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Discussion of etiologic factors in sterility

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A Discussion of Etiologic Factors in Sterility

by

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Definitions

Sterility is the failure or inability to initiate a pregnancy (99). Hence, in this thesis recurrent abortions and other conditions preventing the birth of a live baby will not be included as etiologic factors in the production of sterility. Sterility may be voluntary or involuntary; it is with the latter type that this discussion is concerned. Various authors have arbitrarily injected the time element into the definition; this varies from two to three years. Thus a fitting definition is: Sterility is the failure to initiate a pregnancy within a period of two years, during which time no known contraceptives have been used.

Absolute sterility is said to exist when it is impossible to accomplish a pregnancy; this is usually due to some major type of pathological defect (100). Relative sterility exists when there are several minor factors interfering with the production of pregnancy, but when pregnancy is not impossible (100). Obviously there are all degrees of sterility or infertility up to the point of absolute fertility where there is nothing interfering with the process of conception. Thus, a relatively sterile couple may on remarriage to mates of high fertility, succeed in producing conception (23).

Incidence of Sterility

Most authors place the incidence of sterility between ten and fifteen percent. Glober (23) and Kirtley (36) place the figure at fifteen percent. Curtis (17) states that twelve percent of all marriages are sterile.

Climate, Season, and Race

Climate seems to have some influence on fertility, but not as much as does race. Women, who are new arrivals in the tropics, often have marked menstrual changes. Abortion and sterility among those with these changes are fairly common. Racial characteristics, however, remain strong in spite of climate; thus the North American Indian family is smaller than that of the white. Southern Slavs and Jews have high fertility, while French fertility is low (98).

There have been many attempts to correlate fertility and sterility with the seasons. There is a high frequency of menstrual disorders in the summer months (1). Associated with these disturbances at this time is a high relative sterility (2). The effect of the long winter night on the Eskimos has also been argued. According to Whitaker (106), there is no decrease in fertility at that time.

Civilization

Darwin said, "Any change in the habits of life, whatever these habits may be, if great enough tends to affect in an inexplicable manner the powers of reproduction" (98). The indirect effect of civilization on fertility is, in my opinion, rather immense. Civilization determines our mode of living, and the latter is the point of origin of many constitutional factors in the etiology of infertility. These will be discussed later.

there is delayed coitus associated with a short menstrual cycle. Both women menstruated every twenty-four to twenty-six days. Because of their misinterpretation of an old Jewish law, they abstained from coitus for two weeks after the last day of the menses. Their menses lasted from three to five days; hence coitus did not begin until the date of ovulation had been passed. Pregnancy resulted in both cases when cohabitation was resumed at the correct time.

Because a woman is infertile, so to speak, during a large part of the menstrual cycle, it seems logical to believe that coital frequency plays some part in the production of pregnancy. The semen must be placed on the cervix at just the right time in order for one of the spermatozoa to meet the ovum; hence increased coital frequency, up to a certain degree, will increase the chances of the semen being deposited at the right time. In conjunction with this the chart below, taken from Stix (94), is of interest.

Coital frequency immediately after marriage	Number of women	Mean number of months before conception
Once per week or less	45	4.6
Two to three times per week	212	4.7
Four to six times per week	121	4.3
Seven or more times per week	101	3.7

Length of Menstrual Cycle

A short menstrual cycle seems to have something to do with sterility (10). One author has seldom seen a pregnancy in a woman whose menstrual cycles were regularly shorter than twenty-seven days (10). This is probably a condition associated with some endocrine dysfunction, which is the basic cause of the sterility.

Psychic Factors

Vaginismus and psychic impotence will be discussed under the subject of faulty delivery and reception. McGoogan (57) reported a case, in which the couple apparently despaired of having a child, and adopted one; subsequent to this the woman became pregnant. This may have been due to some unexplainable psychic factor associated with the adoption of the child.

Gravity

Glober has seen several cases become pregnant following Huhner's test; he states it was probably because the patients remained in bed in the prone position instead of arising immediately as they usually did. It is known also that native women on the island of Bali stand up immediately after coitus in the hope that the seminal fluid will flow out of the vagina, thereby, preventing pregnancy (16). Thus, gravity may be a factor in some cases of infertility, by preventing the ascent of the spermatozoa.

Constitutional Factors

That constitutional factors are of extreme importance, is without question. Vose (103) states that they are much more often the cause of subnormal semen than local lesions are. This is also true of female gametogenesis. Pregnancy often follows the correction of constitutional factors without any local treatment; for instance, thirty-three percent of sixty-nine sterile women became pregnant after thyroid treatment was instituted (48). On the other hand, in one series of cases, totaling 150, constitutional factors were not found to be the cause of sterility in any case (38).

Chronic Intoxication

Gametogenesis is probably that part of the reproductive mechanism which is most often affected by chronic intoxication; impotency may also result from intoxication (49). The effect on gametogenesis is either by direct poisoning of the spermatogonium or oogonium or by a primary depression of the endocrine system, which then may fail to give adequate stimulation for normal gametogenesis.

The chronic infectious diseases are frequent offenders. Generalized tuberculosis may cause necrospermia (18). At first thought, it may seem that septic tonsils, infected paranasal sinuses, or abscessed teeth are not associated with sterility. However, the relation is suggested when it is observed that a fair number of people, thus afflicted, show lowered basal metabolic rates and other evidences of depressed vital functions.

Men with these conditions are also found to produce deficient semen (58). The relationship is fairly well proved when, after the eradication of these sources of intoxication, normal metabolic conditions are established, seminal specimens are improved, and pregnancies result. Chronic prostatovesiculitis may also act as any focus of infection. It produces toxins, which enter the blood stream, are carried to the testes, and there produce a depression of the spermatogenic function. These facts are confirmed by the experiments of Vose (103).

Malaria may cause infertility by damage to the testes (98). or by damage to the ovaries (4). Even Hippocrates knew of the poor capacity of the malaric for conception. Sterility among syphilitics is given as high as twenty-three percent.

The continual use of drugs is also a cause of sterility. The most outstanding of these is morphine, and its derivatives (98). They will produce amenorrhea in women. The effects of alcohol are less pronounced; however in dogs, alcohol is secreted by the prostate gland in about the same concentration as by the kidney; some is excreted by the testicle.Alcohol thus excreted by the genital tract of dogs inhibits the motility of the spermatozoa (20). Prolonged alcohol intoxication in rats will cause abnormal spermatogenesis and even atrophy of the seminiferous tubules (58). Alcohol will produce necrospermia in men (18). Little is known about its effects on the female genital system.

