OBSTETRICS AND GYNAECOLOGY CLINICAL PRACTICE GUIDELINE	
# Gestational Trophoblastic Disease [NEW]	
Scope (Staff):	WNHS Obstetrics and Gynaecology Directorate staff
Scope (Area):	WNHS Obstetrics and Gynaecology Directorate clinical areas
This document should be read in conjunction with the Disclaimer.	

Contents

Aim

To provide information on the care and management of women presenting with suspected or confirmed gestational trophoblastic disease (GTD).

Note: These are guidelines and do not preclude the use of clinical judgement and discussion in a tumour board setting for unique cases which may require treatment deviating from this document.

Key points

1. A pregnancy test, quantitative beta hCG (BhCG) should be performed in all cases of persistent or irregular vaginal bleeding after a pregnancy event (including live birth, miscarriage, termination or ectopic pregnancy) to investigate for undiagnosed GTD.[1, 2]
2. Suction evacuation is the preferred initial management for all cases of suspected molar pregnancy.[1, 2] Ideally this should be performed or supervised by an experienced Gynaecologist, under ultrasound guidance, to ensure the uterine cavity is empty at completion and to minimise the risk of perforation.
3. Use of misoprostol to ripen the cervix is appropriate before uterine evacuation.[3] There is insufficient data on the safety of prostaglandins for cervical ripening in later gestations (greater than 15 weeks) and therefore should be used with caution in this situation.[1]
4. Molar pregnancies can cause heavy vaginal bleeding. Tranexamic acid should be considered. The management of haemodynamically unstable patient is emergency uterine evacuation. Oxytocics may be used in theatre ONLY after uterine evacuation has been completed due to the risk of trophoblastic tissue being disseminated throughout the venous system.[1, 2]
5. Although complete moles lack the anti-D antigen, there may be a significant delay in histological confirmation, therefore it is recommended that ALL women who are RhD negative receive RhD Immunoglobulin prophylaxis.[1, 2, 4]
6. All products of conception obtained at evacuation should be sent for histopathology and results to be reviewed in EC admin clinic GYN561[1, 2]

7. Ploidy status and immunohistochemistry staining for P57 may be useful for differentiation between a partial or complete mole.[1, 2] Ploidy studies (FISH) should be requested in cases of possible partial molar pregnancies.
8. Patients should be advised regarding the suspected diagnosis and advised to commence weekly BhCG testing after uterine evacuation.
9. If histopathology confirms a molar pregnancy (possible partial, partial or complete molar), patient should be advised of the diagnosis and referred to the Western Australia Trophoblastic Centre (WATC) for registry and ongoing care. Do not wait for FISH results, referral can be sent based on histopathology recommendations.
10. WATC provides a statewide service with comprehensive counselling, monitoring, treatment and follow up for all patients with GTD.
11. Pregnancy should be avoided until after the completion of the surveillance period. Women should be advised to have protected sexual intercourse. Oestrogen and/or progestogen contraceptives may be used between evacuation of the molar pregnancy and prior to return to normality of BhCG levels. This does NOT appear to increase the risk of invasive mole or choriocarcinoma developing.[1,5,6]
12. To minimise the risk of uterine perforation, insertion of an intrauterine device should be delayed for at least 6 weeks after uterine evacuation and after BhCG levels have returned to normal.[1]
13. A diagnosis of persistent GTD, gestational choriocarcinoma, atypical placental site nodule (APSN), epithelioid trophoblastic disease (ETT) and placental site trophoblastic tumours (PSTT) requires referral to WATC.
14. For women who conceive again after having a molar pregnancy, there is a less than 1 percent chance of recurrence. An ultrasound scan early in pregnancy at 6-8 weeks gestation is recommended. A BhCG level should be completed 6 weeks after the conclusion of any future pregnancy regardless of the outcome (i.e. miscarriage, termination, or delivery).[1]
15. The patient's general practitioner (GP) should be notified of the diagnosis of GTD, and a discharge letter should be sent on conclusion of treatment and/or follow up.

