Introduction

You and your family have learned that you have a condition called gestational trophoblastic disease, or GTD. This is a term used for a group of pregnancy-related tumors. The amount of information you receive at the time of diagnosis can feel overwhelming. We hope this information will help you understand your condition more thoroughly and help you through this difficult time.

Gestational Trophoblastic Disease (GTD): An Overview

Gestational trophoblastic disease (GTD) is a rare group of interrelated tumors that develop following conception that lead to abnormal development of the placenta. More than 80% of GTD cases are non-cancerous. All forms of GTD can be treated, and in the great majority of cases the treatment results in a cure. Most women who have had a single incidence of GTD can go on to have normal pregnancies.

There are three main types of GTD:

1. Hydatidiform Mole
A hydatidiform mole (also called a “molar pregnancy”) is a form of GTD that arises when fertilization of an egg cell results in an abnormal pregnancy. There are two types of molar pregnancies, complete and partial. A complete molar pregnancy develops when the fertilized egg cell lacks maternal genes. The pregnancy that results contains no fetal tissue and resembles grape-like cysts that fill the uterine cavity. A partial molar pregnancy occurs when more than one sperm fertilizes a normal egg resulting in a pregnancy where both the fetus and placenta are abnormal. The term partial is used because the placenta contains both normal tissue and grape-like cysts similar to that seen in complete moles. 80% of molar pregnancies are benign in that they cause no further trouble after they are removed from the uterus. However, in approximately 20% of complete molar pregnancy and 1-4% of partial moles the molar tissue either spreads locally within the muscular wall of the uterus (called invasive mole) or spreads more widely to other parts of the body, most commonly the lungs (called metastases), which requires treatment. Hydatidiform moles occur in only one of every 1000-1200 pregnancies in the United States.

2. Choriocarcinoma

Choriocarcinoma is a highly malignant form of GTD that spreads rapidly throughout the body and requires vigorous treatment. It may have begun as a molar pregnancy or from tissue that remains in the uterus following a miscarriage or childbirth. Choriocarcinoma is even less common, arising in only one of every 20,000-40,000 pregnancies.

3. Placental-Site Trophoblastic Tumor
Placental-site GTD is a very rare form of the disease that arises in the uterus at the site where the placenta was attached. These tumors penetrate the muscle layer of the uterus and usually do not spread to other parts of the body.

**Risk Factors**

Although doctors cannot always explain why a woman develops GTD, there are a number of factors that may increase a woman’s risk of developing the disease:

- **Age** Since GTD develops from pregnancy this disease only occurs in women in the childbearing age group. The risk of developing GTD increases with age, particularly after age 40.

- **Prior GTD** Women who have had a previous molar pregnancy or choriocarcinoma are at increased risk of another. For example, a second molar pregnancy occurs ten times more frequently than the first mole.

- **Diet** Women whose diets are low in beta carotene or vitamin A appear to have a higher risk of developing complete molar pregnancy.

- **Use of Oral Contraceptives** Long-term use of contraceptives appear to increase the risk of partial molar pregnancy.

- **Irregular periods** Women who have irregular periods appear to have an increased risk of partial molar pregnancy.

- **Fertility problems** Women who have had spontaneous abortions appear to have an increased risk of complete and partial molar pregnancy.
Symptoms

The most common symptoms of hydatidiform mole are feeling pregnant and vaginal bleeding, which can be either bright red or watery brown discharge. Other symptoms are:

- Abdominal bloating
- Nausea and vomiting which is generally more severe than in normal pregnancy
- Fatigue, shortness of breath and lack of energy due to anemia, if there has been a great deal of blood loss
- Signs of an overactive thyroid gland including rapid heartbeat, warm skin, and mild shaking seen rarely in patients with complete mole.
- High blood pressure due to pre-eclampsia (also called toxemia of pregnancy) which can develop if the molar pregnancy continues beyond twelve weeks

Women who develop choriocarcinoma may be symptom-free or experience symptoms based on which organ(s) are involved:

- **Uterus**: Vaginal bleeding, discharge
- **Lung**: Coughing up blood, shortness of breath, chest pain
- **Liver**: Abdominal pain
- **Brain**: Headache, trouble with vision, weakness or loss of function, convulsion
- **Kidney**: Blood in urine
- **Bowel**: Blood in stool

Diagnosis
The diagnosis of **hydatidiform mole** is most commonly made by an ultrasound, a test which uses sound waves to show the contents of the uterus. The ultrasound picture of a **complete hydatidiform mole** will show the uterus filled with cysts. There is no evidence of a fetus.

