Some etiological factors in sterility

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SOME ETIOLOGICAL FACTORS IN STERILITY

by

P. HAMILTON JENKINS

April 1932
Sterility is the inability to conceive or if conception does take place, the inability to give birth at term to a viable or living child. Synonymous with the term "sterility" are the terms "barrenness" and "infertility".

Prior to the consideration of Sterility, I shall present a sufficient outline of Embryology, Physiology, and Anatomy of the generative organs to show the normal development and function of this system; thus I shall lay a foundation for the discussion of the abnormalities and pathological processes of these organs in the production of Sterility.

Due to the close relationship in the embryological development of the male and female generative organs it will be convenient to consider their formation together.

In origin and development the ovaries and testes are identical. The urogenital fold is the anlage of the genital glands as well as the mesonephros. There is proliferation of the fold and it forms two parallel ridges extending the length of the coelomic cavity. Due to the construction of the mesonephric fold there is a fusion of the two genital folds to form a stalk. This mesenterial attachment extends lengthwise and forms, in the male, the mesorchium; in the female, the mesovarium. The mesonephric ducts with the degeneration of the mesonephroi become the primitive genital ducts. For a time both sexes have as a result of development a pair of female ducts. These are the Mullerian ducts and they form as thickened ventro-lateral grooves in the urogenital epithelium near the head ends of the mesonephroi. Near the tail ends of the mesonephroi there is a closing over to form tubes. Cranially however, it remains open as the funnel.
shaped ostium abdominale of the Mullerian ducts. The Mullerian ducts grow caudally to reach the urogenital sinus and open into it on its medial dorsal wall. At this stage there is as yet no differentiation of sexes. Arey (3).

Internal sexual transformations now occur and in male embryos of 13 mm., the genital glands show two characteristics that mark them as testes: (1) the occurrence of branched anastomosing cords of cells, the testes cords; (2) the occurrence between epithelium and testes cords of a layer of tissue, the anlage of the tunica albuginea. Arey (3). The testes cords round up and are marked off by connective tissue sheaths from the intermediate cords, columns of undifferentiated tissue lying between them. The testes cords are made up of indifferent cells and a few larger germ cells. The cells gradually group themselves radially about the connective tissue as a many celled epithelium. About the seventh month a lumen appears extending toward the rete testes to meet the lumen that has formed there. Arey (3). In this manner both tubes are connected, the distal ends of which go to form the convoluted tubules of the testes and the proximal ends remain straight and form the tubuli recti. This net work of tubules in the rete testes then unite with the efferent ductules. The intermediate cords disappear but the connective tissue sheaths unite with the tunica albuginea and extend to the mediastinum testis to give the septa that are present in the adult testes. The primordial germ cells present in the testes go to form the spermatogonia of the seminiferous tubules. The indifferent cells go to form the sustentacular cells of Sertoli, while the cells of the intermediate cords form the interstitial cells of the testes.

In the development of the female embryo the ovaries like the testes consists of an inner epithelial mass, but form more slowly. At about ten to eleven weeks there is a dense cortex formed and a clear medullary zone containing large germ cells. There is neither epithelial cords nor tunica albuginea at this stage as in
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the testes. Arey (3).

At a later period there follows the development from the hilus, an ingrowth of connective tissue and blood vessels which form the mediostinum and septula of the ovaries. The cells from the inner epithelial mass go to form the young ova and as will be pointed out, this process extends toward the periphery of the ovary. At four or five months the tunica albuginea develops as a peripheral zone around the ovary supposedly derived from the peritoneal layer of epithelial cells. This peripheral zone is a single layer of cells. Arey (3). When this new peripheral zone of cells is formed there is degeneration of the young ova of the medulla and a filling in with a stroma of fibrous connective tissue. Follicles develop late in fetal life as a result of the young ova being surrounded by cells of the cortex. These follicles at first primordial later develop into vascular follicles to be described at a later point in this paper.

We must now go back and pick up our thread where we left it at the indifferent stage and trace the development of the mesonephric tubules and ducts and the transformation of the Mullerian ducts. In the case of the mesonphros there is a gradual degeneration until in both the male and female embryos at 21 mm. [Arey (3)] there are only twenty six tubules which are separated into a caudal and caranial group.

In the male the lumina of the rete and the collecting tubules of the mesonphros are continuous. The caranial collecting tubules becoming the ductuli efferentes of the epididymis. At the fifth month (Arey (3)) the efferent ductules coil at their proximal ends and form the lobuli epididymidis. The lower group of collecting tubules persist as the paradidymis and ductuli abberantes. The efferent ducts convey spermatozoa from the testes to the mesonphric ducts which by this time are the male genital ducts. The caranial portion is coiled to form the ductus epididymis;
and its blind caranial end persists as the appendix epididymis. The caudal portion of the male duct remains straight and is known as the ductus deferens and ejaculatory duct. They extend from the epididymis to the urethra. As it opens into the latter it dilates to form the ampulla. The seminal vesicles are formed by evagination of the walls of the ampulla.

In the female the rete ovary is always vestigual but it joins with the mesonephric collecting tubules to form the epoophoron, a rudimentary structure of adult life. The paraoophoron is formed from the caudal portion of the collecting tubules. The rest of the mesonephric duct atrophies but some remnant of it may be found as Gartner's ducts of the epoophoron.

The female genital ducts are known embryologically as the Mullerian ducts. They follow the course of the mesonephric ducts lying at first lateral to them and then crossing over the mesonephric ducts to enter the genital cord on the medial side of the mesonephric ducts. According to Arey (3) in embryos of two months their caudal ends are dorsal to the urogenital sinus and extend as far as the Mullerian tubercle. This tubercle marks the site of the hymen in the adult. It is formed when the mesonephric duct enters the median dorsal wall of the urethra. Before the Mullerian ducts have entered the urethra and open into it, their caudal ends have fused and in both male and female embryos is the site of the anlage for the vagina and uterus. The paired Mullerian ducts at their caranial ends give rise to the uterine tubes and make a descent in the body cavity.

In the male the above structures degenerate, the vaginal portion remaining vestigual as the vagina masculina or prostatic utricle; and as was stated the extreme end of the Mullerian duct becomes the appendix testis.

In developing the vagina and uterus the Mullerian ducts at their caranial ends after fusion bulge outward and the middle portion is thus taken up into the
body of the uterus and aids in forming the fundus. The cervix and vagina arise from the original utero-vaginal anlage spoken of above. As the entrance of the vagina is still some distance from the urogenital sinus some elongation of both takes place and thus forms the vestibule into which vagina and urethra both open.

The lower limit of the vagina lies at the level of Mullerian tubercle where the utero-vaginal anlage enters the urogenital sinus. The tubercle is compressed as a disc lined on the inside with vaginal epithelium and on the outside by epithelium of the urogenital sinus or future vestibule.

This flattened knob lined on one side with vaginal epithelium and on the other side with urogenital epithelium and in the middle with mesenchyme is the hymen. The Mullerian tubercle in the male becomes the colliculus seminalis from the top of which the prostatic utricle forms. From Arey (3) we learn that at ten weeks the serosa, muscularis and mucosa are indicated. The first circular muscle fibers appear during the fifth month while the other fibres develop later. The epithelium of the uterine tubes and corpus remains simple; that of the cervix and vagina becomes stratified at nine weeks. The tubular glands of the corpus appear about the seventh month. The uterus shortens greatly at birth and does not regain this length until about the eleventh year. The vagina is for a time without a lumen, and solid epithelium fills its fornices. The vaginal lumen reappears in feti after five months through degeneration of the central epithelial cells.

It has been stated before that the gonads form from the genital groove; and as has been pointed out this structure extends from the diaphragm toward the pelvis. The growth is at the caudal end and for this reason there is a gradual moving downward in the body of the ovaries and testes. The atrophy of the caudinals ends and the growth of the caudal ends gives a wave like progress of these organs toward the pelvis but not an actual internal descent or mass movement. When the process of
growth and degeneration are complete the caudal ends of the testes lie at a point between the pelvis and abdomen; where as, the ovaries lie in the pelvis where they remain. In its descent the ovary rotates about its center as an axis and finally lies transversely in the pelvis. It further rotates thru a 180 degrees about the Mullerian duct as an axis and thus finally lies caudal to the uterine tube.

The first evidence of the preparation for the descent of the testes in the male is an outpocketing on the ventral aspect of the abdomen. These are the anlage of the vaginal sacs. The testes lie close to these and as the sacs emerge thru the inguinal ring and evaginate over the pubis the testicles descend along the same course due to the pull of the gubernaculum testes. There is shortening of the gubernaculum and a drawing downward of the testes into the scrotum which is usually accomplished sometime between the seventh and ninth months. The descending testicles take with them the layers of the abdomen thru which they pass and the tunica vaginalis of the testes is formed by the vaginal sacs becoming isolated from their peritoneal attachments. The canals that were formed by the descent of the testes are closed off and their epithelium absorbed with in a few months after birth. The ductus deferens, blood vessels and nerves descend with the testes and are surrounded with connective tissue and make up the spermatic cord.

In the female, shallow peritoneal pockets frequently exist as diverticula of Buck and correspond to the vaginal sacs of the male; and it has been known for a more or less complete ovary to descend into the labia majora. The interposition of the uterus between the ovarian and round ligaments is responsible for the re-tension of the ovaries within the abdomen. Arey (3)

From Williams (7) for the sake of summarizing I have included the following table.
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Indifferent embryonic type  Male  Female
Genital gland  Testes  Ovary
Mesonephros  Epididymis  Epoophoron
Mesonephric ducts  Vasa deferentia  Disappears
Mullerian ducts  Appendix of the testes  Fallopian tubes
Uterus and Vagina

Following the above discussion of the development of the internal sexual organs I shall give a little insight into the development of the external genitalia in order to clarify certain development anomalies that will later be referred to in the causation of sterility.

