
The Face

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Normal Anatomy of the Face

The fetal face can be studied with ultrasound very early in gestation. Several elements of the normal anatomy (orbits, forehead) can be identified as early as the 12th week of gestation. Before 14 weeks, the soft tissues of the face are too thin to be reliably imaged with current ultrasound equipment. After this time, forehead, orbits, nose, lips, and ears can be consistently identified^{1,4} and studied in detail. A systematic approach to the examination of the fetal face should include sagittal, axial, and coronal planes.

SAGITTAL PLANES

Sagittal planes of the fetal face are useful in the assessment of the normality of the profile: forehead, nose, and jaw (Fig. 2-1). Ears are well visualized in parasagittal scans tangential to the calvarium. In late gestation, significant details of the anatomy of the external ear can be seen. The helix, scaphoid fossa, triangular fossa, concha, antihelix, tragus, antitragus, intertragic incisure, and lobule can be identified (Fig. 2-2).

AXIAL PLANES

An axial scan slightly caudal to the one commonly used for the determination of the biparietal diameter easily reveals both orbits. This view (Fig. 2-3) can be used for determination of the ocular biometry.^{2,3} Nomograms for binocular distance, interocular distance, and ocular diameter (Fig. 2-4, Table 2-1) are available. One type of nomogram is utilized for the evaluation of ocular biometry when the gestational age is known (Figs. 2-5, 2-6, 2-7). If the gestational age is uncertain, nomograms constructed with the biparietal diameter as the independent variable can be utilized (Figs. 2-8, 2-9, 2-10). By moving the transducer caudally, the anterior palate can be visualized, and a slight angulation will allow visualization of the tongue within the oral cavity (Fig. 2-11).

CORONAL PLANES

The coronal planes are the most important ones in the evaluation of the integrity of facial anatomy. Figure 2-12 illustrates a sequence of scans tangential to the

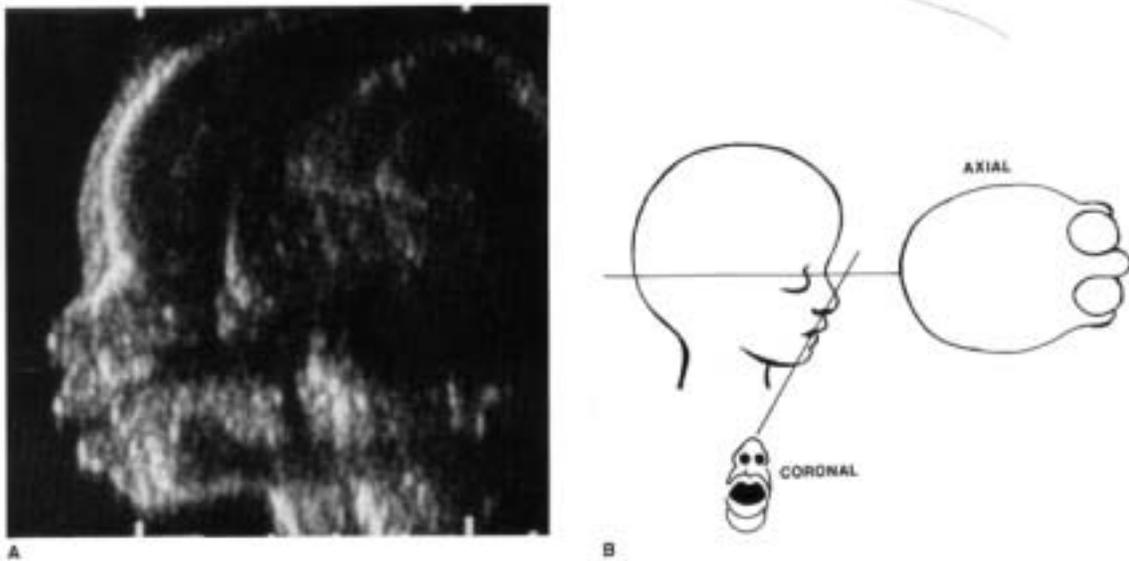


Figure 2-1. A. Fetal profile at 25 weeks. B. Schematic representation of the scanning planes to be used for obtaining axial and coronal views of the fetal face. (Figure A reproduces with permission from Pilu et al: *Am J Obstet Gynecol* 155:45, 1986.)

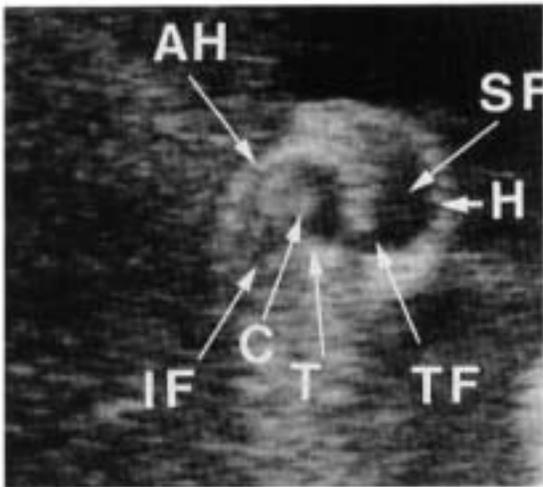


Figure 2-2. The helix (H), scaphoid fossa (SF), triangular fossa (TF), concha (C), antihelix (AH), tragus (T), and intertragic incisure (IF) can be seen in this view of the fetal ear.

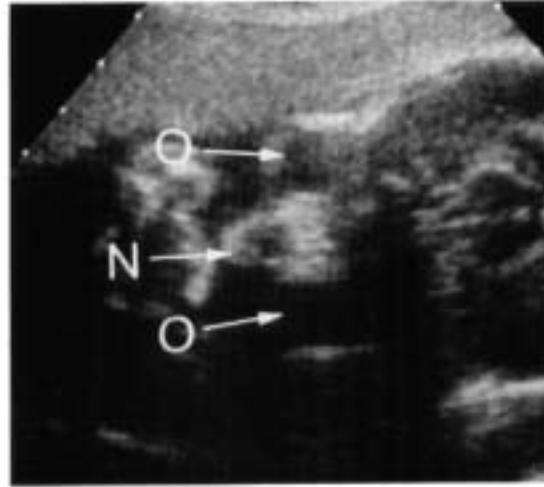


Figure 2-3. Axial scan passing through the orbits (O) of a normal third trimester fetus. N, nasal process. (Reproduced with permission from Pilu et al.: *Am J Obstet Gynecol* 155:45, 1986.)

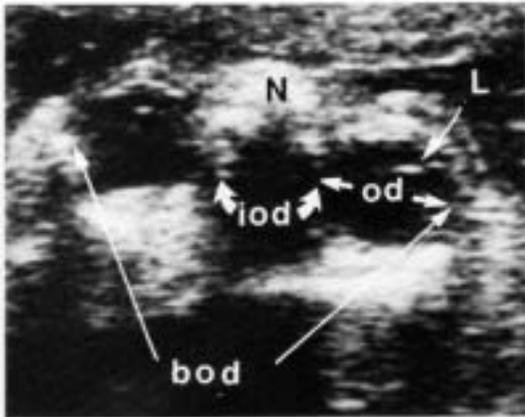


Figure 2-4. The ocular diameter (od), interocular distance (iod), and binocular distance (bod) are demonstrated in this scan. The lens (L) is visible in the eye. N, nasal process.

forehead. Orbits, eyelids, nose, and lips are well visualized. The tip of the nose, the alae nasi, and the columna are seen above the upper lip. The nostrils typically appear as two little anechoic areas (Fig. 2-13). In this scanning plane, it is possible to evaluate movements of the mouth, including protrusion of the tongue, "chewing" movements, and wide opening of the mouth (Fig. 2-14). By tilting the transducer, it is sometimes possible to visualize the intranasal portion of the upper airways (Fig. 2-15).

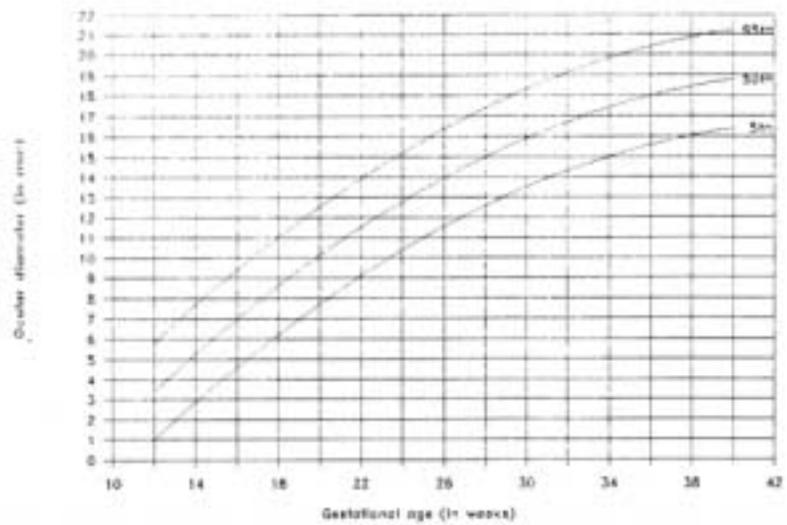
The lens, iris, pupil, cornea, and extraocular structures such as muscles, retro-orbital fat, and optic nerve may be visualized. Movements of both eyes are not synchronous and conjugated, limiting the possibility of the prenatal diagnosis of strabismus.^{1a}

This chapter focuses on the anomalies more frequently found during the course of prenatal diagnosis. It is divided into anomalies of the orbits, nose, lip, palate and mandible. Besides these dysmorphic

TABLE 2-1. GROWTH OF THE OCULAR PARAMETERS

Age (weeks)	Binocular Distance (mm)			Interocular Distance (mm)			Ocular Diameter (mm)		
	5th	50th	95th	5th	50th	95th	5th	50th	95th
11	5	13	20	—	—	—	—	—	—
12	8	15	23	4	9	13	1	3	6
13	10	18	25	5	9	14	2	4	7
14	13	20	28	5	10	14	3	5	8
15	15	22	30	6	10	14	4	6	9
16	17	25	32	6	10	15	5	7	9
17	19	27	34	6	11	15	5	8	10
18	22	29	37	7	11	16	6	9	11
19	24	31	39	7	12	16	7	9	12
20	26	33	41	8	12	17	8	10	13
21	28	35	43	8	13	17	8	11	13
22	30	37	44	9	13	18	9	12	14
23	31	39	46	9	14	18	10	12	15
24	33	41	48	10	14	19	10	13	15
25	35	42	50	10	15	19	11	13	16
26	36	44	51	11	15	20	12	14	16
27	38	45	53	11	16	20	12	14	17
28	39	47	54	12	16	21	13	15	17
29	41	48	56	12	17	21	13	15	18
30	42	50	57	13	17	22	14	16	18
31	43	51	58	13	18	22	14	16	19
32	45	52	60	14	18	23	14	17	19
33	46	53	61	14	19	23	15	17	19
34	47	54	62	15	19	24	15	17	20
35	48	55	63	15	20	24	15	18	20
36	49	56	64	16	20	25	16	18	20
37	50	57	65	16	21	25	16	18	21
38	50	58	65	17	21	26	16	18	21
39	51	59	66	17	22	26	16	19	21
40	52	59	67	18	22	26	16	19	21

