8 Normal First Trimester of Pregnancy

Kalesha Hack and Phyllis Glanc

Introduction

The first trimester conventionally refers to the stage of pregnancy occurring prior to 14 weeks gestational age (GA). First trimester ultrasound may be used to refer to all scans performed prior to the 14 week mark [1] or to scans occurring between confirmation of an intrauterine pregnancy and 13+6 weeks gestation [2]. With the advent of highly sensitive home pregnancy tests, more women are presenting for a dating ultrasound before ultrasound is able to show confirmatory evidence of an early intrauterine pregnancy [3]. For this reason, we have chosen to include a discussion of all ultrasounds performed in a woman with a positive β-subunit of human chorionic gonadotropin (β-hCG) pregnancy test prior to 14 weeks in this chapter.

All dates in this chapter are referred to in menstrual age which, hereafter, will be considered synonymous with GA. GA is defined as the conceptual age + 2 weeks. Pregnancy dating can also be described based on timing of conception, known as the conceptual age or embryonic age, where day 1 refers to fertilization. This dating method may be used by assisted reproductive technology specialists.

There are several important stages in early pregnancy development that occur before they can be resolved by current commercial ultrasound technology.[1] Fertilization typically takes place around day 14 of the menstrual cycle when the sperm and mature ovum unite to form a zygote in the outer portion of the fallopian tube. Initially, the zygote undergoes rapid cellular division and migrates toward the uterus. Implantation typically is complete by 10 days post-fertilization and, in a normal pregnancy, occurs within the central portion of the uterine cavity. The embryo begins to flatten out and form a bilaminar disc that lies between the amniotic cavity and exocoelomic cavity. The primitive yolk sac develops at 9 days post-fertilization, however, it is not visible sonographically.

The primitive yolk sac subsequently breaks off and is extruded, around 4 weeks GA, to form

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[1] See also Chap. 5.

J. S. Abramowicz, R. E. Longman (eds.), *First-Trimester Ultrasound*,
https://doi.org/10.1007/978-3-031-24133-8_8

the secondary yolk sac which can be seen at early ultrasound. Subsequent use of the term yolk sac in this chapter refers to the secondary yolk sac. In the 5th gestational week, gastrulation occurs and results in the formation of the three germ cells layers: ectoderm, mesoderm, and endoderm, each giving rise to different organ systems. Closure of the neural tube is generally completed by the end of the 6th week. The developing heart begins to form in week 5 of the pregnancy. Development of the internal and external organs occurs during the first 8–10 weeks of pregnancy, known as the *embryonic period* or *organogenesis*. Recent advances in 3D imaging techniques have enabled detailed images of the developing embryo to be obtained and correlated to embryonic anatomy sections and micro-CT images increasing the body of knowledge of early normal and abnormal imaging appearances [4]. Prior to the end of the 10th week, the developing pregnancy is referred to as an *embryo*. After this time, once the organogenesis phase is completed, the term *fetus* is used.

Gestational Sac

The earliest sonographically visible evidence of an intrauterine pregnancy is the appearance of an intrauterine gestational sac [1, 5, 6]. With modern high-frequency transvaginal transducers, the gestational sac can first be seen as early as 4 weeks 1 day gestation and is typically seen around 4.5–5 weeks at which time it measures 2–3 mm [7–10]. The gestational sac is a round or ovoid fluid-filled structure identified within the central echogenic portion of the uterus, i.e., the decidualized endometrium. On closer inspection, one can identify that the sac is eccentrically located within the decidua, as opposed to in the endometrial cavity itself and has a peripheral echogenic rim (Fig. 8.1a).

An important distinction in early pregnancy ultrasound is the ability to differentiate a true intrauterine gestational sac, before the yolk sac or embryo is seen, from an intrauterine fluid collection such as a subendometrial cyst, decidual cyst, or fluid collection in the setting of an ectopic pregnancy. Careful interrogation will demonstrate that subendometrial cysts are external to the decidualized endometrium (Fig. 8.2). A decidual cyst is also a benign finding but is more challenging to distinguish from an early IUP. The key distinction will depend on the relationship of the early IUP, which should abut the interstitial line of the collapsed endometrial cavity (Fig. 8.1b), whereas the decidual cyst may not be anatomically related to the collapsed endometrial cavity. Decidual cysts also typically have a thinner wall and may be multiple. In cases where there is doubt, follow-up imaging will demonstrate appropriate growth of the early intrauterine gestational sac, with development of a yolk sac to confirm an early IUP.

It is equally important to ensure the "cyst" is not actually within the endometrial cavity. In most cases, fluid within the endometrial cavity can be distinguished from fluid outside of the endometrial cavity on the basis of shape, location, and contents. Whereas endometrial cavity fluid collections may be angular, complex with internal echogenic debris, or elongated, conforming to the uterine cavity, the early gestational sac will be anechoic and typically rounded or ovoid [11]. In cases where there is uncertainty, the differential diagnosis will include a pregnancy of unknown location or intracavitary fluid collection, accompanying early pregnancy loss.

It has been shown that intrauterine fluid, commonly referred to as a "pseudogestational sac," in the setting of ectopic pregnancy occurs much less frequently than previously thought and may be seen in only around 10% of ectopic pregnancies [12, 13]. Doubilet et al. reported in an editorial on pregnancy of unknown location that given the relatively low incidence of ectopic pregnancy (approximately 2%) and low likelihood of intrauterine fluid with an ectopic pregnancy, the probability that any intrauterine fluid collection in a woman with a positive pregnancy test represents a gestational sac is 99.5% [14]. This led to a change in thinking with respect to early pregnancy such that, **in the absence of sonographic evidence of ectopic pregnancy, any fluid col-**

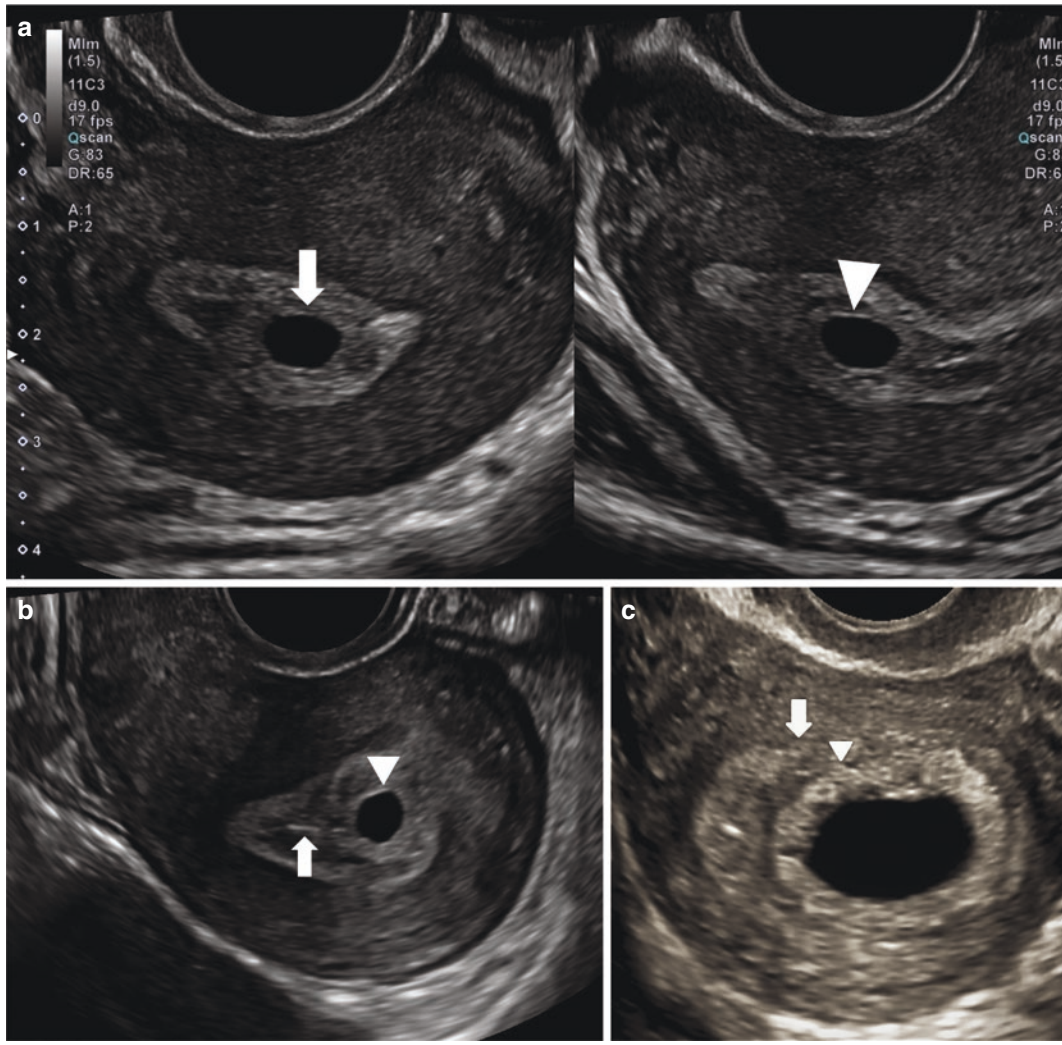


Fig. 8.1 Normal early gestational sac: (**a**) 5 weeks 2 days transvaginal transverse and sagittal images showing an oval intrauterine fluid collection (white arrow) eccentrically located within the endometrial cavity in a woman with a positive serum B-hCG. Note the faint surrounding echogenic rim (white arrowhead) typical of an early gestational sac. Although there is no yolk sac or fetal pole identified, findings should be reported as an early intrauterine pregnancy of unknown viability. (**b**) 5 weeks 2 days transverse sagittal image shows an eccentric round fluid collection with an echogenic rim (white arrowhead) adjacent to the thin echogenic line (white arrow) of the collapsed endometrial cavity demonstrating the "intradecidual sign." (**c**) 6 weeks 5 days transvaginal transverse image showing an intrauterine fluid collection surrounded by two concentric echogenic rings (white arrowhead inner and white arrow outer) forming the so-called double sac sign

lection with curved edges in a woman with a positive pregnancy test should be thought of as an early intrauterine gestational sac [14]. In a study of 649 women presenting with a positive β-hCG and an intrauterine sac-like structure without a yolk sac or embryo on ultrasound, none of the intrauterine fluid collections represented a pseudogestational sac [15]. In the setting of a suspected early intrauterine pregnancy, follow-up imaging can be obtained, to confirm subsequent appearance of embryonic structures including a yolk sac and an embryo with cardiac activity. The role of follow-up β-hCG serology in this setting will be discussed separately.

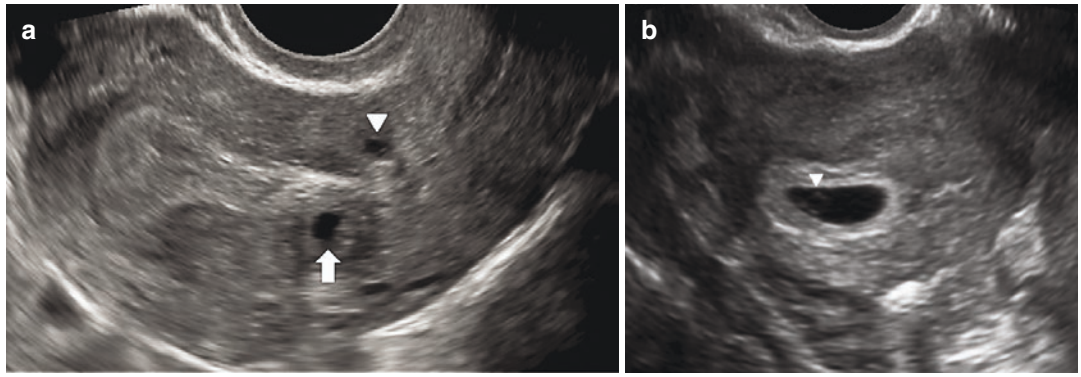


Fig. 8.2 Subendometrial cysts in a patient with a positive pregnancy test and unknown dates, transvaginal images: (**a**) Sagittal image of the uterus showing two round fluid collections outside of the echogenic endometrial cavity (arrow and arrowhead). These can be identified as decidual cysts due to their location outside of the endometrial cavity. Note that these cysts also demonstrate a thin imperceptible wall in contrast to the echogenic rim typically seen around an early gestational age. No intrauterine gestational sac is identified. (**b**) Transverse image from follow-up study 9 days later shows an intrauterine gestational sac with visible yolk sac (arrowhead) confirming an intrauterine pregnancy

The **double sac sign (DSS)** and **intradecidual sign (IDS)** have historically been described as useful in differentiating a true IUP from a non-gestational intrauterine fluid collection [16, 17]. The DDS, first described in 1982, refers to the appearance of two echogenic rings around the gestational sac felt to represent the inner and outer layers of the decidua, the decidua capsularis and decidua basalis (Fig. 8.1c) [17]. The IDS, initially described in 1986, refers to a fluid collection with an echogenic rim in an eccentric location on one side of the uterine cavity (Fig. 8.1b) [16]. Both of these signs were initially described on transabdominal ultrasound and considered to be early reliable signs of an IUP with the DSS seen in 77% of the initial study population with an IUP and the IDS seen in 92% [14, 16, 17]. Currently, with the advent of high resolution, high-frequency transvaginal transducers, subsequent studies have shown that in normal IUP the DSS may be absent in 50–60% and the IDS absent in up to 50% [14, 18, 19]. With improvements in technology, it is no longer infrequent that the yolk sac is visible prior to DSS and IDS and, consequently, these signs are now felt to be of limited utility. The absence of a DSS or IDS should not be used to exclude one [20] and similarly should not be interpreted as a poor prognostic factor. In 2020, Phillips et al. reported that the likelihood of an early intrauterine gestational sac progressing to a live pregnancy by the end of the first trimester was better in women when an intradecidual sign was present (46% vs 35%), however, neither the intradecidual sign or double sac sign proved to be of clinical value in predicting the outcome of an early pregnancy [15].

