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

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- TRAUMATIC ICH (ICH T)

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.
ETIOLOGY

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

Any age - acute disseminated encephalomyelitis (s. acute hemorrhagic leukoencephalopathy, Westin-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 s. arteriolosclerosis = fibroinoid necrosis and S. hyalinization.
   - 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 capsular/putamen - classic for hypertensive hemorrhage:

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!).
   - diagnosed only postmortem by Congo red staining ("congophilic angiopathy").
   - multiple small subcortical haemorrhages.
   - probably amyloid potentiates plasminogen.
   - there is no way to control risk of bleeding from amyloid angiopathy!!!

3. Structural lesions – most common etiology in lobar hemorrhages (vs. only rarely affect basal ganglia, thalamus, pons)
   - 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!).
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   - probably amyloid potentiates plasminogen.
   - there is no way to control risk of bleeding from amyloid angiopathy!!!

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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)

5. Hyperperfusion after carotid stenting / endarterectomy.

6. Venous sinus thrombosis.

7. Spät apoplex - delayed ICH post TBI.

**PATHOLOGY ACCORDING TO PATIENT'S AGE**

**YOUNG PERSONS** – vascular disorders (AVM, aneurysm, vasculitis), drug abuse (amphetamine, 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.
2. Acute BP rises (can cause ICH even in absence of preexisting severe hypertension!), e.g. sympathomimetic 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).
5. Heavy alcohol consumption (acute or chronic).
6. Drug abuse (amphetamine, 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 Mefloxicain (RR 1.27; 95% CI, 1.02–1.59 and RR 1.27; 95% CI, 1.08–1.50, respectively).

**PATHOLOGY, PATHOPHYSIOLOGY**

- hematomas are at first soft and dissect along white matter fiber tracts (rather than destroying brain tissue locally).
- hematomas 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
- bleed 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 hematomas 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.

Source of picture: “WebPath – The Internet Pathology Laboratory for Medical Education” (by Edward C. Klatt, MD)
INTRACRANIAL HEMORRHAGE (ICH)

EPIDEMIOLOGY

- $\approx 10$-$15\%$ of all strokes (up to $30\%$ in blacks and Asians).
- men $\geq$ women.
- peak incidence (for spontaneous ICH) $\approx 60$ 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. Cortical involvement
     2. Age > 65 y
     3. Volume > 10 mL
     4. Early seizures
     ≥ 2 present – epilepsy risk?

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

<table>
<thead>
<tr>
<th>CLINICAL FEATURES</th>
<th>SITE OF HEMORRHAGE</th>
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<tr>
<td></td>
<td>Putaminal</td>
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<tr>
<td>Unconsciousness</td>
<td>Later</td>
</tr>
<tr>
<td>Hemiparesis</td>
<td>Yes</td>
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<tr>
<td>Sensory change</td>
<td>Yes</td>
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<tr>
<td>Hemianopia</td>
<td>Yes</td>
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<td>Pupils (Size / Reaction)</td>
<td>Normal / ±</td>
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<tr>
<td>Gaze paresis</td>
<td>Contralateral (eyes look to ICH)</td>
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<tr>
<td>Response to caloric</td>
<td>Yes</td>
</tr>
<tr>
<td>Ocular bobbing</td>
<td>–</td>
</tr>
<tr>
<td>Gait lost</td>
<td>–</td>
</tr>
<tr>
<td>Vomiting</td>
<td>Occasional</td>
</tr>
</tbody>
</table>

Ocular signs are rapid method of localizing hemorrhages!

DIAGNOSIS

Lumbar puncture can 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), electrocardiogram screen.

EEG

- polymorphic slow waves over region.

IMAGING

CT/MRI EFFECT

- 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 (≥ 180 HU) + mass effect (vs. hemorrhagic infarctions - areas of increased density [blood] interspersed with areas of decreased density [infarction]).

  - acute hematoma: volume ≥ 80 cm³ is usually fatal.
  - no edema around fresh clot (!!!); but clot retraction → fine rim of low density.
  - in severely anemic patients (Hct ≤ 20%), hematoma 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!

