This care process model (CPM) was developed by clinical experts from Intermountain Healthcare’s Women and Newborns Clinical Program. The CPM recommends diagnosis, treatment, and follow-up processes to improve care in the emergency department for patients with ectopic pregnancies.

**Why Focus on ECTOPIC PREGNANCY?**

In the United States, the annual incidence of ectopic pregnancy is approximately 2% and rising. The incidence varies among populations, with most ectopic pregnancies occurring in multigravid women. The overwhelming majority of ectopic pregnancies occur in the fallopian tubes.

**Ectopic pregnancy is always serious.** Despite improved methods leading to earlier detection and treatment, hemorrhage from ectopic pregnancy is the leading cause of pregnancy-related maternal death in the first trimester and accounts for 4% to 10% of all pregnancy-related deaths. Other morbidity associated with ectopic pregnancy includes infection, repeat ectopic pregnancy, and infertility.

**Ectopic pregnancy can be difficult to diagnose.** Between 40% and 50% of ectopic pregnancies are not diagnosed during an initial visit to an emergency department. Delay in diagnosis increases the chance of tubal rupture and may reduce options for nonsurgical treatment.

**Why Focus on NONSURGICAL MANAGEMENT?**

Ectopic pregnancy can be treated surgically or nonsurgically. Nonsurgical treatment includes expectant management (“watchful waiting”) and medical treatment with the drug methotrexate (MTX). This CPM focuses on nonsurgical management for the following reasons:

- **Nonsurgical management is appropriate in many cases of ectopic pregnancy.** Approximately 35% of women with ectopic pregnancy are eligible for medical management; a small number are eligible for expectant management. For patients meeting recommended criteria, nonsurgical approaches are generally preferred for preserving fertility, decreasing recovery time, and lowering cost. The overall success rate for medical treatment is nearly 90%. Because MTX is a potent antimetabolite medication, take measures to minimize staff exposure during drug handling and administration. This CPM supports Intermountain’s MTX-handling procedure, found page 50 of the Sterile, Nonsterile, and Hazardous Drug Compounding Manual, available at intermountain.net/policy.

- **Special handling measures must be used for MTX.**

- **Safe, nonsurgical management requires continuity of care.** Most patients with ectopic pregnancy are first evaluated in the hospital emergency department (ED). This CPM outlines a process to ensure that patients are also evaluated by an obstetric provider while in the ED and that this provider counsels the patient and carefully monitors her throughout the course of her treatment outside the ED.
Patient presents to ED with signs / symptoms of ectopic pregnancy (a)

Ectopic pregnancy diagnosed?

no

EXPLORE causes of symptoms
Early ectopic pregnancy should still be considered and a 48-hour follow-up arranged as necessary

yes

ASSESS for ectopic pregnancy (b)

REFER to provider with appropriate training*

MANAGE ectopic pregnancy

• EVALUATE patient to confirm diagnosis
• DETERMINE if patient meets criteria for nonsurgical management with either of the following:
  – Administration of methotrexate (MTX) (c)
  – Expectant management (d)

SCHEDULE surgery

no

Does patient meet criteria for nonsurgical management?

yes

DETERMINE appropriate plan

MTX treatment

INITIATE MTX treatment

• EDUCATE patient on the condition, planned treatment with MTX, and follow up (e)
• ORDER MTX**; a verbal order is NOT acceptable
• ADMINISTER MTX per Intermountain guidelines (f)

DISCHARGE from ED with follow-up surveillance instructions (g)

Expectant management

INITIATE expectant management

EDUCATE patient on the condition, planned treatment with MTX, and follow up (e)

DISCHARGE patient from ED with follow-up instructions to measure hCG levels twice weekly until resolution

* Obstetrician, gynecologist, family practice physician with obstetric training and surgical privileges, or a midlevel provider with surgical back-up — preferably one with an established relationship with the patient.