Measurement of the Gestational Sac[2]

Measurements of the gestational sac can be obtained and used to estimate gestational age and predict appearance of normal embryonic structures. The mean sac diameter (MSD) is obtained by averaging the transverse, sagittal, and anteroposterior dimensions of the gestational sac and can be correlated with expected GA and with β-hCG levels (Fig. 8.3). There is variability in gestational sac size measurements between different observers. In a study of 54 patients by Pexsters et al. [21] interobserver

[2] See also Chap. 9.

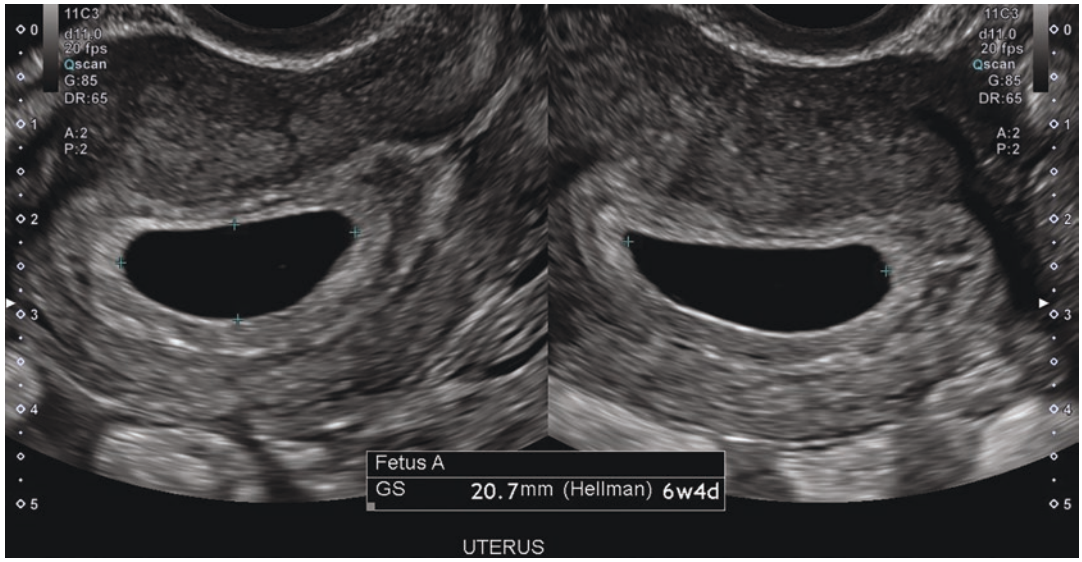


Fig. 8.3 Mean sac diameter: 6 weeks 4 days transvaginal sagittal and transverse images of the uterus measuring the gestational sac in three orthogonal dimensions which are averaged to obtain the mean sac diameter (MSD). Care should be taken to place calipers directly on the white line around the sac to ensure accurate measurements

variability for MSD was reported as being up to ±19%. Expected rate of growth of the gestational sac has previously been reported as approximately 1 mm/day [8]. However, in a study of 359 women, Abdallah et al. [22] found overlap in MSD growth rate in viable and non-viable early IUP and were unable to define a rate of gestational sac size that can be considered normal in early pregnancy [22]. A small gestational sac with less than 5 mm difference between crown rump length and gestational sac length has been referred to as first trimester oligohydramnios and considered to be associated with poor outcome [23]. However, this has only been examined in a small population and as an isolated finding likely warrants follow-up imaging (Fig. 8.4). It is important to note that in addition to growth, the shape of the gestational sac may change on serial ultrasound from a round to more irregular appearance. This may be the result of maternal factors such as uterine contractions, over-filled bladder, fibroids, or subchorionic hematomas and should not necessarily be interpreted as a sign of an impending loss (Fig. 8.5).

Mean Sac Diameter and Viability

Much attention has been given to the maximum size at which an empty gestational sac, i.e., a sac without a visible yolk sac or embryo, can be considered normal. While a yolk sac is usually seen with a MSD >8 mm, the MSD at which a yolk sac and embryo can be sonographically detected is variable and caution should be exercised if using MSD to determine viability [24]. Historically, the upper limit at which an empty gestational sac was considered a normal early pregnancy finding was a transvaginally measured MSD between 16 and 20 mm [25, 26]. However, several recent studies have shown that a small percentage of viable pregnancies may exist with empty sac size up to 18–19 mm [27, 28] and given interobserver variability in sac size measurement, **an empty gestational sac should be considered a potentially normal early pregnancy finding up to a MSD of 25 mm on transvaginal ultrasound** [22, 25, 26, 28, 29] (Fig. 8.6). This is discussed further in Chap. 10 which refers to new discriminatory criteria for defining early viability. One caveat of using more stringent criteria to diagnose early

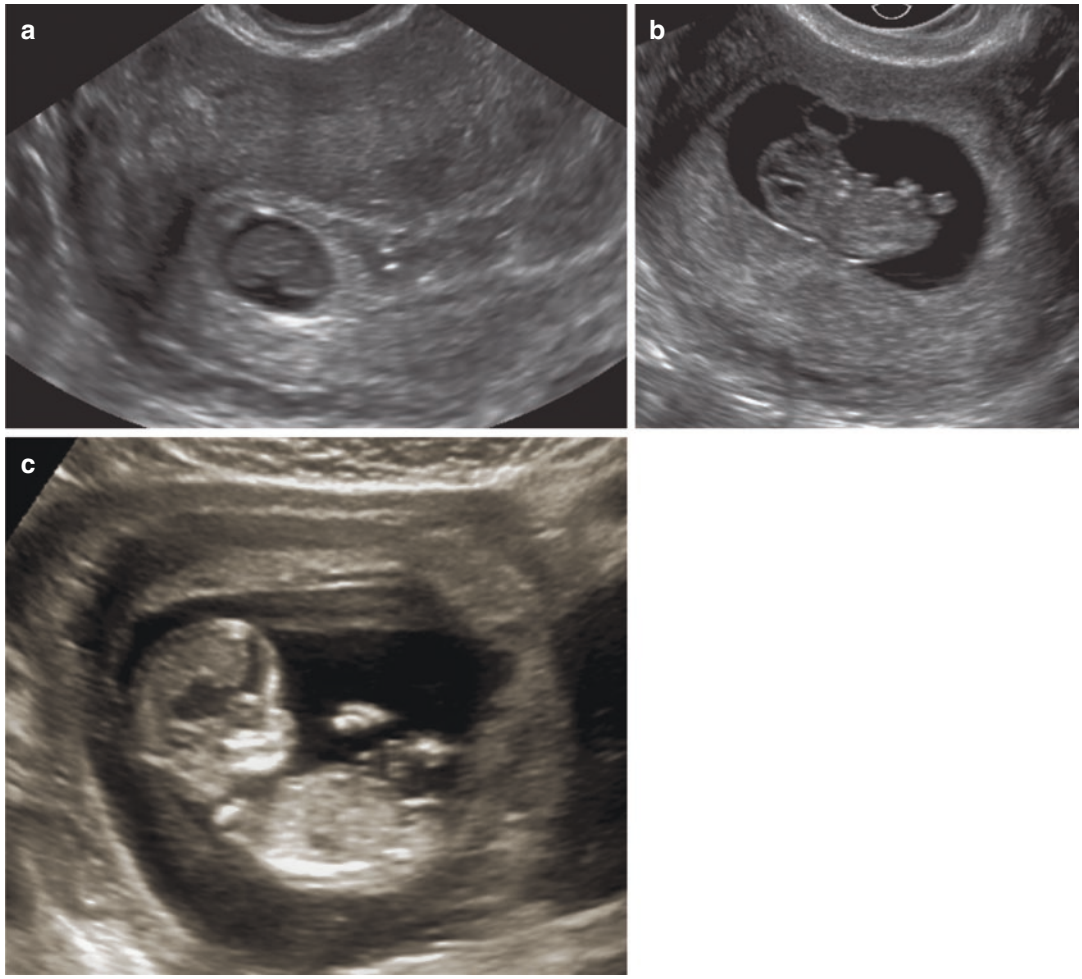


Fig. 8.4 First trimester oligohydramnios: (**a**) 7 weeks 4 days transvaginal image showing small sac size (MSD 12.4 mm) for CRL (8.1 mm) in keeping with "first-trimester oligohydramnios." (**b**) 8 weeks 1 day transvaginal follow-up scan shows live embryo with persistent discordant GS size. (**c**) 12 weeks 0 days transabdominal image shows live fetus with interval growth of both sac and fetus; however, sac continues to be small

pregnancy loss is that it may cause delayed diagnosis in patients who wish to have expedited treatment for various reasons. In such cases, it may be reasonable to apply a lower threshold such as a MSD ≥21 mm or CRL ≥6 mm when measurements are close to threshold and patients wish to proceed with urgent management. Detection of peritrophoblastic flow demonstrating high velocity and low impedance around the gestational sac is a normal finding that has been described as an aid in confirming a very early intrauterine pregnancy [30]. However, caution is recommended in the use of color and, particularly, spectral Doppler imaging in early pregnancy, due to increased power output and potential risk to developing pregnancy [9, 31].

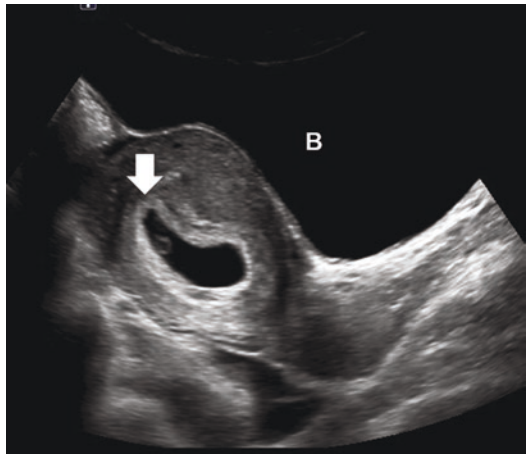


Fig. 8.5 Eccentric appearance of gestational sac: 6 weeks 2 days transabdominal sagittal image shows an intrauterine gestational sac with yolk sac confirming an intrauterine pregnancy. The superior aspect of the sac has a pointed appearance due to compression by the over-filled maternal bladder (B). This should not be presumed to be an abnormal finding or worrisome for a subsequent pregnancy loss

Gestational Sac Appearance and β-hCG in Early Pregnancy

A gestational sac is usually visible in an intrauterine pregnancy when the β-hCG level is between 1000 and 2000 mIU/mL [5]. Historically, much attention has been paid to the concept of a discriminatory β-hCG level above which an intrauterine gestational sac should always be seen in a normal IUP. This number was initially around 2000 mIU/mL; however, it is now recognized that there is considerable overlap of β-hCG levels in viable IUP, nonviable IUP, and ectopic pregnancy [32, 33]. Doubilet et al. have reported that, in rare instances, even with an absent gestational sac on transvaginal ultrasound and β-hCG level >4000 mIU/mL, follow-up ultrasound can show a normal pregnancy [32]. Practically speaking, it is unlikely to have a normal IUP develop when no gestational sac is seen with a β-hCG level >3000 mIU/mL. This can-

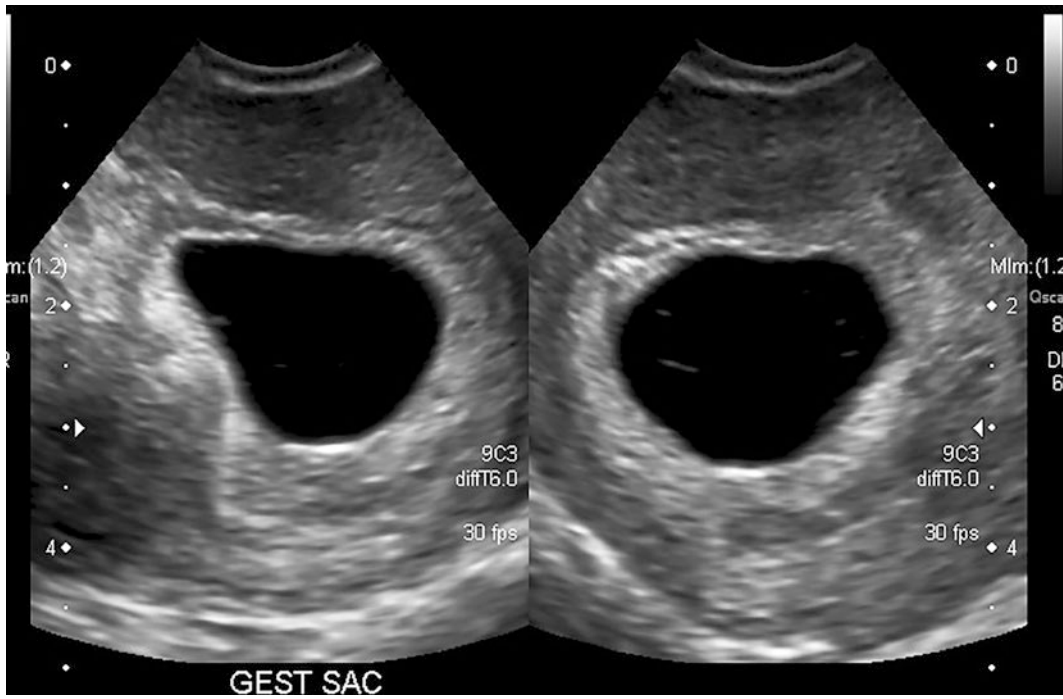


Fig. 8.6 Empty gestational sac: 7 weeks 0 days transvaginal sagittal and transverse images show an intrauterine gestational sac with MSD 19.5 mm. No yolk sac or fetal pole is identified. These findings are suspicious but not diagnostic for early pregnancy loss as the MSD is <25 mm. Findings should be reported as an early intrauterine pregnancy of unknown viability and follow-up scan performed

not, however, be considered diagnostic criteria for early pregnancy loss with 100% specificity. Consequently, the use of a single discriminatory β-hCG level to guide management in the setting of pregnancy of unknown location (PUL) is not recommended [32, 34]. There is emerging evidence that the incremental increase in serum β-hCG over 48 h, expressed as a ratio, may be a useful predictor of IUP when ultrasound findings are inconclusive [35–37]. β-hCG levels obtained 48 h apart should typically double, i.e., increase 100%. Various thresholds can be used to achieve greater diagnostic certainty with a rise of <67% predictive of an abnormal outcome with 95% certainty and a rise of ≤35% predictive of an abnormal pregnancy with 99.9% certainty [38–40]. Bignardi et al. [35] have reported that a β-hCG ratio >2.0 is suggestive of a viable IUP with sensitivity of 77%, specificity of 96%, and a positive predictive value of 87%. However, the use of β-hCG ratio as a predictor of viability in the setting of early pregnancy is not routine practice in all centers.

