Haemorrhagic stroke in children

Finbar O'Callaghan
Institute of Child Health, UCL
&
Great Ormond Street Hospital, London

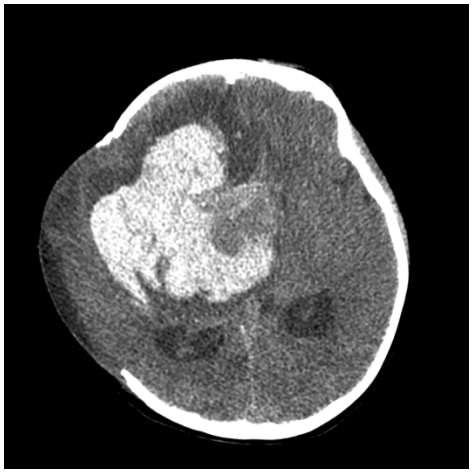
Definition

- Acute neurological deficit secondary to focal haemorrhage in the brain.

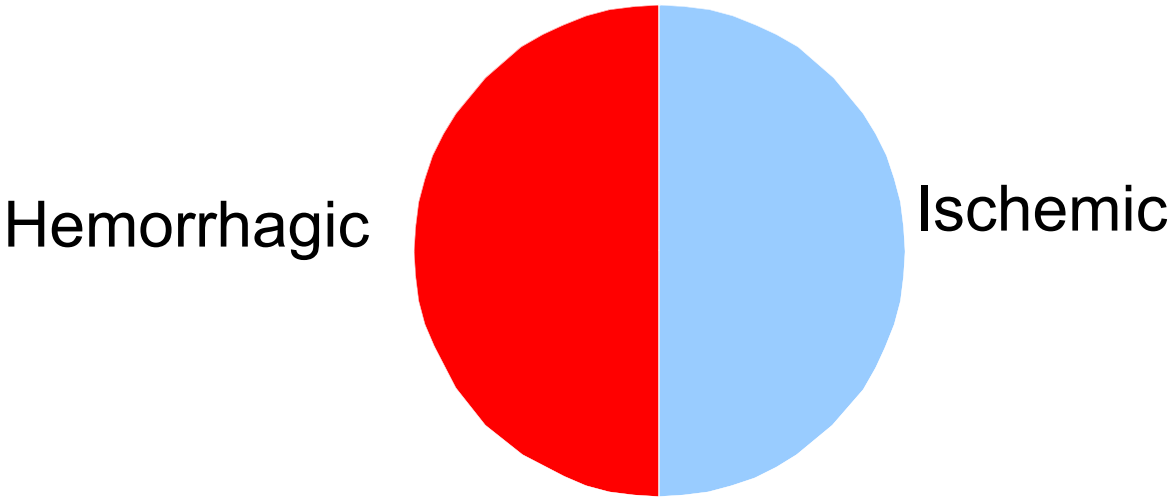
What are we talking about?

- Hemorrhagic stroke (HS):
  - Intracerebral hemorrhage (ICH)
  - Subarachnoid hemorrhage (SAH)
  - Intraventricular hemorrhage (IVH)

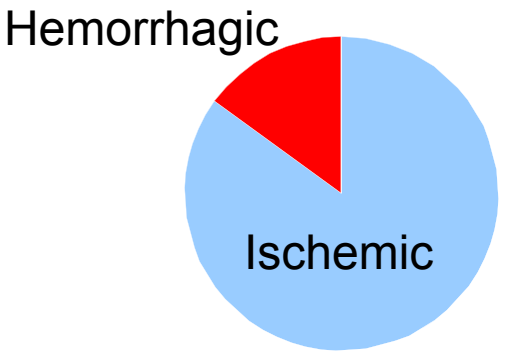
- Excluding:
  - Hemorrhagic infarcts
  - Neonatal IVH
  - Subdural hemorrhage (SDH)
  - Epidural hemorrhage (EDH)



The Relative Importance of Hemorrhagic Stroke in Kids



Children



Adults

Broderick, et al, J Child Neurol 1993

Background

- In adults haemorrhagic stroke (HS) – 15% strokes
- Children HS : 45% - 50% stroke
- Mortality rate HS x5 higher than ischaemic stroke
- High risk of serious life-long disability
  - Affecting multiple domains

Previous Studies

- Very little study of HS in children
- 10 times more ischaemic stroke publications than HS publications since 2000
- Sparse outcome data
- No population based outcome data

