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ECTOPIC PREGNANCY WITH SPECIAL REFERENCE
TO TUBAL PREGNANCY AND ITS DIAGNOSIS

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"There is no serious intra-abdominal condition which has the diagnosis written all over its face more clearly than has extra-uterine pregnancy, and at the same time has been more often over-looked."

Hunner

ECTOPIC PREGNANCY WITH SPECIAL REFERENCE TO
TUBAL PREGNANCY AND ITS DIAGNOSIS

Introduction and History

Ectopic pregnancy is pregnancy outside of the uterine cavity. "With few exceptions the developing embryo is in the beginning located in the Fallopian tube. Consequently the term 'tubal pregnancy' is applicable in most cases. (8).

Tubal pregnancy is the condition which arises when the fecundated ovum lodges and imbeds itself within the Fallopian tube. Nidation proceeding in the aberrant site for a variable period.

Extra-uterine pregnancy as such was apparently unknown to the ancients, there being no allusion to the subject in the works on Greek or Roman medicine. The first recorded case is that of one Albucasis, an Arabian physician living in Spain and flourishing about the middle of the eleventh century. (45). This was undoubtedly a case of secondary abdominal pregnancy, since no mention was made as to the placental site.

The first mentioned case of Cesarean section was that done by a swine spayer, Jacob Nufer on his own

wife. The literature does not state whether the pregnancy was intra or extra-uterine. (45)

The first authentic operation abdominal pregnancy was performed by Primerose in 1594, and the first record of tubal gestation with rupture was that of Riolan in 1604. (45) Lawson Tait (11,53) an English gynecologist, performed the first operation for ectopic pregnancy in the latter part of the 19th century. There has been an enormous amount of literature presented on this subject discussing its many phases since these reports were made.

Frequency:

There is much controversy as to the frequency of ectopic pregnancy. The average is about .003% of all pregnancies. This figure is compiled from statistics gathered in formulating this material.

The frequency of the occurrence of ectopic pregnancy is not positively known, (24) but they occur about as frequently as do twin pregnancies. (22). The frequency is variable as indicated by the works of these observers; Scheffey (44), 2.19%; Urdan (55), 1.5%; Wynne (11), 1.3%; Hunner (26), 92%; Schumann (11,45), 3%; Johnson (27), 152 out of 10,002 cases;

Bandl (11), one case in 20,000.

The age incidence may be anywhere within the stage of sex life, but the majority occur between the ages of 23 and 35 years. (31,44).

Etiology:

The etiology or actual causes of ectopic pregnancy are unknown but there are many speculations as to the contributing causes and many arguments are given for and against each. The thought, which stand out is that there is some interference with the passage of the ovum, fertilized or unfertilized, in its journey from the fimbriated extremity of the tube to the uterine cavity. This may be developmental, perhaps associated with hypoplasia and abnormalities; it may be due to peritubal adhesions, post operative or post inflammatory; to pressure on the tube; or to distortion of its lumen from without. (19)

The most frequently assigned factor is an obstructive change in the tubal lumen, the result of prior salpingitis of varying degree. Salpingitis acts in two ways; one by glueing the folds of mucosa together and thus forming blind pouches in which the ovum

may become caught, and the other by destroying the cilia that are used to propel the ovum through the tube. (19, 31, 55, 58)

There are two schools of thought as to what the primary causes may be, whether it is the ovum or the tube itself, The work of His, Bischoff, and Strassman would seem to indicate that the causes is in the ovum and occurs in the Fallopian tube. If their supposition is true, then every pregnancy is extra-uterine in its beginning, and ectopic implantation may be claimed to be due to the retarded advance of the fertilized ovum. (31) The other group believe it is due to obstruction of the Fallopian tube which may be (1) salpingitis, (2) pressure of tumors from within or without, (3) adhesions, strictures, kinks, or inflammatory masses in the pelvis. Any of these conditions may have been present for years previous to the ectopic pregnancy. This is the more prevalent thought and is supported by such investigators as Nos. 2, 8, 14, 27, 30, 32, 40, 55, 56, 57, and 58.

Factors related to the etiology of ectopic pregnancy as listed by Williams (58) are:

1. A histological examination of the implicated

Fallopian tube in cases of ectopic gestation is of more value in the explanation of the etiological factor or factors than simple clinical observation.

2. Clinical examination of the structures may reveal no evidence of an inflammatory reaction nor or anatomical malformations which, however, are possible to demonstrate by microscopic examination.

3. Microscopic examination may show no adhesions surrounding the Fallopian tubes, whereas microscopically the mucosa and muscularis of the same tubes may show the evidence of a pre-existing inflammatory reaction.

4. In all specimens evidences of an inflammatory reaction which had preceded the onset of the ectopic gestation were demonstrable. The observations of Opitz in a series of 23 cases coincides with those of Williams.

