Early pregnancy bleeding:

1. Abortion
2. Ectopic pregnancy
4. Other local and systemic
GTD (gestational trophoblastic disease)

It is a spectrum of diseases arises from abnormal fertilization event leading to an abnormal pregnancy
CLASSIFICATION:

1- Benign hydatidiform mole which further subdivided into partial and complete mole.
2- Invasive mole (chorioadenoma destruens) which can metastasize.
3- Choriocarcinoma (frankly malignant).
4- Placental site trophoblastic tumour (PSTT).
The majority of the patients follow a benign course and their disease remitting spontaneously.
The disease is characterized by the sensitive tumour marker (β-hCG) which is secreted by the tumour cells and allows accurate diagnosis and follow up of the disease.
# Risk factors for gestational trophoblastic disease (GTD)

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>↑ &lt;16 years, ↑↑↑ &gt;45 years</td>
</tr>
<tr>
<td>Geographic</td>
<td>↑ Asia</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>↑ American Indians, ↑ Asians</td>
</tr>
<tr>
<td>Previous GTD</td>
<td>↑ one episode, ↑↑↑↑ two or more episodes</td>
</tr>
<tr>
<td>Dietary</td>
<td>↑ carotene deficiency</td>
</tr>
<tr>
<td>Genetic</td>
<td>Rare family clusters and repetitive moles</td>
</tr>
</tbody>
</table>
Etiology and epidemiology

- Blood group A women if married to a man with blood group O (there is 10 folds higher risk of choriocarcinoma), and if the woman of bl.gp AB it carries a relatively worse prognosis.
- Diet may play a role: low dietary intake of carotene, low protein, animal fat and folic acid intake predispose to GTN.
- Low estrogen status?
Genetics of H. mole

**complete**

**partial**
## Pathological features of hydatidiform mole

<table>
<thead>
<tr>
<th></th>
<th>Complete</th>
<th>Partial</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Macroscopic</strong></td>
<td>Often recognizable, with characteristic grape-like structures</td>
<td>Can resemble hydropic abortion; may have recognizable fetal tissues</td>
</tr>
<tr>
<td><strong>Microscopic</strong></td>
<td>Diffusely hydropic villi</td>
<td>Focal hydropic swelling of villi</td>
</tr>
<tr>
<td></td>
<td>Atypical and hyperplastic trophoblast</td>
<td>Focal trophoblastic hyperplasia</td>
</tr>
<tr>
<td></td>
<td>Usually diagnosable from uterine products</td>
<td>Often misdiagnosed as hydropic abortion or complete mole</td>
</tr>
<tr>
<td><strong>Karyotype</strong></td>
<td>Usually diploid (paternally derived)</td>
<td>Usually triploid (maternal contribution)</td>
</tr>
</tbody>
</table>
Clinical features of hydatidiform mole

<table>
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<tr>
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<th>Complete</th>
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</thead>
<tbody>
<tr>
<td><strong>Features</strong></td>
<td>May be severe and/or accompanied by paraneoplastic sequelae</td>
<td>Often mild, resembling spontaneous miscarriage</td>
</tr>
<tr>
<td><strong>Diagnosis</strong></td>
<td>Usually suspected on clinical or ultrasound scan findings</td>
<td>Often unsuspected and retrospectively diagnosed after uterine evacuation</td>
</tr>
<tr>
<td><strong>Persistent trophoblastic disease</strong></td>
<td>In up to 20% of cases</td>
<td>In &lt;0.5% of cases</td>
</tr>
</tbody>
</table>
Diagnosis of H.Mole:

1) Symptoms and signs:
- Abnormal vaginal bleeding in the 1st and the beginning of the 2nd trimesters in > 90% of the patients.
- Anemia: dilutional or may be due to hemorrhage.
- Large for date uterus with soft (doughy) in consistency
- No fetal parts with negative fetal heart tones
**Symptoms and signs:**

- **Pre eclampsia** early before 20\textsuperscript{th} week of gestation.

- **Hyperemesis** in 1/3 of the patients.

