# ECTOPIC PREGNANCY

Dr. Marta Larroya, Dr. Teresa Cobo, Dr. Silvia Escura, Dr. Silvia Ferrero, Dr. Montse Creus, Dr. Marta López, Dr. Montse Palacio

## 1. INTRODUCTION

We define pregnancy as extrauterine when the pregnancy is not located in the uterine cavity. According to the 2012 NICE guidelines, 11 out of every 1000 pregnancies are ectopic, the most frequent location being the tubal pregnancy, in 95% of cases, specifically in the ampullar region (80%). The remaining 5% have a non-tubal origin. The 6 main locations of non-tubal ectopic pregnancies are: cervical, interstitial, cornual, on caesarean scar (Caesarean scar pregnancy (CSP)), ovarian and abdominal (*Figure 1*) (1).

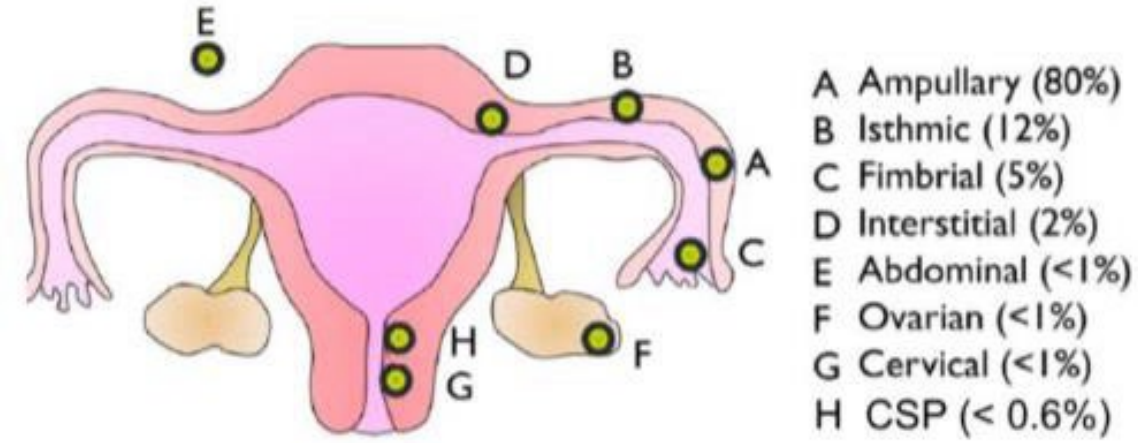



***Figure 1**: Different possible locations of extrauterine pregnancies.*

Nowadays, with the determination of β-hCG hormone and the technological progress in ultrasound, the diagnosis is usually made early. A universal consensus does not exist on the optimal treatment of this type of pregnancy. If a woman wants to preserve her fertility, medical treatment is usually the treatment of choice, unless there is haemodynamic instability or other signs of active bleeding.

## 2. RISK FACTORS

Main risk factors are resumed in table 1:

| *RISK FACTOR* | *ODDS RATIO* |
|---|---|
| *Previous ectopic pregnancy* | |
| - *One* | 12.5 |
| - *More than one* | 76.6 |
| *Previous salpingectomy* | 8.8 |
| *Infertility history (≥2 years)* | 5.0 |
| *Pelvic inflammatory disease history* | 3.4 |
| *Conception with intrauterine device (IUD)* | 3.0 |
| *Smoking habit* | 2.9 |
| *Maternal age* | |
| - *35-39 years* | 2.1 |
| - *≥40 years* | 5.7 |
| *Previous abdominal surgery* | 3.8 |
| *Previous miscarriage* | |
| - *Surgical miscarriage* | 2.6 |
| - *Medical and surgical miscarriage* | 8.9 |
| *≥3 Spontaneous miscarriages* | 4.7 |
| *Assisted reproductive technology* | 1.9 |

***Table 1**: main risk factors and their Odds ratio for ectopic pregnancy. Adapted from Parker V.L. ArchGynecolObstet (2016) 294:19–27).*

## 3. DIAGNOSIS

### 3.1. CLINICAL DIAGNOSIS

The symptoms of ectopic pregnancy are unspecific. The most frequent are amenorrhea, vaginal bleeding, and abdominal pain during the first trimester of pregnancy. in about 10% of ectopic pregnancies, symptoms are very mild or absent.

In cases of ectopic pregnancy rupture, more severe symptoms are usually seen, such as abdominal distention, peritonism, haemoperitoneum, or haemorrhagic shock.

### 3.2. ULTRASOUND DIAGNOSIS

Transvaginal ultrasound is the most sensitive tool for the early diagnosis of ectopic gestation, with a sensitivity of 87-99% and a specificity of 94-99% according to different studies. The resolution of the ultrasound machine, experience of the sonographer, elevated body mass index, or presence of fibroids and/or ovarian pathology can decrease its diagnostic accuracy.

The final diagnosis of ectopic gestation is performed by extrauterine visualisation of a gestational sac with vitelline vesicle and/or embryo with or without heartbeat (20% of cases).