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

INTRACEREBRAL HEMORRHAGE (ICH)

Vas20 (5)
INTRACRANEAL HEMORRHAGE (ICH)

- blend sign - blending regions of high and low density with clear boundary within the hematoma - predicts hematoma expansion:
  
  (a) blend sign (+); (b) blend sign (−)

- 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, from periphery towards centre (therefore appears smaller), vasogenic edema develops in surrounding white matter (IV contrast → ring enhancement*).
- 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.

- 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.

- MRI - picture depends on precise sequence used and age of hemorrhage (hemoglobin degradation products 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.

- 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:

MRI:

- picture depends on precise sequence used and age of hemorrhage (hemoglobin degradation products 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.
Clinical presentation

1. CT at 24 hours – uniform hypodensity
2. T1-MRI at 72 hours – mild hypointensity (schematic infarction would have hyperintensity).
3. T2-MRI at 72 hours – hypointense core of hematoma; rim of hyperintensity represents edema.

Hypertensive putaminal hemorrhage:
A. CT at 24 hours – uniform hypodensity
B. T1-MRI at 72 hours – mild hypointensity
C. T2-MRI at 72 hours – hypertensive core of hematoma; rim of hyperintensity represents edema.

VASCULAR IMAGING (angiography / CTA / MRA):

- indications (to exclude treatable causes - AVM, aneurysm, vasculitis, tumor):
  a) low patient ICH (e.g., children) (i.e. amyloid angiopathy is unlikely)
  b) no history of hypertension
  c) hematoma in location apyrtic for hypertensive ICH (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:

- timing of angiography – delay until hematoma has resolved (vascular lesions can be compressed by acute hematoma - not apparent angiographically).
- Ipipal sign - CTA marker of contrast extravasation within hematoma – highly predictive of hematoma expansion and poor outcome – such patients could be selected for hemostatic therapies.
- Leukopenic sign - defined as > 10% increase in Hounsfield units in hematoma in delayed phase of CTA – 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. Raptured aneurysm
4. Tumor
5. Hypertensive

PENETRATING 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 hemiparesis (incl. face) with small hemisensory loss (with small hematoma, there can be pure motor hemiparesis).
2) homonymous hemianopia
3) conjugate horizontal gaze palsy (eyes “look toward hematoma and away from hemiplegic”)
4) global aphasia (dominant hemisphere) / hemineglect (nondominant hemisphere).

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

EXCLUDING HEMORRHAGE:

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

Clinical presentation (resembles putaminal ICH):

1) contralateral hemisensory deficit of all modalities with later* & lesser degree hemiparesis (hemianthesia precedes hemiparesis! – vs. putaminal ICH) + dissection into internal capsule
2) homonymous hemianopia (often clearing quickly)
3) Ocular signs (extension into upper midbrain): unimpaired upward gaze → downward- inward deviation of eyes (depression-convergence syndrome - eyes “look down at nose”), skew deviation (eye opposite hemisphere displaced downward and medially), small unisaccadic and light-nonreactive pupils (papillary 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.
Non-dominant thalamus → neglect, apragnosia or mutism.

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

**Common causes:**
1. *infarcted angioopathy* - most common cause in elderly
2. tumor
3. *subdural malformation, hematologic malignancy* – young person
4. extension of deep hemorrhage
5. hemorrhagic transformation of ischemic infarct
6. 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** occurring 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, discrete cerebellar
3. pinpoint infarct **(1 mm** reactive pupils (check with magnifying glass)
4. grossly disconjugate centrally positioned eyes (gaze paresis) with **absent oculocephalic & neuvestibular reflexes**
5. *5 ocular bobbing.***
6. *axial 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 intracerebral ophthalmoplegia, *one-and-a-half syndrome*, ipsilateral misiss, 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 **oculovestibular reflexes**, pupillary findings (ipsilateral dilatation, miosis, skew deviation, **astasia abatis** - 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) - max cause brain stem compression:
  1. **cranial** findings: caloric resistant ipsilateral gaze palsy → eye deviation toward opposite side; small reactive pupils, skew deviation (Maggiw-Hertwig sign), gaze-paretic nystagmus, ocular bobbing
  2. **cerebellar signs:** (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 hematomas, 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!)

