

The Role of Ultrasound in Chorionic Villus Sampling

A Review

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The use of ultrasound as a guidance tool for chorionic villi sampling for prenatal diagnosis in the first trimester is discussed. Three sampling techniques used in the first trimester are reviewed: endoscopy, blind aspiration, and the combination of endoscopy and aspiration with ultrasound guidance. A review of the literature found that ultrasound guidance provided the highest success rate in obtaining chorionic villi for chromosomal analysis and enzyme determination. Concerns regarding proper scanning technique for localizing the implantation site for sampling are discussed.

Key words: chorion biopsy, chorionic villi sampling, early prenatal diagnosis.

At present, prenatal diagnosis is available in the second trimester by ultrasound, amniocentesis, or, less frequently, fetoscopy. These techniques over the last few years have proven reliable in diagnosing a multitude of intrauterine abnormalities and diseases.¹⁻⁶ However, these methods are not usually employed until the middle of the second trimester (16-20 weeks).

Ultrasound is now widely used in obstetric care, and although some anomalies can be detected from the 12th to the 14th week of gestation, there are many conditions which cannot be recognized until later in pregnancy.

Genetic amniocentesis is performed at approximately the 16th week of gestation for three reasons: the uterus is readily accessible transabdominally; there is usually a sufficient amount of amniotic fluid; and cell growth is optimal, with accurate curves for α -fetoprotein analysis. However, results from the cell culture are often not available for 3 weeks, and in case of culture failure, the decision on

the management of a possible anomaly is carried into mid-pregnancy. This may cause considerable parental distress, especially because the mother may have perceived the onset of fetal motion.

Fetoscopy allows for diagnosis of morphologic and hematologic disorders. Blood sampling is frequently delayed until about the 18th to 20th week of gestation. Before 18 weeks, it has been demonstrated that pure fetal blood was not easily obtainable for proper analysis.² Direct visualization of fetal parts may be difficult because of fetal positioning and the clarity of the amniotic fluid. It has also been observed that bleeding occurs frequently after fetoscopy, which may contribute to the 1% fetal loss rate.³ In the situation where congenital abnormalities or hemoglobinopathies are detected and termination of the second trimester pregnancy is undertaken, the mother is subjected to increased risks from complications such as cervical and uterine trauma and hemorrhage, as well as the emotional anxiety.^{1,4}

To eliminate some of these problems, recent interest has been focused on developing a method for sampling and culturing tissues in the first trimester. The most accessible tissue at this stage of pregnancy is the chorionic villi. The role of ultrasound is to act as a guidance tool for the physician to obtain the chorionic villi. First trimester (chorionic villi sampling) diagnosis will in most cases give the same information presently obtained by second trimester techniques. According to Simoni et al.⁵ and Rodeck et al.,⁴ if an abnormality is diagnosed in the first trimester and the mother wishes to terminate the pregnancy, aspiration termination of pregnancy at a gestational age less than 14 weeks has less morbidity than second trimester abortions.

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EARLY PLACENTAL DEVELOPMENT

At approximately 4 menstrual weeks, the implantation process by invasive action on the part of the trophoblast cells is complete. The endometrium has undergone the decidual reaction, resulting in the development of three distinct regions. The region beneath the conceptus is the decidua basalis (the future placental site); the decidua capsularis surrounds the rest of the blastocyst; and the decidua vera or parietalis lines the remainder of the uterine cavity.

During the formation of the embryonic disk, the cytotrophoblast and syncytiotrophoblast (trophoblast cells) continue to develop and expand around the chorionic sac and the decidua basalis region. This leads to the beginning stages of primary chorionic villus development and the uteroplacental circulation.

By the fifth week, the increased development of chorionic villi in the decidua capsularis and basalis regions greatly enhances the surface area of the chorion for exchange of nutrients and other substances between the maternal and embryonic circulations.

Prior to the ninth to tenth week, the chorionic sac is covered with villi. As the sac grows, the blood vessels in the decidua capsularis become compressed

and degenerate, leaving a relatively avascular base area called the smooth chorion. During the same period, the villi in the decidua basalis region branch and increase dramatically in number and size to form the chorion frondosum, the fetal component of the future placenta. Ideally, this is the location where chorionic villus samples should be obtained.