## 4. ECTOPIC PREGNANCY TYPES

### 4.1. TUBAL PREGNANCY

Tubal pregnancy is the most frequent location of ectopic pregnancies.

#### 4.1.1. Ultrasound diagnosis

The most common finding (60% of cases) is the heterogeneous image that moves separately from the ovary. It is generally spherical or elongated (if there is a hematosalpinx) and it is called “blob sign” (*Figure 2A).* In 20% of cases, the image is similar to a pseudo-extrauterine sac and it is called “bagel sign” (*Figure 2B*). The sensitivity and specificity of these images for the diagnosis of tubal ectopic pregnancy is 89% and 83%, respectively, for “blob sign” and 95% and 99%, respectively, for “bagel sign”. Colour Doppler does not contribute effectively to the diagnosis of ectopic pregnancy.

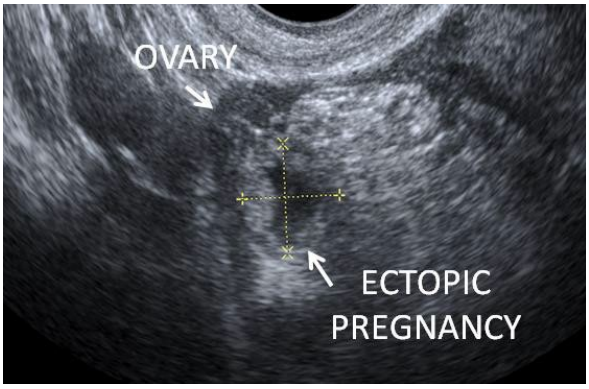



*Figure 2A*

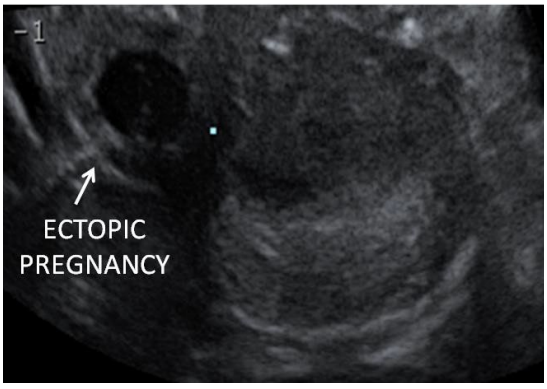



*Figure 2B*

*Figure 2A: “Blob sign”. From Hospital Clínic de Barcelona. Figure 2B: “Bagel sign”.*

In the endometrium there is no specific image or thickness that reliably contributes to the diagnosis of tubal ectopic pregnancy. In more than 20% of cases, an image of fluid collection can be seen inside the uterine cavity, classically known as "pseudosac", but a similar image can also correspond to an initial intrauterine pregnancy.

The presence of hyperechogenic fluid in the pelvis is seen in 28-56% of cases of ectopic pregnancy and corresponds to haemoperitoneum.

The visualisation of an intrauterine gestational sac does not definitively exclude the existence of a tubal ectopic pregnancy. There is a possibility of heterotopic pregnancy, especially in those patients whose pregnancy is the result of treatment using assisted reproductive techniques (1-3%).

### 4.1.2. Treatment

The most important thing is to make an early diagnosis, in order to reduce the risk of tubal rupture and improve the results of conservative treatment.

**a) Watchful waiting**

Watchful waiting is possible in selected cases:
- Asymptomatic patient
- β-hCG <1000 IU/L. The lower the initial β-hCG level, the greater the probability of favourable evolution without treatment (example: in 88% of women with β-hCG levels <200 IU/L, the ectopic pregnancy resolves spontaneously).
- Absence of fluid in the pelvis.

In cases of expectant management, a clinical and β-hCG control will be carried out within 48 hours. If a β-hCG decrease greater than 50% is observed, a weekly follow-up is recommended until the β-hCG level is less than 20 IU/L. An active approach (medical or surgical) will be chosen if symptoms appear or β-hCG levels increase or do not decrease adequately.

**b) Medical treatment**

In patients with good general condition and who are clinically stable, intramuscular treatment with Methotrexate (MTX) has shown to be as effective as surgical treatment.

MTX is a folinic acid antagonist that interferes with DNA synthesis and therefore with the generation of trophoblastic tissue. β-hCG levels may increase in the first few days of its administration. For this reason, to assess the efficacy of MTX treatment, we have to compare the β-hCG levels on day 4 and day 7 after treatment. Approximately 75% of patients have abdominal pain crises between 3 and 7 days after starting treatment with MTX, which usually disappears in 4-12 hours.

As general recommendations, non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided as an analgesic treatment in these patients since they interact with MTX and increase its toxicity.

