



Gestational Trophoblastic Disease

What is cancer?

The body is made up of hundreds of millions of living cells. Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries.

Cancer begins when cells in a part of the body start to grow out of control. There are many kinds of cancer, but they all start because of out-of-control growth of abnormal cells.

Cancer cell growth is different from normal cell growth. Instead of dying, cancer cells continue to grow and form new, abnormal cells. Cancer cells can also invade (grow into) other tissues, something that normal cells cannot do. Growing out of control and invading other tissues are what makes a cell a cancer cell.

Cells become cancer cells because of damage to DNA. DNA is in every cell and directs all its actions. In a normal cell, when DNA gets damaged the cell either repairs the damage or the cell dies. In cancer cells, the damaged DNA is not repaired, but the cell doesn't die like it should. Instead, this cell goes on making new cells that the body does not need. These new cells will all have the same damaged DNA as the first cell does.

People can inherit damaged DNA, but most DNA damage is caused by mistakes that happen while the normal cell is reproducing or by something in our environment. Sometimes the cause of the DNA damage is something obvious, like cigarette smoking. But often no clear cause is found.

In most cases the cancer cells form a tumor. Some cancers, like leukemia, rarely form tumors. Instead, these cancer cells involve the blood and blood-forming organs and circulate through other tissues where they grow.

Cancer cells often travel to other parts of the body, where they begin to grow and form new tumors that replace normal tissue. This process is called metastasis. It happens when the cancer cells get into the bloodstream or lymph vessels of our body.

No matter where a cancer may spread, it is always named for the place where it started. For example, breast cancer that has spread to the liver is still called breast cancer, not liver cancer. Likewise, prostate cancer that has spread to the bone is metastatic prostate cancer, not bone cancer.

Different types of cancer can behave very differently. For example, lung cancer and breast cancer are very different diseases. They grow at different rates and respond to different treatments. That is why people with cancer need treatment that is aimed at their particular kind of cancer.

Not all tumors are cancerous. Tumors that aren't cancer are called benign. Benign tumors can cause problems – they can grow very large and press on healthy organs and tissues. But they cannot grow into (invade) other tissues. Because they can't invade, they also can't spread to other parts of the body (metastasize). These tumors are almost never life threatening.

What is gestational trophoblastic disease?

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. (Tropho- means "nutrition," and -blast means "bud" or "early developmental cell.") Early in normal development, the cells of this layer form tiny, finger-like projections known as *villi*. These 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.

Most GTDs are benign (non cancerous) and they don't invade deeply into body tissues or spread to other parts of the body. But some are cancerous. Because not all of these tumors are cancerous, this group of tumors may be referred to as gestational trophoblastic disease, gestational trophoblastic tumors, or gestational trophoblastic neoplasia. (The word *neoplasia* simply means "new growth.")

All forms of GTD can be treated. And in most cases the treatment 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

Hydatidiform mole

The most common form of GTD is called 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. Hydatidiform moles are not cancerous, but they may develop into cancerous GTDs.

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

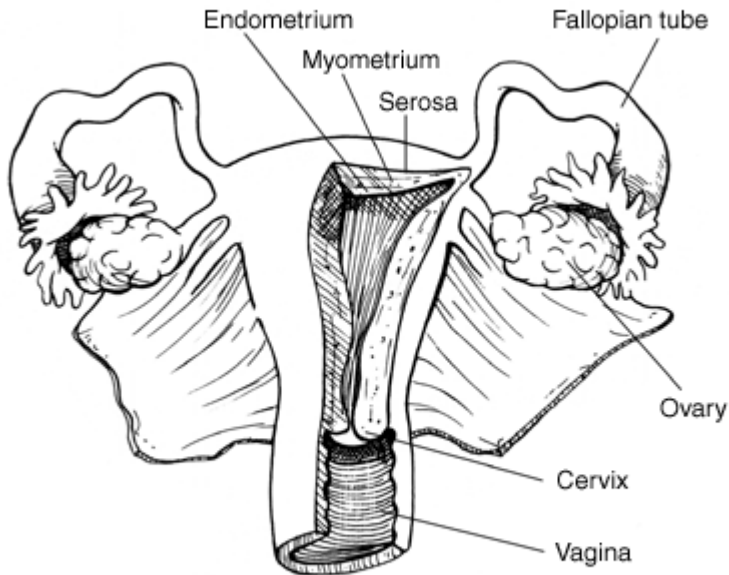
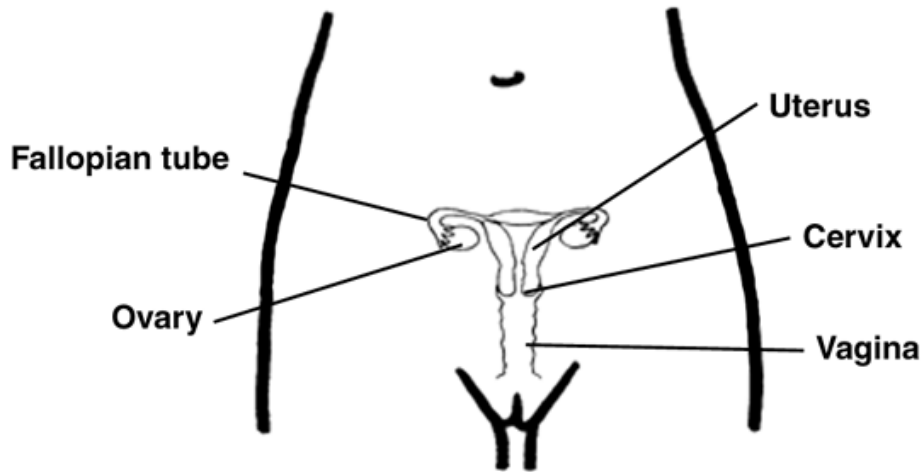
A **complete hydatidiform mole** most often develops when either 1 or 2 sperm cells fertilize an "empty" egg cell (a cell that contains no nucleus or DNA). All the genetic material comes from the father's sperm cell. Therefore, there is no fetal tissue.

Surgery can totally remove most complete moles, but in as many as 1 in 5 women there will be some persistent molar tissue (see the section, "Persistent gestational trophoblastic disease" 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 are usually 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 a term used to describe GTD that is not cured by initial surgery. Persistent GTD occurs when the hydatiform mole has grown from the surface layer of the uterus into the muscle layer below (called the *myometrium*). The surgery used to treat a hydatiform mole (called suction dilation and curettage, or D&C) involves scraping 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 a little 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 the last menstrual period and treatment.
- The uterus has become very large.
- The woman is older than 40 years.
- The woman has had GTD 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 may 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 GTD. It is much more likely than other types of GTD to grow quickly and spread to organs away from the uterus.

Choriocarcinoma most often develops from a complete hydatidiform mole, but it can also occur after a partial mole, a normal pregnancy, or a pregnancy that ends early (such as a miscarriage or an elective abortion).

Rarely, choriocarcinomas can develop that are not related to pregnancy. 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 our documents, *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, aimed at completely removing disease.

What are the key statistics about gestational trophoblastic disease?

Hydatidiform moles occur in about 1 pregnancy out of 1,000 in the United States and Europe. In very rare cases (less than 1%), a normal fetus can develop along with the hydatidiform mole.

In about 15% of cases, a hydatidiform mole will progress to become an "invasive" mole. Overall, invasive moles occur at an estimated rate of 1 pregnancy in 15,000.

Choriocarcinoma, a malignant form of gestational trophoblastic disease (GTD), is even less common, affecting approximately 1 pregnancy out of 40,000 in the United States. Like other forms of GTD, choriocarcinoma is more common in many Asian and African countries.

About 2% to 4% of hydatidiform moles progress to become choriocarcinoma. But only half of all gestational choriocarcinomas start off as molar pregnancies. About one-quarter of all choriocarcinomas 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 one-quarter occur after normal pregnancy and delivery.

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 the section "Treatment of GTD by type and stage."

What are the risk factors for gestational trophoblastic disease?

A *risk factor* is anything that affects your chance of getting a disease such as cancer. Different cancers have different risk factors. For example, exposing skin to strong sunlight is a risk factor for skin cancer. Smoking is a risk factor for cancers of the lung, mouth, larynx (voice box), bladder, kidney, and several other organs.

But risk factors don't tell us everything. Having a risk factor, or even several risk factors, does not mean that you will get the disease. And some people who get the disease may not have any known risk factors. Even if a person has a risk factor, it is often very hard to know how much that risk factor may have contributed to the cancer.

