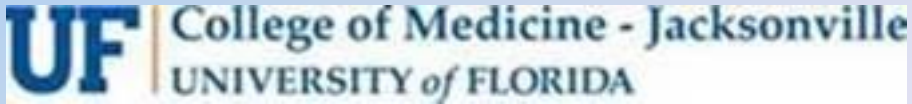
Application of Transcranial Doppler Ultrasound in Spontaneous Pediatric Subarachnoid Hemorrhage

Darryl Miles , MD
Assistant Professor, Department of Pediatrics
Division of Critical Care
UT Southwestern Medical Center – Children's Medical Center Dallas

Karen Lidsky MD
Associate Professor, University of Florida Jax
Division of Pediatric Critical Care
Wolfson Children's Hospital , Jacksonville Fla



DISCLOSURES

No Disclosures

ASN 42ND ANNUAL MEETING
JANUARY 24-26, 2019
PUERTO RICO

Objectives

- Discuss mechanisms of action in SAH induced vasospasm
- Describe the role of TCD in the management of pediatric SAH vasospasm
- Present a clinical case of subarachnoid hemorrhage due to ruptured AV fistula complicated by cerebral artery vasospasm
- Correlation TCD findings with conventional neurovascular imaging such as cerebral angiography and CT angiography
- Present case report pediatric use of intra-arterial milrinone therapy for acute vasospasm management

Background

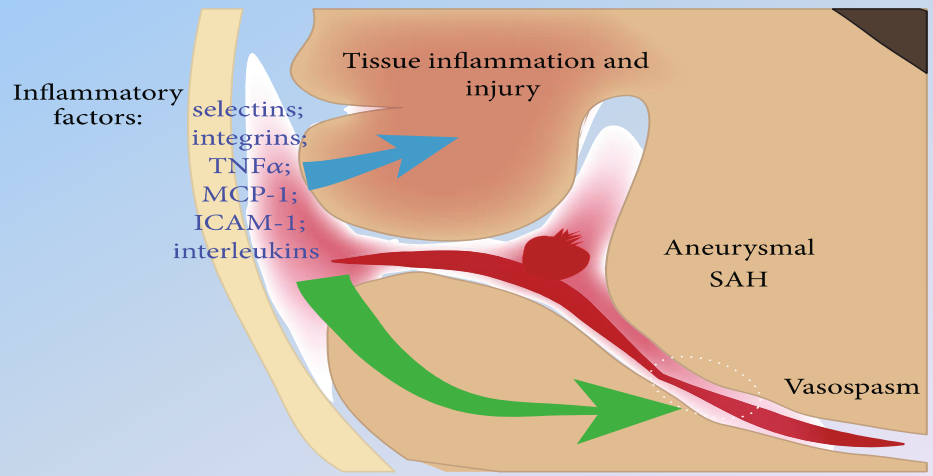
- Causes spontaneous SAH
  - Arteriovenous malformation (AVM):
    - Rarity: 3% of all AVMs but extremely high rupture rate
    - Most frequent abnormality ; most common cause spontaneous hemorrhage
    - Headaches, seizures , hemorrhage
  - Aneurysm
    - Gain rare: < 2% aneurysms; extremely rare under 5yrs; predominate teens
    - Males to females: 1.8 :1 : suggests differences in pathogenesis
    - Occurrence in the ICA bifurcation in 25%; giant size and posterior circulation 17%
    - Infectious etiology
  - Miscellaneous
    - Trauma
    - Infection
    - Tumor

Vasospasm: Mechanism of Action

- Vasospasm: “reversible reduction caliber of the lumen of conducting artery in the subarachnoid space
- Cerebral vasospasm leading determinate delayed cerebral ischemia (DCI)
- Mechanism of action
  - Endothelial damage
  - Smooth muscle contraction
  - Change in vascular responsiveness
  - Inflammatory process

Vasospasm: Mechanism of Action

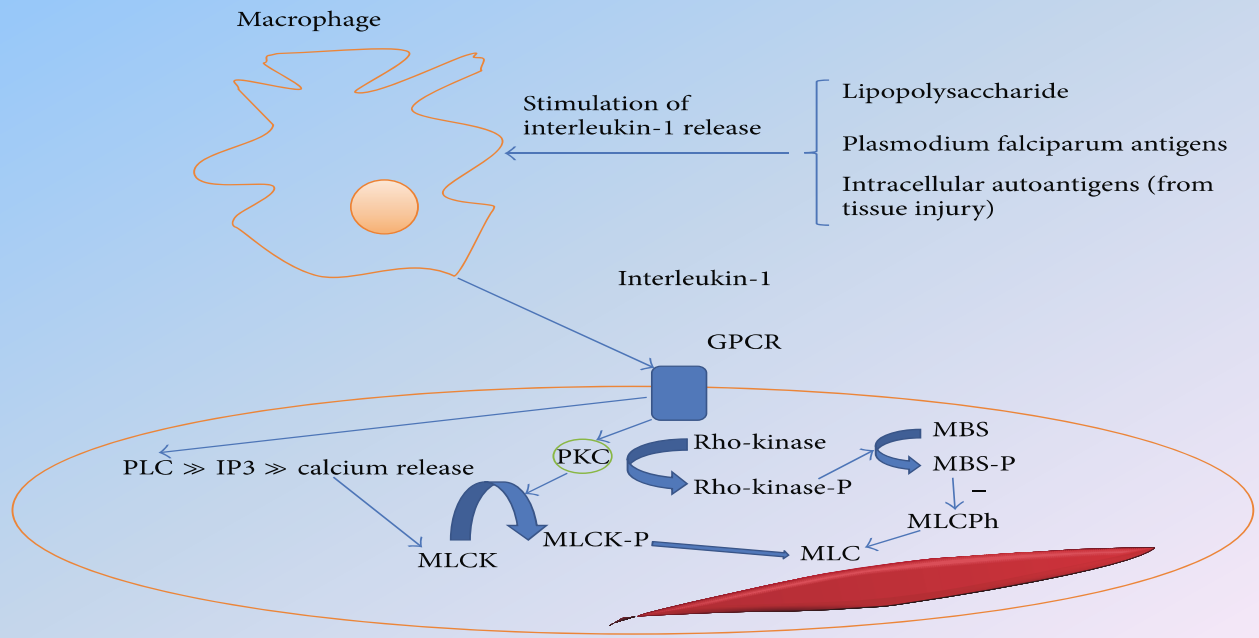
- Nitric Oxide (NO)
  - NO released from endothelium----stimulates guanylate cyclase in vascular smooth muscle ---- increase intracellular cGMP ----- muscle relaxation
  - Reduction neuronal nitric oxide synthase
  - Dysfunction of endothelial NO synthase
  - Hemoglobin scavenging of NO
- Inflammatory Mediators
  - Endothelin -1 (ET-1)
  - IL-1, TNFα



