1958

Review of the causes of spontaneous abortion : with special mention of the changes seen in chorionic villi

Allan Campbell Landers
University of Nebraska Medical Center

A REVIEW OF THE CAUSES OF SPONTANEOUS ABORTION WITH SPECIAL MENTION OF THE CHANGES SEEN IN CHORIONIC VILLI

Allan Campbell Landers

Submitted in Partial Fulfillment for the Degree of
Doctor of Medicine

College of Medicine, University of Nebraska

March 10, 1958

Omaha, Nebraska

TABLE OF CONTENTS

I. INTRODUCTION

Spontaneous abortion should be of prime concern to every physician who has dedicated himself to the preservation and prolongation of life; for herewith lies the greatest single cause of death. This is obvious when one considers that of 4,000,000 pregnancies occurring in this country in 1955, 400,000 resulted in spontaneous abortion. During the same year, cardiovascular disease and cancer killed approximately 400,000 and 200,000 respectively. Javert (1) states approximately one-half of the adult female population of this country, of child bearing age, is affected by spontaneous abortion. Thus, in terms of incidence, this is our greatest public health problem.

The literature has many data on abortion. Numerous authors have expressed one or more facets of the problem as they see it, ranging from psychological impact on the mother to management. There is comparatively little written on the pathology of spontaneous abortion. It is the purpose of this paper to consolidate and briefly review the causes of spontaneous abortion as well as to summarize the scant literature on the changes seen in the chorionic villi in association with this condition. An attempt will be made to correlate a cause and effect relationship insofar as possible.

II. DEFINITIONS

There are conflicting ideas in the literature as to the definitions of abortion and related terms. An important point of difference concerns the placement of the dividing line between abortion and premature birth. Therefore, in any discussion of the subject, it seems advisable to establish which definitions are being used.

Abortion is the termination of pregnancy prior to the time the fetus reaches a stage of viability.(2) A fetus weighing 500 grams or more and having reached a gestational age of 22 weeks is considered to have reached a stage of viability. These criteria are used by the United States Public Health Service as a basis for their vital statistics.(1) Eastman (2) uses a weight of 400 grams and a gestational age of 20 weeks. However, no fetus weighing under 500 grams has survived in his clinic. One authenticated case of a fetus weighing less than 500 grams and surviving is reported in the literature; this was a baby which weighed 397 grams at birth.(1) (2) Formerly, a weight of 1000 grams and gestational age of 28 weeks was considered the stage of viability. The downward revision of this figure is a reflection of advances in the field of Pediatrics.

A premature infant is one attaining a birth weight of 501-2500 grams or a gestational age of 22-36 weeks.

Miscarriage is synonomous with abortion but a poor medical term. Nevertheless, it is probably advisable for the physician to use this term when communicating with laymen, because the latter generally tend to interpret abortion as a criminal act.

Spontaneous abortion is one occurring of natural causes without resort to medicinal or mechanical agents.(2)

Therapeutic abortion is the deliberate termination of pregnancy because of some grave condition that would make continued pregnancy extremely hazardous to the mother.

Criminal abortion is the deliberate termination of pregnancy without legal or medical justification.(2)

Complete abortion is the expelling of the entire products of conception, and most commonly occurs prior to the tenth week of gestation.

Incomplete abortion is the retention of part of the products of conception (most often the placenta), and most commonly occurs after the tenth week of gestation.

Missed abortion is the retention, in utero, of the products of conception for a period of at least two months following death of the fetus.

Habitual abortion is that condition in which three or more successive pregnancies are terminated by spontaneous abortion.(1)

Threatened abortion is defined as vaginal bleeding prior to the 22nd week of gestation, with or without concurrent uterine cramping.

III. INCIDENCE OF ABORTION

The overall incidence of abortion is not accurately known for obvious reasons. As Fisher (3) states, the possibility exists many pregnancies are terminated with the next menstruation; and, therefore, many pregnancies are never recognized. Some patients will abort, recognize what has transpired, have no ensuing complications, and never report to a doctor. Others may interpret vaginal bleeding, which in actuality is abortion, merely as delayed or irregular menstruation. Criminal abortion, because of its nature, is very difficult to appraise.

The experience of many very reliable authorities, such as Hertig,(4) Eastman,(2) Javert,(1) Rock,(5) Hudson,(6) and others, would indicate spontaneous abortion occurs in very close to ten per cent of all pregnancies. This is based upon observations of many thousands of private and clinical patients; and tends to show that race, parity, and social status do not affect the incidence. Nevertheless, Reis (7) maintains 14-16 per cent is more nearly the true incidence of spontaneous abortion.

The most accurate estimates in the medical literature report criminal abortion to occur in 11-12 per cent of all pregnancies.

