

Neurologic aspects of PHACE

PHACE Family Conference, 2018

Geoffrey L. Heyer, MD
Pediatrics and Neurology
and The Ohio State University

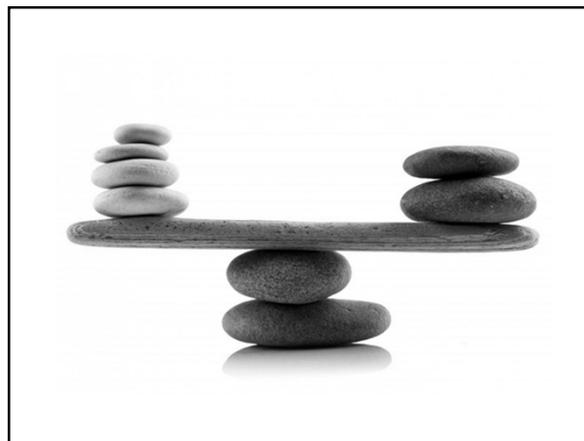


Topics to discuss

1. Potential risks of early childhood anesthesia
2. Aspirin therapy for vascular abnormalities of PHACE
3. Headache treatments (including magnesium)

Anesthesia and the developing brain

- Certain anesthesia medicines cause changes in the brain cells of developing animals
- Human studies suggest that anesthesia exposure can affect childhood brain development
- Studies in humans are not conclusive



Anesthesia study results

Always have a healthy degree of skepticism when reading (or hearing about) any research study.

There is no such thing as a perfect study in clinical medicine.

Anesthesia studies (Ing et al., 2014)

Compared children with anesthesia exposure before age 3 years to children without anesthesia exposure:

“Cases” had an increased risk of lower scores on neuropsychological testing.

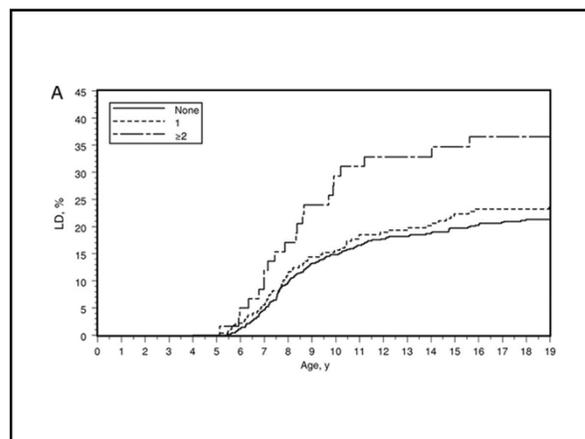
There were no differences in scholastic achievement test scores.

Anesthesia studies (Flick et al., 2011)

Compared 350 children with anesthesia exposure before age 2 years to 700 children without anesthesia exposure:

“Cases” with multiple anesthesia/surgery exposures had an increased risk of learning disorders.

Single exposures were not different than no exposure.



Anesthesia studies (pitfalls)

1. The *effects* of surgery (as opposed to anesthesia) were not analyzed.
2. The analyses do not account for specific *reasons* for multiple surgeries (and anesthesia exposures).
3. Other risk factors for learning disorders were analyzed in some studies, but not exhaustively.

Anesthesia studies (Sun et al., 2016)

Compared 105 sibling pairs where one sibling had inguinal hernia surgery with anesthesia before 3 years of age:

There were no statistically significant differences in IQ scores later in childhood (8-15 years of age)

Anesthesia studies (References)

1. Sun LS, Li G, Miller TL, et al. Association Between a Single General Anesthesia Exposure Before Age 36 Months and Neurocognitive Outcomes in Later Childhood. *JAMA*. 2016 Jun 7;315(21):2312-20.
2. Backeljauw B, Holland SK, Altaye M, Loepke AW. Cognition and brain structure following early childhood surgery with anesthesia. *Pediatrics*. 2015;136(1):e1-e12.
3. Ing C, DiMaggio C, Whitehouse A, et al. Long-term differences in language and cognitive function after childhood exposure to anesthesia. *Pediatrics*. 2012;130(3):e476-e485.
4. Hansen TG, Pedersen JK, Henneberg SW, et al. Academic performance in adolescence after inguinal hernia repair in infancy: a nationwide cohort study. *Anesthesiology*. 2011;114(5):1076-1085.
5. Flick RP, Katusic SK, Colligan RC, et al. Cognitive and behavioral outcomes after early exposure to anesthesia and surgery. *Pediatrics*. 2011;128(5):e1053-e1061.
6. Bartels M, Althoff RR, Boomsma DI. Anesthesia and cognitive performance in children: no evidence for a causal relationship. *Twin Res Hum Genet*. 2009;12(3):246-253.

Gadolinium (contrast) with MRI risks

Studies suggest that gadolinium can deposit in some brain structures when it is given at an early age.

This finding seems to be most prominent among patients treated for brain tumors.

It is not clear whether this occurs in all children or what the consequences are when this occurs.



“Feed and wrap”

Alternatives to anesthesia exist for MRI.

The feed and wrap technique refers to the use of swaddling and feeding a young child to induce natural sleep.

