

AMNIOCENTESIS AND WOMEN WITH HEPATITIS B, HEPATITIS C, OR HUMAN IMMUNODEFICIENCY VIRUS

This guideline has been reviewed by the Genetics Committee and approved by Executive and Council of the Society of Obstetricians and Gynaecologists of Canada.

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Abstract

Objective: To review the risk of *in utero* infection through amniocentesis in women with hepatitis B, hepatitis C, or human immunodeficiency virus (HIV).

Outcomes: Fetal and neonatal morbidity and mortality.

Evidence: Review articles, meta-analyses, and MEDLINE searches from 1966 to 2002 for English-language articles related to amniocentesis, fetal and neonatal infection, and hepatitis B, hepatitis C, or HIV.

Values: The evidence collected was reviewed by the Genetics Committee of the Society of Obstetricians and Gynaecologists of Canada (SOGC) and quantified using the Evaluation of Evidence guidelines developed by the Canadian Task Force on the Periodic Health Exam.

Recommendations:

1. The risk of fetal hepatitis B infection through amniocentesis is low. However, knowledge of the maternal hepatitis B e antigen status is valuable in the counselling of risks associated with amniocentesis. (II-1C)
2. Amniocentesis in women infected with hepatitis C does not appear to significantly increase the risk of vertical transmission, but women should be counselled that very few studies

have properly addressed this possibility. (II-2C)

3. In HIV-positive women all noninvasive screening tools should be used prior to considering amniocentesis. (II-2D)
4. For women infected with hepatitis B, hepatitis C, or HIV, the addition of noninvasive methods of prenatal risk screening, such as nuchal translucency, triple screening, and anatomic ultrasound, may help in reducing the age-related risk to a level below the threshold for genetic amniocentesis. (II-2C)
5. For those women infected with hepatitis B, hepatitis C, or HIV who insist on amniocentesis, every effort should be made to avoid inserting the needle through the placenta. (II-1B)

Validation: These guidelines have been approved by the SOGC Genetics Committee, SOGC Executive, and SOGC Council.

Sponsors: The Society of Obstetricians and Gynaecologists of Canada.

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INTRODUCTION

These guidelines are designed to review the risks of *in utero* infection through amniocentesis in women with hepatitis B, hepatitis C, or the human immunodeficiency virus (HIV), so that obstetric care providers may better counsel these women about the option of genetic or therapeutic amniocentesis.

Key Words

Pregnancy, genetics, amniocentesis, hepatitis, human immunodeficiency virus, prenatal diagnosis

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The quality of evidence reported in these guidelines has been described using the Evaluation of Evidence criteria outlined in the Report of the Canadian Task Force on the Periodic Health Exam (Table).¹

AMNIOCENTESIS AND HEPATITIS B

In women presenting for prenatal care, hepatitis B has a prevalence of 0.34% to 1.1%.²⁻⁴ The rate of vertical transmission in hepatitis B surface antigen (HbsAg) positive women without immunoprophylaxis is approximately 15%, and may be as high as 90% in those women who are HbsAg and hepatitis B e antigen (HbeAg) positive. With appropriate immunoprophylaxis, the rate of vertical transmission drops to 1.5% for women who are HbsAg positive and to 10% for women who are HbsAg and HbeAg positive.⁵ There have been 115 HbsAg positive women reported to have had genetic amniocentesis.⁶⁻⁹ All the infants of these pregnancies received hepatitis B vaccination and immunoprophylaxis commencing at birth. In one series, 3 infants (2.6%), delivered of mothers who were HbeAg positive, demonstrated postnatal seroconversion.⁹ This rate of immunoprophylaxis failure is consistent with rates seen in women who have not undergone amniocentesis.¹⁰ These findings would suggest that the risk of fetal hepatitis B infection through amniocentesis is low. However, knowledge of the maternal HbeAg status would be valuable in the counselling of risks associated with amniocentesis.

