Ultrasonographic diagnosis of miscarriage

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Summary
Miscarriage is the most frequent complication in pregnancy. Ultrasound is the main diagnostic tool used in diagnosing the various types of miscarriage and, to some extent, in the diagnosis of the cause. Knowledge of the normal sonographic features of early pregnancy is essential for diagnosing pathologic development. The physiologic development of the endometrium, of the gestational and yolk sac, of embryonic growth and heartbeat are sonographically documented. The sonographic signs of miscarriage and their prognostic value for pregnancy outcome are discussed in this article.

If there is only a single sonographic sign of miscarriage and the clinical features are asymptomatic, a follow-up examination should be offered before the abortion is confirmed. The only sonographic sign that is a confirmation of miscarriage is the loss of fetal heart action. Doppler examination of the uterine arteries shows a large overlapping of the normal and pathologic velocity flow profiles in normal pregnancies and pregnancies that end in miscarriage. This examination is, therefore, of no prospective value in the diagnosis of fetal loss. 3D studies reveal additional information in the first trimester of pregnancy. Nevertheless, there are very few data on the subject.

Abortion – definition, classification and epidemiology
Miscarriage is the most common complication to occur during pregnancy. It is defined as the non-artificial loss of pregnancy before the fetus has developed sufficiently to survive. The limits of fetal viability are based on a fetal weight of 500 g. If the fetal weight is not known, the 22nd week of pregnancy post menstruationem (p.m.) is used as a basis. There are several classifications specifying miscarriage, which are, however, of varying clinical relevance: abortions can be classified as sporadic or habitual, according to their frequency, the latter being defined as “at least three consecutive abortions”. Some authors favour an alternative definition that describes habitual abortion as two consecutive abortions in women over the age of 30 (Brock and Holloway 1990; Knudsen et al. 1991; Scott and Branch 1998).
According to the stage of the pregnancy at which they occur, abortions are classified either as early (during the 1st trimester) or late abortion (the miscarriage occurs at a later stage).

Both the above-mentioned classifications are clinically relevant, as not only do the causes of sporadic and habitual abortion differ, but the causes of early and late abortion also vary. This has consequences for diagnostic management, as well as for the prophylactic and therapeutic measures taken.

Depending on the clinical stage at which it occurs, abortion is classified as follows: abortus imminens, abortus incipiens, abortus incomplectus, abortus completus, and missed abortion. Sonography is the method of choice in the diagnosis of these different types of miscarriage. This classification is of clinical importance as the various types of miscarriage require different methods of treatment.

The incidence of clinically symptomatic spontaneous abortion is 10% to 15%, and that of habitual abortion 3% to 5% (Petrozza 2006). So-called preclinical abortions (there is no clinical recognition of the miscarriage) are characterized by the loss of the embryo before implantation or between implantation and the next menstruation. The rate of preclinical abortion is correspondingly higher (>50% to 5%) (Edmonds et al. 1982; Petrozza 2006).

The incidence of miscarriage increases with the age of the mother and the presence of certain predispositive factors that are possible etiological causes of abortion. The latter are mainly found in the group of women that experience habitual abortion. These include anatomic alterations of the uterus, immunologic and endocrinologic factors, thrombophilia, genetic aberrations and possibly microbiologic causes (Table 1). The fear of a repeated miscarriage after a previous abortion is also discussed as being a negative prognostic psychological factor.

Table 1: Habitual abortion: predispositive factors (according to Heilmann 2008)

<table>
<thead>
<tr>
<th>Anatomic Factors</th>
<th>Genetic factors</th>
<th>Endocrinologic factors</th>
<th>Immunologic factors</th>
<th>Thrombophilia</th>
<th>Microbiologic factors***</th>
<th>Psychological factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Uterus septum</td>
<td>• Balanced translocation</td>
<td>• Hyper-/hypothyroidism</td>
<td>• Alloimmunologic***</td>
<td>• Factor V Leiden mutation</td>
<td>• Ureaplasma urealyticum</td>
<td>• Is more likely to be the cause of a late abortion</td>
</tr>
<tr>
<td>• Bicornate uterus</td>
<td>• Trisomy**</td>
<td>• PCO syndrome/metabolic syndrome</td>
<td>• Autoimmunologic</td>
<td>• Prothrombin mutation</td>
<td>• Chlamydia trachomatis</td>
<td>• More common in sporadic abortion</td>
</tr>
<tr>
<td>• Uterus duplex</td>
<td>• X0-monosomy**</td>
<td></td>
<td>• Antiphospholipid antibody syndrome</td>
<td>• Protein S deficiency</td>
<td></td>
<td>• Controversial discussion/inconclusive data</td>
</tr>
<tr>
<td>• Intrauterine adhesions</td>
<td>• Polyplody**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>• Myomatous uterus</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>• Insufficient closure of the cervix*</td>
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</tr>
</tbody>
</table>

