Cranial & Vertebral Anomalies

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SKULL

Head circumference measurement - occipital-frontal circumference (OFC) - is routine part of physical assessment of all children ≤ 2 yrs.

• stimulus for head growth is increase in volume of intracranial contents.

NORMAL DEVELOPMENT

FONTANELLES

Anterior fontanelle: largest fontanelle, diamond shaped, size 4 (AP) x 2.5 (transverse) cm at birth.

• closes by age 2.5 yrs.

Posterior fontanelle: triangular.

• closes by age 2-3 mos.

Sphenoid and mastoid fontanelles: small, irregular.

• sphenoid closes by age ~ 2-3 mos, mastoid by age 1 year.

Cranial & Vertebral Anomalies

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SKULL

Head circumference measurement - occipital-frontal circumference (OFC) - is routine part of physical assessment of all children ≤ 2 yrs.

• stimulus for head growth is increase in volume of intracranial contents.
growth essentially ceases at age 7 yrs.

LeFort skull is unilaminar at birth.

diophe appears by 4 yrs and reaches maximum by age 35 yrs (when diaphysis forms).
Partial bossing is formed by motor cortex growth.

Material presence: formation commences by age 2 yrs, air cell formation occurs during 6th yr.

SUTURES

calvarial sutures serve 2 important functions:
 1) head malleability during passage through birth canal.
 2) separation of calvarial bones during intrauterine – early perinatal growth.
 3) ossification of cranial vault starts in central region of each cranial bone and extends outward toward cranial sutures.
 4) by end of 2nd yr, bones have interlocked at sutures and further growth occurs by accretion and absorption (sutures serve as site of bone deposition in growing calvarium).
 5) Skull growth occurs perpendicular to suture!
 6) primary factor that keeps sutures open is ongoing brain growth.
 7) suture closure occurs by age ≤ 12 yrs, but completion continues into 3rd decade.

CRANIOSYNOSTOSIS

- premature fusion of one or more of 6 cranial sutures → abnormal growth of cranium.
 1) primary defect of ossification (PRIMARY CRANIOSYNOSTOSIS)
 2) primary brain growth failure (SECONDARY CRANIOSYNOSTOSIS) - more common (92-98%)

overall incidence – 0.6 – 1/1000 live births.
N.B. craniosynostosis is in utero event!

ETHIOPATHOGENESIS

80-90% are sporadic ISOLATED cases; 10-20% cases are PART OF SYNDROME (syndromic craniosynostoses); > 70 syndromes include craniosynostosis.

1. Many cases are of unknown etiology.
2. Nongenetic causes:
   1) metabolic conditions that can lead to premature fusion of cranial sutures (hyperthyroidism, hypercalcemia, hypophosphatasia).
   2) hematologic disorders that cause bone marrow hyperplasia (e.g. uclele cell disease, thalassemia).
   3) severe constraints in utero (e.g. amniotic band rupture sequence).
3. Mutations (10-20% cases) in family of FIBROBLAST GROWTH FACTOR RECEPTORS (FGFR):
   FGFR1 gene - Pfeiffer's syndrome.
   FGFR2 gene (chromosome 7) - Cronn's syndrome, Apter's syndrome, Jackson-Weiss syndrome, Pfeiffer's syndrome.
   FGFR3 gene - thanatophoric dysplasia, achondroplasia.
    – mutations in other genes are rare (e.g. homeobox gene MSX2 - Boston type of craniosynostosis).
    – gene locus for SINGLE SUTURE craniosynostosis has not been identified.

PATHOPHYSIOLOGY

prevaling hypothesis suggests that abnormal development of skull base creates exaggerated forces on dura that act to disrupt normal cranial suture development.
N.B dysfunctional osteoblasts or osteoclasts are not responsible!

CLINICAL FEATURES

- commonly present a birth (but not always noticeable), certainly manifests as clinical deformity in first few months of life.
N.B. it is PRENATAL abnormality!

1) abnormal skull growth → cosmetic facial and cranial deformity (often with visible/ palpable ridging of closed suture); worsen over time!
    skull growth restricted - in plane perpendicular to affected suture (‘hand grabs and holds skull at suture’).
    skull growth enhanced - in plane parallel to affected suture.

skull base growth is different in various types of craniosynostosis - important for final skull shape; morphology of cranial base has been shown to be normalized following cranial expansion surgery in some synostoses!

2) ICP - only when > 1° suture is affected (cause and mechanism is not well understood* - may be present even in cases where absolute intracranial volume is increased) → adverse effects on development (sun-setting eyes, headaches, vomiting, school performance), gradual visual failure.

*esp. in syndromic cases (some experts say – up to 11% of single suture cases cause ICP!)*

*anomalies of cerebral venous drainage due to maldevelopment of foramina at skull base
N.B. papylinea is rarely seen even in presence of intracranial hypertension!
N.B. hydrocephalus is rare (assertion that CSO may follow CSF shunting for HCP is unproven)

3) airway problems in syndromic cases (hypoplastic maxilla → dental malocclusion, difficulty breathing through nose; sleep apnea).

