Ectopic Pregnancy

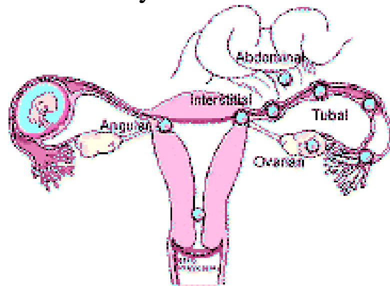
Greek word Ektopos=out of place

Definition Implantation of the fertilized ovum outside the uterine cavity.

Frequency increased since 1970 6 times with incidence of 2% of all pregnancies. It is the leading cause of maternal mortality in the first trimester.

Sites

95% in the fallopian tube,
*80% in ampullary portion, *12%isthmus -5%fimbria -2%cornual
less common sites include *intraabdominal 1.4% *cervical and ovarian .2%each or rudimentary horn.



Risk factors for ectopic pregnancy

In theory anything that delays the migration of the embryo to the endometrial cavity could predispose to ectopic pregnancy

1-Pelvic inflammatory disease
2-history of prior ectopic
3-history of tubal surgery and conception after tubal ligation
4-Use of fertility drugs or Assisted Reproductive technology
5-Use of intrauterine device
6-increased age
7-smoking
8-salpingitis isthmica nodosum
9-others…history of exposure to diethylstilbestrol(DES) in uterus, prior abdominal surgery, failure with progestin-only contraceptive pills, rupture appendix, broad ligament tumor stretching or partially obstructing the tube.

1-Pelvic inflammatory disease

It is the commonest risk factor for ectopic pregnancy. Infection may lead to:
-destruction of the tubal epithelium with reduction or loss of ciliary current
-intratubal adhesions resulting in partial tubal obstruction
-peritubal adhesions resulting in restricted tubal motility.
*Commonest organism is Chlamydia trachomatis, other may be Neisseria gonorrhoea.

The incidence of tubal damage increases after successive episodes of PID i.e. 13% after 1 episode, 35% after 2 episodes and 75% after 3 episodes

2-Prior history of ectopic pregnancy

Patients with history of previous ectopic has a 10-25% chance of another ectopic pregnancy.

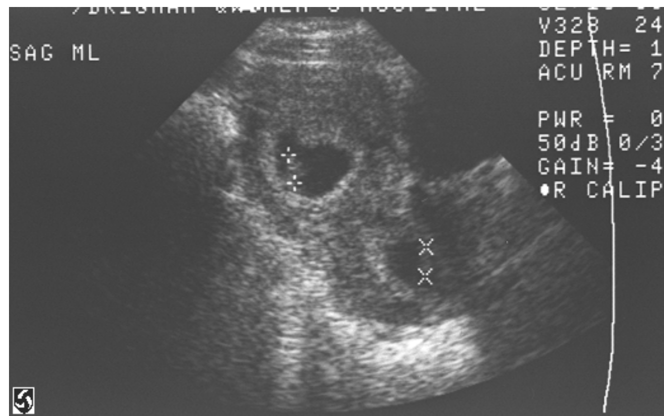
3-History of tubal surgery and conception after tubal ligation

Surgeries carrying higher risks for ectopic include salpingostomy, neosalpingostomy, fimbriostomy, tubal reanastomosis and lysis of peritubal or periovarian adhesions

*35-50% of patients who conceive after tubal ligation are reported to experience ectopic pregnancy. The use of bipolar tubal cautary carries more risk than sutures, ring or clips

4-Use of fertility drugs and ART

Ectopic pregnancy increases 4-folds in patients using drugs for ovulation induction, may be due to multiple ova and increases in hormonal level. Patients undergoing IVF or GIFT have 5% risk of ectopic pregnancy.
Heterotopic pregnancy presence of intrauterine and ectopic pregnancy together occur in 1:30,000 pregnancies but it occurs in 1% of cases with GIFT or IVF.



5-Use of Intrauterine device

Copper devices do not increase the incidence of ectopic but if pregnancy occurs the incidence of ectopic is increased. Medicated IUD with progestogin increases the risk 3-4%.

6-Increasing Age
The incidence of ectopic was shown to increase with maternal age, with an incidence 4- folds higher in the age goup 35-44 years compared to the age group 15-24 years.
Aging may result in loss of myoelectrical activity of the tube.

7-smoking
Ectopic pregnancy was shown to occur more common in smoker with a risk of 1.6-3.5% times that of non-smoker.A dose-response effect has been suggested. Several mechanisms have been postulated:
*delayed ovulation * altered tubal motility and uterine motility *altered immunity

8-Salpingitis isthmica nodosum
Defined as the microscopic presence of tubal epithelium in the mesosalpinx or beneath the tubal serosa. These pockets of epithelium protrude through the tube, similar to diverticula. Studies showed that 50% of tubes removed for ectopic show this finding. The cause of this condition is not clear but it could be postinflammatory or endometriosis.

