

The Ectopic

by Dr. Gys Roux



Release of a ripe egg from the ovary

This is a review of ectopic pregnancy from the recent literature.

Definition:

Ectopic pregnancy (syn. eccyesis) is any intra/extra uterine gestation in which the fertilised ovum implants at an aberrant site inconducive to growth and development. These aberrant sites are:

- a) Cornu of the uterus
- b) Fallopian tubes
 - interstitial
 - isthmus
 - ampulla
 - fimbriae
- c) Ovaries
- d) Other, such as the broad ligament, the cervix and any other place in the abdominal cavity.

Incidence:

The incidence varies from one author to the other, but all are convinced that the incidence is rising, eg:

- 1) 1/126 normal deliveries in 1962
1/90 normal deliveries in 1968
1/69 normal deliveries in 1978
- 2) 1/160 normal deliveries in 1970
1/100 normal deliveries in 1977

The reason for this increase is thought to be due to the rising incidences of gonorrhoea, or to the relative greater effectiveness of the intra uterine contraceptive device to prevent intra uterine pregnancy rather than extra uterine pregnancy.

The mean age in the U.S.A. in one study was found to be 26,6 years.

The mean parity in the same study was found to be 1,8 (ranging from 0,9).

Mortality:

Most authors put it between 5,7% of perinatal maternal deaths, though some give figures as high as 15,4%. It is the major cause of maternal death in the first trimester of pregnancy — even worse than with abortions!

Most cases die at home before medical attention can be reached.

Many of those dying have been seen at least once by a doctor before the terminal episode. An early diagnosis could have prevented death.

Etiology

Pathophysiology of Conception:

A normal ovum survives up to 24 hours (probably only 8 - 12 hours) before it starts to degenerate - i.e. it has to be fertilised before that time to prevent degeneration.

A normal spermatozoon is capable of fertilising an ovum 48 hours (up to 72 hours if in a favourable environment) after ejaculation.

Fertilisation usually takes place in the distal part of the ampulla, and from there the fertilised ovum is transported to the uterine cavity by means of the ciliary current of the endosalpinx, as well as by peristaltic movement. Secretions of the endosalpinx help with the nourishment of the fertilised ovum.

In about four days it reaches the uterine cavity and lies there free for another 2 - 3 days before it implants into the endometrium after 7 days from conception. The endometrium is then in its progestational secretory phase.

From the above it can be seen that up to 3 days after coitus fertilisation of an ovum can still take place. The fertilised ovum then has a long way to travel, over a prolonged time span, during which its progress can be halted at any place to cease embedding at an ectopic site. The reasons for such an implantation can be:

1. Malfunctioning of the tube due to, for instance: Congenital or hormonal influences or infections.
2. Anatomical deformities of the tube of the endosalpinx such as caused by infections, tumours, diverticuli, etc.
3. Ectopic placental tissue such as in endometriosis causing implantation at these ectopic sites.
4. The "migrating ovum" theory, which means that a fertilised ovum from the

Pregnancy



contralateral tube migrates to the tube where it implants transperitoneally.

During its migration it has become too big, and has been retarded to such an extent, that it cannot get to the uterine cavity, but implants earlier.

5. The "regurgitation" mechanism. This theory is also based on the fact that the corpus luteum of pregnancy is often found in the tube contralateral to that of the ectopic pregnancy.

It is said that the fertilised ovum reaches the uterine cavity in the normal way, but then is regurgitated again before its implantation into one of the tubes, where it implants causing an ectopic pregnancy.

6. "Tubal spasm" is mentioned as a theoretical cause, but has never been proven.

From the above a number of etiological factors can be isolated. The importance of each could vary from society to society and from cultural group to cultural group. They are as follows:

1. Pelvic Infections:

This is the largest single factor according to most authors. The incidence given is between 25% and 50%. In one series 81% of these pelvic infections were due to salpingitis, 11,5% were due to puerperal sepsis, and 7,6% were due to complications of abortion.

In a series where operative evidence of

P.I.D. (Pelvic inflammatory disease) was found, 40% of these cases had denied ever having had P.I.D.!

2. Previous abdominal surgery:

This is, according to one author, the second most common cause of ectopic pregnancy - normally 26% of cases.