Sonography is a basic tool in the diagnosis of the causes of abortion and predispositive factors when searching for anatomic alterations and genetic anomalies. Ultrasound plays an accompanying therapeutic role as a form of “tender loving care” when a patient fears a repeated miscarriage. Regular examinations providing evidence of an intact pregnancy have a prognostically favorable effect on the outcome of the pregnancy and also strengthen the patient’s confidence in an uncomplicated course of the pregnancy (Jauniaux et al. 2006; Li 1998).

The rate of abortion increases with the number of previous abortions. The rate is between 10 and 15% in every pregnancy, increasing to 12% to 24% after one, to 19% to 35% after two, and to 25% to 46% after three abortions (Marzusch 2004).
Sonography of undisrupted early pregnancy and prognostically unfavorable parameters

Diagnosis and classification of a pathologic state are impossible without thorough knowledge of normal findings. Furthermore, it is indispensable to generate accurate reference data according to the specified guidelines, to provide an accurate diagnosis of abortion. The sonographic characterization of a normal early pregnancy is therefore illustrated below, and the sonopathology of abortion during the 1st trimester is subsequently described.

The patient should undergo a transvaginal sonographic examination, and the bladder should be empty. A full bladder displaces the uterus from the pelvis, thus reducing the assessability of the organs of the small pelvis and the examination may be unpleasant for the patient. The patient should be placed in the lithotomic position, if possible in a gynecological chair; a wedge may be placed under the patient’s pelvis. This should ensure sufficient mobility of the transducer.

Secretory transformation of the endometrium

Even before the gestational sac is visible, the secretory transformation of the endometrium may be regarded as a condition of undisrupted implantation. The secretory transformation of the endometrium is characterized by an echogenic homogeneous structure, with the loss of the middle-echo that is characteristic of ovulation. The endometrial thickness is a maximum of 15 mm between the 20th and 25th day of the cycle, thereafter decreasing slightly (Deichert et al. 1986) (Fig. 1).

Figure 1: Secretory transformation of the endometrium, longitudinal section of the uterus

A decrease in the thickness of the endometrium or an inhomogeneity in the endometrial structure and the loss of the echogenic texture and a verified β-HCG are evidence of a preclinical abortion, even before the gestational sac can be shown.

Gestational sac

It is not possible to show the gestational sac until it has grown to at least 2 mm, in the 5th week p.m. (32nd-36th day p.m.). At this early stage, the gestational sac is shown as an echogenic ring structure, corresponding to the trophoblastic seam, and the chorionic cavity, which is echo-free (Fig. 2). In contrast to the “pseudo-gestational sac” at the border of the endometrial cleft in extrauterine pregnancy, the gestational sac is located either in the front or back endometrial lobe, therefore off-center. An undisrupted placenta and embryo are found in a cranial position in the inner cervix. In the sonographic image it is found over the insertion point of the uterine arteries (Jurkovic and Mavrellos 2007). To determine whether the intrauterine position of the gestational sac is correct an exact sagittal image of the uterus should be made to trace the continuity of the endometrium from the cervix to the fundus (Fig. 2). A coronary plane or TUI (“Tomographic Ultrasound Imaging”) in 3D ultrasound may also be helpful.