Background[7]

GTD is a rare group of placental related disorders derived from a pregnancy. The incidence of molar pregnancies is in the order of 1:300-1000 pregnancies. They form a spectrum of diseases characterised by their origin in trophoblastic cells.[20] Because human chorionic gonadotrophin (hCG) is secreted from trophoblastic cells, GTD can be accurately monitored. Trophoblastic diseases range from the usually benign partial and complete molar pregnancy and atypical placental site nodule through to invasive mole, choriocarcinoma, epithelioid trophoblastic tumour and placental site trophoblast tumour.[1,4,20]

The use of ultrasound in early pregnancy has led to the earlier diagnosis of molar pregnancy, as opposed to the common clinical presentations of irregular vaginal bleeding, hyperemesis, excessive uterine enlargement, early failed pregnancy or

persistent vaginal bleeding following a completed pregnancy. Rarer presentations may include hyperthyroidism, early onset pre-eclampsia or the presence of theca lutein cysts. BhCG levels greater than two multiples of the median may also contribute to the diagnosis.[1, 2]

Gestational trophoblastic neoplasia (GTN) is a term used to describe GTD requiring chemotherapy or excisional treatment because of the persistence of hCG or the presence of metastases. GTN may follow a hydatidiform mole (60%), a previous miscarriage / abortion (30%), a normal pregnancy or ectopic gestation (10%).[1] Patients with a partial molar pregnancy have a 1–4% risk of progression to GTN, patients with a complete molar pregnancy have a 15-20% risk of progression to GTN. Patients with APSN have a 15% risk of co-existing or developing PSTT or ETT.

GTN is chemo-sensitive and highly curable when treated adequately and patients benefit from coordinated monitoring and treatment from dedicated GTD multi-disciplinary teams.

Risk factors

- Extremes of reproductive age[1]
    - Age 35 years and over
    - Age 20 years and under
- Previous GTD
- Patients of Asian descent have a higher incidence of GTD (1:390) compared to Caucasian patients (1:750).[1] There may be a higher incidence of molar pregnancies in Africa and Asia. However, the varying standards in the frequency and accuracy of histopathology makes it difficult to make accurate comparisons.[8]

Classification

Gestational trophoblastic diseases are divided into pre-malignant and malignant forms:

- **Pre-malignant**
    - Partial Hydatidiform Molar (PHM)
    - Complete Hydatidiform Molar (CHM)
    - Atypical placental site nodule (APSN)
- **Malignant**
    - Invasive mole (Persistent GTD)
    - Choriocarcinoma
    - Placental site trophoblastic tumours (PSTT)
    - Epithelioid trophoblastic tumour (ETT)

Pre-malignant trophoblast disease

Hydatidiform moles are separated into CHM and PHM based on genetic and histopathological features. In early gestational products of conception, it may be difficult to differentiate the two on histopathology. Immunohistochemistry p57 gene is a paternally imprinted but maternally expressed gene. The p57 protein is expressed in the cytotrophoblasts and villous stromal cells of normal placental tissue and PHM, but not in CHM as there is no maternal genetic material.
Cytogenetic testing such as Fluorescence In Situ Hybridization (FISH) allows the determination of ploidy of the pregnancy but will not necessarily distinguish diandric from digynic triploidy.

Partial Hydatidiform Mole PHM

PHM are usually triploid with 2 sets of paternal and 1 set of maternal chromosomes (XXX, XXY, XYY) but may be tetraploid or mosaic in 10% of cases[4]. Macroscopically partial moles may resemble the normal products of conception as they contain embryonic or fetal material. As a result, the diagnosis of partial mole can often be missed after an apparently straightforward miscarriage or termination. Partial moles rarely become malignant with an overall risk of 1 - 4%.[2]

In cases of possible partial mole, cytogenetic testing such as Fluorescence In Situ Hybridization (FISH) may be requested. FISH allows the determination of ploidy of the pregnancy but will not necessarily distinguish diandric triploidy from digynic triploidy. Digynic tripoloidy pregnancies are non-molar, usually present with second trimester pregnancy loss and do not carry any risk of malignancy, and they do not require BhCG monitoring.

Complete Hydatidiform Mole CHM

Complete moles are diploid and androgenic in origin with no evidence of fetal tissue. The genetic material is entirely male in origin and results from the fertilisation of an empty ovum lacking maternal genes. The chromosome complement is most commonly 46XX, which results from one sperm that duplicates its DNA, or less frequently 46XX or 46XY from the presence of two different sperm in an empty ovum.[3] Patient with CHM have a 15-20% risk of progressing to invasive molar (GTN) requiring chemotherapy.[1, 2]

Atypical Placental Site Nodule

Placental site nodules (PSN) are a benign finding of little clinical significance, whereas Atypical Placental Site Nodules (APSN) have a 15% risk of co-existing PSTT or ETT.[17] Patients often present with vaginal bleeding resulting in endometrial biopsy. The pathology should be centrally reviewed, and staging investigations performed to determine further management. Patients who have completed their family may wish to consider a hysterectomy. If further pregnancies are desired, careful counselling and testing is advised.