Researchers have found several risk factors that may increase a woman's chance of developing gestational trophoblastic disease (GTD).

Age

GTD occurs most often in women of childbearing age. The risk of complete molar pregnancy is highest in women over age 40 and younger than 20. The risk is even higher for women over the age of 50. In this age group, one-third of pregnancies results in a complete hydatiform mole. Age is less likely to be a factor for partial moles.

Prior molar pregnancy

Once a woman has had a hydatidiform mole, she has a higher risk of having another one. The overall risk for later pregnancies is about 1% to 2%. This risk increases further if she has had more than one molar pregnancy.

Prior miscarriage(s) or problems getting pregnant

Women with either of these have a higher risk of GTD, but their overall risk is still low.

Blood type

Women with blood type A or AB are at slightly higher risk than those with type B or O.

Birth control pills

Women who take birth control pills may be more likely to get GTD when they do become pregnant. The link between the use of birth control pills and GTD is weak, and may be explained by other factors. This risk seems to be higher for women who took the pills longer. But the risk is still so low that it doesn't outweigh the benefit of using the pills.

Socioeconomic status

Some studies have found that women who have lower income or education level have an increased risk, but the reasons for this are not clear. Some researchers have suggested that diet may play a role.

Diet

A few studies have found that a low level of beta-carotene (a nutrient converted to vitamin A in the body) in the diet may be linked with a higher risk of complete molar pregnancies. More research is needed to confirm this.

Family history

Very rarely, several women in the same family have one or more molar pregnancies.

Do we know what causes gestational trophoblastic disease?

Normally, the sperm and egg cells each provide a set of 23 chromosomes (bits of DNA that contain our genes) to create a cell with 46 chromosomes. This cell will start dividing to eventually become a fetus. This normal process does not occur with gestational trophoblastic disease (GTD).

In *complete hydatidiform moles*, the problem most often arises when a sperm cell fertilizes an abnormal egg cell that contains no nucleus (or chromosomes). The reason the egg contains no chromosomes is not known. After fertilization, the chromosomes from the sperm duplicate themselves, so there are 2 copies of identical chromosomes that both come from the sperm. When this happens, normal development cannot occur, and no fetus is formed. Instead, a complete hydatidiform mole develops. Less often, a complete mole forms when an abnormal egg without any chromosomes is fertilized by 2 sperm cells. Again, there are 2 copies of the father's chromosomes and none from the mother, and no fetus forms.

Partial hydatidiform moles result when 2 sperm cells fertilize a normal egg at the same time. The fertilized egg contains 3 sets of chromosomes (69) instead of the usual 2 sets (46). An embryo with 3 sets of chromosomes cannot grow into a normally developed infant. This situation leads to an abnormal (malformed) fetus along with some normal placental tissue and a partial hydatidiform mole.

Invasive moles are hydatidiform moles that begin to grow into the muscle layer of the uterus. They develop more often from complete moles than from partial moles. It's not clear exactly what causes this to happen.

Most *choriocarcinomas* develop from persistent hydatidiform moles (usually complete moles). They can also develop when bits of tissue are left behind in the uterus after a miscarriage, an intended abortion, or the delivery of a baby following an otherwise normal pregnancy. Researchers have found changes in certain genes that are commonly found in choriocarcinoma cells, but it's not clear what causes these changes.

Placental-site trophoblastic tumor (PSTT) is an uncommon type of GTD. Unlike choriocarcinomas and hydatidiform moles, they do not contain villi. They occur most often after pregnancies that have gone to term.

Can gestational trophoblastic disease be prevented?

The only way to avoid the rare chance of developing gestational trophoblastic disease (GTD) is to not get pregnant. But a first case of GTD is so rare that its prevention should not be a factor in family planning decisions.

Women with a prior history of one or more molar pregnancies should speak with their doctor to be sure they understand their risk for future molar pregnancies.

Can gestational trophoblastic disease be found early?

Most cases of gestational trophoblastic disease (GTD) are found early during routine prenatal care. Usually, a woman has certain signs and symptoms, like vaginal bleeding, that suggest something may be wrong. (These symptoms are discussed in the section, "How is gestational trophoblastic disease diagnosed?") These signs will prompt the doctor to look for the cause of trouble.

Often, moles or tumors cause swelling in the uterus that seems like a normal pregnancy. But a doctor can usually tell that this isn't a normal pregnancy during a routine ultrasound exam. A blood test for human chorionic gonadotropin (HCG) can also show that something is abnormal. This substance is normally elevated in the blood of pregnant women, but it may be very high if there is GTD.

Fortunately, even if it is not detected early, GTD is a very treatable (and usually curable) form of cancer.

Because women who have had one molar pregnancy are at increased risk, doctors can be especially careful in checking their future pregnancies with beta-HCG tests and transvaginal or pelvic sonograms. (These tests are described in the next section.)

How is gestational trophoblastic disease diagnosed?

Gestational trophoblastic disease (GTD) is most often found either as a result of abnormal signs or symptoms during pregnancy or from the results of certain tests during routine prenatal care.

Signs and symptoms

It's important to let your doctor know about any abnormal symptoms you are having during pregnancy. Your doctor may suspect that GTD is present based on a typical pattern of signs and symptoms. Many of these may also be caused by conditions other

than GTD. Still, if you have any of these, it's important to see your doctor right away so the cause can be found and treated, if needed.

Complete hydatidiform moles (molar pregnancies)

Most of these signs and symptoms (except for bleeding), are seen less commonly now than in the past because they tend to occur late in the course of the disease. Most women with GTD are now diagnosed early because of the use of blood tests and ultrasound early in pregnancy.

Vaginal bleeding: Almost all women with complete hydatidiform moles have irregular vaginal bleeding during pregnancy. It occurs a little less often with partial moles. Bleeding typically starts during the first trimester (13 weeks) of pregnancy. Women with GTD often pass blood clots or watery brown discharge from the vagina. Sometimes, pieces of the mole resembling a cluster of grapes become dislodged from the uterus and are discharged through the vagina. This bleeding often leads the doctor to order an ultrasound (discussed later in this section), which leads to the diagnosis of a molar pregnancy.

Anemia: In cases of serious or prolonged bleeding, a woman's body is not able to replace red blood cells as fast as they are lost. This can lead to anemia (low red blood cell counts). Symptoms can include fatigue and shortness of breath, especially with physical activity.

Abdominal swelling: The uterus and abdomen can get bigger faster in a complete molar pregnancy than they do in a normal pregnancy. Abnormal uterine enlargement occurs in about 1 out of 4 women with complete moles but rarely in women with partial moles.

Ovarian cysts: Human chorionic gonadotropin (HCG), a hormone made by the tumor (see below), may cause fluid-filled cysts to form in the ovaries. These cysts can be large enough to cause abdominal swelling. They only occur with very high levels of HCG. Even though they can become quite large, they usually go away on their own about 8 weeks after the molar pregnancy is removed. Sometimes they can twist on their blood supply (called *torsion*). This can cause severe pain and needs to be treated with surgery (to remove the cyst) or a procedure to drain the fluid inside the cyst.

Vomiting: Many women have nausea and vomiting during the course of a typical pregnancy. With GTD, however, the vomiting may be more frequent and severe than normal.

Pre-eclampsia: Pre-eclampsia (toxemia of pregnancy) can occur as a complication of a normal pregnancy (usually in the third trimester). When it occurs earlier in pregnancy (like during the first or early second trimester), it can be a sign of a complete molar pregnancy. Pre-eclampsia may cause problems such as high blood pressure, headache, exaggerated reflexes, swelling in the hands or feet, and too much protein leaking into the urine. It affects a small number of women with complete moles but is rare in women with partial moles.

Hyperthyroidism: Hyperthyroidism (having an overactive thyroid gland) occurs in some women with complete hydatidiform moles. It occurs only in women with very high HCG blood levels. Symptoms of hyperthyroidism can include rapid heartbeat, warm skin, sweating, problems tolerating heat, and mild tremors (shaking). This occurs in less than 10% of women with complete molar pregnancy.

Partial hydatiform moles

The signs and symptoms of partial hydatidiform moles are similar to those of complete moles, but often are less severe. Some symptoms, such as frequent vomiting or an overactive thyroid gland, rarely, if ever, occur with partial moles.

Partial moles are often diagnosed after what is thought to be a miscarriage. The molar pregnancy is found when the uterus is scraped during a suction dilation and curettage (D&C) and the products of conception are looked at under a microscope.

