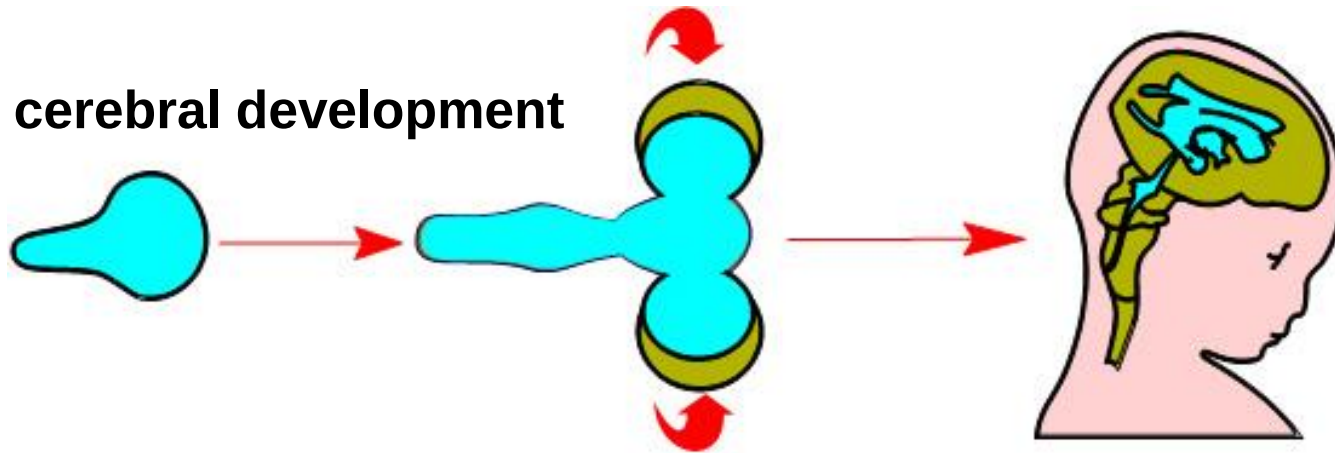
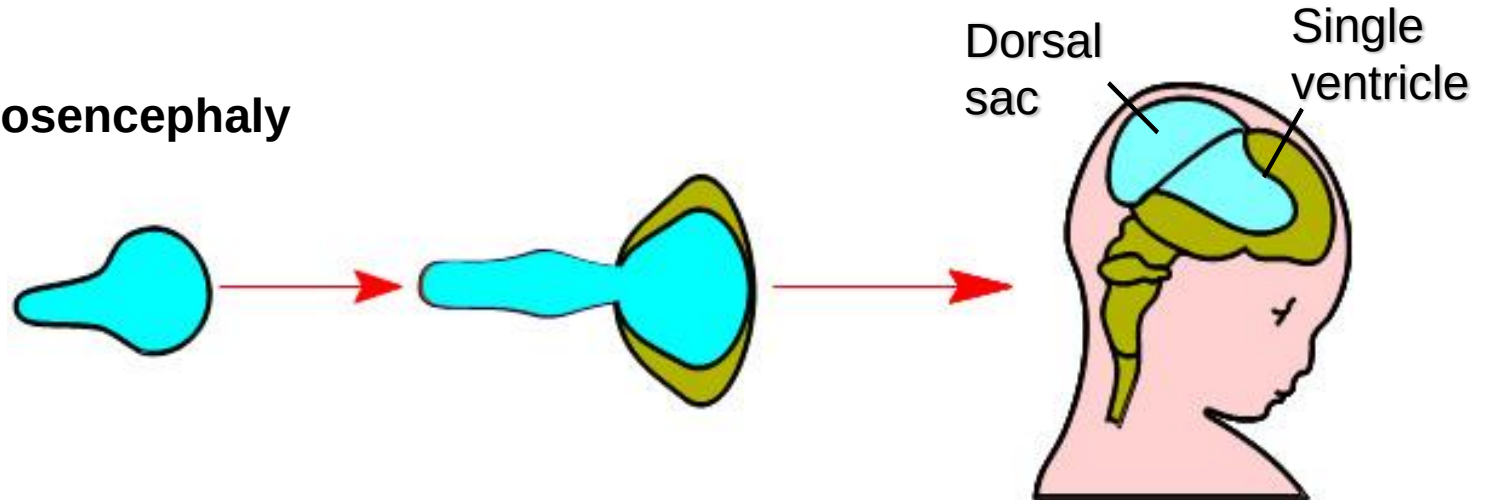


Embryology of holoprosencephaly

Normal cerebral development

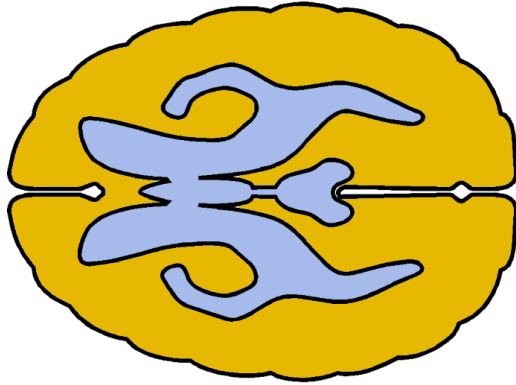


Holoprosencephaly

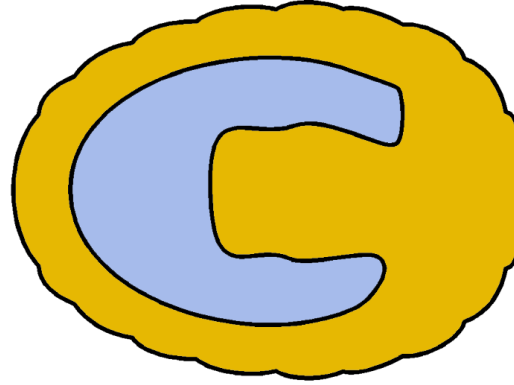


Results from a failure of the process of cleavage and rotation of the embryonic brain

