

Cancer Association of South Africa (CANSA)



Fact Sheet on Gestational Trophoblastic Disease

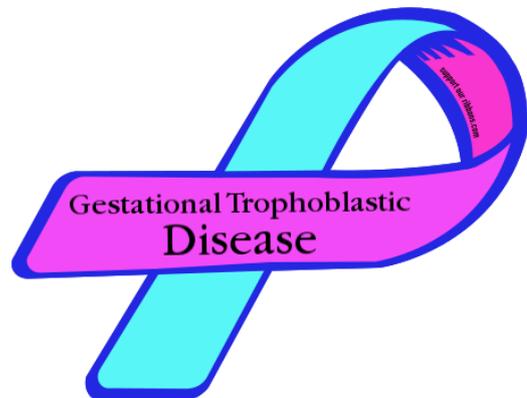
Introduction

Cancer is a term for diseases in which abnormal cells divide without control and can invade nearby tissues. Cancer cells can also spread to other parts of the body through the blood and lymph systems. There are several main types of cancer. Carcinoma is a cancer that begins in the skin or in tissues that line or cover internal organs. Sarcoma is a cancer that begins in bone, cartilage, fat, muscle, blood vessels, or other connective or supportive tissue. Leukaemia is a cancer that starts in blood-forming tissue, such as the bone marrow, and causes large numbers of abnormal blood cells to be produced and enter the blood. Lymphoma and multiple myeloma are cancers that begin in the cells of the immune system. Central nervous system cancers are cancers that begin in the tissues of the brain and spinal cord. Cancer is also referred to 'malignancy'.

[Picture Credit: Gestational Trophoblastic Disease]

Gestational Trophoblastic Disease (GTD)

Gestational Trophoblastic Disease (GTD) is a group of rare tumours that involve abnormal growth of cells inside a woman's uterus. The tumours do not develop from cells of the uterus like endometrial cancer (cancer of the lining of the uterus). Instead, these tumours develop from cells that surround an egg after it is fertilised. This tissue is made of trophoblast cells, which connect the fertilised egg to the wall of the uterus and form the placenta. Trophoblast cells are cells forming the outer layer of a blastocyst, which provide nutrients to an embryo and develop into a large part of the placenta. The placenta is the organ that develops during pregnancy to feed the foetus. The term 'gestational' refers to pregnancy (Medline Plus Medical Encyclopedia; American Cancer Society; National Cancer Institute; Wikipedia).



Types of Gestational Trophoblastic Disease (GTD)

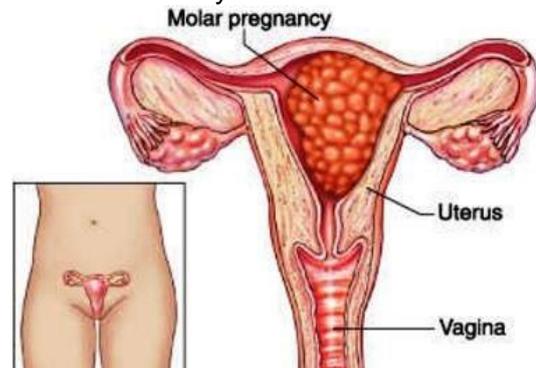
There are three main types of Gestational Trophoblastic Disease (GTD).

Hydatidiform Mole - a hydatidiform mole (also called a "molar pregnancy") is a form of GTD that arises when fertilisation of an egg cell results in an abnormal pregnancy. There are two

types of molar pregnancies, complete and partial. A complete molar pregnancy develops when the fertilised egg cell lacks maternal genes. The pregnancy that results contains no foetal tissue and resembles grape-like cysts that fill the uterine cavity.

[Picture Credit: Molar Pregnancy]

A partial molar pregnancy occurs when more than one sperm fertilises a normal egg resulting in a pregnancy where both the foetus and placenta are abnormal. The term partial is used because the placenta contains both normal tissue and grape-like cysts similar to that seen in complete moles. 80% of molar pregnancies are benign in that they cause no further trouble after they are removed from the uterus. However, in



approximately 20% of complete molar pregnancy and 1-4% of partial moles, the molar tissue either spreads locally within the muscular wall of the uterus (called invasive mole) or spreads more widely to other parts of the body, most commonly the lungs (called metastases), which requires treatment.

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

Placental-Site Trophoblastic Tumour - placental-site GTD is a very rare form of the disease that arises in the uterus at the site where the placenta was attached. These tumours penetrate the muscle layer of the uterus and usually do not spread to other parts of the body. (Foundation for Women's Cancer; National Cancer Institute).

Incidence of Gestational Trophoblastic Disease (GTD) in South Africa

The National Cancer Registry (2011) does not provide any information regarding Gestational Trophoblastic Disease.

Signs and Symptoms of Gestational Trophoblastic Disease (GTD)

It is essential that the woman talks to the physician if any abnormal symptoms occur during pregnancy since GTD might be suspected based on its common pattern of signs and symptoms.

