
بسم الله الرحمن الرحيم

management of tubal ectopic pregnancy

Dr.Parvin hakimi
Fellowship of infertility
tabriz university of medical sciences

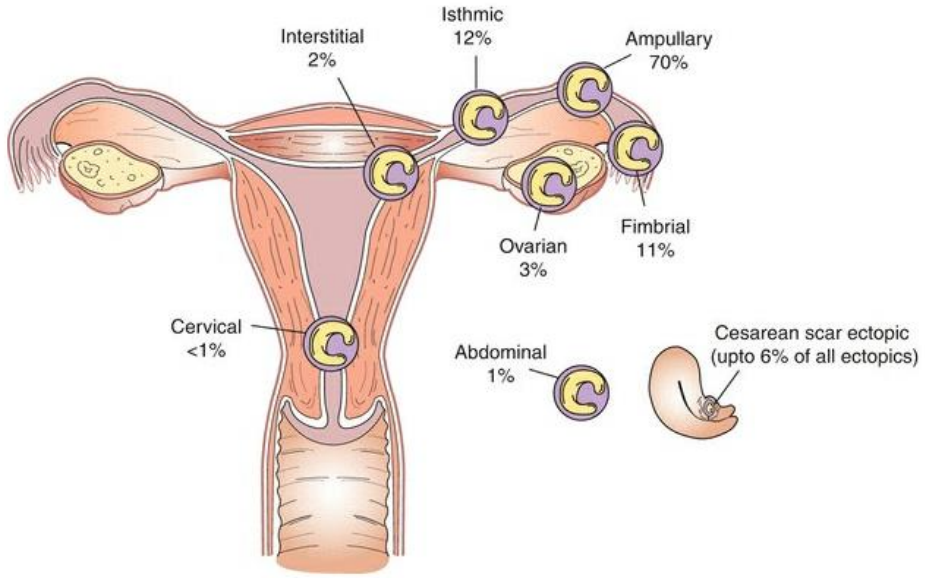
An ectopic pregnancy is an extrauterine pregnancy

Almost all ectopic pregnancies occur in the fallopian tube (96 percent)
but other possible sites include cervical, interstitial, hysterotomy (cesarean) scar, ovarian, or abdominal

In rare cases, a multiple gestation may be heterotopic (include both an intrauterine pregnancy [IUP] and an extrauterine pregnancy

Ectopic pregnancy is associated with a **classic triad of symptoms**

- delayed menses,
- vaginal bleeding
- lower abdominal pain



The diagnosis of ectopic pregnancy should be **suspected** in a pregnant patient with no evidence of an intrauterine pregnancy on transvaginal ultrasound (TVUS) and any of the following:

Visualization of

- A **complex inhomogenous** extraovarian adnexal mass
- an extraovarian adnexal mass containing an **empty gestational sac**
- **intraperitoneal bleeding** on TVUS

A serum human chorionic gonadotropin (hCG) that is **rising abnormally**

- ✓we generally define an abnormal rise as <35 percent over two days
- ✓The actual expected rate of rise is dependent on initial hCG level

Abdominal pain and/or vaginal bleeding, especially in those patients with risk factors for ectopic pregnancy

over 50 percent of patients are asymptomatic before tubal rupture and do not have an *identifiable risk factor for ectopic pregnancy*

The diagnosis of ectopic pregnancy can be **confirmed** when any of the following are present:

- Visualization of an *extrauterine gestational sac with a yolk sac or embryo* (with or without a heartbeat) on TVUS

- A positive serum hCG and *no products of conception on uterine aspiration with subsequent rising or plateauing hCG levels*

- *Visualization at surgery* (usually performed for patients with hemodynamic instability) with histologic confirmation following resection of ectopic pregnancy tissue

DIAGNOSTIC EVALUATION

Any pregnant patient with vaginal bleeding and/or abdominal pain should be evaluated for ectopic pregnancy

The main goals and steps of the evaluation are to:

- Confirm that the patient is pregnant
- Evaluate the patient for hemodynamic instability
- Determine the site of the pregnancy

The Serum β-hCG Concentration

- In pregnant patients, hCG can be detected in serum as **early as six days** after the luteinizing hormone surge
- The hCG concentration in a normal IUP rises in a **curvilinear fashion** until **approximately 41 days of gestation**, after which it **rises more slowly** until **approximately 10 weeks**, and then **declines until reaching a plateau in the second and third trimesters**
- In general, levels **double every 1.4–2.1 days** in early pregnancy and peak between **50,000 and 100,000 IU/L at 8–10 weeks of gestation**
-
- At or near the time of the **first missed menses**, serum *levels between 50 and 100 IU/L are typical*
- It also is important to note that **interassay variation** in β-hCG measurements ranges between **10% and 15% in most laboratories**
- Consequently, for most confident interpretation, serial concentrations should be performed in **the same laboratory** whenever possible

The concept of a “discriminatory zone”

the **minimum serum β-hCG** concentration *above which a gestational sac always should be detected* in a viable intrauterine pregnancy

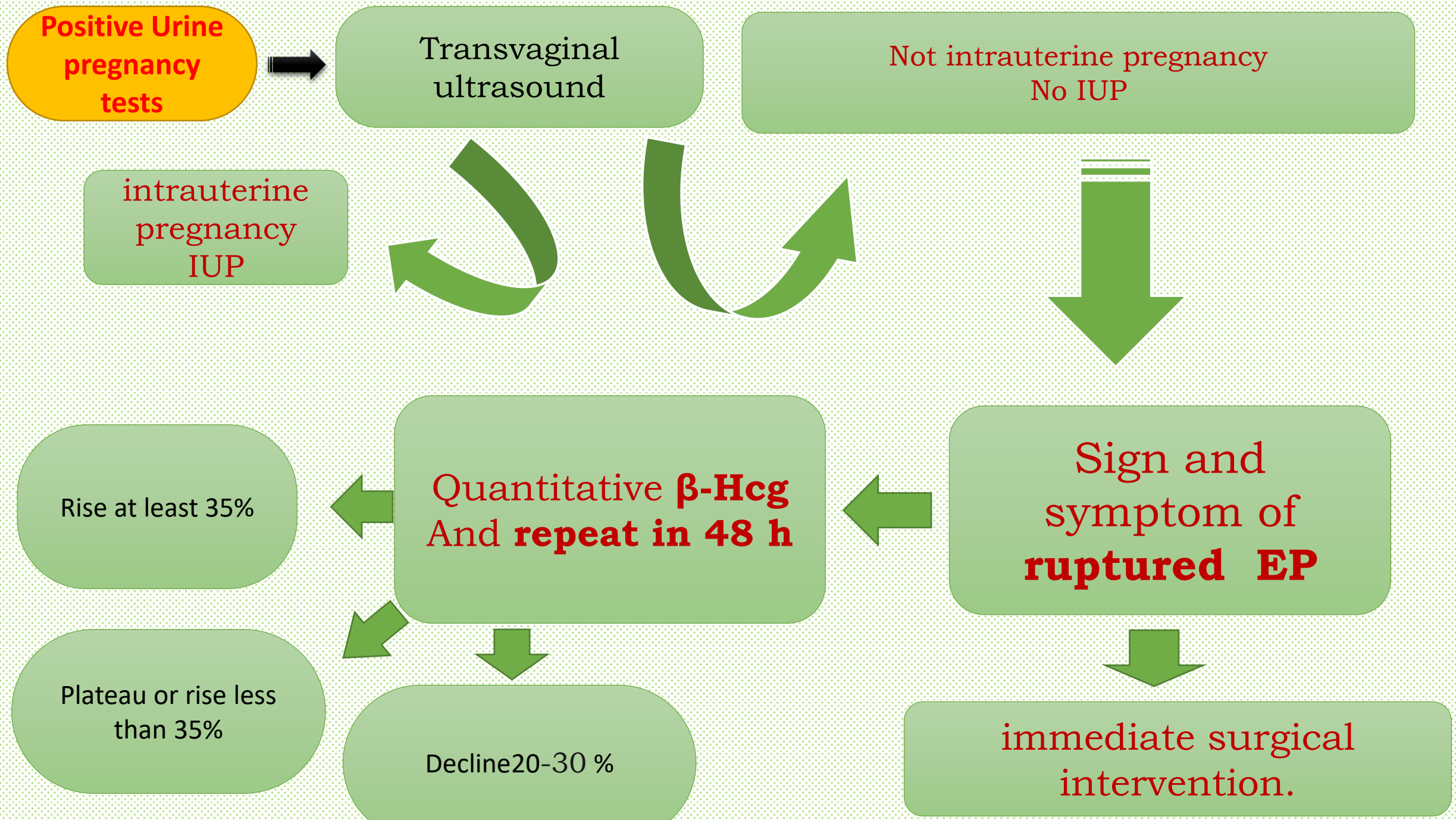
- we use a **discriminatory zone of 3510** milli-international units/Ml

