3 Normal Early Pregnancy (First Trimester)

Pregnancy Dating

Menstrual age and conceptual age. Because the date of conception is not precisely known, it is customary in obstetrics to date a pregnancy in terms of menstrual age, which is counted from the first day of the last menstrual period. This is commonly referred to as the gestational age. In embryology, the conceptual age is used to designate the true age of the embryo counted from the date of conception (i.e., days postconception). Since the advent of reproductive medicine in the early 1980s, we are able to examine embryos of which the date of conception is precisely known.

Carnegie classification. For the first time, high-resolution transvaginal real-time ultrasound has been used to examine dated human embryos without disturbing their physical integrity or development. The Carnegie classification of the developmental stages in human embryos (5) is based on the parameters of maximum body length, external body shape, and the degree of development of the internal organs. Today this staging system can be correlated with the sonomorphologic findings of body length and body shape in living human embryos. The accurate dating of embryos examined in vivo enables us to check the gestational age figures in the Carnegie classification.

The normal development of the living human embryo will be reviewed in this chapter. Gestational age figures are based on conceptual age, but 14 days are added to obtain the menstrual age that is customarily used in obstetrics. Embryonic morphogenesis through 10 weeks’ postmenstrual age is summarized in Table 3.1.

<table>
<thead>
<tr>
<th>Table 3.1 Synopsis of human embryonic development (10)</th>
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Technique of Transvaginal Ultrasound

Modern ultrasound technology, including the use of high-resolution vaginal transducers, makes it possible to study ultrasound embryology in vivo. Several conditions must be satisfied, however, in order to accomplish this:

- The maternal bladder should be empty. A full bladder would lift the pregnant uterus out of the lower pelvis, and this would require applying an uncomfortable degree of pressure to obtain acceptable images.
- The patient is placed in a lithotomy position or supine with the buttocks elevated on a cushion. This increases the mobility of the vaginal probe in situ.

- Variable-frequency transducers should be set to the highest possible frequency, since higher frequencies correlate with higher image resolution.
- Ultrasound scanners for use in embryology should have a zoom feature that magnifies the image with minimal degradation.
- The examination should be done within the focal zone of the transducer to ensure that very small embryonic structures can be resolved. External pressure may have to be applied in some cases to move the uterus into the focal zone.

In principle, these conditions apply to all applications of transvaginal ultrasound. They are reviewed here because they are of fundamental importance in ultrasound embryology.

Ultrasound Embryology

Embryonic Development in the 5th Week of Menstrual Age (Day 15–21 Postconception)

Today the earliest phase of human development from conception to the initial cell divisions can be observed under the microscope within the framework of reproductive medical procedures (in-vitro fertilization/embryo transfer, IVF/ET; intracytoplasmic sperm injection, ICSI). When natural conception has occurred in the fallopian tube, we cannot directly observe the earliest stages of human embryonic development (Carnegie stages 1–5), and the conceptus can be visualized only after it has implanted in the uterine mucosa.

Chorionic sac. The earliest that we have been able to detect an implanted chorionic sac was on day 16 postconception. The sac diameter at that time was 2 mm (Figs. 3.1, 3.2). Two days later, the chorionic sac had doubled in size and already contained a recognizable yolk sac. The chorion appears as a circular echogenic structure bordering directly on the decidua. High-resolution color Doppler imaging can define maternal blood vessels between the decidua and chorion (Figs. 3.3, 3.4). By establishing this connection with the maternal circulation, the embryo secures the nutritional supply that is necessary for its further development.

Chorion frondosum. A hypoechoic structure in the uterine cavity can be identified as a chorionic sac only if it is surrounded by hyperplastic endometrium and displays an echogenic border, the chorion frondosum. If these signs are disregarded, a fluid collection in the uterine cavity (= pseudogestational sac) in an ectopic pregnancy may be misinterpreted as an intrauterine pregnancy.