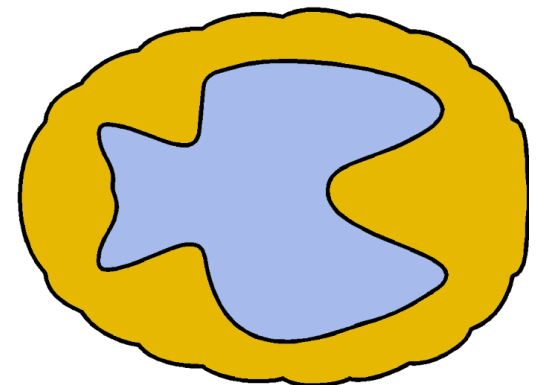
Classification of holoprosencephaly



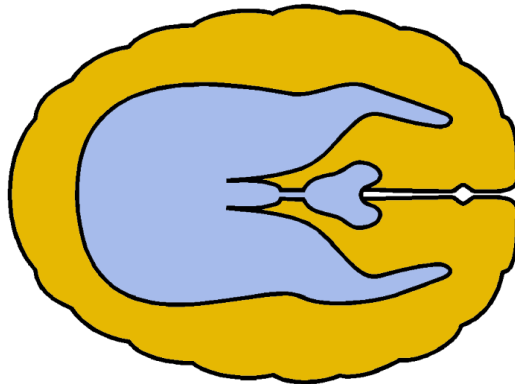
Normal brain



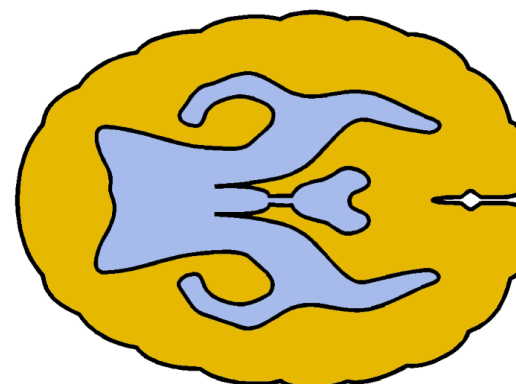
Alobar



Middle variant



Semilobar



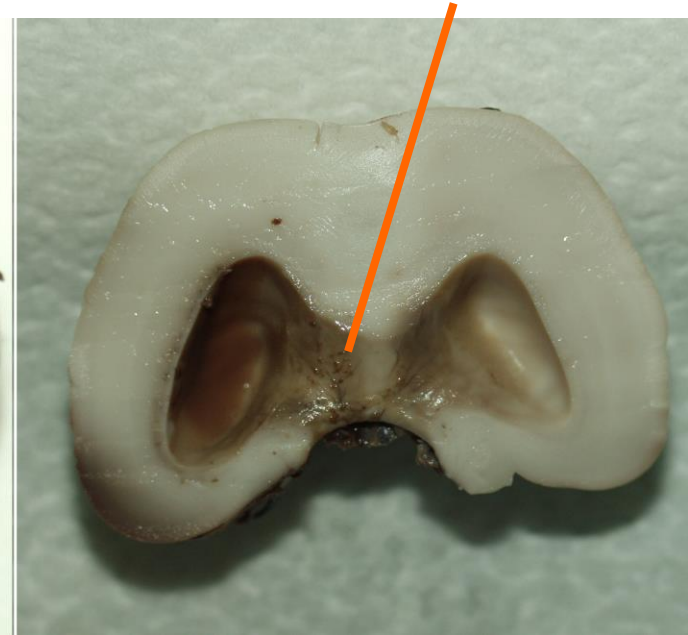
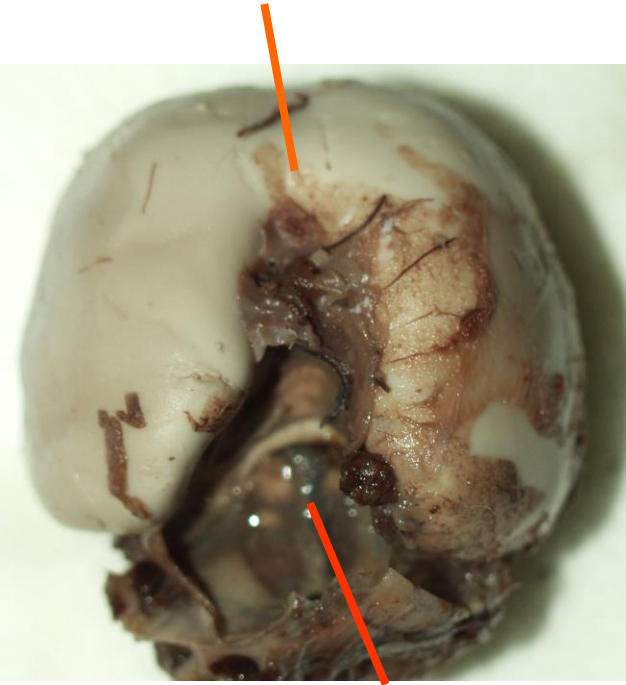
Lobar

Alobar holoprosencephaly

Fusion of cerebral hemispheres

Absence of olfactory tracts

Single ventricle



A cyst atop the posterior part of the brain (dorsal sac) may be present

Facial anomalies with holoprosencephaly

Cyclopia



Otocephaly



Ethmocephaly



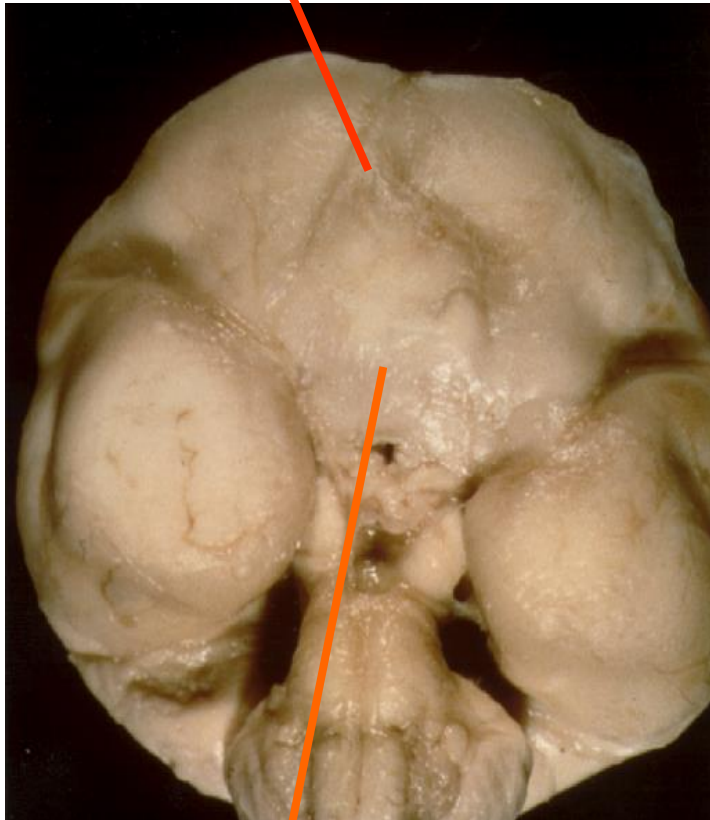
Median cleft



Severe holoprosencephaly is typically associated with facial malformations including cyclopia, hypotelorism, proboscis and median cleft lip