Invasive moles and choriocarcinoma

These more invasive forms of GTD sometimes develop after a complete mole has been removed. They occur less commonly after a partial mole. Choriocarcinoma can also develop after a normal pregnancy, ectopic pregnancy (where the fetus grows outside of the uterus, such as inside a fallopian tube), or miscarriage. Symptoms can include:

Bleeding: The most common symptom is vaginal bleeding. Rarely, the tumor grows through the uterine wall, which can cause bleeding into the abdominal cavity along with severe abdominal pain.

Infection: In larger tumors, some of the tumor cells may die, creating an area where bacteria can grow. Infection may develop, which can cause vaginal discharge, crampy pelvic pain, and fever.

Abdominal swelling: Like hydatidiform moles, more invasive forms of GTD can expand the uterus, causing abdominal swelling. Human chorionic gonadotropin (HCG), a hormone made by the tumor (see below), may cause fluid-filled cysts (called theca lutein cysts) to form in the ovaries, which can be large and may also contribute to abdominal swelling.

Lung symptoms: The lung is a common site for distant spread of GTD. Spread to the lungs may cause coughing up of blood, a dry cough, chest pain, or trouble breathing.

Vaginal mass: These tumors can sometimes spread to the vagina, which can cause vaginal bleeding or a pus-like discharge. The doctor may also notice a cancerous growth on the vagina during a pelvic exam.

Other symptoms of distant spread: Symptoms depend on where the spread occurs. If GTD has spread to the brain, symptoms can include headache, vomiting, dizziness, seizures, or paralysis on one side of the body. Spread to the liver can cause abdominal pain and a yellowing of the skin or eyes (jaundice).

Placental site trophoblastic tumors

Placental site trophoblastic tumors (PSTTs) rarely spread to distant sites. More often, they grow into the wall of the uterus

Bleeding: As with other forms of GTD, the most common symptom of PSTT is vaginal bleeding. If the tumor grows all the way through the wall of the uterus, it can cause bleeding into the abdominal cavity with severe abdominal pain.

Abdominal swelling: As they grow within the wall of the uterus, PSTTs may cause the uterus to enlarge.

Blood and urine tests

Blood and urine tests can be used to help diagnose GTD.

Human chorionic gonadotropin (HCG)

Trophoblastic cells of both normal placentas and GTD make a hormone called human chorionic gonadotropin (HCG), which is vital in supporting a pregnancy. HCG is released into the blood, and some of it is excreted in the urine. This hormone consists of 2 chemical components, and the commonly-used blood and urine tests measure one of these, called *beta-HCG* (β HCG).

HCG is normally found only in the blood or urine of pregnant women. In fact, finding HCG in urine is the basis of most pregnancy tests.

A complete mole usually releases more HCG than a normal placenta, so finding higher than expected HCG levels in the blood can be a sign that a complete mole is present.

However, not all women with GTD have HCG levels that are higher than those seen in a normal pregnancy. For example, most women with partial moles or placental site trophoblastic tumors have normal or only slightly increased HCG levels.

HCG tests can also help tell if GTD may be present after a pregnancy or miscarriage, as the level of HCG should normally fall to an undetectable level soon afterward.

Along with helping to diagnose GTD, blood HCG levels are also very useful in women already known to have GTD. They can be used to:

- Help estimate the amount of GTD that is present in a patient's body. Higher levels of HCG may mean that there are more tumor cells present in the body.
- Determine if treatment is working. HCG levels should drop to normal levels after treatment.
- Detect GTD that has come back after treatment

It's especially important to monitor HCG levels during treatment and follow-up to make sure the disease is going and has gone away, or has not returned. The HCG test is

generally very accurate. In rare cases, patients may have abnormal substances (antibodies) in their blood that interfere with the HCG test. When these patients' blood samples are tested, the HCG levels appear higher than they really are, a situation known as *phantom HCG*. In some cases, women have been diagnosed with GTD when it is not actually present. A sign of phantom HCG is having high blood levels of HCG, but normal urine levels (because the abnormal antibodies are not present in urine). If doctors notice that the blood (or serum) levels of HCG are high but the urine levels are not, they can order special tests to distinguish between truly elevated HCG levels and phantom HCG.

Other blood tests

Other tests may provide indirect evidence of GTD. For example, red blood cell counts can detect anemia (having too few red blood cells), which can be caused by uterine bleeding. Human placental lactogen (hPL) is a marker that may be used to follow patients with PSTT.

For women diagnosed with GTD, blood tests are often used to watch for side effects from chemotherapy. Blood cell counts are done to watch the health of the bone marrow (where new blood cells are made), and blood chemistry tests can be used to check the condition of the liver and kidneys.

Tests of spinal fluid

If symptoms suggest that there may be spread to the brain or spinal cord or if there is a high HCG level but there are no tumors seen on any radiology studies, samples of spinal fluid may be removed to check for signs of tumor spread. This procedure is called a lumbar puncture or spinal tap. For this test, the patient may lie on their side or sit up. The doctor first numbs an area in the lower part of the back over the spine. A small, hollow needle is then placed between the bones of the spine to withdraw some of the fluid.

Imaging tests

Imaging tests use sound waves, x-rays, magnetic fields, or radioactive substances to create pictures of the inside of your body. Imaging tests may be done to help find out whether a tumor is present and to learn how far it may have spread.

Ultrasound (sonogram)

Ultrasound can identify most cases of GTD that are in the uterus, and will likely be the first test done if your doctor suspects there may be a problem.

How it works: This test uses sound waves to produce images of internal organs. A small microphone-like instrument called a *transducer* gives off sound waves and then picks up the echoes they make as they bounce off body tissues. The echoes are converted into a black and white image by a computer. That image is then displayed on a computer screen.

What it's like to have the test: Ultrasound is an easy procedure. It uses no radiation, which is why it is often used to look at developing fetuses. During an ultrasound exam, you simply lie on a table while a technician or doctor moves the transducer on the part of your body being examined. Most ultrasounds are done with the transducer placed on the skin after it is first lubricated with gel.

To diagnose GTD, a different type of ultrasound called *transvaginal ultrasonography* is most often used. In this procedure, a small transducer is placed into the vagina. This allows for good images of the uterus for women suspected of having GTD during the first trimester of their pregnancy.

What doctors look for: In a normal pregnancy, ultrasound imaging shows a picture of the developing fetus inside the womb.

In a complete molar pregnancy, however, no fetus can be seen on an ultrasound. Instead, the ultrasound detects the large, grape-like swollen villi that are typical of GTD. Rarely, the ultrasound may show a "twin" pregnancy in which one of the twins is a normal fetus and the other is a hydatidiform mole. This occurs less than 1% of the time.

In a partial molar pregnancy, ultrasound can show an abnormally formed placenta. If a fetus is seen, it is often deformed.

Ultrasound can also be used to help find out if a mole is invading local tissues. If blood levels of HCG are still elevated after the mole has been removed, more exams may need to be done.

Chest x-ray

A chest x-ray may be done in cases of persistent GTD to see if it has spread to your lungs, which is very unlikely unless your cancer is far advanced. However, CT scans of the chest are done more often if your doctor suspects persistent or advanced disease outside of the uterus. Either test can be done in an outpatient setting.

Computed tomography (CT) scan

The CT scan is an x-ray test that produces detailed cross-sectional images of your body. Instead of taking one picture, like a regular x-ray, a CT scanner takes many pictures as it rotates around you while you lie on a table. A computer then combines these pictures into images of slices of the part of your body being studied. Unlike a regular x-ray, a CT scan creates detailed images of the soft tissues in the body.

Before any pictures are taken, you may be asked to drink 1 to 2 pints of a liquid called "oral contrast." This helps outline the intestine so that certain areas are not mistaken for tumors. You may also receive an IV (intravenous) line through which a different kind of contrast dye (IV contrast) is injected. This helps better outline structures in your body.

The injection may cause some flushing (a feeling of warmth, especially in the face). Some people are allergic and get hives. Rarely, more serious reactions like trouble breathing or low blood pressure can occur. Medicine can be given to prevent and treat

allergic reactions. Be sure to tell the doctor if you have ever had a reaction to any contrast material used for x-rays.

CT scans take longer than regular x-rays. You need to lie still on a table while they are being done. During the test, the table moves in and out of the scanner, a ring-shaped machine that completely surrounds the table. You might feel a bit confined by the ring you have to lie in while the pictures are being taken.

This test may be done to see if the GTD has spread outside the uterus, such as the lungs, brain, or liver.

