CHAPTER XIII

MALFORMATIONS

The growth of an organ may be simply arrested or it may grow in the wrong way. In either case there results a malformation. Most genital deformities are due to partial arrest of development. To understand these malformations, it is necessary to understand something about the development of the organs.

POINTS IN DEVELOPMENT

The first structures indicative of the genitourinary organs are the **wolffian ducts,** which appear in the embryo about the fifteenth day, and the **wolffian bodies,** which appear on the eighteenth day. These structures represent the future kidneys and genital apparatus. They lie on each side of the median line.

During the fourth week another duct appears near the wolffian body on each side. These are the **muellerian ducts.** The wolffian ducts go to form the excretory ducts of the genital apparatus in the male. The muellerian ducts go to form the excretory ducts of the genital apparatus in the female. A part of the wolffian body of each side finally forms the genital gland of that side, i.e., the ovary in the female and the testicle in the male.

At the end of the first month the middle part of each wolffian body shows thickening and proliferation, resulting in the formation of elevated bands called "genital ridges." These are the earliest traces of the genital glands. For a few days they remain indifferent. Very soon, however, a difference in the two sexes is noticed. The primitive female gland "possesses a large number of the primitive sexual cells and evidences a tendency of its elements to arrange themselves into groups, in which the large primitive ova become central figures." The primitive male gland, on the other hand, shows a tendency to the formation of a network of cell cords—the forerunners of the seminiferous tubules. "Microscopic examination of the sexual primitive glands even at the end of the fifth week is capable of distinguishing the future sex of the being." In a short time there is a difference in the gross appearance of the gland, with a difference in the arrangement of the ducts.