Malignant Trophoblast Disease

Gestational trophoblastic neoplasm (GTN) may develop after a molar pregnancy, a non-molar pregnancy or a live birth. Any patient who develops abnormal or persistent vaginal bleeding after a pregnancy event is at risk of having GTN. Patients may also present with a wide variety of symptoms from distant metastases to the lungs, liver and central nervous system.[9] Locally invasive GTN is most commonly located in the vaginal fornices or suburethrally. Due to their highly vascular nature, biopsy should be avoided.[1]

As this disease crosses the placenta, in all suspected and confirmed cases of postpartum GTN, the neonate should have a urine test for quantitative hCG.[1]

Invasive mole (Persistent GTD)

Invasive moles usually arise from a complete mole and is characterised by the invasion of the myometrium. Microscopically, invasive moles have a similar benign histological appearance as complete moles but is characterised by the ability to invade into the myometrium and the local structures and metastasis out of the pelvis if left untreated.

The usual presentation of an invasive mole is with hCG elevation or plateau during surveillance following a molar pregnancy.[10]

Gestational choriocarcinoma

Choriocarcinoma is clinically and histologically overtly malignant and hCG levels are always elevated. The diagnosis most frequently follows a complete mole (25-50%) when the patients are usually in a surveillance programme but can also arise within 12 months after a non-molar abortion (25%) or after a normal term pregnancy (25-50%).[1,10]

Placental Site Trophoblastic Tumour & Epithelioid Trophoblastic Tumour

Placental site trophoblast tumours (PSTT) and Epithelioid trophoblastic tumour (ETT) are very rare and are the least common forms of GTD comprising less than 2% of all cases[18].

Patients with PSTT/ETT usually present later in comparison to other forms of GTD. The average interval between the pregnancy event and presentation of disease is 3.4 years. The clinical presentation of PSTT/ETT can range from slow growing disease limited to the uterus, with abnormal uterine bleeding to more rapidly growing metastatic disease with behaviours similar to choriocarcinoma. Other presentations may include amenorrhea, hyperprolactinemia or nephrotic syndrome.[11]

ETT/PSTT are often indolent tumours associated with low serum hCG levels, chemoresistance and poor correlation of clinical outcomes with FIGO staging[18]. Due to the rarity and unique clinical-pathological behaviours of ETT/PSTT all cases should be managed by a dedicated specialised GTD unit such as WATC.[18]

Management of patients with suspected GTD

The Gynaecology Consultant rostered in EC at time of presentation must be notified for all suspected or confirmed molar pregnancies.

Initial management for suspected molar pregnancy

1. Perform initial blood tests for
    - BhCG levels
    - Blood group and hold (G&H)
    - FBC
2. Arrange suction evacuation; recommended for complete and partial molar pregnancies. Consider evacuation under ultrasound guidance due to increased perforation risk.
    a. Notify consultant and/or registrar assigned to the theatre list. If possible, book the case at the beginning of the list due to risk of excessive bleeding.
    b. Ensure that there is a current G&H
    c. Misoprostol may be given prior for cervical ripening[3]
3. Avoid the use of oxytocics until after uterine evacuation has been completed. This reduces the risk of causing trophoblastic embolism from the placental bed and disseminated disease.
4. Send all products of conception for histology examination
5. Administer RhD immunoglobulin to Rh-negative patients after surgery
6. Histopathology results are to be reviewed in EC admin clinic GYN561
7. Provide patient request form for BhCG to be done one week post evacuation and weekly thereafter until histopathology confirmed molar or non-molar or WATC takes over care.
8. Provide initial patient education and provision of information brochures.
9. Provide information about pregnancy loss services and/or referral to psychological medicine if required.

Management of 'confirmed' complete and partial mole on histopathology

1. Ring patient and advise of diagnosis and referral to WATC. (Please refer to; **"Follow Up"**)
2. Advise against pregnancy until end of surveillance period (Please refer to; **"Contraception Advice**")
3. Advise patient of need for weekly hCG and provide blood form. Patients may choose to have their bloods taken at a collection centre most convenient for them. They must go to the same laboratory centre each week. Please notate on referral which laboratory the patient has elected to have their blood tests.
4. Arrange eReferral to WATC **"Outpatient referral > Site: KEMH > Unit: MOWT > Responder: Allanson, Emma or Ayres, Chloe"**
5. Health care providers and patients can directly contact WATC at watc@health.wa.gov.au or call the WATC CN on 0403 137 408. (Options for referrals to WATC include:
    - **Option 1 Registry and WATC care** – WATC will contact the patient, provide full medical, nursing, psychological care and support; care can be provided via

telehealth, text, email and/or in-person depending on patient preference. WATC to inform GP and referrer of patient progress.