Magnetic resonance imaging (MRI) scan

Like CT scans, MRI scans provide detailed images of soft tissues in the body. But MRI scans use radio waves and strong magnets instead of x-rays. The energy from the radio waves is absorbed and then released in a pattern formed by the type of body tissue and by certain diseases. A computer translates the pattern into a very detailed image of parts of the body. A contrast material called gadolinium is often injected into a vein before the scan to better see details.

MRI scans are a little more uncomfortable than CT scans. First, they take longer -- often up to an hour. Second, you have to lie inside a narrow tube, which is confining and can upset people with claustrophobia (a fear of enclosed spaces). Newer, "open" MRI machines can sometimes help with this if needed. The machine also makes buzzing and clicking noises that you may find disturbing. Some centers provide headphones with music to block this out.

MRI scans are most helpful in looking at the brain and spinal cord. They are most likely to be used to scan the brain if GTD has already been found to have spread elsewhere, such as to the lungs. Sometimes they are used to look to see if the tumor has grown into the wall of the uterus.

Positron emission tomography (PET) scan

PET scans involve injecting a form of radioactive sugar (known as fluorodeoxyglucose or FDG) into the blood. The amount of radioactivity used is very low. Cancer cells in the body grow rapidly, so they absorb large amounts of the radioactive sugar. A special camera can then create a picture of areas of radioactivity in the body. The picture is not finely detailed like a CT or MRI scan, but it provides helpful information about your whole body.

PET scans are sometimes useful if your doctor thinks the cancer may have spread (or returned after treatment) but doesn't know where. PET scans can be used instead of several different imaging tests because they scan your whole body. Still, these tests are rarely used for GTD.

Some machines are able to perform both a PET and CT scan at the same time (PET/CT scan). This allows the radiologist to compare areas of higher radioactivity on the PET with the appearance of that area on the CT.

Other tests

Doctors can often be fairly certain of a diagnosis of GTD based on symptoms, blood test results, and imaging tests, but the diagnosis is often made after a D&C in patients with abnormal bleeding. The cells from the tumor are removed and viewed under a microscope. The cells from different types of GTD each look different under the microscope. Sometimes complete and partial moles may be hard to tell apart when they are examined under the microscope early in the first trimester. If so, other tests may be needed to distinguish the 2 types of mole. Some tests, called *cytogenetics*, look at the number and type of chromosomes of the mole. Other tests may look at certain genes that only come from the mother to see if it is a partial mole versus a complete mole. (D&C is described in the section, "Surgery.")

How is gestational trophoblastic disease staged?

Staging is the process of finding out how far a cancer has spread. This information helps doctors choose the type of treatment that offers the best possible results.

Molar pregnancies (complete and partial moles) are usually completely removed during a D&C (or, rarely, a hysterectomy), so they don't need to be surgically "staged." Staging is more useful for persistent GTDs, including invasive moles and choriocarcinomas.

Gestational trophoblastic disease (GTD) classification

The stage of most cancers depends on how large they are and whether they have spread to lymph nodes or distant sites. This is part of staging for GTD as well (and is described below). But because treatment is usually effective regardless of the extent of the disease, other factors such as a woman's age, length of time from the pregnancy, and HCG level are more useful in predicting a woman's outlook (prognosis). These factors are taken into account in a scoring system.

Prognostic scoring system

In the United States, most cancer centers use a system that describes women with persistent GTDs according to their prognosis, based on several factors.

Age	Score
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Younger than 40	0
40 or older	1
Preceding pregnancy	Score
Molar pregnancy	0
Abortion (includes miscarriage)	1
Birth (term pregnancy)	2
Time since pregnancy	Score
Less than 4 months	0
At least 4 months but less than 7 months	1
7 to 12 months	2
More than 12 months	4
Blood HCG level (IU/L) before treatment	Score
Less than 1,000	0
1,000 - 9,999	1
10,000 - 99,999	2
100,000 or more	4
Largest tumor size, including the original one in the uterus	Score
Less than 3 cm (1.2 inches) across	0
At least 3 cm but less than 5 cm (2 inches)	1
5 cm or more	2

Site of metastases (if any)	Score
Lung	0
Spleen, kidney	1
Gastrointestinal tract	2
Brain, liver	4
Number of metastases found	Score
0	0
1 to 4	1
5 to 8	2
More than 8	4
Prior failed chemotherapy	Score
None	0
Single drug	2
2 or more drugs	4

The numbers are then added up, and the overall score determines a woman's risk level.

- Women with a score of 6 or less are at low risk and tend to have a good outlook regardless of how far the cancer has spread. The tumor(s) will usually respond well to chemotherapy.
- Women with a score of 7 or more are at high risk, and their tumors tend to respond less well to chemotherapy, even if they haven't spread much. They may require more intensive chemotherapy.

FIGO anatomic staging

The International Federation of Gynecology and Obstetrics (FIGO) has developed a staging system based on the extent of the GTD as follows:

Stage I: The tumor is still within the uterus.

Stage II: The tumor has grown outside of the uterus to involve other genital structures (like the vagina or ovaries). It has not spread outside the pelvis.

Stage III: The tumor has spread to the lungs; it may or may not also involve genital structures such as the vagina or vulva.

Stage IV: The tumor has spread to distant organs such as the brain, liver, kidneys, and/or gastrointestinal tract.

Stage grouping

Stage grouping is a process that some doctor use that combines the prognostic score and the anatomic stage. This is listed as the anatomic stage, followed by the letter A if the prognostic score was low risk or B if the prognostic score resulted in high risk.

Stage IA: The tumor has not spread outside the uterus, and the prognostic score puts you at low risk.

Stage IB: The tumor has not spread outside the uterus, and the prognostic score puts you at high risk.

Stage IIA: The tumor has grown outside of the uterus but not beyond the vagina or pelvis, and the prognostic score puts you at low risk.

Stage IIB: The tumor has grown outside of the uterus but not beyond the vagina or pelvis, and the prognostic score puts you at high risk.

Stage IIIA: The tumor has spread to the lungs, and may or may not also involve genital structures such as the vagina or vulva. The prognostic score puts you at low risk.

Stage IIIB: The tumor has spread to the lungs, and may or may not also involve genital structures such as the vagina or vulva. The prognostic score puts you at high risk.

Stage IVA: The cancer has spread to distant organs such as the brain, liver, kidneys, and/or gastrointestinal tract. The prognostic score puts you at low risk.

Stage IVB: The cancer has spread to distant organs such as the brain, liver, kidneys, and/or gastrointestinal tract. The prognostic score puts you at high risk.

Another option is to combine the anatomic stage with the actual prognostic score number (separated by a colon). An example of this is II:5.

If GTD comes back after treatment (recurs), the disease is "restaged." This takes into account where the disease is in the body, along with the prior treatment.

How is gestational trophoblastic disease treated?

This information represents the views of the doctors and nurses serving on the American Cancer Society's Cancer Information Database Editorial Board. These views are based on their interpretation of studies published in medical journals, as well as their own professional experience.

The treatment information in this document is not official policy of the Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor.

Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask him or her questions about your treatment options.

The first part of this section describes the various types of treatments used for gestational trophoblastic disease (GTD). This information is followed by a description of the most common approaches used for these cancers based on the type and classification of GTD.

Making treatment decisions

After GTD is diagnosed and staged, your medical team can recommend one or more treatment options. Choosing a treatment plan is an important decision, so be sure to take time and think about all of the choices.

No matter what type or stage of GTD a woman has, treatment is available. Your treatment choice depends on many factors. The location and the extent of the disease are very important. Other important factors include the type of GTD present, the level of human chorionic gonadotropin (HCG), duration of the disease, sites of metastasis if any, and the extent of prior treatment. In selecting a treatment plan, you and your medical team will also consider your age, general state of health, and personal preferences.

It is important to begin treatment as soon as possible after GTD has been detected. The main methods of treatment are surgery, chemotherapy, and less frequently radiation therapy. Sometimes the best approach uses a combination of 2 or more of these methods.

Surgery for gestational trophoblastic disease

Suction dilation and curettage (D&C)

This procedure is often used to diagnose a molar pregnancy and may be the first treatment given for a hydatidiform mole. It can be the only treatment needed. . It is done in an operating room in a hospital or other type of surgical center.

Most often, general anesthesia is used (where you are asleep). Using a special instrument, the doctor enlarges (dilates) the opening of the uterus (the cervix) and then inserts a vacuum-like device that removes most of the tumor. The doctor then uses a long, spoon-like instrument (curette) to scrape the lining of the uterus to remove any molar tissue that

remains. During this procedure you may receive an intravenous (IV) infusion of a drug called oxytocin. This causes the uterus to contract and expel its contents.