- **Ovarian cysts:** multiple theca leutin cyst due to high hCG.

- **Hyperthyroidism:** it is mild or subclinical

- **Expulsion of vesicles vaginally**
2) **Investigations**

1. **(β-hCG):**
   It is higher than normal pregnancy values and can be detected in the serum or urine of all patients (its level correlate closely with the number of viable tumour cells). (>200 000 U/L)

2. **U/S it is the diagnostic method of choice (snow storm appearance)**

3. **CXR to show metastatic disease**
**Treatment:**

- Evacuation of the uterus preceded by **B hCG level**, complete blood count, renal function test, liver function test, coagulation profile, ECG and chest X-ray.
- Blood loss is moderate **SO** (prepare blood)
The **GOLD standard** for termination of pregnancy is by **suction curettage** which is safe, rapid and effective method. When the conceptus nearly totally evacuated we start the oxytocin to induce uterine contractions and avoid perforation.
Treatment: (continued)

* **Hysterectomy** is done in certain situations:
  1. the woman >35 years completed family
  2. high risk of persistent GTN may be lowered by hysterectomy from 20% to 3.5% only.

Medical induction is **not** recommended because fear of showering emboli through the blood stream.

**Hysterotomy** is not recommended.

All Rh negative women should receive anti-D immunoglobulin
Complications

1. perforation
2. hemorrhage
3. Deportation of trophoblastic tissues to the lungs is frequent which may regress spontaneously but sometime postevacuation acute pulmonary insufficiency may result leading to dyspnoea, and cyanosis 4-6 hours after evacuation.
4. Pulmonary edema from high output heart failure, pre eclampsia, anemia, and hyperthyroidism.
5. Sepsis.
Surveillance following molar pregnancy

- Following evacuation (β-hCG) titers should be estimated serially because of the 20-30% risk of persistent disease.
- The determination should be started 48 hours after the evacuation and weekly until it becomes undetectable (< 5mIU).
- Effective contraceptive measures is essential
The titer remission should occur spontaneously by 12 - 14 weeks then the patient should be followed up monthly for 6-12 months before the patient is released from close medical supervision.
- Gynecological examination 1 week after evacuation for uterine size, adnexial mass, vulval and vaginal deposits (metastasis).

- 1 year after negative titers pregnancy is allowed
GTD

2nd PART
Prophylactic chemotherapy in molar pregnancy for those with high risk of persistent disease and risk of GTN

- High initial hCG > 100,000 mIU/ml
- Age > 40
- Large for date uterus
- Big ovarian cysts
- Presence of embolizations
- Poor compliance to follow up
- Unavailability of health services and hormonal follow up
Invasive mole:

1. It occurs in 20% of patients with H.mole,
2. pathologically it is the same as hydatidiform mole but penetrates deeply into the myometrium or the adjacent structures
3. C/F: profuse hge, lower abd pain, hematuria, rectal bleeding, intra peritoneal bleeding, emboli to the lung
4. It may regress spontaneously
Malignant GTN

The malignant GTN can be classified into:
- the non-metastatic: invasive mole
- and the metastatic: choriocarcinoma and the PSTT
Malignant disease can be suspected when

1- Plateauing or rising B-hCG value over a period of 3 consecutive weeks.
2- A rise of B-hCG over a period of 2 weeks.
3- Persistence of a detectable B-hCG after 6 months of evacuation
4- Appearance of metastasis during follow up
The frankly malignant disease is further subdivided into

1. Good prognosis group (low risk group)
2. And the poor prognosis group (high risk group).
Choriocarcinoma

The *anteecedent pregnancy* is
1- H. mole in 50%,
2- normal pregnancy in 25%
3- abortion or ectopic pregnancy in 25%.
Clinical Presentation

1- Vaginal bleeding is the most common symptom.

2- Lower abdominal pain because of invasion of the surrounding structures.

3- Abdominal AND/OR vaginal mass.

