

# Canadian Guidelines for Prenatal Diagnosis

## TECHNIQUES OF PRENATAL DIAGNOSIS

*The following guidelines for prenatal diagnosis have been prepared by the Prenatal Diagnosis Committee of the Canadian College of Medical Geneticists (CCMG) and the Genetics Committee of the Society of Obstetricians and Gynaecologists of Canada (SOGC) and approved by the Board of Directors of the CCMG and Executive and Council of the SOGC. These guidelines are an update of the guidelines previously published (Canadian College of Medical Geneticists and Society of Obstetricians and Gynaecologists of Canada, 1993).*

*These guidelines will also be available on the Internet at [www.sogc.org](http://www.sogc.org) and will be updated regularly.*

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FOR INFORMATION ON THE SELF-DIRECTED LEARNING EXERCISE SEE PAGE 635.

## **INTRODUCTION**

Invasive prenatal diagnosis techniques include chorionic villus sampling (CVS), amniocentesis, cordocentesis or percutaneous umbilical blood sampling (PUBS), fetal tissue sampling, as well as embryoscopy and fetoscopy (Table 1). Some diagnostic results may be obtained by more than one technique: for example, fetal karyotype can be obtained from cells from amniocentesis, chorionic villus sampling or fetal blood sampling.

## **AMNIOCENTESIS**

Amniocentesis is an ultrasound-guided invasive prenatal diagnosis procedure usually performed after 14 weeks gestational age for determination of fetal karyotype, molecular, and biochemical abnormalities. Other genetic diagnoses can be made from cultured amniocytes or by measurement of specific substances in the amniotic fluid. Results can generally be obtained prior to 20 weeks gestational age. The fetal karyotype will usually take one to three weeks from the time of amniocentesis, depending on the cytogenetic laboratory. The major disadvantage of amniocentesis is that results of the prenatal diagnosis are not available until 17 to 20 weeks gestational age. If genetic abnormalities are identified and the patient requests termination of pregnancy, the techniques of pregnancy termination carry a greater emotional and physical risk to the woman than a first trimester termination.

## **PROCEDURE**

Ultrasound is performed prior to amniocentesis to determine fetal gestational age, location of placenta, amniotic fluid volume, fetal cardiac activity, number of fetuses, and other uterine factors such as fibroids, amnion-chorion separation or contractions. More detailed fetal biometry may be included, depending on the centre. The needle insertion site is identified by the ultrasound information regarding fetal position, amniotic fluid volume, and placental location. Avoidance of the placenta is recommended. Although published results regarding transplacental amniocentesis have not shown significant increased risks for miscarriage,<sup>1</sup> increased risk of fetal-maternal transfusions has been reported.<sup>2</sup> The concurrent use of ultrasound with amniocentesis is recommended to allow continuous observation of the fetus, amniotic fluid, and needle tip.

Sterile technique, including sterile gloves and a procedure tray with antiseptic solution, gauze pads, forceps, and sterile drape should be used. The skin insertion site is cleaned with an antiseptic solution. The use of local anesthetic in the abdominal wall is not generally necessary. The procedure is usually performed with a 20 to 22 gauge spinal needle using a single continuous movement of the needle through the abdominal and uterine wall. It is important that entry into the amniotic sac is a sharp thrust to avoid "tenting" of the amnion. A 10 to 20 cc syringe is used to aspirate the amniotic fluid following removal of the needle stylet. The volume of amniotic