After the procedure, most women can go home on the same day. Potential complications of a suction D&C are not common but can include reactions to anesthesia, bleeding from the uterus, infections, scarring of the cervix or uterus, and blood clots. A rare but serious side effect is trouble breathing caused when small pieces of trophoblastic tissue break off and travel to the blood vessels in the lungs. Most women will have cramping for up to a day after the procedure.

Hysterectomy

This type of surgery removes the uterus (womb). It is an option for women with hydatidiform moles who do not want to have any more children, but it isn't often used. It is also the standard treatment for women with placental site trophoblastic tumors. Removing the uterus ensures that all of the tumor cells in the uterus are gone -- including any that had invaded the muscle layer (myometrium). But since some tumor cells may have already spread outside the uterus at the time of surgery, it does not guarantee that all tumor cells are removed from the body.

The ovaries are usually left in place. Rarely, when there are theca-lutein cysts (fluid-filled sacs) in the ovaries, these cysts will be removed in an operation called an ovarian cystectomy.

There are 3 approaches to remove the uterus:

Abdominal hysterectomy: During this operation, the uterus is removed through an incision that is made in the front of the abdomen.

Vaginal hysterectomy: Less often, if the uterus is not too large, it may be detached and removed through the vagina. In some cases, the surgeon may make a small cut in the abdomen to insert a laparoscope -- a long, thin instrument with a video camera on the end -- to aid with the operation. This is known as a *laparoscopic-assisted vaginal hysterectomy*. Because there is no large abdominal incision, recovery is often quicker than with an abdominal hysterectomy.

Laparoscopic hysterectomy: For this surgery, several small holes are made in the abdomen and long, thin instruments (including one with a video camera on the end) are inserted into them to perform the operation. The uterus is then removed through a small hole made in the vagina. Again, recovery is usually quicker than with an abdominal hysterectomy.

For all of these operations, the patient is either asleep (general anesthesia) or sedated and numbed below the waist (regional anesthesia). A hospital stay of about 2 to 3 days is common for an abdominal hysterectomy. Complete recovery takes about 4 to 6 weeks. The usual hospital stay for a vaginal hysterectomy is 1 to 2 days with a recovery time of 2 to 3 weeks. A similar recovery is expected for a laparoscopic hysterectomy.

Hysterectomy results in the inability to have children. Some pain is common after surgery but can usually be well controlled with medicines. Complications of surgery are unusual but could include reactions to anesthesia, excessive bleeding, wound infection, or damage to the urinary tract, the intestine, or to nerves.

Surgery (suction D&C or hysterectomy) removes the source of disease within the uterus, but it does not get rid of cancerous cells that may have already spread outside the uterus to other parts of the body. To be certain that no cancer cells remain, blood HCG levels are carefully checked at regular time points after surgery. If HCG levels stay the same or start to rise, doctors often recommend that women receive chemotherapy. Most women with hydatidiform moles do not require chemotherapy.

Surgery for metastatic tumors

Even when GTD has spread to distant areas of the body, it can often be treated effectively with chemotherapy. But in some rare cases, surgery may be used to remove tumors in the liver, lung, brain, or elsewhere, especially if chemotherapy is not shrinking the tumor(s).

Chemotherapy for gestational trophoblastic disease

Chemotherapy (chemo) uses anti-cancer drugs that are injected into a vein or given by mouth. These drugs enter the bloodstream and reach all areas of the body, making this treatment useful for cancers that have spread to distant organs (metastasized). GTD is one of the few cancers that can almost always be cured by chemo no matter how advanced it is. The best indicator of which drug to use is the prognostic score.

The drugs that can be used to treat GTD include:

- Methotrexate (with or without leucovorin)
- Actinomycin-D (dactinomycin)
- Cyclophosphamide (Cytosan®)
- Chlorambucil
- Vincristine (Oncovin®)
- Etoposide (VP-16)
- Cisplatin
- Ifosfamide (Ifos®)
- Bleomycin
- Fluorouracil (5-FU)

To reduce the risk of side effects, doctors try to give the fewest drugs at the lowest doses that will still be effective. As a general rule, women who need to get chemo and fall into the low-risk group (see the section, "How is gestational trophoblastic disease staged?")

are given a single chemo drug. Women who fall in the high-risk group usually receive combinations of drugs, often at higher doses.

Single drug treatment

Methotrexate: Chemotherapy with methotrexate alone can be used in most women with low risk disease. The methotrexate can be given as an injection into a vein or a muscle every day for 5 days. This can be repeated again after a rest period based on the HCG level. Another way to give methotrexate is to give a larger dose once a week. Again, the treatment is continued as long as needed based on the HCG level. Another option is to give methotrexate along with folinic acid (also called leucovorin). Leucovorin is not a chemo drug, but instead is a type of vitamin related to folic acid that reduces the toxic effects of methotrexate. In this course of treatment, methotrexate is given on days 1, 3, 5, and 7, and leucovorin is given on days 2, 4, 6, and 8. Each cycle has 8 days of drug treatment, followed by a rest period. This method involves more treatment days, so it may be less convenient. In all cases, methotrexate is given in cycles that are repeated until blood levels of HCG remain normal for a few weeks. Vitamins such as folic acid can make methotrexate less effective and so should not be taken with this drug unless directed by your doctor.

Actinomycin-D: Another option is to give actinomycin-D instead of methotrexate. This drug may be especially useful in patients with liver problems, because it is less toxic to the liver than is methotrexate. Actinomycin-D is given in a vein (intravenously, or IV) every day for 5 days, followed by several days without treatment. It is also given as a larger single dose once every 2 weeks. This schedule seems to have fewer side effects while still working well. Either way, the cycles are repeated until HCG levels have stayed in the normal range for several weeks.

Combinations of drugs

Women with higher-risk disease will receive combinations of drugs such as methotrexate, actinomycin-D, and cyclophosphamide. Other drugs such as etoposide, vincristine, and cisplatin may also be used.

Some of the more commonly used combinations include:

- MAC: methotrexate/leucovorin, actinomycin-D, and cyclophosphamide or chlorambucil
- EMA-CO: etoposide, methotrexate/leucovorin, and actinomycin-D, followed a week later by cyclophosphamide and vincristine (Oncovin)
- EMA-EP: etoposide, methotrexate/leucovorin, and actinomycin-D, followed a week later by etoposide and cisplatin ("platinum")
- VBP: vinblastine, bleomycin, and cisplatin
- BEP: bleomycin, etoposide, cisplatin

Possible side effects

Chemo drugs work by attacking cells that are dividing quickly, which is why they work against cancer cells. But other cells in the body, such as those in the bone marrow, the lining of the mouth and intestines, and the hair follicles, also divide quickly. These cells are also likely to be affected by chemotherapy, which can lead to some side effects.

The side effects of chemo depend on the type and dose of drugs given and the length of time they are taken. Common side effects of chemotherapy drugs include:

- Hair loss
- Mouth sores
- Loss of appetite
- Nausea and vomiting
- Low blood counts

Because chemotherapy can damage the blood-producing cells of the bone marrow, the blood cell counts might become low. This can result in:

- Increased chance of infections (due to low white blood cell counts)
- Easy bruising or bleeding (due to low blood platelet counts)
- Fatigue (due to low red blood cell counts)

Most of these side effects are short-term and tend to go away after treatment is finished. There are often ways to lessen these side effects. For example, drugs can be given to help prevent or reduce nausea and vomiting. Do not hesitate to discuss any questions about side effects with the cancer care team.

Along with the effects listed above, some side effects are specific to certain medicines:

Common side effects of methotrexate are diarrhea and sores in the mouth. This drug can also cause mild liver damage which is seen as changes in certain blood tests (liver enzymes). Some women experience inflammation of the eye (conjunctivitis), pain in the chest or abdomen, irritation in the genital region, or skin rash. Hair loss and blood side effects do not usually occur with single-drug methotrexate therapy.

Actinomycin-D can cause fairly severe nausea and vomiting. This can be prevented by medications given before chemo. Treatment with actinomycin-D or combination therapy is more likely to result in hair loss. Your bone marrow's ability to produce blood cells may be affected, which in turn may lower the ability of your immune system to fight infection.

Bleomycin can cause lung problems. These occur more often in patients who smoke.

Cyclophosphamide can cause some nausea and hair loss. It can also cause bladder irritation and rarely causes severe lung problems.