Figure 2: Gestational sac (>), located in the back endometrial lobe, diameter 2.6 mm, longitudinal section of the uterus

The inner to inner margin measurements are taken, i.e. only the chorionic cavity is measured, without the trophoblastic seam. The measurements should be taken on two planes with three measurements, the lines horizontal to one-another, to arrive at the mean value. It is practical to show both planes in a double image (Fig. 3). In the early stages, the gestational sac is round, it then takes on an ellipsoid shape. The growth of the chorionic cavity is linear, increasing at 1.1 mm per day (Jauniaux and Jurkovic 1997; Nyberg et al. 1987) and correlates closely with the increase in the β-HCG level.
After the gestational sac can be shown in the sonogram, the abortion rate is still as high as 11% (Goldstein 1994). Signs that indicate an abortion include a gestational sac that is too small (Nyberg et al. 1987; Varelas et al. 2008), malformation of the placenta and embryo (Fig. 4), an inadequate pace of growth (significantly below 1.1 mm per day) (Nyberg et al. 1987) and an atypical location (Table 2). Any of these signs found individually or in combination, are prognostically unfavorable for the further course of the pregnancy. However, if the clinical symptoms are normal and an abortion is not confirmed by the sonographic findings, a follow-up examination is recommended. Before the miscarriage is confirmed on the basis of the follow-up examination, the individual abnormal sonographic findings should not be discussed with the pregnant woman.

Gestational sacs that are too small are also found in pregnant women with chromosomal anomalies (connection with triploidy and trisomy 16) (Dickey et al. 1994; Jauniaux et al. 2003a).

Yolk sac
The secondary yolk sac is the first structure in the gestational sac that is visible in the sonogram image as a thin, echogenic circular ring structure, even before the embryo (Fig. 5). There should always be evidence of the yolk sac when the chorionic cavity has reached a mean diameter of 10 mm (Bree and Marn 1990; Jauniaux et al. 1991). The yolk sac is situated in the extra-embryonic coelum, which

Table 2: Early pregnancy: normal and pathological findings of abortion

<table>
<thead>
<tr>
<th></th>
<th>Normal findings</th>
<th>Characteristic signs of abortion</th>
</tr>
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<tbody>
<tr>
<td><strong>Endometrium</strong></td>
<td>Secretory transformation</td>
<td>Inhomogeneity</td>
</tr>
<tr>
<td></td>
<td>Echogenic, homogeneous</td>
<td>Loss of the echogenic texture</td>
</tr>
<tr>
<td></td>
<td>a.p. ca. 15 mm</td>
<td>Decrease in a. p. size</td>
</tr>
<tr>
<td><strong>Chorionic cavity</strong></td>
<td>Location: off-center</td>
<td>Displacement</td>
</tr>
<tr>
<td></td>
<td>(front/back endometrial lobe)</td>
<td></td>
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<tr>
<td></td>
<td>Cranial to the inner cervix</td>
<td></td>
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<tr>
<td></td>
<td>Shape: round – ellipsoid</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Growth: 1.1 mm/day</td>
<td></td>
</tr>
<tr>
<td><strong>Yolk sack</strong></td>
<td>Size: ca. 2 mm</td>
<td>Lack of yolk sac</td>
</tr>
<tr>
<td></td>
<td>(5th week of pregnancy)</td>
<td>Size: &gt; &gt; 7 mm*, very small*</td>
</tr>
<tr>
<td></td>
<td>Shape: circular/ball-like</td>
<td>Irregular shape*</td>
</tr>
<tr>
<td><strong>Embryo/crown-rump length</strong></td>
<td>Latest findings from the 6th week of pregnancy</td>
<td>Lack of embryo</td>
</tr>
<tr>
<td></td>
<td>Growth within the reference range</td>
<td>CRL is too small (Cave: accurate gestational age)</td>
</tr>
<tr>
<td><strong>Cardiac activity</strong></td>
<td>Latest findings from 5 mm</td>
<td>Lack of cardiac activity</td>
</tr>
<tr>
<td></td>
<td>CRL/18 mm CCV</td>
<td>Brady-/tachycardia</td>
</tr>
<tr>
<td><strong>Hematoma</strong></td>
<td>Location: subchorial/retroplacental, retroamnial</td>
<td>Prognostic factors: size, location</td>
</tr>
</tbody>
</table>

* Controversial discussion/inconclusive data

CCD: diameter of chorionic cavity; CRL: crown-rump length
corresponds to the chorionic cavity. When it is possible to determine the amnion in the sonogram, the extra-embryonic coelum and the yolk sac are located in the cleft between the amnion and the chorion (Fig. 6).

The outer to outer margins of the yolk sac are measured. Growth is initially linear, flattening out after the 8th week p.m. In the 5th week p.m., the size of the yolk sac is ca. 2 mm, increasing to a maximum of ca. 7 mm (Bahlmann et al. 1997). After the 13th week p.m., there is no trace of the yolk sac. This is possibly due to mechanical factors (convergence of the amnion and chorion) as well as to physiologic degenerative processes (Jauniaux et al. 2005).