5. An infection of gonorrhoea more than any other kind of infection predisposes to the formation of false diverticula. A tuberculous process does not produce the ideal condition for the retention and especially for the development of an ovum in the tube.

6. The inflammatory changes were shown to be bilateral in all cases where both tubes were removed. Diverticula were present in the supposedly normal

tube as well as in the tube which lodged the ovum.

7. The statistics of cases of tubal pregnancy occurring so frequently in the opposite Fallopian tube a few months to a year after an operation for the removal of an ectopic pregnancy in the other side would warrant us in advising the patient that the retention of the apparently sound or slightly diseased tube may possibly lead to the development of another ectopic pregnancy.

8. Williams believes in saving the opposite tube if it is capable of functioning or if the occlusion or other pathological lesion can be corrected. He always warns the patient as to the possibility of another ectopic pregnancy and lets her decide as to the advisability of removing the other tube.

9. Williams found that with the development of false diverticula or mucous-lined channels such as were histologically demonstrable in his series of cases and those of Opitz, the chances for an ectopic pregnancy as against a normal uterine pregnancy are in the proportion of from 2 to 8 to 1.

10. In a routine examination of many thousands of specimens, Williams has noted the presence of true

anatomical diverticula in a few instances. The other possible factors ascribed as etiological factors are many times rarer than cases of ectopic pregnancy.

11. From an exhaustive study of the subject and from the analysis of a series of cases Williams believes that the presence of these false mucous-lined channels or diverticula produced by an inflammatory reaction in the tubes is the chief predisposing cause of tubal pregnancy in at least 95 to 98% of all cases.

"Any change which delays the ovum in its progress will favor tubal pregnancy." (2, 38).

Falk (14) from his own observations and an extensive study of the literature gives the incidence of follicular salpingitis as 90 to 95% of the cause of tubal pregnancy. Van Etten (56) found only 10.8% of his cases showed signs of previous or concurrent tubal inflammation. Ahfeld, Grove, and De Lee (12) state that the low incidence of ectopic gestation in rural communities is due to the rarity of gonorrhoea. Any pathological or abnormal condition of the female genitals may be a focus or cause of this accident. (6, 7, 53). The tube must not be entirely occluded or the spermatazoa cannot reach the ovium. (8)

Schumann (45) lists the following as the cause:

1. "Obstruction of the tubal lumen from without.
2. Obstruction of the tubal lumen from within.
3. Anamolies of the tubal lumen, assessorry tubes etc., into which the ovum falls and hence cannot be propelled further.
4. Decidual reaction in the tube.
5. The growth of a fertilized ovum outside the tube to such extent that when the ovum does finally enter the tube its size precludes its transit through the lumen. (External immigration of ovum.)"

Physiology and Pathology:

Decidua vera or partialis takes place in the uterus while in the tube only small isolated islands of decidua are found, and these may even be found in the opposite tube. Implantation in the tube takes place in the same way as in the uterus or by the eroding action of the trophoblast bringing choriomic villi into direct contact with tubal mucosa and musculature. The rapidity with which the cell divides or the ovum grows is not known and the ovum may become too large for the lumen of the tube. Another unknown fact is how soon the ovum reaches the trophoblastic stage in which it has

the power to digest its way in the wall of the tube. The amount of membrane granuloma adherent to the ovum which may make it very difficult for it to pass through the Fallopian tube is also unknown. As the ovum develops it bulges into the lumen of the tube, pushing part of the wall of the tube before it. When this part of the tube comes in contact with the opposite wall, this is stretched and bulges in the opposite direction, the whole lumen being greatly dilated. (31)

The hypertrophy of the muscle of the tube is usually insufficient to accommodate the ovum, and the muscle fibres at the site of the placenta are separated and destroyed by the erosive action of the villi; and thus a weak spot at this point is the result. Any traumatism, as straining at stool, coitus, a jar, or bimanual examination may cause a slight hemorrhage at this site, with a rupture, leaving the villi free in the peritoneum where they may reattach or the fetus may die.

If the nulliparous woman has been married fairly recently, the occurrence of ectopic pregnancy suggests the possibility of a developmental defect. If, however, the conception occurs relatively late in her married career and the history suggests an earlier genital in-

fection, then changes in the Fallopian tube due to inflammation must be considered. Also adhesions must be kept in mind for all patients that have had previous operations.

In the parous woman, the probability of an inflammatory cause is greater than in the nullipara, because of post-partal infections or intercurrent genital tract diseases. Many will give definite histories of abortions. The so-called lengthy "sterility," or "one child sterility," periods were previously thought to be indicative of long standing inflammatory changes resulting from infection, the lumen not being sufficiently closed to keep out the sperm but closed enough not to allow the descent of the ovum. This may occur by regeneration. Many recent analyses by different observers of numerous series of cases fails to substantiate this contrasted period of infectility. (55).