Miller BA et al. BioMed Research International Volume 2014 ID#384342

Vasospasm : Mechanism of Action

- ET-1:
  - Produced cerebral endothelium and mediates effect via Endothelin A receptors – vascular smooth muscle
  - Increased intracellular calcium concentrations
- IL -1: G-protein coupled receptors



Eisenhut M. International J Inflammation Volume 2014 ID#509707

Vasospasm: Mechanism of Action

Mediator	Function of mediator
(i) Nitric oxide	(i) Vasodilator (ii) Inhibitor of endothelin-1 expression
(i) Endothelin-1	(i) Vasoconstrictor
(i) Interleukin-1 (ii) Interferon gamma (iii) Tumor necrosis factor	(i) Activators of protein kinase C (ii) Stimulators of release of endothelin-1

Application TCD in Pediatric SAH

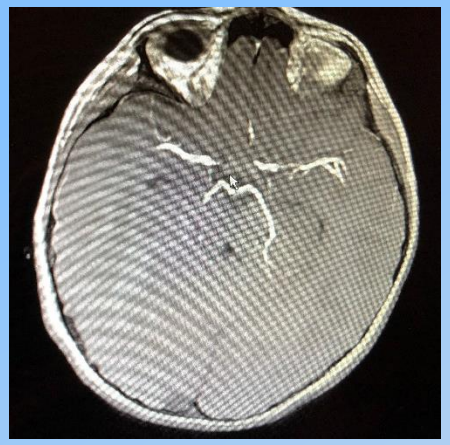
- Angiography assesses arteries > 1mm; small vessel contribution undetected
- Lindegaard – defined cerebral blood flow velocities for cerebral vasospasm
  - Inverse relation between angiography determined vessel size and cerebral blood flow velocity
  - Adult criteria:
    - Mean MCA velocity > 120cm/s plus Lindegaard ratio ≥ 3
    - Mean BA velocity >90 cm/s
    - Concerning DCI: increase ≥ 50cm/s/day or increase> 65cm/s/day 3-7
    - Systematic review : 99% sensitivity, 67% specificity VSP ≥ 25%
- WHAT ABOUT PEDIATRICS?

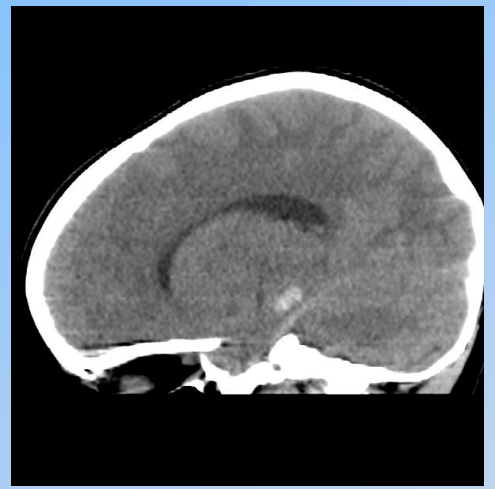
Application TCD in Pediatric SAH

- Pediatric flow velocities elevated baseline compared to adults- overestimate VSM using adult criteria
- Pediatric definition
  - Mean MCA or BA flow velocity ≥ 2 SD above normal values based on sex and age
  - Lindegaard ratio remains the same
- Consideration impact critical illness, sedation , mechanical ventilation has on velocities
  - Obrien(2015): MCA flow velocities lower