The early diagnosis of a **partial hydatidiform mole** will look like a miscarriage or show an abnormal fetus with an abnormal placenta depending upon the number of weeks pregnant. In most cases of partial mole the diagnosis is made by the pathologist. A blood test will also be done to look for a hormone called human chorionic gonadotropin (known as hCG or beta-hCG) which is also present in normal pregnancy. This hormone is an important test which will be used to determine whether the molar pregnancy will become malignant, to determine if treatment is working, and to find out if the GTD has returned.

The diagnosis of **choriocarcinoma** is usually made when the patient develops abnormal vaginal bleeding or other symptoms, or on rare occasions when a pregnancy test is found to be elevated and there is no pregnancy.

**Treatment**

After the diagnosis of **complete or partial hydatidiform mole** is made or suspected, the uterine contents are removed by suctioning (called Dilation and Evacuation, D&E)

Hysterectomy may be advisable in older patients who have completed childbearing to reduce the risk of malignancy. After the uterus is emptied, testing for human chorionic gonadotropin should be performed every week in order to determine if the molar pregnancy is malignant. If
the molar pregnancy is benign the hormone level will become undetectable in 8-12 weeks.

Hormone testing should be continued until three weekly negative levels are obtained, then followed by monthly tests for six months, after which pregnancy is permitted. During the six month follow-up it is important to avoid pregnancy. The use of oral contraceptives is safe.

A rise in the hormone level indicates that the molar pregnancy is malignant GTD (also called gestational trophoblastic neoplasia, GTN). More tests will be done to find out if the cancer has spread from the uterus to other parts of the body (called staging). Even if GTD has spread to other parts of the body it is still highly curable. The stages of malignant GTD are:

- Stage I. The cancer has not spread from the uterus
- Stage II. The cancer has spread from the uterus to other structures in the pelvis
- Stage III. The cancer has spread to the lungs
- Stage IV. The cancer has spread to other organs

The treatment of malignant GTD depends on the stage and number of risk factors which determine the type of drugs that will most likely cure the disease. The factors that are characteristic of women who are likely to be cured by one or more single chemotherapy drugs (called **low-risk malignant GTD**) are:

1. The last pregnancy was less than 4 months ago
2. The level of hCG in the blood is low
3. The cancer has not spread to the liver, brain and/or other distant organs
4. The patient has not received chemotherapy treatments earlier
The risk factors of women who develop malignant GTD who are NOT likely to be cured by one or more single chemotherapy drugs and who require treatments containing multiple agents to effect cure (called **high-risk malignant GTD**) are:

1. The last pregnancy was more than 4 months ago
2. The level of hCG in the blood is high
3. The cancer has spread to the liver, brain and/or other distant organs
4. The patient received chemotherapy earlier and the cancer did not go away
5. The tumor began after completion of a normal pregnancy

Three kinds of treatment are used for malignant GTD: surgery (removing the cancer), chemotherapy (using drugs to kill the cancer), and radiation therapy (uses high energy x-rays to kill cancer cells and shrink tumors). The most common operation used for malignant GTD is hysterectomy, an operation to take out the uterus. Surgery may also be used to remove cancer involving the lungs and other organs which have not gone away with drug therapy.