In rare cases, etoposide treatment has been linked with the development of leukemia several years later. But doctors still consider it important to use because its benefit in curing the cancer outweighs the small risk of leukemia.

Vincristine and cisplatin can damage nerves (called *neuropathy*). Patients may notice tingling and numbness, particularly in the hands and feet. Cisplatin can also cause hearing loss and kidney damage. These side effects may persist after treatment is stopped.

You should report any side effects or changes you notice while getting chemotherapy to your medical team so that they can be treated promptly. In some cases, the doses of the chemotherapy drugs may need to be reduced or treatment may need to be delayed or stopped to prevent the effects from getting worse.

Radiation therapy for gestational trophoblastic disease

Radiation therapy uses focused high-energy x-rays that penetrate the body to reach and destroy cancerous cells.

Radiation isn't often used to treat GTD, unless it has spread and is not responding to chemotherapy. Radiation may then be used to treat sites where the cancer may be causing pain or other problems. It may also be used when GTD has spread to the brain. If radiation is used, combination chemo is often used as well.

The type of radiation therapy most often used in treating GTD is called *external beam radiation therapy*. In this type of radiation therapy, the radiation is aimed at the cancer from a machine outside the body. Having this type of radiation therapy is much like having a diagnostic x-ray, except that each treatment lasts longer and the treatments are usually repeated daily over several weeks.

Clinical trials for gestational trophoblastic disease

You may have had to make a lot of decisions since you've been told you have cancer. One of the most important decisions you will make is choosing which treatment is best for you. You may have heard about clinical trials being done for your type of cancer. Or maybe someone on your health care team has mentioned a clinical trial to you.

Clinical trials are carefully controlled research studies that are done with patients who volunteer for them. They are done to get a closer look at promising new treatments or procedures.

If you would like to take part in a clinical trial, you should start by asking your doctor if your clinic or hospital conducts clinical trials. You can also call our clinical trials matching service for a list of clinical trials that meet your medical needs. You can reach this service at 1-800-303-5691 or on our Web site at www.cancer.org/clinicaltrials. You can also get a list of current clinical trials by calling the National Cancer Institute's Cancer Information Service toll-free at 1-800-4-CANCER (1-800-422-6237) or by visiting the NCI clinical trials Web site at www.cancer.gov/clinicaltrials.

There are requirements you must meet to take part in any clinical trial. If you do qualify for a clinical trial, it is up to you whether or not to enter (enroll in) it.

Clinical trials are one way to get state-of-the-art cancer treatment. They are the only way for doctors to learn better methods to treat cancer. Still, they are not right for everyone.

You can get a lot more information on clinical trials in our document called *Clinical Trials: What You Need to Know*. You can read it on our Web site or call our toll-free number (1-800-227-2345) and have it sent to you.

Complementary and alternative therapies for gestational trophoblastic disease

When you have cancer you are likely to hear about ways to treat your cancer or relieve symptoms that your doctor hasn't mentioned. Everyone from friends and family to Internet groups and Web sites offer ideas for what might help you. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

What exactly are complementary and alternative therapies?

Not everyone uses these terms the same way, and they are used to refer to many different methods, so it can be confusing. We use *complementary* to refer to treatments that are used *along with* your regular medical care. *Alternative* treatments are used *instead of* a doctor's medical treatment.

Complementary methods: Most complementary treatment methods are not offered as cures for cancer. Mainly, they are used to help you feel better. Some methods that are used along with regular treatment are meditation to reduce stress, acupuncture to help relieve pain, or peppermint tea to relieve nausea. Some complementary methods are known to help, while others have not been tested. Some have been proven not to be helpful, and a few have even been found harmful.

Alternative treatments: Alternative treatments may be offered as cancer cures. These treatments have not been proven safe and effective in clinical trials. Some of these methods may pose danger, or have life-threatening side effects. But the biggest danger in most cases is that you may lose the chance to be helped by standard medical treatment. Delays or interruptions in your medical treatments may give the cancer more time to grow and make it less likely that treatment will help.

Finding out more

It is easy to see why people with cancer think about alternative methods. You want to do all you can to fight the cancer, and the idea of a treatment with no side effects sounds great. Sometimes medical treatments like chemotherapy can be hard to take, or they may no longer be working. But the truth is that most of these alternative methods have not been tested and proven to work in treating cancer.

As you consider your options, here are 3 important steps you can take:

- Look for "red flags" that suggest fraud. Does the method promise to cure all or most cancers? Are you told not to have regular medical treatments? Is the treatment a "secret" that requires you to visit certain providers or travel to another country?
- Talk to your doctor or nurse about any method you are thinking about using.
- Contact us at 1-800-227-2345 to learn more about complementary and alternative methods in general and to find out about the specific methods you are looking at.

The choice is yours

Decisions about how to treat or manage your cancer are always yours to make. If you want to use a non-standard treatment, learn all you can about the method and talk to your doctor about it. With good information and the support of your health care team, you may be able to safely use the methods that can help you while avoiding those that could be harmful.

Treatment of GTD by type and stage

The following lists the standard treatment options according to the type of GTD and the stage and prognostic group of the disease. These treatments are discussed in more detail in separate sections about surgery, chemotherapy, and radiation therapy.

Hydatidiform moles (complete and partial moles)

The standard treatment for women who may wish to have children in the future is to remove the tumor by suction dilation and curettage (D&C). Women who no longer wish to have children usually have the option of choosing either suction D&C or hysterectomy (removal of the tumor and entire uterus). A hysterectomy ensures no tumor remains within the uterus but, like a D&C, it does not treat tumor cells that may have already spread outside the uterus.

Rarely, a hydatidiform mole occurs as part of a "twin" pregnancy, where there is a normal fetus along with the mole. In this case, the pregnancy is watched closely and typically allowed to continue. The mole is then treated after delivery.

Once the tumor is removed, a pathologist will look at it under a microscope for signs of choriocarcinoma or other malignant changes in the specimen. If there are none, then patients are carefully monitored with frequent measurements of blood HCG levels. The levels should drop and become undetectable within several months. If not, there may still be mole tissue deep in the uterus (an invasive mole) or elsewhere in the body.

Doctors recommend that women avoid becoming pregnant during the first year after diagnosis because pregnancy would raise HCG levels. Oral contraceptives may be used, but intrauterine devices (IUDs) should not be used at this time because of the risk of

bleeding, infection, or other problems. Sometimes IUDs can cause problems that can look like tumor left in the uterus.

Chemotherapy will likely be needed if the blood HCG level begins to rise or is still detectable after a reasonable time (often around 4 to 6 months), or if the pathologist finds choriocarcinoma in the tissue sample. About 1 in 5 women will need chemotherapy after a molar pregnancy.

Stage I low-risk gestational trophoblastic tumors

This can be either persistent GTD (where the HCG level hasn't dropped to normal after treatment of a molar pregnancy) or a choriocarcinoma or placental site trophoblastic tumor that was found in the curettage specimen. The tumor is still confined to the uterus, and the prognostic score is less than 7.

Chemotherapy with either methotrexate (with or without leucovorin) or actinomycin-D is the recommended treatment for stage 1, low risk disease. Hysterectomy may also be advised, particularly for women who no longer want to have babies. It may reduce the amount of chemotherapy needed.

Chemotherapy is given until there are no longer any signs of cancer, based on levels of HCG in the blood (the HCG level should return to normal after treatment). If the initial chemotherapy drug does not get rid of the tumor, a second drug may be tried. If the HCG level is still detectable at this point, more intensive chemotherapy with a combination of drugs may be needed.

Placental-site trophoblastic tumor is treated with hysterectomy. Chemotherapy is usually not helpful. Since HCG is often not found at high levels in the blood with PSTT, blood levels of another hormone called human placental lactogen (hPL) may be checked and followed.

Stage II/III low-risk gestational trophoblastic tumors

These tumors have spread to the genital structures or to the lungs, but the prognostic score is less than 7. Chemotherapy with either methotrexate (with or without leucovorin) or actinomycin-D is curative in most cases. If a single drug does not get rid of the tumor, treatment with combination chemotherapy is usually effective. In rare cases, surgical removal of the tumors plus chemotherapy may be used. Blood HCG levels are measured after treatment and should return to normal.

Stage II/III high-risk gestational trophoblastic tumors

These tumors have spread to the genital structures or to the lungs, and the prognostic score is 7 or higher. Standard treatment is usually an intensive combination chemotherapy regimen such as EMA-CO. Other drug combinations, such as EMA-EP, may also be used, although they may be reserved for use if the EMA-CO regimen isn't effective. In rare cases, surgical removal of the tumors plus chemotherapy may be used. Blood HCG levels are measured after treatment and should return to normal.

