Management of Gestational Trophoblastic Neoplasia

Key Document code:	WAHT-TP-027
Key Documents Owner:	Miss Mamta Pathak Consultant Gynaecologist
Approved by:	Gynaecology Governance Meeting
Date of Approval:	10th December 2020
Date of review: **This is the most current version and should be used until a revised document is in place**	20th February 2025

Key Amendments

Date	Amendment	Approved by
14th December 2020	Documents extended for 3 years	Alex Blackwell
10th December 2020	Amendments made to document	Gynaecology Governance Meeting
29th December 2023	Document extended for another 6 months whilst under review.	Alex Blackwell
20th August 2024	Document extended for another 6 months whilst under review.	Alex Blackwell

Introduction

Hydatidiform mole can be subdivided into complete (CHM) and partial mole (PHM) based on genetic and histopathological features. Complete moles are diploid and androgenetic in origin, with no evidence of fetal tissue. Complete moles usually arise as a consequence of duplication of the haploid sperm following fertilisation of an empty ovum. Some complete moles arise after dispermic fertilisation of an empty ovum. Partial moles are triploid in origin with two sets of paternal haploid genes and one set of maternal haploid genes. They occur in almost all cases, following dispermic fertilisation of an ovum. There is usually evidence of a fetus or fetal red blood cells.

The widespread use of ultrasound has led to earlier diagnosis of pregnancy and has changed the pattern of molar pregnancy. The majority of women present with symptoms of early pregnancy failure while presentation with hyperemesis, early severe pre-eclampsia and hyperthyroidism is very rare.

Classic features of molar pregnancy are irregular vaginal bleeding, hyperemesis, excessive uterine enlargement and early failed pregnancy. Rarer presentation includes hyperthyroidism, early severe pre-eclampsia or abdominal distension due to luteal cysts.

The WHO classification of Gestational Trophoblastic disease (GTN) as follows:

Hydatidiform Mole – complete (CHM)	Pre-malignant
Hydatidiform Mole – partial (PHM)	Pre-malignant
Invasive mole	Malignant
Choriocarcinoma	Malignant
Placental site trophoblastic tumour	Malignant

The incidence of GTN in the UK is 1:714 live births.

It does occur more commonly in parts of Asia, Africa, and Latin America.

Evidence of ethnic variation in UK as incidence in Asian women is 1:387.

It is also more common in women <16 years or > 40 years.

Increased risk of hydatidiform mole in women with a previous molar pregnancy:

Previous CHM X 1	Risk = 1:76
Previous CHM X 2	Risk = 1:6.5

The risk of a further molar pregnancy in women with previous molar pregnancy is 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 high risk of obstetric complications.

Complete Hydatidiform Mole
Usually presents with first trimester bleeding (as threatened or complete miscarriage).

Uterus may be larger than dates.

The ultra sound appearances are classical (like a bunch of grapes-multiple sonolucent cystic areas of variable size between 5 – 25mm diameter).

Presentation can however be as follows:
Hyperemesis
Theca lutein cysts
Hyperthyroidism
Severe pre-eclampsia

CHM could potentially develop into an invasive mole and there is a 2 – 3% risk of chorocarcinoma or placental site trophoblastic tumour.

Partial Hydatidiform Mole
In this condition there may be a co-existing fetus. There is an increased risk of triploidy. The ultrasound diagnosis of a partial mole is more complex and requires the finding of soft markers, including both cystic spaces in the placenta and a ratio of transverse to AP dimension of the gestation sac of greater than 1.5.

Advice should be sought from the Regional Fetal Medicine Unit or the relevant Trophoblastic Screening Centre. Women should be counselled about risk of perinatal morbidity and outcome for GTN.

In twin pregnancies where there is one viable fetus and the other pregnancy is molar, the pregnancy should be allowed to continue if the mother wishes after appropriate counselling. The probability of achieving a viable pregnancy is 40%. There is a risk of complications however, in the form of pulmonary embolism and pre-eclampsia.

There is no further increased risk of developing persistent gestational trophoblastic neoplasia after such a twin pregnancy and the outcome after chemotherapy is unaffected.

Management

- Suction curettage is the management of choice.
- A suction catheter up to a maximum of 12mm should be sufficient to evacuate all complete molar pregnancies.
- Preparation of the cervix immediately prior to evacuation is safe.
- Excessive vaginal bleeding can be associated with molar pregnancy and a senior surgeon directly supervising the surgical evacuation is advised. The use of oxytocic infusion prior to completion

of evacuation is not recommended. If the women is experiencing significant haemorrhage prior to evacuation, evacuation should be expedited and need for an oxytocic infusion weighed against risk of tumour and embolism.