Other behavioral techniques (practice and desensitization) have been used in young children who are awake during the scan.

When should aspirin be given?



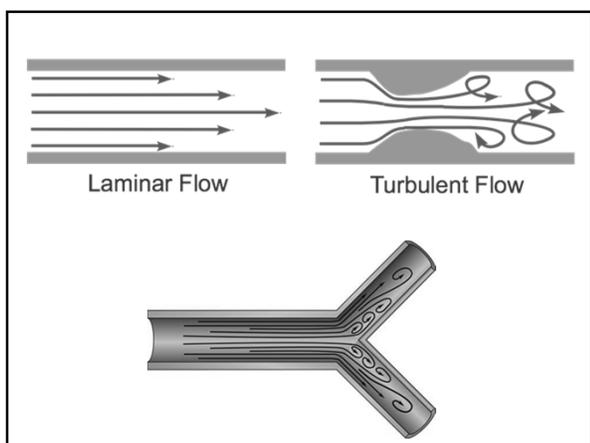
Question: When should a patient with PHACE syndrome and cerebral vascular abnormalities be prescribed aspirin?

Correct answer: Nobody knows.

Remainder of discussion: Opinions about aspirin therapy

Opinions about aspirin therapy

- ▶ Certain blood vessel changes can increase the risk of clot formation.
- ▶ Aspirin is given to decrease that risk.
- ▶ Other medicines also decrease clot risks.
- ▶ Potential benefits should outweigh potential risks (much like anesthesia exposure)



Opinions about aspirin therapy

- ▶ Most pediatric neurologists will start aspirin (or a different medicine) if there are arterial changes that suggest an increased stroke risk
 - ▶ Moyamoya changes
 - ▶ Some cases of artery narrowing (stenosis)
 - ▶ Arterial changes that cause excessive turbulence
 - ▶ Rare cases where blood flow changes direction

Opinions about aspirin therapy

- ▶ When patients have had prior strokes, have known clots in the arterial system, or have high-risk heart problems, medicines other than aspirin are usually considered.
- ▶ The primary risk of aspirin therapy is bleeding (easy bruising, excessive bleeding, stomach ulcer)
- ▶ Other risks (Reye syndrome) may be discussed.

Headaches and PHACE



- ▶ Patients with PHACE may have an increased vulnerability to headaches.
- ▶ Results from a prior survey suggest that more than 60% of patients with PHACE have headaches
- ▶ The average age of headache onset was 48.8 months

Headache classification

- ▶ Headaches can be categorized as primary or secondary
- ▶ Categories are defined by the absence or presence, respectively, of a clear underlying cause
- ▶ Primary headaches may have a genetic cause. Mom or dad might have headaches also

Migraine (and migraine-like) headaches

- ▶ Nausea with or without vomiting
- ▶ Sensitivity to bright light and loud noise
- ▶ Throbbing pain, usually on one side of the head
- ▶ Pain aggravated by activity
- ▶ Headaches last at least a few hours
- ▶ Some patients have aura

Tension-type headaches

- ▶ Sensitivity to bright light or loud noise may be present
- ▶ Tension-type pain without throbbing
- ▶ Usually affects both sides of the head
- ▶ Pain is less intense than migraine pain
- ▶ Aura is never present

When to treat headaches

- ▶ Whenever headaches interfere with normal activities (sleep, school, play, etc.), some form of treatment should be considered.
- ▶ Treatments include medicines that are taken as soon as the headache starts (abortives) and treatments that are taken every day to prevent headaches (prophylaxis).
- ▶ "Behavioral" treatments are also helpful

Behavioral treatments

- ▶ Good sleep practices
- ▶ Good fluid hydration
- ▶ No missed meals
- ▶ Stress management techniques
- ▶ Trigger avoidance

Abortive treatments (treating at onset)

- ▶ Simple analgesics (e.g., ibuprofen)
- ▶ Combination analgesics (sometimes include caffeine)
- ▶ Triptan medicines (neurology prescribed).
 - ▶ It is important that an expert prescribe this medicine when patients have or may have vascular abnormalities.

Prophylactic treatments (headache prevention)

- ▶ Magnesium
- ▶ Riboflavin (vitaminB2)
- ▶ Amitriptyline (Elavil)
- ▶ Topiramate (Topamax)
- ▶ Propranolol (Inderal)
- ▶ Cyproheptadine (Periactin)

Does magnesium help headaches?

Different magnesium formulations have demonstrated effectiveness in decreasing headaches.

Magnesium is taken every day.

A single pediatric study (ages 3 to 17 years) showed a decrease in headache frequency and severity using magnesium oxide.

Diarrhea is the most common side effect.

Does magnesium help headaches?

Adult studies use different forms of magnesium.

Magnesium oxide may have lower bioavailability (meaning less magnesium goes into the bloodstream).

It is unlikely that funding will be available for pediatric studies of magnesium and headache, so we rely on adult studies.

Headache “Red Flags”

- ▶ New-onset headaches
- ▶ Change in neurologic exam
- ▶ Change in headache character
- ▶ Headaches caused by positional change
- ▶ Underlying illness (including PHACE)

Questions?

.....

.....