SOCS Study Area

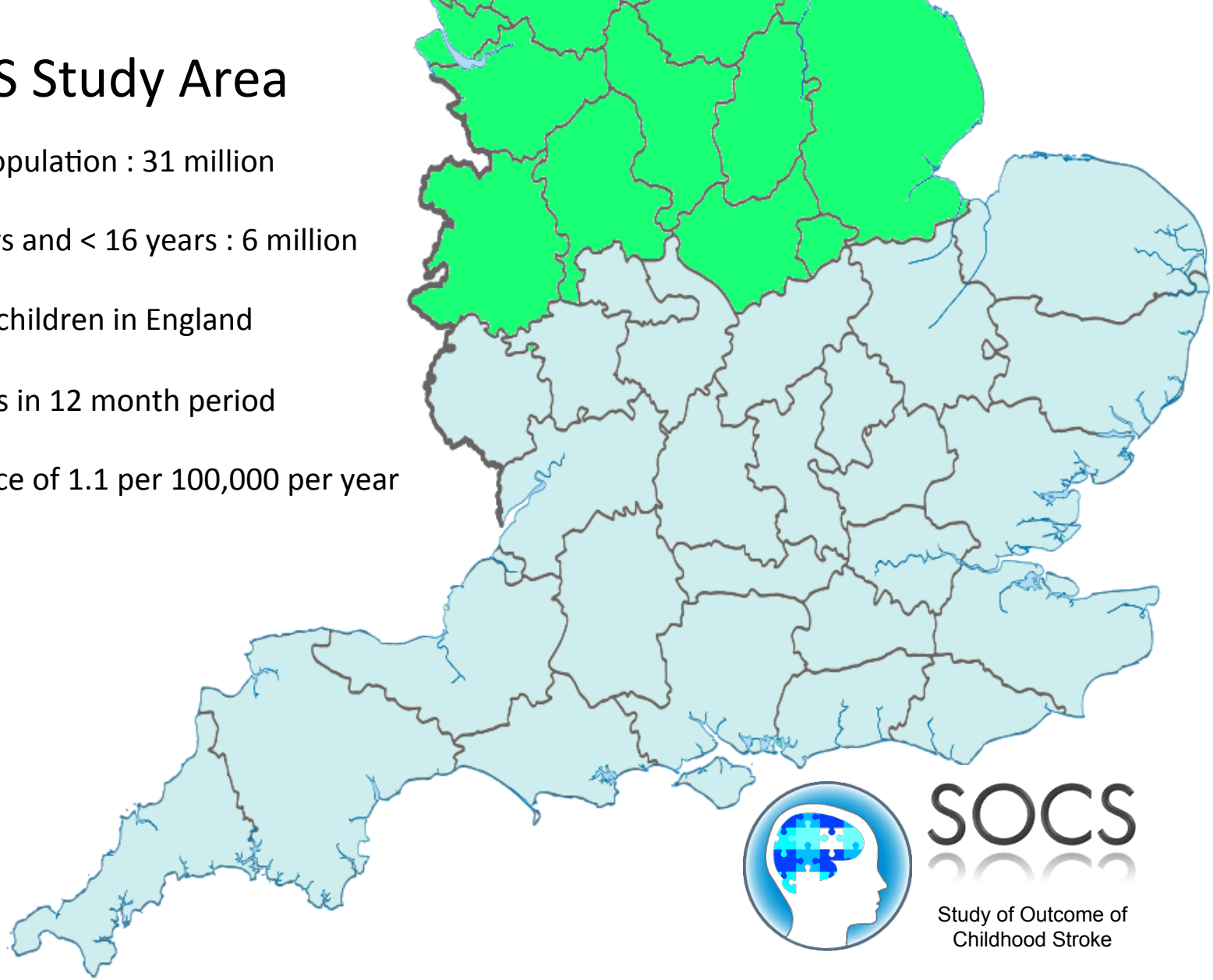
Total population : 31 million

>27 days and < 16 years : 6 million

63% of children in England

65 cases in 12 month period

Incidence of 1.1 per 100,000 per year



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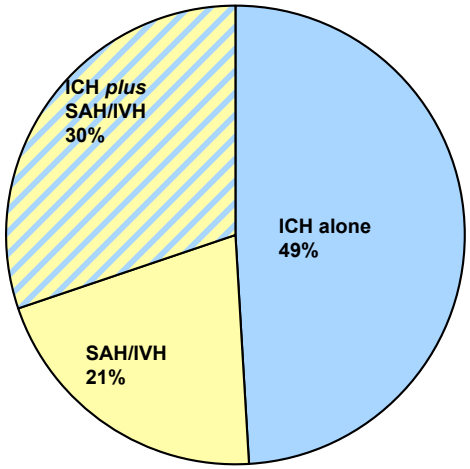
Study of Outcome of Childhood Stroke

Pattern of Haemorrhage

- 153 haemorrhagic stroke cases



- Mean age:

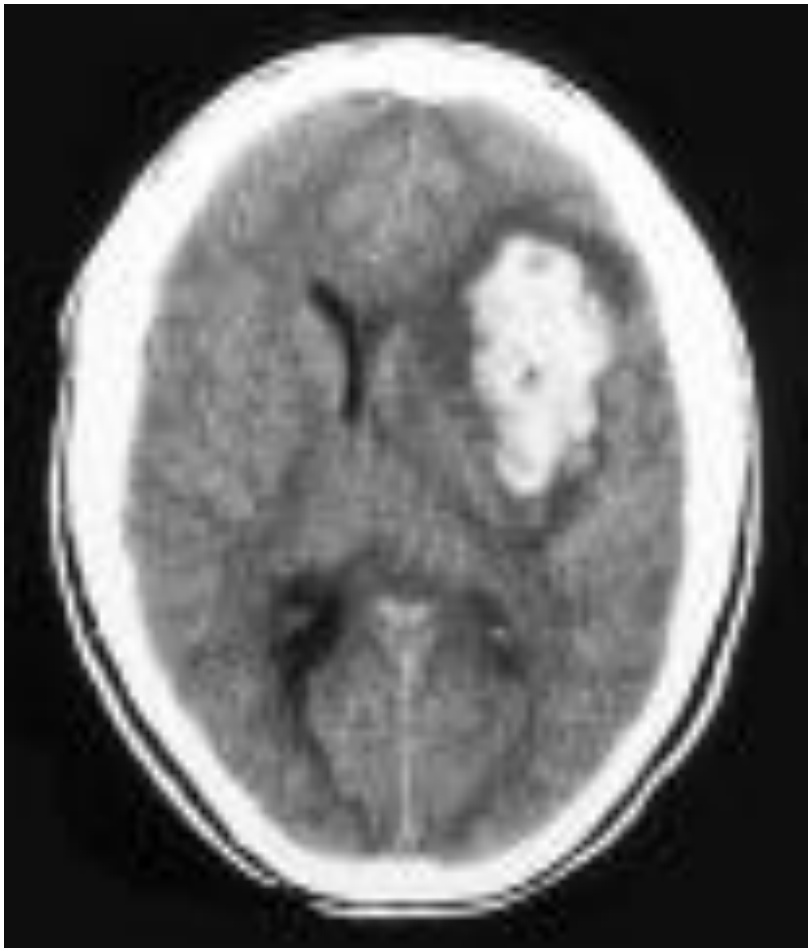
  11.8 years (SD 6.5)

Fullerton, *Stroke*, 2007

Clinical Presentation

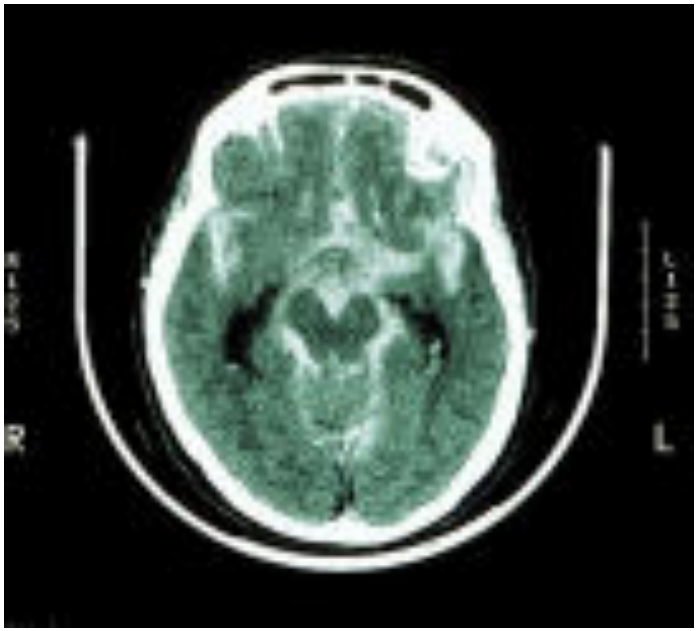
- **Headache: thunderclap**
- Vomiting
- Syncope
- **Seizures**
- Focal deficits
- **Altered mental status**
- Hypertension

