

Intracerebral Hemorrhage

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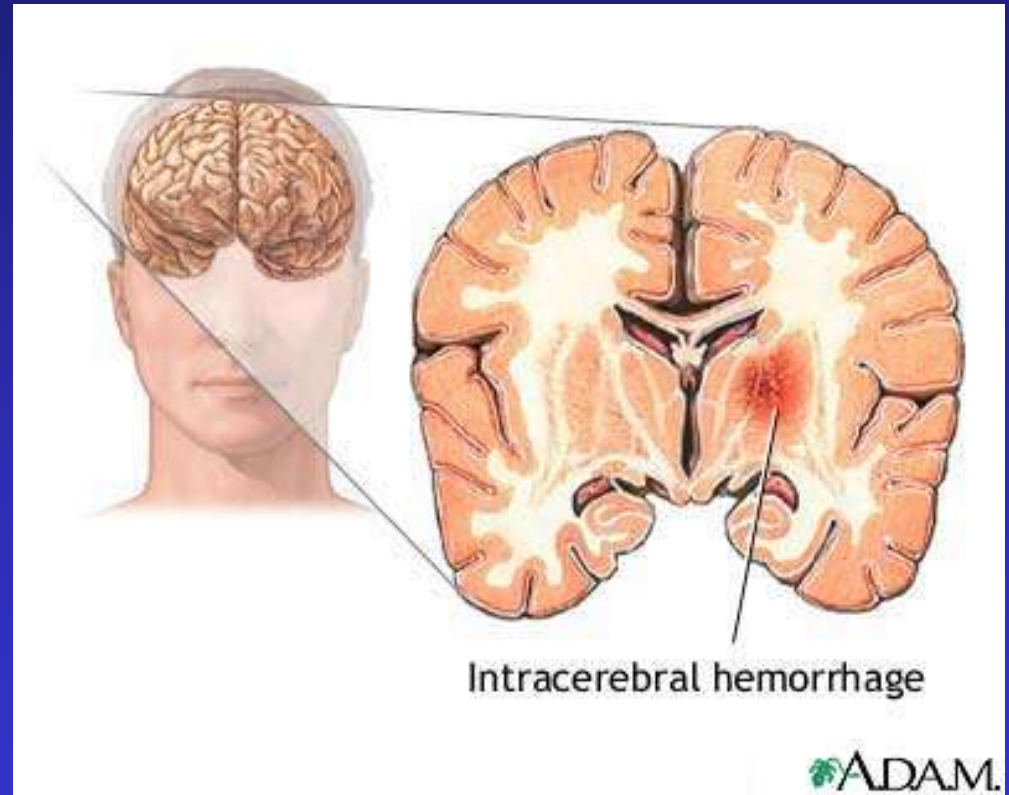
Disclosure: I have received consulting fees and served on an advisory board for CSL Behring.

ICH - Order of lectures

- Joshua N. Goldstein, MD:
 - Initial evaluation, diagnosis, stabilization in the ED.
- Steven Messe, MD:
 - Initial management, early hospitalization, surgical therapy, ICP management.
- Eric E. Smith, MD:
 - Determining underlying cause, secondary prevention, discharge preparation and care.

Outline

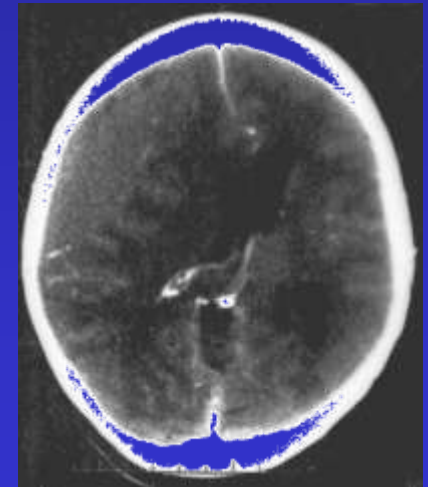
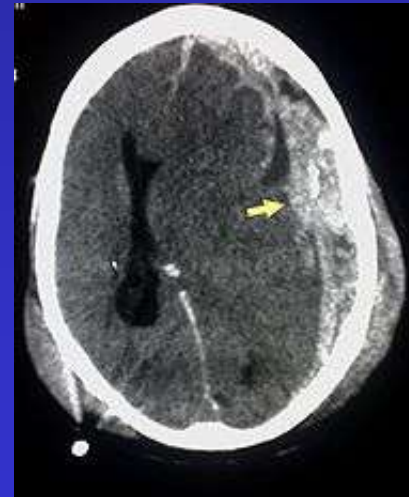
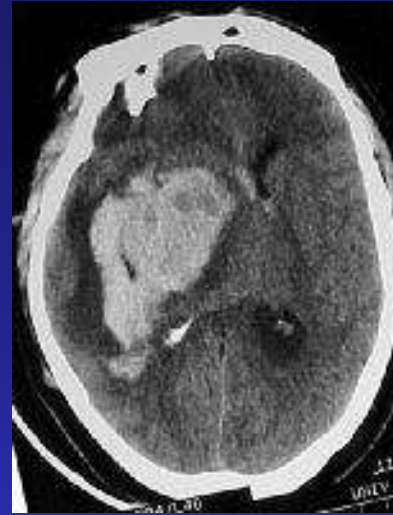
- I. ICH- epidemiology, outcomes
- II. Acute diagnosis
- III. Initial stabilization
- IV. EMS transport



Recommendations in this talk are based on those from the American Heart Association: Morgenstern LB, Hemphill JC, 3rd, Anderson C, Becker K, Broderick JP, Connolly ES, Jr., Greenberg SM, Huang JN, Macdonald RL, Messe SR, Mitchell PH, Selim M, Tamargo RJ. Guidelines for the Management of Spontaneous Intracerebral Hemorrhage. A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2010 July 22