Tubal pregnancy usually terminates early, either by rupture of the tube wall, or a so-called tubal abortion, in which blood escapes through the tube lumen and the ovum is sometimes seen protruding from the end of the tube. (11)

The term rupture includes internal rupture or tubal abortion as well as rupture through the tubal

wall. However, a few cases have been known to go through to full term. (49)

The majority of the ruptured specimens contain normal embryos according to Mall, (32) Joachimsthal, Leopold. However, Martin, Veit, Orthmann, Ruge, and Olshansen (38) state that monsters are much more common in tubal pregnancies than in uterine pregnancies.

Von Winchel (38) found 14% of the feti that were normal in the beginning became monstrous, while in uterine pregnancies the per cent is below 1. He also makes the statement that one half of the feti in ectopic pregnancies are deformed in some way. The most frequent deformities are of the hands, feet, and head.

Diagnosis:

The words of Hunner (22, 26) are very appropriate for a start of this subject. He states, "there is no serious intra-abnormal condition which has the diagnosis written all over its face more clearly than has Extra-uterine pregnancy, and at the same time has been more often overlooked."

In 1907 Harris (21) wrote (according to Schumann (45), "When any woman after puberty and before menopause, who as menstruated regularly and painlessly, goes four, five, six eight, ten, fifteen, to eighteen days or over the time at which menstruation is due, sees blood from the vagina differing in quality, color quantity or continuance from her normal or usual menstrual flow, and has pains, generally severe, in one side of the pelvis or other, or possibly in the hypogastric region, extopic pregnancy may be presumed."

The diagnosis can be roughly divided into three divisions as follows:

1. Before rupture of the tube.
2. Beginning rupture or abortion.
3. After rupture of the tube.

Symptoms of early ectopic pregnancy may simulate any abdominal condition, and the best diagnosis is made by complete and careful history. (45) In order to help support this statement other features of diagnosis will be discussed.

Polak (11,39) says, "When any woman has an anomal^uous menstruation, she should be carefully examined to determine if she has an ectopic pregnancy."

Amenorrhea of 5 to 6 weeks followed by bleeding associated with pain is very common. (55) Scheffey (44) disagrees with the statement about amenorrhea, stating 80% of his cases were regular in periodicity.

Howard Taylor (45) gives 81% as having a disturbance in menstruation. Polak (39) gives 96%. Johnson (27) states that many patients take no notice of their menstrual period and this will account for the variation in statistics found by the various observers. However, a missed period is always a presumptive sign of pregnancy. (12,58) A patient often wants "to wait until next month and see if menstruation will take place then." (27) Some patients believe they are normally pregnant and wish to wait until next month before consulting a physician. (8) Postponed, prolonged, or otherwise abnormal menstruations are very suggestive. (11,27,55) Subjective symptoms and vaginal bleeding are rare before rupture. Small cramp like pains, slight discomfort and soreness are some of the complaints, but are not severe enough to cause the patient to consult a physician. (27)

The bleeding from the vagina is of venous origin and arises from the endometrium of the uterus and does not come from the involved Fallopian tube. It is a

manifestation of the regressive stage of involution. This regressive stage of involution is in the majority of cases prolonged because the termination of the pregnancy is rarely completed with the first attack of pain and as long as the pregnancy is not terminated and its activity influences the uterus, a condition of sub-involution exists and uterine bleeding usually persists. (45) Kline (30) states that vaginal bleeding in ectopic pregnancy probably depends upon changes other than the casting off of uterine decidua tissue.

Taylor and Schumann (45) says "The hemorrhage is usually due to some separation of decidua membrane from the interior of the uterus and is moreover a sign that the vitality of the pregnancy is endangered or that the vitality of the pregnancy is endangered or destroyed. So long as the pregnancy, although out of place, is growing and uninjured, there is, as a rule, no uterine bleeding. External hemorrhage, therefore, is not so much a sign of extra-uterine pregnancy as of some secondary disease or injury, which has affected the pregnancy; but as the great majority of cases suffer accidental changes during earlier months, it becomes a sign of great importance."

Concomitant signs of pregnancy in early weeks, both objective and subjective may be listed as: (12,58)

1. Amenorrhea as described above
2. Morning sickness or nausea and vomiting
3. Softening of the cervix
4. Enlargement of the uterus
5. Increased anteflexion of the uterus
6. Cyanosis of the vaginal mucosa
7. Pain and tingling in the breasts; may also find colostrum present
8. Increased pigmentation in various skin areas as of Cullen's sign or the bluish discoloration about the umbilicus
9. Frequency in urination
10. Pregnancy tests as the Aschheim-Zondek, Freidman test or the Abderhalden reaction

In general it may be said that these signs and symptoms are less marked in ectopic or tubal pregnancies than in ^{an}uterial pregnancies and in many instances only one or two of them may be found in any one case. Even if they are present they do not prove the pregnancy to be extra-uterine, but if they are all outstandingly present they at least suggest a normal implantation within the uterus. Every observer remarks

on these findings in his reports and the majority of them are absent.