The indications for treatment with MTX in tubal ectopic pregnancy are:
- Haemodynamically stable patient
- Absence of severe or persistent abdominal pain
- Possibility of monitoring until the process is resolved
- Normal liver and kidney function
- Negative embryo cardiac activity (with positive cardiac activity the success of the treatment decreases drastically).
- Diameter of the ectopic pregnancy less than 4 cm assessed by ultrasound
- β-hCG less than 5000 IU/L

Contraindications for MTX:
- Intrauterine pregnancy
- Presence of significant haemoperitoneum (outside pouch of Douglas)
- History of ipsilateral ectopic pregnancy with prior conservative treatment
- Heterotopic pregnancy
- Immunodeficiency
- Leukopenia, anaemia, moderate to severe thrombocytopenia

- Sensitivity to MTX
- Active lung disease
- Active gastric ulcer
- Alcoholism, liver disease and/or nephropathy
- Breastfeeding
- Rejection of eventual blood transfusion
- When the other criteria mentioned in the indications are not met.

The treatment and tests are summarised in the table above:

| Day | Medical test | Treatment |
|---|---|---|
| 0 | Ultrasound<br>β-hCG<br>Blood count, renal and liver function, Rh, coagulation test. | MTX 50 mg/m$^2$ (intramuscular)<br>Anti-D Immunoglobulin (if Rh negative)<br>Avoid NSAIDs |
| 4 | β-hCG | None |
| 7 | Ultrasound<br>β-hCG | Comparing β-hCG on day 4 and 7:<br>- Decrease >15% → weekly control until β-hCG <20 IU<br>• Decrease ≤15%<br>○ Repeat MTX (same dosage) → β-hCG on day 11<br>○ Surgical treatment |
| 11* | β-hCG | Compare β-hCG on day 7 and 11<br>• If there is not a decrease of β-hCG levels, surgical treatment must be performed. |

*Only if second dose of MTX is needed.

### c) Surgical treatment

The indications for surgical treatment are:

- Ectopic pregnancy with a diameter > 4 cm
- β-hCG greater than 5000 IU/L
- Positive embryo cardiac activity.
- Presence of significant haemoperitoneum
- Heterotopic pregnancy with one of the sacs in the tube
- History of ipsilateral ectopic pregnancy treated conservatively
- Difficulty in subsequent follow-up of the patient
- Contraindication to MTX
- When the patient does not want conservative treatment
- Failure of medical treatment

The first option for surgical treatment is a laparoscopic unilateral salpingectomy. The laparotomic route will be reserved for those patients in whom a laparoscopy cannot be performed, because of the patient's haemodynamic situation or in the presence of multiple adhesions that complicate access to the tubes by laparoscopy.

## 4.2. INTERSTITIAL PREGNANCY

This is the most common non-tubal ectopic pregnancy (1-11%). It is defined as being when the pregnancy implants itself at the junction between the interstitial part of the fallopian tube and the myometrium. In cases where it is located in a bicornuate uterus or in the rudimentary horn of a unicornuate uterus, we will call it a cornual ectopic pregnancy.

It is the ectopic localisation with a higher maternal mortality (20% of maternal deaths secondary to ectopic pregnancies). It has a great capacity to grow before rupture occurs, which is why asymptomatic cases have been described up to week 16 of gestation. However, it is usually diagnosed earlier, between 6-8 weeks. Vaginal bleeding is less frequent than in other types of ectopic pregnancies and this explains its later clinical onset.

### 4.2.1. Ultrasound diagnosis (2,3,4)

1. Uterine cavity without the presence of a gestational sac (empty uterine cavity).
2. Gestational sac located ≥ 1 cm from the endometrial line and surrounded by myometrium, whose thickness is less than 5 mm (specificity 88-93%, sensitivity only 40%). Figure 3A and 3B.
3. Echogenic interstitial line between the gestational sac and the endometrium (this ultrasound marker has a sensitivity of 80% and a specificity of 98%). Figure 3C