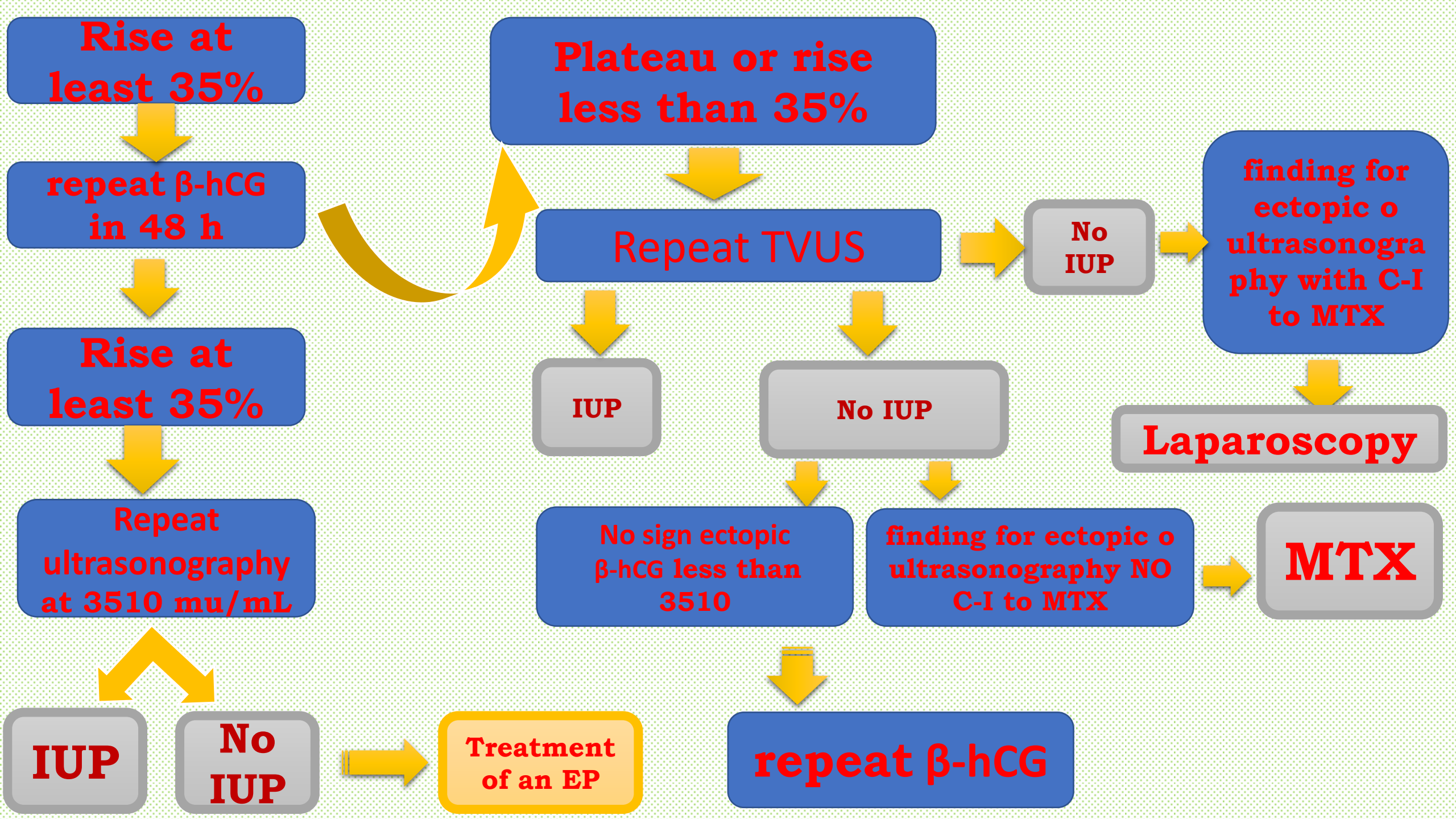
some institutions set the discriminatory zone at 2000 milli-international units/mL