The next most important diagnostic sign is pain, which may be either in the abdomen or pelvis and may be located anywhere therein or may radiate to different points as the shoulder, epigastrium, thorax or back. The most predominant type of abdominal pain is irregular, lancinating or colicky, and usually subject to remissions. (34) Other terms used to describe the pain are: sharp, bearing down, tearing like, intermittent labor-like, dull ache, severe cramp, extreme agony, gas-like, pressure sensation, feeling of weight in the rectum, bladder or back, and they may occur during sleep, walking, riding, intercourse, or after eating.

The etiology of the pain is: (45)

1. The separation of the embryonal envelopes from their abnormal decidua may begin, or the ovum may die. In either case the ovum is a foreign body and the tube will make an effort to expel it by means of contractions of a peristaltic nature of the muscular coat of the Fallopian tube. Colicky pain in the region of the diseased tube is the clinical manifestation

of this condition. This pain may be transmitted to the uterus and have it contracting after a time.

2. The procedure mentioned above usually causes bleeding of variable amounts into the peritoneal cavity, and because of the irritative effect of this blood on the peritoneum, will cause a generalized dull lower abdominal pain, which is a very important symptom.

3. This blood that extrudes from the tube accumulates in the most dependent part, which is the cul de sac of Douglas, and this gives rise to pain especially noted on defecation or coitus, or, if the blood happens to be collecting in the folds of the broad ligament, the increase in pressure will be noted as a dull throbbing pressure pain.

Pain is very variable in its occurrence according to different observers, as it is present in 96% of Farrar's (16) cases, 84% of Wynn's (31), and 58.4% of Hendry's (24) cases. However, Hendry (24) states that pain is the most important symptom, even though he does get a very low percentage of cases showing this symptom clinically. Faulkrod (17) states that unruptured tubal pregnancy is very painful, being much more so than a pus tube or other conditions found in the pelvis.

Recurring pain is one of the most reliable signs according to Behney. (4) Johnson (27) agrees, but qualifies his statement by stating that any pain or soreness on defecation if not present previously must be considered, especially if it is followed by relief for a few hours, several days, or even weeks, and then recurring should be a very significant indication of tubal pregnancy.

Lavell (31) states that abdominal pain of a recurring nature and vaginal bleeding accompanied by the symptom of fainting or its minor manifestation of sudden weakness, will establish a diagnosis in the majority of cases. Urdan (55) says pain and vaginal bleeding are the two most important and common symptoms, and when coupled with shoulder pain and fainting make the diagnosis almost absolute. Grier (19) lists his symptoms as, first, irregular bleeding, second, amenorrhea, and third, sudden pain. Heaney (22) supports Grier in his view as to the relative importance of these symptoms, while Culbertson (9) lists metrorrhagia as the symptom of most importance.

It can be appreciated from the above discussion that a very careful and complete history is most essential to bring out all of the salient points as to the

time and severity of the pain; its radiations or location, the history of the periods and any bleeding between them, any irregularity in the length of the period or change in the amount of flow, and any fainting or weakness that may have been sudden in onset and accompanying the other symptoms. Parry (Schumann 45) brings out another significant point in the history by stating, "Ectopic conception occurs most frequently in women showing previous inaptitude for conception." This statement is supported by such observers as Farrer (13) who found 13.6% of her patients showing a sterility of five or more years; Taylor (31, 45) found 8.6%; Rongy (40) found 20%; Boulware (5) found 20%; and Danforth (10) found 10%. One must also watch for and ask about one child sterilities as they are widely mentioned throughout the literature and represent about 30% of the cases reported. As noted in the etiology, it is important to inquire as to the previous pelvic diseases, and any pelvis or abdominal operative procedures as they are found to be present in from 10 to 20% of the cases. (13,27,45)

Other signs and symptoms which are very important and in many cases indispensable, but not as frequently

mentioned or discussed are as follows:

Syncope was found in 26.7% of Scheffey's (44) cases, 53% of Grier's (19) cases, and is mentioned by several other observers who gave no statistical data in their reports.

Grier (19) found nausea and vomiting in 43% of his cases. These were mentioned by several other observers but no statistical data was given, probably because many normal uterine pregnancies and many abdominal conditions will also give rise to nausea and vomiting in the patient.

Important signs found on physical examination are usually not found until late or until after rupture of the tube, or abortion, as before this time the physical signs are generally negative as far as an ectopic pregnancy is concerned (45). However, just preceding the rupture, a mass may be palpable in one of the tubes which is very tender. The tenderness of this mass is out of all proportion to its size and density, and traction on the cervix or active manipulation of the uterus generally aggravates the pain and tenderness. (6)

Farrar (16) found a pelvis mass or definite enlargement of the adnexa in 86% of her series of cases;

Frank (18) and Oastler (36) found a mass in the adnexa of 86% of their cases; Grier (19) found a mass or fullness present in the adnexa of 51.2% of his cases; Johnson (27) says the mass is more often missed than found because of its small size at this stage of development.