**Cerebral Hemorrhage**
- ≈45% 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)

**INTRACEREBRAL HEMORRHAGE (ICH)**
- 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
- ICH is independent factor associated with poor outcome (risk of death increased from 20% without ICH to 51% with ICH).
- **etiologies** - head trauma, vascular malformation, aneurysm, tumor, hypertension, and clotting disorders.

**INTRACEREBRAL HEMORRHAGE (IVH)**

- **a)** primary (confined to the ventricles)
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**NEUROLOGICAL EXAM:**
- pupils – *2, reactive; 1, asymmetrical*;
- **light reflex:** (ask if patient sees light)
- **pupils:** (ask if patient sees two)
- **extraocular movements**:
  1. *abduction deficit (ipsilateral)*
  2. *adduction deficit (contralateral)*
  3. *conjugate gaze palsy (ipsilateral)*
  4. *ipsilateral internuclear ophthalmoplegia (check with magnifying glass)*
  5. *nystagmus (ipsilateral)*

**speech: (see Table 4, p. 185)**
- **dysarthria** - most common following large ICH
- **dysphasia** (includes Wernicke, Broca, global, conduction, von Economo)
- **aphasia** - * (see Table 4, p. 185)*

**cranial nerve findings**:
- *ophthalmic nerve losses* → *ipsilateral hemianopia, ipsilateral orbital pain.*
- *motor cranial nerve defects* → *ipsilateral abulia, contralateral hemiparesis, conjugate gaze palsy toward side of hemorrhage.*
- *2nd cranial nerve:\* (ipsilateral) → *ipsilateral papilledema.*
- *3rd cranial nerve:\* (ipsilateral) → *ipsilateral oculovestibular reflexes.*
- *4th cranial nerve:\* (ipsilateral) → *ipsilateral oculovestibular reflexes.*
- *5th cranial nerve:\* (ipsilateral) → *ipsilateral oculovestibular reflexes.*
- *6th cranial nerve:\* (ipsilateral) → *ipsilateral oculovestibular reflexes.*
- *7th cranial nerve:* (ipsilateral) → *ipsilateral facial weakness, ipsilateral absence of corneal reflex.*
- *8th cranial nerve:* (ipsilateral) → *ipsilateral oculovestibular reflexes.*

**incontinence:**
- *urinary incontinence:***
- *faecal incontinence:***

**other examination:**
- *head trauma:* (ask if patient saw light)
- *vascular malformation:* (ask if patient sees two)
- *aneurysm:* (ask if patient sees two)
- *tumor:* (ask if patient sees two)
- *hypertension:* (ask if patient sees two)
- *clotting disorders:* (ask if patient sees two)
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% of 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 day of hospitalization is probably recommended (Class IIa, Level of Evidence B). Patients with preexisting DNR 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 intermittent pneumatic compression stockings same day, low-molecular-weight heparin 3-4 days following bleeding cessation
- treatment of fever may be reasonable (Class Ib, Level of Evidence C).
- maintain normoglycemia (< 100 mg/dL), both hyperglycemia and hypoglycemia should be avoided (Class I, Level of Evidence C); target glucose level remains to be clarified.
- rapid blood pressure reduction (MAP < 70) lowers CPP.
- normoglycemia (≤ 110 mg/dL; Class IIa; Level of Evidence C).
- SBP 150 mmHg with 20% increase in mortality and 16% increase in chance of worse functional outcome.

- rapid blood pressure reduction in patients with acute intracerebral hemorrhage (ICH) does not compromise functional outcomes.
- early intensive lowering of BP on presentation (sustained > 180, MAP > 130) increases bleeding and rises ICP.
- for patients presenting with SBP > 220 mm Hg, it may be reasonable to consider aggressive reduction of BP (Class Ib, Level of Evidence C).

