CHAPTER 1

Craniofacial development and the body axis: normal and pathological aspects from early prenatal to postnatal life

Body axis pre- and postnatally

Germ disk and notochord
If you ask a dentist or a medical professional “From where does the cranium develop in its initial phase?” they will probably not be able to answer you. Going back to basic embryology, recall your memory of the germ disk. From this very early two-layered disk, the whole body arises. Gradually the mesoderm forms the third layer in the body and the notochord develops. The notochord is an axial row of cells of ectodermal origin which are decisive for the closure of the neural tube, formation of the central nervous system and visceral and skeletal development. The germ disk folds and begins to close centrally at approximately day 18 of gestational age (GA) and openings in the cranial and caudal ends arise (Figure 1.1). These openings are called neuropores.

Formation of the vertebral column
The ridges (left and right) that surround the cranial neuropore are called the neural crest (Figure 1.2). The neural crest cells are ectodermally derived and represent a “contact ridge” between the outer surface ectoderm and the inner neuroectoderm. The tissues that are derived from the neural crest are called the ectomesenchyme – having ectodermal origin with the ability to differentiate into various cell types, including connective tissue (e.g. cartilage, bone). From different regions on the neural crest, different ectomesenchymal cell groups migrate anteriorly through the fold between the neuroectoderm and the surface ectoderm, bulging out and gradually forming the craniofacial skeleton.

More posterior parts of the cranium arise from tissue located laterally to the notochord, called paranotochordal tissue.

Gradually, the neuropores close and the germ disk forms the brainstem. From here the cerebral hemispheres develop from the foramen of Monro. Figure 1.3 depicts the craniofacial skeleton and the central nervous system.

The notochord forms the body axis at a very early stage (Figure 1.4). The notochord is essential for the folding and closing of the germ disk and for formation of body structures and the vertebral column. The bodies of the individual vertebrae form around the notochord (Figure 1.5). Remnants of notochordal tissue remain in the intervertebral disks after birth but not in the vertebrae. In the cranial portion of the body axis, the notochord ends in the region of the posterior wall of the sella turcica (Figure 1.6). Thus the notochord also organizes the main parts of the occipital bone and parts of the sphenoid bone corpus.

The sequence in which the vertebral bodies ossify is always the same, starting with the lumbar region and gradually moving cranially. The arches in the vertebrae protecting the medulla spinalis develop in a sequence which is also constantly the same, but the ossification of the arches starts cranially and moves gradually caudally. The region in which the ossification of the vertebral bodies and vertebral arches meet each other is near to the upper thoracic vertebra (Figure 1.7). In summary, the development of the head and brain is completely integrated with body axis development.

Fetal pathology
Malformations in the vertebral bodies occur in relation to the notochord. These malformations could be twin bodies (completely separated body units) or partially cleft vertebral bodies. Also fusion between bodies or the absence of a vertebral body may occur. Different types of abnormal vertebrae are demonstrated in Figure 1.8.

The mapping of the body axis in fetuses with different genetic abnormalities demonstrates that abnormal development often occurs regionally in so-called developmental fields. Thus fetuses with trisomy 18 predominantly have abnormalities in the thoracic and lumbar vertebral fields and not in the cervical field. This is not the case in trisomy 21, trisomy 13 or triploidy. Mapping of the body axis shows that the different genotypes affect the different fields in the vertebral column (Figure 1.9).

Cervical spine pre- and postnatally
The bony bodies (corpora) of the cervical spine are formed by ossification of the cartilage encircling the early notochord. Remnants of the notochord may persist in the nucleus pulposus in the intervertebral disks. The arches of the vertebrae encircle
the spinal cord. The atlas, which is the upper vertebra of the cervical spine, articulates with the occipital condyles on the external cranial base.

Figure 1.10 demonstrates the normal cervical spine in a child.

Clinical relevance
Prenatal defects are always present postnatally as well. Mapping of the malformations in the vertebral column is therefore essential for clinical diagnostics of postnatal vertebral development. Figure 1.11 demonstrates examples of malformations of the cervical column observed in children with known and unknown diagnoses.

The interrelationship between the body axis and the cranium
In 1974, Nicole Le Douarin published a study on cell migration in animals from the front-most part of the neural crest field to the cranium and face. Le Douarin found that the face and cranium had different regions with tissues that stem from different parts of the neural crest. The original research involved radioimmune marking which is a method not possible in human studies. Research on the early, embryological, facial development from the neural crest can therefore only be conducted on animals.

