

Protocol for Treatment of Ectopic Pregnancy

If ectopic pregnancy has been diagnosed and the patient is clinically stable with a non-ruptured ectopic pregnancy, there are options for either medical management with methotrexate or surgical management (salpingostomy or salpingectomy) based on initial quantitative-HCG, ultrasound findings, and individual patient factors and preferences. Patients who are exhibiting signs or symptoms of ruptured ectopic pregnancy (hemodynamic instability, free fluid in the cul-de-sac on ultrasound, significant abdominal pain, or adnexal tenderness) should be emergently transferred to the care of a surgeon for immediate surgical intervention.¹

Medical Management

Methotrexate interrupts actively proliferating tissues, including the rapidly dividing cells of the ectopic pregnancy. This allows them to then be resorbed by the body. The success rate of methotrexate decreases with higher initial quantitative beta-HCG levels.²

Contraindications to outpatient medical management → urgent referral to surgery as below:

- Any sign of ruptured ectopic pregnancy (hemodynamic instability, free fluid in the cul-de-sac on ultrasound, significant abdominal pain, adnexal tenderness)
- Visible ectopic pregnancy **with** fetal cardiac activity on ultrasound
- Medical conditions including liver disease or alcoholism, moderate-to-severe anemia/leukopenia/thrombocytopenia, immunodeficiency, breastfeeding, active peptic ulcer disease, pulmonary disease, renal insufficiency
- Initial quantitative beta-HCG >10,000
- Inability to establish close cell phone communication and follow up

Importantly, patients should be counseled that risk of ruptured ectopic pregnancy persists until beta-HCG levels are undetectable and should be given strict ectopic precautions.

Side effects of methotrexate include: abdominal pain 2-3 days after administration (can be managed expectantly as long as no signs of ruptured ectopic pregnancy), other gastrointestinal symptoms (nausea, vomiting), vaginal spotting, alopecia, and neutropenia.³

¹ Tubal ectopic pregnancy. ACOG Practice Bulletin No. 193. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2018; 131;e91-103.

² Medical treatment of ectopic pregnancy: a committee opinion. Practice Committee of American Society for Reproductive Medicine. *Fertil Steril* 2013;100(3):638–44

³ Barash JH, Buchanan EM, Hillson C. Diagnosis and management of ectopic pregnancy. *Am Fam Physician*. 2014;90:34–40

One-Dose Treatment Protocol and Follow Up:

This carries the lowest risk of adverse effects however is less efficacious than the two-dose protocol in patients with higher initial quantitative beta-HCG levels.

Day 1:

- Ensure reliable cell phone access and provide patient with 24/7 emergency number to call.
- Obtain baseline CBC, BMP, LFTs, blood type, and quantitative beta-HCG.
- Administer single dose of methotrexate 50mg/m² intramuscularly (m² is also known as the body surface area (BSA): it can be calculated in many EHRs using a smartphrase or using this [BSA calculator](#))

Day 4:

- Measure quantitative beta-HCG level (it is common to see an increase from day 1 levels and does not represent treatment failure)

Day 7:

- Measure quantitative beta-HCG level and compare level to day 4 level:
 - If decrease from day 4 to day 7 is < 15%: readminister methotrexate 50mg/m²
 - If decrease from day 4 to day 7 is > 15%, measure quantitative beta-HCG levels weekly until they are undetectable OR once HCG <50 can consider having a phone check-in in 1 week with continued ectopic precautions and home urine pregnancy test in 2 weeks. If negative home urine pregnancy test at that time, no need for further follow-up.

If quantitative beta-HCG does not decrease after four doses, consider surgical management.

Two Dose Treatment Protocol and Follow Up

Consider two-dose methotrexate regimen for patients with an initial high quantitative beta-HCG level (i.e. over 5000). Resolution of HCG levels is significantly faster in patients treated with two-dose MTX compared with one-dose.

Day 1:

- Ensure reliable cell phone access and provide patient with 24/7 emergency number to call.
- Obtain baseline CBC, BMP, LFTs, blood type, and quantitative beta-HCG.
- Administer dose of methotrexate 50mg/m² (m² is also known as the body surface area (BSA): it can be calculated in many ESRs using a smartphrase or using this [BSA calculator](#))

Day 4:

- Administer second dose of methotrexate 50mg/m².

- Measure quantitative-HCG level post-administration of methotrexate.

Day 7:

- Measure quantitative-HCG level and compare level to Day 4 level:
 - If decrease from day 4 to day 7 is < 15%: readminister methotrexate 50mg/m² and recheck quantitative-HCG levels on day 11.
 - If decrease from day 4 to day 7 is > 15%: measure HCG weekly until undetectable OR once HCG <50 can consider having a phone check-in in 1 week with continued ectopic precautions and home urine pregnancy test in 2 weeks. If negative home urine pregnancy test at that time, no need for further follow-up.

If quantitative beta-HCG does not decrease after four doses, consider surgical management.

Surgical Management

Indicated if any of the conditions mentioned under contraindications for medical management exist. Process of referral to surgery may vary by health system and this system should be worked out prior to offering treatment for ectopic pregnancy in the office. A system for tracking the patients to assure that there is one clinician prepared to call with follow up results and reminders is also important.