Development and anomalies of the cranio-vertebral junction

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What is the Cranio-Vertebral Junction

- A segment of the spine dedicated to head motion
  - vision, smell, earing, seizing, eating, fighting
- Interposed between the “standard” spine and the “cephalized” spinal segment that constitutes the bony posterior fossa
- Derived from occipito-cervical somites

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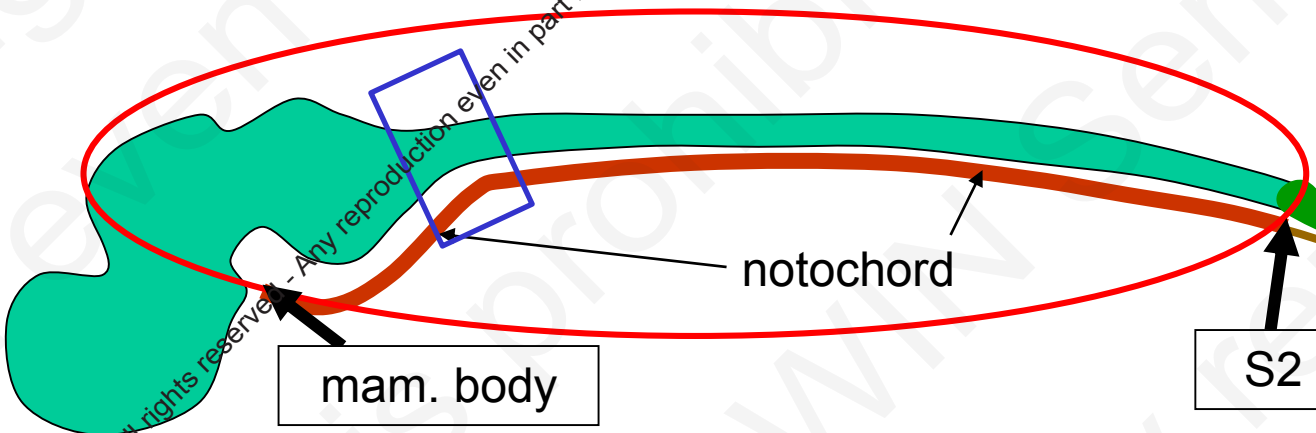
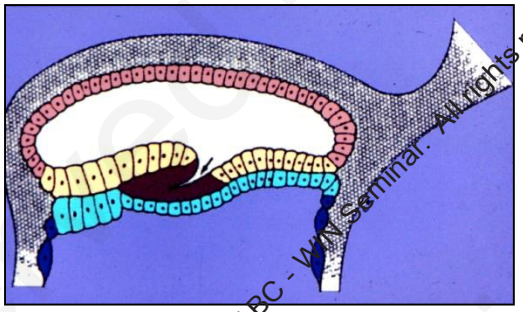
Malformations at the cranio-vertebral junction

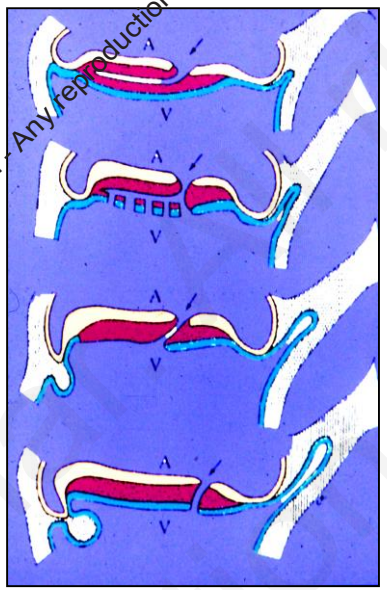
1. Gastrulation: notochord development and malformations
   → neuro-enteric canals/cysts
   → diplomyelia/diastematomyelia
2. Neurulation: neural tube differentiation and closure
   → Chiari III
3. Somitic/vertebral segmentation disorders
4. Bony growth disorders
   → Chiari 1 deformity commonly associated to both

