clots - awaiting a funding application.

Side of EVD

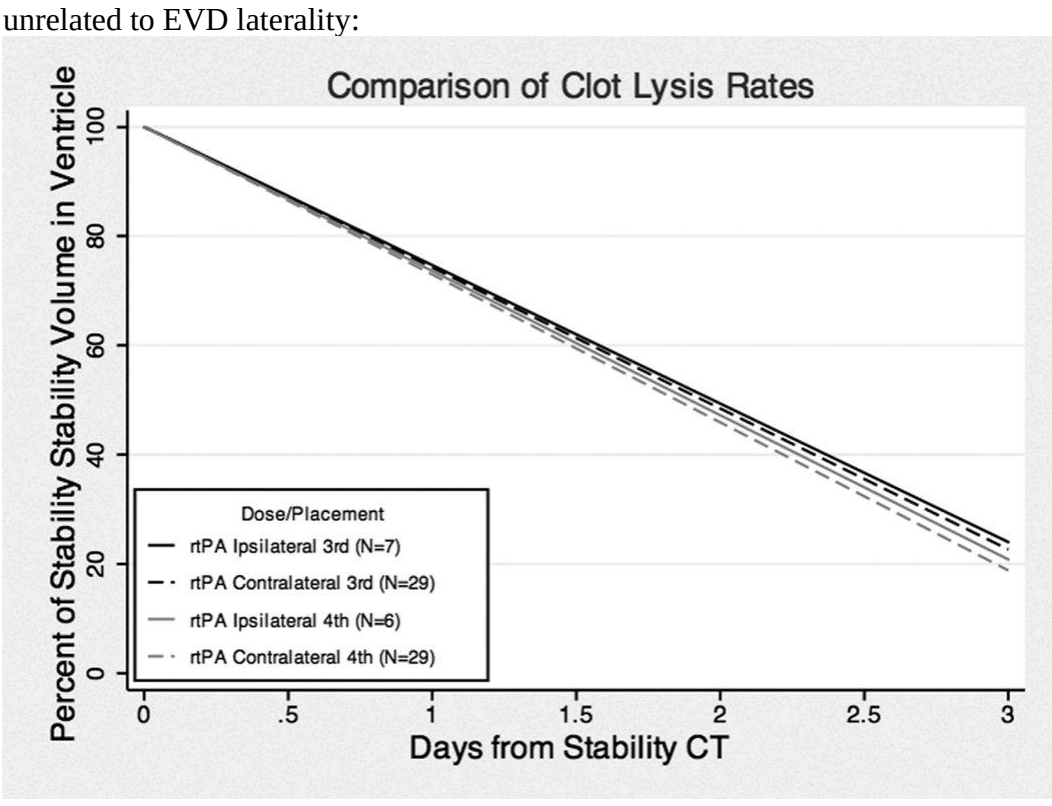
Jennifer Jaffe et al. Ventricular Catheter Location and the Clearance of Intraventricular Hemorrhage. Neurosurgery. 2012 May ; 70(5): 1258–1264.

- EVD location was ***retrospectively assessed*** in 100 patients in two CLEAR Phase II trials.
- side of EVD placement was at the discretion of treating neurosurgeon.
- laterality of catheter was correlated with IVH clearance rates over the first 3 days.
- results:
  - clearance of IVH was significantly greater when thrombolytic was administered as compared to placebo (saline), regardless of catheter laterality ($p < 0.005$, CI −14.0, −4.14 for contralateral EVD and CI −24.7, −5.44 for ipsilateral EVD).
  - EVD ***catheter clogging rate*** was unaffected by EVD laterality.
  - when thrombolytic was administered, there was a trend of more rapid clearance of total IVH through EVD placed on side of dominant intraventricular blood as compared to an EVD on the side with lesser blood (P = 0.09; CI −9.62, 0.69); this was not true when placebo was administered.

    N.B. mean total rt-PA dose administered during the 3-day index period was significantly larger in contralateral EVD as compared to ipsilateral cases (11.8 mg vs 5.21 mg, p = 0.02).