Lobar holoprosencephaly

Fusion of frontal lobes



Absence of olfactory tracts

Fusion of frontal horns with absence of septum pellucidum

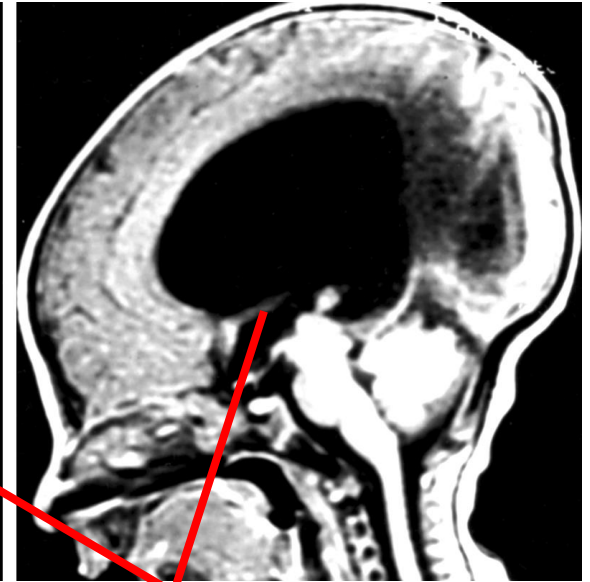


Holotencephaly

Interhemispheric fissure



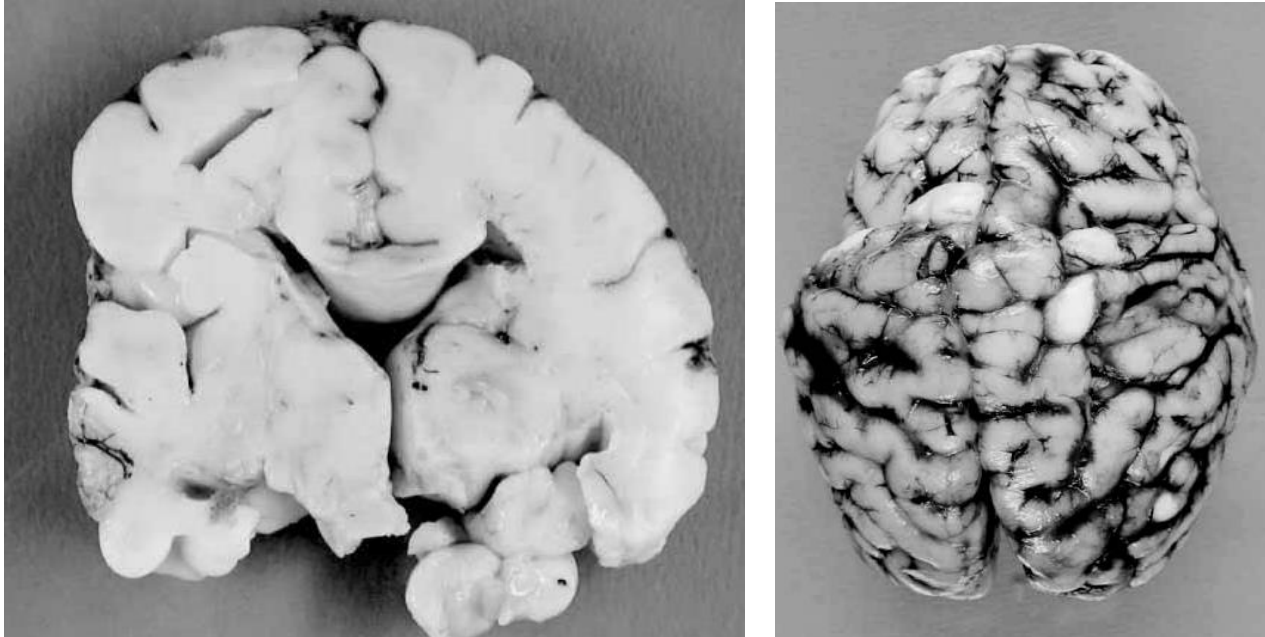
Fused frontal horns with flat roof



fused fornices

Holotencephaly is the mildest variation of holoprosencephaly. The cerebral hemispheres are almost completely cleaved, but the frontal horns are fused centrally and with the third ventricle inferiorly, the fornices may be fused and appear as a solid fascicle running within the ventricular cavity

Middle interhemispheric variant

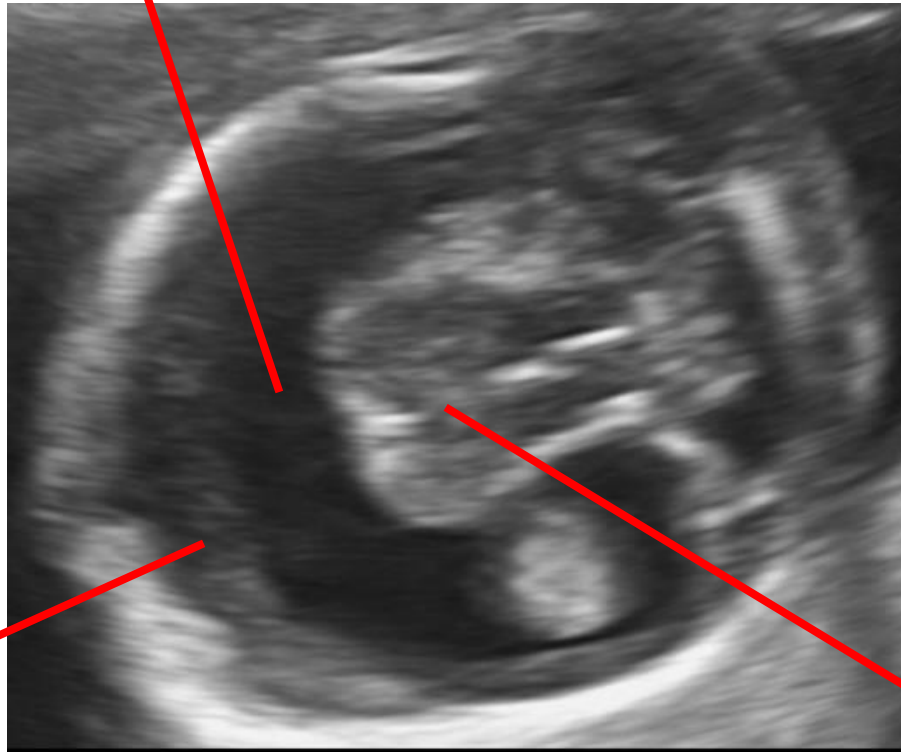


The middle interhemispheric variant of holoprosencephaly is intermediate between the alobar and lobar type: the frontal horns are well formed but the two hemispheres are posteriorly fused.

Reproduced from: Picone O et al: Prenatal diagnosis of a possible new middle interhemispheric variant of holoprosencephaly using sonographic and magnetic resonance imaging. *Ultrasound Obstet Gynecol.* 2006 Aug;28(2):229-31

Sonography of severe holoprosencephaly

Rudimentary ventricular cavity



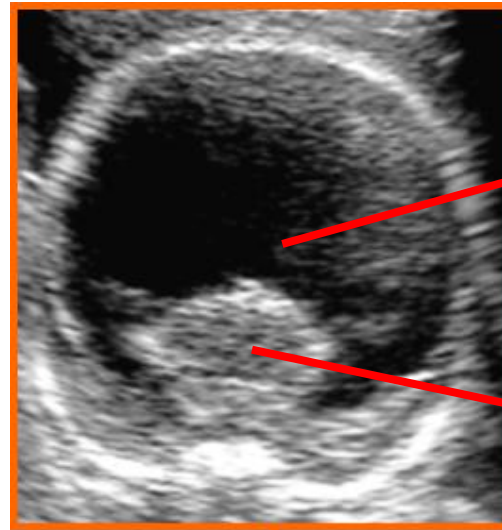
No midline

Bulb-shaped thalami

Diagnosis relies upon the demonstration of a single crescent shaped ventricular cavity. The hypoplastic and fused thalami have a typical bulb-shaped appearance

The dorsal sac

The single ventricular cavity may be connected posteriorly with a large cystic structure: the dorsal sac