- **Option 2 Registry only** – patient details will be added to the state-wide registry. Treating doctor must agree to monitor and follow up the patient. Patient should be re-referred if escalation of care is required. WATC will not contact the patient unless requested.
- **Option 3 For discussion at WATC MCC/MDT meeting** – cases requiring advice on management may be referred for discussion at the WATC MDT, held every Thursday lunchtime. Patients will not be contacted, but the referring doctor will be notified with a clear recommended management plan.
- **Option 4** Patient already registered (as per option 2), WATC to take over care (a per option 1)

Management of "possible partial molar pregnancy" or "unable to exclude a molar pregnancy" on histopathology

Histopathology may report "unable to exclude a molar pregnancy" or "possible partial molar pregnancy". Ploidy studies (fluorescence in situ hybridisation - FISH) should be requested to assist in the diagnosis. The patient will continue to be managed as a molar pregnancy with weekly hCG levels. FISH results may take up to six weeks. The patient can still be referred to WATC, who will continue management, hCG monitoring and care of the patient while awaiting the FISH results. WATC will follow up the FISH results and inform the patient.

Management of a molar pregnancy with a coexisting viable twin pregnancy

Twin pregnancy with a suspected molar pregnancy is estimated to occur in 1:20,000-100,000 pregnancies.[20] Cases should be discussed with Maternal Fetal Medicine (MFM) team to consider a tertiary level ultrasound and discuss management:

- If ultrasound reveals an abnormal co-twin fetus, patient can be counselled, and a termination of pregnancy may be arranged as per suspected molar pregnancy care.
- If the tertiary level ultrasound suggests co-twin is normal, patient may be counselled on options of termination or continuation of pregnancy[16]:

GTN risk	Obstetric and fetal risk
- risk of GTN 24% - risk of GTN higher than singleton pregnancy - Risk of GTN not increased by continuing pregnancy - Increased risk of multi-agent chemotherapy treatment of GTN	- high risk pregnancy requiring MFM management - high chance PV bleeding - hyperthyroidism - increased and early risk of hypertensive disorders - high risk (>40%) of pregnancy loss <24 weeks - high risk preterm birth - 25% chance of live birth >24 weeks

References: 16, 20,

Contraception Advice

Pregnancy should be avoided in the follow up period. Patients should be counselled on contraceptive options.

- Patient should be advised to use barrier contraception
- Any of the oestrogen and/or progestogen contraceptives may be used. The combined contraceptive pill does not appear to increase the risk of invasive mole or choriocarcinoma developing.[21, 25, 26]
- Intrauterine contraceptive devices should be avoided for at least 6 weeks following uterine evacuation and normalisation of BhCG levels due to the risk of uterine perforation.[21] If an IUD was placed at time of evacuation, before histopathology reported molar pregnancy, the IUD may remain.

Follow up of GTD and BhCG monitoring

Following diagnosis of complete or partial mole, patients should be followed with weekly serial serum hCG levels. The blood test can be performed at any pathology collection centre most convenient to the patient. Advise patient to attend the same pathology centre each week for consistency of hCG assay to aid with interpretation of hCG levels. Please advise WATC which pathology centre patients have elected to have their blood tests.

Interpreting hCG during monitoring of GTD/GTN

The hCG levels are measured weekly, with serum sample sent to the same laboratory each week. Each hCG level is compared with the level from the previous week to determine if the level is increasing, decreasing or plateauing.

Complete mole hCG monitoring

Weekly quantitative hCG levels should be undertaken until 3 consecutive weekly normal levels are achieved. When patient has had 3 normal hCG levels they then switch to monthly hCG levels.

- If hCG level has normalised within 56 days of uterine evacuation, only one further hCG in a month is required. If hCG is still < 5 iu/L monitoring is complete.[19]
- If hCG levels take more than 56 days to normalise, it is recommended the patient have 6 months of monthly hCG levels from normalisation.[19]

Partial mole hCG monitoring

Weekly quantitative hCG levels should be taken until < 5 iu/L, and then one further hCG level is checked in one month. If hCG is still < 5 iu/L monitoring is complete.

