

Pregnancy: Expecting a Child with OI

Sometimes, women who do not have osteogenesis imperfecta (OI) become concerned about it during pregnancy. Two situations typically give rise to this concern.

1. The woman's partner has OI.
2. Prenatal testing suggests the presence of OI symptoms in the fetus.

In both situations, the woman and her partner should seek advice from a geneticist.

Osteogenesis imperfecta is the result of a mutation in one of the two genes that carry instructions for making type 1 collagen -- the major protein in bone and skin. The mutation may result in either a change in the structure of type 1 collagen molecules or in the number of collagen molecules made. Either of these changes results in weak bones that fracture easily and other connective tissue symptoms. Results of studies in recent years show that the great majority of people with OI, even those who are the only affected person in a family, have dominantly inherited forms of the disorder. For more detailed information about the genetics of OI inheritance, see the OI Foundation fact sheet, *OI Issues: Genetics*.

1. When the woman's partner has OI

A person with OI has a 50 percent chance of passing on the disorder to each child. The child will have the same OI-causing mutation as the parent, although the child's symptoms may be milder or more severe than the parent's symptoms. It is possible that the child of a person with OI will have a spontaneous genetic mutation resulting in a different type of OI, but the chances of this happening are no greater for a parent with OI than they are for the general population. Some individuals with very mild OI have been known to have a child with more severe symptoms. In these cases it is believed that the parent is a mildly affected mosaic for OI. Mosaicism means that the individual carries a mutation for OI in only some of his or her cells. This can cause very mild symptoms of OI, or none at all in the carrier. Excluding OI, the risk of other congenital disorders in pregnancies in which one parent has OI is the same as that of the general population.

Genetic Counseling

It is recommended that couples at risk of having a child with OI seek genetic counseling before conception, or as early in the pregnancy as possible. A genetic counselor can provide information on OI genetics and prenatal diagnosis. Collagen testing of the partner with OI can be a useful tool to diagnose the child. Because collagen testing takes months to be completed, it should be initiated before conception if the person with OI was not been previously biopsied. A geneticist can also provide information about preimplantation genetic testing.

Preimplantation genetic testing or preimplantation genetic diagnosis is a new procedure. It involves in vitro fertilization plus the added step of "embryo analysis." After a couple has gone through the initial stages for in vitro fertilization and embryos have been formed, a single cell is removed from the dividing cells at the 8-cell stage and is tested for a single genetic condition, in this case, OI. If the embryo does not show any signs of OI, it is then implanted in the mother to continue normal development. At this time there is no known adverse effect on the fetus to having one cell removed at this stage. To be a candidate for this procedure, the parent's exact genetic mutation must be identified, usually through a collagen biopsy or DNA analysis and a mutation-specific test developed. This procedure cannot remove the OI gene (or the gene for any other condition), but only embryos without the mutation are implanted.

Undergoing prenatal diagnosis does not obligate parents to elect pregnancy termination, and the information may be useful in managing pregnancy and delivery. There are three techniques for prenatal diagnosis of OI in a fetus; ultrasound, chorionic villus sampling (CVS) and amniocentesis. None of these techniques can detect OI in 100

percent of the cases in which it occurs. Individualized assessment by a genetic counselor and/or geneticist is necessary to determine which techniques are most useful for a particular pregnancy.

It is also recommended that couples discuss their genetic history with the obstetrician. Parents may want to make arrangements, prior to the due date, to have a cord blood saved for DNA analysis. It can be helpful for families at risk for OI Type I or Type IV to have the question of OI inheritance answered as soon as possible.

2. When prenatal testing suggests the presence of OI symptoms in the fetus

Sometimes, through routine ultrasound, OI is suspected in the fetus of an unaffected mother. This often leads to additional ultrasound tests at higher levels and/or referral to a center for high-risk pregnancies. In the majority of cases, there is no previous history of OI. In a few instances, the ultrasound may have been ordered because of a previously affected pregnancy. In either situation, the finding presents certain medical and ethical questions to be addressed by the couple and their medical team. The questions include accuracy of the diagnosis, severity of the disorder, and prognosis for survival and development. The answers will help direct the remainder of the prenatal care and mode of delivery. It should be noted that it can be difficult to tell from an ultrasound whether the fetus has OI Type II or Type III.

Prenatal Diagnosis

Ultrasound can be used to examine the fetal skeleton for bowing, fractures, shortening, or other bone abnormalities consistent with OI. Ultrasound is generally most helpful for prenatal diagnosis of the more severe forms of OI. The fetal skeleton shows signs of OI as early as 16 weeks in OI Type II, and 18 weeks in OI Type III. Fetuses with mild OI seldom show evidence of fractures or deformity before birth. Ultrasound is a noninvasive, low-risk procedure. There are different levels of ultrasound, some of which are more useful than others in detecting OI.

Chorionic villus sampling (CVS) and **amniocentesis** analyze cells obtained from the fetus for collagen defects and/or a genetic mutation that causes OI. CVS looks at placental cells, while amniocentesis examines fetal cells (amniocytes) shed into the amniotic fluid. Both of these procedures carry a risk of miscarriage (about 1 in 200 for amniocentesis and about 1 percent for CVS). These prenatal tests are useful if the parent who has OI already has the results of his or her own collagen or DNA tests. When faced with these findings, couples are typically advised that Type II OI is most often lethal at birth or in early infancy and that Type III is associated with significant disability and at times early mortality. Because it is sometimes difficult to distinguish Types II and III OI prenatally, parents have sometimes been given a lethal prognosis for a fetus that actually had Type III OI.

Managing the Pregnancy

All pregnant women are encouraged to talk with a physician about appropriate diet and exercise during pregnancy to ensure optimum health for both themselves and their babies. To date, research indicates that the standard amount of calcium and vitamin D and other minerals is appropriate for a pregnancy where OI is suspected. At this time, there are no treatments or dietary supplements that can prevent the child from having OI or that will make the type of OI milder.

Delivery Options

In general, decisions about the best mode of delivery (vaginal vs. cesarean) should be made on an individual basis. Though it has been suggested that cesarean section is less traumatic than vaginal delivery when a baby with OI shows evidence of long-bone fractures, there are no data to confirm that this assumption is correct. Some physicians believe it is appropriate, when planning a mode of delivery, to assess the degree of mineralization of the baby's skull. Theoretically, there is an increased risk of central nervous system injury with vaginal delivery when the baby's skull is poorly mineralized.

According to a recent study (Cubert et al), cesarean delivery did not decrease fracture rates at birth in infants with nonlethal forms of OI, nor did it prolong survival for those with lethal forms. This study also found that most cesarean deliveries were done for the usual obstetric indications and not specifically because OI was detected in the fetus.

Planning for the delivery should also include conferring with the hospital's neonatologist, chief obstetrical nurse and nursery staff. Medical personnel who have experience with premature infants often have the skills necessary to handle a tiny, fragile baby who has OI.

Information is available from the Osteogenesis Imperfecta Foundation regarding caring for an infant who has OI.

Resources

Cubert, Rachel, M.D., Edith Y. Cheng, M.D., Sarah Mack, Melanie G. Pepin, MS, Peter H. Byers, M.D. Osteogenesis Imperfecta: Mode of Delivery and Neonatal Outcome. *Obstetrics & Gynecology*. Vol. 97, No. 1, January 2001.

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