Diagnosis: CT sensitive for intracerebral hemorrhage

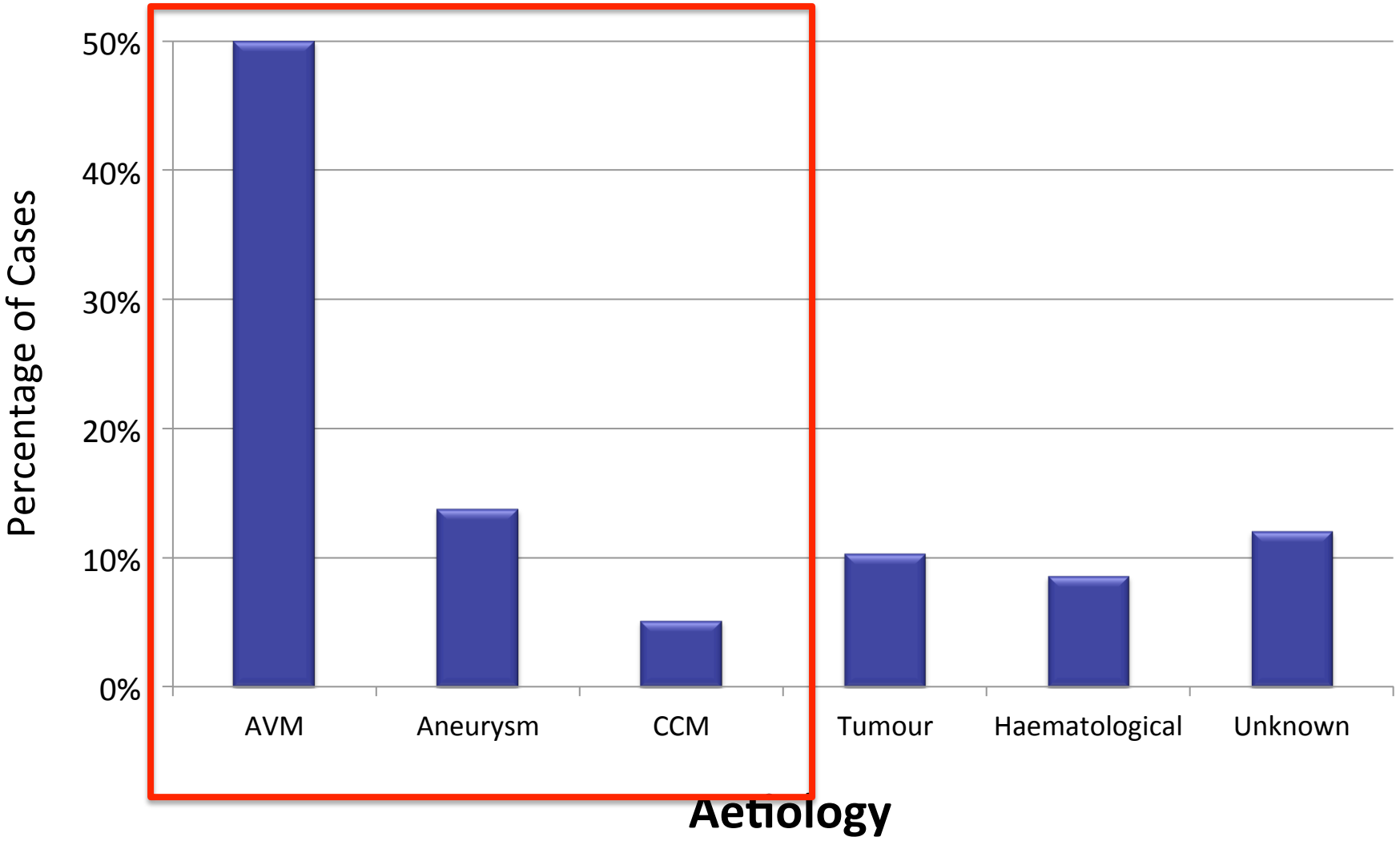


Diagnosis: CT also sensitive for subarachnoid hemorrhage

- But not 100%
- Gold standard is LP
- Consider when convincing story

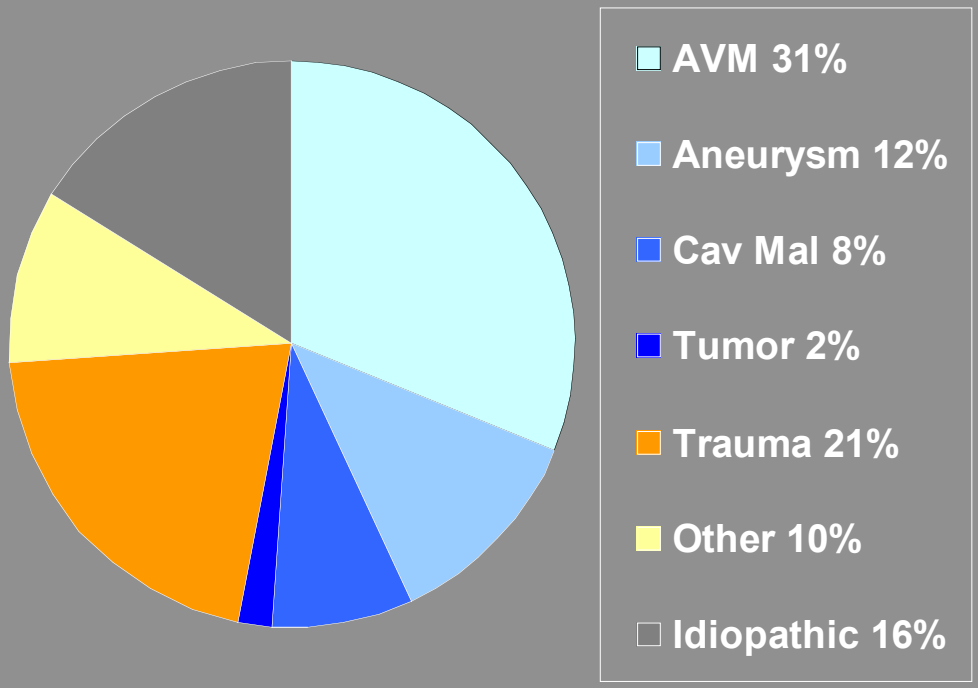


Aetiology


50%
40%
30%
20%
10%
0%
Percentage of Cases
AVM
Aneurysm
CCM
Tumour
Haematological
Unknown
Aetiology

