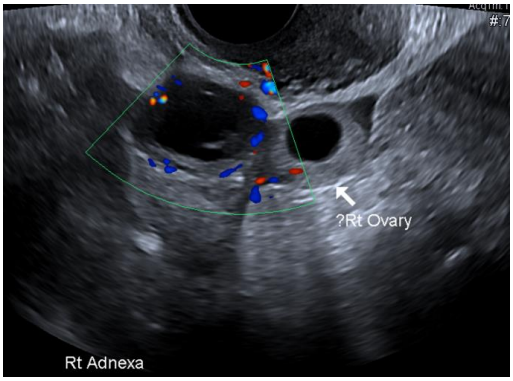
Clinical update no. 530
6 February 2019

Case: 33yr-F initially presenting at 5wk gestation with PV spotting. Serial HCGs as follows; the slow rise concerning for ectopic:

Index visit	+2 d	+4 d	+ 8 d	
1283	1667	2258	4096	IU/L

An ultrasound + 9 days from the index visit showed an empty uterus and right sided adnexial mass suggestive of an ectopic. Methotrexate was given.



She subsequently presented with further bleeding and pain, and went to theatre for removal of right tubal ectopic.

DIAGNOSIS
A. UTERINE CURETTINGS: DECIDUA AND HYPERSECRETORY ENDOMETRIUM
B. RIGHT FALLOPIAN TUBE: ECTOPIC TUBAL GESTATION

How successful is methotrexate for management of ectopic pregnancy?

Canadian Journal of Emergency Medicine

Methotrexate for the treatment of unruptured tubal ectopic pregnancy

Published online: 08 October 2018

What did this study find?

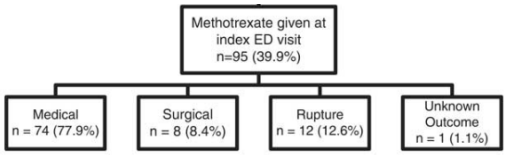
Of patients treated with methotrexate, 18% went on to require surgical management, with 11.2% having ruptured on surgical evaluation.

This single centre study with a high acuity obstetric program evaluated 612 patients with suspected ectopic pregnancy. About half had an ectopic pregnancy confirmed.

At the index visit to ED, 95 received methotrexate, 124 underwent expectant management, and 21 underwent surgical management.

After the index ED visit, 28 went on to have a ruptured ectopic pregnancy, 17 of whom were initially treated with methotrexate.

13.2% of patients received methotrexate despite having relative contraindications.



Despite access to a high acuity obstetric service, many patients represented to ED. Of those given methotrexate there was a mean 1.7 return visits to ED. ED doctors need to be aware of potential complications and risk of rupture following methotrexate therapy.

Patients may represent to ED after methotrexate therapy with ongoing symptoms including pain and bleeding. The ectopic may also rupture. A high index of suspicion is required with close O&G involvement to follow up and manage complications.

The Royal Australian and New Zealand College of Obstetricians and Gynaecologists
Excellence in Women's Health

https://www.ranzcog.edu.au/Statements-Guidelines

Ectopic pregnancy and miscarriage

Diagnosis and initial management in early pregnancy of ectopic pregnancy and miscarriage

Issued: December 2012

NICE clinical guideline 154
guidance.nice.org.uk/cg154

The RANZCOG refer to the NICE Guildeines.

1.6 Management of ectopic pregnancy

Surgical and medical management

1.6.3 Offer systemic methotrexate[H] as a first-line treatment to women who are able to return for follow-up and who have all of the following:

- no significant pain
- an unruptured ectopic pregnancy with an adnexal mass smaller than 35 mm with no visible heartbeat
- a serum hCG level less than 1500 IU/litre
- no intrauterine pregnancy (as confirmed on an ultrasound scan).

Offer surgery where treatment with methotrexate is not acceptable to the woman.

Methotrexate is recommended as first line treatment when criterion outlined are met including an HCG <1500 IU/L.

Of note, there may be a viable gestation with an HCG <1500 and no intrauterine gestation seen on ultrasound, so there needs to be some certainty before giving methotrexate.

