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Etiology and treatment of recurrent abortion

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THE ETIOLOGY AND TREATMENT
OF
RECURRENT ABORTION

by

John T. Snyder

SENIOR THESIS

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OUTLINE

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HISTORY

Abortion, from the Latin verb aboriri signifying something that has been detached from its site, is now considered to be defined as detachment or expulsion of the previable products of conception although considered by the laity to be the willful attempt to terminate pregnancy before the fetus is viable.

Historically speaking, abortion has been known as far back as human records can be traced. Abortifacients were used by the ancients, both in religious practices and to limit the number of offsprings. More than 4,600 years ago Tang Shen-wei made reference to mercury causing abortion.

The Jewish race, from the earliest days, stressed the importance of increasing its numbers, and so frowned on any attempts to produce abortion and severely punished anyone participating in the act.

Hippocrates mentions softening of the breasts as a sign of threatened abortion. For treatment, he ordered parsley as it produced gas which was thought to be good for pregnancy. Plato and Aristotle, in their writings, gave the idea that if a woman, after bearing the prescribed number of children, discovered herself

pregnant before she noticed fetal movement, could have the child driven from her. It was not considered a criminal act to effect an abortion before life was felt or interrupt pregnancies that occurred after a woman became forty years of age.

As to the causes of spontaneous abortion, Hippocrates cited many forms of external violence which might produce abortion. He also suggested that fevers, vomiting, abdominal pains, too little or too much nourishment, drastic purgatives and too large an opening in the uterus might be responsible for premature expulsion of the ovum. He suggested that habitual abortion was due to insufficient development of the uterus. Some of these views are accepted today.

With the advent of Christianity, the views previously set forth by the Jews were upheld, and their teachings held that the fetus in the womb acquired animation and became an immortal being and hence to destroy it was a murderous act. During the Renaissance the morality of the church was very loose, but even then poor people were punished by death for the crime, usually by crucifixion. In contrast the wealthy could, by paying a large sum of money, free themselves of the crime.

There is to a certain degree, racial predisposition to spontaneous abortion. In some countries,

it seems that no amount of physical exertion is able to bring about an interruption of pregnancy. In China, for example, women row for long periods of time without deliterious effect, as is the case in Persia where women ride long distances on horseback. On the other hand, in New Zealand and parts of Australia, where it is the custom to give abdominal massage during the prenatal period, spontaneous abortion is quite common. Also among the wealthy women of China who engaged in foot-binding and led a more or less sedentary life, abortion was quite common. In countries where malaria and tropical fevers are prevalent, the abortion rate is quite high.

SCOPE

An estimate of the prevalence and number of abortions in any country is most difficult, and hence all figures are highly speculative. In Germany the per annum figure is estimated to be between 1,000,000 and 3,000,000. Taussig (38), estimates, from the averages in large series of cases, the number of abortions a year in the United States to be about 681,000. Of these 278,000 are rural and 403,200 urban. The abortion rate is estimated to be about the ratio of one miscarriage to each five confinements in the country and about one to two and five-tenths cases among city dwellers. Maternal deaths in this country have been estimated by Taussig to be about 4,000 or from 2-4% of cases. Reports vary as to the type of institution reporting and in many instances deaths actually due to abortion are written on the death certificate as pneumonia, septicemia, or some terminal condition rather than the real cause. Taking these facts into account, Taussig feels that a more accurate estimate of registered and concealed abortion deaths would be close to 8,000 per annum in the United States alone.

CLASSIFICATION OF ETIOLOGY OF ABORTION

The causes of abortion may be divided at first into two major groups; namely, those causes attributed to the mother and those brought about by the death or malformation of the fetus or its attachments.

According to Meaker (30), every abortion includes three events:

1. Death of the ovum
2. Separation of the ovum from its attachments
3. Expulsive uterine contractions

Any one of the above may be the leading event in a given case. For example, he cites the case of the fetus being killed by Roentgen rays, dislodgement with a curette or inducing uterine contractions with a bougie.

