GESTATIONAL TROPHOBLASTIC DISEASE (Complete and partial molar pregnancy)

This LOP is developed to guide clinical practice at the Royal Hospital for Women. Individual patient circumstances may mean that practice diverges from this LOP.

1. AIM

- To monitor patients with a molar pregnancy to allow early detection of progressive disease

2. PATIENT

- Woman with a diagnosis of complete hydatidiform molar pregnancy, partial molar pregnancy, microscopic or macroscopic changes suggestive of possible partial or early complete molar change

3. STAFF

- Medical Staff
- Registered Nurses
- Registered Midwives
- Student Nurses
- Student Midwives

4. EQUIPMENT

- Size 10-12 suction curette

5. CLINICAL PRACTICE

- Obtain histological diagnosis of molar pregnancy. This will occur as a result of histological examination of routine evacuation of retained products of conception (ERPC) or in a patient with high suspicion of molar pregnancy. In the latter case suction curettage with size 10-12 suction curette is recommended as primary treatment
- Consider the risk of intraoperative haemorrhage based on clinical assessment and take necessary medical precautions including group and hold, cross match and the availability of uterotonics and senior medical staff help as appropriate.
- Ensure RhD immunoglobulin 250IU is given intramuscular (IM) to Rh-negative patients post operatively
- Explain diagnosis and monitoring. Provide patient information leaflet. Provide Social Work contact details if appropriate.
- Ensure patient returns to early pregnancy clinic one week post curette for ongoing monitoring or as soon as possible after diagnosis confirmed on retained products post routine ERPC
- Recommend contraceptive for duration of monitoring as pregnancy should be avoided. Options include: barrier contraception or oral contraceptive pill (combined or progesterone only)
- Weekly serum molar BhCG performed in endocrine laboratory

Complete molar pregnancy

- Monitor for 6 months from date of evacuation with monthly BhCG, if BhCG returns to normal (<5) within 8 weeks (56 days) from curettage
- Monitor for 6 months from when BhCG is<5 with monthly BhCG, if BhCG has not normalised within 8 weeks (56 days) from curettage

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GESTATIONAL TROPHOBLASTIC DISEASE (Complete and partial molar pregnancy) cont'd

Partial molar pregnancy

- Cease monitoring once BhCG has normalised
- Refer to Gynaecology Oncology:
    - 4 values or more of plateau (<10% fall) of BhCG over at least 3 weeks
    - Rise of BhCG of 10% or greater for 3 values or longer over at least 2 weeks
    - Persistence of BhCG 3 months after mole evacuation
    - Presence of histologic choriocarcinoma
    - Evidence of metastases

- Obtain chest X-ray +/- CTabdo/pelvis (as directed by gynaecology oncology fellow)
- Discuss case with gynaecology oncology fellow and ensure written referral completed

Subsequent pregnancy

- Perform early ultrasound to confirm the presence of a normal pregnancy
- Send the placenta for histopathology to exclude the presence of molar disease
- Perform a repeat BhCG 6 weeks post-partum to ensure there is no persistent trophoblastic disease

6. DOCUMENTATION

- Integrated clinical notes

7. EDUCATIONAL NOTES

- Gestational trophoblastic disease occurs in 1-1.5 per 1000 pregnancies. Gestational trophoblastic disease forms a group of disorders including complete and partial hydatidiform moles, invasive mole, choriocarcinoma and placental site trophoblastic tumours.
- Complete molar pregnancies are formed when a sperm fertilises an empty ovum then duplicates. With exclusively derived paternal DNA there is no presence of embryonic or fetal tissue. Up to 20% will become persistent requiring chemotherapy.
- Partial moles are triploid following dispermic fertilisation of an ovum. Embryonic or fetal tissue is usually present. Partial moles are less often persistent (2-4%).
- Risk factors for molar pregnancy include extremes of age with women over forty having a 5-10 fold higher risk. Prior spontaneous miscarriage is a risk factor for both complete and partial moles. Women with prior molar gestation have a 10 times increased risk of subsequent molar pregnancy. However, 98% of women will have a normal subsequent pregnancy.
- Clinical signs and symptoms may include:
    - Abnormal vaginal bleeding, enlarged uterus, hyperemesis
    - Complete molar pregnancy rarely includes:
        - Hyperthyroidism, early onset gestational hypertension, theca lutein cysts, respiratory distress, anaemia
- Ultrasound is not diagnostic of molar pregnancy but may reveal a 'snow storm' appearance. In complete molar pregnancies, theca lutein cysts may be present.
- BhCG levels are often markedly elevated in complete molar pregnancies >100 000.
- Histology:

GESTATIONAL TROPHOBLASTIC DISEASE (Complete and partial molar pregnancy) cont'd

Risk

- Combined OCP use: A systematic review, including two large randomised control trials, showed no increased risk of developing gestational trophoblastic neoplasia. A large UK case series suggests a RR of 1.19.
- Monitoring: A large Victorian case series (2006) followed >300 women and found no relapse after achieving normal levels of BhCG in women with partial moles. This is in keeping with previous case series of >9000 patients in the UK.

	Complete	Partial
Swelling chorionic villi	Diffuse	Focal
Trophoblastic hyperplasia	Diffuse	Focal
Scalloping chorionic villi	Absent	Present
Trophoblastic stromal inclusions	Absent	Present
P57 stain	Negative	Positive
Embryonic tissue	Absent	Present

8. RELATED POLICIES / PROCEDURES / CLINICAL PRACTICE LOP

- Rh D Immunoglobulin in Obstetrics
- Maternity – Early Pregnancy Complications (DoH Policy) PD2009_58

9. RISK RATING

- Low

10. NATIONAL STANDARD

- Standarda 5 – Comprehensive Care

11. REFERENCES

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GESTATIONAL TROPHOBLASTIC DISEASE (Complete and partial molar pregnancy)

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APPENDIX A
Patient Information Leaflet

TROPHOBLASTIC DISEASE

This pamphlet has been adapted for the Royal Hospital for Women from the patient information provided by the International Society for the Study of Trophoblastic Diseases adapted from the publication "Hydatidiform Mole and You" from the Yale Centre for Trophoblastic Disease, Department of Gynecology, Yale University School of Medicine, New Haven, Connecticut, USA

1. WHAT IS A HYDATIDIFORM MOLE?

A hydatidiform mole occurs when there is an abnormal union between eggs and sperm. There are two types of hydatidiform mole - complete and partial moles. A complete mole occurs when there are no genes inside the egg and a sperm fertilises this empty egg. We do not know why empty eggs occur or how the egg can be fertilised in this situation. Either one or two sperm can join with this empty egg and the resulting pregnancy has no embryo (fetus, baby). The placenta does grow and this is abnormal and forms lots of cysts and has no blood vessels. These cysts look like a cluster of grapes when they are passed out of the uterus or on an ultrasound and that is why it is called a hydatidiform mole (grape like). A hydatidiform mole will often miscarry by about 16 to 18 weeks if there is no intervention, however since the diagnosis may be made by ultrasound before that time, it is better for you to have the tissue removed from the uterus (a D&C). This is so the tissue can be removed in a controlled manner with a lower risk of bleeding and infection. A blood test that measures the level of a hormone that is produced by the placenta called Human chorionic gonadotropin (hCG) may assist in making the diagnosis and monitoring following treatment.

The other type of hydatidiform mole is called a partial mole and this is also the result of a genetically abnormal pregnancy. In a partial mole there are three sets of chromosomes instead of the usual two (this is called triploidy). An egg is usually fertilised by two sperm to give the three sets of chromosomes and in this situation, a fetus may be present, however since there are three sets of genetic information, this fetus is always very abnormal and will not survive.

2. WHAT KIND OF SYMPTOMS WOULD SOMEONE WHO HAS A HYDATIDIFORM MOLE HAVE?

Symptoms of a molar pregnancy usually appear in the second or third month of pregnancy. There may be abnormal bleeding or cramps or the passage of tissue. There may be severe vomiting, more than would occur in a normal pregnancy, due to a very high level of pregnancy hormone (hCG).

