This lecture was very straightforward. Most slides are completely on point with what he said. Lots of example pictures.

Congenital Malformations of the CNS

APPROVED

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- **I have no financial interests or relationships to disclose**

- **Reference:**
  - **Robbins and Cotran Pathologic Basis of Disease 8th Edition**

Objective of Today's Lecture

- **At the end of the lecture be able to recognize and describe the basic pathology of some common congenital CNS disorders:**
  - **Neural Tube Defects**
  - **Forebrain Anomalies**
  - **Posterior Fossa Anomalies**
  - **Syringomyelia, Hydromyelia**
  - **Perinatal Brain Injury**

Forebrain= everything supra (above)-tentorial

CNS Malformations

- **Pathogenesis and etiology largely unknown**
- **Genetic and environmental factors**
  - **Toxins, infectious agents**

these are theories of causation, but overall we don't really have definitive, provable reasons for these malformations

Neural Tube Defects

- **Failure of a portion of the neural tube to close**
- **May involve a combination of neural tissue, meninges, overlying bone and soft tissues**

Embryologically:
2-4th wk of gestation
CNS begins developing.
What was once a flat piece of tissue has to role up into a tube that is your spinal canal/cord

Neural Tube Defects

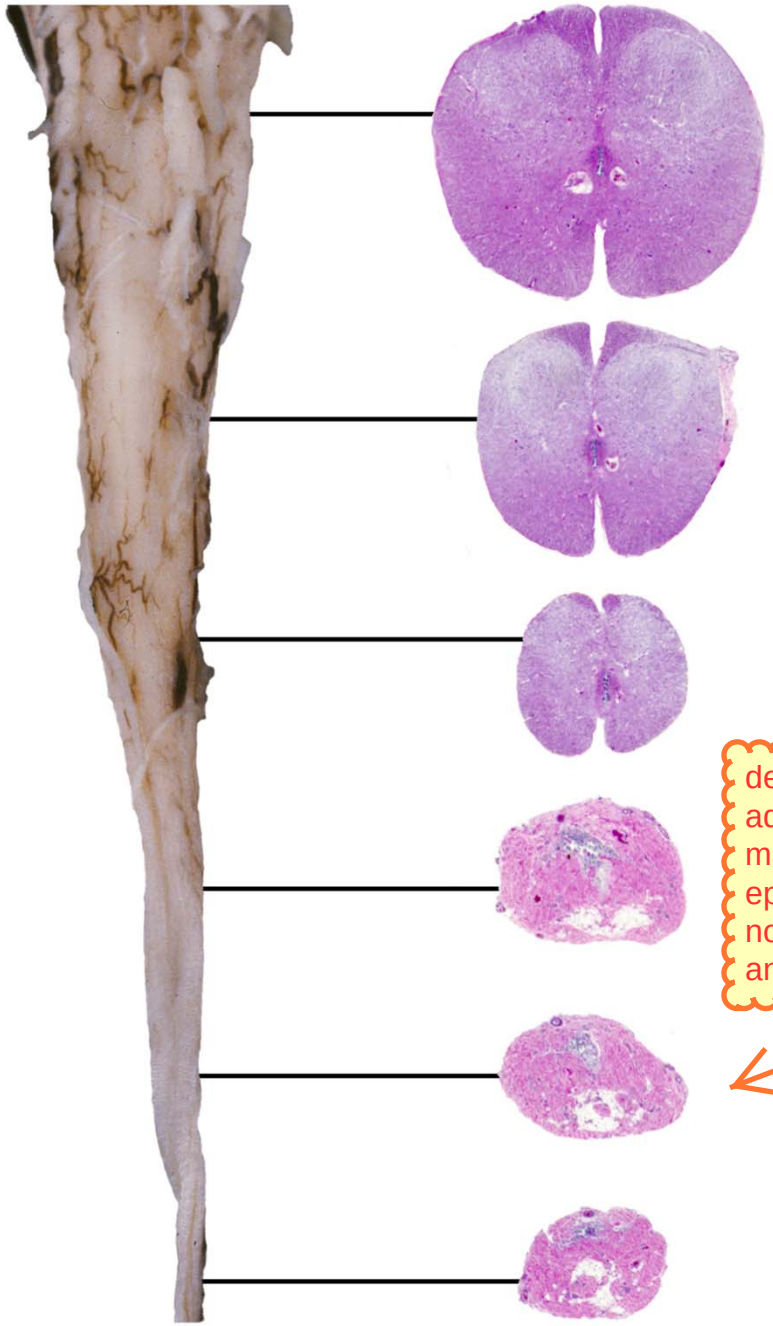
- **Primary neurulation:**
  - **Elevation, approximation and closure of the neural folds to form the neural tube**

- **Secondary neurulation:**
  - **Neural development caudal to the caudal neuropore after the termination of primary neurulation**
  - **Formation of conus medullaris and filum terminale**

distal spinal cord

fibrous termination of the dural mater that will insert into sacrum

Conus medullaris



dense fibrous and adipose tissue, maybe some ependymal canal. no spinal cord anymore

Filum terminale

Common operable lesion is a TETHERED CORD, where the filum terminale is stretched and may be thickened or contain too much adipose. (If not fixed as a child, could lead to spinal cord injuries while growing into an adult.

Neural Tube Defects

- **Anencephaly**
- **Encephalocele**
- **Spinal Dysraphism**
  - **Spina bifida occulta**
  - **Meningocele**
  - **Myelomeningocele**
  - **Lipomyelomeningocele**

complete absence of a brain

herniation of brain through skull defect

he'll go into further explanation of these later in the lecture.

Anencephaly

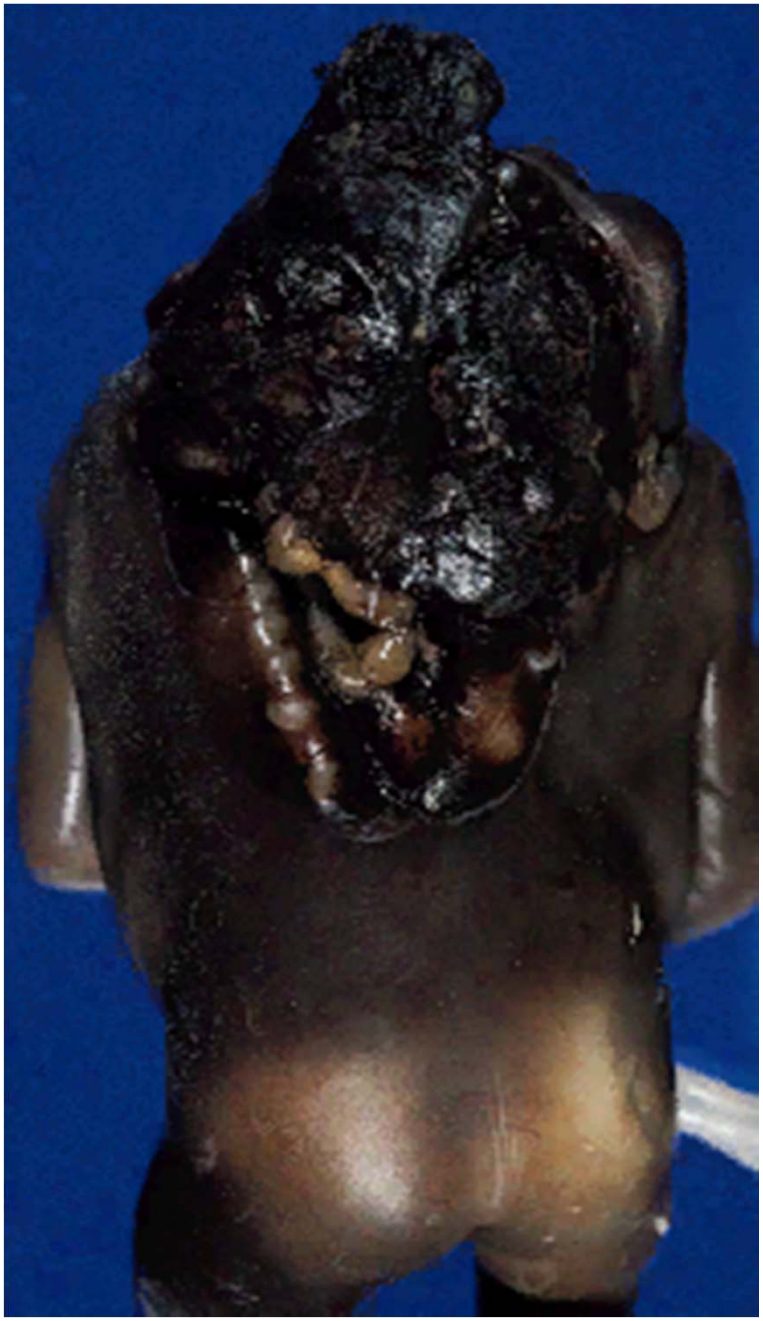
not compatible with life- duh.

with this, as well as many other neural tube defects, they usually occur very early, before the woman even knows she is pregnant

- **Absence of the brain and calvarium**
- **1 to 5 per 1000 births**
- **More common in females**
- **Develops at approximately 28 days gestation**
- **Area cerebrovasculosa:**
  - **vascularized and disorganized brain tissue**

you would see this histologically

example of anencephaly

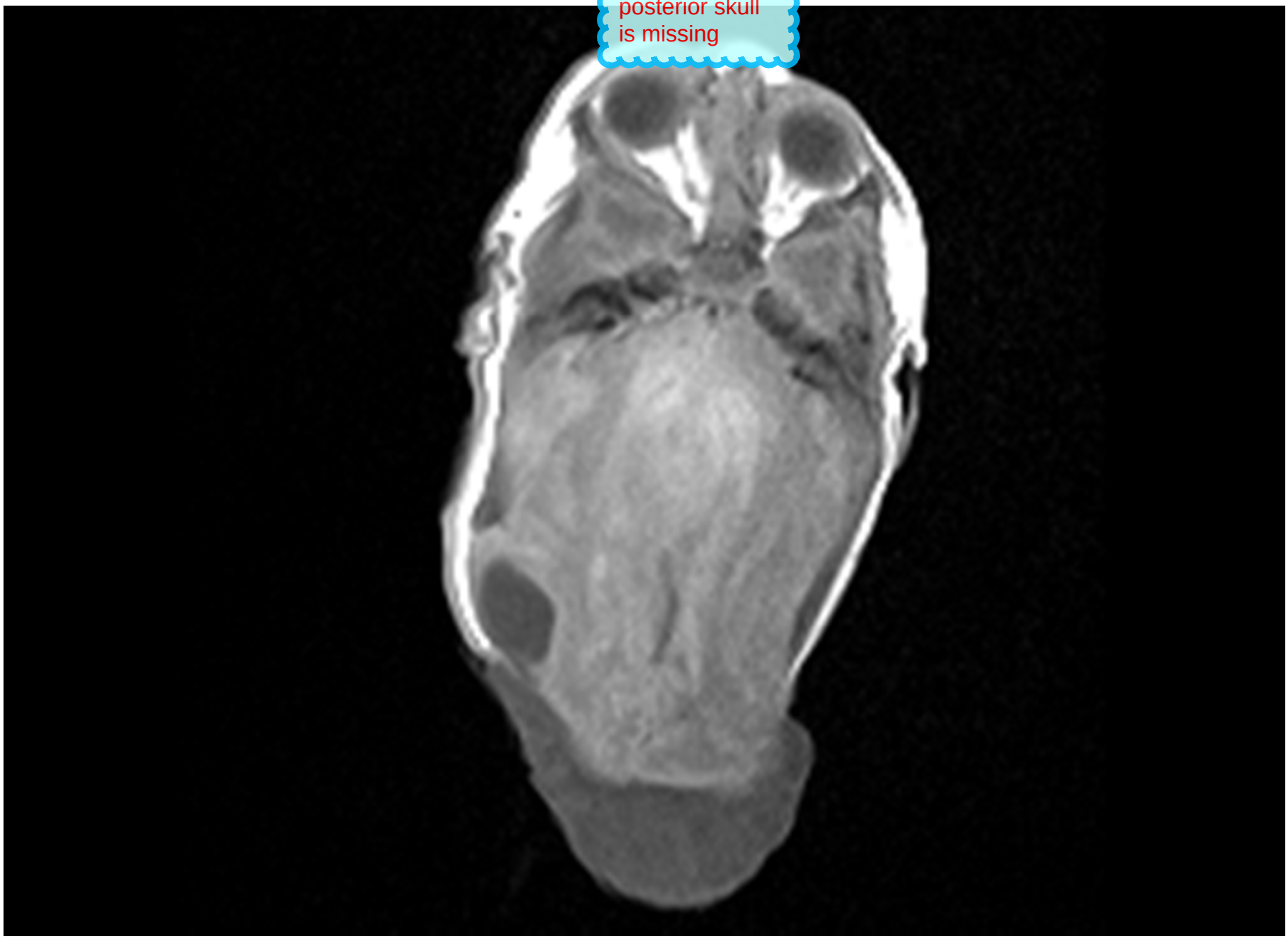


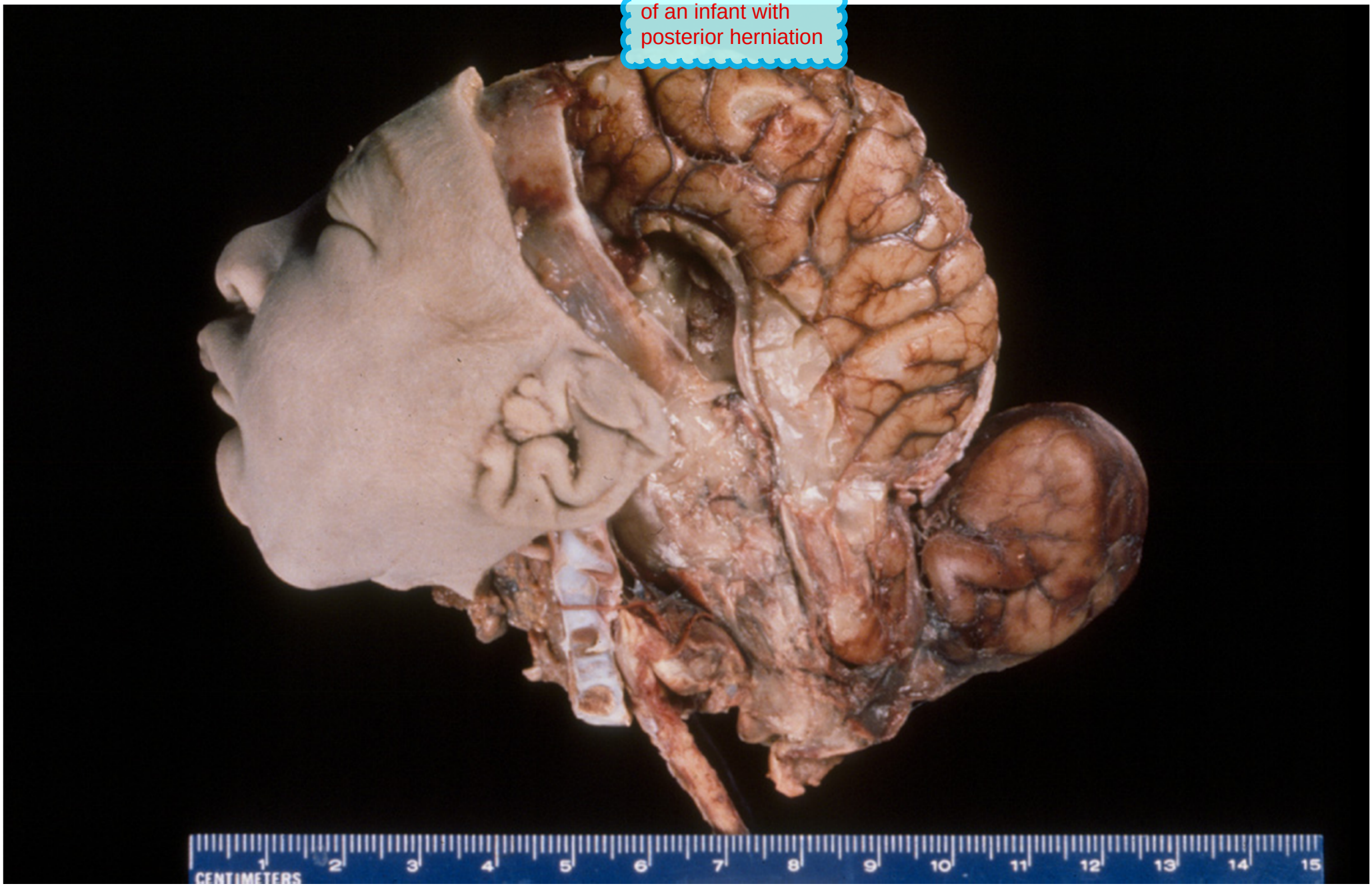
another one- note: no spinal cord

Encephalocele

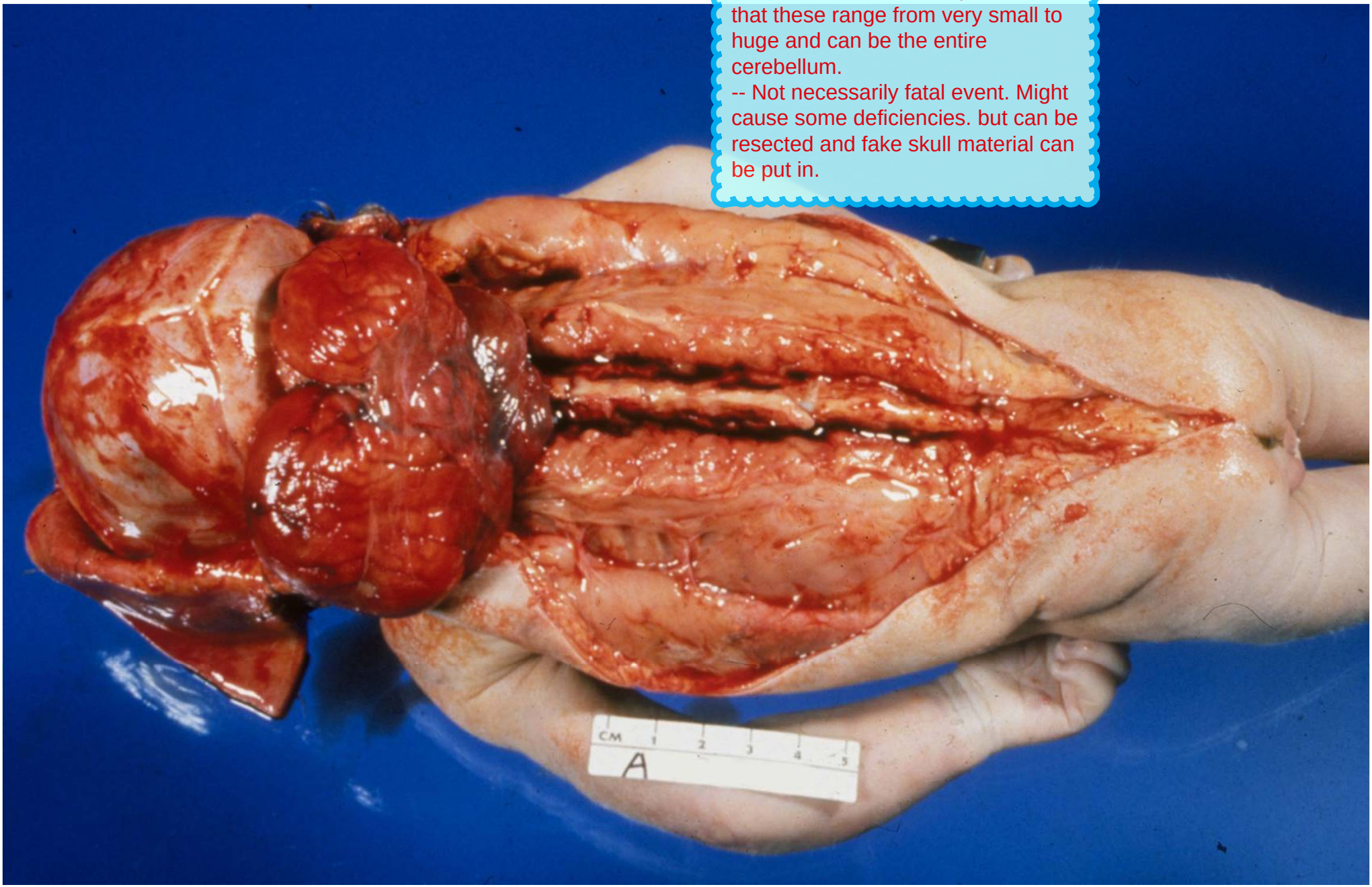
- **A diverticulum (‘herniation’) of malformed and disorganized neural tissue extending through a defect in the cranium**
- **Most common in the occipital region or the posterior fossa**

