About Gestational Trophoblastic Disease

Overview and Types

If you have been diagnosed with gestational trophoblastic disease or are worried about it, you likely have a lot of questions. Learning some basics is a good place to start.

- What Is Gestational Trophoblastic Disease?

Research and Statistics

See the latest estimates for cases of gestational trophoblastic disease in the US and what research is currently being done.

- What Are the Key Statistics About Gestational Trophoblastic Disease?
- What's New in Gestational Trophoblastic Disease Research and Treatment?

What Is Gestational Trophoblastic Disease?

Tumors can grow anywhere in the body and happen when cells in the body begin to grow out of control. Some tumors might have cancer cells within them, and some might not. Cells in nearly any part of the body can become cancer, and can spread to other
areas of the body. To learn more about how cancers start and spread, see What Is Cancer? ¹

Gestational trophoblastic disease (GTD) is a group of rare tumors that involve abnormal growth of cells inside a woman's uterus. GTD does not develop from cells of the uterus like cervical cancer or endometrial (uterine lining) cancer do. Instead, these tumors start in the cells that would normally develop into the placenta during pregnancy. (The term gestational refers to pregnancy.)

GTD begins in the layer of cells called the trophoblast that normally surrounds an embryo. (Trophi- means nutrition, and -blast means bud or early developmental cell.) Early in normal development, the cells of the trophoblast form tiny, finger-like projections known as villi. The villi grow into the lining of the uterus. In time, the trophoblast layer develops into the placenta, the organ that protects and nourishes the growing fetus.

You might hear GTDs called gestational trophoblastic disease, gestational trophoblastic tumors, or gestational trophoblastic neoplasia. (Neoplasia simply means new growth. Most GTDs are benign (not cancer) and they don't invade deeply into body tissues or spread to other parts of the body. But some are malignant (cancerous).

All forms of GTD can be treated. And in most cases the treatment² produces a complete cure.

**Types of gestational trophoblastic disease**

The main types of gestational trophoblastic diseases are:

- Hydatidiform mole (complete or partial)
- Invasive mole
- Choriocarcinoma
- Placental-site trophoblastic tumor
- Epithelioid trophoblastic tumor

**Hydatidiform mole**

The most common form of gestational trophoblastic disease (GTD) is a hydatidiform mole, also known as a molar pregnancy. It is made up of villi that have become swollen with fluid. The swollen villi grow in clusters that look like bunches of grapes. This is called a molar pregnancy, but it is not possible for a normal baby to form. Still in
rare cases (less than 1 in 100), a normal fetus can develop alongside the molar pregnancy. Hydatidiform moles are not cancerous, but they can develop into cancerous GTDs.

There are 2 types of hydatidiform moles: complete and partial.

A complete hydatidiform mole most often develops when 1 or 2 sperm cells fertilize an egg cell that contains no nucleus or DNA (an “empty” egg cell). All the genetic material comes from the father’s sperm cell. Therefore, there is no fetal tissue.

Surgery can totally remove most complete moles, but as many as 1 in 5 women will have some persistent molar tissue (see below). Most often this is an invasive mole, but in rare cases it is a choriocarcinoma, a malignant (cancerous) form of GTD. In either case it will require further treatment.

A partial hydatidiform mole develops when 2 sperm fertilize a normal egg. These tumors contain some fetal tissue, but this is often mixed in with the trophoblastic tissue. It is important to know that a viable (able to live) fetus is not being formed.

Partial moles usually are completely removed by surgery. Only a small number of women with partial moles need further treatment after initial surgery. Partial moles rarely develop into malignant GTD.

Persistent gestational trophoblastic disease is GTD that is not cured by initial surgery. Persistent GTD occurs when the hydatidiform mole has grown from the surface layer of the uterus into the muscle layer below (the myometrium). The surgery used to treat a hydatidiform mole (called suction dilation and curettage, or D&C) scrapes the inside of the uterus. This removes only the inner layer of the uterus (the endometrium) and cannot remove tumor that has grown into the muscular layer.
Most cases of persistent GTD are invasive moles, but in rare cases they are choriocarcinomas or placental site trophoblastic tumors (see below).

