GTD : Gestational Trophoblastic disease

- Group of disorders spanning the conditions of complete and partial molar pregnancies through to the malignant conditions of invasive mole, choriocarcinoma and the very rare placental site trophoblastic tumour (PSTT).
- There are reports of neoplastic transformation of atypical placental site nodules to placental site trophoblastic tumour.

– Here all the symp. r exagerated cuz very ↑ B-HCG, Prey but Here is a Baby

Types

- Molar Pregnancies:
  - Complete Moles (CM)
  - Partial Moles (PM)

Based on genetic histopathological features

— parents will ask is there there something wrong in our sides? ANS: No

*very aggressive

Complete Moles (CM)

- Complete moles; diploid , androgenic in origin, with no evidence of fetal tissue.
  - ↳ paternal genetic make up only
- 75-80% of complete moles; consequence of duplication of a single sperm following fertilisation of an 'empty' ovum.
- 20-25% can arise after dispermic fertilisation of an 'empty' ovum.

Partial Moles (PM)

- 90% of partial moles; triple in origin, with two sets of paternal haploid genes and one set of maternal haploid genes
- In almost all cases, dispermic fertilisation of an ovum (Normal, But fertilized by 2 sperms)
- 10% represent tetraploid or mosaic conceptions
- There is usually evidence of fetus or fetal red blood cells (2 genetic make up → Paternal, → Maternal)

Moles

- A rare event; in the UK, incidence of 1/714 live births
- Women from Asia having a higher incidence than non-Asian
- Under represent the incidence of the disease; problems with reporting, particularly in regard to partial moles
- GTN may follow a molar pregnancy, non-molar pregnancy or a live birth
- The incidence after a live birth is estimated at 1/50 000
- In the UK; effective registration and treatment programme
- The programme has achieved impressive results, with high cure (98-100%) and low (5-8%) chemotherapy rates

↳ eg: she birthed normally but still symp? send for B-HCG or preg test after 6 weeks

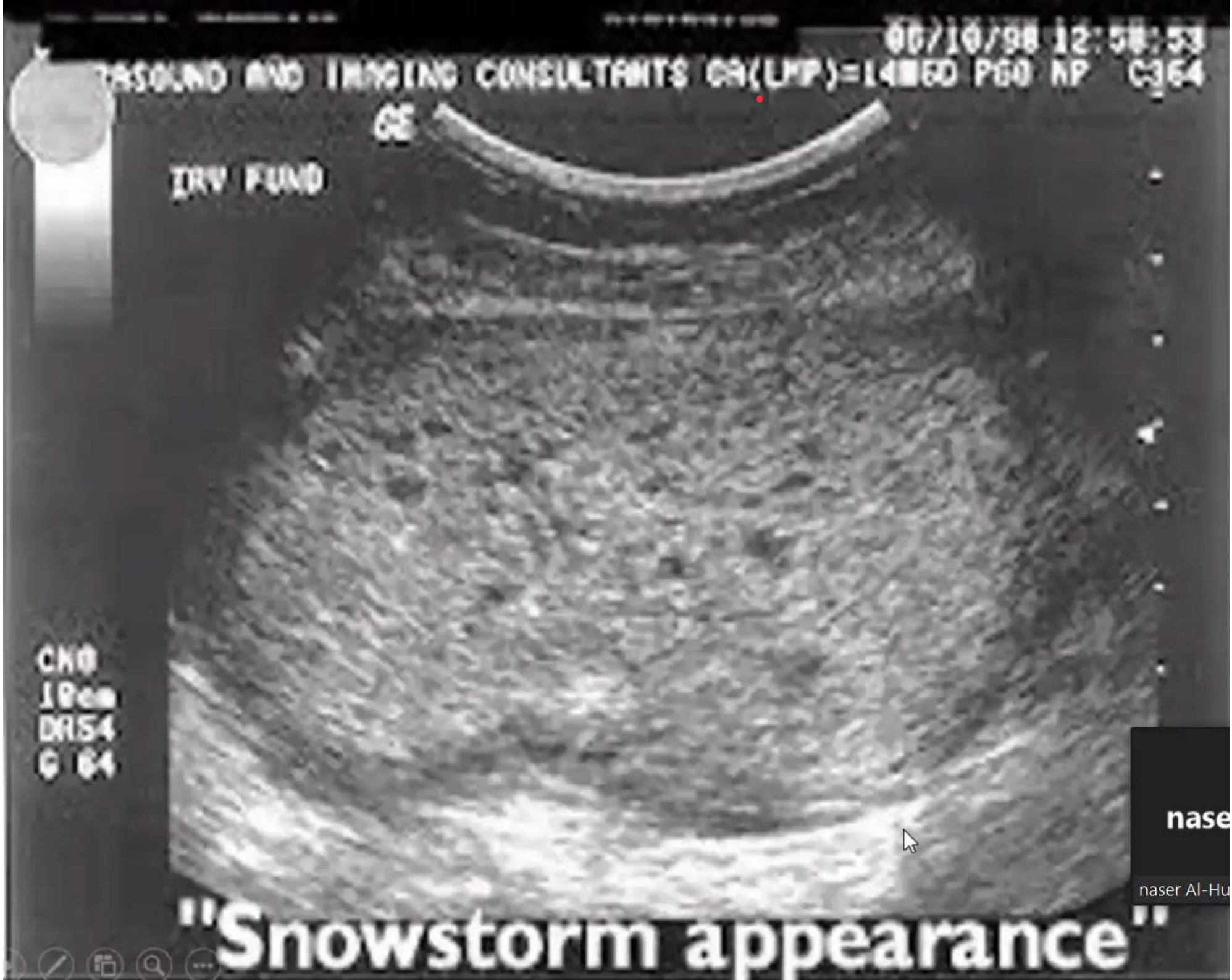
* Many Undiagnosed (cuz most spont. resolved)

