Fetal hydrocephalus

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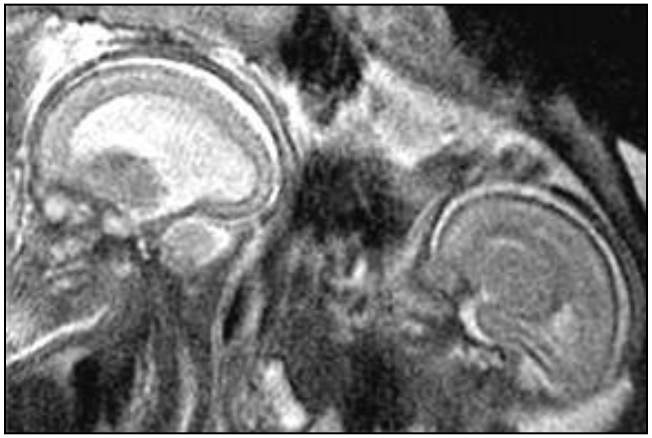
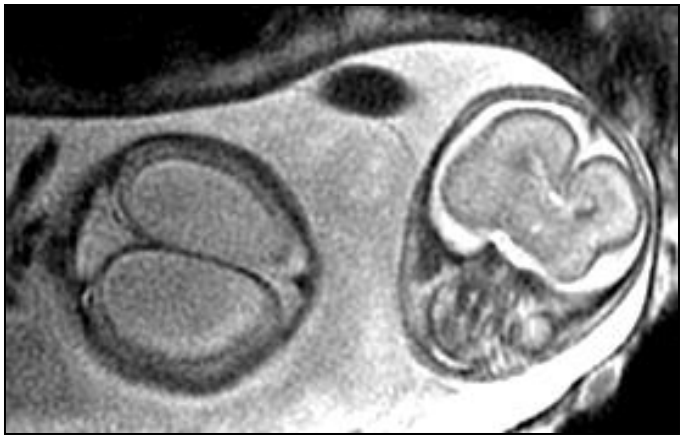
Fetal hydrocephalus





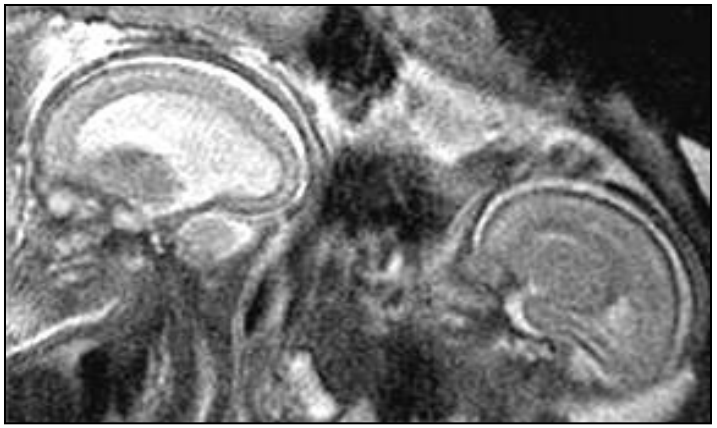
- Not uncommon (MMC/Chiari 2 excluded)
- Either mid- or late gestation, never acute
  - ultrasonography at 12w, 22w, 32w,
- Definition: hydrocephalus versus “ventriculomegaly”
- Ability to recover
- Aqueductal stenosis as the major etiology

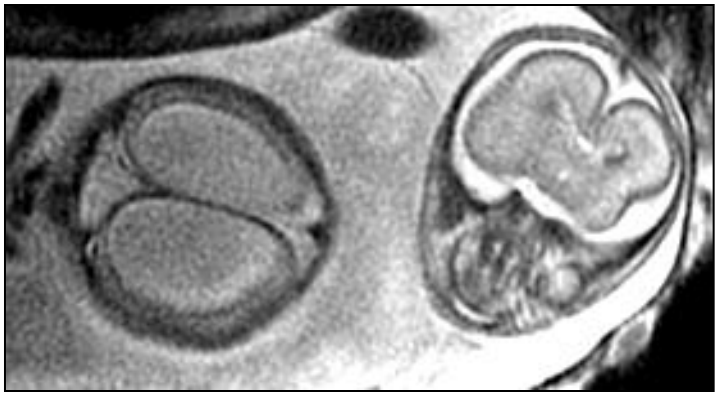
Fetal hydrocephalus: material

- 41 cases in two groups, no overlap
  - 30 cases mid-gestation (19.4w-26.4w)
  - 11 cases late gestation (32.2w-38.4w)
- Follow-up, treatment: 8 cases
  - 5 cases mid-gestation (22.5w-26.2w)
  - 3 cases late gestation (38w-38.4w)

Fetal hydrocephalus vs fetal ventriculomegaly

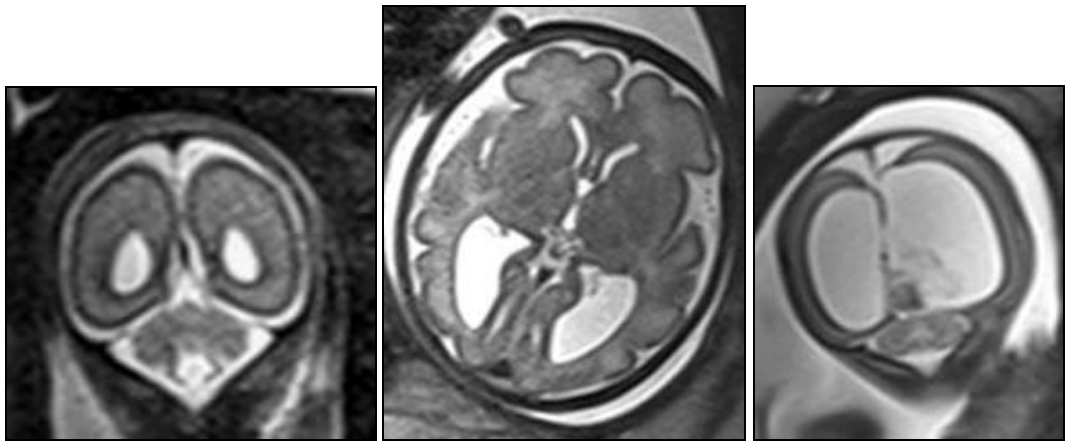
1. Disproportionate ventriculomegaly
2. Effacement of pericerebral spaces
3. Cerebral mantle: thinning, dehiscence
4. An identified cause
5. Rupture of septum pellucidum
6. Macrocephaly
7. Follow-up and response to treatment