Yolk Sac

The appearance of the yolk sac provides the first *definitive* confirmation of an intrauterine pregnancy. **Although visualization of an intrauterine gestational sac with an echogenic rim is likely to represent an IUP, it is not as accurate at confirming an IUP as detection of the yolk sac.**

The yolk sac can first be visualized within the gestational sac at approximately 5.5 weeks gestation [1, 6, 9, 41] as a thin echogenic circular ring within the gestational sac on transvaginal scanning. It is usually visible by the time the MSD reaches 8 mm. If the yolk sac is not identified by this stage, a careful interrogation of the gestational sac with image optimization may assist in the ability to detect it. These may include narrowing the sector width, image zoom, appropriate placement of the focal zone, choice of a higher frequency, or other vendor specific post-processing settings (Fig. 8.7).

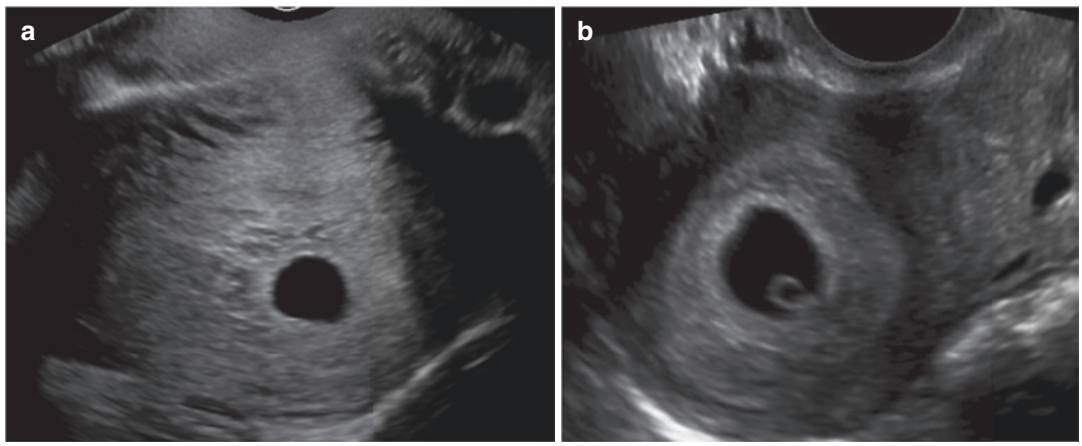
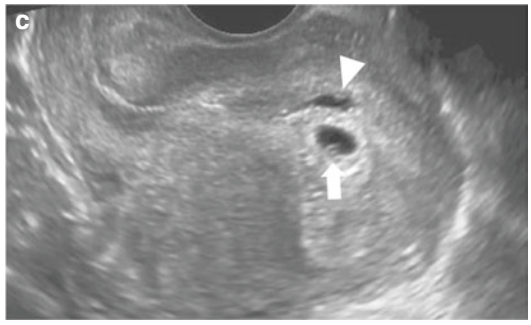


Fig. 8.7 Normal yolk sac: (**a**) 6 weeks 1 day transvaginal transverse images show an apparently empty gestational sac. (**b**) Same patient as above with transvaginal transverse image with narrow sector width is able to detect a circular echogenic ring representing the yolk sac thus confirming an early IUP. (**c**) 5 weeks 3 day transvaginal images show a very small circular echogenic ring (white arrow) within the gestational sac representing a normal yolk sac and confirming an IUP. This patient also has a small subchorionic hematoma at the posterior aspect of the gestational sac (white arrowhead)



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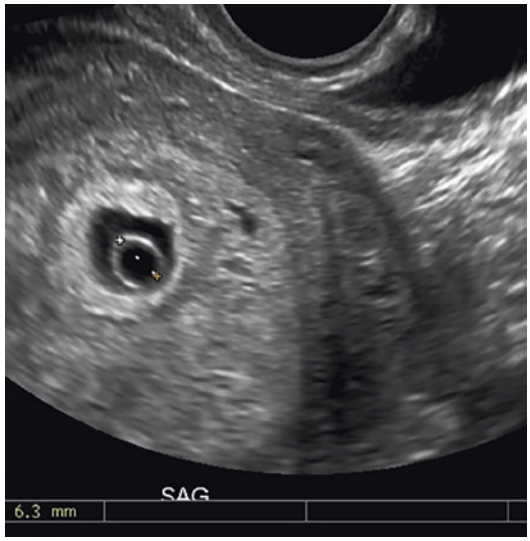

Fig. 8.8 Enlarged yolk sac: 5 weeks 6 days transvaginal sagittal image shows an enlarged yolk sac measuring 6 mm

Normal yolk sac measurement between 5 and 10 weeks GA is around 5 mm [9]. An enlarged yolk sac greater than 5 mm may be associated with poor pregnancy outcome. As an isolated finding, however, it cannot be considered definitely abnormal (Fig. 8.8) [42]. Typically, the yolk sac will gradually decrease in size after the 10th week of gestation and usually disappears by the end of the first trimester.

Embryo

The embryo is first visualized alongside the yolk sac at approximately 6 weeks gestation. Initially, it appears as a featureless linear echogenic structure without discernible limb buds and with no distinct cranial or caudal end (Fig. 8.9a). At this stage, a quantitative assessment of the embryo is achieved by obtaining the longest length measurement. Once the crown and rump are distinguishable, it is ideal to acquire the crown rump length (CRL) which is defined as the longest length excluding the limbs and yolk sac (Fig. 8.9b). The CRL can be measured on transabdominal or transvaginal. The ideal plane of measurement is midsagittal, with the embryo or fetus in a neutral position. Presence of fluid between the fetal chin and chest can be used as a sign to ensure that the fetus is not hyperflexed [2]. In practical terms, prior to 7 weeks gestation, measurement is actually of the longest length of the embryo that can be seen, but, after 7 weeks, a concerted effort should be made to measure the embryo in the midsagittal plane, excluding the yolk sac [43]). The smallest detectable embryo transvaginally has a CRL of 1–2 mm. Normograms are available to correlate CRL with gestational age [44–47]. A 2014 publication by Papageorghiou et al. established a CRL chart for pregnancy dating, based on a multi-center international trial, thereby providing an international standard for evaluating CRL linear growth in the first trimester [48].

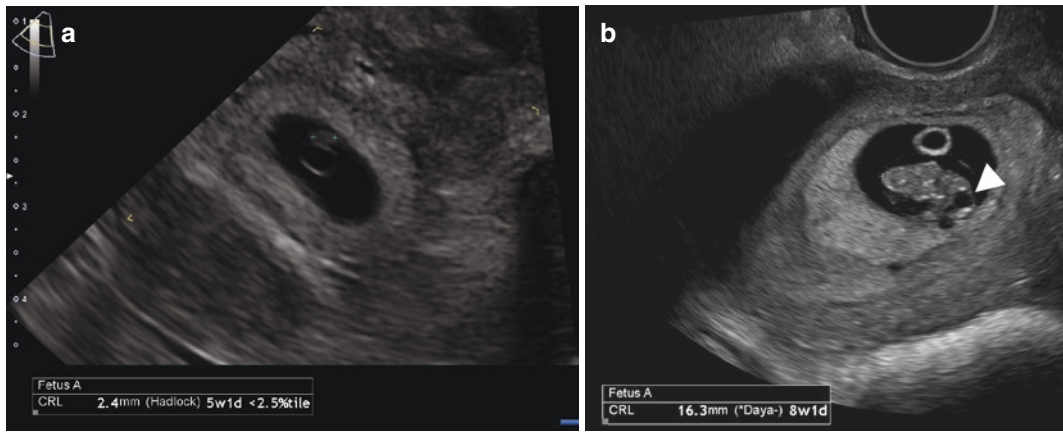

Fig. 8.9 Early embryo and crown rump length: (**a**) 5 weeks 1 day transvaginal image showing yolk sac and a 2 mm embryo. At this stage, the embryo has no discernible features and the longest length is measured to obtain the crown rump length (CRL). (**b**) 8 weeks 1 day transvaginal images showing a single embryo with CRL 16.3 mm. Note the clearly visible rhombencephalon (white arrowhead) identifying the fetal cranium as distinct from the caudal end. Calipers must be carefully placed to exclude yolk sac and flexed limbs

Embryonic and Fetal Cardiac Activity

Embryonic cardiac activity (ECA) is usually visible as soon as the embryo is detectable and can be seen with a CRL as small as 1 mm [5]. **Although ECA is virtually universally identified by CRL of 4–5 mm, the absence of ECA cannot be considered abnormal until the embryo reaches 7 mm** [25, 26]. This number is chosen to achieve as close to 100% specificity as possible for diagnosing early pregnancy loss based on absence of embryonic cardiac activity while taking into account the potential ±15% interobserver variability in CRL measurement [49].

Embryonic cardiac activity is documented using motion mode (M mode) to determine a heart rate (Fig. 8.10). ECA is considered normal if greater than 100 beats per minute (bpm). Doubilet et al. [50] suggested a lower limit of normal embryonic heart rate of 100 bpm up to 6.2 weeks gestation and 120 bpm between 6.3 and 7 weeks. Embryonic heart rates <100 bpm were thought to be associated with an increased risk of demise. In a 2018 meta-analysis on prediction of miscarriage in women with viable intrauterine pregnancy up to 15+6 weeks, fetal bradycardia had a sensitivity of 68% and specificity of 98% and likelihood ratio of 32 in predicting pregnancy loss [51]. Sensitivity and specificity greatly increased if vaginal bleeding was also present. In this study, a cut-off of ≤100 bpm showed the best predictive value for miscarriage. However, there is also data from a review of early first trimester pregnancies with slow embryonic heart rate revealing that this may not necessarily be a poor prognostic factor [50, 52, 53]. High embryonic heart rate in early pregnancy has been defined by Benson et al. [54] as >135 bpm before 6.3 weeks and >155 bpm between 6.3 and 7 weeks. This, generally has a good prognosis with high likelihood of normal outcome.

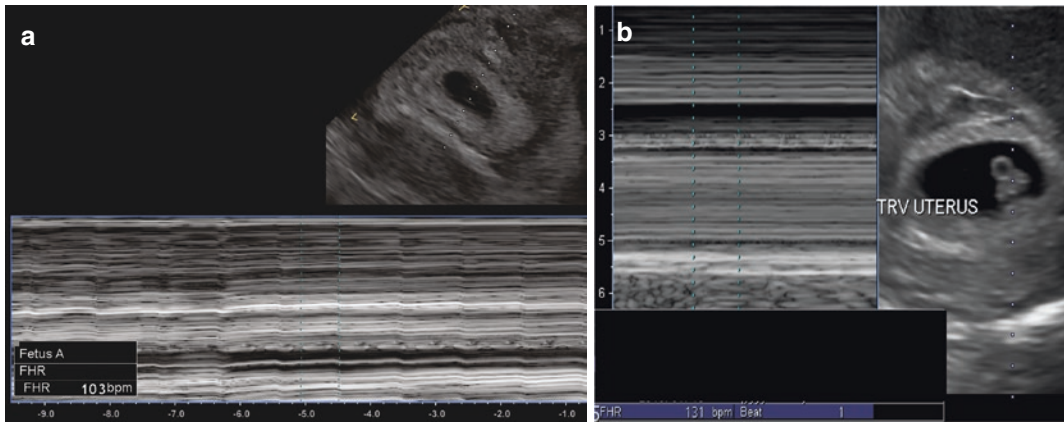

Fig. 8.10 M mode of embryonic cardiac activity: (**a**) 5 weeks 1 day transvaginal image showing embryonic cardiac activity detected with M mode in an embryo with CRL 2 mm. Note that even at this small size, ECA can be clearly demonstrated although its absence is not considered an abnormal finding until the embryo has reached a CRL of 7 mm. (**b**) 6 weeks 6 days transvaginal image where they embryo is more clearly visualized with FHR 131 bpm as detected with M mode

Multiple Gestations and Chorionicity[3]

Globally twins are approximately 1–3% of all pregnancies [55]. Twin rates have doubled between 1980 and 2009 from 18.9 to 33.2 per 1000 births [56]. In some areas of the US, the prevalence of multiple gestations is as high as 1 in 30 pregnancies. This is thought to be related to a combination of assisted reproductive technologies and increasing maternal age. Two-thirds of twin pregnancies are dizygotic, and one-third are monozygotic. The rate of intrapartum complications including pregnancy loss due to twin-twin transfusion syndrome or selective fetal growth restriction is far greater in monochorionic twins [57]. For optimal care, monochorionic pregnancies should be identified as early as possible to allow for closer surveillance and early detection of these conditions. **Assignment of chorionicity is therefore a mandatory and vital component of first trimester ultrasound with multiple gestations.** However, surprisingly in a review by Wan et al., only 44% of pregnancies referred to a tertiary care center had accurate diagnosis of amnionicity and chorionicity [58]. It is therefore important that practitioners be familiar with signs used to assess amnionicity and chorionicity in the first trimester.

