BMJ Best Practice

Molar pregnancies

Straight to the point of care

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Summary

Molar pregnancies (MPs; hydatidiform moles) are chromosomally abnormal pregnancies that have the potential to become malignant.

There is a higher possibility of MP in women less than 20 years of age or over 35 years of age, and in those who have experienced MP in a previous pregnancy.

The most common presenting symptom is vaginal bleeding.

Suction evacuation (electrical or manual) is the preferred management option in women who desire preservation of fertility.

Hysterectomy may be considered in women who do not want to preserve fertility.

The risk of post-molar neoplasm is 15% to 20% for those with complete hydatidiform mole and 1% to 5% for those with partial hydatidiform mole.

Over 95% of women with post-molar gestational trophoblastic neoplasia attain remission, often with preservation of fertility.

Definition

Molar pregnancies (hydatidiform moles) are chromosomally abnormal pregnancies that have the potential to become malignant (gestational trophoblastic neoplasia). If a MP or other conception gives rise to a persistent locally invasive and/or metastatic trophoblastic tumour, this is considered to be gestational trophoblastic neoplasia (GTN). Gestational trophoblastic disease includes tumours, such as hydatidiform moles and GTN, arising from placental trophoblasts. Syncytiotrophoblasts secrete human chorionic gonadotrophin and, therefore, this hormonal product is used as a tumour marker for the disease.[1] [2] [3]

Epidemiology

The incidence of hydatidiform mole is expressed as molar gestations per number of pregnancies. In the US, molar pregnancy (MP) is identified in 1 in 1000 to 1200 pregnancies, and in 1 in 600 therapeutic abortions.[5] The incidence seems to be higher in Latin American and Asian countries, although the aetiological factors involved have not yet been determined.[5] [6] [7] Women with a previous diagnosis of hydatidiform mole have a 1% to 2% chance of molar gestation in subsequent pregnancies.[8] [9] There is a modestly increased incidence of MP among women less than 20 years of age, but women over 35 years of age have a significantly higher risk of MP, which increases progressively as maternal age advances.[10] [11] [12] [13] [14] [15] Despite these findings, most molar pregnancies occur in women between 20 and 30 years of age because there is a larger total number of pregnancies in this age group.

Aetiology

The underlying mechanism for molar pregnancy (MP) is not entirely understood. An important component is the presence of excess paternal chromosomes. There is a greater risk of malignant transformation in the presence of a diandric diploid homozygous conception, suggesting a genetic component for the more aggressive form of the disease.[16] Rare hereditary forms of recurrent MP suggest an imprinting defect may be an important contributor to disease pathogenesis.[17] [18] [19]

Pathophysiology

Complete hydatidiform moles have a 46 XX or 46 XY karyotype that is derived entirely of paternal DNA.[20] This is typically the result of fertilisation either of a chromosomally empty egg with a haploid sperm that then duplicates its chromosomes by two sperm. By contrast, partial hydatidiform moles contain a karyotype of either 69 XXX or 69 XXY, and contain both maternal and paternal genetic material.[20] This pathology usually arises from fertilisation either of a haploid ovum by a single sperm, and duplication of paternal haploid chromosomes, or by two sperm.

Partial moles may contain histological or macroscopical evidence of fetal parts, fetal circulation, and fetal red blood cells. Complete moles do not contain these elements.[21]

Both partial and complete molar pregnancies contain abnormal and hydropic chorionic villi, which produce high levels of human chorionic gonadotrophin (hCG); however, the villi of a complete mole are more oedematous, more diffuse, and the increased volume of trophoblast produces more hCG.[22] The hCG glycoprotein hormone is a heterodimer, composed of alpha and beta subunits. The alpha subunit is common to other hormones, such as luteinising hormone, follicle-stimulating hormone, and thyroid-stimulating hormone, but the beta subunit is unique to hCG.[3] The higher elevations in serum hCG levels seen in complete molar pregnancies are associated with a greater incidence of severe medical sequelae such as hyperemesis gravidarum, early-onset gestational hypertension, pre-eclampsia, theca lutein cysts, and hyperthyroidism.[23] [24] [25] [26]

Classification

Clinical classification[4]

Gestational trophoblastic disease (GTD)

- Benign trophoblastic tumours
    - Subtle abnormalities in placental pathology such as exaggerated placental sites, and placental site nodules (PSN) and PSN with atypical features (ASPN).

Hydatidiform moles

- Partial hydatidiform mole
- Complete hydatidiform mole

Gestational trophoblastic neoplasia (GTN)

- Malignant invasive mole
- Choriocarcinoma
- Placental site trophoblastic tumour (PSTT)
- Epithelioid trophoblastic tumour (ETT)

Case history

Case history #1

A 24-year-old woman presents 8 weeks after her last menstrual period. She reports one episode of vaginal spotting during the past week. Urine pregnancy screen is positive, and serum human chorionic gonadotrophin (hCG) is elevated. Ultrasound of the pelvis reveals an apparent missed abortion, with no identifiable fetal pole.

Case history #2

An 18-year-old pregnant woman presents at 10 weeks' gestation with vaginal bleeding. Vital signs indicate sinus tachycardia and hypertension. On pelvic examination the uterus is enlarged to 16 weeks' gestational size with a palpable left adnexal cyst of about 9 cm diameter. Pelvic ultrasound reveals a mixed echogenic (snow-storm) pattern with no fetus and thin-walled cysts in the left ovary.

Approach

Although there are several classic symptoms and signs typical of molar pregnancy, such as vaginal bleeding, hyperemesis, or hyperthyroidism, most women with molar pregnancy in modern clinical practice are diagnosed incidentally at histological examination of the products of miscarriage or on findings from early maternal ultrasound.[30] [31]

History

Women with molar pregnancy typically present in the first trimester of pregnancy with a history of a missed menstrual period, and are found to have positive urine test for pregnancy and elevated serum human chorionic gonadotrophin (hCG) levels on laboratory evaluation. Women are commonly at the extremes of reproductive life (younger than 20 years of age or over 35 years of age), and may relate a history of prior MP.[8] [9] [10][11] [12] [13] [14] [15][32]

The most common presenting symptom is vaginal bleeding.[33] [34] This may vary in its degree from light spotting to heavy bleeding, and may even include passage of hydropic villi. Heavy or persistent bleeding can lead to anaemia, with symptoms of dizziness and fatigue.

Women may report exacerbated symptoms of pregnancy (as a result of abnormally high serum hCG levels) that include severe nausea and emesis (hyperemesis gravidarum), palpitations, insomnia and diarrhoea (from thyrotoxicity), and headache and photophobia (from early-onset pre-eclampsia).[24] [25] [35] High-output cardiac failure from hyperthyroidism, severe pre-eclampsia, and, less commonly, anaemia may lead to dyspnoea and respiratory distress. Dyspnoea may also indicate trophoblastic emboli or pulmonary metastases. Because it is accompanied by significantly higher levels of serum hCG, complete hydatidiform mole is more likely to be associated with these symptoms than partial molar pregnancy.[23] Women with molar pregnancies may also experience pelvic pain secondary to ovarian theca lutein cysts.

Hydatidiform moles with severe medical complications occur less frequently because of early diagnosis from the widespread use of ultrasound in the first trimester of pregnancy. About 50% of women with molar pregnancies are diagnosed while still asymptomatic. However, earlier diagnosis has not been associated with a lower occurrence of post-molar gestational trophoblastic neoplasia (GTN), and prognosis is still a clinical challenge.[24] [25]

Physical examination

The uterine size is greater than expected for gestational age in approximately 25% of complete molar pregnancies.[36] [37] There may be active bleeding from the cervical os, and there may be spontaneous evacuation of hydropic vesicles from the cervix.[4]

Other signs include pallor, tachycardia, tremor, hypertension, and respiratory distress. Because of the molecular homology between subunits of thyroid-stimulating hormone and hCG, serum hCG may stimulate the production of thyroid hormone with the clinical symptoms and signs of thyrotoxicosis.[26] [38][39] However, the absence of ophthalmopathy differentiates molar pregnancy from thyrotoxicosis due to Graves' disease.[40]

Laboratory investigations

Most molar pregnancies (MPs) are diagnosed incidentally at pathological evaluation of a suction evacuation (electrical or manual) specimen for missed abortion or from early maternal ultrasound screening in the first trimester of pregnancy.[31] Many women who are diagnosed with MP at an early maternal ultrasound screening in the first trimester of pregnancy terminate pregnancy before the development of the classic signs and symptoms.[24] [25] [35] For this reason, most authorities consider it mandatory to conduct histological examination of miscarriage tissue.[4] [34]

