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# Prenatal Screening for and Diagnosis of Aneuploidy in Twin Pregnancies

**This clinical practice guideline has been prepared by the Genetics Committee of the Society of Obstetricians and Gynaecologists of Canada (SOGC) and the Prenatal Diagnosis Committee of the Canadian College of Medical Geneticists (CCMG) and approved by the Executive and Council of the Society of Obstetricians and Gynaecologists of Canada and the Board of Directors of the Canadian College of Medical Geneticists.**

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## Abstract

**Objective:** To provide a Canadian consensus document with recommendations on prenatal screening for and diagnosis of fetal aneuploidy (e.g., Down syndrome and trisomy 18) in twin pregnancies.

**Options:** The process of prenatal screening and diagnosis in twin pregnancies is complex. This document reviews the options available to pregnant women and the challenges specific to screening and diagnosis in a twin pregnancy.

**Outcomes:** Clinicians will be better informed about the accuracy of different screening options in twin pregnancies and about techniques of invasive prenatal diagnosis in twins.

**Evidence:** PubMed and Cochrane Database were searched for relevant English and French language articles published between 1985 and 2010, using appropriate controlled vocabulary and key words (aneuploidy, Down syndrome, trisomy, prenatal screening, genetic health risk, genetic health surveillance, prenatal diagnosis, twin gestation). Results were restricted to systematic reviews, randomized controlled trials, and relevant observational studies. Searches were updated on a regular basis and incorporated in the guideline to August 2010. Grey (unpublished) literature was identified through searching the websites of health technology assessment and health technology assessment-related agencies, clinical practice guideline collections, clinical trial registries, and national and international medical specialty societies. The

**Key Words:** Prenatal screening, twin pregnancy, prenatal diagnosis, amniocentesis, nuchal translucency, maternal serum screening, chorionic villus sampling

previous Society of Obstetricians and Gynaecologists of Canada guidelines regarding prenatal screening were also reviewed in developing this clinical practice guideline.

**Values:** The quality of evidence was rated using the criteria described in the Report of the Canadian Task Force on Preventive Health Care (Table 1).

**Benefits, harms, and costs:** There is a need for specific guidelines for prenatal screening and diagnosis in twins. These guidelines should assist health care providers in the approach to this aspect of prenatal care of women with twin pregnancies.

#### Summary Statements

1. Fetal nuchal translucency combined with maternal age is an acceptable first trimester screening test for aneuploidies in twin pregnancies. (II-2)
2. First trimester serum screening combined with nuchal translucency may be considered in twin pregnancies. It provides some improvement over the performance of screening by nuchal translucency and maternal age by decreasing the false-positive rate. (II-3)
3. Integrated screening with nuchal translucency plus first and second trimester serum screening is an option in twin pregnancies. Further prospective studies are required in this area, since it has not been validated in prospective studies in twins. (III)
4. Non-directive counselling is essential when invasive testing is offered. (III)
5. When chorionic villus sampling is performed in non-monochorionic multiple pregnancies, a combination of transabdominal and transcervical approaches or a transabdominal only approach appears to provide the best results to minimize the likelihood of sampling errors. (II-2)

#### Recommendations

1. All pregnant women in Canada, regardless of age, should be offered, through an informed counselling process, the option of a prenatal screening test for the most common clinically significant fetal aneuploidies. In addition, they should be offered a second trimester ultrasound for dating, assessment of fetal anatomy, and detection of multiples. (I-A)
2. Counselling must be non-directive and must respect a woman's right to accept or decline any or all of the testing or options offered at any point in the process. (III-A)
3. When non-invasive prenatal screening for aneuploidy is available, maternal age alone should not be an indication for invasive prenatal diagnosis in a twin pregnancy. (II-2A) If non-invasive prenatal screening is not available, invasive prenatal diagnosis in twins should be offered to women aged 35 and over. (II-2B)
4. Chorionicity has a major impact on the prenatal screening process and should be determined by ultrasound in the first trimester of all twin pregnancies. (II-2A)
5. When screening is done by nuchal translucency and maternal age, a pregnancy-specific risk should be calculated in monochorionic twins. In dichorionic twins, a fetus-specific risk should be calculated. (II-3C)
6. During amniocentesis, both amniotic sacs should be sampled in monochorionic twin pregnancies, unless monochorionicity is confirmed before 14 weeks and the fetuses appear concordant for growth and anatomy. (II-2B)
7. Prior to invasive testing or in the context of twins discordant for an abnormality, selective reduction should be discussed and made available to those requesting the procedure after appropriate counselling. (III-B)
8. Monitoring for disseminated intravascular coagulopathy is not indicated in dichorionic twin pregnancies undergoing selective reduction. (II-2B)

## ABBREVIATIONS

| | |
|---|---|
| AFP | alpha fetoprotein |
| CVS | chorionic villus sampling |
| DR | detection rate |
| FPR | false-positive rate |
| hCG | human chorionic gonadotropin |
| NT | nuchal translucency |
| PAPP-A | pregnancy-associated plasma protein A |
| uE3 | unconjugated estriol |

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## OVERVIEW OF TWIN PREGNANCIES: EPIDEMIOLOGY, ZYGOSITY, AND CHORIONICITY

### Epidemiology

In Canada and other developed countries, the incidence of multiple pregnancies has increased dramatically since the 1980s. Over the period 1995 to 2004, the rate of multiple births showed a steady increase from 2.2% to 3.0%.[1] The two major reasons for this increase are the rising maternal age because of delayed childbearing, and the increasing use of assisted reproductive technologies and ovulation induction.

### Zygosity and Chorionicity

Zygosity refers to the genetic identity of each twin in the pregnancy, and chorionicity relates to its placentation. In monozygotic twins, a single fertilized oocyte splits into 2 distinct individuals after a variable number of divisions. Such twins are almost always genetically identical and therefore of the same sex. On rare occasions, mutations or chromosomal non-disjunction cause genetic discordance, resulting in phenotypic and chromosomal differences between monozygotic twins.[2] When 2 separate oocytes are fertilized, dizygotic twins result. These individuals are genetically distinct and usually discordant for chromosomal anomalies. The incidence of spontaneous monozygotic twins is remarkably stable worldwide at approximately 4 per 1000 births. It is now clear that infertility treatments are associated with a 2- to 12-fold increased risk of monozygotic twinning.[3–5] The exact mechanisms of this association remain elusive.[2] The incidence of dizygotic twinning varies greatly with factors such as maternal age, ethnicity, and infertility treatments, sharing a common mechanism of increased FSH maternal serum levels. Overall, about 66% of twin pregnancies are dizygotic and 33% are monozygotic.

The determination of chorionicity of a twin pregnancy is of paramount importance, and it should ideally be assessed in the first trimester,[6] when its accuracy is 96% to