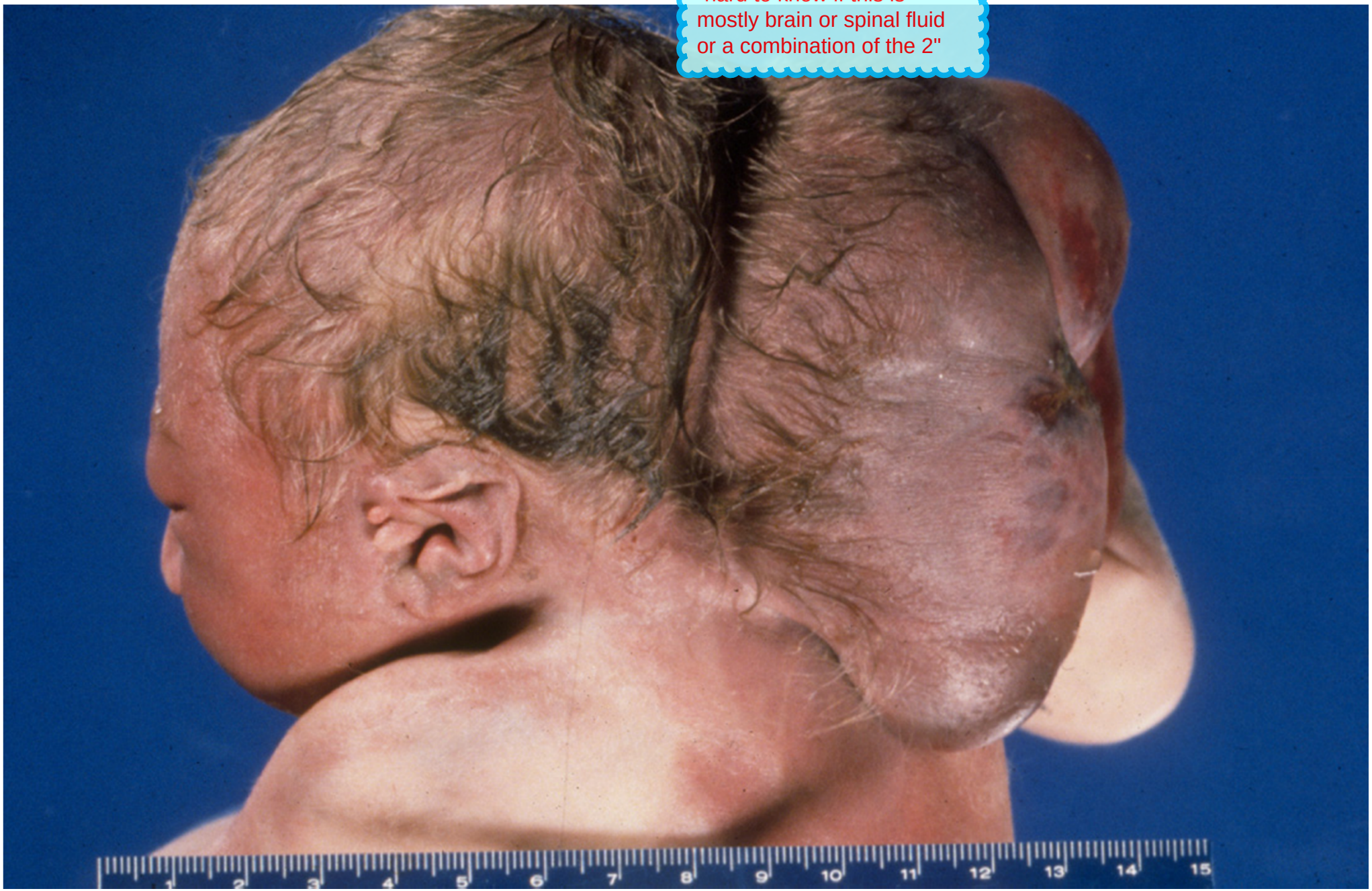
can also happen in frontal nasal region.
- usually happens in children, but recently at Duke they operated on an adult w/one of these

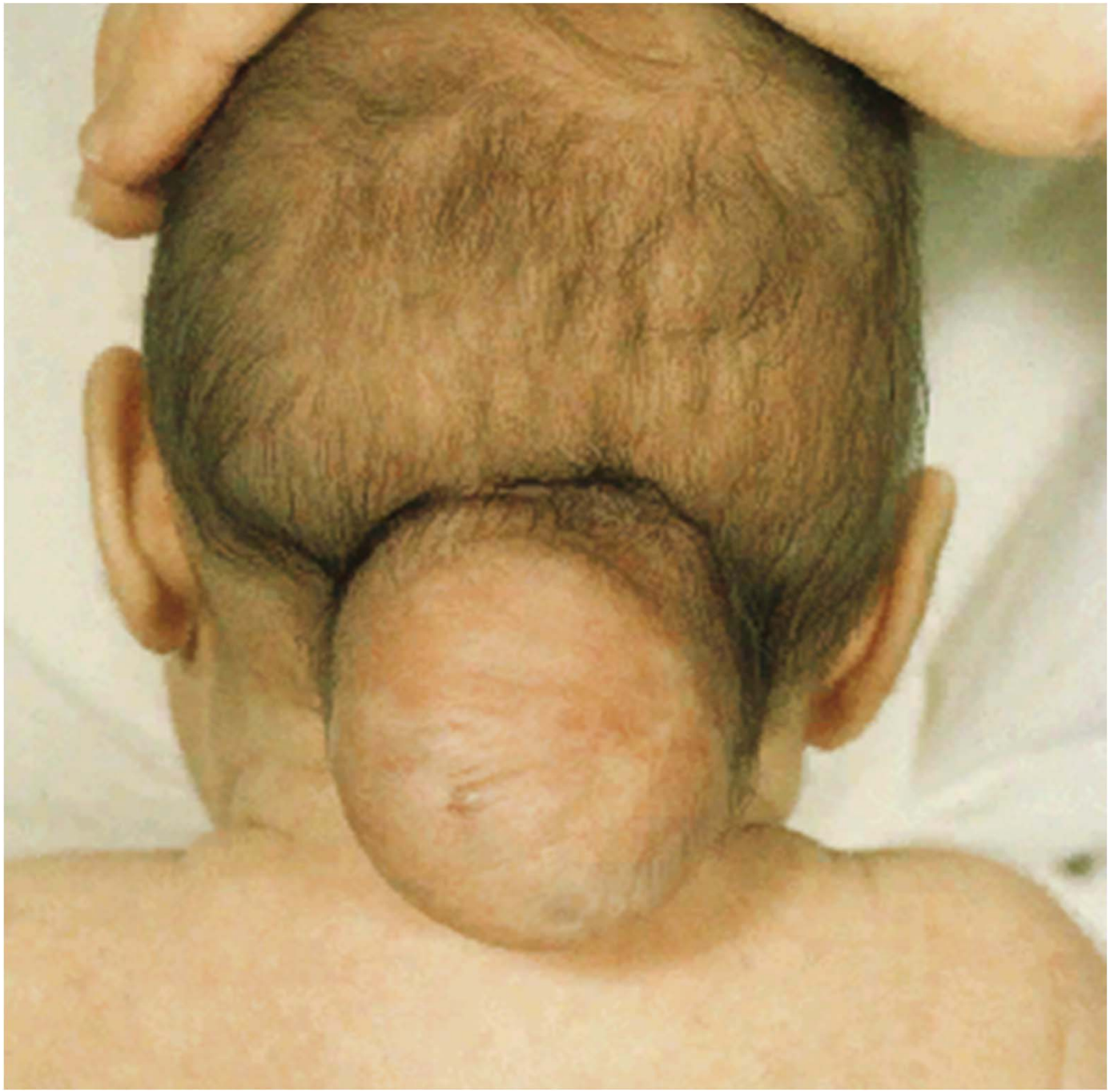

child MRI of brain- part of posterior skull is missing


autopsy specimen
of an infant with
posterior herniation
CENTIMETERS
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15

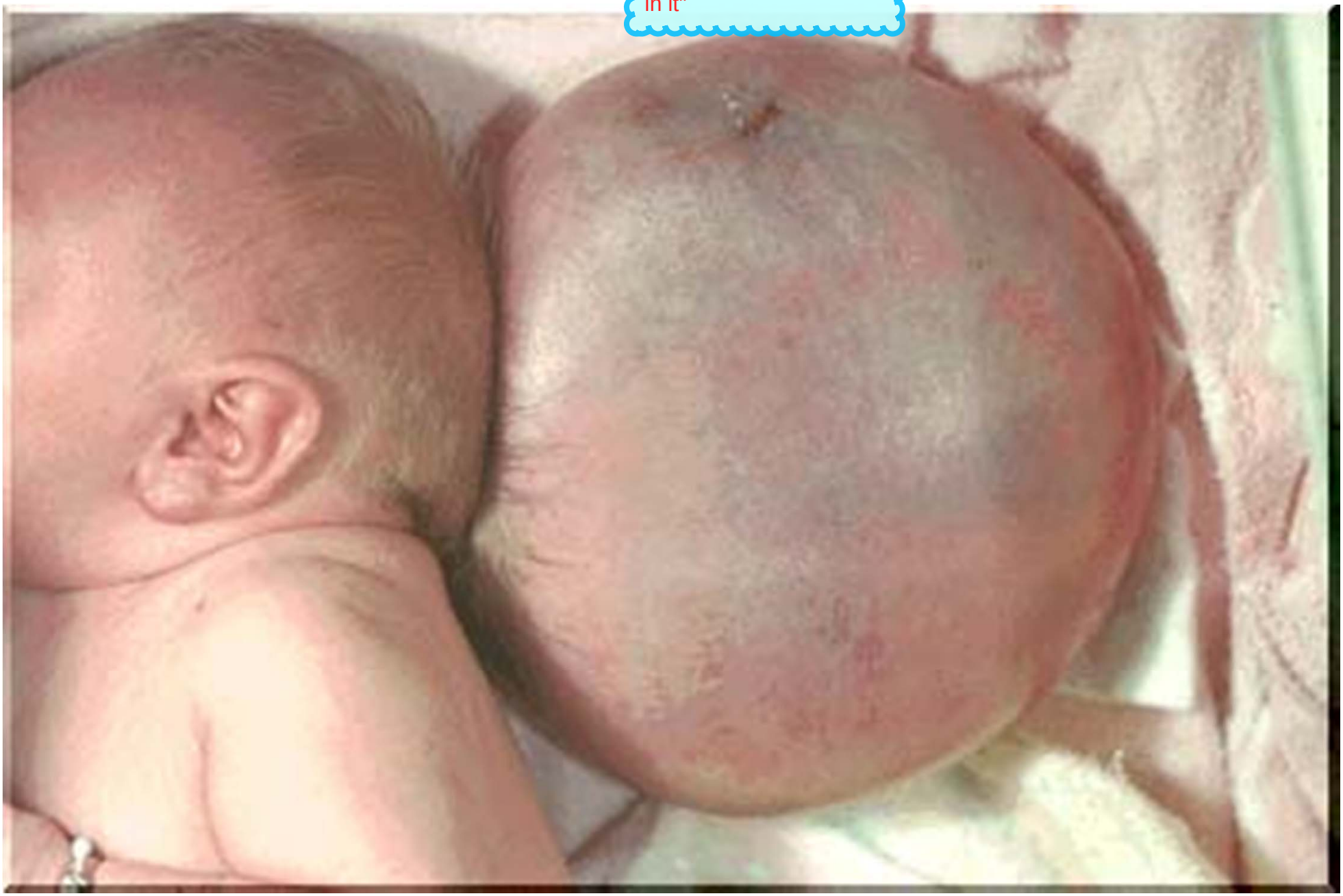
there was a question here that I couldn't hear but his response was that these range from very small to huge and can be the entire cerebellum.
-- Not necessarily fatal event. Might cause some deficiencies. but can be resected and fake skull material can be put in.




"hard to know if this is
mostly brain or spinal fluid
or a combination of the 2"



"might have a lot of fluid in it"



sorry guys- there wasn't a lot to say about these. just examples.

Spinal Dysraphism

incomplete closure

may or may not be recognizable

determine via X-ray. spinal cord and meninges usually normal.

- **Spina Bifida Occulta:**
  - **Defect of lamina // posterior elements**
  - **Asymptomatic or chronic back pain**

herniate

- **Meningocele**
  - **Meninges extend through a defect in the vertebral column**
  - **Spinal cord remains in place**

Spinal Dysraphism

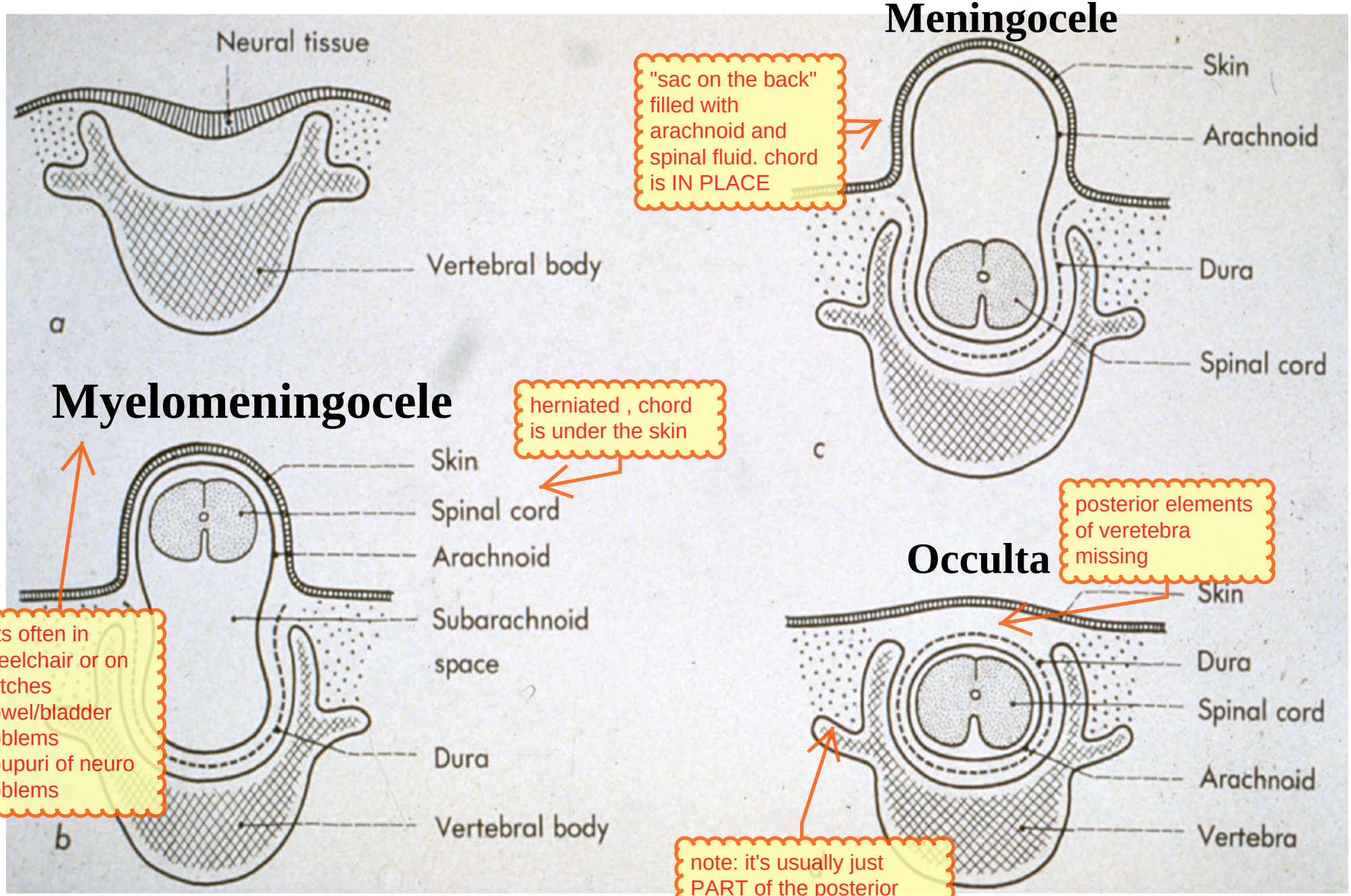
spinal cord equivalent of encephalocele of the brain

most severe

- **Myelomeningocele**
  - **Meninges and spinal cord tissue extend through a defect in the vertebral column**

- **Lipomyelomeningocele**
  - **Meninges and spinal cord tissue extend through a defect in the vertebral column**
  - **Associated with lipomatous tissue**

adipose tissue herniating with the spinal cord tissue


Neural tissue
Vertebral body
a
Meningocele
"sac on the back" filled with arachnoid and spinal fluid. chord is IN PLACE
Skin
Arachnoid
Dura
Spinal cord
c
Myelomeningocele
herniated , chord is under the skin
- pts often in wheelchair or on crutches
-bowel/bladder problems
-poupuri of neuro problems
Skin
Spinal cord
Arachnoid
Subarachnoid space
Dura
Vertebral body
b
Occulta
posterior elements of veretebra missing
note: it's usually just PART of the posterior lamina that's missing. this is an exaggerated cartoon.
Skin
Dura
Spinal cord
Arachnoid
Vertebra

general term for spinal dysraphism, neural tube defect

Incidence of Spina Bifida

- **1980: 4.8 / 1000 live births Ireland**
- **Currently: 1 / 1000 live births Ireland**

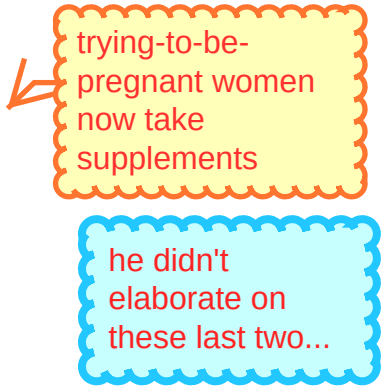
- **0.6-1.3 cases / 1000 live births USA**
  - **6-11,000 /year**
  - **Declined 50% in recent decades**
  - **In US, highest rate in Boston of Irish descent**

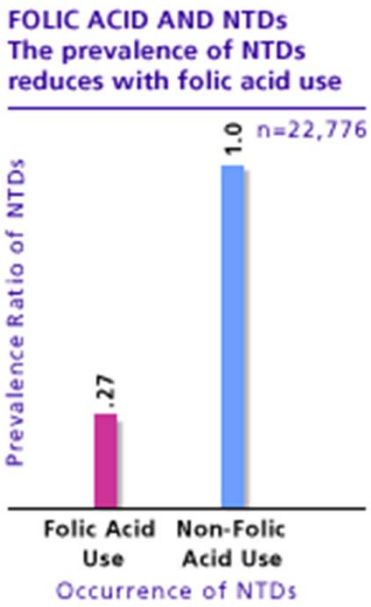
- **3.7 cases / 1000 live births Northern China**

incidence is going down due to folic acid- see next slide

Causes

- **Several genetic and environmental factors have been implicated:**
  - **Folate deficiency (diet)**
  - **Season of conception**
  - **Socioeconomic status**