TABLE 1

**SUMMARY OF AMNIOCENTESIS AND CHORIONIC VILLUS SAMPLING INFORMATION**

	<b>Amniocentesis</b>	<b>CVS</b>
Procedure	Amniotic fluid removed by needle and syringe	Chorionic villi removed by transcervical (TC) catheter and syringe or transabdominal (TA) needle insertion
Timing	15 to 17 weeks	10 to 11-6/7 weeks (greater than 12 weeks TA CVS only)
Added risk of miscarriage due to procedure	0.5-1.0%	TA 1-2% TC 2-6%
Fetal malformation risks	—	1 in 3000 vascular limb malformation (suggested but not proven)
Chance of successful sampling	Approximately 99%	Approximately 99%. If unsuccessful, can follow with amniocentesis
Time required for cytogenetic diagnosis	1 to 3 weeks (FISH may be available)	2-3 weeks (rapid direct technique may be considered in specific situations)
Accuracy (chromosomes) Aneuploidy and major structural rearrangement	Highly accurate	Highly accurate
Mosaicism	Level 3 — Rare	Confined placental — 1.0-2.0%
Open neural tube defects	AFP in amniotic fluid detects approximately 95% of NTDs	Other tests required for detection

fluid removed is 15 to 30 cc and depends on the indication for prenatal diagnosis. The removal of the spinal needle uses a similar technique to insertion.

The two most common tests performed on the amniotic fluid are the fetal karyotype from fetal and membrane cells in the amniotic fluid after tissue culturing or direct fluorescent *in situ* hybridization (FISH) techniques, and direct measurement of amniotic fluid  $\alpha$ -fetoprotein (AFAFP). Other genetic diagnoses can be obtained by biochemical or molecular techniques after discussion with the local prenatal diagnosis centre.

Removal of the amniotic fluid generally takes less than one minute. The patient may experience some mild uterine cramping and pressure sensation. The amniotic fluid is generally similar in appearance to white wine. Occasionally blood-tinged amniotic fluid may be obtained, generally due to maternal bleeding into the amniotic cavity at the time of the procedure. If the patient has previously had a history of antepartum bleeding, the amniotic fluid may be brown or dark red in colour due to blood pigments being absorbed across the chorio-amnion membranes. The presence of discoloured fluid on amniocentesis is associated with an increased risk of pregnancy loss.<sup>3</sup>

No more than two uterine needle insertions into or through the uterine wall are recommended. If the procedure is unsuccessful, further attempts can be made with a delay of at least 24 hours.

Freshly blood-stained amniotic fluid should be separately analyzed by a Kleihauer test and cell count to determine whether the new blood is maternal or fetal. If the blood is fetal, the AFAFP value may be elevated without a congenital anomaly as the etiology.

## **DISADVANTAGES AND RISKS OF AMNIOCENTESIS**

### **A) FETAL LOSS**

Fetal loss after amniocentesis is estimated to be one in every 100 to 200 procedures above the background loss rate.<sup>4-10</sup>

### **B) INFECTION**

The risk of infection introduced at the time of the amniocentesis is estimated to be one to two in 3000 procedures.<sup>11</sup> Recent information indicates that approximately 10 to 50 percent of post-amniocentesis losses have evidence of low grade infections at the time of the procedure with increased cytokine levels in the amniotic fluid.<sup>12-13</sup>

### **C) FETAL INJURY**

Serious fetal injuries at the time of amniocentesis are rare with or without continuous ultrasound guidance. Small skin dimpling lesions have been reported following contact of the fetus with the needle, but these are generally minimal and the specific anatomic location may be the only consideration.<sup>14-16</sup> Patients are generally requested to have limited activity for 12 to 24 hours following the amniocentesis procedure but this has not been well studied.

### **D) MINOR COMPLICATIONS**

Minor complications without fetal loss following amniocentesis include continued leakage of amniotic fluid, bleeding, and uterine irritability. These minor complications are estimated to occur in one to five percent of procedures.<sup>10,17,18</sup> These complications are generally self-limited. Recommendations may include bedrest and additional serial ultrasound monitoring if continued amniotic fluid leakage is present. The benefit of antibiotic use with amniotic fluid leakage has not been evaluated.

### **TWIN PREGNANCY**

The risk of pregnancy loss following twin amniocentesis is estimated to be one to two percent.<sup>19-21</sup> It is necessary to define placental location and presence or absence of separating membranes. Good descriptive localization of twin A or B (right- or left-sided twin with placental location) is necessary, especially when an abnormality is identified in only one twin.

