Intracerebral Hemorrhage (ICH)

Etiology

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- Caudate Hemorrhage
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- LVAD (left ventricular assist device)
- Traumatic ICH

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, 20% thalamus & subcortical white matter

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ETIOLOGY

Multiple microbleeds
- Elderly - chronic hypertension or amyloid angiopathy
- Children - cavernous or hematologic abnormalities

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1. Arterial hypertension - most common cause of ICH (called hypertensive ICH).
ICH accounts for ≈ 15% deaths in chronic hypertension
• chronic hypertension causes hyaline arteriolosclerosis (lipohyalinosis) 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.

2. Cerebral amyloid angiopathy (s. congophilic angiopathy)
• appears in Alzheimer’s disease (rare in patients < 55, except in Down syndrome).
• 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 nonhypertensive lobar hemorrhages.
• 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)
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).


5. Hyperperfusion after carotid stenting / endarterectomy.

6. Venous sinus thrombosis.
**ICHTHREbral HEMORRHAGE (ICH)**

**Vas20 (3)**

**ITIOLOGY 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).

**PRECIPIITATING 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. sympatheticoimetic 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. TrH >>
5. **Heavy alcohol consumption** (acute or chronic).
6. **Drug abuse** (amphetamine, cocaine)

**RISK FACTORS**

1. **Age > 70** (increases ICH risk 7x)
2. **Male sex**
3. **Non-Caucasian race**
4. **Previous CVA** (23x)
5. **NSAID use** – only COX-1 > COX-2 (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).
- 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 → distortion 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.

**PATHOLOGY, PATHOPHYSIOLOGY**

- Hemorrhage tissue effect with ending shift:

**Source of picture:** WebPath - The Brain Tumor Laboratory for Medical Education (by Edward C. Klatt, MD) >>

- **Hypertensive basal ganglia hemorrhage**:

**Source of picture:** WebPath - The Brain Tumor Laboratory for Medical Education (by Edward C. Klatt, MD) >>
INTRACRANIAL HEMORRHAGE (ICH)

Hypertensive basal ganglia hemorrhage, hemorrhage has ruptured into ipsilateral ventricle.

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 30-90 minutes (66%) - because hemorrhages arise from tiny vessels; further clinical evolution is due to brain swelling.

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%)
- nausea & vomiting (40-50%)
2) 
- normotensive or 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 (6-10%*)
*more common with lobar hemorrhage (~25% patients) - cortical irritation by blood.
4. Meningeal irritation – if bleeding extends to subarachnoid space.

<table>
<thead>
<tr>
<th>CLINICAL</th>
<th>SITE OF HEMORRHAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patunal</td>
<td>Thalamic</td>
</tr>
<tr>
<td>Unconsciousness</td>
<td>Late</td>
</tr>
<tr>
<td>Hemiparesis</td>
<td>Yes</td>
</tr>
<tr>
<td>Sensory change</td>
<td>Yes</td>
</tr>
<tr>
<td>Hemianopia</td>
<td>Yes</td>
</tr>
<tr>
<td>Pupils (Size / Reaction)</td>
<td>Normal /</td>
</tr>
<tr>
<td>Gaze paresis</td>
<td>Contralateral (eyes look to ICH)</td>
</tr>
<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 hematomas!

**DIAGNOSIS**

**Lumbar puncture is contraindicated!** – may cause herniation; CSF does not provide definitive diagnostic information
- CSF is usually bloody several hours after hemorrhage, but sometimes it is normal initially.

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

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

**EEG**
- polymorphic slow waves over region.

**IMAGING**

**NON-CONTRAST 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 (~ 100 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%), hematomas can be isointense to surrounding brain.
- multifocal hemorrhages at poles (frontal, temporal, or occipital) suggest Traumatic etiology.
- TUMORS can acquire similar density in contrast CT!