Embryonic Development in the 6th Week of Menstrual Age (Day 22–28 Postconception)

Fetal pole. A fetal pole can usually be seen adjacent to the yolk sac at the start of the 6th week of menstrual age. Starting on day 23 postconception, we are consistently able to define a fetal pole in a normal pregnancy (10). It is still broadly adherent to the yolk sac at this time, initially appearing only as an echogenic structure about 1 mm long on the surface of the yolk sac.
**Notochord.** In subsequent days the early embryo appears pear-shaped in coronal section and contains a central notochord (Fig. 3.5). The neural tube begins to close from the rostral direction. This process concludes on day 38 of menstrual age with closure of the inferior neuropore.

**Heart activity.** Embryonic heart beats may be detected as early as the 23rd day postconception and are consistently detected by the 26th day (Fig. 3.6). The development of the cardiac pump and the parallel development of the vascular system provide a mechanism for distributing nutrients throughout the body of the embryo, enabling its further development during subsequent weeks.

### Embryonic Development in the 7th Week of Menstrual Age (Day 29–35 Postconception)

**Separation from the yolk sac.** At the start of week 7 menstrual age, the embryo measures approximately 4 mm in length and its rostral pole begins to fold away from the yolk sac. The increasing longitudinal development of the embryo, made possible by acquiring a nutrient supply from the mother and distributing it via the cardiovascular system, leads to an increasing separation of the embryo from the yolk sac. At first this involves only a curling of the embryo, which is still broadly adherent to the yolk sac (Figs. 3.7, 3.8). But as the connecting stalk develops, the embryo increasingly separates from the yolk sac. Meanwhile the yolk sac is extruded into the extra-amniotic coelom, with only the vitelline duct connecting it to the embryonic vascular system (Figs. 3.10, 3.11).

**C-shaped embryo.** The embryo appears as a C-shaped figure at the end of 7 weeks’ menstrual age (Figs. 3.8, 3.9). The amniotic membrane is still closely attached to the embryo, which consists of a dominant rostral pole and a smaller inferior pole (Fig. 3.12). Viewed in coronal section, limb buds can be distinguished on the lateral aspects of the body at the end of 7 weeks’ menstrual age (Fig. 3.13).

### Embryonic Development in the 8th Week of Menstrual Age (Day 36–42 Postconception)

**Brain.** The external shape of the head changes rapidly during this period, accompanied by rapid development of the embryonic brain. The maximum body length of the embryo is approximately 9 mm. M-mode scanning can already define two cardiac chambers separated by a distinct interventricular septum (Fig. 3.14). As early as day 36 postconception, we have been able to detect body movements reflecting the function of the embryonic central nervous system (10). Brain development proceeds rapidly during this period. By the end of the 8th postmenstrual week, the brain comprises approximately 50% of the total body length. The axis of the head is roughly perpendicular to the axis of the trunk (Figs. 3.15, 3.16). The telencephalon can always be identified by day 40 postconception. It first appears as a rostral, symmetrical outpouching from the prosencephalon and later envelops the diencephalon. Ultrasound confirms the development of the telencephalon by demonstrating the choroid plexus, which appears as a symmetrical, echogenic feature (Fig. 3.17). The rhombencephalon can be identified in the occipital head region (Fig. 3.18). The brain, then, is the first fetal organ system to undergo extensive structural differentiation, consistent with its central regulatory function.

**Limbs.** Brain development is paralleled by an initial segmental development of the embryo, which shows a marked increase in trunk width. Concomitant with this development of the mesoderm, the limbs begin to unfold and can be clearly identified with ultrasound (Fig. 3.19).

### Embryonic Development in the 9th Week of Menstrual Age (Day 43–49 Postconception)

**Limb differentiation.** The embryo measures approximately 16 mm at the start of the 9th postmenstrual week. This stage is marked by changes in external body shape, characterized by longitudinal growth and differentiation of the limbs (Fig. 3.21). Differentiation of the upper limbs precedes that of the lower limbs by several days. But in all cases the upper limbs are clearly subdivided into an upper arm, forearm, and hand, and the lower limbs into a thigh, lower leg, and foot.

**Physiologic umbilical hernia.** A sagittal scan through the umbilical cord insertion at the end of this developmental stage demonstrates the physiologic umbilical hernia, which appears as a hyperechoic structure located in front of the embryonic abdominal wall (Figs. 3.22–3.24).