O'Brien NF. Nerv Syst (2015) 31:2269-2276

Application TCD in Pediatric SAH

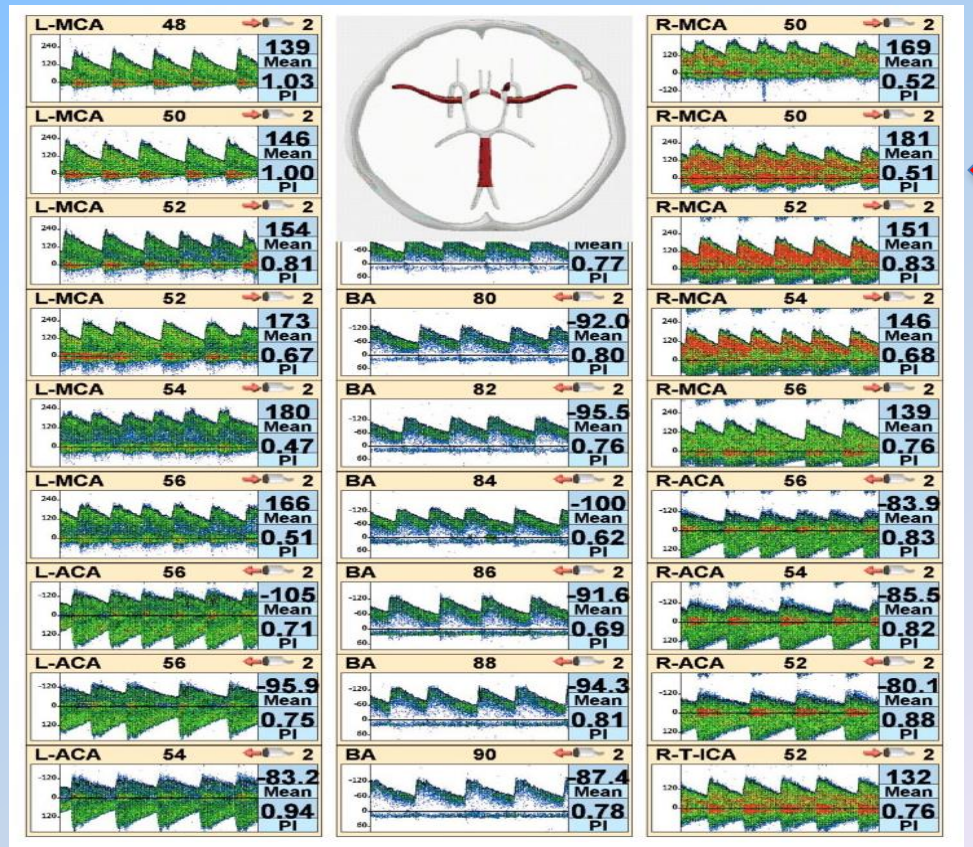




Application TCD in Pediatric SAH

TCD	01/23/2017	01/24/2017	01/25/2017	01/26/2017	01/27/2017	01/28/2017
R MCA	111 cm/s	126 cm/s	143 cm/s	181 cm/s	164 cm/s	127 cm/s
R ACA	78.9 cm/s	66 cm/s	81.6 cm/s	83.3 cm/s	83.3 cm/s	99 cm/s
R ICA	88.6 cm/s	92 cm/s	110 cm/s	132 cm/s	135 cm/s	111 cm/s
R PCA	72 cm/s	76.2 cm/s	103 cm/s	105 cm/s	104 cm/s	90 cm/s
R VA	53.9 cm/s	78.5 cm/s	110 cm/s	91.2 cm/s	91 cm/s	62 cm/s
L MCA	97.4 cm/s	141 cm/s	153 cm/s	180 cm/s	155 cm/s	125 cm/s
L ACA	58.1 cm/s	80.5 cm/s	91.6 cm/s	103 cm/s	83.3 cm/s	71 cm/s
L ICA	86.6 cm/s	105 cm/s	99.7 cm/s	109 cm/s	111 cm/s	105 cm/s
L PCA	55.4 cm/s	58.1 cm/s	94.7 cm/s	100 cm/s	104 cm/s	82 cm/s
L VA	35.4 cm/s	74.3 cm/s	87.8 cm/s	84.3 cm/s	83.5 cm/s	61 cm/s
Basilar	54.7 cm/s	83.5 cm/s	107 cm/s	100 mc/s	97.8 cm/s	79 cm/s

TCD	01/29/2017	01/30/2017	01/31/2017	02/01/2017	02/02/2017
R MCA	131 cm/s	131 cm/s	130 cm/s	130 cm/s	129 cm/s
R ACA	71 cm/s	72.4 cm/s	70.8 cm/s	82.4 cm/s	89.7 cm/s
R ICA	92 cm/s	91.6 cm/s	97.8 cm/s	99.3 cm/s	103 cm/s
R PCA	78 cm/s	77.8 cm/s	97.8 cm/s	95.9 cm/s	93.2 cm/s
R VA	74 cm/s	73.5 cm/s	79.3 cm/s	79.3 cm/s	67 cm/s
L MCA	119 cm/s	119 cm/s	142 cm/s	135 cm/s	117 cm/s
L ACA	69 cm/s	77 cm/s	91.2 cm/s	84.7 cm/s	80.8 cm/s
L ICA	99 cm/s	98.6 cm/s	104 cm/s	104 cm/s	105 cm/s
L PCA	85 cm/s	84.7 cm/s	96.3 cm/s	94.7 cm/s	94.7 cm/s
L VA	78 cm/s	72.8 cm/s	63.1 cm/s	85.1 cm/s	68.5 cm/s
Basilar	99 cm/s	98.6 cm/s	92 cm/s	87.4 cm/s	76.6 cm/s