Intracerebral Hemorrhage

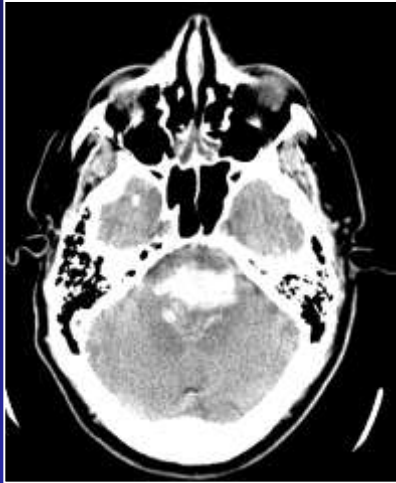
- Primary intraparenchymal hemorrhage (intracerebral hemorrhage, or ICH)
- Subarachnoid hemorrhage
- Subdural hematoma
- Epidural hematoma
- This talk will focus on primary ICH



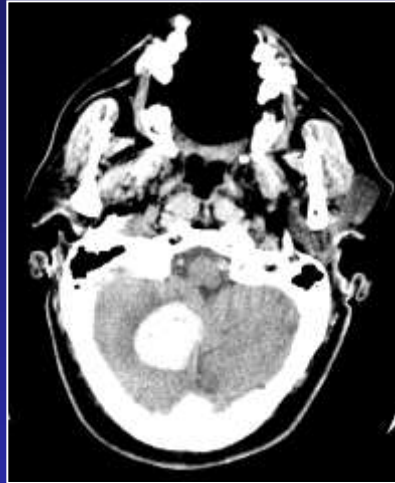
Primary Intracerebral Hemorrhage

- Constitutes 10-15% of strokes.
- Affects approximately 65,000 patients per year.
- Mortality rate is 35 to 52%.
- Only 20% of survivors are functionally independent at 6 months
- ICH is expensive:
 - Average hospitalization cost of non-survivors is \$16,466
 - Average hospitalization cost of survivors is \$28,360
 - Average post-discharge cost is \$16,035 during the first year.
- Of survivors, 41% require inpatient rehabilitation, and 8% require repeat hospitalizations.

Intracerebral Hemorrhage (ICH)



Brainstem



Cerebellum



Thalamus



Basal Ganglia



Lobar

Initial diagnosis

- Initial presenting symptoms can include
 - Abrupt onset of headache
 - Vomiting
 - Seizure
 - Altered mental status
 - Any focal or generalized neurological symptoms.
- Symptoms should be considered the same as those for acute stroke
- The public should be educated to call 911 for symptoms.

Prehospital management

- The role of EMS is highly emphasized by AHA.
- Patients transported by EMS have shorter time to presentation, and more rapid time to physician evaluation and neuroimaging.

EMS evaluation

- ABCs
- Cardiac monitoring
- IV access
- O2 as needed
- Fingertick glucose
- NPO
- Alert the receiving ED
- **Rapid transport to a stroke center!**

Initial care

- Before diagnosis, this is the same as early stroke care, as this patient has a “suspected stroke”.
- Airway management
 - Balance the risk of losing the patient’s airway vs. loss of the neurologic exam.
- Diagnosis – usually head CT

ICH - diagnosis

- Noncontrast CT scan – effectively 100% sensitive for ICH.
- CTA – CT angiography to examine the cerebrovasculature
- MRI – is equally sensitive, but can also pick up very small prior bleeds (“microbleeds”)
- MRA – another means of examining the arteries.



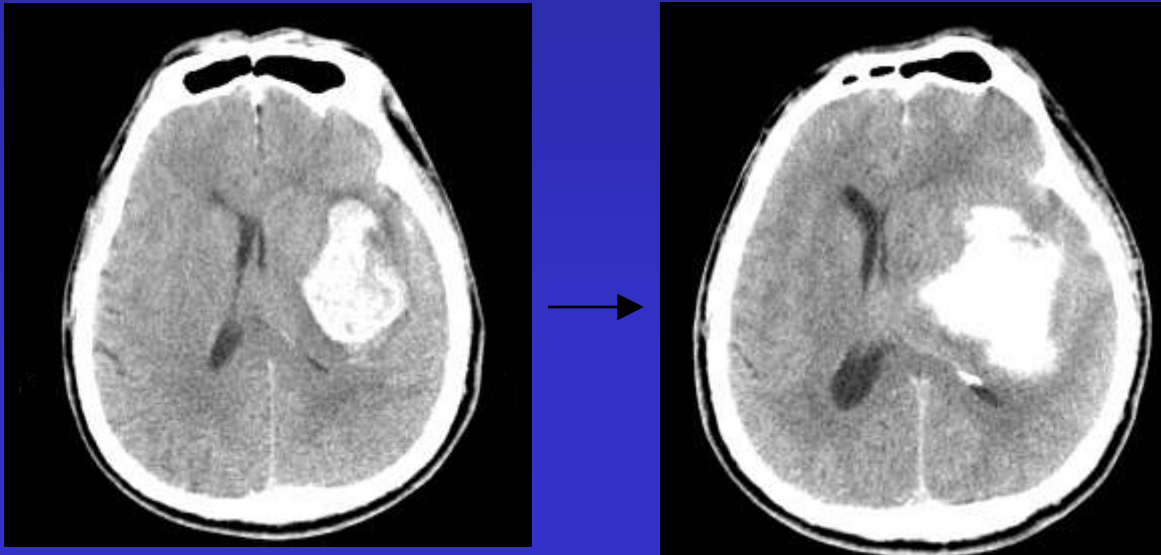
ICH – Initial management

- A number of factors are associated with poor outcome – older age, history of diabetes, worse GCS score – that we cannot change.
- What factors are associated with poor outcome that we CAN fix?
 - Hematoma expansion
 - Hyperglycemia
 - Large hematoma volume