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

- layering in clot (as if fluid-blood layer) or mixed iso-hypodense picture:
  a) hyperacute / ongoing bleeding
  b) coagulopathic patient
- 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*),
- 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 (ICH): hematoma (high-density signal in thalami [left arrows] with extension into 3rd ventricle [top arrow] and occipital horns of lateral ventricle [bottom arrow] and contralateral [right arrow] lateral ventricles;
INTRACEREBRAL HEMORRHAGE (ICH)

**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.

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 hypodensity
B. T1-MRI at 72 hours - mild hyperintensity (ischemic infarction would have hypointensity).
C. T2-MRI at 72 hours - hypointense core of hematoma - rim of hyperintensity represents edema.
Clinical presentation

Infection

Hemorrhages at gray

Weston

Uncommon

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).

Spot sign - CTA marker of contrast extravasation within hematoma - highly predictive of hematoma expansion and poor outcome – such patients could be selected for hemostatic therapies.

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 – rare
4. Tumor – very rare

PUTAMINAL HEMORRHAGE

- most common form of ICH (putamen is most common site of hypertensive ICH) ≈ 0.15-0.20%

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

1) rapidly progressing contralateral hemiplegia (incl. face) with severe hemisensory deficit and homonymous hemianopsia (extension into upper midbrain): skew deviation (eye opposite hemorrhage displaced downward and medially), convergence-retraction nystagmus, pseudo-Frenzel sign.
2) homonymous hemianopsia (extension into upper brainstem compression → lethargic / comatose within minutes to hours) with deep, irregular respirations.
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 hours to days).

TALAMIC 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) pupillary changes (impairment upward gaze → downward-inward deviation of eyes (depression-convergence syndrome – eyes “lock down at nose”), skew deviation (eye opposite hemorrhage displaced downward and medially), small anisocoria and light-nonreactive pupils (pupillary light-near dissociation).
4) small anisocoria and light-nonreactive pupils (pupillary light-near dissociation).
5) slow (extension into upper brainstem compression → lethargic / comatose within minutes to hours) with deep, irregular respirations.

LOBAR HEMORRHAGE

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

Common causes:

1) amyloid angiopathy - most common cause in elderly
2) junior
3) vascular 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, Westph-Hunt disease).

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

Clinical presentation (resembles thromboembolic infarction!):
**Pontine Hemorrhage**

- 10-15% of all ICHs
- usually placed symmetrically at junction of basis and tegmentum (paramedian vessels from basilar artery).
- hematomata 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, decrease rigidity
3. pinpoint (1 mm) reactiv pupils (check with magnifying glass)
4. groggy disorientation, centrally positioned eyes (gaze paresis) with absent oculocephalic & oculovestibular reflexes
5. aocral bobbing
6. aatic Hachne-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 interuncular ophthalmoiopia, “one-and-a-half” syndrome, ipsilateral miosis, ocular bobbing, ipsilateral hemihematusia with crossed hemiisensory deficits.

**Cerebellar Hemorrhage**

- 90% 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 ptd staxia (ataxia-abaosa), vertigo, dysarthria, nystagmus.

"gait (truncal) ataxia may be only neurololgic 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 brainstem compression.

1. **ocular findings**: colorless-resistant isplatal gaze palsy → eye deviation toward opposite side; small reactive pupils, skew deviation (Magenode-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 brainstem compression, cerebellar herniation → death (H: prompt clot evacuation!)

**Caudate Hemorrhage**

- 4-5% 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), hypophalumus (Homer’s syndrome)

**Intraventricular Hemorrhage**

- isolated or as ICH extension.
- **cerebellum**, head trauma, vascular malformation, aneurysm, tumor, hypertension, and clotting disorders.

- **clinical features**: meningsimius, headache, vomiting, mental status changes with few motor or ocular findings, "bormorhory" (periodic tonic spasms of limbs & atonic pauses),

- **complications**: obstructive hydrocephalus, delayed communicating hydrocephalus, thrombocytopenia and inflammation in reaction to ventricular blood.

**TREATMENT**

Current guidelines for ICH recommend initial CONSERVATIVE MEASURES!

ICH is the least treatable form of stroke!

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

hematomata expansion occurs in 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**

Avoid activites after ICH – increase risk of ICH recurrence!