The lack of a yolk sac is regarded as being prognostically unfavorable as it is an indication of a blighted ovum. There is controversial discussion in the reference literature as to whether an abnormally sized yolk sac is evidence of an abortion. Some authors have found a connection between a yolk sac that is too large and abortion and chromosomal anomaly, which has, however, not been confirmed by other studies (Kucuk et al. 1999; Lindsay et al. 1988; Reece et al. 1988; Rempen et al. 1988; Stampone et al. 1996) (Fig. 7). A significantly smaller yolk sac appears to be an indication of a disrupted pregnancy (Rempen et al. 1988), as is a yolk sac with an irregular shape (Lindsay et al. 1988).

If the size or shape of the yolk sac is the only abnormal sonographic or clinical finding, a further examination is indicated. This should be discussed very carefully with the pregnant woman in order not to unduly unsettle her.

Embryo and crown-rump length (CRL)

The earliest evidence of the embryo is available when the CRL reaches a size of 1 to 2 mm in the 6th week p.m. Initially, the embryo appears as a thickening directly on the yolk sac (see Fig. 5). In the 7th week, the embryo moves away from the yolk sac by developing a hypophysial stalk, taking on a C-shape (Fig. 8). At this point, the amnion is still located close to the embryo (Merz 2002).

The CRL can be measured accurately by a mediosagittal section from the cranial to the caudal pole of the embryo (Fig. 8). Initially, however, it is not the CRL that is measured, but the total length of the embryo. It is only possible to measure the actual CRL when the extremities develop. Mistakes in measurement can occur if there is a great flexion

Figure 5: Yolk sac with adjacent embryo
Figure 6: Yolk sac in the extra-embryonic coelum, amniotic membrane and embryo
Figure 7: Enlarged yolk sac in a missed abortion, 3D image

Figure 8: Measurement of the crown-rump length (8th week of pregnancy)
or deflexion of the embryo or fetus, or if the yolk sac is included in the measurement (Merz et al. 2002). The CRL is the parameter best suited to determine the gestational age in the 1st trimester. In the interval between the 5th and 95th percentile the age of gestation (+/- 6 days) can be established by measuring the CRL, while the variability using the measurement of the chorionic cavity is 10 days and 8 days if the biparietal diameter is measured (Rempen 1991). Accurate knowledge of the gestational age forms the basis of obstetric management. The question as to whether there has been a missed abortion or blighted ovum can also only be answered in correlation with an accurate gestational age.

The rate of abortion in cases where the CRL is greater than 5 mm is still 7.2%. It decreases to 3.3% when the CRL is between 6 to 10 mm or to 0.5% if the CRL is over 10 mm (Goldstein 1994).

It is presumed that there is a connection between a CRL that is too small for the gestational age and aneuploidy (Bahado Singh et al. 1997). A small CRL is also a prognostically unfavorable sign for miscarriage. If the CRL deviates by more than –2 standard deviations (SD) from the expected size, spontaneous abortion occurs in up to 13.7% of the pregnancies (Reljic 2001). Differential diagnostics must be performed to distinguish this early delay in growth from an inaccurate due date. This is carried out by further monitoring the growth dynamics at intervals of one to two weeks. Other signs of abortion or a chromosomal anomaly should be excluded. If an early restriction in growth is suspected, further ultrasonographic examinations are indicated, according to the recommendations of the German Society for Ultrasound in Medicine (DEGUM) (Merz et al. 2004).

Cardiac activity
Embryonic cardiac pulse activity can be shown by sonography from the 36th day p.m. at the earliest, or from a CRL of 2 mm, and should be evident, at the latest, after the 40th day p.m., when the CRL is 5 mm or when the chorionic cavity has reached a mean diameter of 18 mm (Tezuka et al. 1991). Cardiac frequency is dynamic in the first trimester. At the first sign of cardiac activity the frequency is ca. 110 beats per minute (bpm), increasing to up to 180 bpm around the 9th week and then decreasing up to the 13th week to 150 to 160 bpm (Tezuka et al. 1991). These dynamics are caused by the variation in the development of the sympathetic and parasympathetic nervous systems during this period.