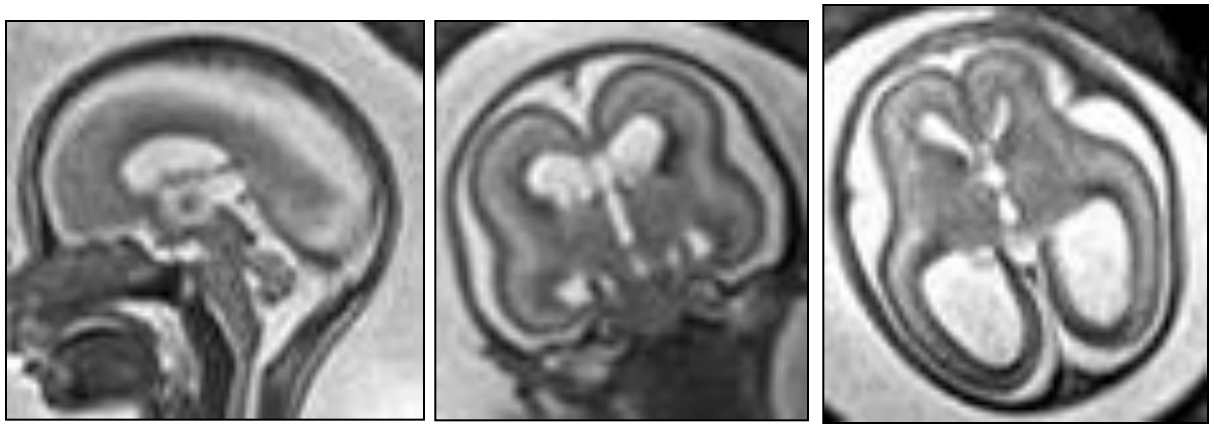
Fetal ventriculomegaly

- Measured at the atrium, on largest side
- Usually 5-8mm throughout gestation
- May be benign (reversible) or destructive
- By convention
  - normal <10mm
  - mild VM 10-15mm
  - moderate 15-20mm
  - severe > 20mm



Fetal hydrocephalus

- Measured at the atrium, on the largest side
  - symmetric in 9/41
- Active expansion of ventricles (obstructive)
- Cases of hydrocephalus
  - in 34/41: at, or larger than, 20mm
  - smallest 14.1mm (familial aqueductal stenosis)



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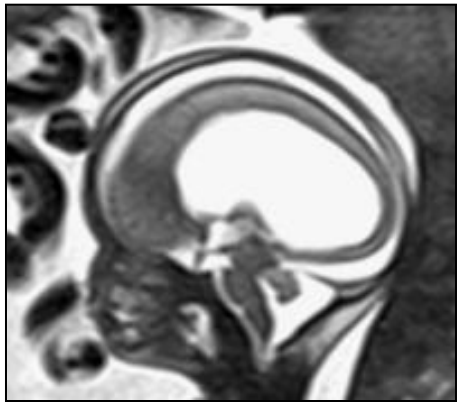

Fetal hydrocephalus vs fetal ventriculomegaly

1. Disproportionate ventriculomegaly
2. Effacement of pericerebral spaces
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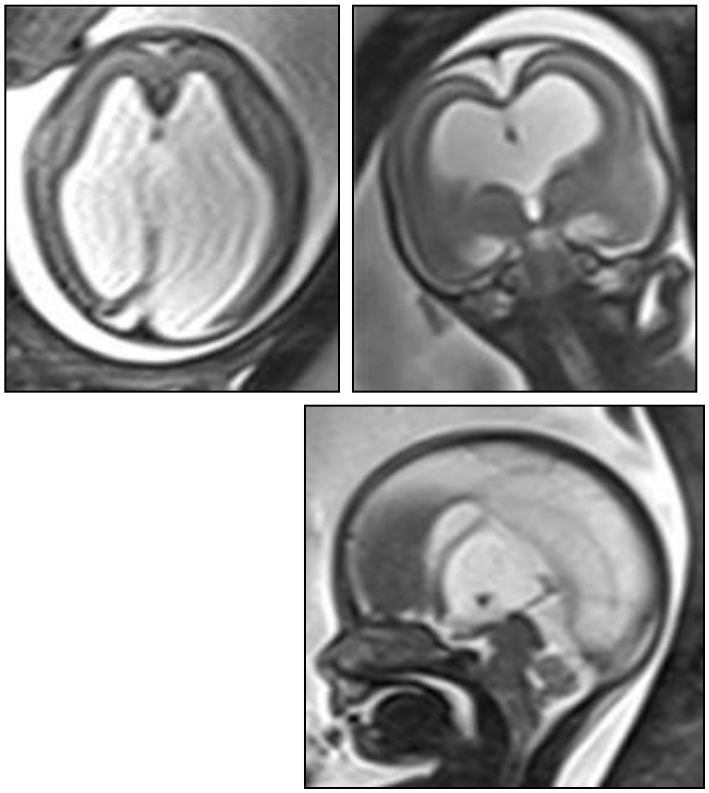