4) vision loss (coronal synostosis can cause amblyopia).

DIAGNOSIS

1. Skull XR
   initially - 4-view Towne.
   to visualize all sutures, special Waters views must be taken.
   N.B. make sure you see suture of interest on XR before patient leaves radiology facility
   then request radiology report on that suture.
   – sutures - straight with heaped-up sclerotic margins or completely absent (invisable).
   – indentations of inner table (evidence of ICP).
   – any suture is functionally closed even if it has closed only short over distance.
   – several indices have been devised and used for comparisons (most popular - cranial index described by Cronqvist).

2. CT with 3D reconstruction (method of choice, esp. before surgery) - fused sutures are clearly identified; abnormal contour of skull is better appreciated; skull base is clear; 3D-CT is especially indicated in multiple-suture synostosis - to assist surgery.
3. Direct mutation analysis of FGFR genes.

4. PRENATAL detection with 3D ultrasonography.

**SINGLE-SUTURE SYNOSTOSES**

- can be very mild phenotypically; majority are sporadic; only rarely causes neurologic deficit.

<table>
<thead>
<tr>
<th>Sagittal</th>
<th>Coronal</th>
<th>Metopic</th>
<th>Lambdoid</th>
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<tr>
<td>50-60%</td>
<td>20-30%</td>
<td>4-10%</td>
<td>2-4%</td>
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Sagittal synostosis → scaphocephaly

- elongated skull with compensatory frontal bossing and exaggerated occiput (occipital bathtosephaly), absent anterior fontanelle.

N.B. DOLICHOCEPHALY term is reserved for normal anatomic variant!

- head circumference is above 95th percentile (although biparietal diameter is low) - actual intracranial volume is normal or even increased - brain growth impairment does not occur (although ICP may be elevated in some cases) - no neurological deficits!

- normal face.

- often causes labor difficulties (cephalopelvic disproportion).

- frequent in premature infants.

- 80% are males.

- 3D-CT scan - complete fusion of sagittal suture, with patent coronal suture and elongated cranial contour; apparent holes in posterior parietal regions are due to normal thinning.
Coronal synostosis → brachycephaly
(18-30% of all cases)
- foreshortened skull and corresponding enlargement of bitemporal and biparietal diameter:
  - variable degree of exophthalmus (shallow orbits)!!!
  - orbits may be elliptical (i.e. Harlequin features).
  - fronto-orbital bar is recessed; consequently, supraorbital rim is more posterior to corneal plane (normally, rim is 2 mm ventral to corneal plane).
  - higher incidence of neurological complications:
    1) optic atrophy (traction of chiasm and optic nerves due to upward displacement of chiasm = ICP↑)
    2) mental retardation.
- often syndromic (e.g. Apert’s syndrome).
- more common in females.

Note bilateral harlequin configuration of orbits and slitlike appearance of coronal suture (arrow); margins of coronal suture are densely sclerotic.
Unicoronal synostosis → anterior plagiocephaly
- flattening of ipsilateral frontal and parietal bones, bulging of contralateral frontal region, and bulging of ipsilateral temporal bone; displacement of eyebrow downwards on that side; asymmetric orbits, nose curvature (nasal root deviated toward fused suture).

Unilateral cases outnumber bilateral forms by 2:1

- parents often like affected HARLEQUIN eye (bigger) more than normal eye.
Metopic synostosis
(4-10% of all cases) - prominent midline frontal ridge (keel-shaped forehead), recessed orbital rims, hypotelorism (indicates early fusion of metopic suture*).

*Physiologically, metopic suture is first suture to close (as early as 3rd postnatal month)
- often occurs in syndromic context (e.g., 19 chromosome, Opitz trigonocephaly syndrome) or in conjunction with holoprosencephaly.
- abnormality is usually mild and requires no surgical intervention.
Cranial & Vertebral Anomalies

Lambdoid synostosis
(2-4% of all cases)

Unilambdoid synostosis → posterior plagiocephaly
1) ipsilateral occipital flattening and enlargement of ipsilateral mastoid process - pathognomonic for lambdoid synostosis!!!
2) compensatory bulge at contralateral parietal eminence
3) in most serious cases, ear on affected side is displaced forward and out.

Combined-Suture Synostoses
- strongly suggests craniofacial syndrome!

Coronal + sagittal synostosis → oxycephaly
- high, conical head with sharp bossing in region of anterior fontanelle (Gr. oxys - sharp).
- microcephaly with crowding of intracranial contents – elevated ICP!

Sclerotic margins and heaped-up bone of fusing sagittal suture. Note flattening of right side of calvaria (plagiocephaly) and right harlequin orbit: The same patient: right coronal suture is abnormally straight (large arrow) and narrow in appearance, whereas left is normal (small arrow).

3D CT (vertex view) - normal lambdoid suture with complete fusion of sagittal and coronal sutures:

Coronal + sagittal + lambdoid synostosis → triphyllocephaly, or kleeblattschädel
(cloverleaf, or trilobed, skull) – calvarial bone between sutures is expanded by developing brain but held at area of sutures - bilateral constrictions at sylvian fissures, very prominent temporal bones, bulging forehead, ocular proptosis (resulting from shallow orbits).
Cranial & Vertebral Anomalies

N.B. metopic and squamosal sutures are normal!

