PROMISE MIDWIFERY SERVICES, LLC

TITLE:          GESTATIONAL TROPHOBLASTIC DISEASE

EFFECTIVE DATE:  November 11th, 2013

POLICY STATEMENT
Certified nurse-midwives need to have a comprehensive understanding of GTD, including its different clinical presentations, diagnostic tests, disease management, and essential post-treatment follow-up and surveillance. While treatment of these conditions is typically beyond the scope of midwifery practice, it is crucial that the disease is recognized early and that women be referred immediately for appropriate therapy. Additionally, there are many situations in clinical practice in which a midwife could become involved in the care of a woman who experiences GTD. A knowledgeable midwife can be beneficial in educating the woman about her status and treatment options. Midwives are well prepared to aid affected women in negotiating their way through the emotional turmoil of the diagnosis and guide them along the road to recovery. Compassionate midwifery care can provide the extra emotional support that is needed during this difficult time.

BLOOD BORNE PATHOGEN
EXPOSURE CATEGORY:   I (Involves exposure to blood, body fluids, or tissues)

FUNCTION:  Care of Clients

EQUIPMENT:
1. Doppler
2. Ultrasound
3. Laboratory supplies

POINTS OF EMPHASIS:
Gestational trophoblastic disease (GTD) is a term that encompasses a wide range of conditions arising from abnormal development of placenta tissue. These disorders include hydatidiform moles, invasive moles, gestational chorioncarcinoma, and placental site trophoblastic disease. These conditions have the potential to develop into gestational trophoblastic neoplasm, which can progress into a malignant, life-threatening illness.

Gestational trophoblastic neoplasm had a high rate of fatal outcomes in the past but currently has a 98% cure rate with proper diagnosis and treatment. The development of sensitive serum assay testing for the hormone hCG and advances in effective chemotherapy agents have contributed to the reduced mortality rate.

Hydatidiform Mole
Hydatidiform mole is a disease resulting from an atypical growth of the trophoblastic cells that would normally develop into the placenta; it is not a deviation from an otherwise normal pregnancy. It starts at the time of fertilization due to a defective union of the sperm and ovum, which causes an aberrant proliferation of trophoblastic tissue that rapidly fills the uterine space. Placental villi fill with fluid and become edematous, grape-like structures.

In the US, hydatidiform moles occur in approximately 1 in 600 therapeutic abortions and 1 in 15,000 pregnancies. Maternal age appears to be the major risk factor for developing HM, especially for complete molar pregnancies. Women at both ends of the reproductive age spectrum are the most vulnerable. Those aged younger than 16 years have a 6-fold higher risk of HM than those aged 16 to 40 years. Women aged over 40 years have a 5- to 10-fold higher risk of developing HM, and those aged 50 years or older have a 1 in 3 chance of having a molar pregnancy.

A molar pregnancy is classified as either a complete mole or partial mole. These 2 entities differ in the ways in which they are formed and have distinct variations in histologic features, genetic coding, and clinical symptomatology. In spite of these differences, the management and treatment of clients with either type of molar pregnancy is comparable.
A complete mole occurs when a haploid sperm fertilizes an empty ovum. As a result, the genetic material in the sperm replicates itself. The resultant tissue is completely paternal in origin, usually with a 46XX karyotype. Characteristics of a complete mole include generalized hyperplasia and swelling of the trophoblastic tissue, with marked atypia of the trophoblastic tissue at the implantation site. There is no identifiable fetal tissue in a complete molar pregnancy.

A partial mole is the result of a normal ovum being fertilized by two sperm. The genetic component of the tissue contains both maternal and paternal chromosomal material, but the replication of the cells results in a triploid karyotype, usually 69XXY. The trophoblastic tissue has only diffuse areas of trophoblastic hyperplasia and swelling, with only mild atypia of the trophoblastic cells at the implantation site. A partial mole also has identifiable fetal tissue associated with it. A fetus that develops a partial molar pregnancy is nonviable and exhibits congenital anomalies associated with triploidy.

The effects of excessive amounts of hCG on the pregnant woman can lead to several medical problems such as pregnancy-induced hypertension, hyperthyroidism, anemia, and hyperemesis gravidarum. Women with a complete mole also may present with ovarian enlargement and theca lutein cysts secondary to the hyperstimulation from elevated hCG levels. Most of these traditional symptoms will not be evident until the woman reaches her second trimester.

One of the first symptoms of a complete molar pregnancy may be vaginal bleeding during the first trimester. As some of the trophoblastic tissue deteriorates, blood clots may form between the trophoblastic villi and the endometrial lining. As these blood clots disintegrate, the woman will experience dark red vaginal bleeding and possibly the passage of some of the trophoblastic tissue. Since many of these pathological sings and symptoms are generally not as pronounced in early pregnancy, a complete mole might be diagnosable after histologic and/or genetic evaluation of the products of conception.