Wall defect: always early hydrocephalus with effaced pericerebral spaces

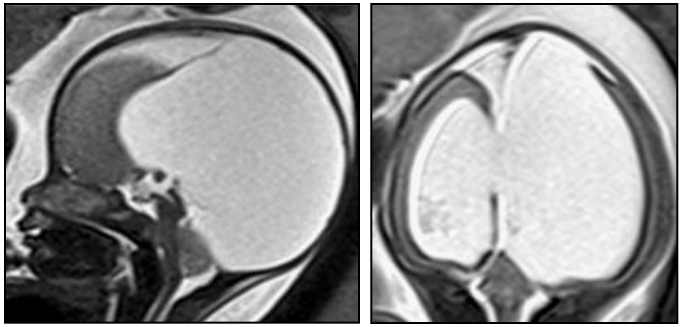
Fetal hydrocephalus: an identified cause

- Mid-gestation
  - aqueductal stenosis 28/30
    - hemorrhage in 1
  - others 2/30: AVF torcular (1), retro-cerebellar cyst (1)
- Late gestation
  - aqueductal stenosis 6/11
    - hemorrhage in 4
  - others 5/11:
    - vermian mass (1),
    - cysts (1 each): suprasellar, quadrigeminal, latero- and retro-cerebellar

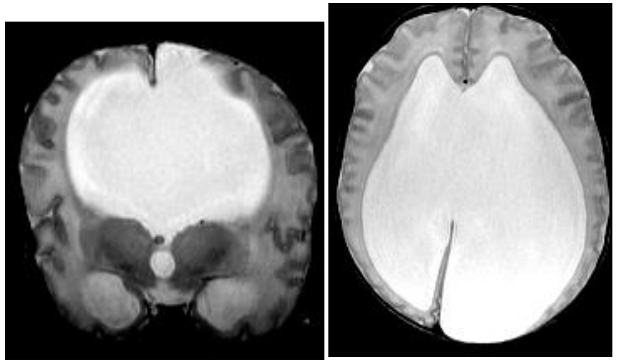
Fetal hydrocephalus: head measurements

- Evaluation of macrocephaly
  - from BPD and HC
  - HC = ½ (BPD+ FOD) x 3.14
- Quantified in weeks from average
  - but wide variations from average
- Results
  - BPD consistently above average
  - for HC, mostly increased but 6/40 are at, or slightly below average
    - poor cerebral growth due to hydrocephalus?

Normal twin	Hydro twin
+ 0.2	+ 3
+ 2.4	+ 4.3
+ 4.3	+ 3.5
+ 2.2	+ 4

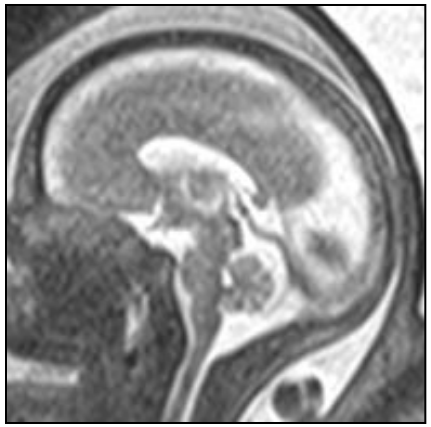


Fetal hydrocephalus: severity

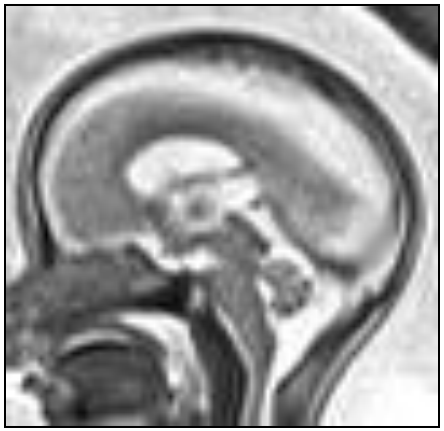


- Moderate:
  - patent cerebral mantle
  - patent pericerebral spaces
- Severe:
  - effaced pericerebral spaces
  - dehiscent cerebral mantle: postero-medial mantle thinning and disruption (early only?)
- Mid- versus late gestation

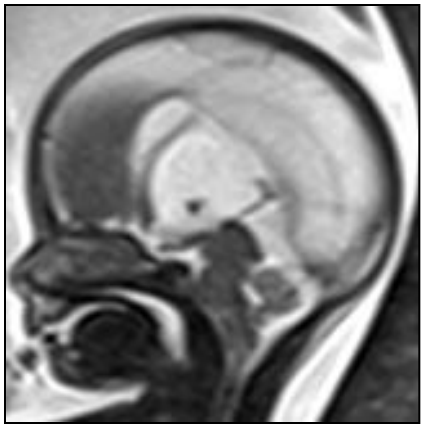
Humphreys et a. Focal cerebral mantle disruption in fetal hydrocephalus. Pediatr Neurol 2007, 36 (4):236-243



normal (24w)