RECOMMENDATION

1. The risk of fetal hepatitis B infection through amniocentesis is low. However, knowledge of the maternal

hepatitis B e antigen status is valuable in the counselling of risks associated with amniocentesis. (II-1C)

AMNIOCENTESIS AND HEPATITIS C

The prevalence of hepatitis C varies greatly, depending on the population studied. Generally, the prevalence in women of reproductive age is 1% to 2%.^{11,12} In women in the Canadian federal penitentiary system, however, the prevalence is 40%.¹³ The prevalence in antenatal clinics in Scotland is 0.6%.¹³ The rate of vertical transmission is approximately 5% to 10%.¹⁴⁻¹⁷ The exact timing of vertical transmission is unknown, but elective Caesarean section does not appear to be preventive.¹⁷ The risk of vertical transmission appears to be increased in women whose hepatitis C is associated with active liver disease, in those whose levels of hepatitis C virus ribonucleic acid (HCV RNA) are greater than 10⁶/mL, and in women co-infected with HIV.^{14,17}

The only series reporting the use of amniocentesis in hepatitis C positive women describes 22 women, of whom 16 had HCV RNA identified in their serum. All women (median age 39 years) underwent amniocentesis in the fourth month of pregnancy.¹⁸ The amniotic fluid samples were tested using polymerase chain reaction for HCV RNA. Of the 16 viremic women, HCV RNA was detected in the amniotic fluid of 1 patient. The placenta was anterior in this case. None of the children from these pregnancies, including the child from the pregnancy with HCV RNA positive amniotic fluid, was found to be HCV RNA positive on postnatal testing.¹⁸ Although somewhat reassuring, little is learned from this series, as the expected number of seropositive children would be only 1 or 2,

QUALITY OF EVIDENCE ASSESSMENT ¹	CLASSIFICATION OF RECOMMENDATIONS ¹
<p>The quality of evidence reported in this document has been described using the Evaluation of Evidence criteria outlined in the Report of the Canadian Task Force on the Periodic Health Exam.</p> <p>I: Evidence obtained from at least one properly randomized controlled trial.</p> <p>II-1: Evidence from well-designed controlled trials without randomization.</p> <p>II-2: Evidence from well-designed cohort (prospective or retrospective) or case-control studies, preferably from more than one centre or research group.</p> <p>II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category.</p> <p>III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.</p>	<p>Recommendations included in this document have been adapted from the ranking method described in the Classification of Recommendations found in the Report of the Canadian Task Force on the Periodic Health Exam.</p> <p>A. There is good evidence to support the recommendation that the condition be specifically considered in a periodic health examination.</p> <p>B. There is fair evidence to support the recommendation that the condition be specifically considered in a periodic health examination.</p> <p>C. There is poor evidence regarding the inclusion or exclusion of the condition in a periodic health examination, but recommendations may be made on other grounds.</p> <p>D. There is fair evidence to support the recommendation that the condition not be considered in a periodic health examination.</p> <p>E. There is good evidence to support the recommendation that the condition be excluded from consideration in a periodic health examination.</p>

thus it may be by chance that no seroconversion was identified. Amniocentesis in women infected with hepatitis C does not significantly increase the risk of vertical transmission, but women should be counselled that very few studies have properly addressed this possibility.

RECOMMENDATION

2. Amniocentesis in women infected with hepatitis C does not appear to significantly increase the risk of vertical transmission, but women should be counselled that very few studies have properly addressed this possibility. (II-2C)

HUMAN IMMUNODEFICIENCY VIRUS

The prevalence of HIV in an obstetric population varies greatly, depending on the population studied. The reported prevalence in British Columbia is 0.03%, while in some inner city populations in the United States, the prevalence is as high as 1.5%.^{19,20} The AIDS Clinical Trials Group 076 study clearly demonstrated a 26% vertical transmission rate, which was lowered to 8% in women who received antepartum, intrapartum, and neonatal zidovudine therapy.²¹ Many HIV-positive women are now taking multidrug therapy.²² In one French series of 1,632 HIV-positive women in which only 5% received antenatal zidovudine therapy,²³ the rate of vertical transmission was 19%.²³ Amniocentesis was performed on 13 women and amniocentesis on 26 women, with a vertical transmission rate of 36%. This rate was significantly elevated, compared to that observed in women who did not have invasive needling procedures. The rate of vertical transmission of HIV after amniocentesis in women who have received zidovudine or combined therapy antenatally has not been described. Given the significant elevation in vertical transmission described, efforts should be made to avoid amniocentesis in HIV-positive women.