It can be observed from the chorionic development that villi may be obtained from either the implantation site (chorion frondosum) or from the surrounding chorionic sac prior to degeneration at the tenth week (Fig. 1). Either location has proven successful in chorionic sampling applications.⁶⁻⁸

Sampling of chorionic tissue should yield adequate cellular cultures for chromosomal analysis, without maternal tissue contamination and with minimal risk to the mother and fetus.⁴

CLINICAL REVIEW

The success of obtaining a good sample without complications depends on the biopsy technique. There have been numerous methods employed to gather chorion samples. They include:

1. endoscopic direct vision biopsy
2. blind aspiration
3. lavage and blind aspiration
4. ultrasound guided needle aspiration or biopsy forceps
5. a combination of endoscopy and ultrasound guidance
6. transabdominal biopsy under ultrasound guidance.

Table 1 summarizes the success rate of obtaining chorionic samples with different techniques. It shows that ultrasound guidance, whether it is used in conjunction with endoscopy or alone, provided an improved success rate. Because the risks of chorionic sampling to fetal and maternal well-being are not yet known, most investigations were conducted on patients who were undergoing therapeutic abortion.

The first chorionic sampling was reported in 1968 by Mohr and Hahnemann,⁹ who introduced the concept of transcervical chorion biopsy by endoscopy. With further investigation of this method, Hahnemann⁹ in 1974 sampled 95 patients with a success rate of only 38%. Kullander and Sandahl¹⁰ and Simoni et al.⁵ similarly used the endoscope technique, with success rates of 51% and 76%, respectively. The difference in success rates may be

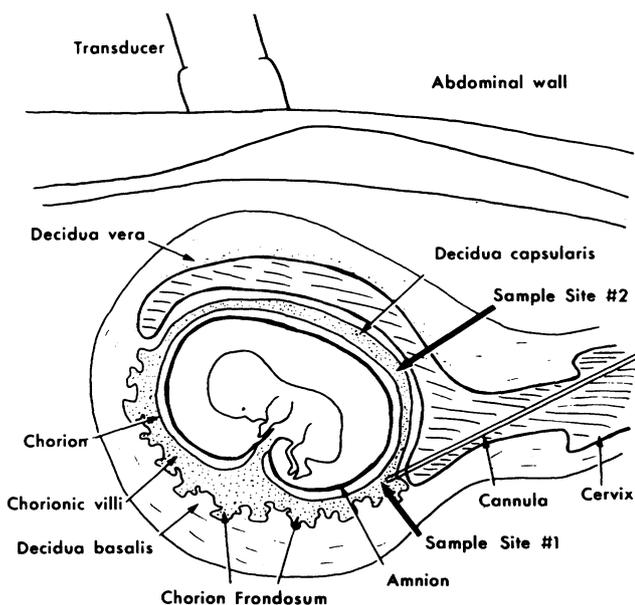


FIG. 1. Graphic illustration of the embryo in relation to the cannula insertion and chorionic sampling site. Sample site 1 is the ideal location for aspiration. Sample site 2 is an alternative location for aspiration of chorionic villi prior to the tenth week of gestation.

due to user familiarity with the technique. Some of the major problems encountered were infection, amniotic sac punctures, maternal tissue contamination from the decidua within samples, and bleeding.^{7,9,10} However, both Hahnemann⁹ and Simoni et al.⁵ attributed these failures to the difficulty in recognizing the sample site, particularly in early gestation, which led to sac disruption, bleeding, and obscured vision.

A relatively simple approach is used for the blind aspiration technique. The aspirator is inserted transcervically until resistance is felt in the expected region of the gestational sac. Aspiration follows. The success rate is in the 60% to 70% range,^{5,8,11,12} but again, similar complications have arisen.

A Chinese group from Tietung Hospital¹¹ first used the blind aspiration technique and achieved a success rate of 73% on 100 patients. However, 86% of the samples contained blood, and amniotic sac puncture occurred in 3% of the samples. The inadequacy of blind aspiration was further demonstrated in studies by Lui et al.,⁸ Howell et al.,¹² and Simoni et al.,⁵ with success rates of 33%, 40%, and 64% to 66%, respectively.

With the introduction of real-time ultrasound guidance of the aspirator or forceps or in conjunction with endoscopy, successful sampling of the chorion frondosum was improved.

Kazy et al.⁷ were the first to utilize ultrasound to locate the chorion frondosum and guide the biopsy forceps. One hundred sixty-five patients between 6 and 12 weeks' gestation were sampled, and the success rate was 77%. Twenty-nine patients continued the pregnancy. No amniotic sac punctures were recorded.