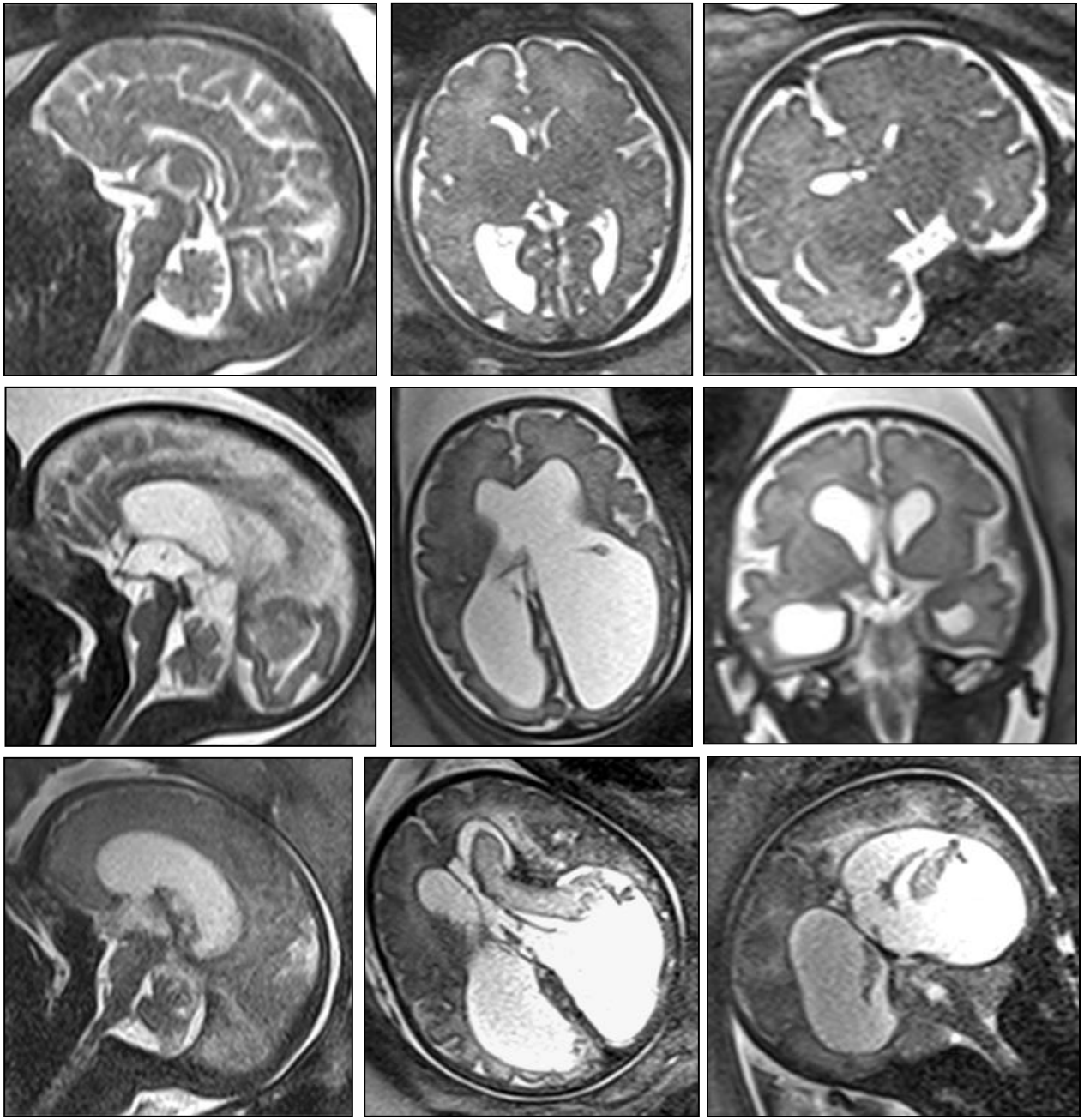


moderate (23w)
aqueductal stenosis



severe (21.5w)
aqueductal stenosis

Mid-gestation



normal (35w)

moderate (32.4w)
aqueductal stenosis

severe (35.4w)
hemorrhage
aqueductal stenosis

Late gestation

Fetal hydrocephalus: morphological severity

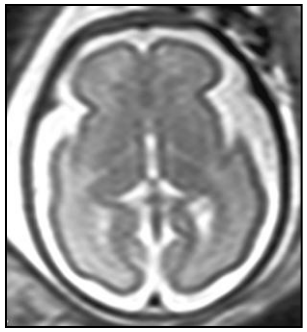
- Moderate:
  - patent cerebral mantle,
  - patent pericerebral spaces
- Severe:
  - defect cerebral mantle
  - effaced pericerebral spaces
- Mid- versus late gestation

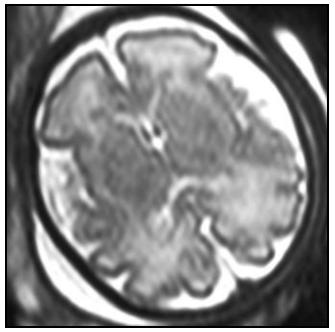
	moderate	severe
Mid-gestation	13/30	17/30
Late gestation	5/11	6/11

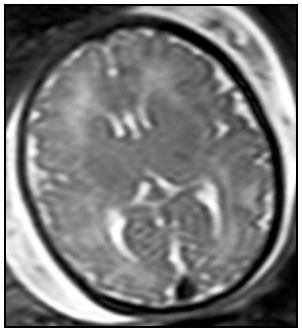
- What is the fetal pericerebral space due to?
- Wide in fetuses, not in preterms
  - post-natal CBF change: pulmonary, atrial foramen, ductus arteriosus
    - → drop of venous pressure
  - different absorption mechanisms? (absorption routes, AQPs)
  - elastic skull, amniotic pressure

FETUS

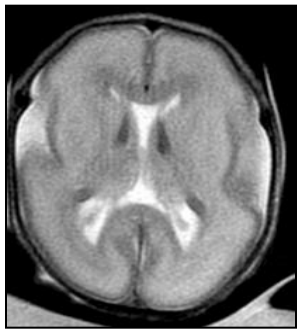

24w


28w

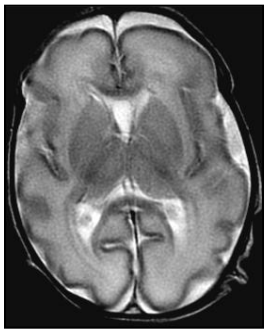

33w


37w

PREM


25w


28w


33w

Fetal hydrocephalus: morphology summary

- Mid-gestation: 30 cases
  - overwhelmingly idiopathic aqueductal stenosis (27/30)
    - 1 each: AVF, midline cyst, hemorrhage
  - more often severe (17 vs 13)
- Late gestation 11 cases
  - idiopathic aqueductal stenosis 2/11 only
    - other 9: hemorrhagic 4, tumor 1, midline cysts 4
  - slightly more often severe
- Mantle dehiscence: specific for early occurrence?