N.B premature implantation or delayed implantation of fertilized ovum could be a factor for ectopic pregnancy.
-premature shedding of zona pellucida from the fertilized egg may be due to delayed ovulation
-transperitoneal migration of ova to be implanted in the contralateral tube, as it takes long time to reach the other tube. Cases with ectpoic in one tube and corpus luteum in the other ovary support this mechanism.

Pathogenesis

- The trophoblast develops in the fertilized ovum and invades deeply into the tubal wall.

- Following implantation, the trophoblast produces hCG which maintains the corpus luteum.

- The corpus luteum produces estrogen and progesterone which change the secretory endometrium into decidua. The uterus enlarges up to 8 weeks size and becomes soft.

- The tubal pregnancy does not usually proceed beyond 8-10 weeks due to :

*lack of decidual reaction in the tube, *the thin wall of the tube, *the inadequacy of tubal lumen, *bleeding in the site of implantation as trophoblast invades.

- Separation of the gestational sac from the tubal wall leads to its degeneration, and fall of hCG level, regression of the corpus luteum and subsequent drop in the estrogen and progesterone level. - This leads to separation of the uterine decidua with uterine bleeding.

Fate of tubal pregnancy:

(I) Tubal mole:

The gestational sac is surrounded by a blood clot and retained in the tube.

(II) Tubal abortion:

- This occurs more if ovum had been implanted in the ampullary portion of the tube.

- Separation of the gestational sac is followed by its expulsion into the peritoneal cavity through the tubal ostium.

- Rarely, reimplantation of the conceptus occurs in another abdominal structure leads to *secondary abdominal pregnancy*.

- If expulsion was complete the bleeding usually ceases but it may continue due to incomplete separation or bleeding from the implantation site.

(III) Tubal rupture

- More common if implantation occurs in the narrower portion of the tube which is the isthmus.- Rupture may occur in the anti-mesenteric border of the tube. Usually profuse bleeding occurs with intraperitoneal hemorrhage.

- If rupture occurs in the mesenteric border of the tube a broad ligament hematoma will occur.

Clinical Picture

General symptoms:

1- Short period of amenorrhoea:

usually does not exceed 8-10 weeks. This may be lacking if the ectopic pregnancy is disturbed before the next menstruation. This may occur particularly with ectopic pregnancy in the interstitial portion of the tube.

2- Pain:

is present in almost every case and precedes vaginal bleeding. It may be:

a. Aching due to tubal distension.

b. Colicky in tubal abortion.

c. Stabbing in tubal rupture.

d. Shoulder pain if blood accumulates under the diaphragm.

e. Bladder and rectal irritability in pelvic hematocele.

3- Vaginal bleeding:

Due to shedding of the decidua. It is usually slight and follows the pain.

General signs:

General examination: general condition depends on twhether tubes has ruptured or not.

Breast signs of pregnancy.

Abdominal examination:

Lower abdominal tenderness and rigidity especially on one side may be present.

Vaginal examination:

- Bluish vagina and bluish soft cervix. - Uterus is slightly enlarged and soft.- Marked pain in one iliac fossa on moving the cervix from side to side.- Ill defined tender mass may be detected in one adnexa in which arterial pulsation may be felt. The other manifestations depend upon the clinical variety of the ectopic pregnancy:

(A) Undisturbed Tubal Pregnancy

It is the same general symptoms and signs mentioned before. The pain is aching in nature and there is no vaginal bleeding.

(B) Tubal Abortion

The more common so it is called the classical picture of ectopic pregnancy.

Symptoms:

1. The general symptoms and signs are present.
2. Fainting attacks due to pain and intraperitoneal hemorrhage.
3. Nausea and vomiting due to peritoneal irritation.

Signs:

General examination:

1. Anemia of varying degree depending upon the blood loss.
2. Pulse is usually rapid.
3. Temperature slightly higher (up to 38°C) due to absorption of blood from the peritoneal cavity.
4. Blood pressure: falls in proportion to the amount of internal hemorrhage.

Abdominal examination:

Cullen's sign: a periumbilical bluish discoloration may be present due to absorption of the blood in the peritoneal cavity by lymphatics. It is a late sign.

Local examination:

Boggy swelling in the cul-de-sac if pelvic hematocele is present.

(C) Tubal Rupture

The most dramatic although not the most common.

Symptoms:

Short period of amenorrhoea (6-8 weeks) or even there is no missed period.