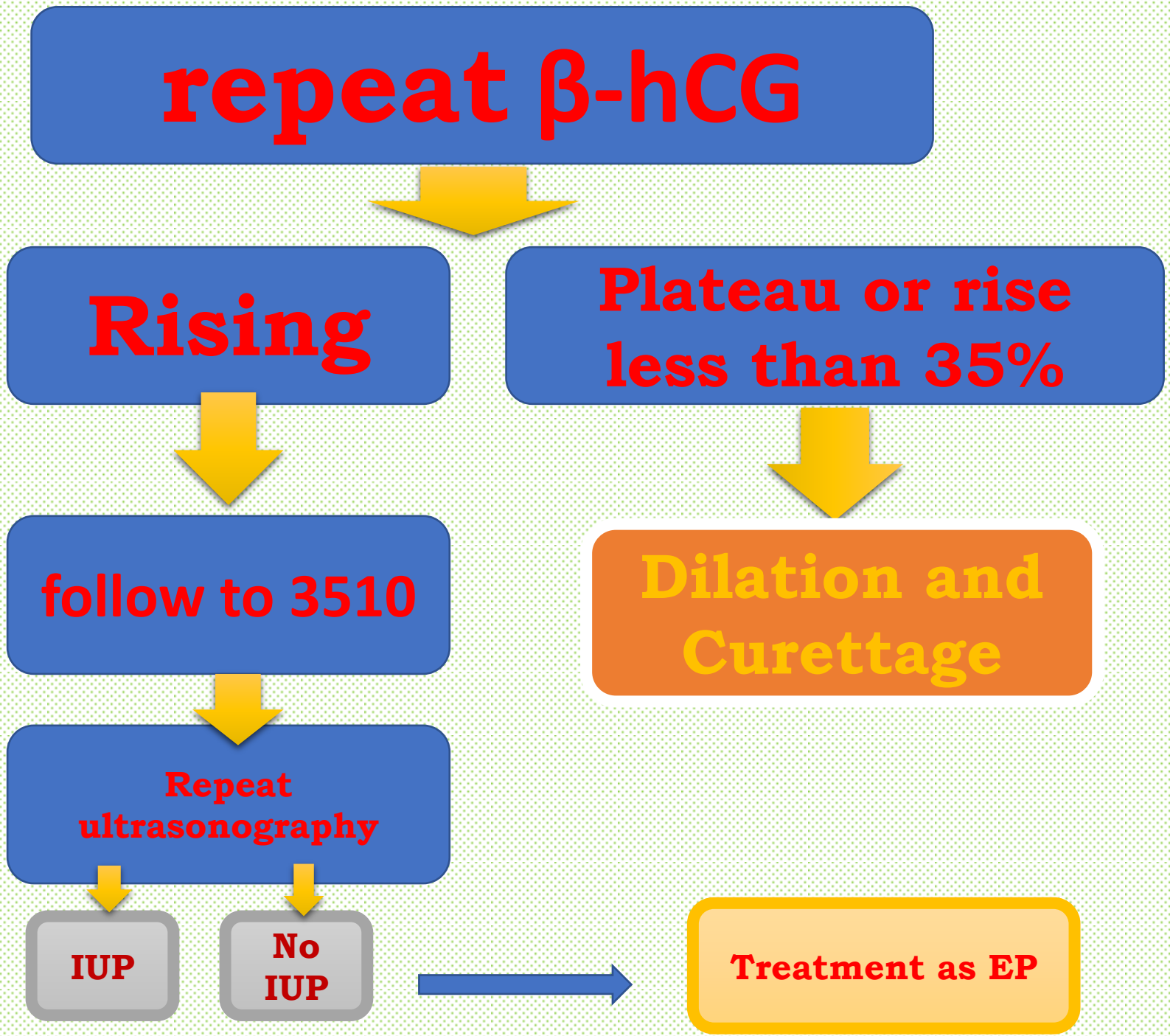
It is important to emphasize that a patient **should not be diagnosed** or treated for an ectopic pregnancy based **on a single serum hCG level**