Etiologies of Pediatric HS

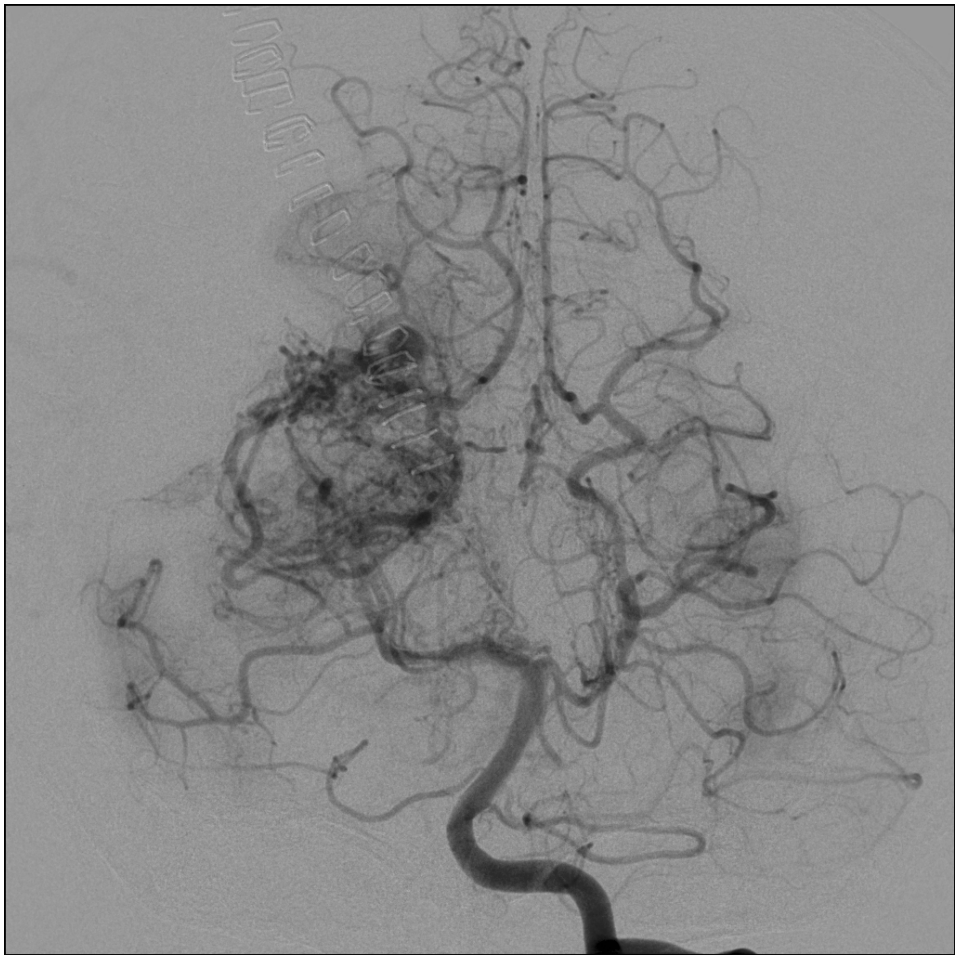
- Structural 53%



  - Other 10%
    - Hypertension, drug use, thrombocytopenia, hemophilia, leukemia

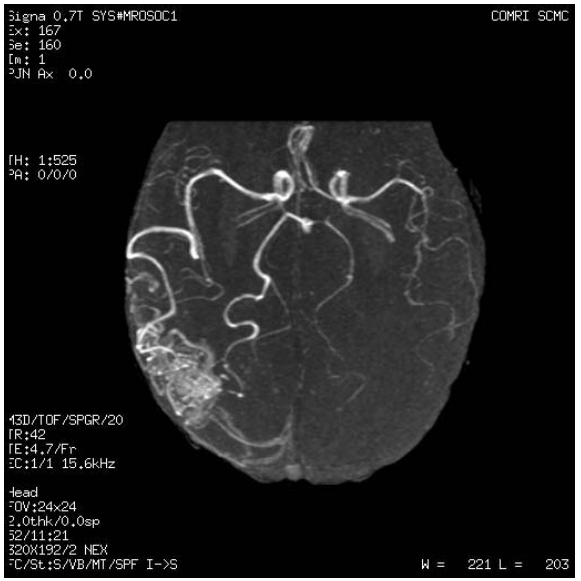
Fullerton, *Stroke*, 2007

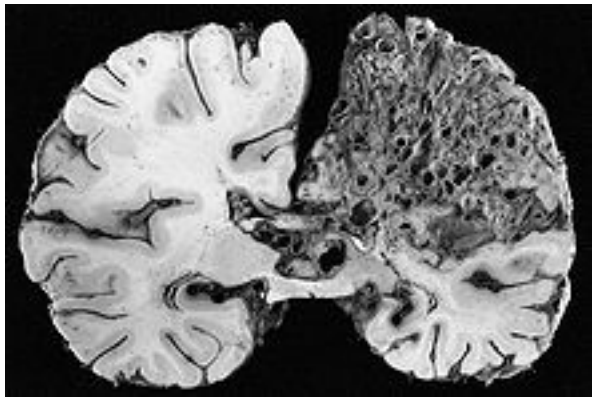
AVM: the most common cause



Arteriovenous Malformations (AVM's)

- Def: collection of abnormal thin walled vessels connecting arteries to veins
- Over time, feeding arteries and draining veins dilate
- Later, veins can stenose (risk for hemorrhage)





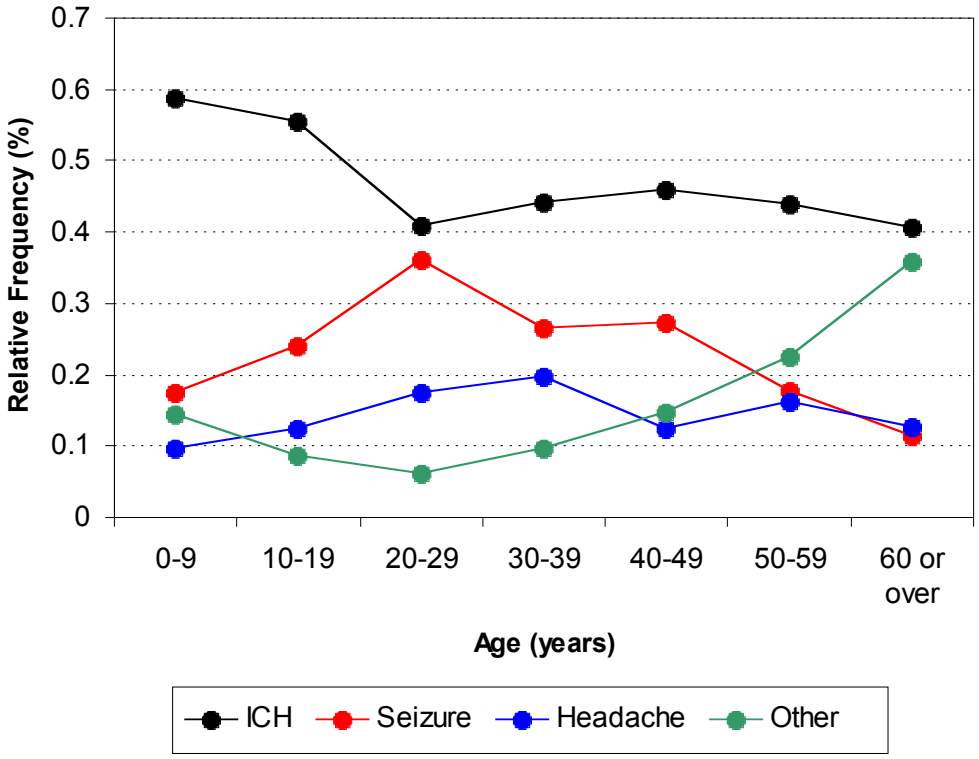
AVM's: Presentation & Dx

- Miller 1994, 56 children, newborns to 18yo:
  - hemorrhage (50%)
  - seizures (9%)
  - recurrent HA's (3.5%)
  - hydrocephalus (9%) — Infants
  - CHF (18%) — Neonates
  - Other, including progressive neuro deficits (11%)