RECOMMENDATION

3. In HIV-positive women all noninvasive screening tools should be used prior to considering amniocentesis. (II-2D)

RISK OF AMNIOTIC FLUID

CONTAMINATION AT AMNIOCENTESIS

Contamination of the fetal amniotic cavity with maternal blood at amniocentesis is common.²⁴ In a study by Giorlandino *et al.*, 20 women underwent a second amniocentesis two weeks after the original amniocentesis because of cell culture contamination.²⁴ At the second amniocentesis all 20 were found to have amniotic fluid contamination based on red blood cell and hemoglobin concentrations.²⁴ Women undergoing their first amniocentesis were used as matched controls and no blood con-

tamination was found at the onset of the procedure. The amount of blood in the amniotic fluid was significantly increased when an anterior placenta was present.²⁴

ASSESSMENT OF RISK AND AMNIOCENTESIS

For women infected with hepatitis B, hepatitis C, or HIV, the addition of noninvasive methods of prenatal risk screening, such as nuchal translucency, triple screening, and anatomic ultrasound, may help in reducing the age-related risk to a level below the threshold for genetic amniocentesis. For those women infected with hepatitis B, hepatitis C, or HIV who insist on amniocentesis, every effort should be made to avoid inserting the needle through the placenta.

RECOMMENDATIONS

- 4. For women infected with hepatitis B, hepatitis C, or HIV, the addition of noninvasive methods of prenatal risk screening, such as nuchal translucency, triple screening, and anatomic ultrasound, may help in reducing the age-related risk to a level below the threshold for genetic amniocentesis. (II-2C)**
- 5. For those women infected with hepatitis B, hepatitis C, or HIV who insist on amniocentesis, every effort should be made to avoid inserting the needle through the placenta. (II-1B)**

CONCLUSION

There is a critical lack of evidence to determine the impact of amniocentesis on the risk of vertical transmission in women with hepatitis B, hepatitis C, or HIV. For this reason, the addition of noninvasive methods of prenatal risk screening, such as nuchal translucency, triple screening, and anatomic ultrasound, may help in reducing the age-related risk to a level below the threshold for genetic amniocentesis. The available evidence suggests the risk of vertical transmission through amniocentesis in women with hepatitis B and hepatitis C is not greatly increased. In contrast, the risk of vertical transmission of HIV appears to be increased through amniocentesis. Efforts should be made to avoid inserting the needle through the placenta in all cases.

REFERENCES

- Woolf SH, Battista RN, Angerson GM, Logan AG, Eel W. Canadian Task Force on the Periodic Health Exam. Ottawa: Canada Communication Group; 1994. p. xxxvii.
- Delage G, Montplaisir S, Remy-Prince S, Pierri E. Prevalence of hepatitis B virus infection in pregnant women in the Montreal area. *Can Med Assoc J* 1986;134:897-901.
- Healy CM, Cafferkey MT, Butler KM, Cahill I, McMorrow J, Philbin M, et al. Antenatal hepatitis B screening – is there a need for a national policy? *Ir Med J* 2001;94:111-2, 114.