Stage IV gestational trophoblastic tumors

These tumors have spread to distant sites such as the liver or brain. Intensive treatment is needed for these tumors. Combination chemotherapy such as the EMA-CO regimen is the standard treatment. If the cancer has reached the brain, radiation therapy to the head is often used as well. In some cases, surgical removal of tumors may be used along with chemotherapy. Again, blood HCG levels are measured after treatment and should return to normal.

Recurrent gestational trophoblastic tumors

A tumor is called recurrent when it come backs after treatment. Recurrence can be local (in or near the same place it started) or distant (spread to organs such as the lungs or bone). The type of treatment used depends on where the cancer recurs and what treatment the woman has already received.

For tumors that were first treated with surgery, single-drug chemotherapy may be used, unless a new risk factor puts the patient at high risk (in which case combination chemotherapy would be used). In women who have already had chemotherapy, a more intensive chemotherapy regimen would be used. Several different combinations of drugs might be tried, if needed. Again, if the cancer has reached the brain, radiation therapy to the head is often used. In some cases, surgical removal of tumors may be used as well.

Cure rates for GTD

Nearly 100% of women with complete or partial moles and low-risk GTD can be cured of their disease with appropriate treatment. While PSTT has high cure rates, the outlook isn't as good if the disease spreads outside of the uterus. Even for high-risk GTD, cure rates are as high as 80% to 90%, but they will likely require more intensive treatment (combination chemotherapy, sometimes together with radiation and/or surgery).

More treatment information

For more details on treatment options -- including some that may not be addressed in this document -- the National Cancer Institute (NCI) is a good source of information.

The NCI provides treatment guidelines via its telephone information center (1-800-4-CANCER) and its Web site (www.cancer.gov). Detailed guidelines intended for use by cancer care professionals are also available on www.cancer.gov.

What should you ask your doctor about gestational trophoblastic disease?

It is important to have honest open discussions with your medical team. You should feel free to ask any question, no matter how minor it might seem. Among the questions you might want to ask are:

- What kind of gestational trophoblastic disease do I have?
- Has my cancer spread beyond the uterus?
- Can the stage of my cancer be determined and what does that mean? What is my prognostic score?
- How much experience do you have treating this type of disease?
- Are there hospital centers that specialize in the treatment of this disease?
- What treatment choices do I have? Which do you recommend? Why?
- Am I eligible for a clinical trial?
- Does one type of treatment reduce the risk of recurrence more than another?
- What are the side effects and other risks of each treatment?
- How will you monitor my response to treatment?
- Based on what you've learned about my cancer, what are my chances of being cured?
- What should I do to be ready for treatment?
- How long will it take me to recover from treatment?
- When can I go back to work after treatment?
- How soon after treatment can I have sex? Will I need to use birth control?
- What are the chances that my cancer will come back (recur)? What would we do if this happens?
- Will a specialist in gynecologic oncology be involved in my care?
- Will I be able to have a normal pregnancy later on?
- How soon after treatment can I get pregnant?

What happens after treatment for gestational trophoblastic disease?

Completing treatment can be both stressful and exciting. You may be relieved to finish treatment, but find it hard not to worry about cancer coming back. (When cancer comes back after treatment, it is called *recurrence*.) This is a very common concern in people who have had cancer. It is a very real concern for some women with gestational trophoblastic disease (GTD). The risk of GTD returning is very small for molar pregnancies and low-risk GTD, but may be as high as 10% to 15% in women with high-risk GTD. For this reason, follow-up is very important.

It may take a while before your fears lessen. But it may help to know that many cancer survivors have learned to live with this uncertainty and are living full lives. Our document, *Living With Uncertainty: The Fear of Cancer Recurrence*, gives more detailed information on this .

Follow-up doctor visits

When treatment ends, your doctors will still want to watch you closely. It is very important to go to all of your follow-up appointments. During these visits, your doctors will ask questions about any problems you may have and may do exams and lab tests or x-rays and scans to look for signs of cancer or treatment side effects. Almost any cancer treatment can have side effects. Some may last for a few weeks to months, but others can last the rest of your life. This is the time for you to talk to your cancer care team about any changes or problems you notice and any questions or concerns you have.

Your medical team will set up a program of follow-up visits and tests to make sure that everything is all right. The exact steps in the follow-up program depend on the type of GTD you had and the treatment you received.

In all cases, the most basic test involves measuring levels of HCG (or hPL for PSTT) in the blood. Rising HCG levels may indicate that the disease is growing again in the uterus (if hysterectomy was not done) or that it has spread to another location and is growing there. Different treatment centers follow different schedules. For molar pregnancies, blood HCG levels are usually taken weekly until the results are normal for at least 3 consecutive weeks, then monthly for at least the next 6 months. For other forms of GTD, the follow-up period may be extended to a year or 2 following treatment for those who have metastatic GTD with risk factors.

Your doctor will most likely recommend that you have a physical exam about every 3 to 6 months for the first year, then about every 6 months. Depending on your situation, you may need to have certain tests or procedures, such as chest x-rays or other imaging tests, from time to time. Ask your doctor what kind of follow-up schedule you can expect.

It is important to keep health insurance. Tests and doctor visits cost a lot, and even though no one wants to think of their cancer coming back, this could happen.

If cancer does recur, it will most likely be detected with blood HCG tests before it causes any symptoms. Still, if you notice any new symptoms you should report them right away so that the cause can be determined and treated, if needed.

If GTD does come back, in most cases it can be treated successfully. For more information, see “Recurrent gestational trophoblastic tumors” in the section, “Treatment of GTD by type and stage.” Also, our document, *When Your Cancer Comes Back: Cancer Recurrence* can give you information on how to manage and cope with this phase of your treatment.

Avoiding pregnancy during follow-up

If you did not have a hysterectomy, it is important to avoid getting pregnant during the follow-up period. Talk with your doctor about how long this should last and whether oral contraceptives (birth control pills) or a barrier method of birth control (such as a diaphragm or condoms) might be best for you. Most doctors advise against using intrauterine devices (IUDs), as they may increase the risk of bleeding, infection, or puncturing of the uterine wall if tumor is still present.

Later pregnancies

Most women who have had a molar pregnancy can have normal pregnancies later. Studies have found that women treated for GTD have near normal risks of problems such as stillbirths, birth defects, premature babies, or other complications. However, if you do get pregnant and have had GTD once before, there is about a 1% to 2% chance that another molar pregnancy will occur. It can be a complete or partial molar pregnancy. You should have a pelvic ultrasound exam within the first 13 weeks (first trimester) of pregnancy to make sure everything is proceeding normally.

If you give birth, your doctor may request a microscopic examination of the placenta to look for any lingering signs of GTD. You will also need to have your HCG level measured about 6 weeks after the end of any subsequent pregnancy, whether it was a normal birth, abortion, or miscarriage.

Later cancers

One question many women ask is whether they are more likely to get another type of cancer later on. Having had gestational trophoblastic disease does not raise your risk of getting other cancers. However, some chemotherapy drugs sometimes used to treat GTD can increase the risk of certain other types of cancer (most often leukemia). This is rare after treatment of low-risk GTD but is slightly more common with certain drugs used for high-risk GTD, such as etoposide and cyclophosphamide.

Seeing a new doctor

At some point after your cancer diagnosis and treatment, you may find yourself seeing a new doctor who does not know anything about your medical history. It is important that you be able to give your new doctor the details of your diagnosis and treatment. Make sure you have this information handy:

- A copy of your pathology report(s) from any biopsies or surgeries.
- If you had surgery, a copy of your operative report(s).
- If you were hospitalized, a copy of the discharge summary that doctors must prepare when patients are sent home.

- If you received chemotherapy, a list of the drugs, drug doses, and when you took them.
- If you had radiation therapy, a copy of the treatment.

It is also helpful if you have copies of reports for any imaging tests (ultrasounds, CT scans, etc.) you have had.

The doctor may want copies of this information for his records, but always keep copies for yourself.

Lifestyle changes

You can't change the fact that you have had cancer. What you can change is how you live the rest of your life – making choices to help you stay healthy and feel as well as you can. This can be a time to look at your life in new ways. Maybe you are thinking about how to improve your health over the long term. Some people even start during cancer treatment.