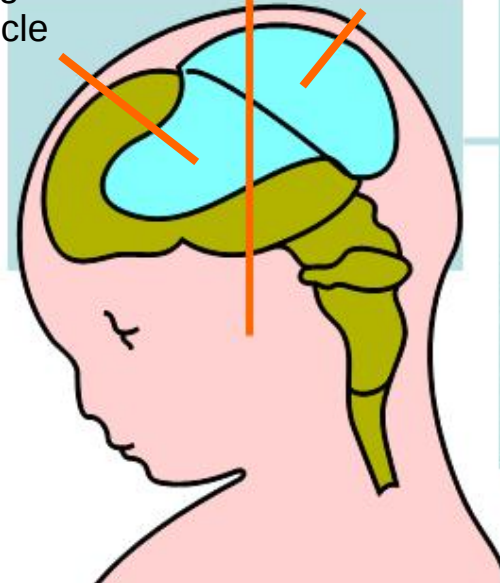
Coronal view

Single ventricle + Dorsal sac

thalami

Single ventricle

Dorsal sac



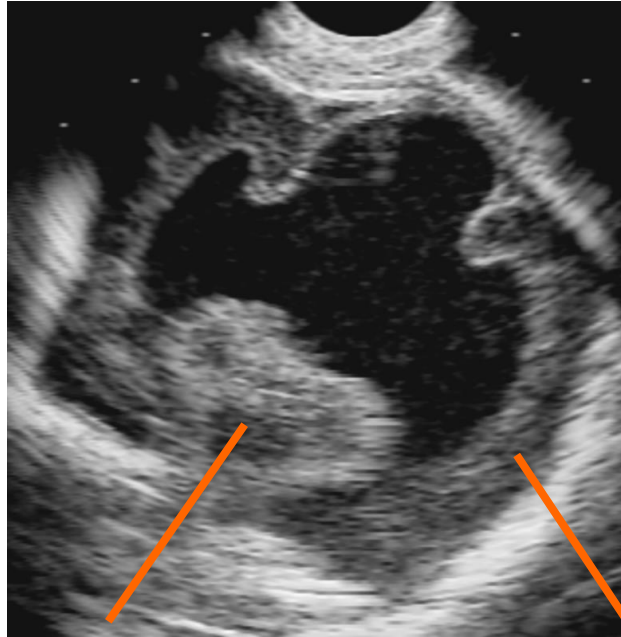
Sagittal view

Varieties of alobar holoprosencephaly

'pancake'



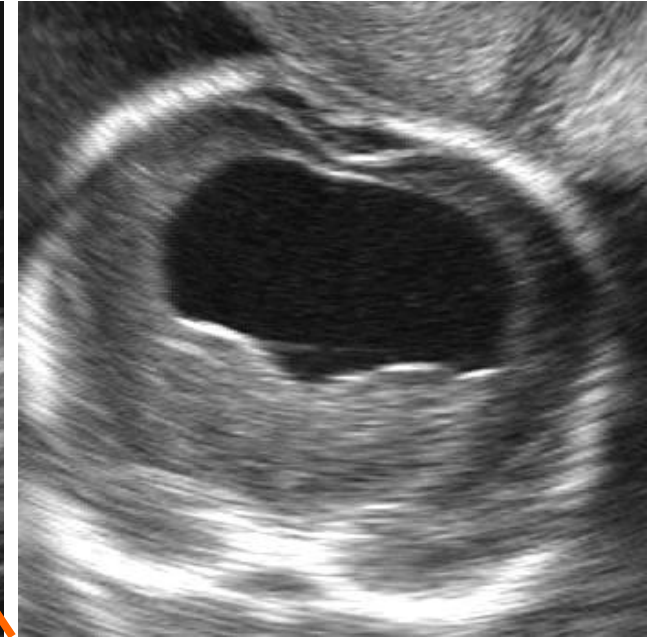
'cup'



thalami

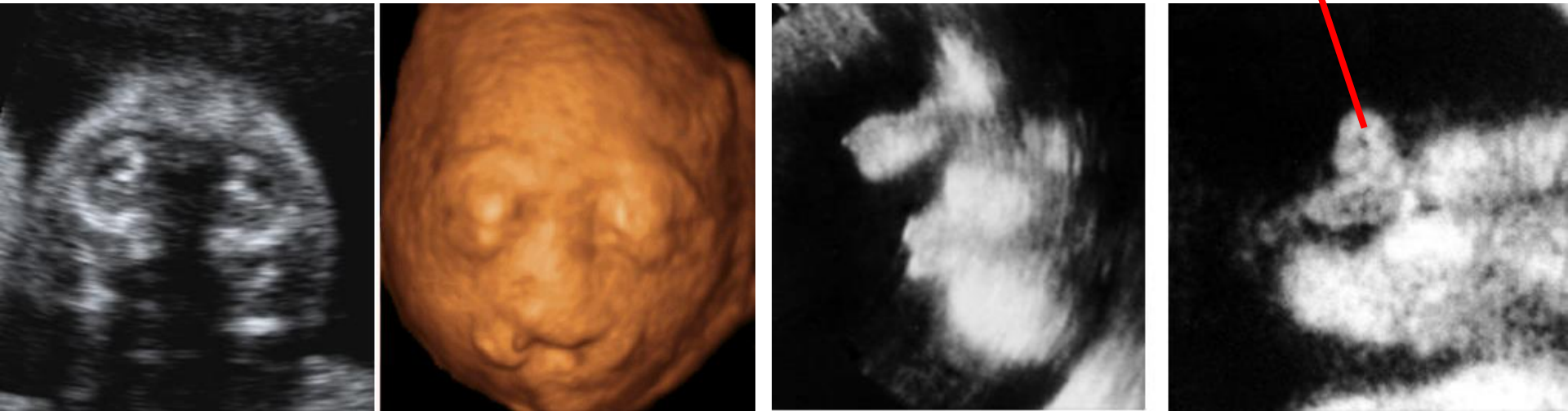
cortex

'ball'



Depending upon the degree of enfoldment of the cortex over the ventricular cavity three varieties can be distinguished

Hypotelorism and proboscis



The most common facial anomaly encountered with severe holoprosencephaly is hypotelorism, that is featured by a marked decrease in the distance between the orbits. The proboscis that is associated with some forms of holoprosencephaly is an appendage with a single opening that does not communicate with the nasal fossae; it can be found above the orbits (ethmocephaly) or below (cebocephaly).

Ethmocephaly

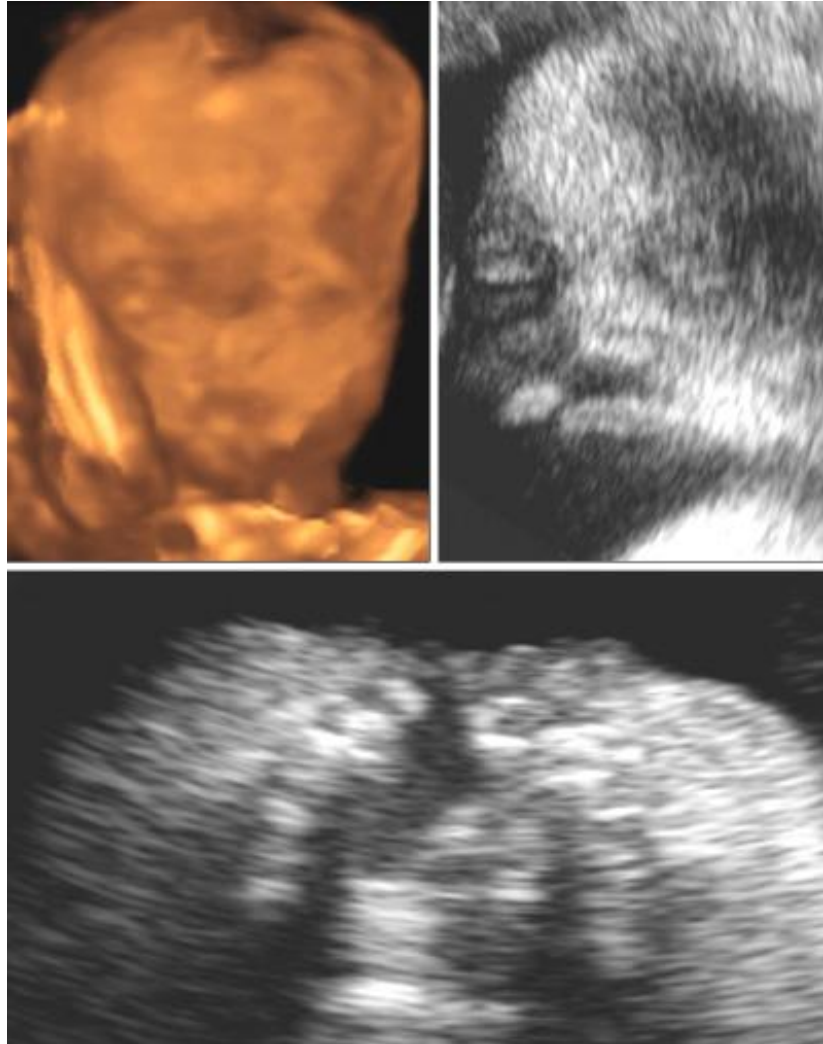
Is featured by a combination of severe hypotelorism and a proboscis implanted above the level of the orbits