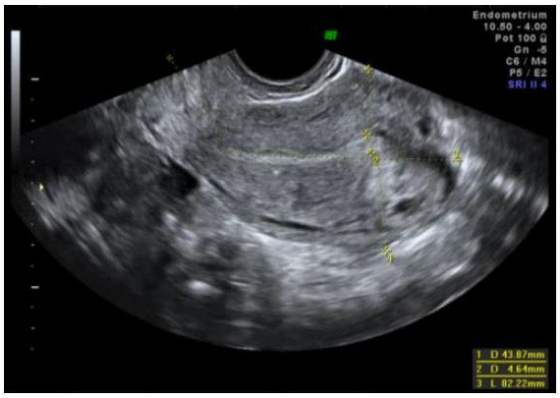



*Figure 3A*

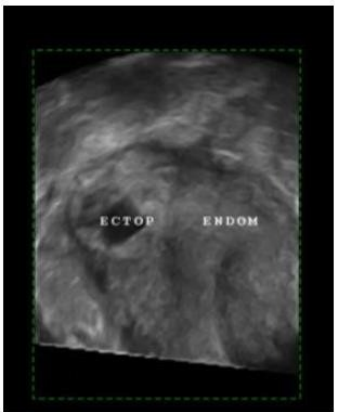



*Figure 3B*

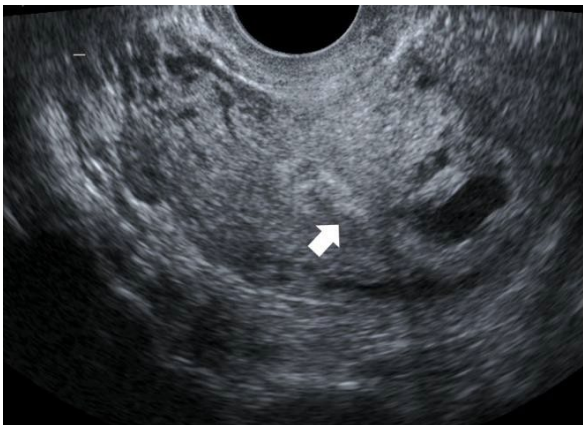


*Figure 3C*

*Figure 3A: interstitial pregnancy with the visualisation of an empty uterine cavity and a gestational sac located ≥ 1 cm from the endometrial line surrounded by myometrium.*
*Figure 3B: 3D-ultrasound image of the endometrial cavity and gestational sac. Figure 3C: Echogenic interstitial line between the gestational sac and the endometrium marked with the white narrow.*

### 4.2.2. Differential diagnosis

An interstitial ectopic pregnancy can be confused with an angular intrauterine pregnancy, which is the one that is implanted in one of the angles. It differs because the angular gestation is medial to the utero-tubal junction. In addition, the myometrium surrounding the sac is usually > 5 mm thick. It is associated with a high risk of miscarriage due to its very lateral implantation (38%). As associated complications: persistent pelvic pain, irregular and recurrent bleeding, retention of placental remains. It is rarely a cause of uterine rupture.

### 4.2.3 Treatment

**a) <u>Medical treatment</u>**

Conservative treatment with systemic MTX associated with intrasaccular injection of potassium chloride (KCl) in cases with positive embryo cardiac activity is considered the treatment of choice in clinically stable patients who wish to preserve fertility.

- **Intramuscular MTX**

  Medical treatment with intramuscular MTX presents an overall success rate of 89% (5). The dose, duration of treatment with MTX, and management of these pregnancies will differ depending on the initial level of β-hCG:

  **I. β-hCG < 5000 IU at diagnosis:**
  In these cases, hospital admission is not necessary. A single dose of intramuscular MTX 50 mg/m$^2$ (according to body surface area) will be administered (7).
  The management is summarised in the table below:

| Day | Medical test | Treatment |
|---|---|---|
| 0 | Ultrasound<br>β-hCG<br>Blood count, renal and liver function, Rh, coagulation test. | MTX 50 mg/m$^2$ (intramuscular)<br>Anti-D Immunoglobulin (if Rh negative)<br>Avoid NSAIDs |
| 4 | β-hCG | None |
| 7 | Ultrasound<br>β-hCG | Comparing β-hCG on day 4 and 7:<br>- Decrease >15% → weekly control until β-hCG <20 IU<br>• Decrease ≤15%<br>  ○ Repeat MTX (same dosage) → β-hCG on day 11 |
| 11* | β-hCG | Compare β-hCG on day 7 and 11<br>• If there is not a decrease of β-hCG levels, surgical treatment must be performed. |

*Only if second dose of MTX is needed.

  **II. β-hCG ≥ 5000 IU at diagnosis:**
  When the β-hCG level ≥ 5000 IU at diagnosis, hospital admission and the administration of multiple doses of intramuscular MTX (1 mg/kg weight/day every 48 h for 4 doses) are

recommended (5). During treatment with MTX at multiple doses, it will be recommended to avoid sex, drinking of alcohol, sun exposure, and foods and vitamins that contain folic acid. The management is summarised in the table above:

| Day | Medical test | Treatment |
|---|---|---|
| 0 | Ultrasound<br>β-hCG<br>Blood count, renal and liver function, Rh, coagulation test. | Admission to hospital<br>MTX 1 mg/kg (intramuscular)<br>Anti-D Immunoglobulin (if Rh negative)<br>Avoid NSAIDs |
| 1 | | Calcium levofolinate 5 mg (oral) |
| 2 | Ultrasound | MTX 1 mg/kg (intramuscular)<br>Hospital discharge if clinically stable patient |
| 3 | | Calcium levofolinate 5 mg (oral) |
| 4 | β-hCG | MTX 1 mg/kg (intramuscular) |
| 5 | | Calcium levofolinate 5 mg (oral) |
| 6 | | MTX 1 mg/kg (intramuscular) |
| 7 | Ultrasound<br>β-hCG | Calcium levofolinate 5 mg (oral)<br>Comparing β-hCG on day 4 and 7:<br>- Decrease >15% → weekly control until β-hCG <20 IU<br>• Decrease ≤15%<br>○ Repeat MTX on day 8 → β-hCG on day 11 |
| 8* | | MTX 1 mg/kg (intramuscular) |
| 11* | β-hCG | Compare β-hCG on day 7 and 11<br>- Decrease >15% → weekly control until β-hCG <20 IU<br>• Decrease ≤15%<br>○ Surgical treatment |

*Only if there is a decrease ≤ 15% between levels of β-hCG on day 4 and 7.