Taking the male first it is found early, ten weeks Arey (5), that the edges of the urethral groove progressively fold together thus converting the open urogenital sinus into the tubular urethra. The fused edges are represented by the median raphe. The scrotal swellings shift to their final position which is caudal from where they start and each makes up one half of the adult scrotum, separated from its fellow by the raphe and underlying scrotal septum. While this is going on, the shaft of the penis elongates and by the fourteenth week (Arey 3) the urethra has closed as far as the glans. This closing process continues and the urethra extends thru the glans by the glans rounding over it.

The frenum is formed by a part of the anal epithelium becoming attached just posterior to the glans and growing deep into the substance of the shaft. The attachment with the anus degenerates and the edge of the epithelium surrounds the glans to become the prepuce. The corpora cavernosa penis arise as paired mesenchymal columns while the corpora cavernosum urethra rises from the linking of similar unpaired anlages, one in the glans and the other in the shaft.

In the case of the female the changes are less profound and slower in development. The Phallus which is the genital tubercle, and elongates noticeably in the
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Male to give the shaft and glans of the penis, lags in development and becomes the clitoris with its glans and prepuce. The short urethra of the female never extends into glans as in the male, but remains open at the vestibule. The labia minora is made up by the urethra folds that grow along the side of the groove. The labio-scorotal swellings move caudad to fuse in front of the anus to form the posterior commissure, while the original lateral portions of the groove enlarge to form the labia majora. The structure so far forms a horseshow shaped rim opening toward the front. The mons pubis seems to develop independently and arises later. As in the case of the internal generative organs I will summarize the adult form with the indifferent stage for the sake of clarity. (Arey 3)

<table>
<thead>
<tr>
<th>Male</th>
<th>Indifferent stage</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Prostatic and membranous urethra</td>
<td>1. Urogenital sinus</td>
<td>1. Urethra and vestibule</td>
</tr>
<tr>
<td>2. Cavernous urethra</td>
<td></td>
<td>2. None</td>
</tr>
<tr>
<td>3. Prostatic gland</td>
<td></td>
<td>3. Paraurethral ducts</td>
</tr>
<tr>
<td>4. Bulbo urethra glands</td>
<td></td>
<td>4. Vestibular glands</td>
</tr>
<tr>
<td>5. Penis</td>
<td>5. Phallus</td>
<td>5. Clitoris</td>
</tr>
</tbody>
</table>

Having traced the embryological development of the generative systems of the male and female, I will consider the development from birth to puberty, and the normal physiological function of these organs at maturity.

At birth the boy and girl are quite similar but as the years go on they grow rapidly apart. The girl develops more rapidly mentally and physically. The
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Secondary sexual changes start manifesting themselves at eight to ten years in the case of the girl and a few years later in the case of the boy. The approximate age of fourteen marks the advent of puberty. DeLee (2), Arey (3). The changes during this period are much more rapid especially in the girl. The mother instinct develops and the whole sex life is more intense. She rapidly passes into womanhood both physically and psychically, as is shown by the appearance of secondary sex characteristics. There is general rounding out, the pelvis enlarges, and the breasts fill out and are more noticeable. The activity of the skin is increased and the subaceous glands pour out an excess of secretion often resulting in acne. The external genitals grow larger and darker while hair grows around the mons and under the arms.

In the case of the boy there is a deepening of the voice, a realization of sex instinct, and the appearance of hair on the chest, under the arms and around the pubis. There is noticeable increase in the size of the testes and penis with erection of the organ with no apparent cause. About this time nocturnal emissions occur.

This external change is but the manifestation of the internal glands of secretion. DeLee (2). The internal changes in the female are the lengthening of the vagina, the development of rugae, the elongation of the tubes, and signs of life in the ovaries shown by the development and consequent enlargement of the Graffian follicles.

The period of puberty is marked by the appearance of menstruation. This show of blood proves the functioning of the awakened ovary for ovulation has begun. DeLee (2), Arey (3).

Ovulation is the discharge of the ovum from its follicle. Arey (3). It signifies that the ovum is ripe and ready for the sperm cell or male element to couple with it and start the development of new individual.
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The ovary is almond shaped and is attached to the broad ligament by two bands of peritoneum into a cavity, Fossa Ovarica, on the posterior aspect of the broad ligament. The right is usually larger than the left and is more apt to become pathologically involved because of the close approximation of the appendix. The outer end of the ovary is attached to the fallopian tube by one of the fimbriated ends of the tubes.

The size of the ovaries vary in different individuals of different ages without any apparent relation to fertility. DeLee (2). The growth of the ovary from birth is dependent upon increase in connective tissue, blood vessels and upon the enlargement of the pre-existing primordial follicles. When menopause occurs, the ovary atrophies and may be found only as a small navy bean like structure.

The structure of the ovary from within outward is that of a stroma of white and elastic fibers and unstriped muscle fibers which are more dense at the hilus. These surround the lowest layer of ova which are the large ova in the process of ripening, and the next layer, the small unripe ova which are covered with a tough tunica albuginea. Surrounding the tunica albuginea is the germinal epithelium which is the germinal epithelium which is made up of low columnar epithelium and is without lustre.

The ova form very early in fetal life from the multiplication of the primordial germ cells within the ovary itself. According to Arey (3), at birth or shortly thereafter the ova cease to form. The number at this time is placed at 100,000 to 300,000. Cellular degeneration reduces this number until at eighteen years there are but 35,000 to 70,000, and several years after the menopause none are to be found. The ova develop in follicles which enclose the primordial germ cells as they approach the germinal epithelium. When the female reaches puberty the follicles ripen one at a time. During this ripening process there is an increase in size of the follicle due to rapid proliferation of the cells of the stratum granulosum.
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As this proliferation increases there is a liquid, liquor folliculi, that appears among the cells thus distending the follicle even more, causing the ova surrounded with its proliferating cells, discus proligerus, to be forced to the periphery of the follicle. While all this is going on, the follicle is growing larger and for this reason coming closer to the surface of the ovary. There is also increased blood supply to the ovary and a local congestion around the rapidly proliferating follicle. Now at a point nearest to the surface of the ovary there is a thinning and necrosis of the follicle and the ova with its surrounding cells is shot out of the follicle. This is ovulation. The ova is a cell and contains all the morphology of the cell. The final mature stage is reached when the cell has halved the number of chromosomes that are found in the primary oocytes of large ripening ova at the inner part of the ovary which is accomplished by cell division. When the follicle bursts the fluid gushes out carrying with it the ovum torn loose from its cumulus oophorus. The ovum is now swept into the tube by means of the inwardly stroking cilia of the tubal fimbriae. The ovum altho ready for fertilization is not technically speaking mature, for the last polar body division awaits the stimulus of fertilization. Arey (3).

After ovulation the empty follicle fills with a blood clot, the corpus hemorrhagicum, the cells of the stratum granulosum proliferate, enlarge and produce a yellow pigment. This structure then composed of connective tissue cells and lutein cells is called the corpus luteum. In the advent pregnancy does not take place the corpus luteum grows for two weeks and is then gradually replaced by fibrous tissue. The resultant silvery white scar is known as the corpus albicans. After several weeks, the site of the corpus luteum is represented only by a small retracted scar. According to Arey (3) "In pregnancy the corpus luteum verum continues its growth until, at the thirteenth week, it reaches its maximum diameter
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of 15 to 30 mm.; at term it is still a prominent structure in the ovary. The corpus luteum is believed to produce an important internal secretion, for if removed the ovum fails to attach to the wall of the uterus, or if the ovum is already imbedded, development ceases. (Fraenkel) An influence in retarding ovulation and stimulating the mammary gland function has also been shown experimentally (L. Loeb; O'Donaghue).

It is known that ovulation and menstruation start at puberty and for this reason the two must be related. It was supposed for a time that they were synchronous but this has been found not to be the case. Curtis (6) states as follows: "It is generally believed that ovulation occurs twelve to fourteen days previous to menstruation. Rather sharp unilateral pain lasting for a few minutes occurs in certain individuals at the time of the rupture of the follicle." Arey (3) states that "Ovulation occurs between the fourth and fourteenth day after the menstrual onset, while correct as a generalization, this correlation is not rigid and often ova are liberated at other times." This is shown by the fact that girls who have not yet started to menstruate sometimes become pregnant and women after the menopause are likewise impregnated.

Menstruation is the periodic flow from the vagina that occurs from puberty until menopause. According to DeLee (2) "The flow begins as a whitish discharge, but soon becomes bloody and contains red and white corpuscles, degenerated, ciliated, and columnar epithelium, vaginal and uterine secretions, and many microorganisms, some of them pathogenic."

The stages of menstruation are very aptly expressed by Curtis (6).

Post Menstrual Stage. The mucosa is low and tends to pallor. The glands are narrow and straight. Marked formation of new epithelial cells is noted.

Interval Stage. The cells become higher. The endometrium increases much in
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depth. The glands become tortuous. The connective tissue is loose meshed and contains many round cells.

Premenstrual Stage. There is a differentiation of the mucosa into compact and spongy layers, enlargement and marked tortuosity of the glands develops and decidua like changes are evident in the stroma cells. Some glandular secretions are present at this time.