Milunsky et al showed a 73 percent reduction in the risk of NTDs in fetuses of women who used folic acid during the first six weeks of pregnancy.

shouldn't wait until after a positive preg test to start taking these, cause at that point it's usually too late and neural tube defects have already happened. Women who are trying to get pregnant are counseled to supplement this into their diet

Supplement Facts

Serving Size: 1 tablet

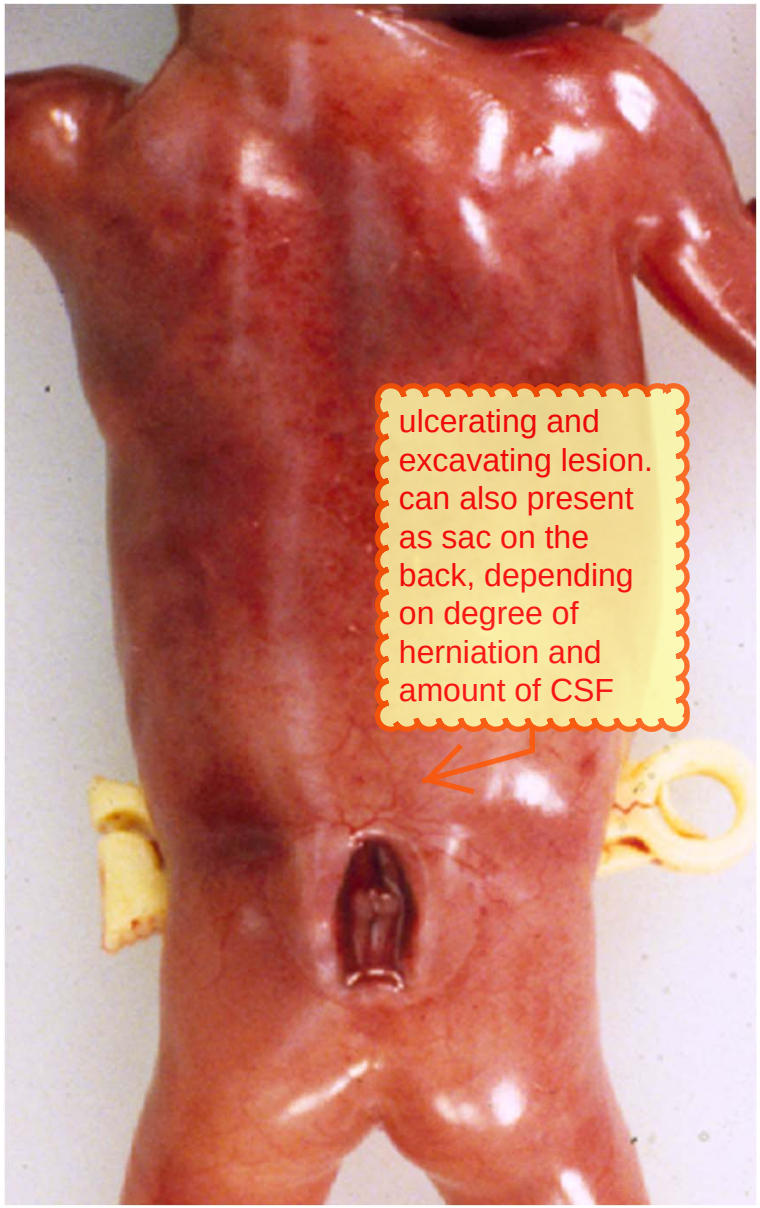
Amount Per Serving	% Daily Value	
Vitamin A	5000IU	100
Vitamin C	60mg	100
Vitamin D	400 IU	100
Vitamin E	30 IU	100
Thiamin	1.5mg	100
Riboflavin	1.7mg	100
Niacin	20mg	100
Vitamin B6	2mg	100
Folic Acid	400mcg	100
Vitamin B12	6mcg	100
Biotin	30mcg	10
Pantothenic Acid	10mg	100
Calcium	162mg	16
Iron	18mg	100
Iodine	150mcg	100
Magnesium	100mg	25
Zinc	15mg	100
Selenium	20mcg	100
Copper	2mg	100
Manganese	3.5mg	175
Chromium	65mcg	54
Molybdenum	150mcg	200
Chloride	72mg	2
Potassium	80mg	2

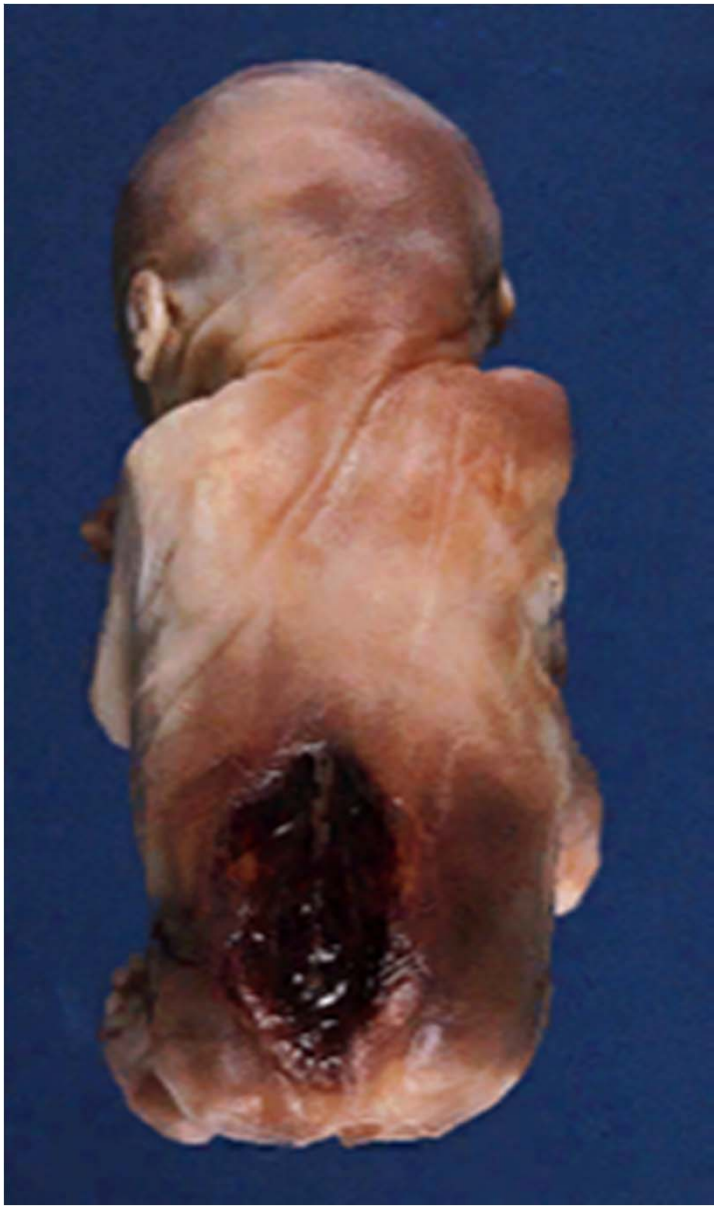
Myelomeningocele

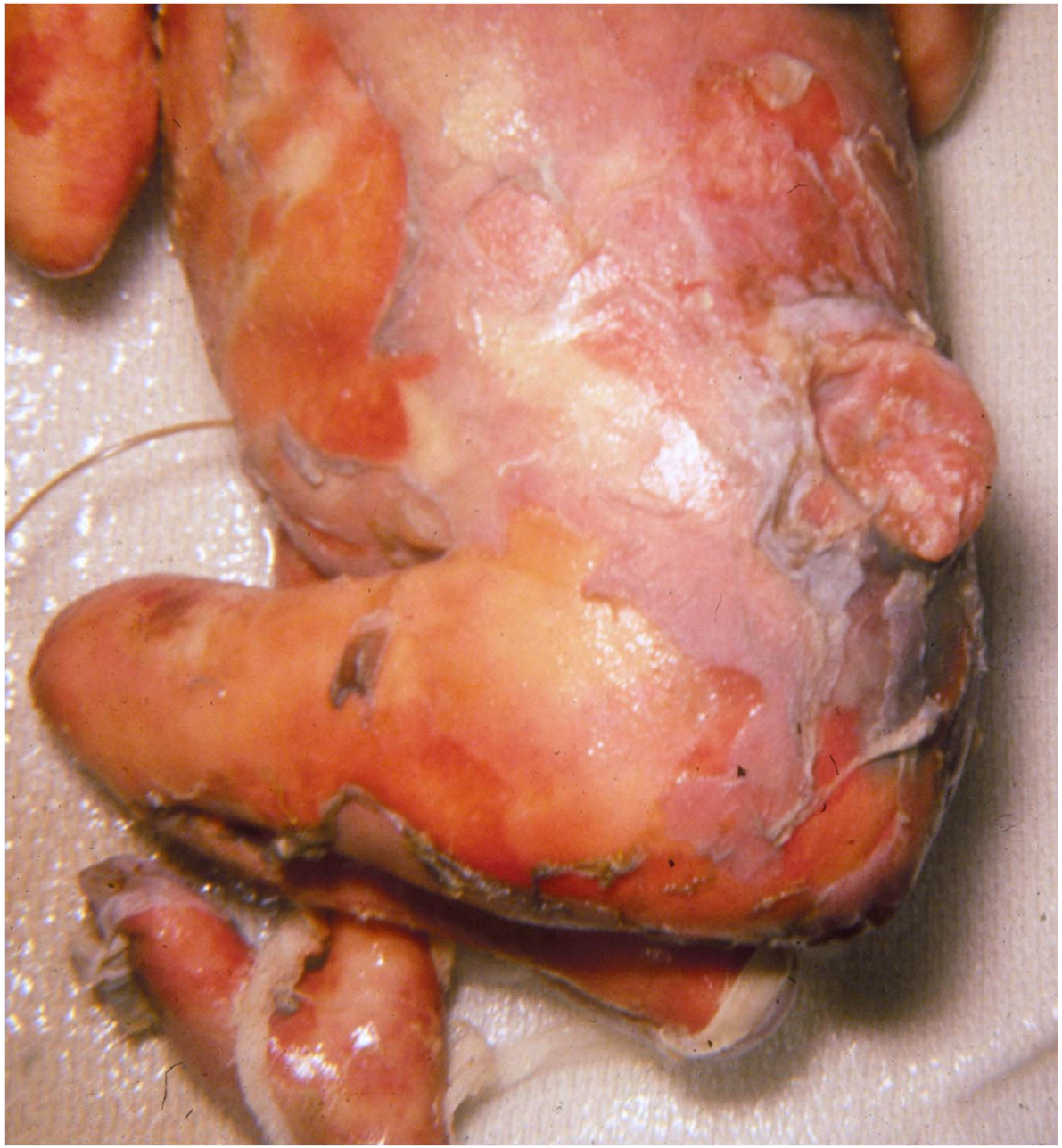
- An extrusion of meninges and CNS tissue through a defect in the vertebral column
- More common in lumbosacral region
- Sensory and motor deficits
- Bowel and bladder dysfunction
- Arnold-Chiari type II

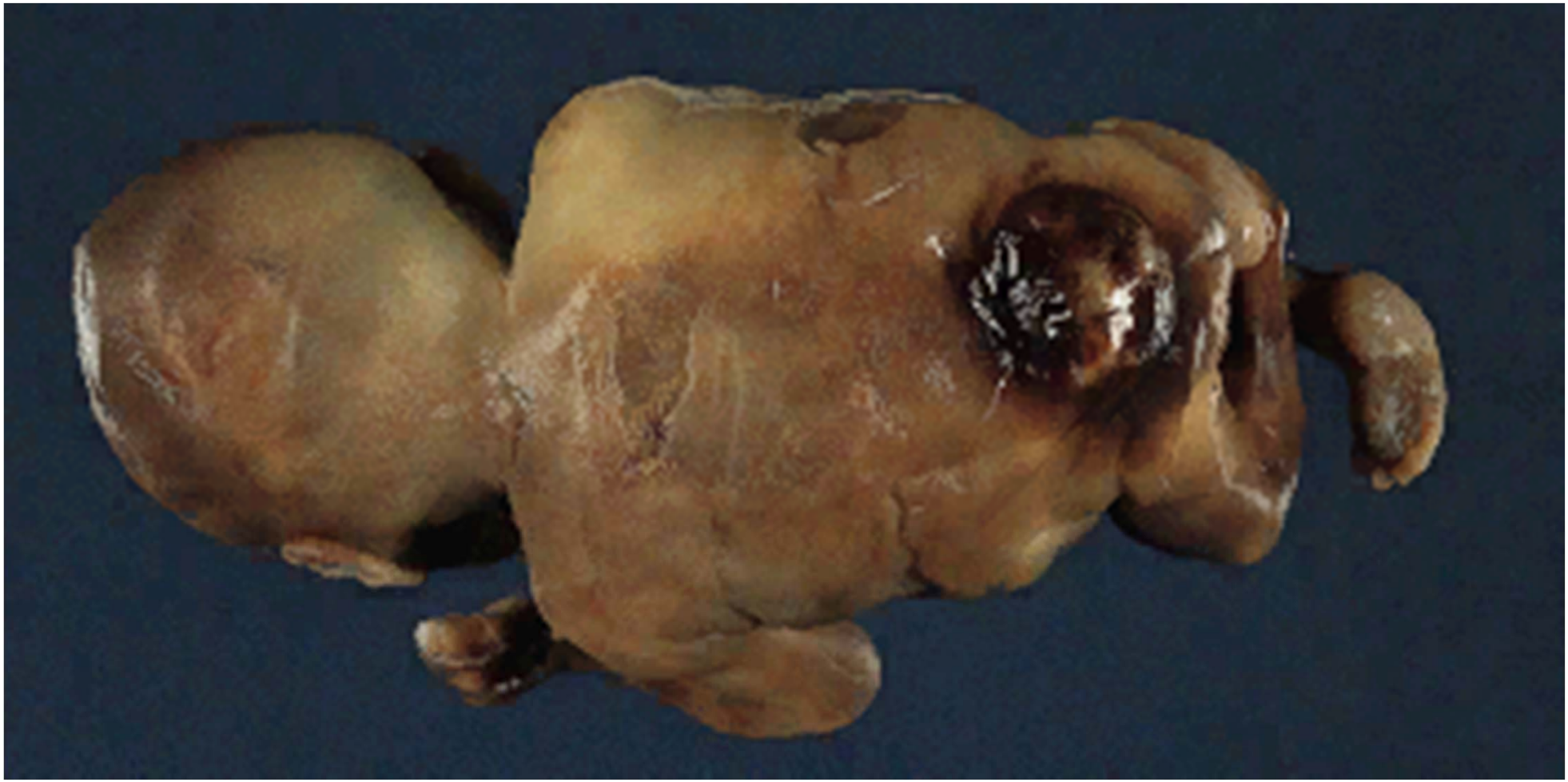
can sometimes happen in thoracic region as well