- **A negative (normal)** quantitative BhCG level is less than 5 iu/L
- **Note: BhCG of 5 is still elevated.**
- **Normalisation** is confirmed with three consecutive weekly normal BhCG levels (i.e. three consecutive weekly BhCG levels less than 5 iu/L).

Diagnosis of Persistent/Invasive molar (GTN) or a plateau in hCG

The diagnosis of persistent or invasive molar disease (GTN) is usually made in the following hCG monitoring situations:

a. A BhCG increase of more than 10% over two consecutive weekly levels (a persistently rising hCG);
b. A BhCG decrease of less than 10% over three consecutive weekly levels (a plateau in hCG);
c. An elevated BhCG levels (> 5iu/L) following initial normalisation during the surveillance period (note: must exclude new pregnancy).

These cases should be referred to WATC for counselling, examination, staging and treatment management options.

Increasing hCG level

- >10% rise in level compared with week prior
- Rising hCG that progressively increases >10% across three values during at least a two-week period (e.g. on days 1, 7 and 14) meets criteria for GTN staging.

Decreasing hCG level

- >10% decline in level compared with week prior
- hCG returns to 'normal' once reaches <5 iu/L (hCG of 5 is still elevated, level must <5)

Plateau and unusual hCG level

- Plateau in hCG is four measurements that remain +/- 10% over a three-week period (e.g. days 1, 7, 14 and 21)
- A plateau in hCG meets criteria to be considered for GTN staging.
- Persistently low positive hCG warrants further investigation to determine cause.
- Raised hCG level months after D&C, patient should be reviewed and individualised decision regarding care determined.

Unexplained Persistent Low-Level Elevated hCG [20]

A low level unexplained hCG can be a diagnostic dilemma and requires careful history taking and a structured workup. It is important to remember an elevated hCG may be related to pregnancy, GTD, pituitary hCG, non-GTD tumour, renal failure, exogenous hCG use or false positive caused by circulating heterophile antibodies.

Approach to patient with unexplained raised hCG [16,20]:

- Review criteria above regarding diagnosis of persistent hCG
- Careful history including previous pregnancies and exogenous hCG
- Patients with unexplained elevated hCG may be referred to the WATC multidisciplinary case conference for advice on investigations and management.
- Discuss with PathWest QEII biochemistry to arrange serum hCG sample to be analysed on different hCG assays and dilution testing to exclude heterophile antibodies.
- A negative quantitative urine hCG suggests a false-positive serum result
- Pelvic ultrasound (consider serial scans if indicated) extra/intra uterine pregnancy or placental tissue

- Consider endometrial sampling (endometrial pipelle biopsy or hysteroscopy with direct visualisation tissue removal system such as Myosure).
- Additional tumour markers for germ cell tumours (hCG, AFP, LDH), hormones to identify menopause/pituitary hCG (LH, FSH, estradiol) and kidney function to exclude renal failure.
- Consider CT chest/abdomen/pelvis to assess potential sites of GTN and non-gynaecological malignancy (e.g. liver, lung, pancreas, stomach).
- Familial elevated hCG is a rare inheritable syndrome where mutated nonfunctional forms of hCG are produced.
- Combined oral contraceptives will normalise hCG in the case of menopausal-induced pituitary hCG production. If clinically safe, consider high dose combined contraceptive pill (ethinylestradiol 50mcg/levonorgestrel 125mcg) for one month.

Management of Gestational Trophoblastic Neoplasia (GTN)

Patients who meet criteria for GTN with rising or persistent hCG, unusual or abnormal pathology or high-risk pathology, should be referred to WATC for counselling, examination, staging and treatment management options.

WATC will arrange an urgent patient appointment and full GTN metastatic work up to determine the extent of disease. Investigations include:

- Chest Xray
- Pelvic ultrasound
- CT chest/abdomen/pelvis
- MRI brain (only if CT chest indicates presence of lung metastases or there are concerning neurological symptoms. Brain metastases in the absence of lung metastases are extremely rare.)
- Pelvic MRI may be considered in some cases
- Blood tests - hCG, FBC, EUC, eGFR, LFT, HepB/HepC, Ca/Mg/Ph
- Speculum examination to detect vaginal metastasis

All cases of GTN will be reviewed at WAGCS Tumour Conference for calculation of FIGO staging and WHO prognostic risk score, imaging may be reviewed at WAGCS Radiology Meeting, and all monitoring and care will be coordinated via WATC.