Reports as high as 20 per cent may be the result of studies in too limited an area of this country. Spelman (8) makes the startling statement that 69 per cent of all abortions are criminally induced. Thus, even the conservative estimate would indicate a daily rate far in excess of 1000 per day for the United States.

Therapeutic abortion, for this country as a whole, is fairly accurately estimated as occurring in a ratio of one to every 200 live births.(2) In a series of 10,000 deliveries in Eastman's clinic, the ratio was one to 147. Javert's (1) series disclosed an incidence of one to 241 or 0.41 per cent. These figures agree quite closely with the reported incidence in Sweden and Denmark. That therapeutic abortion may be a highly abused procedure seems evident when one considers, as reported by Cosgrove,(9) that the ratio was one to 16,750 deliveries at the Margaret Hague Maternity Hospital. Assuming these figures are correct and assuming the maternal death rate did not increase, the writer feels this wide discrepancy points clearly to a need for the medical profession to be more reluctant in concluding a therapeutic abortion is indicated.

The foregoing paragraphs seem to substantiate Rock's statement(5): "It is apparent that an abortion rate of 25 per cent of pregnancies is a conservative estimate." Henry (10) feels one-third of all fertilized ova abort.

IV. CAUSES OF SPONTANEOUS ABORTION

In the discussion to follow, we are going to divide the causes of spontaneous abortion into two broad categories: (1) Causes primarily attributable to abnormalities in the genital system and products of conception, and (2) Causes primarily attributable to other factors. This is done in the interest of organization and clarity of presentation. The writer is aware there is considerable overlap of and multiplicity of causes.

Spontaneous Abortion due to Abnormalities of the Genital System and Products of Conception.

Ovary and Uterus

Retroversion and retroflexion of the uterus has been seen, by several authorities, with greater frequency in spontaneously aborting than in non-aborting obstetrical patients. The overall incidence of this condition in the female population is thought to be 11-15 per cent. Hudson and Rucker (6) found 26 per cent of their term patients had this condition as opposed to 44 per cent of their abortion patients six weeks postpartum. Javert (1) reported an incidence of 38 per cent in a large number of habitual aborters. Wall and Hertig (11) found this condition in 37 per cent of their habitual aborters. Although it is generally agreed impaction of the uterus due to retroversion and retroflexion will almost always lead to abortion, some writers are not willing to agree that simple retroversion and retroflexion is an important cause.(2) (5)

Leiomyomata of the uterus undoubtedly play some etiologic role in abortion. Javert (1) reports an incidence of 12 per cent, in a series of 1769 spontaneous abortions, as compared to an overall incidence of 1.8 per cent in women of child bearing age diagnosed by pelvic examination. Eastman (2) summarizes the problem as follows: "The position which the fibroid occupies is more likely to affect the issue than the size of the tumor. Submucosal tumors and those situated in the lower segment are the most likely to cause abortion. It is amazing how sometimes the most gnarled and nodular uterus carries a pregnancy to term. The only way one can determine how a uterus with fibroids will behave in pregnancy is to give it the clinical test."

Masters (12) reports patients with bicornuate uterus or uterus didelphys tend to abort about three times as frequently as women with normal uteri. In a review of the literature, it was found in 418 cases of uterus didelphys there were 213 abortions occurring in 735 pregnancies for an incidence of 29 per cent.(1) Other congenital anomalies are more apt to be a cause of sterility than abortion.(2)

Congenitally short cervix or one which is surgically amputated during the child bearing years is associated with slightly higher incidence of abortion. There is extensive reference in the literature to incompetent cervical os as an occasional complication of pregnancy. However, studies indicate this complication

almost always arises after the twenty-second week of gestation; and thus, by definition, causes premature birth rather than abortion.(13)

Hertig and Livingstone (4) found acute bacterial endometritis to be the cause of 1.3 per cent of 1000 cases of spontaneous abortion. A similar report is given in a later article by Wall and Hertig.(11) Rock (5), and Hudson and Rucker (6) disagree with this theory, as does Henry (10) who states: "Endometritis is not the cause of abnormal development and abortion, but is their direct result."

There appears to be general agreement that hemorrhage into the decidua basalis is the most common histologic change seen in spontaneous abortion. Formerly this was thought to be an important cause of abortion; Javert (1) still believes this to be a cause in some cases. However, most writers now label this condition a result rather than a cause.

Endometrial fibrosis, according to Masters,(12) secondary to postpartum or postabortal infection, is a primary cause in some cases. This is a condition in which the endometrium undergoes varying degrees of replacement by fibrotic tissue. A somewhat related condition has recently been described by Netter, et al(14), which he labels traumatic uterine synechiae. This is obliteration of parts of the uterine cavity by scar tissue following myometrial injury. He summarizes the problem as follows: "Curretage,

especially during the postpartum or postabortal period, results not infrequently in adhesions of the uterine wall, adhesions which can cause, in extreme cases, complete disappearance of uterine, cervical, and isthmic cavities. He proves the diagnosis by hysterometry and hysterography. Netter et al.(14) further states: "If by chance pregnancy occurs, abortion and premature delivery are more likely to occur as well as low insertion of the placenta. Delivery of the placenta is difficult and dangerous on account of abnormal placental adhesions."