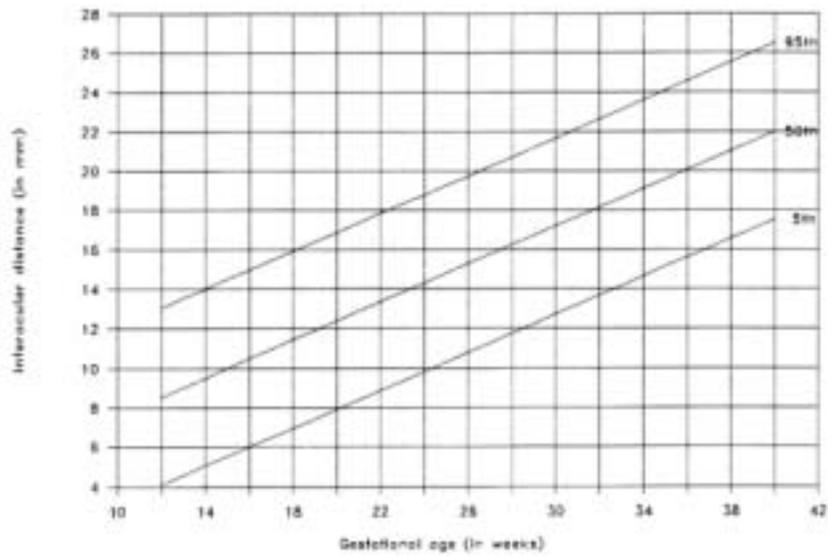
Figure 2-5. Ocular diameter versus gestational age. This nomogram and the one displayed in Figure 2-8 are utilized for the diagnosis of microphthalmia.



anomalies, ultrasound examination of the face can identify less common and more benign anomalies such as lacrimal duct cysts and hemangiomas.^{1b} Congenital obstruction of the nasolacrimal duct results in cystic dilatation of the proximal part of the duct (dacryocystocele). It has been identified prenatally as a hypoechogenic mass inferior to the globe. The differential diagnosis includes an anterior cephalocele, hemangiomas, and dermoid cyst. Hemangiomas generally have a solid appearance or multiple septae. Dermoid cysts usually have a superolateral location. Anterior cephaloceles may be difficult to differentiate

from these lesions. The presence of hydrocephaly should raise the index of suspicion for a cephalocele. Dacryocystoceles resolve spontaneously in 78 percent of cases by 3 months and in 91 percent of cases by 6 months. Hemangiomas of the fetal face have been recognized prenatally. They appear as exophytic lesions with echogenicity similar to the placenta. Pulsation may be identified. The differential diagnosis includes cephaloceles and teratomas of the face. The cavernous variety of hemangiomas generally disappears spontaneously. A giant hemangioma may be associated with thrombocytopenia (Kasabach-Merritt

Figure 2-6. Interocular distance versus gestational age.



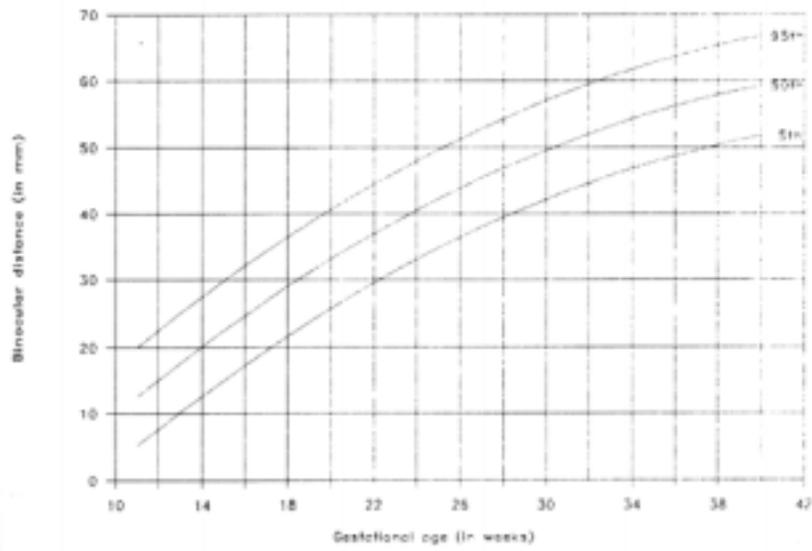


Figure 2-7. Binocular distance versus gestational age.

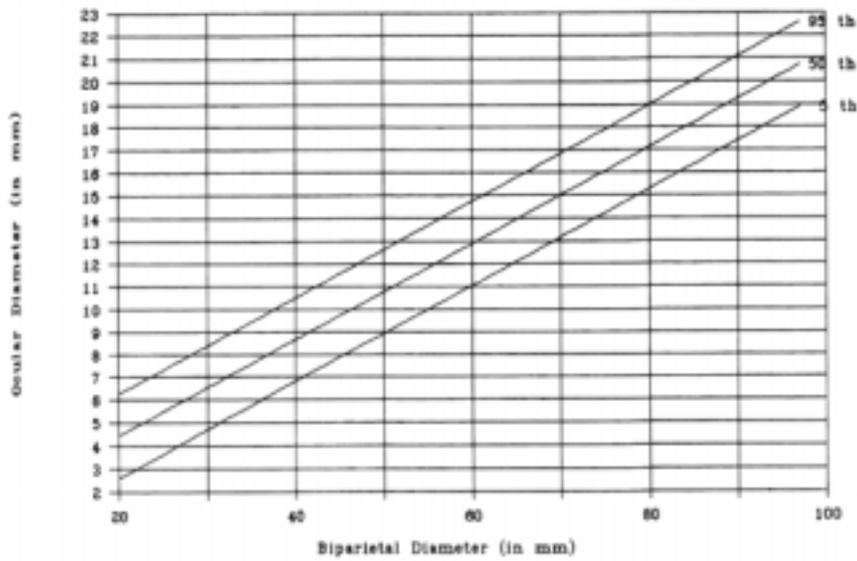


Figure 2-8. Ocular diameter versus biparietal diameter.

Figure 2-9. Interocular distance versus biparietal diameter

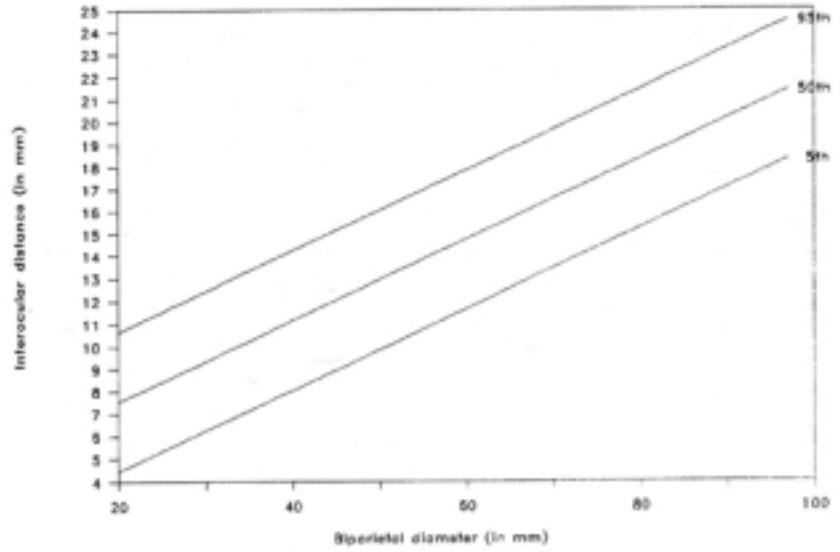
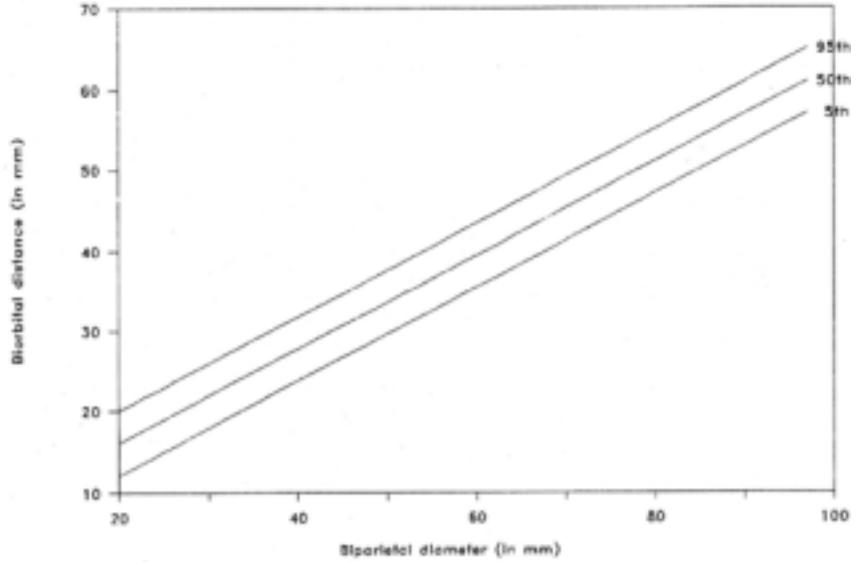


Figure 2-10. Binocular distance versus biparietal diameter



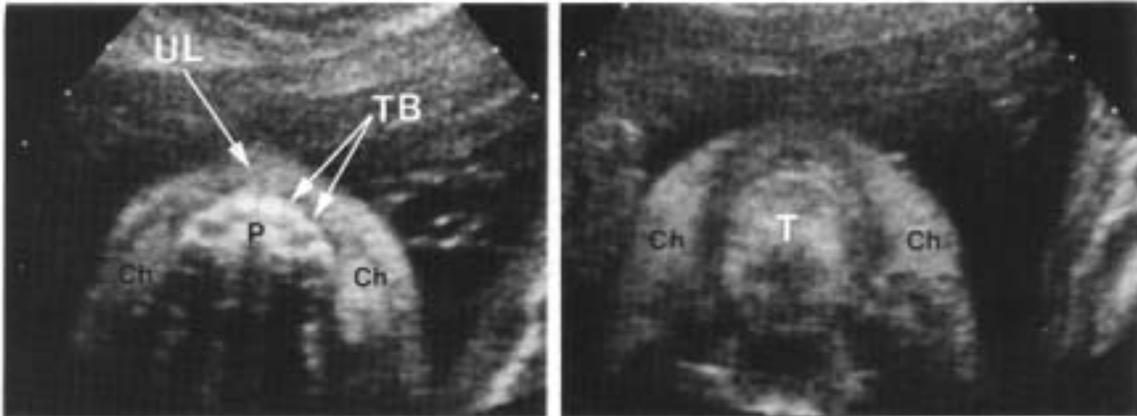


Figure 2-11. Axial scan of the lower fetal face demonstrating the upper lip (UL) and the anterior palate (P). The teethbuds (TB) and cheeks (Ch) can be seen. At a slightly lower level, the tongue (T) is seen filling the oral cavity. (Reproduced with permission from Pilu et al: *Am J Obstet Gynecol* 155.-45, 1986.)

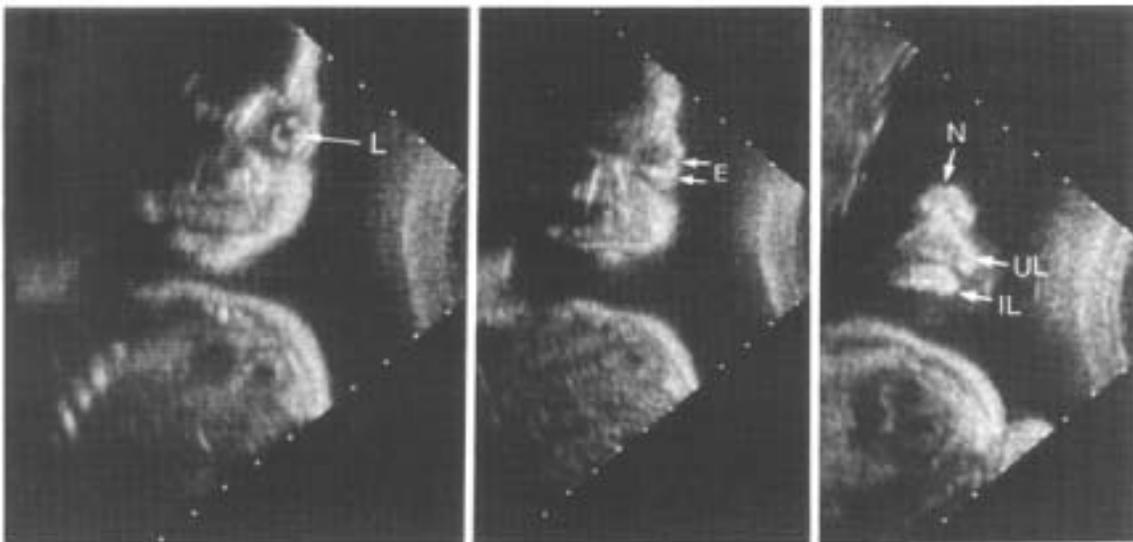


Figure 2-12. Cross sectional sweep from posterior to anterior, demonstrating the lens (L) inside the corpus vitreum, the eyelids (E), the upper and inferior lip (UL and IL), and the nose (N). (Reproduced with permission from Pilu et al.: *Am J Obstet Gynecol* 155.-45, 1986.)