The cells from the neural crest are multipotent and can form cartilage, bone, muscles, nerves, and vessels. In 1997, the knowledge gained by Le Douarin was applied to human cranial and facial development. Figure 1.3 is a schematic drawing of how the neural crest might influence the development of various parts of the cranium and face. Immunohistochemical markings of the body axis in rat embryos have demonstrated how gene expression differs in the different fields of the body axis. For example, the Pax9 gene is expressed in the lumbosacral body axis and also in the craniofacial region (see Chapter 13).

Clinical relevance
Occipitalization is a postnatal condition in which the upper vertebra (atlas) is fused to the occipital condyle (see Chapter 13). This is an abnormality observed postnatally which could be explained by a prenatal fusion or by nonseparation of the cartilage which forms both the atlas and the occipital bone.
**Figure 1.3** A schematic drawing of the skeleton of a human fetus about GA 17 weeks. The spinal cord and the brainstem (not the cerebellum) are marked dark yellow, and the hemispheres of the cerebrum and cerebellum are marked beige. Green arrows indicate paths of neural crest cell migration to the jaws forming the green jaws and facial bones. White indicates the theca bones and the vertebral column. Red lines mark structures with an ectodermal origin which includes the notochord within the vertebral bodies. Peripheral nerves to the jaws are marked in orange.

**Figure 1.4** Midsagittal section of a part of the body axis of a human embryo GA 24 days demonstrating the early morphology of the notochordal cells (red).

**Figure 1.5** A midsagittal section of the developing vertebral column in a human embryo GA 7 weeks. The cartilaginous vertebral bodies are marked purple. The notochord is a lightly marked (nearly white) cell structure centrally and vertically located within the vertebral bodies.

**Figure 1.6** Profile radiograph of a child. The red line indicates the former location of the notochord from the vertebral bodies, through the basilar part of the occipital bone to the rostral location in the posterior wall of the sella turcica.
Craniofacial development pre- and postnatally

Bone tissue develops after the embryo has reached GA 7 weeks (Figure 1.12). The main components of the cranium are the bones in the cranial base, the maxilla, the mandible, the vomeral bone, the nasal bone, and the temporal bone (Figure 1.13). These and other bones will be described in this section. It is characteristic for bone development that the individual ossification sites always develop in a constant sequence at the same locations and with the same morphology. The prenatal skeleton can therefore be used as a map to reveal where a malformation is located and when it arose.

Cranial base (excluding the sella turcica)

We now focus on the horizontal plane and midaxial plane of the cranial base (Figure 1.14). The bones ossify midaxially in the following sequence: basilar part of the occipital bone, sphenoid
bone corpus, ethmoid bone, lower part of the frontal bone. The sequence is always the same. The morphology of the individual bone components differs with age. The developmental outline of the basilar part of the occipital bone at GA 20 weeks is seen in Figure 1.14.

All parts of the osseous cranial base has been formed from cartilage before birth. Between the bone components there are multiple cartilaginous synchondroses. In a five-month-old fetus, there are synchondroses between the sphenoidal bone and occipital bone (sphenooccipital synchondrosis) and three synchondroses between the different sphenoidal components (pre-sphenoid, intersphenoid, and basisphenoid synchondrosis). There are also two synchondroses between the occipital components (anterior and posterior intraoccipital synchondroses). Synchondroses also exist between the occipital bone and temporal bone (petrooccipital synchondrosis), and between the temporal bone and sphenoid bone (sphenopetrosal synchondrosis). These synchondroses allow growth of the cranial base in the sagittal and transversal planes.

At birth, the synchondroses are significantly diminished. Only the sphenopetrosal and sphenooccipital synchondroses are maintained.
At puberty, there is only one active synchondrosis left – the sphenoooccipital synchondrosis. This synchondrosis is a relatively common finding on a profile radiograph (Figure 1.15). It is difficult to analyze the amount of growth in this synchondrosis, which was studied in detail by Melsen in 1974. The growth of the cranial base has also been attempted in an anthropological analysis (Figure 1.16). This study shows that the central part of the cranial base that supports the brainstem only grows until approximately four or five years of age. This was determined by analyzing the distance between the stable innervation foraminens in the cranial base (see Chapter 2).