**Invasive mole**

An invasive mole (formerly known as chorioadenoma destruens) is a hydatidiform mole that has grown into the muscle layer of the uterus. Invasive moles can develop from either complete or partial moles, but complete moles become invasive much more often than do partial moles. Invasive moles develop in less than 1 out of 5 women who have had a complete mole removed. The risk of developing an invasive mole in these women increases if:

- There is a long time (more than 4 months) between their last menstrual period and treatment.
- The uterus has become very large.
- The woman is older than 40 years.
- The woman has had gestational trophoblastic disease in the past.

Because these moles have grown into the uterine muscle layer, they aren't completely removed during a D&C. Invasive moles can sometimes go away on their own, but most often more treatment is needed.

A tumor or mole that grows completely through the wall of the uterus might result in
bleeding into the abdominal or pelvic cavity. This bleeding can be life threatening.

Sometimes after removing a complete hydatidiform mole, the tumor spreads (metastasizes) to other parts of the body, most often the lungs. This occurs about 4% of the time (or 1 in 25 cases).

**Choriocarcinoma**

Choriocarcinoma is a malignant form of gestational trophoblastic disease (GTD). It is much more likely than other types of GTD to grow quickly and spread to organs away from the uterus.

Half of all gestational choriocarcinomas start off as molar pregnancies. About one-quarter develop in women who have a miscarriage (spontaneous abortion), intentional abortion, or tubal pregnancy (the fetus develops in the fallopian tube, rather than in the uterus). Another quarter (25%) develop after normal pregnancy and delivery.

Rarely, choriocarcinomas that are not related to pregnancy can develop. These can be found in areas other than the uterus, and can occur in both men and women. They may develop in the ovaries, testicles, chest, or abdomen. In these cases, choriocarcinoma is usually mixed with other types of cancer, forming a type of cancer called a mixed germ cell tumor.

These tumors are not considered to be gestational (related to pregnancy) and are not discussed in this document. Non-gestational choriocarcinoma can be less responsive to chemotherapy and may have a less favorable prognosis (outlook) than gestational choriocarcinoma. For more information about these tumors, see [Ovarian Cancer](#) and [Testicular Cancer](#).

**Placental-site trophoblastic tumor**

Placental-site trophoblastic tumor (PSTT) is a very rare form of GTD that develops where the placenta attaches to the lining of the uterus. This tumor most often develops after a normal pregnancy or abortion, but it may also develop after a complete or partial mole is removed.

Most PSTTs do not spread to other sites in the body. But these tumors have a tendency to grow into (invade) the muscle layer of the uterus.

Most forms of GTD are very sensitive to chemotherapy drugs, but PSTTs are not. Instead, they are treated with surgery, to completely remove disease.
Epithelioid trophoblastic tumor

Epithelioid trophoblastic tumor (ETT) is an extremely rare type of gestational trophoblastic disease that can be hard to diagnose. ETT used to be called atypical choriocarcinoma because the cells look like choriocarcinoma cells under the microscope, but it is now thought to be a separate disease. Because it can be found growing in the cervix, it can also sometimes be confused with cervical cancer\textsuperscript{9}. Like placental-site trophoblastic tumors, ETT most often occurs after a full-term pregnancy, but it can take several years after the pregnancy for the ETT to occur. Also, like placental-site trophoblastic tumors, ETT does not respond very well to chemotherapy drugs, so the main treatment is surgery\textsuperscript{10}. It might have already metastasized when it is diagnosed which carries a poorer prognosis (outlook).

Hyperlinks


References

See all references for Gestational Trophoblastic Disease (https://www.cancer.org/content/cancer/en/cancer/gestational-trophoblastic-disease/references.html)
What Are the Key Statistics About Gestational Trophoblastic Disease?

Gestational trophoblastic disease (GTD) occurs in about 1 pregnancy out of 1,000 in the United States. Most of these are hydatidiform moles.

Choriocarcinoma, a malignant form of gestational trophoblastic disease (GTD), is even less common, affecting around 2 to 7 of every 100,000 pregnancies in the United States.

Choriocarcinoma and other forms of GTD are more common in many Asian and African countries.

Overall, gestational trophoblastic tumors account for less than 1% of female reproductive system cancers.

Cure rates depend on the type of GTD and its stage, as described in Treatment of Gestational Trophoblastic Disease, by Type and Stage.