Other investigators^{4-6,13-16} similarly found ultrasound guidance to play an important role in obtaining chorionic tissues with relatively little difficulty.

Rodeck et al.¹³ compared six different methods of chorionic sampling: blind aspiration, contact hysteroscopy, microbiopsy forceps under direct vision, aspiration biopsy under direct vision, microbiopsy forceps under direct vision with ultrasound control, and aspiration biopsy under direct vision with ultrasound control. They found that the last technique provided the best result, with a 100% success rate. This is attributed to the fact that ultrasound provides recognition of the implantation site in advance, therefore allowing accurate guidance to the proper site with minimal maneuvering.

Simoni et al.⁵ compared three different methods: endoscopy, blind aspiration, and a combination of

TABLE 1. Success Rate of Chorionic Sampling with Different Techniques

Technique	No. of Patients	Success Rate
Endoscopy	95	38% ⁹
	39	51% ¹⁰
	62	76% ⁵
Blind aspiration	137	33% ⁸
	82	40% ¹²
	157	64% ⁵
	48	66% ⁵
	100	73% ¹¹
Ultrasound and biopsy forceps	165	77% ⁷
Ultrasound and transabdominal biopsy	58	84.5% ¹⁸
Ultrasound and aspiration	155	84% ¹⁶
	47	89% ⁶
	40	90% ¹⁷
	100	93% ¹⁶
	103	96% ⁵
Ultrasound and endoscopy	48	100% ¹³
	13	100% ¹⁵

aspiration and ultrasound guidance. The last technique achieved a success rate of 96%.

Investigators^{5-7,13-17} have used real-time ultrasound either alone or with endoscopy and have achieved very high success rates (Table 1). However, the ultimate decision on the best method depends on user familiarity and experience.

In a recent study by Smidt-Jensen and Hahnemann,¹⁸ transabdominal fine-needle biopsy monitored by ultrasound achieved a success rate of 84.5%. This technique was employed because of patients' displeasure with transcervical sampling.

In light of the current research in chorionic sampling, the employment of ultrasound has proven invaluable. This has been specifically stressed by investigators who have previously used only blind aspiration techniques.^{8,12}

METHODS AND PROCEDURES

The ultrasound examination, prior to the sampling of chorionic tissue, provides useful information for the investigator. Gestational age is determined by crown-to-rump measurements to ensure that dates are correct. Fetal heart rate, the number of fetuses, and the position of the fetus in relation to the chorionic frondosum are recorded (Fig. 2).

With the patient in the lithotomy position, disinfectant is applied to the vagina and cervix, and either the endoscope or the aspirator is inserted through the internal os. The real-time transducer,

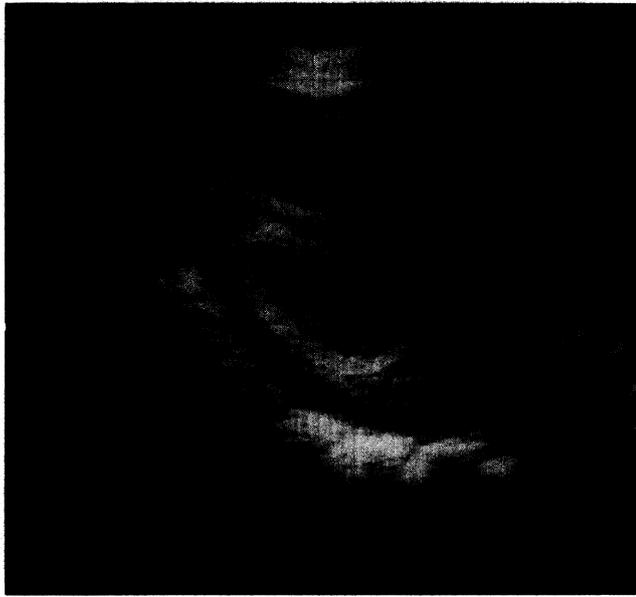


FIG. 2. Sonographic illustration of the embryo in relation to the cannula and the chorion frondosum. *Small black arrows, chorion frondosum; black arrow, cannula; white arrow, embryo* at 9 weeks' gestation.

placed on the lower abdomen, localizes the uterus in a sagittal view for assessment of the implantation site. The cannula is easily detected ultrasonically and guided toward the lowest border of the chorion frondosum so that amniotic sac disturbances can be avoided⁵ (Fig. 3).