Fetal pathology
Different prenatal malformations can be traced in the basilar part of the occipital bone. As an example, different occipital bone malformations related to specific diagnoses are shown in Figure 1.17. There may also be signs of early fusion of bone components in the cranial base (see Chapter 13). These early malformations indicate early phenotypic characteristics for a given disease.

Clinical relevance
If the cartilaginous tissue is abnormal, as seen in dwarfism (with short extremities), then the cranial base is also short. This results in a large, rounded, protruding frontal bone in order to provide enough space for proper brain development (Figure 1.18).

Figure 1.14  A horizontal and midaxial views of a normal prenatal human cranial base. (Upper) The figure demonstrates the internal cranial fossae (left) seen from above (note the large sella turcica; arrow) and a horizontal histological section (right) of the caudal part of the cranial base, larynx, and mandible from a fetus GA 15 weeks. Note the cartilage surrounding the foramen magnum (star), the cartilage of the hyoid bone (black arrow), and the mental lower part of the mandible (red arrow). (Center) A radiograph of the cranial base from a fetus GA 20 weeks. (Inset) A deviscerated basilar part of an occipital bone from a fetus GA 20 weeks. (Lower) Midsagittal section (anterior direction to the left) of a human cranial base GA 15 weeks demonstrating ossification of the basilar part of the occipital bone and the morphology of the sella turcica formed in cartilage (purple, marked by arrow). The sella contains the pituitary gland marked dark blue for the adenopituitary gland (anteriorly) and light blue for the neuropituitary gland (posteriorly).
Clefting of the basilar part of the occipital bone can also arise prenatally and persist through adulthood. This is observed in the anthropological case provided in Figure 1.19.

Sella turcica
The sella turcica is formed by cartilage which gradually ossifies from the lower aspects and progresses cranially. The posterior wall, the dorsum sellae, may retain remnants from the rostral end of the notochord (see Figure 1.6). The sella turcica is the only part of the medial cranial fossa which appears on a profile radiograph.

Fetal pathology
The mapping of the sella turcica in malformed fetuses with known and unknown genotypes has demonstrated that some conditions are associated with an abnormality in the anterior wall, some with abnormality in the posterior wall and some with an opening in the floor. Examples are given in Figure 1.21. Irregular cartilaginous walls have also been described.

Clinical relevance
When observing a profile radiograph, it is important to notice the posterior and anterior walls of the sella turcica. Absence or malformation of the posterior wall may be associated with abnormalities in the spine due to the notochordial relationship between the spine and the posterior wall of the sella (Figure 1.22). Meanwhile, abnormalities in the anterior wall are often associated with malformations of the facial bones. In several skeletal malocclusions, the sella often has an overlying bridge between the posterior and anterior walls (Figure 1.23). This is a sign which often appears early in postnatal life and indicates a malocclusion with a grade of severity that cannot be corrected orthodontically but which should rather be treated surgically.

The sella turcica appears as a border region in the cranial base between the anterior, neural crest-formed cranial base and the posterior, notochord-related cranial base (see Figure 1.20).
is important to bear in mind in cases where deviations are restricted to the anterior or posterior sella wall. As the cranial end of the notochord ends in the posterior sella wall, it is important in clinic to determine whether deviations in the posterior sella wall are related to deviations in the basilar part of the occipital bone and/or in the vertebral bodies which are also formed around the notochord. Examples of sella turcica malformations are demonstrated in Figure 1.23.

**Maxilla**

The maxilla is attached through the ethmoid bone and the vomeral bone to the cranial base. Ossification of the maxilla appears in week 9 GA starting in the canine region. Again, there is a completely reproducible sequence in the formation of the different bony elements. The orbital foramen is bound by bone tissue encircling the maxillary nerve. The infraorbital canal develops gradually as a result of external bone apposition. The palate is formed by vertically located, soft tissue palatal processes on each side of the tongue (Figure 1.24). These processes shift from a vertical to a horizontal position at the time when the tongue is lowered. This process is explained in further detail in the section on the mandible. The midpalatine suture arises gradually, as does the transverse palatine suture (see Figure 1.24). The transverse palatine suture is a layer of connective tissue between the slanted edges of the horizontal processes of both the palatal bones and the maxillary bones. This suture allows the maxilla to move downward and forward during growth. The palatal sutures are demonstrated in Figure 1.24.