Bradydysrythmia or deviations from the normal pattern of cardiac frequency are symptomatic signs of abortion (Tezuka et al. 1991). A loss of cardiac activity is a sure sign of an abortion. Deviations from the normal pattern of cardiac frequency during the 1st trimester have, however, also been found in fetuses with aneuploidy (Liao et al. 2000). If an abnormal pattern of cardiac frequency is suspected, the practical procedure is identical to that in the case of a CRL that is too small (see above).

Amniotic cavity
The amnion first appears as an echogenic membrane from the 7th week p.m. onwards, when it no longer closely surrounds the embryo. The amniotic fluid is echo-free. The fluid in the chorionic cavity can produce fine inner echoes. The growth of the amniotic cavity is also linear, like the chorionic cavity, but grows more quickly due to the onset of metanephric urine production. Thus, in the 14 - 0 week of pregnancy, at the latest, the amniotic and the chorionic membrane become fused, and the chorionic cavity is no longer depicted filled with fluid (Bahlmann et al. 1997; Jauniaux and Gulbis 2000).

There is discussion that amniotic cavities that are too large and a lack of fusion of the amnion and the chorion after the 15th week p.m. are prognostically unfavorable factors for the course of pregnancy 1992).

Correlation of clinical symptoms and the ultrasonographic images of various types of abortion

Vaginal Bleeding
This is the main symptom of a disrupted pregnancy. The sonographic correlate of vaginal bleeding may be a subchorial, retroplacental or retroamniial hematoma, a chorion or placenta in a low position that affects the inner cervix, or bleeding associated with different kinds of abortions. In a prospective study, vaginal bleeding was registered in 21% of the pregnancies examined. Of these, 57.3% ended in abortion (Everett 1997). On the other hand, vaginal bleeding is seen in ca. 50% of intact intrauterine pregnancies, 20% to 35% are cases of blighted ova and a further 25% to 30% are cases of missed abortion. Among the women who experience vaginal bleeding, in 1% to 3% it is a symptom of extraterine gravidity and in 1% to 3% a symptom of a hydatid mole (Hansmann et al. 1985).

Causes of genital or extragenital bleeding that are not connected with the pregnancy should also be excluded.

Subchorial hematoma
The sonographic image of a subchorial hematoma shows a hypoechoic or echo-free halfmoon- or wedge-shaped structure between the chorionic cavity and the myometrium (Fig. 9). Fresh hematomas are echo-free, whereas with increasing organization of the hematoma, hypoechoic, inhomogeneous internal structures develop. Differentiating between a hematoma and the placenta sometimes presents difficulties, which can, however, be solved by using the color Doppler (which can depict intraplacental vessels). There is no evidence of vessels in a hematoma. Various studies have made different evaluations of the
prognostic significance of subchorial hematoma. The main point examined was the correlation between the size of the hematoma and the outcome of the pregnancy or the complications that arose (Abu Yousef et al. 1987; Ball et al. 1996; Bennett et al. 1996; Mantoni and Pedersen 1981). Depending on the stage of pregnancy at which the hematoma develops, the overall rate of abortion is between 3% and 44% (Pearlstone and Baxi 1993).

It would also appear, however, that the location of the hematoma has a prognostic significance with regard to the future course of the pregnancy. A hematoma cranial to the gestational sac (fundus or corpus uteri) appears to be associated with a worse prognosis than a hematoma in a caudal position (Kurjak et al. 1996). Furthermore, a hematoma in a peripheral position, situated at a distance to the attachment of the umbilical cord, is more often found in threatened abortion and has a better prognosis than a hematoma in a central position (Jauniaux et al. 2005). The preterm loss of closure of the spiral arteries by trophoblast cells is the pathophysiological explanation of this observation. The resulting intervillous vascularization increases the oxygen partial pressure in the intervillous space at an unphysiological early stage. As a result, oxygen radicals interfere with placentation. In contrast, an undisrupted pregnancy develops in an environment low in oxygen until about the 10th week because the spiral arteries are closed by trophoblast cells. The spiral arteries do not open until the 10th week, initially on the periphery and then progressively towards the center of the chorionic cavity. The disruption of placentation appears to be more pronounced the sooner the central spiral arteries open and intervillous vascularization of the part of the chorion close to the umbilical cord takes place. Additional effective pathophysiological factors of subchorial hematoma include mechanical compression and chronic inflammation (Jauniaux et al. 2005).

