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ECTOPIC PREGNANCY

GENERAL INFORMATION Normally, at the beginning of a pregnancy, the fertilized egg travels from the fallopian tube to the uterus, where it implants and grows. But in about 2% of diagnosed pregnancies, the fertilized egg attaches to an area outside of the uterus, which results in an ectopic pregnancy (also known as a tubal pregnancy or an extrauterine pregnancy). An ectopic pregnancy cannot support the life of a fetus for very long. But an ectopic pregnancy can grow large enough to rupture the area it occupies, cause heavy bleeding, and endanger the mother. A woman with signs or symptoms of an ectopic pregnancy requires **immediate** medical care and is one of the leading causes of death in pregnant women. In most ectopic pregnancies, the fertilized egg has implanted in a fallopian tube.

In rare cases: The egg attaches and grows in an ovary, the cervix, or the abdominal cavity (outside of the reproductive system). One or more eggs grow in the uterus, and one or more grow in a fallopian tube, the cervix, or the abdominal cavity. This is called a heterotopic pregnancy.

COMPLICATIONS OF ECTOPIC PREGNANCY

Ectopic pregnancy can damage the fallopian tube, which can make it difficult to become pregnant in the future. Ectopic pregnancies are usually detected early enough to prevent deadly complications such as severe bleeding. A ruptured ectopic pregnancy requires emergency surgery to prevent heavy bleeding into the abdomen. The affected tube is partially or fully removed. The increased incidence of ectopic pregnancy is partially attributed to improved ability in making earlier diagnosis. Ectopic pregnancies that previously would have resulted in tubal abortion or complete, spontaneous reabsorption and remained clinically undiagnosed are now detected.

TREATMENT OPTIONS

Some investigators have questioned the need for unnecessary surgical or medical intervention in very early cases and have advocated EXPECTANT MANAGEMENT in select cases. However, distinguishing patients who are experiencing spontaneous resolution of their ectopic pregnancies from patients who have proliferative ectopic pregnancies requires an experienced physician. Candidates for successful expectant management should be asymptomatic and have no evidence of rupture or hemodynamic instability. Furthermore, they should demonstrate objective evidence of resolution, such as declining beta-human chorionic gonadotropin (β -HCG) levels. They must also be fully compliant and be willing to accept the potential risks of tubal rupture.

Approximately one fourth of women presenting with ectopic pregnancies have declining β -HCG levels, and 70% of this group experience successful outcomes with close observation (and no treatment), as long as the gestation is 4cm or less in its greatest dimension. An initial low β -HCG titer also correlates with successful spontaneous resolution. Although data are limited on this matter, initial β -HCG titers below 1000 mIU/mL have been demonstrated to predict a successful outcome in 90% chance that the pregnancy will resolve without therapy. Note that no cutoff value below which expectant management is uniformly safe has been established. Furthermore, rupture despite low and declining serum levels of β -HCG has been reported, making close follow-up and *patient compliance* of paramount importance.

METHOTREXATE is an antimetabolite chemotherapeutic agent that binds to the enzyme dihydrofolate reductase, which is involved in the synthesis of purine nucleotides. This interferes with deoxyribonucleic acid (DNA) synthesis and disrupts cell multiplication (ie kills growing cells). Methotrexate has long been known to be effective in the treatment of leukemia, lymphomas, and carcinomas of the head, neck, breast, ovary, and bladder. It has also been used as an immunosuppressive agent in severe psoriasis and rheumatoid arthritis.

The effectiveness of methotrexate on trophoblastic tissue has been well established and is derived from experience gained in using this agent in the treatment of hydatiform moles and choriocarcinoma (cancer of the placenta). As used in the treatment of ectopic pregnancy, methotrexate is administered in a single or in multiple intramuscular (IM) injections.

Treatment with methotrexate is an especially attractive option when the pregnancy is located on the cervix or ovary or in the interstitial or the cornual portion of the tube. Surgical treatment in these cases is often associated with increased risk of hemorrhage, often resulting in hysterectomy or oophorectomy. Successful medical treatment using methotrexate has been reported in the literature with good subsequent reproductive outcomes. By avoiding surgery, the risk of tubal injury is reduced.