Death of the Ovum. In certain cases the embryo dies days or even weeks before there are any expulsive efforts or signs, such as bleeding or cramp-like pains. In other cases an already moribund embryo dies after a minimum of bleeding and cramps, but before these symptoms are established. In the first case, the trouble is probably hereditary and is present from the

moment of conception. Like anatomic defects, they simply lead to a state of insufficient vitality. Mall (27), Streeter, Huntington (20), and others have found that upward of 50% of abortion embryos are pathological. Huntington also brings out the analogy that it is impossible to tell by looking at hen's eggs, which ones will hatch and that in any given number of eggs, only a certain percentage will produce living chicks.

Mall (27) feels that the deformities present are due, in the most part, to faulty nidation and subsequent malnutrition of the fetus. On the other hand, Levine feels that it is on a hereditary basis. His work on the Rh factor can be summed up as follows: If an Rh negative woman marries an Rh positive man, the offspring may inherit Rh positive blood in a certain number of cases. The factor is thought to be carried by the red cell which is in a constant state of break-down and regeneration. This may be the explanation of how the fetal factor gets into the maternal circulation. At any rate, the mother builds up anti-agglutinins which pass into the fetal circulation and hemolizes the erythrocytes of the fetus.

The most commonly accepted cause of fetal weakness is the relative infertility of the sperm and/or ovum, probably chiefly due to debilitating conditions, such as endocrine disturbances, chronic intoxications and generally poor hygiene.

Of the second case, that is of a moribund embryo which dies after slight bleeding and cramps, the fetus most likely dies from poor nourishment, either due to faulty implantation or the result of acute or chronic disease of the mother. However, it is surprising as to how sick a woman can be without losing her pregnancy. Chemical poisoning and toxemias of focal infection especially predispose to abortion through death of the fetus, the same being true of diabetes, thyroid disorders, malnutrition and acute febrile diseases. In some of these cases the leading event is uterine contraction, but in far the majority, the fetus dies first. Syphilis is relatively harmless in the first half of pregnancy while it is quite disastrous in the last semester.

In the literature of the past few years, we find reports of from 50% to 80% success in the treatment of both threatened and habitual abortion. This should be positive proof that all embryos that abort are not defective.

Séparation of the Ovum. According to Meaker, the commonest event in spontaneous abortion is ovular separation, and that bleeding was noted before cramps in over 80% of his series of cases. Implantation is dependent upon two factors, the first being a proper endocrine balance for stimulation and a healthy endometrium capable of responding. The actual mechanism of premature separation is not clearly understood. It is known, however, that the corpus luteum degenerates and the placenta takes over its function between the seventieth and nintieth days and it is during this period that abortion from these causes is most likely to occur.

It might be well to mention here the inability of the endometrium to respond to endocrine stimulation, the so-called hypoplastic endometrium. This condition is usually accompanied by under-development of the rest of the sex organs, hence pregnancies are quite rare. Finally, according to Mall, defective trophoblastic cells leading to faulty implantation may occur. This, he feels, may be either due to poor nutrition leading to degeneration or is on an inherent basis.

Contractions of the Uterus. In a fewer number of cases this is the leading symptom and is usually noted as low back pain of cramp-like character and a sense of

weight in the pelvis by the patient which, if not checked, may develop into rhythmic contractions and lead to evacuation of the uterus.

The causes of uterine irritability will be considered later but here it may be said that they may be initiated by external violence such as falls, blows on the abdomen, by increased irritability and mobility of the lower bowel as would be found in the diarrheas and dysenteries, by mechanical hindrances to proper accommodation such as retroversion, fibromyomata, adhesions and scars from previous operations upon the uterus and lastly, by acute febrile infections of the mother. Coitus is also considered here but it is well tolerated under normal conditions. It is, however, contra-indicated in the presence of pathology or a history of previous abortions.

A complete list of the maternal causes of abortion would be too lengthy for practical purposes but Edwards (5) lists them under the following headings: First, as to general causes, he considers acute infections such as typhoid, pneumonia, measles, scarlet fever, Malta fever, diphtheria and meningitis, nephritis, diabetes and asthenia brought on by Addison's disease, a marked hypothyroidism or hyperthyroidism or pernicious anemia.

As to local causes, Edwards considers fibroids, intra-mural or submucous and rarely subserous uterine polyps, ovarian cysts, mechanical factors such as retroflexion of the gravid uterus or other malpositions, lacerations of the cervix, juvenile uteri and congenital malformations such as septate uterus and didelphus uterus. It might be well to add diet and avitaminosis to the general list.