**Heart.** Also at this time, the embryonic heart completes its complex structural development (1). The ostium primum regresses during the 9th postmenstrual week, and the membranous interventricular septum closes (8), completely separating the systemic circulation from the pulmonary circulation. Further development is manifested by an increase in the epimyocardial mantle. Cardiogenesis is accompanied by a steady rise in the embryonic heart rate, culminating in a maximum rate that is about twice that of the maternal heart rate (Fig. 3.25).

**Brain.** During this stage the embryonic trunk straightens and the head begins to assume a more upright position. The midbrain flexure and dominant rhombencephalic fossa are clearly visible in a midsagittal scan (Fig. 3.26). Also, the contours of the telencephalon becomes increasingly distinct. A coronal scan from the posterior side demonstrates the structures of the axial skeleton (Fig. 3.27). The rhomboid fossa can be defined rostrally by tilting the coronal scan into the transverse plane.

### Embryonic Development in the 10th Week of Menstrual Age (Day 50–56 Postconception)

**Completion of organogenesis.** Organogenesis is completed during the 10th week of menstrual age, and the major embryonic vessels can be defined with power color Doppler (Fig. 3.28). The embryo has a maximum body length of 23–31 mm.

**Limbs.** The limbs, which can be brought together only at the fingers and toes in the 9th postmenstrual week, lengthen and flex at the elbows and knees and can now reach across the fetal midline (Fig. 3.29). Details of the fingers and toes can be appreciated (Fig. 3.30). Isolated arm and leg movements can also be seen and are no longer attributable to spinal reflex actions (11).

**Head.** It is possible to discern the maxilla and mandible, which form the basic framework for the embryonic facial skeleton (Fig. 3.31). Development of the telencephalon becomes increasingly distinct, and the two hemispheres are separated by the falx cerebri (Fig. 3.32).

**Trunk.** A transverse Doppler scan through the embryonic trunk below the liver can clearly demonstrate the umbilical vessels and the adjacent bowel loops that have herniated into the umbilical cord insertion.
(Fig. 3.33). The initially oblong amniotic cavity has expanded to a circular-shaped structure (Fig. 3.33), with a corresponding reduction in the size of the extra-amniotic coelom. The yolk sac is still clearly visible in the extra-amniotic coelom.

### Fetal Development in the 11th Week of Menstrual Age (Day 57–63 Postconception)

**Body shape.** The organs that develop during organogenesis become sonographically visible during the coming weeks of fetal development. The maximum body length measures between 31 and 40 mm, and the BPD ranges from 14 to 18 mm (10) (Fig. 3.34). The contours of the fetal profile become more distinct, although the frontal prominence of the calvaria is still the dominant feature (Fig. 3.35).

**Trunk.** The fetal urinary bladder can be seen in the lower part of the trunk (Fig. 3.36), at this stage consisting only of connective tissue and epithelial cells with no contractile elements (4). The amniotic cavity has expanded markedly, compressing the yolk sac in the extra-amniotic coelom.

### Fetal Development in the 12th Week of Menstrual Age (Day 64–70 Postconception)

The maximum body length in this week is 41–53 mm, and the BPD increases from 18 to 21 mm. The stomach and bladder can be identified within the fetal abdomen (Fig. 3.38), and both kidneys can be seen in the retroperitoneum (Fig. 3.39). Thoracic scans can demonstrate the heart with its two chambers, which can be clearly visualized with color Doppler (Fig. 3.40). In a coronal scan of the face, both eyes can be identified (Fig. 3.41).

### Fetal Development in the 13th Week of Menstrual Age (Day 71–77 Postconception)

**Face.** The fetus at the end of the first trimester has a maximum length of 71 mm and a BPD of 24 mm. The facial physiognomy is clearly discerned on a midsagittal scan through the head owing to the development of the facial skeleton and soft tissues (Fig. 3.42).

**Abdomen and pelvis.** The physiologic umbilical hernia can no longer be seen (Fig. 3.43). Discontinuities in the abdominal wall must now be classified as fetal pathology (6). Color Doppler imaging can define the principal blood vessels (Fig. 3.44). Smooth-muscle cells can be detected in the wall of the urinary bladder, but they still lack an autonomous nerve supply (3). The external genitalia are grossly visible at the end of 13 weeks (9).