Medical therapy for ectopic pregnancy involving methotrexate may be indicated in certain patients. To determine acceptable candidates for methotrexate therapy, first establish the diagnosis by one of the following criteria:

- Abnormal doubling rate of the beta-human chorionic gonadotropin (β -HCG) level and ultrasonographic identification of a gestational sac outside of the uterus OR
- Abnormal doubling rate of the β -HCG level, an empty uterus

Also:

- The patient must be hemodynamically stable, with no signs or symptoms of active bleeding or blood in the belly
- The patient must be reliable, compliant, and able to return for follow-up care
- The size of the gestation should not exceed 4cm at its greatest dimension (or exceed 3.5 cm with cardiac activity) on ultrasonographic measurement - Exceeding this size is a relative, but not absolute, contraindication to medical therapy
- Absence of fetal cardiac activity on ultrasonographic findings - The presence of fetal cardiac activity is a relative contraindication
- No evidence of tubal rupture - Evidence of tubal rupture is an absolute contraindication
- β -HCG level less than 5000 mIU/mL - Higher levels are a relative contraindication

Although patients with β -HCG levels above 5,000 IU/L and fetal cardiac activity have been treated successfully with methotrexate, these patients require much greater surveillance and carry a higher risk of subsequent operative intervention. There is an inverse association between β -HCG levels and successful medical management of an ectopic pregnancy. Other contraindications to the use of methotrexate include the following:

- Documented hypersensitivity to methotrexate
- Breastfeeding
- Immunodeficiency
- Alcoholism
- Alcoholic liver disease
- Any other type of liver disease
- Blood disorders
- Leukopenia
- Thrombocytopenia
- Anemia
- Active pulmonary disease
- Peptic ulcer disease
- Renal, hepatic, or hematologic dysfunction

Treatment effects of methotrexate include an increase in abdominal pain (occurring in up to two thirds of patients), an increase in β -HCG levels during the first 1-3 days of treatment, and vaginal bleeding or spotting.

The medical treatment of ectopic pregnancy requires compulsive compliance. The physician must emphasize the importance of patient follow-up and have patient information on hand, including the patient's home address, telephone numbers at home and work, and the means to reach a contact person in case attempts to reach the patient directly are unsuccessful. Proper documentation of attempts to reach the patient, including records of telephone calls and certified mail are important medical-legal considerations.

Most patients experience at least 1 episode of increased abdominal pain, which usually occurs 2-3 days after the injection. Increased abdominal pain is believed to be caused by the separation of the pregnancy from the implanted site. It can be differentiated from tubal rupture in that it is milder, of limited duration (lasting 24-48 h), and is not associated with signs of acute abdomen or hemodynamic instability.

Advise patients to avoid alcoholic beverages, vitamins containing folic acid, nonsteroidal anti-inflammatory drugs (NSAIDs), and sexual intercourse, until advised otherwise.

SALPINGOSTOMY AND SALPINGECTOMY

Within the last 2 decades, a more conservative surgical approach to unruptured ectopic pregnancy using minimally invasive surgery has been advocated to preserve tubal function. The conservative approaches include linear salpingostomy (cutting open the tube and removing the pregnancy), milking the pregnancy out the end of the tube (high risk for failure and tubal damage), resecting the segment of the fallopian tube that contains the gestation (removing the ectopic and tube). Laparoscopy has become the recommended approach in most cases. Laparotomy is usually reserved for patients who are hemodynamically unstable or for patients with cornual ectopic pregnancies; it also is a preferred method for surgeons in patients in whom a laparoscopic approach is difficult (eg, secondary to the presence of multiple dense adhesions, obesity, or massive amounts of blood in the belly). Multiple studies have demonstrated that laparoscopic treatment of ectopic pregnancy results in fewer postoperative adhesions than laparotomy. Furthermore, laparoscopy is associated with significantly less blood loss and a reduced need for analgesia. Finally, laparoscopy reduces cost, hospitalization time, and convalescence period.