**General care**

- bedrest during first 24 hours; clinically stable patients → progressive increase in activity (avoid strenuous exertion).
- N.B. all ICH patients with limited mobility need early enteral feeding.

**Brain stem**

- maintain normoglycemia (< 300 mg/dL).

Glucose should be monitored. Both hyperglycemia and hypoglycemia should be avoided (Class I, Level of Evidence C).

**drypahgia screening** for all ICH patients before they start oral intake – to reduce risk of pneumonia (Class I, Level of Evidence B) - most common medical sequelae seen in this patient population; if failed → early enteral feeding.

**BP control**

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

Keep MAP 70-110 mmHg

Target SP < 140 mmHg

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Death occurs within few ho
For ICH patients presenting with SBP between 150 and 220 mm Hg and without contraindication to acute BP treatment, acute lowering of SBP to 140 mm Hg is safe (Class I, Level of Evidence A) and can be effective for improving functional outcome (Class IIa, Level of Evidence B). (Revised from the previous guideline)

- **hypertension** (systolic > 180, MAP > 130) increases bleeding and rises ICP. H: IV Labetalol or Sodium Nitroprusside or Termediphan Camysylate.

- **hypotension** (MAP < 70) lowers CPP.

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


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


**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.

**INTERACT 2** - intensive blood pressure reduction is safe, but does not significantly reduce death or major disability.

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

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicardipine</td>
<td>1.25-5 mg IV over 60 minutes</td>
<td>Can be restarted within 2 hours after randomization using NICARDIPINE. Labetalol may also be used if maximum amounts of nicardipine are used.</td>
</tr>
<tr>
<td>Hydralazine</td>
<td>5 mg IV</td>
<td>Rapid blood pressure reduction (in conditions where a maximum amount of immediate effect is preferred).</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>25-50 mg IV</td>
<td>Reduces stress-induced tachycardia commonly associated with rapid blood pressure reduction.</td>
</tr>
<tr>
<td>Amlodipine</td>
<td>2.5 mg IV</td>
<td>Lowers CPP.</td>
</tr>
<tr>
<td>Amodiaquine</td>
<td>100 mg IV</td>
<td>For use in ICH with hemoglobin levels of 65–80 g/L and cardiac output of 5-30 mL/s.</td>
</tr>
</tbody>
</table>

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

### ICP CONTROL

- elevating head of bed, analgesia, sedation, hyperventilation, Mannitol, etc. see p. 550.

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

* steroids - no evidence of benefit or harm!

**Fondaparinux** (sodium-1-phosphate receptor modulator approved for MS) may improve outcomes of ICH.


One randomized 0.5 mg kg for 4 consecutive days for patients with surgical intracerebral hemorrhage and isomolar volume of 5-30 mL - safe and effective in reducing perihematoma edema and neurologic deficits, with enhanced recovery.

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### REVERSAL OF BLEEDING DIASTHESES

- patient on warfarin → factor (II, VII, IX, X) prothrombin complex concentrate PCC (KOMPASS) is first line treatment, then H: INR 1.2-1.5 mg/100 U IV.

- patients on heparin INR → PROTHAMINE - dose depends upon duration of time since heparin administration (do not exceed 50 mg IV over 10 min).

- 30-60 min: 0.5-0.75 mg/100 U of heparin

- 2 h: 0.25-0.375 mg/100 U of heparin

- if heparin was administered by deep SC injection, 1-1.5 mg/100 U of heparin.

- patients on LMWH → PROTHAMINE but reversal is incomplete.

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

- thrombocytopenia → PLATELET TRANSFUSION.

- thrombolysis-associated bleeding → CRYOPRECIPITATE 10 units IV, replacement of clotting factors*, AMINOCAPROIC ACID (5 g over 30-60 minutes → 1 g 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 3-30 days if risk for thromboembolism is very high)

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### AED

Short-term gephyrolyc anticonvulsants for lobar hemorrhages extending to cortex (e.g. PHENYTOIN, LEVITIRACETAM).

- some studies suggest anticonvulsants may be linked to fever and poor outcomes; therefore, continuous EEG monitoring may provide rational way to direct therapy.