### **EARLY AMNIOCENTESIS**

Findings from the large Canadian multicentred prospective randomized trial<sup>10,22</sup> comparing early amniocentesis (11 to 12 weeks 6 days) and mid-trimester amniocentesis (15 to 16 weeks 6 days) have confirmed the findings from smaller randomized trials. Significant differences for early amniocentesis compared with mid-trimester amniocentesis were found for: 1) total fetal losses including pre-procedure, post-procedure, stillbirth, and neonatal death, (7.6% for early amniocentesis vs. 5.95% for mid-trimester amniocentesis,  $p = 0.012$ ), newborn clubfoot (incidence of 1.3% in early group compared with the background 0.1% for the mid-trimester group,  $p = 0.0001$ ), and post-procedural amniotic fluid leakage (3.7% for the early group compared to 1.5% for the mid-trimester group,  $p = 0.0007$ ). Cytogenetic culture failures were also more likely in the early amniocentesis group (1.8% for early amniocentesis vs. 0.2% for mid-trimester amniocentesis,  $p < 0.0001$ ), requiring additional invasive prenatal diagnosis techniques for these women if further diagnosis was requested. There was no significant difference in the incidence of neonatal respiratory disease or congenital hip dislocation when comparing the two groups.

Early amniocentesis does not appear to be appropriate for routine prenatal diagnosis at gestational ages of 11 to 12 weeks 6 days gestation. The exact safety of amniocentesis for gestational ages 13 and 14 weeks has not been established by randomized trials.

### **CHORIONIC VILLUS SAMPLING**

Chorionic villus sampling (CVS) is the most common first trimester invasive prenatal diagnosis technique for evaluation of fetal karyotype, molecular, and biochemical abnormalities. CVS is an ultrasound-guided technique that is usually performed in the first trimester between 10 and 11 weeks 6 days gestation. Although the procedure was initially developed as a

transcervical technique, both transcervical and transabdominal techniques have recently become available. The upper gestational age of 12 weeks is generally considered for the transcervical technique but as more experience is gained with transabdominal CVS, the procedure may be undertaken at a gestational age of 10 weeks gestation or greater. In contrast to amniocentesis, which obtains amniotic fluid, the CVS obtains chorionic tissue from the developing placenta.

## PROCEDURE

The transcervical chorionic villus sampling technique uses a flexible plastic catheter with a plastic or metal obturator whose shape can be moulded to allow the catheter to pass, under continuous ultrasound guidance, through the cervix and into the placental tissue. Prior to insertion of the catheter, a speculum is placed in the vagina and the cervix and vaginal walls are cleansed with antiseptic solution. In the majority of cases, further manipulation of the uterus and cervix by a tenaculum is not necessary. The transabdominal chorionic villus sampling technique generally utilizes a freehand technique with continuous ultrasound guidance, similar to amniocentesis or cordocentesis. A 19 or 20 gauge spinal needle is used for the transabdominal technique; other needle options include a two needle set with an outer gauge of 18. Both the transcervical and transabdominal technique usually obtain five to 25 mg of chorionic tissue which is aspirated into the catheter or needle by applying negative pressure to a 20 to 30 cc syringe attached to the end of the catheter or needle. The catheter is withdrawn through the placental tissue or the needle is moved back and forth (5-10 movements) in the placental tissue to obtain the specimen with negative pressure by the syringe for both techniques. The transcervical technique is used for the majority of the posterior placental locations, while the transabdominal technique is better suited for the fundal and anterior placental locations. An adequate amount of chorionic villus tissue is generally obtained with one aspiration but two attempts do not increase the risk of post-procedure loss.<sup>23</sup>

Both transabdominal and transcervical chorionic villus sampling have similar accuracy.<sup>24</sup> The transcervical technique is associated with a greater risk of post-procedural spotting or minimal bleeding (10-20%)<sup>25</sup> while the transabdominal technique has increased uterine discomfort and cramps.<sup>26</sup> Infection has not been identified as a significant factor in the large number of patients having transcervical procedures.<sup>22</sup>

Some genetic centres will use CVS techniques for both singleton and twin pregnancies. The safety and accuracy of CVS and twins is reported by a small number of centres.<sup>27,28</sup> Rh disease prophylaxis should be done similarly to the method described for amniocentesis; however, the optimum schedule is not known.