Presentation

- **The classic features; irregular vaginal bleeding, hyperemesis, excessive uterine enlargement and early failed pregnancy.**
- **Clinicians should check a urine pregnancy test in women presenting with such symptoms.**
- Rarely; include hyperthyroidism, early onset pre-eclampsia or abdominal distension due to theca lutein cysts.
- Very rarely, women can present with acute respiratory failure or neurological symptoms such as seizures; these are likely to be due to metastatic disease

Diagnosis

- **Ultrasound examination is helpful .snowstorm appearance**
- **The definitive diagnosis , histological examination of the products of conception**
- Ultrasound in early pregnancy ; the earlier diagnosis
- The majority of histologically proven complete moles are associated with an ultrasound diagnosis of delayed miscarriage or anembryonic pregnancy.
- In one study, the accuracy of pre-evacuation diagnosis of molar pregnancy increased with increasing gestational age, 35–40 % before 14 weeks increasing to 60% after 14 weeks.
- A further study ; 56% detection rate for ultrasound examination.
- The ultrasound diagnosis of a partial molar pregnancy is more complex; the finding of multiple soft markers, including both cystic spaces in the placenta and a ratio of transverse to anterioposterior dimension of the gestation sac of greater than 1.5, is required for the reliable diagnosis of a partial molar pregnancy.
- Estimation of hCG levels may be of value in diagnosing molar pregnancies: hCG levels greater than two multiples of the median may help.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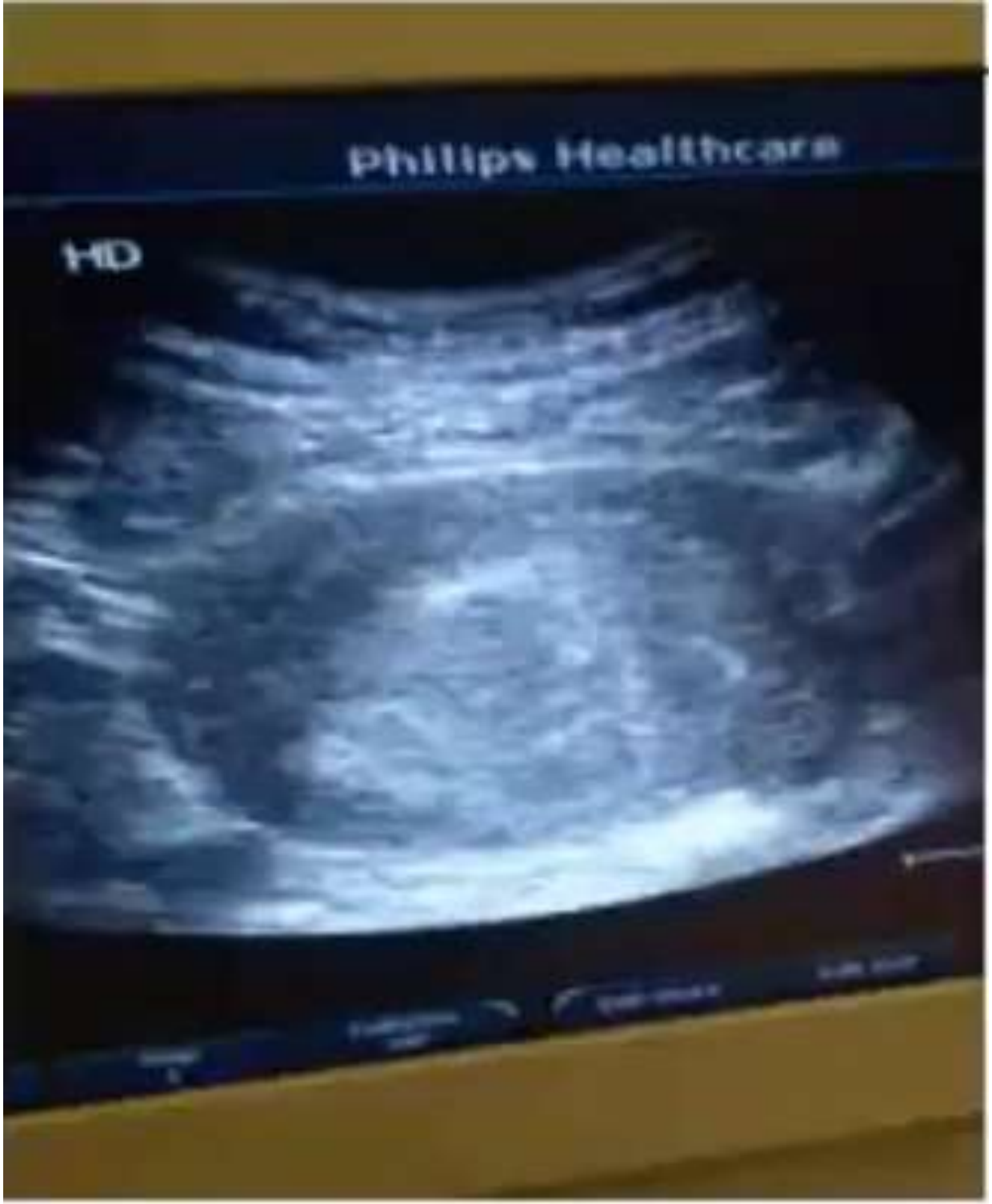
Philips Healthcare
HD

curable +↓ compli

Tx (elective)

Surgical evacuation

→ D&C
here we mechanically dilate cervix

1. Suction curettage ; complete molar pregnancies.
2. Suction curettage : partial molar pregnancies except when the size of the fetal parts deters the use of suction curettage and then medical evacuation can be used.
3. A urinary pregnancy test should be performed 3 weeks after medical management of failed pregnancy if products of conception are not sent for histological examination.
4. Anti-D prophylaxis is required following evacuation of a molar pregnancy.
   - esp. partial

Normally only evacuate
+ β-HCG
CBC
Blood G
LFT
KFT
(Pt, PTA)
→ imp (2)
+ CXR (ex choriocarci to lung)
+ check