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### NEUROPROTECTIVE STRATEGIES

Candidates:
SURGICAL TREATMENT

A. Open surgical evacuation via craniotomy (ultrasound can confirm clot localization) – esp. for lobar clots within 1 cm of interhemispheric fissure.

- surgery between 24-48 h is the best time - vessel has stopped leaking (either spontaneously, or after hematostatic therapy); if earlier - increased risk of rebleeding.
- aspirate, irrigate; clot lysis methods:
  a) lytic agent instillation (e.g. urokinase into clot cavity within 72 h reduces clot burden and risk for death; but rebleeding → functional outcome is not improved).
  b) mechanical rotors.

INDICATIONS

1. Cerebellar hemorrhages compressing vital structures in midline (suggested by declining level of consciousness, posturing, altered respiration, shifted or obliterated 4th ventricle, hydrocephalus) - surgical removal of hematoma as soon as possible (Class I; Level of Evidence B).
   - most cerebellar hematomas > 3 cm require surgical evacuation within hours.
   - surgery not indicated - GCS score ≥ 14 (some investigators say ≥ 9) with small hematoma (< 5-3 cm) without hydrocephalus.
   - contiguity (poor surgery results) - large midline hematoma with lost all brain stem functions and flaccid coma.

2. Supratentorial hematomas with signs of herniation, declining sensorium (esp. if clot is on nondominant side and ≤ 1 cm from cortical surface) – surgical evacuation and/or decompressive craniectomy might be considered life-saving (Class IIb; Level of Evidence C).

Routine evacuation of supratentorial ICH by standard craniotomy within 96 hours of symptom onset with GCS 9-12 is better off with early surgery! – STICH II trial

STICH II trial - craniotomy is as safe as medical treatment and small trend (2%/4%) mRS benefit favored surgery.

STICH II trial - no clear benefit from early surgery! MISTIE (Minimally Invasive Surgery Plus rt-PA for ICH Evacuation) III trial - minimally invasive surgery aspiraion plus 1 mg rt-PA through intracranial catheter q4h (up to 9 doses total) vs. medical therapy alone; inclusion: spontaneous, non-traumatic supratentorial ICH ≥ 80 ml with or without intraventricular hemorrhage (IVH) not requiring EVD, with GCS ≥ 14 or NIHSS ≥ 6, in 18-80 year-patients 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. surgery is not beneficial for hemorrhages in putamen, thalamus, andpons.

In general, surgical evacuation is seldom justified:
- does not substantially improve mortality or considerably increases risk of severe residual neurologic disability if patient survives.
- best candidates are patients with increasing moderate + large hematomas who are still awake (GCS ≥ 9).
- N.B. patients with massive hematoma who are in coma are not likely to benefit!

OTHER SURGICAL MEASURES

1. Hemicraniectomy - option for younger patients with rapidly declining conscious state and imminent herniation.

2. Ventricular drainage for acute obstructive hydrocephalus (esp. in cerebellar hematomas, intraventricular hemorrhage); endoscopic neurosurgical techniques for IVH evacuation may be advantageous compared with EVD.

N.B. INTRAVENTRICULAR HEMORRHAGE must be treated with EVD and can be treated with low-dose intraventricular fibrinolytics (clot-buster based clot lysis) to dissolve clot quicker (e.g. 1.0 mg rt-PA q 8-12 h) - dramatically reduced morbidity & mortality!!!

- EVD must go into clot
- clump ventriculostomy 30-60 minutes and monitor for increased ICP
- monitor daily with CT.
- does not improve good functional outcome (mRS 0-3: 48% in alteplase group, 45% in saline group), but does give 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 of IVH blood loss ≤ 20 ml to start).

CLEAR (Clot Lysis Evaluating Accelerated Resolution of Intraventricular hemorrhage) III trial – intraventricular tPA in patients with small ICH 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 does give 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 of IVH blood loss ≤ 20 ml to start).

- complications (IPA, frequent EVD access).