Enlargement of the uterus itself is of little value since the diagnosis should be made early, and in the first few weeks the uterus enlarges practically the same in intra and extra uterine gestation, but as the ectopic pregnancy progresses the uterus does not enlarge as rapidly and rarely reaches a size larger than that corresponding to a normal uterine pregnancy of three months, even though the ectopic pregnancy reaches full term (52). The uterus is physiologically enlarged after one or more pregnancies and thus is of little value in an early diagnosis. (12) The majority of ectopic or tubal pregnancies are terminated by rupture or abortion by the sixth or eighth week. (31, 45, 48)

Hegar's sign is not elicited in tubal gestation and is important only in differential diagnosis, in that when it is present along with other signs, it shows almost conclusive evidence of an intra-uterine

gestation. (27, 31, 45)

Grier (19) found rigidity of the abdomen in 58% of his cases; Scheffey (44) found 41.4%, and Schumann (45) states these cases of ectopic pregnancy are usually rigid to some degree, the rigidity naturally effecting more definitely the rectus muscle on the side of the effected tube. Other observers do not give any definite data about abdominal rigidity. Bleeding in the abdominal cavity or any inflammation or irritation to the peritoneum will cause a rigidity of the abdominal muscles. (29)

Cullen's sign, which is a dark discoloration of and about the umbilicus, may be noted in some cases, but was mentioned by only two observers. Bubis (6) found it in 4% of his cases, and Scheffey (44) did not find it in a single case; therefore, this is probably of little or no importance in diagnosis.

Farrar (16) found pain and colostrum in the breasts of 13% of her cases, Taylor (Schumann 45) found enlarged and tender breasts in 44% of his cases, however, as these conditions are found in normal intra-uterine pregnancy, they are of little or no importance in the diagnosis of ectopic gestation as an indication of pregnancy. (59)

Increases in pigmentation and the appearance of lines nigra along with darkened mammary areola are very frequently absent in intra-uterine pregnancy, and therefore, are of little or no value in the determination of extra-uterine pregnancy. This sign is of value when present, as it is an indication of pregnancy and will differentiate pregnancy from some other abdominal or pelvic condition. (12)

Jaundice is of little or no importance in early diagnosis, (6) and was mentioned by only two or three observers. Mc Googan states that when jaundice is found it is usually from an old hemorrhage which is being absorbed, the constituents of the disintegrating blood being carried in the peripheral blood stream producing this transitory jaundice.

Schumann (45) and De Lee (12) states that in ectopic pregnancy shifting dullness in the flanks is never found. Bubis (6) found shifting dullness in 14.7% of his cases, but they all had marked intra-abdominal hemorrhage. Mc Googan states shifting dullness should be found in most cases of ruptured tubal pregnancy and will be more marked in those patients having excessive intra-abdominal hemorrhages.

The temperature is rarely above 101° Fahrenheit

(31, 38, 55) in cases of ectopic pregnancy, and the pulse rate is proportionately increased, the average being from 90 to 110 unless actual bleeding is present. The relatively low temperature and fast pulse are expressions of the mild peritoneal reaction to the presence of free blood and a consequent mild pelvic peritonitis^s thus produced. Both of these findings are true only in cases that are not complicated by infections or concomitant diseases as the characteristics of the other disease or infection may be that of a high temperature and fast pulse.

The blood pressure is also very rarely changed except in cases where the hemorrhage has been severe or there is an intercurrent infection. (31). Therefore, this procedure is of little diagnostic aid in ectopic pregnancy (36, 45). Several observers use the blood pressure findings in determining the correct time to terminate ectopic pregnancy by surgery.

Urinary frequency is also encountered in many cases of ectopic pregnancy, because of the irritation caused by the abnormally placed ovum. (5) Farrar (16) found urinary retention in 2% of her cases. It is probably possible for both of these observers to be correct in that the position of the ovum in the Fallopian

tube and the position of the Fallopian tube in the pelvis could in some cases cause urinary frequency by irritating the bladder or urinary retention by direct pressure on the trigone of the bladder.

It should also be possible to have a retention of feces or an increased desire to defecate for the same reason as those stated under urinary frequency and retention. Neither of these are of definite value in the diagnosis of ectopic pregnancy because any tumor mass in the pelvis could give the same findings (27).

There may be shock due to the loss of blood and in this case there will be a change in the blood picture as will be outlined later.