With a partial molar pregnancy, the proliferation of the trophoblastic tissue is less dense than that seen in a complete mole; therefore, the woman with a partial mole will usually have hCG levels that are within a normal range for the gestational age. Uterine size is not significantly larger than would be expected. Most women with a partial mole present clinically with dark red vaginal bleeding and symptoms of a missed or incomplete abortion.

**Gestational Trophoblastic Disease**

Gestational trophoblastic neoplasia encompasses a group of related disease entities that develop from abnormal proliferation of trophoblastic tissue. These conditions can occur after a molar or a normal pregnancy. It is essential that affected women are identified immediately and referred for thorough evaluation and appropriate treatment. GTN is characterized by the trophoblastic tissue invading the myometrium, with the potential for the tissue to enter uterine blood vessels and metastasize to other areas of the body. There are three types of GTN: invasive mole, choriocarcinoma, and placental site trophoblastic tumor. Each of these diseases have their own distinct clinical presentation.

**Invasive moles** cause the edematous chorionic villi to extend directly into the myometrium. These rarely metastasize beyond the uterus. This condition occurs after evacuation of complete hydatiform moles in approximately 20% of clients. Although uncommon, an invasive mole can also occur after other pregnancies as well. Clinical signs of invasive mole include prolonged vaginal bleeding and persistent levels of hCG. Chemotherapy is used to treat invasive moles.

**Choriocarcinoma** develops when abnormal trophoblastic tissue evolves into an epithelial malignancy, which occurs in approximately one in 20,000 to 40,000 pregnancies. There is a high incidence of vascular invasion, with the resultant high risk of early systemic metastasis. The most common site for choriocarcinoma metastasis (80%) is in the lungs. The next most common site for metastasis (30%) is in the vagina. Brain and liver metastasis accounts for another 10%, respectively. The trophoblastic tumors in choriocarcinoma develop a vascular system that contains fragile blood vessels. Hemorrhage is a frequent symptom of choriocarcinoma metastasis. Unusual bleeding such as hemoptysis, cerebral bleeding, or hepatic hematoma can be a sign of choriocarcinoma metastasis. Choriocarcinoma also may present as tumors located high in the vaginal fornices. A client with vaginal metastasis may present with unusual or
irregular bleeding. Choriocarcinoma is treated with either single-agent or multiple-agent chemotherapy, depending on the extent of the disease.

*Placental site trophoblastic tumor* is a rare form of GTN. This tumor arises from the placental implantation site and can occur after any pregnancy whether it is an intrauterine gestation, an ectopic pregnancy, or a spontaneous or induced abortion. Placental trophoblastic tumor does not contain chorionic villi, and there is a limited amount of hCG secreted. Levels of hCG are lower than the levels of hCG observed in other forms of GTN. A unique feature of a placental site tumor is slow growth; symptomatology may not appear until after the pregnancy has ended. It may present with irregular postpartum vaginal bleeding, uterine subinvolution, or persistent unexplained low serum levels of hCG after the completion of a pregnancy. Placental site trophoblastic tumor is usually resistant to chemotherapy and is commonly treated with hysterectomy.

**PROCEDURE:**

1. When a woman experiences an early pregnancy loss, the possibility of a molar pregnancy should be considered. In any first trimester loss, the products of conception should be sent to a pathology laboratory for a histologic examination to obtain a definitive diagnosis. Prolonged postpregnancy vaginal bleeding that is not responsive to usual treatment measures should alert the practitioner to suspect trophoblastic disease and initiate serial monitoring of hCG levels.

2. In midwifery practices, it isn’t customary for clients to obtain first trimester ultrasounds; therefore, molar pregnancies may not be discovered until the early second trimester when absent fetal heart sounds and/or a larger than expected uterus are the first indicators of a problem. The CNM may be the practitioner who initiates the medical assessment and diagnostic evaluation of the woman with a suspected molar pregnancy. Attention should be paid especially to the respiratory system because pulmonary complications are most often seen in women with uterine enlargement greater than 14 to 16 weeks’ size. Thyroid, renal, and liver function also are essential components of the medical evaluation.

3. Trophoblastic tissue releases RhD antigens, and thus women who are Rh negative must receive Rh immune globulin at the time of uterine evacuation.

4. Midwives should also be suspicious of the possibility of GTN after any type of pregnancy. Any women who exhibits persistent postpartum bleeding and/or uterine subinvolution that does not respond to conventional methods of treatment should be assessed for GTN. Any elevation of hCG levels during the postpartum period should alert the CNM to the need for immediate referral for GTN evaluation.