- hypertension (systolic > 180, MAP > 130) increases bleeding and rises ICP.
- hypertension (MAP > 70) lowers CPP.

- Propofol or Ketamine with midazolam (maximum 1 mg/kg/h) may be reasonable (Class IIb; Level of Evidence C).

BP CONTROL (wide BP swings are common in initial period)

<table>
<thead>
<tr>
<th>Keep MAP &gt; 90±10 mmHg</th>
<th>Target SBP &lt; 140 mmHg</th>
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<tbody>
<tr>
<td>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 Ib, Level of Evidence B), see INTERACT 2.</td>
<td></td>
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<td>– for patients presenting with SBP &gt; 220 mm Hg, it may be reasonable to consider aggressive reduction of BP (Class Ib, Level of Evidence C).</td>
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<tr>
<td>drugs: IV NACRIDINE/ Labetalol/ Combination Nitropressure/ Esmolol, Administration of perihematoma CABILICS,</td>
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Early intensive lowering of BP does not result in significant reduction of death or major disability, but improves functional outcomes.

(interhemispheric decompression during ICH)

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 mm Hg:

- 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%.
- 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 0.66±0.39 versus standard group 0.55±0.40, P=0.02).

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 or < 180 mmHg within 15 hours of symptom onset; BP targets are to be maintained for 24 hours after randomization using NACRIDINE/ Labetalol may also be used if maximum amounts of nicardipine are used.

PeriOperative 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, MAINTOL, etc. etc. see p. 330 >>

Small hematomas and limited ICH usually do not need ICP treatment! (the higher the Glasgow Coma Scale, the lower the risk for differential pressures/gradient 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, transient herniation, significant ICH 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 ICH

2. no 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 for further deterioration from secondary damage (including hemiation) for up to a week - monitor for ICP! (esp. with cerebellar hematomas)

• "steroids 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 and thrombosis

[RECOMMENDANT Factor VIIa (rFVIIa) (NovoSeven®. N.B.): 40-120 μg/kg g/h 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 → factor (II, VII, IX, X) prothrombin complex concentrate (PCC) (Kcentra) is first line treatment; then vit. K (PHENOXADONE 20-40 mg IV), FFP.

• patients on heparin IV → PROTHAMS - does depend 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: 0.50-0.75 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 → PROTHAMS but reversal is incomplete.

• hemophilia → Factor VIII (to achieve level of 80-100% of normal).

• thrombocytopenia → PLATELET TRANSFUSION.
A. 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 cortices!

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

For most supratentorial ICH, 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 may 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).

### TRIALS

**International Surgical Trial in Intracerebral Hemorrhage (STICH)**

- cf. STICH trial – traumatic ICH – see p. ThH >>


**STICH I** – early (within 24 hrs of randomization) surgery (cortioriomy or CT-guided aspiration) vs. best medical management; class I evidence (1033 patients, 83 centers in 27 countries).
- **craniorrhexis 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!

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Early surgery group</th>
<th>Best medical management group</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Favourable outcome</td>
<td>26%</td>
<td>24%</td>
<td>None</td>
</tr>
<tr>
<td>Unfavourable outcome</td>
<td>74%</td>
<td>76%</td>
<td>None</td>
</tr>
<tr>
<td>Mortality</td>
<td>36%</td>
<td>37%</td>
<td>None</td>
</tr>
</tbody>
</table>


**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 hematoma (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 hematomas 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 or large hematomas who are *still awake* (GCS ≥ 9).

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

**ENRIC (Early Minimally-Invasive Removal of ICH)**

see below >>

### SURGICAL MEASURES

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 hematoma.

- **hemostasis:** bipolar coagulation, cotton balls with peroxide, SurgiFoam / FloSeal; may finish by Surgicel on hematoma walls.

B. Evacuation via **transcranial approach** using BrainPath.

**ENRIC (Early Minimally-Invasive Removal of ICH)** trial
C. Stereotactic aspiration via burr hole; clot mobilization methods:
   a) mechanical rotors.
   b) fibrinolytic agent instillation.