The best time to determine chorionicity is prior to 14 weeks gestational age [57]. The classic features to determine a dichorionic gestation include two separate gestational sacs or placental masses, a thick inter-twin membrane in association with the lambda (λ) sign and different fetal genders. The λ sign refers to a triangular shaped projection of tissue which extends into the inter-twin membrane and is synonymous with the "twin-peak" sign (Fig. 8.11). With respect to triplet pregnancies, the upsilon zone representing the interface of the three amniotic membranes has been identified as useful to assign chorionicity in triplet pregnancies (Fig. 8.12) [59]. A recent study of 55 triplet pregnancies showed that the upsilon zone was identifiable in 95% of scans and demonstrated interobserver agreement of 100% [60].

Prior to 10 weeks the presence of two distinct, separated gestational sacs will confirm a dichorionic-diamniotic (DCDA) pregnancy. After 10 weeks, the most reliable signs for assessing chorionicity are a combination of placental number and the λ sign [57] given that gender cannot be reliably determined prior to 12 weeks. In a

[3]See also Chap. 14.

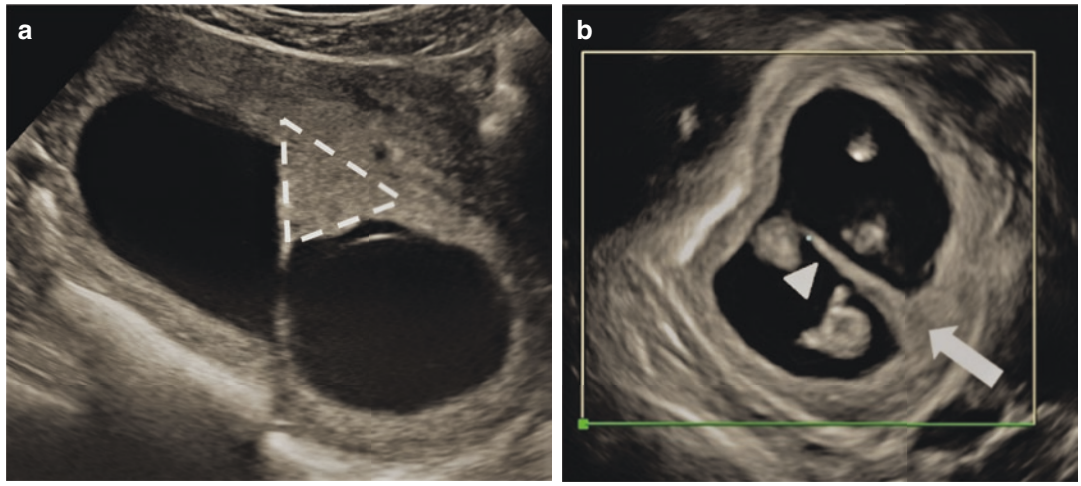

Fig. 8.11 Lambda sign in 11 weeks 3 days dichorionic twin gestation: (**a**) Transabdominal image showing triangular shaped tissue projecting into the inter-twin membrane (white outline) representing the lambda sign. (**b**) 3D representation showing the lambda sign (arrow) and thick inter-twin membrane (arrowhead)

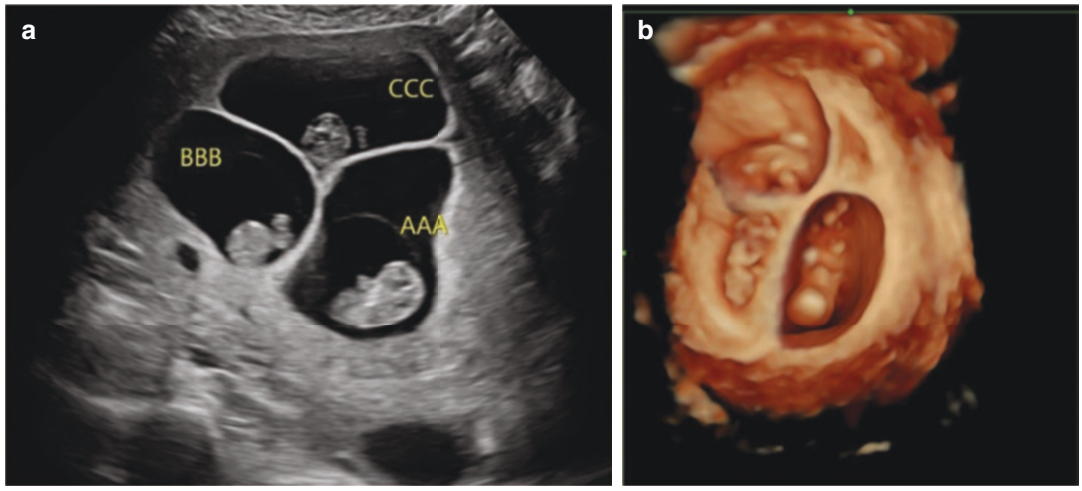

Fig. 8.12 Upsilon zone in triplet gestation 9 weeks 4 days: (**a**) Transabdominal images showing "upsilon zone" which demonstrates thick inter-fetal membranes and their intersections in a trichorionic triamniotic (TCTA) first trimester pregnancy. (**b**) 3D representation of upsilon zone showing thick inter-fetal membranes in a TCTA pregnancy at 9 weeks

study of 648 twin pregnancies, the number of placental masses and the presence of either the T or λ sign is virtually 100% accurate for determining chorionicity between 11 and 14 weeks [57]. A study by Bora et al. suggests that evaluation for chorionicity at 7–9 weeks had very high agreement with the 11–14 week scan and can be attempted; however, challenges were noted with respect to differentiating monochorionic monoamniotic pregnancies from monochorionic diamniotic pregnancies as the appearance of the inter-twin membrane may be delayed [61].

With respect to differentiating monoamniotic from diamniotic pregnancies, it is important to recognize that the temporal development of the yolk sac and the amnion is variable [62]. The appearance of the amniotic sac can be as late as 8–10 weeks with the thin membranes making it

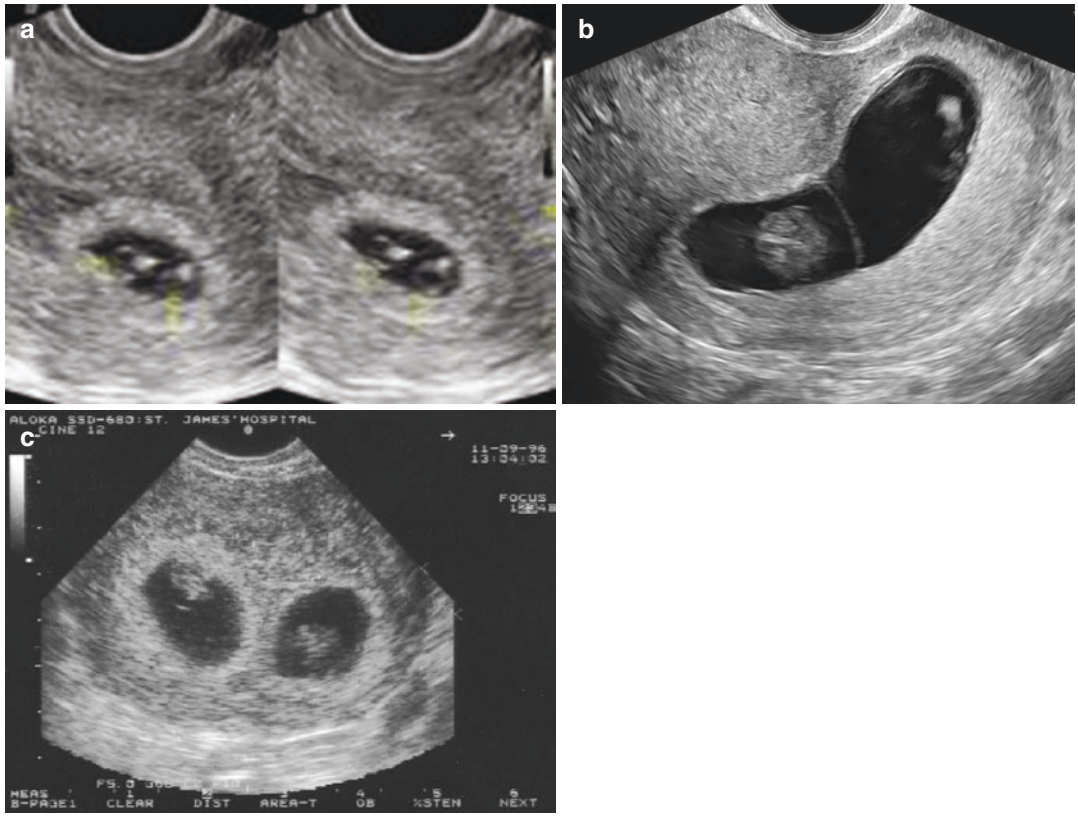

Fig. 8.13 Early monochorionic diamniotic twin pregnancy: (**a**) 8 weeks 0 days transvaginal transverse image showing two yolk sacs in keeping with twin gestation. No clear dividing membrane is seen. (**b**) Follow-up scan at 13 weeks showing thin inter-twin membrane and T-sign confirming monochorionic diamniotic twin pregnancy. (**c**) 3D representation of MCDA twins at 8 weeks

challenging to identify, even with the higher resolution of transvaginal ultrasound (Fig. 8.13). In the setting of multifetal pregnancies, the number of yolk sacs was previously thought to be a reliable way to assign amnionicity; however, it is less reliable than once presumed [62, 63]. While the presence of two yolk sacs is highly predictive of a diamniotic pregnancy and is seen in approximately 85% of monochorionic diamniotic (MCDA) twins, the presence of only one yolk sac can be seen with both monoamniotic and diamniotic twin pregnancies [62]. On rare occasion, a monochorionic monoamniotic twin pregnancy may present with two yolk sacs. If uncertain that a membrane is present separating the fetuses, it is prudent to repeat the test 1–2 weeks later. Alternatively, direct visualization of umbilical cord entanglement may provide early confirmation of the monoamniotic status of a twin gestation.

Heterotopic Pregnancy

Prior to the more widespread use of assisted reproductive techniques (ART), the presence of an intrauterine gestational sac with a yolk sac was felt to virtually exclude the diagnosis of ectopic pregnancy. Nonetheless, heterotopic pregnancy can occur where an ectopic pregnancy coincides with an otherwise normal IUP. The estimated incidence of this occurrence is between 1 in 8000 and 1 in 30,000 (Fig. 8.14) [64]. The incidence may be higher in gestations after

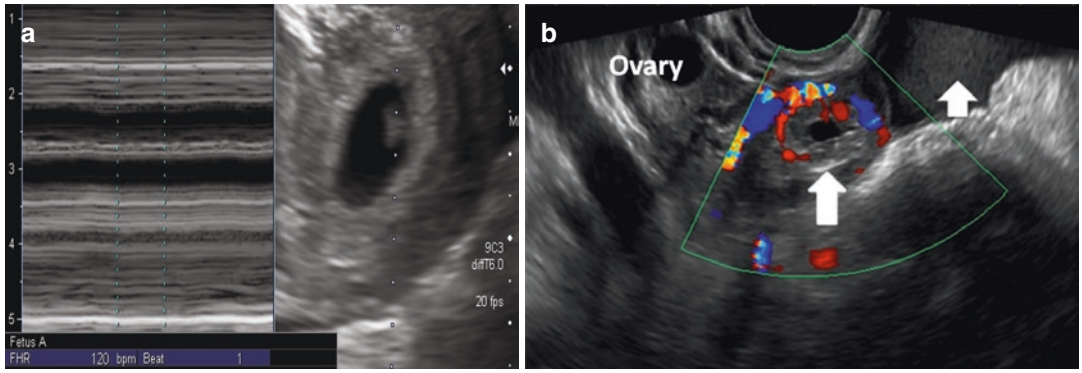

Fig. 8.14 Heterotopic pregnancy: (**a**) 6 weeks 5 days transvaginal image showing live intrauterine pregnancy. (**b**) Transvaginal sagittal image of right adnexa showing a hypoechoic mass (long arrow) with peripheral vascularity separate from the normal ovary with follicles which is seen at the upper margin of the image. Complex free fluid is seen in the pelvis (short arrow) representing hemorrhagic fluid

assisted fertility [65] and has been estimated as high as 1 in 100 in this population [45]. Thus, in patients who have undergone ART, despite the presence of an IUP, a thorough interrogation of the adnexae is recommended, to rule out a heterotopic pregnancy.

Early Pregnancy Dating

One of the indications of first trimester ultrasound is to confirm dating of pregnancy. Accurate pregnancy dating is critical to prenatal management for a variety of reasons including: to prevent preterm induction of supposed postdates pregnancies, to determine viability in the setting of premature delivery, to interpret growth patterns, to optimize prenatal screening for aneuploidy, and to appropriately time diagnostic interventions such as chorionic villus sampling and amniocentesis [66, 67]. Evidence has shown early ultrasound dating of pregnancy to be more accurate at predicting the expected due date than menstrual history [2, 68, 69]. Pregnancy dating is most accurate in the first trimester and can be determined using MSD, CRL, or fetal biometry. MSD can be used for dating when the embryo is not seen but shows greater variability in predicting GA compared to CRL [70] and should not be used when an embryo is visible. **The most accurate estimation of gestational age is achieved in the first trimester by using the CRL somewhere between 8 and 13+6 weeks [47, 67, 71, 72]**. At earlier gestations, the relatively small size of the embryo may lead to more significant measurement error. The reported accuracy of the CRL measurement for dating is within 3–8 days [8], with the most accurate results reported when CRL measures [73] between 7 and 60 mm [46, 47, 71]. CRL continues to be the most reliable predictor of gestational age until 12–14 weeks, when CRL and biometry begin to achieve similar accuracy [74–77]. Based on current recommendations by the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG), CRL is recommended for dating until the embryo measures 84 mm. Beyond 84 mm, the use of head circumference has been shown to be slightly more accurate than BPD [2]. Given the increased accuracy of ultrasound for pregnancy dating and the clinical importance of accurate dating, it has been suggested that a first trimester dating ultrasound be performed in all pregnancies [73, 78–81]. Dating of the pregnancy may be performed concurrently with the 11–14 week nuchal translucency scan.