In the frontal region, the incisive fissure borders the posterior aspect of the incisors. This fissure is not a suture where growth occurs, nor is it a structure which borders the frontonasal region from the maxillary region (see Chapter 3). The fissure extends from the midpalatine suture to the region behind the canine and has a function during the enlargement of the incisive tooth buds.
and later during eruption of the incisors. After eruption has occurred, the fissure has no known function.

The maxilla is composed of two, bilateral, osseous, hemimaxillary components which meet the axial plane where they form the midpalatine suture. This midpalatine suture is named differently in different regions: anteriorly – interincisal suture; centrally – intermaxillary suture; posteriorly – interpalatine suture. The midpalatine suture forms the base for transverse growth of the palate.

The height of the maxilla depends on the growth of the sutures between the maxilla and the neighboring bones (nasal bone, frontal bone, zygomatic bone, and palatine bone). In the palatine process of the maxilla, there is resorption of the surface facing the nasal cavity and apposition on the palatine surface. All sutures that are responsible for growth in height have an orientation which is mostly oblique and which ensures that the maxilla moves downward and forward. Lastly, the growth of the maxilla must also support the development of the alveolar process for erupting teeth. The growth in the transpalatine suture with an oblique orientation ensures that the maxilla during growth is transported forward and downward. During this sutural growth, there is a gradual apposition of the maxillary tuber (Figure 1.25).

The palatine nerve is located in a groove in the horizontal part of the palatine bone. The palatine foramen is therefore located on the opposite side of the first molar in early childhood, but due to the gradual forward movement of the maxilla, as a result of growth in the transpalatine suture, it appears at the level of the second molar during puberty (see Figure 1.25). One can therefore appreciate that space for the third molar depends on the growth in the transverse palatine suture and on bone apposition in the tuber region.

The infraorbital canal arises gradually during the early growth period by apposition at the anterior maxillary surface. The direction of the canal reflects the transverse and sagittal growth pattern in the maxilla. This direction also is supported by radiographic studies by Bjørk and by Solow of maxillary growth. Solow found that the midpalatine suture has a fan-shaped growth with more growth in the posterior than the anterior region. The incisive fissure is not a growth zone but a fissure which merely adapts to the gain in size of the incisors, and thus this fissure functions only until the permanent incisors have attained their full crown size (see Figure 1.25).

**Fetal pathology**

The most commonly observed malformations in the maxilla are clefts. Some of these are very severe and may extend all the way to the sella turcica region where the entire floor may be absent. Other midaxial malformations may involve a malformed palate, having a round shape as opposed to the normal horseshoe formation. This “round” palate is associated with abnormalities in the nasal cavity and the anterior cranial fossa and the absence of the anterior part of the midpalatine suture.
Clinical relevance

Fetal pathology is important not only for understanding of the depth and posterior extent of a cleft formation but also for understanding that the growth pattern of the two hemimaxillary.
components can be different. Such a difference in hemimaxillary growth results in maxillary asymmetry which is demonstrated in Figure 1.26. This figure displays how unilateral abnormal growth influences the shape of the palate and the nasal floor.

What is a premaxilla?
The term *premaxilla* does not indicate an individual bone but is used to describe the anterior maxillary region. This region is the frontonasal area which is formed by the frontonasal neural crest cells. The border between the frontonasal area and the maxillary area cannot normally be observed on the bone. In anthropological cases, a slight crease may appear, indicating the border

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**Figure 1.24** Developmental aspects in the human maxilla. (*Upper left*) Frontal section of a human fetal head demonstrating the two soft tissue palatal shelves bordering the tongue. The palate has not yet formed. GA 11 weeks. (*Upper right*) Frontal section of the nasal cavity after palate formation. GA 15 weeks. (*Lower*) Radiographic appearance of the ossified palate. GA 17 weeks. (*Inset*) A schematic drawing of the sutures in the palate and a sagittal cut (*dotted line*) demonstrating specifically the transverse palatine suture and the direction of growth in this suture (*arrow*). Source: Kjær et al. (1999). Reproduced with permission of John Wiley & Sons.