Chemotherapy is the main treatment for malignant GTD and is generally highly effective. Chemotherapy uses drugs to kill cancer cells. It may be taken by pill, or by a needle in vein or muscle. It is called systemic treatment because the drugs enter the bloodstream, travel through the body, and can kill cancer cells outside the uterus. Chemotherapy may be given before or after surgery or alone. Patients can preserve fertility and still be cured with chemotherapy even in the presence of widespread disease.
Radiation may infrequently be used in certain cases to treat cancer that has spread to other parts of the body, particularly the brain. Radiation may come from a machine outside the body (external-beam radiation therapy) or from putting materials that produce radiation (radioisotopes) through thin plastic tubes into the area where the cancer cells are found (internal radiation).

**Placental site trophoblastic tumors**, unlike choriocarcinoma, are not very sensitive to chemotherapy. Since in most cases the tumor is localized to the uterus, hysterectomy is generally curative. When the disease spreads outside the uterus, high dose chemotherapy is used with some success.

**Once You Have Been Treated, Then What?**

Hormone follow-up by measuring the level of human chorionic gonadotropin (hCG) in blood continues until the hormone level is normal for three weeks, then should continue monthly for 12 months (24 months or patients with Stage IV disease). During that time the patient should avoid pregnancy. Women who conceive within 12 months of completing chemotherapy have an increased risk of miscarriage, particularly if they have received multiple chemotherapeutic agents. If pregnancy occurs before follow-up is complete, tumor relapse may be difficult to detect and diagnosis of relapse may be delayed.
The chemotherapy used for the treatment of malignant GTD is generally well tolerated without long-term side effects with two exceptions: 1) the use of multi-agent chemotherapy is associated with an earlier menopause, and 2) women with high-risk GTN who require multi-agent chemotherapy which includes a drug called etoposide and survive for more than 25 years should be advised that they may be at increased risk of developing secondary tumors, particularly acute myeloid leukemia, colon cancer, melanoma, and breast cancer.

**Recurrent Disease**

GTN is a highly curable disease. Women with hydatidiform mole have an excellent prognosis and women with malignant GTD (called GTN) usually have a very good prognosis. Choriocarcinoma, for example, is an uncommon, yet almost always curable cancer. Although choriocarcinoma is a highly malignant tumor and life-threatening disease, it is very sensitive to chemotherapy. 85-90% of women with low-risk malignant GTD are cured by the initial chemotherapy and the remaining are cured by the use of stronger combinations of drugs, or surgery. Similarly, 85-90% of women who develop high-risk malignant GTD are cured by chemotherapy used together with the selective use of surgery and radiation. Approximately 10-15% of women with high-risk malignant GTD will develop drug resistance after prolonged chemotherapy. This group is made up of patients with stage IV disease that involves distant organs such as the brain, liver and bowel. Specially designed chemotherapy treatments using drugs that have been shown to be effective against other cancers are being employed to salvage many of these women.
**Becoming Pregnant Again**

After completing hormone follow-up for **hydatidiform mole** women may try for pregnancy whenever they wish. The risk of another molar pregnancy is low. More than 98% of women who become pregnant following a molar pregnancy will not have a further hydatidiform mole or be at increased risk for complications. Since patients with hydatidiform mole are at increased risk of another molar pregnancy it is advisable for them to undergo ultrasound examinations at 10 weeks of gestation to determine if the pregnancy is progressing normally.

Most women who require treatment for **malignant GTD** can become pregnant again and can have normal pregnancy outcomes. After chemotherapy is completed women should postpone pregnancy for 12 months (24 months for women with stage IV disease) while they are being followed with hormone testing to make sure the tumor does not recur. There does not appear to be an increase rate of congenital malformation irrespective of the chemotherapy used. Following GTD the expectation of normal future pregnancy is about comparable to the general population.

**Summary**

Gestational trophoblastic disease, although highly curable, is an emotionally traumatic event in a women’s life, not only because of the pregnancy loss, but also because of the fear of cancer. Treatment of malignant GTD can impact significantly on her self-image, relationship with her spouse/significant other, family and friends. It is important for women to make use
of all available psychological and social services and spiritual support to help them through this difficult time.