- severe neurological impairment:
  - shallow orbits, traction & compression in optic canals → proptosis → optic atrophy (22%), legal blindness (7%).
  - conductive hearing loss (55%).
  - headaches, seizures.
  - mental deficiency is rare.

- occurs in Crouzon's syndrome, thanatophoric dysplasia.

**SYNDROMIC SYNOSTOSES**

- craniosynostosis + other body deformities.
  - Crouzon's and Apert's syndromes account for 2/3 of syndromic craniosynostoses cases.
  - midface retrusion is associated with Apert or Crouzon syndrome.
  - all are AUTOSOMAL DOMINANT!

**CROUZON'S SYNDROME (S. CRANIOFACIAL DYSOSTOSIS)**

- autosomal dominant KLEEBLATTSCHÄDEL

  - incidence: - 1 case in 60,000 live births.
  - 25 mutations in FGFR2 gene; 25% cases sporadic.
  - 60% patients have intracranial hypertension.
  - normal limbs.

Note hypoplastic maxilla, which is severely disproportionate to normal mandible:

**APERT'S SYNDROME (S. ACROCEPHALOSYNDACTYLY)**

- autosomal dominant or sporadic BRACHYTURRICEPHALY = BRACHYCEPHALY + TURRICEPHALY, S. TURMSCHÄDEL = short and high skull; prominent forehead and flat occiput.

  - incidence: - 1 case in 10,000 live births.
  - almost all cases are due to 1 of 2 described mutations of FGFR2 gene (chromosome 7); sporadic in 95% cases.
  - intracranial volumes tend to be higher than normal! (but 45% patients have intracranial hypertension)
  - in infancy, wide and gaping sagittal and metopic sutures.
  - frequent platybasia, maxillary hypoplasia, C5-6 vertebral fusion (68% patients).
  - proptosis of eyes, hypertelorism, downward slanting palpebral fissures, small nose, low-set ears.
  - optic atrophy and conductive hearing loss can occur.
  - 50% patients have IQ < 70; but normal (or above average) intelligence is not exception.
  - CNS can be affected in number of ways (esp. agenesis of corpus callosum, migrational anomalies).
  - acrosyndactyly - osseous* syndactyly of hands & feet (mitten hands and sock feet) is prominent feature.

  *progressive calcification and fusion of bones.
abnormal configuration of brain parenchyma; distortion of corpus callosum and ventricular system; posterior fossa is shallow and hindbrain herniation is present:

postoperative photograph of 4-year-old girl (she had fronto-orbital advancement when aged 2 months): orbits are well covered, but ears remain low-set and turricephaly has not changed significantly:

- PFEIFFER syndrome
  - autosomal dominant or sporadic coronal and perhaps sagittal suture closure (perhaps TURCICHEPhALy)
    - mutations of both FGFR1 and FGFR2 genes.
    - down slanting of palpebral fissures is characteristic.
    - hypertelorism, narrow maxilla.
    - broad distal phalanges (esp. of thumb and great toe), polydactyly.
    - 3 types:
      - type I (most common) – moderate/severe hearing loss (auditory canal stenosis or atresia, hypoplasia or enlargement of middle ear cavity).
      - type II - severe proptosis, ankylosis of elbows.
      - type III - ocular proptosis, hydrocephalus, hearing defects, short stature, cervical fusion, cone-shaped epiphysis and hypoplastic bones about elbow.

- SAETHRE-CHOTZEN syndrome
  - autosomal dominant asymmetric coronal suture closure (→ PLAGIOCEPhALy).
    - bilateral ptosis is common (usually requires surgical treatment).
    - facial asymmetry, maxillary hypoplasia, shallow orbits, hypertelorism, small ears.
    - shortened fingers + cutaneous syndactyly, short stature.
    - cervical fusion is often seen at C2-3.

- CARPENTER syndrome
  - probably autosomal recessive synostosis of coronal and often sagittal and lambdoid sutures (→ KLEEBLATTSCHÄDEL).
    - shallow supraorbital ridges, laterally displaced inner canthi.
    - neurosensory and conductive hearing loss; mental retardation is common.
    - brachydactyly & soft-tissue syndactyly of hands and feet.

- JACKSON-WEISS syndrome
  - coronal and basal skull synostosis.
    - mapped to same gene as Crouzon disease.
    - enlarged great toes and craniofacial abnormalities similar to Pfeiffer syndrome but in absence of thumb abnormalities.

- AUTLEY-BINLER syndrome
  - autosomal recessive multiple sutures closure.
    - midfacial hypoplasia, poorly formed ears.
    - mental deficiency.
    - radial hypoplasia, and other preaxial limb anomalies.
    - anal malformation.

- BEARE-STEVENSON syndrome
  - autosomal recessive one or more suture synostosis (usually metopic)
    - car diac and genitourinary defects.
    - metopic suture closure.