OBSTETRICS AND GYNECOLOGY/CLINICAL POLICY

Clinical Policy: Critical Issues in the Initial Evaluation and Management of Patients Presenting to the Emergency Department in Early Pregnancy

Volume 69, no. 2 : February 2017 Annals of Emergency Medicine 241

A discriminatory HCG threshold is defined as the level at which the sensitivity of US approaches 100% for detecting an IU gestation, with the presumptive diagnosis of ectopic pregnancy if an intrauterine pregnancy is not seen. The threshold is considered about 1,000 – 2,000 mIU/ml for a formal transvaginal US, but applicability of a discriminatory threshold to ED practice is not clear, and not used in the ACEP Policy. Errors can occour if using that threshold.

There is some variation and a viable gestation can be present in about 2% with an HCG >2,000 and an indeterminate scan.

Diagnostic Criteria for Nonviable Pregnancy Early in the First Trimester

N ENGL J MED 369;15 NEJM.ORG OCTOBER 10, 2013

among women with a pregnancy of unknown location and hCG levels of 2000 to 3000 mIU per milliliter, there will be 19 ectopic pregnancies and 38 nonviable intrauterine pregnancies for each viable intrauterine pregnancy.

1.6.4 Offer surgery as a first-line treatment to women who are unable to return for follow-up after methotrexate treatment or who have any of the following:

- an ectopic pregnancy and significant pain
- an ectopic pregnancy with an adnexal mass of 35 mm or larger
- an ectopic pregnancy with a fetal heartbeat visible on an ultrasound scan
- an ectopic pregnancy and a serum hCG level of 5000 IU/litre or more.

Surgery is recommended for criteria outlined, which include an HCG > 5000 IU/L.

1.6.5 Offer the choice of either methotrexate[H] or surgical management to women with an ectopic pregnancy who have a serum hCG level of at least 1500 IU/litre and less than 5000 IU/litre, who are able to return for follow-up and who meet all of the following criteria:

- no significant pain
- an unruptured ectopic pregnancy with an adnexal mass smaller than 35 mm with no visible heartbeat
- no intrauterine pregnancy (as confirmed on an ultrasound scan).

Advise women who choose methotrexate that their chance of needing further intervention is increased and they may need to be urgently admitted if their condition deteriorates.

A choice can be offered if stable with an HCG 1500–5000 IU/L, with close follow up required

1.6.6 For women with ectopic pregnancy who have had methotrexate, take 2 serum hCG measurements in the first week (days 4 and 7) after treatment and then 1 serum hCG measurement per week until a negative result is obtained. If hCG levels plateau or rise, reassess the woman's condition for further treatment.

Follow up with serial HCG until –ve.

1.7 Anti-D rhesus prophylaxis

1.7.1 Offer anti-D rhesus prophylaxis at a dose of 250 IU (50 micrograms) to all rhesus negative women who have a surgical procedure to manage an ectopic pregnancy or a miscarriage.

1.7.2 Do not offer anti-D rhesus prophylaxis to women who:

- receive solely medical management for an ectopic pregnancy or miscarriage **or**
- have a threatened miscarriage **or**
- have a complete miscarriage **or**
- have a pregnancy of unknown location.

1.7.3 Do not use a Kleihauer test for quantifying feto–maternal haemorrhage.

Give anti-D 250 IU (50 mcg) if Rh –ve if having surgery; it is <u>not</u> required if managed medically, nor for threatened or complete miscarriage. Kleihauer test is not required.

The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL PRACTICE

Ectopic Pregnancy

N ENGL J MED 361;4 NEJM.ORG JULY 23, 2009

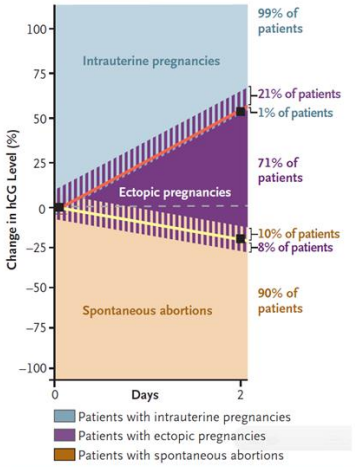


Figure 2. Change in the hCG Level in Intrauterine Pregnancy, Ectopic Pregnancy, and Spontaneous Abortion.

These updates are a review of current literature at the time of writing. They do not replace local treatment protocols and policy. Treating doctors are individually responsible for following standard of care.