Notochordodysraphism

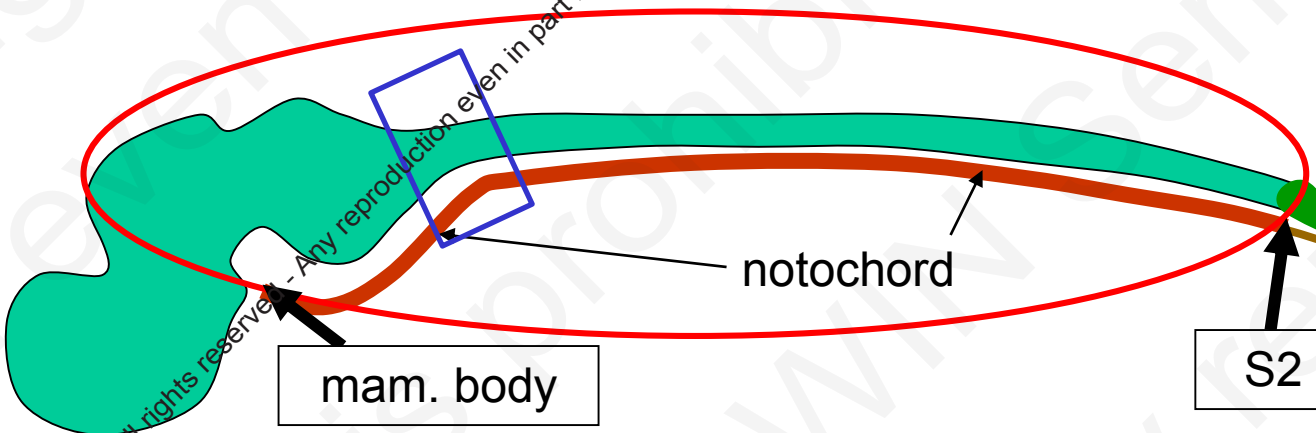


Formation of the notochord
Neuro-enteric canal and cyst

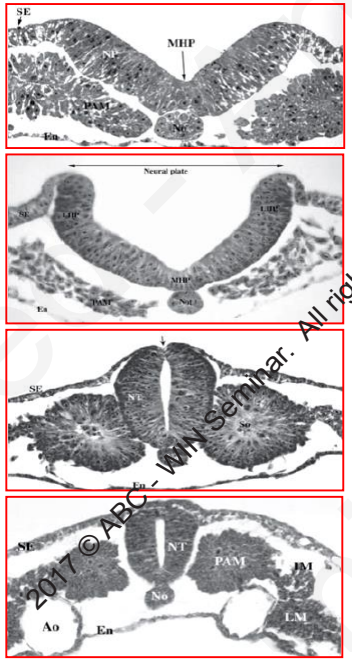


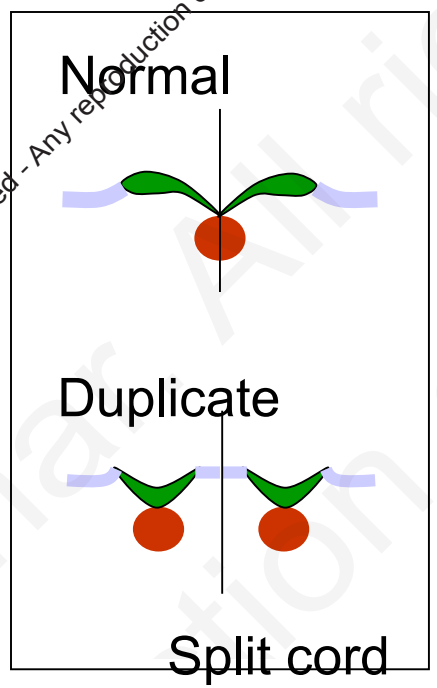


Notochordodysraphism

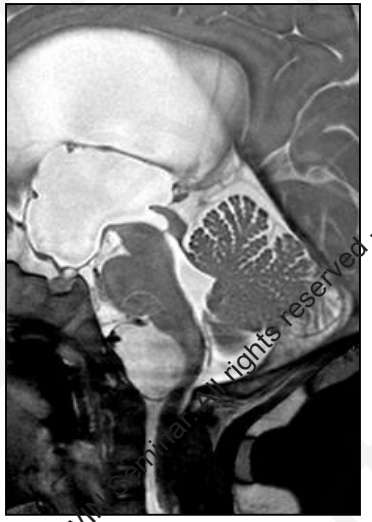


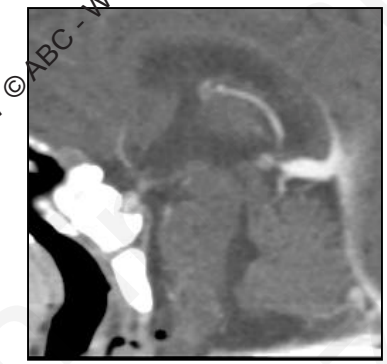
Induction of the neurulation



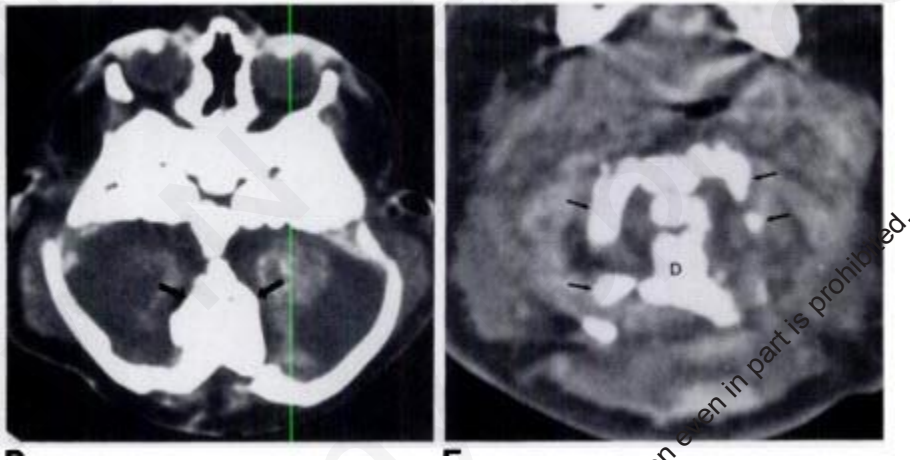


Notochordodysraphism at the CVJ

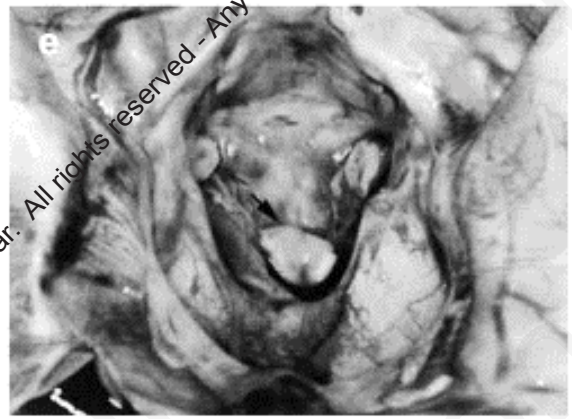




Neuro-enteric canal and cyst

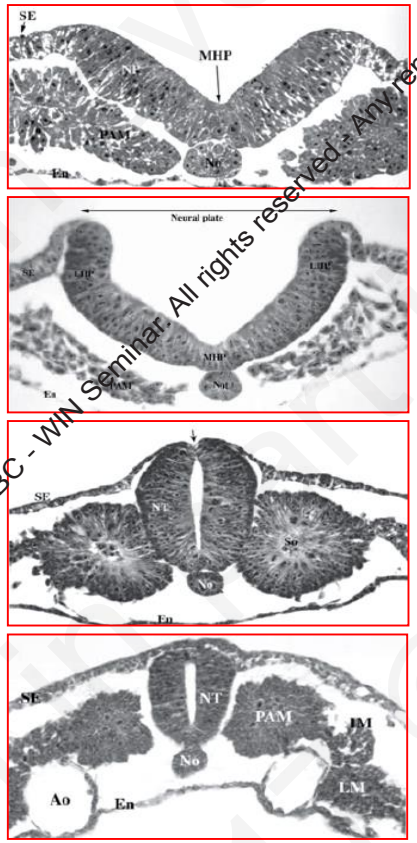


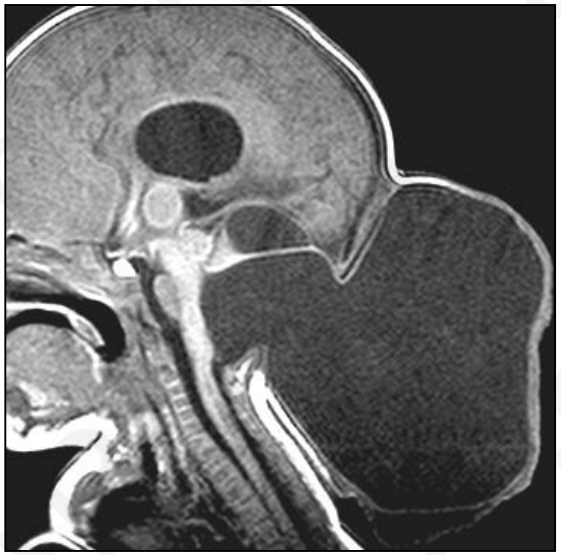
Diastematobulbia Herman, AJNR 1990

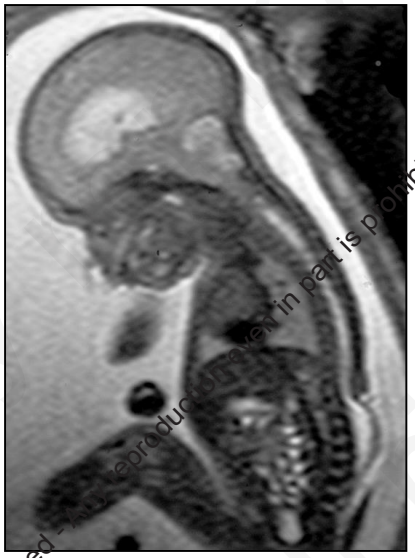


Foramen magnum diastematobulbia with triplobulbia
Sandberg CNS 2007

Open neurodysraphysm (neural tube defect) at the CVJ

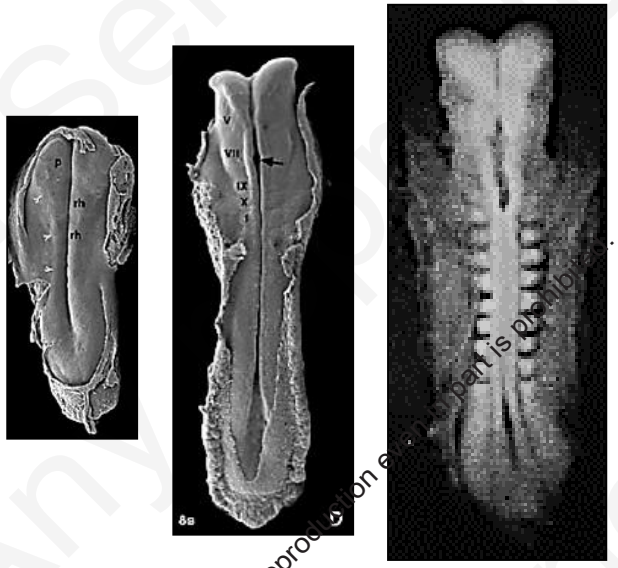






- Myelobulbo-meningocele = Chiari 3
- (Chiari 2 is a deformity secondary to a myelomeningocele, not a malformation)

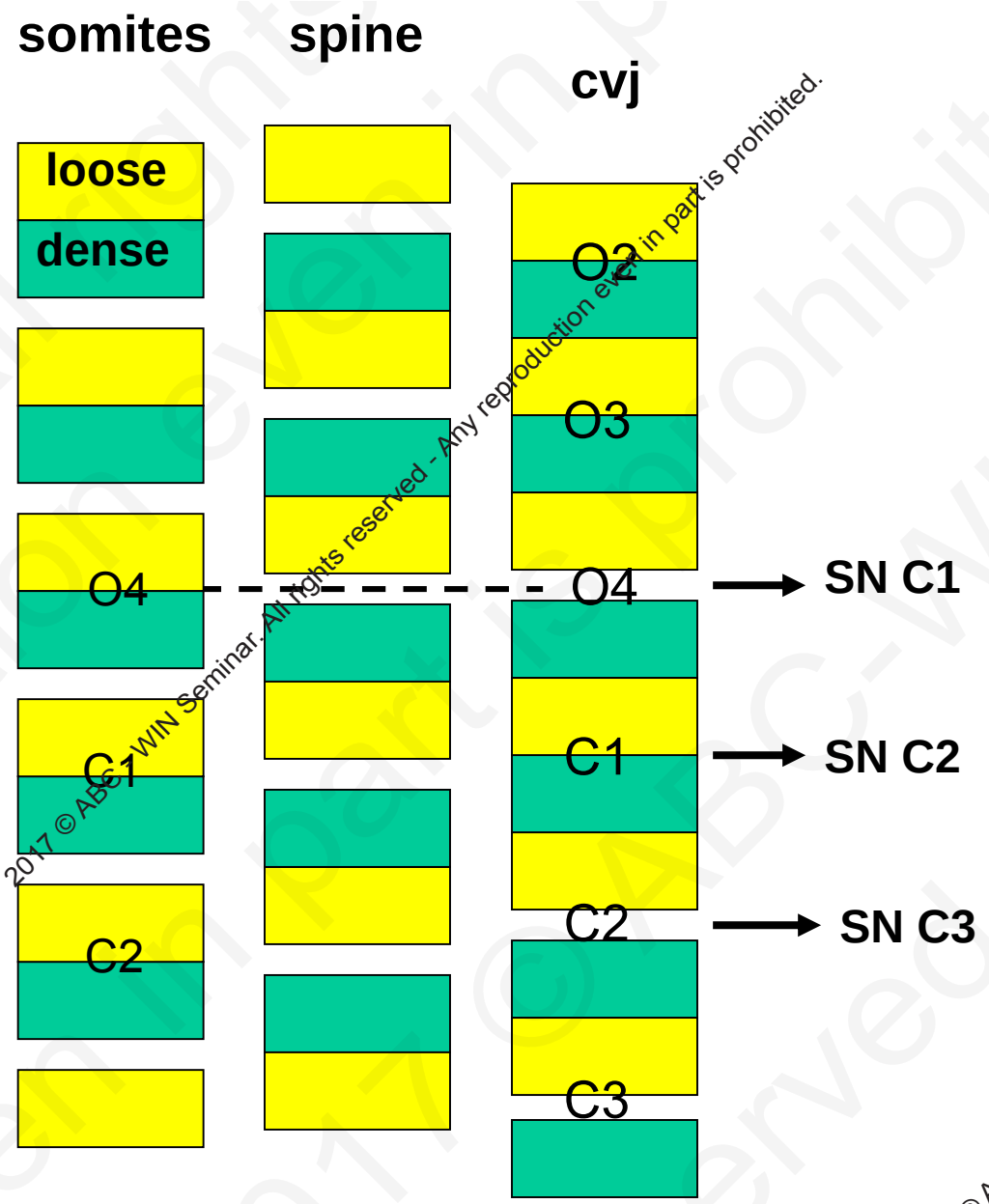
Somitic segmentation process

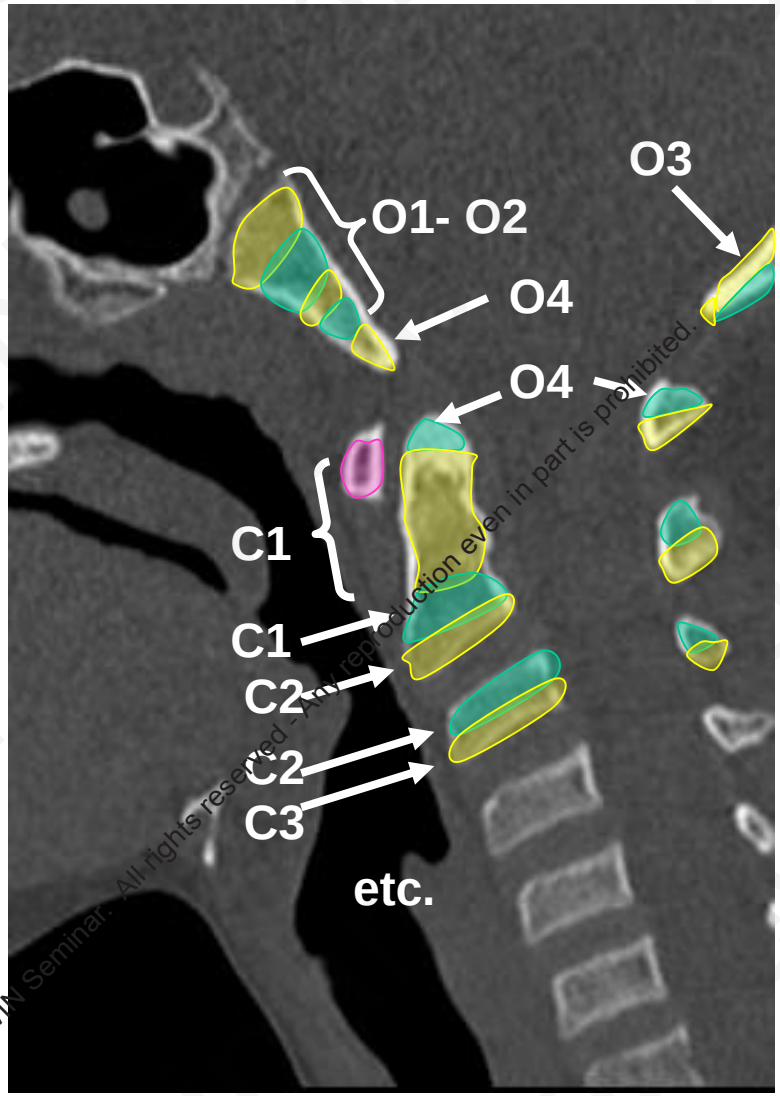


- Ventral induction *SHH*
- Segmentation genes: Homeobox genes
- "Segmentation clock" genes:
  - cyclic activation of *Notch, Wnt, FGF* makes up the somites
  - cyclic inhibition by *MESP2* = intersomitic-boundaries

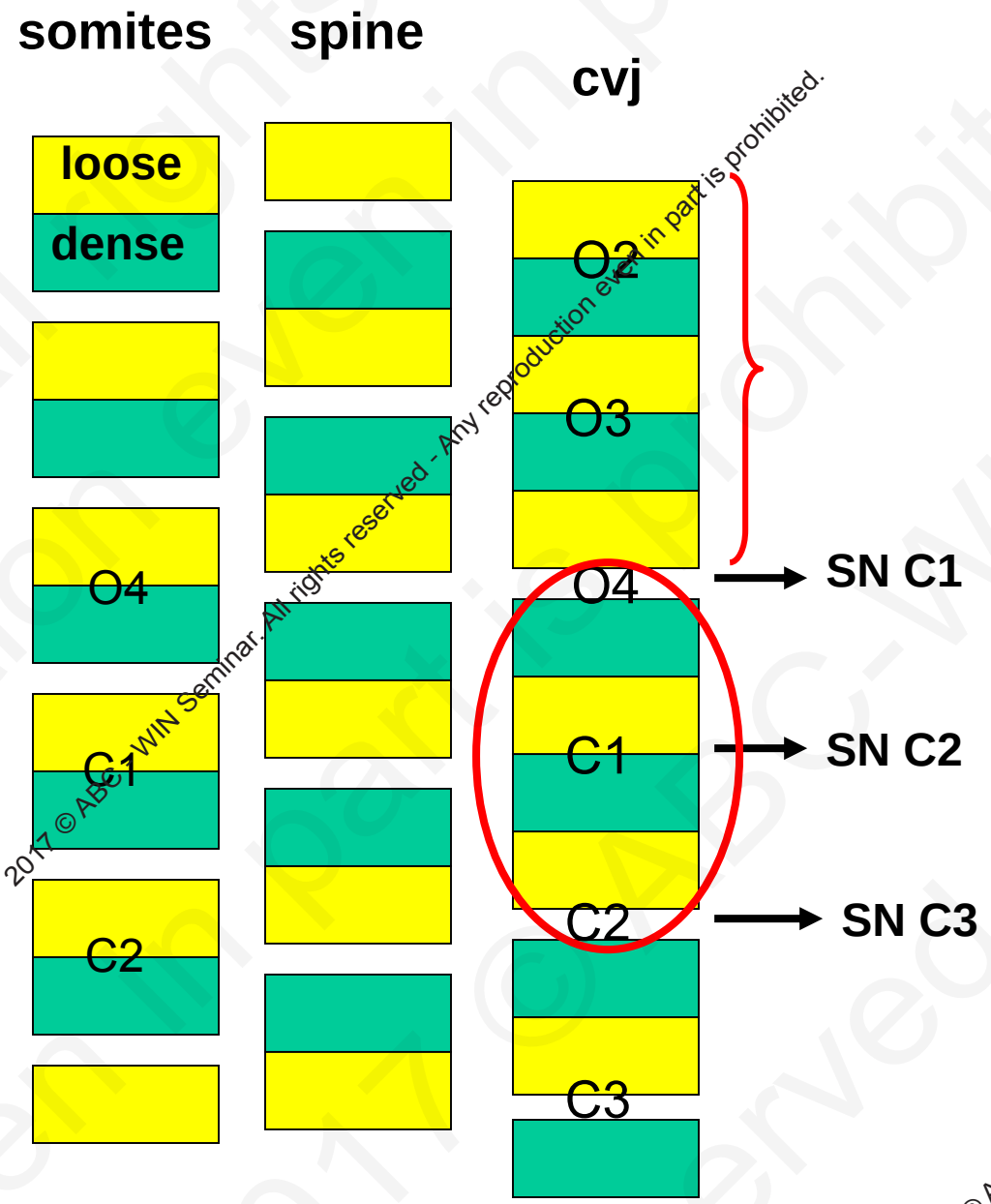
Bony cranio-vertebral junction segmentation