Bouvocque (38) stated that after the explosion of a powder mill he was called to see ninety-two patients, either aborting or threatening due to psychic trauma.

Kent (23) states that in the Lillooet River valley, near Vancouver, the diminished amount of iodine in the soil was responsible for abortion and stillbirths in the livestock. Surveying the Vancouver hospital records, he found that in 19,730 deliveries, there were 330 stillbirths in which no definite cause could be found. Giving small oral doses of iodine in 741 pregnancies resulted in no idiopathic abortions while a control group receiving no medication showed fifty abortions in 4,073 pregnancies.

PATHOLOGY

The pathology of uncomplicated abortion has been studied most completely by several Russian investigators, both spontaneous and induced cases having been considered.

Jakowleff, quoted by Taussig (38), studied the uterine mucosa of forty post-abortive cases ranging from the third to the twenty-first day. He showed that after termination by curettement, regeneration was comparatively slow.

Epithelization starts on the eighth or ninth day and is not completed until about the twentieth day and decidual tissue remains up to sixteen days. Greenhill (12) cites a case in which placental tissue was recognizable after sixteen years retention. Regeneration of the uterine glands usually starts on about the fourth or fifth day.

Complicated abortions present a more variable picture and often if it occurs early in the first trimester, is merely considered as a heavy menstrual flow. The products of conception are rarely found except in the case of blighted ova where the products come out fairly intact.

In the second trimester, the picture is somewhat varied. Macerated soft feti are quite common which is essentially a non-bacterial softening and often shows multiple blisters to blebs over the body which may be infiltrated with blood. The internal viscera has lost most of its substance and contour.

Quite the opposite picture may be seen in which the fetus undergoes fluid loss or mummification. Finally, the fetus may become infiltrated with calcium salts over a period of many years and is known as a lithopedion. This condition is very rare.

The chorionic villi may be small and in insufficient numbers as to adequately support the fetus. Infarcts are quite numerous and probably produce a diminished nourishment to the ovum. Their pathology is not clearly understood. Some investigators, (Curtis 10), feel that implantation can occur over a chronically infected endometrium which later involves the secundines to produce a deciduitis, but the part it plays in abortion is still under discussion. Syphilitic invasion of the placenta is usually not in evidence before the twenty-fourth week and is characterized by club-shaped chorionic villi and end-arteritis.

PREVENTION AND TREATMENT

Before considering treatment of threatened or habitual abortion, it is well to consider the prevention of the underlying causes that are understood to be contributory. At this time I feel that, although the term habitual abortion is still in common usage, it is not adequate nomenclature. It is more often defined as a condition whereby a woman aborts two or more times without apparent reason, which could mean any one of several common causes. Repeated or recurrent abortion seems a little less subtle means of describing the condition.

Any patient who presents a history of repeated abortion deserves a thorough history and physical examination. The history should bring out any family predisposition to abortion, past diseases, accidents and operations which have bearing on the condition. It is also well to know her habits of eating and the use of narcotics, sedatives, stimulants and tobacco. Her general condition should be noted with special emphasis on signs of endocrine upsets such as thyroid upsets, obesity or dwarfism. A basal metabolic rate may or may not be needed. The chest, heart and abdomen should be examined and special emphasis placed on the pelvic

examinations noting the external genitalia, vagina, cervix, pelvic floor, uterus and adnexia for signs of pathology from infection or displacement. Any evidence of focal infection of the teeth, paranasal sinuses, tonsils or abdominal viscera should be ruled out or corrected if possible and present. Any relaxation of the pelvic floor or cervical tears should be repaired and retroversion corrected by a Smith-Hodge pessary or suspension of the round ligaments. Evidence of hyperplasia of the endometrium should be treated by dilatation and curettage. Cervical stenosis must be considered.

Blood and urine analysis should be routine and any anemia corrected by antianemic therapy. Diabetes and Bright's disease can be ruled out by urinalysis.