Titus (99) reported one case of inactive spermatozoa due to lead poisoning. Excessive use of tobacco may also be an underlying

and may have some bearing on male sterility. The clinical results obtained in the treatment of certain sterility cases. with vitamin E would seem to indicate that vitamin E is a large factor in the etiology of these cases; however, these results may have been purely coincidental with the use of the vitamin E. (53). At any rate, it is difficult to obtain proof that vitamin E is of value in the treatment of sterility in human beings (107).

Lack of a properly balanced diet and especially overfeeding diminish fertility(97). Dietary excesses may lead to abnormal obesity and finally to the production of sluggish sex cells (98). Diets lacking in certain mineral salts, especially calcium, and lacking in proteins and vitamin A have a detrimental effect upon fertility (98)(97). Protein deficiency is the only type of dietary lack which is encountered with any degree of frequency, and is a factor of considerable importance because the sex cells are among the first to suffer from protein starvation as is evidenced by semen examination in male patients; such conditions may be present when the general nutrition of the patient from external appearances is good (58). Reynolds and Macomber (80) have shown that a moderate decrease in the percentage of protein, calcium, and fat-soluble vitamin in an otherwise adequate diet produces a definite decrease in the fertility of rats.

Carbohydrate metabolism must also be considered. Disturbed or suspended menses were encountered by Rabinowitch (76) in ninety percent of untreated diabetics. When the diabetes was brought under control by insulin, the normal menstrual cycle

returned. Sterility may be associated with disturbed sugar tolerance curves when no other evidence of diabetes is present; these cases may become pregnant incidental to the use of insulin (75). In these cases of disturbed sugar metabolism and cases of hyperthyroidism, protein catabolism is increased; hence an increased protein intake is necessary (76).

When rats are fed a diet, which is practically free of fats, but which do contain all the known essential food elements, there is still satisfactory growth and reproduction (50). Also of interest is the fact that massive doses of vitamin B 1 produces sterility in rats. There is no evidence to show that these factors are of importance in human sterility.

Lack of exercise should be mentioned here because of the role it plays in the production of obesity; Obesity is likely to result in deficient gametogensis, amenorrhea, and sterility (58). Obesity also has an endocrine etiology.

General Malconditions without the Intoxicating Factor

The relation of these conditions to the etiology of sterility is usually much more obscure. The effect of the general debility on reproduction varies a good deal with different individuals. Anemia has often been given as a cause of infertility (99). Even the milder types may produce striking depressions of spermatogenesis and "presumably" oogenesis, according to Meaker (58). However, in fourty-three percent of 1,500 women there was a relative anemia without disturbance of the menstrual cycle or pregnancy (75).

General debilitated conditions following acute illnesses may cause sterility for a time. But severe cachetic states, such as those associated with pulmonary tuberculosis and malignancies, may have little or no influence on fertility. Insanity may also be accompanied by sterility; melancholia in particular is associated with anovulation. In fifteen cases of schizophrenia, reported by Williams (108), the average abnormal spermatozoa count was fourty-eight percent. Early cranial sclerosis with poor development of the accessory sinuses is sometimes associated with menstrual disorders and apparent sterility in the female (10). This would have its effect through the medium of the pituitary gland.

Fertility and potency may be decreased by great responsibilities with their accompanying worries, overwork, and improper hours of rest; infertility of this type is found most often among business and professional men(98).

Constitutional Inadequacy and Infertility

When no other apparent cause for a given case of sterility is discernable, constitutional inadequacy or inferiority may be the factor concerned. There are only a few cases, to which this is applicable. The entire idea is pure speculation. People of this type give general physical as well as mental evidences of inadequacy; hence the condition is more than a local genital factor. It is well that people of this type are sterile, for they are poor specimens of human beings; they may be the result

of in-breeding, which according to the Mendelian laws would tend to bring out the undesireable recessive characteristics. In experimental work the fly, Drosphilia, has been produced as a result of breeding. Any two members of this strain will always produce a sterile mating, but when bred with members of another strain, they will be fertile. Such factors asthese may explain a few of the otherwise inexplainable cases of human infertility.

Endocrine Factors

These are rather frequent factors in both sexes. The hypofunctional types are seen more frequently than hyperfunction.

Pituitary gland: Because this gland is the center of control for all the endocrine glands of the body, it is evident that any disturbance here will have a profound influence on the endocrine system as a whole. Primary pituitary deficiency is probably the chief endocrinopathy. Atrophy of the anterior lobe may be due to tumors, emboli, and inflammatory processes (115), or arteriosclerosis, thrombosis, and chronic systemic infection (114). Pseudo-infantilism is found in hyperfunction, as in pituitary giants; this is accompanied by genital atrophy and premature impotence. Pseudo-infantilism is also found in hypofunction, as in pituitary dwarfs (115); this is associated with amenorrhea, impotence, and sterility (114). Frolich's syndrome has an indefinite etiology, but it also shows sexual infantilism (55); this is the most common anterior pituitary dysfunction associated with sterility (15). In Dercum's disease there is amenorrhea and sexual frigidity, but this would rarely be seen as a cause of

sterility because the disease is not often seen before the menopause. Simmon's disease may be caused by tumors, emboli, or inflammatory lesions; This disease is characterized by decreased libido, amenorrhea, and sterility (115). The Laurence-Biedl syndrome is another condition of hypofunction wherein there is genital underdevelopment (114). Basophilic adenoma of the pituitary gland is accompanied by precocius sex development and later by amenorrhea (55), frigidity, and sterility (114). In some cases infantilism and genital underfunction are found in persons with acidophilic or chromophobe tumors of the pituitary gland.

Thyroid gland: Hypofunction is much more common than hyperfunction in the production of sterility; fifty-six percent of Litzenberg's (48) sixty-nine sterile women had a low basal metabolic rate. Woods (115) reported a low basal metabolic rate in practically every man with deficient spermatozoa. There may even be a normal basal metabolic rate, and still sterility will persist till thyroid treatment is given. There may be recurrent abortions and menorrhagia due to endometrial hyperplasia, accompanying hypofunction of the thyroid; however menstruation may be scanty or absent altogether.

Thymus gland: A persistent thymus has been supposed by some to cause genital infantilism, but the relationship has not been definitely established. The genital infantilism may be a symptom of some other glandular dyscrasia, the persistent thymus being coincidental (115).