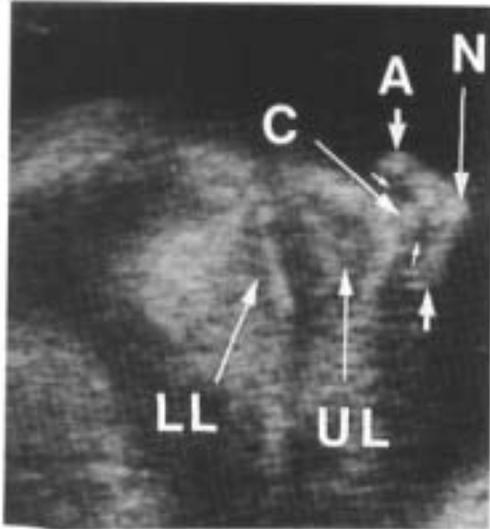


Figure 2-13. The tip (N) of the nose, the alae nasi (A), and the columna (C) are seen above the upper lip (UL). The nostril typically appears as two little anechoic areas (*tiny arrows*). LL, lower lip.

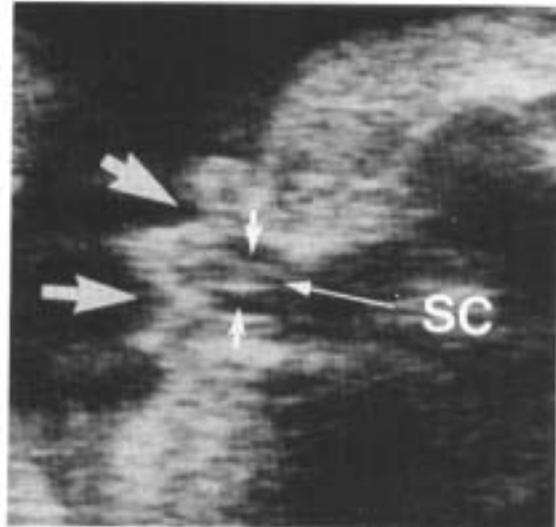
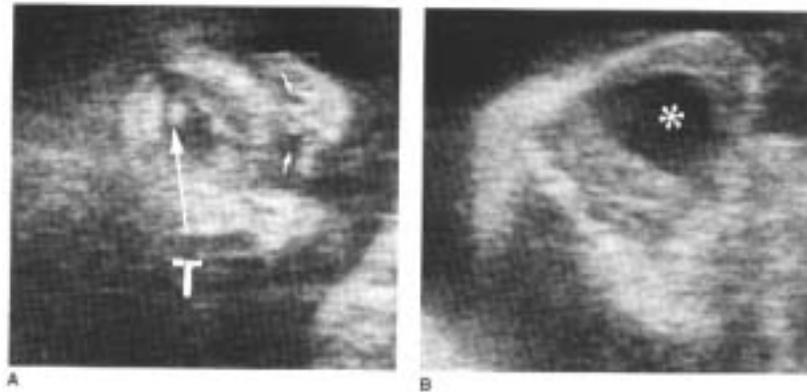


Figure 2-15. Transverse sections reveal the intranasal portion of the upper airways (*small arrows*) between the concha and the septal cartilage (SC). Large arrows, nostrils.

Figure 2-14. **A.** Coronal scan permits the visualization of the tongue (T) protruding. *Small arrows*, nostrils. **B.** Wide opening of the mouth (*) in the same fetus.



syndrome). Complications of hemangiomas include ulceration, bleeding, infection and scar formation.^{3a}

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ANOMALIES OF THE ORBITS

Hypertelorism

Synonym

Euryopia.

Definition

Hypertelorism is an increased interocular distance.

Incidence

Rare.

Embryology and Pathogenesis

In early developmental stages of the human embryo, the eyes are placed laterally in the primitive face in a fashion similar to that of lower animals with panoramic vision. As gestation progresses, they migrate toward the midline, creating favorable conditions for the development of stereoscopic vision (Fig. 2-16). Three different mechanisms have been postulated to be responsible for hypertelorism²³: (1) primary arrest in the forward migration of the eyes, (2) secondary arrest due to the presence of a midline tumor, such as a frontal meningoencephalocele, or (3) abnormal growth vectors of the skull bones manifested through an enlargement of the lesser wings of the sphenoid.⁴² Another hypothesis is that hypertelorism is due to abnormal growth of the splanchnocranium associated with maldevelopment of the bones derived from the first branchial arches.⁴¹

Pathology

Three parameters have been used to quantitate ocular spacing in infants and adults: interpupillary distance,^{30,55,58,61,88} canthal distance, and interorbital dis-

tance. Canthal measurements include the distance between the two medial canthi (intercanthal) and the distance between the two external canthi (outer canthal). These measurements are obtained from frontal view photographs.^{12,30,45,55,61,69,93,94} Another commonly used parameter is the canthal index, which is the ratio between the inner and outer

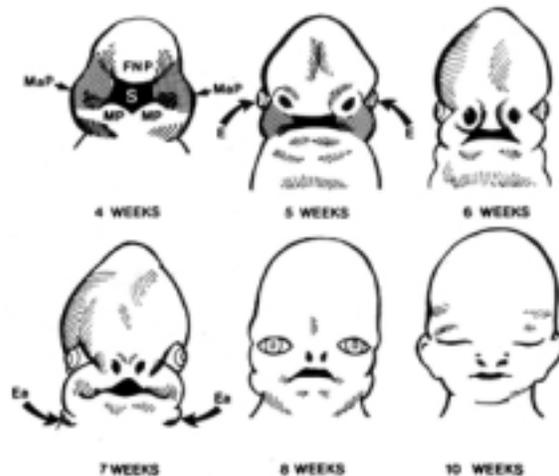


Figure 2-16. Schematic representation of the development of the facial structures from the 4th to the 10th week of gestation. In the earliest stages, the primitive eyes (E) are positioned on both sides of the cephalic pole. As gestation progresses, they migrate toward the midline. FNP, frontonasal prominence; MaP, maxillary prominence; MP, mandibular prominence; Ea, ears; S, stomodeum.

TABLE 2-2. MALFORMATIONS AND SYNDROMES ASSOCIATED WITH HYPERTELORISM

Hypertelorism with other median plane facial malformations	Rieger syndrome of iris dysplasia, hypodontia, and questionable myotonic dystrophy ^{19,62}
Median cleft face syndrome: V-shaped frontal hairline (widow's peak), cranium bifidum occiput, median cleft nose (bifid nose, Doggenase), median cleft lip and palate ^{14,20,84,95}	With heterotopia of the macula and pseudoexotropia
Frontal, ethmoidal, or sphenoidal meningoencephalocele	Fraser syndrome of cryptophthalmia, ear and genital malformations
Frontal, ethmoidal, or sphenoidal dermoid-lipoma-teratoma	Iris dysplasia and mental retardation ¹⁹
Nasal glioma	Stickler syndrome of arthroophthalmopathy: myopia, retinal detachment, micrognathia, cleft palate, and marfanoid habitus, with hyperextensible joints ⁶¹
Nasofrontal mucoceles, segmental vitiligo, and porencephaly ¹⁰⁶	Wildervanck I-Waardenburg-Franceschetti-Klein syndrome, cervicocoloacoustic syndrome of congenital deafness, abducens paralysis, frequently other face and tooth deformities and heterochromia of the irises ⁶⁴
Hypertelorism with miscellaneous facial defects	Wildervanck II syndrome of microphthalmia and blepharophimosis with facial dysmorphism, dysostosis zygomatica-maxillomandibulofaciatis ⁶⁴
Proboscis lateralis ²⁰	Mohr syndrome of conduction deafness, short stature, and multiple minor facial and skeletal malformations; autosomal recessive; patients probably have only dystopia canthorum and not true hypertelorism
Facial clefts other than median ²⁰	Freeman-Sheldon whistling face syndrome of short stature, whistling, pursed appearance of lips, blepharophimosis, ptosis, strabismus, subcutaneous ridge across lower forehead, and scoliosis ⁶⁶
Facial hemangioma ⁶⁰	Familial telecanthus-hypospadias-multiple minor malformations syndrome—see under hypertelorism with sex organ malformations
Extra nares ²⁸	Nyctalopia and tremor ⁶³
Hypertelorism with other prominent skull dysplasias	Miscellaneous ocular defects ⁹
Craniosynostosis with or without syndactyly ⁶³	Corneal ulceration, pseudoexophthalmos, bifid tongue, and extremity and digital malformations ⁶⁸
Apert ¹⁴	Microphthalmus, iris dysplasia, corneal opacity, severe retardation, and spastic cerebral tetraplegia ⁶⁶
Crouzon syndrome	Hypertelorism with cleft lip/palate
Pfeiffer syndrome	Ordinary cleft lip and palate ^{3,32,74}
Carpenter syndrome	Robert syndrome of cleft lip and palate with tetraphocomelia and genital enlargement ^{29,47}
Kleeblattschaedel	Cleft lip, iridochoroidal coloboma, and deafness ⁹⁰
Thickened skull	Juberg-Hayward syndrome of oral-cranial-digital anomalies ⁶⁶
Albers-Schonberg disease	Orofaciodigital syndrome I and II ²⁹
Cranioetaphyseal dysplasia of Pyle	Meckel-Gruber syndrome ²²
Metopism ¹⁰⁵	Median cleft face syndrome ^{14,20,95}
Hypertelorism with teeth defects²⁸	Cleft lip/palate, tetrasperomelia, deformed pinna, scarcity of hair, and hypoplastic nipples ²⁹
Rieger syndrome with teeth hypoplasia ⁶²	Oral duplication (two hard palates and dental arches) ²⁹
Hypertelorism with prominent neurologic and brain defects	Hypertelorism, microtia, and facial clefting (HMC syndrome) ⁹
Hydrocephalus, any prenatal type including myelomeningocele (Chiari malformation, Arnold-Chiari malformation)	Cleft lip with otitis gyrata and acanthosis nigricans ⁷
Megalencephaly with generalized skull enlargement ²⁷	Hypertelorism with prominent skin manifestations and frequent mental retardation
Anatomic megalencephaly: simple autosomal dominant ²⁷	Riley-Day syndrome ⁴⁷ ; true hypertelorism doubtful
Metabolic megalencephaly, particularly mucopolysaccharidosis	Albinism syndrome ⁶⁴
Familial neurovisceral lipidosis syndrome	Segmental vitiligo, porencephaly, and nasofrontal mucoceles ¹⁰⁶
Lissencephaly ⁶⁰	Leopard syndrome of multiple lentiginos, pulmonary stenosis, and cardiac conduction defects with dysrhythmia ⁶⁸
Agenesis of the septum pellucidum ⁶²	Basal cell nevus syndrome ⁴⁷
Agenesis of the corpus callosum ⁶⁴	Hypohidrotic ectodermal dysplasia syndrome
With microcephaly and mild extremity malformation ^{47,75}	Sjogren-Larsen syndrome
Arhinencephaly; hypertelorism with arhinencephaly very rare; hypotelorism very common ^{22,24}	G-syndrome of dyschondroplasia, cutis laxa, trigonocephaly (?), polysyndactyly, and kewpie doll facies ⁶⁰
Possibly patients with Meckel-Gruber dysencephalia splanchnocystica syndrome ²²	
Peripheral neuritis, ulnar ¹⁰⁴	
G syndrome of dysphagia-dysphonia, ear anomalies, and hypospadias ⁶⁰	
Essential tremor and nyctalopia ⁶⁴	
Bilateral deafness-microtia 5 (Mengel-Konigsmark-Berlin-McKusick syndrome) ⁶⁴	
Pinsky-DiGeorge-Harley-Baird oculocerebral syndrome of microphthalmus, iris dysplasia, severe retardation, and spastic tetraplegia ⁶⁸	
Cerebrohepatorenal syndrome of high forehead, hepatomegaly, hypotonia, mild skeletal malformation; patients may have only canthal rather than orbital hypertelorism ⁴⁷	
Cerebral gigantism ^{96,108}	
Familial mild mental retardation ²⁹	
Hypertelorism with other prominent ocular defects	
Waardenburg syndrome of dystopia canthorum, white forelock, and deafness ¹⁰⁷	