- OTHER
  - 9p monosomy (deletion of distal portion of short arm chromosome 9) - metopic suture closure.
  - long middle phalanges of fingers with extra flexion creases, short distal phalanges with short nails.
  - cardiac and genitourinary defects.
**DIFFERENTIAL DIAGNOSIS**

**SECONDARY CRANIOSYNOSTOSIS:**
- retarded brain growth/atrophy is primary abnormality, i.e. secondary craniosynostosis is frequent with microcephaly (e.g. unilateral destructive brain lesions, microencephaly, shunt placement in hydrocephalus?; ICP is normal, and surgery seldom is needed.

Secondary craniosynostosis in cerebral atrophy:

**POSITIONAL POSTERIOR PLAGIOCEPHALY**, "LAZY LAMBDOID"; OCCIPITAL PLAGIOCEPHALY
- not progressive flattened posterior part of head; due to position head takes during sleep*, normal lambdoid sutures, frequently associated with torticollis (may be the cause of specific head position in bed!)

*Since American Academy of Pediatrics recommended that infants sleep on their backs to reduce SIDS

N.B. OCCIPITAL (NOT LAMBDOID) to stress that suture is normal!

N.B. true lambdoid synostosis is rare (≈ 2% posterior plagiocephaly cases!)

View from above ("bird’s-eye view"):
1) head shape is parallelogram (rhomboid) - skull is pushed ventrally on one side.
2) ear position is more anterior on side of flattening.
3) frontal bossing is ipsilateral.

TRUE CRANIOSYNOSTOSIS:
1) head shape is trapezoid - growth is restricted on side of fused suture.
2) ear position is more posterior on side of flattening.
3) frontal bossing is contralateral (if any).

**TREATMENT**

**INDICATIONS**
1. Cosmetic problems (the only consideration in single-suture nonsyndromic synostosis cases!).
2. Elevated ICP (in some units, routine measurement of ICP is performed in all syndromic cases).

N.B. if any restriction of brain growth by skull occurs, it is only in first 6 months of life; after infant is > 6 months, effect of craniosynostosis becomes exhausted (burnt out); i.e. maximum constrictive effect of craniosynostosis occurs at birth when difference in intracranial volume between healthy neonates and neonates with craniosynostosis is maximal!

3. Progressive exophthalmos threatening eyes.

**CONTRAINDICATIONS**
- only absolute contraindication is microcephaly.

**SURGERY TIMING**

a) EARLY SURGERY - soon after birth (minimized risk of mental impairment due to restricted brain growth, bones grow rapidly and easily cover surgical defects - best cosmetic results, but high risk of recurrent deformity).

b) LATE SURGERY - at age 12 months.

Surgery is recommended as soon as child can safely tolerate physiological stress of surgery, usually best is – 6 weeks/6 months of age.

Do not operate in patients without raised ICP until considering following:
- infants have large head relative to body size - deformity appears more prominent in young infant and may be less obvious with age.
- as infant grows and more hair appears, visible abnormality may decrease.
- head shape does not improve by age 2-4 months, then abnormality is unlikely to resolve with age.

**SURGICAL PROCEDURE**
- see p. Dev15 >>
A. Open surgery – at age 4–10 months (Dr. Ritter prefers 10 mos.) – better withstands anesthesia stress, has no Hib, no harm with waiting so long), bone fragments are replaced back and secured with plates.

B. Minimally invasive surgery (mostly for single suture synostosis) – at age ≤ 5 months:


Main principle – OVERCORRECT (as head grows back to original shape)!!!

Complex forms of craniosynostosis - more complex cranial expansion & remodeling procedures (linear craniotomies have been abandoned!)

- in earlier years, tendency was for monoblock facial advancement (forehead and midface in one osteons block) – now waned in popularity (extensive surgery with considerable morbidity, less than superior results).
- most modern procedures constitute various forms of fronto-orbital advancement (cranial vault remodeling) – mobilization of supraorbital bar with series of facial osteotomies – (advancement and stabilization of supraorbital bar in new more anterior position (results in expansion of floor of anterior fossa and roof of orbits).)
- with this technique, connection of coronal suture complex with skull base is disrupted: – problem often encountered after any type of fronto-orbital advancement is persistent narrowing in temporal regions (difficult to correct).

**FLAGEcephaly**  - although only one suture is prematurely fused, in fact, deformity is bilateral because normal side is attempting to compensate - bilateral correction is usually necessary (i.e. both ipsilateral and contralateral suture lines must be surgically corrected to allow for smooth and symmetric correction).

**EUBLERATISCHADER** - early subfetal cranioectomy is only reasonable attempt at correction:
- a) not sutures are resected, skull is morcellized – bone fragments replaced and sutured loosely to dura.
- b) alternative surgical approach - remove all bone!

Progressive maxillary hypoplasia (midface hypoplasia) – maxfacial advancement at 10-15 yrs:
- a) Le Fort III osteotomy and advancement in one operation.
- b) maxfacial distraction (patient wears external frame for several weeks) - gaining popularity – better, long-lasting result.