6,3% — 11% of cases of ectopic pregnancy had had a previous ectopic pregnancy. This means that your chances are quite high to get a second ectopic if you've had one. In fact, different authors put it between 23,7% and 30% (i.e. 1:3 - 1:4 pregnancies!)

3,0 — 12% of ectopics had a tubal sterilisation procedure carried out on them before. What's more, this incidence is increasing! If you take the incidence as 7,4% it means that \pm one in every thirteen ectopics are due to a sterilisation operation.

In one series 99% of these were Pomeroy procedures, and 45% were laparoscopy procedures (especially tubal fulguration).

Internal procedures were rarely implicated. The mechanism of failure was either that recanalisation had taken place to such an extent as to allow spermatozoa to pass through, but not a fertilised ovum, and therefore trapping the ovum in the distal segment of the tube, or that a peritoneal fistula had occurred,

leading to transperitoneal migration of spermatozoa to the ovum, and then to entrapment of the ovum in the distal segment of the tube.

In only one out of five ectopics after tubal sterilisation was the implantation in the peritoneal segment of the tube - in all the others it was in the distal segment.

One of the reasons for the formation of a proximal fistula, can be the use of non-absorbable sutures. It is therefore suggested by the author that the proximal stump should be buried (in the corpus/broad ligament) or that non-absorbable sutures are used (it has been shown that the last measure does not prevent ectopics, though)

4,0% of ectopics take place after previous tubal reconstructive surgery (i.e. "tuboplasty" etc.)

Other operations mentioned are Hysterectomy, Appendicectomy, Ovarian cystectomy, etc.

3. Contralateral ovulation:

It is said to occur in 2 - 50% of cases of ectopic, depending on the author. It has never been proven conclusively to be the cause of ectopic pregnancy, however.

As already mentioned, the contribution of contralateral ovulation to ectopic pregnancy can be explained either

through the regurgitation theory or the transperitoneal migration theory.

4. Contraception:

- a) Intra uterine Contraceptive Device (I.U.C.D.): In one series I.U.C.D.'s were present in 10,5% of ectopic pregnancies. Where the highest incidence of ectopics quoted is between 1:60 to 1:100 pregnancies that of ectopics in I.U.C.D. failures is 1:23! There is therefore a 2,5 - 10 fold increase in risk of a pregnancy being ectopic if you are an I.U.C.D. user!

The importance for the G.P. in the above lies there in that ectopics in I.U.C.D. users are often missed (!) because they commonly complain of lower abdominal pain and abnormal vaginal bleeding in the normal course of events.

- b) As far as hormonal contraception is concerned, nothing has been proven either. Experimentally, oestrogen in low dosages has been shown to increase tubal motility in animals, and in high dosages to decrease it.

It is important to note that "the morning after contraception" consists of a high dosage of oestrogens given as a stat dose, and that this could theoretically therefore predispose to ectopic pregnancy. Progesterone before ovulation increases tubal motility and afterwards either has no effect or decreases it.

5. "Tubal deformities" — due to various reasons, could all predispose to ectopic pregnancy. A leiomyoma of the tube, diverticulae of the tube, endometriosis, extrinsic tumours pressing on the tube, T.B. of the tubes and pelvis, and intratubal growth have all been implicated.

6. Ovulation induction with clomiphene — could lead to multiple pregnancies of which some could be in an ectopic location.

7. Infertility: Between 2% and 18,8% (depending on the author) of patients with ectopic gestation had primary infertility and 2,5 were primigravidae. In another series 20% of patients had had fertility investigation, and 40% had no children who had lived. The author concludes that ectopic pregnancy is usually a disease of low parity, except in developing countries.

8. Other factors mentioned are psychogenic, tubal spasm, an abnormal zygote, and previous therapeutic abortions.

9. "No reason" could be found in 40% in two series.

From the above certain high risk groups emerge where one has to seriously bear the possibility of ectopic pregnancy in mind. These are:

- 1) History of previous episodes of P.I.D.
- 2) Previous ectopic (chances 1:3 - 1:4 to have a second one!)

- 3) Sterilisation procedures (1:13 ectopics!)