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<p>Hypertelorism with miscellaneous facial defects</p> <p>Proboscis lateralis²⁰</p> <p>Facial clefts other than median²⁰</p> <p>Facial hemangioma⁶⁰</p> <p>Extra nares²⁸</p>	
<p>Hypertelorism with other prominent skull dysplasias</p> <p>Craniosynostosis with or without syndactyly⁶³</p> <p>Apert¹⁴</p> <p>Crouzon syndrome</p> <p>Pfeiffer syndrome</p> <p>Carpenter syndrome</p> <p>Kleeblattschädel</p> <p>Thickened skull</p> <p>Albers-Schonberg disease</p> <p>Cranio-metaphyseal dysplasia of Pyle</p> <p>Metopism¹⁰⁵</p>	
<p>Hypertelorism with teeth defects²⁸</p> <p>Rieger syndrome with teeth hypoplasia⁶²</p>	
<p>Hypertelorism with prominent neurologic and brain defects</p> <p>Hydrocephalus, any prenatal type including myelomeningocele (Chiari malformation, Arnold-Chiari malformation)</p> <p>Megalencephaly with generalized skull enlargement²⁷</p> <p>Anatomic megalencephaly: simple autosomal dominant²⁷</p> <p>Metabolic megalencephaly, particularly mucopolysaccharidosis</p> <p>Familial neurovisceral lipidosis syndrome</p> <p>Lissencephaly⁶⁰</p> <p>Agenesis of the septum pellucidum⁶²</p> <p>Agenesis of the corpus callosum²⁴</p> <p>With microcephaly and mild extremity malformation^{47,75}</p> <p>Arhinencephaly; hypertelorism with arhinencephaly very rare; hypotelorism very common^{22,24}</p> <p>Possibly patients with Meckel-Gruber dysencephalia splanchnocystica syndrome²²</p> <p>Peripheral neuritis, ulnar¹⁰⁴</p> <p>G syndrome of dysphagia-dysphonia, ear anomalies, and hypospadias⁶⁰</p> <p>Essential tremor and nyctalopia⁶⁴</p> <p>Bilateral deafness-microtia S (Mengel-Konigsmark-Berlin-McKusick syndrome)⁶⁴</p> <p>Pinsky-DiGeorge-Harley-Baird oculocerebral syndrome of microphthalmus, iris dysplasia, severe retardation, and spastic tetraplegia⁶⁶</p> <p>Cerebrohepatorenal syndrome of high forehead, hepatomegaly, hypotonia, mild skeletal malformation; patients may have only canthal rather than orbital hypertelorism⁴⁷</p> <p>Cerebral gigantism^{66,108}</p> <p>Familial mild mental retardation²⁹</p>	
<p>Hypertelorism with other prominent ocular defects</p> <p>Waardenburg syndrome of dystopia canthorum, white forelock, and deafness¹⁰⁷</p>	
	<p>Hypertelorism with cleft lip/palate</p> <p>Ordinary cleft lip and palate^{3,32,74}</p> <p>Robert syndrome of cleft lip and palate with tetraphocomelia and genital enlargement^{28,47}</p> <p>Cleft lip, iridochoroidal coloboma, and deafness⁹⁰</p> <p>Juberg-Hayward syndrome of oral-cranial-digital anomalies⁶⁴</p> <p>Orofaciodigital syndrome I and II²⁹</p> <p>Meckel-Gruber syndrome²²</p> <p>Median cleft face syndrome^{14,20,95}</p> <p>Cleft lip/palate, tetrapheromelia, deformed pinna, scarcity of hair, and hypoplastic nipples²⁹</p> <p>Oral duplication (two hard palates and dental arches)²⁹</p> <p>Hypertelorism, microtia, and facial clefting (HMC syndrome)⁹</p> <p>Cleft lip with cutis gyrata and acanthosis nigricans⁷</p> <p>Hypertelorism with prominent skin manifestations and frequent mental retardation</p> <p>Riley-Day syndrome⁴⁷; true hypertelorism doubtful</p> <p>Albinism syndrome⁶⁴</p> <p>Segmental vitiligo, porencephaly, and nasofrontal mucoceles¹⁰⁶</p> <p>Leopard syndrome of multiple lentigines, pulmonary stenosis, and cardiac conduction defects with dysrhythmia²⁸</p> <p>Basal cell nevus syndrome⁴⁷</p> <p>Hypohidrotic ectodermal dysplasia syndrome</p> <p>Sjogren-Larsen syndrome</p> <p>G-syndrome of dyschondroplasia, cutis laxa, trigonocephaly (?), polysyndactyly, and kewpie doll facies⁶⁰</p>

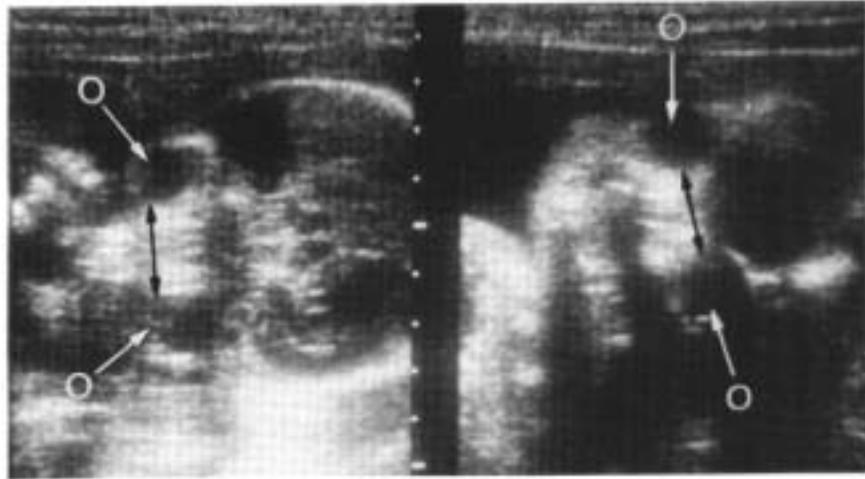


Fig. 2-17. Axial and coronal scans passing through the orbits (O) of a 26-week fetus with hypertelorism. The inter-orbital distance (black arrows) is increased.

canthal distance.⁸⁴ Interorbital distance is measured on posteroanterior radiograms.^{12,16,37,46,74,97}

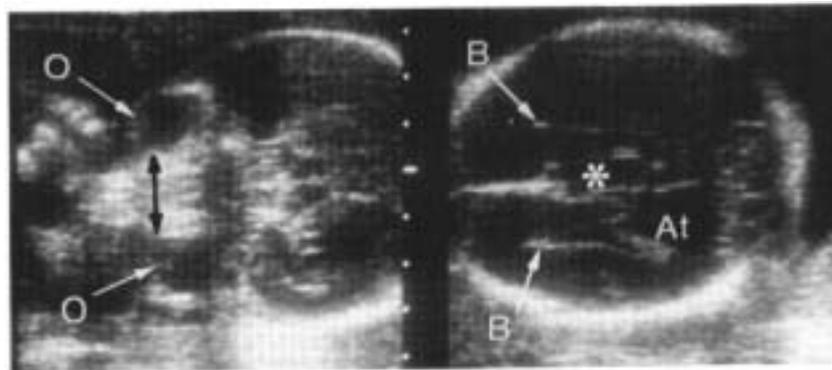
Analysis of the literature is somewhat confusing, and many authors have used intercanthal distance to define hypertelorism. However, there are anomalies of the soft tissues of the face that can lead to changes in intercanthal distances without affecting interorbital distance (epicanthal folds, dystopia canthorum, cryptophthalmus). It is now well established that the definition of hypertelorism is based on radiographic interorbital measurements.²³

In the overwhelming number of cases, hypertelorism is bilateral, although some unilateral cases have been reported in such conditions as plagiocephaly and proboscis lateralis.^{23,26}

Hypertelorism can be either an isolated finding or associated with other clinical syndromes or malformations. Table 2-2 is an exhaustive classification, provided by DeMyer, of hypertelorism according to associated abnormalities.²³

A few entities deserve to be considered in more detail. The most common syndromes with hypertelorism are the median cleft syndrome and craniosynostoses. The median cleft face syndrome, or frontonasal dysplasia, is characterized in its most severe expression by hypertelorism, median cleft lip with or without a median cleft of the hard palate and nose, and cranium bifidum occultum. At the other end of the spectrum is the infant with only mild hypertelorism and broad nasal root.^{14,20,23} Agenesis of the corpus callosum has been described in these infants.^{20,34} The median cleft face syndrome is usually a sporadic disease, although a few familial cases consistent with an autosomal dominant form of inheritance have been reported.¹⁴ Among the craniosynostoses, hypertelorism can be consistently found in Apert, Crouzon, and Carpenter syndromes. For a more detailed discussion of the subject the reader is referred to the section on craniosynostoses, page 369.

Figure 2-18. In the same fetus as in Figure 2-17, an axial scan passing through the lateral ventricles demonstrates the typical enlargement of the atria (At), widely separated bodies (B), and upward displacement of the third ventricle (*) pathognomonic of agenesis of the corpus callosum. O, orbits.



Diagnosis

Nomograms indicating the normal values of the ultrasound measurements of the interorbital distance in the fetus are now available.^{54,68} By using these nomograms, the prenatal diagnosis of hypertelorism in a case of median cleft face syndrome has been reported.¹¹ We have been able to identify hypertelorism in one fetus with agenesis of the corpus callosum, Dandy-Walker malformation, double outlet right ventricle, bilateral clubfeet, and normal chromosomes (Figs. 2-17, 2-18). However, the accuracy of sonography in the diagnosis of hypertelorism has not been established in a large series of cases.

Prognosis and Obstetrical Management

Hypertelorism per se results only in cosmetic problems and possible impairment of stereoscopic binocular vision. For severe cases, a number of operative procedures, such as canthoplasty, orbitoplasty, surgical positioning of the eyebrows, and rhinoplasty, have been proposed. It should be stressed that "hypertelorism by itself has little or no status as an entity, does not serve to identify a unitary group of syndromes, and by itself it does not constitute a diagnosis."²³ Therefore, a careful survey for associated anatomic anomalies and a karyotype is mandatory. The obstetrical management depends on the precise diagnosis. Hypertelorism per se does not require a change in standard obstetrical care. The median cleft face syndrome is usually associated with normal intelligence and life span. However, there is a high likelihood of mental retardation when either extracephalic anomalies or an extreme degree of hypertelorism is found.²³ The severity of the cosmetic disturbance should not be underestimated, because this syndrome may be associated with extremely grotesque features.

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Hypotelorism

Synonym

Stenopia.

Definition

Hypotelorism is a decreased interorbital distance.

Incidence

Very rare.