- **Intrasaccular injection of KCl**

  In cases of positive embryo cardiac activity, intrasaccular injection with KCl (2 mL = 2 mEq/mL) is important to induce embryo asystole. The combined treatment (intrasaccular KCl + intramuscular MTX) is associated with a success rate of 66-100%.

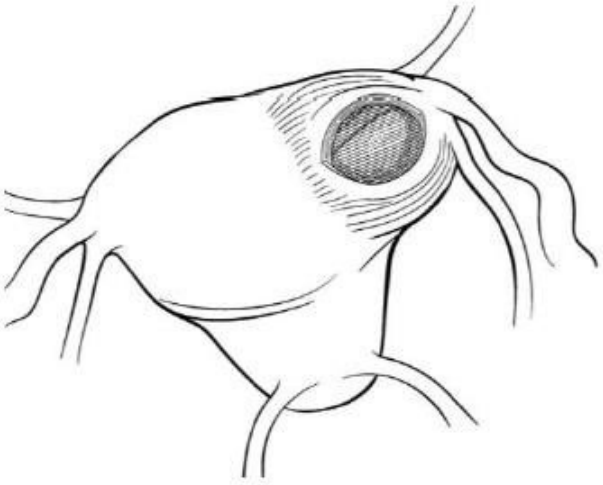
  The ultrasound-guided intrasaccular puncture will be performed with a 20 g needle adapted to the transvaginal ultrasound transducer with a puncture guide (6). Prior to the injection, the content of the sac has to be aspirated.

  In cases where it is not possible to perform intrasaccular puncture at the time of diagnosis (for example, inexperience of the team), treatment with intramuscular systemic MTX will be started and intrasaccular puncture will be postponed until it is technically feasible, ideally within the first 24-48 hours of diagnosis.

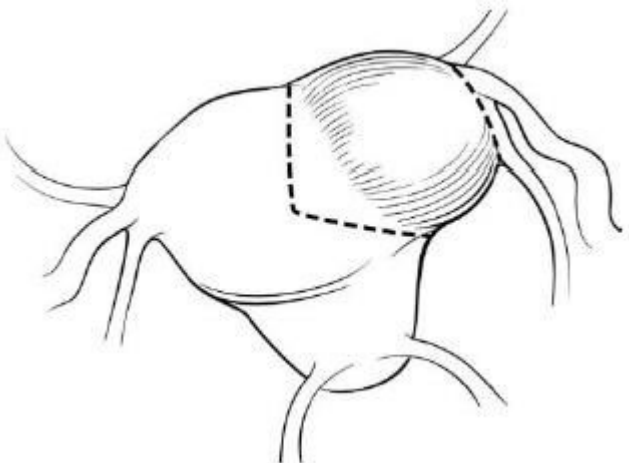
**b) Surgical treatment**

In cases of uterine rupture with hemodynamic instability, the approach route (laparotomy vs. laparoscopy) as well as the surgical technique will be discussed with the gynaecology team. The most frequently described techniques are:

- **Cornuostomy:** linear incision over the ectopic pregnancy with electrosurgical scalpel looking for the dissection plane to reach a full resection of the ectopic pregnancy without compromising the surrounding myometrial tissue. After careful haemostasis, the uterine scar can be closed with a continuous suture of absorbable material. In these cases, a prophylactic dose of intramuscular MTX 50 mg/m$^2$ can be considered immediately after surgery.



- **Wedge resection**: V-shaped resection, including ectopic pregnancy and surrounding myometrium. It is considered a more aggressive option with greater surgical complexity.



- **Hysterectomy**: this would be indicated in cases of uncontrollable bleeding or cases where conservative surgical treatment is not possible.

In all cases that require surgery, it is advisable to perform ipsilateral salpingectomy to reduce the risk of future ectopic pregnancy.

It is important to remember that, in cases of surgical treatment, an inter-pregnancy period of at least 12 months and the performance of an elective caesarean section at term, if there is a new pregnancy, will be recommended.

### 4.3. CERVICAL PREGNANCY

Ectopic pregnancies located in the cervix are rare and constitute <1% of the total number of ectopic pregnancies. The proximity between the uterine arteries and the cervix, and the potential trophoblast invasion makes them ectopic pregnancies with a very high risk of bleeding. The main risk factor is a history of aspiration curettage, which has been associated in up to 70% of cases.

#### 4.3.1. Ultrasound diagnosis

1. Suspicious cervical image (haemorrhagic mass, gestational sac, or embryo).
2. Hourglass-shaped uterus.
3. Dilated or barrel-shaped cervix
4. Absence of "sliding sign": applying pressure to the cervix with the transvaginal ultrasound probe, the sac pregnancy does not move separately from the cervix, a fact that would occur in cases of spontaneous abortion.