The ovary per se (the ovum will be discussed subsequently) probably plays very little part in the etiology of abortion except that a functioning corpus luteum of pregnancy is necessary for at least the early months of gestation. However, the writer feels few authorities would be as zealous as Henry (10) in ascribing omnipotence to the corpus luteum, to the exclusion of other factors, when he concludes: "the maternal uterine environment in all its components - its blood supply, its myometrial, and more obviously important, its decidual development - is completely dependent, from the moment of implantation, upon the maternal corpus luteum's ability to respond to demands made upon it by fetal tissues developing in the uterus."

Uteroplacental Organ

Under this heading will be discussed the causes of spontaneous abortion which bear a direct relationship to the intimate

attachment the fetal placenta makes to the maternal uterus.

Premature separation of the placenta is most commonly a complication of the third trimester of pregnancy. However, Javert (1) found this to be a cause, in 32 of 2000 cases of spontaneous abortion.

Likewise, in the literature placenta previa is referred to as a third trimester complication of pregnancy. Studies of the site of placentation, in a large series of therapeutic abortion cases, showed placenta previa to be more frequent than is seen in the third trimester or at term. This discrepancy suggests many of the early cases of placenta previa are lost to spontaneous abortion. Javert (1) observed 35 such conditions in his series of 2000 abortions. Hertig and Livingstone (4) report this as the cause in 5.6 per cent of 1000 spontaneous abortions. Rock, (5) Reis,(7) and Wall (11) also count this as an important cause.

Cervical pregnancy, although rarely seen, is almost certain to proceed to abortion, because it is actually an exaggeration of placenta previa.

In a study of 100 cases of habitual abortion, Wall and Hertig (11) found circumvallate placenta and placenta membranacea to be the cause in 3 and 1 case respectively. Eastman (2) also reports a slightly higher incidence of abortion in association with circumvallate placenta. Torpin,(15) in reporting recently on his study of placental anomalies, came to this startling conclusion:

"The deepest implantation results in circumvallate placenta or membranaceous placentas of which my clinical studies have indicated that 80 per cent of circumvallates and almost 100 per cent of membranaceous abort. If this is true, and there are approximately 40,000 term circumvallate placentas annually in the United States, there should be 160,000 spontaneous abortions associated with this anomaly. J. Whitridge Williams in 1927 concluded that placenta circumvallata had no clinical significance, and most American textbooks tend to agree and, consequently, devote few lines to the subject."

Ovum, Embryo, and Fetus

The vast majority of writers agree this area of pathology explains most cases of spontaneous abortion. In view of this, it is interesting to note there seems to be the least amount of published literature explaining the pathologic nature of these cases. This writer feels this suggests a fundamental deficit in our knowledge of the most important cause of spontaneous abortion. Defects in the ovum, embryo, or fetus apparently cause 50 per cent or more of all spontaneous abortions. Rock (5) placed the figure at 50 per cent. Hertig and Livingstone (4) report a figure of 61 per cent. Huber et al (16) report this as a cause in excess of 50 per cent of cases.

Overworked terms in the literature are "defective germ plasm" and "defective germ cell" used apparently in reference to defects

in the ova and spermatozoa. Shettles (17) in a recent article reports pathologic ova to be the cause of 62 per cent of all spontaneous abortions. He states: "Recently the view has been expressed that the most common cause of abortion is a defective ovum, a bad spermatozoon or both, which is accepted by many not as a mere hypothesis, because it is based on the microscopic findings in many conceptuses."

Joel (18) reports an interesting study which tends to incriminate the spermatozoa as a causative factor in abortion rather than just in sterility as is sometimes considered to be the case. He studied the sperm of 114 male partners of marriages plagued by repeated spontaneous abortion. Forty-six of these had subnormal sperm. Twenty-six of the latter group were eliminated, because theirs was only a low to moderate degree of hypospermia which was not considered to be severe enough to reliably account for the abortions. Of the remaining 20, six had a very high degree of pathologic changes in the spermatozoa, and their marital situation was uniquely suited to this type of study in that each of their wives had a history of significant sexual exposure to other than the single individual. All six wives of these men had normal pregnancies and deliveries in marriages contracted with other men. Two successive marriages of one of these men resulted only in abortions, but the second wife had a normal pregnancy and delivery following artificial insemination. Joel (18) concludes, "Although

the contribution of the male is of obvious importance, no clear-cut relationship between the external morphology of the spermatozoa and abortion has been found." The importance of ova and spermatozoa is summarized by Henry (10) who believes spontaneous abortion, in the majority of cases, is determined by genetic factors carried in chromosomes of one or both germ cells; further, if either germ cell is abnormal, the conceptus will be abnormal and will nearly always be aborted.