Repeat uterine evacuations

The role for repeat uterine evacuation in confirmed cases of GTD/GTN is controversial. The procedure may be considered if the hCG level is <5000 IU/L with disease confined to the cavity (no myometrial spread or metastatic disease). However, the low efficacy of repeat evacuation, the risk of haemorrhage, perforation and uterine damage should be considered in comparison with an almost 100% cure rate and the relative safety of chemotherapy.[1, 2, 4]

In selective cases, a secondary evacuation has showed a cure rate of GTN of 40%.[20] **If** a repeat evacuation is considered, the use of hysteroscopy to locate[1], and direct visualisation tissue removal system (e.g. Myosure) to resect the foci of persistent disease is recommended. Hysterectomy is also an alternative treatment in women who have completed fertility and disease is confined to the uterus. Post-procedure WATC will continue to provide close hCG surveillance.

GTN staging

Patients with GTN are staged according to the FIGO anatomical staging and classification, stage I – IV and the World Health Organisation (WHO) prognostic score is calculated to guide chemotherapy regimen.

FIGO staging of GTN[13]

FIGO stage	Description
Stage I	Gestational trophoblastic tumours strictly confined to the uterine corpus
Stage II	Gestational trophoblastic tumours extending to the adnexae or to the vagina but limited to the genital structures.
Stage III	Gestational trophoblastic tumours extending to the lungs, with or without genital tract involvement.
Stage IV	All other metastatic sites

WHO prognostic score[14]

	Score			
Prognostic factors	0	1	2	4
Age (years)	<40	>40	-	-
Antecedent pregnancy	mole	abortion	term	-
Interval from index pregnancy (evacuation), in months	<4	4 to 6	7 to12	more than 12
Pre-treatment serum hCG (iu/L)	$<10^3$ <1,000	10^3-10^4 1,000 to 9,999	10^4-10^5 10,000 to 100,000	$>10^5$ >100,000
Site of metastases including uterus	lung	spleen, kidney	gastrointestinal tract	brain, liver
Largest tumour size, including uterus (in cm)	-	3-4	>/= 5	-
Number of metastasis identified	0	1 to 4	5 to 8	more than 8
Previous unsuccessful chemotherapy	none	none	single drug	two or more drugs

GTN staging and chemotherapy

The prognostic score predicts the potential for developing resistance to single-drug chemotherapy with methotrexate or dactinomycin. A score of 0 to 6 is considered low risk and therefore a single chemotherapeutic agent is indicated. A score of 7 or greater indicates high risk of resistance and requires multi-agent chemotherapy regime[14].

Prescribing of chemotherapeutic agents for GTN is arranged by WATC. Multi agent chemotherapeutic regimes for resistant GTD or WHO high risk scoring patients requires specialised chemotherapeutic regime protocols that is organised by Medical Oncology in collaboration with WATC.

GTN is very responsive to chemotherapy, and associated cure rates are greater than 90% even in women with metastatic disease[15]. Fertility is not harmed after treatment for low-risk GTN, and even after high-risk chemotherapy regimens such as EMACO, fertility is generally unchanged.[20] Women who receive chemotherapy may experience menopause earlier by 1 year for single agent, and 3 years for multi-agent chemotherapy.[2, 4, 10]

Post GTD/GTN care:

- WATC will coordinate all monitoring and follow up as required. The patients GP will be sent a letter when the patient is registered with WATC and on discharge from WATC.
- Patients with GTD are advised to avoid pregnancy during hCG monitoring, and WATC will advise patents when their monitoring is complete. Patients with GTN are advised to avoid pregnancy for 12 months following completion of chemotherapy.[1, 2,10]
    - Early pregnancy during monitoring of hCG can make diagnosis of recurrence of GTD/GTN difficult.

  - Early pregnancy during follow-up is not associated with a higher risk of recurrence or unfavourable pregnancy outcome.[20]
  - Fertility rate is not affected following chemotherapy.

