

# 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 the 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.

**Bruce, S. & Sorosky, J.** 2020. Gestational Trophoblastic Disease. *In*: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan. 2020 Aug 26.

"Gestational trophoblastic disease (GTD) is a group of tumors defined by abnormal trophoblastic proliferation. Trophoblast cells produce human chorionic gonadotropin (hCG). GTD is divided into hydatidiform moles (contain villi) and other trophoblastic neoplasms (lack villi). The non-molar or

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malignant forms of GTD are called gestational trophoblastic neoplasia (GTN). They include the invasive mole, choriocarcinoma, placental site trophoblastic tumor, and epithelioid trophoblastic tumor. These malignancies can occur weeks or years following any pregnancy but occur most commonly after a molar pregnancy.”

### **Incidence of Gestational Trophoblastic Disease (GTD) in South Africa**

The National Cancer Registry (2016) does not provide any information regarding Gestational Trophoblastic Disease.

### **Risk Factors for Gestational Trophoblastic Disease (GTD)**

Risk factors include:

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Two factors have consistently been associated with an increased risk of GTD:

- Maternal age.
- History of hydatidiform mole (HM).

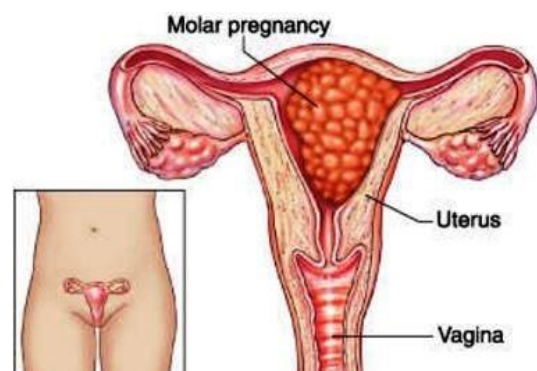
“If a woman has been previously diagnosed with an HM, she carries a 1% risk of HM in subsequent pregnancies. This increases to approximately 25% with more than one prior HM. The risk associated with maternal age is bimodal, with increased risk both for mothers younger than 20 years and older than 35 years (and particularly for mothers >45 years). Relative risks are in the range of 1.1 to 11 for both the younger and older age ranges compared with ages 20 to 35 years. However, a population-based HM registry study suggests that the age-related patterns of the two major types of HM—complete and partial HM—are distinct. However, the rates of partial HM increased for the entire age spectrum, suggesting possible differences in etiology. The association with paternal age is inconsistent. A variety of exposures have been examined, with no clear associations found with tobacco smoking, alcohol consumption, diet, and oral contraceptive use.”

### **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.

[Picture Credit: Molar Pregnancy]



Choriocarcinoma - is a highly malignant (cancerous) form of GTD that spreads rapidly throughout the body and requires vigorous treatment. Choriocarcinoma is less common, arising in only one of every 20 000 to 40 000 pregnancies.

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Placental-Site Trophoblastic Tumour - 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.

### **Signs and Symptoms of Gestational Trophoblastic Disease (GTD)**

It is essential that affected women talk 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

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GTDs contain paternal chromosomes and are placental, rather than maternal, in origin. The most common presenting symptoms are vaginal bleeding and a rapidly enlarging uterus, and GTD should be considered whenever a premenopausal woman presents with these findings. Because the vast majority of GTD types are associated with elevated human chorionic gonadotropin (hCG) levels, an hCG blood level and pelvic ultrasound are the initial steps in the diagnostic evaluation. In addition to vaginal bleeding and uterine enlargement, other presenting symptoms or signs may include the following:

- Pelvic pain or sensation of pressure.
- Anemia.
- Hyperemesis gravidarum.
- Hyperthyroidism (secondary to the homology between the beta-subunits of hCG and thyroid-stimulating hormone (TSH), which causes hCG to have weak TSH-like activity).
- Preeclampsia early in pregnancy.

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

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.

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- 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.

### **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.

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  $\beta$ -hCG detected during pregnancy testing
- Unexplained complications of pregnancy

### **Treatment of Gestational Trophoblastic Disease (GTD)**

Treatment may include:

- 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. (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

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##### Cancer Wall

[https://cancerwall.com/gestational-trophoblastic-disease/#Causes\\_Pathology](https://cancerwall.com/gestational-trophoblastic-disease/#Causes_Pathology)

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

##### Gestational Trophoblastic Disease

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