Usually these parents are very cooperative and desirous of bearing children so an examination of the husband may be helpful. Greenhill (12) states that in sterility, it is traceable to the male partner in 30%, and the feasibility of defective germ plasm as mentioned previously under causes of abortion. Emphasis should be placed on finding and treating evidences of malnutrition, chronic intoxications, and

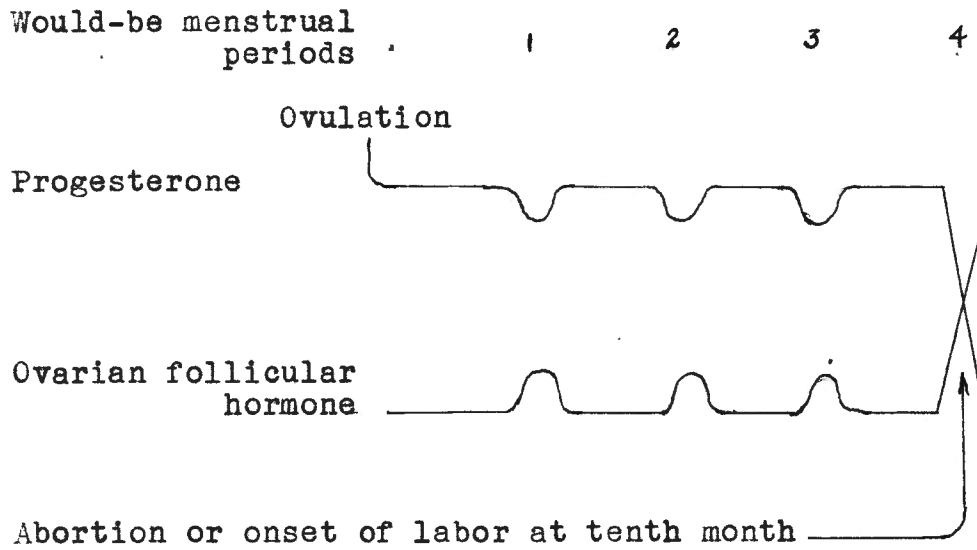
congenital malformations. Contributory history may be that of an old gonorrhoeal infection or orchitis following epidemic parotitis, the latter being responsible for 90% of sterility in males. Semen examination may be helpful, both before and after it has come in contact with the vaginal mucosa as incompatibility is now considered as a factor.

Assuming that the above mentioned conditions have been corrected or ruled out, we can start laying the ground work for the next pregnancy. It is best that from three to six months have elapsed since the previous abortion or serious illness or operation has ensued. Both partners should be receiving adequate rest, nutrition and exercise and there should be no marital discord or emotional factors to complicate the conception or pregnancy. Taussig (38), and other workers feel that preconceptive endocrine therapy may be helpful and suggest for hypothyroidism that the patient be given 1-3 grains desiccated thyroid for about one month before the expected conception. No results of this type of treatment were encountered in the literature but it seems quite logical and is being used quite widely by Hamblin (18), who feels that progesterone is not the answer to the solution and tends to upset the effects of the thyroid medication.

By far, the most prevalent type of case seen by either practitioner or specialist is that of a patient in her second, third or fourth month of pregnancy complaining of bleeding and/or cramps, and a sense of weight in the pelvis or a patient who has a history similar to that above, and having experienced one or more abortions and being desirous of bearing children. Before discussing active treatment, I feel that it would be well to review the hormonal factors responsible for changes which take place during the menstrual cycle and pregnancy.

Immediately following menstruation, the endometrium has been disquamated until only the basal layer remains on the uterine musculature. The glands are straight, widely spaced and lined with a single layer of low columnar or cuboidal cells with a central nuclei. By this time, the premordial follicle has begun to develop in the ovary. During this period of its development, estrin is elaborated, which is responsible for the hyperplasia of the endometrium, including marked increase in thickness, increase of vascularity and hypertrophy and hyperplasia of the uterine glands. Somewhere near mid-interval the follicle ruptures, the ovum is extruded and the ruptured follicle is converted into corpus luteum. The elaboration of

HORMONAL CONTROL DURING EARLY PREGNANCY



From: Witherspoon (42)

estrin is continued by this body but the characteristic hormone of the corpus luteum is progesterone. Its influence on the endometrium is shown by the marked secretory appearance of the epithelium, that is, columnar cells with basal nuclei, vacuolization of the cells, distension of the lumina with secretion and a "fuzziness" of the inner gland borders. The development of the Graffian follicle and subsequent corpus luteum is dependent on the hormones of the anterior hypophysis. Although not proven, the mechanism is more clearly understood if we postulate that two hormones are elaborated, a follicle stimulating hormone and a luteinizing hormone. A normal premenstrual endometrium, therefore, presupposes a normal ovarian cycle with a normal elaboration of, and balance between, estrin and progesterone.