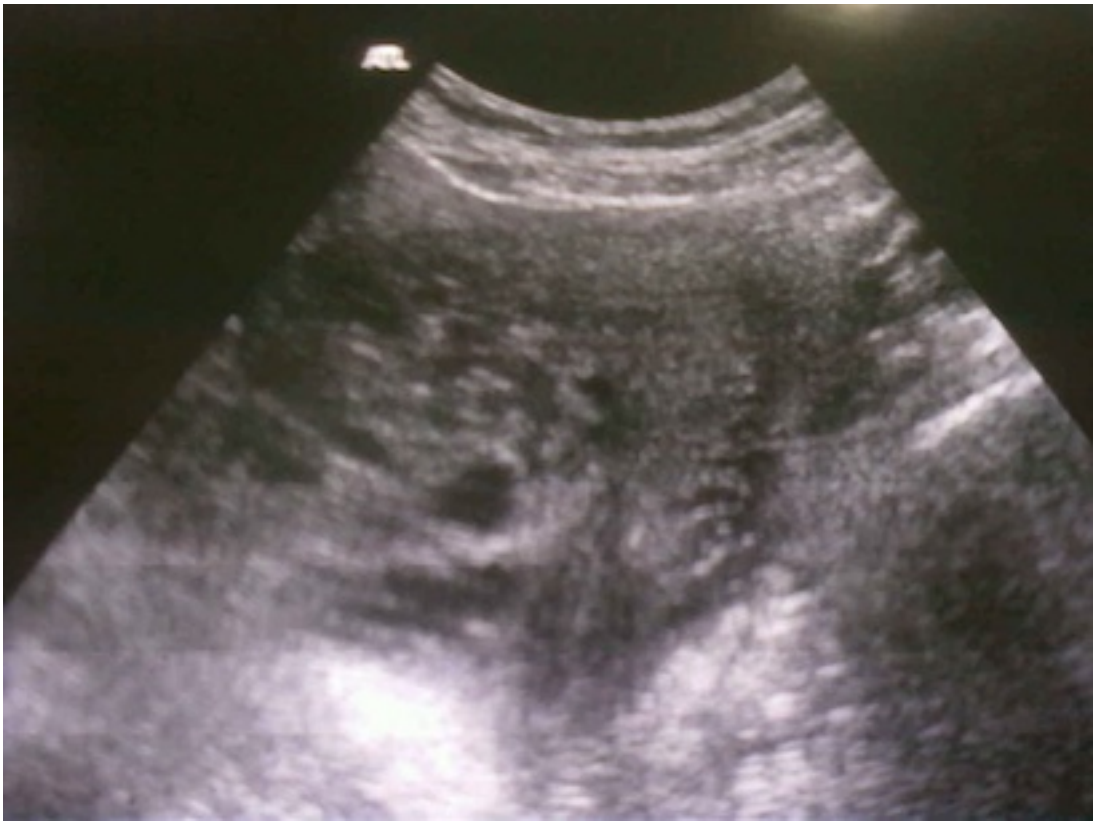
hCG is secreted by syncytiotrophoblasts, which proliferate excessively in molar pregnancy, and so it is a sensitive biomarker for diagnosis of MP, response to treatment and follow-up monitoring for GTN.[22] Normal pregnancies are associated with a peak serum hCG level of <100,000 mIU/mL.[23] However, hCG levels alone should not be used to infer the presence of a molar pregnancy because greater than expected hCG levels may be seen in multiple gestations. Serum hCG acts as a tumour marker to follow post-molar regression and to identify post-molar gestational trophoblastic neoplasia. In the absence of histopathology, post-treatment measurement of hCG levels should be performed weekly until normalisation of hCG levels or diagnosis of GTN. The duration of monitoring varies by country.[3] The International Federation of Gynecology and Obstetrics recommends monitoring hCG every 1-2 weeks post-treatment until levels return to normal, followed by a single confirmatory normal measurement within a month for partial hydatidiform moles and monthly hCG measurements for 6 months for complete hydatidiform moles.[4] [41] In the UK, the Royal College of Obstetricians & Gynaecologists (RCOG) recommends monitoring hCG levels post-treatment until there are two normal measurements at least 4 weeks apart for partial hydatidiform moles. For complete hydatidiform moles, RCOG recommends monitoring hCG levels every month for 6 months either post-treatment if normalisation took up to 56 days or from the date of normalisation if this took more than 56 days.[34]

Anaemia may result from heavy or persistent vaginal bleeding and the dilutional effects of increased blood volume. There is a greater risk for serious bleeding at the time of evacuation for MP, with a risk of disseminated intravascular coagulation from blood loss or trophoblastic embolism, although these are the rarest complications of molar pregnancy.

About 15% to 20% of women with complete molar pregnancies and 0.5% to 5% of women with partial molar pregnancies develop GTN and require chemotherapy.[4] [42] These chemotherapy agents require normal liver and renal function for optimal dosing. Women undergoing evacuation of molar pregnancies are at increased risk of bleeding significant enough to require a blood transfusion. Blood typing ensures that type-appropriate blood can be made available in the event of haemorrhage.

Imaging

Pelvic ultrasound is the mainstay of diagnosis and an essential component in the evaluation of suspected GTN.[31] [43] Typical ultrasound findings for a complete molar pregnancy include a diffuse echogenic pattern described as a snow-storm pattern, which is created by intermingling of hydropic villi and blood clots.[3] [42] The presence of a smaller volume of abnormal placenta with partial fetal development, without fetal cardiac activity, is characteristic of a partial molar pregnancy.[3] [42] Cystic enlargement of the ovaries may represent theca lutein cysts.[3]



Ultrasound showing multiple cystic areas in the uterine cavity giving a 'snowstorm appearance' suggestive of molar pregnancy.
Nigam A, Kumari A, Gupta N. Negative urine pregnancy test in a molar pregnancy: is it possible? Case Reports 2014;2014:bcr2014206483.

Advanced imaging, such as CT scan or MRI, is not typically required for benign moles, unless the woman has signs or symptoms of pulmonary or brain metastases.[4]

Women with an established diagnosis of gestational trophoblastic neoplasia (GTN)

The FIGO diagnostic criteria for post-molar GTN without symptoms are based on surveillance of hCG levels and histopathology:[4]

- Four or more measurements of plateaued hCG levels over a 3-week period (on days 1, 7, 14, and 21).
- An increase in hCG levels for three or more consecutive weekly measurements over a period of at least 2 weeks (on days 1, 7, and 14).
- A histopathological diagnosis of choriocarcinoma.

Women with an established diagnosis of GTN following molar pregnancy should be evaluated with a pelvic examination and chest x-ray.[3] Pulmonary congestion, oedema, alveolar infiltrates, and metastatic nodules may be visible on the chest radiograph. If the chest x-ray is inconclusive, if there are metastases ≥1 cm or the woman has a signs or symptoms of metastatic disease, computed tomography scans of the chest, abdomen, and pelvis should be performed and magnetic resonance imaging of the brain should be obtained to further evaluate and stage metastases.[3] [4]

History and exam

Key diagnostic factors

presence of risk factors (common)

- The patient may be at the extremes of reproductive age (<20 years of age, >35 years of age), or have a history of prior molar pregnancy.[10] [27] [44] [45] [46]

first trimester of pregnancy (common)

- Women typically present in the first trimester of pregnancy with a history of a missed menstrual period.
- Most molar pregnancies are diagnosed incidentally at pathological evaluation of an evacuated dilation and evacuation (D&E) specimen for missed abortion, or from early maternal ultrasound screening in the first trimester of pregnancy.[30] [31]

vaginal bleeding (common)

- Vaginal bleeding is the most common presenting symptom of molar pregnancies (58% to 84%).[30] [34] This may vary in its degree from light spotting to heavy bleeding, and may include passage of hydropic villi. Heavy or persistent bleeding can lead to anaemia.

unusual uterine size for gestational age (common)

- The uterine size is greater than expected for gestational age in approximately 25% of complete molar pregnancies.[36][37]
- However, the uterine size may be smaller than anticipated in partial molar pregnancies because of fewer hydropic villi and abnormal fetal development (e.g., slow growth of a fetus with triploidy).

Other diagnostic factors

early-onset pre-eclampsia (uncommon)

- Exacerbated signs and symptoms of pre-eclampsia such as hypertension, headache, and photophobia may be present before 20 weeks' gestation (as a result of abnormally high serum human chorionic gonadotrophin [hCG] levels).
- Ophthalmopathy is absent.

shortness of breath and respiratory distress (uncommon)

- High-output cardiac failure from hyperthyroidism, severe pre-eclampsia and, less commonly, anaemia may lead to dyspnoea and respiratory distress.

severe nausea and emesis (uncommon)

- Women with complete hydatidiform moles report exacerbated symptoms of pregnancy (as a result of abnormally high serum hCG levels) that include severe nausea and emesis (hyperemesis gravidarum).[47]

tachycardia, tremor, insomnia, and diarrhoea (uncommon)

- There is molecular homology between subunits of thyroid-stimulating hormone and hCG. As a result, serum hCG may stimulate the production of thyroid hormone with the clinical symptoms and signs of thyrotoxicosis.[26] [38][39]
- Ophthalmopathy is absent.

pallor (uncommon)

- Anaemia may result from heavy or persistent vaginal bleeding and the dilational effects of increased blood volume.

pelvic pain (uncommon)

- Women with molar pregnancies may experience pelvic pain secondary to ovarian theca lutein cysts.

uterine bleeding (uncommon)

- There may be active bleeding from the cervical os, and there may be spontaneous evacuation of hydropic vesicles from the cervix.[4]

Risk factors

Strong

extremes of maternal age

- There is a significantly higher chance of MP among women over 35 years of age, which increases progressively as maternal age advances.[10] [11] [12] [13] There is a modestly increased risk of MP among women with a maternal age of less than 20 years.[14] [15]

prior molar pregnancy

- Women with a previous diagnosis of hydatidiform mole have a 1% to 2% (or about 10 times the baseline) risk of a molar gestation in a subsequent pregnancy.[8] [9]

Weak

diminished dietary fat and carotene

- It has been suggested that reduced dietary animal fat and carotene intake in certain geographic areas (e.g., Latin America and Southeast Asia) might account for the higher rate of MP in these populations.[27] [28] [29]

Investigations

1st test to order

Test	Result
histological examination of placental tissue • Many women with hydatidiform mole terminate pregnancy before the development of the classic signs and symptoms.[35] [48] For this reason, most authorities consider it mandatory to conduct histological examination of miscarriage tissue.[4] [34]	**placental villi with irregular architecture, oedema with true villous cavitation, and trophoblast hyperplasia**
serum human chorionic gonadotrophin (hCG) • Abnormally elevated serum hCG levels for gestational age.	**often >100,000 IU/L (100,000 mIU/mL)**
pelvic ultrasound • May demonstrate snow-storm appearance of the uterine cavity and the absence of fetal parts (complete molar pregnancy); or a small placenta with partial fetal development (partial molar pregnancy).	**abnormal with uterine enlargement, may demonstrate ovarian cysts**

Other tests to consider

Test	Result
FBC • Anaemia may result from heavy or persistent vaginal bleeding and dilutional effects of increased blood volume.	**may show anaemia**
serum PT, PTT • A greater risk for serious bleeding at the time of evacuation for MP.	**may be prolonged**
serum metabolic panel • Normal liver and renal function may be essential for optimal dosing of chemotherapeutic agents.	**may show renal or hepatic dysfunction**
serum thyroid-stimulating hormone (TSH) • Cross-reactivity of beta hCG and TSH may lead to thyrotoxicosis in the absence of elevated levels of TSH.	**normal**
blood type with antibody screen • Blood typing ensures that type-appropriate blood can be made available in the event of haemorrhage.	**A, B, AB, O; Rhesus status may be negative or positive**
CXR • Pulmonary oedema may be secondary to high-output cardiac failure from severe pre-eclampsia and, less commonly, from anaemia or hyperthyroidism. • Alveolar infiltrates may be a sign of respiratory distress syndrome. • Pulmonary nodules may represent metastatic disease.	**may show Kerley B lines, fluid within pulmonary fissures, interstitial markings, alveolar infiltrates,#pulmonary nodules**