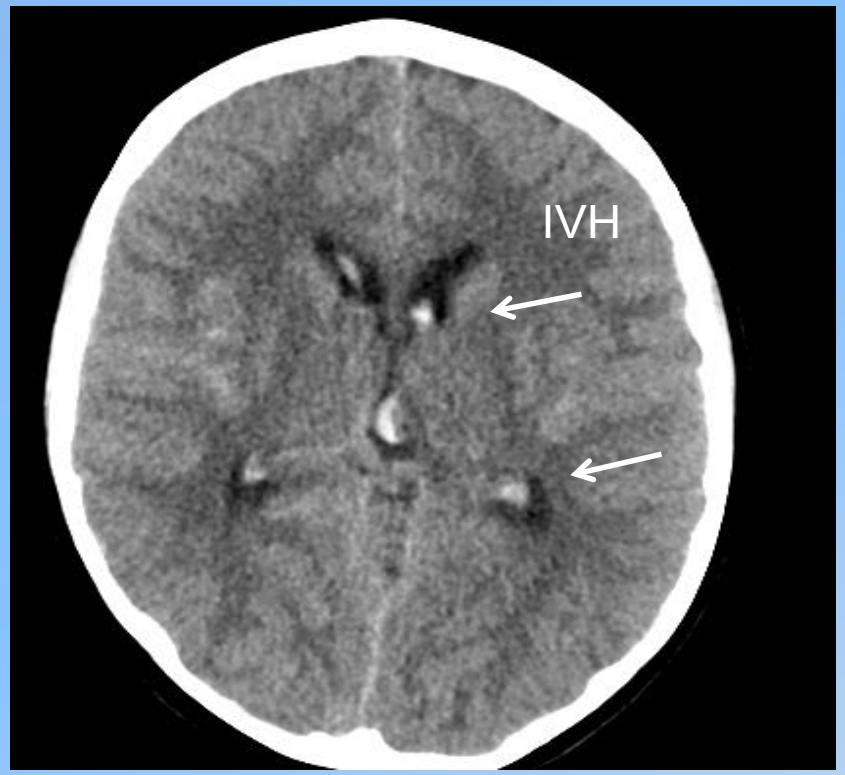


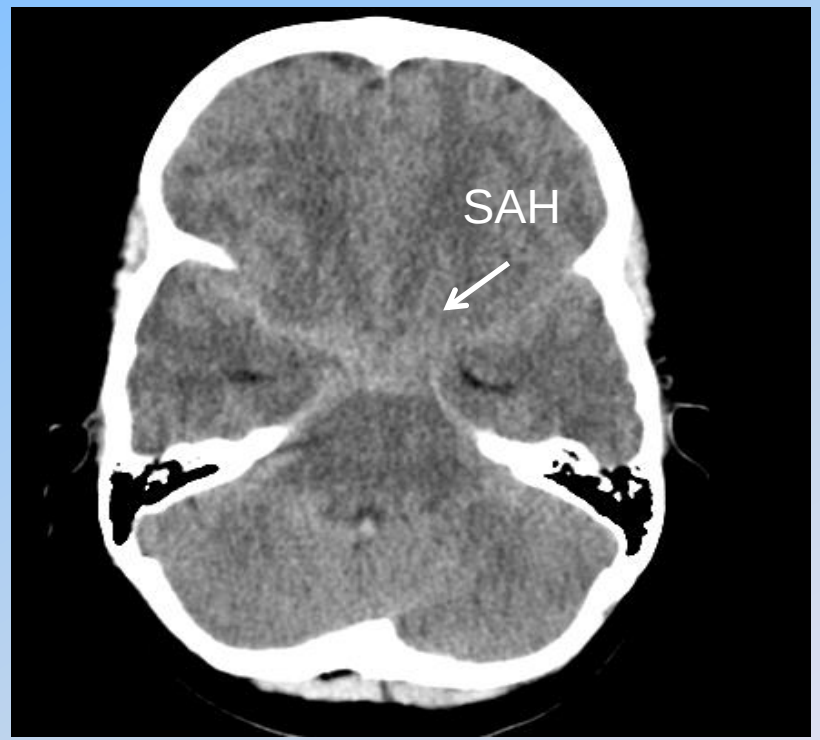
Age Norm: MCA 94(SD 10)

Clinical Case

- 8 year old previously healthy girl presented with acute onset of headache, altered mental status and respiratory failure
- Intubated for neurogenic pulmonary edema, started on epinephrine infusion for LV dysfunction (2 min CPR)
- Head CT - diffuse edema, extensive SAH and IVH
- CTA - complex AV fistula malformation arising from a ectatic left vertebral artery

Initial CT Head



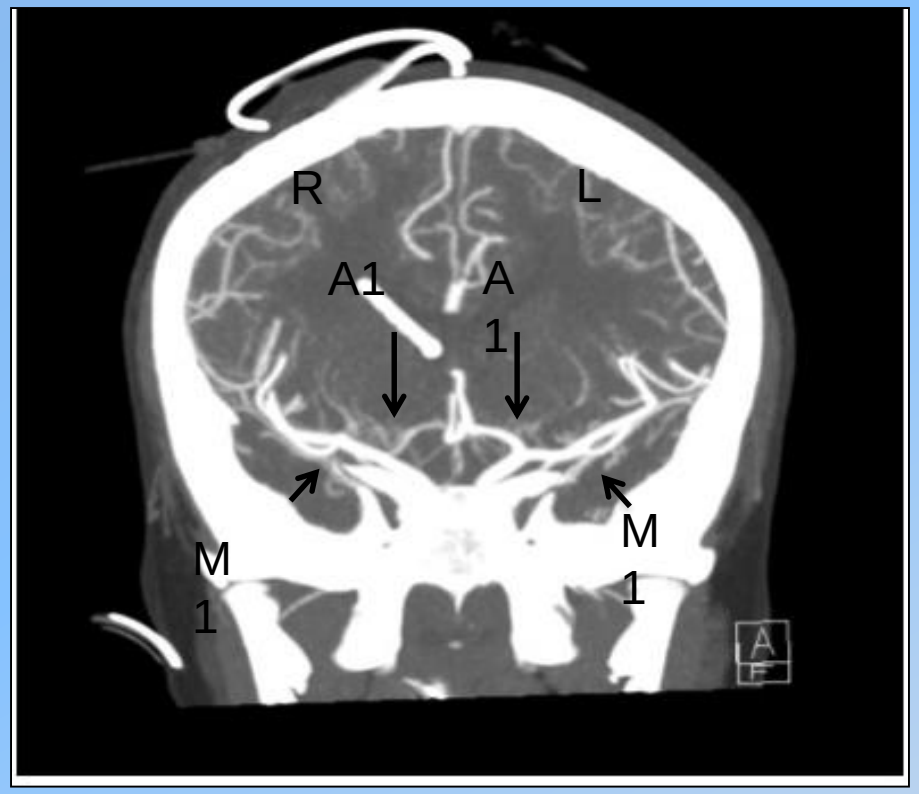


Complex AV fistula vascular malformation with multiple intranidal aneurysms (up to 8mm) with superficial and deep venous drainage