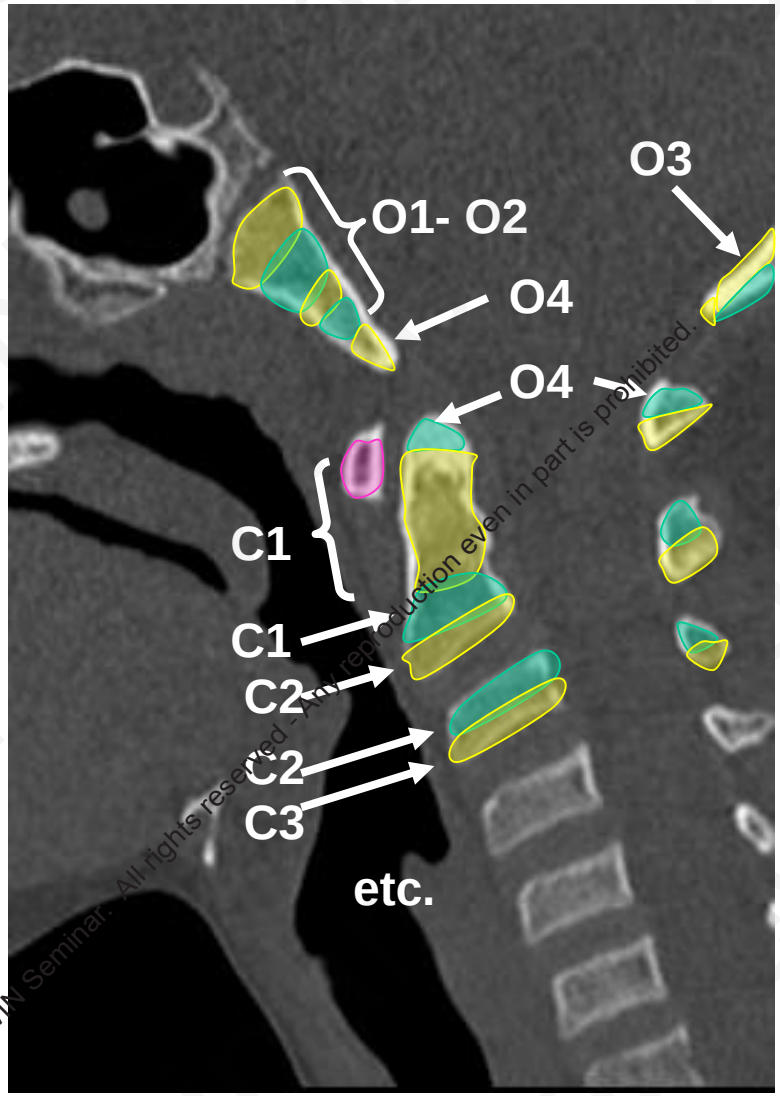
- Vertebral “resegmentation” process
  - Somites = nerves, vertebrae between nerves
- Three cranio-vertebral specificities
  1. cephalized rostral “spine”: unsegmented posterior fossa
  2. bidirectional cranio-vertebral joint: un-divided C1-C2
  3. retention of C1 hypo-centrum for rotation socket



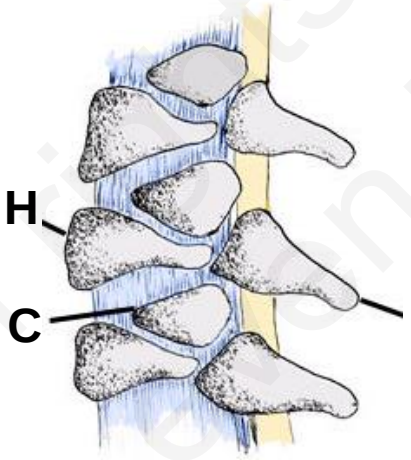


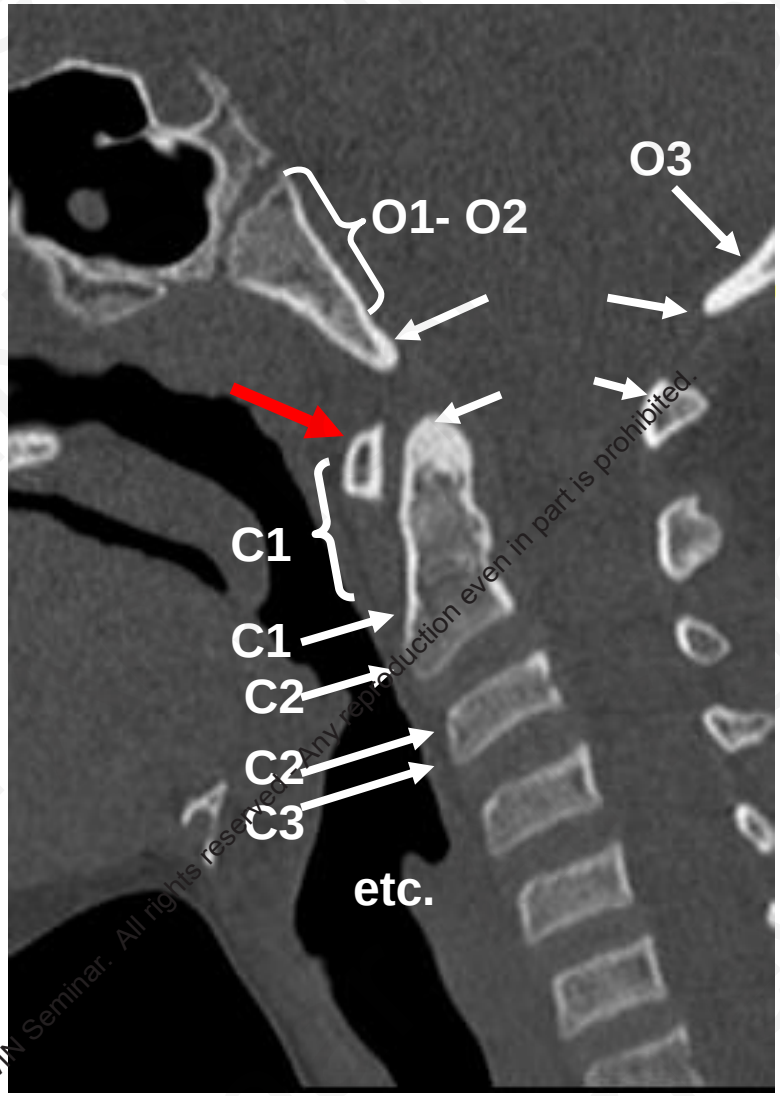
1) somitic levels correspond to nerves – vertebrae are between nerves





2) unsegmented occipital – CVJ segment – resegmented spine





3) retention of the O4 - C1 segmental hypocentra (hypochordal arches) to complete the multidirectional articulation (socket for the axis)

Segmentation process: beyond the somites

- Axial skeleton, paraxial mesoderm, neural tube are segmented
- Rostral-most notochord extends to mesencephalon
- Rhombomere 0 = isthmic organizer starts the segmentation
- Segments = somitomeres correspond to neuromeres
  - pharyngeal (branchial) arches = ventral portion of incomplete somites: no dorsal sclerotome, myotome, dermatome
  - occipital somites 1-3: no dorsal myotomes
  - pro-atlas: no dorsal sclerotome
  - C1: no dorsal dermatome (no sensory C1)

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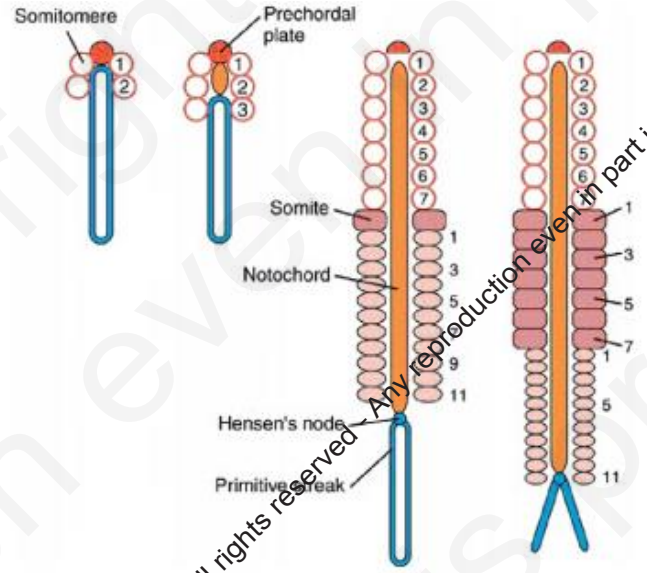

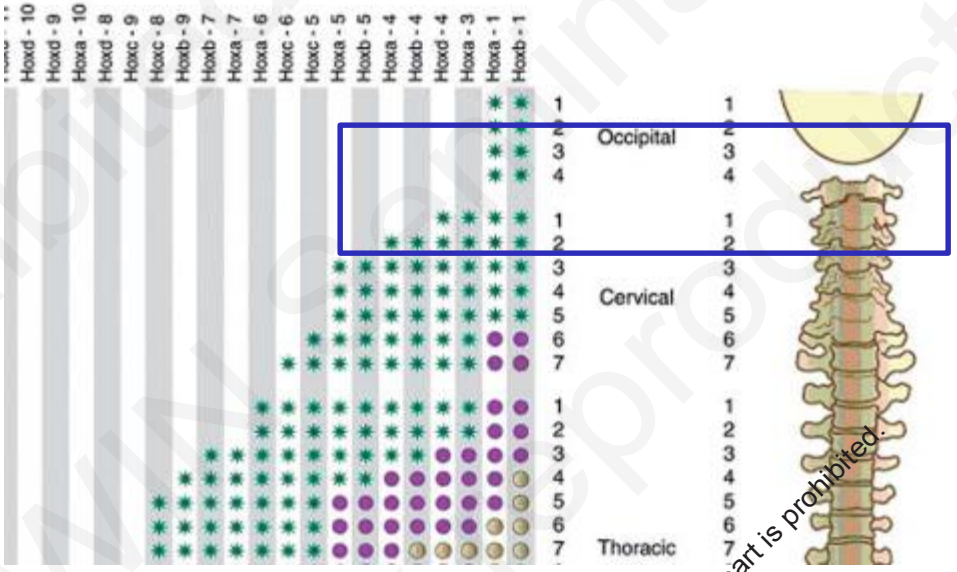

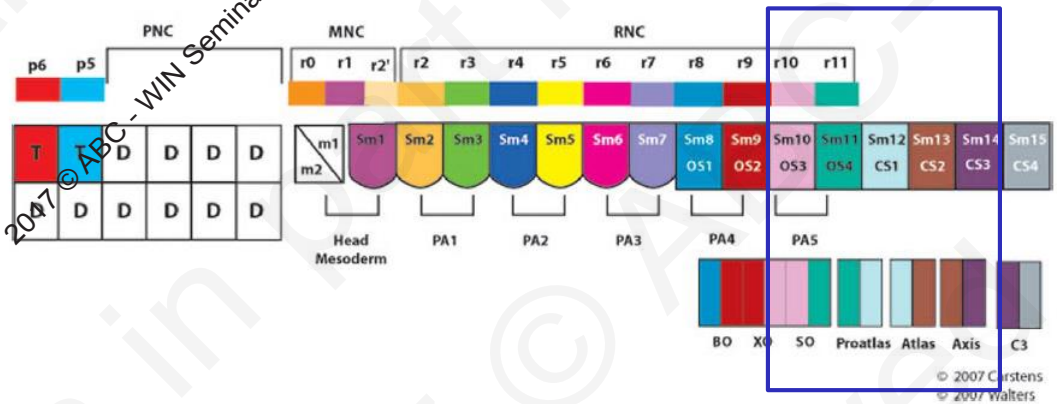

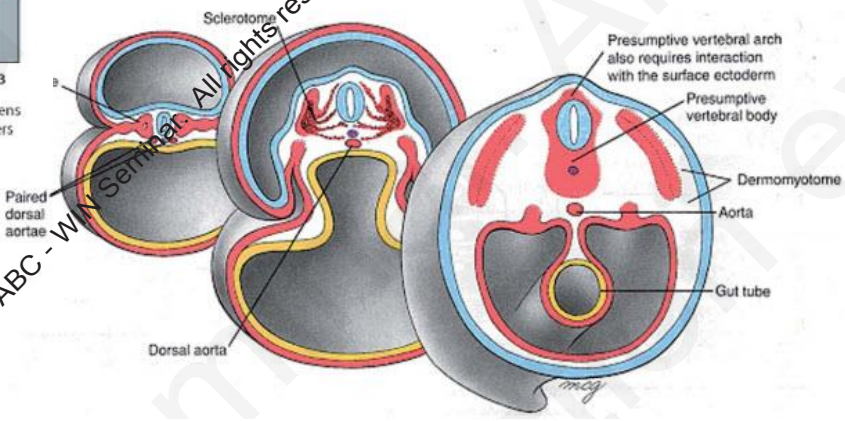

MH Carstens
Handbk Clin Neurol, Malf. Nerv. Syst
Chapt 16-17, 2008

neuro-mere	neural tube	somito-mere	somite	derivative 1	derivative 2
r0				NC: prechordal mesoderm?	
r1	pons-cerebellum	1		NC: orbital muscles and walls	
r2	open medulla 1	2		Phar. arch 1	
r3		3			
r4	open medulla 2	4		Phar. arch 2	
r5		4			
r6	open medulla 3	6		Phar. arch 3	pyramid
r7		7			mastoid
r8	closed medulla	8	OS1	Phar. arch 4	occiput
r9		9	OS2		
r10	closed medulla	10	OS3	Phar. arch 5	
r11		11	OS4		foramen magnum
m1	cord	12	CS1		C1-C3
m2		13	CS2		
m3	cord	14	CS3		
m4		15	CS4		

Segmentation process

- Ventral induction *SHH*
- Segmentation genes: Homeobox genes
- "Segmentation clock" genes:
  - cyclic activation of *Notch, Wnt, FGF* makes up the somites
  - cyclic inhibition by *MESP2* = intersomitic-boundaries
- Specific causes, pathways, processes to explain why segmentation is abnormal in a given patients are lacking
- Specifics of CVJ unknown
- Segmentation disorders may be syndromic or sporadic