- Diagnosis: conventional angiography

AVM presentation

- Children are more likely to present with ICH



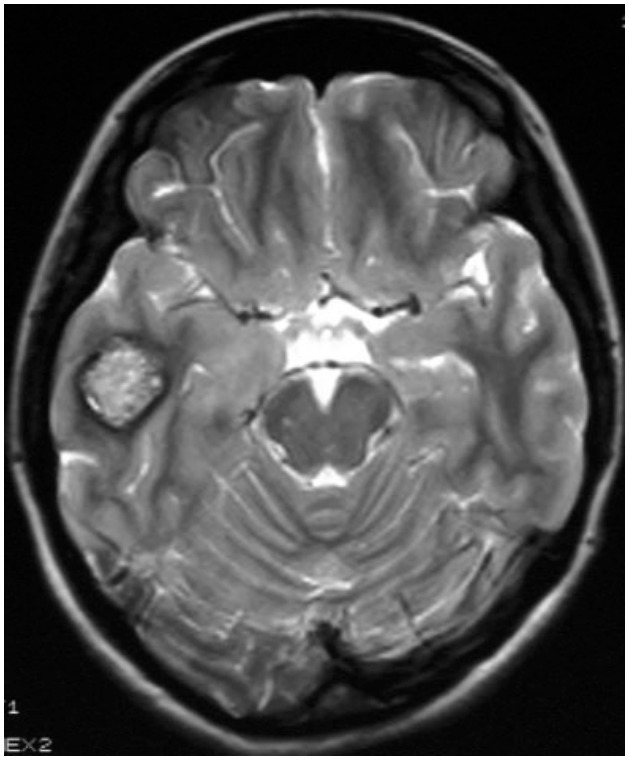
Fullerton, et al, Stroke, 2005.

Treatment of Brain AVMs

- **Embolization**—usually just to decrease surgical risk, but not curative
- **Surgical resection**—risk based on size, location, deep venous drainage; tx of choice for an AVM that has bleed
- **Radiosurgery** (Gammaknife)—delayed effect (6 mo to 3 years), reserved for high surgical risk or unruptured

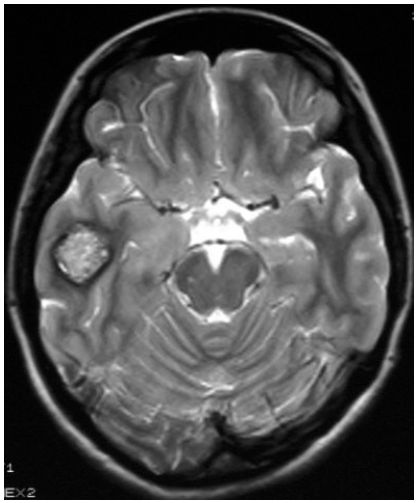
Cavernous Malformations (Haemangiomas)

- Spherical collections of endothelial lined sinusoidal (cavernous) vascular spaces
- feeding arteries and draining veins have normal calibre



Cavernous malformations

- Presentation:
  - Seizures
  - Symptomatic hemorrhage
  - Incidental
- **Diagnosis:**
  - **MRI**
  - **Most are angiographically occult**



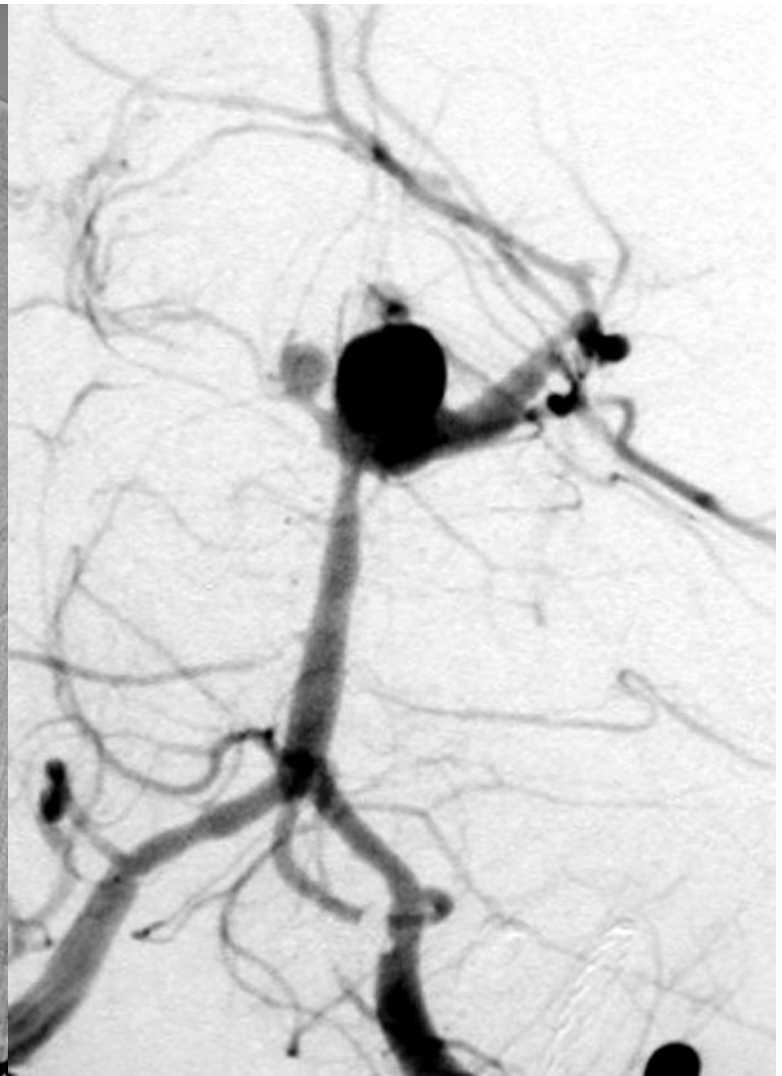
Cav mal: Management

- Management:
  - Surgical
  - Observation
  - Radiosurgery not effective
- Goals of surgery:
  - Prevention of hemorrhage
  - (Seizure control)
- Indications for tx:
  - Symptomatic hemorrhage
  - (Uncontrolled epilepsy)
- Risks of surgery vs natural history risk