Fetal hydrocephalus: evolution, outcome

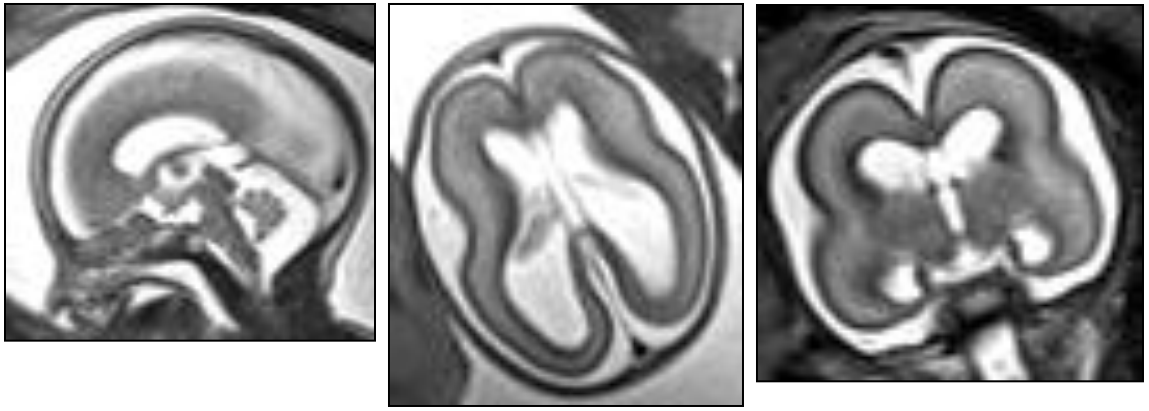
- Only 8/40 cases F/U and treatment
  - 5 cases mid-gestation
  - 3 cases late gestation
- Mid-gestation 5
  - 2 moderate hydrocephalus → fair/good morphologic outcome 2
  - 3 severe hydrocephalus → poor morphologic outcome 2, deceased 1
- Late gestation 3
  - 3 moderate hydrocephalus → good morphologic outcome 3

Mid-gestation histogenesis

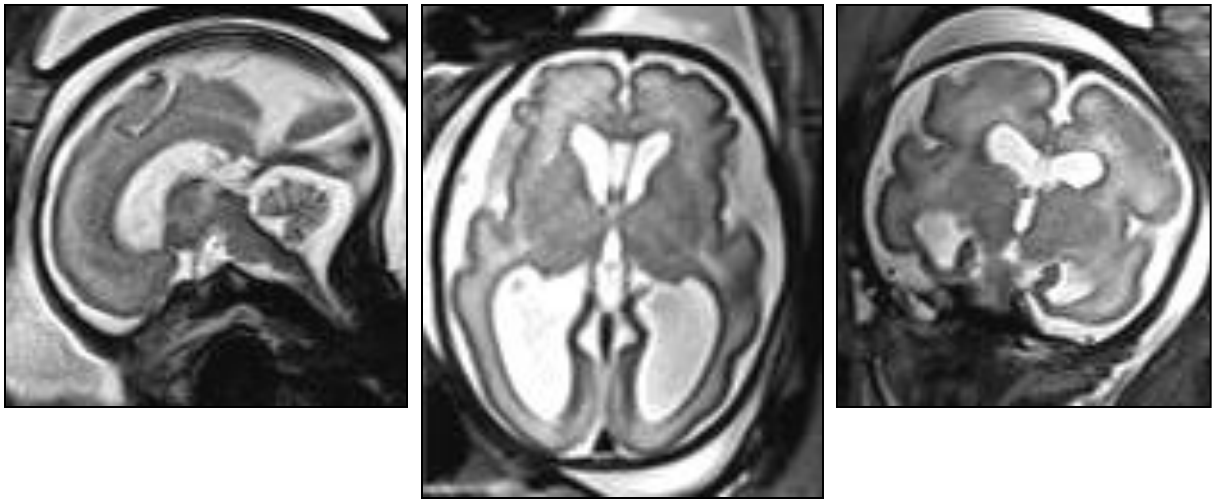
- Weeks 20-27
- Neuronal migration essentially completed
  - period of thalamo-cortical connectivity (weeks 22-27)
  - initiates cortical organization with later association-commissural connectivity
- Early cortical vascularization
  - week 22 onward
- Germinal matrices
  - mantle matrix → 28w

Late gestation histogenesis

- Weeks 31-47
- Intense connectivity-synaptogenesis
  - cortical organization with long association-commissural (27-32w) and short association (32-47w)
  - associated developing sulcation
- Intensely developing oligodendroglia
- Developing cortical vascularization
- Germinal matrices
  - ganglionic eminence matrix regresses <36w

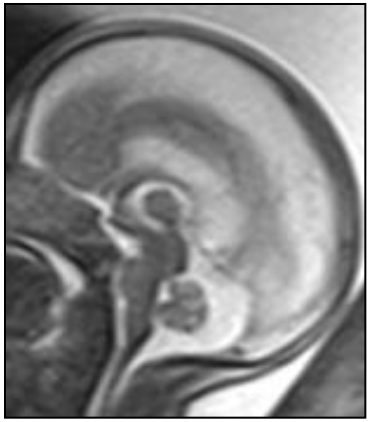
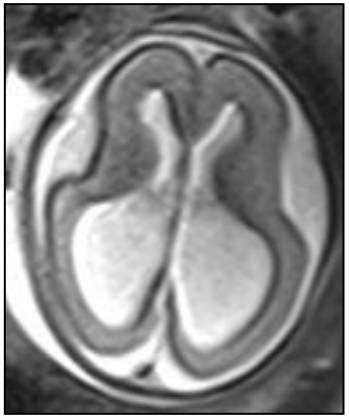
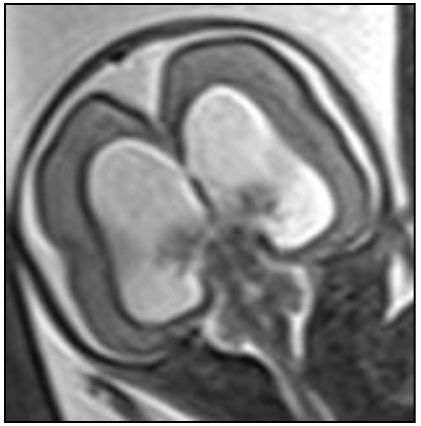


moderate, 23w
(aqueductal stenosis)