Etiology

With exceedingly rare exceptions,^{1,7} hypotelorism has always been found in association with other severe anomalies (Table 2-3). The main association is with the holoprosencephalic malformation sequence.

Embryology and Pathogenesis

The craniofacial skeleton originates from a mesenchymal mass that has a dual origin: the mesoderm and the neural crest that migrate into the region. There is a close correlation between the development of the midline facial structures (forehead, nose, interorbital structures, and upper lip) and the differentiation process of the forebrain. Both events are probably induced by the prechordal mesenchyma, the tissue interposed between the prosencephalon and the roof of the primitive mouth (stomodeum). Therefore, midline defects of the face, such as hypotelorism, are frequently associated with cerebral anomalies, mainly holoprosencephaly.^{6,8,9}

Although there is some controversy about the precise nature of the process,^{6,8} an interference with the activity of the prechordal mesenchyma would lead to defects in both areas, brain and face. The facial anomalies encompass a broad range of defects that are due to aplasia or varying degrees of hypoplasia of the median facial structures. Underdevelopment of the skeleton of the face would result in medial dis-

placement of the orbits. The cerebral anomalies are mainly due to varying degrees of failure of cleavage of the prosencephalon, with incomplete division of the cerebral hemispheres and underlying structures (see pp. 59-65).

Hypotelorism can also be found in association with trigonocephaly,⁸ microcephaly,⁸ Meckel syndrome,⁵ and chromosomal aberrations.^{2,10,12,16} It is unclear from some of the reports of hypotelorism whether it occurred as an isolated finding or as a part of a holoprosencephalic malformation sequence.

Pathology and Associated Anomalies

The interorbital distance is reduced, and severe associated anomalies are almost always present.⁷ Other facial anomalies can occur as a part of the holoprosencephalic sequence. The classification suggested by DeMyer⁹ is shown in Table 1-17.

Diagnosis

The diagnosis is based on demonstration of a reduced interocular distance (Table 2-1, Figs. 2-6, 2-9, 2-19). The prenatal diagnosis of hypotelorism, always in association with holoprosencephaly, has been reported in the literature several times.^{3,4,13,14,15}

Prognosis and Obstetrical Management

Prognosis and management depend entirely on the associated malformations. A careful survey of the fetal anatomy and karyotyping must be performed.

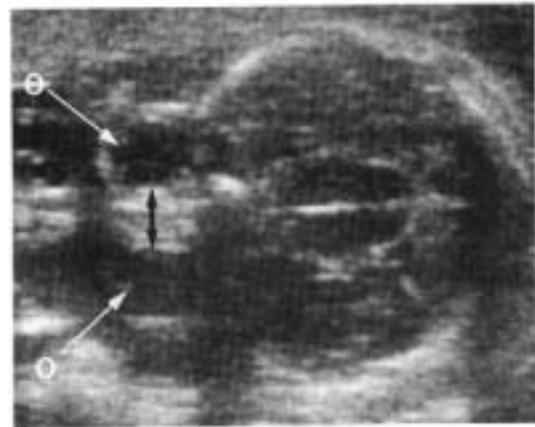


Figure 2-19. Axial scan passing through the orbits (O) in a 22-week fetus with alobar holoprosencephaly. The interorbital distance (black arrows) is obviously decreased. (Reproduced with permission from Pilu et al.: *Am J Obstet Gynecol* 155:45, 1986.)

TABLE 2-3. ANOMALIES ASSOCIATED WITH HYPOTELORISM

Holoprosencephaly ^{5, 6, 8, 9}
Trigonocephaly ⁸
Oculodentodigital dysplasia ¹¹
Microcephaly ⁸
Meckel syndrome ⁵
Maternal phenylketonuria ¹⁶
Chromosomal aberrations
Trisomy 13 ¹⁶
Trisomy 21 ¹⁰
18 p ⁻¹⁶
5p ⁻²
14 q ⁺¹²

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Microphthalmia

Definition

Decreased size of the eyeball. The term "anophthalmia" refers to absence of the eye. However, it should be reserved for the pathologist, who must demonstrate not only absence of the eye but also of optic nerves, chiasma, and tracts.

Incidence

The incidence is difficult to define. Microphthalmia/anophthalmia is responsible for 4 percent of cases of congenital inheritable blindness.⁵

Etiology/Pathology

Microphthalmia is generally associated with other anomalies. On rare occasions it occurs in the absence of other ocular and systemic malformations and the term "nanophthalmous" is used. Microphthalmia can occur as a sporadic disorder or as a condition inherited with an autosomal dominant, recessive, or X-linked pattern.⁴ Microphthalmia can be unilateral or bilateral. The term "cryptophthalmia" refers to a condition in which there is fusion of the eyelids, and it is frequently associated with microphthalmia.

Diagnosis

The diagnosis can be suspected by demonstrating an orbital diameter below the 5th percentile for gestational age (Table 2-1, Fig. 2-5). It should be stressed that this is a statistical definition of microphthalmia. Some normal infants will fall within this range. A careful examination of the intraorbital anatomy is indicated to identify lens, pupil, and optic nerve.¹ The diagnosis of this condition has been reported twice. One fetus had Fraser syndrome, and the other hemifacial microsomia (Goldenhar-Gorlin syndrome). In the former case, the diagnosis was made in a patient at risk for this autosomal recessive condition.² In the latter case, the diagnosis was possible by detecting unilateral microphthalmia and a deformed ipsilateral ear.³ Table 2-4 illustrates conditions associated with microphthalmia that can be diagnosed in utero. Once the diagnosis is suspected, a search for associated anomalies is indicated. The sonographer should concentrate on the identification of microtia, micrognathia, syndactyly, camptodactyly, median cleft, feet abnormalities (rockerbottom and talipes), hemivertebrae, and congenital heart defects. Karyotyping is indicated, because several

ANOMALIES OF THE NOSE

Arhinia

Definition

Absence of the nose.

Incidence

Unknown. It is an extremely rare condition.

Etiology and Associated Anomalies

Unknown in most cases. It may occur as an isolated malformation or be part of a malformation complex, such as holoprosencephaly² or mandibulofacial dysostosis (Treacher Collins syndrome).¹

Embryology

The nasal cavity originates from the nasal sacs which are paired invaginations of the ectoderm. The nasal sacs are originally separated from the oral cavity by the oronasal membrane, which subsequently undergoes reabsorption. At about 6 weeks of gestation, the primitive nasal and oral cavities communicate freely through an opening that is then progressively closed by the developing palate. At about 12 weeks gestation, when the lateral palatine processes fuse medially with the nasal septum, the oral and the two nasal cavities are formed and separated. The external nose derives from the lower portion of the frontonasal prominence, which merges on both sides with the maxillary processes (Fig. 2-16).

Failure of development of the frontonasal prominence results in complete or partial nasal aplasia. In the holoprosencephalic sequence, this defect is part of a complex spectrum of midfacial anomalies that are thought to arise from a primitive defect of the pre-

chordal mesenchyma, the tissue responsible for the induction of both facial and cerebral structures (see p. 60).

Pathology

In arhinia, a concavity extending from the forehead to the upper lip is usually seen in the position normally occupied by the nose. In unilateral aplasia, a small pit is often seen in the area of the nostril.

Diagnosis

The diagnosis can be easily made by using both axial and longitudinal scans of the fetal face.³ A careful survey for associated anomalies is mandatory. (see Fig. 2-25).

Prognosis and Obstetrical Management

These depend on the associated anomalies. Isolated arhinia is compatible with life and does not require alteration in obstetrical care.

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Proboscis

Definition

A proboscis is a trunklike appendage with either one or two internal openings, usually associated with absence of the nose.

Incidence

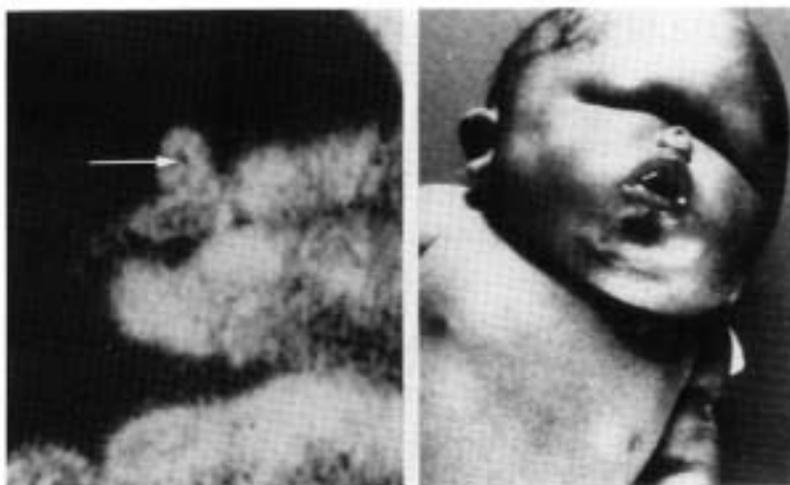
Unknown. Cyclopia and cebocephaly, two of the main conditions in which a proboscis is present, have

been reported to occur in 1:40,000 and 1:16,000 births, respectively.^{3,7}

Embryology

Normal development of the nose is discussed above. The presence of a proboscis is almost always found in association with holoprosencephaly. It has been suggested that in these cases, a primary disorder of the

Figure 2-20. Anterior coronal scan of the face of a fetus with cebocephaly. The presence of a proboscis is inferred by the tubular appearance of the nasal appendage and by the presence of a single median nostril (arrow). An image of the stillborn infant is provided for comparison. (Reproduced with permission from Pilu et al.: *Am J Obstet Gynecol* 155:45, 1986.)



prechordal mesenchyma results in an abnormal induction of the midfacial structures. Abnormal development of the nasal prominences may lead to a fusion of the olfactory placodes and formation of a proboscis. Derangement in the morphogenesis of the medial facial structures may lead to different positions of the proboscis with regard to the eye(s).²⁻⁴

Pathology and Associated Anomalies

The proboscis usually has a single central opening. According to the classification of holoprosencephalic facies suggested by DeMyer (Table 1-17), the proboscis may be inserted either above the orbit(s) (cyclopia, ethmocephaly) or in a normal position between the orbits (cebocephaly). The openings of the proboscis have no connection with the choanae. The ethmoid, the nasal conchae, and the nasal and lacrimal bones are absent. Typically, in cyclopia, ethmocephaly, and cebocephaly, there is no cleft of the lip and palate. The presence of a proboscis has rarely been reported in the absence of holoprosencephaly.⁸ In these cases, there is usually unilateral nasal aplasia, and the proboscis is found in the position normally occupied by the missing nasal structures. In rare cases, a bilateral proboscis has been found.⁸

Diagnosis

The diagnosis relies on the demonstration of a trunklike structure, usually with a single central opening either occupying the normal position of the nose⁶ or hanging above the orbits,^{1,5} (Fig. 2-20).

Prognosis and Obstetrical Management

Most cases will be associated with holoprosencephaly, which was discussed in the previous chapter (see pp. 59-64). A karyotype should be performed.

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ANOMALIES OF THE LIP AND PALATE

Facial Clefting

Synonyms

Cleft lip and cleft palate.

Definition

This term refers to a wide spectrum of lateral clefting defects usually involving the upper lip, the palate, or both. Median cleft lip and palate is a different entity and will be discussed separately (see p. 105).

Incidence

Facial clefting is the second most common congenital malformation, accounting for 13 percent of all anomalies.⁸ Its incidence in the United States has been estimated to be 1:700 live births.⁸ In 50 percent of patients, both lip and palate are defective, whereas either the lip or the palate alone is involved in 25 percent of patients each.²

Etiology

In the vast majority of patients, cleft lip (CL) and cleft palate (CP) have a multifactorial etiology, with both genetic and environmental factors accounting for the defect.⁷ The empiric risks of recurrence for these cases are reported in Table 2-5. CL with or without CP and isolated CP are two different anomalies. With exceedingly rare exceptions, recurrences are type specific. If the index case has CL-CP, there is no increased risk for isolated CP, and vice versa. In some cases, facial clefts are a part of well-established mendelian, chromosomal, and nongenetic syndromes. Gorlin et al.⁸ list 72 possible associations (Table 2-6).