## ADVANTAGES OF CVS

The major advantage of CVS is the earlier gestational age at sampling, affording earlier results. If a chromosomal or DNA

abnormality is detected and pregnancy termination is requested, some of the physical and emotional stresses of pregnancy termination may be less than when termination follows amniocentesis at a later gestational age. A second advantage is related to specific molecular diagnoses with DNA extracted directly from the villi, allowing an earlier result with no cell culturing for these genetic disorders. A third advantage is that direct chromosomal analysis may be used in certain situations for rapid results in less than 24 hours by either cytogenetic or FISH techniques.

## DISADVANTAGES AND RISKS OF CVS

### A) CONFINED PLACENTAL MOSAICISM

Confined placental mosaicism, a discrepancy between the chromosomes in the chorionic and fetal tissues, is a biologic placental factor which is present in one to two percent of pregnancies.<sup>29-31</sup> Although this finding is usually limited to the placental tissue and is not usually present in the fetus, additional amniocentesis should be offered for further evaluation. The additional procedure may increase pregnancy complication risks. Clinical effects of the confined placental mosaicism can vary depending on the specific chromosome involved. The concerns that need to be considered in this situation are uniparental disomy and risks of placental dysfunction with intrauterine growth restriction and fetal death.

### B) MATERNAL CONTAMINATION

Contamination by maternal decidual tissue is possible, but this potential problem can be minimized with very careful attention to cleaning or stripping of the chorionic villi of maternal decidual cells under the dissecting microscope prior to tissue culturing. This has not been a significant problem in most cytogenetic laboratories with long term experience in CVS.<sup>32,33</sup>

### C) PREGNANCY LOSS

The background risk of spontaneous pregnancy loss in the advanced maternal age group, after ultrasound has confirmed a viable pregnancy at 10 weeks gestational age when no procedure is undertaken, is estimated at two to three percent.<sup>34</sup> The CVS procedure adds approximately one to two percent above the background in comparison to the 0.5 to 1.0 percent risk for amniocentesis.<sup>9,35,36</sup> Vaginal bleeding occurring prior to the procedure increases the risk of pregnancy loss following CVS by either route. The risk of pregnancy loss increases with the number of attempts needed to obtain the chorionic tissue and should be limited to two attempts. Uterine and placental location may alter procedural risk factors depending on the CVS technique used. Uterine fibroids may cause some additional risks of technique success and pregnancy loss. Transcervical and transabdominal CVS techniques differ in the post-procedure loss rate risk. Risks are approximately doubled with transcervical technique (3-6%).<sup>17,37,38</sup>

#### D) LIMB OR FACIAL ANOMALIES

The risk of limb or facial anomalies is higher if CVS is done at a gestational age earlier than nine weeks. CVS is generally restricted to greater than or equal to 10 weeks gestational age in most centres. The incidence of transverse limb (minor or major) in the general population is estimated at nine in 10,000 live births. One-third of these anomalies may be due to a vascular disruption sequence such as CVS. The risk of a limb or facial abnormality related to the CVS procedure could be as high as one in 3000 fetuses.<sup>39-45</sup> A recent report from the World Health Organization (WHO) registry concluded that CVS is not associated with an increased risks for fetal loss or anomalies.<sup>46</sup>

#### **CORDOCENTESIS**

Cordocentesis or percutaneous umbilical blood sampling (PUBS) can be used to obtain fetal blood from as early as 12 weeks gestational age until term, but is usually used after 16 weeks.<sup>47</sup> Indications for cordocentesis include: fetal karyotyping when congenital malformations or intrauterine growth retardation are identified by ultrasound, viral infections, hematological abnormalities including Rh or other immune hemolytic disease, maternal or fetal platelet disorders, and inborn errors of metabolism. In addition, physiological assessment of the fetus can be evaluated by measuring components such as fetal blood gases, glucose, and lactate. The procedure can be used for fetal therapy when intravascular transfusions are required, as well as for the introduction of medications for fetal treatment and in the future for fetal therapy protocols.