Tissue movement into the cannula during aspiration and a small echo-free space at the sample site after withdrawal of the cannula can be detected by ultrasound. It is important to continue monitoring this region for any signs of hematoma formation.

After the sample is obtained, the fetal heart rate is observed and any disturbances of the gestational sac are noted. At present there are a large number of ongoing pregnancies worldwide.

Kazy et al.⁷ stated that ultrasonic surveillance presented a distinct vision of the target so that the biopsy was taken with the least possible harm to the amniotic sac. The screen clearly showed the shape of the biopsy forceps, and all stages of the procedures could be monitored.

Transabdominally,¹⁸ the use of static and real-time scanners with puncture needles attached to the sides were used with a high success rate. With static scanning, the combination of A-mode and B-mode delineated the demarcation and depth of the gestational sac. This method was replaced by continuous real-time surveillance.

DISCUSSION

It has been suggested by some authors^{5,7,18} that the best time to sample chorionic villi is between 8 and 9 weeks, because the amnion is still separated from the chorion by the embryonic coelom, which acts as a buffer against amnion damage.⁸ Other investigators^{6,8,17,19} suggest that between the 10th and 11th week the chorion frondosum is well developed, allowing for easy ultrasound recognition and access to the villi.

Some information that has currently been obtained from chorion sampling includes sex determination by X and Y chromatin analysis,^{7,11} fetal karyotype analysis and enzyme determination,⁵ and DNA analysis such as sickle cell disease or thalassemia by enzyme analysis.¹⁴ Further research and refining of technological aspects will provide information comparable to that obtained with amniocentesis and fetoscopy but within a shorter time interval.^{5,20}

Many pregnancies have continued after sampling, with normal deliveries and birth weights between 3100 and 4250 g. It has been estimated that the chorion mass is 16 to 25 g at 8 to 10 weeks of pregnancy, while the biopsy specimen is 0.07% to 0.1% of the entire chorionic mass. It appears that a sample of this size does not represent a significant risk to the fetus.⁷

It has been demonstrated in studies^{11,14,20} where the pregnancies were allowed to continue that the



FIG. 3. Sonographic illustration demonstrating the cannula in the lowest portion of the chorion frondosum. *Black arrow, cannula tip; white arrow, embryo* at 9 weeks' gestation.

spontaneous abortion rate was 6%. While more data is needed for us to obtain accurate risk figures, presently the risks are no higher than the documented risk (5-10%) of spontaneous abortion in the first trimester of pregnancy.^{6,20} Perry et al.¹⁶ suggest that a spontaneous abortion rate following chorionic villus sampling be compared with the rate among fetuses ultrasonically proven viable at the time when chorionic villus sampling would have been performed but not subjected to the sampling. This will provide valuable information for the physician as well as for parents who are concerned about the risks of chorionic villus sampling. A preliminary analysis of questionnaire responses showed that if the spontaneous abortion rate were similar to amniocentesis, women would prefer chorion villus sampling.¹⁶

Niazi et al.²¹ suggest that the abortion rate of 5% may be lowered by using ultrasound to locate the chorion frondosum easily. If ultrasound is the key to lower abortion rates, proper teamwork and scanning technique are essential. For optimal ultrasonic scanning during transcervical biopsy, it has been demonstrated that linear-array monitoring causes frequent reverberation artifact due to the high acoustic impedance of the cannula. Also, beam width artifact commonly produces the appearance of sac perforation. It has been found that sector real-time scanning eliminates this problem.¹³

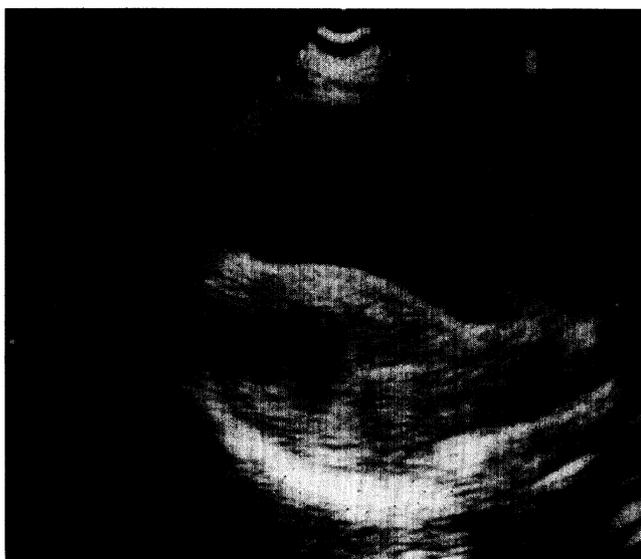


FIG. 4. Sonographic illustration demonstrating the importance of maintaining the tip of the cannula in the field of view to avoid amniotic sac puncture. *Black arrow*, tip of cannula; *white arrow*, embryo at 9 weeks' gestation.