  - ***clearance of 3rd and 4th ventricular blood*** (main cause of obstructive HCP) was unrelated to EVD laterality:



- conclusion and discussion:

  Bilateral EVD: contralateral for ICP control → ipsilateral for tPA

  - if not using tPA, side does not matter.
  - if using tPA, probably better use ipsilateral side (also lower tPA doses may be used) for clot clearance speed; but:

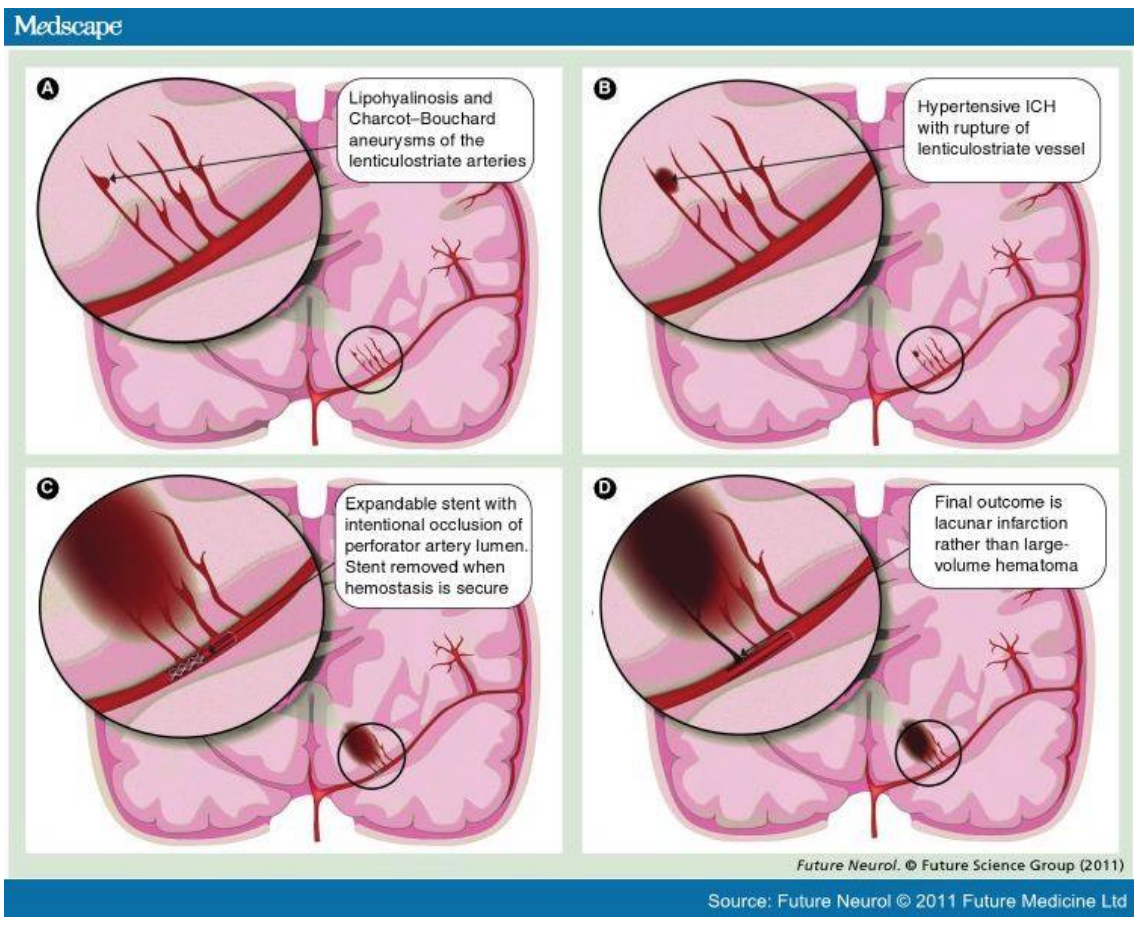
    N.B. currently favored practice [and recommended strategy in CLEAR III] of placing initial EVD contralateral to dominant lateral ventricular IVH would still seem to be justified (esp. from ICP control standpoint).
  - **bilateral EVD** is also justified – may lead to even greater IVH clearance.