ICH – Hematoma Expansion

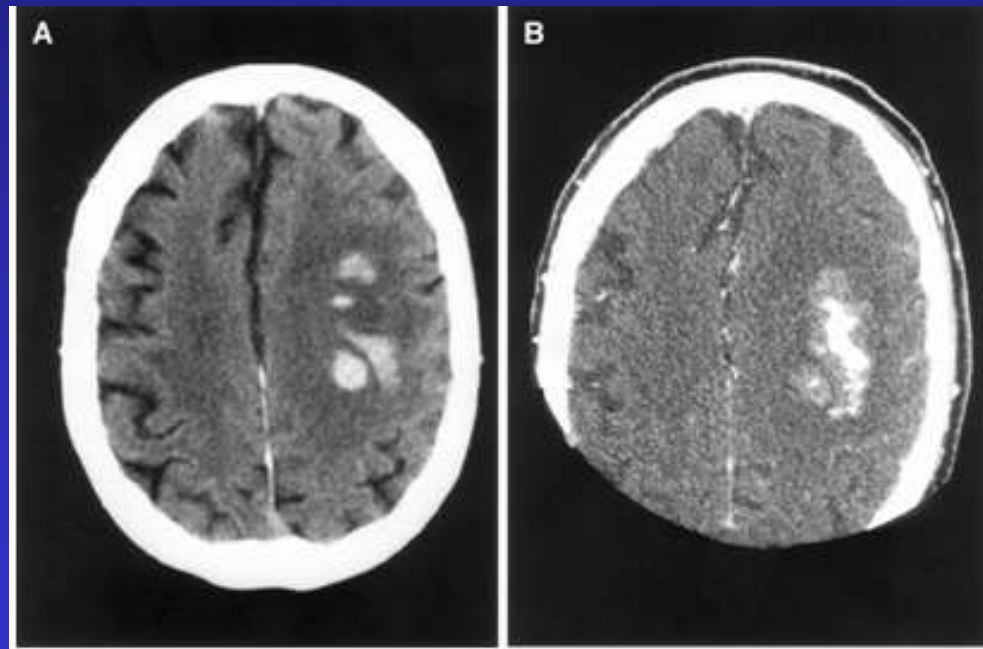
Expansion Occurs Early!

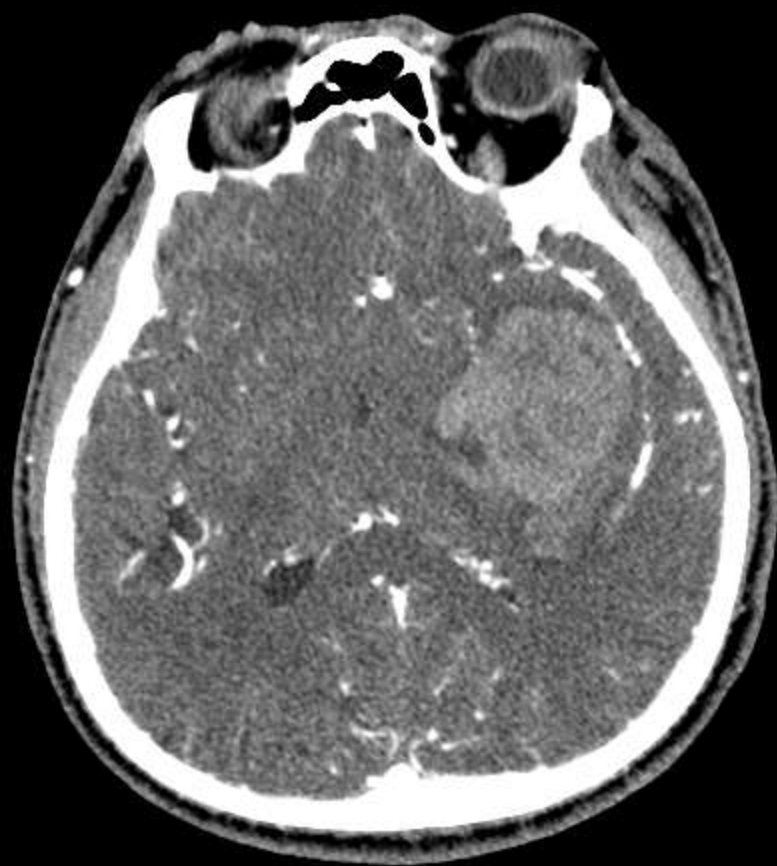
- Of patients presenting within 3 hours,
 - 38% have **significant** hematoma growth (>33% increase in volume)
 - – 26% within 1 hour
 - – 12% between 1 and 24 hours
 - Associated with clinical deterioration
- Therefore, therapies that target hematoma expansion may improve outcome, and much of this benefit would occur in the acute phase.