3. HOW DOES THE DOCTOR MAKE THE DIAGNOSIS OF HYDATIDIFORM MOLE?

At an examination, your doctor may find that the uterus is larger than normal for the duration (age) of the pregnancy. An ultrasound examination will make the diagnosis and will help distinguish a molar pregnancy from other early pregnancy situations that may be normal including more than one baby (twins, triplets or more). A blood test that measures hCG may also be used for diagnosis or monitoring.

4. HOW IS A HYDATIDIFORM MOLE TREATED?

The treatment for a hydatidiform mole is to remove the tissue from the uterus by a procedure called a Suction Curettage or "D&C". In this procedure the cervix (the neck of the womb) is gently and progressively opened or "dilated" by rods of increasing size in order to allow a thin plastic tube with an opening on one side to to enter the uterus. Suction is then applied through this tube and this removes all of the abnormal tissue from the uterus. An alternative to this simple treatment if you are sure you do not want any more children could be a hysterectomy (the removal of the uterus), however this is a major procedure and is not usually recommended as primary treatment.

5. WHAT KIND OF SYMPTOMS SHOULD I WATCH OUT FOR AND REPORT TO MY DOCTOR AFTER THE D&C?

You should report any new bleeding, fever, or if you pass any tissue from your vagina.

6. THAT IS THE CAUSE OF HYDATIDIFORM MOLE?

As yet, we still do not know the cause of hydatidiform moles. There are some studies that have linked hydatidiform mole to dietary or genetic factors, and is more common in women from South East Asia.

7. HOW COMMON IS IT TO HAVE A HYDATIDIFORM MOLE?

Hydatidiform mole occurs approximately in 1 out of 1000 pregnancies in Australia. It is three times more common in some countries of South East Asia.

8. IF I DO HAVE A HYDATIDIFORM MOLE, WHAT IS MY CHANCE OF HAVING ANOTHER HYDATIDIFORM MOLE?

The chance for a hydatidiform mole occurring in a subsequent pregnancy is low at 1%.

9. I HAVE HEARD THAT IF SOMEONE HAS A HYDATIDIFORM MOLE IT MIGHT LEAD TO CANCER. DO I HAVE CANCER?

If you have had a hydatidiform mole, it does not mean you have cancer. Up to one in five or 20% of patients who have had a hydatidiform mole have tissue that may regrow and continue to produce hormones and symptoms of pregnancy. This happens because the molar tissue may be invasive and grow into the wall of the uterus, so that even though the tissue is removed from inside the uterus there are cells that are out of reach of the surgeon. It is these cells that may spread to other parts of the body through the bloodstream. If this occurs it is called "trophoblastic neoplasia" or "persistent trophoblastic tumour". Trophoblastic disease may be a form of cancer but is very treatable cancer with chemotherapy. When treated early with chemotherapy trophoblastic disease has a 99.9% cure rate. It is because of this possibility that ongoing monitoring is so important following diagnosis and treatment of a molar pregnancy.

10. HOW WILL MY DOCTOR AND I KNOW IF THERE IS STILL MOLAR TISSUE REMAINING?

The tissue of the hydatidiform mole or trophoblastic tissue produces the hormone Human Chorionic Gonadotrophin (hCG), which is found in both the blood and urine. The blood level can be measured and the level of hCG hormone acts as a measure of the response to treatment.

11. HCG AND FOLLOW UP

Monitoring following a molar pregnancy is essential and you will need to have a blood test to check the level of hCG initially every week following your treatment. Once the blood level is <5 (this is the normal level), then the frequency of the tests will decrease usually to monthly. This continues for up to 6 months.

12. WHEN WILL I KNOW WHETHER OR NOT I WILL NEED CHEMOTHERAPY?

You must have blood collected weekly (without fail) to measure your hCG hormone. You need to be carefully followed to make sure each week that the blood level of hCG continues to fall until it is at a normal level of <5. If,your hCG level stays the same for several weeks or starts to increase, then this may mean that there is growing molar tissue and then chemotherapy will be necessary. You will also be referred to a Gynaecology Oncologist (specialist in gynaecology related cancers).