CL-CP and isolated CP can occur as a component of a well-defined syndrome in 3 percent of the cases (syndromic) and in 97 percent of cases is non-syndromic. Of nonsyndromic defects, CL-CP represents 75 percent of all clefting malformations (25 percent isolated CL and 50 percent CL+CP), and isolated cleft palate represents 25 percent. CL-CP can occur as a result of a multifactorial defect or the combination of an autosomal dominant with incomplete expressivity and penetrance (25 percent) or a sporadic disorder (75 percent). The male:female ratio is 2:1, and the left side is involved twice as often as the right.

The genetic basis of isolated CP is less well established but is thought to be similar to CL-CP. The

female:male ratio is 2:1. If the parent affected is the mother, the recurrence risk is decreased, and if it is the father, the recurrence risk is increased.⁶ The opposite is true for CL-CP. The claimed risk associated with diazepam and steroidal agents intake has not been confirmed in carefully controlled studies. Chromosomal abnormalities are present in less than 1 percent of clefting abnormalities.¹³

Embryology

Shortly after the third week of gestation, outgrowths of mesenchyma result in the formation of ectodermal elevations that surround the primitive oral cavity or stomodeum. These structures (frontonasal prominence, maxillary prominence, and mandibular prominence) are separated by grooves (Fig. 2-16). Progressive growth of the prominences obliterates the grooves. Cleft lip results from the persistence of the grooves. Collapse of the mesenchymal tissue under the groove leads to the formation of the cleft (Fig. 2-21).¹²

The palate originates from the fusion of three palatine processes. The median originates from the medial nasal prominences, and the two lateral ones originate from the maxillary processes. The palatine processes fuse also with the nasal septum, which divides the nasal cavities (Fig. 2-22). Cleft palate is the consequence of lack of fusion of these structures.¹²

TABLE 2-5. INCIDENCE OF CLEFT LIP/PALATE AND ISOLATED CLEFT PALATE IN RELATIVES OF SIMILARLY AFFECTED PERSONS

Affected Parents	Affected Siblings	Affected Relatives	Percent Risk for Each Subsequent Child	
			Cleft Lip/Palate	Isolated Cleft Palate
None	None	None	0.1	0.04
None	1	None	4	2
None	1	1	4	7
None	2	None	9	1*
1	None	None	4	6
1	1	None	17	15

* The authors have no explanation for this puzzling observation. Adapted from Curtis et al.: *Am J Dis Child* 102:853, 1967.

TABLE 2-6. MALFORMATION AND SYNDROMES ASSOCIATED WITH FACIAL CLEFTING

Autosomal dominant cleft syndromes	
1. Cleft lip or palate or both and lip pits (Van der Woude syndrome)	8. Cleft palate, retinal detachment and myopia
2. Cleft lip or palate or both and ankyloblepharon filiforme adnatum	9. Cleft palate, retinal detachment and joint hypermobility
3. Cleft lip/palate, lobster claw deformity, dacrocystitis, and hypodontia (most sporadic cases)	10. Cleft lip or palate or both and multiple nevoid basal cell carcinoma
4. Cleft lip or palate or both and enlarged parietal foramina (uncertain)	11. Cleft palate and the Apert syndrome
5. Cleft lip or palate or both and congenital neuroblastoma	12. Cleft palate and the Marfan syndrome
6. Cleft lip or palate or both and popliteal pterygia	13. Cleft lip or palate or both and the Waardenburg syndrome
7. Cleft palate and hereditary arthrophthalmopathy	14. Cleft palate and mandibulofacial dysostosis
	15. Cleft palate and congenital spondyloepiphyseal dysplasia
	16. Cleft lip/palate, hypohidrosis, thin wiry hair and dystrophic nails
	17. Cleft palate, camptodactyly, and clubfoot
Autosomal recessive cleft syndromes	
1. Cleft lip/palate, tetrachomelia, and penile or clitoral enlargement	10. Cleft lip or palate or both and cryptophthalmia syndrome
2. Cleft lip/palate and pseudothalidomide syndrome	11. Cleft lip/palate, ocular hypertelorism, and microtia
3. Cleft palate and Klippel-Feil syndrome (genetic pattern uncertain)	12. Cleft lip/palate, microcephaly, and hypoplasia of radii and thumbs
4. Cleft palate and chondrodysplasia punctata	13. Cleft lip/palate, tetrapromelia, deformed pinna, and ectodermal dysplasia
5. Cleft palate and multiple congenital dislocations (Larsen syndrome)	14. Cleft palate, stapes fixation and oligodontia
6. Cleft palate and diastrophic dwarfism	15. Cleft palate and cerebrocosto mandibular syndrome
7. Cleft palate and the Smith-Lemli-Opitz syndrome	16. Cleft palate and orofaciocigital syndrome II
8. Cleft palate and the Meckel syndrome	17. Cleft palate and new chondrodysplasia
9. Cleft palate and the multiple pterygium syndrome	18. Cleft palate, median cleft lip, and unknown lethal chondrodysplasia
X-Linked cleft syndromes	
1. Olopalatodigital syndrome (probably XLR)	4. Cleft palate, micrognathia, talipes equinovarus, atrial septal defect, and persistence of left superior vena cava (XLR)
2. Orofaciodigital syndrome I (XLD, lethal in male)	
3. Cleft uvula, familial nephrons, deafness, congenital urinary tract, and digital anomalies (XLR, ?)	
Nongenetic cleft syndromes	
1. Robin syndrome (rare familial occurrence)	11. Cleft lip/palate and lateral proboscis
2. Cleft lip/palate and cleft larynx	12. Premaxillary agenesis (may also occur with trisomy 13 and 18p-)
3. Cleft lip/palate and laryngeal web	13. Cleft lip or palate or both and encephalomeningocele
4. Cleft lip or palate or both and thoracopagus twins	14. Cleft lip or palate or both and median cleft face syndrome
5. Facial clefts and amniotic band syndrome	15. Cleft palate and congenital oral teratoma
6. Cleft lip or palate or both and forearm bone aplasia	16. Cleft palate and buccopharyngeal membrane persistence
7. Cleft lip or palate or both and congenital heart disease	17. Cleft palate and oral duplication
8. Cleft lip or palate or both and anencephaly	18. Cleft palate and bilateral femoral dysplasia
9. Cleft palate and Brachmann-DeLange syndrome	
10. Cleft palate and glossopalatine ankylosis	
Gross chromosomal cleft syndromes	
1. 4p-	9. 18q-
2. 5p-	10. Trisomy 21
3. Trisomy C mosaicism	11. XXXXY syndrome
4. Trisomy 13	12. Various translocations
5. Dp-	13. Supernumerary G-sized fragment
6. 14q-	14. Monosomy G
7. Trisomy 18	15. Triploidy
8. 18p-	

XLR, X-linked recessive; XLD, X-linked dominant.
Adapted from Gorlin et al: *Birth Defects 7 (7): 3, 1971.*

Pathology

Facial clefts encompass a broad spectrum of severity, ranging from minimal defects, such as a bifid uvula, linear indentation of the lip, or submucous cleft of the soft palate, to large deep defects of the facial bones and soft tissues (Fig. 2-23). The typical CL will appear

as a linear defect extending from one side of the lip into the nostril. CP associated with CL may extend through the alveolar ridge and hard palate, reaching the floor of the nasal cavity or even the floor of the orbit. Isolated cleft palate may include defects of the hard palate, the soft palate, or both or the submuco-

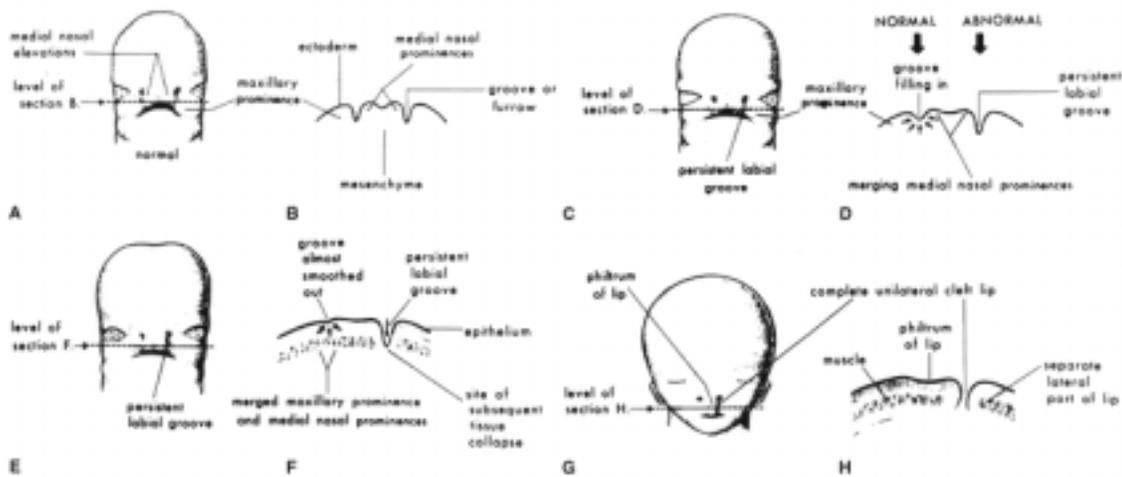


Figure 2-21. Drawings illustrating the embryologic basis of complete unilateral cleft lip. **A.** Five-week embryo. **B.** Horizontal section through the head, illustrating the grooves between the maxillary prominences and the medial nasal prominences. **C.** Six-week embryo, showing a persistent labial groove on the left side. **D.** Horizontal section through the head, showing the disappearance of the groove on the right side because of proliferation of the mesenchyma (arrows). **E.** Seven-week embryo. **F.** Horizontal section through the head, showing that the epithelium on the right has almost been pushed out of the groove between the maxillary prominence and medial nasal prominence. **G.** Ten-week fetus with a complete unilateral cleft lip. **H.** Horizontal section through the head following stretching of the epithelium and breakdown of the tissues in the floor of the persistent labial groove on the left side.¹² (Reproduced with permission from Moore: *The Developing Human: Clinically Oriented Embryology*, 2d ed. Philadelphia, Saunders, 1977.)

sal tissue. CL is bilateral in 20 percent of patients, whereas CL-CP is bilateral in 25 percent of cases.¹¹

Associated Anomalies

Associated anomalies are found in 50 percent of patients with isolated CP and in only 13 percent of those with CL-CP.⁹ An incidence of 60 percent has been found in embryos and fetuses with facial clefting.¹⁰ In the majority of patients, the associated anomalies do not conform to an established syndrome. In cases of either isolated CL or CP, the most frequent anomaly is clubfoot, whereas in cases of CL-CP, it is polydactyly.⁸ Of particular importance is the association with congenital heart disease.³ No specific pattern could be identified.¹⁸ Specific associations with well-described syndromes are shown in Table 2-6.

Diagnosis

The sonographic diagnosis of CL-CP in the fetus depends on demonstration of a groove extending from one of the nostrils inside the lip and possibly the alveolar ridge. Both axial and coronal planes can be used. In our experience, coronal scans have proved to be the most informative (Fig. 2-24). Several cases of prenatal diagnosis of CL-CP have been reported in the literature.^{1,4,5,14,15,17} However, it must be stressed that in all these cases, the facial lesions were quite

large. The accuracy of ultrasound in detecting small lesions has not been established. At present the ultrasound diagnosis of isolated CP appears difficult¹⁴ in cases at risk for mendelian syndromes associated with isolated CP, fetoscopy could be diagnostic.¹⁶ We have seen several cases of both CL and CP associated with polyhydramnios, and, therefore,

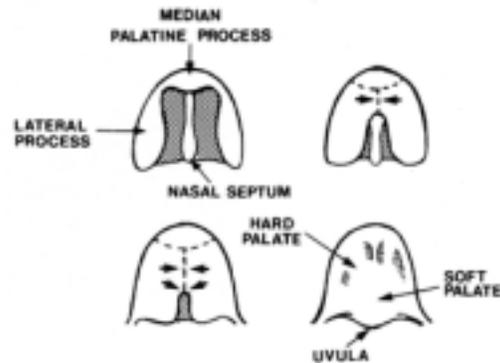


Figure 2-22. The palate derives from the fusion of the median and lateral palatine processes. Merging with the outgrowing nasal septum results in the separation of the oral and nasal cavities.