**Figure 1.25** Different aspects of the human maxilla under development. (*Upper*) An anthropological maxilla in the occlusal view from a child approximately five years of age. Note that the horizontal process of the palatine bone is absent on the left side. Also notice the incisive fissure and the vague marking of the borderline between the frontonasal area and the maxillary area of the maxilla (*arrows*). (*Center*) Schematic drawing of the sutures in the palate. A sagittal cut (*dotted line* in Fig. 1.24) demonstrates the transverse palatine suture which makes the direction of growth downward and forward possible. The three figures are from three different ages (left, six years; middle, 14 years; right, 20 years). Red marks the horizontal processes of the palatine bone. Green marks the maxillary and palatine alveolar processes including the tuber maxillae. White marks newly formed bone and the small circles within the red area (palatine bone) mark the palatine foraminae. Note that the forward growth of the maxilla occurs predominantly at the maxillary edge of the transverse palatine suture. The stable position of the red squares indicates why the palatine foramen appears opposite to the first molar at six years, and later opposite the second or third molar. (*Lower*) A right hemimaxilla from a child approximately three years of age (*left*) and a left hemimaxilla from an adolescent (*right*) demonstrating the difference in bone size and bone apposition at the alveolar process and resorption in the floor of the nasal cavity and of the orbital cavity. Source: Damgaard (2011). Reproduced with permission of Taylor & Francis Publishing Group.
between the two areas (see Figure 1.25). In pathological cases, a cleft may appear at this borderline.

An infection in childhood manifested in a localized region of the mucosal palate can disturb the appositional growth in that region. If the palatine bone apposition continues normally in the region surrounding the infection site, a hole will gradually develop at the initial infection starting point. This can occur in the condition called segmental maxillary dysplasia described in Chapter 10.

**Mandible**

The mandible is the first bone to ossify in the cranium at around week 7 GA. Before the osseous mandible, there is a cartilaginous structure, Meckel’s cartilage, extending from the ear region to the mental region. The bone is first laid down in the canine region from where bone formation stretches anteriorly and posteriorly. From the canine region and anteriorly, bone is also developed lingually to Meckel’s cartilage. This is not the case posteriorly to the canine region. There is a muscle insertion in the inner aspects of the mandible of the geniohyoidei and genioglossi muscles. Around GA 12 weeks, these muscles contract and draw the tongue downwards. It is this downward movement of the tongue which gives the palate shelf the possibility of moving to the horizontal position. When motion occurs, the cartilage bends to an S-shape and the mandible moves forward, resulting in a protrusion of the tongue between the lips, and later the mandible retracts to a position behind the lips. After these movements of the developing mandible, the mandibular condyle begins development from early cartilaginous tissue which appears in the dorsal aspects of the bony mandible at GA 15 weeks (see Figure 1.27). During...
further development, the cartilage undergoes different changes, resulting in the appearance at birth of a mushroom-shaped, condylar cartilage covering the bony condyle (see Figure 1.27). The condylar fossa and the condylar disk with the lower and upper joint chambers occur around GA 19 weeks. Special attention should be given to the germinative cell layer located between the cartilage and the perichondrial layer protecting the cartilage. This germinative layer produces prechondroblasts and fibroblasts in the inner layer of the perichondrium (Figure 1.28). The vessels nourishing the cartilage appear in the germinative layer and in older fetuses also in the intracartilaginous canals.

The symphysis menti is the anterior midaxial joint structure connecting the left and right mandibular formations. This symphysis in the early stages is bordered by Meckel’s cartilage, later by Meckel’s cartilage covered on the labial surface by bone, and thereafter by bone labially as well as lingually. In the mental region (chin region), the cartilaginous Meckel’s cartilage gradually disappears due to resorption. New cartilage formations appear on the bone surfaces and the characteristic structure of the symphysis occurs. The symphysis menti is characterized by bilateral, endochondral, bony ends covering an interosseous connective tissue layer. The symphysis menti is richly vascularized and is a site for prenatal, transverse, mandibular growth.

The bony components of the mandible with the main mandibular body and the three processes (condylar process, coronoid process, and alveolar process) are also formed before birth (Figure 1.29). The mental foramen forms early by bone tissue encircling the mental nerve. The mental canal arises gradually by apposition at the mandibular surface. The mandibular foramen develops in the later part of prenatal life (see Chapter 2).