The parts played by the wolffian ducts and muellerian ducts differ in the two sexes. In the **female** the muellerian ducts are the most important. The lower portions of the ducts of Mueller become fused and form the vagina and uterus, and the upper portions remain separated and form the fallopian tubes (Figs. 1034 to 1036). The lower end of the canal (future vagina) formed by the fused muellerian tubes is closed at first. Later the lower part of the septum, which shuts off this canal from the urogenital sinus, breaks down, permitting the canal (vagina) to communicate with the urogenital sinus. If this septum fails to break down, imperforate hymen results. The very end of
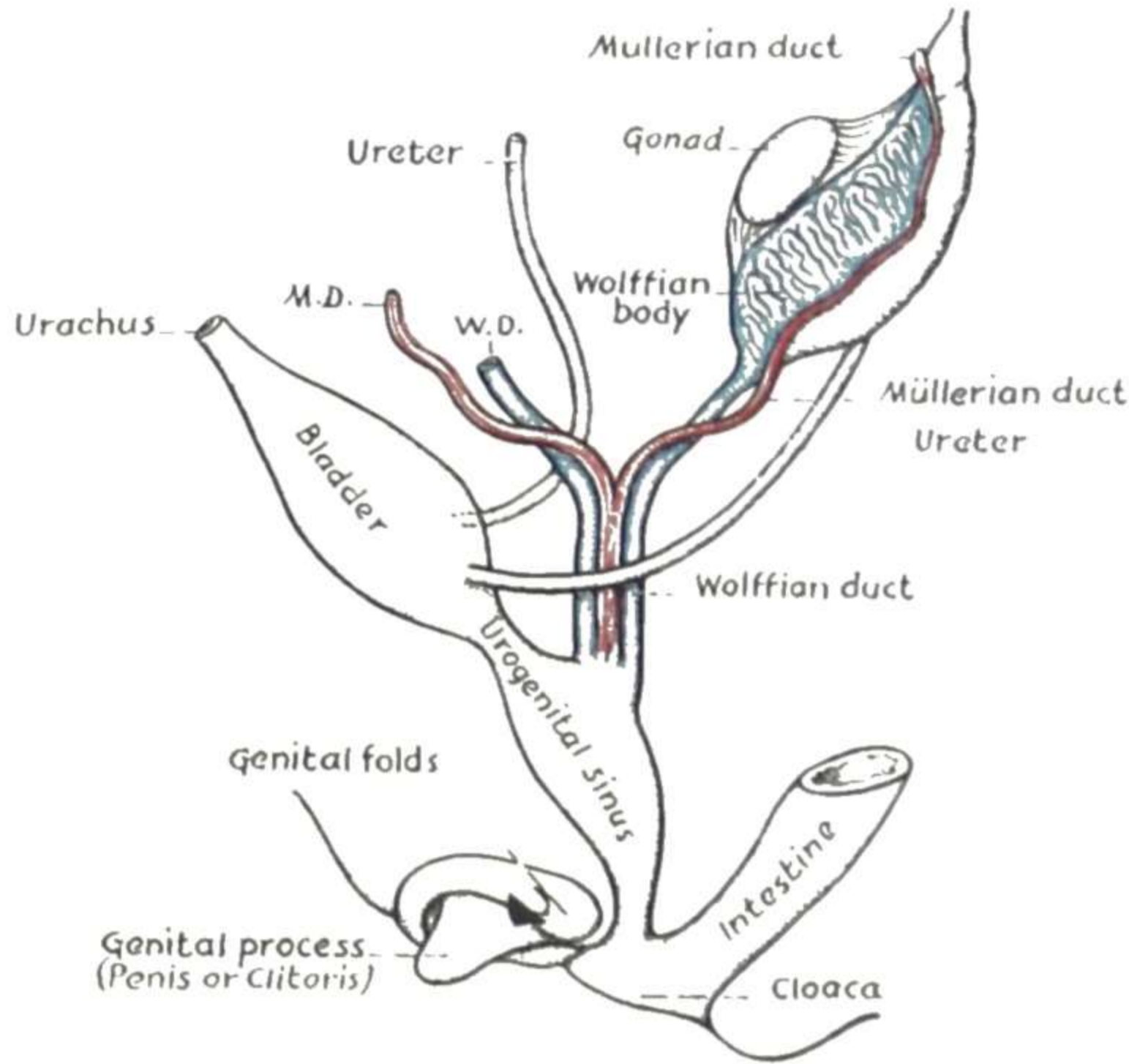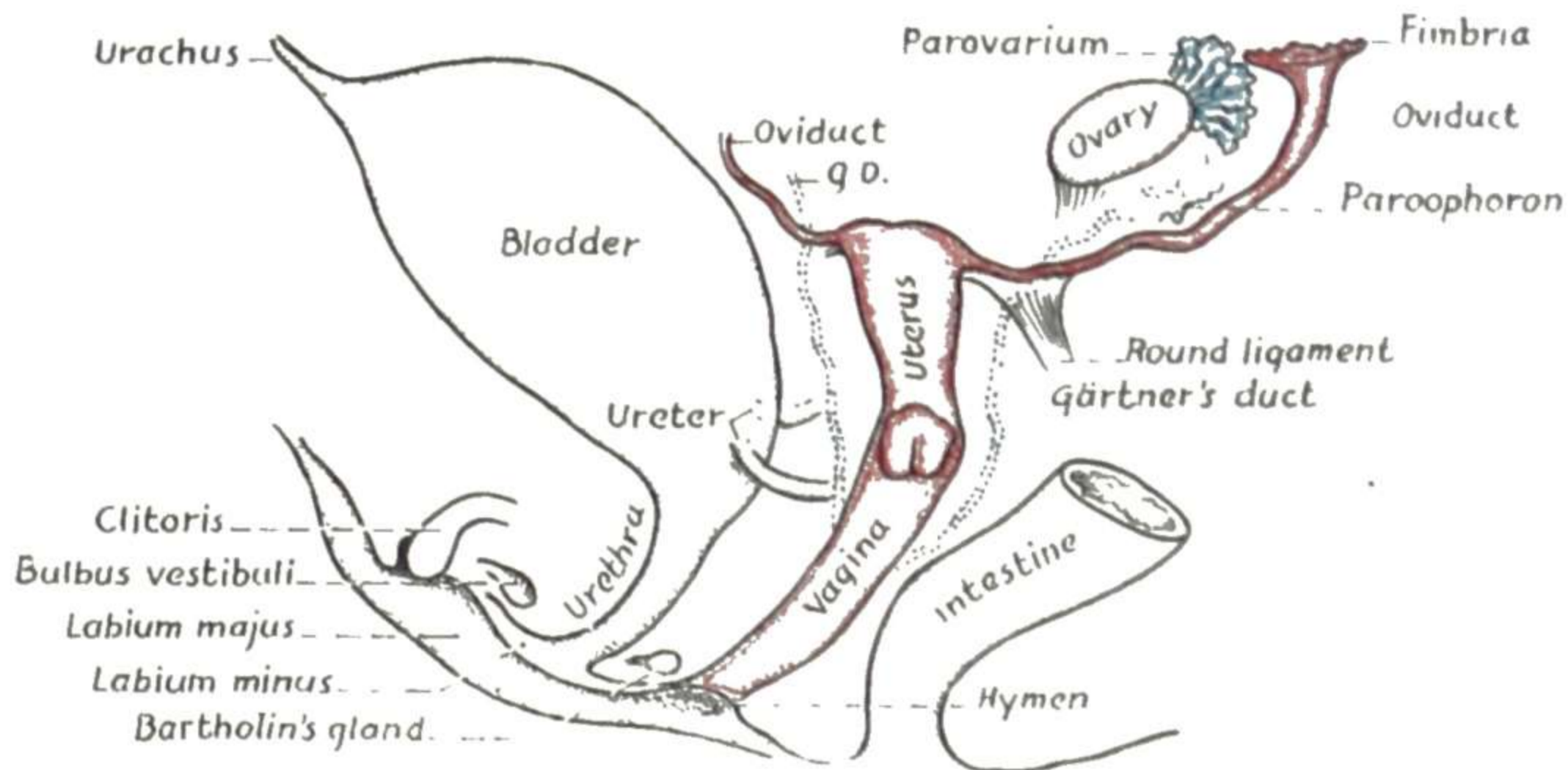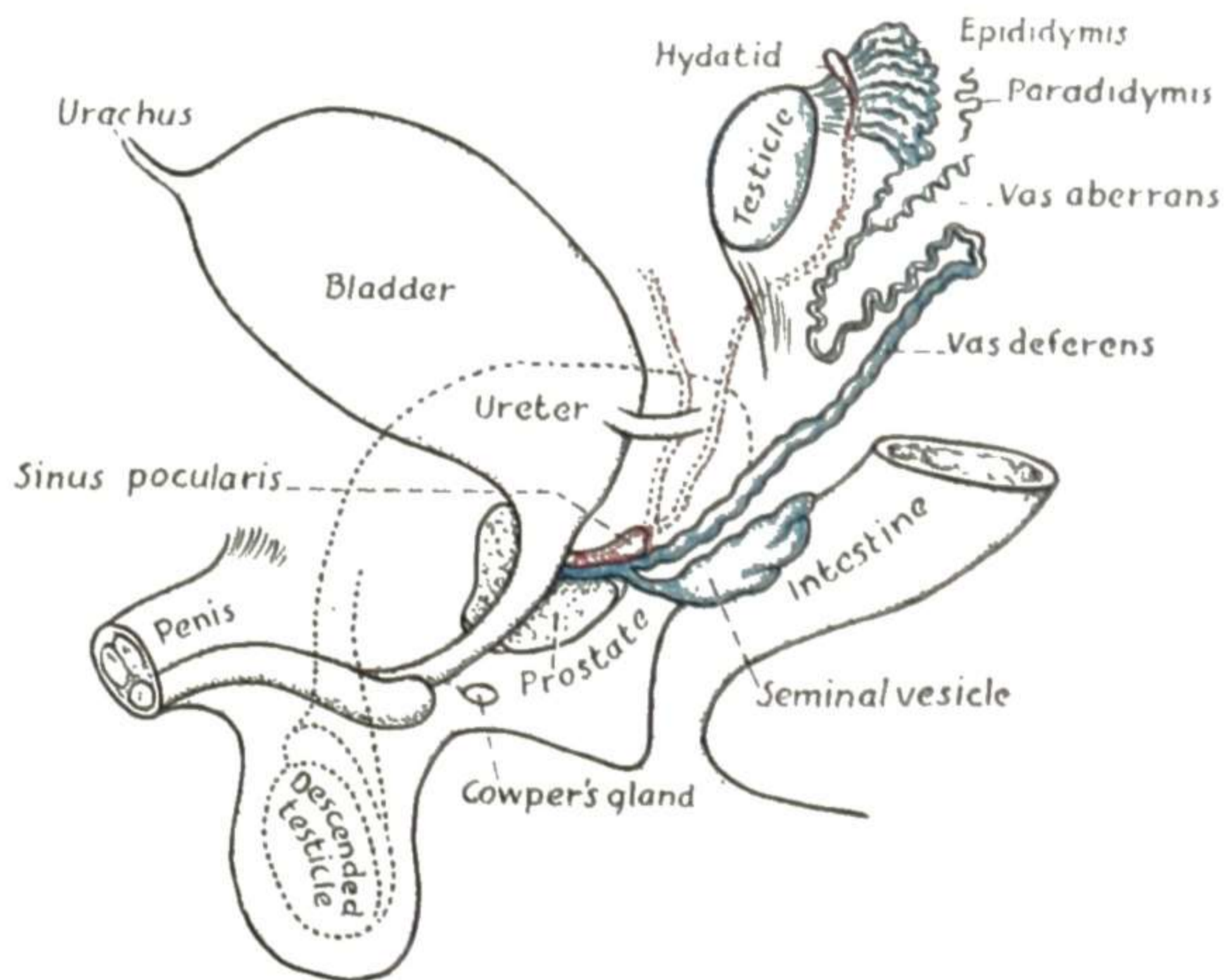
Fig. 1034.