Abortus imminens
The main clinical symptom of an imminent abortion is vaginal bleeding and/or abdominal pain. In the sonogram one finds an intact pregnancy and possibly, in addition, a subchorial hematoma (see above), a retroamnial hematoma, or the chorion or placenta is in a low position.

Apart from diagnosing an abortus imminens, sonography has the task of monitoring the progress, i.e. the dynamics of the size and structure of the hematoma and the normal or abnormal development of the embryo, yolk and gestational sacs.

Abortus incipiens
The clinical characteristics of this type of abortion are vaginal bleeding and pain. The characteristic sonographic sign is malformation of the amniotic cavity, which is located in an atypical low position (see Fig. 4). The decidualized endometrium is, depending on the strength of the bleeding, already inhomogeneous (Merz 2002). The loss of the pregnancy can no longer be avoided.

Abortus completus
Vaginal bleeding and abdominal pain are clinically notable factors of a complete abortion. The sonogram shows an endometrium that is less than 15 mm in width, and there is no longer any evidence of the pregnancy. The color Doppler and frequency spectral analysis may be an aid in the search for traces of the pregnancy (Merz 2002). Such residues are characterized by increased vessel density with low impedance. If no residues can be found in the sonogram, curettage is unnecessary. Thus, superfluous curettage may be avoided with the aid of sonography (Nielsen and Hahlin 1995).
Abortus incompletus
The clinical correlate of incomplete abortion is vaginal bleeding and/or pain. In the sonogram the contents of the cavity are inhomogeneous to a varying degree, which corresponds to the presence of blood, blood clots, and residual tissue from the pregnancy. Residual tissue is echogenic, while fresh blood is echo-free; older blood clots are, in contrast, hypoechoic. There may still traces of the amniotic sac. Residual tissue from the embryo/fetus can also be identified by using the color Doppler (see above).

Blighted ovum
Bleeding and pain are less frequent in this type of miscarriage. Some patients describe the loss of pregnancy symptoms. In the sonogram one usually finds a (for the stage of the pregnancy) normally developed but empty amniotic cavity: the yolk sac and embryo are lacking. A blighted ovum should not be diagnosed at too early a stage. If the mean diameter of the chorionic cavity is < 10 mm, the calculated date of conception may have been inaccurate; thus, the pregnancy may simply be at an early stage, a stage at which the yolk sac is not necessarily physiologically detectable. If the clinical symptoms are normal, a follow-up examination should be carried out a week later, at the earliest.

Missed abortion
The clinical symptoms of the so-called missed (delayed) abortion correspond to those of a blighted ovum. Sonographic criteria are either a lack of cardiac activity and a CRL of ≥ 6 mm or a lack of embryonic growth and a CRL of ≤ 6 mm. The CRL is also usually too small for the calculated gestational age (Fig. 11). As the chorionic cavity may continue to develop despite the death of the embryo, a chorionic cavity is often found that is too large for the CRL. Color Doppler sonography may also be useful in confirming the lack of cardiac activity. Due to its high ultrasonic intensity, the color Doppler should not be used routinely, nor should it be used if the B-image shows cardiac activity, but only to secure a diagnosis when the findings are ambiguous. In such cases, a follow-up examination is recommended if the gestational age is unclear, if there is no definite evidence of a missed abortion, and the clinical symptoms are normal.

Sonography in the diagnostics of the causes of miscarriage
There are a series of predispositive factors that may lead to miscarriage (see Table 1). There is, hereby, a great difference in the weighting of the causes of sporadic and habitual abortion. For instance, numerical chromosomal aberrations are responsible for 50% to 70% of sporadic abortions but only for 3% to 5% of habitual abortions. Anatomic factors are more often the cause of habitual abortion than of sporadic abortion. In both types of miscarriage, however, in the majority of cases the cause cannot be determined. 40% to 60% of the cases of habitual abortion are idiopathic in type. There follows a description of the causes that can either be identified using sonography or for which sonography may provide evidence.

Genetic causes
As there is a strong natural selection against embryos with chromosomal anomalies, this is the most common cause of miscarriage.

The earlier an abortion takes place, the more likely that it is due to chromosomal causes. In cases of sporadic spontaneous abortion in the 1st trimester, chromosomal aberrations are found in about 50% of the cases and in abortions in the 2nd trimester the figure is about 20%. The main cause is trisomy, the frequency of which increases with maternal age, as well as polyploids, monosomy, and structural aberrations. Structural chromosomal aberrations are found (Wieacker et al. 2005) in about 5% of the spontaneous abortions associated with chromosomal findings.