Menstrual Stage. During this stage endometrium is cast off, the cells flatten, and the glands become less tortuous. Until relatively recent years most investigators have maintained that the endometrium remains almost intact during menstration; it is now recognized that there is a loss of practically all of the superficial layer and a considerable portion of the deeper spongy layer. The mucosa is shed in small particles, the individual cells of which retain their vitality to a varying degree. Regeneration occurs chiefly from the bases of the uterine glands.

The above stages are passed thru periodically in all women of the child bearing age, except in those cases where there is some pathological condition present or some congenital anomaly that would make it impossible to occur. The periodicity varies in different individuals. Figures from DeLee (2) show that 71% of women menstruate every twenty eight days; 2% every twenty one days; 14% every thirty days; 1% every twenty seven days and some healthy women flow every six weeks. Other variations than the above are pathological and are evidence of some genital disturbance or anomaly. The amount of flow is estimated at from 5 to 10 ounces. Curtis (6).

It is now necessary to mention some of the adult anatomy, function and uses of the adult sexual organs and the method by which conception takes place. Copulation is the act of union of the male and female. The result in some cases is that of conception; but this is, as is well observed, not always the case. It is not entirely necessary for the male organ to be introduced into the vagina of the female for
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conception to take place. The depositing of the semen by artificial methods (Davis 4) in the vagina will often accomplish the same results; and there are cases on record where young females with an intact hymen become pregnant.

In the male the penis is the organ of copulation and urination. We are primarily interested in the former function. The penis is made up of erectile tissue which is placed in three bodies, two corpora cavernosa and one corpus spongiosum. These are made up of fibrous tissue and contain many spaces which are called blood sinuses. The urethra passes thru these bodies and has numerous muciparous glands which open by means of ducts and are the follicles of Littre, crypts of Morgagnii and Cowpers glands. Taylor (8). Cowpers glands are located just behind the anterior layer of the triangular ligament and have ducts opening into the bulbus urethra; the other two sets of glands open into the penile portion of the urethra and they secrete a clear viscid mucus which is alkaline in reaction. The fluid is secreted more during sexual excitement and serves as a lubricant of the urethreal mucous membrane, and possibly (Taylor 8) serves to neutralize the acidity of the urine that remains in the urethra thus preventing destruction of the spermatozoa by this acid medium. Cowpers glands secrete copious amounts of secretion which make up the bulk of the seminal fluid during intercourse.

The prostate gland is an accessory sexual organ. It is glandular in structure, made up of three lobes, which are composed of fibrous connective tissue and unstriated muscle fibers and is located at the beginning of the male urethra surrounded by a dense fibrous connective tissue derived from the pelvic fascia. Cunningham (9). The gland is compound tubular in structure and opens into the urethra. The contents of the gland is squeezed out by the contraction of the unstriated muscle fibers during ejaculation. The ducts of the seminal vesicles pass thru the gland to open into the prostatic urethra, which goes thru the middle of the gland and is about an inch in length.
The seminal vesicles according to Taylor (8) "are two elongated and lobulated membranous pouches situated at the base of the bladder just beyond the prostate and in front of the rectum." The vesicles are about two and one half inches in length, while the ducts of the vesicles merge to form the ejaculatory duct entering the prostate to open into the prostatic urethra as before stated. The function of the seminal vesicles according to Taylor (8) is that of liberating large quantities of mucous during coitus which due to its volume and force carries along with it and dilutes the seminal fluid.

In close approximation to and joining with the first part of the duct of the seminal vesicles are the ampullated ends of the vas deferens. They have the same glandular histology as the seminal vesicles. Taylor (8). The testes and ampulla are connected by two long tubes called the vas deferens.

The next step in our development is the physiology of the sexual function in the male. During intercourse the penis must be in a state of erection which is brought about by the vaso-dilator action of the nervi erigentes (Taylor 8 and Lydström 10) which causes the corpus of the penis to become engorged with blood thus making it stiff.

The state of erection is brought about by psychic or tactile influences or a combination of both. The sexual center is located in the lower lumbar region of the spinal cord. Taylor (8) states that "This center is stimulated into functional activity by impressions or sensations which originate in the brain, and are transmitted through the pedunculi cerebri and the pons down to the spinal cord to it, and also by excitation and frictional influences, which are applied to some part of the penis." By these sensations the genital center is thrown into a condition of excitation which stimulate the nervi erigentes causing rigidity of the penis and activity of the accessory sexual organs. In the case of foreign contact with the
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penis the peripheral nerves are stimulated and the stimulus is transmitted back to the genital center by means of the sensory nerves. This causes the center to be further stimulated and this irritation is reflected back over the nervi erigentes to increase rigidity. It is quite obvious that anything but a healthy genital center would result in a block and a failure of erection and the proper normal sexual function.

Erection is maintained by the compression of the large longitudinal veins of the penis, by the increased amount of blood in the sinuses and by the direct action of the extrinsic muscles namely: (1) bulbo cavernous muscle, which compresses the bulb and dorsal vein of the penis; (2) erector penis and transverse perinei, which compresses the crus penis and slows down the return blood supply; (3) the levator ani, which also has a compressor action. Taylor (8).

Erection is culminated and a flacid condition of the penis results when ejaculation has taken place. During the time that the penis is in erection the testicles assume activity as is shown by their being drawn up close to the body by the action of the cremasteric muscles. The semen is then forced into the vas and carried to the ampulla by the contraction of the circular muscle fibers. At this time there is a strong contraction of the vesicles adding the vesicular fluid to the semen and forcing the whole quantity to the prostatic urethra, thru the ejaculotery ducts. While this has been going on the prostatic gland has been actively functioning and due to the strong contraction of the musculature of this gland the whole admixture is forced thru the prostatic urethra into the penile urethra where the circular muscle fibers of this structure with wave-like contractions aided by the contraction of the accelerator urinai muscle on the bulbus urethra; in this manner the entire quantity of semen thus far formed is forcibly shot along the urethra and out of the meatus.
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The semen is made up of the combined secretions of the testicles, seminal vesicles, prostate, Cowper's glands and the muciperous glands of the urethra. Microscopically, the sperm cells, seminal bodies and granules, some epithelial cells and crystals of phosphates are noted. Taylor (8). The chemical reaction of the semen is alkaline.

The sperm cells are the male element for reproduction and their maturation is essentially the same as the maturation of the ova which is by cell-division of the spermatogenic cells. The sperm cells when mature have an appearance similar to that of a tad-pole. They are composed of a head and tail, and have a wriggling like motion. There are from three to five hundred million in a single ejaculation. Macomber (11). The length varies from fifty to sixty mm., while the head varies from three to five mm. Taylor (8).

It should be remembered that the male is the aggressive partner of the sex act and that he has more or less continuous desire; and that, while the female can be aroused by proper stimulation on the part of the male, she normally has desire for the sex act only just before or just after her menstrual period. Gardner (12).

The female, when aroused, has much the same sensations as the male. There is an increased turgescence of the female generative organs, dilatation of the entroitus and an increase in secretion from Bartholins and Skenes glands and also from the cervical glands. The friction of the penis causes in the female the stimulation of the same nerve centers as described in the male. The clitoris becomes erect as does the penis in the male. The friction of the male penis against the clitoris stimulates the nerve endings lying in this organ, causing the woman to reach an extreme degree of excitement with the pouring out of secretions from her generative tract. According to Marshall (13) and Lydstron (10) the uterus has a peculiar behavior as it seems to descend down into the pelvis and assumes a more perpendicular position; then as the uterus becomes softer, the
labia of the uterus seem to alternately project and contract causing a sucking-like action.

The vaginal secretion is normally acid while the secretion from the cervix, uterus and tubes is normally alkaline.

Now assuming we have had a successful intercourse and ovulation has occurred and the sperm cell has met the ovum in the tube and fertilization has resulted. There remains now implantation of the fertilized ovum, which will be discussed only for the purpose of pointing out the possibility of failure to implant as a cause of sterility.

The uterine mucosa has been prepared for the reception of the ovum by the corpus luteum. The mucosa is thickened and more velvety in appearance. It is softer and the vascularity is much increased while the glands are filled with a thick clear mucous secretion. DeLee (2). He further states "that the condition of the ovum as it enters the uterine cavity is unknown; probably it is in the blastula or gastrula formation. The zona pellucida has disappeared, and with it the cells of the cumulus oophorus, the corona radiata." When the ovum reaches an optimum spot in the uterus, probably one without cilia (DeLee 2), the ectodermal covering of the ovum begins to eat into the epithelium due to the tryptic-like action of the surrounding cells of the fertilized ovum; and in this way the ovum arrives in the sub-epithelial layer of the uterus. By this tryptic action the ovum sinks to the compacta, while the opening thru which it passes, closes after it either by a mushroom-like cap or by the decidua and epithelium growing after it. The cells surrounding the developing ovum are called the trophectoderm and are the epithelial cells of the chorion. Trophectoderm erodes into other cells and provides the ovum with nourishment. The invasion of all surrounding cells including blood vessels soon causes the ovum covered with its cells to be bathed
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in blood which causes swelling of the cells and the formation of a monogeneous mass around them known as the syncytiun. As the ovum grows there follows a bulging into the uterine cavity. The cellular portion covering the developing ovum is called the decidua reflexa; that part on which the ovum rests is called the decidua basalis while all the rest lining the uterine cavity is called the decidua vera. We now have a growing individual who draws his food from the mother thru the cells of the trophoderm. The cells later become located on the basal side and form the placenta which is the future organ of food and respiration for the developing fetus.

