

# Vasospasm after aneurysmal SAH: prevention & treatment

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# Definition

## angiographic vasospasm:

transient arterial narrowing visualized on cerebral angiogram 4-12 days after SAH

## symptomatic vasospasm:

delayed cerebral ischemia resulting from angiographic vasospasm

# Incidence

67% develop angiographic vasospasm

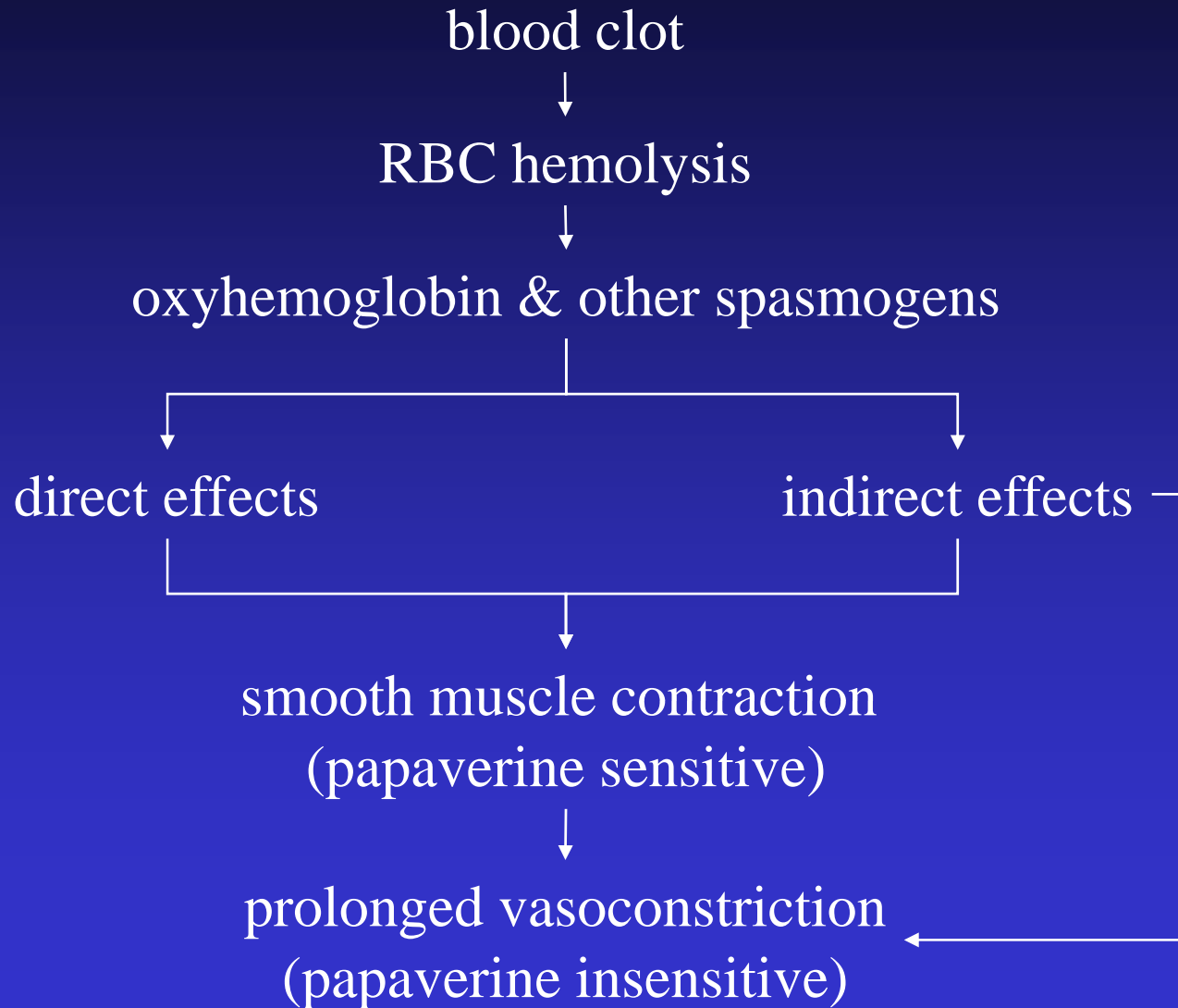
32% develop symptomatic vasospasm

## M & M of vasospasm

Vasospasm increases mortality after SAH by  
1.5- to 3- fold in the first 2 weeks after SAH

Morbidity and mortality has been reduced  
from 30% to 15% since the 1960's

# Pathogenesis



# Purported indirect reactions

1. Production of vasoactive free radicals
2. Inhibition of endothelium-dependent relaxation (NO mediated)
3. Increased endothelin release
4. Increased arterial wall eicosanoid release (calcium and/or calmodulin mediated)
5. Damage perivascular nerves

Risk of vasospasm correlates  
with severity of SAH

Fisher Grade

# Fisher Grade

grade I: no blood

grade II: diffuse, thin SAH layers ( $< 1$  mm)

grade III: localized clot and/or  
thick SAH layers ( $> 1$  mm)

grade IV: ICH or IVH (no significant SAH)

# Fisher grade & vasospasm risk

grade I/II = 5.6%

grade III = 96%

grade IV = rare

# Window of risk

# Window of risk

a-vasospasm:

4-12 days after SAH (peak 5-7 d)

s-vasospasm:

lags behind a-vasospasm by 1-2 days (peak 7-10 d)

*However . . .*

- may develop as early as 2 to 3 days or as late as 3 weeks after SAH
- 3-4% of patients develop s-vasospasm > 13 days after SAH