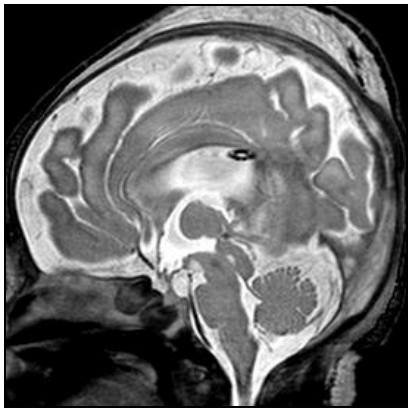
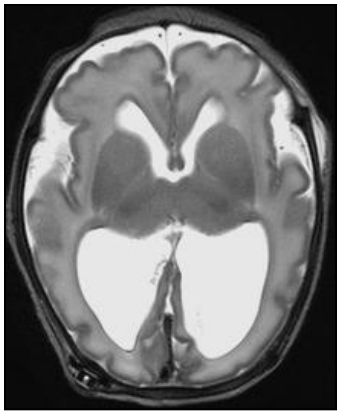
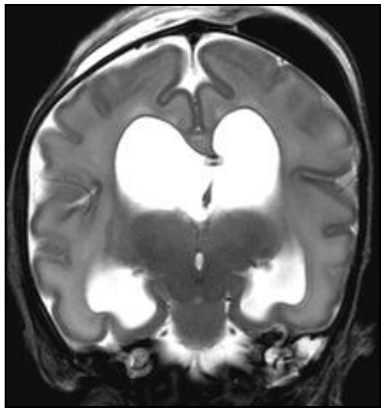


same 30w, delayed but
developing sulcation

Early hydrocephalus does not prevent, or only in part, the development of connectivity and sulcation