One cannot say with certainty that congenital malformations per se lead to abortion. A congenitally malformed fetus that aborts may, in actuality, be the result of a defective ovum or spermatozoon whose pathology is of a degree that will permit intrauterine life to progress a significant length of time but not to the time of viability.

One may justifiably question, at this point, whether or not the treatment of threatened abortion (which is beyond the scope of this paper) will result in a higher incidence of seriously deformed babies. Studies seem to prove such is not the case. Burge (19) in a study of some 12,000 deliveries plus a review of the literature, concluded: "a patient whose pregnancy survives a threat to abort has at least a 98.5 per cent chance of delivering a baby without major or life-threatening defects." He feels there is no evidence the treatment of spontaneous abortion increases the incidence of congenital defects and that we, fortunately, cannot

significantly change the incidence of abortion due to abnormal conceptuses. This appears to support Henry's (10) contention that spontaneous abortion due to defective ovum, embryo, or fetus "is essentially conservative in nature."

Umbilical Cord and Fetal Membranes

Javert (1) attaches great significance to abnormalities of the umbilical cord as a cause of intrauterine death and consequent spontaneous abortion. This is in contrast to most writers in the field who seldom implicate this structure as a primary cause. In 297 cases of abortion which he attributed to defects in the cord, Javert (1) lists achordia as the cause in 181 or 61 per cent. Other authors would class this as a defect in the development of the fertilized ovum. This writer would agree with the latter, for how can one assign an etiologic role to a defect in a non-existent structure? Javert (1) and Novak (20) describe coarctation of the cord as a cause; the former describes this in 15 of his 297 cases. He goes on to say extremely long cords (three times the length of the standing fetus) predispose to involvement in prolapse, looping, torsion and knots. Certainly, extreme degrees of any of these could lead to fetal anoxia and death. However, it appears Wharton's jelly, by virtue of its consistency, protects the vessels from complete occlusion due to these factors in many instances. This is evidenced by the frequency with which these complications are seen in apparently normal term babies. While Javert (1) considers pathologic torsion to be the second most

common cord complication leading to abortion, Hertig and Sheldon (21) and Eastman (2) consider this to be a postmortem phenomenon and not the cause of death of the fetus.

Rupture of the membranes in premature and term deliveries is most often followed by onset of labor. In view of this, one might be inclined to believe an intrinsic weakness of the fetal membranes might lead to rupture and abortion. Jeffcoate (13) studied the strength of freshly obtained fetal membranes by placing them unsupported over various sized apertures and then applying pressure to the point of bursting. He concluded normal membranes will withstand a pressure much higher than could conceivably be reached in utero, during pregnancy. This appears to rule out intrinsic weakness as a cause. On the other hand, membranes weakened by infection may be predisposed to early rupture and, hence, abortion. In a study by Javert (1) chorionitis and amnionitis was six and ten times more frequent respectively in spontaneous abortion than in his control material consisting of unintentional and therapeutic abortions.

Spontaneous Abortion due to Factors Other than Abnormalities of the Genital System and Products of Conception

Trauma, in spite of the importance ascribed to it by the general public, is probably one of the rarest causes of spontaneous abortion. To be effective in producing abortion, trauma must actually initiate one of the following according to Rock:(5)

"disturbance of the choriodecidual relation; interference with the uterine blood supply to the nidatory site; damage to membranes; serious injury to the very young corpus luteum; or activation of the neuromuscular mechanism of uterine evacuation by local irritation or by cerebral disturbance." Hertig and Sheldon,(21) in a very convincing article, reported the experience of seven obstetricians in Boston, all of whom were members or emeritus members of the Obstetrical Society of Boston. These specialists had seen seven cases of bona fide traumatic abortion in a total of 157 years of obstetrical experience; four had seen no cases in a total of 64 years experience. These specialists were also unanimous in agreeing the onset of signs and symptoms leading to abortion follow the causative trauma within minutes to hours. On the basis of these findings, Hertig and Sheldon (21) concluded: "A bona fide traumatic abortion is one in which the abortus was anatomically normal in development up to the time at which the external trauma and/or psychic shock occurred. If this predicate cannot be proven, we must regard the evidence of traumatic causation as conjectural and speculative, and suspect that the abortion was a spontaneous one due to pathologic causes." In most cases of so called "traumatic etiology," if the abortuses are examined, virtually all of them will be seen to have suffered their lethal damage days or weeks before the designated injury and subsequent abortion.(5) Tupper et al.,(22) and Whitley and Green (23) believe trauma,

exercise, and stress may be the trigger mechanism to an already unstable pregnancy, but they believe it rarely to be the basic cause of any abortion.