#### **PROCEDURE**

Cordocentesis is an ultrasound-guided freehand or needle guide technique which allows insertion of a 22 gauge spinal needle into the umbilical cord vessels at either the placental insertion of the umbilical cord or into a free loop of umbilical cord. Fetal chromosomes can usually be obtained within 48 to 72 hours by culturing fetal white blood cells. The technique will vary depending on the placental position as well as fetal position and activity. Fetal paralysis (pancuronium) is sometimes required. Fetal blood specimens can usually be obtained in less than five to 10 minutes. Depending on the indications for the test and the gestational age of the fetus, one to three ml of blood are removed for analysis. Confirmation of fetal blood is required and can be done by an initial Apt test (a bedside test for differentiating fetal from maternal hemoglobin) followed by laboratory confirmation of fetal hemoglobin (Kleihauer). The reported success rates for cordocentesis range from 93.7 to 98.5 percent.<sup>48-51</sup>

#### **ADVANTAGES OF CORDOCENTESIS**

The major advantage of cordocentesis is that it allows direct access to the fetus, not only for diagnostic but also for therapeutic management.

#### **DISADVANTAGES AND RISKS OF CORDOCENTESIS**

##### **A) PREGNANCY LOSS**

Procedure-related pregnancy loss following cordocentesis has been linked to several factors, including procedure indication, fetal distress (bradycardia), and prolonged cord bleeding.<sup>52,53</sup> The procedure indication greatly increases the risk of procedure-related pregnancy loss. The procedure-related pregnancy loss risk with fetal anomalies or intrauterine growth restriction is approximately 3.2 percent compared to 1.25 percent in a group of fetuses with normal growth and anatomy.<sup>53,54</sup> The incidence of post-cordocentesis pregnancy loss with normal fetal structures, abnormal fetal structures, fetal physiological assessment (IUGR), and non-immune hydrops, excluding therapeutic abortions, was reported to be one, seven, 14, and 25 percent respectively.<sup>55</sup> Other reported factors increasing the risk of fetal loss include longer procedures (more than 14 minutes) and placental position (anterior placenta increased over posterior placenta).<sup>49,51,56</sup>

##### **B) FETAL BRADYCARDIA**

Fetal bradycardia (fetal distress) at or following the procedure may result in fetal morbidity and mortality. The risk of fetal bradycardia is variable but can be estimated at five to 10 percent. The risk of bradycardia is greater when the umbilical artery is punctured (17%) compared with venous puncture (2%).<sup>57,58</sup>

##### **C) BLEEDING**

Bleeding from the cord puncture site varies from 10 to 40 percent but in the majority of cases the duration is less than 90 seconds.<sup>49</sup>

#### **OTHER FETAL TISSUE SAMPLING**

Techniques to obtain tissue from fetal skin and liver or fluid from the fetal urinary tract, abdomen, thorax or cystic hygroma are similar to freehand ultrasound-guided techniques, such as amniocentesis and cordocentesis. Needle insertion into specific fetal areas requires appropriate fetal positioning. Fetal paralysis may be required. Protocols for fetal paralysis may vary from centre to centre.<sup>59</sup> Risks and complications of the procedures are similar to those quoted for cordocentesis, with the risks of fetal death being increased if major congenital malformations and growth retardation are present. The accuracy of the test is dependent on the tissue being obtained and the specific analysis required. For urinary tract evaluation, urinary specimens for osmolality, electrolytes, and other urinary factors can be obtained by bladder aspiration. Thoracic and abdominal fluids can be evaluated for cell and protein content, as in a chylothorax. Lymphatic fluid from cystic hygroma can be used for chromosome analysis. Liver, muscle, and skin have been sampled for evidence of specific genetic syndromes.<sup>59</sup> These procedures are rare and should be discussed with regional genetic and perinatal consultants.