Thresholds for Assessing Viability

The criteria for assessing viability of pregnancy early in the first trimester including thresholds for establishing a sonographic diagnosis of early pregnancy loss will be discussed further in a separate. These values have been chosen to include almost all

normal pregnancies in an effort to "do no harm" and prevent the small risk of erroneously reporting early pregnancy loss in the setting of a viable pregnancy.

The criteria, which are based on transvaginal ultrasound assessment, have increased the thresholds at which nonvisualization of ECA and embryonic structures may be considered normal and are summarized as follows:

- Absence of cardiac activity in an embryo <7 mm *may be normal*.
- Absence of an embryo with a MSD < 25 mm *may be normal*.

Follow-up in 1 week's time is recommended in the above two scenarios.

Nuchal Translucency Evaluation[4]

Assessment of nuchal translucency is routinely offered in many countries, including the United States, as a component of prenatal screening and when combined with maternal age and maternal serum biochemistry (β-hCG and pregnancy associated plasma protein-A [PAPP-A]) can be an effective method of screening for chromosomal abnormalities [82]. Even in the setting of a normal non-invasive cell-free DNA test for aneuploidy, 11 to 13+6 week ultrasound including nuchal translucency assessment is recommended to assess for structural anomalies which may not be associated with a detectable chromosomal abnormality [83]. Nuchal translucency (NT) refers to the sonolucent area posterior to the fetal neck. For the purpose of prenatal screening, the NT should be assessed between 11 and 13+6 weeks gestational age, when the embryo measures between 45 and 84 mm by transabdominal ultrasound technique. The NT should be seen transabdominally in about 80% of cases [82]. Transvaginal assessment of the NT can be attempted if visualization is inadequate by transabdominal approach; however, it is more challenging due to limited ability to maneuver the probe to obtain a true midline sagittal image. If the NT is not adequately seen transabdominally, our routine is to either bring the patient back later the same day or on a subsequent day, rather than perform a transvaginal study. However, many centers will prefer to proceed to a transvaginal examination immediately following an unsuccessful transabdominal NT evaluation.

Criteria for NT Measurement

Accurate measurement of nuchal translucency is required to optimize results of screening tests. Both the American Institute of Ultrasound in Medicine (AIUM) and ISUOG have published guidelines outlining proper technique for NT measurement [2, 6]. The NT should be evaluated in the midsagittal plane of the face, defined by visualization of the echogenic tip of the nose and rectangular shape of the palate [2]. The fetus should be in a neutral position, neither hyperflexed nor extended. The image should be magnified, such that the fetal head and upper thorax fill the screen. Margins of the NT edges must be clear enough for proper placement of calipers which should be placed directly on the edges of the NT. Equipment used should allow for precise measurement up to 0.1 mm. The amnion should be seen as a separate echogenic line from the NT (Fig. 8.15). The NT should be measured at the

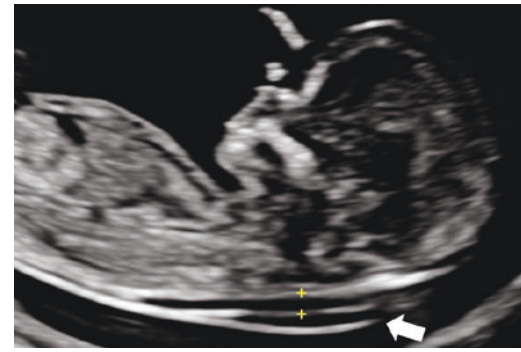

Fig. 8.15 Nuchal translucency at 12 weeks 6 days: transabdominal sagittal midline image showing normal nuchal translucency (between yellow calipers). The thin echogenic line of the amnion can be seen as separate from the NT

[4]See also Chaps. 8 and 9.

widest space and, if multiple measurements meeting the criteria are obtained, the largest measurement should be used for risk assessment. It is important that individuals who perform a NT evaluation have undergone training and are associated with an appropriate quality assurance program.

Significance of Elevated NT Measurement

Normal nuchal translucency is defined as a measurement less than 3 mm, if the 95th percentile is used or 3.5 mm, if the 99th percentile is chosen [82]. Nuchal translucency increases with increasing gestational age, and higher measurements are associated with greater risk of abnormality [84]. When combined with maternal age and serology (including PAPP-A and maternal serum β-hCG), NT thickness successfully identified 89% of fetuses with trisomy 21, with a false positive rate of 5% [82]. Elevated nuchal translucency can also be associated with other chromosomal abnormalities, including trisomy 13, 18 and Turner's syndrome [82]. Even in normal karyotype fetuses, an elevated NT confers a greater risk of fetal structural anomalies, most commonly congenital heart anomalies [85]. The prevalence of congenital heart disease with an NT >95th percentile is 1/48 and is 1/19 with NT >99th percentile [85]. A meta-analysis of 2271 singleton euploid fetuses, with NT >3 mm at 10–14 weeks, reported structural anomalies in 10.6% and genetic syndromes and single-gene disorders in 15% [86]. The prevalence of abnormal outcome was shown to increase with increasing NT measurements.

It is important to note, however, when counselling patients, that not all elevated NT pregnancies are necessarily associated with congenital or structural anomalies. In one report, 90% of pregnancies with NT measurement below 4.5 mm and normal karyotype resulted in healthy live births [82]. Normal outcome was seen in 80% of pregnancies with NT between 4.5 and 6.4 mm and 45% of pregnancies with NT greater than 6.5 mm [87]. In the previously described meta-analysis evaluating outcome of elevated NT above 3 mm, chromosomally normal fetuses had a 68% overall chance of normal outcome. Long-term neurodevelopmental outcomes have also been evaluated in children who had an increased fetal NT and normal karyotype. In a systematic review of 17 studies and 2458 patients, there was no significant difference in the rate of neurodevelopmental delay in this group, when compared to the general population. Nonetheless, further large-scale prospective studies are needed to predict neurodevelopmental outcome in this population with greater certainty [88].

Recommendations in the setting of increased NT include detailed early anatomic assessment to look for structural anomalies, fetal echocardiography, and discussion regarding cell-free DNA analysis and/or invasive diagnostic testing such as chorionic villus sampling and amniocentesis.

Assessment of the Nasal Bone During the NT Evaluation

Evaluation for presence or absence of the nasal bone can be performed at the time of NT scan [82, 89, 90]. Nasal bone ossification first becomes apparent at a crown rump length of approximately 42 mm [90] or 11 weeks gestation and nasal bone length progressively increases with gestation. Assessment for presence of the nasal bone is performed in the midsagittal plane and, as for NT measurement, requires strict adherence to proper technique and operator experience to be reliable. The nasal bone appears as an echogenic line parallel to and thicker than the echogenic skin line overlying the nasal bridge. It is best seen when the footplate of the transducer is parallel to the long axis of the nasal bone. The two parallel lines of the nasal bone and skin line comprise the "equal sign" (Fig. 8.16). The nasal bone is considered absent if the deeper line is not present. Nasal bone assessment appears to be more difficult than NT assessment. Nevertheless, there are reports that, with adequate training and experience, assessment for presence or absence of nasal bone can be performed with success in up to 99% of fetuses [91].

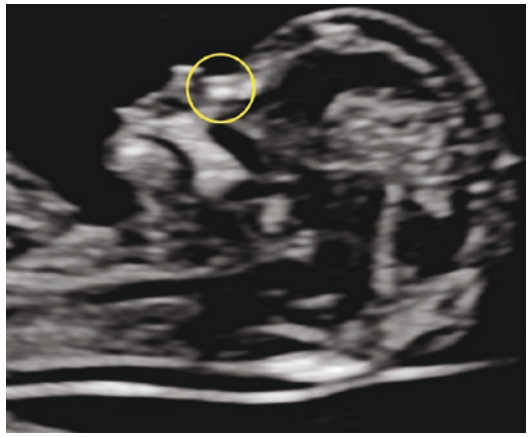

Fig. 8.16 Nasal bone at 12 weeks 5 days. Transabdominal sagittal midline image shows the nasal bone as an echogenic line posterior to the skin line resulting in two parallel echogenic lines often referred to as the "equal sign" (yellow circle)

Significance of Absent Nasal Bone

As mentioned, an absent nasal bone is seen more frequently in trisomy 21 as compared to the general population. In a study of over 21,000 fetuses between 11 and 14 weeks, absence of the nasal bone was noted in 62% of fetuses with trisomy 21 as compared to 0.6% of unaffected fetuses [91]. Absence of nasal bone has been shown to be an independent finding with respect to serum β-hCG and PAPP-A and can, therefore, be added to routine combined prenatal screening for trisomy 21 [90]. When combined with routine NT screening and serum β-hCG and PAPP-A, addition of nasal bone presence may decrease the false positive rate for trisomy 21 from 5% to 2.5% [90]. Absence of the nasal bone has also been reported in approximately 55% of fetuses with trisomy 18, 35% of trisomy 13, and 10% of Turner's syndrome [92].

However, it is important to be aware that an absent or hypoplastic nasal bone does not necessarily imply pathology and can be a normal variant. The prevalence of absent nasal bone decreases with gestational age and absence of the nasal bone prior to a crown rump length of 42 mm should not be considered abnormal. If there is question of nasal bone absence between 11 and 12 weeks, a repeat scan can be obtained to ensure that lack of visualization represents true absence, as opposed to late ossification. Additionally, there is ethnic variation in presence and size of the nasal bone, and an absent nasal bone may be more prevalent in certain ethnic groups, particularly African and Asian populations. A prospective study of nearly 4000 fetuses reported prevalence of absent nasal bone to be 5.8% in patients of African origin, 3.4% in patients of Asian origin, and 2.6% in patients of Caucasian origin [93].

In some instances, the nasal bone may be present but seen to be shortened or hypoplastic. Nasal bone length has not been shown to be a useful first trimester measurement for screening of trisomy 21 [90].

Screening for Neural Tube Defects at the Time of the NT Evaluation

Neural tube defect with open spina bifida is a relatively uncommon condition affecting approximately 1 in 2000 fetuses [94]. Traditionally open spina bifida was diagnosed via a combination of alpha-fetoprotein from maternal serum or amniocentesis and second trimester ultrasound evaluations. With the move to first trimester screening and earlier anatomic ultrasound evaluations, a number of investigators have proposed parameters to assess for these conditions in the first trimester.

Open spina bifida may be accompanied by sonographically visible changes in the posterior fossa at the time of the NT evaluation [95–97]. In these cases, the combination of CSF leakage with a gradual shift of the brainstem toward the occipital bone may result in obliteration of the intracranial translucency or developing fourth ventricle and thickening of the brainstem as it prolapses caudally.

The developing fourth ventricle can be identified as an intracranial translucency (IT) or fluid containing space which is parallel to the nuchal translucency in the midsagittal plane at 11–14 weeks. The IT borders are defined anteriorly by the posterior border of the brain stem and posteriorly by the anterior border choroid plexus

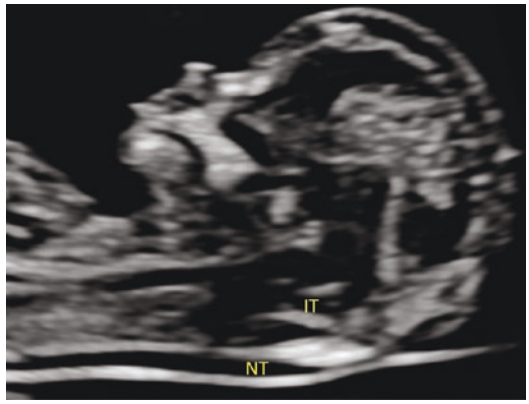

Fig. 8.17 Intracranial translucency 12 weeks 6 days. Transabdominal image showing normal intracranial translucency (IT) anterior to the nuchal transluency (NT). The anterior border of the IT is the brainstem and the posterior border is the choroid plexus

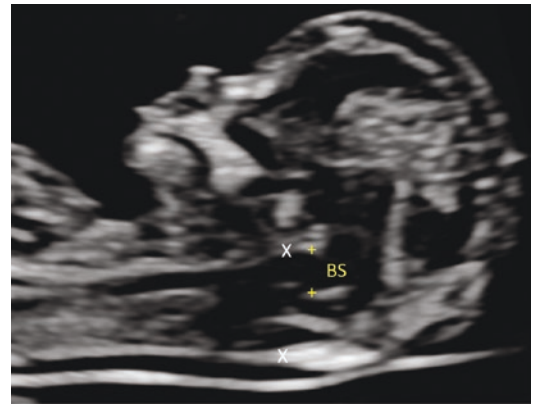

Fig. 8.18 Brainstem to brainstem-occipital bone ratio 12 weeks 6 days. Transabdominal image showing measurement of the brainstem (yellows calipers) and the brainstem to occipital bone distance (white x). Although the brainstem and brainstem to occipital bone measurements are obtained in the same plane as the nuchal translucency, it is not routine practice to measure these structures in all fetuses

(Fig. 8.17). The IT may be absent in cases of open spina bifida and can be assessed between 11 and 14 weeks at the time of NT screening. Initially, it was felt that IT evaluation would be a simple addition to routine NT evaluation given that the structures to be evaluated are in the same plane. However, on further evaluation, IT measurement may be more technically challenging than previously thought [98]. It is currently not routine practice in all centers [95–97].