- Once hCG monitoring is complete, patients may consider trying to conceive if desired.
- WATC counsels patients for their next pregnancy. The risk of a second molar pregnancy is less than 1%.[20] We offer an early ultrasound at 6 –8 weeks gestation to confirm viability, and recommend a hCG level 6 weeks after the conclusion of any subsequent pregnancy event regardless of the outcome (i.e. miscarriage, termination, or delivery).[1]

The Women and Newborn Health Service (WNHS) endorses the use of this Clinical Practice Guideline in conjunction with the Practical Guidelines for the Treatment of Gestational Trophoblastic Disease (European Organisation for the Treatment of Trophoblastic Disease (EOTTD); European Society of Gynaecological Oncology (ESGO): Gynaecologic Cancer Intergroup (GCIG), International Society for the Study of Trophoblastic Disease (ISSTD) (2025):

https://ascopubs.org/doi/pdf/10.1200/JCO-24-02326

Flow chart: GTD Management

Western Australia Trophoblastic Centre (WATC) Management of Complete / Partial Mole

*FISH = FLUORESCENCE IN-SITU HYBRIDISATION

Suspected Gestational Trophoblastic Disease on ultrasound
Arrange evacuation of uterus
If unexpectantly high βhCG or any concerning features recommend discussion with WATC to confirm appropriate management

Procedure considerations
- Prostaglandins (misoprostol) may be used for cervical ripening
- Oxytocic use may be used, if required, after evacuation
- Experienced practitioner, perform under ultrasound guidance
- All products of conception obtained to be sent for histology
- Rhesus negative patients to receive anti-D
- Recommend discussion with WATC prior to performing repeat curettage for RPOC in GTD

Arrange weekly βhCG and follow up of histology results.
Advise contraception until histology confirmed and monitoring complete.
No imaging (i.e. CXR/CT) required unless GTN suspected, recommend discussion with WATC

Non molar pregnancy

Advise patient of results. No hCG monitoring required

Histology reports partial mole
(NB: "possible partial mole" request *FISH to confirm diagnosis. *FISH results may take six or more weeks, refer to WATC while awaiting result)
→ refer to WATC for registry +/- ongoing care.
WATC will follow up *FISH results

*FISH Confirms Non molar pregnancy pregnancy

Advise patient of results. No βhCG monitoring required

Partial mole confirmed (histology/*FISH)
→ refer to WATC for registry +/- ongoing care

Monitoring of patient with partial mole:
- Advise and educate patient on diagnosis, advise contraception and offer psychological support
- Arrange weekly βhCG (at same lab)

βhCG rise or plateau
→ refer to WATC

Weekly βhCG until < 5 then one further βhCG in 4 weeks

Histology confirms complete mole
→ refer to WATC for registry +/- ongoing care

Monitoring of patient with complete mole:
- Advise and educate patient on diagnosis, advise contraception and offer psychological support
- Arrange weekly βhCG (at same lab)

Continue weekly βhCG until 3 consecutive weekly βhCG < 5

βhCG rise or plateau
→ refer to WATC

If βhCG normalise within 56 days of uterine evacuation, then one further βhCG in 4 weeks

If βhCG normalise within 56 days of uterine evacuation, then one further βhCG in 4 weeks

Histology GTD/GTN including:
- Atypical Placental Site Nodule (APSN)
- Choriocarcinoma
- Placental Site Trophoblastic Tumour (PSTT)
- Epithelioid Site Trophoblastic Tumour (ETT)
- Or any atypical/unusual/unknown GTD

→ refer to WATC

When βhCG monitoring completed patient may consider trying to conceive if desired. Risk of recurrence of molar pregnancy is very low (less than 1%).
Offer early ultrasound (6-8 weeks gestation) to confirm viability. Recommend repeat βhCG 6 weeks after conclusion of any subsequent pregnancy.

WESTERN AUSTRALIAN TROPHOBLASTIC CENTRE (WATC)

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REFERRALS:
Please fax or email all referral and attachments (copies of results etc)
WATC@health.wa.gov.au

If urgent please contact the on-call Gynae-Oncology Fellow or on-call Gynaecologic Oncologist through (08) 6458 2222 to discuss case.