** Only the obstetric provider — not an ED attending or other physician — may order MTX.
ALGORITHM NOTES

(a) Signs / symptoms of ectopic pregnancy
Maintain a high degree of suspicion in any female of reproductive age (regardless of contraceptive method) presenting with:
- Common symptoms: Abdominal pain, possibly with vaginal spotting 6–8 weeks after last menstrual period (may be later if nontubal)
- Less common: Pain radiating to shoulder, vaginal bleeding, syncope

(b) Assessment for ectopic pregnancy
- Medical history. Determine presence of risk factors for ectopic pregnancy, chiefly:
  - Pelvic inflammatory disease
  - Previous ectopic pregnancy
  - Endometriosis
  - Previous tubal or pelvic surgery
  - Infertility or infertility treatments
  - Uterotubal anomalies
  - History of iatrogenic exposure to diethylstilbestrol
  - Cigarette smoking
- Physical exam. Findings often unremarkable, especially for small, unruptured ectopic pregnancies. Suggestive findings include:
  - Normal or slightly enlarged uterus
  - Pelvic pain with movement of cervix
  - Palpable adnexal mass
  - Signs of leaking or ruptured ectopic pregnancy: hypotension, marked abdominal tenderness with guarding and rebound tenderness
- Labs:
  - Quantitative serum hCG
  - Imaging: Transvaginal ultrasound

(c) Considerations for medical treatment with MTX
Absolute MTX contraindications (ANY of the following):
- Intrauterine pregnancy
- Immunodeficiency
- Pre-existing blood dyscrasias
- Known sensitivity to MTX
- Active pulmonary disease
- Peptic ulcer disease
- Alcoholism or liver disease
- Abnormal creatinine (> 1.3 mg/dL) or elevated AST (SGOT)
- Breastfeeding
- Ruptured ectopic pregnancy
- Hemodynamically unstable with active bleeding or signs of hemoperitoneum
- Patient unwilling to return for follow-up care

Relative MTX contraindications (ANY of the following):
- Fetal cardiac activity
- Beta-hCG > 5,000 mIU/ml
- Unruptured mass > 4.0 cm
- Patient unwilling to accept blood transfusion

(d) Considerations for expectant management
INCLUSION criteria (must meet ALL):
- Hemodynamically stable
- Experiencing minimal pain
- Initial hCG level < 1,500 mIU/ml
- Falling hCG levels measured twice weekly until resolution
- Reliable patient willing to complete follow-up instructions

(e) MTX patient / family education
- For treatment with MTX, use Intermountain fact sheet, Methotrexate to Treat Ectopic Pregnancy, to facilitate a conversation with patient and family. (Document that patient has received fact sheet and given verbal consent to treatment; a signed informed consent form is NOT necessary.) See page 4 for ordering instructions.
- Discuss possible side effects of MTX including:
  - More common: Nausea, vomiting/stomatitis, gastric distress, dizziness, and fatigue.
  - Less common: Skin photosensitivity, inflammation of the membrane covering the eye, sore mouth and throat, pneumonitis, reversible alopecia (rare), and severe neutropenia (rare).
- Instruct patient to avoid the following during MTX administration:
  - Vitamins containing folic acid (found in prenatal vitamins and most multivitamin supplements)
  - Alcohol
  - NSAID medication
  - Penicillin
- Emphasize importance of follow-up visits and determine schedule.

(f) MTX administration guidelines
- Ordering: MTX must be ordered by a qualified provider (obstetrician, gynecologist, family practice physician with obstetric training and surgical privileges, or a midlevel provider with surgical back-up) who agrees to follow the treatment course with the patient in his/her office or another setting. (ED department should NOT be used for follow-up unless complications mandate an emergency evaluation.)
- Administration and setting: MTX must be given only by a nurse qualified to give chemotherapeutic agents. MTX may be given wherever staff have been appropriately trained. For timely administration, the patient may need to be transferred to a site where qualified providers are available.
- Dose: 50 mg/m2 given IM.
- Drug interactions that may:
  - Increase MTX concentrations: Ciprofloxin, penicillin, omeprazole, cyclosporine, probenecid, and NSAIDS.
  - Cause MTX toxicity: Doxycycline, sulfa antibiotics, amiodarone, and phenytoin.