Laboratory findings; Grier (19) found the study of the white blood cell count to be the most valuable laboratory aid, Farar (15) found in the study of 150 cases that the white blood count increased rapidly with the escape of blood into the peritoneal cavity and to drop quickly to or near normal as the blood is absorbed or walled in. This fluctuating of the leucocyte count together with the moderate elevation of temperature differentiated ectopic gestation in the 150 cases from

purulent salpingitis with its more uniformly high leucocyte count and fluctuating temperature. She believes that the rapidly increasing leucocyte count in a hemorrhaging tubal pregnancy is of better diagnostic aid of the condition than the fall in number of red blood cells or hemoglobin. Peterson (38) agrees with Farrar (15) about the leucocyte count and states that a high leucocyte counts means hemorrhage. Danforth (10) also agrees with Farrar (15) on the leucocyte count and states it is chiefly due to the extravasation of blood rather than to tissue damage.

Scheffey (44) found 22% of his patients had a leucocyte count of from 3000 to 8000; 39% showed 8000 to 11,000 and 18.3% showed 11,000 to 15,000, the others being above or below these figures.

Schumann (45) says it is common to have a leucocytosis of a low degree because of the blood which has been extravasated into the peritoneal cavity, and is usually between 10,000 and 12,000. If the hemorrhage is large the leucocyte count rises within a few hours after the bleeding begins, while the red cells do not appreciably diminish in number and the hemoglobin is unaffected. In one of two days the blood picture

is back to normal. With a sudden profuse hemorrhage the white count may go to 20,000 or 25,000 or more.

Johnson (27) agrees with Farrar (15) that the white count is usually low and with Schumann (45) that the red blood cell count and hemoglobin remain the same. Behney (4) states there is no change in the leucocyte count in ectopic gestation. Sovak (49) agrees with Behney (4). Hendry (24) states that a white count of 15,000 or over signifies intra-peritoneal rupture of the tube. There is no change in eosinophilia.

Schumann (45) states that after a few days the red blood cell count and hemoglobin both show a decrease. Scheffey (44) found a red count of from $2\frac{1}{2}$ to 4 million in 53.7% of his cases, above 4 million in 22%, and above or below these figures in the remainder. He found the hemoglobin to be between 55 and 85% in 60% of his cases, below 55% in 32.7% the remainder being above or below these figures.

These blood counts are really of very little value as far as statistical data is concerned for use in a diagnostic survey, because there is no mention of the different methods used in making the blood counts

and hemoglobin determinations, and the observers do not state whether or not there was hemorrhage present, nor the amount of blood found in the peritoneal cavity. Therefore, we must use conjecture in evaluating their results in using them to our own advantage in the future diagnosis of cases.

Mc Glinn (34) states the urobilinogen test was effective in determining the presence of free blood in a serous cavity in 100% of his cases. The blood may be in the pleural cavity, the pericardial cavity or in the head, as well as being in the peritoneal cavity.

Symptoms differ depending on the location of the hemorrhage. Therefore, this test may be of value in the diagnosis, but not conclusive, as the blood may be from a ruptured Graafian follicle or some cause other than a ruptured ectopic pregnancy. The treatment in any case is surgery to stop the hemorrhage if possible.

Scheffey (44) and Lavill (31) state the sedimentation time is of no value in differentiating ectopic pregnancy from other abdominal or pelvic conditions, while Urdan (55) believes the sedimentation time of 30 minutes or more favors ectopic pregnancy rather than inflammatory adnexal disease. Other observers

mention the sedimentation time but do not believe it to be as important in the diagnosis of ectopic pregnancy as a careful history, physical examination, etc.

The different hormonal pregnancy tests are of value in differential diagnosis but they will not differentiate between intra and extra-uterine pregnancy. (59)

The X-ray may be used to differentiate pregnancy from other abdominal and pelvic conditions, by finding the fetal skeleton, but this in many instances will not determine whether or not it is intra or extra-uterine. Greenhill (De Lee 12) has found the report of seven cases in which iodized oil was injected into the uterine cavity for diagnosis. He states that if the child is alive this may be dangerous, but if the child is found to be dead, the procedure is safe, simple, and presents absolute evidence of ectopic pregnancy.

Hope (25) tells of the use of the peritoneoscope by Jacobus in 1910 to visualize the contents of the abdominal cavity. The peritoneoscope is a small instrument containing mirrors and an electric bulb which is inserted into the abdominal cavity somewhere between

the umbilicus and symphysis. After inserting the peritoneoscope, air is injected to raise the abdominal wall from the viscera and thus allow visualization. He states it is a safe procedure, not likely to cause abortion, and is very helpful in a differential diagnosis.

Hall (20) says, "The main reason why ectopic pregnancies are so often overlooked is because many of the men who see these cases first, the family physician, have an idea that it is a very rare condition. Hence, when they are confronted with an acute pelvic condition they at once think of the more common lesions, such as an intestinal colic, appendicitis, threatened abortion, or a salpingitis, and make their diagnosis accordingly."

Treatment:

About 50 years ago Parry (Bubis 6) stated the theory that the accident of ectopic gestation was almost fatal and that there were no reliable means to combat its dangers.