Clip holo_2



Median cleft

Most fetuses with severe holoprosencephaly identified prenatally will demonstrate a combination of hypotelorism, flat nose and median cleft lip/palate



Cyclopia



Otocephaly



Cyclopia is the most severe end of the spectrum of facial anomalies and is characterized by the presence of a single orbital cavity that may contain one or two eye-bulbs; *otocephaly* is a severe cranio-facial malformation characterized by extreme hypoplasia or absence of the mandible and abnormal horizontal displacement of the ears that are frequently fused (synotia). It may be isolated but is frequently associated with holoprosencephaly

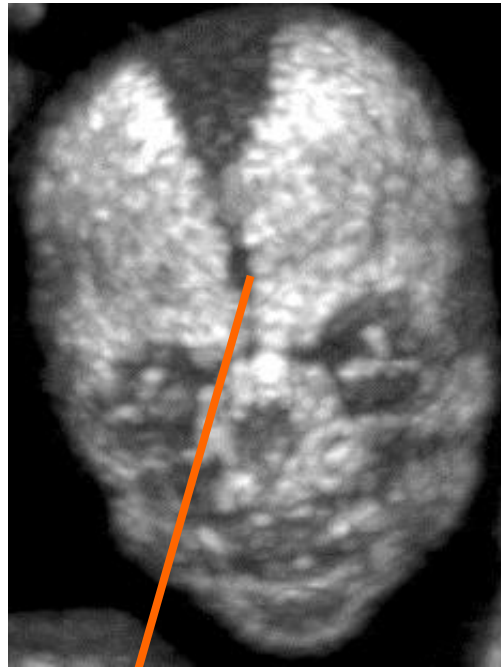
Cyclopia

Clip holo_1



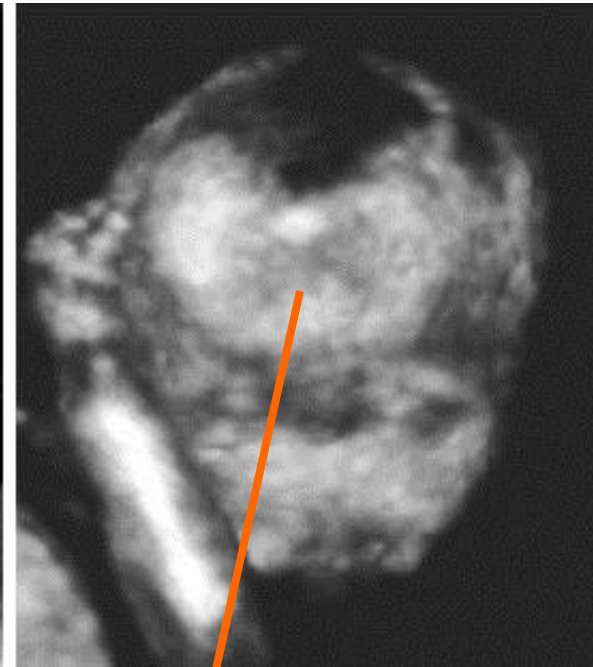
Absence of frontal suture

Normal fetus
20 weeks



Frontal suture

Holoprosencephaly
18 weeks



Fused frontal bone

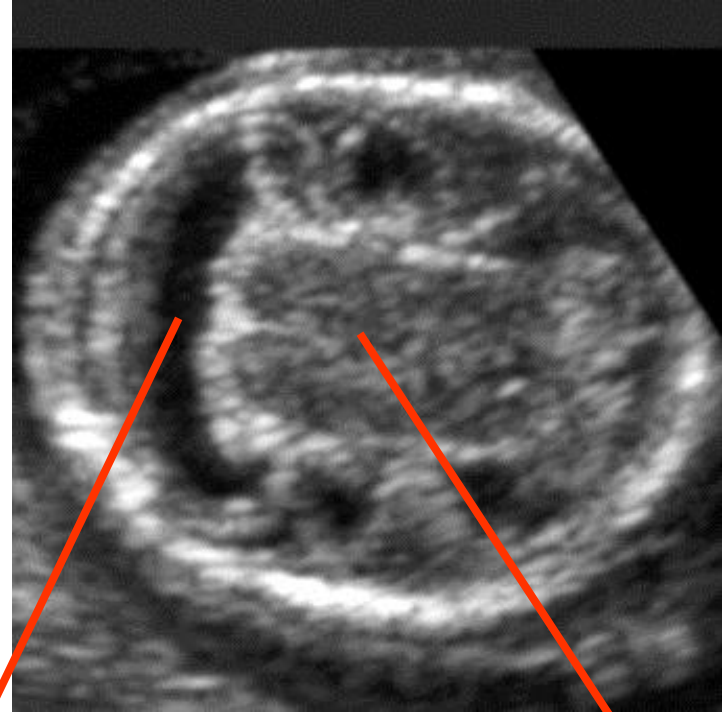
Using 3D maximum mode it has been demonstrated that fetuses with severe holoprosencephaly have fusion of the frontal bone since the first trimester