- 4) Tubal reconstructive surgery performed.

- 5) Primary infertility

- 6) I.U.C.D. users (2,5 - 10 fold increased risk if they should fall pregnant)

- 7) Pelvic T.B., Endometriosis.

Clinical Picture:

The classical triad consists of:

- 1) Pelvic pain
- 2) Abnormal (irregular) vaginal bleeding
- 3) A period of amenorrhoea — in a woman of child bearing age.

One author goes as far as to say that the diagnosis has to be thought of whenever pelvic pain and irregular bleeding are found together.

The history therefore, is the most important factor in the diagnosis.

The problem is, however, that it is often misdiagnosed. In two series 50% of cases had been misdiagnosed by a general practitioner and had been seen before by him without making the diagnosis, 36% were wrongly diagnosed by the hospital doctor. More than 30% of patients were sent to general surgical wards and 1,2% to medical wards, 10% went home again before the diagnosis of ectopic pregnancy was made, often having had a curettage for suspected incomplete abortion.

What then, is the clinical picture?

Symptoms:

- 1) The most common symptom by far is **Pelvic Pain** (96% - 98% - 99,3% - 100%)

In 44% of cases the pain was of < 24 hours duration

In 28% of cases the pain was of 1 - 7 days' duration

In 26,2% of cases the pain was of > 1 week duration

The site of the pain was general in 44,3% of cases and unilateral in 32,7%. It radiated to a shoulder in 22,3% of cases.

The onset of pain varied from the typical sudden onset, to a gradual and progressive onset.

- 2) **Abnormal vaginal bleeding** was present in 68,4% of cases to 90% of cases, depending on the author, which means that 10 - 31,6% of cases had had NO vaginal bleeding since the onset of amenorrhoea! (or since their last normal period).

The duration was usually 1 - 5 days, and varied from intermittent spotting to frank continuous bleeding with or without the passage of clots or tissue.

- 3) **Amenorrhoea** is the third of the triad mentioned earlier. The incidence also varies from author to author. Many people are of the opinion that the more thorough your history taking is, the more likely you are to elicit a history of "missed" or "scanty" menstrual flow. According to one author it was present in 80% of cases in his series.

Last normal menstrual period 4 - 8/52 ago - 53%

Last normal menstrual period 8 - 12/52 ago - 16,8%

Last normal menstrual period > 12/52 ago - 9,4%

According to another author, in 68% of cases a period will have been missed for at least 2/52. Yet another author puts the incidence at 63%, the most common period of amenorrhoea being 5 - 8/52.

In conclusion then, one author states that in 94% of cases there will be some form of menstrual abnormality - amenorrhoea or abnormal P.V. bleeding or a combination. Only 6% will have a normal menstrual history.

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4. Other symptoms

Classically **nausea, vomiting and syncope** is associated with the onset of lower abdominal pain - i.e. when the tube "ruptures", or when some other bleeding intraperitoneally occurs. Nausea was present in 20% of cases in one series, vomiting in 15%, syncope in 13% (37% by another author), and dizziness in 9%. Weakness was present in 9%, passage of tissue "cast" in 5 - 6.7%, breast engorgement in 3%, fever and chills in 3%, diarrhoea in 3%, and a sensation of abdominal fullness in 1%. Dyspareunia is also mentioned by one author as a commonly occurring complaint.

Signs:

The most significant findings are supposed to be:

Abdominal pain and tenderness;
Severe pain on pelvic examination;
Adnexal mass/fullness; according to one author.

1) General observation:

Blood pressure

In 78% of one series it was normal. In 16% it was borderline (systolic 80 - 100/diastolic 40 - 60)

In 6% there was overt shock (Systolic < 80/Diastolic 40 - 0).

According to another author shock was present in 17% of cases.

Shock is not at all a common finding in ectopic pregnancy, as one is inclined to think.

Temperature:

Usually normal (in 80 - 95% of cases) In one series 6.81% were - 37.8°C and in another 5% were 37.6°C.

It is important to note though, that it can be elevated! - according to one author a low degree of fever was present in 17% of cases and a high fever in 2%. In 0.3% of one series the temperature was 38.2 - 39.2°C.