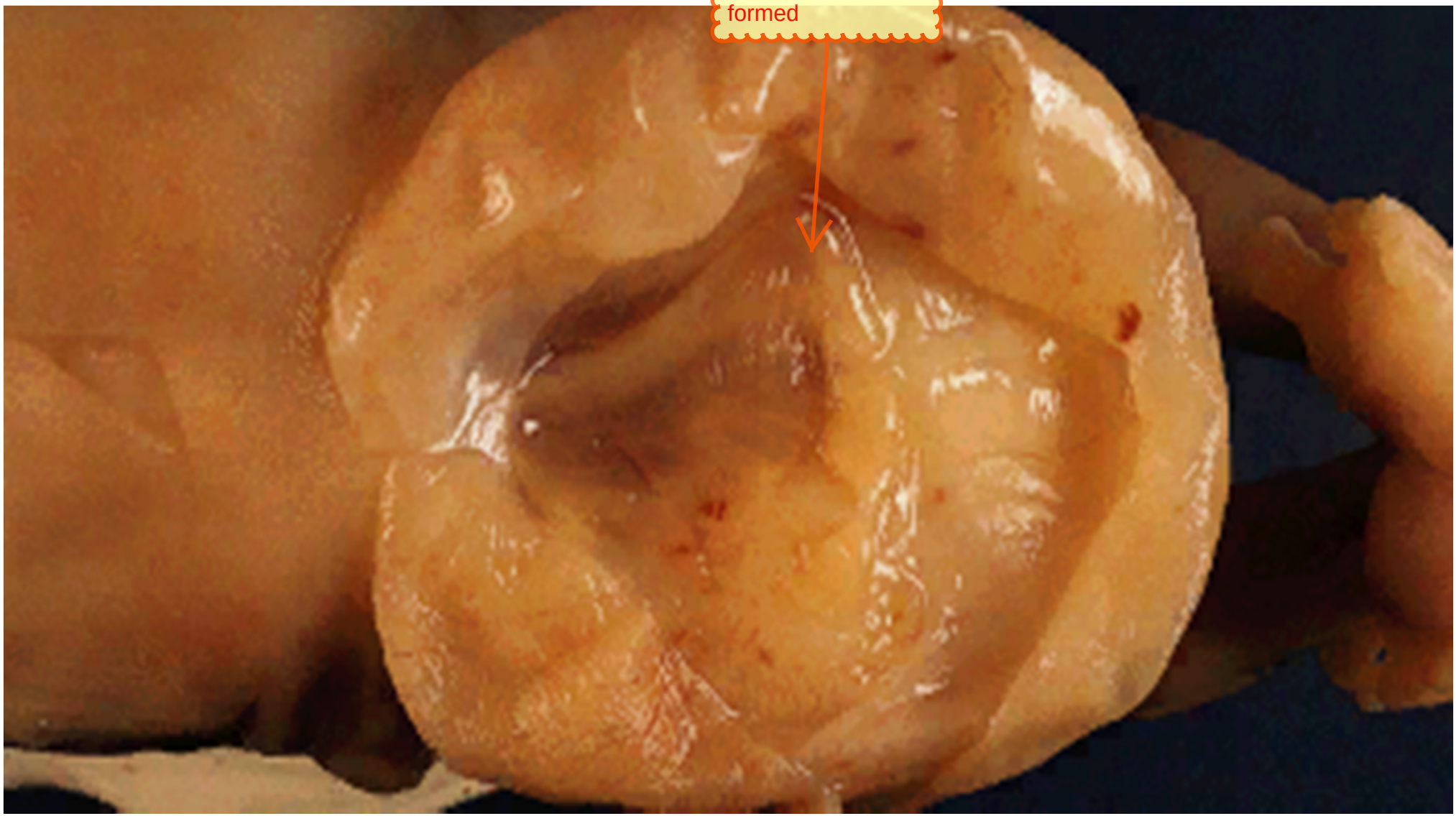
and orthopedic

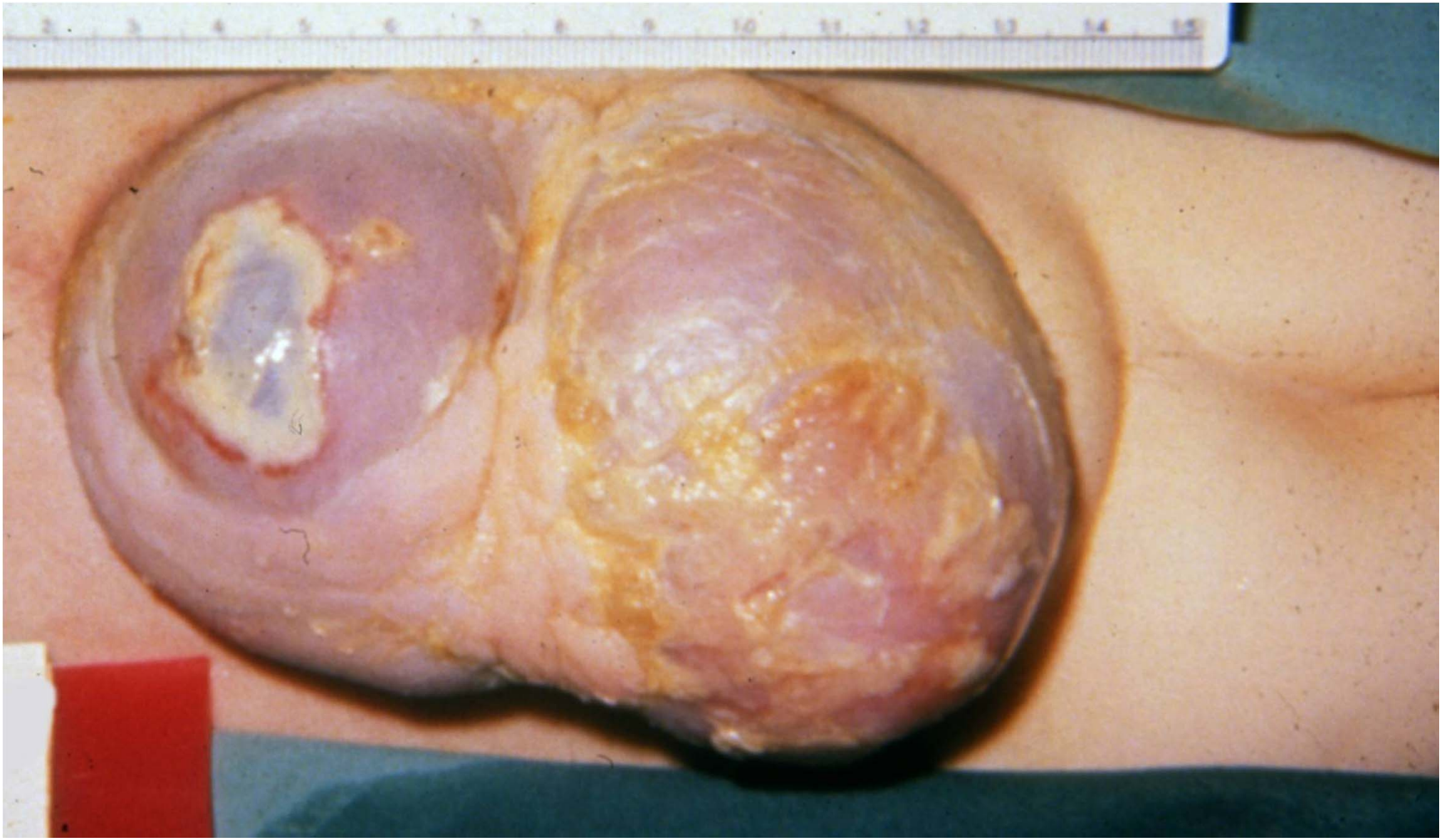

ulcerating and excavating lesion. can also present as sac on the back, depending on degree of herniation and amount of CSF







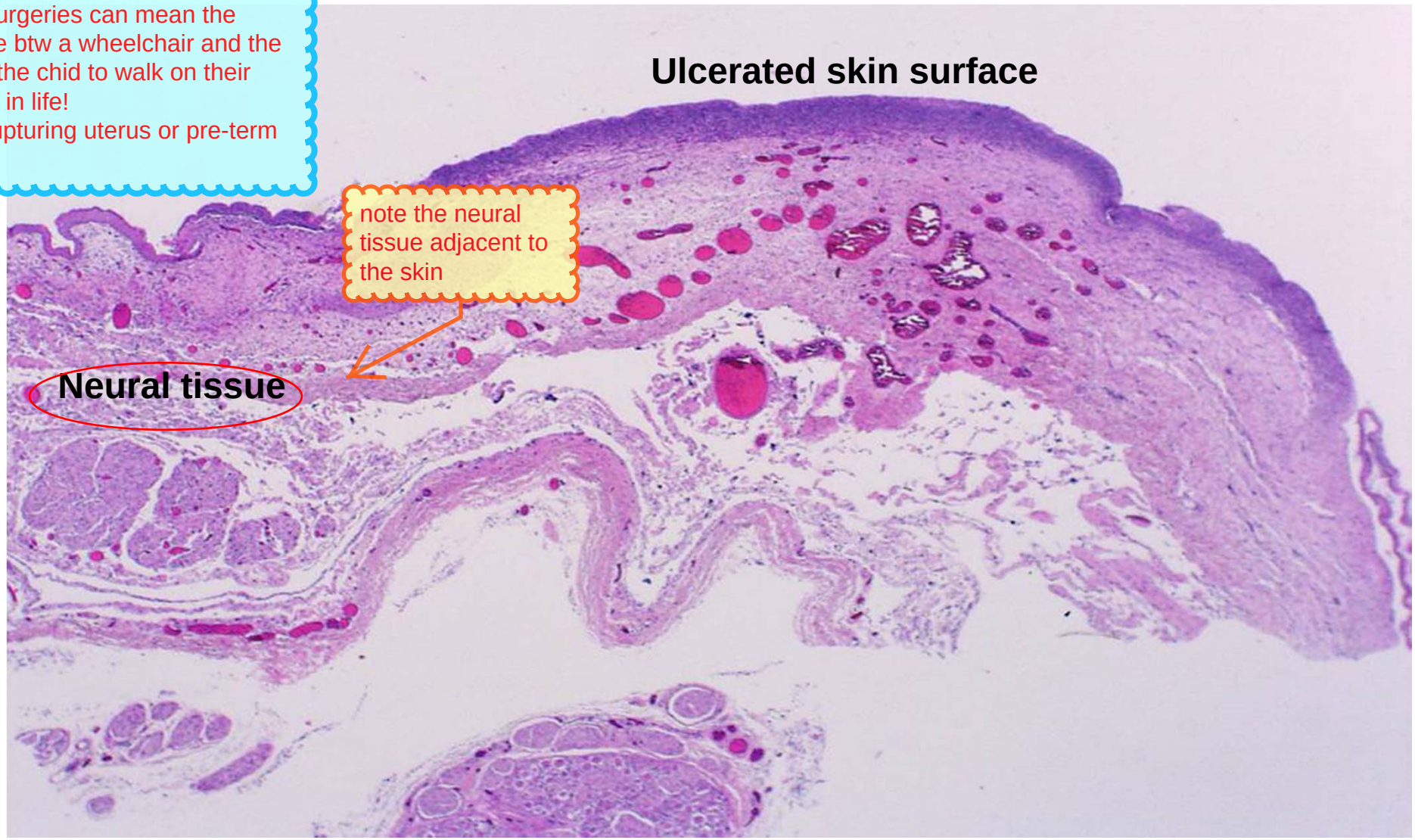

here you can see the placode- disorganized mass of neural tissue that's improperly formed



autopsy specimen- showing roots and spinal cord tissue protruding

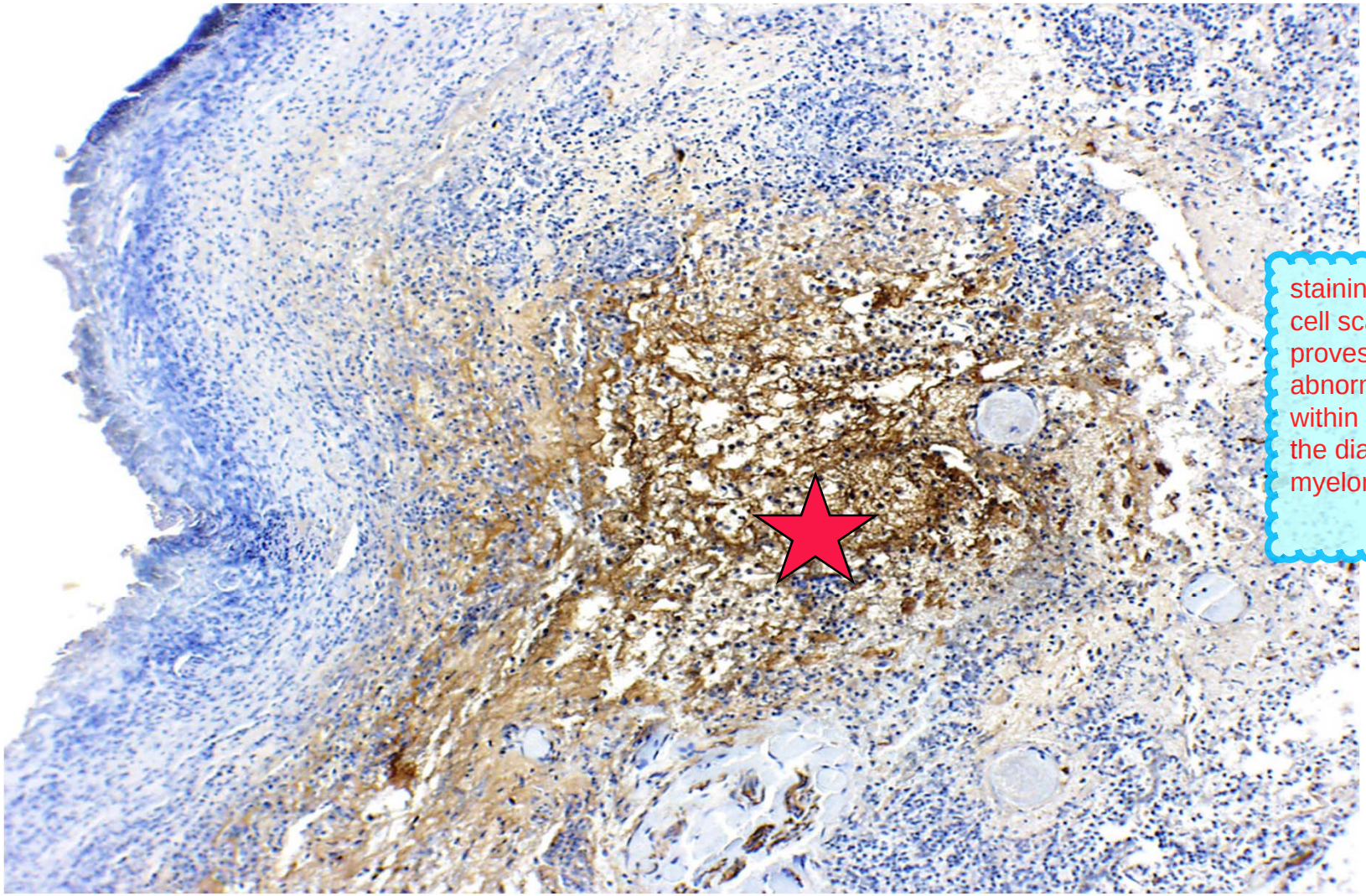
They are now performing in-utero surgeries during the second trimester to repair these defects, reducing long term deficits.
It is thought the amniotic fluid may be contributing to a negative outcome by attacking or in a way poisoning the lesion.
* these surgeries can mean the difference btw a wheelchair and the ability of the chid to walk on their own later in life!
*risk of rupturing uterus or pre-term delivery.

Placode histology



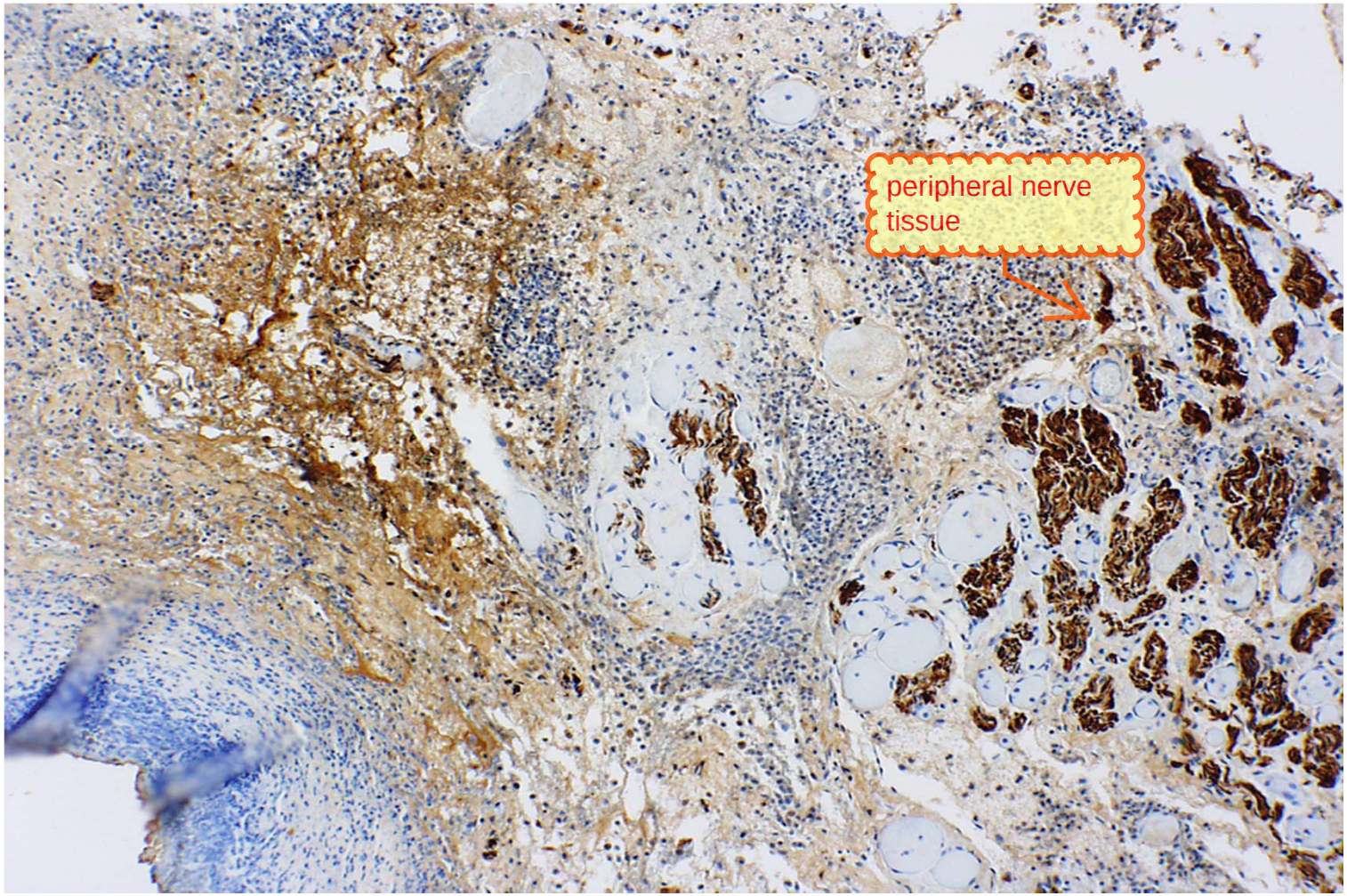
scaffolding protein!

Immunohistochemical stain (brown) for GFAP (glial fibrillary acidic protein: the intermediate filament in the cytoplasm of glial cells (astrocytes, oligodendrocytes, ependymocytes)

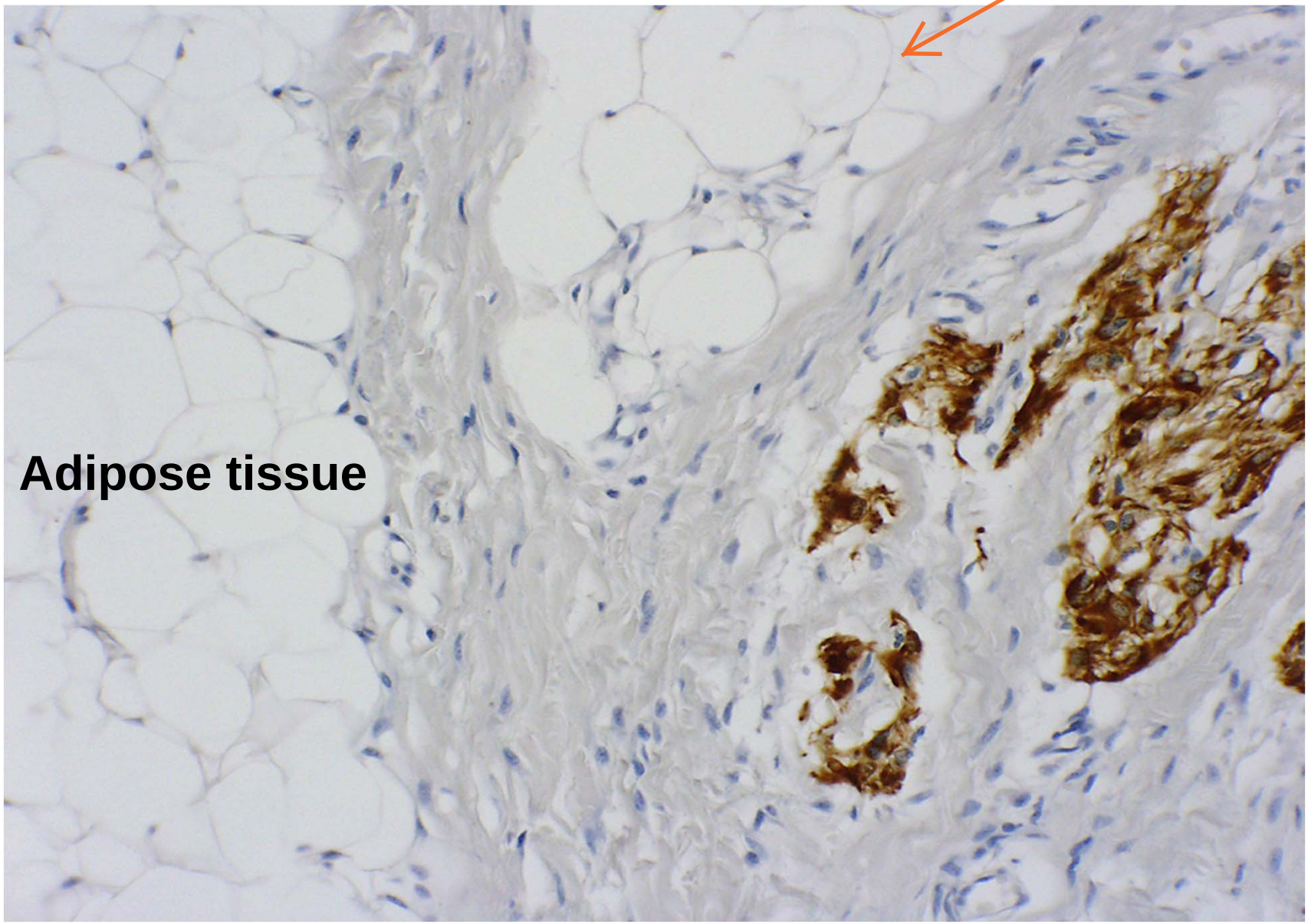


staining for GFAP (glial cell scaffolding protein)- proves that there is abnormal glial tissue within the skin, making the diagnosis of a myelomengiocele

S-100 protein: an immunohistochemical stain for central and peripheral nervous tissue (neural crest tissues)



Lipomyelomeningocele



Forebrain Anomalies

- **Holoprosencephaly**
- **Agenesis of the Corpus Callosum**
- **Polymicrogyria**
- **Megalencephaly**
- **Microencephaly**
  - **Fetal alcohol syndrome, HIV**