**POSTOPERATIVE**

- pediatric intensive care unit for 24 hours.
- considerable edema may be encountered, but it quickly resolves in following days.
- some restriction in activity to avoid head injury.
- optional CT on 4* postoperative day – discharge.
- routine postoperative follow-up: 3 weeks, 6 weeks, 3 months, 6 months, and 1 year, with annual visits until age 6 yrs – every 2-3 yrs.
- MRI at yearly intervals (in syndromic cases) - exclude development of hindbrain hernia.
- continue head circumference measurements, watch for signs of raised ICP.
- minor asymmetries are encountered, H. HYDROXYVAPITAN presentation.
- brain is slow to expand - new space is mostly occupied by CSF (± extradural collections).
- children (aged 5–10 years) may develop recurrent craniosynostosis – repeat operations (> 7%)
- features of craniosynostosis (copper-beaten appearance (localized or generalized).
- sclerotic hyperdense bands of bone in calvarium.
- some loss of advancement is normally expected in first few years after operation.

**MACROCEPHALY**

Head circumference (related to age, sex, and body size):
- a) > 2 standard deviations above mean for age.
- b) above 98th percentile for age.

**ETIOLOGY**

- Down’s infant + young child (closed sutures in pubertal child prevent skull enlargement!):

1. Pressure-inducing disorders (ICP), (rapidly increasing head circumference):

- progressive hydrocephalus
- mass lesions (e.g. chronic subdural collections, tumour, expanding arachnoyd cyst)

2. Syndromes (normal ICP; head grows at ≈ normal rate; commonly, child is macrosomic):

- mucopolysaccharidoses, osteopetrosis, achondroplasia
- syndromes with microencephaly (see p. Dev 7) >>
- thickened cranium (e.g. chronic anemia, rickets, osteogenesis imperfecta, epiphyseal dysplasia).
- fragile X syndrome (all patients with macrocephaly should be evaluated for mental retardation!)
- trisomy 18 syndrome – macrocephaly with somatic and genital growth delay; facial, hand & feet deformities, perisutural muscle hypoplasia, delayed bone maturation; severe mental retardation.
- Robinow syndrome – macrocephaly with macroglossia and other facial deformities; hemivertebrae and limb defects; genital hypoplasia; n seizes, variable degree of mental deficiency.
- Greig cephalo-ocysteovacanty – autosomal dominant macrocephaly, frontalbossing and hypertelorism, broad thumbs.

3. BENG syndrome (bilateral enlargement of subarachnoidal space) - no signs of raised ICP, infants develop normally clinically.
- shows initial rapid growth followed by normal rate (larger than normal head growing at normal pace).
- positive history in one or both parents.
- imaging (ultrasound / CT / MRI) – wider than normal ventricular system, wider than normal subarachnoid spaces (particularly over frontal lobes); brain is otherwise normal - findings compatible either with communicating hydrocephalus (microcephaly + hydrocephalus ex vacuo), megalencephaly or atrophy.
- N.B. imaging is impossible to interpret without knowledge of previous head growth and circumference measurements, i.e. radiologist is unable to make correct interpretation without knowledge of clinical history.
- larger than normal intracranial fluid-containing spaces will eventually reduce and become normal in size.

**DIAGNOSIS**

- CT / MRI – mildly dilated lateral ventricles and increase in subarachnoidal fluid.

*CSF shunts are reserved for progressive enlargement of CSF spaces and evidence of neurologic dysfunction.

**MICROCEPHALY**
Head circumference (related to age, sex, and body size): 1) ≥ 2-3 standard deviations below mean. 2) below 5th percentile.

• very small head circumference implies process that began early in embryonic or fetal development.

ETIOLOGY

Common cause is abnormal brain development with subsequent reduction in brain volume (microencephaly)!

A. Secondary (nongenetic) microcephaly - noxious agents that affect fetus or infant during first 2 yrs of life:

1. Conditions that restrict brain growth:
   a) craniosynostosis
   b) skeletal dysplasias
   c) external restriction of skull growth in utero

2. Conditions that destroy brain substance before completion of brain growth:
   a) hypoxic-ischemic insults
   b) congenital infections (esp. CMV, rubella, toxoplasmosis)
   c) meningitis/encephalitis
   d) drugs & toxins (alcohol, hydantoin)
   e) radiation
   f) endocrinopathies (maternal diabetes mellitus, maternal hyperphenylalaninemia)
   g) hyperthermia
   h) malnutrition (?)

B. Primary (genetic) microcephaly - conditions that intrinsically impair brain growth; manifest at birth:

1. Microcephalia vera - autosomal recessive significant microcephaly (up to 5 standard deviations below mean);
   a) not associated with other malformations
   b) brain size < 300 g (normal 1200-1500 g)
   c) primitive gyral pattern, cortex thickened and disorganized without clear laminations.
   d) severe mental retardation (no recognizable speech but relatively preserved personality).
   e) may also be less severe autosomal dominant.

2. Chromosomal syndromes (Down, Edwards, cri-du-chat)

3. CEREBELLO-PALSY SYNDROME - prenatal & postnatal growth delay, synphryns, thin down-turning upper lip, proximally placed thumb.

