Introduction

- The term gestational trophoblastic disease describes a group of inter-related disease, including complete and partial molar pregnancy, choriocarcinoma, placental site trophoblastic tumor and invasive mole, which vary in their propensity for local invasion and metastasis.
- Although persistent GTD (now often termed gestational trophoblastic neoplasia) most commonly follows a molar pregnancy, it may also be seen after any type of gestation, including term pregnancy, abortion and ectopic pregnancy.
- Gestational trophoblastic tumor produce human chorionic gonadotrophin (hCG), which is important in the diagnosis, management and follow up of these patients, providing an example of an ideal tumor marker.

Epidemiology

- The WHO classification for GTT divides trophoblast tumours into premalignant partial and complete hydatidiform mole and the malignant diagnosis of invasive mole, choriocarcinoma and PSTT.
- Worldwide, the incidence of GTD reportedly varies between 0.5 and 8.3 cases per 1000 live births. The highest incidence occurs in Asian women and also in Native American Indians. There is also significantly higher incidence in Asian women living in the UK.

Risk Factors

1. Maternal age appears to be the most consistent risk factor associated with molar gestation. Age-specific incidence reports a (J curve) with extremes of reproductive life associated with an increased incidence. Pregnancies below 15 years have a moderately increased risk, whereas those occurring over the age of 50 years are associated with substantially increased.
2. Women who have had previous mole, have an increased risk of further molar pregnancies. Following one mole the risk is less than 2%, but following two molar pregnancies it increase substantially up to one in six; following three moles the risk may be as high as one in two.
3. Occasionally, family clusters have been seen, implicating an underlying genetic disorder in such cases.
4. Nutritional and socioeconomic factors also appear to be risk factors for molar pregnancy in some population. For example, low dietary intake of carotene and animal fat may be associated with an increased incidence of complete mole.

Pathophysiology

- Hydatidiform mole may be complete or partial and histopathological features differ.
- Complete mole is recognized by the presence of characteristic grape like structures, which represent swollen chorionic villi, and the absence of a viable fetus. The chorionic villi are diffusely hydropic and enveloped by hyperplastic and atypical trophoblast. The conceptus is entirely paternally derived, resulting from the fertilization of an empty anucleated oocyte lacking maternal DNA. The chromosome complement is most commonly 46XX, which results from one X chromosome-carrying sperm that duplicate its DNA.
- In contrast, partial mole usually has recognizable embryonic and fetal tissues, with focal hydropic swelling of the chorionic villi and focal trophoblastic hyperplasia. Partial moles are generally triploid, for example 69XXY; they result most often from dispermic fertilization of normal ovum. When the fetus is present it often has the features of triploidy, including growth retardation and multiple congenital malformations.
- The clinical entity of invasive mole occurs when a complete or, less commonly partial mole invades deeply into the myometrium.
Clinical Features

- The clinical presentation of partial mole is most frequently via a failed pregnancy rather than irregular bleeding or by detection on routine ultrasound. Partial mole rarely transforms into malignant disease, and there is an overall risk of 0.5-1% of patients requiring chemotherapy after a partial mole.
- The clinical presentation of complete mole is often by first-trimester bleeding or an abnormal ultrasound. Although now it's rarely seen, however complete mole may present as excessive uterine size, anaemia, hyperemesis, pre-eclampsia, theca lutein cysts and hyperthyroidism specially in under developed countries. Complete mole has an appreciable risk of proceeding to invasive disease, with approximately 15% requiring chemotherapy.

Diagnostic Investigation

- While the ultrasound diagnosis of complete mole is usually reliable, that of partial mole is more difficult. In complete mole a classic pattern is seen, consisting of multiple small sonolucencies, representing the numerous hydropic villi (snow storm). The finding of focal multiple cystic spaces in the placenta is suggestive of partial mole. Fetal part may be seen. In over half of the patient the diagnosis of partial mole is done after evacuation of conceptus been diagnosed as a missed miscarriage.
- Trophoblastic disease is virtually unique in that it produces a specific marker (hCG) which can be measured in urine and or blood and correlate precisely with the amount of disease present. The measurement of hCG allows estimation of tumor bulk, forms an important part of the assessment of the patients disease risk and provide a simple method to follow the response to treatment.

Treatment of Molar Pregnancies

- Suction curettage is the method of choice for evacuation of complete molar pregnancies because of the lack of fetal parts, a suction catheter of up to 12 mm is usually sufficient. Sharp curettage is now not generally recommended because of the possibility of uterine perforation and of increasing the risk of Ashermans syndrome.
- Medical termination of complete mole should be avoided where possible. There is a theoretical concern about the routine use of potent oxytocic agents because of the possibility of forcing trophoblastic tissue into the venous space of the placental bed and disseminating the disease to the lung. Its recommended that when necessary, oxytocic therapy is only commenced once evacuation is complete. If there is significant bleeding prior to or during evacuation, such agent may be used according to clinical judgment. Mifepristone is best avoided.
- Partial mole is also better to be treated by suction evacuation, but when the size of fetal part is large, medical termination can be used.
- Sine persistent trophoblastic disease may develop after any pregnancy; all products of conception, obtained after evacuation should be histologically examined.

Registration & Follow-up

- Post-evacuation, all cases must be registered with trophoblast screening center for hCG surveillance to ensure early detection of post molar GTN. Serum hCG levels are measured fortnightly until normalization, and urine levels analysed monthly after this. The risk of developing GTN is highest in the first 6 months following diagnosis of partial mole and one year after complete mole after spontaneous hCG normalization. Post- HM surveillance for all cases has, therefore, been reduced to the above mentioned time period accordingly.
- Women should avoid becoming pregnant during this period, the only extra monitoring recommended in subsequent pregnancies are hCG checks at 6 and 10 weeks post-delivery. The oral contraceptive pill should not be used until hCG levels have returned to normal (it may act as a growth factors for trophoblastic tissue) but it's safe after that.
Routine second evacuation is not needed, except for:

1. Post-evacuation high hCG.
2. Recurrent of severe bleeding
3. Recurrent molar tissue confirmed on ultrasound.

Persistent Trophoblastic Disease

• In a proportion of patients (10%), trophoblastic disease persists, as evidenced by continuing clinical symptoms particularly vaginal bleeding and/or elevation of hCG levels, excessive uterine size and prominent theca lutein cysts.
• Because of routine registration and good follow-up, the great majority of patients requiring chemotherapy for persistent disease are recognized early.

Indication for Initiating Chemotherapy

1. High, plateau or rising hCG level after evacuation.
2. Persistent vaginal bleeding with raised hCG.
3. hCG > 20000IU/L more than 4 weeks after evacuation.
5. Pulmonary, vulval or vaginal metastases unless the hCG level is falling.
6. Brain, liver, gastrointestinal metastases or lung metastases >2cm on chest radiography.