BIG brain

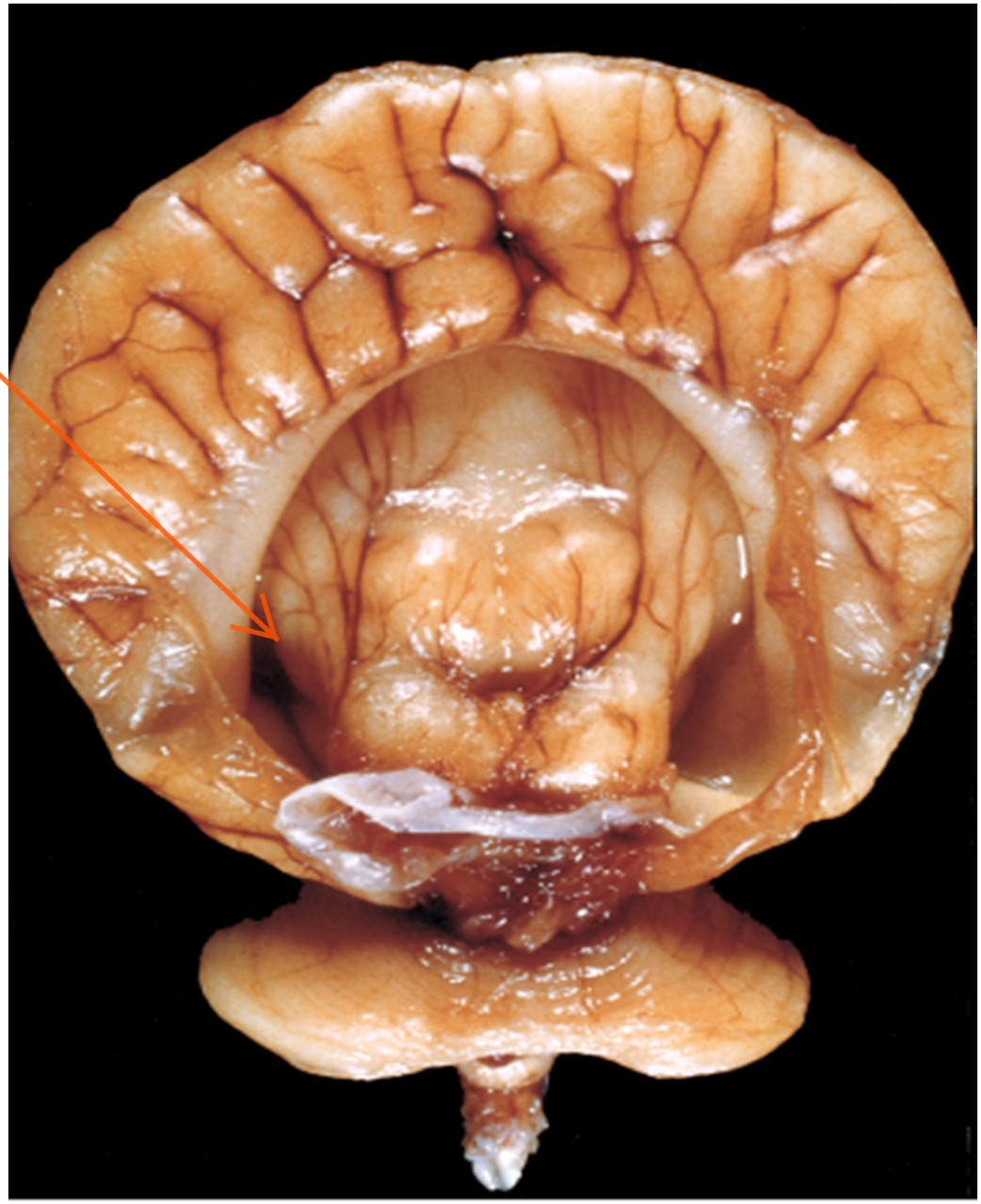
little brain

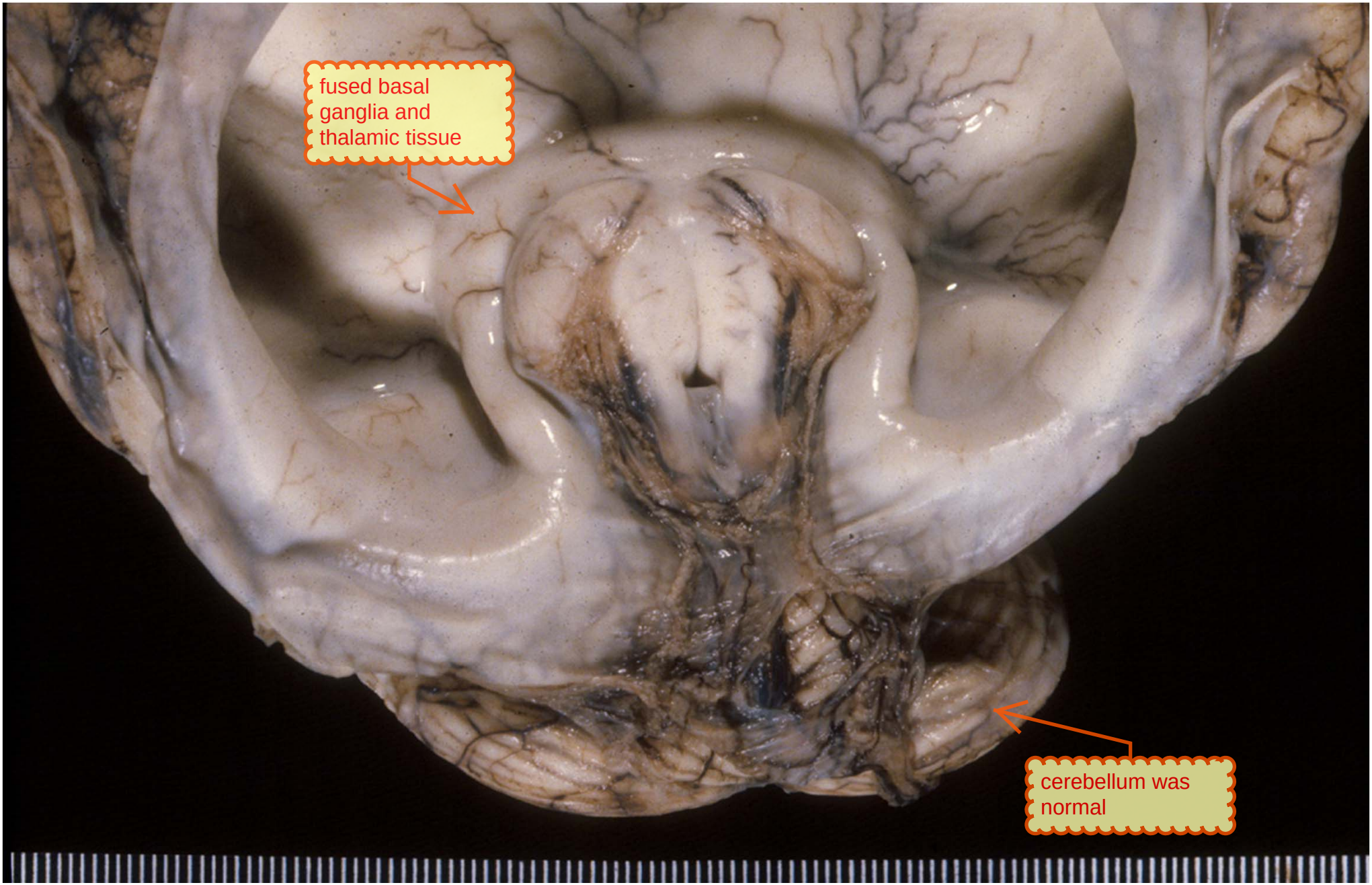
these are the major risk factors for microencephaly development

Holoprosencephaly

- **Monoventricular brain** lateral ventricles are one giant ventricle
- **Fused basal ganglia**
- **Posterior fossa unremarkable**
- **Trisomy 13, 18** association

monoventricle




fused basal ganglia and thalamic tissue
cerebellum was normal

Agenesis of the Corpus Callosum

- Patients range from
  - Mentally retarded
  - Clinically normal

benign tumor of fat

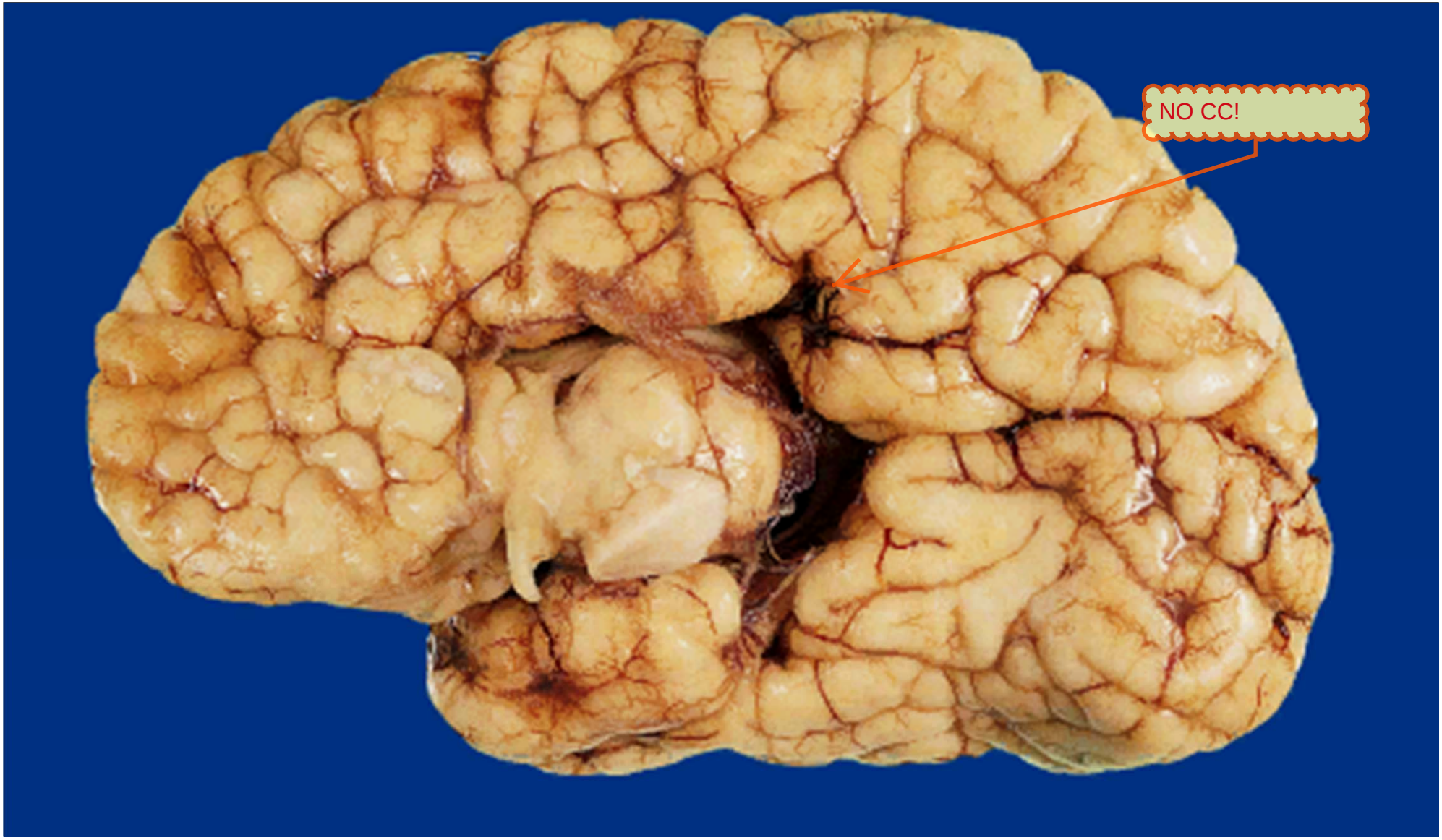
- Can present in isolation or with other abnormalities
  - Lipoma of the corpus callosum

- Can be complete or partial

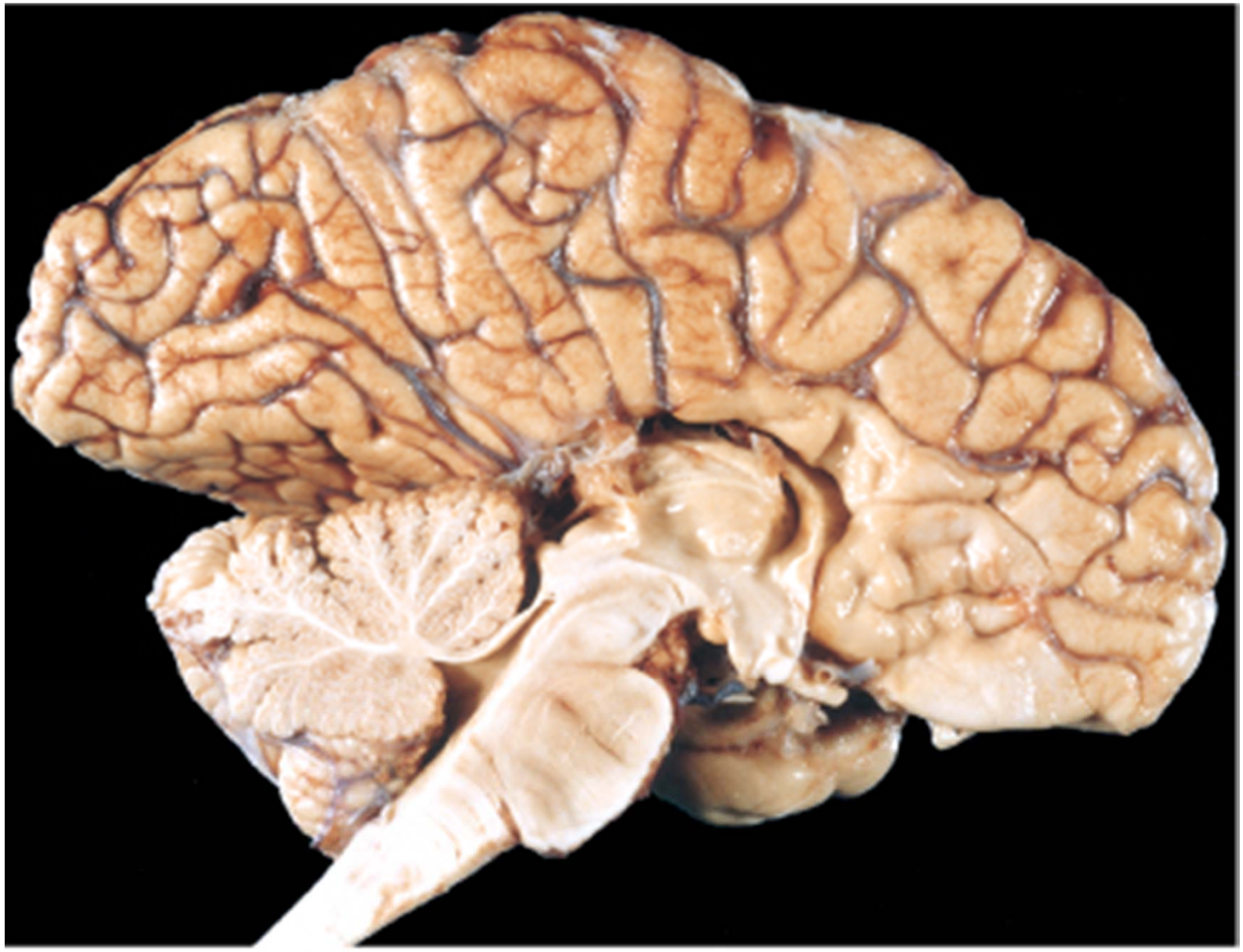
- Aicardi syndrome
  - X-linked, lethal in males
  - Chorioretinal defects
  - Seizures

didn't say anything additional to this....