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Missegmentation of the bony CVJ

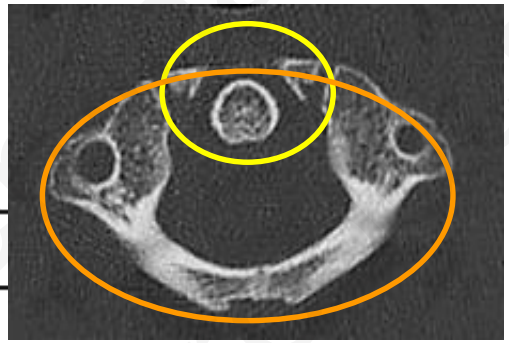
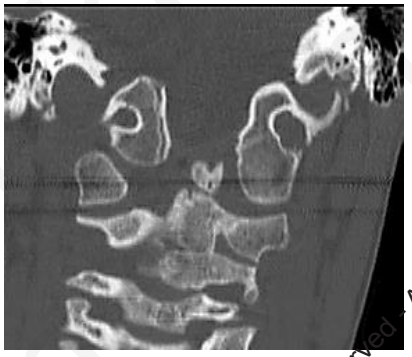
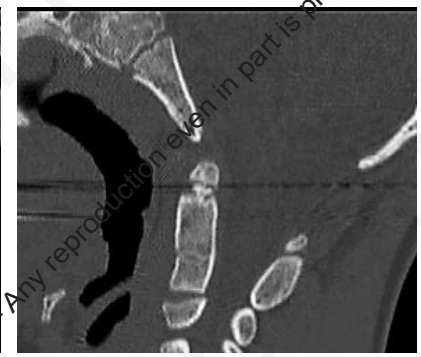
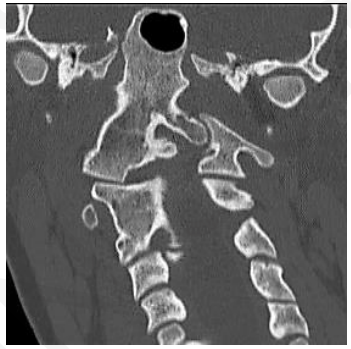
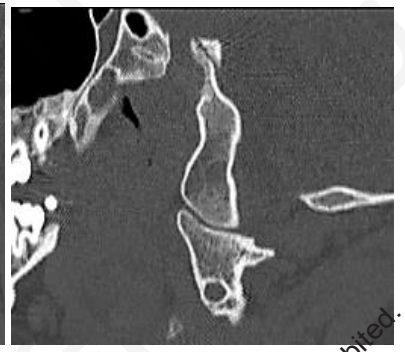
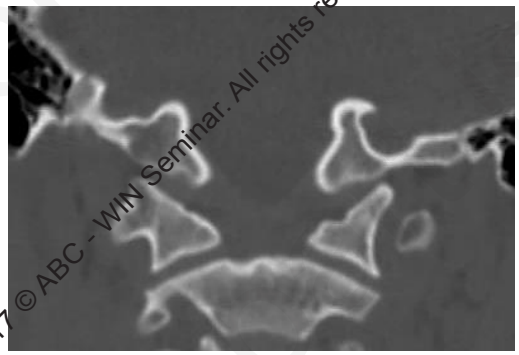
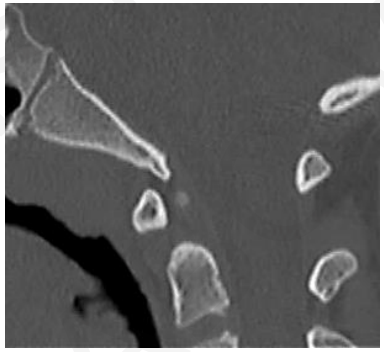
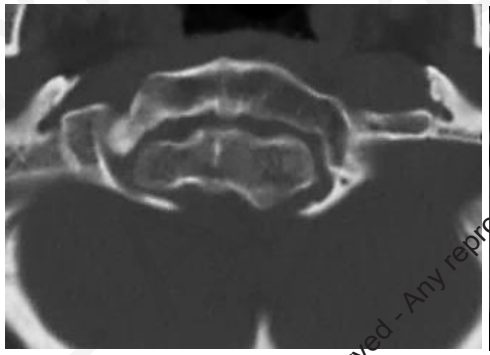
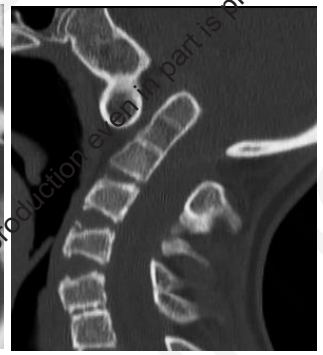
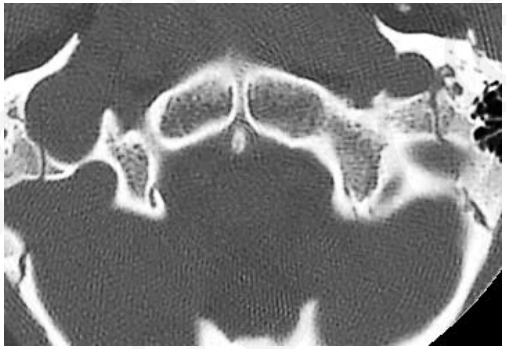
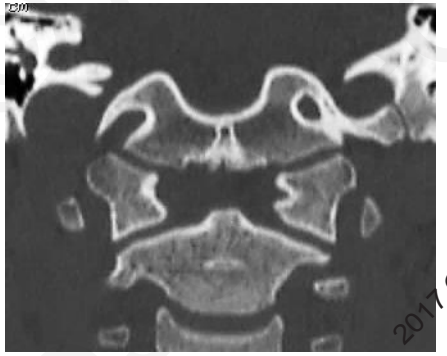
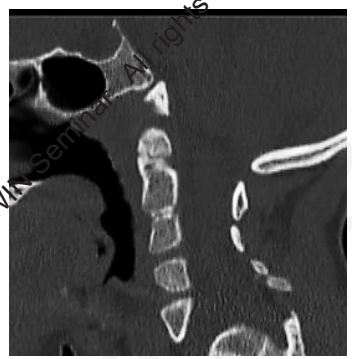
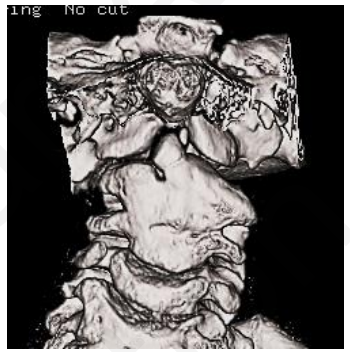


Table 1 Classification of bony malformations of the CVJ according to embryogenesis

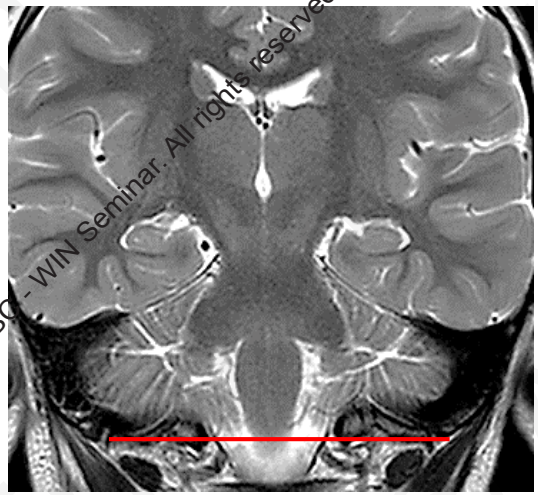
Clinically significant CVJ bony malformations			
Malformations of central pillar		Malformations of surrounding rings	
Disturbance of axial component of occipital sclerotome, proatlas and C_1 resegmented sclerotome		Disturbance of lateral component and hypochordal bows of proatlas and C_1 resegmented sclerotome	
Odontoid dysgeneses	Basioccipital dysgeneses	Proatlas anomalies	C_1 sclerotome anomalies
▪ Aplasia/hypoplasia of odontoid components	▪ Failed midline integration of basioccipital primordium	▪ Hyperplasia of hypochordal bow of proatlas	▪ Aplasia of hypochordal bow of C_1
▪ Disturbance of odontoid synchondroses (IBZ)	– Bifid clivus	– Third occipital condyle	– Aplasia and hypoplasia of anterior C_1 arch
– Os odontoideum	▪ Basioccipital dysplasia	– Pre-basioccipital arch	▪ Aplasia/hypoplasia of lateral sclerotome
– Ossiculum terminale persistens	– Basilar impression	▪ Hyperplasia of exoccipital sclerotome	– Posterior C_1 arch agenesis
▪ Abnormal resegmentation of proatlas centrum	– Platybasia	– Hypertrophic occipital condyle	▪ Combined hypochordal bow and lateral sclerotome dysplasia
– Os avis	– Retroflexed dens	▪ Non-resegmentation of proatlas (anterior homeotic transformation)	– Aplasia of lateral mass and anterior C_1 arch
▪ Failed midline integration of basal dental segment	– Basilar invagination	– Atlas assimilation	– Combined anterior and posterior C_1 arch defects
– Bifid dens	– Basilar kyphosis	▪ Posterior homeotic transformation	– Bifid anterior and posterior C_1 arch

Pang and Thompson Childs Nerv Syst 2011

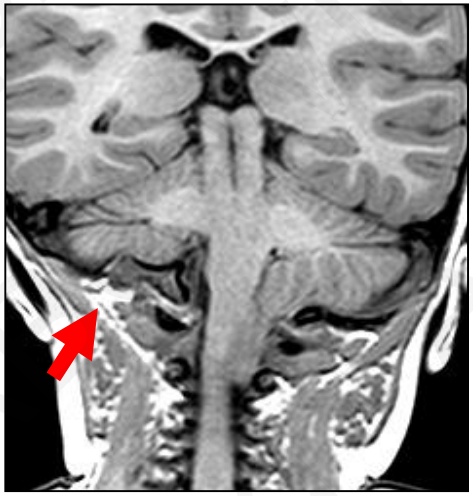
Missegmentation of the bony CVJ

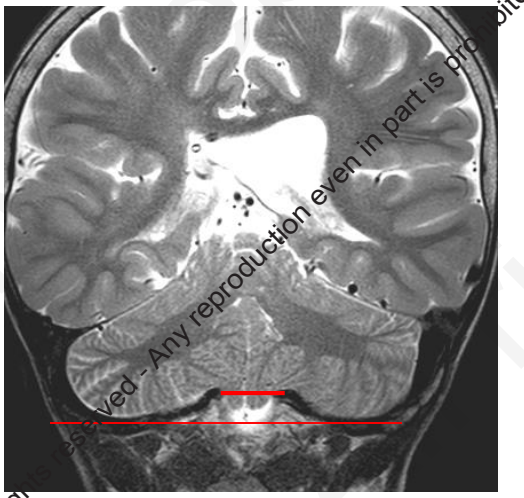
Abnormal bony posterior fossa



Normal occipital alignment

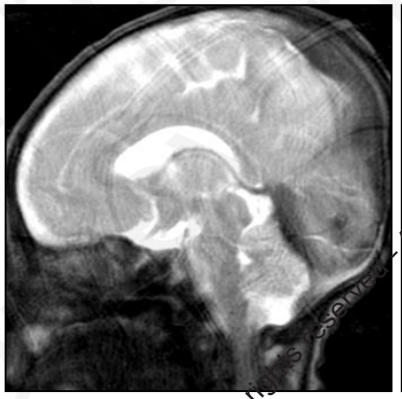


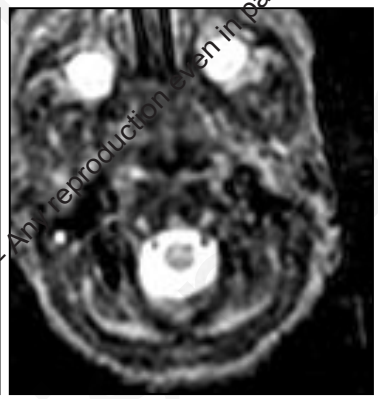
Unilateral occipital hypoplasia



Basal impression (invagination)

Neural CVJ: Chiari 1 deformity





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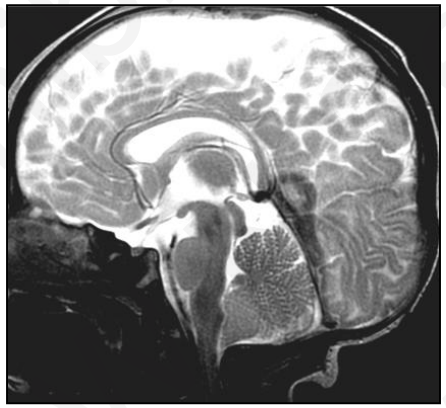
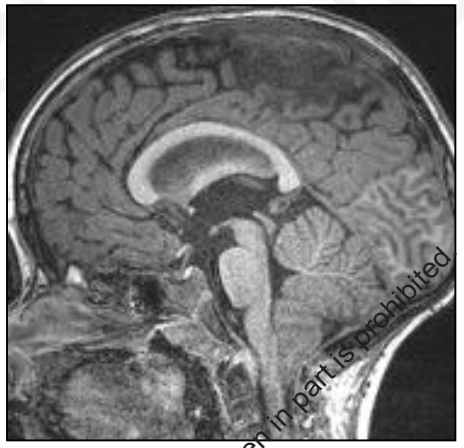
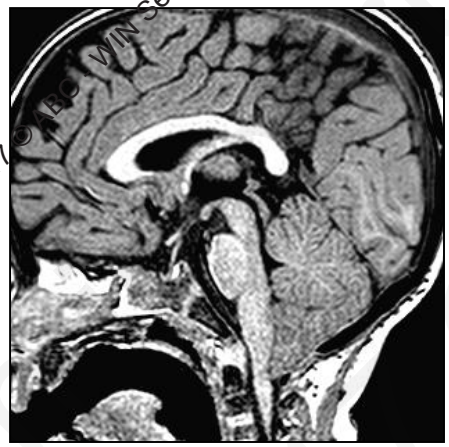