The growth center of the mandible is the germinative cell layer covering the condylar cartilage in both prenatal and postnatal life (see Figures 1.27 and 1.28). During prenatal life, the mandible is a relatively flat bone compared to the postnatal mandible. It is backward tilted and without a fully developed ramus (see Figure 1.29). After birth, the ramus develops gradually, possibly due to mastication. Cephalometric studies of postnatal mandibular growth have shown that there are vertical as well as sagittal growth patterns, and that these growth patterns are related to development of the occlusion. In the mandible, the mandibular and mental canals indicate the directional growth of the mandible (see Figure 1.29), just as the infraorbital canal indicates the maxillary directional growth. Also in the mandible, space should be gained in the alveolar process for the erupting teeth (see Figure 1.29). Gain in length of the alveolar process occurs by anterior resorption of the mandibular ramus and at the same time, a posterior apposition occurs on the posterior aspect of the ramus. The bone apposition and resorption patterns in the mandible are closely linked to the directional growth of the mandibular condyle. Space for the third molar depends on the condylar growth pattern and the associated ramus resorption.

**Fetal pathology**

The different parts of the mandible arise by cartilaginous ossification (anteriorly), by intermembranous ossification (medially), and cartilaginous condylar growth (posteriorly). If one of these ossification processes malfunctions then the result is visible on prenatal radiographs (Figure 1.30). If the condylar cartilage does not develop then the mandible cannot gain in size. If this happens bilaterally, then agnathia (see Chapter 3) arises which is a lethal condition.

**Clinical relevance**

Asymmetrical development of the mandible and condylar ankylosis can be a congenital or acquired, unilateral, condylar, abnormal development. Asymmetrical development of the mandible and condylar malformations are exemplified in the cases...
demonstrated in Figure 1.31. Unilateral condylar hypoplasia and unilateral condylar ankylosis result in mandibular asymmetry during postnatal life. An anthropological analysis of the direction of the mental canal can indicate when the defect in the condylar region arose. If the affected side of the mandible has arrested growth, then the canal direction will be different from the other side. If this occurs later in life, the asymmetry is less and the direction of the two canals more symmetrical. Figure 1.31 shows a cranium in which an early condylar growth arrest contributes to severe asymmetry.
The uppermost part of Meckel’s cartilage produces the malleus and incus of the inner ear. It is logical to associate deviations in these small bones with deviations of the mandible which is also dependent on Meckel’s cartilage.

A median cleft in the mandible and/or nonclosure of the symphysis menti are very rare findings shown in Figure 1.32. If the bilateral hemimandibles do not fuse correctly in the midaxial plane, a midline mandibular cleft can occur (see Figure 1.32). This abnormality and the persistence of the symphysis menti are rarely observed.

Diseases such as juvenile arthritis result in complete or partial arrest of mandibular growth which leads to asymmetry or retrognathia. Other forms of congenital or acquired conditions can also result in deviant mandibular growth.

Congenital absence of mandibular incisors appears in Ellis–van Creveld syndrome which involves malformation of cartilaginous tissue (Figure 1.33). This might indicate the influence of the surrounding endochondral tissue (ectomesenchyme) anteriorly in the mandible on tooth formation in this region.

**Theca cranii**

The theca cranii protecting the brain ossifies first in the most anterior and lower part of the frontal bone and in the posterior part by the occipital squama. Later, thin, porous bone membranes appear in the protuberantia frontalis and protuberantia parietalis. The intramembranously formed bone structure radiates out from these protuberantiae (Figure 1.34). The theca sutures do not develop until after GA 22 weeks. Between the
squamous bones (frontal squama, parietal sqama, sphenoidal squama and occipital squama), there are large sheets of connective tissue called fontanelles, which allow cerebral growth. At birth, these fontanelles (especially the frontal fontanelle) are still very large. The pattern of sutures and fontanelles differs in different craniofacial malformations. The postnatal thickness and size of the theca cranii increase gradually and can be measured by cephalometry. The thickness varies under normal conditions and normal malocclusions. The lower part of the occipital squama has a cartilaginous origin.

Clinical relevance
Different craniofacial malformations are interrelated with various malformations in the theca cranii (Figure 1.35). It has been debated whether the theca cranii has a neural crest origin or paranotochordal origin or a mixture of the two (the last being the more probable theory). The different theca malformations observed in different craniofacial malformations cannot clearly identify the relationship between the malformations of the theca and malformations in other regions of the cranium.