2. Abdomen:

76% had peritoneal signs in one series! with localised tenderness in 51% and a palpable abdominal mass in 6.6%.

3. Vaginal examination:

The classical finding of Cervical excitation tenderness is present in 38 - 85% of cases, depending on the author.

Much more common (94.2 - 96%) it seems is **Adnexal tenderness** - in 40% unilateral and in 60% bilateral. A pelvic mass could be felt in 36 - 53% of cases!

In many cases however, it was felt on the side to the ectopic pregnancy (19.5%). The reason for this is said to be either the corpus luteum of pregnancy, coincidental pelvic inflammation, or accumulated blood/clots.

Adnexal fullness was present in 17.8% of one series.

An enlarged uterus was present in 14.1%. In another series it was present in 29.3%, the sizes being:

25% 6 - 8/52 pregnancy size
3.3% 9 - 12/52 pregnancy size
0.3% 25/52 pregnancy size (fibroid)

Diagnostic Procedures:

1. **Culdocentesis** (Syn. Colpopuncture, aspiration of Cul de Sac). This is the classical diagnostic procedure, and still regarded as "the simplest and probably most rewarding procedure".

Depending on the author it is said to be positive in between 75% and 95% of cases.

The procedure is to put a needle under direct vision (with a wide open Cusco vaginal speculum to tense the posterior fornix of the vagina; good light necessary) into the Pouch of Douglas through the posterior fornix. Go in posterior to the fold caused by the reflexion of the vaginal wall from the cervix, and in the **midline** so as to miss the bloodvessels coming from the parametria. Keep on suctioning while putting the needle in through the vaginal wall, and also on retrieving it.

Before introducing the needle, clean the vagina in Savlon/Hibitane in WATER. Infiltration with lignocaine is probably not necessary since it is likely to be as painful as the aspiration itself, and takes extra time.

The colpopuncture is said to be positive if there are blood clots present (squirt blood out on a piece of gauze) or if the Haematocrit is < 15%. It must be non clotting blood. One author found the Haematocrit to be > 15% in 97.5% of positive colpopunctures. If the Haematocrit is < 15% the puncture could presumably have been produced by a ruptured follicle cyst, or infection or something else.

NB. A colpopuncture is **NEGATIVE** when the ectopic is still **UNRUPTURED**, and that is actually the time you want to pick it up!

2. Pregnancy Test:

It is generally taken to be positive in 50% of cases, but some find it positive in as high as 82% of cases and some find it negative in as much as 87% of cases.

Positive in 13% - 50% - 82%. It is probably dependent on the type of kit used.

The old bioassay urine test (sensitivity of 3 000 I.U. HCG/l) is positive in 33 - 66%.

The newer agglutination inhibition test has a sensitivity of \pm 2 000 I.U./l. (1 500 - 2 500 I.U./l) and is more sensitive than the above. It can become positive five days after a skipped period, but pregnancy is usually diagnosed only twelve days after a missed period.

The problem with the pregnancy tests on urine (agglutination inhibition test) is that in ectopic pregnancies the H.C.G. concentration in urine is usually less than 50% of that of a normal pregnancy. It usually, in a normal pregnancy, becomes positive, as mentioned above, 5 - 12 days after the missed period.

It is therefore understandable why there is a percentage of false negative results, especially if one bears it in mind that an ectopic pregnancy usually presents 1 - 4 weeks after the missed period.

3. Serum H.C.G.:

There are two measurements here — Radio immune assay and Radioceptor assay.

Radioceptor assay has a sensitivity of 100 I.U. of H.C.G./l and is positive in 87 - 90% of cases. It is almost 100% sensitive, one day after the missed

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period. It takes about an hour to do, but is only available in very specialised institutions.

Radio immune assay is more sensitive than the above (5 I.U./l) but takes about 36 - 48 hours to do. It is positive in 95 - 100% of cases, and becomes positive a few days after implantation of the fertilised ovum.

(P.S. Radioceptor assay for H.C.G. cross reacts with L.H., and one therefore has to determine the β -subunit concentration.