B. **Ventriculoperitoneal shunt** for chronic hydrocephalus.

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

OTHER 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%)

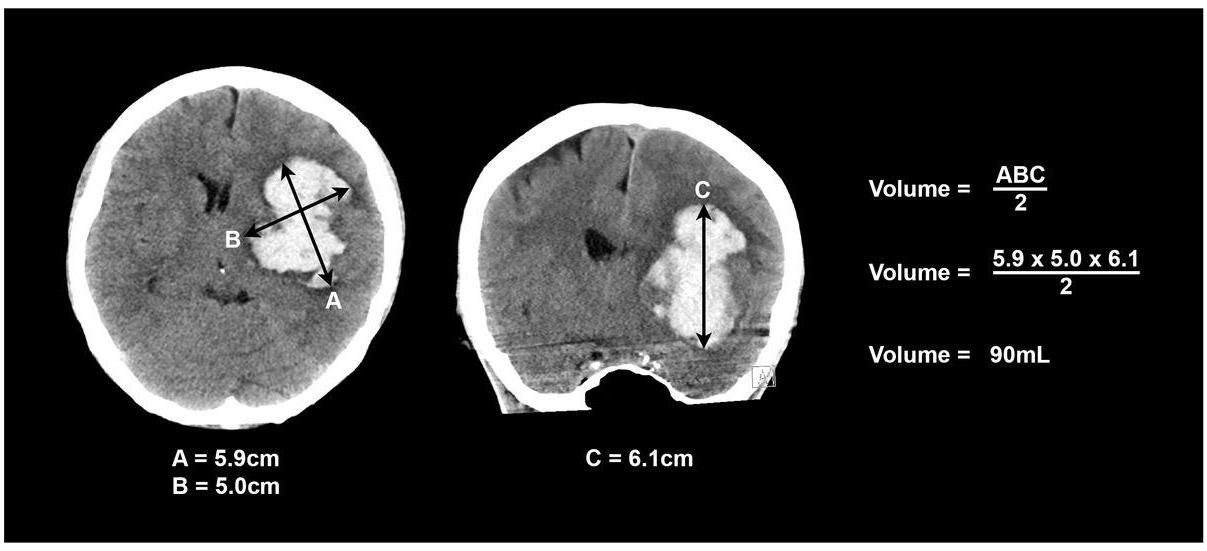
ICH is most deadly form of stroke!
Half of deaths occur *within the first 24 hours*

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2015)
Aggressive care and postponement of new DNAR 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 DNAR orders. DNAR status should not limit appropriate medical and surgical interventions unless otherwise explicitly indicated (Class III; Level of Evidence C).

ICH

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2015)
A baseline severity score should be performed as part of the initial evaluation of patients with ICH (Class I; Level of Evidence B).

- although the optimal severity scale is not yet clear, the most widely used and externally validated is the **ICH Score**.
- **NIHSS score** - commonly used for ischemic stroke, may also be useful in ICH; however, ICH patients often have depressed consciousness on initial presentation, and this may diminish the utility of the NIHSS.



- 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)

PROGNOSTICATION SCALES

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2022)
Baseline severity scales can be useful to provide an overall measure of hemorrhage severity but *should not be used as the sole basis* for forecasting individual prognosis or limiting life-sustaining treatments.

ICH Score

J C Hemphill 3rd et al. The ICH score: a simple, reliable grading scale for intracerebral hemorrhage. Stroke . 2001 Apr;32(4):891-7.