- Prostaglandin analogues should be reserved for cases where oxytocin is ineffective.
- In cases of partial mole where the size of the fetal parts may be too large for the use of suction curettage medical termination can be used.
- In patients with retained products of conception, consultation with the trophoblastic screening centre is recommended prior to second evacuation.

ALL PRODUCTS OF CONCEPTION OBTAINED AFTER EVACUATION (medical or surgical) should undergo histological examination. The histologist request form must include information that a molar pregnancy is suspected.

N.B. In cases where there are persisting symptoms such as vaginal bleeding after initial evacuation consultation with the screening centre should be sought before surgical intervention. There is no clinical indication for the routine use of a second uterine evacuation in the management of molar pregnancies.

Registration

Registration of any molar pregnancy by the Consultant is essential. The **on-line** Registration Form for Patients having Hydatidiform Mole should be completed. See appendices 1 and 2 for details.

Women following molar pregnancies should be registered and require follow up for 6-24 months as determined by the screening centre.

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

Treatment of persistent GTN

Women with persistent GTN should be treated at a specialist centre with appropriate chemotherapy.

Placental site trophoblastic tumour

Advice on the management of these rare tumours should be sought from the appropriate registration centre.

Surgery and multi-agent chemotherapy play a major role in the clinical management of this tumour.

Future pregnancy

Women should be advised not to conceive until hCG level has been normal for 6 months. Women who undergo chemotherapy are advised their follow-up is complete and not to conceive for one year after completion of treatment.

Contraception and hormone replacement therapy

The combined oral contraceptive pill and HRT are safe to use **only** after hCG levels have returned to normal. Alternative forms of contraception should be suggested.

The small risk of using emergency hormonal contraception in women with raised hCG levels is outweighed by the potential of pregnancy to women.

Vaginal metastasis-vaginal nodules should not be biopsied as there is a risk of haemorrhage.

Patient information

Patients may find the websites www.hmole-chorio.org.uk and www.miscarriageassociation.org.uk helpful.

Trophoblastic Screening Centres

TROPHOBLASTIC TUMOUR SCREENING AND TREATMENT CENTRE
Department of Medical Oncology
Charing Cross Hospital
Fulham Place Road
London
W6 8RE
Tel: 020 884 61409
Fax: 020 874 856665

See appendix 3 – The Miscarriage Association leaflet "Hydatidiform Mole" to be used to complement discussions with patients available via link below.
http://www.miscarriageassociation.org.uk/ma2006/information/leaflets/hydamole.pdf

Appendix 1

TROPHOBLASTOC TUMOUR SCREENING & TREATMENT CENTRE
Dept of Cancer Medicine, Charing Cross Hospital, Fulham Palace Rd, London, W6 8RF
Helpline & Advisory Service:
Tel: 020 8846 1409
Fax: 020 8383 5577
On Line Registration: https://nww.h-mole.nhs.uk

HYDATIDIFORM MOLE FOLLOW-UP
(Revised March 2004)

The following notes have been prompted by enquiries we have received relating to these patients. hCG follow-up will start with serum and urine assays every 2 weeks until normal then four weekly urine only assays. The patient is contacted directly to send in her samples and is also sent information about molar pregnancy, contraception and future pregnancies. This information can be found on our Website: www.hmole-chorio.org.uk. We offer a telephone advisory service to clinicians and health professionals as well as to patients registered for follow-up with us.

If the patient's hCG levels reach the normal range within 56 days of evacuation, follow-up will be limited to just 6 months. Sequelae has not so far been observed in these patients. The majority of patients with partial hydatidiform mole, and patients with lesions suspicious of HM, fall into this short-term follow-up group. It also includes some patients with complete hydatidiform mole. For patients who do not reach normal values within 56 days of evacuation follow-up will continue until sixx months of normal tests have been seen after the first normal value.

This laboratory requests **SERUM** samples at 2 weekly intervals post-evacuation, until normal values are obtained. Following this, **URINE** samples are requested at 4 weekly intervals until the end of the follow-up period. Further **SERUM** samples are requested if subsequent hCG become abnormal. **(Normal values: Urine hCG 0 - 24 IU/L. Serum hCG 0 - 4 IU/L).** Patients who fail to comply with requests for samples will be sent two reminders, at fortnightly intervals after which we will inform the Gynaecologist and GP.