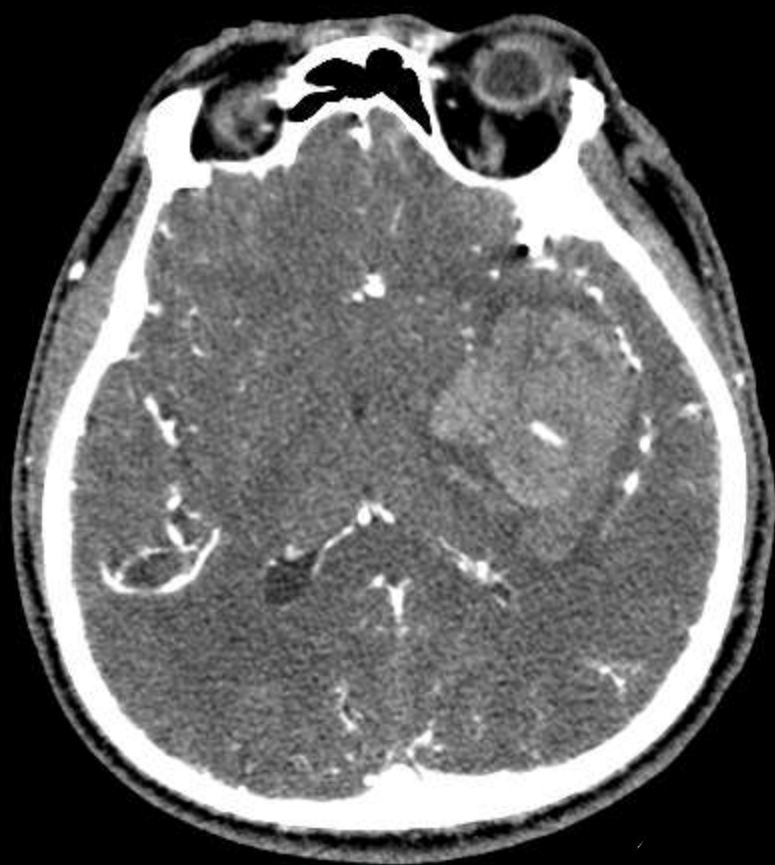


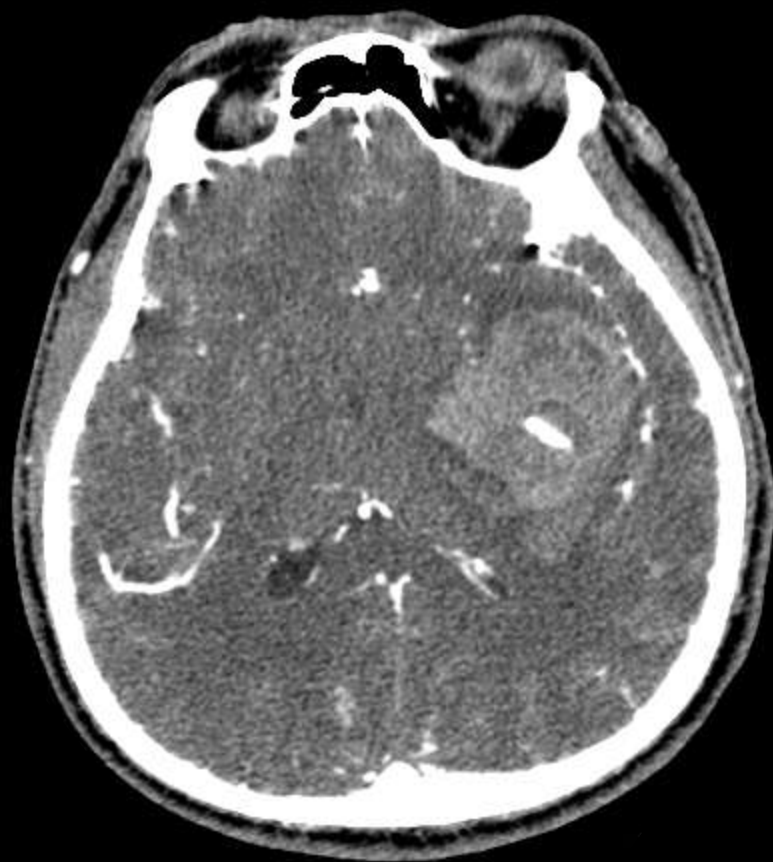
Which people will expand?

- Patients with intracerebral hemorrhage (ICH) often undergo radiological studies using contrast.
- In some patients, contrast leaks into the hematoma.