Maternal disease, such as pneumonia, pyelitis, influenza, and typhoid fever may lead to abortion.(2) It is said either toxins or bacterial invasion may destroy the fetus and result in abortion. In some cases, severe toxic conditions of the mother may initiate labor and abortion without demonstrable pathologic evidence of damage to the fetus. Hertig and Livingstone (4) believed that 2 per cent of their 1000 cases of spontaneous abortion were the result of febrile and inflammatory disease. They state: "That general febrile states can and do cause spontaneous abortion is attested by the number of pregnant patients who aborted during the influenza epidemic of 1918-1919." Reis (7) made the same observation. Tuberculosis is a rare cause of abortion.(5) Syphilis is no longer thought to be a cause of abortion, because studies have shown the spirochete does not cross the placental barrier until after the 20th week of gestation. It is, however, an important cause of premature stillbirth. Toxemia of pregnancy is not a cause of abortion because, by definition, toxemia does not occur until after the 24th week of pregnancy.

There is little evidence imbalance of sex hormones plays a frequent causative role in spontaneous abortion. As stated by Eastman (2): "Endocrine dyscrasias or imbalances, which are

occasionally convenient terms to cloak ignorance of exact factors, may also cause abortion." Tupper et al,(22) found no correlation between levels of sex hormones in aborters and non-aborters. The empirical use of thyroid extract in obstetrical patients to prevent habitual abortion would suggest hypothyroidism is a more common clinical cause of abortion than other endocrine disturbances. (24)

Psychosomatic etiology of spontaneous abortion can be inferred from statistics and reports of cases, but it is a difficult factor to prove. The details of this problem are too extensive to go into at length in this paper, but a few suggestive data will be presented. Based on statistically reliable comparisons as to age groups, total pregnancies and abortions, Javert (1) reports spontaneous abortion to occur ten times as frequently in married women as in unwed prospective mothers! This implies some stressful situation in the marriage relationship as a causative factor in some abortions. Weil and Stewart (25) report the case of a married woman who had had seven consecutive spontaneous abortions. She was considered to be in normal health from an obstetric, gynecologic, and general medical point of view. When she became pregnant the eighth time, she was placed under a psychiatrist's care for weekly sessions of psychotherapy. Urinary gonadotrophic hormone determinations were done weekly and found to be at the lowest level following periods of emotional stress. At one time the

psychiatrist was out of town and could not be present for an appointment. The patient during that week had to be hospitalized for threatened abortion with vaginal bleeding and cramping. She recovered from this episode and went on to deliver a normal baby at term.

Malnutrition, avitaminosis, and insufficient calcium intake, while extremely detrimental to the mother's health during pregnancy, are rarely, if ever, the sole cause of spontaneous abortion. Rock (4) points out that one must not be misled by results obtained in animal laboratories,for deficiency states imposed there are seldom reached in human beings.

Advancing age plays a part in the frequency of abortion; to label this a cause is perhaps erroneous. McMahon et al,(26) made a study of this problem with results of high statistical significance. (The reader is referred to the original article for details.) They concluded: "The percentage of cases in which a normal living fetus (at or shortly before time of abortion) was found decreased steadily with increasing maternal age, from 33.0 per cent in material from mothers under age 25 to 3.2 per cent in mothers aged 40 and over." Javert (1) also found that the incidence of spontaneous abortion per total number of pregnancies by age groups, steadily increased from age 15 and under to age 45-49. In this latter age group, the incidence was 29 per cent in his series.

Radiation, in excess of that needed for limited roentgenography will cause abortion. In fact, this has been proposed as a means of therapeutic abortion.(5)

Finally, lead and other heavy metals may cause abortion by passing through the placental barrier to poison the fetus.(2) More frequently, however, lead causes abortion by first exerting its effect on the ovum or spermatozoon in such a manner that the zygote is incapable of growing to maturity.(5)

V. PATHOLOGIC CHANGES SEEN IN THE CHORIONIC VILLI

Pathologists have known for a long time that in a large percentage of abortuses there are characteristic changes seen in the chorionic villi. The significance of these changes has been, in general, poorly understood. However, recent studies, particularly by Huber (16) and his group at Indianapolis, have given us a more accurate description of these changes and suggest that guarded conclusions may be drawn concerning the meaning of these changes. Specifically, these alterations of the chorionic villi concern what is referred to as molar change. Huber et al,(16) established certain criteria that must be met in order to make the diagnosis of molar change. These are as follows:

(1) Avascular villi or relatively avascular villi.

(2) Edema of the stroma with or without increase in size of the villi with the development of cystic spaces which

tend to coalesce.

(3) Proliferation of trophoblastic cells in excess of the usual two-cell layer in at least some of the villi, excluding the anchoring villi. These findings should be seen in several villi in the specimen.