The value of the H.C.G. determinations (urine or serum) is that the more sensitive they are, the more accurately one can diagnose pregnancy - albeit intra or extra uterine pregnancy. A positive result therefore **does not imply EC-TOPIC pregnancy** - especially as far as the urine pregnancy test is concerned.

4. Sonar:

Sonar is of special value in those cases where a woman presents with an adnexal mass, lower abdominal pain and possibly vaginal bleeding in the first trimester of pregnancy. If an intrauterine pregnancy can be demonstrated, **extrauterine pregnancy can be ruled out.**

New techniques are more sensitive than older ones and extrauterine pregnancies can be picked up more accurately with a diagnostic error of 7.7% (1/36 false positive and 2/36 false negative). It must be stressed though that older techniques have a diagnostic error of 25.6% - and that is what we have in most hospitals at the moment!

The only function therefore remains that of the exclusion of extrauterine pregnancy by demonstrating intra uterine pregnancy. (NOTE: in a very small percentage one can have both!)

5. Laparoscopy/Culdoscopy

Could be useful especially in those cases in which there is a negative colpopuncture, but suspicious clinical findings. It should not be used in the acute case though.

It should be noted that through a laparoscope on ovarian pregnancy can look like an ovarian cyst - and the incidence of that is rising with the increasing use of the I.U.C.D.

6. Haematocrit/Hb

Some people say that it correlates poorly with the degree of shock, while others say that it correlates well with the amount of haemoperitoneum found at operation. One thing is sure enough, that a decreasing Hb if done serially, every hour, is definitely significant and means that internal haemorrhage is taking place.

It is also a fact that if hypovolemia resulting from internal haemorrhage has not been corrected by haemodilation (as is the case in acute bleeding), the Hb would be normal. In one series the haematocrit was

> 30% in 73% of cases

21 - 30% in 23% of cases

< 21% in 4.7% of cases

A normal Hb (or haematocrit) therefore does not exclude an ectopic at all!

7. Examination under anaesthesia:

It is seldom done these days when an ectopic pregnancy is suspected, because there are so many other aids in the diagnosis (eg. laparoscopy) and there is always the danger of rupturing the ectopic while doing the examination.

8. The White Cell Count and E.S.R. —

Can be higher and confuse the issue.

In conclusion, I must say that the stress falls more and more on the early diagnosis of ectopic pregnancy before rupture, because that enables one to attempt reconstructive surgery on the tube and therefore improve the patient's chance of subsequent conception, and it also decreases the mortality and morbidity attached to the disease. The newer development in diagnostic aids (Sonar, laparoscopy, serum H.C.G. determination) have made this more of a possibility.

Management

1. Operative:

To get consent, especially in the Black population, one has to take time to explain the reason, and one must be honest. One also has to give the patient time to think the matter over. They very often have deep-seated fears of operations, and it may help to have the sister or a nurse - somebody speaking their language - speaking to them. They also usually do not like to take quick decisions, but want to think it over, and like to have the same thing repeated to them, in different ways, until they are convinced.

If one does not give them that time, it happens what has happened in some

cases - where forced into decisions they were not entirely convinced were the right ones, they changed their minds later on - even in theatre just before the operation. I would say it is much better to try and establish a relationship of trust and understanding with a patient, so that the patient understands that you care about her, and still think that an operation is necessary.

Findings:

1. Haemoperitoneum was present in 86% of cases in one series

- < 500 ml blood 52.7%
- 500 ml - 1000 ml 28.7%
- 1000 - 1500ml 9.7%
- 1500 - 2000 ml 3.7%
- > 2000 ml 5.3%

2. Only 6% of cases were unruptured in one series. This number is increasing due to better diagnostic aids.

3. Site of ectopic pregnancy:

Tubal in 96% of cases:—

- 9% proximal 1/3
- 24% middle 1/3
- 65% distal 1/3

— 2.4% fimbrial end.

most occur in the distal ampulla.

Ovarian: 0.3% to 2.7% (rising incidence due to the I.U.C.D.)

Cornual pregnancy: 2 - 4%

Abdominal: 2.7%

Cervix and broad ligament - seldom (no number available)

As already mentioned earlier microsurgical repair (especially in unruptured cases, but also in selected ruptures with very little distortion of the anatomy) of the involved tube, if it was a tubal pregnancy, is nowadays the aim. It happens however, in a very selected few. As seen in the quoted series, 99% of ectopics were ruptured at the time of operation.