Differentials

Condition	Differentiating signs / symptoms	Differentiating tests
Hyperemesis gravidarum	• A common presenting symptom. Nausea and vomiting might develop earlier and be more severe because of unusually high hCG levels.	• Routine early maternal screening ultrasound has enabled earlier diagnosis of molar pregnancy, before severe clinical symptoms develop. Hyperemesis associated with a molar gestation resolves promptly after evacuation, roughly in parallel to the decline in hCG levels.
Spontaneous abortion	• Risk factors include older parental age, infection, and thrombophilias. • Cramp-like discomfort may signify the process of expulsion of the fetus.	• Ultrasound findings of a complete mole are characteristically different from spontaneous abortion. A partial mole may contain a fetal pole or fetus, usually without cardiac activity, and may be more difficult to discriminate from a missed abortion. • Inspection of evacuated tissue for hydropic villi, and chromosome testing of evacuated tissue may be confirmatory.
Multiple gestation	• The uterus is larger than expected for dates, and there is an elevated serum hCG level with corresponding symptoms of nausea and emesis. Multiple gestations can be complicated with a complete or partial mole and a co-existing viable fetus, but it is rare for molar pregnancies to be associated with multiple gestation.	• Ultrasound with uterine enlargement greater than expected for gestational age and multiple fetuses.
Ovarian cysts	• Elevated levels of hCG or hypersensitivity to hCG causes gross cystic enlargement of the ovaries. Ovarian cysts may present with pelvic or abdominal masses or ovarian torsion. Pelvic pressure and abdominal extension are common. The theca lutein	• Theca lutein cysts are difficult to diagnose by palpation because of uterine enlargement. However, ultrasound identifies enlarged ovaries with cysts >6 cm in diameter. After evacuation of the MP, ovarian cysts spontaneously

Condition	Differentiating signs / symptoms	Differentiating tests
	cysts of molar pregnancies are typically a painful condition.	regress within about 12 weeks.
Uterine fibroids	• Symptoms include an enlarged uterus on examination, pelvic pain and pressure, and bleeding.	• Pelvic ultrasound shows well-defined uterine tumours.
Hyperthyroidism	• History of heat intolerance, palpitations, and anxiety.	• Enlarged and possibly tender thyroid and thyroid nodules on palpation. • Decreased thyroid-stimulating hormone and elevated thyroxine (T4).
Pre-eclampsia	• New-onset, persistent hypertension (defined as a systolic blood pressure ≥140 mmHg and/or a diastolic blood pressure ≥90 mmHg), usually after 20 weeks' gestation, with new-onset proteinuria (protein:creatinine ratio of ≥30 mg/mmol and albumin:creatinine ratio of ≥8 mg/mmol) or evidence of systemic involvement.	• In molar pregnancy, symptoms of pre-eclampsia might develop earlier and be more severe because of unusually high hCG levels.
Ectopic pregnancy	• Missed menstrual period, lower quadrant pain, or pelvic pain with some degree of vaginal bleeding or spotting. Cervical motion tenderness may be present on pelvic examination.	• Elevated hCG levels. • Ultrasound reveals an empty uterus and may show a mass in the fallopian tubes.
Pelvic tumour	• May present with an enlarged uterus and painless bleeding of uterine and adnexal masses. • Nausea, emesis, and hyperthyroidism are not typically seen in pelvic malignancies.	• Serum hCG levels are rarely elevated with pelvic tumours. • Ultrasound of the pelvis demonstrates a uterine mass or abnormal adnexal organs. • Pelvic computed tomography generally is diagnostic. • Pathology of the products of dilation and suction evacuation may confirm tumour histology.

Screening

Routine early maternal screening ultrasound is recommended for a variety of reasons, including evaluation of the cause of vaginal bleeding or suspected gestational trophoblastic disease (such as hydatidiform moles), assessment of gestational age, and identification of multiple gestations.[43] [49]

Approach

Care of women with molar pregnancy generally requires the expertise of a consultant. Women who desire preservation of fertility should undergo suction evacuation (electrical or manual), usually under ultrasound guidance.[3] [4] [34] Hysterectomy may be considered in women who do not want to preserve fertility.[3] [4] [34] [42]

Supportive care

Women with unevacuated hydatidiform moles generally require stabilisation of associated comorbidities (e.g., respiratory distress, pre-eclampsia/eclampsia, hyperthyroidism, or severe anaemia) before definitive treatment. Using a large-bore intravenous catheter is appropriate in women with uterine enlargement greater than 14 weeks' gestational size, in anticipation of the need to rapidly administer intravenous fluids and blood products at the time of evacuation.

Oxytocics or other means of inducing labour should not be given before cervical dilation intraoperatively.

Prophylactic antibiotics are not considered mandatory, and are reserved for clinical concerns of infected products of conception.

Sequential compression stockings, as a single modality, is considered adequate for venous thrombo-embolism prophylaxis.

High-output cardiac failure may be secondary to hyperthyroidism or thyroid storm, severe pre-eclampsia, gestational hypertension, pulmonary oedema, and, less commonly, anaemia.[50] This condition is usually self-limiting, and resolves over time after complete removal of the molar pregnancy. It is best treated with supportive care, including mechanical ventilation tailored to minimise barotrauma, and central haemodynamic monitoring.

Women desiring future pregnancy

Suction evacuation (electrical or manual) is the preferred management option for women with molar pregnancies who desire preservation of fertility.[3] [4] [34]

Technique

- General anaesthesia is achieved, and beta-blockade given if the women is clinically hyperthyroid.[51] Women who are Rho (D)-negative should receive anti-D immunoglobulin.[52] After the cervix is gently mechanically dilated with tapered Pratt dilators, intravenous oxytocin may be given to facilitate involution of the uterus. A suction cannula is advanced gently to the uterine fundus, and rotated while mechanical suction is applied. Sharp uterine curettage is not recommended because of the risk of uterine perforation, and equivalent outcomes with the suction method.[53]

In the absence of histopathology, post-treatment measurement of human chorionic gonadotrophin (hCG) levels should be performed weekly until normalisation of hCG levels or diagnosis of gestational trophoblastic neoplasia (GTN). The duration of monitoring varies by country.[3] (see Monitoring)

During the period of follow-up after evacuation of the mole, strict adherence to contraception should be advised.[3] [34][54] Unless contraindicated for separate medical conditions, women should commence a reliable method of hormonal birth control, such as an oral contraceptive, immediately after uterine

evacuation.[55] [56] However, intrauterine devices (medicated or not) are contraindicated in women with active, invasive tumours or persistently elevated hCG levels because of the risk of uterine perforation.[54] (see Patient discussions)

Women not desiring future pregnancy

Hysterectomy may be more desirable for the management of molar pregnancy than suction evacuation in women who have completed childbearing.[57] It is associated with an increased risk of postoperative complications compared with suction evacuation, but a decreased risk of postoperative GTN.[57] Women undergoing hysterectomy for the management of molar pregnancy should also be monitored postoperatively with the measurement of serial hCG levels.

With hyperemesis gravidarum

The objectives of managing a woman with molar pregnancy complicated by hyperemesis revolve around symptomatic control of emesis with an anti-emetic and/or an H2 antagonist and intravenous hydration with electrolyte replacement, while moving towards prompt removal of the hydatidiform mole. Hyperemesis associated with a molar gestation resolves promptly after removal, roughly in parallel with the decline in hCG levels. Complete hydatidiform mole, because it is accompanied by significantly higher levels of hCG, is more likely to be associated with these symptoms than partial hydatidiform mole.[23][24] [25] [26]

With active bleeding

Bleeding can complicate hydatidiform mole, as acute haemorrhage before treatment, surgical management, or as delayed haemorrhage during follow-up of a patient after evacuation of a molar pregnancy. It is important to establish the baseline haemogram in women with molar pregnancy before treatment. Women who are Rho (D)-negative should receive anti-D immunoglobulin.[52] Women with severe anaemia or haemodynamic instability require transfusion before treatment.

If acute haemorrhage occurs before or during surgical management, the procedure should be completed promptly and the benefit of oxytocic infusion considered against the risk of embolisation and dissemination of trophoblastic tissue through the venous system.[34] The use of oxytocic agents or methylergometrine will control bleeding after surgical management in most women.[34] Prostaglandins can be considered, if acute bleeding during or after evacuation is encountered. Bleeding around the time of uterine evacuation rarely requires uterine artery embolisation or hysterectomy. Delayed haemorrhage after uterine evacuation (while hCG levels are still elevated) is often a sign of trophoblastic proliferation. Rarely, a woman will require a second suction evacuation to control symptomatic haemorrhage after the initial molar evacuation.[34]

In women with an established diagnosis of post-molar GTN, chemotherapy will usually control bleeding.

Very rarely, women with normal hCG levels develop delayed bleeding after molar evacuation. These women will often have a history of heavy menstrual bleeding preceding the episodes of spontaneous bleeding. Pelvic-transvaginal Doppler ultrasound or contrast magnetic resonance imaging studies of the uterus may be helpful to exclude post-molar uterine arteriovenous malformation. Depot medroxyprogesterone and tranexamic acid, selective embolisation, myometrial wedge resection and repair, or hysterectomy may be required to treat these lesions.[58]

With thyrotoxicity

Thyrotoxicosis in molar pregnancy is typically self-limited and best treated with supportive care. Beta-blockers should be given with the induction of anaesthesia at the time of surgical management, if the woman is clinically hyperthyroid. Carbimazole can be added, if a faster clinical response is needed or there is a thyrotoxic storm.[51]

With pre-eclampsia

Anti-hypertensive therapy should be started if systolic BP is persistently between 140 and 159 mmHg and/or diastolic BP is persistently between 90 and 109 mmHg, or if there is severe hypertension (systolic BP ≥160 mmHg and/or diastolic BP ≥110 mmHg).[59] [60]

In the US, magnesium sulfate is recommended for all women with severe pre-eclampsia.[59] In other countries, including the UK, a more targeted approach is recommended, allowing the physician to exercise individual judgment based on the woman's specific risk factors (e.g., presence of uncontrolled hypertension or deteriorating maternal condition).[60] Seizures reflect progression to eclampsia, and are both treated and prevented with magnesium sulfate. The Food and Drug Administration (FDA) and MHRA recommend that maternal administration of magnesium sulfate should not last longer than 5-7 days during pregnancy due to the risk of skeletal adverse effects, hypercalcaemia, and hypermagnesemia in the neonate.[61] [62] Despite the recommendation, magnesium sulfate is usually only used for 24-48 hours in clinical practice.