References

1. The Royal Australian and New Zealand College of Obstetricians and Gynaecologists. RANZCOG Statement for the management of gestational trophoblastic disease. 2017. www.ranzcog.edu.au/wp-content/uploads/Management-Gestational-Trophoblastic-Disease.pdf. Available from: https://www.ranzcog.edu.au
2. Royal College of Obstetricians and Gynaecologists. The Management of Gestational Trophoblastic Disease: Green-top Guideline No. 38. RCOG. 2010.
3. Flam F LV, Pettersson F. Medical induction prior to surgical evacuation of hydatidiform mole: is there a greater risk of persistent trophoblastic disease? Eur J Obstet Gynecol Reprod Biol. 1991;42(1):57-60.
4. Seckl MJ, Sebire NJ, RS B. Gestational trophoblastic disease. The Lancet. 2010;376:717-29.
5. Curry SL SJ, Kohorn EI, Boyce JB, Gore H, Twiggs LB , et al., . Hormonal contraception and trophoblastic sequelae after hydatidiform mole (a Gynecologic Oncology Group Study). Am J Obstet Gynecol. 1989;160(4):805-9 discussion 9-11.
6. Dantas et al. Does hormonal contraception during molar pregnancy follow-up influence the risk and clinical aggressiveness of gestational trophoblastic neoplasia after controlling for risk factors? Gynecologic Oncology 2017.
7. Charing Cross Hospital. Trophoblast disease service: Info for clinicians Available from: http://www.hmole-chorio.org.uk/index.html
8. Lurain J. Gestational trophoblastic disease I: epidemiology, pathology, clinical presentation and diagnosis of gestational trophoblastic disease, and management of hydatidiform mole. American Journal of Obstetrics and Gynecology. 2010;203(6):531– 9.
9. Seckl MJ, Fisher RA, Salerno G, Rees H, Paradinas FJ, Foskett MA, et al. Choriocarcinoma and partial hydatidiform moles. Lancet 2000;256:36-9.
10. Seckl MJ, Sebire NJ, Fisher RA, Golfier F, Massuger L, Sessa C, et al. Gestational trophoblastic disease: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2013;24(suppl 6):vi39-50.
11. Schmid P, Nagai Y, Agarwal R, Hancock B, Savage PM, Sebire NJ, et al. Prognostic markers and long-term outcome of placental-site trophoblastic tumours: a retrospective observational study. Lancet. 2009;374(9683):48-55.
12. Shih IM, RJ K. Epithelioid trophoblastic tumor: a neoplasm distinct from choriocarcinoma and placental site trophoblastic tumor simulating carcinoma. Am J Surg Pathol. 1998;22(11):1393-403.
13. FIGO Oncology Committee. FIGO staging for gestational trophoblastic neoplasia 2000. Int J Gynaecol Obstet. 2002;77:285-7.
14. Ngan HY, Bender H, Benedet JL, Jones H, Montruccoli GC, Pecorelli S, et al. Gestational trophoblastic neoplasia, FIGO 2000 staging and classification. Int J Gynecol Obstet. 2003;83(Supp 1):175-7.
15. Seckl MJ, Sebire NJ, Berkowitz RS. Gestational trophoblastic disease. Lancet. 2010;376(9742):717–729. DOI: 10.1016/S0140-6736(10)60280-260280-2)
16. Sebire NJ, Foskett M, Paradinas FJ, Fisher RA, Francis RJ, Short D, et al. Outcome of twin pregnancies with complete hydatidiform mole and healthy co-twin. Lancet. 2002;359(9324):2165-6.
17. Management of Gestational Trophoblastic Disease: RCOG Green-top Guideline No. 38. 2020. BJOG - An International Journal of Obstetrics & Gynaecology. DOI: https://doi.org/10.1111/1471-0528.16266
18. Filicko A, Verma R, Barber E, Strohl A, Hinchcliff E. Surveillance of epithelioid trophoblastic tumors and placental-site trophoblastic tumors - Gynecologic Oncology (gynecologiconcology-online.net). 2024;190(Supp 1):S353. DOI: 10.1016/j.ygyno.2024.07.529
19. Coopmans L, Swift B, Coyle C, Singh K, Winter M, Seckl M. #248 How long do we need to monitor HCG after evacuation of a complete hydatidiform mole? International Journal of Gynecological Cancer. 2023; Volume 33, A33. DOI: 10.1136/ijgc-2023-ESGO.50

References

20. Lok C, Van Trommel N, Braicu EI, PLanchamp F, Berkowitz R, Secki M. Practical Guidelines for the Treatment of Gestational Trophoblastic Disease: Collaboration of the European Organisation for the Treatment of Trophoblastic Disease (EOTTD)–European Society of Gynaecologic Oncology (ESGO)–Gynecologic Cancer InterGroup (GCIG)–International Society for the Study of Trophoblastic Diseases (ISSTD). June 2025: Vol 43, No. 18. Journal of Clinical Oncology.
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Version History

Number	Date	Summary
1.0	September 2025	First version. Gestational trophoblastic disease content removed from (now superseded) WNHS Clinical Guideline “Pregnancy Care: First trimester Complications”. Major review of content.

The health impact upon Aboriginal people has been considered, and where relevant incorporated and appropriately addressed in the development of this policy.

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