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

N.B. surgery is not beneficial for hemorrhages in putamen, thalamus, andpons.

In general, surgical evacuation is seldom justified:
- does not substantially improve mortality or considerably increases risk of severe residual neurologic disability if patient survives.
- best candidates are patients with increasing moderate + large hematomas who are still awake (GCS ≥ 9).
- N.B. patients with massive hematoma who are in coma are not likely to benefit!
3. Aneurysm repair, removal of bleeding AVM or tumor, i.e. bleeding structural / vascular lesion is also indication for surgery.
4. Ventriculoperitontial shunt for chronic hydrocephalus – predictors of development of shunt-dependent hydrocephalus after ICH: thalamic ICH, persistently elevated ICP.

FUTURE APPROACHES

Hypertensive lipohyalinosis results in a Charcot–Bouchard aneurysm. 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.

\[ \text{Feature} \]
\[ \text{Finding} \]
\[ \text{Points} \]
\[ \text{Score} \]
\[ \text{30-day mortality} \]
\[ \text{GCS} \]
\[ 3-4 \]
\[ 5-12 \]
\[ 13-15 \]
\[ 2 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ Age \]
\[ \geq \ 80 \]
\[ < 80 \]
\[ 1 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ Location \]
\[ infratentorial \]
\[ supratentorial \]
\[ 1 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ ICH volume \]
\[ < 30 \ mL \]
\[ \geq 30 \ mL \]
\[ 1 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ Intraventricular bleeding \]
\[ yes \]
\[ no \]
\[ 1 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]

\[ \text{Total score} \]
\[ 30 \]
\[ 20 \]
\[ 10 \]
\[ 5 \]
\[ 0 \]

- **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.
- 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 (<.30%) when initial hematoma volumes are >20-30 mL.
- 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)
  5. risk of recurrent hemorrhage is relatively low; exception - AVMs (can rebleed 2% annually), LVAD (risk of rebleed 1% up to 5-fold).

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 mm Hg systolic and 72 mm Hg diastolic) - Class I, Level of Evidence A

**IVH**

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

**SPECIAL SITUATIONS**

**LVAD (LEFT VENTRICULAR ASSIST DEVICE)**

\[ \text{Feature} \]
\[ \text{Finding} \]
\[ \text{Points} \]
\[ \text{Score} \]
\[ \text{30-day mortality} \]
\[ \text{Location} \]
\[ infratentorial \]
\[ supratentorial \]
\[ 1 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ ICH volume \]
\[ < 30 \ mL \]
\[ \geq 30 \ mL \]
\[ 1 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ Intraventricular bleeding \]
\[ yes \]
\[ no \]
\[ 1 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]

\[ \text{Total score} \]
\[ 30 \]
\[ 20 \]
\[ 10 \]
\[ 5 \]
\[ 0 \]

**PROGNOSIS**

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

\[ \text{Feature} \]
\[ \text{Finding} \]
\[ \text{Points} \]
\[ \text{Score} \]
\[ \text{30-day mortality} \]
\[ \text{GCS} \]
\[ 3-4 \]
\[ 5-12 \]
\[ 13-15 \]
\[ 2 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ Age \]
\[ \geq 80 \]
\[ < 80 \]
\[ 1 \]
\[ 0 \]
\[ 0 \]
\[ 0 \]
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\[ 0 \]
\[ Location \]
\[ infratentorial \]
\[ supratentorial \]
\[ 1 \]
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\[ 0 \]
\[ 0 \]
\[ ICH volume \]
\[ < 30 \ mL \]
\[ \geq 30 \ mL \]
\[ 1 \]
\[ 0 \]
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\[ 0 \]
\[ 0 \]
\[ 0 \]
\[ Intraventricular bleeding \]
\[ yes \]
\[ no \]
\[ 1 \]
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\[ 0 \]
\[ 0 \]

\[ \text{Total score} \]
\[ 30 \]
\[ 20 \]
\[ 10 \]
\[ 5 \]
\[ 0 \]
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 Assoc 2015 “Guidelines for the Management of Spontaneous Intracerebral Hemorrhage”