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

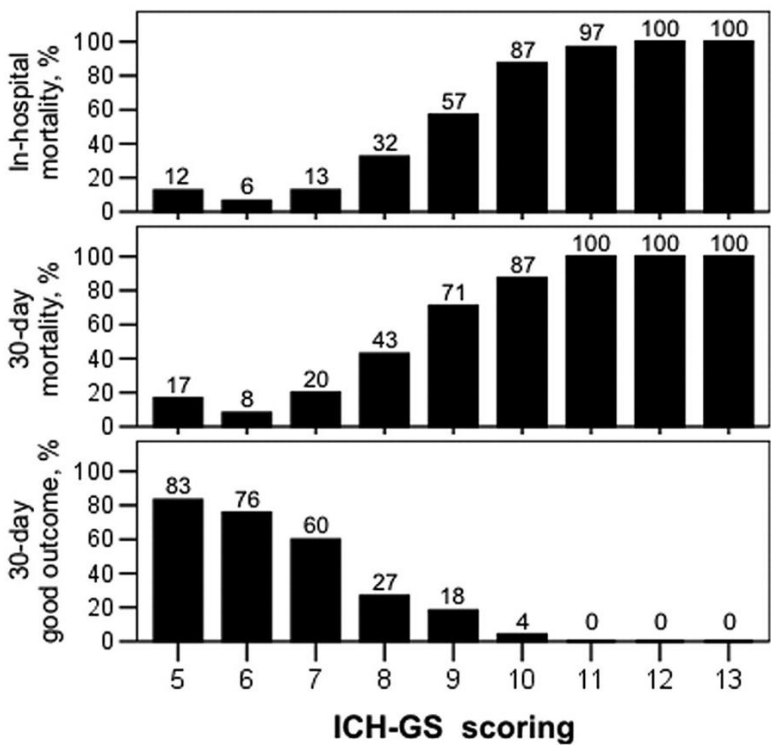
Score	30-day mortality
0	0%
1	13%
2	26%
3	72%
4	97%
5	100%
6	100%

	< 30 mL	0
Intraventricular blood	yes no	1 0
	Total score	

ICH-Grading Scale

José L. Ruiz-Sandoval et al. Grading Scale for Prediction of Outcome in Primary Intracerebral Hemorrhages. Stroke. 2007;38:1641–1644

Characteristic	Points
Age, years	
<45 years	1
45–64 years	2
≥65 years	3
GCS score at hospital admission	
13–15	1
9–12	2
3–8	3
ICH location	
Supratentorial	1
Infratentorial	2
ICH volume	
For supratentorial location	
<40 mL	1
40–70 mL	2
>70 mL	3
For infratentorial location	
<10 mL	1
10–20 mL	2
>20 mL	3
Extension into ventricles	
No	1
Yes	2