(g) Follow-up surveillance after MTX therapy
Check hCG levels as follows:
- On day 4: 4 days after MTX is given, hCG levels usually decline but may plateau or even rise.
- On day 7: Expect a decrease in hCG levels. If day 7 levels do not show a decrease of at least 15%, a second dose of MTX may be given if criteria are still met. A second dose is necessary for 15% to 20% of patients.
- Weekly thereafter until resolution (hCG < 15 mIU/mL). The average time to resolution is 34 days.
If necessary, repeat transvaginal ultrasound. Abdominal pain is experienced in 60% of patients and may be due to tubal placental separation and a resultant small tubal hematoma. As a result, subsequent ultrasound may show increasing tubal diameter.

Hemodynamically stable
Weekly thereafter
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NSAID medication that may:
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Dose:
Penicillin
Medical history .
Initial hCG level < 1,500 mIU / ml
Reliable patient willing to complete follow-up instructions
Previous ectopic pregnancy
Patient unwilling to accept blood
Immunodeficiency
Experiencing minimal pain
Infertility or infertility treatments
Patient unwilling to return for
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FACT SHEET FOR PATIENTS AND FAMILIES

Methotrexate to Treat Ectopic Pregnancy

What is ectopic pregnancy?

Ectopic pregnancy is when a fertilized egg grows outside the uterus (the womb). The most common location for an ectopic pregnancy is in a fallopian tube. It won’t result in a live birth. An ectopic pregnancy won’t result in the uterus having the right conditions and the space needed for the egg to develop normally.

An ectopic pregnancy won’t result in a live birth. An ectopic pregnancy can cause severe, life-threatening bleeding inside the abdomen. It can be ended with a medicine called methotrexate. In this case, the medicine removes the fertilized egg before a rupture occurs. Sometimes, a second or third injection is necessary in the ectopic pregnancy.

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Provider tools

Access this CPM and other resources from the “Ectopic Pregnancy” topic page, available from intermountainphysician.org/CPM/CPM033.

Tools to ensure safe handling of methotrexate

Order form

Ectopic Pregnancy Methotrexate Chemotherapy
Order form (available at intermountain.net/forms)

Procedure

Sterile, Nonsterile, and Hazardous Drug Compounding Manual, available at intermountain.net/policy.

For select RNs in the ED and in rural facilities who will administer MTX, the following must be completed PRIOR to administration for indication of ectopic pregnancy:

- Administering Methotrexate for Ectopic Pregnancy (LMS Course #29085) — Pass-off (annual; 0.25 hours).
- Caring for the Patient Who has Received Hazardous Drugs (LMS Course #13726).

For specific information on the safe handling procedure or on staff training to support it, contact Pharmacy Services, (801) 442-3308.

Patient tools

Order and access patient education tools, including Methotrexate to Treat Ectopic Pregnancy fact sheet, available in both English and Spanish.

REFERENCES


CPM DEVELOPMENT TEAM

Ware Branch, MD
Wes Davis, MD
David Jackson, MPH (Medical Writer)
Jean Millar, MBA, RN
Sara Jane Pieper, MD (Chair)
Douglas Richards, MD

This CPM presents a model of best care based on the best available scientific evidence at the time of publication. It is not a prescription for every physician or every patient, nor does it replace clinical judgment. All statements, protocols, and recommendations herein are viewed as transitory and iterative. Although physicians are encouraged to follow the CPM to help focus on and measure quality, deviations are a means for discovering improvements in patient care and expanding the knowledge base. Send feedback to Sara Jane Pieper, MD, Gynecology Development Team Lead, Intermountain Healthcare, (gyn@mail.org).