### Clinical Importance of Ultrasound Embryology

Diagnostic ultrasound in the first trimester gives doctors and parents a detailed look at early human development and provides impressive documentation of this period. A knowledge of the normal development of the human embryo on ultrasound images forms the basis for the early detection of embryofetal pathology.

Because the morphogenesis of the embryo proceeds at a rapid pace, it is very useful for the dating of embryos. This requires a very high degree of morphologic expertise, however, and so the age of a pregnancy in routine settings is determined by measuring the greatest embryonic length and the BPD. The essential aspects of morphologic development are reviewed in Table 3.2.

### Table 3.2 Developmental milestones in the first trimester (adapted from 7, 9, and 10)

<table>
<thead>
<tr>
<th>Ultrasound finding</th>
<th>Earliest visualization (menstrual age)</th>
<th>Definite visualization (menstrual age)</th>
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<tbody>
<tr>
<td>Chorionic cavity</td>
<td>Day 30</td>
<td>Day 32</td>
</tr>
<tr>
<td>Yolk sac</td>
<td>Day 32</td>
<td>Day 34</td>
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<tr>
<td>Fetal pole</td>
<td>Day 35</td>
<td>Day 37</td>
</tr>
<tr>
<td>Heart activity</td>
<td>Day 37</td>
<td>Day 40</td>
</tr>
<tr>
<td>Limbs</td>
<td>Day 47</td>
<td>Day 53</td>
</tr>
<tr>
<td>Telencephalon</td>
<td>Day 50</td>
<td>Day 54</td>
</tr>
<tr>
<td>Movements</td>
<td>Day 50</td>
<td>Day 56</td>
</tr>
<tr>
<td>Stomach</td>
<td>Week 10</td>
<td>Week 11</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>Week 11</td>
<td>Week 12</td>
</tr>
<tr>
<td>Genitalia</td>
<td>Week 12</td>
<td>Week 14</td>
</tr>
</tbody>
</table>

### References

Week 5 of menstrual age

Fig. 3.1 Transvaginal sonogram of an embryo that implanted in the decidua of the posterior uterine wall on the 17th day after conception (from 10, with permission of Springer Verlag, Heidelberg).

Fig. 3.2 Embryo prior to reorganization (after 2).

Fig. 3.3 Two days later, the embryo from Fig. 3.1 shows the development of a yolk sac. The implantation vessel is also definable by color Doppler imaging (from 10, with permission of Springer Verlag, Heidelberg).

Fig. 3.4 Embryo after reorganization (after 2).

Week 6 of menstrual age

Fig. 3.5 Embryo implanted in the uterus on postmenstrual day 40. The pear-shaped fetal pole is visible on the yolk sac.

Fig. 3.6 Embryo implanted in the uterus on postmenstrual day 40. The M-mode trace indicates an embryonic heart rate of 105 bpm.

Week 7 of menstrual age

Fig. 3.7 Embryo on postmenstrual day 43. The body is still broadly opposed to the yolk sac and exhibits lوردosis.

Fig. 3.8 By postmenstrual day 47, the embryo has separated from the yolk sac and shows a C-shape curvature.
Fig. 3.9 Development of the umbilical cord, viewed from the left side (after [2]).

Fig. 3.10 On postmenstrual day 48 the yolk sac is in the extra-amniotic coelom and is linked to the embryo by the vitelline duct (arrow).

Fig. 3.11 Course of the vitelline vein and umbilical vein (after [2]).

Fig. 3.12 The embryo is closely enveloped by the amniotic membrane (arrow) on postmenstrual day 48.

Fig. 3.13 Coronal scan through the embryo on postmenstrual day 48 demonstrates upper and lower limb buds (arrows).

**Week 8 of menstrual age**

Fig. 3.14 M-mode scan of the biventricular embryonic heart on postmenstrual day 55. The cardiac diameter is 1.8 mm.

Fig. 3.15 Midsagittal scan through the embryo on postmenstrual day 53 shows the dominance of brain development.
Fig. 3.16 Embryo 9.6 mm long, viewed from the right side (after [2]).