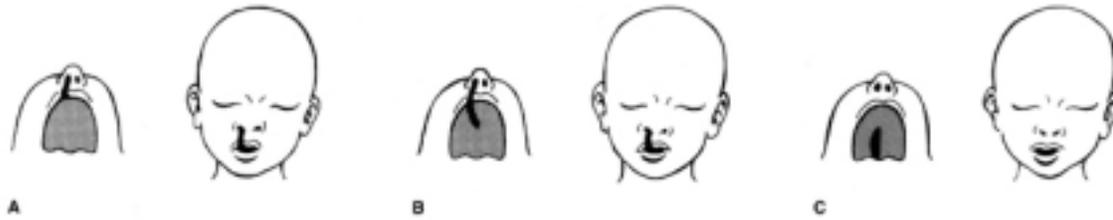


Figure 2-23. Schematic representation of various types of cleft lip and cleft palate. **A.** Unilateral cleft lip. **B.** Unilateral cleft lip and palate. **C.** Unilateral cleft palate.

we believe that an increased amount of amniotic fluid is an indication for careful examination of the fetal face.

Prognosis

Minimal defects, such as lineal indentations of the lips or submucosal cleft of the soft palate, may not require surgical correction. Larger defects cause cos-

metic, swallowing, and respiratory problems. Recent advances in surgical technique have produced good cosmetic and functional results. However, prognosis depends primarily on the presence and type of associated anomalies.¹³

Obstetrical Management

A careful survey for associated anatomic defects is indicated. The advisability of karyotype is controversial in view of the low incidence of chromosomal anomalies in clefting defects. In the absence of other anomalies, fetal CL-CP does not require a change in standard obstetrical care. Infants should be delivered in a tertiary center because of the possibility of respiratory and feeding problems.

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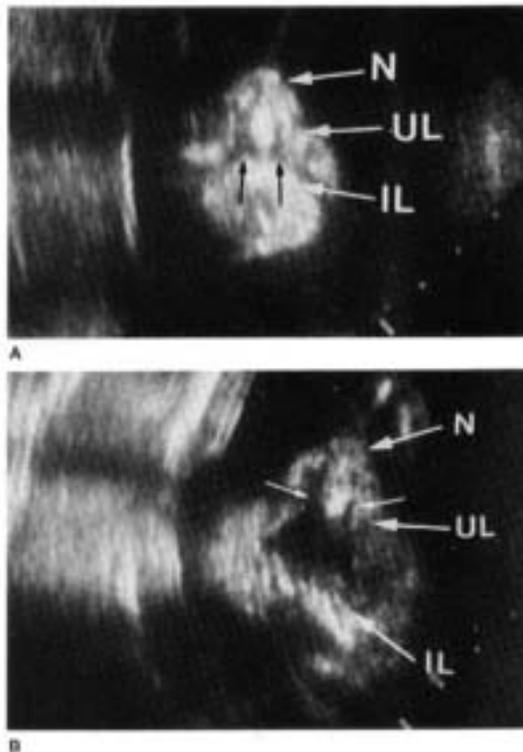


Figure 2-24. **A.** Coronal scan of the face of a 26-week fetus with bilateral cleft lip and palate. Two grooves (*black arrows*) are seen extending from both sides of the upper lip (UL) into the nostrils. N, nose; IL, inferior lip. **B.** A slight posterior angulation of the transducer allows visualization of the defects extending into the hard palate (*thin arrows*).

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Median Cleft Lip

Synonyms

Complete median cleft lip, pseudomedian cleft lip, and premaxillary agenesis.

Definition

A quadrangular or triangular median defect of the upper lip, possibly extending posteriorly to the nose.

Incidence

Median cleft lip (MCL) accounts for 0.2 to 0.7 percent of all cases of cleft lip.^{1,4}

Embryology

The median portion of the upper lip and maxilla derives from the frontonasal prominence, which joins the maxillary prominences (Fig. 2-16). In cases of median cleft lip, there is absence or underdevelopment of this portion.

There is a close correlation between the development of the midline facial structures and the differentiation process of the forebrain. Both events are probably induced by the prechordal mesenchyma, the tissue interposed between the prosencephalon, and the roof of the primitive mouth (stomodeum). Therefore, midline defects of the face, such as MCL,

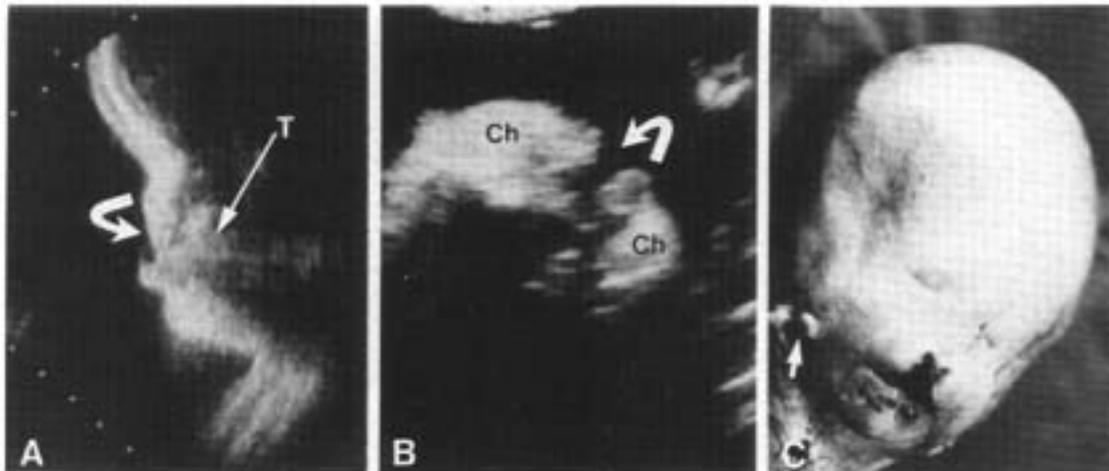


Figure 2-25. Median cleft lip in a third trimester holoprosencephalic fetus. **A.** Midsagittal scan of the face reveals an unusually high position of the tongue (T) inside the oral cavity, as well as absence of the nose (curved arrow). **B.** Axial scan of the palate demonstrating a large quadrangular median cleft (curved arrow). Ch, cheeks. **C.** Postnatal appearance of the stillborn infant. Note the median cleft lip and palate, absence of the nose, anophthalmia, and low set ears (arrow). (Reproduced with permission from Pilu et al.: *Am J Obstet Gynecol* 155:45, 1986.)



Figure 2-26. Axial scan at midfacial level in a third trimester fetus with holoprosencephaly and a large cleft of the palate. The seemingly intact appearance of the palate is due to the tongue (T) filling the defect. A correct diagnosis could be made by observing the midline cleft of the upper lip (curved arrow), as well as the active movement of the tongue.

are frequently associated with cerebral anomalies, such as holoprosencephaly (see Fig. 1-64, Table 1-17)³

Etiology and Pathology

MCL has been described only as part of two distinct syndromes: MCL with orbital hypotelorism,³ which is a synonym for holoprosencephaly, and MCL with orbital hypertelorism.² In the former case, there is absence of the premaxillary bone, nasal septum, nasal bones, and crista galli. The ethmoid bone that sets the interorbital distance is hypoplastic. The secondary palate may or may not be involved. For a detailed description of the other facial and cerebral findings, see the section on hypotelorism in this chapter and the section on holoprosencephaly in Chapter 1. MCL with hypertelorism (also known as "median cleft face syndrome" or "frontonasal dysplasia") is characterized by the presence of a bifid nose and cranium bifidum occipitum. The premaxilla is usually present. The brain is normal in most cases.

Diagnosis

The diagnosis relies on the demonstration of a wide central defect involving both the upper lip and the palate.^{5,6} In our experience, the defect is better demonstrated in axial scans of the palate (Fig. 2-25). A useful hint for the diagnosis is the visualization of the tongue in a higher than normal position within the oral cavity. The sonographer should be alerted to a possible pitfall in the diagnosis of MCL. On occasion, the defect may be filled by the tongue, giving a false impression of an intact palate (Fig. 2-26). Recognition of MCL should immediately prompt a careful ultrasound investigation of the entire fetal anatomy, with special attention to the intracranial contents. Orbital measurements will identify hypotelorism or hypertelorism.

Prognosis and Obstetrical Management

Prognosis depends entirely on the association with other anomalies. MCL syndrome is associated in 80 percent of cases with normal intelligence.⁸ Radical cosmetic surgery may be required. Alobar holoprosencephaly is uniformly lethal.

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Epignathus

Definition

A teratoma that arises from the oral cavity or pharynx.

Incidence

Two percent of all pediatric teratomas occur in the nasopharyngeal area (including oral, tonsillar, and



Figure 2-27. Sonogram of a 32-week fetus, demonstrating a complex mass with solid (S) and cystic (C) components. The arrow points to areas of calcification with acoustic shadowing. (Reproduced with permission from Chervenak et al: *J Ultrasound Med* 3.-235, 1984.)



Figure 2-29. Mass arising from the palate, obstructing the mouth opening and nostril of the neonate. (Reproduced with permission from Chervenak et al.: *J Ultrasound Med* 3.-235, 1984.)

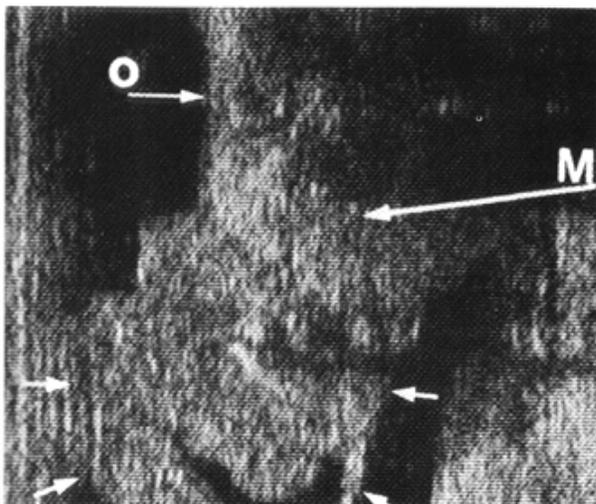


Figure 2-28. Coronal scan of the same fetus as in Figure 2-27, with arrows outlining the mass. O, orbit; M, mouth area; mouth not visualized. (Reproduced with permission from Chervenak et al: *J Ultrasound Med* 3.-235, 1984.)



Figure 2-30. Appearance of mass after resection. (Reproduced with permission from Chervenak et al.: *J Ultrasound Med* 3.-235, 1984.)



Figure 2-31. Radiograph showing the relation of the mass to the skull and calcifications in the mass. (Reproduced with permission from Chervenak et al: *J Ultrasound Med* 3:-235, 1984.)

basicranial areas).⁵ Most of approximately 100 cases have been reported in newborns.^{6,8}

Pathology

Most tumors arise from the sphenoid bone. Some arise from the hard and soft palate, the pharynx, the tongue, and jaw. From their sites of origin, the tumors grow into the oral or nasal cavity or intracranially. Most tumors are benign. Histologically, they consist of tissues derived from any of the three germinal layers. Most often they contain adipose tissue, cartilage, bone, and nervous tissue. These tumors can fill the mouth and airways and lead to acute asphyxia immediately after birth. Obstruction of the mouth is responsible for polyhydramnios.

