Objectives

1. Describe how the amniocentesis procedure has changed over the years and the best approach currently for performing the procedure to minimize complications.
2. Explain the various risks and complications associated with amniocentesis.
3. Explain the significance of brown colored fluid that may be obtained at the time of genetic amniocentesis and the use of amniocentesis in Rh negative women.
4. Describe how intra-amniotic bleeding that can occur at the amniocentesis site, may appear sonographically.

Introduction and History:

The first amniocentesis procedures were reported by Von Schatz, Lambl, and Prochownick in the 1870’s and early 1880’s. These early procedures were used to relieve patients that were suffering from severe polyhydramnios. In 1930, Menees reported performing the procedure on pregnant women for the purpose of amniography.

The main focus of the amniocentesis changed to that of a diagnostic procedure in the mid 1950’s. These early procedures were for fetal gender determination based in part on the research of the Canadian anatomist, Murray Barr, who described the “barr body” in 1949. When more than one X-chromosome is present, one is usually active and the other is inactivated. The inactivated X-chromosome forms a chromatIn mass called a barr body. The sex chromosome makeup for females is two Xs and for males is an X and a Y. Therefore, females will have a barr body and males do not. In 1956, Fuchs and Riis reported performing amniocentesis procedures to determine fetal sex by analysis of the presence or absence of the barr body.

In the mid 1960’s, Steele, Bregs, and Nadler described the performing of amniocentesis procedures in order to culture cells for a full chromosome analysis and also the measurement of alphafetoprotein (AFP). Hence the birth of the genetic amniocentesis. Since the late 1960’s, amniocentesis has become a very common obstetrical procedure, not only for genetic
evaluation, but also for diagnosing other issues such as infections, fetal maturity, relieving polyhydramnios, and in analyzing Rh sensitized women.

The Risks of amniocentesis:

From a statistical point of view, amniocentesis is a very safe procedure with an overall complication rate that is very low (usually less than 1%). However, the complications that might occur can be devastating to a family such as injury to the fetus or loss of the pregnancy. Therefore, the procedure should never be taken lightly. The pregnant couple should understand the reason why they might have the procedure performed and agree to having it done. This is especially true for pregnancies that have not reached viability (such as the majority of genetic procedures).

The complications related to amniocentesis include pregnancy risks of rupturing the membranes, causing bleeding, and introducing infection – all of which might result in the loss of the pregnancy. The fetal risks can include trauma from the needle and/or death (primarily due to the pregnancy delivering prior to viability), while the maternal risks reported have included intra-abdominal infections, sepsis, amniotic fluid embolus, and endometriosis in the needle track.

The majority of studies that have analyzed the pregnancy loss rate related to the procedure have focused on the genetic amniocentesis performed prior to viability or less than 23 weeks gestation. When evaluating these studies, multiple factors come into play including the use of ultrasound and how ultrasound is utilized, the gauge of the needle, experience of the performer, fluid color, the number of procedures required in order to obtain enough fluid, transplacental approach, and maternal history.

Another difficulty that is encountered when looking at the various studies is how “a pregnancy loss” was defined. There are well over 50 studies in the literature that have analyzed the loss rate following amniocentesis. Some of these have compared the survival rate all the way up to 7 days after delivery, whereas others have analyzed the loss rate up to 28 weeks gestation. Still others have only compared the loss rate up to 24 weeks or only within 1 to 4 weeks following the procedure. As
you can, it is difficult to determine the true definition of a loss following the procedure. In addition, some of these studies only report their outcome with no comparison or controls. Furthermore, nearly all of them are retrospective meaning that the data was collected at a later date.

To compare the loss rate differences all the way to delivery including the first 7 days of life of the newborn between pregnancies that had an amniocentesis versus those that did not seems quite long. This brings into play the differences in how pregnancies were handled once viability was reached and may not be a true indication of the actual risk of the procedure. If one analyzes only the prospective controlled studies that evaluated the loss rate up to 28 weeks gestation, the difference between the two groups (those with amniocentesis versus those without) is about 0.4% to 0.5% which is 1 in 200 to 1 in 250. This risk of 1 in 200 to 1 in 250 is probably the most often used risk rate quoted for amniocentesis and was the rate found in the United States Collaborative study.

Many other studies are in print that have listed loss rates ranging from 1 in 150 to 1 in 500, but again, most of these are retrospective without controls and vary on the use of ultrasound, experience of the performer, the needle size, and number of attempts. Currently there is only one prospective randomized study on genetic amniocentesis and this will probably never be performed again for ethical reasons. The study by Tabor, et al, was published in 1986 and involved 4,606 low risk women ages 25 to 34 who were randomized to have a genetic amniocentesis versus no amniocentesis and the loss rate difference was 1 in 100 or 1%. The original study reported the use of an 18 gauge needle but this was later described as a 20 gauge needle in a letter to the editor.