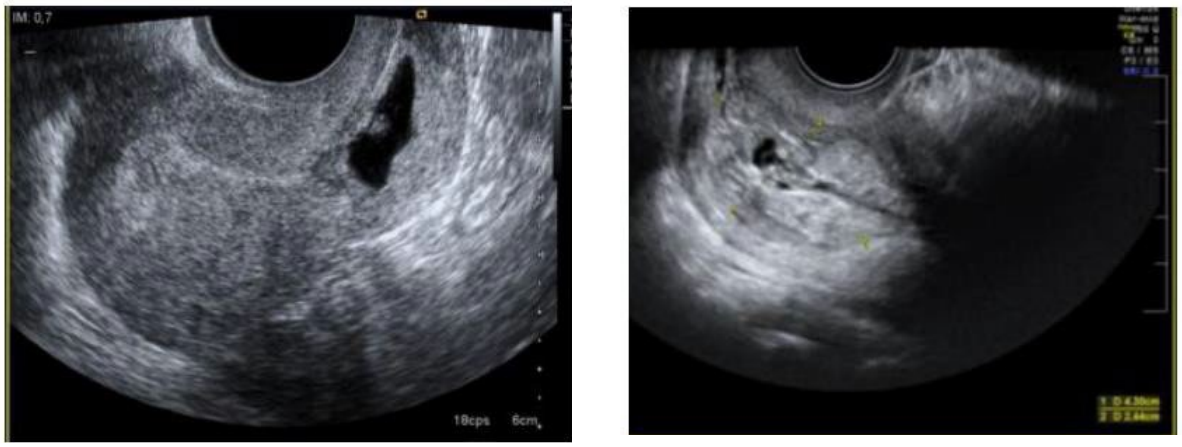


*Figure 4: cervical ectopic pregnancies diagnosed by ultrasound.*

#### 4.3.2. Treatment

The medical treatment is **intramuscular MTX at multiple doses** (1 mg/kg weight/day) every 48 h for 4 doses + Calcium levofolinate 5 mg/day every 48 h for 4 alternate doses.

If there is a positive embryocardia, intrasaccular puncture with 2 mL of KCl must be performed. The management will be the same as described for interstitial pregnancy with β-hCG ≥ 5000 at diagnosis. The success rate of the combined treatment is 60-90%.

In cases of acute bleeding, a Foley catheter placed intracervically can be used, insufflating between 5-30 mL of saline, to control bleeding. If the bleeding is not controlled, a CT angiography is recommended, evaluating the option of embolisation of the uterine arteries. In cases where the patient presents haemodynamic instability, an emergency hysterectomy is the best option.

### 4.4. CAESAREAN SCAR PREGNANCY

Caesarean section scar ectopic pregnancies (CSP) are extremely rare, representing 0.4% of total pregnancies and 6% of all ectopic pregnancies in patients with a history of a previous caesarean section.

They constitute a continuous pathology, from pregnancy with implantation on a properly healed scar (superficial CSP) to those implanted in a dehiscent scar ("niche") (deep CSP), whose prognosis is worse than those implanted over the scar (*Figure 5*).

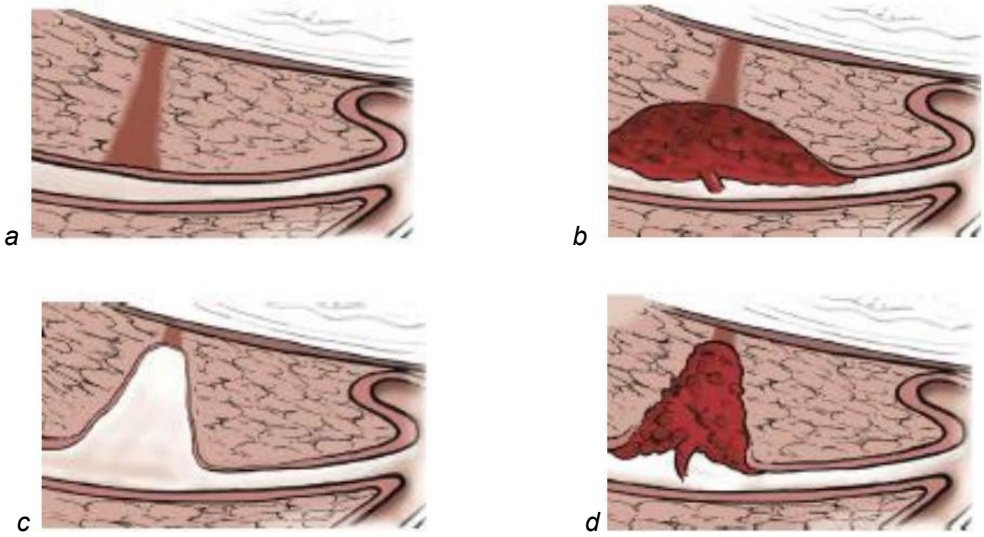



*Figure 5a: properly healed caesarean section scar. Figure 5b: superficial CSP: placenta implanted on a properly healed scar. Figure 5c: Dehiscent caesarean section scar image ("niche"). Figure 5d: deep CSP: placenta implanted on "niche".*

In addition to a medical history of caesarean section, the main associated risk factors are: myomectomy, need for manual removal of the placenta in previous gestation, adenomyosis and aspiration curettage.