Making healthier choices

For many people, a diagnosis of cancer helps them focus on their health in ways they may not have thought much about in the past. Are there things you could do that might make you healthier? Maybe you could try to eat better or get more exercise. Maybe you could cut down on the alcohol, or give up tobacco. Even things like keeping your stress level under control may help. Now is a good time to think about making changes that can have positive effects for the rest of your life. You will feel better and you will also be healthier.

You can start by working on those things that worry you most. Get help with those that are harder for you. For instance, if you are thinking about quitting smoking and need help, call the American Cancer Society for information and support. This tobacco cessation and coaching service can help increase your chances of quitting for good.

Eating better

Eating right can be hard for anyone, but it can get even tougher during and after cancer treatment. Treatment may change your sense of taste. Nausea can be a problem. You may not feel like eating and lose weight when you don't want to. Or you may have gained weight that you can't seem to lose. All of these things can be very frustrating.

If treatment caused weight changes or eating or taste problems, do the best you can and keep in mind that these problems usually get better over time. You may find it helps to eat small portions every 2 to 3 hours until you feel better. You may also want to ask your cancer team about seeing a dietitian, an expert in nutrition who can give you ideas on how to deal with these treatment side effects.

One of the best things you can do after cancer treatment is put healthy eating habits into place. You may be surprised at the long-term benefits of some simple changes, like increasing the variety of healthy foods you eat. Getting to and staying at a healthy weight,

eating a healthy diet, and limiting your alcohol intake may lower your risk for a number of types of cancer, as well as having many other health benefits.

Rest, fatigue, and exercise

Extreme tiredness, called *fatigue*, is very common in people treated for cancer. This is not a normal tiredness, but a "bone-weary" exhaustion that doesn't get better with rest. For some people, fatigue lasts a long time after treatment, and can make it hard for them to exercise and do other things they want to do. But exercise can help reduce fatigue. Studies have shown that patients who follow an exercise program tailored to their personal needs feel better physically and emotionally and can cope better, too.

If you were sick and not very active during treatment, it is normal for your fitness, endurance, and muscle strength to decline. Any plan for physical activity should fit your own situation. An older person who has never exercised will not be able to take on the same amount of exercise as a 20-year-old who plays tennis twice a week. If you haven't exercised in a few years, you will have to start slowly – maybe just by taking short walks.

Talk with your health care team before starting anything. Get their opinion about your exercise plans. Then, try to find an exercise buddy so you're not doing it alone. Having family or friends involved when starting a new exercise program can give you that extra boost of support to keep you going when the push just isn't there.

If you are very tired, you will need to balance activity with rest. It is OK to rest when you need to. Sometimes it's really hard for people to allow themselves to rest when they are used to working all day or taking care of a household, but this is not the time to push yourself too hard. Listen to your body and rest when you need to. (For more information on dealing with fatigue, please see *Fatigue in People With Cancer* and *Anemia in People With Cancer*.)

Keep in mind exercise can improve your physical and emotional health.

- It improves your cardiovascular (heart and circulation) fitness.
- Along with a good diet, it will help you get to and stay at a healthy weight.
- It makes your muscles stronger.
- It reduces fatigue and helps you have more energy.
- It can help lower anxiety and depression.
- It can make you feel happier.
- It helps you feel better about yourself.

And long term, we know that getting regular physical activity plays a role in helping to lower the risk of some cancers, as well as having other health benefits.

How about your emotional health?

When treatment ends, you may find yourself overcome with many different emotions. This happens to a lot of people. You may have been going through so much during treatment that you could only focus on getting through each day. Now it may feel like a lot of other issues are catching up with you.

You may find yourself thinking about death and dying. Or maybe you're more aware of the effect the cancer has on your family, friends, and career. You may take a new look at your relationship with those around you. Unexpected issues may also cause concern. For instance, as you feel better and have fewer doctor visits, you will see your health care team less often and have more time on your hands. These changes can make some people anxious.

Almost everyone who has been through cancer can benefit from getting some type of support. You need people you can turn to for strength and comfort. Support can come in many forms: family, friends, cancer support groups, church or spiritual groups, online support communities, or one-on-one counselors. What's best for you depends on your situation and personality. Some people feel safe in peer-support groups or education groups. Others would rather talk in an informal setting, such as church. Others may feel more at ease talking one-on-one with a trusted friend or counselor. Whatever your source of strength or comfort, make sure you have a place to go with your concerns.

The cancer journey can feel very lonely. It is not necessary or good for you to try to deal with everything on your own. And your friends and family may feel shut out if you do not include them. Let them in, and let in anyone else who you feel may help. If you aren't sure who can help, call your American Cancer Society at 1-800-227-2345 and we can put you in touch with a group or resource that may work for you.

If treatment stops working

If cancer keeps growing or comes back after one kind of treatment, it is possible that another treatment plan might still cure the cancer, or at least shrink it enough to help you live longer and feel better. But when a person has tried many different treatments and the cancer has not gotten any better, the cancer tends to become resistant to all treatment. If this happens, it's important to weigh the possible limited benefits of a new treatment against the possible downsides. Everyone has their own way of looking at this.

This is likely to be the hardest part of your battle with cancer -- when you have been through many medical treatments and nothing's working anymore. Your doctor may offer you new options, but at some point you may need to consider that treatment is not likely to improve your health or change your outcome or survival.

If you want to continue to get treatment for as long as you can, you need to think about the odds of treatment having any benefit and how this compares to the possible risks and side effects. In many cases, your doctor can estimate how likely it is the cancer will respond to treatment you are considering. For instance, the doctor may say that more chemo or radiation might have about a 1% chance of working. Some people are still

tempted to try this. But it is important to think about and understand your reasons for choosing this plan.

No matter what you decide to do, you need to feel as good as you can. Make sure you are asking for and getting treatment for any symptoms you might have, such as nausea or pain. This type of treatment is called *palliative care*.

Palliative care helps relieve symptoms, but is not expected to cure the disease. It can be given along with cancer treatment, or can even be cancer treatment. The difference is its purpose - the main purpose of palliative care is to improve the quality of your life, or help you feel as good as you can for as long as you can. Sometimes this means using drugs to help with symptoms like pain or nausea. Sometimes, though, the treatments used to control your symptoms are the same as those used to treat cancer. For instance, radiation might be used to help relieve bone pain caused by cancer that has spread to the bones. Or chemotherapy might be used to help shrink a tumor and keep it from blocking the bowels. But this is not the same as treatment to try to cure the cancer.

At some point, you may benefit from hospice care. This is special care that treats the person rather than the disease; it focuses on quality rather than length of life. Most of the time, it is given at home. Your cancer may be causing problems that need to be managed, and hospice focuses on your comfort. You should know that while getting hospice care often means the end of treatments such as chemo and radiation, it doesn't mean you can't have treatment for the problems caused by your cancer or other health conditions. In hospice the focus of your care is on living life as fully as possible and feeling as well as you can at this difficult time. You can learn more about hospice in our document called *Hospice Care*.

Staying hopeful is important, too. Your hope for a cure may not be as bright, but there is still hope for good times with family and friends -- times that are filled with happiness and meaning. Pausing at this time in your cancer treatment gives you a chance to refocus on the most important things in your life. Now is the time to do some things you've always wanted to do and to stop doing the things you no longer want to do. Though the cancer may be beyond your control, there are still choices you can make.

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 been applied to developing lab tests that can help identify these 2 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 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 that 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 value of using combination chemotherapy for high-risk metastatic GTD, such as the EMA-CO and EMA-EP regimens. The excellent results with these regimens have made them treatments of choice in many institutions.

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

For tumors that are resistant to standard chemotherapy doses, doctors are studying the use of high-dose chemotherapy 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 ways to give the usual chemotherapy drugs with new schedules that might be more effective, cause less severe side effects, and/or be more convenient for patients.

Additional resources for gestational trophoblastic disease

In addition to the American Cancer Society, other sources of patient information and support include*:

National organizations and Web sites*

Foundation for Women's Cancer (formerly Gynecologic Cancer Foundation)

Toll-free number: 1-800-444-4441 or 1-312-644-6610

Web site: www.foundationforwomenscancer.org

National Cancer Institute

Toll-free number: 1-800-422-6237 (1-800-4-CANCER)

Web site: www.cancer.gov

**Inclusion on this list does not imply endorsement by the American Cancer Society.*

No matter who you are, we can help. Contact us anytime, day or night, for information and support. Call us at **1-800-227-2345** or visit www.cancer.org.

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Last Medical Review: 4/14/2011

Last Revised: 1/26/2012

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