Synostoses are suture closures. They are observed in different syndromes as well as in cases without a syndromic diagnosis (Figure 1.36). The bone thickness of the theca seems to be interrelated with various skeletal malocclusions. One example is observed in skeletal deep bite where the theca is statistically thicker than average. Pathological thickness of the theca appears in skeletal disorders mentioned in Chapter 15.

Vomeral bone
The vomeral bone is made up of two bilateral ossifications on each side of the nasal septum around 13 weeks GA. The two bilateral bone units fuse caudally and develop a broad base which lies above the midpalatine suture (Figure 1.37). The suture
between the vomeral bone and the maxilla allows the maxilla to move forward during growth.

**Clinical relevance**

Be aware of the nasal septum when analyzing an orthopantomogram. Malformations often appear here in relation to facial and dental malformations. When the vomeral bone appears abnormal in morphology, it is often associated with a malformation in the maxillary incisive region. This could be in cases with supernumerary incisors or malformed incisors.

**Nasal bones**

These are formed as bilateral membranous bones supported during ossification by cartilage. A sagittal view of the prenatal, bilateral nasal bones appears in Figure 1.38. A range of normal nasal bone morphologies as they appear on profile radiographs is demonstrated in Figure 1.39.

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**Figure 1.35** The theca field in cranial development. Anterior direction points upwards. (Right) Schematic drawing of the sutures and fontanelles in a cranium without malformations. (Left) (Figures with blue background). Five different malformed crania from the perinatal period seen from above. The crania are from newborns with various severe facial malformations (see Chapter 3). Note the different morphologies of the anterior fontanelle. These crania demonstrate how abnormalities in the neural crest field development are associated with abnormal development of the theca cranii. Whether the thecal malformation is a trait which is part of the neural crest abnormality pattern or whether it is secondary to a brain malformation is not known. It is still debated whether the theca cranii develops from neural crest cell migration or whether it has a paranotochordal origin. It is also possible that the theca development is dependent of both developmental processes. Source: T. Söderqvist, Medicinsk Museion, Copenhagen, Denmark. Reproduced with permission of T. Söderqvist.

**Figure 1.36** Two crania with different synostoses. (Left) Radiograph of a cranium from a young adult demonstrating a short theca cranii (oxycephaly-like) and presumably a synostosis or retarded growth in the coronal suture. (Right) A human cranium with a scaphocephalic shape. (Inset) A view of the same cranium from above where the long and narrow shape can be seen. The etiology behind this shape is early closure of the sagittal suture.

**Figure 1.37** Formation of the vomeral bone. (Left) The black vomeral bone in the center of the figure is shaped like a tuning fork with a broad base which rests on the intermaxillary suture. The cleft of the fork contains the cartilaginous septum from the ethmoid bone (small circles). The shape of the fork allows maxillary growth as well as growth of the nasal bones. (Center) Radiograph of a frontal section of a human fetus GA 15 weeks. Note the fork axially in the nasal cavity. The symphysis menti appears clearly in the lower part of the radiograph. (Right) Histological frontal section of a human fetus GA 17 weeks with a green-blue, axial nasal cartilage supported by the fork of the vomeral bone which again has a broad base resting on the maxillary suture. Lateral aspects indicate the early nasal conchae development.
Fetal pathology
In some malformations, the nasal bone is phenotypically characteristic for the condition. A short nasal bone may be seen prenatally in trisomy 21 and 18 as well as in fragile X syndrome and cleft lip cases. A short nasal bone is not observed in complete cleft lip and palate or triploidy syndromes. In interuterine screening, the nasal bone is a key structure for analysis and assessment of syndromes such as Down’s syndrome but it can also be a symptom of other inherited conditions.

Clinical relevance
Be aware of the nasal bone when analyzing profile radiographs. Figure 1.39 demonstrates different lengths and morphologies of abnormal nasal bones. A short nasal bone may be seen in association with deviations in the dentition and/or the anterior wall of the sella turcica.

In hypophosphatemic rickets, the nasal bone often has a specific morphology (see Chapter 14).

As the nasal bone occurs bilaterally, the observation of two nasal bone contours on a profile radiograph may indicate facial asymmetry see (Figure 1.39).