Early diagnosis

Normal



Holoprosencephaly

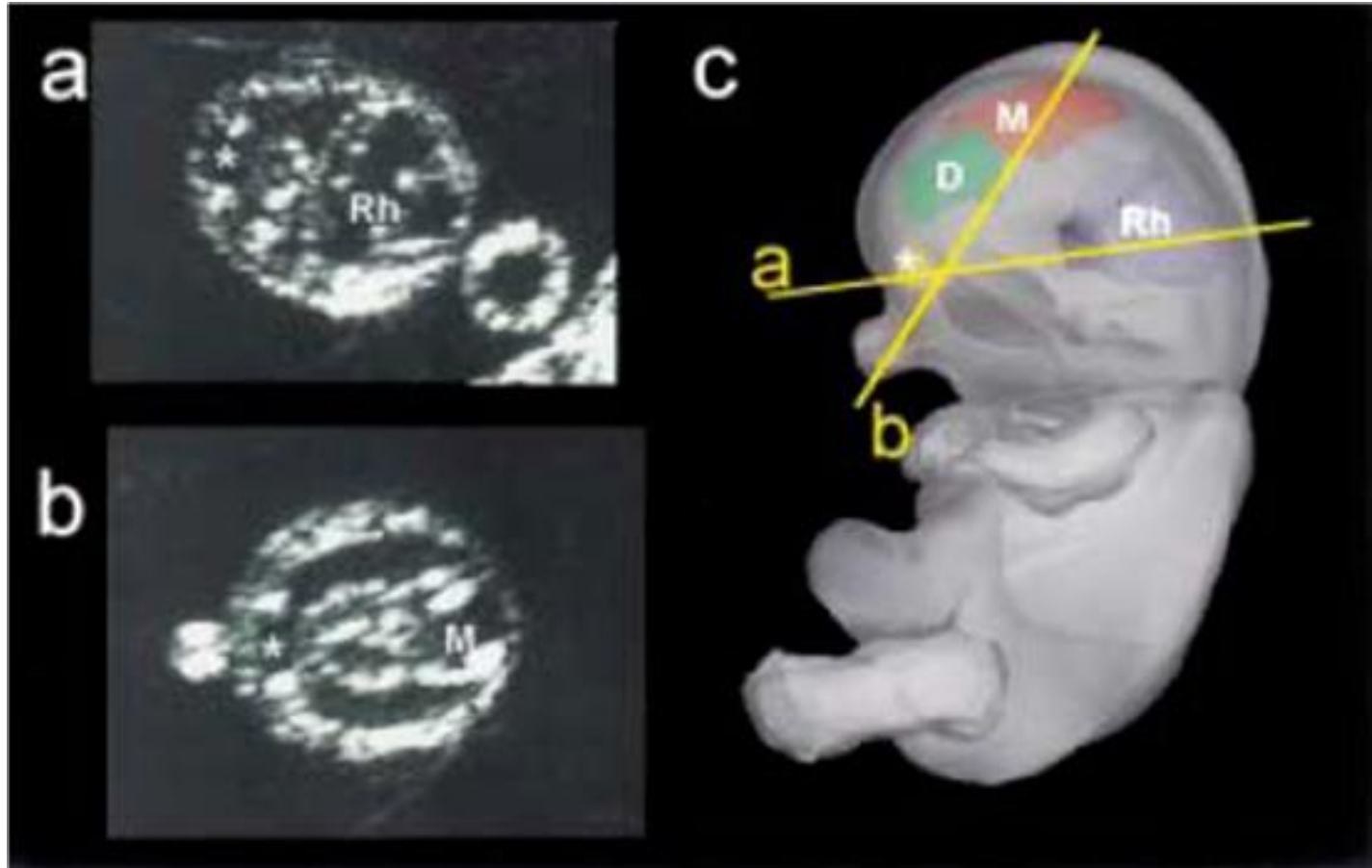


Single ventricle

Fused thalami

Visualization of the single ventricle is usually possible at 11-13 weeks trimester

Diagnosis in first trimester

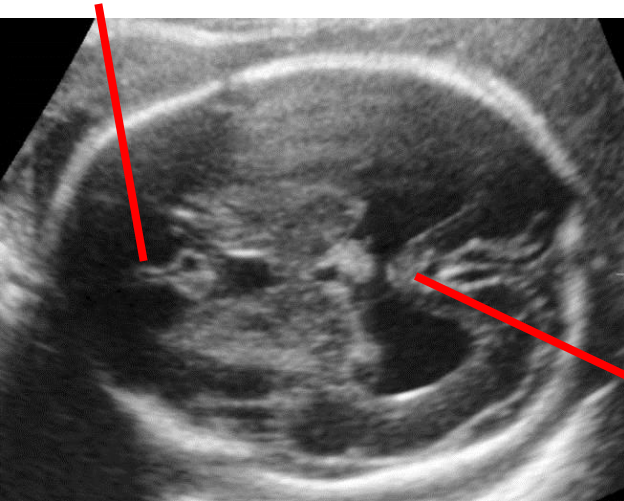


Horizontal section through the head of a 9-week-2-day embryo (CRL 22 mm) showing the nondivision of the forebrain. (b) Tilted section through the head; the mesencephalon and holosphere are visible; in addition, a proboscis can be seen to the left anteriorly to the forehead. (c) Three-dimensional reconstruction of the embryo with volume presentation of body and brain cavities. The lines indicate the sections in (a) and (b). * holosphere (yellow), D diencephalon (green), M mesencephalon (red), Rh rhombencephalon (blue).

Reproduced from: H.-G. K. Blass HG et al.; Alobar holoprosencephaly at 9 weeks gestational age visualized by two- and three-dimensional ultrasound. *Ultrasound Obstet Gynecol* 2000; **15**: 62–65

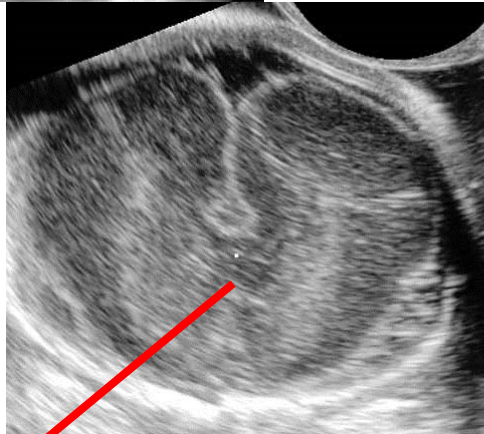
Lobar holoprosencephaly

Midline echo

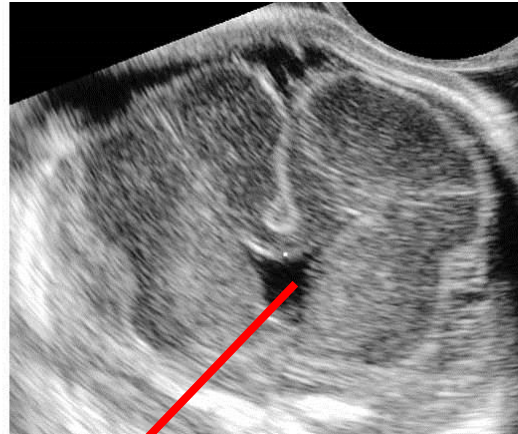


The most informative views are the axial ones demonstrating absence of the septum pellucidum, anterior fusion of lateral ventricles and frontal lobes with poorly developed frontal horns

