## Gestational trophoblastic disease :

Gestational trophoblastic diseases (GTD) covers a spectrum of diseases caused by overgrowth of the placenta. This includes hyatidiform mole, choriocarcinoma, invasive mole, and placental site trophoblastic tumour .

- Incidence:0.6–2.3:1000 pregnancies .

50% of cases follow hyatidiform mole, 25% a normal pregnancy, and 25% a miscarriage or ectopic pregnancy .

## Hyatidiform mole :

*A hydatidiform mole (or molar pregnancy) is a rare, premalignant form of Gestational Trophoblastic Disease (GTD) resulting from abnormal fertilization* Can be subdivided into complete and partial mole based on genetic and histological features .

## Complete mole

Consists of diffuse hydropic villi with trophoblastic hyperplasia .This is diploid, derived from sperm duplicating its own chromosome following fertilization of an 'empty' ovum. This is mostly 46XX with no evidence of fetal tissue .

## Partial mole

Consists of hydropic and normal villi (focal hydropic villi).
This is triploid (69XXX, XXY, XYY) with one maternal and two paternal haploid sets. Most cases occur following two sperms fertilizing an ovum, and a fetus may be present

## Comparison between complete and partial mole

Hydatidiform moles are categorized into two types, which differ in their genetic makeup, pathology, and malignant potential:

| Feature | Complete Hydatidiform Mole (CHM) | Partial Hydatidiform Mole (PHM) |
|---|---|---|
| **Genetic Makeup** | **Diploid** (46,XX or 46,XY), entirely **Paternal** origin (androgenetic). Results from an empty ovum fertilized by one sperm that duplicates its chromosomes, or by two sperm. | **Triploid** (69,XXX, 69,XXY, or 69,XYY), with **Two Paternal** and **One Maternal** set of chromosomes. Results from a normal ovum fertilized by two sperm. |
| **Fetus/Embryo** | **Absent** or only minimal embryonic tissue. | Usually **Present** but non-viable and growth-restricted. |
| **Placental Villi** | Diffuse, marked hydropic swelling ("bunch of grapes" or "snowstorm" appearance on ultrasound), and diffuse trophoblast proliferation. | Focal hydropic swelling and focal trophoblast proliferation. |
| **Malignant Risk** | **Higher** (15-20% risk of progression to Gestational Trophoblastic Neoplasia (GTN)). | **Lower** (1-5% risk of progression to GTN). |
| **hCG Levels** | Typically **Very High** (often >100,000 mIU/mL). | Usually **Lower** than CHM, often resembling spontaneous abortion. |

## *Risk factors for hydatidiform mole :*

- Age: extremes of reproductive life (>40yrs and <15yrs of age).
- Ethnicity: higher in east Asia, particularly Korea and Japan .
- Previous molar pregnancy: x10 higher risk of developing future molar pregnancy.
- Nutritional and socioeconomic factors.

## *Diagnosis*

### *Symptoms and signs :*

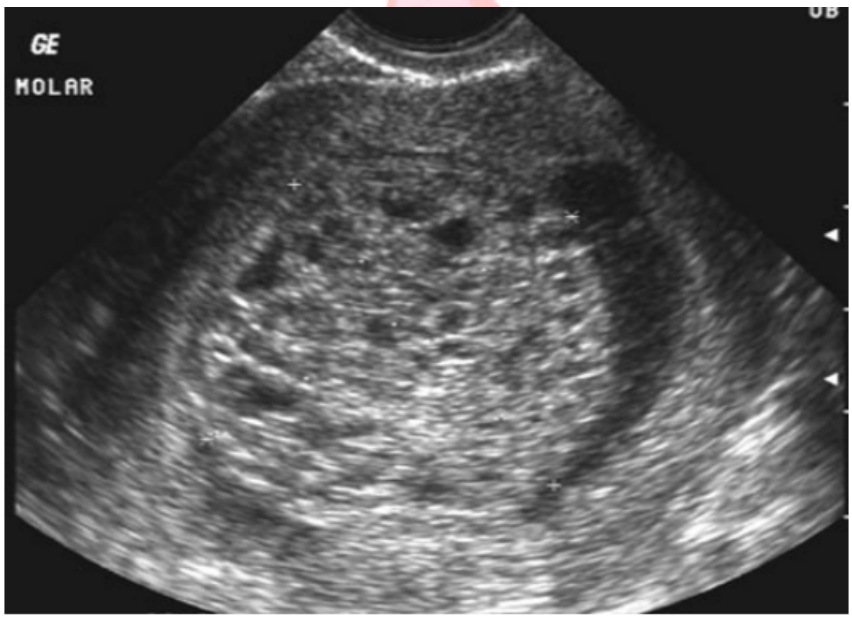
- Irregular first-trimester vaginal bleeding (>90%).
- Uterus large for dates .