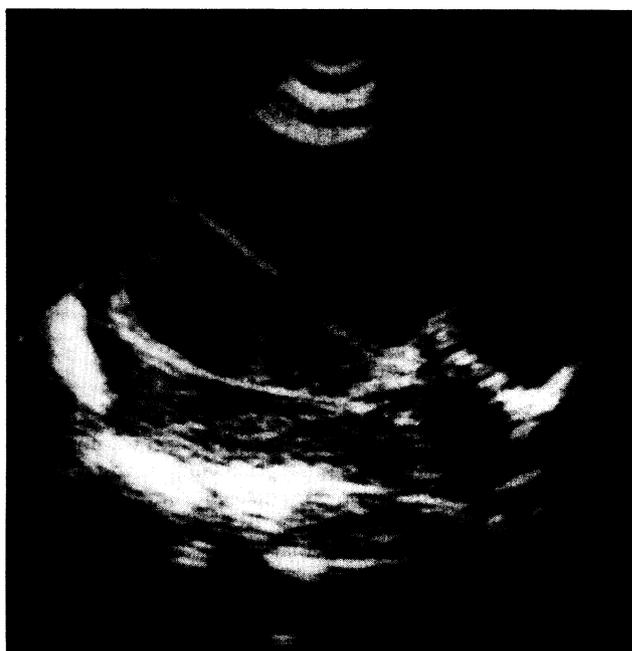


FIG. 5. Sonographic illustration demonstrating the distance to the sample site and the importance of maintaining the cannula in the field of view throughout the entire procedure. *Black arrow*, cannula tip.

Approximately 90% of the investigators failed to mention the necessity of a full bladder in their methods and procedures; this could be a reason some studies demonstrated lower success rates. It is important for the patient to have a relatively full bladder, allowing the focal zone of the ultrasonic beam to be perpendicular to the uterus. The full bladder also straightens out the anteverted uterus to allow easier access to the placental site especially if it is located anteriorly. More importantly, it allows the ultrasonic beam to be perpendicular to the entering cannula so that the tip is maintained in view for proper guidance (Figs. 4 and 5). Improper scanning technique may cause amniotic sac puncture and fetal distress. Furthermore, experience on the part of the clinician and sonographer should show an increase in the success rate of obtaining chorionic villi.⁶ Figure 6 illustrates the dangers of not maintaining the tip of the cannula or needle in view.

SUMMARY

The primary role of ultrasound in chorionic villus sampling is to guide aspirators, needles, or endoscopes to the appropriate sampling region and to

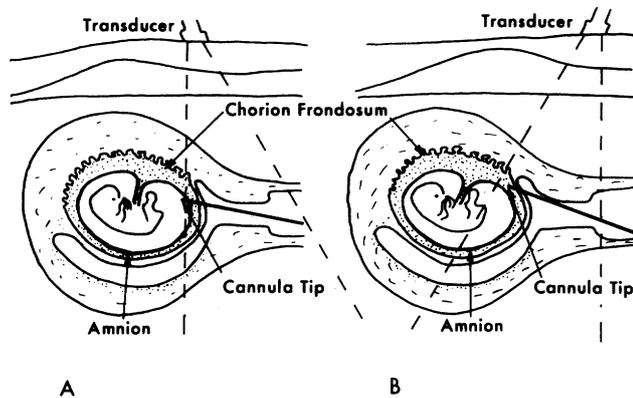


FIG. 6. Graphic illustration demonstrating the dangers of not positioning the transducer perpendicular to the cannula tip. A. The tip of the cannula punctures the amnion because of improper transducer positioning. B. The proper technique places the transducer perpendicular to the cannula tip during chorionic villus sampling.

monitor the site after sampling for signs of hemorrhage. The risks of fetal loss, obstetric complications associated with chorion sampling, and long-term pediatric effects have yet to be assessed. Maternal hazards appear minimal to date.

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