Measurement of the thickness of the brainstem (BS) and the vertical distance between the brainstem anteriorly and occipital bone posteriorly (BSOB) can be obtained between 11 and 14 weeks using the same imaging plane at the NT evaluation (Fig. 8.18). The ratio of the BS/BSOB can be evaluated and is ≤1 in normal fetuses [97]. In cases of open spina bifida, the BS diameter is greater (>95th percentile) and the BSOB is decreased (<5th percentile) resulting in an increased BS/BSOB ratio >1 [97, 99]. This is related to the cerebrospinal fluid leakage and development of the Arnold-Chiari II malformation, with a gradual shift of the posterior brain toward the occipital bone. Several studies [95–97] have showed that evaluation of the posterior fossa may be a useful marker for open spina bifida in the first trimester. It is recommended that a targeted ultrasound of the fetus spine, with transvaginal technique, be performed in order to evaluate directly for open spina bifida, in particular when the IT, BS-BSOB ratio, or BPD findings are suspicious or abnormal. This is not yet, however, routine practice.

These posterior fossa measurements have proven to be challenging and require a high degree of expertise to perform. As such, more recently simpler methods have been described to assist with this challenging diagnosis. Firstly, it has been demonstrated that the BPD will measure below the 5th percentile in fetuses affected with open spina bifida [100] and may ultimately prove to be the simplest way to assess for coexistent posterior fossa abnormalities associated with the Arnold-Chiari malformation. There are also two new signs that have been described which are based on simple pattern recognition of the effects of CSF leakage via an open spine bifida which are visible in the axial plane without requiring specific measurements. The “dry brain” size which compared the size of the choroid plexus to the fetal head is measured in the same plane as the BPD [101]. The “crash sign” represents posterior displacement of the mesencephalon which is compressed against the occipital bone in the axial view, likened to the appearance of a car crashing into a wall [102].

Normal First Trimester Anatomical Assessment

Formation of most major internal and external organs is complete by the end of the 10th week of gestation during the stage of pregnancy commonly referred to as organogenesis. Assessment of fetal anatomy can, therefore, be performed in the first trimester, provided that the fetus is large enough to allow visualization of structures with sufficient resolution for diagnostic evaluation, and that organ development be advanced enough that normal developmental stages can be differentiated from pathology. The performance of a first trimester anatomy scan has become more mainstream practice in many centers, as new high-frequency transducers, as well as increased use and patient acceptability of transvaginal scanning have enabled better visualization of smaller fetal structures, at earlier gestational ages. It is important, however, to be aware that first trimester anatomy evaluation is a specialized examination that requires an in-depth understanding of embryology and a high level of technical expertise, particularly with transvaginal techniques and unique scan planes that may be required to visualize some structures. Advantages of first trimester anatomy assessment include earlier detection of anomalies, earlier patient reassurance in high-risk settings with normal anatomy, and potential for better visualization in certain populations, specifically maternal obesity and patients with abdominal scar tissue from prior surgeries. Some disadvantages include increased cost to the medical system, potential to misdiagnose normal developmental structures for pathology, and potential to miss diagnoses that do not present until later in pregnancy. Evaluation of first trimester transvaginal anatomy is generally reserved for high-risk women, including those with elevated NT, inherited conditions associated with fetal anomalies, previous pregnancy with an anomaly, and maternal hazardous exposure or infection.

Several studies have investigated the feasibility and detection rates of performing first trimester anatomy for anomalies [103–105]. Braithwaite et al. [105] reported that complete first trimester anatomic survey was attainable in 95% of fetuses with transvaginal scanning only required in 20%. A subsequent study of 2876 patients by Ebrashy et al. [106] reported that a complete anatomical survey was obtained in 64% of patients using transabdominal approach only and in 82% using combination of transabdominal and transvaginal scanning. In their study, transvaginal images were particularly useful to evaluate the cranium, spine, stomach, kidneys, bladder, upper and lower extremities. They reported highest rates of nonvisualization for fetal heart and kidneys. Whitlow and Economides found that visualization of first trimester anatomy improved with increasing gestational age and reported 98% visualization at 13 weeks [107]. Monteagudo and Timor-Trisch [108] also support that visualization of first trimester anatomy, while possible at 12 weeks, is optimally performed closer to 13 weeks.

Detection rate of anomalies at first trimester scanning between 11 and 14 weeks has been reported as between 18% and 68% [106, 109]. In a 2014 retrospective cohort of 9692 nuchal translucency scans performed without a dedicated anatomical survey protocol, 41% of major anomalies confirmed on second trimester scan were diagnosed at the time of the first trimester NT scan [110]. A similar detection rate of 45% was found in a 2018 study of 5534 women including 297 at higher risk for a fetal anomaly [109]. In a prospective study of over 100,000 singleton pregnancies, 28% of all anomalies were detected. In this study, anomalies were categorized into those always detectable, those sometimes detectable and those never detectable [111]. This study highlighted an important consideration that the overall detection rate of anomalies in the first trimester may be less relevant than the detection rate specifically for those anomalies that *can* be diagnosed at an earlier gestation, as some anomalies may not develop or be detectable until later in gestation and thus are never detectable at early scan. It is important to note that performing a complete first trimester anatomical survey does not obviate the need for routine anatomical assessment at the 18–22 week stage to assess for such conditions. A systematic approach should

be used keeping in mind that some structures seen at the 18–22 scan may not be fully developed in the first trimester. Various protocols have been suggested with respect to what should be included in first trimester anatomy assessment [112]. In one of the largest prospective studies, including over 45,000 NT evaluations, Syngelaki et al. concluded that certain abnormalities should always be detected during this time period. Specifically they recommended the following conditions should not be missed during a routine NT evaluation: acrania or exencephaly; alobar holoprosencephaly; omphalocele; gastroschisis; megacystis; and body stalk anomaly [113].

In 2013, ISUOG published practice guidelines for first trimester stating that the purpose of the study also includes the detection of gross fetal malformations [72]. The 2013 guidelines from the AIUM state "embryonic/fetal anatomy appropriate for the first trimester should be assessed" [6]. As the 11–14 week ultrasound becomes routine practice in more and more centers, it will become more important for ultrasound practitioners to familiarize themselves with the normal embryology and development of the fetus in the first trimester in order to distinguish normal anatomy from pathology at progressive gestational ages.

Fetal Brain in the First Trimester

Early brain development begins in the 6th week of gestation before formation of the neural tube, with division of the neural groove into three distinct parts: the prosencephalon or *forebrain*, the mesencephalon or *midbrain,* and the rhombencephalon or *hindbrain*. One of the earliest structures to be visualized, at around 7 weeks, is the rhombencephalon. This appears as a cystic area in the posterior brain which should not be mistaken for pathology such as a posterior fossa cyst (Fig. 8.19). At 8–9 weeks gestation, the choroid plexus begins to develop, initially in the fourth ventricle and, subsequently, in the lateral ventricles. At this stage, the cerebral hemispheres can be delineated, as well as the diencephalon and rhombencephalon. The telencephalon and diencephalon are divisions of the forebrain and give rise to the lateral ventricles and third ventricle, respectively. The metencephalon and myelencephalon are formed from the rhombencephalon. With new high-frequency 2D and 3D transvaginal technology, detailed images of the developing fetal brain and ventricular system can be obtained in the first trimester including images depicting the primary brain structures including the telencephalon, diencephalon, mesencephalon, metencephalon, and myelencephalon (Fig. 8.20). The lateral ventricles initially appear as small cystic structures and become more identifiable toward the end of the first trimester, when they are filled by the echogenic choroid plexuses. At 9–10 weeks of gestation, the falx cerebri first becomes apparent and cranial ossification begins. These structures are more readily identifiable, however, closer to 11 weeks gestation and are important landmarks to identify, in order to exclude early diagnosis of anencephaly and alobar holoprosencephaly (Fig. 8.21). Cranial ossification should be seen by the end of the 11th week. It is best visualized in the axial and coronal planes in the frontal region, and may not be visible in the midsagittal plane, typically used for NT assessment (Fig. 8.22).

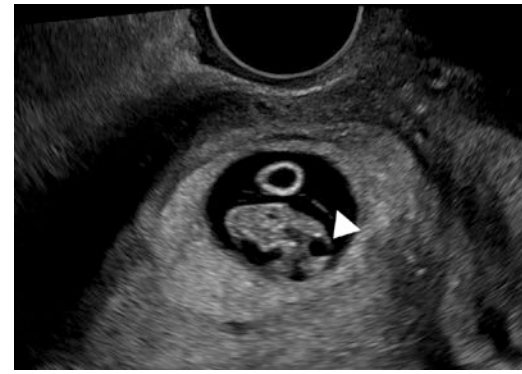

Fig. 8.19 Rhombencephalon 8 week 1 day transvaginal transverse images showing embryo with cystic rhombencephalon in the posterior head (arrowhead). This is a normal findings and should not be mistaken for a pathologic entity such as a posterior fossa cyst or hydrocephalus

The cerebral hemispheres are symmetrical, separated by the interhemispheric fissure and the falx cerebri. The fetal brain has a smooth appearance at this gestation, with sulci and gyri devel-

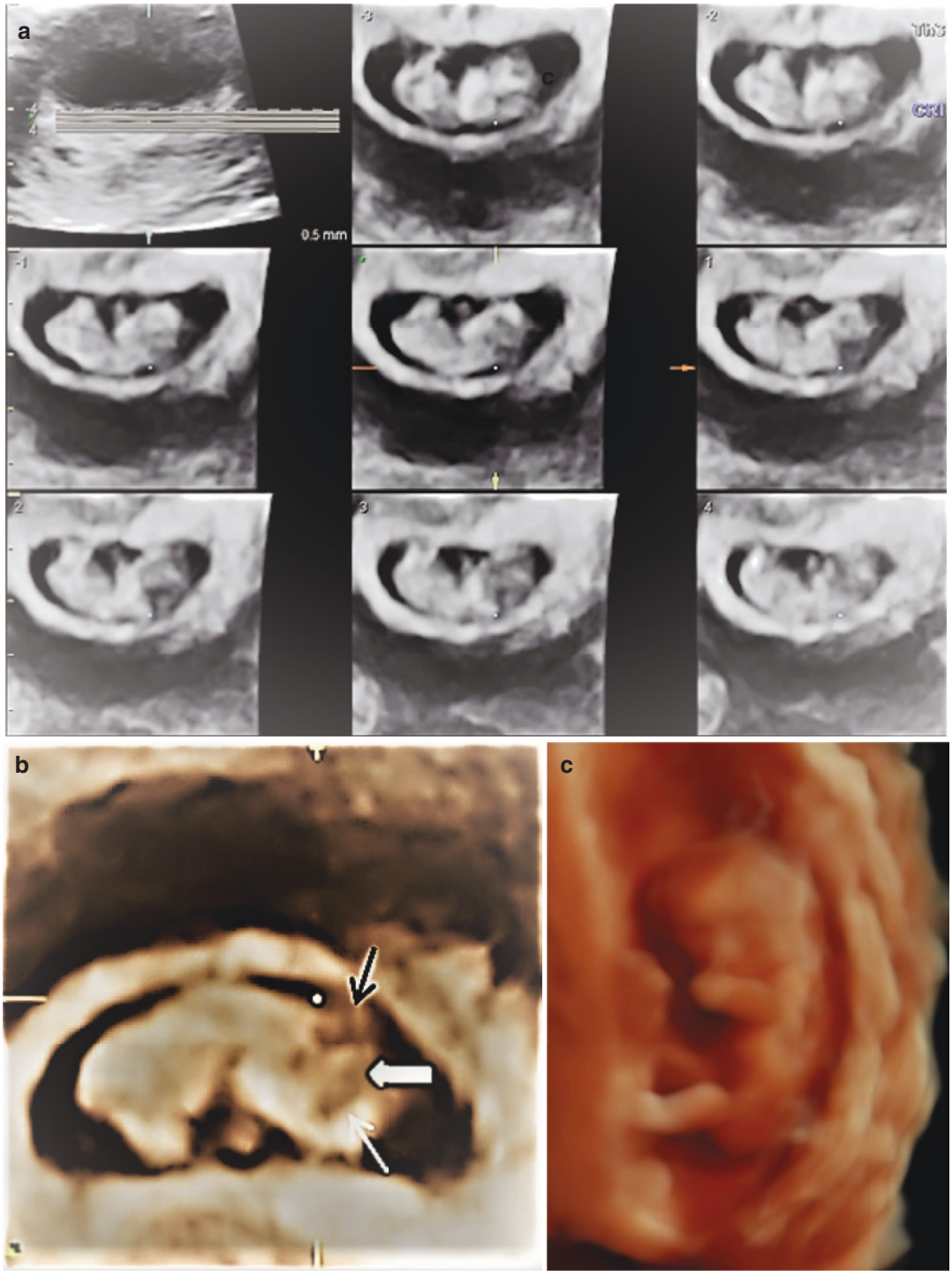

Fig. 8.20 3D Brain at 9 weeks 4 days transabdominal 3D images showing: (**a**) Serial slicing technique through the 3D volume of the embryo. (**b**) Selected 3D sliced image showing early cystic spaces in the cranium representing the developing diencephalon (thin white arrow), mesencephalon (thick white arrow), and metencephalon/myelencephalon (black arrow). (**c**) 3D surface rendered image of the embryo

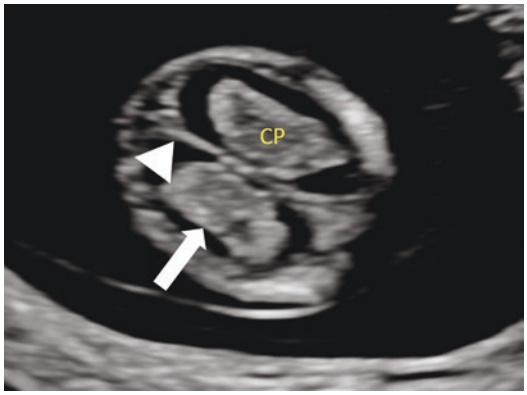

Fig. 8.21 Normal choroid plexus and falx at 12 weeks 6 days on transabdominal images of the fetal head showing bilateral symmetrical echogenic choroid plexuses (CP) which fill the lateral ventricles. White arrow denotes border of the lateral ventricle. The falx cerebri (white arrowhead) divides the cranium at the level of the choroid plexus resulting in a symmetric appearance of the brain