If all three of these criteria were met, the diagnosis of molar change was justifiable. When two of the criteria were present or when one was present with the other two questionably demonstrated, the diagnosis of questionable molar change was justified.

These workers studied only complete abortion specimens, so the pathology of the fetus might be correlated with molar change of the villi. The fetuses were classified as to degree of pathology they exhibited. From greater to lesser degree of pathology they were classified as absent, nodular, cylindrical, stunted, and macerated. It is interesting to note that the percentages of cases showing molar and questionable molar change decreased as the degree of pathology of the fetus decreased. Javert (1), working entirely independently, reports the same phenomenon of decreasing percentage of molar change with decreasing degree of pathology of the fetus, although he did not use as many classifications for fetal pathology.

The results of the studies of Huber et al.,(16) on 90 complete specimens, showed normal fetuses in only 22 instances or 24 percent. Molar change was not present in any of these cases.

Of the remaining 68 fetuses or 76 per cent, all were abnormal. In these 68 specimens, molar change was found in 36, or 53 per cent of the pathologic fetuses. On the basis of molar change alone, Huber then predicts that more than half of people who abort have a pathologic fetus. As reported in Section IV of this paper, this is a correct prediction which correlates with the findings of many authorities studying the embryo and fetus of a vast number of abortions.

Hertig and Edmonds (27) preceded the above group in a very similar type study of what they called hydatidiform degeneration. Their results were quite comparable in that virtually all cases of hydatidiform degeneration were associated with abortions due to pathology of the ovum, embryo, or fetus. They present an hypothesis which would seem to be a logical explanation for the changes seen. Hertig and Edmonds (27) state hydatidiform degeneration begins about the fifth week of pregnancy or at the time the fetal circulation should begin to function. The chorionic vascular system fails in development because of extreme defectiveness of the ovum, and there results avascular villi. The trophoblast continues to play its role of absorption of vital fluids from the maternal circulation. The fluid is absorbed but, in the absence of fetal circulation to carry it to the fetus, accumulates to produce swollen edematous villi. The larger of these villi are described as having a cyst-like appearance with basophilic precipitate in the

center. The walls of the edematous villi are shown to be connective tissue made up of widely separated immature fibroblasts. These authors did not describe proliferation of the epithelium as a constant finding in hydatidiform degeneration, although they report it was frequently present.

Eastman's (2) description of hydatid degeneration is essentially similar to that of Huber et al.,(16) described above. However, Eastman feels the edematous villi are a post fetal death phenomenon and are the result of the imbibition of tissue fluid.

Gray (28) studied the changes in the chorionic villi in 47 cases of spontaneous abortion, on the basis of how the microscopic sections reacted to eight different staining techniques. In 37 cases he demonstrated either collagen, fibrinoid necrosis, or hyalinization; no two of these were found in any one specimen. Nine of the specimens showed none of these changes nor did 22 controls obtained from term or therapeutically interrupted pregnancies. He concluded these stigmas of collagenosis, which he found, suggested the possibility spontaneous abortion should be classified among the collagenoses (connective tissue disease), and that the role of hypersensitivity of ground substance material in the production of spontaneous abortion should be further investigated. Unfortunately, Gray (28) did not have complete specimens, so the cause of the abortion and the condition of the fetus could in no way be correlated with his findings.

We would, at this point, like to speculate on the significance of Huber's (16) findings. If this work could be duplicated in a large number of cases, then one would be reasonably safe in assuming that a pathological report of molar change indicates the abortion, in all probability, is due to a pathologic fetus or defective germ plasm as described in Section IV above. If molar change is not found in the pathologic examination, one is safe in assuming there exists a good chance that defective germ plasm is not the cause of the abortion. Therefore, a pathologist's report following abortion which stated, "Negative for molar change" would be an encouraging sign to the obstetrician. He would be most reluctant to then attribute the abortion to defective germ plasm and would proceed to rule out all other possible known causes of abortion that might exist with this patient. Fortunately, it is these other causes that we are most likely to be able to remedy with our present state of knowledge, and it is these other causes that apparently account for close to 50 per cent of all spontaneous abortions. We feel that such a method of pathologic reporting would be a vast improvement over "Products of Conception" and might, in the future, enable us to reduce the incidence of this major problem.

Wall and Hertig (11) recognized the universal need for pathologic examination when they stated: "Any woman who aborts is potentially an habitual aborter. Therefore, it is important that the very first abortus of any patient should be thoroughly

examined pathologically..... By submitting all abortions to such examination, both the patient and her physician can become intelligently prepared for any subsequent abortions."