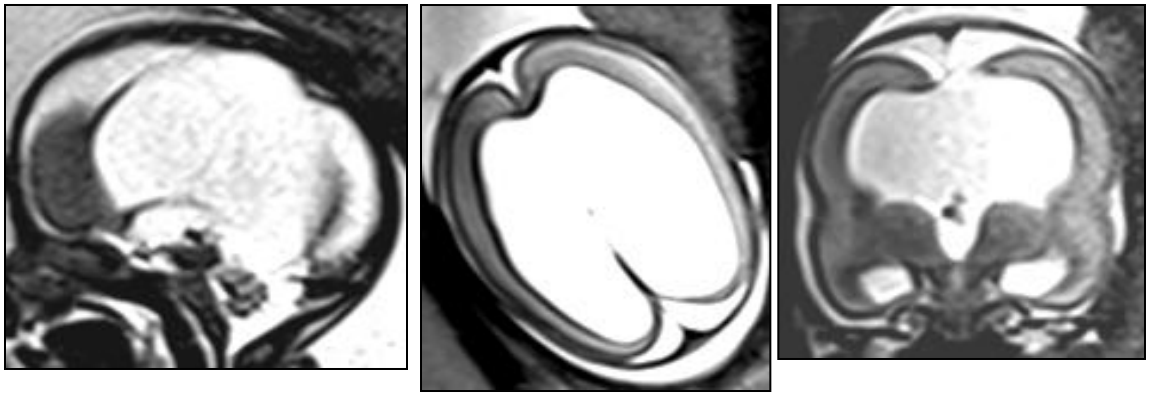
moderate, 25.4w
aqueductal stenosis

same, 3 d
sulcation
post shunt

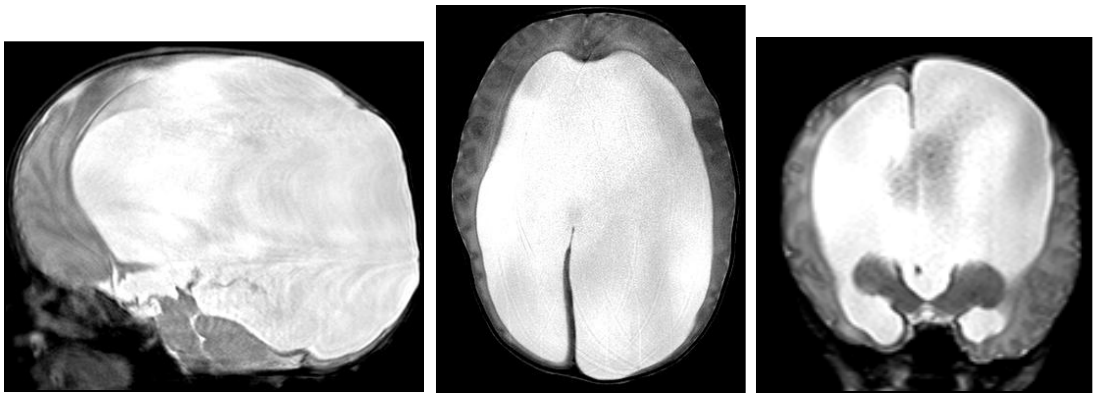
same, 8m/o

Early moderate
Follow-up

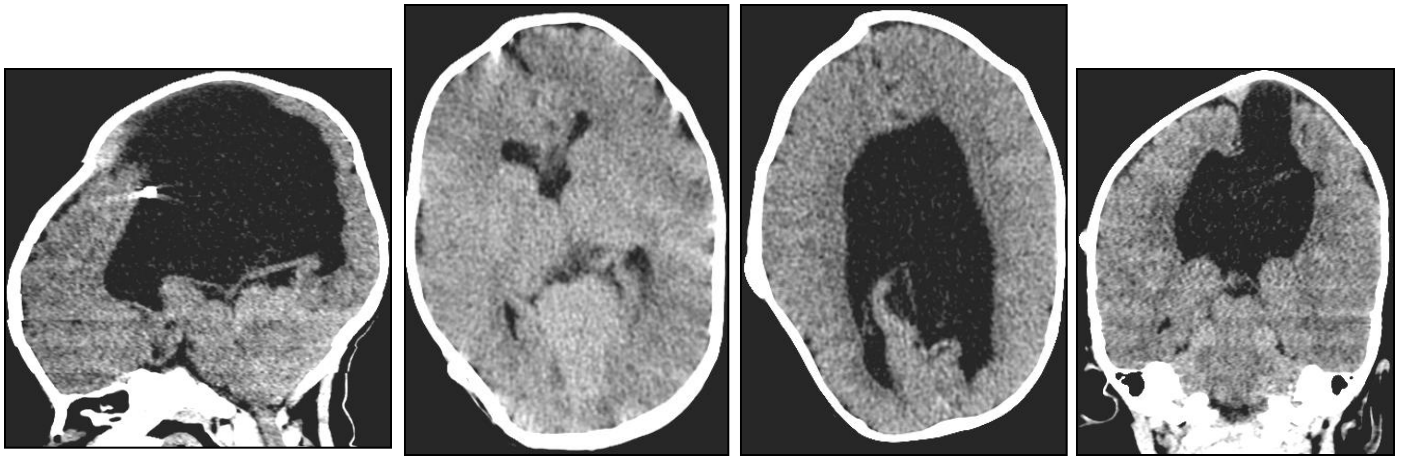


severe, 23.4w
aqueductal stenosis

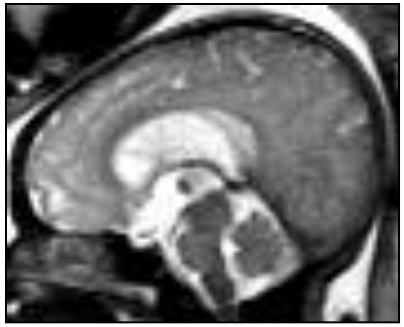
Early severe
Follow-up



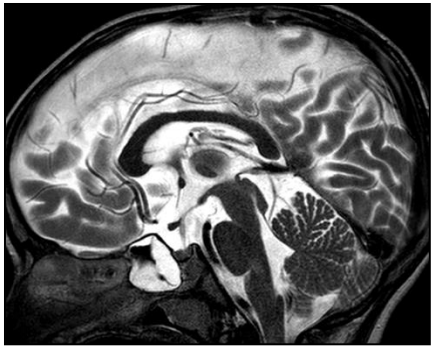
same,1d
change in posterior fossa
partial sulcation



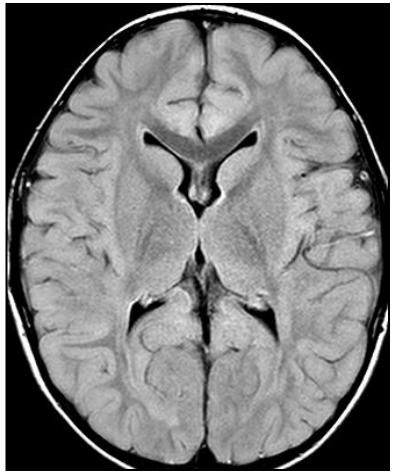
same, 4m
post VP shunt



38w



5y

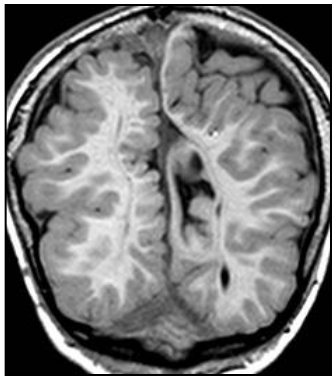


late moderate aqueductal stenosis

Late gestation Follow-up

12d

congenital, but possibly early severe



4y

Potential factors of recovery

- Persistent expression of signaling pathways for axon growth/ branching
- Axonal progression and branching mostly subcortical
- Myelin: most potent inhibitor of axonal development
  - induced by neuronal activity
  - myelin associated inhibitors MAIs limit potential for axon development
    - essentially no hemispheric myelination before term

Bonfanti Prog Neurobiol 2006; Fancy et al Ann Rev Neurosc 2011;
Akbik et al Exp Neurol 2012

Fetal hydrocephalus: causes

- Mid-gestation: 30 cases
  - overwhelmingly idiopathic aqueductal stenosis (27/30)
    - 1 each: AVF, midline cyst, hemorrhage
- Late gestation 11 cases
  - idiopathic aqueductal stenosis only 2/11
    - others: hemorrhagic 4/11, tumor 1,midline cysts 4
    - quite similar to post-natal

Aqueductal stenosis: etiologies

- Possible mechanisms
  - primarystenosis, or secondary to hydrocephalus
  - TORCH: toxoplasmosis, mumps
  - undocumented hemorrhage, inflammation
  - low grade glioma/hamartoma
  - malformative (Dorothy Russell, 1955)
- Context
  - twin pregnancies (10%), siblings (1 family)
- Feto-pathology & animal models
  - subcommissural organ SCO
  - ependymal denudation

- Castañeyra-Perdomo et al. *Alterations of the subcommissural organ in the hydrocephalic human fetal brain*. Devel Brain Res 1994, 79:316-20
- Jimenez et al. *A programmed ependymal denudation precedes congenital hydrocephalus in the hyh mutant mouse*. J Neuropathol Exp Neurol 2001, 60(11):1105-19
- Galarza: *Evidence of the subcommissural organ in humans and its association with hydrocephalus*. Neurosurg Rev 2002, 25:205-15
- Dominguez-Pinos et al. *Ependymal denudation and alterations of the subventricular zone occur in human fetuses with a moderate communicating hydrocephalus*. J Neuropathol Exp Neurol 2005, 64(7):595-604
- Sival et al. *Neuroependymal denudation is in progress in full-term human foetal spina bifida aperta*. Brain Pathol 2011, 21:163-79
- Rodriguez et al. *A cell junction pathology of neural stem cells leads to abnormal neurogenesis and hydrocephalus*. Biol Res 2012, 45:231-41
- McAllister. *Pathophysiology of congenital and neonatal hydrocephalus*. Semin Fet Neonat Med 2012, 17:285-94