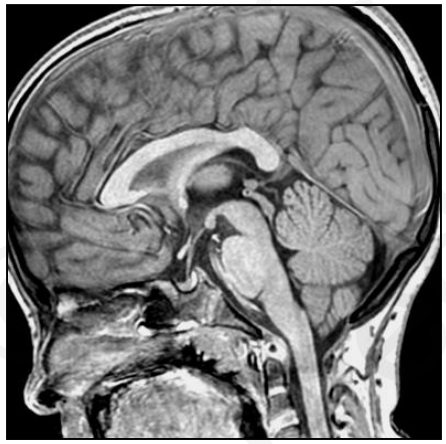
2m



4y



3y



6y

- Chiari 1 may appear or regress spontaneously
- May be secondary to lumbar shunt or CSF over-drainage

Chiari 1 is a deformity, not a malformation

Chiari 1 deformity: terminology

- Hans Chiari 1891
  - Chiari 1: tonsillar ectopia
  - Chiari 2: low, abnormal hindbrain with myelomeningocele
  - Chiari 3: occipito-cervical cephalocele
  - Chiari 4: extreme cerebellar hypoplasia, now PCH (degenerative)
- Tortori-Donati 1996
  - Chiari 4: Chiari 2 + small cerebellum, now “vanished cerebellum”
- Alabama’s group, 2000s
  - Chiari 0: no Chiari but syringomyelia
  - Chiari 1.5: tonsillar + brainstem descent
  - Chiari 5: Chiari 3 + occipital lobes

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Chiari 1: pathogenetic postulates

- Hans Chiari: congenital hydrocephalus
- 1970's-1980's: Chiari 2 in children, Chiari 1 in adults
- 1990's: abnormal ventro-dorsal patterning
- Now: small posterior fossa

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Chiari 1: small posterior fossa

- Poorly developed posterior fossa (Aydin 2005, 60 adults; Sekula 2005, 20 adults)
- posterior fossa normal without syringomyelia, small with syringomyelia (Sgouros 2006, 42 children)
- abnormal skull base morphometry (Sgouros 2007, 30 children)
- small posterior fossa (Trygilidas 2007, 61 children)
- basi-occipital shortness (Noudel 2009, 17 adults; Dagtekin 2011, 15 adults)
- posterior fossa normal in children but abnormal in adults (Furtado 2009, 21 children, 21 adults)

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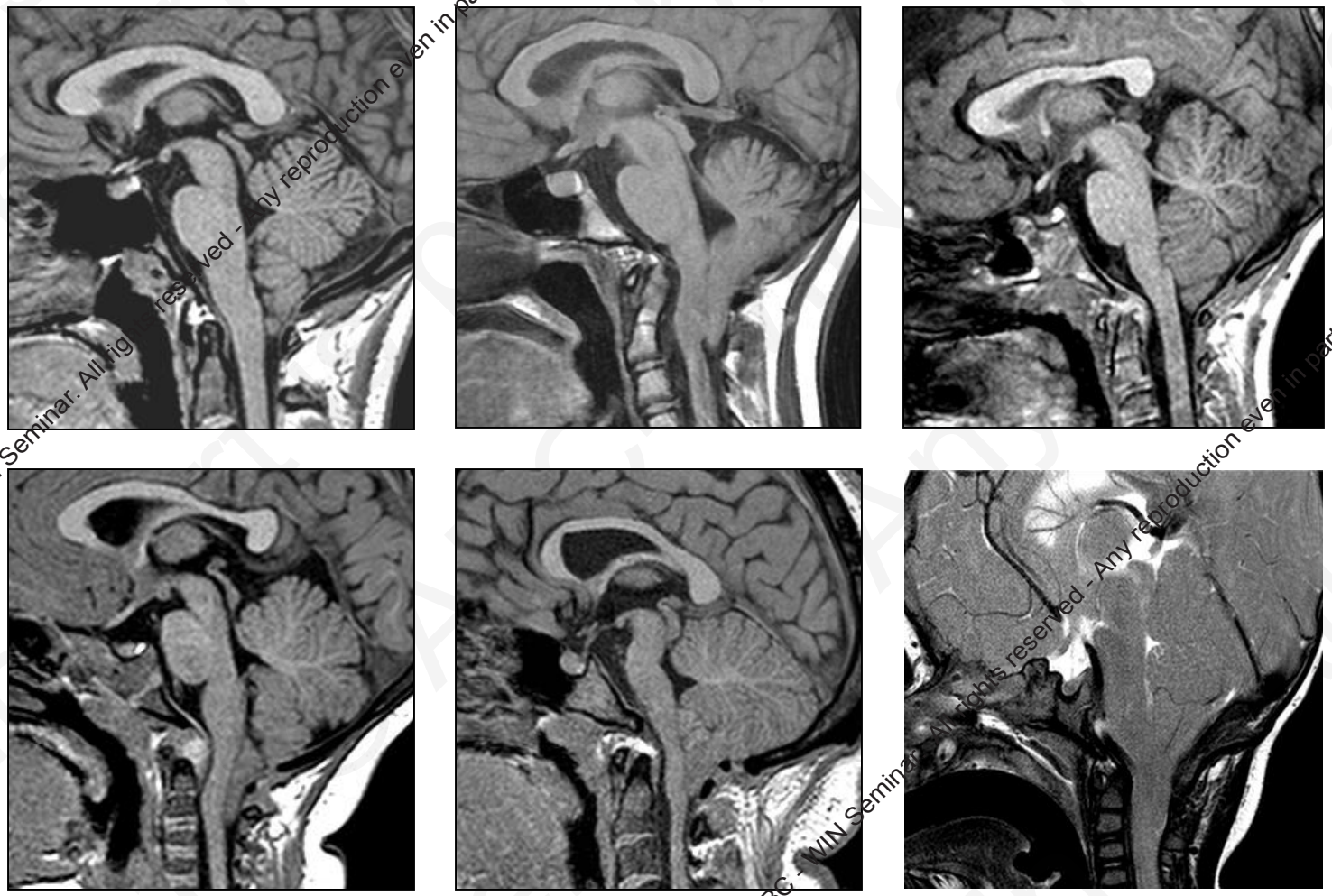
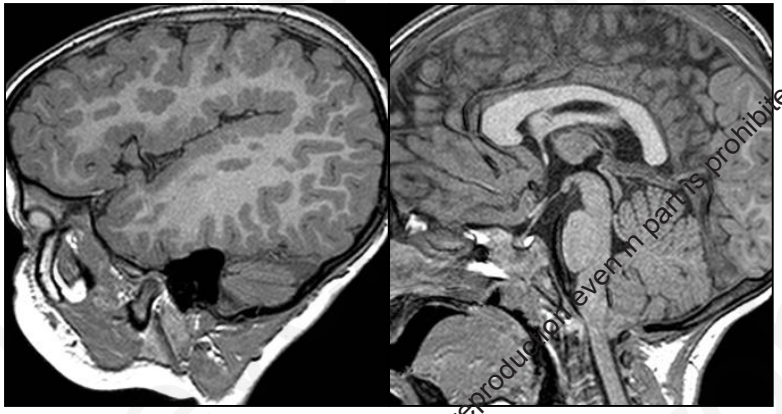
Chiari 1 deformity: a discrepancy content/container

- Large brain/hindbrain
  - Sotos, HME, NF1, congenital hydrocephalus etc.
- Small skull, and / or small posterior fossa
  - craniosynostoses, platybasia, basal impression etc.
- Short clivus (most common)
  - pro-atlas hypoplasia
- Mis-segmentation (e. g., Klippel-Feil)
  - occipital vertebra, other complex malformations

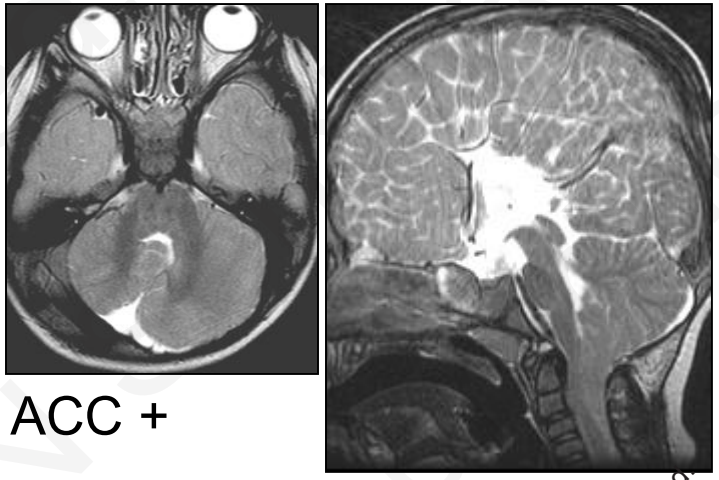
Chiari 1: posterior fossa cisterns



In all, posterior fossa is small, therefore cisterns are effaced and foramen magnum is crowded



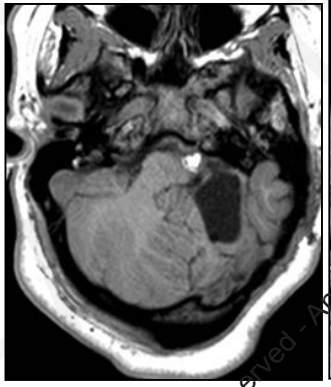
PMG +

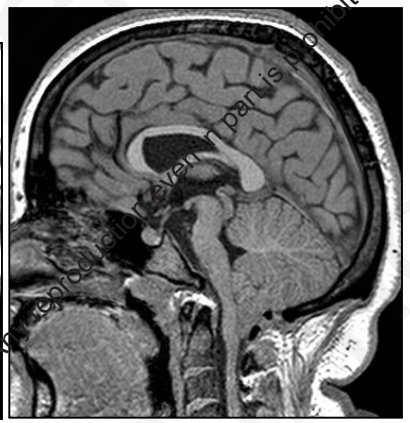


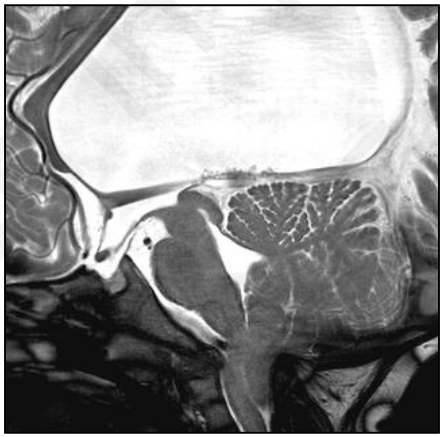
ACC +

Large brains/hindbrains

dysplasia

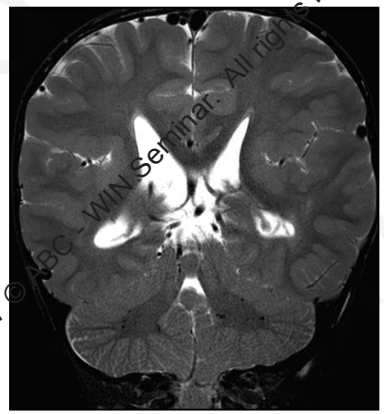


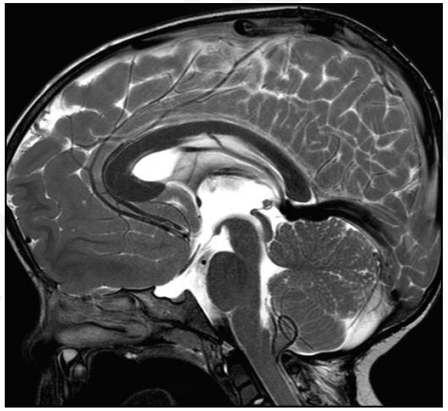




congenital hydrocephalus

Soto's

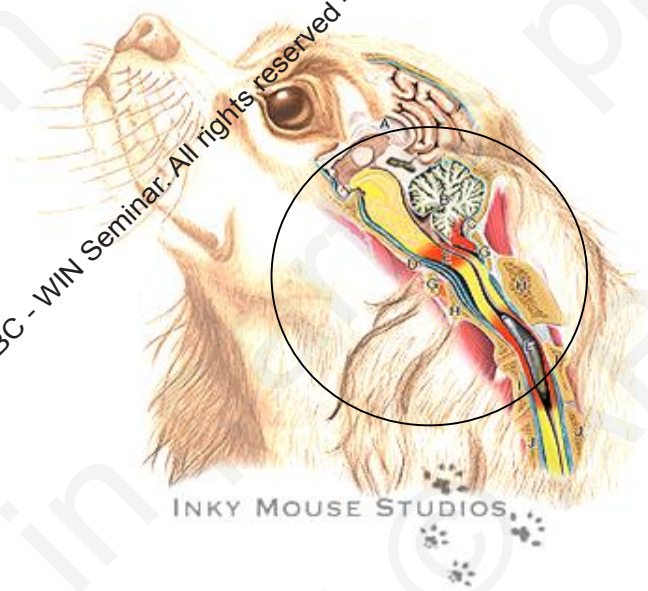




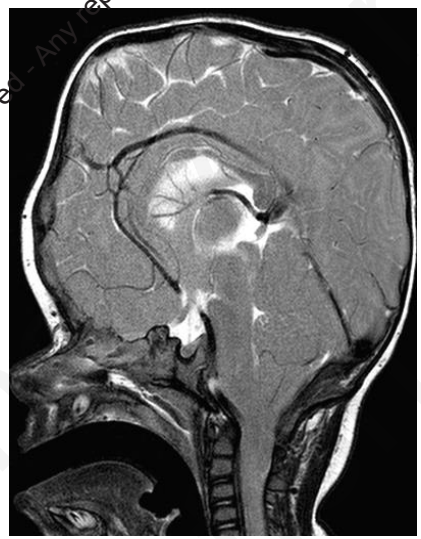
Small skull or small posterior fossa

Cavalier King Charles Spaniel

- small skull
- flat skull base - PF
- Chiari 1 deformity
- syringomyelia (no hydrocephalus)