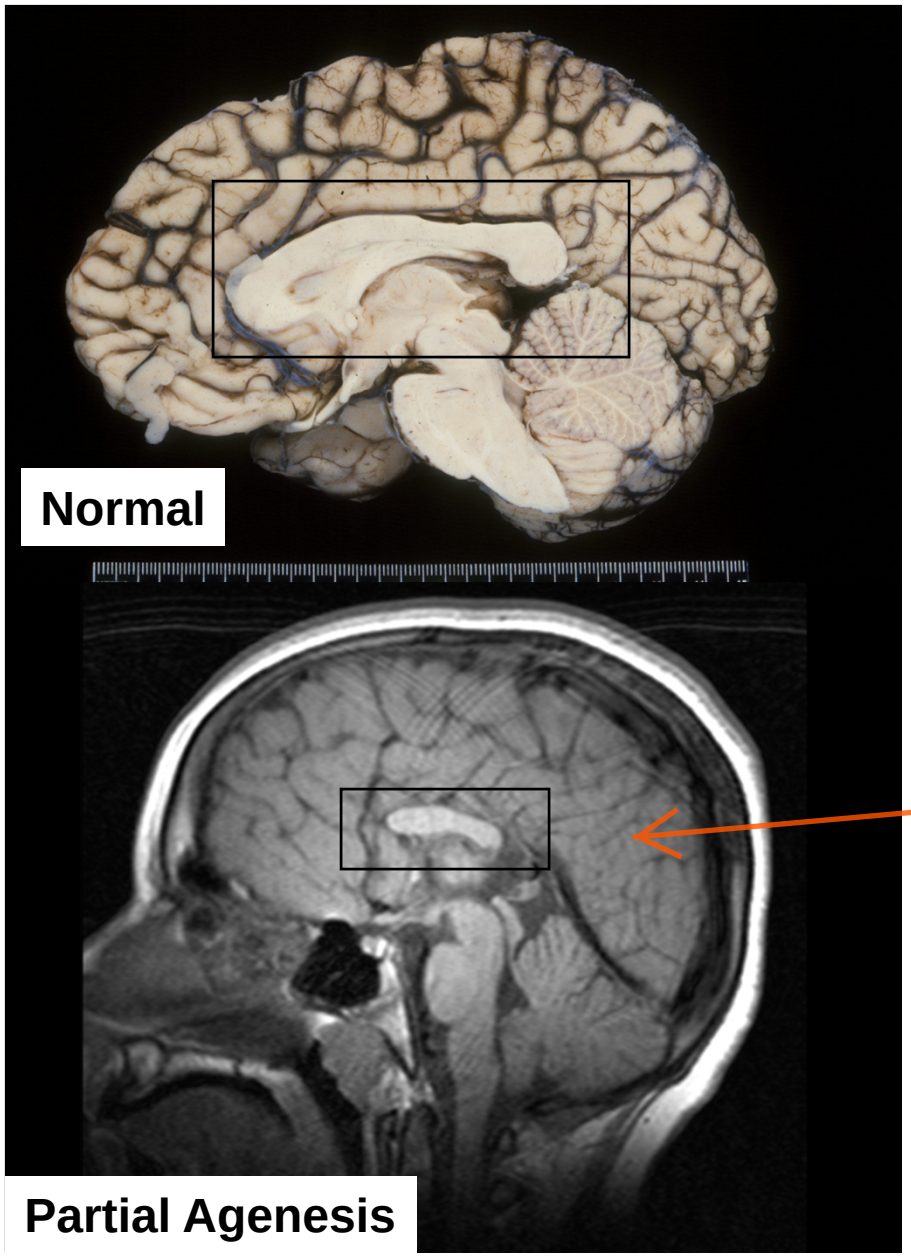
Agenesis of the Corpus Callosum



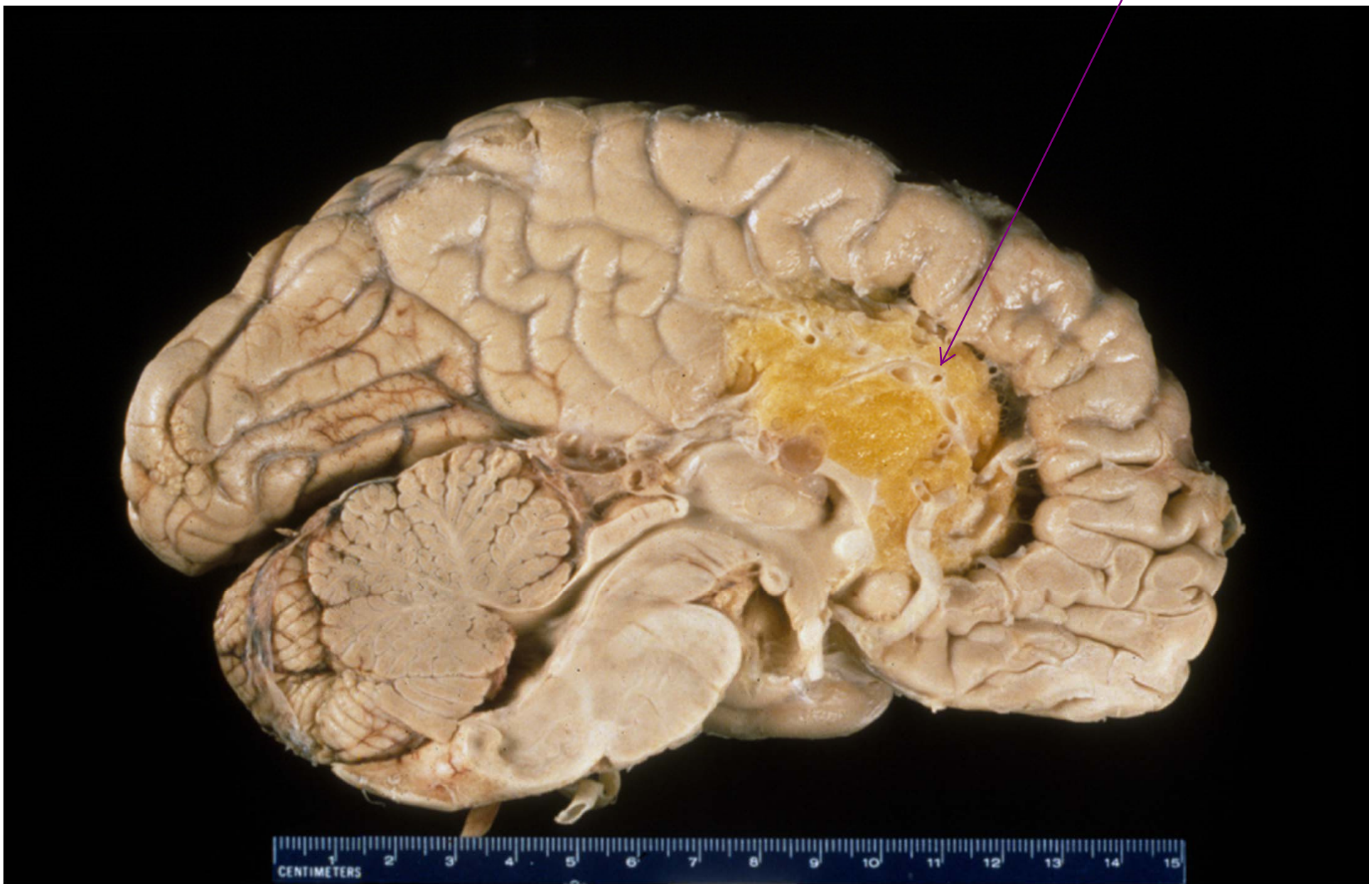
Agenesis of the Corpus Callosum



Agenesis of the Corpus Callosum

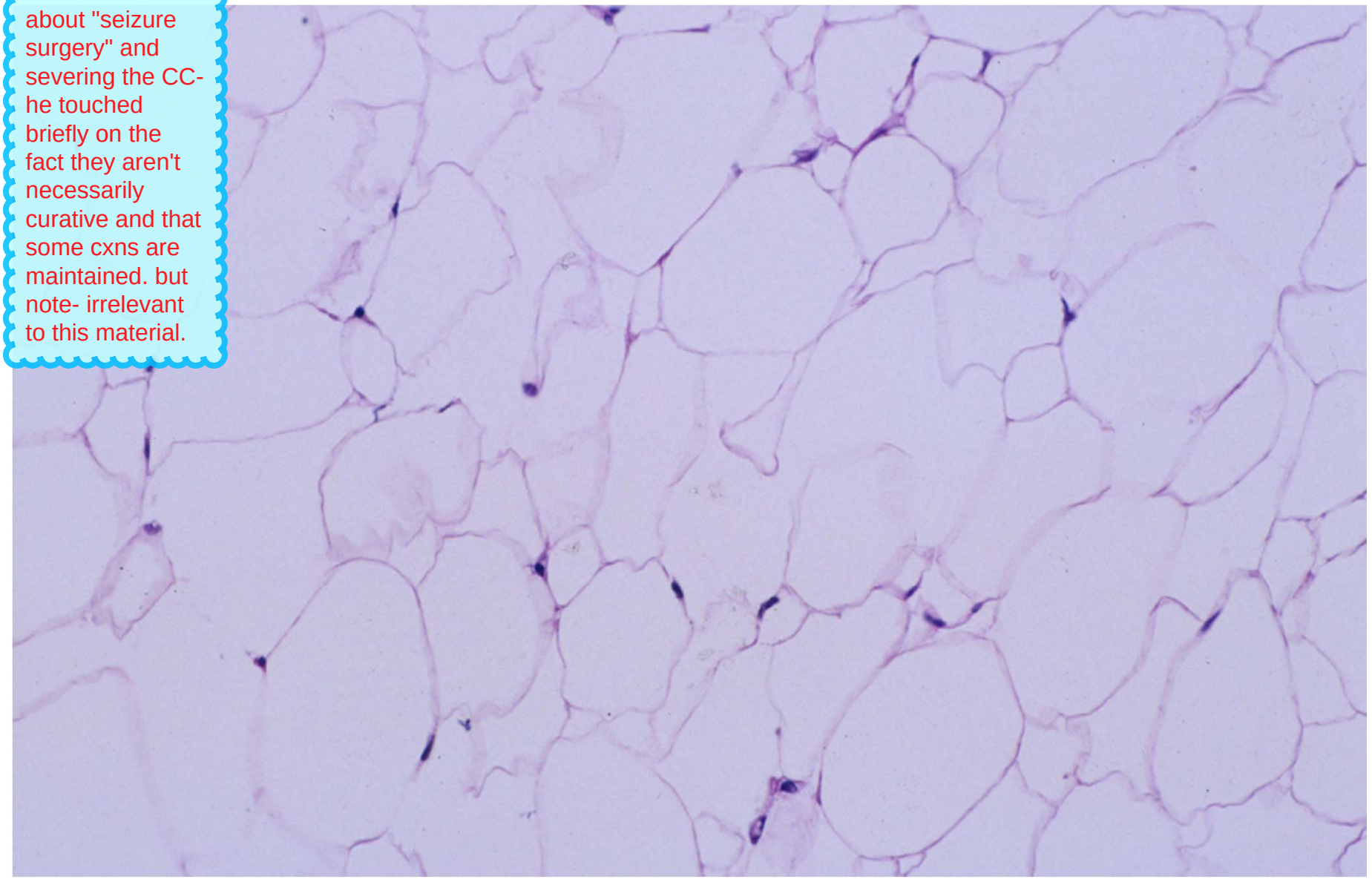


Agenesis of the Corpus Callosum with Lipoma



Adipose tissue, lipocytes

a question was asked here about "seizure surgery" and severing the CC- he touched briefly on the fact they aren't necessarily curative and that some cxns are maintained. but note- irrelevant to this material.



skipped

Posterior Fossa Anomalies

- **Arnold-Chiari malformation**
- **Dandy-Walker malformation**

Arnold-Chiari Malformation

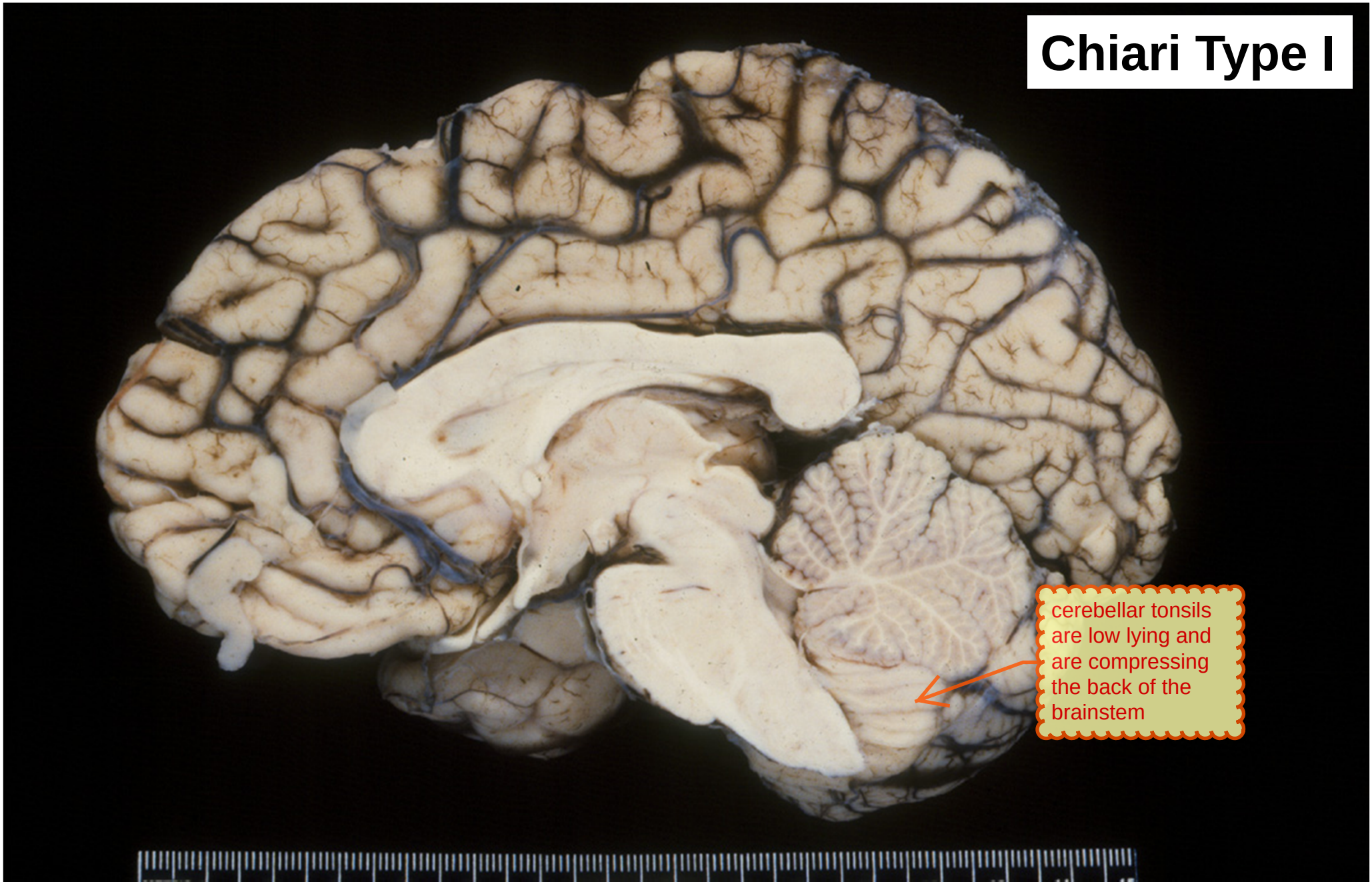
- **Type I**
  - **Adults**
  - **Low-lying cerebellar tonsils extend down into the vertebral canal**
  - **Obstruction of CSF flow**
  - **Medullary // upper cervical spine compression**
  - **Amenable to neurosurgical intervention and decompression of constrictive bone and dura**

Adult that complains of headaches classic presentation

this makes the diagnosis

causes headache

then put a "dura mater patch" and let CSF flow resume normally- pts usually recover


Chiari Type I
cerebellar tonsils are low lying and are compressing the back of the brainstem

Arnold-Chiari Malformation

- **Type II**
  - **Small posterior fossa**
  - **Downward extension of the vermis through the foramen magnum**
  - **Hydrocephalus**
  - **Lumbar myelomeningocele**
  - **Beaking of the tectum**

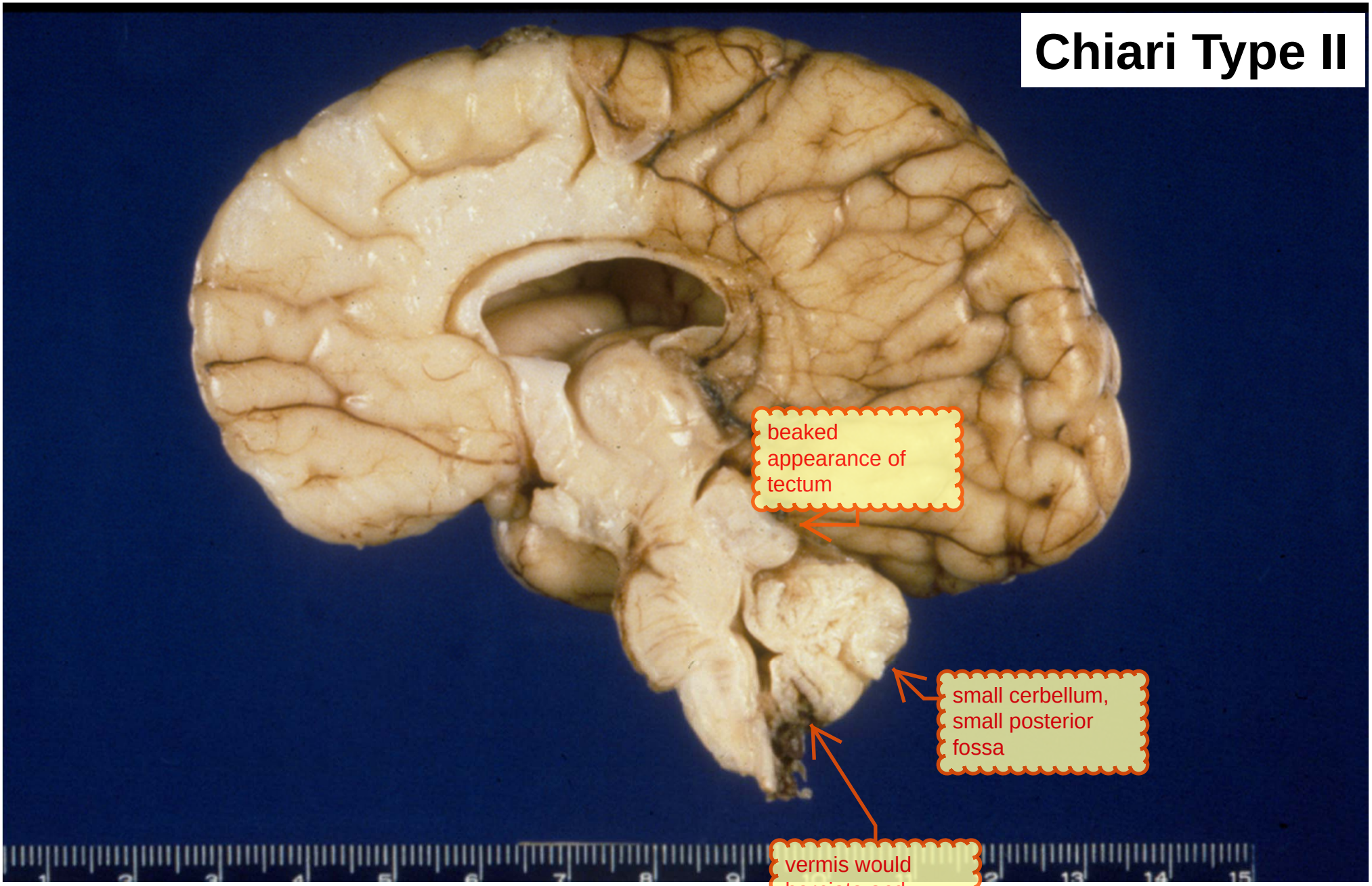
Arnold-Chiari Malformation

- **Type III**
  - **Herniation of the cerebellum and brainstem and formation of an encephalocele**
- **Type IV**
  - **Aplasia // hypoplasia of the cerebellum**