Fused lateral ventricles



Fused frontal lobes



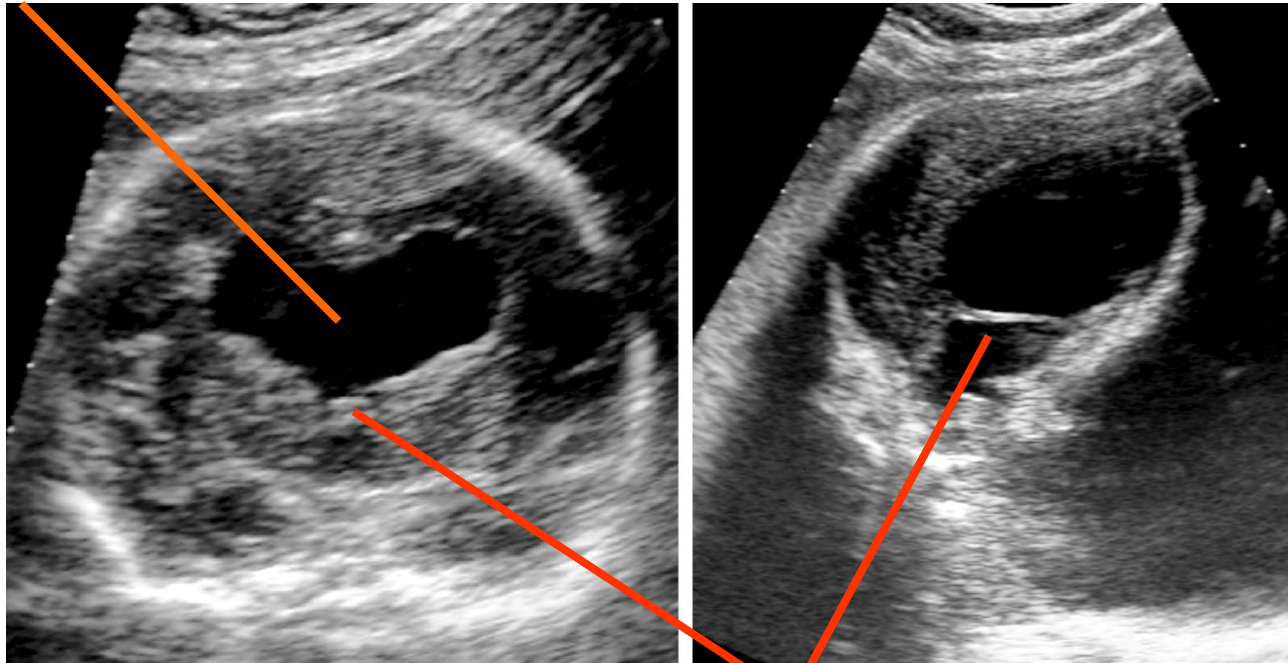
Fused frontal horns



Fused lateral ventricles

Holotelencephaly

fused frontal horns with flat roof

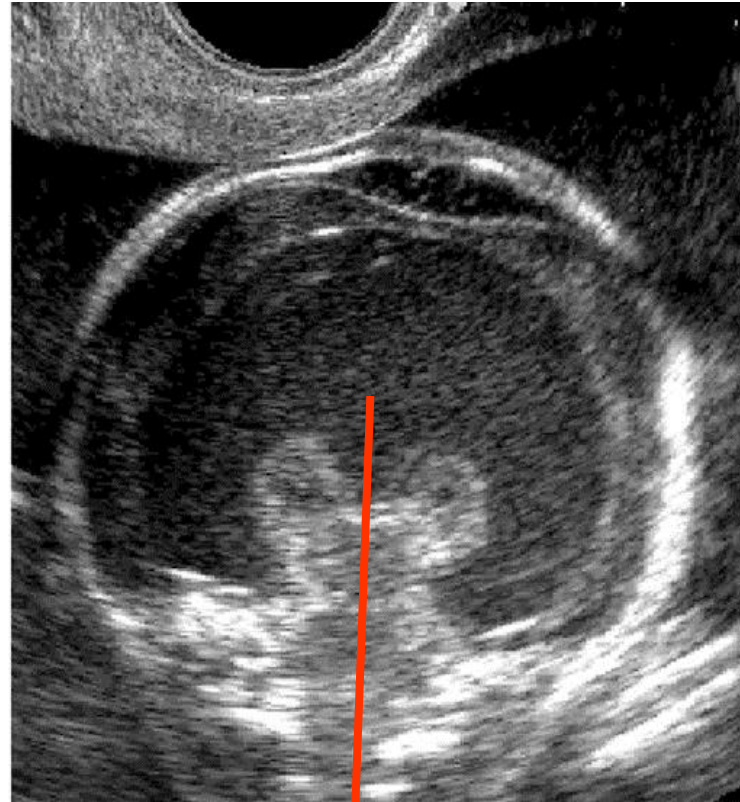
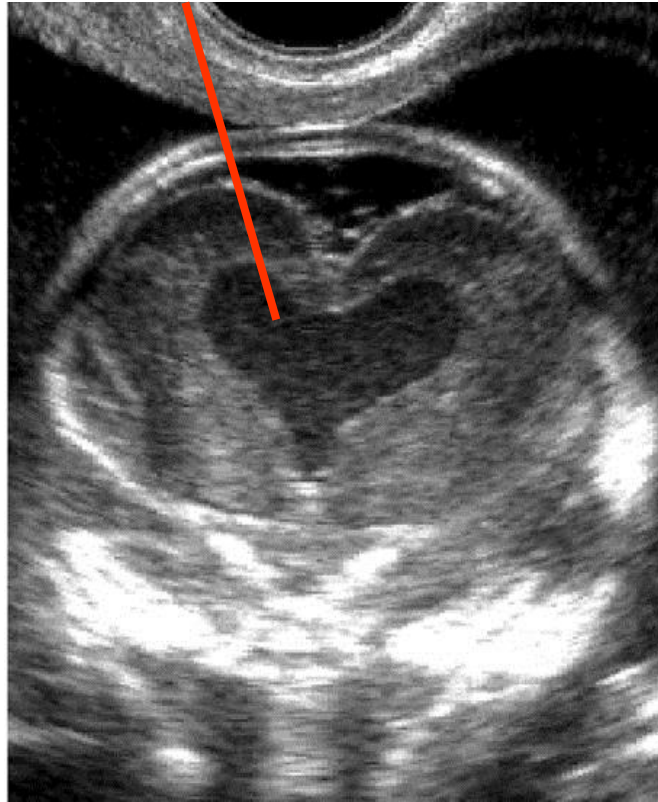


Fused fornices

The frontal horns are fused and have a flat roof, and the fused fornices may be seen as a solid fascicle running within the lateral ventricles

Middle interhemispheric variant

Fused frontal horns

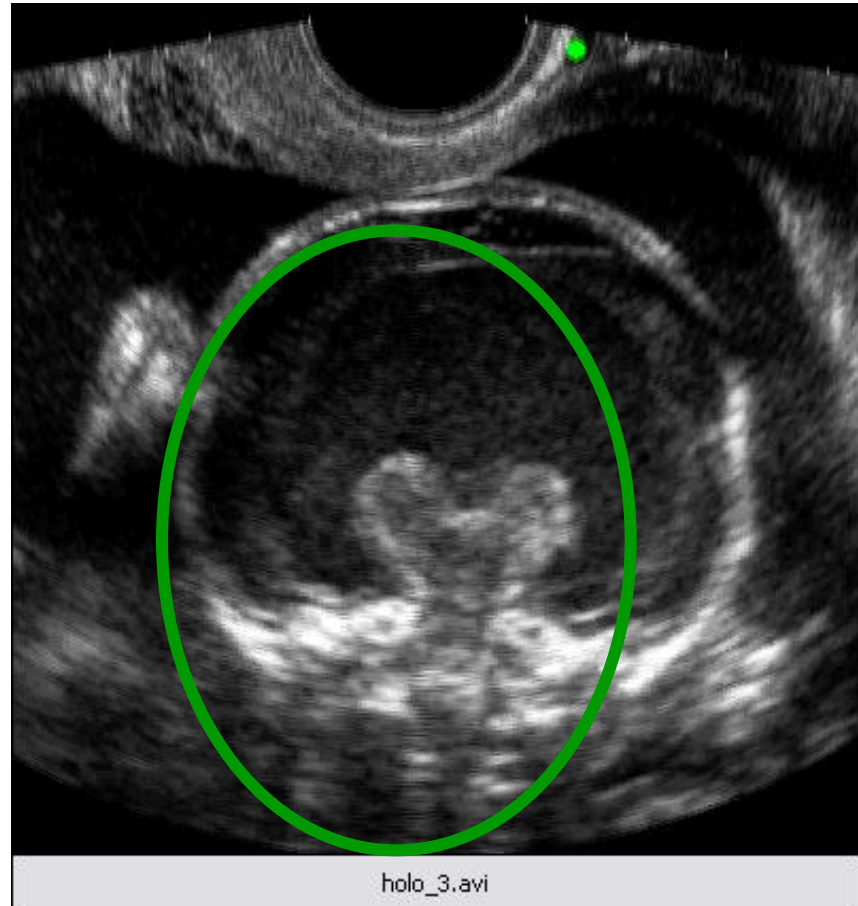


Single ventricular cavity with hypoplastic thalami

the frontal horns are well developed and there is a partial formation of the interhemispheric fissure (but no *falx cerebrii*); posteriorly there is a common ventricular cavity with hypoplastic thalami