VI. SUMMARY

A review of pertinent literature, as regards the causes and incidence of spontaneous abortion, has been undertaken. Furthermore, we have studied the material available concerning histologic changes seen in the chorionic villi coincident to spontaneous abortion. This study was embarked upon in the hope that some correlation might be found between the cause of an abortion and the pathologic findings at time of examination of the specimen. In this regard, we feel we have been only moderately successful.

We have shown that, in terms of incidence, spontaneous abortion is our greatest public health problem in that half of the female population of child bearing age is affected by it.

An attempt has been made to set forth clear concise definitions of some of the terminology used in reference to abortion. It is in this area that a significant amount of confusion appears.

It is pointed out that one-fourth to one-third of all pregnancies terminate in abortion. Unfortunately, more than one-half of these are criminal abortions. Ten per cent of all pregnancies end in spontaneous abortion. Evidence is presented that suggests therapeutic abortion is, perhaps, too common a procedure being

entered into without sufficient justification.

In the discussion of causes of spontaneous abortion, we make no attempt to assign to a specific cause the responsibility for a certain percentage of the abortions, except in very general terms. This information is at present largely unknown. In addition, we do not mean to imply that every cause has been mentioned. Certainly, some causes are too rare to be worthy of mention and others are still unknown. The causes have been divided into those relating to abnormalities of the reproductive system and the products of conception, and those relating to other factors. It is emphasized that there may be overlap of and multiplicity of causes.

In the former group, we further divide our discussion into causes relating primarily to ovary and uterus; uteroplacental organ; ovum, embryo, and fetus; and umbilical cords and fetal membranes. The greatest single cause of spontaneous abortion is found to be defects in the ovum and spermatozoon. Other causes we discuss are retroversion and impaction of the uterus, leiomyomata, congenital anomalies, endometritis, decidual hemorrhage, endometrial fibrosis, and traumatic uterine synechiae. It is suggested that premature separation of the placenta and placenta previa should be considered causes of abortion rather than just third trimester complications of pregnancy. We point out that circumvallate placenta may be of much greater importance than that usually ascribed to it.

Among causes not attributable to abnormalities of the reproductive system, we discuss psychosomatic factors, maternal disease, hormones, maternal age, and others. The role of trauma and nutrition in etiology is shown to be less important than usually considered.

The latter part of this paper describes the changes in the chorionic villi seen with spontaneous abortion. The study of one individual is described in which he finds significant amount of collagenosis in the chorionic villi, and suggests spontaneous abortion might be related to the collagen diseases. We feel his study was not well correlated with the pathology of the fetuses and that his study is, therefore, not too significant.

The findings of other groups, which correlated well with each other, seemed to be of considerable significance. These concern what is called molar change or hydatidiform degeneration of the chorionic villi seen in, roughly, half of the cases of spontaneous abortion. This phenomenon consists of three basic histologic changes as follows: (1) Avascular or relatively avascular villi; (2) Edematous swollen villi with cystic spaces which tend to coalesce; and (3) Proliferation of trophoblastic cells in excess of the usual two-cell layer. There is strong evidence that these changes are not seen except in cases of abortion due to defective germ plasm. On the basis of these findings, we have suggested further study in this area is warrented, and all abortal specimens

should undergo thorough pathologic examination. We feel this might lead to a broad classification as to the cause of the abortion. If the pathologist described molar change, the abortion could almost certainly be ascribed to defective germ plasm. If not described, there exists a strong possibility the abortion was due to other causes. In cases where the latter is true, we feel our present state of knowledge might enable us to assist a mother in avoiding a possible subsequent spontaneous abortion.

VII. CONCLUSIONS

1. Spontaneous abortion, in terms of incidence, is our greatest public health problem.

2. Ten per cent of all pregnancies end in spontaneous abortion, and a greater number in criminal abortion.

3. Therapeutic abortion is, perhaps, too frequent a procedure in this country and should be entered into only when furthered pregnancy is a grave threat to the life of the mother.

4. Defective germ plasm is the most frequent cause of spontaneous abortion.

5. Placenta previa and premature separation of the placenta are causes of abortion as well as third trimester complications of pregnancy.

6. Trauma is a very rare cause of abortion.

7. Psychosomatic factors are occasional causes of abortion.

8. All abortion specimens should be submitted for pathologic diagnosis. Careful histologic study of these specimens to determine the presence or absence of molar change may permit the etiologic classification of abortions into two broad categories; that is, those due to defective germ plasm and those possibly not due to defective germ plasm. Such a separation may be the point of departure for prevention of many needless cases of abortion.

VIII. BIBLIOGRAPHY

1. Javert, C. T., Spontaneous and Habitual Abortion, New York, McGraw-Hill Book Company, Inc., 1957. Chap. 1, 3, 4, 5, 6, 7, 8, 10, and 15.