4. Miranda AE, Alves MC, Neto RL, Areal KR, Gerbase AC. Seroprevalence of HIV, hepatitis B virus, and syphilis in women at their first visit to public antenatal clinics in Vitoria, Brazil. *Sex Transm Dis* 2001;28:710-3.
5. Centers for Disease Control. Protection against viral hepatitis. Recommendations of the Immunization Practices Advisory Committee. *Morb Mortal Wkly Rep* 1990;39:1-26.
6. Towers CV, Asrat T, Rumney P. The presence of hepatitis B surface antigen and deoxyribonucleic acid in amniotic fluid and cord blood. *Am J Obstet Gynecol* 2001;184:1514-8.
7. Alexander JM, Ramus R, Jackson G, Sercely B, Wendel GD Jr. Risk of hepatitis B transmission after amniocentesis in chronic hepatitis B carriers. *Infect Dis Obstet Gynecol* 1999;7:283-6.
8. Grosheide PM, Quartero HW, Schalm SW, Heijtkink RA, Christiaens GC. Early invasive prenatal diagnosis in HbsAg-positive women. *Prenat Diagn* 1994;14:553-8.
9. Ko TM, Tseng LH, Chang MH, Chen DS, Hsieh FJ, Chuang SM, et al. Amniocentesis in mothers who are hepatitis B virus carriers does not expose the infant to an increased risk of hepatitis B virus infection. *Arch Gynecol Obstet* 1994;255:25-30.
10. Centers for Disease Control. Hepatitis B virus: a comprehensive strategy for eliminating transmission in the United States through universal vaccination: recommendations of the immunization practices advisory committee (ACIP). *Morb Mortal Wkly Rep* 1991;40(RR-13):1-19.
11. Healy CM, Cafferkey MT, Conroy A, Dooley S, Hall WW, Beckett M, et al. Hepatitis C infection in an Irish antenatal population. *Ir J Med Sci* 2000;169(3):180-2.
12. Ford PM, White C, Kaufmann H, MacTavish J, Pearson M, Ford S, et al. Voluntary anonymous linked study of the prevalence of HIV infection and hepatitis C among inmates in a Canadian federal penitentiary for women. *Can Med Assoc J* 1995;153(11):1605-9.
13. Goldberg D, McIntyre PG, Smith R, Appleyard K, Dunlop J, Taylor A, et al. Hepatitis C virus among high and low risk pregnant women in Dundee: unlinked anonymous testing. *Br J Obstet Gynaecol* 2001;108(4):365-70.
14. Ohto H, Terazawa S, Sasaki N, Sasaki N, Hino K, Ishiwata C, et al. Transmission of hepatitis C virus from mothers to infants. The Vertical Transmission of Hepatitis C Virus Collaborative Study Group. *N Engl J Med* 1994;330(11):744-50.
15. Hillemanns P, Dannecker C, Kimmig R, Hasbargen U. Obstetric risks and vertical transmission of hepatitis C virus infection in pregnancy. *Acta Obstet Gynecol Scand* 2000;79(7):543-7.
16. Conte D, Fraquelli M, Prati D, Colucci A, Minola E. Prevalence and clinical course of chronic hepatitis C virus (HCV) infection and rate of HCV vertical transmission in a cohort of 15,250 pregnant women. *Hepatology* 2000;31(3):751-5.
17. European Paediatric Hepatitis C Virus Network. Effects of mode of delivery and infant feeding on the risk of mother-to-child transmission of hepatitis C virus. *Br J Obstet Gynaecol* 2001;108(4):371-7.
18. Delamare C, Carbonne B, Heim N, Berkane N, Petit JC, Uzan S, et al. Detection of hepatitis C virus RNA (HCV RNA) in amniotic fluid: a prospective study. *J Hepatol* 1999;31(3):416-20.
19. Patrick DM, Money DM, Forbes J, Dobson SR, Rekart ML, Cook DA, et al. Routine prenatal screening for HIV in a low-prevalence setting. *Can Med Assoc J* 1998;159:942-7.
20. Guinan ME, Hardy A. Epidemiology of AIDS in women in the United States. 1981 through 1986. *J Am Med Assoc* 1987;257:2039-42.
21. Connor EM, Sperling RS, Gelber R, Kiselev P, Scott G, O'Sullivan MJ, et al. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. *N Engl J Med* 1994;331(18):1173-80.
22. Carpenter CC, Fischl MA, Hammer SM, Hirsch MS, Jacobsen DM, Katzenstein DA, et al. Antiretroviral therapy for HIV infection in 1998: updated recommendations of the International AIDS Society-USA Panel. *J Am Med Assoc* 1998;280:78-86.
23. Mandelbrot L, Mayaux MJ, Bongain A, Berrebi A, Moudoub-Jeanpetit Y, Benifla JL, et al. Obstetric factors and mother-to-child transmission of human immunodeficiency virus type 1: the French perinatal cohorts. SEROGEST French Pediatric HIV Infection Study Group. *Am J Obstet Gynecol* 1996;175:661-7.
24. Giorlandino C, Gambuzza G, D'Alessio P, Santoro ML, Gentili P, Vizzone A. Blood contamination of amniotic fluid after amniocentesis in relation to placental location. *Prenat Diagn* 1996;16:180-2.