Signs

General examination:

- Rapidly developed shock, with pallor, sweating, air hunger, rapid thready pulse and hypotension.

- Shoulder tip pain and hiccoughs due to irritation of the phrenic nerve of the diaphragm by accumulated blood when the patient lying down

Abdominal examination:

- The abdomen is distended, rigid with generalized tenderness.

- Shifting dullness and periumbilical bluish discoloration due to intraperitoneal hemorrhage.

Local examination:

The same as in general signs of ectopic, although it is undesirable as it may induce more disruption and bleeding.

(D) Pelvic Hematocele

Symptoms:

1. Symptoms suggesting disturbed tubal pregnancy since a period of time.
2. Pressure symptoms due to accumulation of blood in the Douglas pouch as frequency of micturition, tenesmus and dyspareunia.

Signs:

1. A fixed tender swelling is felt in Douglas pouch.
2. The uterus is slightly enlarged, soft and pushed forwards and the external os is directed downwards.
3. Aspiration of Douglas pouch (*culdocentesis*) may reveal blood which does not clot on standing. If blood clots it means that needle has punctured a blood vessel.
4. Infection may be superadded and a pelvic abscess is formed.

Investigations of Ectopic Pregnancy

(1) Serum b -hCG:

Urine pregnancy tests are positive in only 50-60% of ectopic. Detection of b -hCG in the serum by ELISA or radioimmunoassay are more sensitive and can detect very early pregnancy about 10 days after fertilization i.e. before the missed period.

- If the test is negative, normal and abnormal pregnancy including ectopic are excluded.
- If the test is positive, Ultrasonography is indicated.

Doubling time:

- In normal pregnancy, the b -hCG level is doubling every 48 hours during the first 42 days of gestation.

- Ectopic pregnancy usually shows less than 66% increase in b -hCG level within 48 hours.
- Unfortunately, this is not specific to ectopic pregnancy. In 15% of normal pregnancies as well as in abortions there is also slow doubling time.

N.B. *Alpha-hCG subunit level* is higher in ectopic pregnancy than normal gestations.

(2) Ultrasonography:

In general, a positive b -hCG test with empty uterus by sonar indicates ectopic pregnancy. This is true if the ß-hCG is at or above the threshold level in which an intrauterine gestational sac can be detected. This is called discriminatory zone.

Discriminatory hCG zones:

Diagnosis of ectopic pregnancy is made if there is:

1. An empty uterine cavity by abdominal sonography with b -hCG value above 6000 mIU/ml.
2. An empty uterine cavity by vaginal sonography with b -hCG value above 2000 mIU/ml.

(3) Progesterone:

Serum progesterone level is lower in ectopic than normal pregnancy and usually less than 15ng/ml.

(4) Culdocentesis:

If non-clotting blood is aspirated from the Douglas pouch through a wide pored needle, intraperitoneal hemorrhage is diagnosed. But if not, ectopic pregnancy cannot be excluded.

(5) Curettage:

- If microscopic examination of the products of curettage reveals decidua and chorionic villi, the condition is abortion of intrauterine pregnancy.
- If it reveals decidua only or *Arias Stella reaction* in the endometrium as well (cellular atypism, mitotic activity and glandular proliferation), ectopic pregnancy is diagnosed. The drawback is that in complete abortion also decidua only is curetted.

(6) Laparoscopy:

A good diagnostic aid particularly in disturbed ectopic.

(7) Complete blood picture:

- Hemoglobin and hematocrit ---- to assess anemia.

- Leucocytic count ---- exclude infections as appendicitis and salpingitis.

Uncommon Sites of Ectopic Pregnancy

(I) Cornual angular pregnancy:

- It is implantation in the interstitial portion of the tube.

- It is uncommon but dangerous because when rupture occurs bleeding is severe and disruption is extensive that it needs hysterectomy.

- In some cases, the pregnancy is expelled into the uterus and rupture does not occur.

(II) Pregnancy in a rudimentary horn:

- Pregnancy occurs in the blind rudimentary horn of a bicornuate uterus.

- As such a horn is capable of some hypertrophy and distension, rupture usually does not occur before 16-20 weeks.

- *Treatment:* Excision of the horn. During operation, pregnancy in a rudimentary horn can be differentiated from interstitial cornual tubal pregnancy by finding the attachment of the round ligament lateral to the first and medial to the later.

(III) Cervical pregnancy:

- Implantation in the substance of the cervix below the level of uterine vessels.

- May cause severe vaginal bleeding.

Treatment :

1. Evacuation and cervical packing with haemostatic agent as fibrin glue and gauze.
2. If bleeding continues or extensive rupture occurs hysterectomy is needed.