Initial CT Angiogram and TCD

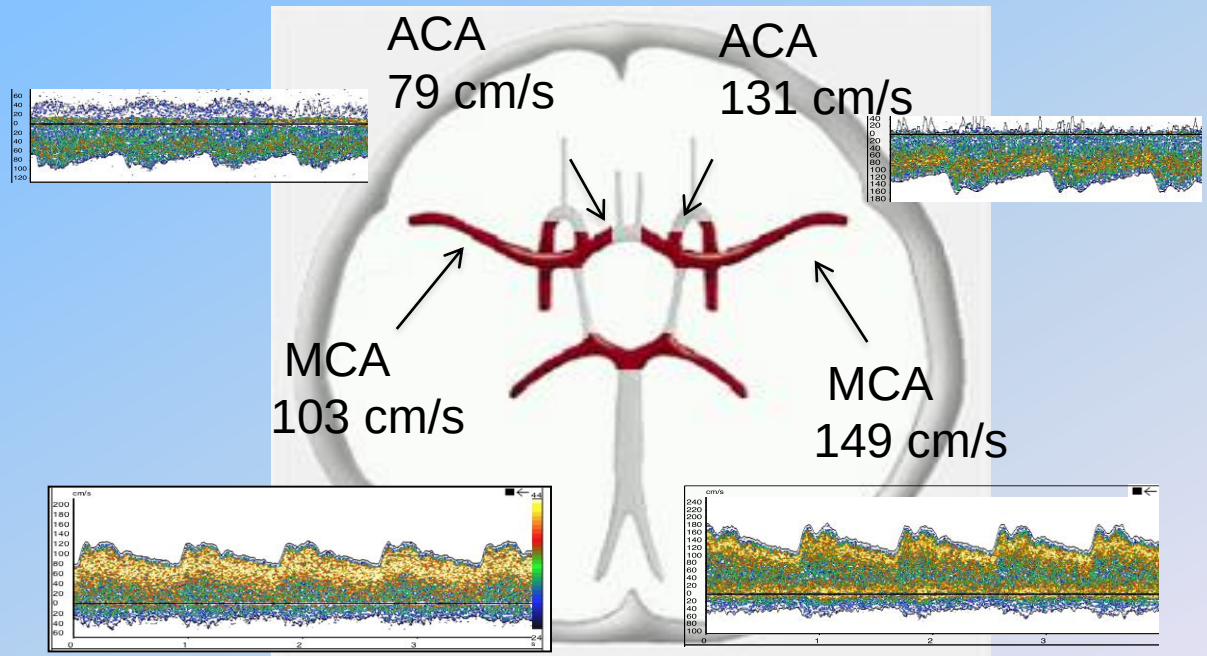
Age based mean TCD values MCA 97 cm/s (9), ACA 65 (13) *Bode H et al, Arch Dis Child 63:606-611, 1988*