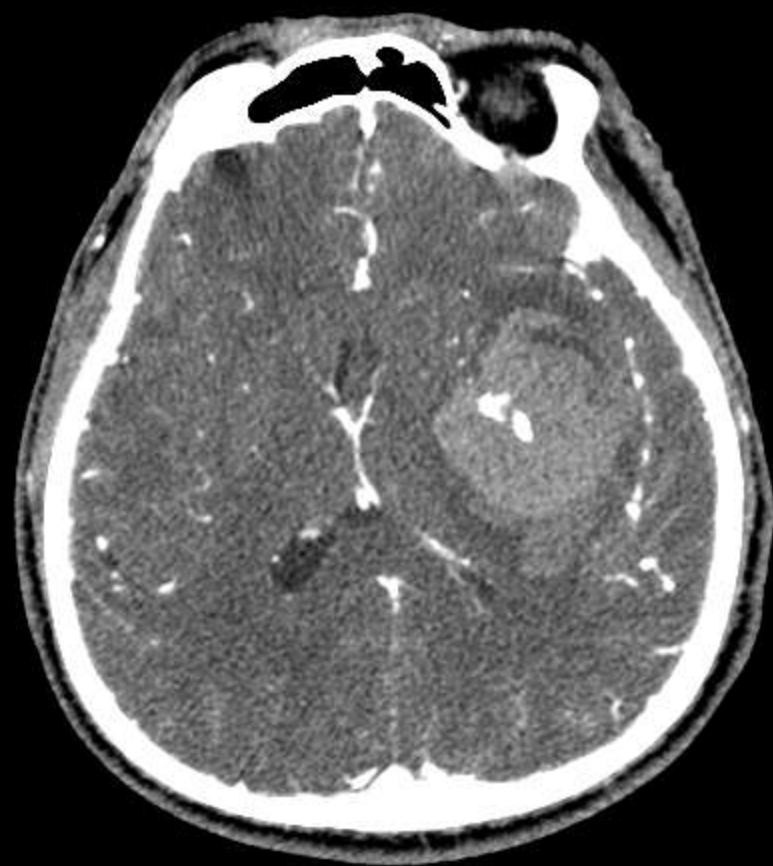


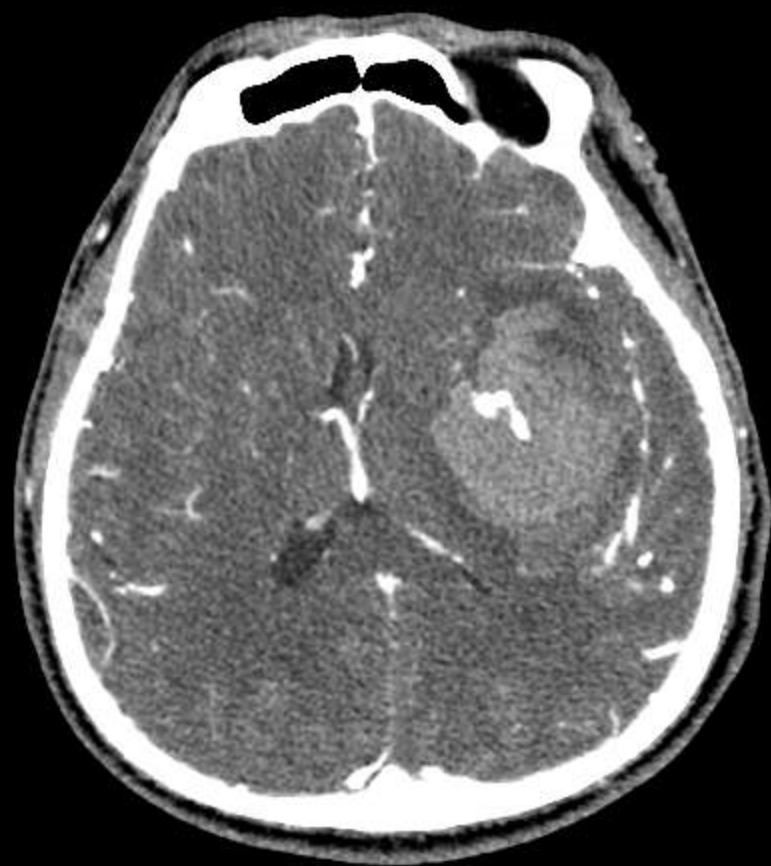


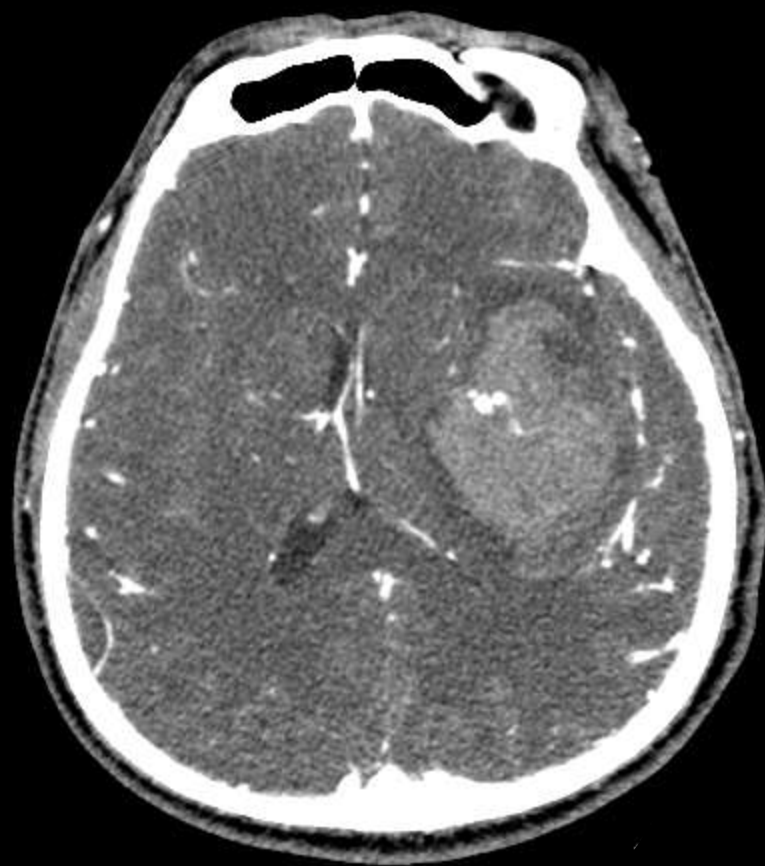


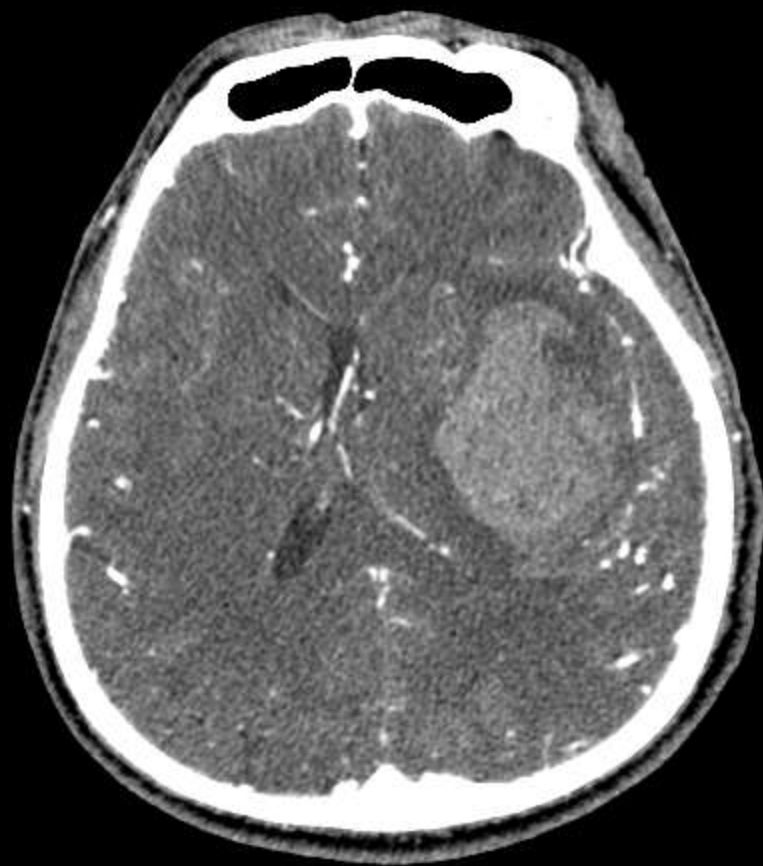
















Contrast Within the Hematoma on CTA Predicts Subsequent Expansion

Goldstein et al:

Sensitivity: 93%

Specificity: 50%

Wada et al:

Sensitivity: 91%

Specificity: 89%

Preventing Hematoma Expansion

- Blood pressure control (to be covered in the next lecture)
- Hemostatic therapy
- Warfarin reversal

Factor VIIa

- Showed some efficacy in hemostasis in animal models.
- It was therefore tested in humans to determine if it can reduce bleeding in intracerebral hemorrhage.