Hyperlinks


References

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What's New in Gestational Trophoblastic Disease Research and Treatment?

Important research into gestational trophoblastic disease (GTD) is being done right now in many university hospitals, medical centers, and other institutions around the country. Each year, scientists find out more about what causes the disease and how to improve treatment.

Causes of GTD

Researchers are studying cells of GTD to learn more about how these tumors develop. Discoveries about chromosome abnormalities of complete and partial moles have helped explain the causes of these types of GTD. These discoveries have led to developing lab tests that can help identify types of moles (partial vs. complete) when routine microscopic analysis does not yield a clear answer.

Epidemiology

Researchers often collect data on how often various forms of cancer occur in different parts of the world and whether these diseases are becoming more or less common. This often provides clues about risk factors and ideas for prevention. Earlier studies suggested that choriocarcinoma and GTDs were 5 to 10 times more common in Asia than in Europe and North America. More recent information indicates that the difference is actually no greater than double and may be even less, and that the original estimates were likely biased by differences in the way births are recorded in different countries.

Staging and prognosis

Newer and more sensitive tests are now able to more accurately determine blood human chorionic gonadotropin (HCG) levels than in the past. Scientists have developed a blood test for a form of HCG known as hyperglycosylated HCG. Early studies suggest that this blood test may help separate patients with active GTD who need treatment from those who have elevated HCG levels but don't truly have GTD, and therefore may not require therapy. More studies are needed to confirm this.

Improvements in the staging systems and prognostic classification systems are making it easier for doctors to recognize which patients will benefit from which treatments.
Treatment

In recent years, a number of studies have shown the benefits of using combination chemotherapy (chemo) for high-risk metastatic GTD, such as the EMA-CO and EMA-EP regimens (these were discussed in the section about chemotherapy). The excellent results with these regimens have made them treatments of choice in many institutions.

Newer chemo drugs including pemetrexed, paclitaxel, and gemcitabine have been studied for use in this disease, as are several new combinations of drugs. Some of these are already being used in women whose GTD doesn't respond to other treatments.

For tumors that are resistant to standard chemo doses, doctors are studying the use of high-dose chemo followed by a stem cell transplant to restore the patient's bone marrow. Some very early results have been promising, but more research is needed.

Researchers are also studying the benefits and risks of giving anti-cancer drugs to prevent future GTDs in women who have had a molar pregnancy in the past.

And researchers are always looking for ways to give the usual chemo drugs with new schedules that might be more effective, cause less severe side effects, and/or be more convenient for patients.

References

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Important research into gestational trophoblastic (jeh-STAY-shuh-nul troh-fuh-BLAS-tik) disease (GTD) is being done right now in many university hospitals, medical centers, and other institutions around the country. Each year, scientists find out more about what causes this disease and how to improve treatment.

Researchers are studying GTD cells to learn more about how these tumors develop. Finding certain chromosome changes in complete and partial moles have helped explain the causes of these types of GTD. These discoveries have led to developing lab
tests that can help identify these 2 types of moles (partial vs. complete) when routine
testing doesn't give a clear answer. As more genetic changes are identified, researchers
hope to be better able to identify and treat GTD.

Studies have suggested that human chorionic gonadotropin (hCG) blood levels may
help separate women with high (hCG) levels with active GTD who need treatment from
those who have high (hCG) levels, but don't have GTD and don't need treatment. More
studies are looking at how this might be useful in women with high (hCG) levels, as well
as in women with low hCG levels who do have GTD.

Improvements in the staging systems and prognostic classification (predicting
outcomes) systems are under discussion. These changes could make it easier for
doctors to recognize which patients will benefit from which treatments. It could also help
researchers when comparing GTD treatments and patient outcomes.

New chemo drugs are being studied for use in this disease, as are new combinations of
drugs. This could lead to more treatment options and better treatment outcomes.
Researchers are also studying ways to give the usual chemo drugs with new schedules
that might work better, cause less severe side effects, and/or be more convenient for
patients.

For tumors that are resistant to standard chemo doses, doctors are studying the use of
high-dose chemo followed by a stem cell transplant to restore the patient’s bone
marrow. So far results have been mixed and more research is needed.

Hyperlinks

1. https://www.cancer.org/content/cancer/en/cancer/gestational-trophoblastic-
disease/treating/chemotherapy.html

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