4. RUBINSTEIN-TAYBI SYNDROME - beaked nose, downward slanting of palpebral fissures, epicanthic folds, short stature with broad thumbs and toes.

5. SNITH-LEVALL-OPZITZ SYNDROME - pnosis, scaphocephaly, inner-epicampic folds, antverted nostrils, low birthweight, marked feeding problems.

• microcephaly is very common in syndromes that have mental retardation and cortical migration abnormalities as component!
• microcephaly is common among mentally retarded population.

DIAGNOSIS

1) head circumference; obtain at birth; serial measurements are more meaningful than single determination; head circumference of each parent and sibling.
2) skull films (to exclude primary craniosynostosis) → CT / MRI
3) karyotype
4) fasting plasma & urine amino acid analysis; serum ammonium.
5) TORCH titers of mother and child.
6) urine culture of CMV.
7) mother's serum & urine culture of CMV & TORCH titers.

TREATMENT

Most intracranial conditions causing microcephaly are untreatable! The only treatable cause is craniosynostosis!

CRANIOCERVICAL JUNCTION (SKULL BASE & CERVICAL VERTEBRAE)

Mechanical compression of neuraxis (lower brain stem & cervical cord):

ichal pain & vertigo may be early nonspecific complaints.
   a) primary downbeating nystagmus (fast component downward)

BASILAR IMPRESSION, BASILAR INVAGINATION, PLATYBASIA, CONVEXOBASIA

- floor of posterior fossa bulges upward in region about foramen magnum (i.e. skull base flattened on cervical spine) 
  - narrowing of foramen magnum.

1. PLATYBASIA
2. BASILAR INVAGINATION (angle* between planes of anterior cranial fossa and clivus > 135-140° on lateral skull x-ray) - generally asymptomatic!
   *i.e. angle formed by line connecting anterior margin of foramen magnum, tuberculum sellae, and nasion.

2. CONVEXOBASIA (more extreme form).

BASILAR IMPRESSION - upward displacement of occipital bone and cervical spine with protrusion of odontoid process into foramen magnum (i.e. odontoid process is above Chamberlain's line [hard palate to base of skull]).

ETIOLOGY

A. Congenital maldevelopment or hypoplasia of basiocipit:
1) Chiari types I and II
2) osteogenesis imperfecta
3) Hajdu-Cheney syndrome
**Clinical Features**
- neck may be short, moxity impaired.
- vertical head diameter.
- compression of pons / medulla / cerebellum / cervical cord. stretching of cranial nerves and blood supply - symptoms begin insidiously in childhood or early adult life:
  1. nuchal pain, neck stiffness, torticollis.
  2. spasticity in lower extremities.
  3. proprioception loss in upper extremities.
  4. ataxic gait, nystagmus.
  5. vertebral artery obstruction may be significant.
  6. brainstem & lower CN dysfunction late in course (incl. sleep apnea, dysautonomia and dysphagia)*.
- in RA patients, it also can be caused by laryngeal arthritis.
- if deformity interferes with CSF circulation → ICP↑; subarachnoid block (partial or complete) is present at lumbar puncture in most cases.

**Diagnosis**
- Skull X-ray + sagittal CT + sagittal MRI.

**Treatment**
- Preoperative halo traction (to reduce vertical instability + C2 compression neuralgia) for 2-5 days with traction force 5 → 25 lbs.
- *wake patient reports if something is going wrong then*
- Surgical decompression at foramen magnum ± C2-3 laminectomies with cervico-occipital fusion (s. occipitoccipital fixation).

Indications for surgery – compression of neural structures (myelopathy, neuropathies)
- suboccipital neuralgia (C2 entrapment between occiput and posterior arch) as sole indication is controversial (but justified if traction eliminates pain – confirms C2 entrapment)

**Atlantoaxial Instability**
- anterior arch of atlas - dens interval > 3 mm.
  - chronic subluxation → remodelling of lateral atlanto-axial joints - enhances instability and prevents reduction.
  - 70% cases are associated with os odontoideum*, most of remainder with cranial assimilation of atlas.
  - abnormal dens ossification (dens not fused with body of axis) secondary to instability and abnormal local stress (i.e. not segmentation anomaly).

**Etiology**
- weakness or absence of structures maintaining stability (e.g. ligament laxity):
  1. Rheumatoid arthritis!!!*
  2. Vertebral metastases, trauma
  3. Mucopolysaccharidoses
  4. Genetic conditions (e.g. 50% Down’s syndrome patients*).
- *screen all trisomy 21 patients at 5-8, 10-12, and 18 years for atlantoaxial instability!

**Clinical Features**
- atlantoaxial subluxation (displacement of atlas anteriorly in relation to axis) → acute or chronic spinal cord compression between dens (mainly thickened ligaments) and posterior rim of foramen magnum.
  - Head movement causes neck pain.
  - children may show head tilt.
  - dislocation can cause immediate death from respiratory failure!

**Diagnosis**
- lateral neck roentgenograms in neutral, flexion, and extension positions - anterior dislocation of atlas.