Fig. 3.17 Coronal scan on postmenstrual day 53 shows the telencephalon with symmetrical development of the cortical anlage. Arrows indicate the choroid plexus on each side.

Fig. 3.18 Coronal scan through the posterior superior fossa on postmenstrual day 55 demonstrates the rhombencephalon.

Fig. 3.19 The limbs are clearly identified on postmenstrual day 56 (short arrows: arms; long arrows: legs).

Fig. 3.20 On postmenstrual day 56, the embryo is surrounded by the amniotic membrane (arrows). The vitelline duct and yolk sac have been displaced into the chorionic cavity.

Week 9 of menstrual age

Fig. 3.21 On postmenstrual day 60, the upper limb of the embryo is seen to consist of three segments.

Fig. 3.22 Transverse scan through the abdomen of the embryo on postmenstrual day 60 shows an echogenic bulge in the umbilical area (arrow).
Fig. 3.23 Embryo 24 mm long on postmenstrual day 65. The physiologic umbilical hernia at this stage has expanded the fetal end of the cord.

Fig. 3.24 Power Doppler at the umbilical ring defines the embryonic vascular system and the physiologic umbilical hernia.

Fig. 3.25 Embryonic heart rate as a function of menstrual age (from [10], with permission of Springer Verlag, Heidelberg).

Fig. 3.26 Sagittal scan through the embryo on postmenstrual day 61 demonstrates the rhombencephalon (long arrow) and telencephalon (short arrow).

Fig. 3.27 Axial skeleton of the embryo on postmenstrual day 60.

Fig. 3.28 Power Doppler on postmenstrual day 66 demonstrates the embryonic vascular system with the heart, aorta, umbilical artery, umbilical vein, and carotid artery.

Fig. 3.29 In a coronal scan on postmenstrual day 66, the arms and legs have grown so long that they can reach across to the contralateral side.
Fig. 3.30  Four fingers (arrows) can be seen on postmenstrual day 66.

Fig. 3.31  Sagittal scan through the embryonic face on postmenstrual day 66 defines the basic structures of the facial skeleton with the mandible and maxilla.

Fig. 3.32  By day 67 the telencephalon has increased markedly in size and is beginning to enclose the diencephalon. Both hemispheres are clearly separated by the falx cerebri.

Fig. 3.33  The amniotic membrane envelopes the embryo on postmenstrual day 66, appearing nearly circular (arrows). The extra-amniotic coelom is considerably more echogenic than the amniotic cavity. The cord insertion is thickened and shows the physiologic umbilical hernia.

**Week 11 of menstrual age**

Fig. 3.34  Transverse scan through the head of the embryo on postmenstrual day 72 for measuring the biparietal diameter. Both halves of the brain are clearly separated, and the cavum septi pellucidi is defined.

Fig. 3.35  Facial profile of an embryo on postmenstrual day 73.

Fig. 3.36  Coronal scan of the embryo on postmenstrual day 72. The urinary bladder appears as a hypoechoic structure in the lower pelvis (arrow).

Fig. 3.37  On postmenstrual day 72 the yolk sac (arrow) is compressed between the amniotic and chorionic membranes and is undergoing regression.
Week 12 of menstrual age

Fig. 3.38  Coronal scan through the embryonic abdomen on postmenstrual day 81. The gastric bubble (long arrow) is visible in the left upper abdomen and the urinary bladder (short arrow) in the lower abdomen.

Fig. 3.39  Coronal power Doppler scan through the retroperitoneum on postmenstrual day 81 demonstrates the aorta, the aortic bifurcation, and both renal arteries. The kidneys are hyperechoic.

Fig. 3.40  Intrathoracic color Doppler scan on postmenstrual day 82 demonstrates the heart with its separate ventricular systems.

Fig. 3.41  Coronal facial scan on postmenstrual day 81 demonstrates both eyes.

Week 13 of menstrual age

Fig. 3.42  Facial profile on postmenstrual day 91.

Fig. 3.43  Umbilical cord insertion on postmenstrual day 88. The abdominal wall is closed.

Fig. 3.44  Thoracoabdominal vessels of a fetus on postmenstrual day 91.