Management of molar pregnancy with a viable twin generally entails close observation for pre-eclampsia as the pregnancy is carried to either voluntary termination, forced delivery, or term. Definitive treatment of pre-eclampsia consists of delivery. The decision about when and how to deliver should only be made after a thorough assessment of the risk and benefits to the mother and co-existing twin.

With theca lutein cyst

Theca lutein cysts result from hCG stimulation of the ovaries and may present with pelvic or abdominal masses, pain, or ovarian torsion. Their incidence is 7% to 9% among women with complete hydatidiform moles.[24] [25] The presence of theca lutein cysts does not necessarily mandate ovarian removal because these cysts are a response to ovarian exposure to elevated hCG levels or hypersensitivity of the ovaries to hCG. They usually involute over time after surgical management of molar pregnancy, and can be drained or, exceptionally, removed, if ovarian torsion with necrosis is confirmed.[50]

With viable twin fetus

Management of molar pregnancy with a viable twin generally entails close observation as the pregnancy is carried to either voluntary termination, forced delivery due to medical complications (e.g., bleeding, severe pre-eclampsia, hyperthyroidism, or acute respiratory distress) or term.[34] Conservative management is not recommended in the presence of choriocarcinoma or fetal aneuploidy.[4] Postnatal, the placenta should be sent for evaluation by a pathologist experienced in the evaluation of GTD, and routine post-molar surveillance should be initiated.[34] Importantly, with careful medical monitoring, about 60% achieve viable live births.[63] Twin pregnancies comprising a viable fetus and a coexisting hydatidiform mole have an increased risk of GTN, with a higher proportion of these women developing metastatic disease or requiring chemotherapy.[63]

With risk of post-molar GTN and non-compliance with follow-up

Chemoprophylaxis is given only after evacuation of a hydatidiform mole and assessment of clinical and social risk factors. A clinical risk assessment is used to identify women at low risk or high risk of developing post-molar GTN.[4] In women who are at high risk of developing GTN (e.g., maternal age >40 years, women with complete hydatidiform moles or hCG levels >100,000 mIU/mL) and in whom hCG monitoring is either unavailable or unlikely to be followed, it may be possible to reduce the risk of GTN by administering chemoprophylaxis with methotrexate or dactinomycin.[4] [64]

Treatment algorithm overview

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

Acute (summary)			
singleton molar pregnancy: desiring fertility			
		1st	suction evacuation
		plus	supportive care
		plus	contraception
		adjunct	anti-D immunoglobulin
	with hyperemesis gravidarum	plus	fluid replacement plus anti-emetic and/or H2 antagonist
	with active bleeding	plus	blood products and cessation of blood loss
	with thyrotoxicity	plus	beta-blocker ± carbimazole
	with pre-eclampsia	plus	anti-hypertensives
		adjunct	magnesium sulfate
	with theca lutein cyst	plus	management of cyst
singleton molar pregnancy: not desiring fertility			
		1st	hysterectomy
		plus	supportive care
	with hyperemesis gravidarum	plus	fluid replacement plus anti-emetic and/or H2 antagonist
	with active bleeding	plus	blood products and cessation of blood loss
	with thyrotoxicity	plus	beta-blocker ± carbimazole
	with pre-eclampsia	plus	anti-hypertensives
		adjunct	magnesium sulfate
	with theca lutein cyst	plus	management of cyst
viable twin fetus: elective termination not desired			
		1st	expectant management
	with hyperemesis gravidarum	plus	fluid replacement plus anti-emetic and/or H2 antagonist
	with active bleeding	plus	blood products and cessation of bleeding

Acute (summary)		
with thyrotoxicity	plus	beta-blocker ± carbimazole
with pre-eclampsia	plus	anti-hypertensives
	adjunct	magnesium sulfate
with theca lutein cyst	plus	management of cyst
viable twin fetus: elective termination		
	1st	suction evacuation
	plus	supportive care
with hyperemesis gravidarum	plus	fluid replacement plus anti-emetic and/or H2 antagonist
with active bleeding	plus	blood products and cessation of bleeding
with thyrotoxicity	plus	beta-blocker ± carbimazole
with pre-eclampsia	plus	anti-hypertensives
	adjunct	magnesium sulfate
with theca lutein cyst	plus	management of cyst

Ongoing (summary)		
following initial management: high risk of gestational trophoblastic neoplasia with completed follow up unlikely		
	1st	prophylactic chemotherapy

Treatment algorithm

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

Acute

singleton molar pregnancy: desiring fertility

1st **suction evacuation**

» General anaesthesia is achieved, and beta-blockade given, if the woman is clinically hyperthyroid.[51] After the cervix has been gently mechanically dilated with tapered Pratt dilators, intravenous oxytocin may be given to facilitate involution of the uterus. A suction cannula should be advanced gently to the uterine fundus, and rotated while mechanical suction is applied.

» Sharp uterine curettage is not recommended because of the risk of uterine perforation, and equivalent outcomes with the suction method.[53]

plus **supportive care**

Treatment recommended for ALL patients in selected patient group

» Women with unevacuated hydatidiform moles generally require stabilisation of associated comorbidities (e.g., respiratory distress, pre-eclampsia/eclampsia, hyperthyroidism, or severe anaemia) before definitive treatment.

» Using a large-bore intravenous catheter is appropriate in women with uterine enlargement >14 weeks' gestational size, in anticipation of the need to rapidly administer intravenous fluids and blood products at the time of evacuation.

» Oxytocics or other means of inducing labour should not be given before cervical dilation intraoperatively.

» Prophylactic antibiotics are not considered mandatory, and are reserved for clinical concerns of infected products of conception.

» Sequential compression stockings, as a single modality, is considered adequate for venous thrombo-embolism prophylaxis.

» High-output cardiac failure may be secondary to hyperthyroidism or thyroid storm, severe pre-eclampsia, gestational hypertension, pulmonary oedema, and, less commonly, anaemia.[50]

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This condition is usually self-limiting, and resolves over time after complete removal of the molar pregnancy. It is best treated with supportive care, including mechanical ventilation tailored to minimise barotrauma, and central haemodynamic monitoring.

plus **contraception**

Treatment recommended for ALL patients in selected patient group

» During the period of follow-up after evacuation of the mole, strict adherence to contraception should be advised.[3] [34] [54]

» Unless contraindicated for separate medical conditions, women should commence a reliable method of hormonal birth control, such as an oral contraceptive, immediately after molar evacuation.[55] [56]

» However, intrauterine devices (medicated or not) are contraindicated in women with active, invasive tumours or persistently elevated hCG levels because of the risk of uterine perforation.[54] (see Patient discussions)

adjunct **anti-D immunoglobulin**

Treatment recommended for SOME patients in selected patient group

Primary options

» anti-D immunoglobulin: consult specialist for guidance on dose
Dose varies between brands.

» Women who are Rho (D)-negative should receive anti-D immunoglobulin.[52]

with hyperemesis gravidarum

plus **fluid replacement plus anti-emetic and/or H2 antagonist**

Treatment recommended for ALL patients in selected patient group

Primary options

» metoclopramide: 5-10 mg intravenously/intramuscularly every 8 hours when required for a maximum of 5 days, maximum 30 mg/day

OR

» prochlorperazine rectal: 25 mg twice daily when required

Secondary options

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» ondansetron: 4 mg intravenously/orally every 8 hours when required

OR

» famotidine: 20 mg intravenously every 12 hours

» The objectives of managing a woman with molar pregnancy complicated by hyperemesis revolve around symptomatic control of emesis with an anti-emetic and/or an H2 antagonist and intravenous hydration with electrolyte replacement, while moving towards prompt removal of the hydatidiform mole. Hyperemesis associated with a molar gestation resolves promptly after removal, roughly in parallel with the decline in hCG levels. Complete hydatidiform mole, because it is accompanied by significantly higher levels of hCG, is more likely to be associated with these symptoms than partial hydatidiform mole.[23] [24][25] [26]

» Metoclopramide should be used for up to 5 days only, in order to minimise the risk of neurological and other adverse effects.[65]

with active bleeding **plus** **blood products and cessation of blood loss**

Treatment recommended for ALL patients in selected patient group

Primary options

» oxytocin: 10 units intramuscularly as a single dose; or 10-40 units by intravenous infusion at a rate to control uterine atony

Secondary options

» methylergometrine: 0.2 mg orally three to four times daily for up to 7 days; or 0.2 mg intramuscularly every 2-4 hours as required

» Women with severe anaemia or haemodynamic instability require transfusion before treatment.

» If acute haemorrhage occurs before or during surgical management, the procedure should be completed promptly and the benefit of oxytocic infusion considered against the risk of embolisation and dissemination of trophoblastic tissue through the venous system.[34] The use of oxytocic agents or methylergometrine will control bleeding after surgical management in most women.[34] Prostaglandins can be

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considered, if acute bleeding during or after evacuation is encountered.

» Rarely, women will require a second suction evacuation to control symptomatic haemorrhage after the initial molar evacuation.[34]

» In women with an established diagnosis of post-molar GTN, chemotherapy will usually control bleeding.

» Very rarely, women with normal hCG levels develop delayed bleeding after molar evacuation.

» Pelvic-transvaginal Doppler ultrasound or contrast magnetic resonance imaging studies of the uterus may be helpful to exclude post-molar uterine arteriovenous malformation.