Normal anterior circulation



R

L



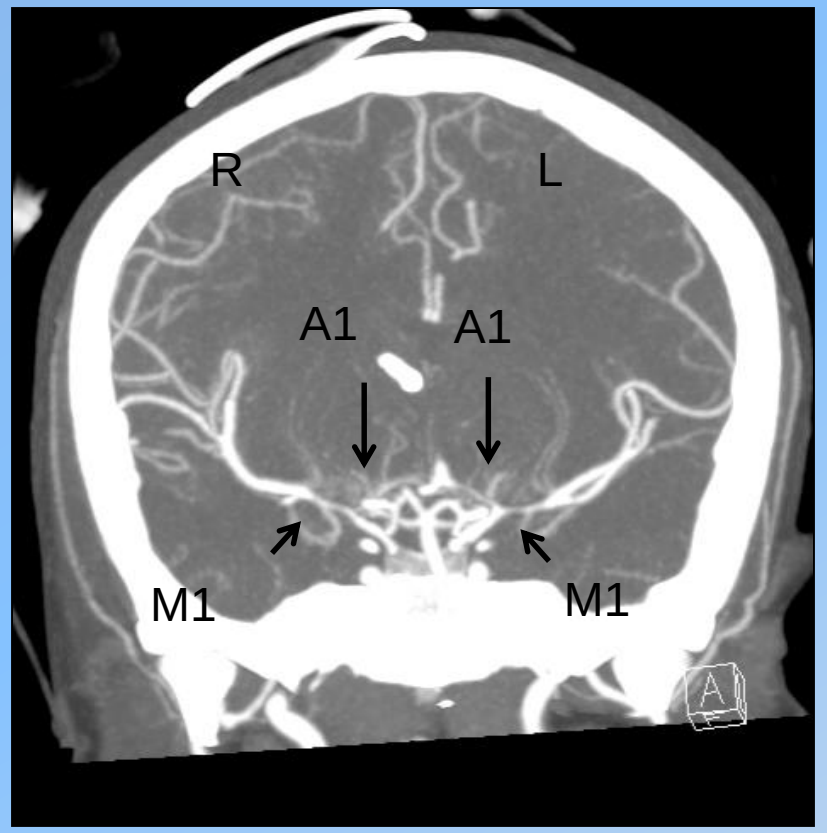
Lindegaard Ratio (EICA/MCA) = 2.4

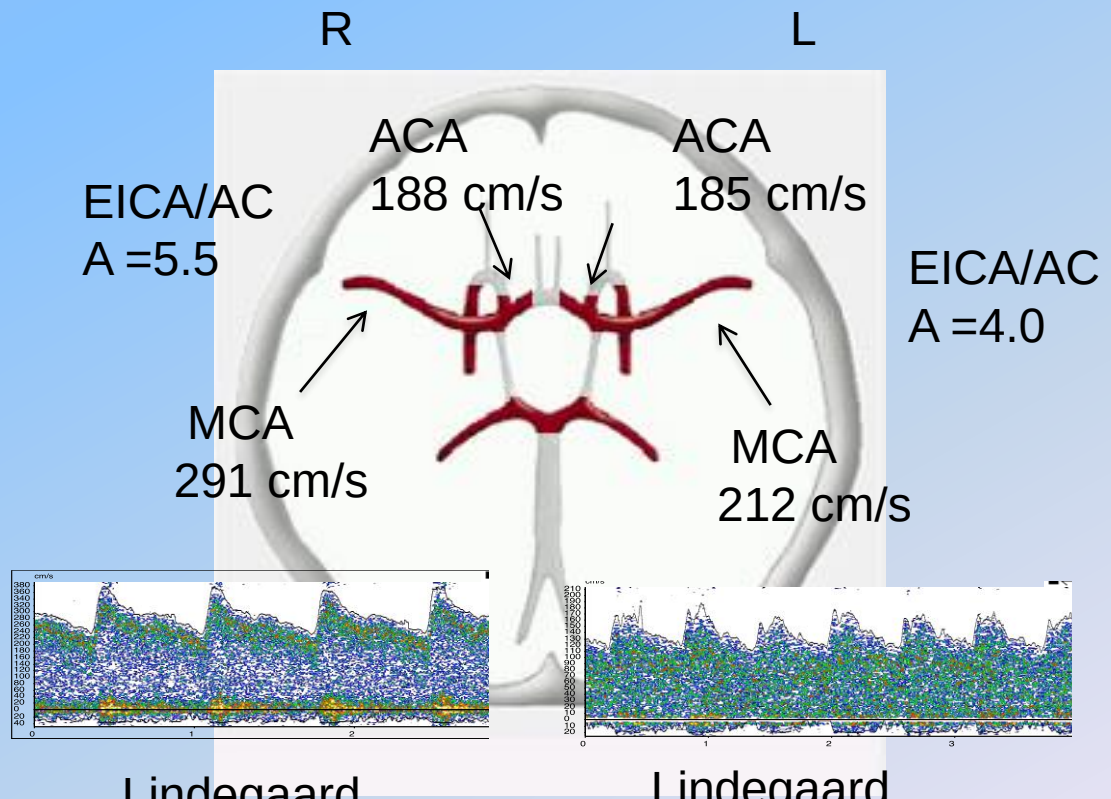
Lindegaard Ratio (EICA/MCA) = 2.9

Clinical Case – Initial Management

- EVD placed, treated for increased intracranial pressure, optimization of systemic cardiac output and cerebral perfusion pressure
- Recovered quickly – by HD#2 following commands, writing on notepad with clinical improved LV function
- HD #2 interventional radiology for embolization of AV fistula malformation
- Complicated by systemic hypertension, recurrent fistula hemorrhage and worsening neurologic exam and intracranial hypertension
- Continued poor neurologic exam - HD # 5 TCD performed by request of medical team consistent with anterior circulation cerebral vasospasm, CTA ordered