Activated Factor VII (NovoSeven)

- Phase II and III trials showed that when given within 4 hours of symptom onset, Factor VII decreases the risk of hematoma expansion:
 - Placebo: 28% expansion
 - Treatment group: 11% expansion ($p < 0.001$)
- However, there was no effect on outcome!
- An increased risk of thromboembolic adverse events may have obviated any benefit.

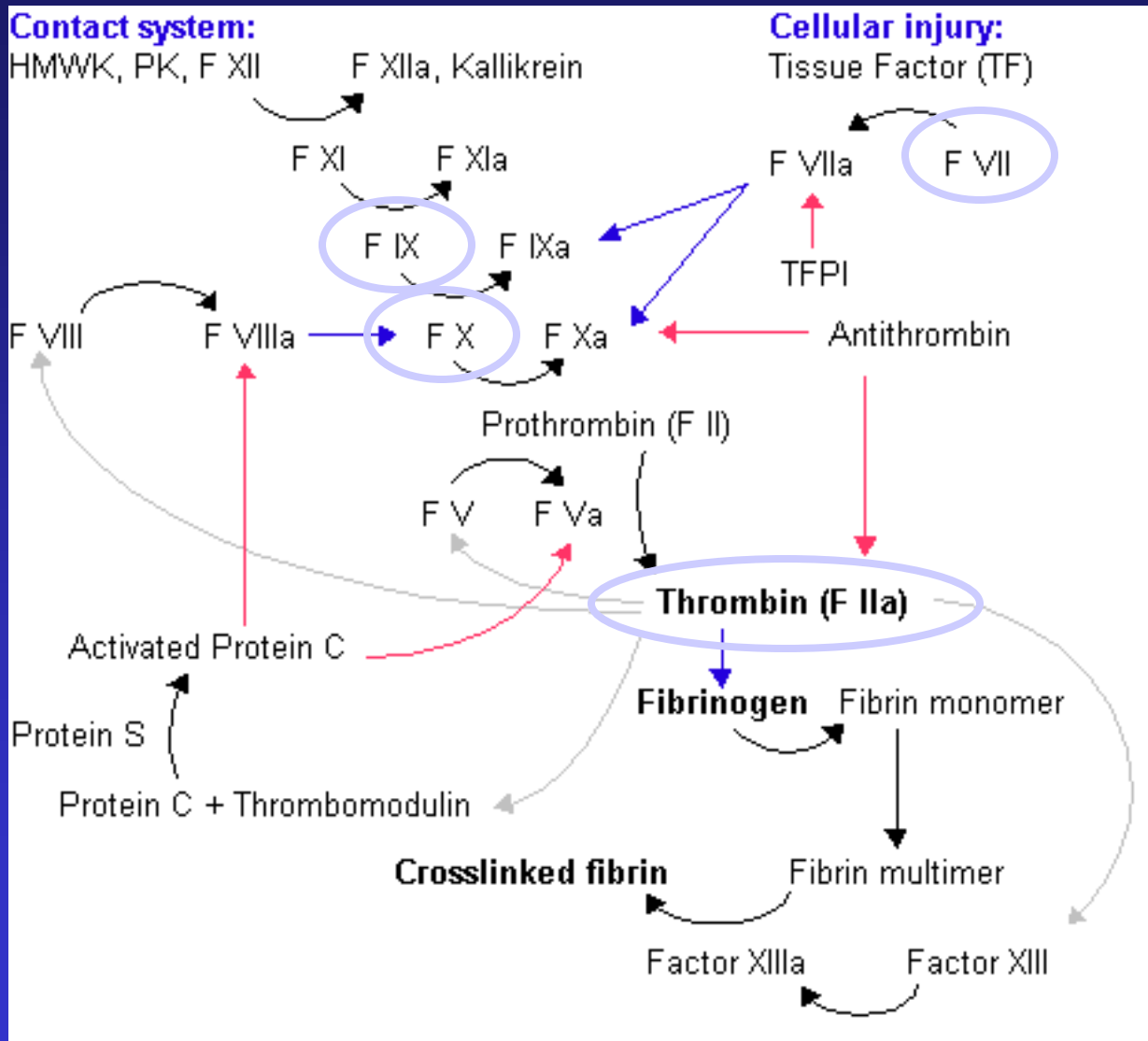
ICH – Anticoagulation reversal

- Most of the time, we are talking about Warfarin (Coumadin™).
- Taken by up to 1.6% of the population.
- **Taken by 4-8% of patients over 65.**
- There are more indications every year.
- The population becomes “grayer” every year.



D. W. Kaufman et al, Recent Patterns of Medication Use in the Ambulatory Adult Population of the United States, JAMA 2002;287:337-344.

Effect of Warfarin



Vitamin K antagonist

Vitamin K is required for carboxylation

Warfarin therefore prevents the synthesis of biologically active factors

ICH – Is anticoagulation bad?