The embryological development, anatomy and function of the sexual organs have been discussed. I shall now consider the subject of sterility.

At a glance then one sees sterility to exist as absolute and relative. By Absolute Sterility one has in mind a woman who has never borne children and never can. It exists of course where the uterus, tubes, or ovaries are not present either from a congenital anomaly or following operative removal. Further, occlusion of the tube thus preventing the sperm from meeting the ova or the ova from entering the tube would result in absolute sterility; and anything that interfered with the ova not being extruded from the ovary, as the accumulations of dense adhesions around the ovary, are of this class.

By Relative Sterility one has in mind a woman who has conceived but for one reason or another the child was not viable or the fetus suffered an early death. As is apparent these two types of sterility are more or less arbitrary and as cases go is not inclusive enough to include the whole situation. For this reason Child (1) saw fit to add a third division namely, that of Conditional Sterility in which class is to be included those cases that have given birth to children but for a time have been unable to become pregnant. This then as is seen is an acquired condition.
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I have taken from Child (1) the following detailed definitions of the types of sterility for they are clearly stated and are helpful in making a classification of the subject.

"Primary Sterility denotes that a woman, while living with a fertile man in her period of sexual maturity, has yet never been pregnant."

"Secondary Sterility indicates those cases where the woman has borne one or more children and becomes sterile thereafter."

"Congenital Sterility includes those women who, from the very beginning of their sexual life have had some condition responsible for sterility."

"Acquired Sterility implies that the woman was originally potentially fertile but later contracted some condition that caused her to become sterile. This division includes both primary and secondary sterility."

"Apparent Sterility also called Functional Sterility and Potential Sterility. In this group are placed those women who, owing to some prohibiting condition of their married life, have never had the proper chance to become pregnant."

As is noted then, absolute sterility is of primary, congenital and acquired type. It is necessary further to include those individuals who for no apparent reason cannot have children. This particular group will be called sex incompatibility and is quite theoretical and not well understood.

In defining the term sterility at the onset of this treatise I have led the reader to believe that the subject of sterility is confined alone to the woman. In former years this was the general opinion but medical science today considers the male just as important a factor as the female in the production of childless homes.

The definitions of sterility as applied to the male are:—

Absolute Sterility signifies a man who, while living with a fertile woman
has never impregnated her. It exists of course, where the testes, vas or penis is absent either from congenital anomalies or from operative removal for some pathological condition.

Relative Sterility signifies a male who, altho able to impregnate one fertile woman, is unable to impregnate another fertile woman.

Conditional Sterility denotes the state where a man while living with a fertile woman has impregnated her once but for one reason or another has been unable to do so again.

Primary Sterility denotes that a man while living with a fertile woman during his period of sexual fertility has never impregnated her.

Secondary Sterility indicates those cases where the man has impregnated a fertile woman one or more time but later is unable to impregnate her again.

Congenital Sterility includes those men who, from the very beginning of their sexual life have had some condition responsible for the sterility.

Acquired Sterility implies that the man was originally potentially fertile but later contracted some condition that caused him to become sterile. This division includes both primary and secondary sterility.

Apparent Sterility also called Functional Sterility and Potential Sterility. In this group are placed those men who owing to some prohibiting condition of their married life have never had a proper chance to impregnate a fertile woman.

Sterility is to be found more frequently among the well-to-do city folk where sexual excess, promiscuous intercourse, disease thus contracted and late marriage are more common among the poorer classes and the country folk where an active healthy life is lead and early marriages are the rule.

Tracing the history of the subject of sterility we find reference to woman alone. The first reference I found was from the Old Testament. Genesis 16:1 "Now Sarai,
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Abram's wife, bore him no children." 16:2 "And Sarai said unto Abram, Behold now, the Lord hath restrained me from bearing--"

Later in the works of Hippocrates - Volume I - Page 220 I find that he has certain standards by which a woman may be judged whether or not she may conceive. "Women may be judged whether they are in fit state for conception or not by attending to the following circumstances. In the first place to their shapes, women of smaller stature more readily conceive than taller persons; the thin than the fat; the white than the ruddy; the dark than the pale; those who have prominent veins than the contrary. In oldish women it is bad to have much flesh, but a good thing to have swelled and large breasts. In addition, inquiry should be made whether or not menstration be regular as to time and quantity. And it should be ascertained whether the uterus be healthy, of a dry temperament, and soft; neither in a state of reaction or prolapsus; and its mouth neither turned aside, nor too closed nor too open. When any of these obstructions come in the way, it is impossible that conception can take place."

"Such women as cannot conceive but appear green, without fever and the viscera is not faulty, these will say that the head is pained, that the menstral discharge is vitiated and irregular. But such of these as have the proper color, are of a fat habit of body, the veins are inconspicuous, they have no pains, and the meneses either never appear at all, or are scanty and intense, and this is one of the most difficult states of sterility to remove. In other cases the health is not to blame, but the fault lies in the position of the womb. The other contingencies in this place are attended with pain, discoloration and wasting."

"Ulceration of the womb from parturation, an abscess of chronic nature, or from other cause, is necessarily accompanied with fevers, buboes, and pains in the place; and if the lochial discharge be also suppressed, all these evils are more intense along with pain in the hypochondrium and head. And when the ulcer
heals the part is necessarily smoother and harder, and the woman is less adapted for conception. If, however, the ulceration be in the right side only, the woman may conceive of a female child, or if in the left side of a male. When a woman cannot conceive, and fever comes on with a slight cough, inquiry should be made whether she has any ulcer about the uterus, or any other of the complaints I have described; for if she has no complaint in that region to account for her loss of flesh and sterility it may be expected that she will have vomiting and the catamenia will be suppressed. But if the fever be carried off with the evacuation of blood, and if the catamenia appear, she will then prove with child. But if looseness of the bowels that have a bad character takes place before there is an evacuation of blood, there is danger less the woman perish before a vomiting of blood can take place." Thus we see that Hippocrates while not saying anything of the male, had quite an insight into the condition that result in sterility in the female.

The next reference obtained was from 1469 by Gronmatea Ferrori da Grado (died 1472) a professor of medicine at Pavia whose Practica (printed 1469-71) and Consilio, contained much original observations on sterility from displacement of the uterus.

The next references occur in the middle 1600 and I will refer to them as I take up the etiology of sterility under its various heads.

A consideration of the congenital absences or mal-formations of certain of the generative organs is now poignant; however it must be remembered that these conditions are not necessarily causes of sterility but may however have some bearing on it such as lowered fertility.

In the case of the female the absence of the ovary or a lobed ovary must be considered as causative factors of sterility. These cases, while not common
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have been known to occur. Arey (3). Further Arey states that "Rarely a more or less complete descent of the ovary into the labum majus occurs." Curtis (6) states that "absence of an ovary is usually associated with rudimentary horn of the uterus. Both ovaries may be present but may not develop." According to Arey (3) "Teratomata, peculiar tumor like growths occur rather frequently in the ovary, less often in the testis and other regions. The simpler types called dermoid cysts, contain such ectodermal derivatives as skin, hair, nails, teeth, and sebaceous glands. They grade into complexes consisting of organ-like masses from all three germ layers, intermingles without order. Missapen representatives of all tissues and organs may be present. Among other explanations of the cause, the isolation and subsequent faulty development of blastomeres has been advanced."

The tubes are subject to frequent abnormalities in development. These heretofore rare conditions are becoming more apparent as a result of the employment of air inflation at the time of abdominal operations for relief of various pathological conditions. This inflation of the tubes reveals frequent diverticula, trumpet shaped tubes, tubes with congenitally small lumen, constricting or deforming congenital bands analogous to Jackson's membranes and absence of one or both uterine tubes.

There are many cases of abnormal uteri and vagina. The more common of which are: (1) duplication of the uterus and vagina due to failure to fuse of the Mullerian ducts. (2) Uterus bicornis also due to incomplete fusion of the ducts. Combined with these defects, the lumen and the vaginal canal may not open to the exterior (Imperfect hymen). (3) The body of the uterus may remain flat or fail to grow to normal size (uterus fetalis or infantalis). Antiflexion of the uterus formally thought to be a cause of sterility due to the acute angle of the organ resulting in impossibility of conception, is now according to Curtis (6) known to indicate a persistence of an infantile type of uterus and this abnormality is the
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is the causative factor in sterility or lowered fertility.

Curtis (6) observes: Absence of the vagina is rare and when present is associated with undeveloped condition of the ovaries and tubes. Atresia of the vagina is more common and is the result of the failure of the Mullerian ducts to reach the surface. Stenosis occurs occasionally. This is a condition where the vagina is congenitally too small to admit the physiological dilator; and an other similar condition is constriction in the mid-third (hour glass contraction).

In the case of the male there maybe congenital absence of the testes or they maybe so poorly developed that function is not possible. At other times the testes may remain in the abdomen undescended, this condition is known as cryptorchism and is associated with sterility.

In many cases of malformation of the penis, coitus is impossible; in others intromission is interferred with; while in others fecundation cannot be accomplished because the opening of the urethra is misplaced so far backward that the semen is deposited outside the vagina. In this group are included absence of the penis, hypospadius and epispadias, abnormalities in size, and double penis. The man maybe potentially fertile due to the proper functioning of the testicles; but due to some impediment cannot engage in successful intercourse.