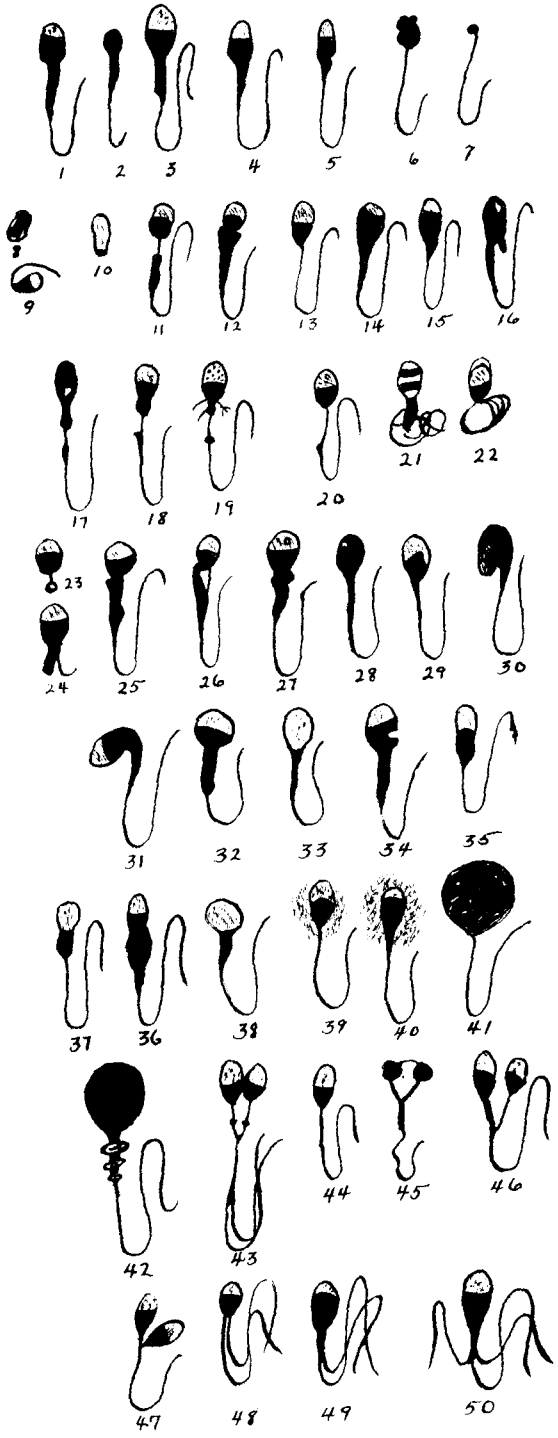
Adrenal glands: Sterility is rarely a result of adrenal cortex deficiency. At any rate, the patient is much more concerned with the systemic condition than with sterility. Degenerative changes in the adrenals may result from hemorrhages into the cortex, chronic intoxications, extensive burns of the skin, or local tuberculosis. These will produce hypofunction, as in Addison's disease, wherein amenorrhea, ovarian atrophy, and sterility may be found. Adrenal adenomata, believed by some to be embryonic testicular cell rests, cause precocious sexual development, masculine traits, and frequent sterility (115).

Pancreas: Liegner (46) has found that pancreatic hypofunction causes atresia of the ovarian follicles, preventing ovulation. The relation of pancreatic function to nutritional and metabolic disturbances has been discussed under dietary factors.

Testes: The anterior pituitary gonadotropic hormone stimulates the testes to hormone secretion and spermatogenesis up to a certain point but not sufficient to produce spermatozoa. The testicular hormone stimulates growth of the prostate, and diminishes the available anterior pituitary hormone. The testicular hormones have no direct effect on the testes, themselves (14); in fact, continuous large doses of this hormone in man may cause loss of sex-desire and the development or increase of oligospermia(15)(25)(84). Injections of testicular hormones into immature, normal, human males causes an increase in the size of the prostate but a decrease in the size of the testes (14); Heckel (25) states that injections of anterior pituitary-like

These functions will not be discussed because the definition of sterility, as used in this thesis, includes only those factors, which prevent the union of the ovum and spermatozoa and not those factors, which influence their subsequent development. These hormones are also essential in the development and maintenance of the adult type of genital organs; thus ovarian dysfunction may result in hypoplastic conditions of these organs. Dyspareunia may result from a hypoplastic vagina. The delicate balance between the several ovarian hormones is easily upset by a number of factors; these factors may be endocrine or non-endocrine. The latter factors include organic lesions of the ovaries.

Ovarian hormone disturbances consist of increases or decreases in the amounts of the various hormones. These may be brought about by other endocrine gland dysfunctions by way of the pituitary gland. Corpus luteum cysts may produce too much progestin, or follicle cysts may produce too much estrogenic hormone. It has also been demonstrated that there is lowered renal threshold for excretion of the female sex hormones in some instances; thus there may be a lack of these substances in the blood stream (21) although the ovaries are functioning properly.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1. Normal spermatozoa
2. Microsperm
3. Megalosperm. End fibril of tail well-pronounced in this specimen.
4. Roughened head membrane.
5. Narrow cell with spheroidal swelling of body.
6. Irregularly solid staining head and absence of body.
7. Aplastic head and absence of body. Such cells have been seen motile.
8. Arrested developement of germ cell, tail tightly coiled about head; head solid staining.
9. Arrested developement of tail.
10. Phantom cell takes almost no stain; head tapers posteriorally due to lack of division of end knobs; no body or tail.
11. Filiform middle piece and spheroidal swelling of posterior end of body.
12. Cytoplasmic extrusion; pseudo-swelling of head.
13. Overdevelopment of end knobs; posterior end of head square.
14. Body tapers, broader anteriorly - form of cytoplasmic extrusion, of no clinical significance.
15. Abaxial implantation of body and tail
16. Abaxial implantation of body and tail. Cell originally double bodied and stump of second body still present.
17. Separation of body (probably artefact).
18. Separation of body
19. Short fibrils seen around abnormal body.

41. Immature, abnormally developed, cell.

42. Large immature cell.

43. Double form showing in each cell the same abnormalities, namely a narrow head, naked body fibril, and thickened end ring.

44. Double neck.

45. Double sperm, immature spermatic veil over and between heads, swelling of body.

46. Double head and body.

47. Double heads, one almost without a body.

48. Single head, double body and tail.

49. Single head, single thickened body, double tail.

50. Single head, single thickened body, triple tail.

Semen

In order to understand the many conditions underlying infertility and sterility of spermatic origin, it is necessary to know what constitutes normal as well as abnormal spermatozoa and seminal fluid.

Number of Spermatozoa

In a study of two hundred fertile men, an average of one hundred and twenty million spermatozoa per cubic centimeter were found (28). Twenty-five percent of these fertile men had counts below sixty million per cubic centimeter. Elsewhere, the same author reports that pregnancy is not apt to occur when the spermatozoa counts are below sixty million per cubic centimeter (29). Rea (79) states that fifty million per cubic centimeter is the point of low normal; he reports an interesting case, in which there was paternity with a count of one and one-half million. The general consensus of opinion isthat loss of fertility begins when there are less than sixty million spermatozoa per cubic centimeter (55).

Morphology of Spermatozoa

The mature human spermium consists of a head, a connecting or middle piece, and a tail. The head is a flattened, almond-shaped object,measuring four to five microns in length and two and one-half to three and one-half microns in width. It is a condensed nucleus. The middle piece is of cylindrical or spindle-shape,and connects the posterior pole of the head with the tail. It has a length of five microns and a thickness of one micron.