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## **RADIOGRAPHY AND MAGNETIC RESONANCE IMAGING**

The use of radiography in prenatal diagnosis has decreased significantly with the introduction of real time ultrasound, but in selected situations there are still appropriate indications for a single plain film radiograph of the maternal abdomen and pelvis. The most common indication for radiography is to add information when major skeletal abnormalities such as dwarfism are diagnosed by ultrasound. A single X-ray may allow a specific diagnosis to be made prenatally from characteristic individual bone involvement and appearance. There appear to be no maternal risks associated with this procedure and no studies to date have shown any increased risk of the fetus developing childhood leukemia.

Fetal anomalies that may be diagnosed with magnetic resonance imaging (MRI) evaluation include: central nervous system (CNS) (cerebral, neural tube defects, holoprosencephaly, hydranencephaly, porencephaly, schizencephaly, ventriculomegaly, AV malformations, tuberous sclerosis, intracranial hemorrhage), cervical teratoma (mass and its relationship to the airway and neck vessels), chest masses (congenital diaphragmatic hernia, congenital cystic adenomatoid malformations, bronchopulmonary sequestration, neuroenteric cyst, myringo-tracheal obstruction), and adrenal neuroblastoma.

The Safety Committee of the Society of Magnetic Resonance Imaging has issued guidelines and recommendations for MRI safety and patient management.<sup>60</sup> MRI may be used in pregnant women if other non-ionizing forms of diagnostic images are inadequate or if the examination provides information that would otherwise require exposure to ionizing radiation.<sup>60</sup> It is recommended that pregnant women be informed that, to date, there has been no indication that the use of clinical MRI during pregnancy has produced deleterious effects. However, as noted by the Food and Drug Administration (FDA), the safety of MRI during pregnancy has not been proved.<sup>60-61</sup>

## **FETOSCOPY/ EMBRYOSCOPY**

There are few indications as yet for fetoscopy in prenatal diagnosis or treatment. The technique allows direct visualization of external fetal features or structures not appreciated by ultrasound, which may assist in non-chromosomal genetic diagnosis. The risks of fetoscopy are greater than the risks of other invasive prenatal diagnosis procedures.<sup>62</sup>

Embryoscopy at present is a research technique and may allow early visualization of the embryo by inserting a rigid scope through the cervix and into the space between the amnion and chorion. Since vaginal ultrasound is able to give similar embryonic and early fetal detail, it is unlikely that this invasive procedure will have any significant indications.

## **ULTRASOUND**

Policy statements have been previously prepared by the Diagnostic Imaging Committee of the Society of Obstetricians and Gynaecologists of Canada on the use of ultrasound in prenatal diagnosis.<sup>63-65</sup> Please see these references for further details.

## **FETAL CELLS IN THE MATERNAL CIRCULATION**

This area of prenatal diagnosis should at present be considered experimental.<sup>66</sup> Many groups continue to refine methods to permit their isolation, identification and genetic analysis.

## **GENERAL PRINCIPLES FOR PRENATAL DIAGNOSIS PROGRAMS**

1. All patients considering prenatal diagnosis should have access to professionals who are knowledgeable in the field and skilled in the procedures.
2. Each region should be integrated so that an entire range of services is available to each patient. Innovations in telemedicine technology promise to offer options for distance face-to-face counselling and ultrasound interpretation that are of particular relevance in a Canadian context.
3. A suggested minimum caseload of 50 invasive procedures per year is recommended per practitioner in order to maintain an appropriate level of competence in the provision of invasive procedures. Exceptions to this minimum caseload may be justified on the basis of unique geographic circumstances; however, informed patient choice is paramount.
4. In order to maintain a high standard of efficiency, a cytogenetic laboratory should have a minimum workload of 100 prenatal specimens.
5. Each patient should have an appropriate assessment of family history and genetic counselling prior to undergoing invasive prenatal diagnosis.
6. Counselling should be given in a non-directive manner in order to allow an informed choice by the couple.
7. The distinction between screening and diagnostic investigations should be clarified, including the frequency of abnormal results, false-positive, and false-negative tests. Accuracy of results, frequency of need for repeat testing, and risk of pregnancy loss are of particular relevance with invasive prenatal diagnosis procedures. The couple should be reminded that normal test results do not rule out every genetic or structural abnormality in their fetus.
8. Prior to embarking on prenatal diagnosis testing, couples should be made aware of the full range of options when confronted with an abnormal test result. Prior commitment to termination of pregnancy following the diagnosis of fetal abnormality is not a prerequisite for prenatal diagnosis. Each