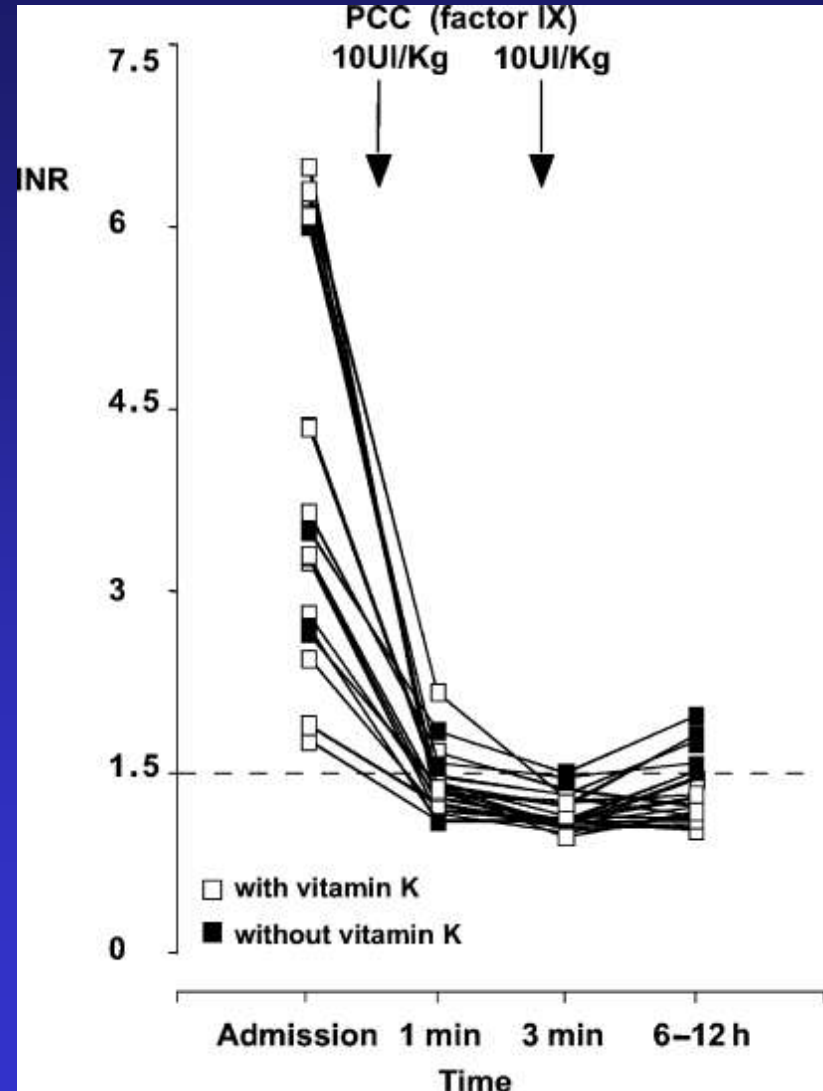
- ICH patients on warfarin suffer *INCREASED morbidity and mortality*, even though ICH volume on arrival is no different.
- Hematoma expansion AFTER the first head CT is seen in:
 - 54% of warfarin users
 - 17% of non-warfarin users

Warfarin Reversal - FFP

- Fresh Frozen Plasma
- FFP contains multiple components of the coagulation system including factors **II**, **V**, **VII**, **IX**, **X**, and **XI** (although factor IX can be difficult to replete)
- No randomized controlled trials. However, widely considered efficacious.
- Total dose of FFP required to reverse INR can be up to 2L (10 units)
- How long does it take for FFP to reverse the INR?
 - Zubkov et al: 7 (2-96) hours
 - Bershad et al: 29 (7-72) hours
 - Goldstein et al: 7 (2-72) hours
 - Brody et al: 32 (10-73) hours
 - Siddiq et al: 8.5 5.6 hours

Warfarin Reversal – PCC

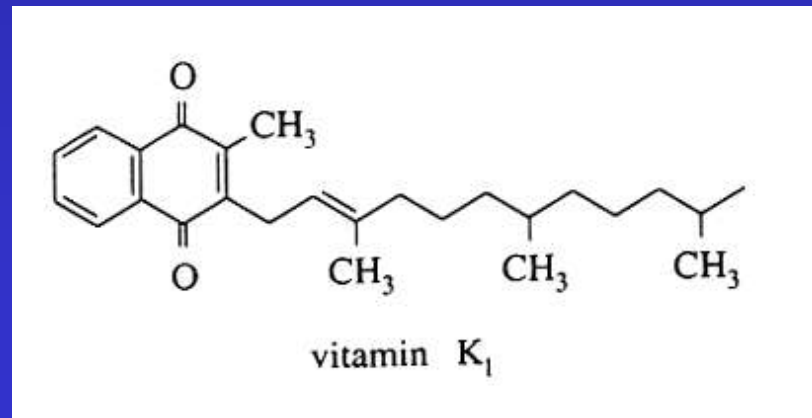
- **Advantages:**
 - Rapid action! Clotting factor repletion within 20 minutes.
 - Reverses INR more rapidly than does FFP
 - Minimal volume required
- **Disadvantages:**
 - Expensive
 - Possible risk of thrombotic complications and disseminated intravascular coagulation



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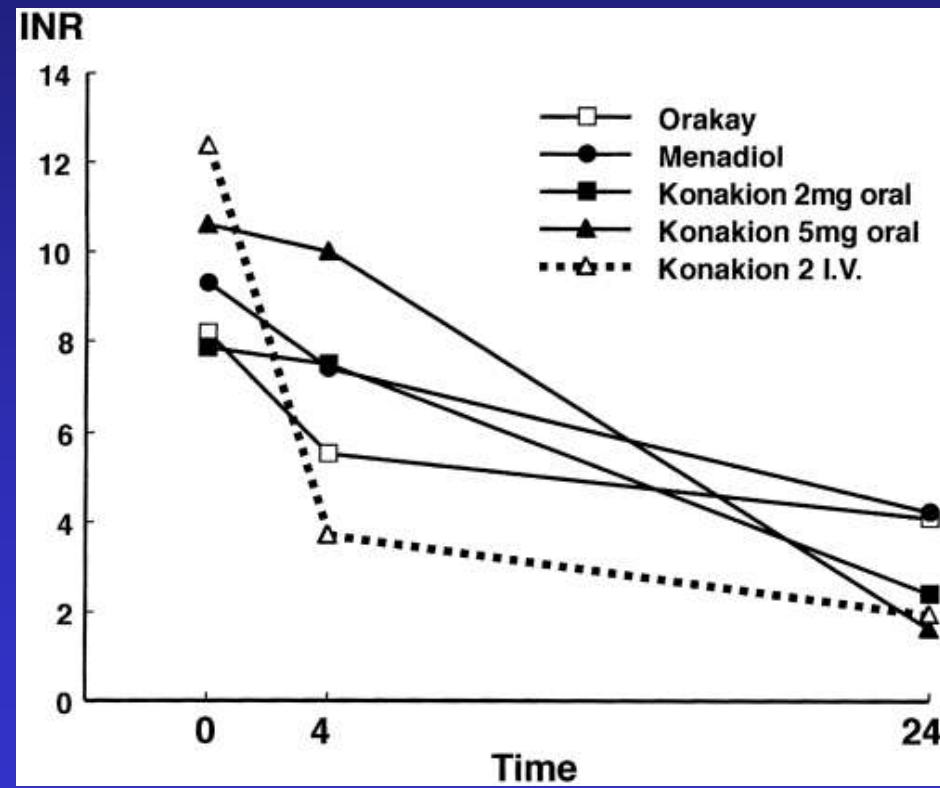
Warfarin Reversal – Vitamin K

- Vitamin K is the ideal warfarin reversal agent.
- **HOWEVER**, it requires time to take effect.
- Allows the liver to synthesize the vitamin K dependent proteins.