The tail has a length of fifty-two microns. At its anterior end it has the same thickness as the middle piece, but gradually tapers down toward the free end. It can be subdivided into the principal part and a short terminal part of extreme thinness. There are many abnormalities of spermatozoa morphology.

Head changes: Abnormalities of the sperm head are by far the most important changes, much more than the body changes or any other aberrant forms, or even the total number of abnormal sperms present. The total number of abnormal spermatozoa shows no relation to the clinical fertility record, except as it is increased by the higher abnormal head count. The body changes also cannot be correlated with the clinical fertility. All head changes are not of equal importance. A slight narrowing of the head, for instance, unless present in most of the cells, usually is of relatively little significance. Somewhat rounded heads should also be considered normal. Truly rounded heads should be considered as abnormal, but whether they are important is still undetermined because they never are present in large enough numbers to allow for their proper evaluation. Distinctly large round cells are probably more or less immature or degenerated cells and distinctly of importance, but are also never seen in sufficiently large numbers to allow of statistical correlation with any clinical abnormalities. In these large cells and large spermatozoa in general, there is not infrequently a tendency to have double form(69). These large and double cell forms have been seen as the result of exposure of the gonads to

to x-ray (45). Tapering and sickle-shaped heads are more sinister types of sperm head changes (67), but distinctly narrow and long heads and rounded heads tapering at the base are most important. In such cells the nuclear material of the head is necessarily reduced, thus impairing the value of the cell. Aside from this, however, the base of the head, where the chromosomes of the spermatozoa are situated, becomes involved.

Body changes: The body may be thickened or doubled. It is rarely absent.

Tail changes: The tail may be coiled or double. It is very rarely absent (69).

Moench (66) has made extensive and significant experiments in the measurement of spermatozoa heads. He measures the length of the heads in millimeters at a magnification of three thousand diameters. From this he obtains the coefficient of variability in length. When this coefficient is from 11.5 to 12.5, there is definite impairment of fertility. When it is above 12.5, there is sterility.

Necrospermia of an intrinsic type is rare in morphologically normal spermatozoa; whereas it is common in some of the highly pathological forms already mentioned. The number of abnormal spermatozoa, which may be present without serious impairment of fertility, varies somewhat, according to the author. In one series of two hundred fertile men, there was an average of ten percent abnormal spermatozoa (28). Meaker (58) states that highly fertile men have an abnormal count well below fifteen percent of

the total count, and that in individuals with poor fertility there may be forty percent or more abnormal forms. Several authors (67)(101)(79) think that certain types of abnormal counts up to twenty percent are consistent with fertility. Twenty-two to twenty-three percent results in impaired fertility, and twenty-five percent causes clinical sterility (69). The difference between twenty and twenty-five percent is a relatively large one. If narrow and tapering heads are marked, and total eight to ten percent or more, sterility may exist. Below is a chart taken from Williams (108), showing the averages of differential cell counts expressed as cells per thousand.

	Number of cases	Normal cells	Pyriform cells	Miscellaneous	Micro sperm	Megal osperm	Percent abnormal
Fertile matings	11	732	56	53	131	25	26
Infertile matings	5	607	80	91	190	29	39

This is a somewhat small group, from which to draw any definite conclusions. Abnormal spermatozoa heads are but an indication of the degree of spermatogenic disturbance, and mean, if of sufficient intensity, that all the other cells would be incapable of fertilizing the ovum, even though they looked normal (67).

Elasticity of the Spermatozoa

Moench's (63) studies in microdissection of the spermatozoa heads revealed the normal forms to have a greater elasticity than the abnormal spermatozoa. This demonstrates the ability of

normal cells to resist physical injury.

Motility of Spermatozoa

In the average fertile case about ten to fifteen percent of the spermatozoa may show no motility; about the same number may be only sluggishly motile, and the rest are actively motile; at least sixty-five to seventy-five percent should be actively motile (101). Ninety percent of the spermatozoa should remain motile for one hour, and ten percent should remain motile for twenty-four hours (55). Length of motility varies according to environmental conditions. In a strong alkaline solution with a lack of oxygen, motility is markedly decreased, but if oxygen is available, ejaculated spermatozoa will ordinarily die at body temperature in less than forty-eight hours (68). Average fertile cells remain motile at room temperature for twelve to twenty-four hours (58). Specimens with high cell counts usually exhibit excellent motility (28). Under special conditions, in vitro, they may remain motile for as long as twenty-one days. Motile spermatozoa have been recovered from the vagina after sixteen days (12)(88), but this does not mean that these cells remain fertile for any where near this length of time (12). If sperm motility is unduly short-lived, it is significant of infertility; otherwise the significance of motility must be judged with a great deal of caution (65).

Motility and the other revelations of the ordinary microscopic examination do not always determine fertility of the spermatozoa. This fact is shown by a case, reported by Seymour(89).

In this case a man of genius mental capacities had a spermatozoa count of ninety-four million per cubic centimeter, three percent abnormal forms, motility for eighteen hours, normal amount of seminal fluid, and no pus cells in the fluid. His semen was used to inseminate fifteen women desirous of having children of the type that he should produce; repeated attempts were unsuccessful in every case. These women all subsequently became pregnant due to spermatozoa from other sources.

Metabolism of Spermatozoa

Mature spermatozoa consume oxygen, and produce lactic acid plus carbon dioxide; thus they tend to alter their environment in an unfavorable manner (33) by increasing the hydrogen ion concentration. They also metabolize glycogen. Meaker (58) has shown that spermatozoa in vitro live longer in glucose solutions. Possibly the increased pH combined with lack of glycogen, causes the death of spermatozoa in vivo.

Heat Resistance of Spermatozoa

The scrotum has a definite temperature-regulating function as is evidenced by the fact that its temperature in man is 2.7 to 7.8 degrees below body temperature, according to Moench (67). He goes on to say that body temperature kills all spermatozoa in not more than forty-eight hours, but he wisely protects himself by stating that these observations are based on loss of motility not fertility. It is well that he did so, for Rea (79) reported two cases of bilateral cryptorchidism, which furnished at least presumptive evidence of absolute fertility because their wives

became pregnant. Rawling (77) found little if any impaired spermatogenesis in forty to fifty percent of bilateral cryptorchids up to thirty to forty years of age. Uffreduzzi (102) also reports cases, which tend to substantiate these facts. Spermatozoa withstand heat more effectively in strong alkaline buffering solutions with a lack of oxygen; these conditions prevail in the epididymis where the mature spermatozoa are stored. Of experimental interest is the work of Young (116) on guinea pigs. He passed water over the scrotum for thirty minutes, maintaining the temperature at 115 degrees. Examination showed that all germinal epithelium except some spermatogonium and cells of Sertoli were lost. Fertility was later regained.