» Depot medroxyprogesterone and tranexamic acid, selective embolisation, myometrial wedge resection and repair, or hysterectomy may be required.[58]

with thyrotoxicity **plus** **beta-blocker ± carbimazole**

Treatment recommended for ALL patients in selected patient group

Primary options

» propranolol: 60-80 mg orally (immediate-release) every 4-6 hours

OR

» propranolol: 60-80 mg orally (immediate-release) every 4-6 hours
-and-
» carbimazole: 15-40 mg orally daily until patient becomes euthyroid, followed by 5-15 mg daily

» Thyrotoxicosis in molar pregnancy is typically self-limited and best treated with supportive care.

» Beta-blockers should be given with the induction of anaesthesia at the time of surgical management, if the woman is clinically hyperthyroid. Carbimazole can be added, if a faster clinical response is needed or there is a thyrotoxic storm.[51]

»

with pre-eclampsia **plus** **anti-hypertensives**

Treatment recommended for ALL patients in selected patient group

MANAGEMENT

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Primary options

» labetalol: 100 mg orally twice daily initially, increase gradually according to response, usual dose 100-400 mg twice daily, maximum 2400 mg/day

OR

» nifedipine: 30-60 mg orally (extended-release) once daily initially, increase gradually according to response, maximum 90-120 mg/day (depending on brand)

OR

» methyldopa: 250 mg orally two to three times daily initially, increase gradually according to response, usual dose 250-1000 mg/day given in 2-4 divided doses, maximum 3000 mg/day

» Anti-hypertensive therapy should be started if systolic BP is persistently between 140 and 159 mmHg and/or diastolic BP is persistently between 90 and 109 mmHg, or if there is severe hypertension (systolic BP ≥160 mmHg and/or diastolic BP ≥110 mmHg).[59] [60]

adjunct **magnesium sulfate**

Treatment recommended for SOME patients in selected patient group

Primary options

» magnesium sulfate: consult specialist for guidance on dose
Dose depends on the indication, route of administration, and local guidelines. High-dose regimens may be recommended for the treatment of eclampsia in some countries such as the US, while low-dose regimens may be recommended in other countries. Consult your local drug formulary or guidelines for further guidance.

» In the US, magnesium sulfate is recommended for all women with severe pre-eclampsia.[59] In other countries, including the UK, a more targeted approach is recommended, allowing the physician to exercise individual judgment based on the woman's specific risk factors (e.g., presence of uncontrolled hypertension or deteriorating maternal condition).[60] Seizures reflect progression to eclampsia,

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and are both treated and prevented with magnesium sulfate. The Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA) recommend that maternal administration of magnesium sulfate should not last longer than 5-7 days during pregnancy due to the risk of skeletal adverse effects, hypercalcaemia, and hypermagnesemia in the neonate.[61] [62] Despite the recommendation, magnesium sulfate is usually only used for 24-48 hours in clinical practice.

with theca lutein cyst **plus** **management of cyst**

Treatment recommended for ALL patients in selected patient group

» Theca lutein cysts result from hCG stimulation of the ovaries and may present with pelvic or abdominal masses, pain, or ovarian torsion. The presence of theca lutein cysts does not necessarily mandate ovarian removal because these cysts are a response to ovarian exposure to elevated hCG levels or hypersensitivity of the ovaries to hCG. They usually involute over time after surgical management of molar pregnancy and can be drained or, exceptionally, removed, if ovarian torsion with necrosis is confirmed.[50]

singleton molar pregnancy: not desiring fertility

1st **hysterectomy**

» Hysterectomy may be more desirable for the management of molar pregnancy than suction evacuation in women who have completed childbearing.[57] It is associated with an increased risk of postoperative complications comapred with suction evacuation, but a decreased risk of postoperative GTN.[57] Women undergoing hysterectomy for the management of molar pregnancy should also be monitored postoperatively with the measurement of serial hCG levels.

plus **supportive care**

Treatment recommended for ALL patients in selected patient group

» Women with unevacuated hydatidiform moles generally require stabilisation of associated comorbidities (e.g., respiratory distress, pre-eclampsia/eclampsia, hyperthyroidism, or severe anaemia) before definitive treatment.

» Prophylactic antibiotics are not considered mandatory, and are reserved for clinical concerns of infected products of conception.

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» Sequential compression stockings, as a single modality, is considered adequate for venous thromboembolism prophylaxis.

» High-output cardiac failure may be secondary to hyperthyroidism or thyroid storm, severe pre-eclampsia, gestational hypertension, pulmonary oedema, and, less commonly, anaemia.[50] This condition is usually self-limiting, and resolves over time after complete removal of the molar pregnancy. It is best treated with supportive care, including mechanical ventilation tailored to minimise barotrauma, and central haemodynamic monitoring.

with hyperemesis gravidarum **plus** **fluid replacement plus anti-emetic and/or H2 antagonist**

Treatment recommended for ALL patients in selected patient group

Primary options

» metoclopramide: 5-10 mg intravenously/intramuscularly every 8 hours when required for a maximum of 5 days, maximum 30 mg/day

OR

» prochlorperazine rectal: 25 mg twice daily when required

Secondary options

» ondansetron: 4 mg intravenously/orally every 8 hours when required

OR

» famotidine: 20 mg intravenously every 12 hours

» The objectives of managing a woman with molar pregnancy complicated by hyperemesis revolve around symptomatic control of emesis with an anti-emetic and/or an H2 antagonist and intravenous hydration with electrolyte replacement, while moving towards prompt removal of the hydatidiform mole. Hyperemesis associated with a molar gestation resolves promptly after removal, roughly in parallel with the decline in hCG levels. Complete molar pregnancy, because it is accompanied by significantly higher levels of hCG, is more likely to be associated with these symptoms than partial hydatidiform mole.[23] [24][25] [26]

Acute

» Metoclopramide should be used for up to 5 days only, in order to minimise the risk of neurological and other adverse effects.[65]

with active bleeding **plus** **blood products and cessation of blood loss**

Treatment recommended for ALL patients in selected patient group

Primary options

» oxytocin: 10 units intramuscularly as a single dose; or 10-40 units by intravenous infusion at a rate to control uterine atony

Secondary options

» methylergometrine: 0.2 mg orally three to four times daily for up to 7 days; or 0.2 mg intramuscularly every 2-4 hours as required

» Women with severe anaemia or haemodynamic instability require transfusion before treatment.

» If acute haemorrhage occurs before or during surgical management, the procedure should be completed promptly and the benefit of oxytocic infusion considered against the risk of embolisation and dissemination of trophoblastic tissue through the venous system.[34] The use of oxytocic agents or methylergometrine will control bleeding after surgical management in most women.[34]

with thyrotoxicity **plus** **beta-blocker ± carbimazole**

Treatment recommended for ALL patients in selected patient group

Primary options

» propranolol: 60-80 mg orally (immediate-release) every 4-6 hours

OR

» propranolol: 60-80 mg orally (immediate-release) every 4-6 hours
-and-
» carbimazole: 15-40 mg orally daily until patient becomes euthyroid, followed by 5-15 mg daily

» Thyrotoxicosis in molar pregnancy is typically self-limited and best treated with supportive care.

» Beta-blockers should be given with the induction of anaesthesia at the time of surgical

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management, if the woman is clinically hyperthyroid. Carbimazole can be added, if a faster clinical response is needed or there is a thyrotoxic storm.[51]

with pre-eclampsia **plus** **anti-hypertensives**

Treatment recommended for ALL patients in selected patient group

Primary options

» labetalol: 100 mg orally twice daily initially, increase gradually according to response, usual dose 100-400 mg twice daily, maximum 2400 mg/day

OR

» nifedipine: 30-60 mg orally (extended-release) once daily initially, increase gradually according to response, maximum 90-120 mg/day (depending on brand)

OR

» methyldopa: 250 mg orally two to three times daily initially, increase gradually according to response, usual dose 250-1000 mg/day given in 2-4 divided doses, maximum 3000 mg/day

» Anti-hypertensive therapy should be started if systolic BP is persistently between 140 and 159 mmHg and/or diastolic BP is persistently between 90 and 109 mmHg, or if there is severe hypertension (systolic BP ≥160 mmHg and/or diastolic BP ≥110 mmHg).[59] [60]

»

adjunct **magnesium sulfate**

Treatment recommended for SOME patients in selected patient group

Primary options

» magnesium sulfate: consult specialist for guidance on dose
Dose depends on the indication, route of administration, and local guidelines. High-dose regimens may be recommended for the treatment of eclampsia in some countries such as the US, while low-dose regimens may be recommended in other countries. Consult your local drug formulary or guidelines for further guidance.

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» In the US, magnesium sulfate is recommended for all women with severe pre-eclampsia.[59] In other countries, including the UK, a more targeted approach is recommended, allowing the physician to exercise individual judgment based on the woman's specific risk factors (e.g., presence of uncontrolled hypertension or deteriorating maternal condition).[60] Seizures reflect progression to eclampsia, and are both treated and prevented with magnesium sulfate. The Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA) recommend that maternal administration of magnesium sulfate should not last longer than 5-7 days during pregnancy due to the risk of skeletal adverse effects, hypercalcaemia, and hypermagnesemia in the neonate.[61] [62] Despite the recommendation, magnesium sulfate is usually only used for 24-48 hours in clinical practice.

with theca lutein cyst — **plus** — **management of cyst**

Treatment recommended for ALL patients in selected patient group

» Theca lutein cysts result from hCG stimulation of the ovaries and may present with pelvic or abdominal masses, pain, or ovarian torsion. The presence of theca lutein cysts does not necessarily mandate ovarian removal because these cysts are a response to ovarian exposure to elevated hCG levels or hypersensitivity of the ovaries to hCG. They usually involute over time after surgical management of molar pregnancy and can be drained or, exceptionally, removed, if ovarian torsion with necrosis is confirmed.[50]

viable twin fetus: elective termination not desired

viable twin fetus: elective termination not desired — **1st** — **expectant management**

» Management of molar pregnancy with a viable twin generally entails close observation as the pregnancy is carried to either voluntary termination, forced delivery due to medical complications (e.g., bleeding, severe pre-eclampsia, hyperthyroidism, or acute respiratory distress), or term.[34] Conservative management is not recommended in the presence of choriocarcinoma or fetal aneuploidy.[4] Postpartum, the placenta should be sent for evaluation by a pathologist experienced in the evaluation of GTD, and routine post-molar surveillance should be initiated.[34] Importantly with careful medical monitoring about 60% achieve viable live births.[63] Twin pregnancies