Cav mal: Natural Hx Annual Hemorrhage Risk

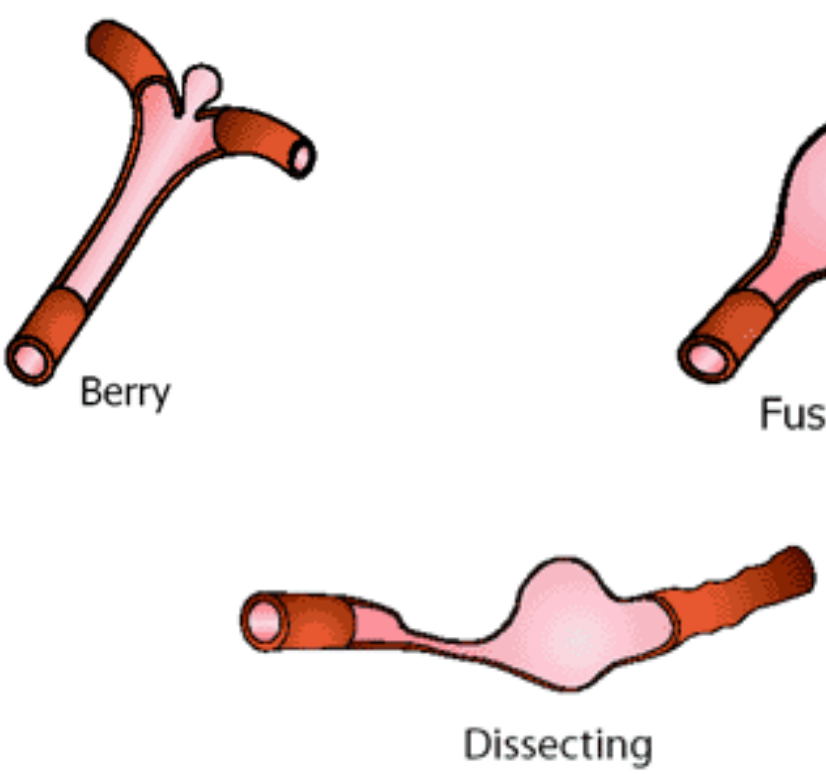
- LIMITED data: retrospective, ? definition of hemorrhage
- Depends on Presentation (Komata 95; Kondziolka 95)
  - Incidental: 0.4%/year
  - Hemorrhagic presentation: 4.5-23%/year
- Depends on location (Wallace 97; Zabramski 99)
  - "Deep" (BS, cerebellar nuclei, deep grey; mostly sx): 5-11%/year
  - "Superficial": 0%

Pediatric Aneurysms




(a)
(b)
(c)

Aneurysm Types



Also mycotic aneurysms

Aneurysms different in children

Paediatric

- 2-5%
- 1-3 M: F
- Internal carotid bifurcation
- Giant 20-40%
- Rarely multiple (except HIV)
- Posterior circulation 20-40%

Adult

- 95-97%
- 3F:1M
- Ant Communicating
- Giant uncommon
- 15% multiple
- Post circulation 5%

Aetiologies of Pediatric Aneurysms

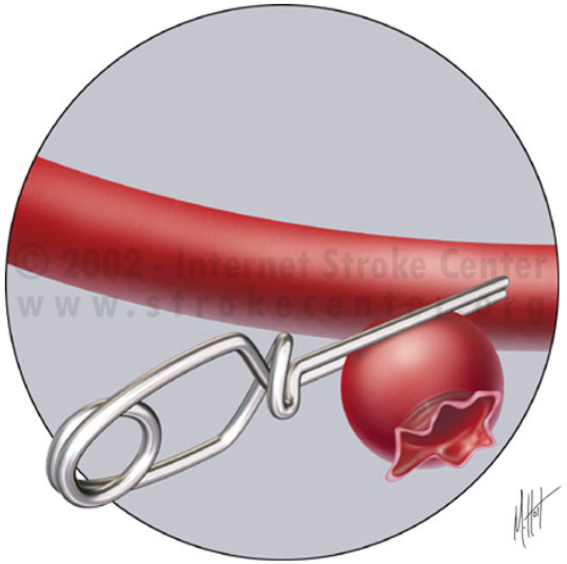
- Childhood aneurysms are expressions of vessel wall dysfunctions, failure to repair wall
- Primary triggers: Trauma, infectious, autoimmune (vasculitis)
- Silent genetic disease: AD polycystic kidney disease, Ehlers-Danlos, Marfan's syndrome, NF1, tuberous sclerosis, MOPD (microcephalic osteodysplastic primordial dwarfism) type 2, moyamoya syndrome

Lasjaunias P. et al(1997) Aneurysmal disease in children. Review of 20 cases. Interv Neuroradiol 3:215– 229