Volume of Seminal Fluid

The volume is normally three to four cubic centimeters, but there may be several cubic centimeters more than this amount. If the volume is less than five tenths of a cubic centimeter, it is insufficient for the survival of the sperm in the vagina and for the formation of an adequate seminal pool near the external os (29). In order to be actively fertile a specimen must have a volume of at least two cubic centimeters (101).

Hydrogen Ion Concentration of Semen

Expressed in terms of pH, this is normally 7.7 to 8.5, according to Hotchkiss (29). Messer and Almquest (60) place the range from 7.0 to 8.0 with an average of 7.2 in sterile men. Because the values for sterile men are so near those for fertile men, their conclusion is that hydrogen ion concentration of the

very hot conditions for several hours continuously; he concluded that these men had no more tendency to be sterile than ordinary men. This does not coincide with work done on experimental animals, as discussed under heat resistance of spermatozoa. Constitutional factors have been discussed under that heading. In some cases gonorrhea may result in a depression of the spermatogenic function; the more common effect of this disease is one of occlusion of the ducts.

Permanently Damaged Testicles

In this instance, testicular function is entirely absent as far as spermatogenesis is concerned. The damage may be due to disease, injury, or atrophy.

Disease: Mumps followed by orchitis is altogether too frequently a cause of permanent damage to the seminiferous tubules (115)(101); where this condition is bilateral, ninety percent of the cases become sterile (58). Testicular tumors, teratoma and seminoma, usually result in sterility. The ravages of local tertiary syphilis are irreparable in some cases. Bilateral tuberculosis is also a causative factor.

Injury: Operation for the repair of bilateral hydrocele, varicocele, or hernia may leave a damaged testicle (37). In one series of herniorrhaphy cases, six percent had post-operative swelling of the testicle on the operated side (13). This swelling probably indicates injury to the blood vessels of the spermatic cord; permanent damage, thus, may result from disturbances of testicular nutrition. Excessive x-radiation over the testicles

will also cause azoospermia. Some individuals are very sensitive to small doses of x-ray; at times even the protective devices used in this region are of no avail (31). Because x-rays first inhibit spermatogenesis without destruction, function is sometimes regained in these testes. Lastly, there are those obvious gross injuries, which need no discussion.

Atrophy: This condition is found in the seminiferous tubules as the normal accompaniment to approaching old age. This, of course, is a gradual process, which has its onset at about the age of thirty-three years (98). If the process has a premature onset, it may be due to endocrinopathies, diseases, or injuries.

Obstructions in the Male Genital Tract

Obstructions may be complete or incomplete, unilateral or bilateral, but in order to produce sterility, the obstructions must be bilateral and fairly complete. These obstructions may occur at most any point along the duct system.

Epididymis: Azoospermia may be due to luetic epididymitis (82). Gonorrhea causes post-inflammatory occlusion more frequently at this point than at any other point in the genital tract (30). The testes may function normally, in spite of bilateral gonorrheal lesions, producing azoospermia. In tuberculous epididymitis azoospermia may be the first apparent sign. Thickening of the epididymis may occur as the result of varicoceles (115).

Vas deferens: There may be bilateral obstruction of the vas deferens due to tuberculosis, syphilis, or gonorrhea. The vas

which the seminal fluid is passed into the bladder, is produced (113).

Obstruction of the passageways may follow a focal infection from an influenza or bronchopneumonia (113).

Hostility of the Prostatovesicular Secretions

It was formerly believed that the seminal vesicles were reservoirs for the spermatozoa, but it is now known that these are the graveyard of the spermatozoa (67); just why this is true the author does not make clear. A normal seminal fluid is necessary to arouse the motility of the spermatozoa (18). There are chemical, bacterial, and mechanical types of hostility.

Chemical: Various types of drugs, poisons, and toxins may be found in these secretions. These factors and the influence of pH changes have already been discussed under constitutional factors and semen, respectively.

Bacterial: Huhner (30) made valuable studies concerning the effects of the gonococcus on fertility. He placed spermatozoa and virulent gonorrheal pus together on a slide; the motility of the spermatozoa remained unaffected. From a clinical viewpoint he sites the mary instances, in which gonorrheal couples succeed in producing conception. Various types of non-specific prostatitis have no direct effect on the spermatozoa, although experimental evidence occasionally shows spermatozoa to be agglutinated by bacterial toxins, especially those produced by special strains of colon bacilli (83); Moench (67) states that colon bacilli do not agglutinate spermatozoa. Vose (103) placed normal spermatozoa in

infected seminal fluid with its poor spermatozoa from men with non-specific prostatovesiculitis; the normal spermatozoa remained unaffected. The conclusion is that the damaged cells already in the fluid are a result of some other factor, testicular or constitutional.

Mechanical: This type of hostility is the most common of the three types, and is concerned with excessively viscid prostatovesicular secretions. This increased viscosity is produced by chronic prostatovesicular infections or congestion. Congestion may come from certain types of exercise, such as horseback riding, but it is more often associated with abnormal sexual excitement; the latter may be due to excessive coital frequency, masturbation, or coitus reservatatus (58). Viscosity may also be increased, relatively by a decrease in mucolysin in the seminal fluid (103). Highly viscid seminal fluid interferes with spermatozoan motility.

Faulty Delivery and Reception

The seminal fluid may not be carried into the vagina due to incomplete coitus or absence of coitus. Even when coitus is complete, cervical insemination does not always occur; if the spermatozoa are not deposited on the cervix, the vaginal acidity may destroy them before the alkaline cervical haven is reached.

Faulty Delivery when Intercourse is Lacking or Incomplete

The method of coitus may be a factor (115). Meaker (58) lists a number of unusual malformations and deformities, which might rarely be factors; these tend to prevent access of the penis to

the vulva: excessive obesity, flexion ankylosis of the hips, and any large scrotal mass, such as hydrocele, hernia, or elephantiasis. Trauma, tumor, or inflammatory changes with scars may distort the penis, thereby, making intromission impossible. Impotence is also a factor here; impotence may be defined as a lack of power, which varies in degree from a condition, in which there is absolutely no manifestation of the physiologic function of erection to cases, in which the erection is partial but insufficient for copulation. In some instances erection is perfect, but of a transitory type, ejaculation occurring prematurely. Impotence may be a result of constitutional factors: endocrinopathy, traumatic shock, debilitating diseases, toxemias, and drugs (49). Injuries to the central nervous system by trauma, tumor, or syphilis may also cause impotence. Exhaustion of the sexual centers by excessive coitus may occur. Psychic impotence is a common disorder (26). It is dependent upon causes of a purely mental or moral character, the sexual organs, so far as can be determined by examination, being perfectly normal. Individuals suffering from this form of impotence usually are of a highly impressionable nervous temperament primarily. Some men in apparent good health find themselves unable to perform the act of copulation as a consequence of a lack of confidence due to recollection of early indiscretions and exaggerated estimates of their effects. Ignorance of sexual physiology often is the foundation for this form of impotence (49).