**Os odontoideum**
- *arise* and atlanto-axial instability (cervical myelography, lateral projections): posterior atlanto-axial subluxation in extension (B) is reduced in flexion (A).

**MORQUIO DISEASE**
- Case 1 - sagittal CT myelography with neck flexed (A) and extended (B): cephalic two-thirds of dens are not ossified, hypermobility in extension (spinal cord is compressed, mainly by thickened ligaments).
- Case 2 (C) - sagittal T2-MRI: carcinosarcoma dens overlying ossified centrum of C1; arrow indicates synchondrosis (disc) between centrum of C1 and C2.


*see also p. 1167 (7a) >>

**References**
- Paget disease, osteomalacia, RA*
- Atlas. - magnum.
- **CASE 1**
- **CASE 2**
- Case 1 - sagittal CT myelography with neck flexed (A) and extended (B): cephalic two-thirds of dens are not ossified, hypermobility in extension (spinal cord is compressed, mainly by thickened ligaments).
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Cranial & Vertebreal Anomalies

TREATMENT
- restrict potentially harmful physical activities (tumbling, diving, football).
- indications for surgery: instability, myelopathy.
- external immobilization alone is unlikely to achieve permanent reduction → surgical arthrodesis (posterior atlanto-axial internal-fixation and fusion).
- all unstable levels must be fused.
- instrumentation provides immediate stability until bony fusion develops.
- Gallie’s fusion technique – becomes standard of care because of high rate of nonunion.

OCCIPITALIZATION of ATLAS (s. ASSIMILATION of ATLAS)
- fusion of anterior arch and ring of C1 with foramen magnum.

ETIOLOGY
1) Chiari type I malformation
2) Klippel-Feil anomaly
3) acrondroplasia.

CLINICAL FEATURES
- cervical myelopathy when AP diameter of foramen magnum (behind odontoid process) decreases to < 19 mm.

DENs HYPOPLASIA
- usually misdiagnosis - os odontoideum in fact being present but overlooked because it is not ossified, small or malplaced.
- TRUE DENS HYPOPLASIA only occurs in association with more complex fusion anomalies (esp. those which restrict rotation at C1/2).

KLIPPEL-FEIL ANOMALY
- congenital fusion of cervical vertebrae into one or more separate masses:
  a) failure of segmentation (most likely)
  b) secondary fusion.
- fusion is most commonly restricted to C2-3 or C5-6 (but can extend beyond cervical spine – esp. upper thoracic vertebrae). *frequently associated with occipital assimilation of atlas.
- size in height of congenitally fused bodies is equal to normal height of two vertebrae plus expected height of intervertebral disc if one were present (vs. fusion due to disease – height is less).
- in cases of PARTIAL fusion, it is anterior aspect that fuses, while rudiment of disc remains in posterior portion.

ETIOLOGY
1) part of syndromes (e.g. Turner's, Noonan's, Wildervanck's)
2) isolated:
   a) sporadic
   b) inherited (autosomal dominant or autosomal recessive).

CLINICAL FEATURES
- fusion of vertebrae in itself is not of any great clinical importance:
  1) short neck
  2) low posterior hairline
  3) limitation of neck movements (esp. rotation and bending to sides).
- accentuation of symptoms in presence of cervical osteoarthritis.

N.B. clinical symptoms are usually due to presence of other developmental defects.

Associated anomalies:
- atlanto-occipital anomalies are frequent (one of major reasons for associated morbidity).
- N.B. main neurological complications result from crano-cervical instability → spinal cord compromise!
- kyphosis & scoliosis are frequent.
- other skeletal malformations (esp. Sprengel's deformity – congenital scapula elevation and medial rotation) can be associated.
- congenital deafness (faulty development of osseous inner ear) – 20-30% patients.
- patients may have GU anomalies (incl. unilateral renal agenesis), cardiovascular anomalies.

MURCS syndrome (Müllerian duct aplasia, renal aplasia, cervicothoracic somite dysplasia) - Klippel-Feil anomaly with absence of vagina & uterus, renal agenesis or ectopy; hearing and GI defects.

ECSOBAR syndrome - autosomal recessive cervical vertebral fusion and other bony defects, ptosis, hypertelorism, pterygia of neck, axillae, and other joints; genital anomalies; small stature.

DIAGNOSIS
ATLANTO-AXIAL ROTATORY FIXATION (AARF)
- rare form of torticollis in children; (rotatory fixation between C1 and C2 within normal range of motion) without subluxation.
- mechanism - lax ligaments and possibly synovium interposition in intervertebral joints.
- clinically - torticollis persisting for > 2 weeks.
- requires careful diagnostic work up - total muscle relaxation (under general anaesthesia) and CT of upper cervical spine in neutral position as well as in maximum rotation to right and left.
- AARF is present if there is asymmetrically reduced rotation between C1 and C2.
- requires aggressive* therapy - traction. *If unsuccessful, AARF will result in permanent rotatory malalignment with ankylosis.