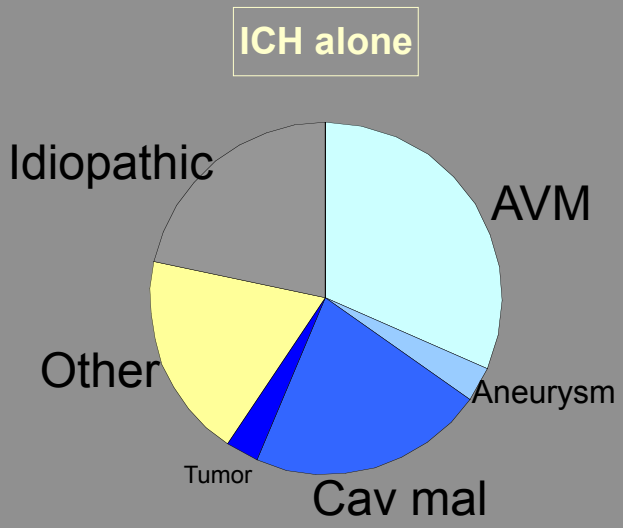
Treatment Options for Aneurysms

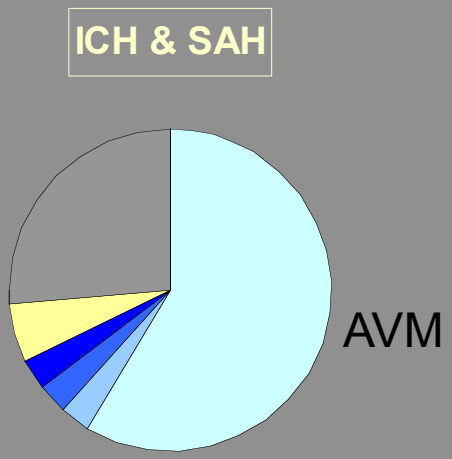
- Endovascular coiling

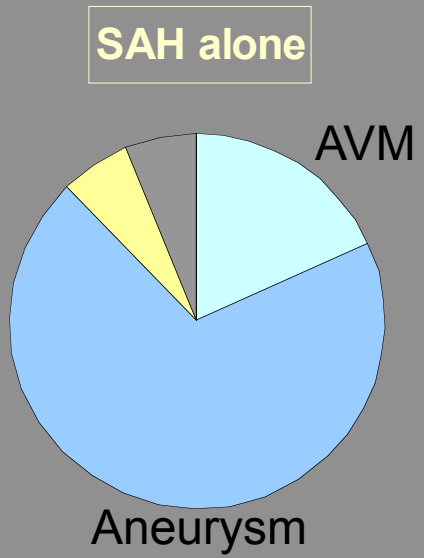
- Surgical clipping



Aetiologies of *Spontaneous* ICH & SAH in children







Fullerton, *Stroke*, 2007

Recurrence risk

Hemorrhagic Stroke Recurrence Kaiser Study

- Follow-up data on **152** of 153 (1 lost to f/u)
- Median f/u period **3.5 years** (4 days - 12 years)
- **16 recurrent hemorrhagic strokes**
- Median of **20 days** (4 days – 5.7 years) after initial event

Fullerton et al, Stroke, 2007

Aetiology of Recurrences

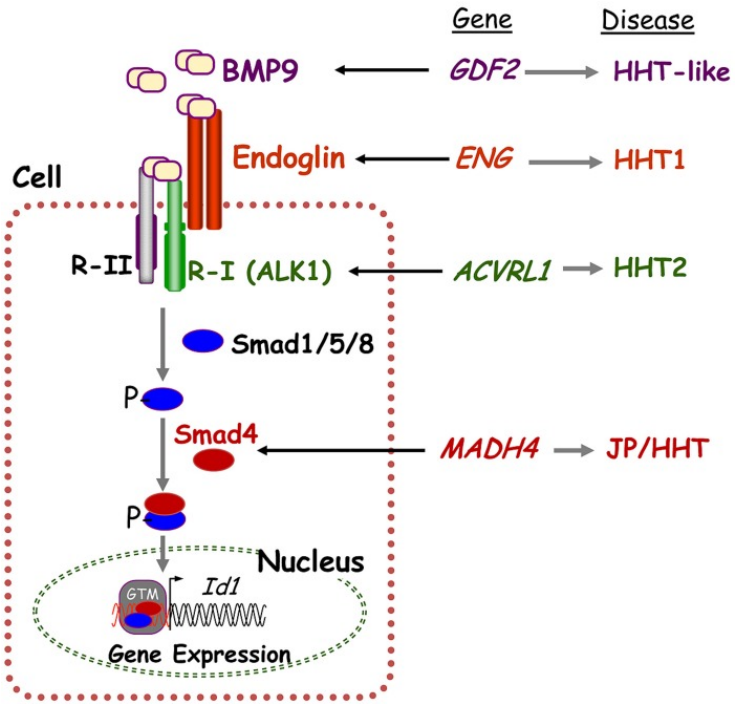
- Structural 12/16
  - 3 AVM
  - 5 cavernous malformations
  - 3 brain tumors
  - 1 aneurysm
- Trauma 1/16
- Other 3/16
  - Hypertension and anticoagulation, thrombocytopenia, moyamoya secondary to SCD (initial SAH, f/u stroke AIS)

Cavernous malformation: Genetics

- Seen on MRI in 0.4% of asymptomatic patients
- Most are sporadic
- Can be inherited: AD
- Three genes identified:
  - Krit1 (role in cytoskeletal/plasma membrane interactions); mutation in 50% familial cases
  - MGC4607/CCM2
  - PDCD10/CCM3

Genetics of AVMs: Hereditary Haemorrhagic Telangiectasia

- 1 in 5000 individuals
- Aka Osler-Weber-Rendu syndrome
- Characterised by abnormal blood vessel formation in multiple organs
- Mutations in transforming growth factor – beta (TGF-β) signalling pathway



Genetics of AVMs: RASA1 mutations

- Port-wine stains (cutaneous capillary malformations) and brain or spine AVMs and AVFs
- Appears to be AD, variable penetrance
- Over-activation of mTORC1 pathway

Eerola, Vikkula, et al, Am J Hum Genet. 2003

Outcome

Parental Impressions

- International Pediatric Stroke Study Recovery and Recurrence Questionnaire
- Recovery from stroke
  - Fully recovered : 15 (26%)
  - Not fully recovered (alive) : 28 (48%)
  - Death (from stroke) : 11 (19%)
  - Death (not stroke) : 4 (7%)
- Dependency (daily activities)
  - No extra help needed : 26 (60%)
  - Extra help needed : 17 (40%)