- Pain from large theca lutein cysts (20%) resulting from ovarian hyperstimulation by high hCG levels .
- Vaginal passage of vesicles containing products of conception (10%).
- Exaggerated pregnancy symptoms :
    - hyperemesis (10% )
    - hyperthyroidism (5% ).
    - early pre-eclampsia (5%).
    - ***Serum hCG*** is excessively high with complete moles, but levels may be within the normal range for partial moles .Extremely high levels (>100,000 mIU/mL) are highly suggestive of a CHM.

***USS findings*** :

1. Complete mole‘ : Snowstorm’ appearance of mixed echogenecity, representing hydropic villi and intrauterine haemorrhage, Large theca lutein cysts .

2. Partial mole :Fetus may be viable, with signs of early growth restriction or structural abnormalities.



**Definitive Diagnosis: Histopathological examination** of the evacuated tissue is required to confirm the diagnosis and classify the mole (complete vs. partial)

**Management**

• ***Complete mole***: surgical evacuation(suction curritage) is advisable and should be performed by an experienced surgeon as risks of uterine perforation and haemorrhage are significant.

Oxytocin may be required to reduce the risk of haemorrhage, but its use is associated with a theoretical risk of tissue dissemination leading to metastatic disease to the lungs or brain and should be avoided until the uterus is evacuated if possible .

• ***Partial mole***: surgical evacuation is preferable, unless the size of fetal parts necessitates medical evacuation .

Histological examination of products of conception is essential to confirm the diagnosis

# Post-Evacuation Surveillance ( follow up )

- All women with a histologically confirmed HM must be registered with a specialized **Gestational Trophoblastic Disease (GTD) Center** for follow-up and central monitoring of hCG levels.
- **β-hCG Monitoring:** Serial β-hCG levels are monitored to detect the development of post-molar GTN.
    - **Complete Mole (CHM):**
        - If hCG returns to normal within 56 days of evacuation, monitoring continues for **6 months** from the date of evacuation.
        - If hCG takes longer than 56 days to normalize, monitoring continues for **6 months** from the date of the first normal hCG level.
    - **Partial Mole (PHM):**
        - Follow-up is concluded once the hCG has returned to normal on **two consecutive samples, at least 4 weeks apart**.

- **Contraception:** Contraception is strictly advised throughout the entire monitoring period because a new pregnancy would produce hCG, obscuring the surveillance of the molar tissue regression.

## Diagnosis of Post-Molar Gestational Trophoblastic Neoplasia (GTN)

## (Indications of chemotherapy)

GTN is diagnosed if the β-hCG follow-up criteria are met:

1. **Plateau:** Four values of β-hCG over a ≥3-week period, with a change of ≤10%. (e.g., days 1, 7, 14, and 21).
2. **Rise:** A ≥10% increase in β-hCG over three values, sustained over a ≥2-week period. (e.g., days 1, 7, and 14).
3. **Persistence:** Persistent detectable β-hCG for ≥6 months after evacuation.
4. **Histological Diagnosis:** Any confirmed histology of choriocarcinoma.

### *Indications of hysterectomy in the management of GTD:*

*1.*Choice (older patient ,localized disease ,family complete).

2.Excessive uterine bleeding (before or during treatment).

3.Chemoresistant (localized) uterine tumour.

4.Placental site trophoblastic tumour.

## *Prognosis*

With effective registration and treatment programed, cure rate is high (98-100

Women should be advised not to conceive until hCG level has been normal for 6 months .

HCG level should be checked 6 and 10 weeks after each subsequent pregnancy .

## *chorio carcinoma*

This is a highly malignant tumour consisting of syncytio- and cytotrophoblast with myometrial invasion. Local spread and vascular metastases to the lung are common, also metastases to the pelvic organs,liver and brain. 50% of cases are preceded by hyatidiform mole.

## Placental site trophoblastic tumour

These tumors have slow growth rate & can present many years after term delivery ,non-molar miscarriage or complete mole.

The usual presentation is with local disease leading to vaginal bleeding or amenorrhea , but they may also metastasize particularly to the lung .

Surgery alone is the treatment of choice for localized disease ,chemotherapy is needed for metastatic tumour.

## *Invasive mole*

Excessive trophoblastic over growth &extensive penetration by the trophoblastic cells including the villi .

Invasive mole penetrate in to the myometrium & sometimes the peritoneum , parametrium &vaginal vault but lack the tendency to widespread metastasis typical of choriocarcinoma

GYNECOLOGY