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During the operation optic instruments and very fine suctioning is used (eg. 6 - 0 Vicril) and tissues are handled atraumatically.

Post operatively peritoneal washouts with anticoagulants is carried out, and antibiotics given prophylactically. A hydrotubation is sometimes done during the operation, and a hysterosalpingogram in the post operative period.

Tubal repair should be attempted especially in those cases where the other tube is damaged.

In most cases, however, microsurgical repair is not possible, and a salpingectomy is carried out if it is a tubal pregnancy. The ovary is not removed unless it is an ovarian pregnancy. If it is a cornual pregnancy the cornu of the uterus is resected.

Abdominal pregnancies can be difficult to handle and if the placenta is implanted at a dangerous site, it is best left insitu and to close the abdomen and wait for its resorption over the next year or two. If an abscess forms, a repeat laparotomy has to be done.

It is also important to note that an extrauterine pregnancy implanted in the abdominal cavity has a very serious risk for the mother and that it should only really be allowed to go to term (eg. when it is the only chance of the mother getting a child of her own).

It should also be remembered that these children have a 50% mortality in the neonatal period, and are badly misshapen, albeit temporarily.

2. Post operative period:

6% in one series developed post operative wound sepsis.

Blood transfusion was necessary in 33 - 66% of cases.

This just shows that severe blood loss is not always associated with ectopic pregnancies although, as mentioned earlier in 5,7% of cases more than 2 000 ml. was thought to be present at the time of laparotomy in the abdominal cavity in the series quoted.

It is also true that the mortality of 5 - 15% associated with the disease mentioned earlier, is said to be almost entirely due to very severe bleeding before being able to get medical attention.

3. Communication:

It is very necessary to communicate with the patient, telling her before the operation what is going to happen to her and why, as mentioned earlier, and also in the post operative period, concerning her outlook regarding future pregnancies.

It is very important that a woman knows what has been done to her - also because she will be able to give that history to a doctor when she presents with a gynaecological complaint to him. A history of a previous ectopic pregnancy is important, because, as mentioned earlier on, the chance of having a second one is between 1:3 and 1:4 (a 25-fold increased risk)!

It is also important that the woman knows what her outlook for future pregnancies are. In one series 36,8% of patients conceived after the ectopic pregnancy. Of

those, 64,3% carried it to term, and 23,7% had a second ectopic pregnancy! 12,5% of the pregnancies ended in an abortion.

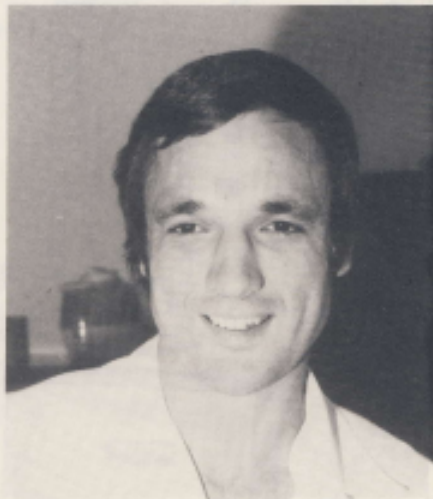
The author concludes that the chances of falling pregnant after an ectopic is not more than 50%, and only about 33% of these ectopics will bring the pregnancy to term! The chances of a repeat of ectopic is increased 30 - 50 fold, according to another author.

All these facts should be known to the woman, so that she will be aware of her chances and of the dangers involved when falling pregnant. It is true that microsurgery and repair of the damaged tube improves one's chances of falling pregnant again, but could also increase the risk of it being ectopic.

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Dr. Gys Roux

M.B.Ch.B. (Stellenbosch) 1976
Intern Ga-Rankua Hospital 1977
Military duty 1978/79
3 months at Charles Johnstone Memorial Hospital, Nqutu, Zululand.
1 year at Jane Furse Memorial Hospital, Lebowa.
Gys is at present a Vocational Trainee in Prof. Sam Fehrsen's Dept of Family Medicine at Ga-Rankua and Medunsa.