Gestational Trophoblastic Disease does not normally cause symptoms during the early stages since it appears like a normal pregnancy.

Symptoms that could indicate a potential problem include:

- Vaginal bleeding
- Weight loss

- Anaemia which is the low count of blood cells that could cause breathing problems, dizziness, an uneven heartbeat, and fatigue
 - A bigger uterus than expected for the duration of the pregnancy
 - Severe sweating or shakiness
 - Pain in the pelvic area
 - Abdominal swelling
 - A pregnancy wherein the movement of the baby has not occurred or changed at the expected time
 - High blood pressure that may be accompanied with oedematous hands and feet and/or headaches
 - Severe vomiting and nausea
- (Cancer Wall).

Clinicopathologic features of gestational trophoblastic disease		
Gestational trophoblastic disease	Pathologic features	Clinical features
Hydatidiform mole, complete	<ul style="list-style-type: none"> • 46,XX (mainly); 46,XY • Absent foetus/embryo • Diffuse swelling of villi • Diffuse trophoblastic hyperplasia 	15-20% trophoblastic sequelae hCG often >100,000 mIU/mL Medical complications
Hydatidiform mole, partial	<ul style="list-style-type: none"> • Triploid (69, XXY; 69, XYY; 69 XXX) • Abnormal foetus/embryo • Focal swelling of villi • Focal trophoblastic hyperplasia 	<5% trophoblastic sequelae hCG usually <100,000 mIU/mL Rare medical complications
Invasive mole	<ul style="list-style-type: none"> • Myometrial invasion • Swollen villi • Hyperplastic trophoblast 	15% metastatic—lung/vagina Most often diagnosed clinically, rather than pathologically
Choriocarcinoma	<ul style="list-style-type: none"> • Abnormal trophoblastic hyperplasia and anaplasia • Absent villi • Haemorrhage, necrosis 	Vascular spread to distant sites—lung/brain/liver Malignant disease
PSTT	<ul style="list-style-type: none"> • Tumour cells infiltrate myometrium with vascular/lymphatic invasion • Intermediate cells/absent villi • Less haemorrhage and necrosis • Tumour cells stain positive for hPL 	Extremely rare hCG levels less reliable indicator Relatively chemoresistant Mainly surgical treatment

hCG, human chorionic gonadotropin; *hPL*, human placental lactogen; *PSTT*, placental site trophoblastic tumour. (Lurain, 2010).

Causes and Risk Factors of Gestational Trophoblastic Disease (GTD)

In most cases, complete hydatidiform mole usually arises when an ovum without maternal chromosomes is fertilised by one sperm that then duplicates its DNA, resulting in a 46XX androgenetic karyotype, in which all chromosomes are paternally derived. About 10% of complete moles are 46XY, arising from fertilisation by two sperm.

Although nuclear DNA is entirely paternal, mitochondrial DNA remains maternal in origin. Findings from some studies show that patients with recurrent disease can have biparental molar rather than typical androgenetic disease, which might be familial or sporadic. Genetic studies in such families showed that the related genes are at chromosome 19q13.3–13.4, and subsequent analysis noted NLRP7 mutations in this region. The function of the normal protein and the mechanism by which mutations are associated with imprinting abnormalities and gestational trophoblastic disease are unknown. Data show clustering of mutations in the leucine-rich region of NLRP7, suggesting that this region is crucial for normal function.

Some androgenetic diploid complete moles and possibly even triploid partial hydatidiform moles might also carry NLRP7 mutations, but confirmation from large studies is needed. Partial hydatidiform moles are almost always triploid, and they result from fertilisation of a seemingly healthy ovum by two sperm; diploid partial moles probably do not exist, with most reported cases being misdiagnosed complete moles. (Seckl, *et al.*, 2010).

The following factors may raise a woman's risk of developing GTD:

- Age. Being younger than 20 or older than 35 when becoming pregnant brings a higher risk of GTD. The risk increases when the woman is over age 45 at the time of pregnancy.
- Previous molar pregnancy. A previous molar pregnancy may increase the risk of developing another GTD.
- Nutrition/diet. Some studies have linked low levels of carotene and vitamin A in a person's diet with a higher risk of molar pregnancy.
- Blood type. Specific blood types – blood type A or AB – may slightly increase the risk of GTD.
- Family history of molar pregnancy. There have been rare cases of women in the same family having 1 or more molar pregnancies.

The only known way to avoid GTD is to avoid pregnancy. When making such family planning decisions, women should remember that GTD is rare. Women who have had a molar pregnancy in the past, or are worried about GTD for any reason, are encouraged to talk with their doctors about the future risk of GTD. (Cancer.Net).

Diagnosis of Gestational Trophoblastic Disease (GTD)

Initial manifestations of a hydatidiform mole suggest early pregnancy, but the uterus often becomes larger than expected within 10 to 16 week gestation. Commonly, women test positive for pregnancy have vaginal bleeding and severe vomiting, and foetal movement and foetal heart sounds are absent. Passage of grapelike tissue strongly suggests the diagnosis. Complications may include uterine infection, sepsis, haemorrhagic shock, and preeclampsia, which may occur during early pregnancy.