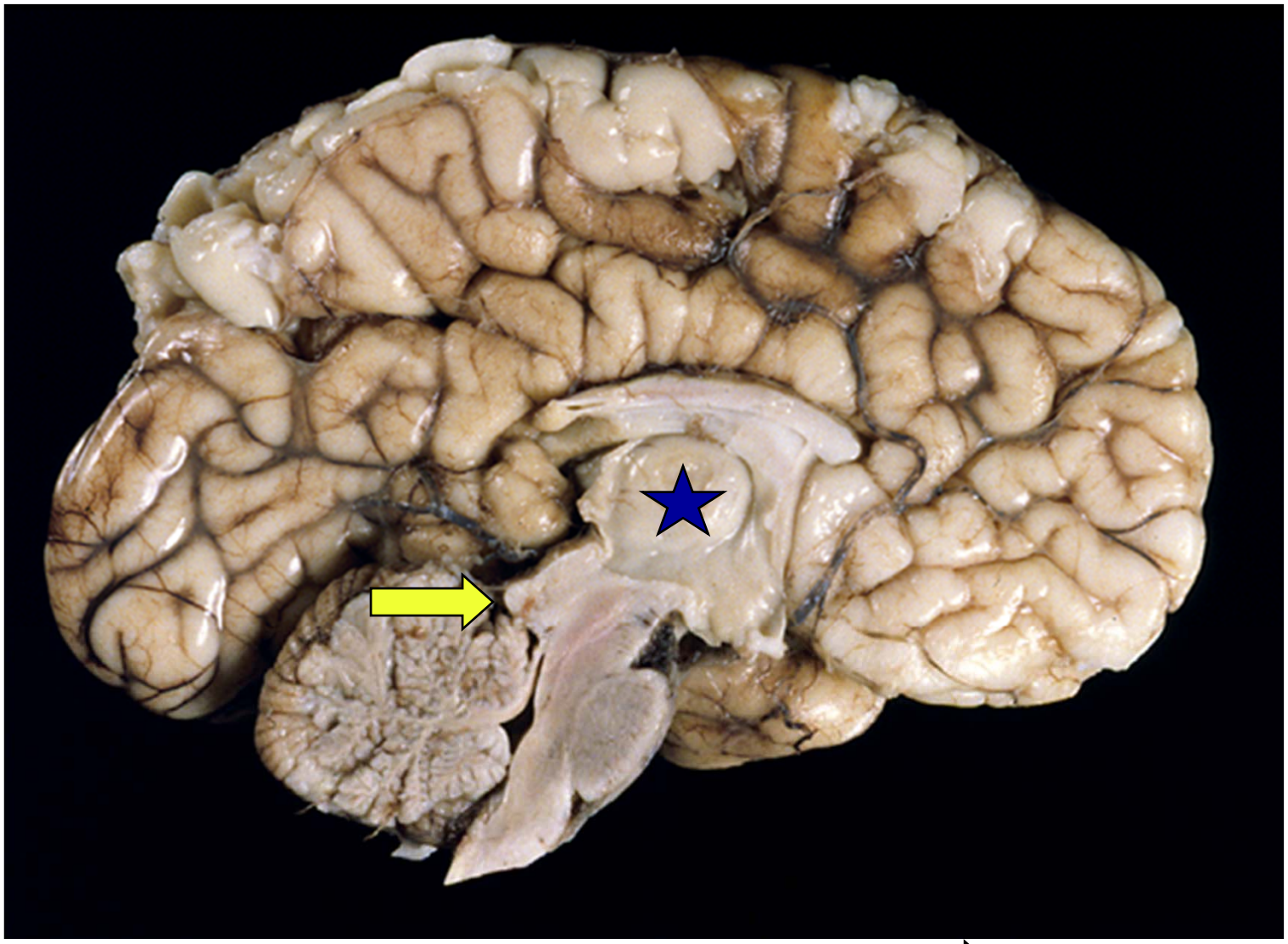
cerebellum fails to develop

these two are very uncommon, much more likely to see type I or II

Chiari Type II



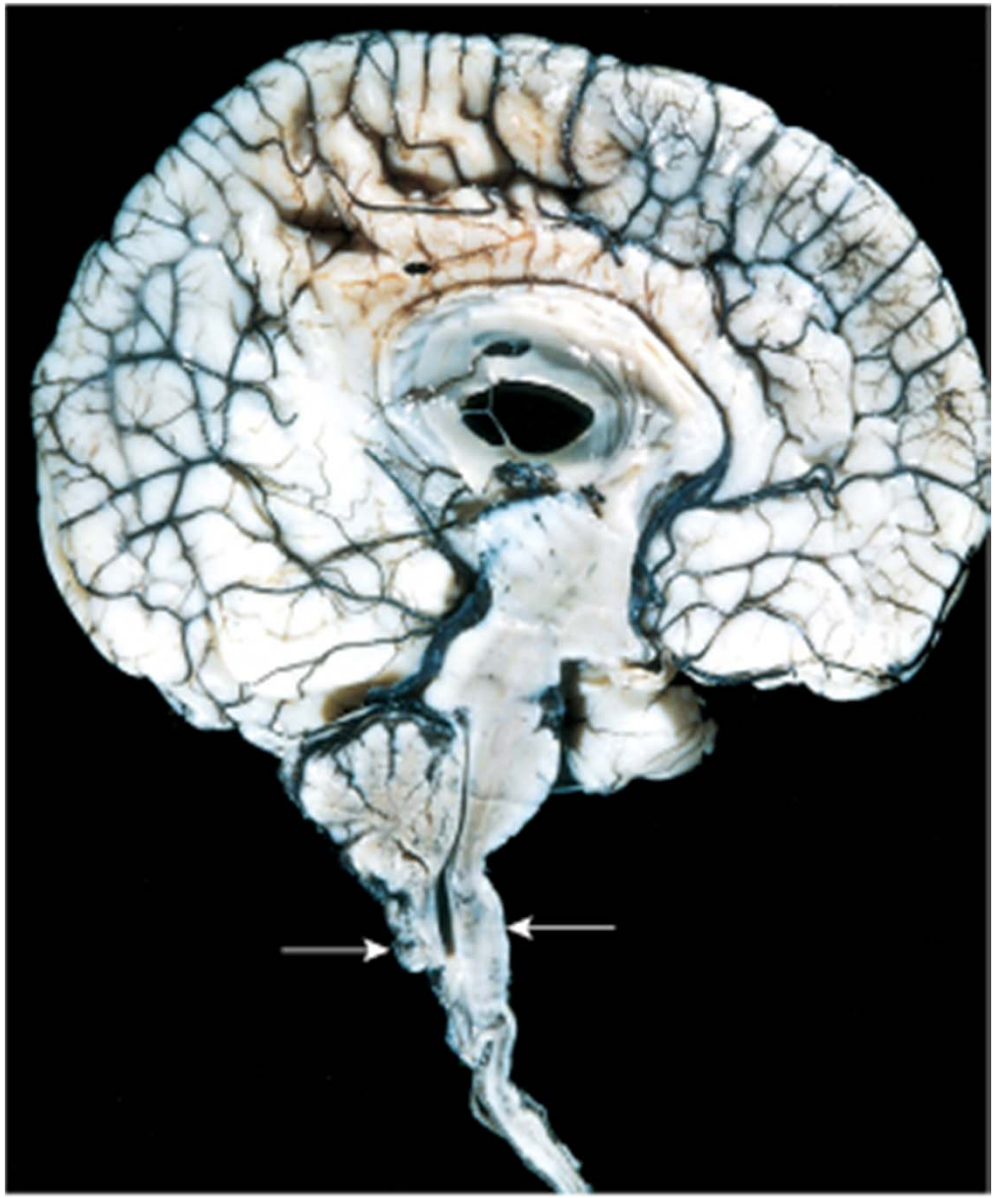
Arnold-Chiari II Malformation



fusion of the thalami

Beaking of tectum

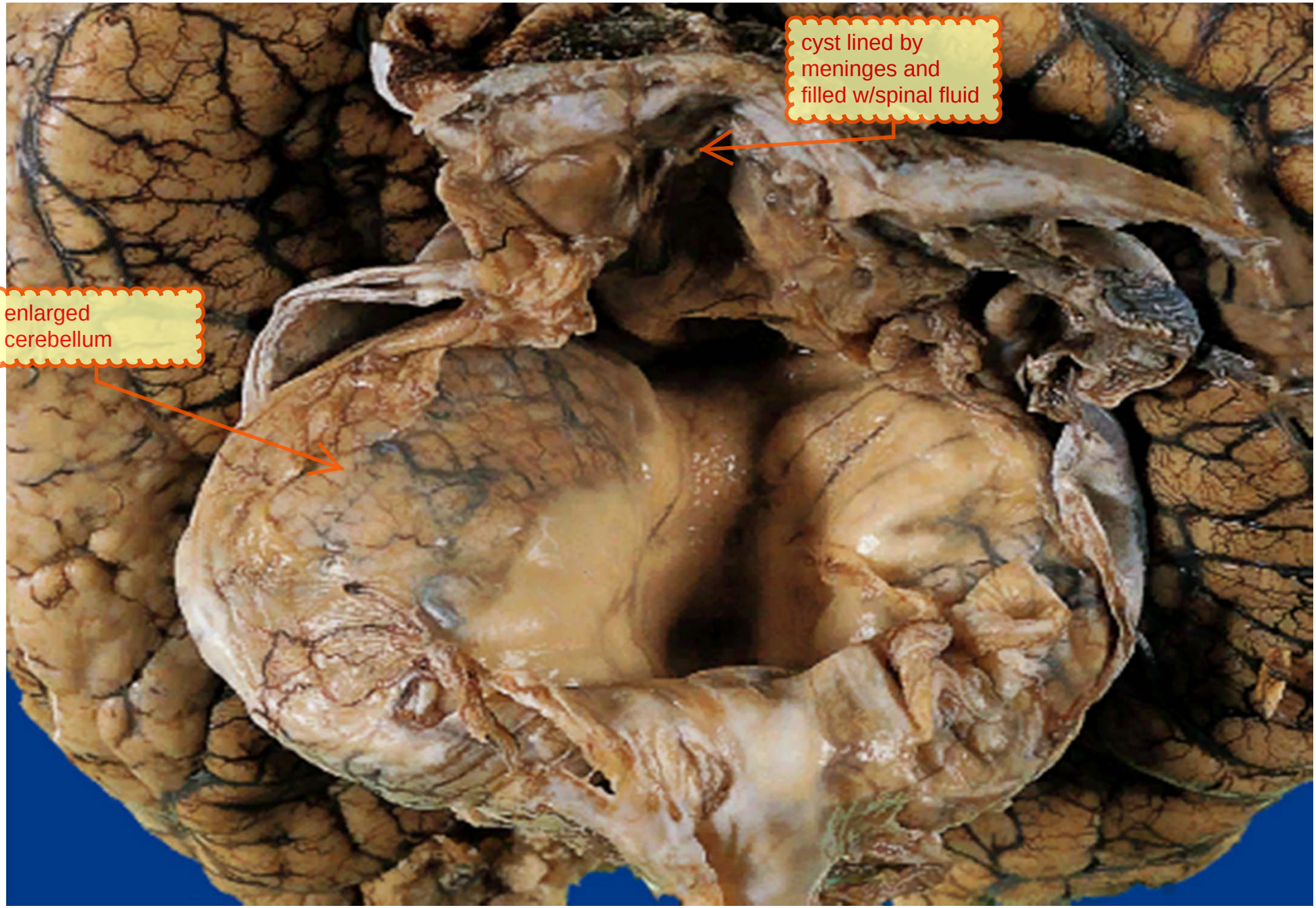
Massa intermedia

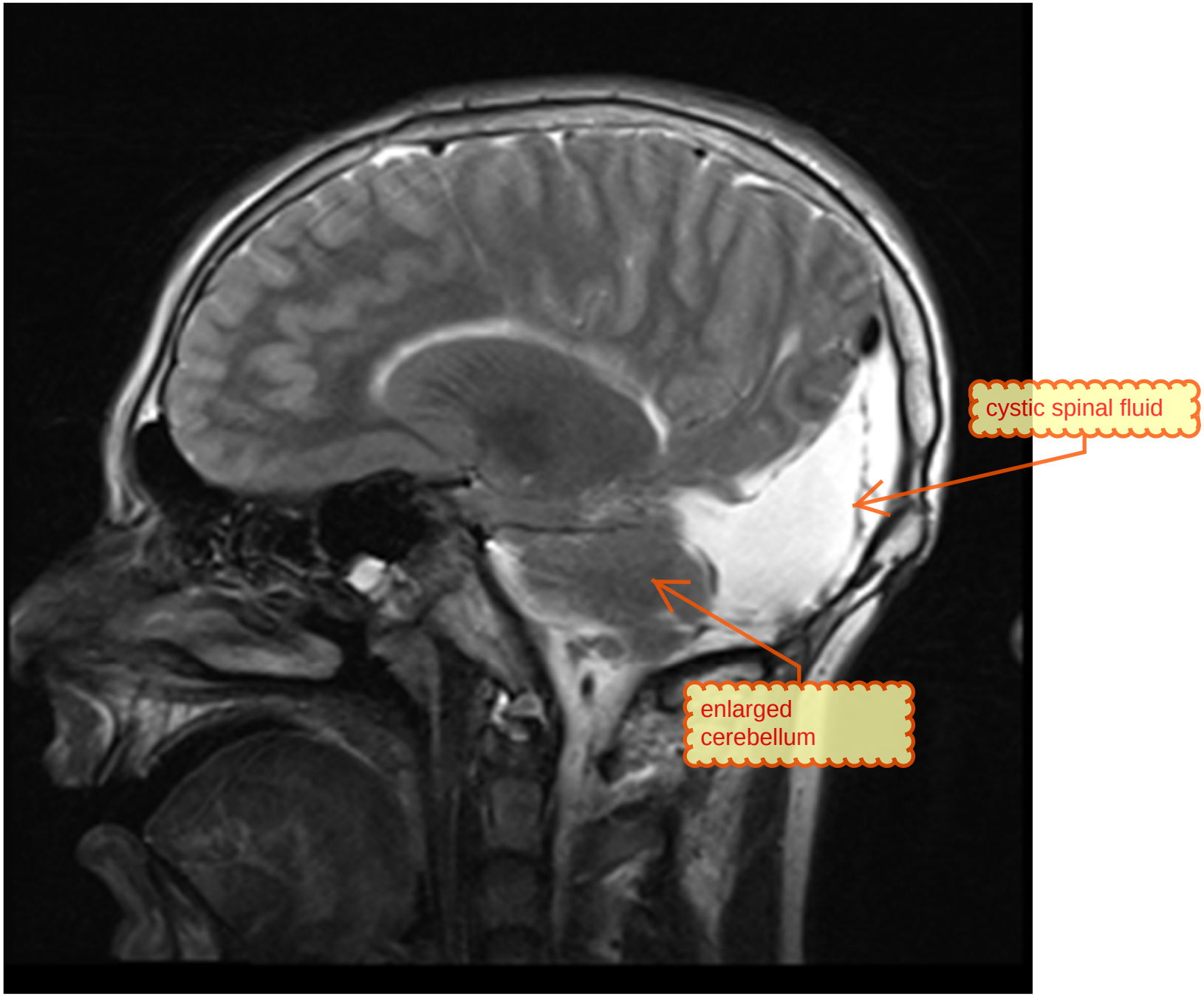


Dandy-Walker Malformation

opposite of
Chiari type II

- **Enlarged posterior fossa**
- **Cerebellar vermis absent or rudimentary**
- **Large midline cyst**

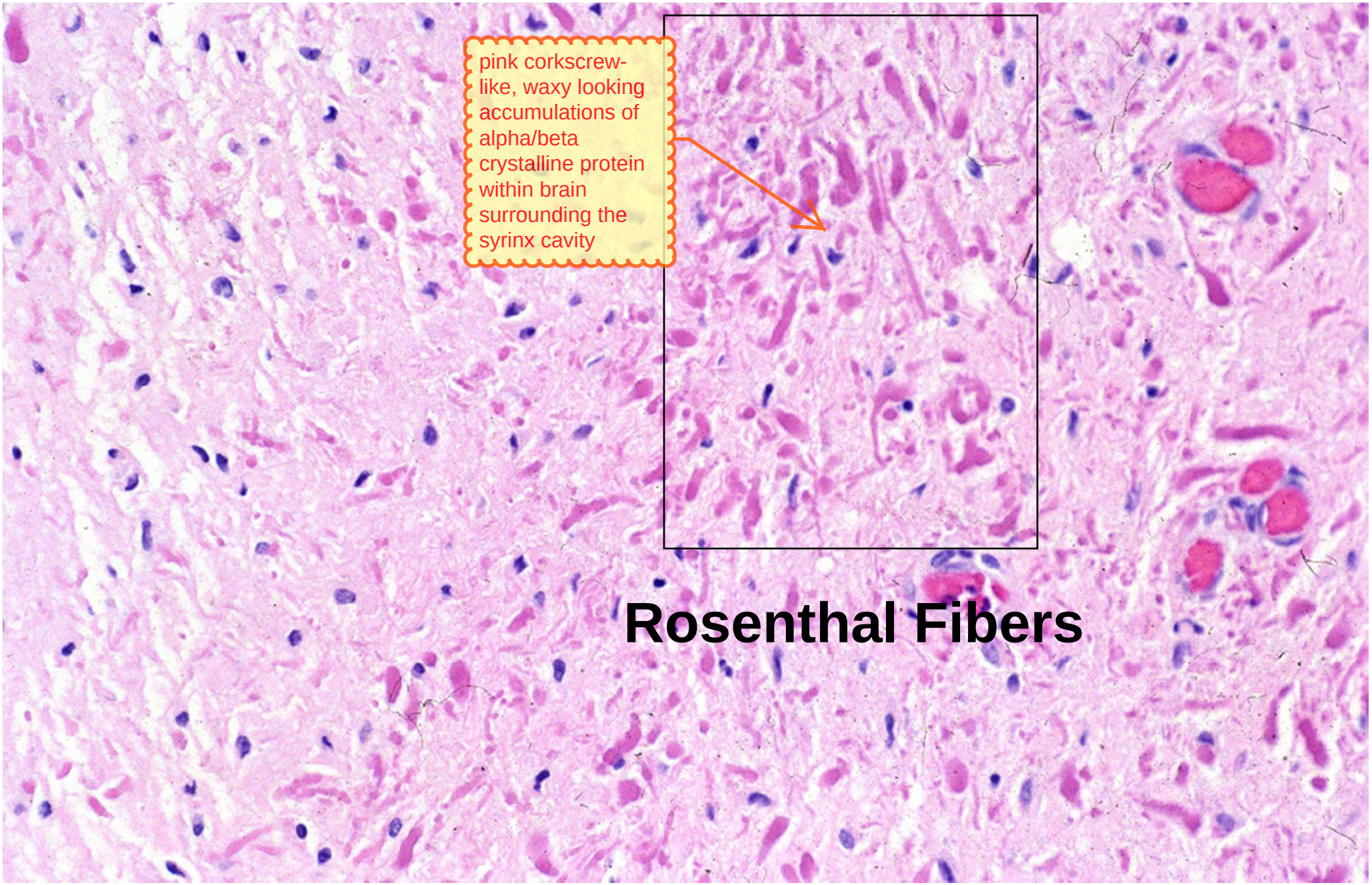

cyst lined by meninges and filled w/spinal fluid
enlarged cerebellum


cystic spinal fluid
enlarged
cerebellum

Syringomyelia

- A fluid-filled cleft-like cavity within the spinal cord parenchyma. Associations:
  - Chiari I malformations
  - Trauma
  - Intraspinal tumors
- Cervical spinal cord most commonly affected
- Cavity may extend up to brainstem: syringobulbia
- Elicits reactive gliosis: Rosenthal fibers

see under microscope- elicits well-defined differential diagnosis, including neoplasms and non-neoplastic things like this

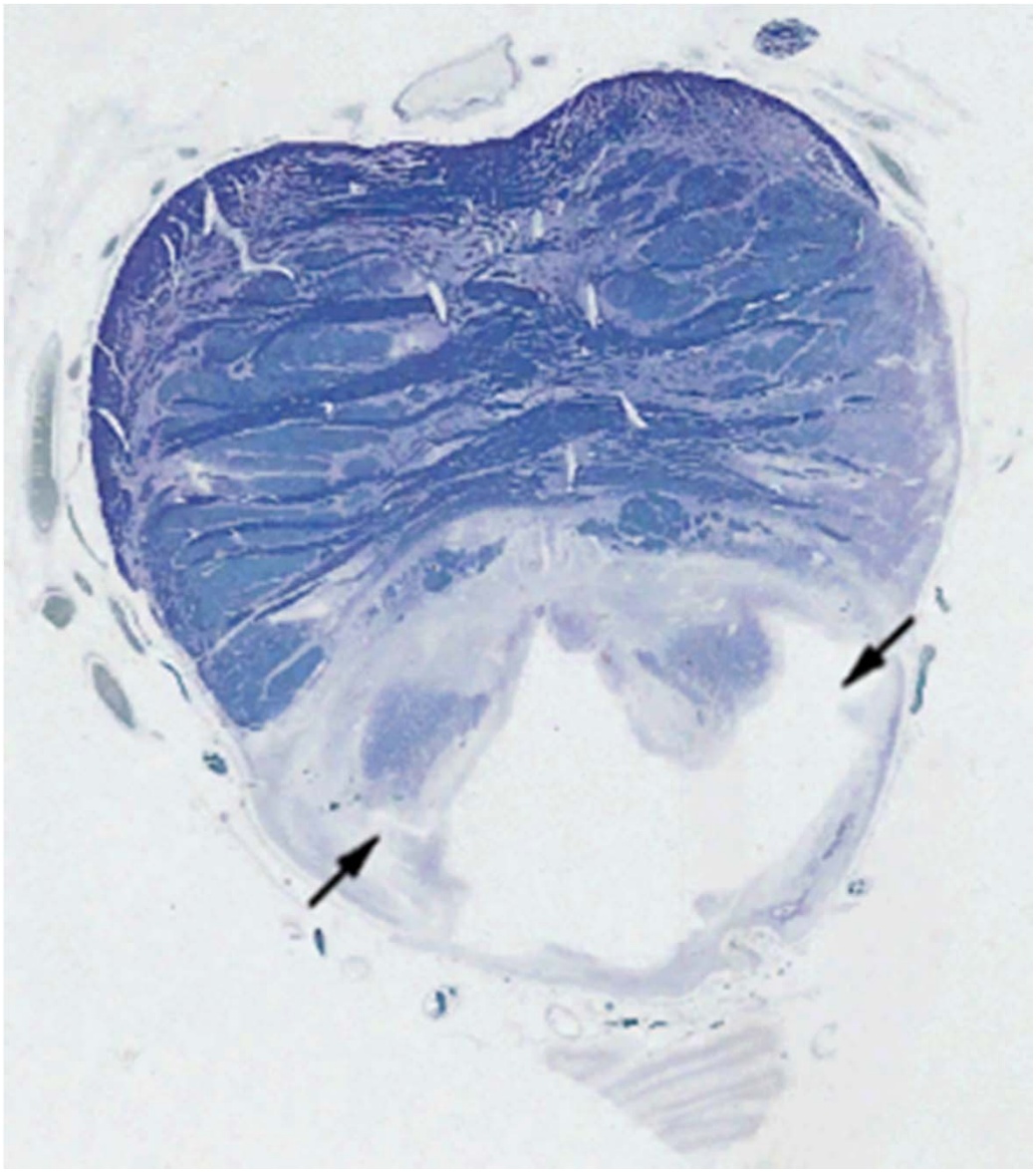

pink corkscrew-like, waxy looking accumulations of alpha/beta crystalline protein within brain surrounding the syrinx cavity
Rosenthal Fibers