It is interesting to note, as brought out by Mason (29), that all departures from normal seem to begin with evidence of diminishing progesterone influence on the uterine glands, which would mean that the corpus luteum is at fault. It is believed by most investigators that corpus luteum is necessary for the continuance of early pregnancy, possibly through the early part of the third month, after which time the placenta assumes its endocrine function and probably elaborates enough pro-

gesterone to maintain the pregnancy. Mason also feels that it is a significant fact that in cases of recurrent abortion, the majority occur between the second and fourth month at about the time of a menstrual period, had the patient not become pregnant. He feels that, either the corpus luteum ceases to function too soon, or that the rise of placental elaboration is too slow, allowing the progesterone level to become so low that the fetus dies. In his series of seven cases, he found evidence of progesterone deficiency in all of the premenstrual endometria. Mason says, "It is evident, therefore, that a threatened abortion may represent, not the beginning of trouble, but the end of a damaging process which is past help."

According to Krohn, Falls and Lackner (14), the first mention of recurrent abortion or an endocrine basis was by Seitz who, in 1913, suggested careful observation of the corpus luteum. Attempts to treat the condition date back to 1919, when Hirst employed aqueous solutions of corpus luteum from pregnant cattle. Hannes, the same year, suggested such treatment might be helpful. In 1920, Hofbauer noted an inhibition of uterine contractions during threatened abortion following the use of a preparation called "ovoglandol." In 1921,

Halban advised the use of corpus luteum preparations and in 1928, Glissman successfully used "lipo-lutin" in recurrent abortion. Krohn feels that, although these men had some degree of success, the preparations they were using were not standardized and were probably quite weak.

In passing it would be well to mention some of the early workers responsible for the endocrinology of the female sex hormones. Weichert, Corner, Allan and Clauberg demonstrated that progestin prepares the endometrium for implantation. Allan and Corner proved the necessity of progestin for the preservation of early pregnancy. Knaus and Manzi showed that progestin maintains the uterus in a state of quiescence during pregnancy and that sensitivity to posterior pituitary extract increases as the corpus luteum extracts are decreased.

Reynolds and Allan inhibited estrus motility in rabbits by the use of projesterone. Hisaw also showed the ability of progestin to nullify the posterior pituitary factor. Parkes, Kelly, Ancheim and Zondek were able to produce abortion in animals with excessive doses of estrogenic substances. The work of Smith and Smith in 1930 indicates that progestin maintains a physiological balance of estrogenic hormone during pregnancy

by promoting its exertion through the kidney. However, this has not been confirmed.

Krohn, et al., feel that as gestation advances, estrogen secretion increases in amount to a maximum at term. In this way, the balance between estrus inducing principle and progestin is disturbed, the estrogen becomes dominant and sensitizes the uterus to the oxytoxic principle of the posterior pituitary secretion.

The above mentioned workers except Krohn, did most of their early work on animals and so their findings do not carry over too accurately in clinical cases. For example, Abarbanel failed to prime the gravid human uterus to oxytoxic principle with dosages of 150-200 mg. orally, of stilbestrol in the first trimester of pregnancy. He did find, however, that 100-150 mg. given orally, in the last trimester, was an excellent priming agent and that patients in the last trimester were very tolerant to large doses of stilbestrol with no adverse effect on the fetus.

Krohn, Falls and Lackner, using progestin, were successful in ten out of eleven cases of threatened abortion, ten of thirteen cases of recurrent abortion and in a series of mixed cases were successful in fourteen out of seventeen cases, giving good results in thirty-four of the forty-one cases treated. They con-

cluded that this treatment was logical and valuable, also they found that by inserting a pneumatic bag in the post-partum human uterus (7 days), that one rabbit unit of progesterone would nullify 1 cc. of posterior pituitary extract. They were unable to note any effect of one-quarter grain of morphine sulphate on contractions produced by posterior pituitary extract. In subsequent reports of series of cases treated in this manner, successful results have been obtained in from 70% to 90% of cases of threatened or recurrent abortion.