- Evacuation of complete molar pregnancies; **oxytocics** should be avoided at present since it increase the sensitivity of the uterus to prostaglandins
- Because of poor vascularisation of chorionic villi and absence of the anti-D antigen in complete moles, anti-D prophylaxis is not required
- Confirmation of the diagnosis of complete molar pregnancy may not be occur for some time after evacuation and so administration of anti-D could be delayed when required, within an appropriate timeframe

- **Preparation of the cervix immediately prior to evacuation is safe.** In a case–control study of 219 patients there was no evidence that ripening of the cervix prior to uterine evacuation was linked to a higher risk for needing chemotherapy. However, the study did show a link with increasing uterine size and the subsequent need for chemotherapy.
- Prolonged cervical preparation, particularly with prostaglandins, should be avoided where possible to reduce the risk of embolisation of trophoblastic cells

- Excessive vaginal bleeding; senior surgeon directly supervising surgical evacuation is advised.
- The use of oxytocic infusion prior to completion of the evacuation is not recommended.
- If the woman is experiencing significant haemorrhage prior to evacuation, surgical evacuation should be expedited and the need for oxytocin infusion weighed up against the risk of tumour embolisation

- **The histological assessment of material obtained from the medical or surgical management of all failed pregnancies is recommended to exclude trophoblastic neoplasia**
- Ploidy status and immuno-histochemistry staining for P57 may help in distinguishing partial from complete moles

- **There is no need to routinely send products of conception for histological examination following therapeutic termination of pregnancy, provided that fetal parts have been identified on prior ultrasound examination**
- The risk of GTN developing after confirmed therapeutic termination is estimated to be 1/20 000.

Follow up B-hCG

Urine or blood test or both every 2 weeks (once normal), a sample taken 4 weeks later.

Contraception for 6-12 months of documented remission. if partial → 6 months; if complete → 12 months

Recurrence in subsequent pregnancies is increased by 10 folds

(so check)

Persisting gynaecological symptoms after an evacuation for molar pregnancy

- Consultation with the relevant trophoblastic screening centre is recommended prior to second evacuation.
- There is no clinical indication for the routine use of second uterine evacuation in the management of molar pregnancies.
- If symptoms are persistent, evaluation of the patient with hCG estimation and ultrasound examination is advised.
- Several case series have found that there may be a role for second evacuation in selected cases when the hCG is less than 5000 units/litre

but

5k

Persistent GTN after a non-molar pregnancy

- **Any woman who develops persistent vaginal bleeding after a pregnancy event is at risk of having GTN.**
- A urine pregnancy test should be performed in all cases of persistent or irregular vaginal bleeding after a pregnancy event.
- Symptoms from metastatic disease, such as dyspnoea or abnormal neurology, can occur very rarely.
- Vaginal bleeding is the most common presenting symptom of GTN diagnosed after miscarriage, therapeutic termination of pregnancy or postpartum.
- The prognosis for women with GTN after non-molar pregnancies may be worse: delay in diagnosis or advanced disease, such as liver or CNS disease, at presentation

Twin pregnancy of a fetus and coexistent molar pregnancy

- Normal pregnancy with a coexisting complete mole; approximately a 25% chance of achieving a live birth.
  early fetal loss 40%.
  premature delivery (36%).
- The incidence of pre-eclampsia is variable, with rates as high as 20% reported. However, in the large UK series, the incidence was only 4% and there were no maternal deaths.
- In the same UK series, there was no increase in the of developing GTN after such a twin pregnancy and outcome after chemotherapy was unaffected

Registration of patients

- Complete hydatidiform mole
- Partial hydatidiform mole
- Twin pregnancy with complete or partial hydatidiform mole
- Limited macroscopic or microscopic molar change suggesting possible partial or early complete molar change
- Choriocarcinoma
- Placental-site trophoblastic tumour
- Atypical placental site nodules: designated by nuclear atypia of trophoblast, areas of necrosis, calcification and increased proliferation (as demonstrated by Ki67 immuno-reactivity) within a placental site nodule

Registration of patients

- After registration, follow-up consists of serial estimation of hCG levels, either in blood or urine specimens
- In the UK, there exists an effective registration and treatment programme. The programme has achieved impressive results, with high cure (98–100%) and low (5–8%) chemotherapy rates.
- Registration forms can be obtained from the listed screening centres or registration can be made online at

  http://www.hmole-chorio.org.uk.