As stated before, several factors need to be examined in regard to amniocentesis and its complications. The following list includes the more significant issues:

1. The use of ultrasound and how it is utilized.
2. The gauge of the needle.
3. The experience of the performer.
4. The number of attempts to be successful.
5. Whether the needle traverses the placenta.
6. Fluid color.
7. Maternal history.

When the literature is analyzed, it becomes very clear that the use of ultrasound and how it is utilized is very important if not the most important factor in minimizing the risk of the procedure. The other factors in the list are important; however, without ultrasound, you are in essence blind. The literature actually shows us how the use of ultrasound with amniocentesis has changed over the years. As previously stated, the first procedures were performed blindly without the use of ultrasound. This was followed by only using ultrasound to identify fetal viability and placental location. The next step in progression was to use ultrasound to mark a site on the abdomen where a pocket of fluid was seen. However, studies showed that these pockets are often transient due to fetal movement and the fullness of the maternal bladder. It is clear based on the literature that the best approach for amniocentesis in order to minimize the number of attempts that are needed in order to obtain enough fluid and to minimize the number of “bloody” taps is to perform continuous ultrasound guidance during the procedure.

A technique that is commonly utilized in continuous ultrasound guidance is to initially use the ultrasound transducer to
identify a pocket of fluid free of the fetus and umbilical cord and to determine the angle of the needle insertion and approximate depth. The transducer can then be placed several centimeters away from the insertion site at an angle that allows the performer to observe the actual needle penetration and path into the pocket of fluid (figure 1). This technique seems to decrease the number of bloody taps and decrease the failure rate.

Currently, before an amniocentesis is attempted, an ultrasound should be performed to determine fetal viability and position, placental location, number of fetuses, and gestational age. In addition, the ultrasonographer should determine the location of amniotic fluid pockets and look for issues that might increase the difficulty of the procedure such as uterine fibroids, etc.

In regard to needle size, it appears that the smaller gauge needles (size 20 or 22) have less problems than larger bore needles such as 18 or 19 gauge needles. In addition, the experience of the performer will decrease the failure rate and the number of bloody taps.

A failure to obtain fluid can occur despite the use of continuous ultrasound guidance with an experienced performer. The more common causes for failure are as follows:

1. Tenting of the membranes.
2. Isolated uterine wall contraction (which distorts the fluid pocket or makes entry into the amniotic sac unsuccessful).
3. Fetal movement that changes the shape of the fluid pocket.

Membrane tenting is a frustrating situation where the needle traverses the uterine musculature, but instead of puncturing the membranes and entering the fluid pocket, the needle actually pushes the membranes off the inner uterine wall.

The issue of transplacental procedures is one of controversy. Several authorities believe that traversing the placenta can increase the complication rate, while others disagree. The majority of studies do not have enough cases of transplacental needle passage to actually make a comparison. It does seem apparent that intra-amniotic bleeding is more common following a transplacental procedure, however, membrane tenting is less common. Most experienced individuals will try to avoid the placenta if possible.

Finally, a common question is whether an amniocentesis is more risky in patients who have a history of pregnancy loss. Very few studies are in existence that have analyzed this question. Most studies outside of amniocentesis have shown that women with a history of first trimester pregnancy loss who make it past the first trimester have no higher complication rate when compared to women who do not have a history of pregnancy loss. This would suggest that the primary problem in these women is the first trimester. In that respect, most amniocentesis procedures occur after the first trimester.

The majority of genetic amniocentesis procedures are performed between 15 and 20 weeks of gestation. One of the arguments against this time period is that the result is obtained later in the pregnancy making it more difficult to act upon. Therefore, an “early amniocentesis” procedure has been reported, which is one that is performed between 11 and 14 weeks gestation. Several studies have looked at the loss rate with early amniocentesis compared to routine amniocentesis and the majority have shown only a slightly higher rate with the early procedure. Therefore, it might be prudent to recommend that women who have a history of first trimester pregnancy loss wait until they go beyond the first trimester before an amniocentesis is performed. This issue, however, is a discussion that should occur between the patient and her healthcare provider.
The Significance of Brown Fluid:

When a genetic amniocentesis is performed, the amniotic fluid should be clear. Periodically, a brown or green colored fluid is encountered. From 30,257 genetic procedures obtained from combining 16 different studies, a total of 677 brown or green fluid samples were identified for an overall occurrence of about 2% (range of 1% to 7%). The pregnancy outcome was reported for 517 of these cases. A total of 62 pregnancies were lost for a rate of 12%. This is higher than the loss rate for pregnancies with clear fluid but not unexpected when the cause for the discoloration is revealed.