Contradictory to this, however, is the work of Bickers (4), who placed an intrauterine bag on a case of inevitable abortion and made tracings before and after the injection of 50 mg. of progesterone. He failed to note any effects of the hormone, but stated that his case went on to abort four hours after the injection. He did, however, agree that uterine contractions under the influence of estrin are of rather high amplitude and relatively long duration, while those of progesterone influence are of short duration and low amplitude. These results should not carry as much weight as those of the previous workers because this was an isolated case.

Hamblin (18), studying blood level titers of pregnandiol during pregnancy and abortion, states that the levels tend to fall previous to abortion and may do

so either gradually or abruptly. He also finds that during the course of a pregnancy prior to the onset of abortion, levels may be either normal or low, and a patient may threaten to abort while her pregnandiol level is normal. He also states that intensive progesterone therapy fails to elevate the titer or prevent the abortion and postulates that large doses may actually depress the level by depressing the intrinsic production. He further states that it may interfere with thyroid therapy and concludes that, "Any benefits from progesterone cannot be explained on a basis of it complimenting progestin-pregnandiol metabolism."

Another argument against the use of progesterone in oil, was that the actual expense to the patient was almost prohibitive to its use, except in the wealthy classes. To carry a recurrent aborter through a pregnancy involved about \$150.00 to \$200.00 for medication alone. Falls, Rezek and Beminsohn (15), ran a series of cases using water soluble preparation with good results. They feel that whole gland preparations are more beneficial in inhibiting uterine contractions and that the water soluble product is as effective as the oil preparation and has the advantages of being cheaper and can be given intravenously, if needed in emergencies.

In their series of 217 threatened and fifty-nine recurrent abortions studied at the Cook County Hospital, they found fifty-one successes and eight failures in the recurrent group. The routine treatment was to give 3 cc. of aqueous corpus luteum extract every four hours for six doses, then three times a day for two days, then 2 cc. twice a day until the patient was discharged. The patients were required to be up and about two days without bleeding before being dismissed. In their control group of eighty-eight cases nothing was used except sedatives and an ice bag placed on the abdomen. Of that group, 61% went on to abort while 39% went home with the diagnosis of pregnancy with a live fetus. Half of the control cases were under three months, one-fourth were under eighteen weeks and the remaining one-fourth were over eighteen weeks. They suggest the use of this preparation before surgery or when a long boat, train or auto ride is contemplated. They also used it in eighteen cases of placenta previa, with but one failure.

Collins, Weed and Collins (7), report a series of twelve patients, on which they used a more general type of therapy. They advocate the use of thyroid, if there is any clinical evidence of hypothyroidism,

some form of corpus luteum extract, but lay more stress on wheat germ oil. Eight of their twelve cases carried to term, one had malaria, one had a missed abortion and one was six and one-half months pregnant at the time the article was written. These twelve cases had collectively a total of twenty-one previous abortions. The interesting phase of their observations was the fact that three of their patients who had stopped taking the wheat germ oil but were continuing on progesterone and thyroid, started to have symptoms of threatened abortion, which promptly stopped on resumption of therapy. They feel that the vitamin E exerts an anti-proteolytic action, or is instrumental in neutralizing estrin.

The above thought was first brought out by Vogt-Miller in about 1930 but was not proven to the satisfaction of the clinicians and challenged by the endocrinologists. It is still under discussion at the present time.

Verzar, according to Shute (36), in 1931, found that concentrated vitamin E, when given in large doses to immature female rats, produced vaginal smears similar to estrus or pro-estrus and uterine enlargement. This was substantiated by Drummond, working with rats, and Underhill, in preliminary experiment on im-

mature mice, but Drummond, Noble and Wright failed to note any results in mice. Bacharach and Chance, in 1940, conclude that dl. alpha-tocopheral produces no cornification in immature white mice.