Faulty Delivery

Intercourse Complete but Cervical Insemination Lacking

Developmental deficiencies may play a part here; among these are hypospadias and epispadias (115). Impotence must also be listed here, for premature ejaculation may fail to inseminate the cervix even though deposition in the vagina takes place. Urethral stricture may cause retrograde ejaculation into the bladder of the male; at best the seminal fluid dribbles out, falling short of the cervix (113). Failure of cervical insemination may also result from removal of the prostate. This is due to a disturbance of the ejaculatory mechanism. Following prostatectomy, the ejaculatory ducts open into a relatively large cavity with non-contractile fibrous walls; in the normal urethra there is a more or less complete muscular tube which will carry the seminal fluid forward by a continuous wave of muscular contraction. The orgasm or ecstatic climax is present but the seminal discharge does not take place until the first micturation after coitus in these cases (24). In the treatment of Hirschprung's disease in children and other diseases lumbar sympathectomy is sometimes done (32); if the first lumbar sympathetic ganglia is removed, as has been done in the treatment of Hirschprung's disease, sterility results because of the fact that the ejaculatory mechanism is upset here also, and a seminal discharge does not take place (44). There may be an absence of seminal discharge as a result of an insensitive glans penis due to local or spinal cord injuries (18).

Faulty Reception with Intercourse Lacking or Incomplete

Here again various malformations and deformities may offer a mechanical obstruction to intercourse. Vulvar tumors, excessive obesity, and ankylosis of the hips may afford poor access to the vagina. A thick vaginal septum may make intromission mechanically impossible (93). Stenosis of the introitus (23), a small introitus, or a short anterior vaginal wall (36) may also result in difficult intromission. Other factors of this type are imperforate hymen, absent vagina, vaginal stenosis, or obliteration of the vaginal cavity by a hypertrophied cervix, prolapsed uterus, or pelvic mass (58)(36)(101). Kraurosis vulvae may also be a factor (8). A more common factor, dyspareunia, is a functional incapacity, usually accompanied by pain. This may have a psychic origin somewhat similar to that of psychic impotence in the male; this type has no local lesionsto account for the pain, and is manifested as vaginismus, a purely nervous phenomenon (97); a clumsy first attempt on the part of the male may furnish a real basis for fear of coitus on the part of the woman. Due to a lack of libido, the woman may not be able to relax for the occasion (115). Pain may be due to superficial local lesions. Certain urethral caruncles are very sensitive (8). Incompletely ruptured hymen, tender hymeneal remnants, ulcerations, fissures, abrasions, eczema vulvae, atrophic changes, and inflammation of any of the vulvar structures are also possibilities for the origin of pain (58). The extremely painful anal fissure is well known. A low pubic arch may cause pain during coitus by compression

of the sensitive urethra and clitoris. Internal pain may be felt during intercourse. All kinds of intrapelvic lesions come up for consideration here. During acute conditions, coitus is not ordinarily attempted anyhow. Chronic pelvic inflammatory disease, prolapsed ovaries, and retrodisplacements of the uterus when associated with either one of the former two factors, may cause internal pain. In the past, it has been believed that female orgasm was necessary for conception; this is, of course, not so (111).

Faulty Reception

Intercourse Complete but Cervical Insemination Lacking

Uterine displacements, flexions, and versions do not play as important a part in the etiology of sterility as has been thought, according to Stein (93). On the other hand, seventeen out of eighteen patients in one series of cases of primary sterility in the female became pregnant within three months after insertion of the Smith-Hodge pessary (27). The theory is that this pessary places the cervix in the correct position for insemination.

Acute anteflexion of the cervix is usually associated with hypoplasia, and indicates that ovarian function is primarily at fault (93). The uterus may beso acutely flexed that the external os is covered by the anterior vaginal wall; this is due to shortness of the anterior cervical attachments associated with shortness of the uterosacral ligaments. If the cervix is elongated as is the case in genital hypoplasia, ejaculation will take place posterior to the cervix; descent of the uterus due to relaxed ligaments will have the same effect. Retroversion of the uterus

without retroflexion places the external os against the anterior vaginal wall; this is usually a result of relaxation of the uterine ligaments, following childbirth, and may result in secondary sterility; however the ligamentsin some instances are congenitally relaxed. An eccentrically placed external os may make insemination of the os more difficult. (7).

Failure of Cervical Insemination due to Mutual Maladjustments

If the penis is relatively long, and the vagina is relatively short, ejaculation into the posterior fornix may occur. If a relatively short penis and long vagina co-exist, ejaculation may fall short of the external os.

Vaginal Conditions Influencing Fertility

The vaginal fluid normally has a volume of less than one-half cubic centimeter; the normal pH range is 4.0 to 5.0, according to Lissimore and Currie (47) and 3.6 to 4.5, according to Williams (109). Mild vaginal acidity has little or nothing to do with production of infertility (86). Moench (62) found that vaginal acidity seldom exceeds that of five tenths percent lactic acid, and that spermatozoa will remain motile for hoursin acid of this strength. The finding of motile spermatozoa in the vagina several daysafter intercourse coincides with this(12)(88). Williams (109) states that the early death of spermatozoa in the vagina is normal. Occasional cases of excessive vaginal acidity may cause sterility (59). This acidity may be increased by the use of acid lubricating jellies during intercourse (99). Mild inflammatory conditions as a result of trichomonas, monilia, or bacterial

Cervical Secretions and Infertility

This seems to be an important factor in the etiology of sterility. Abnormal changes of these secretionsare essentially of three types: bacterial, chemical, and mechanical. In my opinion, the spermatoxins, if there are such, should be included under chemical changes.

Chemical factors: The chief point to be made here is pH. Normal pH varies over a range of 8.0 to 9.0 (59) or 9.0 to 9.6 (61). Meaker and Glaser (59) state that cervical reaction is not notably changed by age, parity, menstrual cycle, endocervicitis, or cervical mucus viscosity; Miller and Kurzrok (61) state that the cervical mucus may become acid during endocervicitis, and repel the spermatozoa. Mazer, Israel, and Charny (55) state they have never seen cervical mucus below an alkalinity of pH 7.5; thus the hydrogen ion concentration is never great enough to kill the spermatozoa, but it may become sufficient to upset the mechanism of orientation. The reaction may be less alkaline in cases of pelvic organ hypoplasia (59). Laffont (43) believes an excess alkalinity of the cervical secretions may cause sterility. It is known that a highly alkaline environment will inhibit spermatozoan motility.