When the pigment is analyzed, the result is hemoglobin in over 90% of the cases. This is consistent with the fact that in over 50% of cases in which discolored fluid is found, a history of bleeding during the pregnancy has occurred. Usually, the hemoglobin content is adult suggesting it is from the mother, but occasionally it can involve fetal hemoglobin. In addition, if the amniotic fluid AFP is elevated in the presence of this fluid, the fetal loss rate is even higher (again suggesting that the discoloration was fetal in origin).

Intra-amniotic Bleeding and Potential Concerns:

In most cases, once the needle has entered the amniotic sac and fluid is obtained, the ultrasonographer will turn their attention to the fetus and other intrauterine contents. However, if the site where the needle penetrates the intrauterine cavity is observed after the needle is removed, intrauterine bleeding can be seen. One prospective study identified intrauterine bleeding in 38% of the cases (in which the placenta was not traversed), but the bleeding stopped in less than 30 seconds over 90% of the time. There were no differences in pregnancy outcome when the pregnancies with bleeding were compared to no bleeding. This would suggest that visible bleeding is a normal occurrence with amniocentesis but is also unavoidable. In fact, in a few cases, the bleeding lasted for several minutes and intrauterine clots developed (figures 2, 3 & 4). If an ultrasonographer is unaware that this can occur, they might misinterpret these clots as fetal malformations, masses, or amniotic bands, etc.

The fact that visible bleeding can occur raises a concern with performing an amniocentesis on pregnant women who have a blood borne infection that may not cross the placenta under normal circumstances. For example, studies have shown that the majority of newborns infected with the hepatitis B virus become infected at the time of delivery. This is why obstetrics tries to identify pregnant women who are carriers of this virus and immunize the baby at delivery to potentially prevent infection. However, an amniocentesis on a hepatitis B carrier might expose the neonate to the virus several weeks to months before the delivery without the benefit of immunization. Unfortunately, at the present time, it is unknown whether an amniocentesis is potentially harmful in exposing the neonate to certain maternal blood borne infections such as hepatitis B or HIV (human immunodeficiency virus) etc.

Amniocentesis and Rh negative women:

Several studies have been performed that have analyzed whether an amniocentesis increases the potential for fetal to maternal hemorrhage. To answer this question, researchers used the Kleihauer-Betke test (an analysis of maternal blood for the presence of fetal cells) or a rise in the maternal serum AFP level. In short, nearly every study has shown that fetal to maternal bleeding does occur with some amniocentesis procedures. For the most part, these fetal to maternal bleeds are very small and do not result in any untoward outcome. However, in a pregnant woman who is Rh negative (who might be carrying an Rh positive fetus), exposure to Rh positive fetal blood could sensitize her to the Rh antigen and lead to significant future obstetrical difficulties. Therefore, the Rh status of pregnant women should be known prior to the procedure and those who are Rh negative should be offered Rhogam to potentially prevent the risk of sensitization. The administration of anti-D immunoglobulin (Rhogam) is recommended by ACOG for pregnant women who are Rh negative.
Summary:

Amniocentesis is a common obstetrical procedure that has a very low complication rate. It is the use of ultrasound that has primarily reduced this rate. An amniocentesis can be used to obtain very important information for the pregnant couple and for healthcare personnel. However, it is important to understand why the procedure is suggested and the couple should have good informed consent. In addition, the information that is to be obtained from the amniocentesis should have the potential of affecting the course of the pregnancy.

Figures:

1. The path of the amniocentesis needle directed into the amniotic sac.
2. The path of the amniocentesis needle through the edge of the placenta.
3. A stream of bleeding seen after the needle was removed.
4. A clot of blood collected next to the fetal head (the baby delivered at term and was entirely normal).

References or Suggested Reading:


About the Author(s)

Dr. Towers is currently Professor and Vice Chair of the Department of Obstetrics & Gynecology at University of Tennessee Medical Center Knoxville in the Division of Maternal-Fetal Medicine. He is still clinically active managing numerous high-risk pregnancies. He is also actively involved in research with over 90 publications in major medical journals. Though his research has spanned many areas in obstetrics, he has primary interests in drugs in pregnancy, infections in pregnancy, fetal heart monitoring, bleeding in pregnancy, and fetal lung maturity.

He has authored a book for consumers regarding the safety of over-the-counter medications that are used in treating the common cold entitled “I’m Pregnant & I Have a Cold – Are Over-the-Counter Drugs Safe to Use?” published by RBC Press, Inc. He is also one of the new Editors of the reference book for clinical care providers entitled “Drugs in Pregnancy and Lactation, published by Wolters & Kluwer.