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comprising a viable fetus and a co-existing hydatidiform mole have an increased risk of GTN, with a higher proportion of these women developing metastatic disease or requiring chemotherapy.[63]

with hyperemesis gravidarum **plus**

fluid replacement plus anti-emetic and/or H2 antagonist

Treatment recommended for ALL patients in selected patient group

Primary options

» metoclopramide: 5-10 mg intravenously/intramuscularly every 8 hours when required for a maximum of 5 days, maximum 30 mg/day

OR

» prochlorperazine rectal: 25 mg twice daily when required

Secondary options

» ondansetron: 4 mg intravenously/orally every 8 hours when required

OR

» famotidine: 20 mg intravenously every 12 hours

» The objectives of managing a woman with molar pregnancy complicated by hyperemesis revolve around symptomatic control of emesis with an anti-emetic and/or an H2 antagonist and intravenous hydration with electrolyte replacement, while moving toward prompt removal of the hydatidiform mole. Hyperemesis associated with a molar gestation resolves promptly after removal, roughly in parallel with the decline in hCG levels. Complete hydatidiform mole, because it is accompanied by significantly higher levels of hCG, is more likely to be associated with these symptoms than partial hydatidiform mole.[23][24] [25] [26]

» The UK Teratology Information Service recommends that ondansetron should be reserved as a second-line agent when first-line agents have failed. This is due to the small increased risk of orofacial clefts noted in one study when ondansetron was taken during the first trimester.[66] [67] The UK Medicines and Healthcare products Regulatory Agency (MHRA)

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also issued a drug safety update for ondansetron that provides similar advice.[68]

» Metoclopramide should be used for up to 5 days only, in order to minimise the risk of neurological and other adverse effects.[65]

with active bleeding **plus** **blood products and cessation of bleeding**

Treatment recommended for ALL patients in selected patient group

Primary options

» oxytocin: 10 units intramuscularly as a single dose; or 10-40 units by intravenous infusion at a rate to control uterine atony

Secondary options

» methylergometrine: 0.2 mg orally three to four times daily for up to 7 days; or 0.2 mg intramuscularly every 2-4 hours as required

» Women with severe anaemia or haemodynamic instability require transfusion before treatment.

» If acute haemorrhage occurs before or during surgical management, the procedure should be completed promptly and the benefit of oxytocic infusion considered against the risk of embolisation and dissemination of trophoblastic tissue through the venous system.[34] The use of oxytocic agents or methylergometrine will control bleeding after surgical management in most women.[34] Prostaglandins can be considered, if acute bleeding during or after evacuation is encountered.

» Rarely, women will require a second suction evacuation to control symptomatic haemorrhage after initial molar evacuation.[34]

» In women with an established diagnosis of post-molar GTN, chemotherapy will usually control bleeding. Very rarely, women with normal hCG levels develop delayed bleeding after molar evacuation. Pelvic-transvaginal Doppler ultrasound or contrast magnetic resonance imaging studies of the uterus may be helpful to exclude post-molar uterine arteriovenous malformation.

» Depot medroxyprogesterone and tranexamic acid, selective embolisation, myometrial wedge resection and repair, or hysterectomy may be required.[58]

»

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with thyrotoxicity **plus** **beta-blocker ± carbimazole**

Treatment recommended for ALL patients in selected patient group

Primary options

» propranolol: 60-80 mg orally (immediate-release) every 4-6 hours

OR

» propranolol: 60-80 mg orally (immediate-release) every 4-6 hours
-and-
» carbimazole: 15-40 mg orally daily until patient becomes euthyroid, followed by 5-15 mg daily

» Thyrotoxicosis in molar pregnancy is typically self-limited and best treated with supportive care.

» Beta-blockers should be given with the induction of anaesthesia at the time of surgical management, if the woman is clinically hyperthyroid. Carbimazole can be added, if a faster clinical response is needed or there is a thyrotoxic storm.[51]

with pre-eclampsia **plus** **anti-hypertensives**

Treatment recommended for ALL patients in selected patient group

Primary options

» labetalol: 100 mg orally twice daily initially, increase gradually according to response, usual dose 100-400 mg twice daily, maximum 2400 mg/day

OR

» nifedipine: 30-60 mg orally (extended-release) once daily initially, increase gradually according to response, maximum 90-120 mg/day (depending on brand)

OR

» methyldopa: 250 mg orally two to three times daily initially, increase gradually according to response, usual dose 250-1000 mg/day given in 2-4 divided doses, maximum 3000 mg/day

» Anti-hypertensive therapy should be started if systolic BP is persistently between 140 and

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159 mmHg and/or diastolic BP is persistently between 90 and 109 mmHg, or if there is severe hypertension (systolic BP ≥160 mmHg and/or diastolic BP ≥110 mmHg).[59] [60]

adjunct **magnesium sulfate**

Treatment recommended for SOME patients in selected patient group

Primary options

» magnesium sulfate: consult specialist for guidance on dose
Dose depends on the indication, route of administration, and local guidelines. High-dose regimens may be recommended for the treatment of eclampsia in some countries such as the US, while low-dose regimens may be recommended in other countries. Consult your local drug formulary or guidelines for further guidance.

» In the US, magnesium sulfate is recommended for all women with severe pre-eclampsia.[59]
In other countries, including the UK, a more targeted approach is recommended, allowing the physician to exercise individual judgment based on the woman's specific risk factors (e.g., presence of uncontrolled hypertension or deteriorating maternal condition).[60]
Seizures reflect progression to eclampsia, and are both treated and prevented with magnesium sulfate. The Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA) recommend that maternal administration of magnesium sulfate should not last longer than 5-7 days during pregnancy due to the risk of skeletal adverse effects, hypercalcaemia, and hypermagnesemia in the neonate.[61] [62]
Despite the recommendation, magnesium sulfate is usually only used for 24-48 hours in clinical practice.

with theca lutein cyst **plus** **management of cyst**

Treatment recommended for ALL patients in selected patient group

» Theca lutein cysts result from hCG stimulation of the ovaries and may present with pelvic or abdominal masses, pain, or ovarian torsion. The presence of theca lutein cysts does not necessarily mandate ovarian removal because these cysts are a response to ovarian exposure to elevated hCG levels or hypersensitivity of the ovaries to hCG. They usually involute over time

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after surgical management of molar pregnancy and can be drained or, exceptionally, removed, if ovarian torsion with necrosis is confirmed.[50]

viable twin fetus: elective termination

1st **suction evacuation**

» General anaesthesia is achieved, and beta-blockade given, if the woman is clinically hyperthyroid.[51] After the cervix is gently mechanically dilated with tapered Pratt dilators, intravenous oxytocin may be given to facilitate involution of the uterus. A suction cannula is advanced gently to the uterine fundus, and rotated while mechanical suction is applied.

» Sharp uterine curettage is not recommended because of the risk of uterine perforation, and equivalent outcomes with the suction method.[53]

plus **supportive care**

Treatment recommended for ALL patients in selected patient group

» Women with unevacuated hydatidiform moles generally require stabilisation of associated comorbidities (e.g., respiratory distress, pre-eclampsia/eclampsia, hyperthyroidism, or severe anaemia) before definitive treatment.

» Using a large-bore intravenous catheter is appropriate in women with uterine enlargement >14 weeks' gestational size, in anticipation of the need to rapidly administer intravenous fluids and blood products at the time of evacuation.

» Oxytocics or other means of inducing labour should not be given before cervical dilation intraoperatively.

» Prophylactic antibiotics are not considered mandatory, and are reserved for clinical concerns of infected products of conception.

» Sequential compression stockings, as a single modality, is considered adequate for venous thromboembolism prophylaxis.

» High-output cardiac failure may be secondary to hyperthyroidism or thyroid storm, severe pre-eclampsia, gestational hypertension, pulmonary oedema, and, less commonly, anaemia.[50] This condition is usually self-limiting, and resolves over time after complete removal of the molar pregnancy. It is best treated with supportive care, including mechanical ventilation

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tailored to minimise barotrauma, and central haemodynamic monitoring.

with hyperemesis gravidarum **plus** **fluid replacement plus anti-emetic and/or H2 antagonist**

Treatment recommended for ALL patients in selected patient group

Primary options

» metoclopramide: 5-10 mg intravenously/intramuscularly every 8 hours when required for a maximum of 5 days, maximum 30 mg/day

OR

» prochlorperazine rectal: 25 mg twice daily when required

Secondary options

» ondansetron: 4 mg intravenously/orally every 8 hours when required

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» The objectives of managing a woman with molar pregnancy complicated by hyperemesis revolve around symptomatic control of emesis with an anti-emetic and/or an H2 antagonist and intravenous hydration with electrolyte replacement, while moving towards prompt removal of the hydatidiform mole. Hyperemesis associated with a molar gestation resolves promptly after removal, roughly in parallel with the decline in hCG levels. Complete hydatidiform mole, because it is accompanied by significantly higher levels of hCG, is more likely to be associated with these symptoms than partial hydatidiform mole.[23][24] [25] [26]

» Metoclopramide should be used for up to 5 days only, in order to minimise the risk of neurological and other adverse effects.[65]

with active bleeding **plus** **blood products and cessation of bleeding**

Treatment recommended for ALL patients in selected patient group

Primary options

» oxytocin: 10 units intramuscularly as a single dose; or 10-40 units by intravenous infusion at a rate to control uterine atony

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Secondary options

» methylergometrine: 0.2 mg orally three to four times daily for up to 7 days; or 0.2 mg intramuscularly every 2-4 hours as required

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Primary options

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Acute

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Primary options

» labetalol: 100 mg orally twice daily initially, increase gradually according to response, usual dose 100-400 mg twice daily, maximum 2400 mg/day

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»

adjunct **magnesium sulfate**

Treatment recommended for SOME patients in selected patient group

Primary options

» magnesium sulfate: consult specialist for guidance on dose

Acute

Dose depends on the indication, route of administration, and local guidelines. High-dose regimens may be recommended for the treatment of eclampsia in some countries such as the US, while low-dose regimens may be recommended in other countries. Consult your local drug formulary or guidelines for further guidance.