Patients in the 6-month follow-up group can start a new pregnancy once follow-up is complete. Patients who do not have normal hCG values within 8 weeks of evacuation should have the longer follow-up. After six months of normal tests it may be judged reasonable to go ahead with a new pregnancy. In this latter group the risk of choriocarcinoma occurring after hCG has been normal for 6 months is 1:286. Further estimations of hCG, 6 weeks and 10 weeks AFTER ANY FUTURE pregnancies are requested because of a small increase in risk of choriocarcinoma developing in such patients. In some cases the choriocarcinoma arises from the new pregnancy.

Assay results are sent to the patient's Gynaecologist and GP, with any relevant comments. All GP's are sent a copy of the follow-up recommendations at registration. The patient is invited to telephone for results and the first normal result is communicated to her on the subsequent form along with the proposed length of follow-up.

Do you need to take any action on results?
We will monitor all patients very closely.

If there is an indication for chemotherapy (see below) the **Gynaecologist** will be contacted in the first instance. Sometimes with the permission of the Gynaecologist we will contact the patient directly to arrange admission to Charing Cross Hospital. We also ensure the GP is informed of the admission.

Indications for chemotherapy

Patients requiring chemotherapy will meet one or more of the following criteria:
1: Serum hCG > 20.000 IU/L at >4 weeks post evacuation.
2: Rising hCG. i.e. 2 consecutive rising serum samples.
3: hCG plateau. i.e. 3 consecutive serum samples not rising or falling significantly.
4: Heavy haemorrhage and/or severe abdominal pain.
5: hCG still abnormal at 6 months post evacuation.

Oestrogen and/or progestogens taken between evacuation of the mole and the return to normality of hCG values appears to increase the risk of invasive mole or choriocarcinoma developing. It is suggested that these be avoided until hCG has become normal in serum (i.e. <5 IU/L). **This advice also applies after any subsequent pregnancy,** until hCG returns to normal.

Appendix 2 – Registration form For information only - registration should be made on-line

REGISTRATION FORM FOR PATIENTS HAVING HYDATIDIFORM MOLE

Please read the supplementary notes overleaf. Completed registration forms should be sent to one of the addresses on the back of this form. Receipt of notification will be acknowledged. 2004

REFERRING CONSULTANT

CONSULTANT
GMC Number
HOSPITAL
ADDRESS

POSTCODE
TEL: FAX:

PATIENT IDENTITY / AFFIX LABEL

SURNAME
FIRST NAMES
Hospital No D.O.B.
ADDRESS

POSTCODE Tel:

OBSTETRIC HISTORY

Number of live births:
Number of pregnancies including this one:
Date of evacuation of hydatidiform mole:
Date of last menstrual period prior to evac:
Gestational age: Uterine size:
Classification of mole(note 4):
Site of mole: Uterine Ectopic
Repeat D&C? YES / NO Date/s
Comment.
Family history of H.Mole? YES / NO

ETHNIC ORIGIN
UNDERSTANDS ENGLISH? YES / NO / LITTLE
MOTHER TONGUE/1st LANGUAGE?

GP NAME

ADDRESS

POSTCODE
Telephone:

EVENTS LEADING TO DIAGNOSIS (Please ring and number sequence of events)

PV bleeding	Histology report	Missed abortion	Foetal abnormality
Ultrasound	Large fo dates	Incomplete abortion	Ectopic pregnancy
Recurrent bleeding-following abortion	Small for dates ^hCG	Termination	Evacuation of uterus

OTHER (please describe in separate letter if preferred)

METHOD(S) OF EVACUATI0N (Please ring as appropriate)

Spontaneous	Curettage	Hysterotomy	Prostaglandins/Analogue
Suction evacuation	Syntocinon	Hysterectomy	Mifepristone

OTHER (please specify)

WAS DIAGNOSIS SUSPECTED PRIOR TO EVACUATION? YES / NO

Please confirm that the need for follow-up has been discussed with the patient, that the procedure has been explained to her and that she has consented to her data being held on computer. Please ask her to notify us of any change of address.

Signed	Name	Pathologist
Consultant or Registrar	Date	Hospital site.
GMC Number		Path.Lab.No.

******PLEASE ATTACH A COPY OF THE HISTOLOGY REPORT******