4- Amenorrhea may precede bleeding caused by the high B-hCG produced by the tumor mass.
Clinical Presentation

5- Pulmonary metastasis may cause dyspnoea and haemoptysis it may be misdiagnosed as pulmonary T.B and it can be diagnosed by CXR.

6- Neurological abnormality may indicate brain invasion.

7- High index of suspicion is required to diagnose it especially if it follows normal pregnancy or abortion.

8- it invade the myometrium and metastasizes to the lungs, brain, liver, and other organs.
On examination:

- Most of the patients have enlarged uterus as well as ovarian enlargement by theca lutein cysts.
- Sites of metastasis should be looked for especially in the vagina cervix and the adnexia.
Investigations:

1- B-hCG level in the serum or the urine. it is very high > 100 000 IU / L
2- U/S for the pelvis, liver, kidneys…
3- CXR.
4- CT for the brain, liver, and pelvic organs metastasis.
5- MRI for the brain metastasis.
6- Lumber puncture: CSF to measure the B-hCG level in the CSF it should be greater than 1:40 (the ratio of the level in the CSF to that in the serum)
7- CBP, LFT, RFT, and the coagulation study.
Confirmation of the diagnosis is made by Histopathology of curettage products but curettage carry high risk of uterine perforation and dissemination of the disease, so it can be diagnosed basically depending on the clinical suspicion and high B-hCG levels.
Classification of the disease according to the prognostic factors:

1- Good prognosis metastatic disease:

2- Poor prognosis metastatic disease:
1- Good prognosis metastatic disease (criteria)

a- short duration (<4 months) between the antecedent pregnancy and chemotherapy.
b- Serum B-hCG <40 000 mIU/ml
c- No metastasis to the brain and the liver.
d- No prior chemotherapy.
2- Poor prognosis metastatic disease (criteria)

a- Long duration from the antecedent pregnancy (>4 months) to chemotherapy.
b- Serum B- hCG >40 000 mIU /ml.
c- Metastasis to the brain.
d- Unsuccessful prior chemotherapy.
e- If the disease is following term pregnancy.
Treatment of GTD

A) For the non metastatic GTD (CM & invasive mole) and for the low risk metastatic disease:

1- Single agent chemotherapy: either methotrexate (MTX) or actinomycin –D (dactinomycin).

2- Combine chemotherapy with hysterectomy in female who not wish to preserve reproductive function and her disease is confined to the uterus.
<table>
<thead>
<tr>
<th>Day</th>
<th>Treatment</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Methotrexate 50 mg im at noon</td>
</tr>
<tr>
<td>2</td>
<td>Folinic acid 30 mg po at 6 p.m.</td>
</tr>
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Important notes:

- When the patient is not responding to this chemotherapeutic agent, this will indicate switching to new agent or combination chemotherapy
- Effective contraception should continue for 1 yr after remission
follow up program:

- B-hCG weekly until 3 consecutive negative titer, then monthly for a year, then 2 monthly for another year, then 6 monthly for life,
- the follow up need Pelvic examination and CXR together with the hCG titer
Poor prognosis (high risk) metastatic disease group:

- Should be treated by combined chemotherapy (multiple agents)
- Usually respond poorly (<40% response rate) to single agent chemotherapy.
- Prior unsuccessful chemotherapy is one of the worst prognostic factors because of considerable toxicity and depleting bone marrow reserves.
IF RESISTANCE OCCURS TO COMBINED CHEMO then

Adjuvant surgery: hysterectomy, thoracotomy or craniotomy for chemotherapy resistant malignant masses.
Prognosis of GTD:

1. For H. Mole the prognosis is excellent,
2. For the good prognostic group the cure rate is 75-85%,
3. the poor prognosis group if there is liver metastases the survival from (0-60%).
4. The survival is <20% if previous failed chemotherapy
Subsequent pregnancy

- There are no extra complication during pregnancy but require good follow up by U/S and B-hCG levels because of the 2% risk of recurrence after 1 mole and 20% after 2 moles and 50% after 3 moles.

- After delivery placenta should be sent for histopathological study, and B-hCG level must be measured 6 weeks postpartum.