HD #5 – Correlation of CT angiogram with TCD





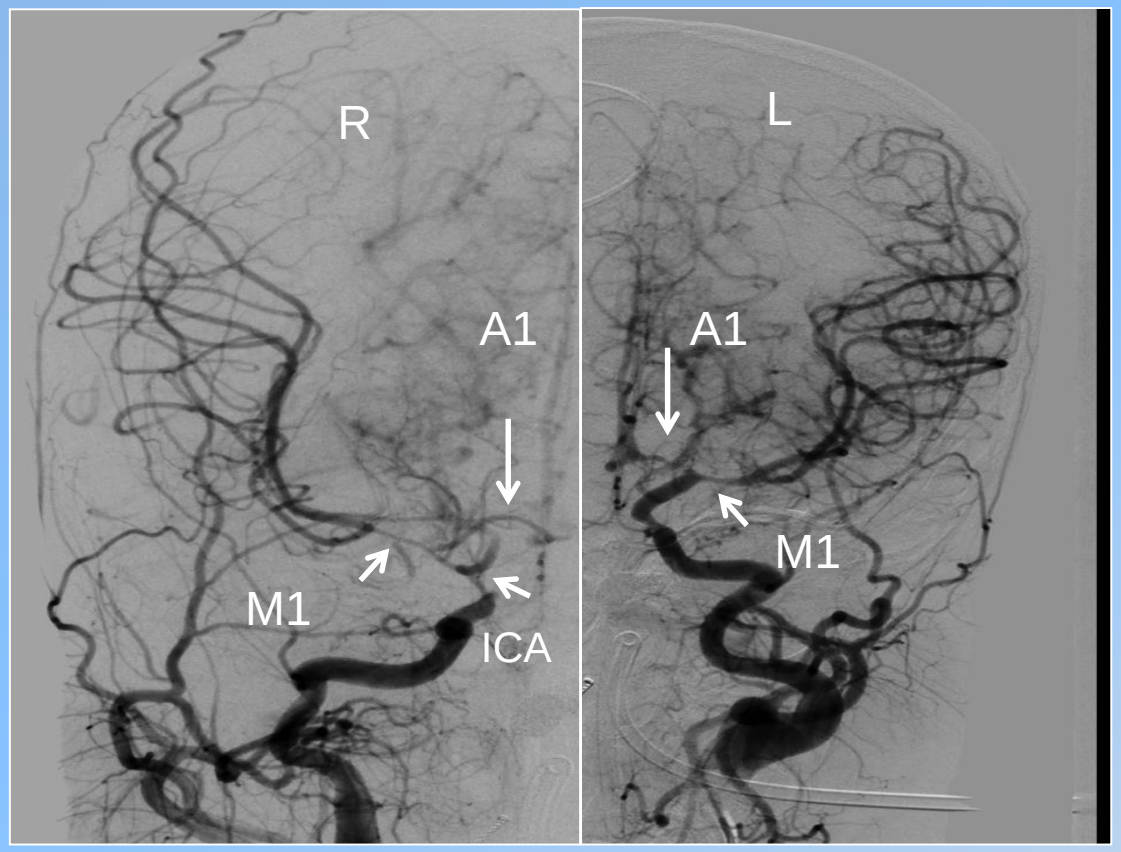
Lindegaard Ratio (EICA/MCA) = 8.5

Lindegaard Ratio (EICA/MCA) = 4.6

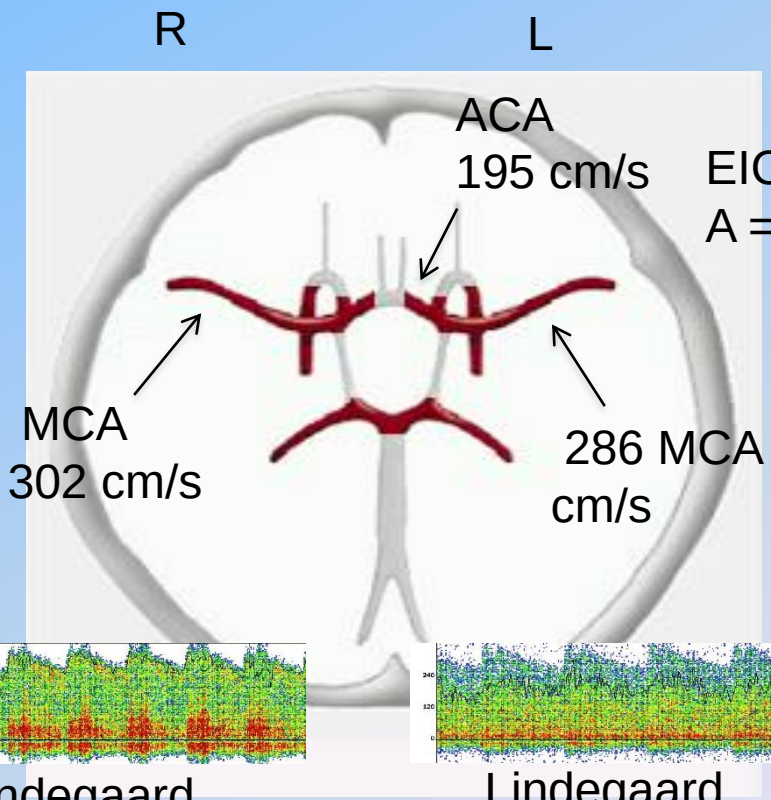
Clinical Case –Vasospasm Management

- Concern for developing ischemic changes in right frontal lobe basal ganglia and parietal convexities
- Induced systemic hypertension- systolic goal of 140-160 mm Hg, peripheral milrinone infusion
- HD #7 continued poor neurologic exam - cerebral angiogram with intra-arterial therapy

HD #7 – Intra-arterial Milrinone Injection and Correlation of Cerebral Angiography with TCD



1.5 mg milrinone into R distal ICA and 0.5 mg milrinone into L distal ICA



Lindegaard Ratio (EICA/MCA) = 10.1

Lindegaard Ratio (EICA/MCA) = 9.5

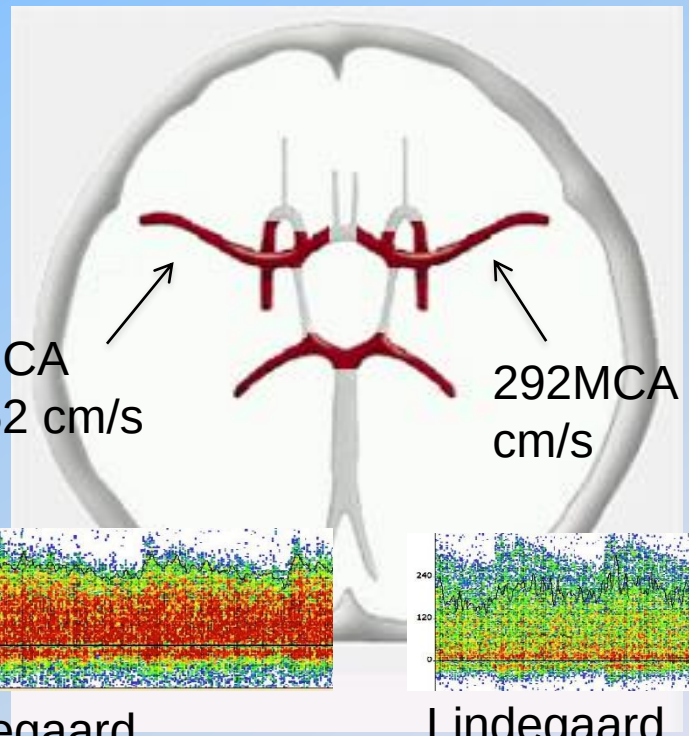
Clinical Case – Continued ICU Course

- 24 hours after IA therapy developed new right basal ganglia hemorrhage and increased ICP
- Left EVD placed
- Pentobarbitol coma for 7 days for refractory intracranial hypertension
- BP goal reduced to systolic 110-130 mmHg

HD #8 – Improving R MCA Vasospasm and New Acute R IVH and Basal Ganglia Parenchymal Hemorrhage