» In the US, magnesium sulfate is recommended for all women with severe pre-eclampsia.[59] In other countries, including the UK, a more targeted approach is recommended, allowing the physician to exercise individual judgment based on the woman's specific risk factors (e.g., presence of uncontrolled hypertension or deteriorating maternal condition).[60] Seizures reflect progression to eclampsia, and are both treated and prevented with magnesium sulfate. The Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA) recommend that maternal administration of magnesium sulfate should not last longer than 5-7 days during pregnancy due to the risk of skeletal adverse effects, hypercalcaemia, and hypermagnesemia in the neonate.[61] [62] Despite the recommendation, magnesium sulfate is usually only used for 24-48 hours in clinical practice.

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»

Ongoing

following initial management: high risk of gestational trophoblastic neoplasia with completed follow up unlikely

1st **prophylactic chemotherapy**

Primary options

» methotrexate: consult local consultant protocol for dosing guidelines

OR

» dactinomycin: consult local consultant protocol for dosing guidelines

» Chemoprophylaxis is given only after evacuation of a hydatidiform mole and assessment of clinical and social risk factors. A clinical risk assessment is used to identify women at low risk or high risk of developing post-molar GTN.[4]

» In women who are at high risk of developing GTN (e.g., maternal age >40 years, women with complete hydatidiform moles ,or hCG levels >100,000 mIU/mL) and in whom hCG monitoring is either unavailable or unlikely to be followed, it may be possible to reduce the risk of GTN by administering chemoprophylaxis with methotrexate or dactinomycin.[4] [64]

Primary prevention

There is no known preventive treatment for gestational trophoblastic disease (GTD).

Secondary prevention

Women should be advised not to conceive again until post-treatment follow-up is complete.[3] [34] [54] Women who previously underwent chemotherapy for GTN should be advised not to conceive for 1 year after completion of treatment.[34] [54]

Subsequent pregnancies in women with prior gestational trophoblastic disease should be evaluated with early sonographic determination of a normal intrauterine gestation.[3] Although controversial, sending material obtained at the end of pregnancy (from an abortion, ectopic pregnancy, or placenta from a preterm/term pregnancy) may be appropriate to exclude cases of repeat GTD. If this is not possible, hCG levels can be measured 6-8 weeks after the end of the pregnancy to detect this serious condition early.[3]

Patient discussions

Strict adherence to contraception is advised after completion of treatment.[3] [34] [54] Most methods of contraception, including oral contraceptives, can be safely used after treatment for GTD and can be

started immediately after uterine evacuation.[55] [56] However, intrauterine devices (medicated or not) are contraindicated in women with active, invasive tumours or persistently elevated hCG levels because of the risk of uterine perforation.[54]

FOLLOW UP

Monitoring

Monitoring

In the absence of histopathology, post-treatment measurement of human chorionic gonadotrophin (hCG) levels should be performed weekly until normalisation of hCG levels or diagnosis of gestational trophoblastic neoplasia (GTN). The duration of monitoring varies by country.[3] The International Federation of Gynecology and Obstetrics recommends monitoring hCG every 1-2 weeks post-treatment until levels return to normal, followed by a single confirmatory normal measurement within a month for partial hydatidiform moles and monthly hCG measurements for 6 months for complete hydatidiform moles.[4] [41] In the UK, the Royal College of Obstetricians & Gynaecologists (RCOG) recommends monitoring hCG levels post-treatment until there are two normal measurements at least 4 weeks apart for partial hydatidiform moles. For complete hydatidiform moles, RCOG recommends monitoring hCG levels every month for 6 months either post-treatment if normalisation took up to 56 days or from the date of normalisation if this took more than 56 days.[34]

Close follow-up aims to maximise the detection of post-molar GTN by identifying plateaued or newly rising hCG levels.

Complications

Complications	Timeframe	Likelihood
pre-eclampsia	**short term**	**medium**

Usually asymptomatic. However, exacerbated symptoms of pre-eclampsia (as a result of abnormally high serum human chorionic gonadotrophin [hCG] levels) may be present. Headache, visual disturbances, epigastric pain, breathlessness, seizures, and oliguria are uncommon and suggest severe pre-eclampsia.

A diagnosis is made if there is new-onset, persistent hypertension defined as a systolic blood pressure ≥140 mmHg and/or a diastolic blood pressure ≥90 mmHg, usually after 20 weeks' gestation, with new-onset proteinuria (protein:creatinine ratio of ≥30 mg/mmol and albumin:creatinine ratio of ≥8 mg/mmol) or evidence of systemic involvement.[69] The significant elevation of hCG associated with complete hydatidiform moles can result in earlier onset of pre-eclampsia (before 20 weeks' gestation).

Antihypertensive therapy should be started if systolic BP is persistently between 140 and 159 mmHg and/or diastolic BP is persistently between 90 and 109 mmHg, or if there is severe hypertension (systolic BP ≥160 mmHg and/or diastolic BP ≥110 mmHg).[59] [60]

In the US, magnesium sulfate is recommended for all women with severe pre-eclampsia.[59] In other countries, including the UK, a more targeted approach is recommended, allowing the physician to exercise individual judgment based on the woman's specific risk factors (e.g., presence of uncontrolled hypertension or deteriorating maternal condition).[60] Seizures reflect progression to eclampsia, and are both treated and prevented with magnesium sulfate infusions. The US Food and Drug Administration and the UK Medicines and Healthcare products Regulatory Agency recommend that maternal administration of magnesium sulfate should not last longer than 5-7 days during pregnancy due to the risk of skeletal adverse effects, hypercalcaemia, and hypermagnesemia in the neonate.[61] [62] Despite the recommendation, magnesium sulfate is usually only used for 24-48 hours in clinical practice.

Management of molar pregnancy with a viable twin generally entails close observation for pre-eclampsia as the pregnancy is carried to either voluntary termination, forced delivery, or term. Definitive treatment of pre-eclampsia consists of delivery. The decision about when and how to deliver should only be made after a thorough assessment of the risk and benefits to the mother and co-existing twin.

hyperthyroidism	**short term**	**medium**

There is molecular homology between subunits of thyroid-stimulating hormone and hCG. As a result, serum hCG may stimulate the production of thyroid hormone with the clinical symptoms and signs of thyrotoxicosis.[26] [38][39] The higher elevations in serum hCG levels seen in complete molar pregnancies are associated with a greater incidence of severe medical sequelae, including hyperthyroidism. The absence of ophthalmopathy differentiates molar pregnancy from thyrotoxicosis due to Graves' disease.[40]

Women with unevacuated hydatidiform moles generally require stabilisation of associated comorbidities, including hyperthyroidism, before definitive treatment. Thyrotoxicosis in molar pregnancy is typically self-limited and best treated with supportive care. Beta-blockers should be given with the induction of anaesthesia at the time of surgical management, if the woman is clinically hyperthyroid. Carbimazole can be added, if a faster clinical response is needed or there is a thyrotoxic storm.[51]

hyperemesis gravidarum	**short term**	**medium**

Women may report earlier and more severe symptoms of pregnancy (as a result of abnormally high serum hCG levels) that include severe nausea and emesis (hyperemesis gravidarum).

FOLLOW UP

Complications	Timeframe	Likelihood
The objectives of managing a woman with molar pregnancy complicated by hyperemesis revolve around symptomatic control of emesis with an anti-emetic and/or an H2 antagonist and intravenous hydration with electrolyte replacement, while moving towards prompt removal of the hydatidiform mole. Hyperemesis associated with a molar gestation resolves promptly after surgical management, roughly in parallel with the decline in hCG levels. Complete hydatidiform mole, because it is accompanied by significantly higher levels of hCG, is more likely to be associated with these symptoms than partial hydatidiform mole.[23][24] [25] [26]		
anaemia	**short term**	**medium**
Anaemia, with symptoms of pallor, dizziness, and fatigue, may result from heavy or persistent vaginal bleeding and the dilutional effects of increased blood volume. Bleeding can complicate hydatidiform mole as acute haemorrhage before treatment, during surgical management, or as a delayed haemorrhage during follow-up after evacuation of a molar pregnancy. There is a greater risk for serious bleeding at the time of evacuation for MP. Women with unevacuated hydatidiform moles generally require stabilisation of associated comorbidities, including severe aaemia, before definitive treatment. Women with severe anaemia or haemodynamic instability, require transfusion.		
invasive mole	**short term**	**medium**
Invasion of hydatidiform mole beyond the normal placentation site (into the myometrium with venous penetration) is followed by persistently elevated serum hCG levels after evacuation of molar pregnancy.[4] [34][42] Persistence is defined as a plateau in hCG levels for four measurements over a period of at least three consecutive weeks (on days 1, 7, 14, and 21) or a rise in hCG levels for three consecutive weekly measurements over a period of at least 2 weeks (on days 1, 7, and 14).[4] The condition is treated with chemotherapy.[4]		
choriocarcinoma	**short term**	**low**
Malignant transformation of molar tissue or a de novo carcinogenesis may evolve from an antecedent normal placenta. Although it is more common after MP, it can occur after any type of pregnancy (e.g., miscarriage, abortion, ectopic pregnancy, or preterm/term gestation).[34] Histological findings include the presence of both cytotrophoblasts and syncytiotrophoblasts, but chorionic villi are absent (which differentiates the condition from an invasive mole).[4] [42] Dysfunctional vaginal bleeding after any pregnancy that does not respond to conventional therapy may indicate choriocarcinoma.[70] Elevated hCG levels in this setting are suggestive of this condition. Pathology confirming the presence of choriocarcinoma is diagnostic, although biopsies are not ordinarily indicated because of the risk of haemorrhage.[4] The hormonal biochemical diagnosis is sufficient for the initiation of treatment.[3] The condition is treated with chemotherapy.[4]		

Complications	Timeframe	Likelihood
placental site trophoblastic tumour	**short term**	**low**

The placental site trophoblastic tumour (PSTT) is a rare type of malignant neoplasia derived from intermediate trophoblastic cells, with low-level production of hCG.[42] [71]

These tumours most commonly arise months to years after a term gestation, but can occur after any pregnancy (e.g., a miscarriage, abortion, ectopic pregnancy, or MP).[71] Benign placental site nodules with or without atypical features (PSNs/ASPNs) can co-exist with or develop into PSTTs, but the association with GTN seems stronger for ASPNs.[72]