5. The CNM may become involved in the post-evacuation surveillance of a woman who has experienced a molar pregnancy. It is important to provide education about molar pregnancy and the potential for further complications in order to ensure compliance with the lengthy time period for the monitoring of declining hCG levels.

**Hydatidiform Mole**

6. A serum assay for hCG may be helpful in the identification of a molar pregnancy, as the rampant growth of trophoblastic tissue in a complete molar pregnancy will produce unusually high levels of hCG; however, it is limited in detecting partial molar pregnancies as rarely do they elevate above normal pregnancy values.

7. Ultrasound is a standard of care in evaluating early pregnancy bleeding and a noninvasive method of diagnosing a molar pregnancy. In early gestation, it is likely that ultrasound will show an echogenic endometrial mass for both complete and partial molar pregnancies. There may be identifiable fetal tissue noted with a partial mole. However, a complete mole demonstrates unique characteristics when the ultrasound is done in the second trimester. During this time, swollen villi and trophoblastic hyperplasia appear as a class “snowstorm pattern.”

**Treatment**

8. A dilation and evacuation procedure is done to remove the molar pregnancy from the uterus. Suction curettage is used to lessen the chance of uterine perforation.

9. Methods such as cervical ripening or labor induction agents are not used because uterine contractions can lead to a trophoblastic embolism.

10. For clients who have completed their childbearing season, a hysterectomy with sparing of the adnexa is another option for treatment of molar pregnancy.
11. After evacuation of a molar pregnancy, hCG levels must be monitored to ascertain that all trophoblastic tissue has been removed as well as to evaluate for the potential development of GTN. Serum hCG levels are measured weekly until levels have been undetectable (<5mIU/mL) for 3 weeks. Levels are then measured monthly until hCG has been undetectable for 6 months. Some specialists are examining whether the 6-month period of monthly testing can be shortened for women who are at low risk for developing malignant disease. Eight-four percent of women with molar pregnancies have complete regression of the hCG titer within 12 to 14 weeks.

12. After evacuation of a molar pregnancy, hCG levels that rise or plateau may be indicative of the development of gestational trophoblastic neoplasia (GTN). In this case, the woman needs immediate evaluation and treatment for postmolar malignant sequelae, which can be seen in 20% of complete molar pregnancies and 5% of partial molar pregnancies. Predictors for the development of neoplasia after a complete mole include markedly elevated hCG levels, an abnormally large uterus prior to evacuation, and theca lutein ovarian cysts larger than 6 cm in diameter. There have been no presenting clinical symptoms that appear to detect women with a partial mole who are at higher risk for developing neoplasia.

**Gestational Trophoblastic Neoplasia**

13. All women who are at risk for the development of GTN need to be monitored closely with serial measurement of hCG levels. If GTN is not diagnosed and treated appropriately, there is increased risk for systemic metastasis.

14. Treatment of GTN is determined by the extent of the disease. This is determined by using a staging/scoring system that is most certainly managed by the consulting physician. High-risk GTN should be managed by an oncologist who is experienced in the treatment of this disease. *Regional GTD treatment centers are located throughout the United States. These facilities offer the services of physicians who are experts in the pathophysiology and treatment of GTD and GTN. Clinicians should consider referral of affected women to such a regional center for the most comprehensive care.*

**Future Fertility**

15. The timing of the next pregnancy will most likely be determined by the obstetrician-gynecologist or gynecologic oncologist.

16. Having a molar pregnancy does not negatively impact future fertility, and even women who have received chemotherapy for GTN can expect their fertility will be preserved.

17. Women must be advised not to get pregnancy while their hCG levels are being monitored after treatment. Until it has been determined that hCG levels have consistently returned to normal levels, any new pregnancy will elevate hCG levels and interfere with the scheduled follow-up hCG testing.

18. Use of an effective contraceptive method is critical during this time period. There are no restrictions for the use of combined methods (pills, patch, ring), progestin-only methods (pills, injectable, implants), and all barrier methods. IUDs however, are not recommended while hCG levels are decreasing or undetectable, and its use is contraindicated in women with persistently elevated hCG levels or malignant disease.

19. In a pregnancy after treatment of GTD, the CNM needs to be diligent in screening for a recurrence of the disease. Midwives can provide emotional encouragement for these women as they contend with their fears and concerns about the potential for another molar pregnancy.

20. Any woman with a history of a molar pregnancy or GTN should be scheduled for a first trimester ultrasound and serum hCG level to provide opportunity for early detection of any recurrence. These women should have serum hCG levels evaluated 6 weeks postpartum, as the pregnancy can possibly reactivate GTD.

**REFERENCES:**


**Originated:** June, 2012