R L

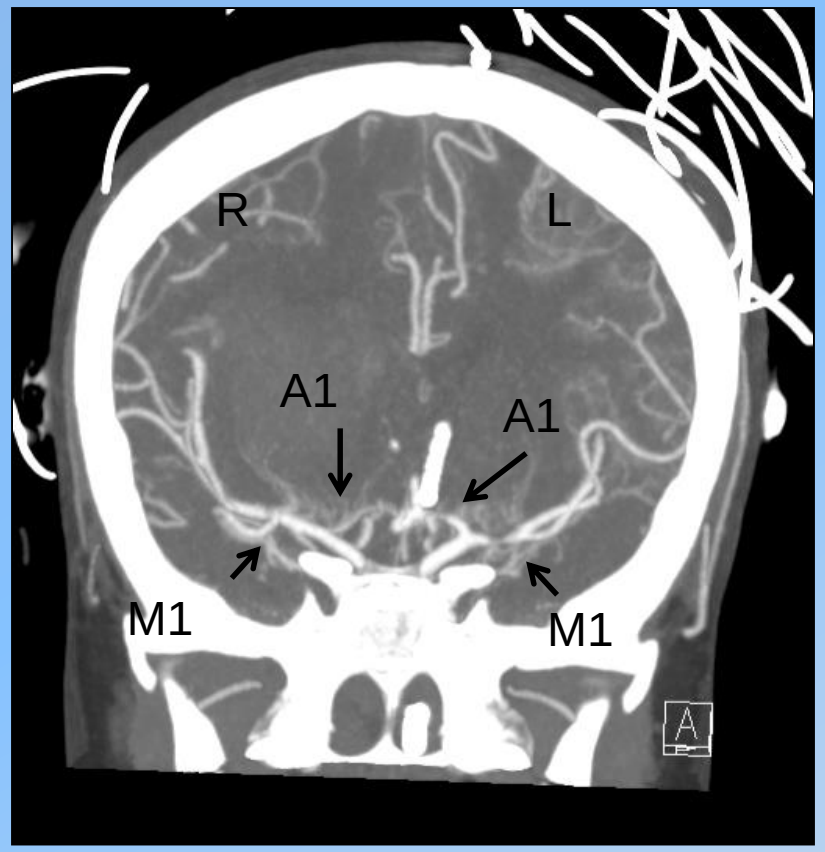
R L

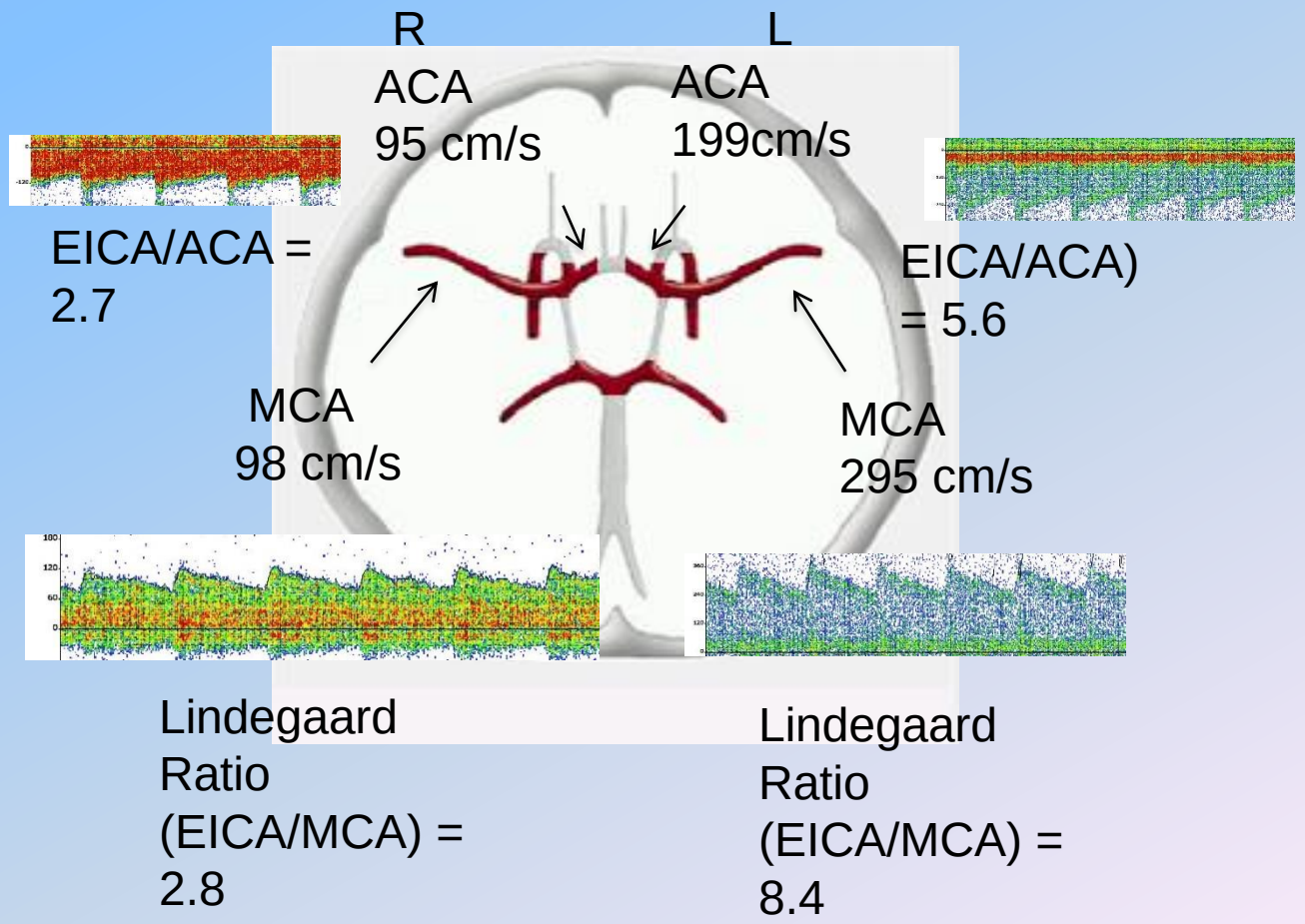


Lindegaard Ratio (EICA/MCA) = 5

Lindegaard Ratio (EICA/MCA) = 9.7

72-96 hrs Post Intra-arterial Milrinone
TCD Resolution of R MCA and ACA Vasospasm





Clinical Case – Outcome

- Continued on IV milrinone infusion with BP goal 100-130 mmHg
- Sonographic evidence of vasospasm in left MCA and ACA resolved by HD #25
- Required tracheostomy, gastrostomy tube, VP shunt and baclofen pump
- Discharged to inpatient rehabilitation
- AV fistula embolization successful with no recurrence

Summary and Conclusions

- Children are at risk for cerebral vasospasm after SAH due to spontaneous rupture of vascular malformations
- TCD can be a valuable tool in pediatric management of SAH
  - non-invasive assessment for cerebral artery vasospasm
  - guide clinical management decisions
  - monitoring response to IA therapy and vasospasm resolution
- Increased TCD velocities for age and a Lindegaard ratio > 4 demonstrated an excellent agreement with conventional gold standards of vasospasm assessment such as CT angiography and cerebral angiography

Summary and Conclusions

- Threshold TCD velocities (age based) and Lindegaard ratios need further validation in pediatric vasospasm with conventional imaging modalities
- Intra-arterial milrinone may be a therapeutic option for pediatric vasospasm management but warrants future study
- Children with spontaneous SAH due to vascular malformation rupture should receive serial TCDs for vasospasm monitoring to prevent delayed ischemic injury