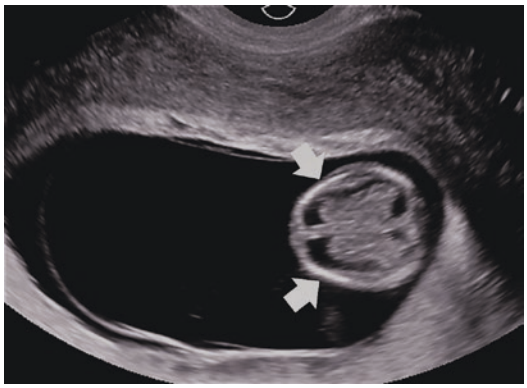

Fig. 8.22 Cranial bone ossification at 12 weeks 3 days transvaginal image of the fetal head shows bilateral normal frontal bone ossification (white arrows)

oping later in the second and third trimester. The cerebral mantle is a thin rim of tissue, seen around the hypoechoic, large lateral ventricles, filled with choroid plexus and occupying most of the cranium at this stage. The posterior fossa structures are not fully developed by the end of the first trimester. The cerebellum and upper vermis can be seen, but the lower vermis is incomplete and persistent communication between the fourth ventricle and cisterna magna is a normal finding at this stage (Fig. 8.23). Structures such as the cavum septum pellucidum and corpus callosum

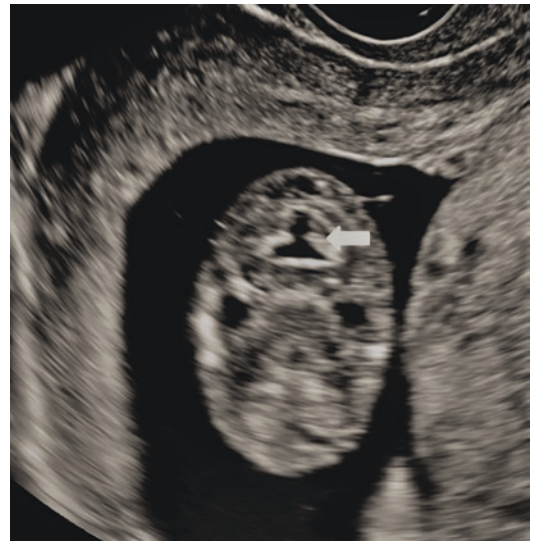

Fig. 8.23 Posterior fossa at 12 weeks 3 days transvaginal image showing normal communication of the fourth ventricle and cisterna magna (white arrow) due to incomplete development of the cerebellar vermis

are not yet developed and should be re-assessed at a later point in the pregnancy.

Face

Structures that can be assessed include the orbits, lens, profile, and nasal bone (Fig. 8.24). The soft tissue structures of the nose and lips are more challenging. Nevertheless, the diagnosis of cleft lip/palate, in particular when bilateral, can be made at this time. Examination in the coronal plane of the retronasal triangle (Fig. 8.25), formed by the two front processes of the maxilla and the primary palate, has been described as a potential way to facilitate detection of cleft palate in the first trimester [114].

Thorax

The lungs appear as echogenic structures in the developing thoracic cavity and should be symmetric. The diaphragm (black arrow) can be seen as an intact structure separating the echogenic lungs from intra-abdominal contents, specifically the stomach and liver (Fig. 8.26).

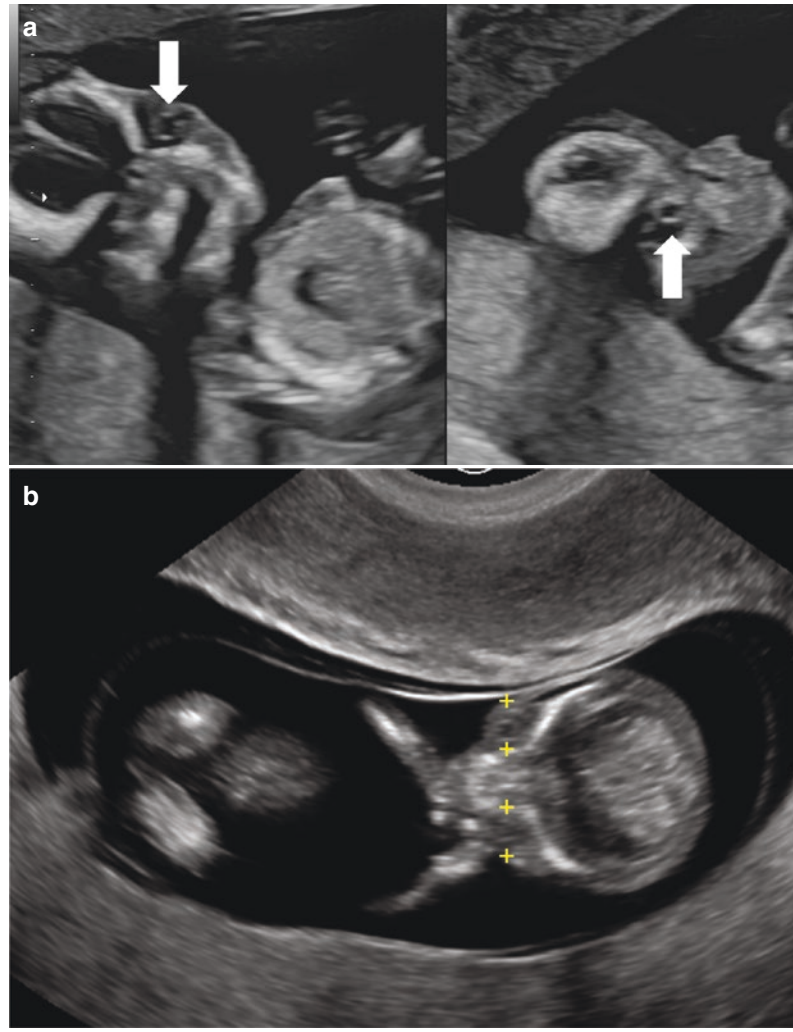

Fig. 8.24 Normal orbits and lenses: (**a**) At 13 weeks 4 days transabdominal image showing fetal lenses. (**b**) At 12 weeks 3 days transvaginal semi-coronal image showing normal inter-orbital distance (yellow calipers)

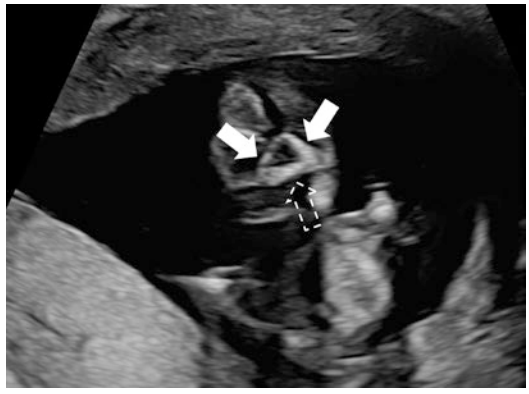

Fig. 8.25 Retronasal triangle at 13 weeks 4 days. Transabdominal coronal image showing the complete retronasal triangle comprised of the two frontal processes of the maxilla (solid white arrows) and the primary palate inferiorly (dashed white arrow)

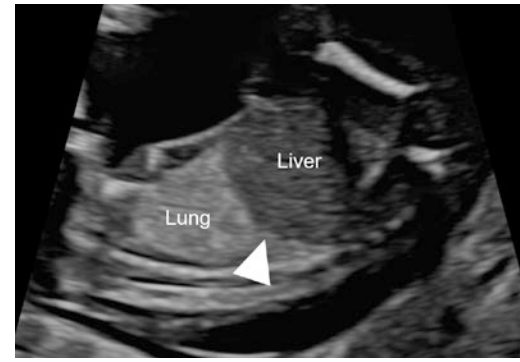

Fig. 8.26 Fetal chest and diaphragm at 13 weeks 1 day. Transabdominal image showing echogenic fetal lungs separated by intact diaphragm (white arrowhead) from the more hypoechoic liver inferiorly

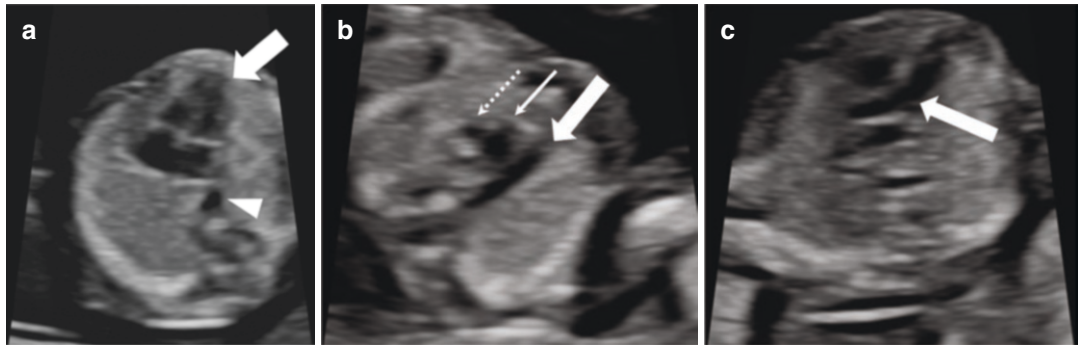

Fig. 8.27 Fetal heart at 13 weeks 4 days. Transabdominal axial images of the fetal chest showing: (**a**) Four-chamber view of the heart demonstrates symmetric cardiac chambers. The apex of the heart (arrow) and the aorta (arrowhead) are to the left of the fetal spine. (**b**) Right ventricular outflow tract (white arrow). Also shown are the aorta (thin white arrow) and SVC (white dashed arrow). (**c**) Left ventricular outflow tract (white arrow)

Fetal Heart in the First Trimester[5]

Development of the fetal heart begins during the 4th week of gestation and the beating heart can be detected sonographically as early as 5 weeks. Heart position can be documented to confirm situs solitus. Normal cardiac structures that can be identified during the first trimester include the four-chamber view which should show symmetry of the atria and ventricles with the cardiac apex directed to the left (Fig. 8.27a). While the four-chamber view may be seen in as many 85% of 11 week fetuses, it is visualized in almost all fetuses by the 13th week of gestation [115]. The cardiac outflow tracts are fully developed and may be visible toward the end of the first trimester (Fig. 8.27b, c), although assessment of these structures may be more technically challenging. There are several studies that now describe first trimester detection of cardiac anomalies as well as early fetal echocardiography [116]. In a systematic review and meta-analysis of first trimester detection of heart anomalies, 767/1445 (53%) of anomalies identified in low-risk patients were detected on first trimester scan [117]. At present, detailed fetal echocardiography is not routine practice in low risks patients. However, a simple screening tool that may be useful is evaluation of the cardiac axis. The cardiac axis can be measured on the four-chamber view of the fetal heart as the angle between a line transecting the thorax in anterior-posterior dimension and a line along the long axis of the heart with normal defined is between 30° and 60° (Fig. 8.28). In a case-control study of 197 fetuses with congenital heart defects, 2/3 of fetuses with cardiac anomalies had an abnormal cardiac axis in the first trimester [118]. While abnormal cardiac axis may not provide a spe-

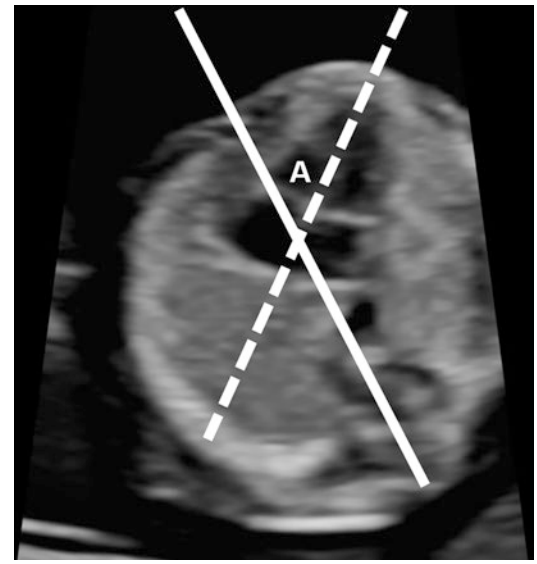

Fig. 8.28 Cardiac axis at 13 weeks 4 days. Transabdominal axial image of the fetal chest at the level of the four-chamber view. The cardiac axis is the angle (A) measured between a line bisecting the fetal chest in anterior-posterior dimension (solid line) and a line drawn along the inter-ventricular septum (dashed line)

[5] See also Chap. 11.

cific diagnosis, this may be a useful screen to identify fetuses who may be at increased risk and require more careful evaluation.

Fetal Kidneys and Urinary Tract System in the First Trimester

The fetal kidneys are sonographically detectable by the 9th week of gestation (Fig. 8.29). The fetal bladder is not reliably visualized until later in the first trimester at around 12 weeks (Fig. 8.30). By 13 weeks gestation, the bladder can be seen in up to 98% of cases and kidneys in up to 99% [119]. Documentation of these structures is important, as urine production does not begin until the 12th or 13th week, and secondary signs of renal agenesis or dysfunction, such as oligohydramnios, may not manifest until later in pregnancy after 16 weeks gestation.