Congenital absence of the penis is rare but does occur according to Taylor (8)

Hypospadius results if the lips of the slit like urogenital opening on the under surface of the penis fail to fuse. Occasionally there is a similar condition on the upper surface of the penis and this is known as epispadius. This condition is usually associated with vesico-abdominal fissure. Of course it is obvious since the conditions maybe present in varying degrees that the degree of fertility would be dependent entirely on the location of the opening in the urethra; if far back near the base of the penis it would be difficult for fecundation to take place
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because of the chance of not getting the semen into the vagina, while on the other hand, if the opening was at the tip it probably would have little ill effect.

Taylor (8) mentions that torsion of the penis while rare does occur and is in association with hypospadius and epispadius. The penis is so twisted on its axis as to render insemination difficult due to misplacement of the urethral orifice.

There maybe variation in the size of the penis so as to render it impossible for proper sexual intercourse. For example, there are cases on record of the rudimentary penis so short as to be as of no value. Lydstron. (10)

The above survey covers the more common congenital anomalies and malformations of the male and female generative organs and while there are doubtless other ones these illustrations will suffice to point out the importance of a careful consideration of these possibilities as influencing fertility. It should be remembered that these congenital anomalies result in the type of sterility classified as Congenital Sterility.

I will now consider the extragenital factors that influence sterility in the human. The first of these will be the glands of internal secretion. It would be impossible to go into the subject any further than to indicate the various possibilities for it is too little understood by the leaders in endocrinology. From a recent paper by Dr. Riddle (20) who has made extensive research on the internal secretions in relation to reproduction, I learn that daily transplantation of anterior lobes of pituitary into infanticile mice and rats effects a definite premature sexual function in them. With this statement in mind, Riddle (20), takes issue with investigators who give ovarian or follicular hormone for resultant sexual maturity, stating that ovarian function is not induced by that hormone as it acts alone on the uterus, vagina and other accessory reproductive organs; but he says that a specific action, on both testes and ovaries is exercised in
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He further states that at the time the thymus is growing most rapidly the ovaries and testes are marked by an exceedingly slow rate of development while at the precise time the thymus begins to involute that the ovaries and testes strike up a new rate of development. And further that the thymus disappears before the first ovulation. Quoting Riddle (20) "The secretions of the anterior pituitary presses for early sexual maturity; a secretion or action of the thymus tends to push the time of beginning reproductive function to a later date. Here there is a reason for regarding the point or time at which maturity is actually attained as a resultant of these two forces." The anterior pituitary not only influences the first ovulation of life as pointed out above but also is probably influential in the re-occurring ovulations.

Meaker (19) considers, in view of the fact that growth and development are under the immediate control of the endocrine glands, that female genital hypoplasia is a result of the pathology of these glands. We can assume therefore that at puberty or during the adolescent years since the reproductive system is the only part of the body that is actively differentiating that it is at this time of life that there is a deficiency or increased activity of the glands of internal secretion. Meaker (19) gives the following figures in support of his theory that genital hypoplasia results in subnormal fertility which it necessarily induces. "In a consecutive series of fifty unmarried adult women, some degree of hypoplasia was observed five times. Of 100 wives whose marriages were sterile, forty-two were demonstrably hypoplastic. Among various women, on the other hand the condition is seldom seen." Meaker (19) agrees with Riddle (20) that the anterior pituitary is the gland most concerned with sexual maturity.

In Meaker (22) - "Discussion on Sterility" I find that besides those patients who have had endocrine failure at puberty with resultant under development of ovaries and testes that there are those patients who have endocrine failure starting in adult life causing suppression of sex cells or if they are produced they are of a
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lowered fertility.

From Curtis (6) we learn that deficient ovarian hormone is indicated by scanty and painful menstruation, lack of sex desire and sterility.

Removal of the anterior pituitary of animals results in general adiposity and atrophy of the genitalia. (Analogous observation of Riddle (2) and Meeker (19)). A corresponding picture is presented by Prolific's syndrome. (dystrophia-adiposogenitalis) in which there is excessive fat, amenorrhea, lack of sexual activity and sterility. Also in the later stages of acromelogy there is frequent amenorrhea, and this disease merges with a Prolific's syndrome.

Tumors of the adrenal cortex are causative factors in female genital hypoplasia with accentuation of the male characteristics. The amenorrhea of Addison's Disease is possibly the result of general constitutional weakness rather than the result of adrenal disease.

That there is a relationship between the thyroid and the genitalia is known but it is not too well understood. Menstrual disturbances occur with pathology of the gland and in the final stages of exophthalmic goitre amenorrhea is common.

Further knowledge of the influence of endocrine glands upon the reproductive system of the male and female is still a matter of research.

It has been maintained for sometime by many authorities that diet plays an important role in sterility and fertility and that certain diets, especially those rich in protein and calcium are markedly beneficial in producing fertility. This has been substantiated by Child (1) who bases his findings on the works of Reynolds and Macomber who state that in their experiments on rats they find:

(1) That a moderate decrease in the percentage of the fat soluble vitamine of the protein or of the calcium contained in an otherwise excellent diet produces a definite decrease in the fertility of individual rats.
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(2) That a slight decrease in the fertility of both partners will produce a sterile mating.

(3) That the fertility of the mating may be stated as the product of the fertility of the individuals concerned.

(4) That if the index so obtained falls below a given point the matings will be sterile, and that this result holds true whether the partners are of equal or of widely different fertility.

(5) That these principles explain the fact that two individuals which are sterile when mated together may nevertheless reproduce freely when mated to new partners (of higher fertility).

(6) That dietary deficiencies produce a lowered fertility which varies in degree with different individuals though of the same parentage and in the same cage.

(7) That diminished fertility sometimes results in the appearance of abortion.

(8) That mere percentage deficiency in both proteins and calcium produce visible ill health and great infertility.

According to Macomber (25) there is production of sterility by alteration in diet. This statement is supported by the analysis of diets of 206 sterile women which showed that these diets deviated in many important ways from normal, and that many of the women showed evidence of nutritional disturbance. Of the 206, forty have become pregnant to date after a correction of diet. The women were first seen two years ago and there is hope that it will not be long before many more of them will be pregnant.

It is also known that chronic intoxications and conditions of general debility are causative factors in sterility if not by themselves occupied with other causes.

Of the chronic intoxications, the most important are those resulting from focal infection. Weaker (24). The depressing influences of focal infections on
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the vital functions is evidenced by the fact that the basal metabolic rate is subnormal in most of these cases. Further, chronic intoxications lowering fertility may result in disturbances of digestion from poisons, such as alcohol, morphine, lead, and arsenic. Syphilis as a chronic intoxicant ranks high.

Conditions of general debility sometimes though not always result in lowered fertility, as seen in anemia, diabetes, tuberculosis or other diseases of a chronic wasting nature.

The types of sterility produced by extragenital disorders maybe Primary, Secondary, or Acquired Sterility.

The four main divisions of extra genital causes of sterility, endocrine gland disorders, nutritional disturbances, chronic intoxications and conditions of general debility, must necessarily now be followed by pathological conditions of the generative tract itself. While up to this time it has seemed advisable to consider the sexes together it now appears necessary to treat them separately. Taking the female first and starting with the vagina and proceeding upward to the ovaries, taking up the various conditions responsible for producing sterility.

It is obvious, of course, for proper fecundation to take place it is necessary for a successful insemination to occur. A condition rendering this impossible is that of Vaginismus. This condition was first described by Sims in 1860. The mechanism of it lies in the production of a nervous spasm of the leg muscles and the muscles around the vaginal orifice so that it is impossible for the penis to be introduced. The more persistent the attempt at entry the greater becomes the spasm.

Kraurosis Vulva, the shrinking of the skin of the vulva and peritoneum, atrophic in nature, and resulting in the cutaneous folds being obliterated, leaving the integument smooth, shiny, dry and glazed, renders intercourse impossible.
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Urethral caruncle and Vaginal cysts when present also lead to dyspareunia.

As was stated at an earlier place in the paper the vaginal secretion is acid, but from the work of Moench (27) we learn that the acidity is never more than .5% and that sperms live for hours in this degree of acidity and that further the alkalinity of the semen dilutes the acidity even more. With this in mind, one sees that vaginal acidity is pretty well ruled out as a cause of sterility; however, it seems to me that if the male was of lowered fertility and his sperms were not overly active or numerous that even this slight acidity might play some part in sterility.

A "Pin hole os" per se never causes sterility. Curtis (1). It is only when this small opening becomes plugged with mucus that sterility is a result. This becomes apparent as soon as one remembers that a pin hole os is never more than macroscopic while the sperm that is to pass thru it is microscopic.

Chronic cervicitis is only to be considered a cause of sterility when the amount of secretion poured out is of great enough quantity to form a continuous block of the cervical canal which even the strongest of spermatozoa can do no more than to spend themselves in an attempt to penetrate this barrier. In the majority of cases chronic cervicitis is a low grade inflammatory reaction confined to the cervical mucosa alone; but as is often the case, it may penetrate deeply into the tissue of the cervix itself. The causative organisms are gonococcus, staphylococcus, streptococcus and occasionally the colon bacillus. Under these conditions the cervical glands are in a state of hyperactivity and pour out great quantities of secretion which block the cervical canal. Laceration of the cervix, a causative factor of acute inflammatory disorders, if severe enough to render the complete closure of the os impossible takes away the normal support of the developing products of conception in the uterus and abortion will result.
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Unrepaired lacerations of the cervix are not only causes of habitual abortion but also the cause of inflammatory condition of the cervix and in these cases may render conception impossible.