13. WHAT IS THE CHANCE I WILL REQUIRE TREATMENT WITH CHEMOTHERAPY?

About 80% or more of patients with hydatidiform mole and 96% of women with partial molar pregnancy have no further problems after the D&C or hysterectomy.

14. MALIGNANCY (CANCER) AND HYDATIDIFORM MOLE.

With complete hydatidiform mole the molar tissue remaining in the uterus may not be destroyed by your body's immune mechanism and may begin to grow into the wall of the uterus. This is called an invasive mole. From the uterus, the molar tissue may spread to the lung and then to other organs like a cancer. This cancer is called choriocarcinoma. Very, very rarely choriocarcinoma may occur after a normal term pregnancy or after an apparently uneventful miscarriage. Invasive mole and choriocarcinoma are treated with chemotherapy with very high success (>99% cure rates).

15. WHAT IS CHEMOTHERAPY?

Chemotherapy is a treatment, which uses medication to attack the abnormal cells that have continued to grow. The amount of chemotherapy you need will depend upon several different factors including your hCG hormone level. Your treatment will continue until the hCG hormone returns to normal in your blood.

16. IF I DO NEED CHEMOTHERAPY, HOW IS IT GIVEN AND WHAT KIND OF SIDE EFFECTS CAN I EXPECT?

The chemotherapy or medications used to treat trophoblastic disease is given either as an injection or through a small needle in a vein in your hand or arm. This treatment is usually done as an outpatient and does not require an overnight stay in hospital. The type of chemotherapy and how often is given will be explained in more detail if you need to have this treatment.

Some of the side effects you might experience are nausea and vomiting but this is nowadays nearly completely prevented by medication. You may have TEMPORARY hair loss (the amount of hair loss will depend on the number of courses of chemotherapy given), some mouth soreness and a skin rash. During the period of chemotherapy you should avoid the use of aspirin and protect yourself from sunlight.
All side effects will be explained to you in much greater detail if it becomes necessary to give you chemotherapy. To remind you again, if it does occur, this disease is more than 99% curable with chemotherapy if followed properly.

17. HOW LONG WILL IT BE NECESSARY TO HAVE BLOOD TESTS?

For complete molar pregnancies monitoring is weekly until blood levels return to normal, then monthly for up to six months. For partial molar pregnancies monitoring is weekly until blood levels return to normal then monitoring ceases. You should use reliable contraception during this time and not become pregnant, since this will affect the pregnancy hormone levels.

18. ONCE MY BLOOD LEVEL BECOMES NORMAL IS THERE A CHANCE OF IT GOING UP AGAIN?

The chance of your hCG blood level going up again after becoming normal is very low.

19. WHY IS IT SO IMPORTANT THAT I DON'T GET PREGNANT DURING MONITORING?

The hCG hormone that measures molar or trophoblastic tissue is the same hormone that is produced during pregnancy. If you do become pregnant, we would not be able to determine whether this hormone is being produced by a normal pregnancy or by remaining molar tissue. Therefore, it is essential that you use reliable birth control such as the oral contraceptive pill or condoms.

20. COULD HAVING A HYDATIDIFORM MOLE CAUSE ME TO HAVE PROBLEMS WITH FUTURE PREGNANCIES?

Any future pregnancy for a woman who has had a hydatidiform mole is likely to be normal, with the same risks as for any woman who has not had a molar pregnancy. In your next pregnancy it is recommended that you have an early ultrasound and after delivery the placenta should be examined by a pathologist for any abnormalities.

21. WILL MY BABY BE NORMAL?

The chance of your baby having any abnormalities is no greater than in the normal population even if chemotherapy was administered.

The information given here is not meant to be comprehensive, particularly in relation to non-hydatidiform trophoblastic disease. If you have questions these may be addressed to your doctor or your nearest trophoblastic disease centre

Additional information is available at www.isstd.org