Women present with abnormal uterine bleeding, a mass in the endometrial cavity, or amenorrhoea.[71]

Serum hCG levels may only be mildly elevated.[71]

The condition is most often treated with surgery (usually hysterectomy) and occasionally with chemotherapy.[4] [71] Although PSTTs are not resistant to chemotherapy, they are less sensitive than other types of GTN (e.g., invasive mole and choriocarcinoma).[3]

epithelioid trophoblastic tumour	**short term**	**low**

Epithelioid trophoblastic tumours (ETTs) are rare but can occur after a prior gestation.[42] [71]

Most of these malignant tumours occur after a term gestation, but they may arise after any pregnancy (e.g., miscarriage, abortion, ectopic pregnancy, or MP).[71] ETTs arise from the intermediate trophoblast. Benign placental site nodules with or without atypical features (PSNs/ASPNs) can co-exist with or develop into ETTs, but the association with GTN seems stronger for ASPNs.[72]

Vaginal bleeding is the presenting symptom in two-thirds of women; about one third of women present with metastatic disease because normal or only mildly elevated levels of hCG and a lack of symptoms contribute to late diagnosis.[71]

The condition is most often treated with surgery (usually hysterectomy) and occasionally with chemotherapy.[4] [71] Although ETTs are not resistant to chemotherapy, they are less sensitive than other types of GTN (e.g., invasive mole and choriocarcinoma).[3]

post-evacuation respiratory distress syndrome	**short term**	**low**

The incidence of complications after post-molar dilation and evacuation increases with uterine size. One of the most serious of these is post-evacuation respiratory distress syndrome. This may occur as a result of pulmonary embolisation of trophoblastic tissue, as well as a high-output cardiac failure secondary to hyperthyroidism, severe pre-eclampsia, and, less commonly, from anaemia.[50]

This condition is usually self-limiting, and resolves over time after complete evacuation of the MP. It is best treated with supportive care, including mechanical ventilation tailored to minimise barotrauma, central haemodynamic monitoring, and beta-blockade to control sequelae of thyrotoxicosis.

Asherman's syndrome	**long term**	**high**

The presence of adhesions and/or fibrosis within the uterine cavity (intrauterine synechiae) due to scars is known as Asherman's syndrome and may form after dilation and evacuation (D&E). This risk is increased after sharp curettage.[73] However, the exact influence of hydatidiform mole itself on the appearance of intrauterine synechiae is unknown because they can occur even if molar evacuation is performed exclusively by suction evacuation and sharp curettage is not used.[53]

Asherman's syndrome may result in infertility, repeated miscarriages, pain from trapped blood, and future obstetric complications, although it can be successfully diagnosed and treated with hysteroscopy.[74]

FOLLOW UP

Complications	Timeframe	Likelihood
metastases	**variable**	**low**

Women with an established diagnosis of GTN should be evaluated with a pelvic examination and chest x-ray, as vaginal and lung metastases are the most common sites of metastatic disease.[3] If the chest x-ray is inconclusive, if there are metastases ≥1 cm, or the woman has a signs or symptoms of metastatic disease, computed tomography scans of the chest, abdomen, and pelvis should be performed and magnetic resonance imaging of the brain should be obtained to further evaluate and stage metastases.[3] [4]

Management is determined by tumour stage and risk classification: low-risk GTN can be treated with single-agent chemotherapy, whereas high-risk GTN or recurrent disease is treated with multiple agent chemotherapy regimens.[4]

Surgery can be incorporated into primary management of women with low-risk disease who desire hysterectomy, as well as resection of isolated brain metastasis, or to resect isolated lesions in women with chemorefractory disease.[4] [42] Radiation is occasionally used to treat high-risk brain metastases.[4]

Prognosis

About 15% to 20% of women with complete molar pregnancies and 0.5% to 5% of women with partial molar pregnancies develop GTN and require chemotherapy.[4][42] However, the cure rate for these conditions exceeds 95%.[34]

Women with a previous diagnosis of hydatidiform mole have a 1% to 2% (or about 10 times the baseline) risk of a molar gestation in a subsequent pregnancy.[8][9] Women should be followed closely in subsequent pregnancies.[3] (see Prevention)

Diagnostic guidelines

United Kingdom

Management of gestational trophoblastic disease (https://www.rcog.org.uk/guidance/browse-all-guidance/green-top-guidelines/gestational-trophoblastic-disease-green-top-guideline-no-38)

Published by: Royal College of Obstetricians & Gynaecologists **Last published:** 2020

International

Diagnosis and treatment of gestational trophoblastic disease (https://obgyn.onlinelibrary.wiley.com/doi/10.1002/ijgo.13877)

Published by: International Federation of Gynecology and Obstetrics **Last published:** 2021

North America

Epidemiology, diagnosis, and treatment of gestational trophoblastic disease (https://www.gynecologiconcology-online.net/article/S0090-8258(21)01421-9/fulltext)

Published by: Society of Gynecologic Oncology **Last published:** 2021

Practice parameter for the performance of obstetrical ultrasound (https://www.acr.org/Clinical-Resources/Practice-Parameters-and-Technical-Standards)

Published by: American College of Radiology (ACR), the American Institute of Ultrasound in Medicine (AIUM), the American College of Obstetricians and Gynecologists (ACOG), the Society for Maternal Fetal Medicine (SMFM), and the Society of Radiologists in Ultrasound (SRU) **Last published:** 2018

Ultrasound in pregnancy (https://www.acog.org/clinical/clinical-guidance/practice-bulletin)

Published by: American College of Obstetricians and Gynecologists **Last published:** 2016 (re-affirmed 2022)

Treatment guidelines

United Kingdom

Management of gestational trophoblastic disease (https://www.rcog.org.uk/guidance/browse-all-guidance/green-top-guidelines/gestational-trophoblastic-disease-green-top-guideline-no-38)

Published by: Royal College of Obstetricians & Gynaecologists **Last published:** 2020

International

Diagnosis and treatment of gestational trophoblastic disease (https://obgyn.onlinelibrary.wiley.com/doi/10.1002/ijgo.13877)

Published by: International Federation of Gynecology and Obstetrics **Last published:** 2021

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Epidemiology, diagnosis, and treatment of gestational trophoblastic disease (https://www.gynecologiconcology-online.net/article/S0090-8258(21)01421-9/fulltext)

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Key articles

- Horowitz NS, Eskander RN, Adelman MR, et al. Epidemiology, diagnosis, and treatment of gestational trophoblastic disease: A Society of Gynecologic Oncology evidenced-based review and recommendation. Gynecol Oncol. 2021 Dec;163(3):605-13. Full text (https://www.gynecologiconcology-online.net/article/S0090-8258(21)01421-9/fulltext) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/34686354?tool=bestpractice.bmj.com)
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- Lok C, van Trommel N, Massuger L, et al. Practical clinical guidelines of the EOTTD for treatment and referral of gestational trophoblastic disease. Eur J Cancer. 2020 May;130:228-40. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/32247260?tool=bestpractice.bmj.com)

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Images

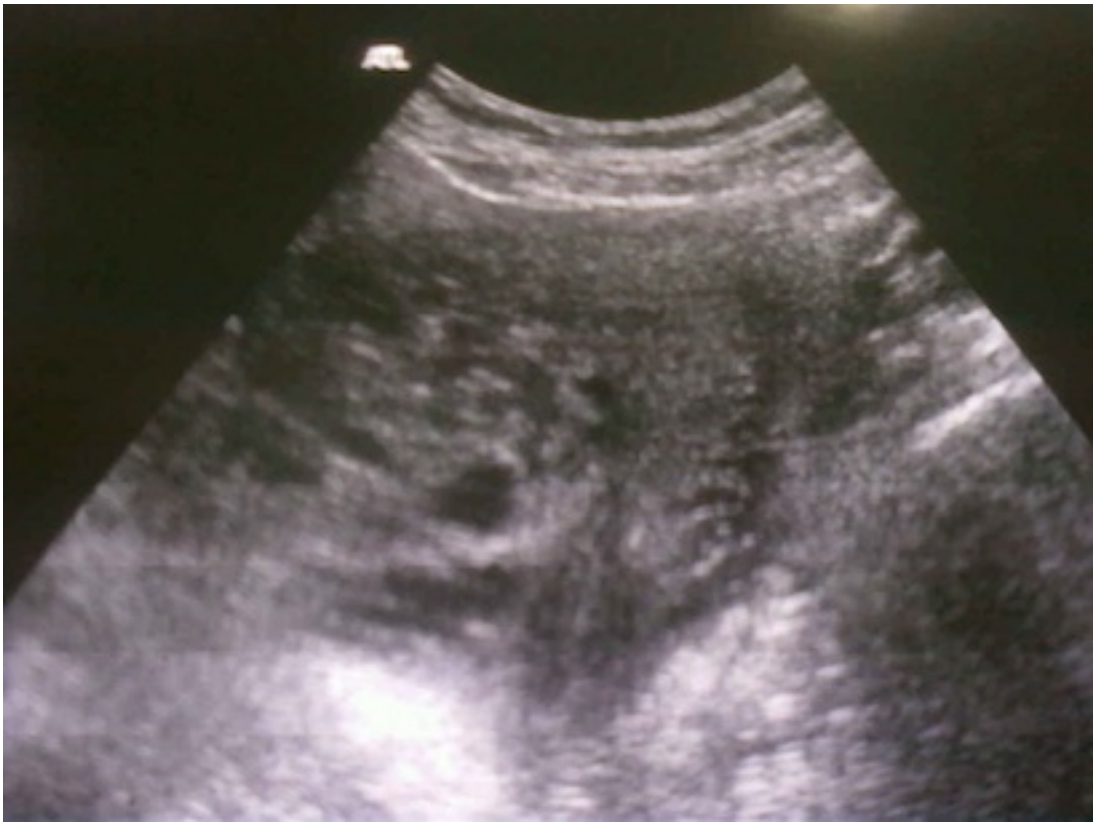

Figure 1: Ultrasound showing multiple cystic areas in the uterine cavity giving a 'snowstorm appearance' suggestive of molar pregnancy.

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Figure 1 – BMJ Best Practice Numeral Style

5-digit numerals: 10,000

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