Retro-displacements of the uterus are considered by some to be a cause of sterility because the unfavorable location of the os is not advantageous to insemination. According to Child (1) too many successful impregnations have resulted in the face of these displacements to prove this particular condition entirely causative in the production of sterility. Meaker (22) states that uterine displacement per se is not the cause of sterility; but that the congestion and inflammation of the adnexa in association with cervical displacement are the causative factors. In fact, Huhner (28) reports a case of retroversion where the cervix was pointed absolutely away from the seminal pool and yet the cervix was found to be swarming with live spermatozoa. The cause here later proved to be occluded tubes. Even tho these references indicate the fact that retroversion is not an absolute cause of sterility it must be borne in mind that the correction of retrodisplaced uteri will in some cases overcome barrenness.

In considering fibroids, I find there is much difference of opinions as to their importance as a cause of sterility. However, Child (1) states that fibroids play a part in about twenty to thirty per cent of all cases while in women who have borne one child the percentage is from twelve to fifteen per cent. To appreciate the etiological factor of fibroids it is well to recall that they are of various types, namely: Mural, Submucous, Subserous and Intra-uterine. The degree of fertility would depend upon their size and location. The submucous fibroid causes bleeding and a thickened endometrium with a tendency to check conception; and, if it does take place, abortion is apt to result. The intra mural fibroid causes mechanical deformities and displacements of the uterus with resultant miscarriage.
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The intra-uterine fibroid acts as a foreign body which causes the uterus to be in a constant state of contraction in an effort to expel it. It is not difficult to imagine the futility of implantation and retention of products of conception. The same thing is true of the intra-mural fibroid. The subserous fibroid while not especially active in causing sterility may certainly be a complicating factor in future delivery at term. The degree of fertility would be dependent on the severity of the condition resultant from the fibroid. Other new growth beside fibroids may affect sterility to a lesser or greater degree.

Subinvolution and superinvolution, resultant from a former pregnancy, cause certain changes within the uterus which are factors in chronic venous congestion exists which produces an increase in connective tissue in the uterine wall and a thickening or over growth of the endometrium known as hyperplasia. This renders the endometrium inhospitable to implantation while if it does take place it usually ends with abortion. In cases of long standing, impregnation becomes nil.

Superinvolution or puerperal atrophy of the uterus, a condition resultant of continued involution past a normal point, may be so severe as to cause thinning of the uterine wall with disappearance of the endometrium and resulting amenorrhea. Causative factors in the production of superinvolution are severe puerperal infections, and outside the puerperal state, conditions of myxedema, tuberculosis, Addison's disease, Grave's disease and in some people emotional upsets.

With the above mentioned uterine disorders it is logical to consider prolapsus uteri. This condition may not cause sterility, but if conception does take place, abortion is usually the rule.

There is voluminous literature on the subject of tubal occlusion, some of which I will attempt to summarize very briefly.

Tubal occlusion is the result of tubal inflammation which may be brought about
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by gonorrheal infection and by acute septic infections following abortion, miscarriage, or labor. In these the etiological factor is either the staphylococcus or streptococcus. A small percentage of closed tubes is the result of some outside involvement, such as the appendicitis or pelvic peritonitis resulting from postpartum infection.

It seems logical that a consideration of gonorrhea be inserted here. It is, I believe, known to all, the sources from which gonorrhea is acquired, the great antiquity of the affliction and the difficulty with which it is controlled. The chief characteristic of the disease is its chronicity and here in lies its importance in the production of sterility. Infections of the vulva, vagina, and urethra yield readily to treatment with no residual involvement but invasion of the cervix, body of the uterus or adnexa is quite another affair, and sterility is the rule in these cases rather than the exception. Infection of Bartholin's glands and Skene's glands are always chronic and result in sterility thru production of dyspareunia.

The gonococcus is a causative factor in from eighty to ninety per cent of the cases (Child 1) in the production of chronic endocervicitis which has been discussed at an earlier point in this paper as to its mechanisms in producing sterility.

Gonorrheal involvement of the uterus itself, usually takes place during menstrual period or shortly postpartum, but spontaneous resolution is the rule. However, with involvement of the metrium there is production of weakness and friability of the uterine wall. Gonorrhea in the tubes usually bilateral, although one may find the process more advanced in one tube than the other. As the infection invades the tube, congestion and edema become marked and rapidly spread thru the layers of the tube and as the inflammatory process proceeds toward the distal end of the tube the fimbria draw in and there is agglutination by the inflammatory process thus sealing the infection within the tube. Nature is usually successful and the process remains
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sealed off where it may absorb or go on to abscess formation.

Nature's success in the sealing of the tube is accomplished at the expense of the woman's fertility, for the tubal occlusion is the cause of absolute fertility.

Statistics from Child (1) show gonorrhea to be responsible for nearly fifty per cent of pelvic inflammatory processes in the female, and for twenty five per cent of the childless homes. Sixty to eighty per cent of abdominal operations for relief of pelvic disease in married women is the result of gonorrhea, while fully eighty per cent tho supposedly cured males suffering from gonorrhe at one time or another will show the evidence of the gonococcus in their semen.

In the case of acute infections resultant from abortion, miscarriage or labor the etiological organism is the staphylococcus or streptococcus and occasionally the colon bacillus. The mode of extension is along the birth canal mucosa with swelling congestion and sealing off of the fimbriated ends of the tubes. It is not sealed off nicely, as in gonorrhea, but is matted and densely adherent to adjacent structures. In still another class of cases of postpartum conditions the infection enters thru some abrasion in the birth canal and travels thru the lymphatics to produce a local pelvic peritonitis with resultant plastering and closing of the tubes by a plastic exudate.

It now seems logical to say something of the method of determining tubal occlusion. This test is called "Peruterine Tubal Insufflation" and was devised in November 1919 by I. C. Rubin. Carbon dioxide is forced thru the uterus from a gas tank with a pressure gauge attached to it; and the physician listens over the tubes with a stethoscope. When he hears air bubbling thru, he is aware the tube is patent. The pressure noted in a study of a group of 650 cases caused Rubin (29) to divide the cases into four groups.

1. The initial pressure rises to 60, 80 or 100 mm of mercury then drops 10 to
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30 points and remains between these levels as long as the air flows in and indicates a normal tube.

2. Initial pressure rises to 200 mm and remains so and indicates an occluded tube.

3. Initial pressure goes over a 100 mm and then gradually falls lower and indicates a stricture.

4. Initial pressure is over a 100 mm and even as high as 200 mm then drops more or less abruptly and indicates a spasm.

From Watkins (30) and Menn (30) we learn that the various sites of occlusion and the percentage of occurrence are as follows: (These determinations were found from injected specimens.)

Intro-mural portion: - The constriction varied from a narrowing to a complete closure. Of the forty-nine tubes studied thirty percent were completely closed while twenty-two percent narrowed.

Isthmian portion: - Occlusions were complete or incomplete and forty per cent were closed while thirty percent were narrowed.

Amputar portion: - As a rule dilated, possibly due to chronic inflammation.

Fimbriated end was closed in thirty eight per cent of the forty nine cases studied.

Dickinson (31) in a sequence of 362 sterile women found a history of appendicitis in 16.3% while Cary (31) found in 410 cases a history of 15.7% and according to them salpingitis takes the lead with 35% occurrence in causing sterility in women.

The next generative organ of the female to be considered is the ovary, and aside from the congenital anomalies and malformation we have the following conditions to consider. Malignancy of the ovary which of course results in absolute
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sterility. Aside from these conditions one frequently finds an ovary completely surrounded by dense adhesions rendering it impossible for the ova to escape, or the ovary may be cystically enlarged with a thickened cortex that shows no evidence of scars of previously ruptured Graffian follicles. In the former case the condition is a result of some pelvic inflammatory process with adhesion formation and possibly an involved and occluded tube. In the later the process affects the ovary alone and seldom the tubes. The thickening of the cortex renders it impossible for the ova to get out and the follicle remains unruptured, the secretion goes on forming, thus producing a cyst. Other follicles do not rupture and the ovary becomes multiple cystic. This condition causes lowered resistance, with resultant inflammation and the ovary becomes many times normal size. The process maybe bilateral or unilateral and if it is unilateral it need not necessarily cause sterility.

The pathological conditions of the male generative organs will be considered from much the same angle as in the female. I will start with the external member and proceed inwardly, merely mentioning the conditions that will cause the individual to be a partner in a childless home. Either because he cannot produce live male elements; or if he can produce them, they cannot be liberated; or possibly, due to some pathological condition, he cannot engage in successful intercourse.

The following conditions are exceedingly rare and are only mentioned to make the etiological factors of sterility in the male more complete.

The first group to be considered will be Sterility resultant from destruction of the integumentum of the penis, either from granulomatous processes, benign or malignant new growths, or preputial calculi.

The integumentum of the penis may be so destroyed thru disease or trauma that
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that when healing occurs the organ is so twisted or contracted as to render it useless sexually. Some of the granulomatous processes are chancroidal ulceration Taylor (8) and Phagedena in syphilis, which usually attacks the glans or prepuce. Under the classes of trauma are Amputation by jealous women or males, Lydstron (10) and severe burns. Under vegetations of the penis which render it incapable of functioning principally because of the large size or scarring are papillary new growth. These may develop in the mucosa as result of irritating secretions or as a result of Chancroid or Chancre. Taylor (8) states that they appear as little redspots which soon develop into papular formations and are cauliflower like. They maybe rounded and sessile, pedunculated, or Indian club shaped. Warts may form and grow to such size as to render the organ incapable of normal function, but the prognosis is usually good. Among the new growths Taylor (8) mentions a rare condition of horns of the penis. Still another is elephantiasis of the penis and scrotum and the picture of such cases are fairly familiar to the minds of all. Then of course there is cancer of the penis, while usually a disease of advanced age, may occur at twenty-five to fifty. Taylor (8). I feel that it is unnecessary to go into the process of development; and the outcome is quite obvious if condition is not taken care of.