(IV) Ovarian pregnancy:

Etiology:

1. Pelvic adhesions.
2. Favorable ovarian surface for implantation as in ovarian endometriosis.

Pathogenesis:

- Fertilization of the ovum inside the ovary or ,

- implantation of the fertilized ovum in the ovary.

Spiegelberg criteria for diagnosis of ovarian pregnancy:

1. The gestational sac is located in the region of the ovary,
2. the ectopic pregnancy is attached to the uterus by the ovarian ligament,
3. ovarian tissue in the wall of the gestational sac is proved histollogically,
4. the tube on the involved side is intact.

Treatment:

Laparotomy and inoculation of the ectopic pregnancy and reconstruction of the ovary if possible. Otherwise, removal of the affected ovary is indicated.

(V) Abdominal (peritoneal) pregnancy:

Types:

1. *Primary:* implantation occurs in the peritoneal cavity from the start.
2. *Secondary:* usually after tubal rupture or abortion. Intraligamentous pregnancy: is a type of abdominal but extraperitoneal pregnancy. It develops between the anterior and posterior leaves of the broad ligament after rupture of tubal pregnancy in the mesosalpingeal border or lateral rupture of intramural (in the myometrium) pregnancy.

Diagnosis:

(A) History:

of amenorrhoea followed by an attack of lower abdominal pain and slight vaginal bleeding which subsided spontaneously.

(B) Abdominal examination:

- Unusual transverse or oblique lie.

- Fetal parts are felt very superficial with no uterine muscle wall around.

(C) Vaginal examination:

- The uterus is soft, about 8 weeks and separate from the fetus.

- No presenting part in the pelvis.

(D) Special investigations:

1. Plain X-ray : shows abnormal lie. In lateral view, the fetus overshadows the maternal spines .
2. Ultrasound : shows no uterine wall around the fetus.
3. Magnetic resonance imaging (MRI): has a particular importance in preoperative detection of placental anatomic relationships.

Differential Diagnosis:

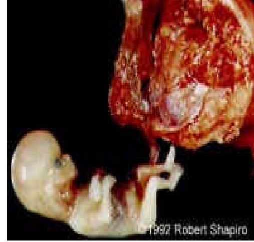
Rupture uterus.

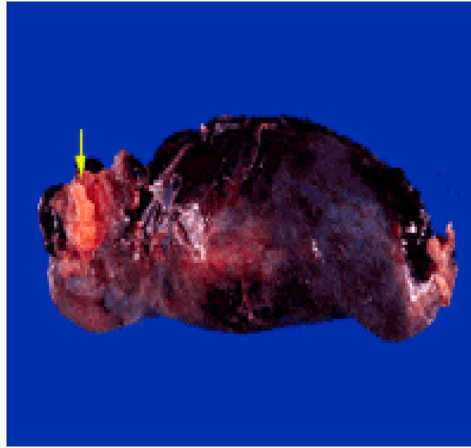
Treatment:

The condition should be terminated surgically through laparotomy once diagnosed as the fetus is malformed in the majority of cases. In addition, there is risk of massive internal hemorrhage if separation of the placenta occurs.

At least 2000 ml of cross-matched blood should be on hand before proceeding to laparotomy. The fetus is removed and if the placenta is attached to an excisable structure as omentum, it is removed with it. If the placenta is attached to an important structure leave it for autolysis which may extend to few months or years. Any attempt to separate placenta will evoke uncontrollable bleeding. In this case, methotrexate 12.5 mg IM daily for 5 days will destroy trophoblastic tissue and accelerates the involution of the placenta.

In rare cases, the fetus may reach full term where spurious (false) labor occurs and the fetus dies if not recognized.





Medical treatment of Ectopic

The use of Methotrexate become widely used to treat patients with ectopic pregnancy. Patient selection is important to avoid rupture of ectopic.

***patient must be hemodynamically stable**

***No symptoms or signs of active bleeding or hemoperitoneum**

***she must be reliable, complaint, and able to return for follow-up**

***best result with 3s…..patient is not more than 3 weeks amenorrhea(i.e. <7weeks pregnant) *B-HCG <3000mIU/ml *size of ectopic <3cm**

Methotrexate 50mg/m2 IM

Measure B-HCG at 4 and 7 days

If levels decreased >15% no need for another methotrexate injection, if less another injection is given.

N.B b-HCG usually rise during first 4 days and pain increase during first week.

Some use misoprostol 600mg a single oral dose with methotrexate with 90% success rate.

*Subsequent the intrauterine pregnancy rate was shown to be:

60% after conservative tubal surgery

87% after medical treatment

40% after salpingectomy

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