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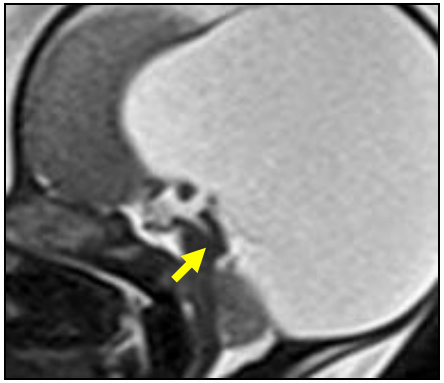
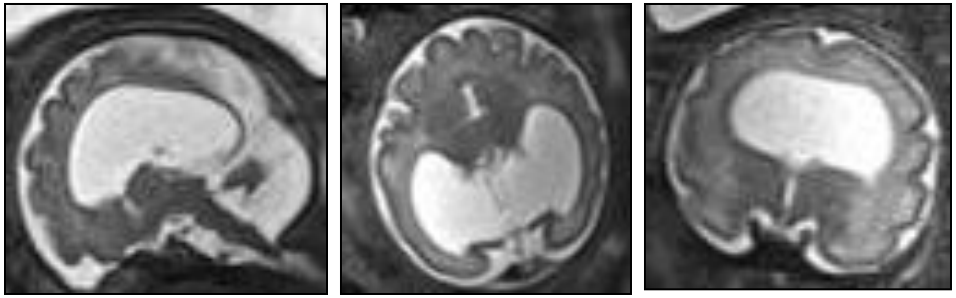
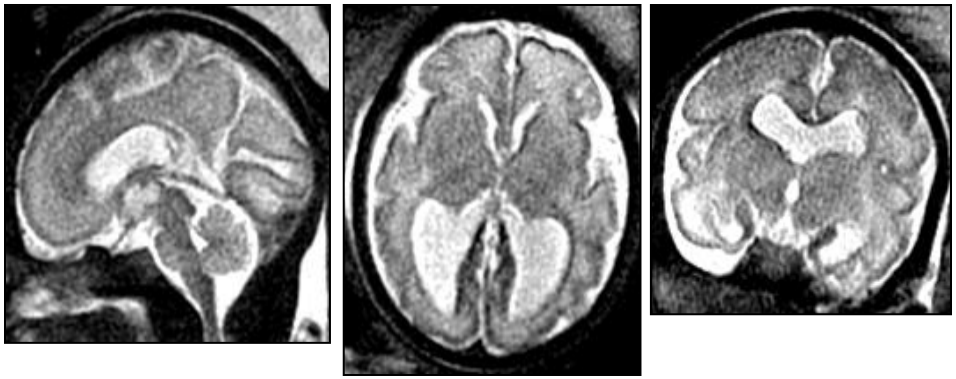


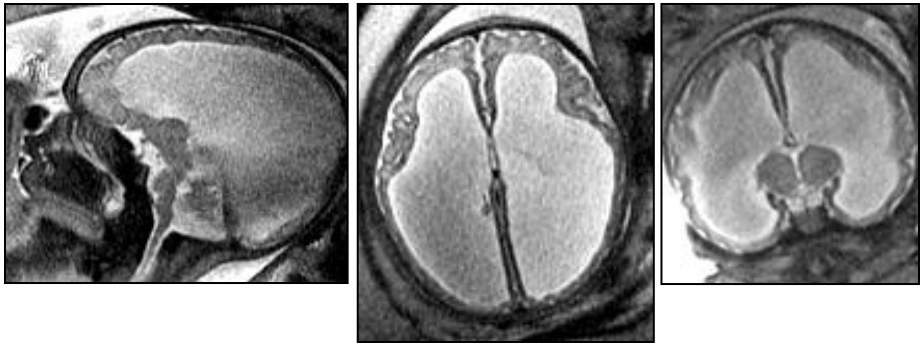


holoprosencephaly
33,5w

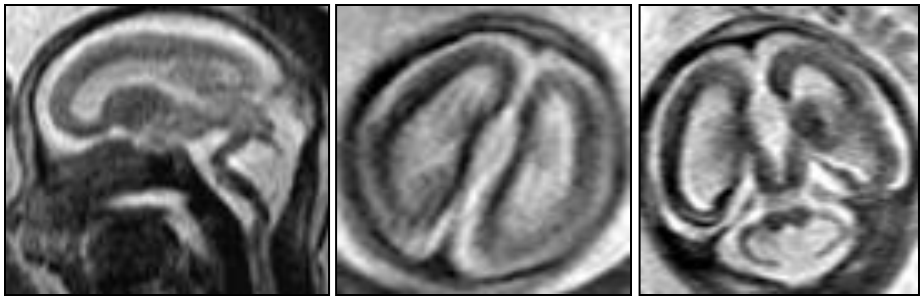


septo-optic dysplasia 30w

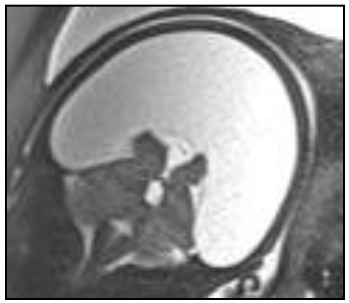
What is not hydrocephalus



L1CAM/CRASH
(X-linked hydrocephalus)



Walker Warburg 31w



hydranencephaly
35w

To try to summarize

- Patterns of early (mid-gestation) fetal hydrocephalus seem to be characteristic
  - overwhelmingly due to “idiopathic” aqueductal stenosis
    - ependymal denudation, SCO
  - well defined severity patterns
    - related morphological recovery potential
- Late fetal hydrocephalus more similar to post-natal
- Pathogenesis still more difficult than in post-natal
- Fairly reliable diagnostic features