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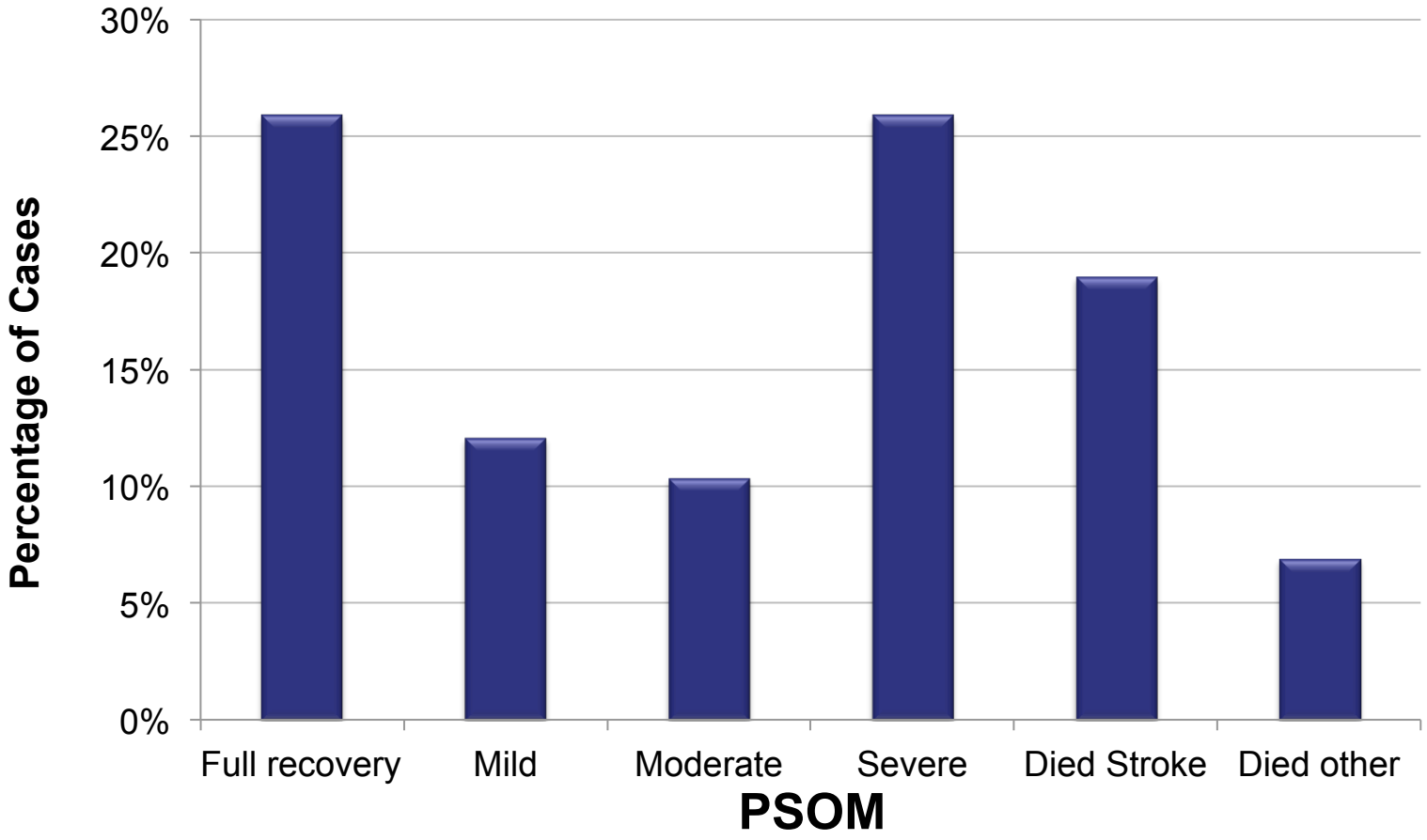
Paediatric Stroke Outcome Measure



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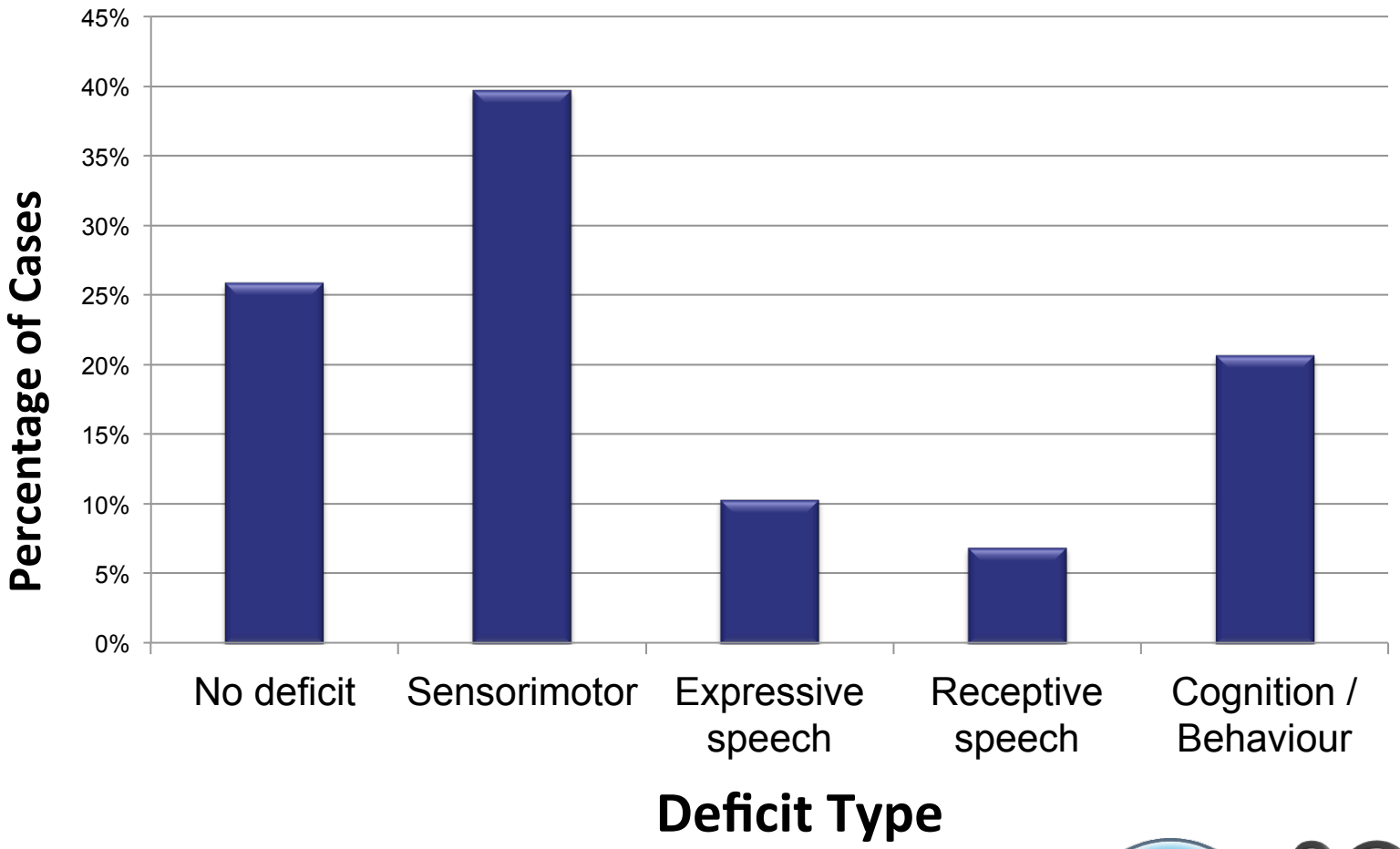
Deficit Type



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Conclusions

- Haemorrhagic stroke not uncommon
- Significant acute management issues
- Half of children with HS dead or dependent at follow-up (significantly worse outcome than AIS)
- Significant recurrence risk
- HS is an important but under researched childhood condition

Should siblings be screened?

- Cav mals: mostly sporadic; consider only if multiple cav mals or strong family hx
- AVMs: mostly sporadic; consider only if pt or family hx suggestive of HHT (eg. nose bleeds) or RASA 1 mutations (port-wine stains)
- Aneurysms: sibs at increased risk, but normal MRI does not rule out aneurysm at later age

Questions

- What is the most common cause of haemorrhagic stroke in children?
- What is the overall recurrence risk for haemorrhagic stroke in children?
- If a child presents with subarachnoid haemorrhage alone – what is the most likely cause?
- Approximately what percentage of children with haemorrhagic stroke will make a full recovery?
- Name one of the genetic mutations associated with hereditary cavenous malformation?