A more conservative cut-off of greater than or equal to 35% was found to adequately **predict a viable intrauterine pregnancy** **and decrease the chance of misclassifying a pregnancy**

- Based on these data the **traditional 66%** should *no longer be used* in diagnosing ectopic pregnancies
- In general, hCG levels in normal early IUPs will **rise by at least 35 percent every two days**
- **having at least three serial values** is helpful, especially if the starting β-hCG level is low
- Follow-up research suggests that the expected rise in β-hCG is dependent upon **starting β-hCG level**
- If the initial a-hCG level is less than 1,500, 1,500 to 3,000, or greater than 3,000 mIU/mL, then the predicted rise at 48 hours is 49%, 40%, and 33%, respectively
- If there is a **plateau or decline in β-hCG levels**, this is usually indicative of a nonviable pregnancy, either intrauterine or extrauterine


Positive Urine pregnancy tests
Transvaginal ultrasound
Not intrauterine pregnancy
No IUP
intrauterine pregnancy
IUP
Sign and symptom of ruptured EP
immediate surgical intervention.
Quantitative β-Hcg
And repeat in 48 h
Rise at least 35%
Plateau or rise less than 35%
Decline20-30 %


Rise at least 35%
repeat β-hCG in 48 h
Rise at least 35%
Repeat ultrasonography at 3510 mu/mL
IUP
No IUP
Treatment of an EP
Plateau or rise less than 35%
Repeat TVUS
IUP
No IUP
No sign ectopic β-hCG less than 3510
repeat β-hCG
No IUP
finding for ectopic o ultrasonography NO C-I to MTX
MTX
No IUP
finding for ectopic o ultrasonography with C-I to MTX
Laparoscopy


repeat β-hCG
Rising
Plateau or rise less than 35%
follow to 3510
Dilation and Curettage
Repeat ultrasonography
IUP
No IUP
Treatment as EP

Dilation and Curettage

Float tissue

No villi

Follow up for completed abortion

repeat β-hCG in 48 h

Plateau or rise β-Hcg

C-I to MTX

Laparoscopy

MTX

Decline β-Hcg

repeat β-hCG 48 h

Decline β-Hcg

Follow to negative

completed abortion or spontaneous ectopic regression

Decline20-30 %

Ultrasound show completed abortion

repeat β-hCG in 48 h

falling

Complete abortion

Ultrasound show unruptured ectopic

repeat β-hCG in 48 h

falling

Plateau or rising

follow<5

Treatment

Ultrasound show No IUP

repeat β-hCG

falling

Plateau or rising

Complete abortion

Dilation and Curettage

Ultrasound show incomplete abortion

stable?