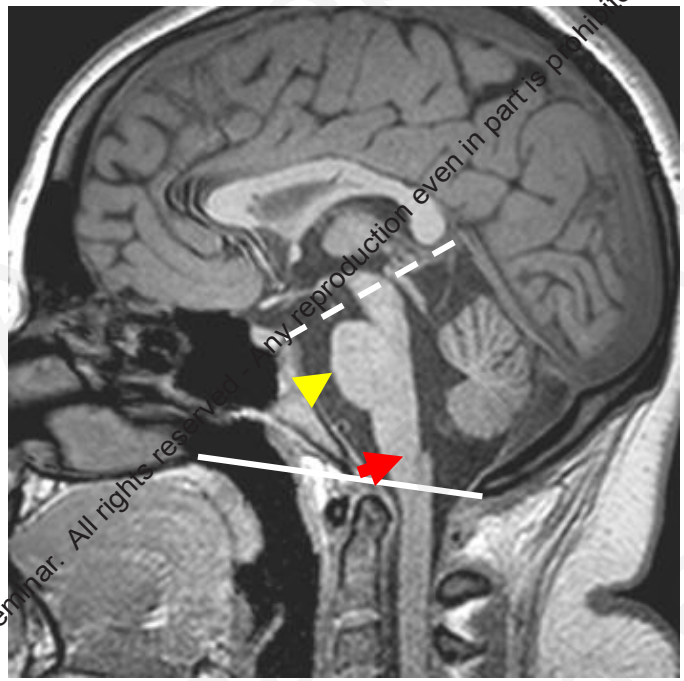


Crouzon
early closure of coronal sutures and basal synchondoses



Anatomic landmarks of bony posterior fossa

- Chamberlain, McRae
  - same plane
- Other landmarks
  - synchondrosis – midpons
  - basion -- obex
- Incisural line



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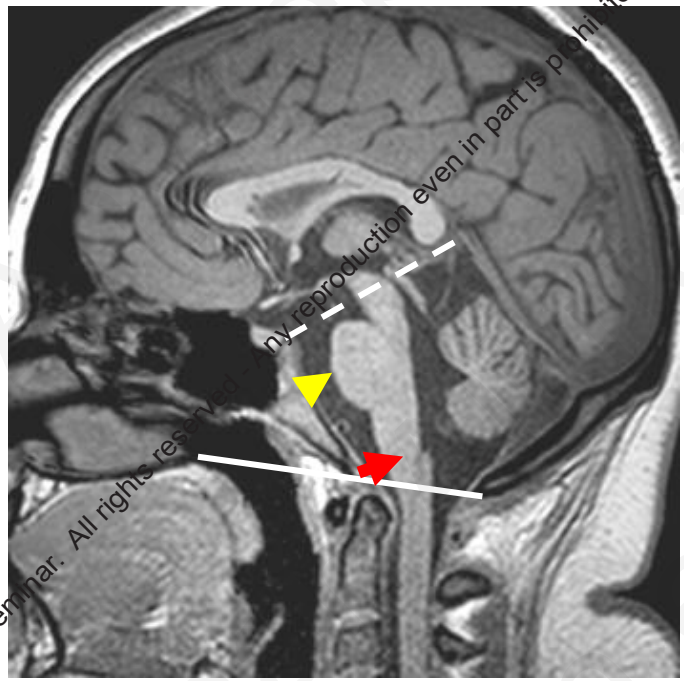
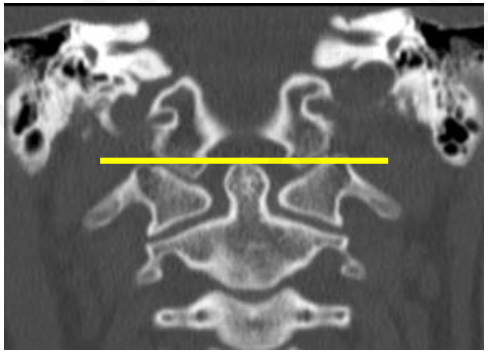
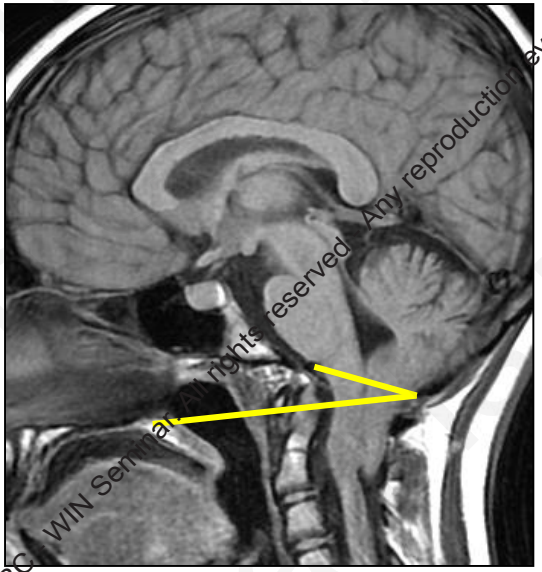
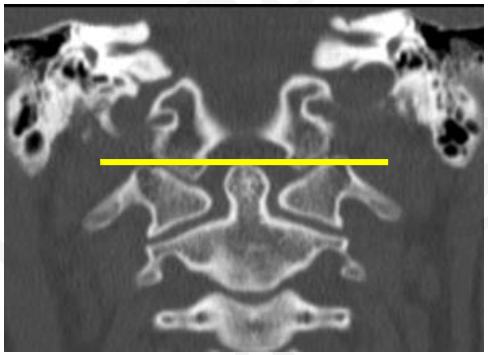




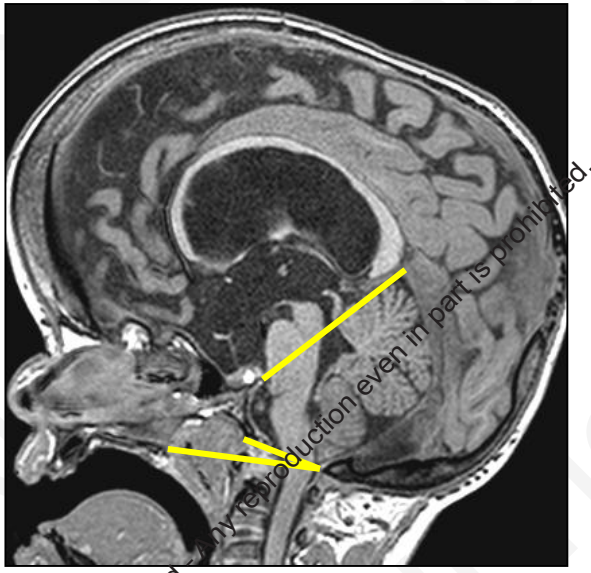
Tip of dens and occipito-atlantal joints are aligned along the flexion axis of the head

Bony abnormalities: posterior fossa landmarks



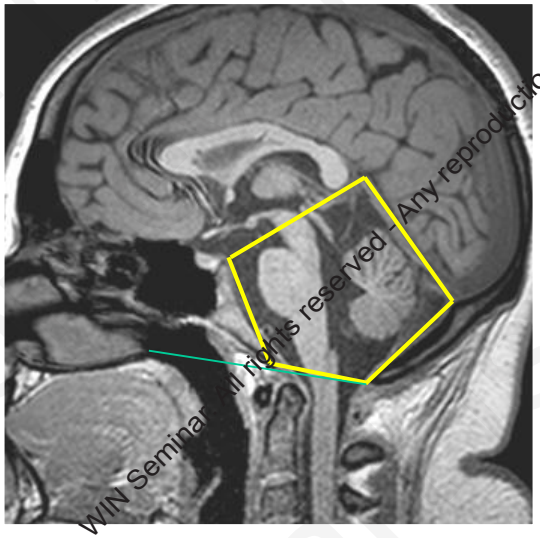


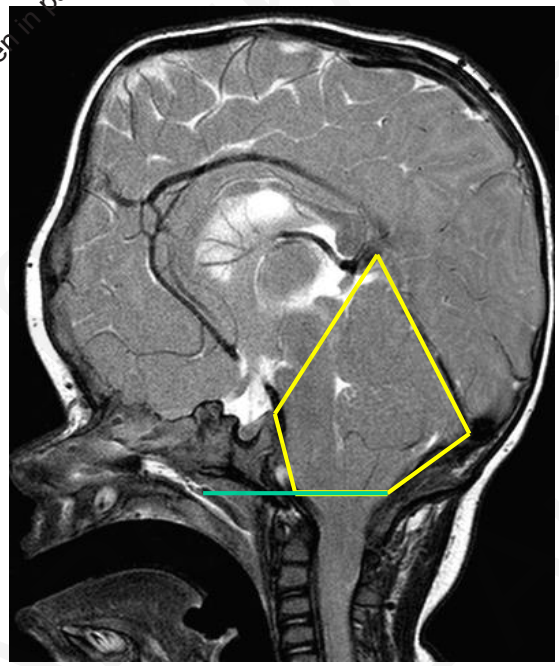
Short clivus
Small posterior fossa
Abnormal CVJ dynamics

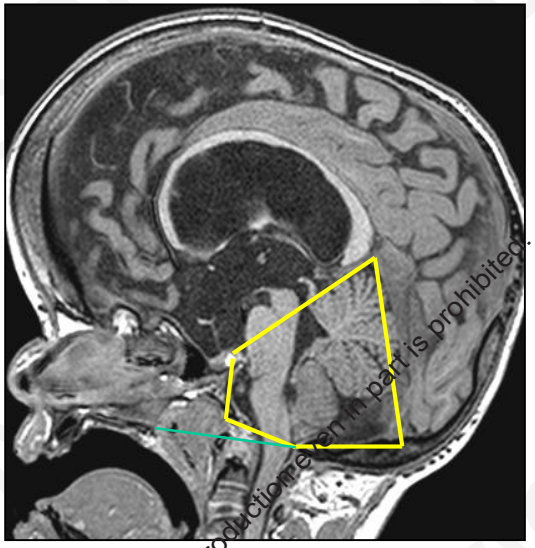


Achondroplasia
Synchondroses closed, not sutures
Posterior fossa small, vault gives way, hindbrain ascends

Anatomical landmarks of posterior fossa

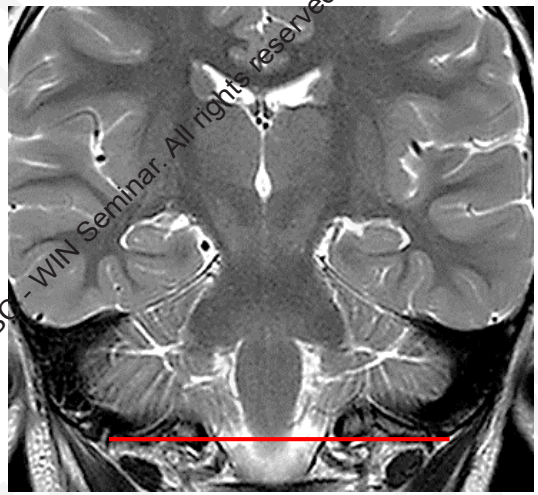




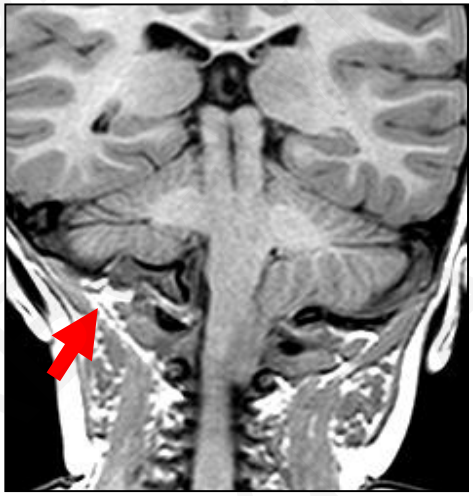


- Posterior fossa sagittal osteo-dural pentagon: regular and symmetric
- Standard measuring bar: clivus