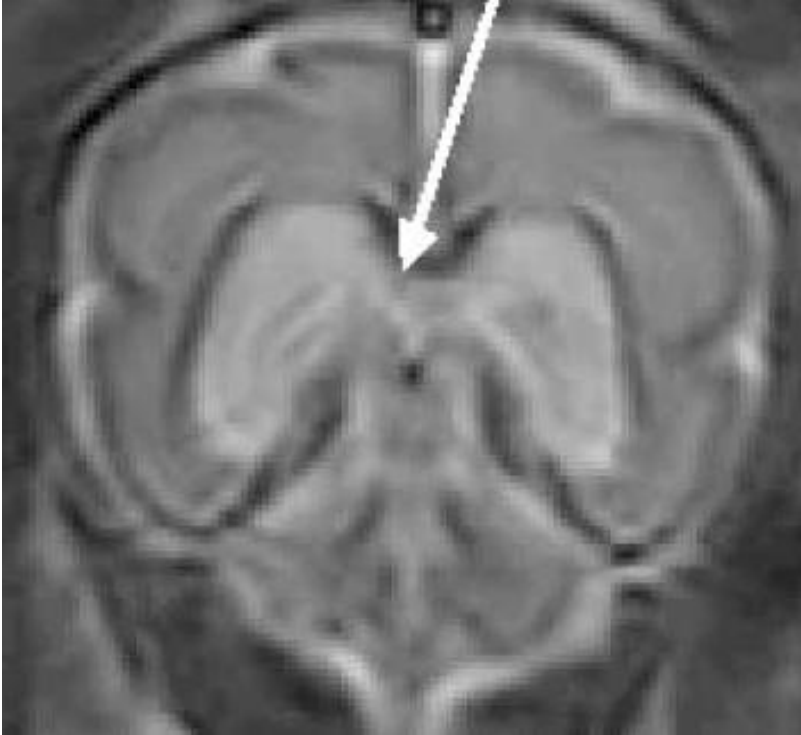
Middle interhemispheric variant

Clip holo_1



MR of middle interhemispheric variant

Single ventricular cavity



An hypoplastic corpus callosum is present



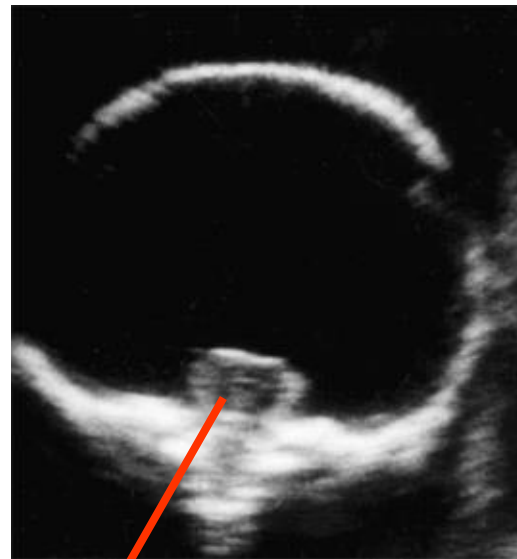
The frontal horns are well developed and there is a partial formation of the interhemispheric fissure; posteriorly there is a common ventricular cavity with hypoplastic thalami.

Reproduced from: Picone O et al: Prenatal diagnosis of a possible new middle interhemispheric variant of holoprosencephaly using sonographic and magnetic resonance imaging. *Ultrasound Obstet Gynecol.* 2006 Aug;28(2):229-31

Differential diagnosis - 1

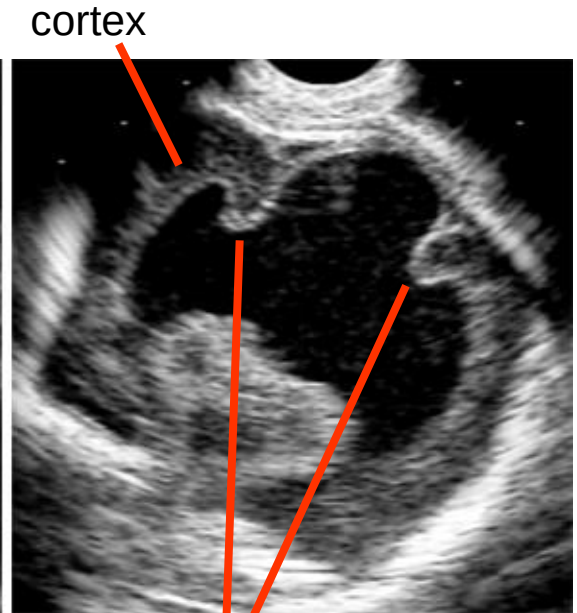
Severe holoprosencephaly with hydrocephalus may have a similar appearance to hydranencephaly; a rim of cortex surrounding the monoventricular cavity and the presence of the hippocampal fornix is suggestive of the former

HYDRANENCEPHALY



Brain stem protruding into fluid filled cranial cavity

HOLOPROSENCEPHALY



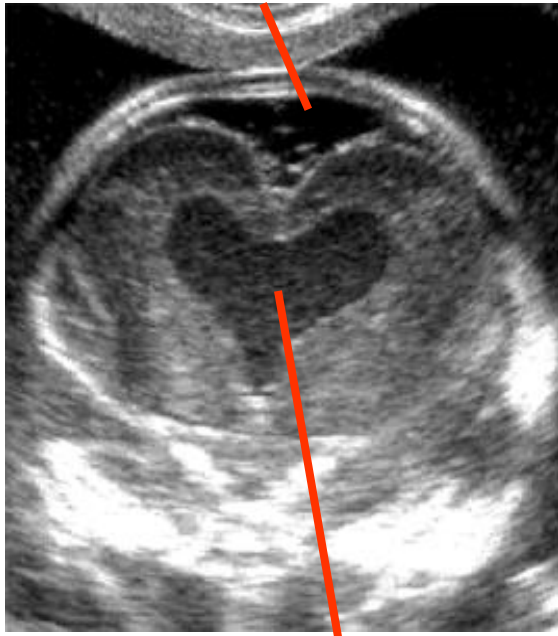
cortex

Hippocampal fornix

Differential diagnosis - 2

HOLOPROSENCEPHALY

No falx



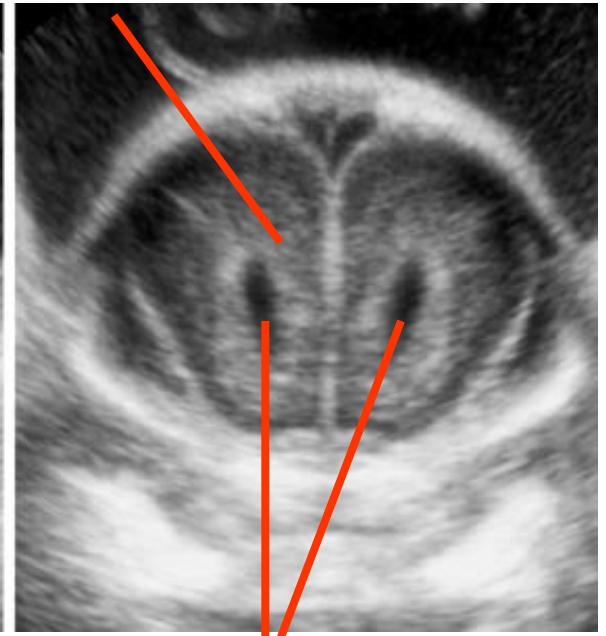
rudimentary ventricles

ABSENCE OF SEPTUM PELLUCIDUM

Falx present



Normal interhemispheric fissure



Anterior separation of frontal horns

Milder forms of holoprosencephaly with well formed frontal horns must be differentiated from absence of the septum pellucidum; in the latter the interhemispheric fissure is complete, the falx cerebri present, the frontal horns are separated anteriorly and the corpus callosum is well formed and complete