In cases of habitual abortion there is an increased likelihood of a balanced structural chromosomal aberration in one parent. It is typical to find Robertson translocations, reciprocal translocations, and inversions (Wieacker et al. 2005).

Due to technical progress in vaginal sonography, differentiated assessment of the embryo and the fetus is possible in the 1st trimester. Furthermore, parallel to the spread of
better technology, the experience potential with regard to normal sonographic anatomy and morphological anomalies, as well as with respect to genetic aberrations in the 1st trimester, has also grown.

The widespread nuchal translucency is the leading marker of chromosomal aberrations, primarily of trisomy 21. If such or other evidence of chromosomal anomaly is identified during a screening examination or prenatal care, or in the nuchal translucency measurement of the risk of trisomy 21, 13 or 18, according to DEGUM recommendations a further sonographic examination is indicated between the 12th and 14th week of pregnancy (Merz et al. 2004). This may result in invasive diagnostics to exclude or to provide evidence of chromosomal anomaly. Other sonographic markers of chromosomal anomaly include dysplasia of the fetal nasal bone, tricuspid regurgitation and a pathological flow in the ductus venosus (Nikolaides 2005; see also www.fetalmedicine.com). Furthermore, major anomalies, which may also provide evidence of chromosomal anomaly or the cause of spontaneous abortion, can be identified during ultrasonographic examination, as early as the 1st trimester.

Anatomic causes
Congenital or acquired uterine anomalies are responsible for about 15% to 30% of habitual abortions (Petrozza 2006). The seriousness of the risk of miscarriage depends on the type of uterine anomaly. The rate of miscarriage in the case of a uterus septum is between 26 and 94%, in the case of a bicornate uterus between 28 and 44%, and in the case of a uterus duplex it is between 13 and 42% (Heilmann 2008). Myoma may also cause abortion. In the reference literature hysteroscopy is often mentioned as the method of choice in the diagnosis of uterine anomalies. Transvaginal sonography is, however, a non-invasive alternative, with an almost comparable sensitivity in diagnosing a double uterus (Kupesic and Kurjak 1998). Sonography should therefore be used in the primary diagnostics of uterine anomalies. The coronary plane of 3D sonography, in particular, allows very precise imaging of uterine anomalies, and provides the possibility of measuring the size of the septum (Fig.12).

Figure 12: Uterus septum, coronary plane

Operative correction is the therapeutic consequence in the case of a combination of habitual abortion and uterine anomalies (Heilmann 2008).

Doppler sonography as a prognostic parameter in the diagnosis of miscarriage
It is known that Doppler sonographic evaluation of the flow pattern in the uterine arteries is of value when predicting the complications of pregnancy, such as preeclampsia and fetal growth retardation. Although disruption of placentation and the adaptation of the spiral arteries guided by trophoblast cells are regarded to be causes of abortion, there appears to be no connection between abortion and alterations in uteroplacental circulation. The overlapping of normal and pathological uterine flow patterns in disrupted and undisrupted pregnancy is too great to be of statistical significance (Alcazar and Ruiz-Perez 2000; Frates et al. 1996; Jauniaux et al. 2005). However, in pregnancies that resulted in abortion, a higher pulsatility index and earlier intervillous flow has been observed in comparison to that seen in normal pregnancies. This difference only occurred in pregnancies which abortion was already in progress and could no longer be averted (Jauniaux et al. 2003b). The Doppler examination of the uterine arteries does not, therefore, seem to provide a suitable technique for the prognosis of abortion.

3D examination in sonographic diagnosis of miscarriage
3D sonographic examinations in obstetrical diagnostics provide additional information, particularly in the diagnosis of dysplasia. Several questions have already been studied with regard to the additive use of 3D ultrasound in the assessment of intact and disrupted pregnancies.