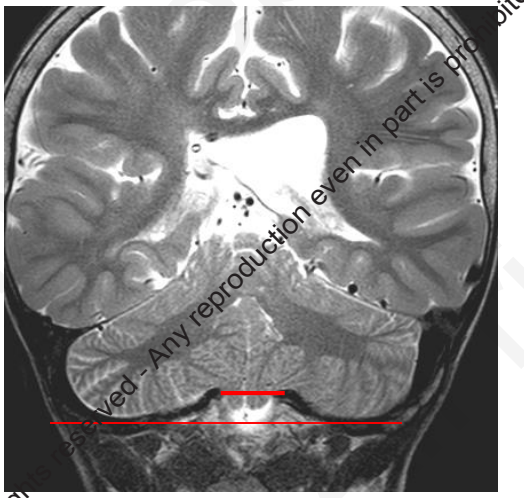
Abnormal bony posterior fossa



Normal occipital alignment

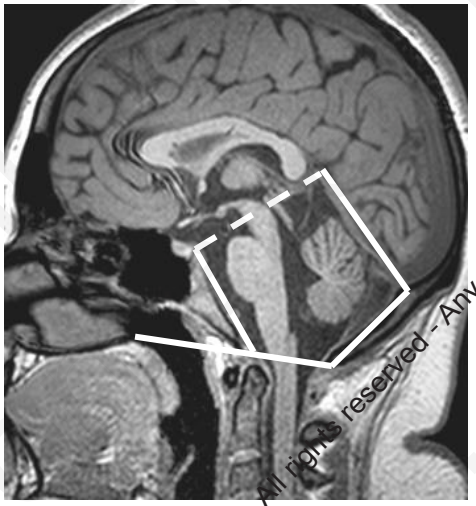


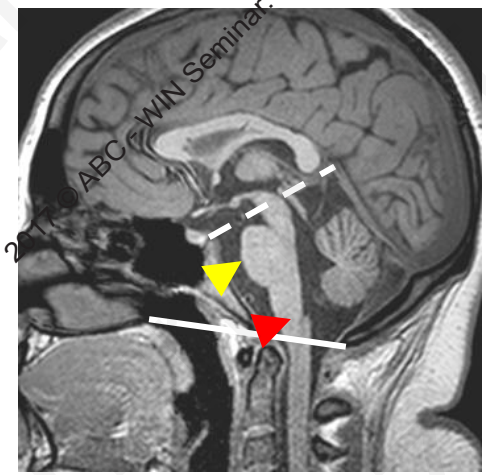
Unilateral occipital hypoplasia

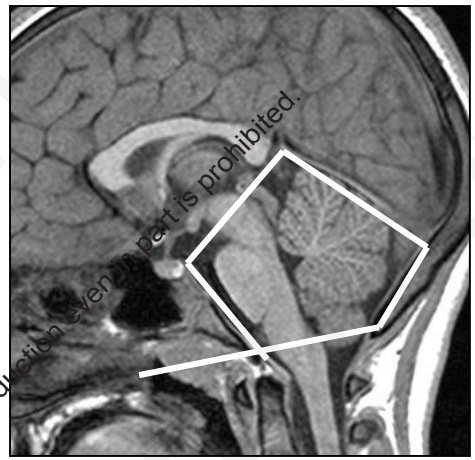


Basal impression (invagination)

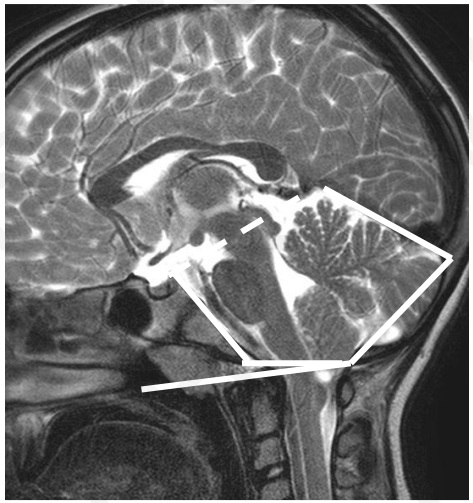
Sagittal pentagon AND coronal evaluation



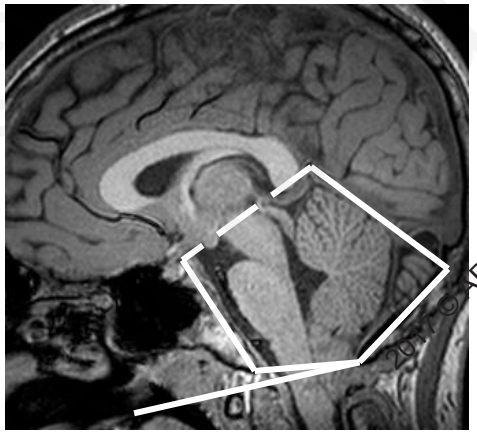




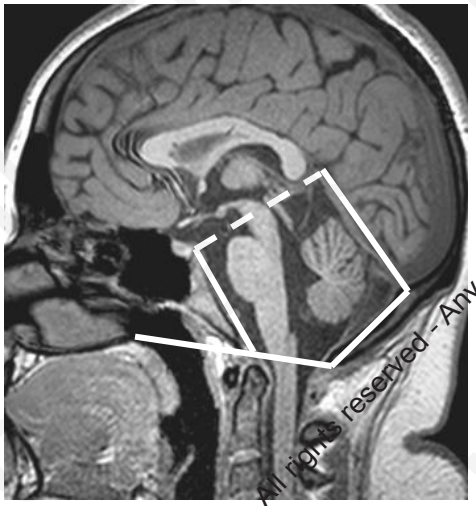
- effaced cisterns
- asymmetric pentagon = short supra-occiput

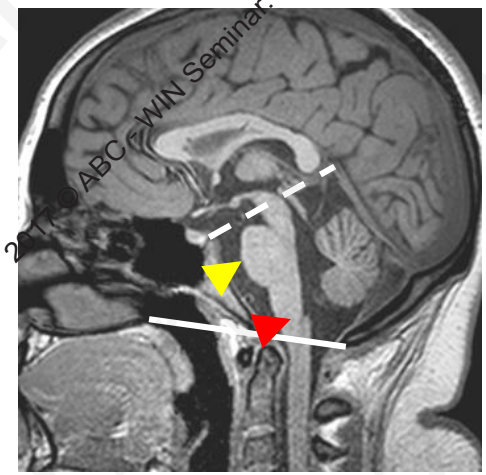


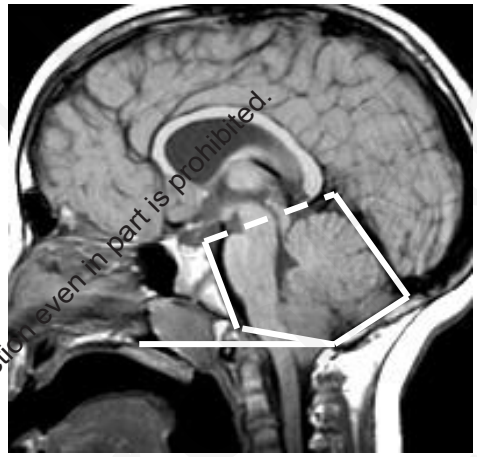
- effaced cisterns
- flat pentagon = flat posterior fossa



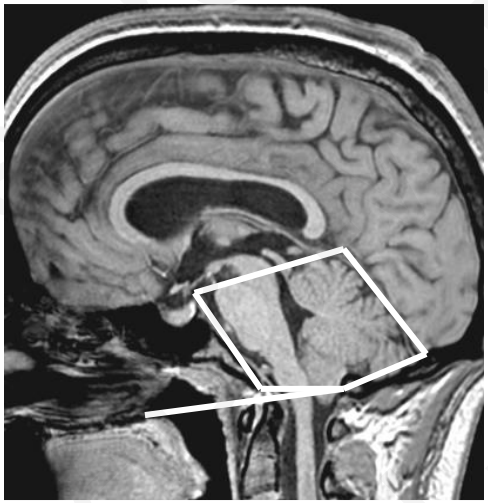
- gelastic seizures
- low forebrain, effaced cisterns, McRae & Chamberlain
- asymmetric pentagon



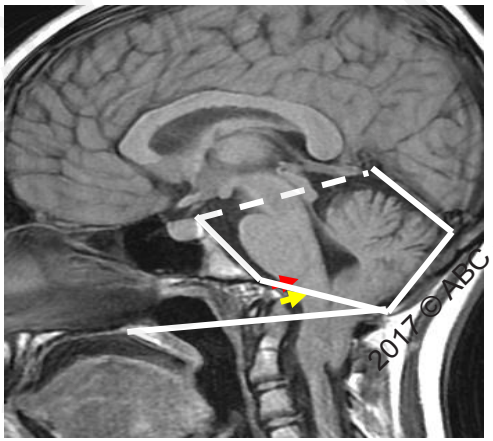




- high midbrain, filled cisterns,
- small, flat pentagon: short clivus & supraoccipital,

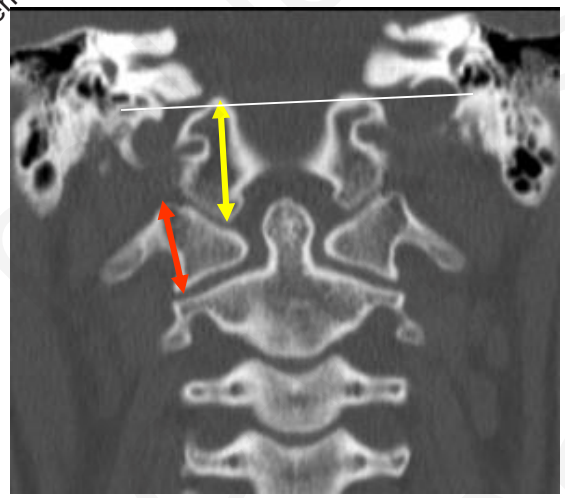


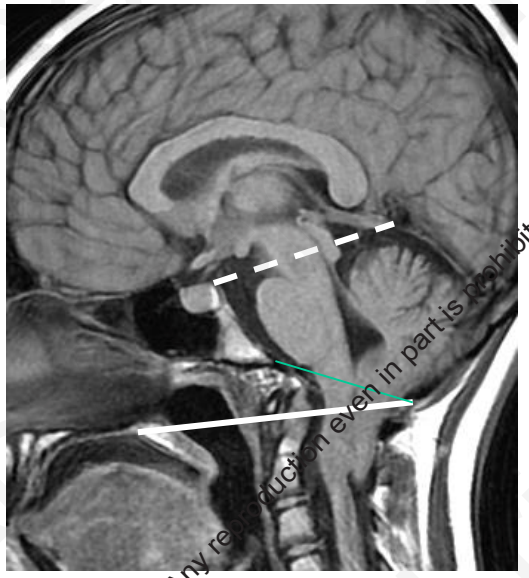
- high midbrain, filled cisterns, wide basal angle
- platybasia, flat asymmetric pentagon & short supraoccipital



- distorted pentagon: short clivus, “retroverted” dens (tilted head)
- = hypoplastic pro-atlas