Placental site trophoblastic tumours tend to cause bleeding.

Choriocarcinoma usually manifests with symptoms due to metastases.

Gestational Trophoblastic Disease does not impair fertility or predispose to prenatal or perinatal complications (e.g., congenital malformations, spontaneous abortions).

- Serum β subunit of human chorionic gonadotropin (β -hCG)
- Pelvic ultrasonography

Gestational trophoblastic disease is suspected in women with a positive pregnancy test and any of the following:

- Uterine size much larger than expected for dates
- Symptoms or signs of preeclampsia
- Passage of grapelike tissue
- Suggestive findings (e.g., mass containing multiple cysts, absence of a foetus and amniotic fluid) seen during ultrasonography done to evaluate pregnancy
- Unexplained metastases in women of child-bearing age
- Unexpectedly high levels of β -hCG detected during pregnancy testing
- Unexplained complications of pregnancy

If gestational trophoblastic disease is suspected, testing includes measurement of serum β -hCG and, if not previously done, pelvic ultrasonography. Findings (e.g., very high β -hCG levels, classic ultrasonographic findings) may suggest the diagnosis, but biopsy is required. Invasive mole and choriocarcinoma are suspected if biopsy findings suggest invasive disease or if β -hCG levels remain higher than expected after treatment for hydatidiform mole.

(Ramirez & Gershenson).

Treatment of Gestational Trophoblastic Disease (GTD)

Treatment comprises:

- Tumour removal by suction curettage
- Further evaluation for persistent disease and spread of tumour
- Chemotherapy for persistent disease
- Post treatment contraception for persistent disease

Hydatidiform mole, invasive mole, and placental site trophoblastic tumour are evacuated by suction curettage. Alternatively, if childbearing is not planned, hysterectomy may be done.

After tumour removal, gestational trophoblastic disease is classified clinically to determine whether additional treatment is needed. The clinical classification system does not correspond to the morphologic classification system. Invasive mole and choriocarcinoma are classified clinically as persistent disease. The clinical classification is used because both are treated similarly and because exact histologic diagnosis may require hysterectomy.

(Ramirez & Gershenson).

Medical Disclaimer

This Fact Sheet is intended to provide general information only and, as such, should not be considered as a substitute for advice, medically or otherwise, covering any specific situation. Users should seek appropriate advice before taking or refraining from taking any action in reliance on any information contained in this Fact Sheet. So far as permissible by law, the Cancer Association of South Africa (CANSA) does not accept any liability to any person (or

his/her dependants/estate/heirs) relating to the use of any information contained in this Fact Sheet.

Whilst the Cancer Association of South Africa (CANSA) has taken every precaution in compiling this Fact Sheet, neither it, nor any contributor(s) to this Fact Sheet can be held responsible for any action (or the lack thereof) taken by any person or organisation wherever they shall be based, as a result, direct or otherwise, of information contained in, or accessed through, this Fact Sheet.

Sources and References

American Cancer Society

<http://www.cancer.org/cancer/gestationaltrophoblasticdisease/detailedguide/gestational-trophoblastic-disease-what-is-g-t-d>

Cancer.Net

<http://www.cancer.net/cancer-types/gestational-trophoblastic-disease/risk-factors>

Cancer Wall

https://cancerwall.com/gestational-trophoblastic-disease/#Causes_Pathology

Foundation for Women's Cancers

<http://www.foundationforwomenscancer.org/types-of-gynecologic-cancers/gestational-trophoblastic-disease-gdt/>

Gestational Trophoblastic Disease

<http://www.supportourribbons.com/custom-ribbon-magnet-sticker/108189/Gestational+Trophoblastic++++Disease+>

Lurain, J.R. 2010. Gestational trophoblastic disease I: epidemiology, pathology, clinical presentation and diagnosis of gestational trophoblastic disease, and management of hydatidiform mole. *Am J Obstet Gynecol*, Volume 203(6): 531-539.

Medline Plus Medical Encyclopedia

<https://medlineplus.gov/ency/article/007333.htm>

Molar Pregnancy

<https://cancerwall.com/gestational-trophoblastic-disease/>

National Cancer Institute

<https://www.cancer.gov/types/gestational-trophoblastic>

Ramirez, P.T. & Gershenson, D.M. Gestational Trophoblastic Disease. MSD Manual.

<http://www.msmanuals.com/professional/gynecology-and-obstetrics/gynecologic-tumors/gestational-trophoblastic-disease>.

Seckl, M.J., Sebire, N.J., & Berkowitz, R.S. 2010. Gestational trophoblastic disease. www.thelancet.com. Published online July 28, 2010. DOI:10.1016/S0140-6736(10)60280-2.

Wikipedia

<https://en.wikipedia.org/wiki/Trophoblast>