Examinations of IVF pregnancies have shown a significantly smaller endometrial volume before a miscarriage occurs (Zohav et al. 2007).
It is possible to measure the volume of amniotic fluid in transvaginal examinations, and thus, to differentiate between pregnancies with a normal course and those in which there is a prognostically unfavorable early reduction in amniotic fluid (Gadelha et al. 2006). Examinations of the volume of the gestational sac have shown that reduced volume is a predictive factor of miscarriage (Babinski et al. 2001; Steiner et al. 1994). A gestational sac with a reduced volume is also found in women with chromosomal anomalies (Falcon et al. 2005). 3D examinations of the yolk sac indicate differences between the volume, shape and vascularization of disrupted and undisrupted pregnancies (Kupesic and Kurjak 2001). Normal values have been suggested (Rôlo et al. 2008) that, as in two-dimensional measurement, only correlate to a slight extent with the gestational age and the crown-rump-length.

The studies show that 3D examinations can provide additional information for the assessment of early pregnancy. The study data are, however, inadequate for the generation of representative reference values. The question of the clinical relevance of deviation from individual parameters is as valid for 3D examination as it is for 2D examination.

In daily practice, the TUI is a useful aid in early pregnancy. The tomographic image of the whole of the chorionic cavity and its contents allows complex evaluation and documentation of all the relevant structures of early pregnancy (Fig. 13, 14).

Figure 13: Tomographic Ultrasound Imaging (TUI) of a missed abortion; in the 2D sagittal plane (picture upper left) the embryo is not clearly shown; * Plane (middle): embryo is clearly shown and is measurable.

Figure 14: TUI of the peripheral hematoma in Figure 10

Keywords
Prenatal sonography, early pregnancy, miscarriage

References


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Conflict of interest
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Ultrasonographic diagnosis of miscarriage

**Question 1**
How great is the incidence of spontaneous clinically manifest abortion?
- a. 5-10%
- b. 10-15%
- c. 5-20%
- d. 20-25%
- e. 25-30%

**Question 2**
How are exact measurements of the diameter of the amniotic cavity made?
- a. Outer to outer margin (including trophoblast) with 2 measurements (1 plane)
- b. Outer to outer margin with 3 measurements (2 planes)
- c. Outer to inner margin with 2 measurements (1 plane)
- d. Inner to inner margin (without trophoblast) with 3 measurements (2 planes)
- e. Inner to inner margin with 2 measurements (1 plane)

**Question 3**
About how many millimeters does the gestational sac grow per day?
- a. 1 mm
- b. 2 mm
- c. 3 mm
- d. 4 mm
- e. 5 mm

**Question 4**
The yolk sac must be apparent in the sonogram when the mean diameter of the chorionic cavity has reached which of the following sizes?
- a. 2 mm
- b. 5 mm
- c. 10 mm
- d. 15 mm
- e. 20 mm

**Question 5**
With respect to the yolk sac, which of the following provides definite evidence of abortion?
- a. A yolk sac size >>7 mm
- b. A very small yolk sac
- c. There is no yolk sac when the size of the chorionic cavity diameter corresponds to the 5th week of pregnancy
- d. There is no yolk sac after the 13th week
- e. The embryo is located close to the yolk sac

**Question 6**
Which is the most exact parameter when determining the gestational age in the 1st trimester?
- a. The diameter of the chorionic cavity
- b. Crown-rump length
- c. Biparietal diameter
- d. Circumference of the head
- e. Circumference of the abdomen

**Question 7**
At which crown-rump length should embryonic cardiac activity be detectable, at the latest?
- a. 2 mm
- b. 5 mm
- c. 10 mm
- d. 15 mm
- e. 20 mm

**Question 8**
Which of the following conditions is most common when there are symptoms of vaginal bleeding?
- a. Missed abortion
- b. Hydatid mole
- c. Blighted ovum
- d. Extrauterine pregnancy
- e. Intact intrauterine pregnancy

**Question 9**
Which of the following conclusions is correct with regard to the following constellation: calculated gestational age 10 + 2 week of pregnancy, sonographic intrauterine pregnancy: CRL 8 mm, CCD 25 mm, yolk sac 8 mm, no cardiac activity?
- a. Intact, normally developed intrauterine pregnancy
- b. Missed abortion
- c. Blighted ovum
- d. Extrauterine pregnancy
- e. Follow-up examination

**Question 10**
Which of the following conclusions is correct with regard to the following constellation: calculated gestational age 10 + 2 week of pregnancy, sonographic intrauterine gravidity: CRL 4 mm, CCD 17 mm, yolk sac 2 mm, cardiac activity negative?
- a. Intact, normally developed intrauterine pregnancy
- b. Missed abortion
- c. Blighted ovum
- d. Extrauterine pregnancy
- e. Follow-up examination