Preputial Calculi most commonly found in China, when well advanced, hinders intercourse. There maybe several of these calculi in the sac of the prepuce.

Other involvements of the penis causing sterility will include degenerative, hyperplastic, and traumatic changes affecting the corpora cavernosa.

A rare condition is ossification of the penis and is usually incident to middle age. The sheaths of the corpora cavernosa are involved in this calcifying process. The onset is insidious and without pain. It causes curvature of the organ and this is usually the thing that brings the patient to the doctor. There
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are several cases on record as Taylor states.

The condition known as fibrous sclerosis of the corpra cavernosa was formerly described by Lydstron (10) under the term Chronic Circumscribed Inflammation of the Corpra Cavernosa. Lydstron's term is a misnomer according to Taylor who states that no inflammatory process has been noted. There is pain on erection and an extreme degree of torsion of the penis rendering coitus impossible.

Syphilitic nodes in the Corpra Cavernosa and corpus spongiosum occur late in syphilis and are the formation of gummata thru out the organ. It is an exceedingly rare involvement. There chief outcome is that of fibrous formation with subsequent deformity. If seen early however, these need not occur.

Extreme curvature of the penis as the result of injury is merely mentioned here to make our etiological factors more complete. Fracture of the penis is quite an uncommon accident and usually occurs during intercourse, it maybe complete with fracture of both the corpra cavernosa and corpus spongiosum or incomplete when only one of the corpra is involved.

I will now consider some of the more relevant causes of sterility in the male. It is only within the last fifty years that sterility in the male has been carefully studied, and, as I have stated, it was assumed that as long as the male seemed well, sexually developed and could engage in the act without difficulty that he was fertile. As medical science was developed the semen was studied and the pathological involvements of the vas deferens, seminal vesicles and prostate were considered.

Then with the aid of the microscope examination was made to bear out the foretold results of pathology of these entities of fertility.

Two conditions were found to be the cause of sterility in the male, namely: Azoospermia, in which, altho the man could perform the act, his semen was infertile, for the reason that, (1), it was lacking in spermatozoa, (2) that these highly vitalized bodies were imperfect in development or (3) that they could not
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reach the sexual tract. The cause of this condition rests in the structural changes in the testes or epididymis by which secretory function was lost, impaired, or possibly an impediment to its outlet existed.

The second condition is that of aspermatism in which there is ability for normal coitus; but there is either (1) no ejaculation of semen, or (2) the quantity is insufficient; or (3) the emission is imperfect or impeded. This condition is the result of block some place between the vesicles and the meatus. Taylor (8).

Azoospermia results from gonorrheal inflammation and syphilis, chronic testicular involvement of nonveneral origin, impairment of the testicular function by hydrocoele or hematocoele, and tuberculosis of the testes or adjacent organs. While it may be bilateral it may also be unilateral and remains as a threat to a man’s verity.

One must recall first, the congenital misplaced or ectopic testes. It is evident that abnormal positions of the testes are associated with sterility in the male. Changes in the epididymis, testes and vas deferens due to gonorrhea are potent causative factors in sterility. Gonorrhea usually attacks the lower part of the epididymis and gives rise to an indurated mass that obliterates the canal of the vas or epididymis. It is obvious in the face of the many convolutions present here that there is much room for residual connective tissue stenosis occurring and thus preventing the sperm from leaving the testes. It is usually quite difficult to locate the seat of trouble as there is very little change evidenced in the testicular substance but there are changes in the seminal fluid that are hostile to the sperm. The prognosis is usually good.

Gonorrheal deferentitis is involvement of the vas deferens with resultant blocking of the vas, thus preventing the sperm from entering the tract.
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Changes in the epididymis testes, and vas deferens due to syphilis involve the globus major where swelling of an indolent nature occurs that may cause sufficient tissue change to block this portion as an outlet to the sperm cells.

Syphilitic orchitis attacks the testes with a slow insidious fibrous or gummatous infiltration causing uniform swelling which results in destruction of the power to form spermatozoa.

Syphilitic deferentitis or involvement of the vas deferens is rare, but does occur, and if left untreated results in occlusion of the vas.

Chronic orchitis or epididymitis often follow gonorrhea, due to the spread of infection to this region with swelling and destruction of interstitial tissue in such quantities as to make further testicular function impossible. They occur in cases of stricture of long standing, prostatitis and cystitis where much manipulation is necessary for a long period of time.

Orchitis and epididymia-orchitis due to general infective processes is usually unilateral but occasionally both glands are involved. I will but mention the conditions in which orchitis has been known to occur. The one of most importance is that of mumps, the others are tonsilitis, variola, scarletina, malaria, grippe and further occasionally during whooping cough, pneumonia, typhoid and grave inflammation of the bone.

Orchitis due to muscular effort is but moderately common and probably is dependent on the fact that the contraction of the abdominal muscles on the spermatic plexes of veins causes injury to them with resultant congestion and induration with subsequent inflammation. The prognosis is good.

The part hydrocele plays is that of producing pressure so as to cause congestion and resultant inflammation with destruction of testicular substance. The same may be said of hematocele.
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Tuberculosis of the testes is one of the most common causes of testicular damage with resultant production of sterility. The age of occurrence is usually at puberty or in early adult life. I feel that little need be said about this condition other than to mention that testicular involvement is usually secondary to some lesion someplace else in the body and that the tuberculosis is probably borne to the testicle by the blood stream.

Having considered the pathological conditions and causes of involvement of the organs of generation, it is now well to consider sterility as resulting from the abnormal conditions of the products of these glands. By this I mean abnormalities of the semen. The number, strength and size of the spermatozoa varies directly with the general physical condition of the man. Taylor (8).

According to Taylor (8), Lydston (10), Macomber (11), Huhner (23) and others it is a known fact that after excessive intercourse over long periods of time the semen may be free from spermatozoa. Any morbid condition which interferes with the normal reaction or integrity of the prostatic secretion is apt to alter the spermatozoa so as to render them infertile. Conditions causing changes in the secretion are Posterior urethritis of venereal and non-venereal origin, Macomber (11), and chronic inflammation of the prostatic tubes. Considered of the same class are plugging of the prostatic ducts with concretions, destruction of the gland by gonorrheal abscess, and the submucous infiltration from chronic posterior urethritis, which so scleroses the tissues as to render the ducts no longer patent. The condition of these organs is brought about by the congestive reaction resultant of gonorrhea, sexual excess, masturbation and failure of sexual satisfaction. Pus as is present in gonorrhea of the urethra does not seem to be compatible to the sperm cell, as they are usually lifeless under these conditions.

General morbid conditions of the body as has been previously stated seems to
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be an important factor in producing sterility. This is due in the case of the male to the general body debility with a failure to produce strong vigorous sperm cells and these weak one quickly succumb due to the toxin produced by the process or because of lesions that are located in the generative tract concurrent with general debility.

Watery semen and colloidal semen is symptomatic evidence of pathology in the ampullations of the seminal vesicles, in the prostate or testes. And in view of the preceding statement it is quite clear that any derangement of the normal substance of these organs would of necessity impair the function of them.

The second condition causing sterility is aspermatism and is meant to indicate those individuals who have the power of performing coitus but fail to ejaculate any semen; and also there is impediment, defective, or imperfect ejaculation. This is a rarer condition than the former and the lesion is usually located between the ampullations of the seminal vesicles and the meatus of the penis. The cause is usually stenosis or destruction of the continuity of the above portions of the genital tract so that rhythmic contractions are so interfered with as to impede the outcoming semen. The condition maybe absolute and permanent or temporary and relative.

Lesions of the seminal vesicles and deferential ampullations which are fistulas are so rare (state Taylor) that they would be looked upon as curiosities.

There are many lesions that occur around the ejaculatory ducts. Plugging of the ducts are of those cases mentioned by Taylor (8). These may be due to concretions or fibrous adhesions resulting from some pathological process at this point. Pain and swelling is the usual symptom and sign found. Gonorrhea is usually the offending agent. In cases of trauma as result of passing sounds the ducts may be so compressed or there position so changed as to render them useless.
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Stricture of the urethra and urethral calculi are also causes of aspermatic and the mere mention of the pathological condition makes it at once clear how the semen maybe prevented from being ejaculated.

Before passing from the pathology of the generative tract producing sterility in the male it is essential that I mention chronic involvement of the prostate. This is undoubtedly one of the most frequent causes of sterility in the male. It is well known that gonorrhea is the most important etiological factor. Non-specific infections caused by streptococcus, staphylococcus and colon bacillus as well as irritation caused by trauma from injections, passing sounds, and other urological instruments, also cause prostitis. I do not feel that it is within the scope of this paper to go into the symptoms of the various conditions. Suffice it to mention the cause and the pathology that results in sterility. Prostatic involvement is usually congestive with a resultant inflammation in connective tissue formation, which results in stricture and plugging of the glandular substance cutting down its functional capacity to such an extent that it is practically without value sexually.