Spermatoxins are of interest although there is no definite proof of their existence in the human being (58). McCartney (56) injected rat spermatozoa subcutaneously into female rats; sterility resulted, lasting for two to twenty-two weeks. The sterility was due to certain substances in the uterine secretions, which

the mucopurulent material entangles and kills the spermatozoa by a purely mechanical action (30). The secretions may become mucopurulent due to lacerations, eversions, or erosions with infection (41). Experiments, in vivo, have shown that spermatozoa will readily penetrate normal cervical mucus; if the cervical mucus is very thick and viscous, the spermatozoa in proximity to it will neither accumulate at its boundary nor attempt to penetrate the mass; there is also a lack of the orientation seen with normal mucus (61). Thus, a thick impenetrable plug may form in the cervix and prevent passage of the spermatozoa. There are several conditions, which alone or in combination may favor the formation of such a plug of mucus: Poor drainage, infection, chronic passive congestion, endocrinopathy, or lack of libido. Poor drainage may be the result of the so-called pin-hole external os, which is usually associated with generalized hypoplasia of the pelvic organs (97); it is practically always found in nulliparae. Due to the lack of drainage the mucusin the cervical canal gradually becomes thicker through inspissation. The lack of good drainage tends to promote infection of the cervical glands; the infection, in turn, perverts the activity of these glands, causing the production of a more viscous mucus. Chronic passive congestion also seems to produce an abnormal function of these glands, perhaps by disturbing their nutrition; the congestion may be produced by constipation, a retroverted uterus, pelvic tumors, or unrelieved sexual excitement. It has been shown that cervical secretions are increased by the administration of estrogenic substances (104);

hence decreased estrogen may result in a lack of the secretion; the mucus may then accumulate in the cervical canal due to an absent or poor flushing of the canal. With a lack of libido there may be but little cervical secretion produced during intercourse; hence the flushing effect will be deficient here also.

Uterine Obstructions

Under this heading only those conditions which might impede the progress of the spermatozoa in their ascent will be discussed.

Cervical Factors

Etiologic factors at this point are quite important. The external os may be of the pin-hole type (97), or the entire cervical canal may be stenosed (23); what degree of stenosis must be present before passage of the spermatozoa is prohibited, is difficult to determine. However, that this is a factor, is shown by the fact that some infertile women become pregnant after dilatation of the cervical canal (57). In a report by Birnberg (7) it seems that any deviation or lack of straightness of the cervical canal may be a factor in sterility; The cervix may be flexed upon itself, or the canal may be crooked without change in the axis of the cervical wall; this condition may be associated with an eccentric external os. The cervical plug of mucus has already been discussed under the subject of cervical secretion. Cervical polyps may occlude the cervical canal (23). Cervical fibroids and other tumors may block the canal by compression. The cervix as well as the fundus may be absent congenitally or as a result of operative procedure.

Fundus Factors

These factors are even more difficult to determine and to evaluate. A number of factors, formerly considered important, are now somewhat discredited. Various types of Mullerian duct fusion defects, such as septate, arcuate, bicornuate, and double uterus, are regarded by Stein (93) as causes of sterility; however, he does not state whether he thinks sterility is caused by obstruction of spermatozoan ascent or by defective implantation of the fertilized ovum. At any rate, Meaker (58) does not regard these fusion defects as factors in infertility. The effect of uterine fibroids on fertilitydepends to a large extent on their position and size. Of course, submucous fibroids are most apt to obstruct the lumen of the uterus; the obstruction may be due to the mass or a thickened, bleeding endometrium; interstial fibroids may enlarge sufficiently to have some effect, while subserous fibroids have practically no effect on the passage of spermatozoa through the uterus. Tumors of many types may obliterate the uterine lumen.

Flexion deformities of the fundus are not as important in themselves as the associated conditions. They may play a small role in the obstruction of the spermatozoan passage. Acutely anteflexed uteri are usually part of a general hypoplastic condition of the pelvic organs. Retroflexed uteri have their chief effect by causing kinking of the tubes, chronic congestion of the pelvic organs, and displacements of the cervix.

Foreign bodies should be mentioned here. The stem pessary might erroneously be considered as an impediment to the ascent of

the spermatozoa. It is more probable that they produce monthly abortions for the length of time that they remain in place (105).

Uterine spasm: In experimenting with strips of fresh uteri and seminal fluid, Kurzrok and Lieb (40) found the following facts. The same uterine muscle may contract under the influence of one semen, and relax under the influence of another semen. The same semen may cause one uterus to contract and another uterus to relax. Uteri from fertile women usually relaxed, while uteri from sterile women of long standing contracted in response to the seminal stimulation. Thus, it may not be going too far into the realm of fantasy to suggest that the latter type of uteri prevent spermatozoan ascent by going into spasm.

Tubal Obstruction

Tubal obstructions may be partial or complete. Obstructions here not only prevent ascent of the spermatozoa but also interfere with the descent of the ovum. Obstruction of the tubes is the most common single cause of sterility (51). A review of the known tubal physiology will throw some light on the present discussion. The tubes undergo a regular and rythmic contraction at a frequency of three to five per minute (19). Parker (74) has shown that the ciliated epithelial cells in the tubal mucosa waft the ovum downward, while the contractions in the tubes appear to force the spermatozoa upward. It is not inconceivable that an exaggeration of the upward-directed force may cause a relative sterility by opposing the descent of the ovum. It has been shown, conclusively, that after the menopause with the gradual cessation of production of

estrogenic hormone, there is a marked impairment in tubal contractility. Administration of estrin resulted in the development of rhythmic contraction waves of high amplitude , similar to those observed in normal females (22). It may be concluded from this that impairment of tubal contractility, due to estrin deficiency, may play a role in some form of tubal pregnancy or sterility (10). The tubes may also show muscle spasm (37)(36). It has been demonstrated by hysterosalpingography that such a condition is existent (35). McGoogan had three cases, in which tubal spasm was the cause of sterility (57).

Inflammatory factors: The most important disease in this group is beyond a question gonorrheal salpingitis, resulting in occlusion of the tubes (101)(97). Next in order of frequency is induced abortion. This emphatically includes the therapeutic type (85)(17). Disease involving the interstitial and isthmal portions of the tube often follows abortion, even of the spontaneous type, resulting in occlusion. Abortion with the use of iodine instillation has an even worse effect on fertility than does curettage (9). In certain cases of abortion there may be regurgitation of blood through the tubes onto the peritoneum, resulting in pelvic peritonitis and occlusion of the tubes due to adhesions. (10). Obstruction of the tubes may also follow puerperal infections and tuberculous salpingitis. Adhesions following mumps or scarlet fever may occlude the tubes (36). Ectopic pregnancy may destroy the tubes and cause adhesions (54). Chemical irritation of the pelvic peritoneum due to high pressure douches or even ordinary

ovary, across the relatively tractless wastes of the peritoneal cavity, and down the opposite tube. The physiological mechanism behind this long treke is not understood, but the entrance of the ovum into the tube is no mere accident.