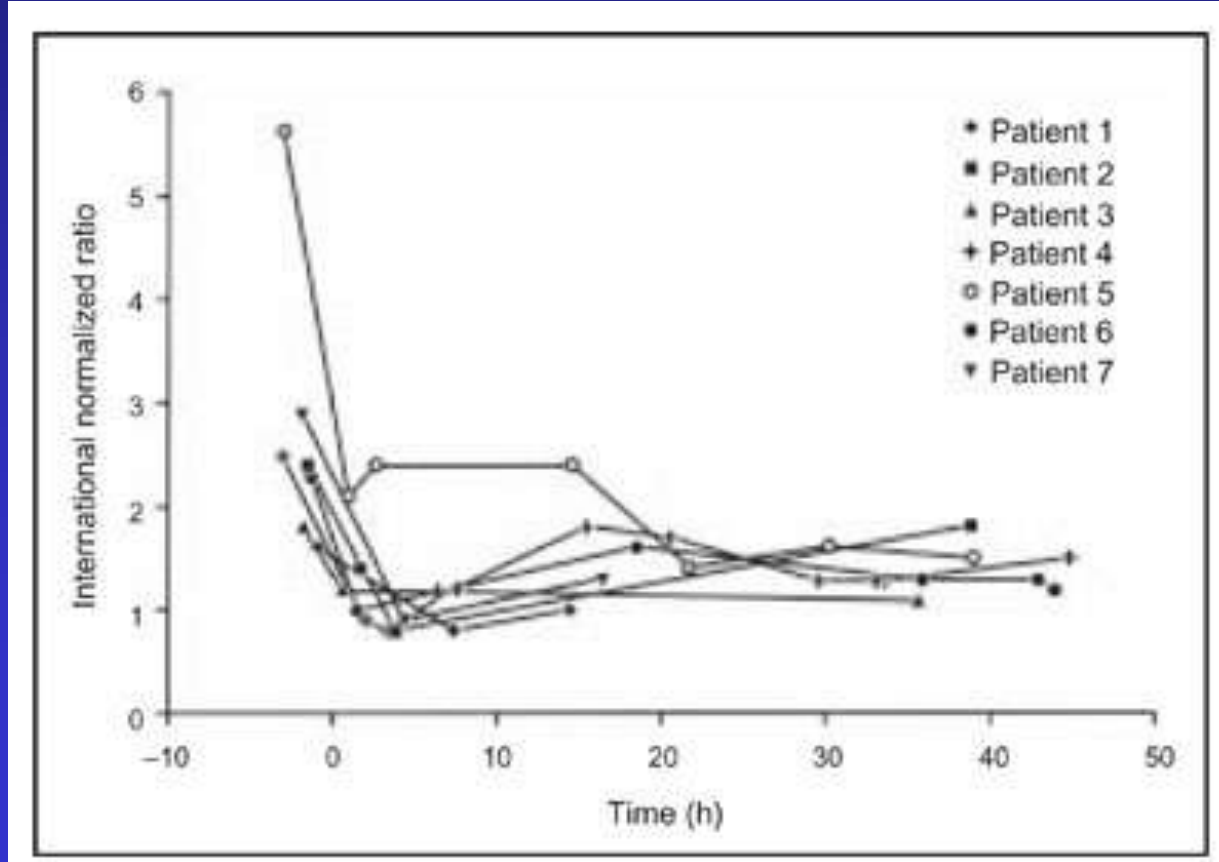
Warfarin Reversal – Vitamin K

- The intravenous form is the most reliable and acts the most quickly.
- There is an effect as early as 4 hours, and it can reverse the INR in as early as 8 hours
- Risks include anaphylaxis (rare)



Warfarin Reversal –Factor VIIa

- Small, uncontrolled studies
- Factor VIIa reduces time to INR correction
- Possible risk of thromboembolic complications.



ICH - Hyperglycemia

- Hyperglycemia is associated with poor outcome, even in the absence of known diabetes.
- This is another factor that we can treat!
- Never been formally tested in ICH patients, but:

Hyperglycemia in critically ill patients

- Two large randomized controlled trials of intensive insulin therapy (Target serum glucose 80-110)
- One in MICU, one in SICU
- Enrolled a variety of patients including neuromedical and neurosurgical
- Reduced morbidity and mortality

Van den Berghe et al, *NEJM* 2006; 354(5)

Van den Berghe et al, *NEJM* 2001; 345(19)

Hyperglycemia in ICH

- No prospective trials of just this group
- However, 2 trials in stroke found no clinical benefit to intensive insulin therapy vs. “standard care” (sliding scale)
- GIST trial – 933 stroke patients, of whom 12% had ICH, were randomized to intensive insulin therapy or standard care. There was no effect on outcome.

ICH - Hyperglycemia

- Hyperglycemia has known neurotoxic effects.
- It is likely that ICH patients benefit from glucose control of some kind.
- While there is no current clear benefit from intensive insulin therapy in the ED, it is reasonable to consider sliding scale insulin

ICH – medical management

- Admission to a stroke unit.
 - Studies of stroke in general and ICH in particular have suggested improved outcomes when patients are admitted to a specialty service.

Next talk: Further ICH management

Questions so far?