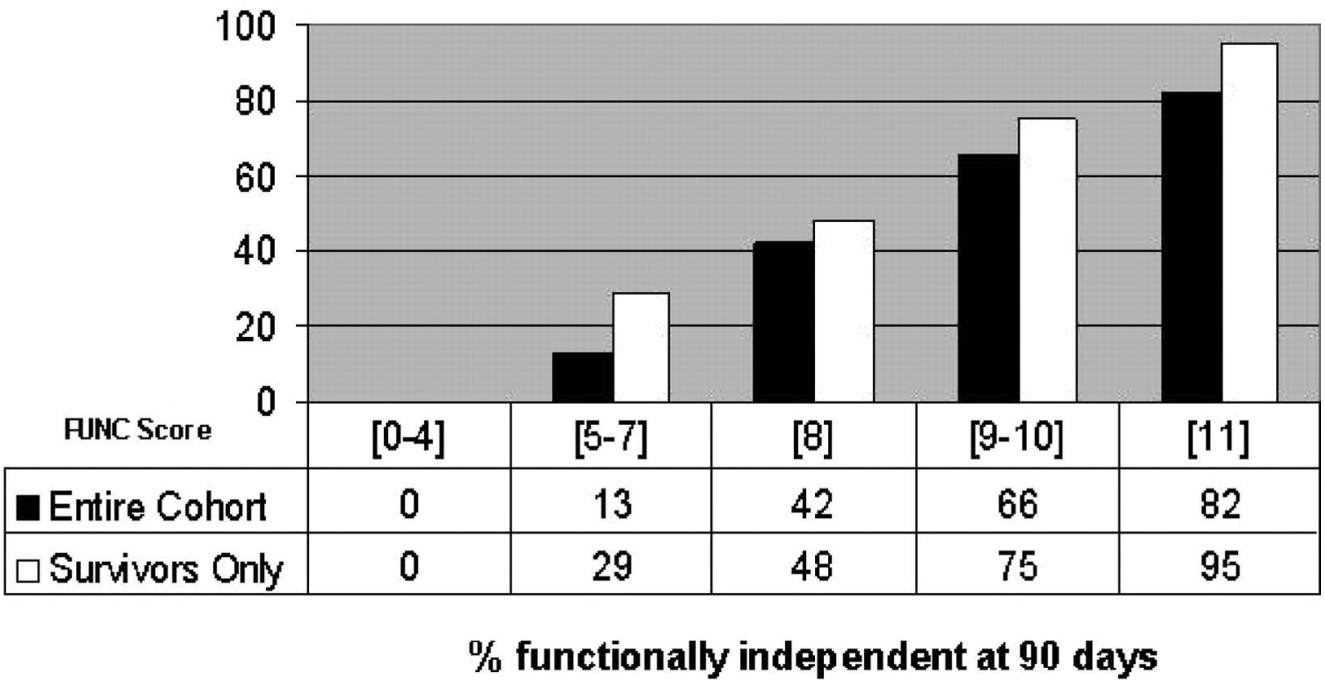
FUNC score

Rost, N. S. et al. Prediction of functional outcome in patients with primary intracerebral hemorrhage: the FUNC score. Stroke (2008), 39(8), 2304–2309

- chances of functional independence (GOS ≥ 4) at 90 days

Component	FUNC Score Points
ICH volume, cm^3	
<30	4
30–60	2
>60	0
Age, years	
<70	2
70–79	1
≥80	0
ICH location	
Lobar	2
Deep	1
Infratentorial	0
GCS score	
≥9	2
≤8	0
Pre-ICH cognitive impairment	
No	1
Yes	0
Total FUNC score	0–11

FUNC score	Chances of functional independence
0-4	0%
5-7	29%
8	48%
9-10	75%
11	95%



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.

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2015)

Given the potentially serious nature and complex pattern of evolving disability and the increasing evidence for efficacy, it is recommended that **all patients** with ICH have access to multidisciplinary rehabilitation (Class I; Level of Evidence A).

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2022)
In patients with spontaneous ICH and **cognitive impairment**, treatment with cholinesterase inhibitors or memantine might be considered to improve cognitive outcomes.

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).

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

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

4) 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

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2022)
AFib: restart anticoagulation in 7-8 weeks or consider left atrial appendage closure.

COR	LOE	Recommendations
2a	C-LD	1. In patients with spontaneous ICH and conditions placing them at high risk of thromboembolic events, for example, a mechanical valve or LVAD, early resumption of anticoagulation to prevent thromboembolic complications is reasonable.[586,587]
2b	B-R	2. In patients with spontaneous ICH with an indication for antiplatelet therapy, resumption of antiplatelet therapy may be reasonable for the prevention of thromboembolic events based on consideration of benefit and risk.[588,589]
2b	B-NR	3. In patients with nonvalvular atrial fibrillation (AF) and spontaneous ICH, the resumption of anticoagulation to prevent thromboembolic events and reduce all-cause mortality may be considered based on weighing benefit and risk.[590–595]
2b	C-LD	4. In patients with AF and spontaneous ICH in whom the decision is made to restart anticoagulation, initiation of anticoagulation ≈7 to 8 weeks after ICH may be considered after weighing specific patient characteristics to optimize the balance of risks and benefits.[596,597]
2b	C-LD	5. In patients with AF and spontaneous ICH deemed ineligible for anticoagulation, left atrial appendage closure may be considered to reduce the risk of thromboembolic events.[598–602]

AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2015)
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).

- 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.
  AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2022)
  In patients with spontaneous ICH, regular long-term use of NSAIDs is potentially harmful because of the increased risk of ICH.

- there are reports that newer anticoagulants may have decreased risk of ICH.
  AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage (2015)
  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
   - 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