Dilation and Curettage Or misoprostole Or expectant management

Dilation and Curettage

The three approaches to the management of ectopic pregnancy are

- surgery (salpingostomy or salpingectomy)
- methotrexate (MTX) treatment
- expectant management

Medical treatment with methotrexate (MTX) for ectopic pregnancy has

- **comparable efficacy to surgery**
- **similar fertility outcomes**

Expectant management

Selection criteria

we offer expectant management only for patients who meet **all the following criteria**:

- Asymptomatic
- Understand the clinical implications and risks of an ectopic pregnancy
- Ready access to a medical facility if emergency surgical treatment is needed.
- Able and willing to comply with close follow-up
- Transvaginal ultrasound (TVUS) does not show an extrauterine gestational sac or demonstrate an extrauterine mass suspicious for an ectopic pregnancy.
- Serum quantitative beta-human chorionic gonadotropin (hCG) concentration is low (≤200 milli-international units/mL) and decreasing

We define decreasing as a **decrease of >10 percent** *across two consecutive measurements*

Some guidelines advise offering expectant management to patients who meet the above criteria and have an hCG <2000 milli-international units/mL

The clinical protocol for expectant management of ectopic pregnancy includes:

- diagnosis of ectopic pregnancy or pregnancy of unknown location with suspicion of ectopic pregnancy
- counseling of patient regarding treatment options
- close monitoring

Close monitoring

- We follow the **hCG level every two days** for **three measurements** to confirm that the **hCG level continues to decrease** (decrease of >10 percent across two consecutive measurements), and then **weekly until it is undetectable**
- **Expectant management should be abandoned** if a patient experiences
  - **a significant increase in abdominal pain**
  - **the serum hCG starts to increase** (increase of >10percent across two consecutive measurements)
  - **fails to decrease** (decrease of >10 percent across two consecutive measurements)

- Asymptomatic patients who are managed expectantly and have **hCG levels that are slowly declining** may be offered continuation of expectant management or MTX injection

- In general, in our practice, **if the hCG has not reached undetectable within 10 weeks, we offer MTX therapy**

MTX

is a folic acid antagonist

Treatment of ectopic pregnancy uses an **intermediate MTX dose (50 mg/m or 1 mg/kg)**

Adverse reactions

Adverse reactions to MTX are usually **mild and self-limited**

The most common are stomatitis and conjunctivitis

Rare side effects include gastritis, enteritis, dermatitis, pneumonitis, alopecia, elevated liver enzymes, and bone marrow suppression

Approximately **30 percent** of patients in the **single-dose protocol** will have side effects

this rate is lower than with **multiple-dose regimens (40 percent)**

MTX is the preferred treatment option when all of the following characteristics are present:

- **Hemodynamic stability**
- Serum beta-human chorionic gonadotropin (hCG) concentration **≤5000 milliinternational units/mL**
- **No fetal cardiac activity** detected on transvaginal ultrasound
- Ectopic mass **size Less than 3 to 4 cm** is also commonly used as a patient selection criterion
- Patients are **willing and able** to comply with post-treatment follow-up and have access to **emergency medical services** within a reasonable time frame in case of a ruptured fallopian tube

MTX is contraindicated and surgery is required when the following are present :

- **Hemodynamic instability**
- **Intrauterine** pregnancy
- Signs or symptoms of **impending or ongoing rupture of ectopic mass**
- Clinically important abnormalities in baseline **hematologic, renal, or hepatic laboratory values**
- Medical conditions such as **immunodeficiency, active pulmonary disease , and peptic ulcer disease**
- **Hypersensitivity to MTX**
- **Breastfeeding**

Pretreatment testing

- a viable intrauterine pregnancy must be excluded
- A history and physical examination are performed. The history should include questions regarding contraindications to MTX
- Serum beta-human chorionic gonadotropin (hCG)
- Transvaginal ultrasound
- Blood type and screen
- Complete blood count and renal and liver function tests