Figure 1.38 Development of the nasal bones. (Left) Prenatal development of the nasal bone (arrow). During development, the bony components rest on the cartilage of the nasal septum. Note the initial calcification of the incisors in the bottom left corner (two white dots). (Right) Normal appearance of a human nasal bone from a child 14 years of age, lateral view. The nose is externally supported by a small rod to secure the correct position in the cephalostat. The nasal bone appears with a broad base and is pointed anteriorly (left side). The shadow of the entire bone is apparent and the suture bordering the maxillary bone is also visible. (Inset) An axial radiograph of the anterior part of the maxilla and nasal bones from a human fetus GA 21 weeks marking the broad and rounded shape of the nasal bones. It is important to remember that the nasal bone is wide and is a bilateral structure.

Temporal bone
The mastoid part of the temporal bone surrounding the inner ear is formed bilaterally in the cranial base from GA 10 weeks. The tympanic membrane is composed of invaginated epithelium on its outer surface. The tympanic ring is seen prenatally as a relatively large, ossified, half moon-shaped ring before the mastoid process ossifies.

Fetal pathology
In rare cases, absence of the tympanic ring can occur.

Clinical relevance
Children with reduced hearing may, among other symptoms, have a cranial base malformation associated with malformation of the inner ear. Also, an ectodermal deviation which involves the tympanic membrane (ear drum) could cause a hearing deficit. In clinic, it is important to observe whether the patient has a hearing aid. An example of a patient with an ectodermal disease involving the ear drum, the skin, and the dentition is shown in Chapter 10.

Figure 1.39 Sections from profile radiographs of three different individuals between 12 and 14 years of age displaying varying nasal bone lengths. The etiology behind these nasal bone lengths is not understood. In all three cases, other associated deviations occur and are described below. (Left) The patient has a severely asymmetrical nasal cavity and agenesis of the maxillary lateral incisors. The nasal bone is short. (Center left) The patient is cross-eyed and has an abnormal sella turcica with a broad bridge from the anterior to the posterior wall. The nasal bone is short. (Center right) The patient has a short, maxillary base and an ectopic maxillary canine. The nasal bone is abnormally long.
Craniofacial morphology and growth

Insight into craniofacial growth has expanded within the last 60 years. Craniofacial morphology has been intensively studied through postnatal, longitudinal, and radiographic studies using cephalometric methods, including three-dimensional (3D) analysis. These studies have documented that tooth position and occlusion are dependent on craniofacial growth. Cephalometric studies are also conducted on prenatal autopsy material. Such studies are cross-sectional and they clearly demonstrate in seemingly normal material how the cranial base angle is very large prenatally and gradually decreases during early childhood development until it stabilizes.

Highlights and clinical relevance

- There is a constant sequence in bone development of the cranium.
- There is coordination between the maxillary and mandibular development controlled by the tongue muscles.
- The mandible fans out transversely before formation of the mandibular condyle. The sella turcica region divides the cranial base in two parts with different origins.
- The etiology of the cranial base behind the sella turcica (posterior cranial fossa) correlates with the notochord while the frontal cranial base anterior to the sella turcica (anterior cranial fossa) develops from the neural crest cells.
- The head is completely integrated with the body axis development.
- The bones in the body axis and the bones in the cranium develop in an interdependent, constant sequence.
- The maxilla and the mandible both start ossification in the canine region.
- The skeleton can be used as a map to reveal where the initial malformation is located and when it arose.
- The palate formation depends on the activity of the tongue muscles.
- The mental canal and the infraorbital canal have a direction which is associated with the direction of mandibular and maxillary growth.
- If the condylar cartilaginous tissue does not appear posteriorly to the bony mandible at about 15 weeks GA, then the condyle will never develop. How and why this cartilage appears is not known but it is essential for postnatal condylar growth.
- The anterior mandibular region is endochondrally formed. Absence of teeth in this region may indicate the importance of the ectomesenchyme for tooth development.
- The anterior and posterior walls in the sella turcica have different origins. The sella morphology must therefore be analyzed on profile radiographs. Deviations in the posterior wall where the rostral end of the notochord appears are related to deviations in the bodies of the cervical column.
- The pattern of sutures and fontanelles differs in different craniofacial malformations.

Further reading