Another condition decidedly pathological is that of inflammation of the seminal vesicles. It is not so common and is the result of gonorrhea, masturbation, and sexual excess. Taylor (8). It may be acute or chronic and is usually accompanied by resolution rather than abscess formation.

I feel that I should say something here of the method of examining the semen but before I do this I would like to quote Macomber (11) "I wish to emphasize the importance and frequency of low fertility in the male and to urge the value of careful study in each case. Such a study must include a microscopic examination of the secretions and of the spermatozoa as well as palpation and inspection of the organs. It is to be supplemented by an exhaustive inquiry into the habits of
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the patient's life, with particular references to those of sex. It is only on the facts accumulated in this manner that a satisfactory opinion as to fertility and a rational plan of treatment can be outlined." If this were strictly adhered to I feel that many of the cases of sterility could be laid at the door of the male instead of being passed off on the female as was so commonly the case not so long ago. This coupled with a thorough examination of the female with the same degree of care would go a long way toward finding a cure for sterility. In examining the semen, the condom specimen is the usual method Moench (33), Macomber (34). Care bringing the sample to the physician must be observed so as to keep the specimen as near body temperature as possible. The specimen is examined under the microscope for motility and abnormal shapes of the spermatozoa, and the semen is examined for normal constituency as far as possible. If these findings are all normal it is safe to assume that the male is not at fault. Moench (33), believes that too much stress maybe laid on the motility and that there are other factors that should be considered. If the sample is repeatedly found to be immotile, then one can assume that the sperms are dead, but mere changes in motility is not enough to allow one to draw this conclusion. The sperm count as given by Macomber and Sanders (34), is as follows: A blood counting chamber is used and a white pipet which is filled to the .5 mark and diluted with a solution made up of 5% sodium bicarbonate plus 1% formalin. The number of cells are computed with this formula. Number of cells in the mm sq. times 10 (depth) times 20 (dilution) equals the number of cells per cu.mm., times 1000 equals the number of cells per cu. cm.. They state that low limits of fertility range from 60 million to 80 million sperms per cc.

The above data was taken from Taylor (3), Child (1), Lydstron (10), Macomber (34) Moench (35, 27), Huhner (28) and others listed in the bibliography. The
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direct quotations have the source following them. The rest of the material was so collected as to render it impossible to very accurately state the source.

I have yet to discuss and briefly so, some conditions that I did not feel could be fitted into my classification. I have called this group Miscellaneous; and it will cover such subjects as: sperm cell immunity, sexual incompatibility, relative fertility, psychic factors, the influence of X-Ray and radium exposure, and self-imposed sterility.

Moench (35) states that it seems little likely to him that the experiments carried out by some on animals producing in them a condition of immunity with sperm cell injections and used by these experimentors to explain those cases of so called unexplainable sterility in the human are true. He believe that a sperm immunity could only occur when excessive intercourse was indulged in over a long period of time; and that in the cases of sterility patients their lives are usually regulated as to frequency of intercourse. He does not find any case where the female blood serum was toxic to the sperm of the husband. While on the other hand, Jarcho (36) is quite enthusiastic about the process and states that while it is still in the experimental state the procedure shows great promise among experimental animals. How applicable it will be to the human remains to be seen.

Sexual incompatibility must be considered as a cause of sterility inasmuch as either partner of a sterile marriage may remarry and be productive with a second partner. Macomber (25). This is explained by his statement that two individuals of lowered fertility when mated with one of higher fertility than themselves will produce offspring. In this class maybe included the case of a fertile man who is successful in impregnating one fertile woman while he fails in the case of another fertile woman. The many theories given as causes of this type of sterility dispute one another and it would seem as yet that the true cause is not known.
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The next condition or conditions is that of psychic factors. The chief result here is impotence rather than any change in the male or female elements. The mechanism lies in the fact there is a block some place between the sexual center and the cerebral cortex so that erection and ejaculation is impossible. The psychical processes are usually emotional. The chief one being that the man fears he cannot prove himself potent. The majority of these patients are of the neurasthenic type, in whom sexual excess in the form of masturbation has robbed them of some of their vigor leaving them with the fear of failure when the final test comes. Further, the husband maybe fearful of impregnating his wife thus subjecting her to later suffering. Child (1). Many other emotions may be etiological in the condition and are apt to be, disgust, fear, and distrust. Such things as past experience, play an important factor too. Ex. Davis (4),

A young man had cohabited with a blond woman who had always insisted on being fully dressed. He had to always have a fully clothed blond for proper intercourse.

Another very important factor is that condition, while dating back into antiquity, but now becoming very prominent, of contraception in the production of self imposed sterility. As is often the case, people expect that after the stoppage of contraception but for a short time to become pregnant at once. It may take some time to re-establish the proper function again and to restore the vitality of the male before pregnancy may result.

And finally I will say something of x-ray. It is known too all the sterilizing effect of long exposure to x-ray. In small doses it may prove stimulating to the gonades but for the most part its use is rather restricted. In the case of long irradiations to the testicles there is apparently some change that takes place, for spermatozoa from these testicles while appearing normal in all ways, either fail to fertilize the ova or they produce monsters. See Dr. Moom.
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From the explanation of each enumerated type given, one can easily determine the class to which the case belongs. In the latter group; that of Pathology, the cases can either be Absolute or Relative depending upon the time when the Pathological condition rendered them sterile; before any conceptions, or after one or more. I am indebted to Mrs. McGoogan and Immert for the following cases that are illustrative of some of the cases of sterility whose etiological factors I have mentioned.

Case 1. Mrs. J. W. age 27, married three years and no children. The first year and a half the patient's husband used a condom. The last year and a half nothing was used; but the patient did not become pregnant. Menstrual History:--Patient started to flow at 14 years of age and flowed every twenty-eight days from four to six days. Has been having dysmenorrhea of increasing severity over a period of year before coming to the doctor. Physical Examination:--Entirely negative. Pelvic Examination:--A normal outlet and no evidence of cervical infection. The cervix was long and conical, the uterus was anteflexed but of normal size and shape and the adnexæ was palpable but normal. Laboratory:--Reaction of the vagina and cervix both acid. Husband's specimen showed about 80 million spermatozoa per cc. which were motile in a hanging drop for two hours and were normal in all other ways. Treatment:--Dilatation of the cervix which was found to be so stenosed as to render the passage of anything but a filiform bougie impossible. A stem pessary was inserted after dilatation and left in four weeks. The patient was instructed to take a soda bicarbonate douche before intercourse. The patient became pregnant one month following the removal of the pessary and was delivered of a full term baby. Diagnosis:--Congenital Stenosis of the cervix and acute anteflexion of the uterus.
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Case II. Male aged 29 admitted to the hospital complaining of sterility.

History: - At the age of fourteen while riding horse back he was thrown from the horse and fell astride a rail fence, suffering injury to his left testicle, which atrophied. At the age of eighteen he enlisted in the army where it was discovered that he had a right inguinal hernia which was repaired. Infection followed and necessitated a repeated repair. During his three years of active service he kept four mistresses and gained the reputation of being able without the use of contraceptives to cohabit with his partners without impregnating them. During this time he did not contract syphilis or gonorrhea. At the age of twenty-six he married and after two years of married life he was unable to impregnate his wife. Physical examination: - Patient normal but for scar in right inguinal region and atrophied left testicle. Diagnosis: - Atrophy of the left testicle and involvement of the right was so as to prevent spermatozoa from entering the urethra.

Treatment: - Both sides of the scrotum were opened and the left was found patent while the right was occluded by the scar in the right inguinal region. An anastomosis was made between the patent part of the left vas and right testicle. One week post-operative spermatozoa were found in the semen for the first time. Three months later his wife became pregnant.

Case III. Mrs. X ages 28 complained of lump in left groin and the inability to have children: History: - Menstrual started to flow at 16 and flowed three days every 28 days. Physical examination: - Presents of mass in upper left labia tenderness over appendix. Pelvic examination: - acute anteflexion of the uterus.

Treatment: - Repaired hernia, removal of the appendix, dilatation and stem pessary to cervix. Impregnation followed soon after the removal of the stem pessary. Apparently the cause here was the anteflexion of the uterus which was corrected by the pessary. Undoubtedly the dilatation of the cervix aided in the cure.
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Case IV. Mrs. MH. Aged 33, married two years without children. History:— Following operation for removal of fibroid from breast she noticed that she had prolonged menstration, increased leucorrheal discharge, back ache and pelvic pain. Physical examination:— A doughy sensation over the abdomen, a mass felt in the pelvis. Pelvic examination:— Cervix chronically inflamed. Treatment:— Dilatation and cauterization of the cervix. Removal of fibroid from anterior wall of the uterus, shortening of the anterior ligaments and removal of the appendix. Patient became pregnant in nine months.

Undoubtedly the chronic inflammation of the cervix acted as a plug to the cervical canal which coupled with the fibroid gives sufficient causes for sterility in this case.

CONCLUSIONS

(1) Both the male and female element must be considered in any given case of sterility.

(2) That there are many cases of sterility that remain unsolved etiologically and therapeutically.

(3) That gonorrhea with its resultant pathology is the greatest causitive factor in the production of sterility in both the male and female.

(4) That occlusion of the tubes in the female and orchitis in the male are the most common conditions rendering conception impossible.

(5) That psychological factors are thought by some to play a more important part in the causation of sterility than was formerly believed to be the case.

(6) That the use of contraceptives often leads individuals to believe that impregnation will occur immediately upon the discontinuance of their use.
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