Hydromyelia

fluid filled canal, arising from central canal rather than spinal paranchyma

- **Expansion of the ependyma-lined central canal of the spinal cord**
- **Combined hydro/syringo-myelia**

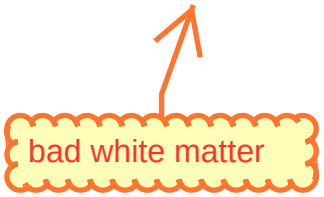
arose from central, expanded into spinal parenchyma



said he couldnt distinguish if this is hydro or syringo but arrows point to fluid-filled space that appears to extend to central canal area

Perinatal Brain Injury

- **Cerebral palsy**
- **Ulegyria**
- **Hemorrhage**
  - **Intraparenchymal**
  - **Intraventricular**
- **Periventricular leucomalacia**



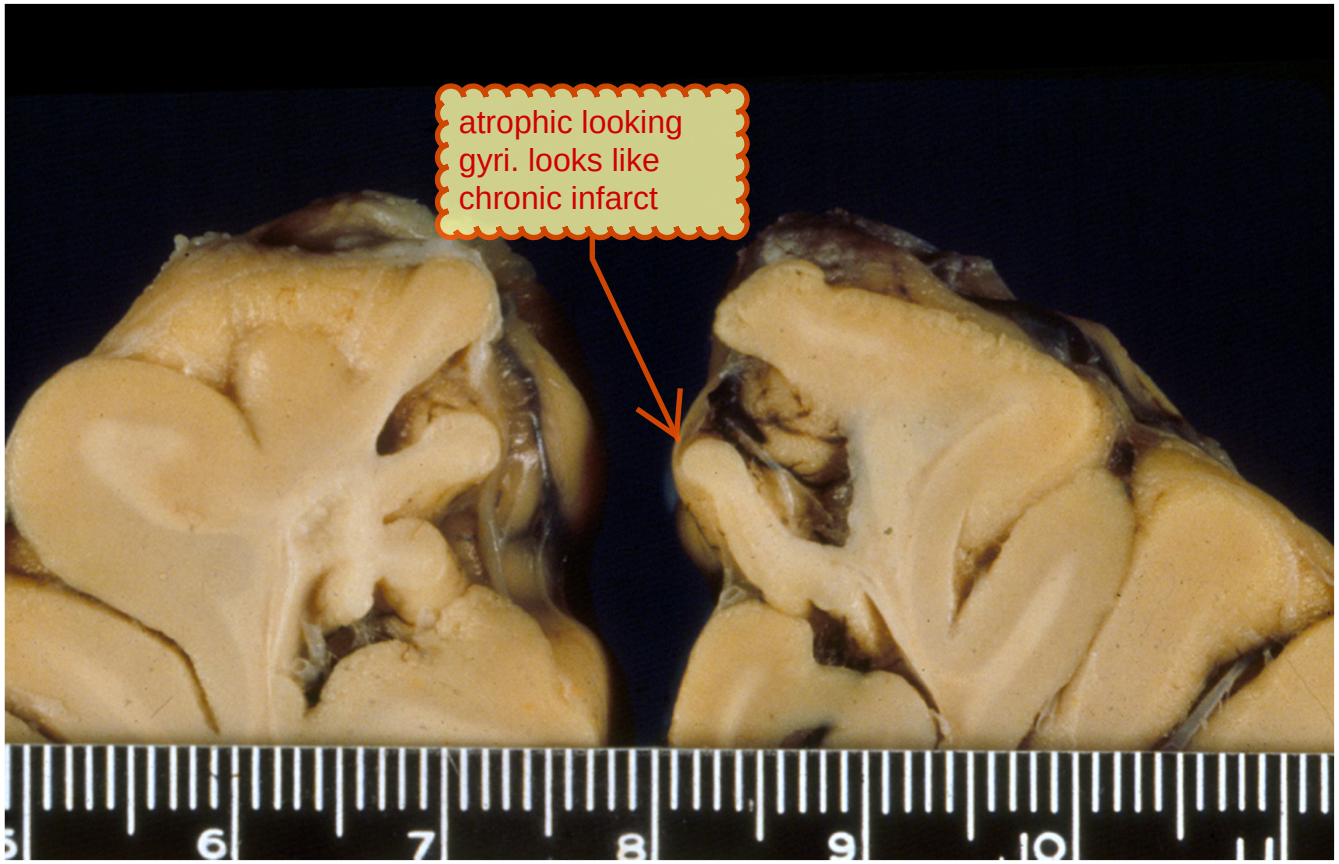
Cerebral Palsy

just read this. typically non-pathological event

- **Clinical term**
- **Non-progressive neurologic deficits**
- **Prenatal // perinatal insults that may result in hemorrhage and infarction**

Ulegyria

- **Thinned, gliotic gyri, perinatal ischemia**



Hemorrhage

- **Premature infants**
- **Germinal matrix**
  - **The periventricular region of neuronal and glial differentiation**
- **Junction of thalamus and caudate nucleus**
- **Hemorrhage may extend into the ventricular system and result in hydrocephalus**

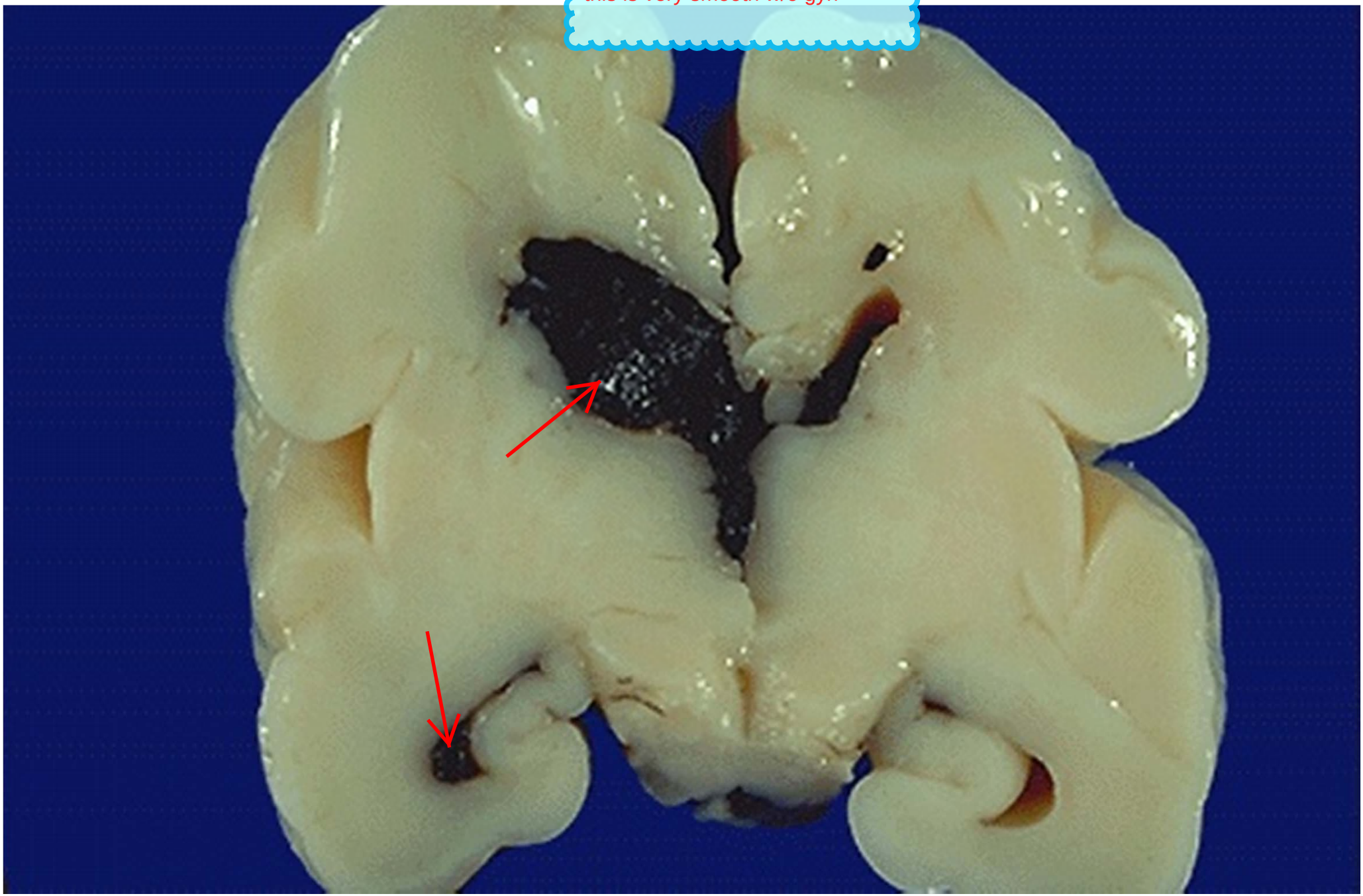
common, if before 34 wks

often occur here in this matrix

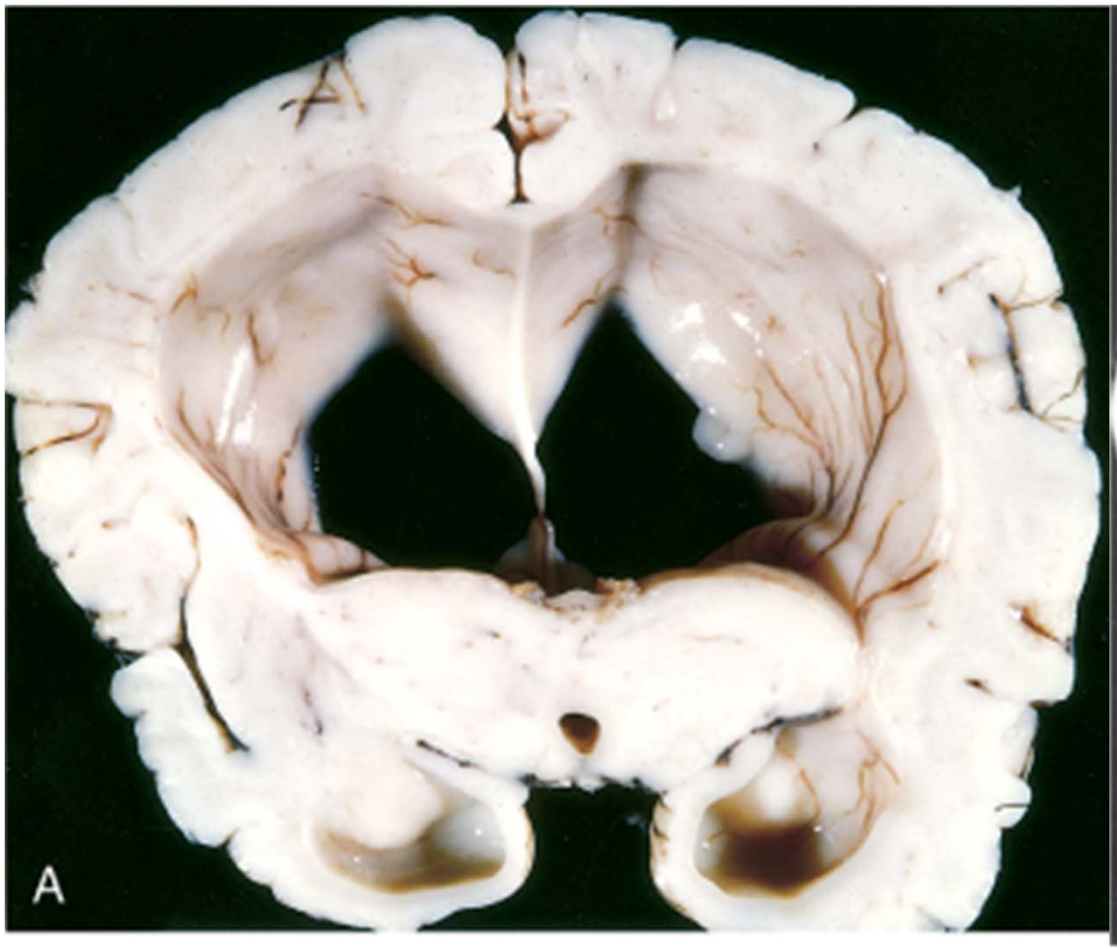
they are there in their primitive state before they migrate out to final place in brain

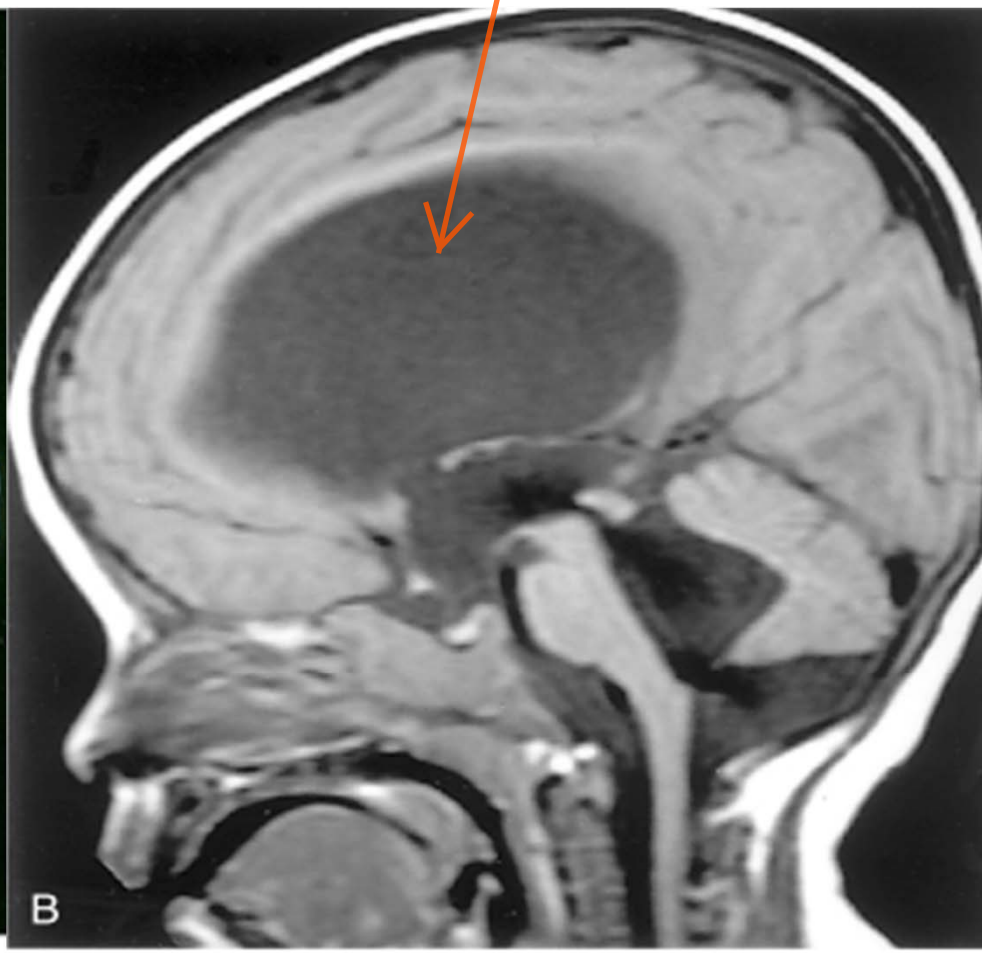
high risk because of strong capillary network

ranked by severity, 1-4. The most severe will result in hydrocephalus and require csf shunting- long term problem


immature brain- can tell because
this is very smooth w/o gyri

Hydrocephalus



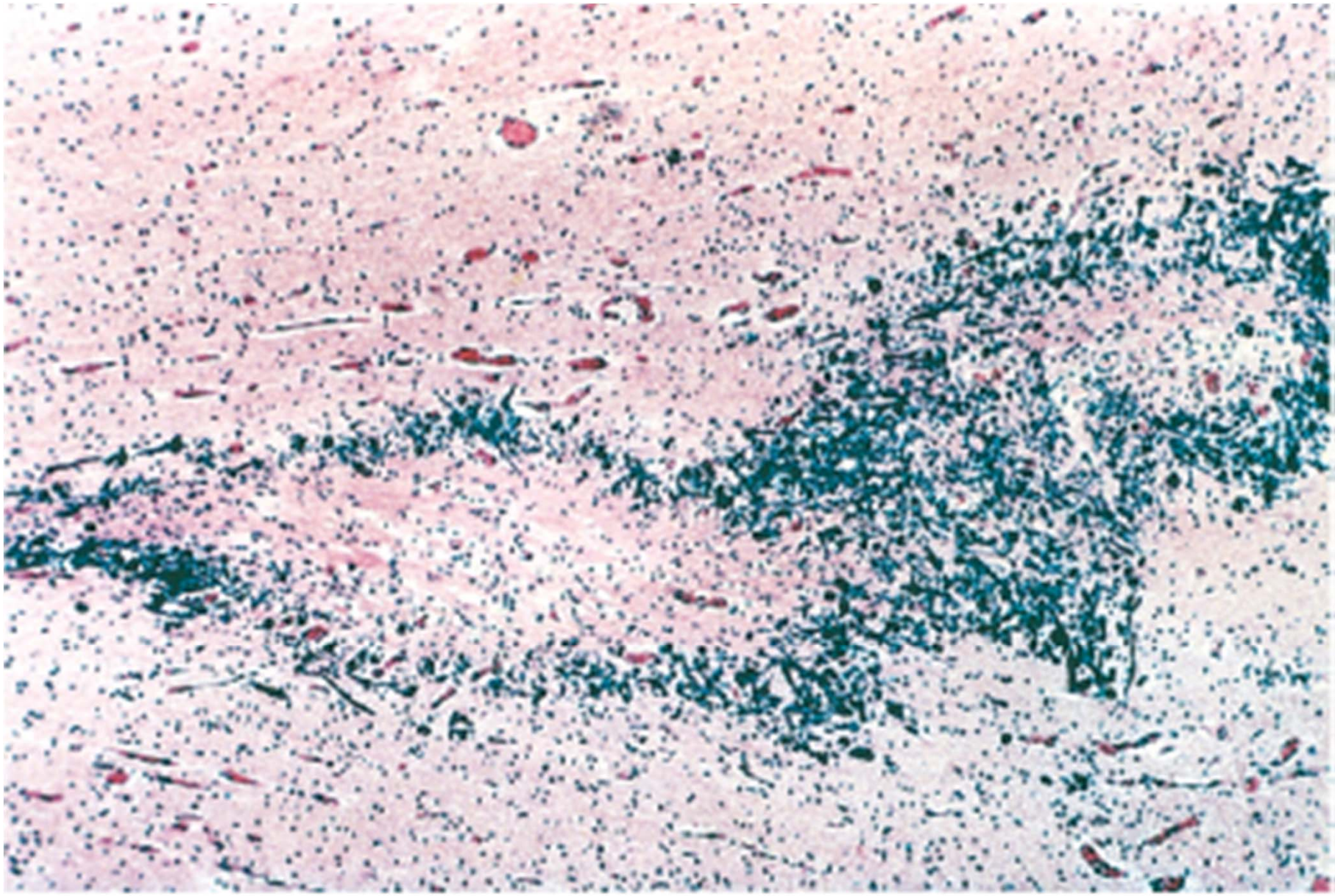


Periventricular Leukomalacia

ischemic event

- **Infarcts of the supratentorial periventricular white matter**
- **Premature infants**
- **Histology:**
  - **necrosis and mineralization**

typical features of ischemic event



The End