Short clivus: proatlantal hypoplasia and retroverted dens

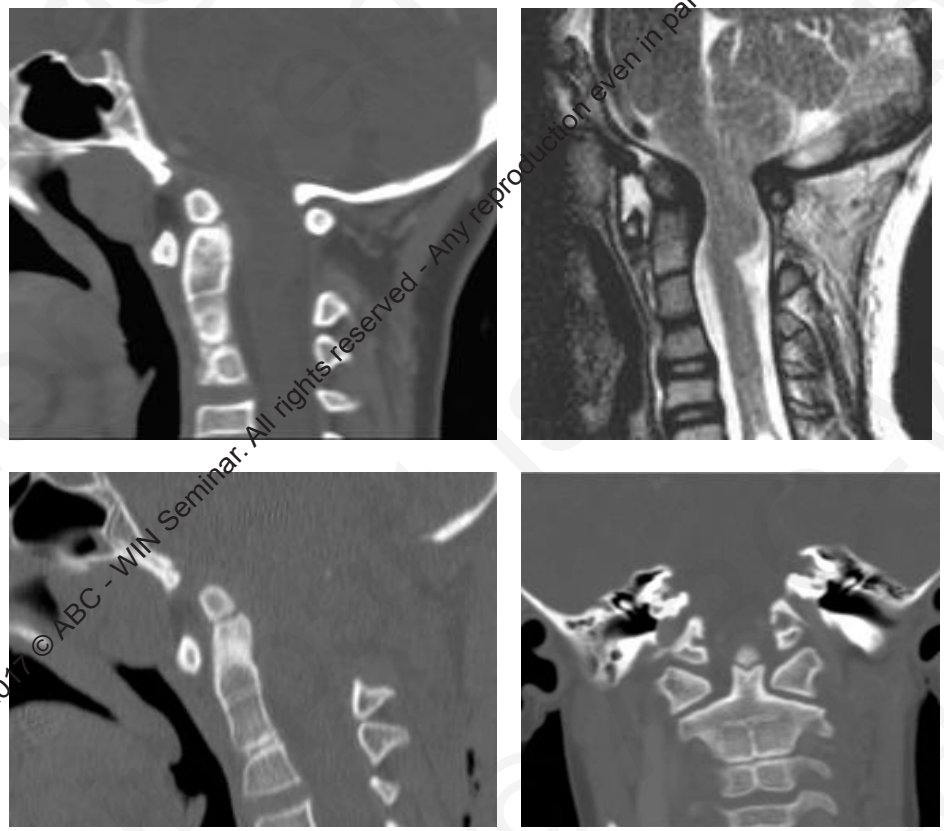


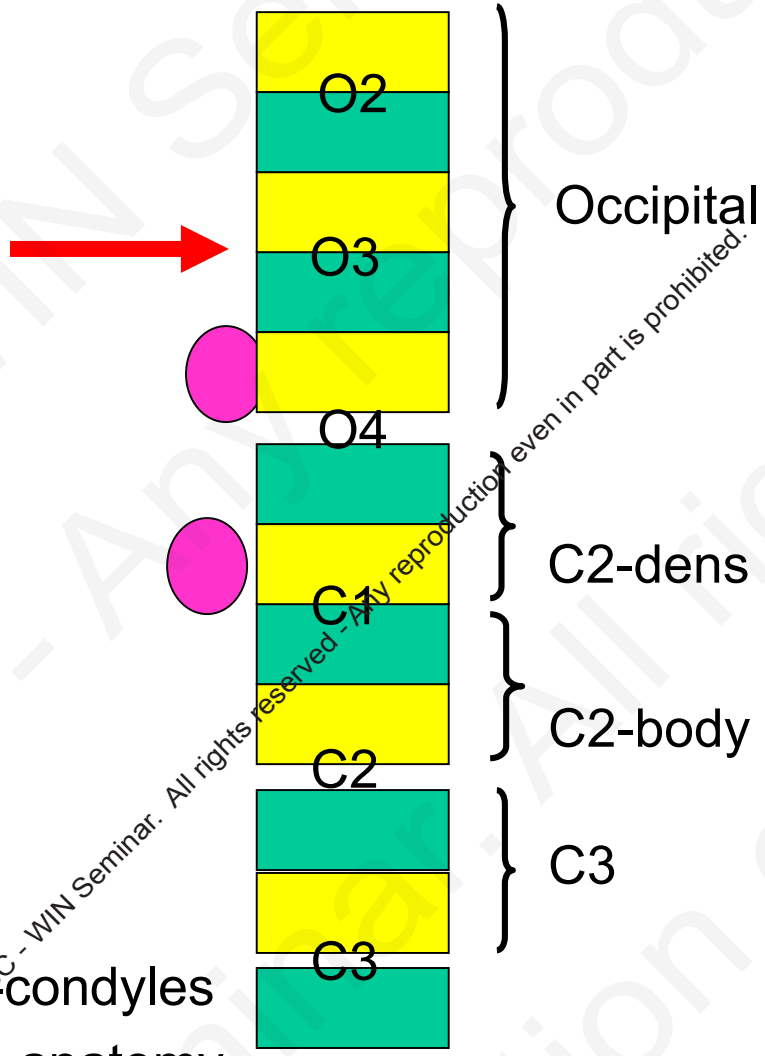


Menezes & Fenoy 2009

- Proatlas: anterolateral margin of foramen magnum
- Hypoplasia of clivus & condyles, not of opisthion
- Head tilted forward, relative ascent of the dens, which abuts medulla
- Occipito-atlantal joints ascend in relation to brainstem
  - not a “basilar impression”

Abnormal segmentation : occipital vertebra



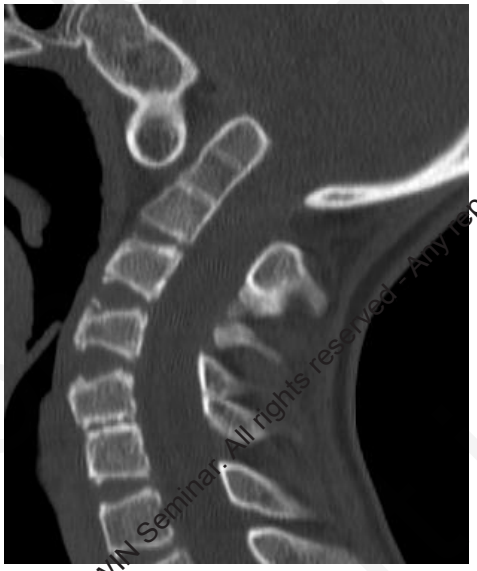


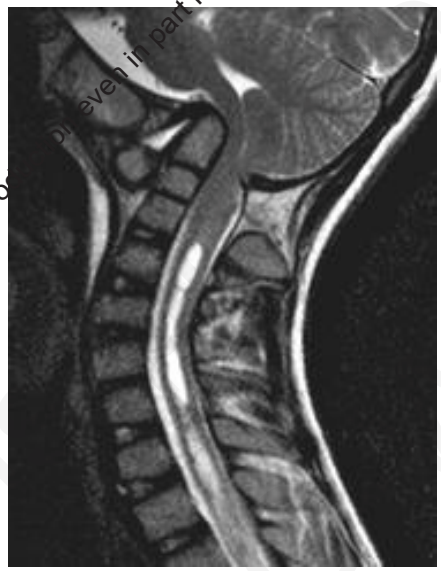
Prominent dens & short clivus

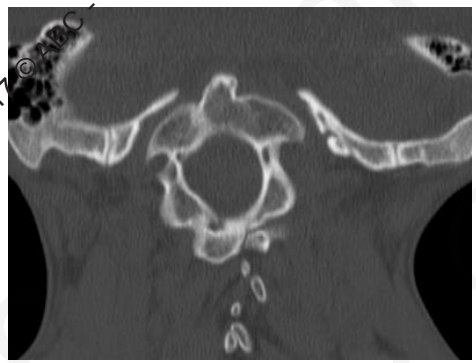
Associated hypoplasia of jugular tubercles-condyles

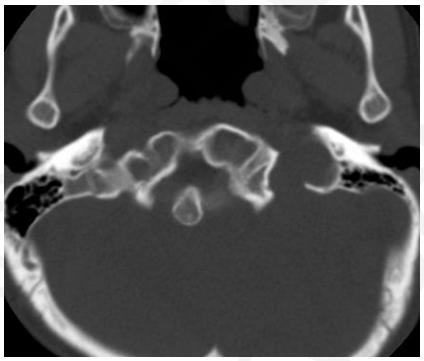
Neo-articulation with unknown ligamentous anatomy

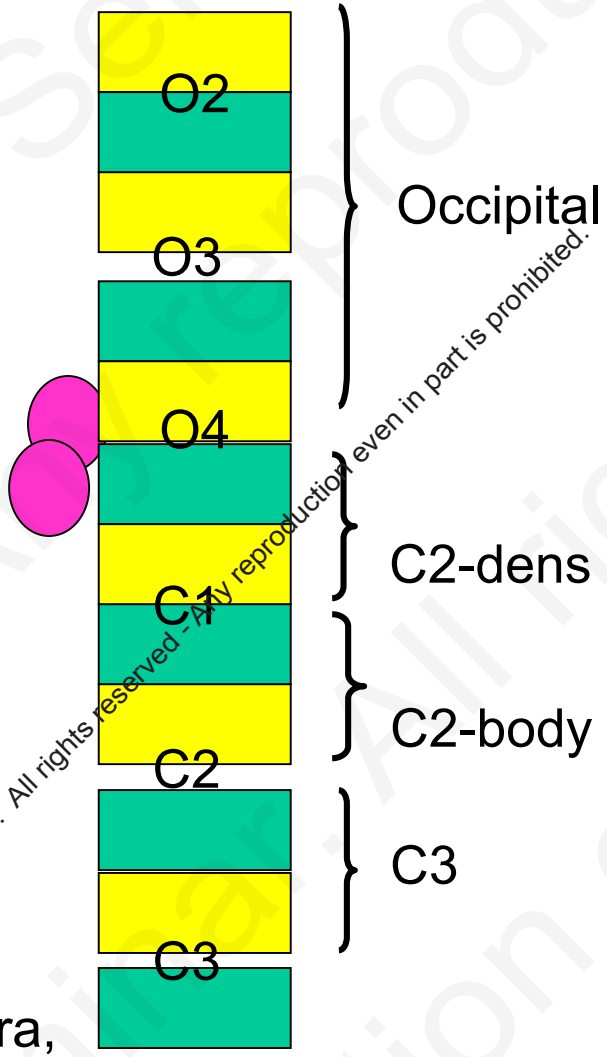
Hypogenesis, condylus tertius: new joint, what ligaments?











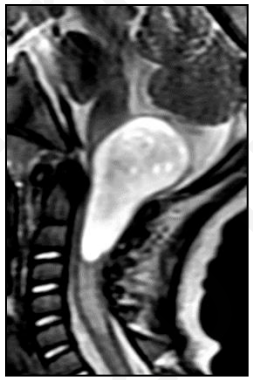
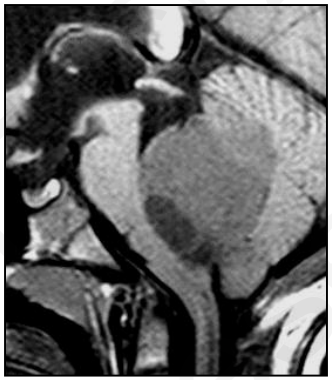
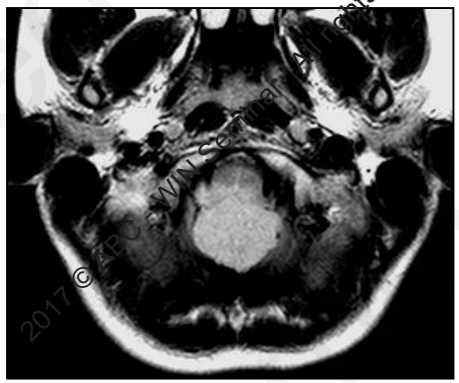
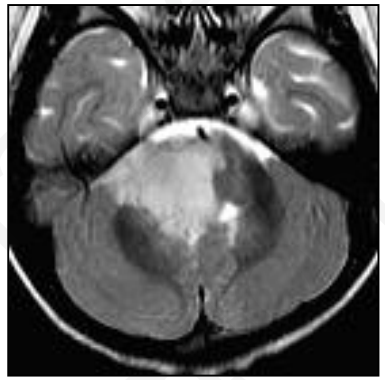
High segmentation, undivided O4, fused hypocentra, prolonged invaginated dens; ligamentous apparatus?

Chiari 1: pathophysiology

- Chiari I deformity : chronic tonsillar downward displacement
  - four main causes: 1) large hindbrain, 2) short / flat posterior fossa, 3) proatlantal hypoplasia, 4) occipital vertebra
- Not a cause of hydrocephalus, but most common cause of hydromyelia and medullary/ low cranial nerve compression (plugging of foramen magnum)
- CVJ *bony malformations* have complex consequences:
  - abnormal osteo-neural biomechanics (specific brainstem exposure)
  - unknown anatomy of ligamentous apparatus (stability)

Neural cranio-vertebral junction: tumors

- Neural cranio-vertebral junction is biologically different from upper medulla
- Like in cord, cranio-cervical gliomas involve the whole neural thickness; upper medullary gliomas are tegmental or ventral
- Genome of ependymomas is different in different locations
  - genetically similar to cord and like them , lower fourth ventricular ependymomas are rather benign (type B)
  - lateral recess ependymomas different, with poor prognosis (type A)

Arterial cranio-vertebral junction: functional adaptation

- Lower medulla and upper cord supplied by anterior midline channel
- Development of the hindbrain first, then of cerebral hemispheres led to capture of the cervical supply through longitudinal paravertebral anastomoses
- The mobility of the CVJ imposed peri-atlantal collateral loops via the pro-atlantal arteries

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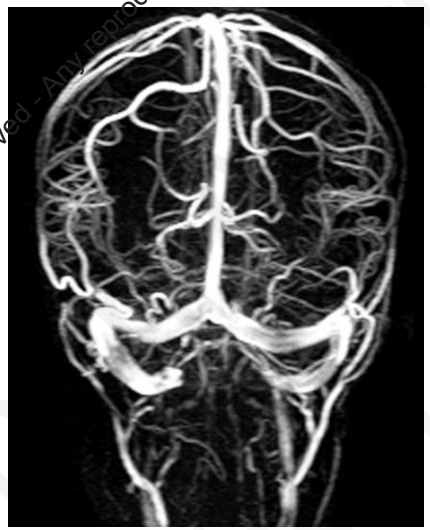
Venous cranio-vertebral junction: cranio-spinal continuity

- Supratentorial venous drainage: through remaining ends of the primary head sinuses: cavernous sinus and jugular foramen, and peripheral dural collaterals (sinuses)
- Like the spine, posterior fossa characterised by an anterior epidural plexus and lateral outlets (mastoid and posterior condylar emissary channels)
- Continuous with sigmoid sinuses and spinal epidural plexuses
- Jugular foraminal stenosis → high ICP
  only if associated with cervical canal stenosis
  (and non-efficient emissary veins)



In summary

- CVJ: a developmentally transitional zone between pharyngeal arch and somitic systems, retaining vestigial hypocentrum
- Bony, neural, arterial and venous transitional segment as well
  - in addition to being a specifically joint for a complex motion
- Chiari deformity a consequence of CVJ abnormalities, not a malformation
  - clinical impact : compression (cord, cranial verves, CSF dynamics) and abnormal biomechanics (osteo-medullary conflict)