Associated Anomalies

Six percent of these tumors have associated anomalies.⁵ They include cleft palate, multiple facial hemangiomas, branchial cysts, hypertelorism, umbilical hernia, and congenital heart defects. Facial anomalies have been attributed to the mechanical effects of the tumor on developing structures.^{1,2,4,9}

Diagnosis

Antenatal sonographic findings have been reported in two fetuses.^{3,7} A solid tumor emanating from the fetal oral cavity is suggestive of this condition (Figs. 2-27 through 2-31). Calcifications and cystic components may be visualized. Differential diagnosis include neck teratomas, cephaloceles, conjoined twins,

and other tumors of the facial structures. Polyhydramnios is usually present.⁸ A careful examination of the CNS anatomy is important because the tumor may grow intracranially.

Prognosis

The outlook depends on the size of the lesion and the involvement of vital structures. Lesions detected antenatally have been very large. Polyhydramnios has been associated with poor prognosis.⁸ Soft tissue dystocia can occur. The major cause of neonatal death is asphyxia because of airway obstruction. Surgical resection and normal postoperative course are possible and have been documented.⁸ There are no reported cases of malignancies. Two cases of epignathus have been diagnosed in our institution, and both infants died. One died immediately after birth and the other after progressive respiratory failure.

Obstetrical Management

Management in the third trimester depends on the size of the lesion. Infants with large tumors are best delivered by cesarean section. An expert pediatric team must be available for intubation of the infant.

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ABNORMALITIES OF THE MANDIBLE

Robin Anomalad

Synonyms

Cleft palate, micrognathia and glossoptosis, and Pierre Robin syndrome.

Definition

This anomalad is characterized by the association of micrognathia and glossoptosis. Frequently, a posterior cleft palate or a high arched palate is present.

Incidence

The frequency is 1:30,000.²

Etiology

In 40 percent of cases, the anomaly is isolated and is mostly sporadic, although familiar cases suggesting both autosomal recessives and autosomal dominant¹ patterns of transmission have been reported. This anomalad is most frequently seen in association with other anomalies or with recognized genetic and non-genetic syndromes (Table 2-7).

Embryology

The mandible arises from the merging of the two mandibular prominences that inferiorly delimit the stomodeum. The palate originates from the fusion of the three palatine processes. The median derives from the frontonasal prominence and the two lateral ones originate from the maxillary processes.

It has been suggested that the three components of the anomalad are related. The primary disorder is probably an early hypoplasia of the mandible. This would lead to posterior displacement of the tongue, thus preventing the normal closure of the posterior palatine processes.⁴

Pathology

The hypoplasia of the mandible leads to foreshortening of the floor of the mouth and reduction of the size of the oral cavity. As a consequence, there is a tendency to glossoptosis, which may alter the development of the palate and lead to a posterior cleft or a high arched deformity.¹

Associated Anomalies

The Robin anomalad is found as an isolated lesion in 39 percent of all patients. In 36 percent, one or more associated anomalies are found, but these do not conform to a well-established syndrome. In 25 percent of patients, a known syndrome is found.²

Diagnosis

Only one case of Robin anomalad has been identified in utero thus far.⁶ The diagnosis relied upon the demonstration of micrognathia in a midsagittal scan of the face (Fig. 2-32). The hypoplasia of the mandible could not be detected in the second trimester. This suggests the possibility of a progressive course, which may preclude an early diagnosis.⁶

Polyhydramnios was seen in the reported case. It is likely to result from failure to swallow as a consequence of the glossoptosis.⁶ Sonographers should suspect Robin anomalad when polyhydramnios is associated with micrognathia. A posterior cleft palate is frequently present, but it may be difficult to detect with ultrasound. The difficulties in imaging this part of the fetal anatomy make this diagnosis unlikely.

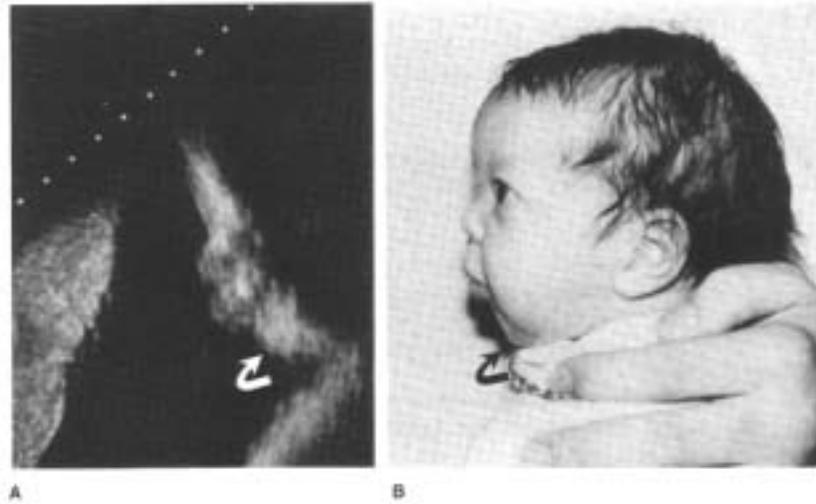
A careful survey of fetal anatomy is indicated. Because congenital heart disease occurs in 10 percent

TABLE 2-7. SYNDROMES ASSOCIATED WITH THE ROBIN ANOMALAD

Genetic syndromes
Monogenic syndromes
Diastrophic dysplasia
Stickler syndrome (congenital myopia associated with irregular articular surfaces)
Spondyloepiphyseal dysplasia
Beckwith-Wiedemann (omphalocele, visceromegaly, macroglossia, neonatal hypoglycemia)
Myotonic dystrophy (weakness of facial, neck, and distal limb muscles)
Campomelic syndrome
Chromosomal
Trisomy 11q+
Nongenetic syndromes
Fetal alcohol syndrome
Fetal hydantoin syndrome
Fetal trimethadione syndrome

Adapted from Cohen: *J Oral Surg* 34:587, 1976.

Figure 2-32. **A.** Midsagittal scan of the face of a 35-week fetus with Robin anomalad. Micrognathia is evident (*curved arrow*). **B.** A side view of the infant is provided for comparison. (Reproduced with permission from Pitu et al.: *Am J Obstet Gynecol* 154:630, 1986.)



of affected neonates,³ fetal echocardiography is recommended.

Prognosis

The Robin anomalad is in many cases a neonatal emergency. Glossoptosis may lead to obstruction of the airways and suffocation. Many cases of sudden death have been described. Infants have difficulties feeding because of the ball valve effect of the tongue in the oropharynx and because of vomiting.^{3,5,8} This leads to failure to thrive. However, with proper assistance, these infants may overcome these difficulties. With time there is some growth of the mandible.

Obstetrical Management

If a prenatal diagnosis is made, the sonographer should look for associated anomalies. It is mandatory that a pediatrician be present in the delivery room and be prepared to intubate the infant. This procedure may be lifesaving. Karyotype should be considered.

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Otocephaly

Synonyms

Synotia and melotia.

Definition

Otocephaly is a grotesque anomaly characterized by absence or hypoplasia of the mandible, proximity of

the temporal bones, and abnormal horizontal position of the ears.

Incidence

Unknown. It seems to be an extremely rare disorder.

Embryology

The mandible arises from the fusion of the two mandibular prominences that inferiorly delimit the stomodeum. The primitive external ears are located laterally and inferiorly to the mandibular prominences, and they migrate (Fig. 2-16). Otocephaly is thought to result from failure of development of the mandible, possibly secondary to a defect in neural crest cell migration.³ Absence or extreme hypoplasia of the mandible leads to an abnormal position of the ears, which are horizontal, with the lobules located close to the midline. A spectrum of anatomic lesions ranging from ears closely apposed to the midline (synotia), agnathia, absence of the mouth to varying degrees of micrognathia and low set ears (melotia) is possible.

Etiology

Unknown. Otocephaly may be part of very severe malformation complexes, such as conjoined twins and holoprosencephaly.⁴ This malformation has been produced experimentally by X-irradiation and administration of streptonigrin in mice.^{2,4}

Associated Anomalies

Holoprosencephaly, neural tube defects, cephaloceles, midline proboscis, hypoplastic tongue, tracheoesophageal fistula, cardiac anomalies, and adrenal hypoplasia.

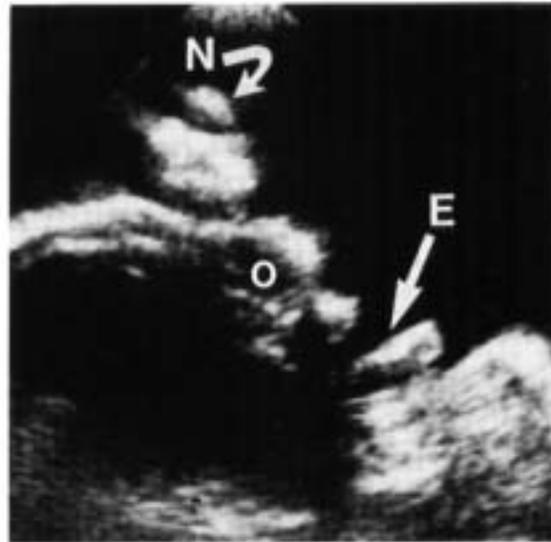


Figure 2-33. A. Midsagittal scan of the face of a fetus with otocephaly and holoprosencephaly. The nasal appendage (N) can be seen arising from the forehead superiorly to the orbits (O). A well-defined ear (E) is seen implanting in the lower face. (Courtesy of Prof. A. Ianniruberto.)

Diagnosis

This condition should be suspected when it is impossible to visualize the jaw and the ears are seen in a very low position (Fig. 2-33). It is likely that this

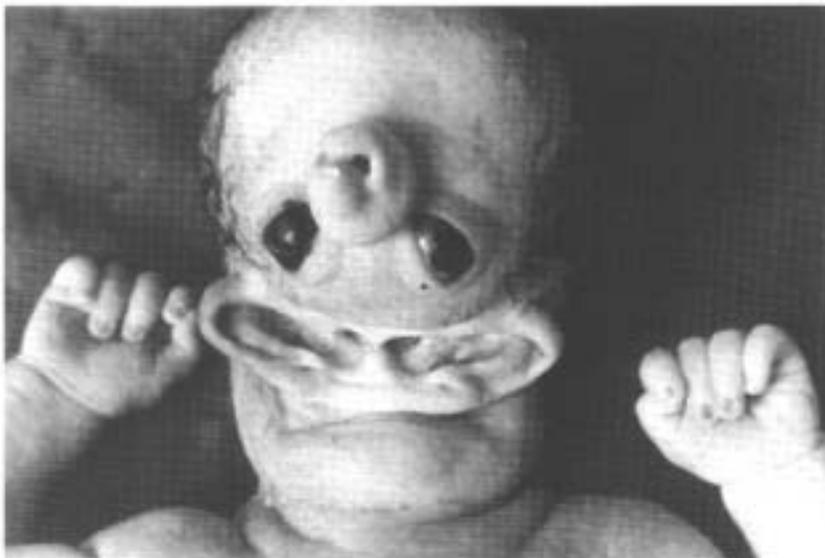


Figure 2-33. B. Frontal view of the stillborn infant. Note synotia, hypotelorism, towering skull, and a proboscis. (Courtesy of Prof. A. Ianniruberto.)

condition will be identified in fetuses with very severe associated anomalies, such as anencephaly, holoprosencephaly, and cephaloceles.¹ Milder expressions of otocephaly may be difficult to distinguish on prenatal ultrasound studies from other conditions characterized by very low set ears, such as Treacher-Collins syndrome.¹

We have recently diagnosed this condition in a fetus with polyhydramnios and an absent stomach. It must be considered, therefore, in the differential diagnosis of esophageal atresia.

Prognosis and Obstetrical Management

This condition is incompatible with life. Pregnancy

termination could be offered any time in a pregnancy when a confident diagnosis is made.

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