Efficacy of single- versus multiple-dose therapy

- For patients with tubal pregnancy treated with MTX, we suggest a **single-dose protocol in most cases**
- The **two-dose protocol** may be beneficial when hCG levels are high **(>3000 international units/L)** or if an adnexal mass measures **>2 cm**
- We reserve the use of **multiple-dose MTX therapy** for **interstitial or cervical pregnancies**
- Approximately **15 to 20 percent** of patients will require a **second dose of MTX**
- **Less than 1 percent** of patients need more than two doses

Single-dose protocol

The dose used is **50 mg per square meter of body surface** area ***maximum dose 100 mg*** *i*n patients with normal renal function

In a commonly used protocol, **on days 4 and 7**, a serum hcg concentration is drawn

If the decrease in hcg between days 4 and 7 is **less than 15 percent**, a second dose of MTX 50 mg/m IM is administered

It is common to observe an **increase** in hcg levels from day 1 through **day 4**

- If an additional dose of MTX is indicated, ***we do not repeat pretreatment laboratory testing***

Follow-up includes:

After day 7, hcg testing is **repeated weekly**. On day 14:

- If there is a **≥15 percent** hcg decline **from days 7 to 14**, check **hcg weekly** until the level is undetectable
- If there is a **<15 percent** hcg decline from days **7 to 14,** an **additional dose** of mtx 50 Mg/m IM is given

If three weekly values are similar, we give an **additional dose of mtx** (50 mg/m)
This typically accelerates the decline of serum hcg

If the hcg does not decline to zero, a **new pregnancy should be excluded**
If the hcg is **rising**, a **transvaginal ultrasound** should be performed

- We give a **maximum of three doses of mtx**

In rare cases in which the hcg **falls <15 percent** between weekly measurements **after a third dose**, we perform a laparoscopic salpingostomy or salpingectomy

Leucovorin rescue is not required for patients treated with the single-dose protocol, even if a few doses are ultimately given

The hCG concentration usually declines to less than 15 milli-international units/mL by **35 days post injection**, but may take as long as **109 days**
some patients have a slow clearance of serum hCG
The risk of **gestational trophoblastic disease** is low

There appears to be no clinical benefit from **routine serial ultrasound examinations**
After treatment, the ectopic pregnancy is often noted to *increase in size* and may *persist for weeks* on serial ultrasound examinations

This probably represents *hematoma* rather than persistent trophoblastic tissue and is *not predictive of treatment failure*
ultrasound evaluation for **peritoneal fluid** is indicated for **patients with severe abdominal pain**

Two-dose protocol

The two-dose protocol includes administration of **MTX 50 mg/m** **on day 1** and a second dose of MTX 50 mg/m **on day 4**

➢ Serum hCG levels are **obtained on day 7**

The goal is for hCG levels to **decline more than 15 percent** from one measurement to the next before moving to the surveillance phase which consists of **weekly measurement** of hCG until it is undetectable

If the serum hCG measurement **declines less than 15 percent**

- a **third dose of MTX** may be administered **on day 7**
- *hCG is reassessed on day 11*

A fourth dose of MTX may be administered **on day 11** for insufficient decline in **hCG**, with subsequent **reassessment on day 14**

If there continues to be an insufficient hCG decline at that point, surgery should be considered

Multiple-dose protocol

The most common multiple-dose regimen is the administration of **MTX 1 mg/kg per day IM or intravenously**

maximum dose 100 mg per day in patients with normal renal function on days **1, 3, 5, and 7 and IM leucovorin (0.1 mg/kg) on days 2, 4, 6, and 8**

hCG levels are drawn on days *1, 3, 5, and 7*
If the serum hCG declines **more than 15 percent** from the previous measurement, treatment is stopped, and a surveillance phase begins
The surveillance phase consists of **weekly hCG measurements**

If the hCG declines **less than 15 percent** from the previous level, the patient is given an additional dose of MTX 1 mg/kg IM followed the next day with a dose of IM leucovorin 0.1 mg/kg