2. Eastman, N. J., Williams Obstetrics, New York, Appleton-Century-Crofts, Inc., 1950. 10th ed., Chap. 20, 21.

3. Fisher, J. J., Spontaneous Abortion, J. Fla. Med. Assoc. 43:992-996,(Apr.) 1957.

4. Hertig, A. T. and Livingstone, R. G., Spontaneous, Threatened, and Habitual Abortion: Their Pathogenesis and Treatment, New England J. Med., 230:797-806, (Jun. 29) 1944.

5. Rock, John, Abortion, New England J. Med., 223:1020-1027, (Dec. 19) 1940.

6. Hudson, G. S. and Rucker, M. P., Spontaneous Abortion, J.A.M.A., 129:542-544, (Oct. 20) 1945.

7. Reis, R. A., The Causes and Treatment of Spontaneous Abortion, Illinois M. J., 80:380-383, (Nov.) 1941.

8. Spelman J. W., Abortions, Post Grad. Med., 17:A36-A44, (May) 1955.

9. Cosgrove, S. A. and Carter, P.A., A Consideration of Therapeutic Abortion, Am. J. Obst. & Gynec., 48:299-314, (Sep.) 1944.

10. Henry, J. S., Some Biological Aspects of Spontaneous Abortion, Am. J. of Obst. & Gynec., 73:1229-1236, (Jun.) 1957.

11. Wall, R. L. Jr., and Hertig, A. T., Habitual Abortion: A Pathologic Analysis of 1000 Cases, Am. J. of Obst. & Gynec., 56:1127-1133, (Dec.) 1948.

12. Masters, W. H., Maze, L. W., and Gilpatrick, T. W., Etiologic Approach to Habitual Abortion, Am. J. of Obst. & Gynec., 75:1022-1034, (May) 1957.

13. Jeffcoate, T. N. A. and Wilson, J. K., Uterine Causes of Abortion and Premature Labor, N. Y. State Jour. of Med., 56:680-690 (Mar. 1) 1956.

14. Netter, A. P., Musset, Rene, Lambert, Alice, and Salomon, Y., Traumatic Uterine Synechiae: A Common Cause of Menstrual Insufficiency, Sterility, and Abortion, Am. J. of Obst. & Gynec., 71:368-375 (Feb.) 1956.

15. Torpin, Richard, Correlation of Placental Anomalies with Spontaneous Abortion or Premature Separation, J. Obst. & Gynec. Brit. Emp., 62:385-389, (Jun.) 1955.

16. Huber, C. P., Melin, J. R., and Vellios, Frank, Changes in Chorionic Tissue of Aborted Pregnancy, Am. J. of Obst. & Gynec., 73:569-578, (Mar.) 1957.

17. Shettles, L. B., The Ovum in Infertility, Abortion, and Developmental Anomaly, Fertil. & Steril., 7:561-572, (Nov.-Dec.) 1956.

18. Joel, C. A., The Role of Spermatozoa in Habitual Abortion, Fertil. & Steril., 6:459-463, (Sep.-Oct.) 1955.

19. Burge, E. S., The Relationship of Threatened Abortion to Fetal Abnormalities, Am. J. of Obst. & Gynec., 61:615-621, (Mar.) 1951.

20. Novak, Emil, Gynecological and Obstetrical Pathology, Philadelphia, W. B. Saunders, 1940. p. 469.

21. Hertig, A. T. and Sheldon, W. H., Minimal Criteria Required to Prove Prima Facia Case of Traumatic Abortion or Miscarriage, Ann. Surg., 117:596-606. (Apr.) 1943.

22. Tupper, C., Moya, F., Stewart, L. C., Weil, R. J. and Gray, J. D., The Problem of Spontaneous Abortion: A Combined Approach, Am. J. of Obst. & Gynec., 73:313-321, (Feb.) 1957.

23. Whiteley, H. J. and Green, H. N., The Role of Trauma in the Aetiology of Abortion, J. Obst. & Gynec. Brit. Emp., 59:829-833, (Dec.) 1952.

24. Novak, Emil and Novak, E. R., Textbook of Gynecology, Baltimore, The Williams and Wilkins Co., 1956. p. 764.

25. Weil, R. J. and Stewart, L. C., The Problem of Spontaneous Abortion: Psychosomatic and Interpersonal Aspects of Habitual Abortion, Am. J. of Obst. & Gynec., 73:322-327, (Feb.) 1957.

26. McMahon, B., Hertig, A. T., and Ingalls, T., Association between Maternal Age and Pathologic Diagnosis in Abortion, Obst. & Gynec., 4:477-483, (Nov.) 1954.

27. Hertig, A. T. and Edmonds, H. W., Genesis of Hydatidiform Mole, Arch. of Pathol., 30:260-291, (Jul.) 1940.

28. Gray, J. D., The Problem of Spontaneous Abortion: Changes in the Placental Villi, Am. J. of Obst. & Gynec., 72:615-621, (Sep.) 1956.