Any upset in the delicate mechanism, which carries ova across this gap, will tend to result in sterility. Some of these upsets are: abnormal peritoneal folds, ovarian adhesions, and abnormal locations of the ovary (115).

Ovarian Dysfunction

The endocrine dysfunction of the ovaries has been discussed under the subject of constitutional factors. The other function of the ovary is ovulation; it is obviously difficult to determine absolutely the presence or absence of ovulation. But about four percent of sterile women may be considered habitually anovulatory, as shown by the condition of the endometrium (81). There are, however, a number of conditions, which undoubtedly have a profound influence on the development and production of ova. Gonorrhea may cause a thickening of the tunica albuginea, making rupture of the Graafian follicle impossible on a purely mechanical basis (97)(30). It is possible that the tunica albuginea may be thick and imperforate as a result of developmental faults; Sheldon (90) reported a case of primary sterility with a thick unscarred tunic. Gonorrhea, tuberculosis, and other infectious diseases may cause such conditions as ovarian abscesses, thus destroying the ovary (93)(8). Ovarian cysts may also cause destruction of ovarian tissue (8);

however, even bilateral cysts do not necessarily cause sterility, provided that there is a portion of healthy ovarian tissue present (97). Other types of tumors involving the ovaries may also cause sterility (115). Roentgen radiation in the region of the ovaries, if given in sufficient dosage, will result in sterility (34). Ovarian disturbances may be due to mumps and less frequently any one of the exanthematous diseases (58). Chronic passive congestion of the pelvic organs, including the ovaries, may interfere with proper nutrition of the follicles as well as compressing them through the medium of edema (115).

Atrophy of the ovary with increasing infertility is a normal process, taking place gradually in all women past the age of about twenty-six (98). This process may be hastened by any of the above local disorders or by constitutional disorders, discussed under that subject.

Hypoplasia of theovary is a condition, which is associated with hypoplasia of all of the generative organs. In this disturbance, the ovary has never attained the true adult type of development, and the case history presents some profound type of constitutional disturbance, taking place sometime before the onset of puberty. The patient recovers, apparently, but there is an upset in the endocrine system, resulting in faulty development of the genitalia.

Incidence of Etiologic Factors

A glance at the literature soon reveals that a case of sterility usually has a multiplicity of factors in the etiology (38). In about seventy percent of the cases Baron (5) states there is no single absolute cause of sterility. Sangree (86) reported an average of four and seven tenths factors in any given case of sterility, but there was usually one outstanding defect. Reports vary as to the degree to which each sex is at fault in the origin of sterility. The male is usually given the benefit of the doubt, being accredited with thirty to fifty percent of the responsibility.

A study of one hundred cases of sterile mating, made by Dr. L.S. McGoogan (57), revealed the following facts. Thirty-four of the cases had had previous pregnancies; these consisted of ectopic pregnancy in three, abortions in twenty, full term pregnancies in nine, and full term pregnancies and abortion in two cases. Criminal induction of abortion was admitted in eight of the twenty cases that had abortion only; of the eight just one subsequently became pregnant. Altogether, four of the full term cases and eight of the abortion cases, totaling twelve, became pregnant during or as a result of study or treatment. The remaining twenty-two cases did not become pregnant again.

Cervical Lesions: There was one cervical polyp; removal by cautery was followed by pregnancy. There were thirteen cases of cervical erosion; removal by cautery was followed by pregnancy in five of these cases; of the remaining eight cases, there were two

cases, in which there were male factors; in another case there was a male factor, and the women had a basal metabolic rate of minus fifteen; one case had salpingitis with a negative Rubin's test, and one had a dermoid cyst; the hypothyroid case and dermoid cyst were treated with thyroid and oophorectomy respectively, but to no avail.

Pelvic findings: There were nine cases of retroversion with retroflexion. Replacements were done in four cases, which then succeeded in producing pregnancy. Pregnancy in one case resulted after use of the fertility period. In four cases the only treatment was Rubin's test, following which pregnancy developed in two of the cases. There was one case with retroflexion and retroversion and erosion; pregnancy followed cauterization of the erosion. There were two cases of retroversion and retroflexion with stenosis of the cervix; in the other case, replacement and dilatation did not result in conception. There were seven cases of cervical stenosis alone; dilatation was done in six of these cases, and pregnancy followed in two; of the four cases in which pregnancy did not occur, one case had a negative Rubin's test. There was one case with cervical stenosis and peritonitis; this was treated with dilatation and use of stem pessary, but without results. There were two cases of fibromyoma; pregnancy followed myomyectomy in one case; the other woman had a basal metabolic rate of minus 30, and was treated with endocrines and X-Ray but without results. There was one uterus didelphus and one prolapsed uterus in which no pregnancies were forthcoming.

Hypothyroidism: There were five cases in the range from minus ten to minus thirty; two of these cases became pregnant. There were three cases in the range from minus five to minus ten; one of these became pregnant.

Patency of uterotubal tract: Rubin's test was done in eighty-one cases; it was found to be negative in eleven instances.

Male factors: These totaled fourteen. In three cases, pregnancy was evolved; in these the male factors were chronic prostatitis, hypogonadism, and a questionable hypogonadism, treated by massage, anterior pituitary-like substance, and nothing, respectively. Eleven cases could not produce pregnancy; seven of these had oligospermia, varying from five thousand to forty million; four had aspermia; of these there was one case of bilateral undescended testicles, one case with bilateral atrophic testes, one with bilateral gonorrheal epididymitis, and one bilateral atrophy of hypopituitary origin.

Pregnancy resulted in a total of forty-one of the cases; of the remaining fifty-nine, the etiology of the sterility was not definitely determined in thirty-four cases; pregnancy was apparently impossible in twenty-five cases. Of these twenty-five, eleven were due to the male factor, aspermia in four and oligospermia in seven cases. The female factors were responsible in fourteen cases out of the twenty-five. These consisted of post-abortal peritonitis three, chronic salpingitis two, ectopic pregnancy three, tubal spasm three, double uterus one, second degree prolapse one, and a fibroid with hyperplasia of the endometrium in one case.

In the forty-one cases, in which pregnancy was later accomplished, the following factors were present.

Male factors: Chronic prostatitis one, hypogonadism two cases.

Female factors: Retroversion and retroflexion three, cervical erosion six, cervical polyp one, cervical stenosis one, fibroid one. In twelve cases, pregnancy resulted after the use of Rubin's test. In four cases, endocrine therapy was followed by pregnancy; theelin and emmenin were used in two cases each. In one case the psychic factor of adoption seemed to result in pregnancy. In eight cases the causative factors were unknown.

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