centre must be aware of the local, regional, national, and international policies and protocols related to termination of pregnancy, and advise the couple of such before undertaking prenatal diagnosis. This is particularly important at gestations beyond 20 weeks.

9. It is recommended that an AFAFP assay be carried out on each sample of amniotic fluid received at the appropriate gestational age, regardless of the original indication for sampling.
10. The decision to karyotype amniotic fluid, chorionic vil-lus, fetal blood or tissue samples obtained where the original indication for testing did not include karyotyping should be decided on an individual basis, with reference to regionally or provincially established policies or guidelines. Although often done, it is not mandatory to do a karyotypic analysis on all samples received. As a minimum requirement, before a final decision is made not to do chromosomal studies, the results of the available screening tests should be reviewed to determine if there is in fact an indication for karyotyping.
11. Determination of fetal sex for the purpose of sex selection procedures on a non-medical basis is inappropriate.
12. In the absence of a medical indication, genetic testing to determine paternity is not an indication for prenatal diagnosis with the possible exception of cases of sexual assault. If an assault has been reported, the police may have an interest in the DNA of the fetus, for example for comparison with the DNA of the sperm found at the place of assault or with the DNA of the suspected assailant. In this case the prenatal diagnosis could be done at the request of the woman and the

law enforcement agency, and the DNA testing would be done at a forensic laboratory. If there are no criminal proceedings and the woman wishes to know whether the father of the fetus is her partner or the assailant, with the intent of abortion in the latter case, prenatal diagnosis could be justified if considered in the best interest of the couple. However, in view of the possibility that lawsuits might subsequently arise, the DNA testing should be done by a private laboratory, following guidelines for civil cases of paternity testing, and with appropriate counselling of the couple. In any case, prenatal diagnosis for paternity testing should not be done without appropriate counselling of the woman, and thorough legal consultation. If a woman has an invasive prenatal test for legitimate medical reasons such as maternal age, she may request that the leftover cells be used for paternity testing. There would normally be no grounds for the laboratory to refuse to give these cells to another lab for paternity testing.

13. Introduction of any new prenatal diagnostic investigation, or alteration of previously established approaches, requires careful follow-up and audit to assess risk, accuracy, and impact.

#### **SUMMARY OF MAJOR RECOMMENDATIONS**

1. It is recommended that women at increased risk for having a child with a chromosomal anomaly be identified based on maternal age. (II-2 A)
2. It is recommended that maternal serum screening be used to identify women at increased risk for having a child with a chromosomal anomaly. Maternal serum screening can be used to modify a woman's age-related risks. (II-2 A)

TABLE 2 QUALITY OF EVIDENCE ASSESSMENT <sup>67</sup>	CLASSIFICATION OF RECOMMENDATIONS <sup>67</sup>
<p>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.<sup>67</sup></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 1940's) 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 these guidelines 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.<sup>67</sup></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>

3. It is recommended that maternal serum AFP screening be used to identify women at increased risk for having a child with a neural tube defect. (II-2 A)
4. It is recommended that an amniocentesis be offered to women at increased risk of having a child with a chromosome anomaly. (I A)
5. It is recommended that CVS be offered to women as an alternative to amniocentesis where resources exist. (I A)
6. Cordocentesis may be offered to high-risk women under certain circumstances. (II-2 B)

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