The hCG is followed until the level is undetectable

Precautions during therapy

- **Avoid vaginal intercourse and new conception** until hCG is undetectable
- **Avoid pelvic examinations** during surveillance of MTX therapy due to theoretical risk of tubal rupture
- **Avoid sun exposure** to limit risk of MTX dermatitis
- **Avoid vitamins containing folic acid**
- **avoid nonsteroidal anti-inflammatory drugs (NSAIDs)**

as the interaction with MTX may decrease renal excretion of MTX and increase the risk of toxicity

Pain after treatment

Mild to moderate abdominal pain of **short duration** (one to two days) at six to seven days after receiving the MTX is common

The pain may be due to tubal abortion or tubal distention from hematoma formation and can usually be controlled with acetaminophen

A patient with **severe pain** should be further evaluated with *transvaginal ultrasonography*

Findings suggestive of **hemoperitoneum** raise clinical suspicion of tubal rupture.

three parameters predicted hemoperitoneum ≥300 mL in patients with ectopic pregnancy:

- Moderate to severe pelvic pain
- Fluid above the uterine fundus or around the ovary
- hemoglobin concentration <10 g/dL

Patients with severe pain should be **closely observed for** hemodynamic changes which may accompany a tubal rupture

Falling hcg levels do not preclude the possibility of tubal rupture

If tubal rupture is suspected, **immediate surgery** is required

Severe pain alone in a hemodynamically stable patient is not an indication for surgery

SUBSEQUENT PREGNANCY

Interval to conception

The safe interval from MTX treatment to conception is **unclear**

Toxicology literature recommends a four- to six-month washout period before attempting to become pregnant

since there is no apparent deleterious effect of previous MTX treatment on the **offspring**, it is reasonable to allow the patients to conceive

residual MTX may be stored in the **liver and kidney for months**

We advise patients **not to conceive for three months**

there is no evidence of teratogenic risk to those who conceive sooner

Obstetric outcome

There is *no evidence of adverse effects of MTX treatment of ectopic pregnancy on future pregnancies*

Surgical treatment

- **Hemodynamically unstable**
- Signs or symptoms of **impending or ongoing rupture** of ectopic mass
- Desire for **sterilization**
- Planned **in vitro fertilization** for future pregnancy with known **hydrosalpinx**
- **Heterotopic pregnancy** with coexisting viable intrauterine pregnancy
- **Contraindications to MTX therapy**
- **Failed MTX therapy**

The choice of salpingostomy or salpingectomy relies upon many factors:

- **Salpingectomy** is the *standard procedure* if the condition of the tube with the ectopic gestation is
  - damaged (ruptured or otherwise disrupted)
  - bleeding is uncontrolled
  - the gestation appears too large to remove with salpingostomy
- Another advantage of salpingectomy is that it avoids the need for further treatment for *persistent trophoblast*
- Based on the risk of retained gestational tissue following salpingostomy, salpingectomy is required in patients who have *contraindications to methotrexate therapy*
- For patients who have *completed childbearing*, bilateral salpingectomy may be performed as permanent sterilization
- *recurrent ectopic pregnancy in the same tube*

salpingostomy is preferred for patients who **desire future childbearing** and in whom the **contralateral tube is absent or damaged**
For patients who undergo salpingostomy, serum human chorionic gonadotropin (hCG) is **measured weekly until the level is undetectable**

If the hCG level does not decline with each measurement or does not reach an undetectable level within a reasonable time period, we treat with **methotrexate**

For cases in which the surgeon is **not certain** whether the entire products of conception have been removed, **a single prophylactic dose** of methotrexate given immediately postoperatively has been proposed
For patients who undergo ***salpingectomy,*** if the pathology evaluation confirms a tubal gestation, many surgeons do not check a postoperative hCG, and others check a single postoperative hCG to confirm a large decline in the level

Interval to conception

There are **no data to establish** the optimal interval to conception following surgical treatment of an ectopic pregnancy
we advise patients that they may try to conceive again following their next menstrual period


Thank You