# Signs and symptoms

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1. focal neurologic deficit
2. ↑ headache
3. ↑ meningismus
4. altered consciousness
5. low-grade fever

# Diagnosis

**Angiogram** is gold standard

**TCD** is an alternative

velocities  $> 120$  cm/sec (mild-mod vasospasm)

velocities  $> 200$  cm/sec (severe vasospasm)

rate of rise  $> 50$  cm/sec/day (perhaps better)

**Microdialysis** is experimental

glucose, lactate, glutamate, and glycerol levels

# Prevention & treatment: avoidance

*Avoid conditions that increase risk for symptomatic vasospasm...*

1. Antifibrinolytic drugs
2. Hypovolemia / hypotension
3. Increased ICP

# Triple-H therapy

# Prevention & treatment: triple-H therapy

1. Hypertension
2. Hypervolemia
3. Hemodilution

*Induced hypertension has the most sound scientific basis...*

# Prevention & treatment: **triple-H therapy**

Stroke Council of AHA conclusions on use of triple-H therapy:

Despite the absence of large, randomized trials, evidence from small series suggests that this approach may decrease morbidity and mortality

Recommended (level of evidence III-IV)

# Prevention & treatment: triple-H therapy

## 1. Hypertension

SBP >150 mmHg (max 200-240 mmHg)

Use phenylephrine & crystalloid/colloid  
(dopamine & norepinephrine are alternatives)

## 2. Hypervolemia

CVP of 10-12 mmHg

PCWP of 15-18 mmHg

## 3. Hemodilution

HCT 30-33%

# Medical therapy

# Prevention & treatment: nimodipine

1. Calcium channel antagonist
2. Does not effect angiographic vasospasm
3. **Improves outcome**
  - reduces infarction after SAH by 34%
  - reduces incidence of poor outcome by 40%
4. Strongly recommended (level of evidence I-II)

# Prevention & treatment: **nicardipine**

1. Calcium channel antagonist
2. Significantly reduced symptomatic and angiographic vasospasm
3. Also reduced need for triple-H therapy
4. **Does not effect overall outcome**
5. An option, but not recommended

# Prevention & treatment: **AT-877**

1. Sulfonamide derivative that antagonizes intracellular calcium
2. Reduced angiographic and symptomatic vasospasm
3. Reduced incidence of poor outcomes
4. Further studies warranted

# Prevention & treatment: **tirilazad**

1. 21-aminosteroid: an antioxidant that inhibits lipid peroxidation
2. **European-Australian multicenter study**  
improved neurologic outcome and lowered mortality
3. **North American multicenter study**  
did not confirm favorable effect

# Prevention & treatment: **other**

1. **Nicaraven:** antioxidant, reduced vasospasm and poor outcome at 1 month (but not at 3 months)
2. **Ebselen:** antioxidant, did not effect vasospasm but trend toward improved outcome
3. **Methylprednisolone:** anti-inflammatory, may reduce delayed ischemic deficits in a small retrospective study

# Prevention & treatment: **other**

1. **Nafamostat mesilate**: inhibits complement activation, improved outcome and reduced delayed cerebral ischemia in a small retrospective study
2. **OKY-1581**: a thromboxane-A<sub>2</sub> synthetase inhibitor, mild reduction in delayed cerebral ischemia & mortality and mild improvement in outcome in a small retrospective study

# Endovascular therapy

# Prevention & treatment: angioplasty

1. Uncontrolled studies only
2. Angiographic improvement in 95%
3. Clinical improvement in 70%
4. Effective for proximal vasospasm
5. Morbidity and mortality: 5-10%
6. Primary therapy vs. salvage therapy??

# Prevention & treatment: **papaverine**

1. Effective for proximal, intermediate, and distal vasospasm
2. Effects are thought to be **transient** (<24 hr)
3. Used primarily as an adjunct to angioplasty, or when angioplasty is unable to be performed

# Prevention & treatment: clot removal and clot lysis

## 1. Surgical clot evacuation

technical difficulties

unclear effect in man

## 2. Pharmacologic fibrinolysis

single center, placebo-controlled study  
showed reduction in severe vasospasm, but  
did not improve outcome at 3 months

# Prevention & treatment: medical tx on the horizon

1. Endothelin antagonists
2. Intrathecal sodium nitroprusside
3. Intra-arterial administration of NO donors
4. Cromakalim (potassium channel activator)
5. Intracisternal slow delivery systems  
papaverine, calcitonin

# In review

## Initial management of SAH

1. Admit SICU / IMC
2. Euvolemia
3. Control BP (<160/100 mmHg); SNP is best
4. Treat increased ICP (ventric at 20 cm)
5. Nimodipine (60 mg PO q6)
6. Seizure prophylaxis
7. Early treatment (surgery vs. endovascular)

# In review

## Vasospasm prophylaxis (aneurysm secured)

### 1. Hypervolemia

IVF at 150 cc/hr; 5% albumin 250 cc q6-12  
consider CVP if high risk

### 2. BP allowed to rise (SBP <200 mmHg)

### 3. Ventriculostomy to 10 cm H<sub>2</sub>O

### 4. Monitor patient through window of risk

# In review

## Delayed neurologic deficit (aneurysm secured)

- Head CT (r/o ICH, edema, HCP, etc.)
- Check AED level, O<sub>2</sub> sats, lytes, etc.
- Drop ventriculostomy to 0 cm H<sub>2</sub>O
- Induce hypertension (phenylephrine)
- Angiogram for diagnosis and therapy
- Place Swan (PCWP 12-15 mmHg; Starling curve)