INIENCEPHALY
- cranial defect at occiput, with brain exposed; often in combination with cervical rachischisis and retroflexion.

SPINE
VERTEBRAL FUSION ANOMALIES
- intervertebral discs are narrow and partly bridged by regions where disc material never developed.
- fused segments show varying degrees of hypoplasia (when multiple segments are involved, marked dysplasias such as hemivertebrae are also often present).
- in marked cases, term SYNSPONDYLISM is used (term Klippel-Feil syndrome is appropriate when cervical region is predominantly involved).
Congenital fusion of two lumbar vertebrae ("block vertebra"): note concavity of anterior vertebral contour at level of expected disc space (not seen in surgical fusions) and posterior remnant of intervertebral disc.


TRANSITIONAL VERTEBRAE

Vertebrae at junction of major divisions of spine have CHARACTERISTICS OF BOTH DIVISIONS:
- C7 may have ribs (unilateral or bilateral) attached to transverse processes (> 0% of normal population);
  - cervical ribs may be short or may be long enough to articulate with sternum.
  - cervical rib may be fused or may form pseudoarthrosis with first rib.
  - cervical rib (as it passes anteriorly) may compress subclavian vessels → venous thrombosis / arterial insufficiency.
  - even if cervical rib is short, fibrous band may extend from its tip to first rib or to sternum (source of compression of subclavian vessels).
- L1 may have rudimentary ribs articulating with transverse processes.
- L5 may be partially sacralized (often one transverse process fused with sacrum, other free) with rudimentary disc between them (> 0% of normal population).
- SI segment may become partially lumbalized:
  - most frequent at thoracolumbar and lumbosacral junctions;
  - transition may be complete (e.g. 6 lumbar vertebrae and 4 sacral segments; 13 thoracic and 4 lumbar); usually, addition of segment to one division of spine is corrected at another level.

Main significance of transitional vertebrae - may result in level being wrongly identified preoperatively (e.g. when MRI is used without X-ray).

Partially sacralized L5 vertebra - left transverse process is enlarged and articulates with sacrum; right transverse process is free.

HEMIVERTEBRAE

LATERAL HEMIVERTEBRA - Incomplete development of lateral half of vertebral body:
- failure of development of one of lateral centers of chondrification.
- in AP radiograph, hemivertebra has triangular shape.
- causes scoliosis with acute lateral angulation of spine.
- hemivertebra in thoracic region has only one rib (on side of ossified center).

Three adjacent hemivertebrae in thoracic spine (arrow) with associated convex rightward scoliosis.


DORSAL HEMIVERTEBRA - Failure of development of ventral fetal ossification center:
- causes progressive kyphosis that may require posterior fusion at level of hemivertebra.

VENTRAL HEMIVERTEBRA (rare) - Failure of development of dorsal ossification center.
BUTTERFLY VERTEBRAE

- failure to fuse of two lateral centers of chondrification for vertebral body → cleft in midsagittal plane (dividing body into two lateral halves)
- more frequently cleft is only partial, resulting in characteristic shape "butterfly vertebra".

Partial sagittal cleft of 10th thoracic vertebra

FAILURE of FUSION of SECONDARY OSSIFICATION CENTERS

- secondary ossification center* fails to unite to vertebral body → persist into adult life as separate bony fragment (esp. at inferior articular process).
- normally, secondary ossification centers appear at tips of all spinous and transverse processes.
- can be confused with fracture*
  - smooth corticated margins of fragment help differentiate this anomaly from acute fracture.

Nonunited apophysis (white arrow) of L4 inferior articular process (oblique lumbar radiograph); smooth, sclerotic margins indicate that this is not acute fracture:

LIMBUS VERTEBRA

- anterior interposition of intravertebrally herniated nuclear material prevents fusion of portion of peripheral ring apophysis with adjacent vertebral end-plate.
- on lateral radiographs: triangle-shaped bony mass along anterosuperior corner with corresponding defect in adjacent vertebral body.
- smooth bony margins and characteristic shape and location differentiate from fracture.

Nonunited accessory ossification center of anterosuperior corner of L4:

PEDICLE ANOMALIES

- absence or hypoplasia of pedicle with compensatory hypertrophy* of opposite pedicle.
- ipsilateral intervertebral foramen is widened; posterior displacement of maldeveloped lateral mass.
- flattening / thinning of pedicles at Th12 / L1 is common anatomic variant.

Absent right pedicle of L2 (arrow); left pedicle shows compensatory sclerosis and hypertrophy:


*normally, secondary ossification centers appear at tips of all spinous and transverse processes.
LATERAL MENINGOCELE SYNDROME

- rare hereditary autosomal dominant connective tissue disorder
- pan-spinal meningoceles secondary to dural ectasia

T2 MRI of thoracolumbar spine (a-c) - intraspinal and paraspinal meningoceles.
Plain lateral radiograph (d) - large neuroforamina, thinned out pedicles and congenital fusion of T10-L4 vertebral bodies.
Axial non-contrast CT (e) - thin stretched out pedicles.

BIBLIOGRAPHY for ch. “Developmental Anomalies” → follow this LINK >>