Optimum follow-up following a diagnosis of GTD

- If hCG has reverted to normal within 56 days of the pregnancy event then follow up will be for 6 months from the date of uterine evacuation.
- If hCG has not reverted to normal within 56 days of the pregnancy event then follow-up will be for 6 months from normalisation of the hCG level

- All women should notify the screening centre at the end of any future pregnancy, whatever the outcome of the pregnancy. hCG levels are measured 6-8 weeks after the end of the pregnancy to exclude disease recurrence

Optimum treatment

- The need for chemotherapy following a complete mole is 15% and 0.5 % after a partial mole. The development of postpartum GTN requiring chemotherapy occurs at a rate of 1/50 000 births
- Women are assessed before chemotherapy using the FIGO 2000 scoring system . Women with scores ≤ 6 are at low risk and are treated with single-agent intramuscular methotrexate alternating daily with folinic acid for 1 week followed by 6 rest days. Women with scores ≥ 7 are at high risk and are treated with intravenous multi-agent chemotherapy, which includes combinations of methotrexate, dactinomycin, etoposide, cyclophosphamide and vincristine.
- Treatment is continued, in all cases, until the hCG level has returned to normal and then for a further 6 consecutive weeks.
- The cure rate for women with a score ≤ 6 is almost 100%; the rate for women with a score ≥ 7 is 95%.
- Placental site trophoblastic tumour is now recognised as a variant of gestational trophoblastic neoplasia. It may be treated with surgery because it is less sensitive to chemotherapy

(حفظ)

FIGO Scoring system

Age

Antecedent pregnancy

Interval months from end of index pregnancy to treatment

Pre-treatment serum hCG (iu/l) → Higher = worse

Largest tumour size, including uterus (cm)

Site of metastases

Number of metastases

Previous failed chemotherapy

Long-term follow up

- **Women who undergo chemotherapy are advised not to conceive for 1 year after completion of treatment**
- The risk of a further molar pregnancy is low (1/80): more than 98% of women who become pregnant following a molar pregnancy will not have a further molar pregnancy nor are they at increased risk of obstetric complications.
- If a further molar pregnancy does occur, in 68–80% of cases it will be of the same histological type

(don't mention it to Pt)

Long term outcome

- **Women who receive chemotherapy for GTN are likely to have an earlier menopause.** single-agent chemotherapy is advanced by 1 year and multi-agent chemotherapy by 3 years
- **Women with high-risk GTN who require multi-agent chemotherapy which includes etoposide should be advised that they may be at increased risk of developing secondary cancers** a 16.6 relative risk of developing acute myeloid leukaemia. 4.6 for developing colon cancer, 3.4 relative risk for melanoma and 5.79 relative risk for breast cancer in women surviving for more than 25 years.
- If combination chemotherapy is limited to less than 6 months there appears to be no increased risk of secondary cancers

who tx is 7 6 mo.

(Imp.)

Contraception after GTD

- **Advised to use barrier methods of contraception until hCG levels revert to normal.**
- **Once hCG levels have normalised, the combined oral contraceptive pill may be used. There is no evidence as to whether single-agent progestogens have any effect on GTN.**
- **If oral contraception has been started before the diagnosis of GTD was made, the woman can be advised to remain on oral contraception but she should be advised that there is a potential but low increased risk of developing GTN.**
- **Intrauterine contraceptive devices should not be used until hCG levels are normal to reduce the risk of uterine perforation**
- A large UK case series reported a 1.19 relative risk for developing GTN after combined oral contraceptives. (Stone M, et al. An analysis of the influence of maternal age, gestational age, contraceptive method and primary mode of treatment of patients with hydatidiform mole on the incidence of subsequent chemotherapy. *Br J Obstet Gynaecol* 1979;86:782–92

HRT

- **Hormone replacement therapy may be used safely once hCG levels have returned to normal.**
- There is no evidence of risk that the use of hormone replacement therapy affects the outcome of GTN.