There has been much controversy as to the treatment of choice in ectopic pregnancy. Observers believe in treatments ranging from that of expectant therapy

to that of immediate surgery.

Diagnosis is the most important point to consider and after it is made the treatment can be determined from the diagnostic findings. As stated by Babis (6) "It is fortunate that the treatment of all conditions with which ectopic pregnancy might be confused is an operation, the only exception would be an acute salpingitis."

Vander Vier (53) in 1889 urged that operation was the treatment of choice and was much better than the then prevalent treatment of killing the child with an electric current and operating a month or more after death of the child. He also suggested removal of the placental tissue, basing his opinion on the success of his own work and the success of Tait. (53)

Crossen (8) says treatment may be roughly divided into:

1. Treatment before rupture
2. Treatment after rupture with free intra-peritoneal hemorrhage
3. Treatment after rupture with repeated slight hemorrhage

4. Treatment of pelvic hematocele

5. Treatment of pelvic hematoma

Marvel (33) says to operate at once on all cases of unruptured ectopic pregnancy, and if ruptured do not operate as the hemorrhage will be self limiting. It is the shock and not the hemorrhage which causes the trouble. It is his opinion that these procedures will conserve life. In these cases prompt operation relieves the period of invalidism. "Significance of delayed operation is exhibited in (1) the greater loss of blood, (2) possible loss of life occasioned by hemorrhage, (3) increased shock depression, (4) recurrent hemorrhage producing worse condition than at first, (5) operation fraught with greater difficulties, (6) more extensive pathology, (7) increased discomforts measured by time and intensity, (8) crippled organs with deficient functions, and (9) protracted invalidism."

Urdan (55) says that once the diagnosis is made operation should be immediate except in those cases where hemorrhage has not been profuse and the patient's condition could be benefited by appropriate preoperative treatment. Transfusion, if necessary should be

and in border-line cases, should be performed to shorten the convalescence, and aid in restoring the patient more rapidly to her normal status.

Beck (3) after a careful search of the literature decided that treatment should always be surgical, and that the proper time depends on the patient's condition and the surgeon's judgment. Hunner (26) says, "If the patient can be operated on with good surroundings and is in condition that promises survival from operation, I prefer early operation, rather than run the risk of repeated hemorrhage." Dugann (13) Frank (18), Harris (21), Hendry (22), Oastler (36), and Rongy (46), believe in immediate operation in all cases, after a diagnosis has been made.

Stillwagen (50) states:

1. "Ectopic pregnancy at any stage is purely a surgical condition.
2. The time of operation, in terminating ectopic pregnancy should be determined entirely by the patient's fitness to withstand surgical interference.
3. The time of operation should be decided by a competent surgeon, each individual case upon its merits.
4. Operation should be done at the earliest period of election.

5. To justify any given course of procedure, a low mortality rate must be shown."

Johnson (27) makes the statement that the only treatment is surgery, and that a patient seen before rupture occurs should have an ordinary laparotomy with removal of the affected tube. The patient being in very good condition, the appendix or any accompanying pathology may be excised at the same time.

After rupture of the tube, the patient being in severe shock, a large hypodermic injection of morphine should be given immediately. Before starting the operation an intravenous solution should be given. The operation should be rapid, the bleeding tube removed and nothing else done in the abdomen.

An autotransfusion may be given at the same time if no infection is found to be present. On the patient's entrance to the hospital donors should be typed for blood transfusion to be given simultaneously or immediately following the operation. The donors should be kept available for possible transfusions some hours later, as frequently a reaction occurs a few hours postoperatively, and a second transfusion may overcome this crisis.

From Johnson's (27) own experience and his observations of other surgeons, he states that spinal anesthesia may be used to advantage in these operations, as it prevents struggling of the patient. This prevents increased bleeding, which is a very important factor in excessive hemorrhage. It has been used in many instances where the patient was in marked shock and with an almost absent blood pressure, with no ill effects.

Cathey (7) says that as soon as an abdominal pregnancy is recognized and the child is living, the patient should be placed in the hospital, if it is thought that the fetus has reached the stage of viability. If possible, wait until the end of the thirty eighth week before delivery. Should the patient develop any symptoms of spurious labor, she should be delivered immediately by opening the abdomen, removing the child, and making every effort to control the blood supply of the placenta and removing it. If feasible, the uterus may be removed with the placenta. Should this be impossible, the edge of the membranes may be stitched to the edges of the abdominal incision, then packed with gauze, the placenta allowed to separate and dis-

charge itself gradually. This method is tedious and trying for the patient, but safer than profuse hemorrhage in an effort to separate the placentas.

When the fetus is dead judgment must be used in determining the type of treatment. In some instances watchful waiting is preferable, while in others surgery is the procedure of choice.