Shute (33), however, who has had a vast experience in the clinical use of vitamin E, feels that it possesses anti-estrogenic activity, because more is required at the time of the pregnant woman's would-be menstrual period and more is required toward term. He feels that it is of doubtful value in recurrent aborters who are already pregnant, but of real value in prophylaxis and threatened abortion and miscarriage, the latter being those of longer than sixteen weeks duration. His data cover 153 pregnancies in 134 women, there being 122 threatened abortions and eighty-seven threatened miscarriages. Of the seventeen threatened abortions having severe pains, 77% were saved, while of the nineteen cases having profuse bleeding, only 47% were saved. Of the twenty-nine threatened miscarriages with severe pains, 93% were saved and three cases as above, showing only profuse hemorrhage, 67% were delivered of living babies. Five of the women had a premature rupture of the membranes and 60% of these were carried to term.

Shute routinely determines the blood estrogen level on all his patients and concludes that a high level means that, the patient will require more E to control, or that trouble is in the offing, if treatment is not instituted. Of his group about 60% showed elevated estrogenic levels. Women with low levels were more easily controlled.

The dosage used must be empirical and Shute feels that most women can tolerate three ounces of wheat germ oil or 125 mg. of alpha-tocopherol acetate. The usual dose is from 1-4 drams daily after a saturation dose. Only one case in his series showed an idiosyncrasy to the medication. He states that women taking E during pregnancy can safely ignore all the traditional cautions about train trips, lifting and laxatives but does urge them to take an added protective dose about twenty hours before such strains are anticipated. He does feel that iron therapy is contra-indicated while E is being given and uses only liver as an antianemic.

To further bear out Shute's (36) contentions that vitamin E has anti-estrogenic properties, he cited five cases of eclampsia or pre-eclampsia where the estrogenic level was known to be low (as is usually the case), where by giving wheat germ oil he was able to produce

an increase in symptoms in all cases.

To merely mention thyroid disorders in relation to abortion again, Litzenburg (25) claims that the conception rate of 255 married women, showing hypothyroidism of negative 10 B.M.R or less, with clinical symptoms, was only about thirty per cent. These same women showed a high degree of impotence and frigidity. Wenkelstein (41), studying in Wisconsin, which is a known goiter area, found in his series that about 25% of women and girls showed more than a plus ten per cent B.M.R, 50% was in the normal range of plus 10 to -10, and the remaining 25% were in the hypothyroid levels. He selected from his series, sixteen of the latter group, which showed no complicating pathology and after a variable period of treatment with the extract of dessicated whole gland, nine patients became pregnant. Seven of these patients carried to term and one of them aborted due to trauma received in an automobile accident. All these patients were kept on treatment throughout their pregnancies. He concludes that it is of definite value, where hypothyroidism is known to exist, and is not indicated in patients within normal limits and without symptoms of decreased thyroid activity. He repeated his finding later in Maryland which is out of the goiter area. Recent literature seems somewhat lacking for

material on the relationship of the thyroid gland to abortion.

Wenkelstein feels that adequate therapy may consist of small doses, insufficient to bring the B.M.R. up to normal limits. Patients showing clinical signs of myxedema with obesity, when given large doses, may have untoward results. He did, however, cite a case of a patient who had been on twelve grains daily of the dessicated gland for over one year with fair clinical results. By accident, she increased her dosage to twenty-four grains a day and after two months became pregnant.

SUMMARY

In the preceding pages, I have tried to present the essentials of recent developments in the field of recurrent or habitual abortion. Its etiology is somewhat illuminated by the past ten years advancement in the field of endocrinology and clinical research. Its treatment, although more scientific and giving a higher percentage of success in the past decade, is still a matter open to discussion and research.

Evaluation of the literature is quite difficult for the following reasons:

1. The clinician feels that his findings must be impressive, and hence is inclined to "throw out" a few border-line cases or "dress up" his series to fit his contentions.
2. Pharmaceutical houses and their detail men, being anxious to sell their products, may take advantage of highly radical articles or results of animal experimentation, thus giving the practitioner an erroneous impression regarding the validity of the preparation.
3. There is no reliable source of statistics to which one can refer to find the actual out-

come in large numbers of collective cases,
as to the relative merits of one form of
therapy over another.

Elimination of the above plus the vigilant
observation and untiring research of the clinician will
do much to unravel another of the preplexing problems
of medicine.

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