The natural history of these pregnancies is the evolution to placenta. The progressive infiltration of the placenta constitutes an important vital risk because it can cause obstetric complications such as severe bleeding and uterine rupture.

#### 4.4.1. Ultrasound diagnosis

1. Empty uterine cavity and endocervical canal.
2. Visualisation of the placenta and/or gestational sac implanted in the hysterotomy scar.
3. Absence or thin layer (1-3 mm) of myometrium between the gestational sac and the bladder.
4. Presence of increased vascularity around or in the area of the caesarean section scar.
5. At early gestation ages, between 5-10 weeks, CSP can be confused with a normal low-lying intrauterine pregnancy (IUP). For the differential diagnosis in these cases Timor-Tritsch et al (8). suggests:

i. Measure the uterine size (mm) in the sagittal plane (from the external os to the fundus) (Distance A). The uterine midpoint is the M point (M=A/2).
ii. If the gestational sac is located between point M and the uterine fundus, it is suggestive of IUP (Figure 6A) and if it is located between M and the cervix it is suggestive of CSP (Figure 6B).

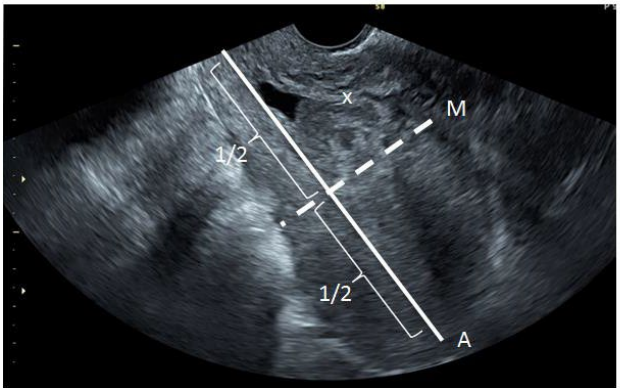



*Figure 6A*

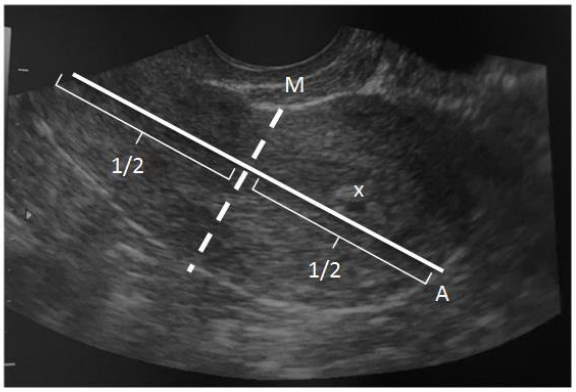



*Figure 6B*

*Figure 6A: IUP. Figure 6B: CSP.*

### 4.4.2. Treatment

**a) <u>Medical treatment</u>**

The medical treatment is **intramuscular MTX at multiple doses** (1 mg/kg weight/day) every 48 h for 4 doses + Calcium levofolinate 5 mg/day every 48 h for 4 alternate doses, following the same protocol as in interstitial pregnancies with β-hCG level ≥ 5000 IU at diagnosis.

However, in cases of positive embryocardia, as an alternative to the injection of 2 mL of KCl, medical treatment can be considered by **combining intra-saccular MTX** (50 mg MTX diluted in 1 mL saline solution) **+ intramuscular MTX** (25 mg) since it is associated with a faster decrease of β-hCG levels, earlier disappearance of the ultrasound image of ectopic pregnancy, and a shorter length of stay in hospital. The intrasaccular puncture procedure is explained in page 8.

Individually, intramuscular treatment has had a success rate of 56%, intrasaccular treatment of 60% and the combination of both of 77% (9).

The follow-up is the same as described for interstitial pregnancies with β-hCG level ≥ 5000 IU at diagnosis.

**b) <u>Surgical treatment</u>**

- **Uterine aspiration curettage**: some authors (10) propose an aspiration curettage as the first therapeutic option in those patients with superficial implantation who meet all of the following diagnostic criteria:

- < 8 weeks of gestation and
- myometrial thickness between bladder and gestational sac > 2 mm and
- haemodynamically stable patient

In the case of uterine aspiration curettage, it will be performed under ultrasound control, with a small cannula and maximum suction pressure of 300 mmHg.

- **Hysteroscopy**: this is a therapeutic option with a low complication rate that could be considered as an alternative to aspiration curettage in patients with the same criteria described for uterine aspiration curettage.

- **Surgical resection**: surgical resection by laparoscopy or laparotomy is an option in cases in which there is bladder infiltration, as well as in case of suspected uterine rupture.

- **Hysterectomy:** indicated in cases of uncontrollable bleeding or when there is no possibility of conservative treatment.

In cases of acute bleeding, **selective uterine arteries embolisation** may be considered prior to carrying out any of the previously proposed therapeutic options.