Polak (39) says to operate early in unruptured cases of ectopic pregnancy, and in cases with rupture place the patient in the Trendelenburg position, watch the pulse and blood pressure, give from one fourth to three eighths of a grain of morphine sulphate; give no atropine or salines intravenously, and no stimulation. When reaction occurs or the pulse has slowed and the blood pressure has gone up, operate removing the involved tube and as much placental tissue as possible. Leave one quart of normal saline solution in the peritoneal cavity and close the abdomen in layers. Polak (39) does not believe in giving infusions because the patient may become dyspnoeic and terminate fatally from acute pulmonary edema. He does not believe in drainage or curettage in treating postoperative hemorrhages.

Bubis (6) places his patients on peritonitis treat-

ment for twenty-four to forty-eight hours. He places the patient in Fowler's position, and gives saline infusions of 1,500 to 3,000 cubic centimeters per day. In some instances he gives 500 cubic centimeters of a 5 to 10% glucose solution in normal saline intravenously, placing hot stupes on the abdomen and giving morphine sulphate to keep the patient comfortable and hold the respirations below twenty per minute. After this preliminary treatment and depending on the reaction of the patient, the time of operation is determined.

Mortality:

The mortality of ectopic pregnancy has ranged from nearly 100%, according to Parry (Bubis (6)), to as low as 2.24% in a series of 1421 cases collected from six teaching clinics. (11) Bubis (6) states the death rate at the time of Tate was 85% or more, and at present is 5%. Davis (11) gives 70% as the early figure, with the present mortality below 5%. Schauta (Duggan 13) collected data from the literature finding 123 operative cases with a mortality of 5.7%. One hundred and twenty one palliatively treated cases with a mortality of 86.89%. Hawks (Duggan 13) reviewed 184 cases of ruptured ectopic pregnancy in three New York

hospitals: one hundred and thirteen of these were operated with a mortality of 8.8%; the seventy-one cases palliatively treated, and not operated until later, showed a mortality of 17%.

Frommott (De Lee 12) gives several reviews on the works of authors reporting on the mortality of patients who were transfused as well as those who were not. In a report of authors on 4354 cases of ectopic pregnancy, the mortality was 5.05%. These authors do not state whether or not transfusions were given. Twenty one authors reporting on 3650 cases, in which auto-transfusion was used, found a mortality of 3.7%. Twelve authors reporting on 1194 cases in which no transfusions were given found a mortality of 2.35%. Eleven authors reporting on 1731 cases in which transfusion was given, found a mortality of 4.8%.

Conclusion and Summary:

Ectopic pregnancy was apparently unknown to the ancients, probably due to their inability to diagnose the condition. Even today the diagnosis is more often missed than found, although it occurs as often as do twin pregnancies which is about .003% of all pregnancies. It may occur any where within the stage of sex life.

The actual causes of ectopic pregnancy are unknown but from a study of the literature, I believe the principle causes to be salpingitis, the pressure of tumors from within or without, adhesions, strictures, kinks, inflammatory masses in the pelvis, or possibly from the excessive growth of the ovum before its entrance into the Fallopian tube.

The most important factor to be considered in a diagnosis of ectopic pregnancy is a very careful and detailed history. The physician should inquire mainly as to any irregularities or changes in the amount or character of the menstrual flow, and associated pain.

The second point of importance in diagnosis is pain in the abdomen or pelvis, of an irregular, lancinating or colicky nature and is usually subject to remissions.

Menstrual changes associated with pain and syncope or its minor manifestation of sudden weakness, will, in the majority of instances, allow the physician to make a diagnosis of ectopic pregnancy. These findings however, should be supported by physical and laboratory examination. The most prevalent physical findings are a palpable tender mass in the pelvis; shifting dullness

in the flank; a slight rise in temperature rarely above 101° Fahrenheit; a pulse rate rarely above 90 to 110; and a blood pressure which is normal except in cases of profuse hemorrhage.

The most important point in the laboratory diagnosis is the slight increase in the white blood cell count. This is in contra-distinction to the high white cell count found in other abdominal and pelvic conditions. The sedimentation time is usually above thirty minutes in ectopic pregnancy. The urobilinogen test is of value in determining the presence of a hemorrhage, and thus like the hormone tests, is of value in making a differential diagnosis. The use of iodized oil in making X-ray examinations is of great value in diagnosis, as one can distinguish extra-uterine pregnancy from intra-uterine pregnancy and from other abdominal or pelvic conditions.

A more recent aid in diagnosis is the use of the peritoneoscope, which should be of definite value in cases in which the differential diagnosis cannot be definitely determined.

The treatment in all cases is surgical, but the physician must use his judgment in determining the time to operate by basing his decisions on the history and the general physical condition of the patient,

points found on physical examination, and the laboratory data.

To justify any given course of procedure, a low mortality rate must be shown, and in many instances where surgery has been used, the mortality rate has been as low as 2.35% but the average is around 5%.

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