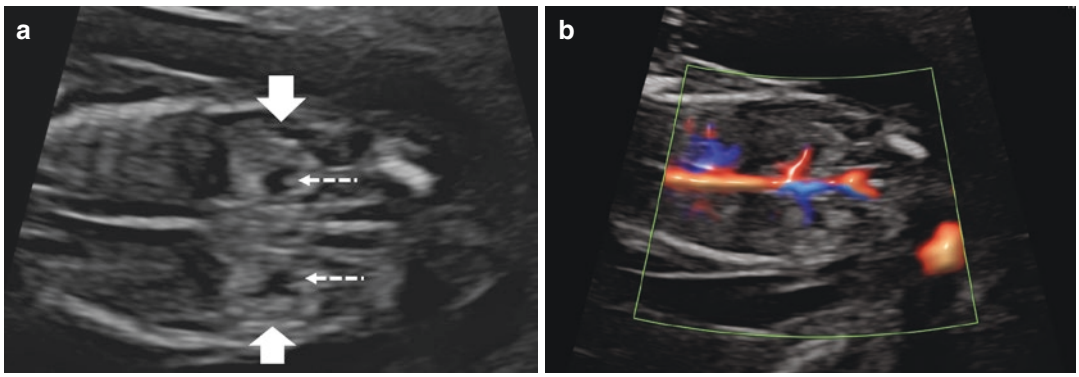

Fig. 8.29 Fetal kidneys at 13 weeks 1 day: (**a**) Transabdominal coronal image of the fetal abdomen demonstrates bilateral kidneys seen as echogenic ovoid structures in a paraspinal location (solid arrows) with central anechoic fluid within the renal pelvis (dashed arrow). The presence of fluid in the renal pelvis helps confirm the structure as a fetal kidney rather than collapsed bowel within the renal fossa. (**b**) Transabdominal coronal image with color Doppler demonstrating bilateral renal arteries arising from the aorta to supply the fetal kidneys

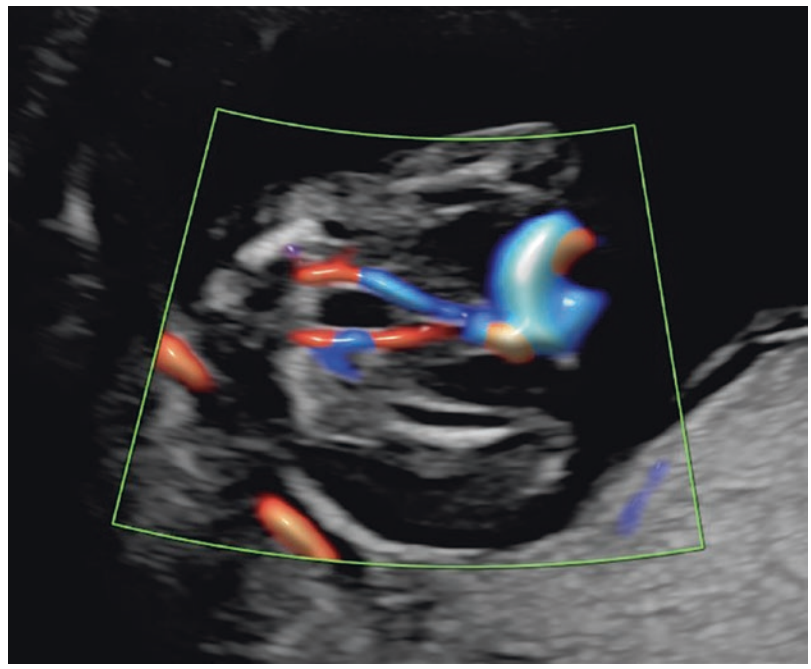

Fig. 8.30 Fetal bladder at 12 weeks 0 days. Transabdominal image showing fetal bladder (**b**) with 2 umbilical arteries coursing adjacent to bladder walls

The normal urinary bladder should measure less than 7 mm in midsagittal dimension at the time of the NT evaluation [119]. When it is greater than 16 mm, the majority of fetuses will have a poor outcome. In the 7–15 mm range, in the euploid group, the majority (>90%) will have a normal outcome [120]. It is felt that this euploid group with transient megacystis may be related to a delay in autonomic innervation of the smooth muscle of the bladder wall. An initial follow-up in 2 weeks is a reasonable approach in this intermediate group.

Fetal Gastrointestinal Tract in the First Trimester

In the embryonic period, the midgut herniates into the umbilical cord at the start of the 8th weeks and, following a 90° rotation, returns to the abdominal cavity by the end of the 12th week. Although normal physiological midgut herniation should measure less than 10 mm prior to 10 weeks and should resolve by 12 weeks, there remains some variability in timing of when the midgut fully returns to the abdomen and herniated bowel may still be present at 12 weeks in up to 20% of fetuses. If midgut herniation is still suspected at 12 weeks, follow-up imaging is recommended to ensure complete return of the herniated bowel into the abdominal cavity. The normal appearance of herniated bowel is an echogenic mass in the central cord, which progressively decreases in size toward the 9th and 10th week [113]. The liver should never be present within the herniated contents. The fetal stomach can be visualized as a fluid-filled structure in the upper abdomen by 12–13 weeks [105]. Absence of the stomach at sonography may be seen in cases of esophageal atresia; however, serial scans documenting persistent nonvisualization of the stomach are required to make this diagnosis.

Abdominal Wall and Umbilical Cord

Normal cord insertion, centrally within the abdomen, can be routinely documented after 12 weeks, following the return of the small bowel into the abdominal cavity. Number of cord vessels can be assessed and normal appearance of two arteries and one vein can be seen, either on gray scale in cross-section, or by using color Doppler to show two arteries adjacent to the urinary bladder. Umbilical cord cysts can be seen and may be associated with chromosomal abnormalities. However, these can also be a normal variant and may resolve on subsequent imaging.

Fetal Skeleton in the First Trimester

Limb buds start to form as early as the 4th week of gestation. They are first identified at ultrasound, however, between 8 and 9 weeks gestation. Ossification of the long bones of the skeletal system can be seen at around 10 weeks. Distal ossification of the phalanges is present by 11 weeks gestation. It is important to document the presence of four limbs, with each limb demonstrating three segments (Fig. 8.31). In normal development, the ratio between upper extremity and lower extremity long bones should approximate 1.0. Disproportionate length of either upper or lower extremities can indicate an underlying skeletal dysplasia and warrants further assessment. Biometry of long bones can be performed with accuracy after 11 weeks and published normograms are available for reference [121].

Assessment of Fetal Genitalia in the First Trimester

In early pregnancy, the genital tubercle is identical in size in male and female fetuses. Accurate sonographic sex determination based on external genitalia can be performed between 12 and 14 weeks [122]. Gender determination at this stage is based upon orientation of the genital tubercle, as seen in the midsagittal plane. The angle of the genital tubercle to a horizontal line through the lumbosacral skin surface is measured. Male gender is assigned if the angle is greater than 30° and female gender if the angle is less than 10° (Fig. 8.32). Gender assignment is considered indeterminate if the angle is between 10°

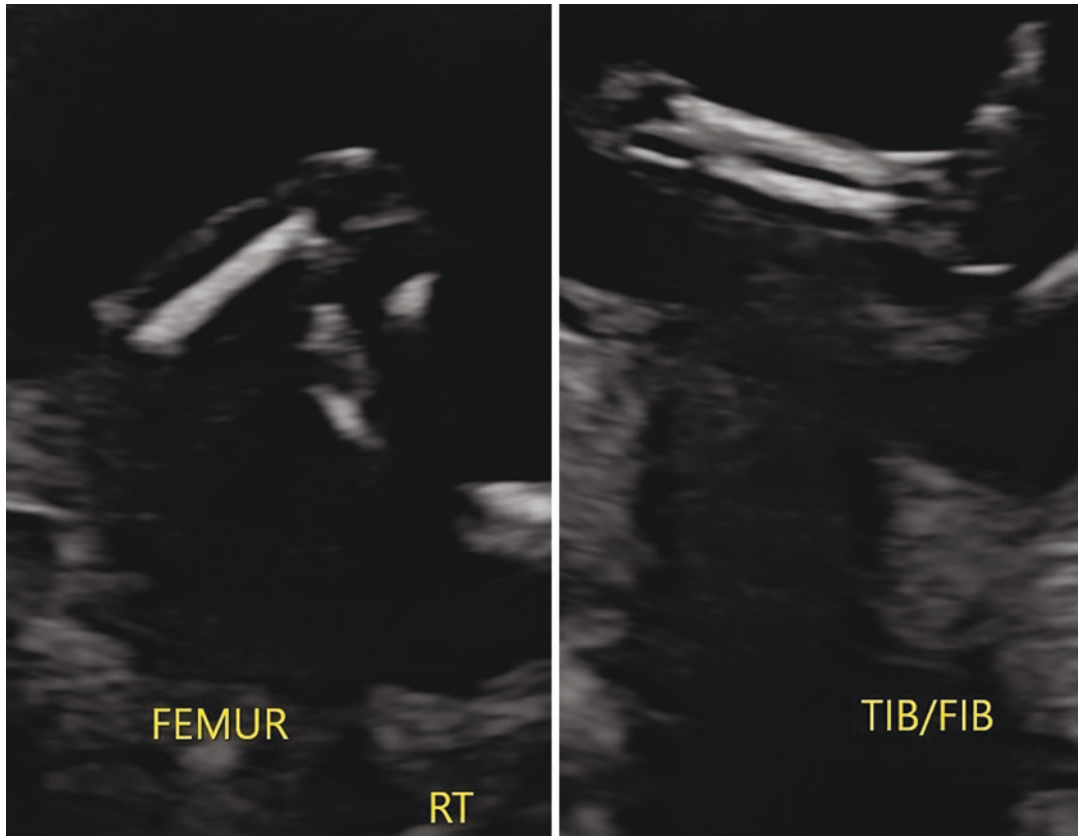

Fig. 8.31 Lower extremity at 13 weeks. Transabdominal image showing three segments of lower extremity (femur, tibia/fibula, and foot)

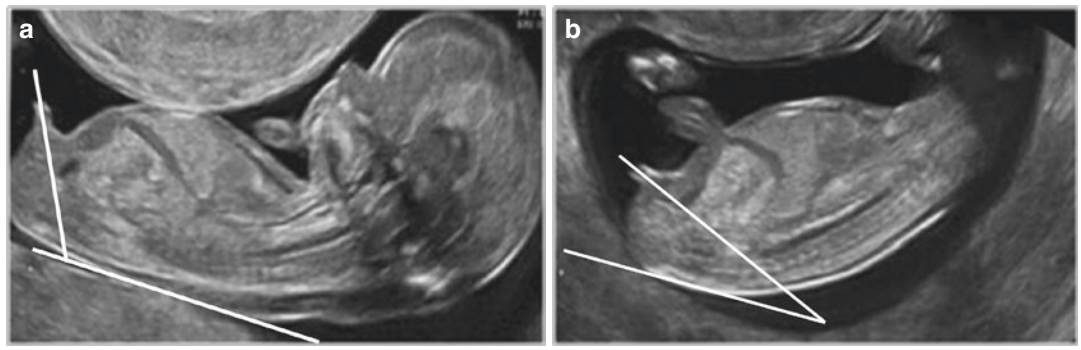

Fig. 8.32 Genital tubercle 12 weeks transvaginal images: (**a**) Vertical orientation of genital tubercle (>30° angulation) in male fetus. (**b**) More horizontal orientation of genital tubercle (<10° angulation) in female fetus

and 30°. Accuracy of gender assignment in higher in male fetuses and accuracy increases with increasing gestational age, with near 100% reliable gender identification possible at 13+6 weeks. Early assignment of fetal gender may be useful in decision-making with regard to invasive testing, such as CVS, in patients at increased risk of sex-linked disorders [123]. It should be noted that fetal sex determination using cell-free fetal DNA in maternal plasma is increasingly performed in

pregnancies at increased risk of X-linked genetic disorders or congenital adrenal hyperplasia. Early reporting of fetal gender is controversial as it may facilitate the practice of sex selection.

Assessment of Spine

Longitudinal and axial views can demonstrate normal alignment and integrity of the overlying skin, in particular toward the end of first trimester. Detailed spine assessment is recommended when the BPD measurements are less than the 5th percentile or a posterior fossa abnormality is suspected [100].

Role of Three-Dimensional (3D) and Four-Dimensional (4D) Ultrasound

Three-dimensional and 4D ultrasound are not part of the routine first trimester care evaluation. Their role remains an area for further research.[6]

Conclusion

In summary, the main goal of a first trimester ultrasound is to provide information which can be used to optimize antenatal care. The establishment of a viable intrauterine pregnancy, accurate dating, and assessment of the fetal number, chorionicity, and amnionicity are crucial components of an early pregnancy evaluation. Evaluation of the nuchal translucency is now routine practice in many centers and, when combined with maternal serology, is useful in assessing aneuploidy risk. Even in the setting of a normal cell-free DNA test excluding fetal aneuploidy, early ultrasound assessment for nuchal translucency and fetal anatomy are of value for detecting structural abnormalities. There is an increasing movement toward a systematic structured and detailed anatomic evaluation of the fetus in the first trimester. Transvaginal ultrasound provides an opportunity for evaluation of the developing embryo as early as 8–9 weeks and is an area of future research interest. It is, therefore, increasingly important to be familiar with the developmental stages of the embryo and fetus at various stages in the first trimester.

[6] See also Chap. 13.

Teaching Points

- Without sonographic evidence of ectopic pregnancy, any fluid collection with curved margins in a woman with a positive pregnancy test should be considered an early intrauterine gestational sac.
- The most accurate sonographic sign for confirmation of an IUP is visualization of the yolk sac.
- An empty gestational sac should be considered a potentially normal early pregnancy finding up to a MSD of 25 mm on transvaginal ultrasound.
- The absence of embryonic cardiac activity should be considered a potentially normal finding up to a measured embryo length of 7 mm.
- Assignment of chorionicity is a mandatory and vital component of first trimester ultrasound with multiple gestations.
- The most accurate estimation of gestational age is achieved in the first trimester by using the CRL between 8 and 13+6 weeks.
- Assessment of nuchal translucency, especially when combined with maternal age and maternal serum biochemistry, can be an effective method of screening for chromosomal abnormalities.
- In euploid fetuses, borderline or mild elevated nuchal translucency may be associated with a normal outcome.
- It is important for practitioners to be familiar with normal anatomy at various gestational ages in the first trimester.

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