MISTIE (Minimally Invasive Surgery Plus rt-PA for ICH Evacuation) III - minimally invasive surgery aspiration + 1 mg rt-PA through intracavit catheter qhrs (up to 9 doses total) vs. medical therapy alone
   • subject: 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.

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

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 Ib; Level of Evidence C).

E. Ventricular drainage for INTRACRANIAL HEMORRHAGE with acute obstructive hydrocephalus (esp. in cerebellar hematomas, intraventricular hemorrhage), trapped ventricle:
   - endoscopic neurosurgical techniques for IVH evacuation may be advantageous compared with EVD
   - EVD and 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 30-60 minutes and monitor for increased ICP
     - monitor daily with CT.
     - clot resolve on average within 3-4 days.
     - clotted intraventricular catheter: alteplase 0.5 mg IT once, reasess complications (IPA, 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 Ib; Level of Evidence B).

CLEAR (Clot Lysis Evaluating Accelerated Resolution of intraventricular hemorrhage) III trial - intraventricular (IPA) 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).

**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.
Intracerebral Hemorrhage (ICH)

Hypertensive lipohyalinosis results in a Charcot–Bouchard aneurysm. Hypertensive ICH results from vessel rupture. (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:

**Message**

‘Sterotactic 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 vessels and ‘activates’ intravascularly 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%).
- ICH is most deadly form of stroke!
- Half of deaths occur within the first 24 hours.
- **Future approaches**

### ICH

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

<table>
<thead>
<tr>
<th>Feature</th>
<th>Finding</th>
<th>Points</th>
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<tbody>
<tr>
<td>GCS</td>
<td>3-4</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>5-12</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>13-15</td>
<td>0</td>
</tr>
<tr>
<td>Age</td>
<td>≥ 80</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>&lt; 80</td>
<td>0</td>
</tr>
<tr>
<td>Location</td>
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<td>1</td>
</tr>
<tr>
<td></td>
<td>supratentorial</td>
<td>0</td>
</tr>
<tr>
<td>ICH volume</td>
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<td>1</td>
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<tr>
<td></td>
<td>&lt; 30 mL</td>
<td>0</td>
</tr>
<tr>
<td>Intraventricular blood</td>
<td>yes</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>no</td>
<td>0</td>
</tr>
</tbody>
</table>

**Total score**

<table>
<thead>
<tr>
<th>Score</th>
<th>30-day mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>1</td>
<td>1%</td>
</tr>
<tr>
<td>2</td>
<td>2%</td>
</tr>
<tr>
<td>3</td>
<td>3%</td>
</tr>
<tr>
<td>4</td>
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<td>5</td>
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<td>6</td>
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<td>7</td>
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<tr>
<td>8</td>
<td>52%</td>
</tr>
<tr>
<td>9</td>
<td>78%</td>
</tr>
<tr>
<td>10</td>
<td>100%</td>
</tr>
</tbody>
</table>

- poor prognostic factors:
  1) **age**
  2) large hemorrhage size (supratentorial > 5 cm, posterior fossa > 3 cm)
  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 5.4 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 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 monitored in all ICH patients (Class E, 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 mm Hg is reasonable (Class Ib, 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) **antiplatelet 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;34:3768-3774]

- antithrombotic 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 antplatelet 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 mechanical heart valves, might decrease the risk of ICH 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.**

CT signs of moderate/severe CAA (vs. absent/mild CAA) in patients with lobar ICH:  

- SAF (89% vs. 42%; P=0.013)  
- intracerebral hemorrhage with finger-like projections (39% vs 0%; P=0.043)  
- presence of APOE ε4 (genotyping from peripheral blood samples) (50% vs 8%; P=0.002)  
- SAH and either presence of APOE ε4 or finger-like projections are 96% sensitive (95% CL 78-100) to risk in CAA-associated lobar ICH.

**IVH**

- no treatment: half die; 20% return home to live independently.

- IVH - 90% of patients live independently at home after 180 days, intracerebral 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 an Italian study but no increased risk in one Canadian study.