### 4.5. OVARIAN PREGNANCY

Ovarian ectopic pregnancies occur in 1-6% of ectopic pregnancies and are usually clinically manifest with unilateral abdominal pain and metrorrhagia. They are highly vascularised and 1/3 start with haemoperitoneum. The main risk factor is endometriosis.

#### 4.5.1. Ultrasound diagnosis

It is usually difficult and is often diagnosed during exploratory surgery as it is mistaken for a haemorrhagic corpus luteum or tubal ectopic pregnancy.

The main findings are:
1. Empty uterine cavity with decidualised endometrium.
2. Cystic image in the ovary with high vascularity and a hyperechogenic halo around it.
3. Unlike tubal ectopic pregnancies, ovarian ectopic pregnancies do not separate from the ovary when pressure is applied with the transvaginal transducer.

#### 4.5.2. Treatment

Since it is most frequently diagnosed intraoperatively, the treatment of choice is surgery, selectively removing the ectopic pregnancy or performing an ovariectomy.

However, if suspected by ultrasound, treatment with multiple doses of IM MTX can be considered following the interstitial ectopic pregnancy protocol with β-hCG > 5000 IU at diagnosis.

### 4.6. ABDOMINAL PREGNANCY

Abdominal ectopic pregnancies are the rarest, occurring in 0.9-1.4% of all ectopic pregnancies and occur when the pregnancy implants in the abdomen, including omentum, liver, spleen, intestine, pouch of Douglas, and other intra-abdominal structures. The viability of the pregnancy will depend on the place of implantation.

However, a high percentage of maternal mortality (20%) is described, with serious complications, such as haemoperitoneum, disseminated intravascular coagulation and intestinal obstruction.

There is no consensus on the management of this type of pregnancies. Some authors suggest, if there is pregnancy viability, adopting a conservative approach until week 34-36 of gestation (having informed the patient of the potential risks). Other authors suggest administering MTX leaving the placenta in situ and adding KCl in case of positive embryocardia. (1).

### 4.7. HETEROTOPIC PREGNANCY

In cases of heterotopic pregnancies (intrauterine pregnancy + ectopic pregnancy), the treatment of choice will depend on the viability of the pregnancies:

a) **Non-viable intrauterine + ectopic** (tubal or non-tubal): a uterine aspiration curettage of IUP will be performed in addition to the ectopic pregnancy treatment based on its location.

b) **Viable intrauterine**
   i. **+ tubal ectopic pregnancy**: salpingectomy
   ii. **+ viable non-tubal ectopic pregnancy**: intrasaccular puncture of KCl in the ectopic gestation sac to achieve cardiac asystole. In these cases, the administration of MTX will be contraindicated.
   iii. **+ non-viable non-tubal ectopic**: expectant management will be considered with clinical monitoring.

## 5. RECOMMENDATIONS AFTER METHOTREXATE

During follow-up, it is important to report that the mean time of β-hCG negativisation is from 19 to 129 days and that the ultrasound image can persist for almost 1 year (3).

It is recommended to avoid pregnancy for the first 6 months (minimum 3 months) after the last dose of MTX due to its teratogenic effect. In exceptional cases, where MTX has not been used, the recommended inter-pregnancy period is 3 months.

In a new pregnancy, it is recommended to perform an early ultrasound 5-6 weeks after the last menstruation period.

## 6. BIBLIOGRAPHY


1. *Parker VL, et al. Non-tubal ectopic pregnancy. Arch Gynecol Obstet (2016) 294:19–27.*
2. *Jafri SZ et al. Sonographic detection of interstitial pregnancy J Clin Ultrasound 1987;15:253-7;*
3. *Timor-Tritsch IE et al. Sonographic evolution of cornual pregnancies treated without surgery. Obstet Gynecol 1992;79:1044-9.*
4. *Ackerman TE et al, Interstitial line: sonographic finding in interstitial (cornual) ectopic pregnancy Radiology 1993;189:83-7*
5. *Moawad N, et al. Current diagnosis and treatment of interstitial pregnancy. AJOG 2010.*
6. *Timor-Tritsch et al. Puncture procedures utilizing transvaginal ultrasonic guidance. Ultrasound Obstet. Gynecol. 1 (1991) 144-150*
7. *Jerny K. The conservative management of interstitial pregnancy. BJOG 2004; 111: 1283-8).*
8. *Timor-TritschIE, et al. Easy sonographic differential diagnosis between intrauterine pregnancy and caesarean delivery scar pregnancy in the early first trimester. Am J ObstetGynecol 2016; 215: 225. E1-7.*
9. *Cheng LY, et al. Outcomes of primary surgical evacuation during the first trimester indifferent types of implantation in women with caesarean scar pregnancy. Fertility and Sterility 2014; 1085-90.*
10. *Maheux-Lacroix, S et al. Caesarean Scar Pregnancies: a systematic review of treatment options. JMIG 2017 Sep-Oct;24(6):915-925. doi: 10.1016.*