Fig. 1035.

Fig. 1036.

Figs. 1034, 1035, and 1036.—Development of the Genital Organs. Diagrams illustrating the transformation of an indifferent primitive genital system into the definite female and male types. (Modified from Arey, after Thompson—*Developmental Anatomy.*)

the other extremity of the muellerian duct is usually represented by a minia-ture cyst attached to one of the fimbria and called the "hydatid of Morgagni."

The wolffian body forms the ovary and also contributes the transverse tubules of the parovarium. The upper part of the wolffian duct remains as the "head tube" of the parovarium. The lower part of the wolffian duct some times remains in whole or in part, and is then known as "Gärtner's duct"
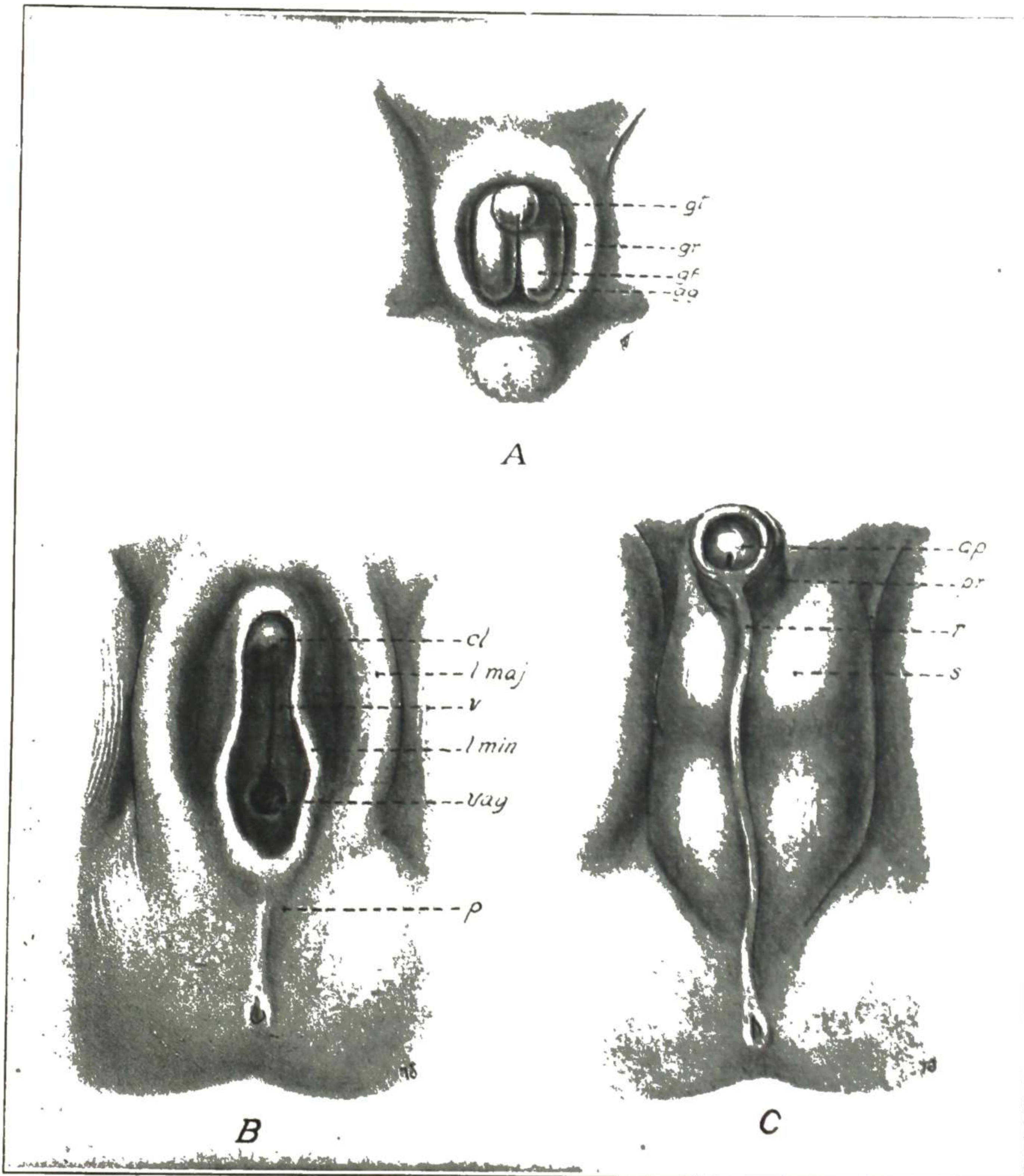

Fig. 1037.—Development of the external genitals (after Ecker-Ziegler models). A, Indif-ferent stage (eighth week) ; gt, genital tubercle; gr, genital ridge; gf, genital fold ; gg, genital groove. B, Female type; cl, clitoris; l. maj., labia majora; v, vestibule; l. min., labia minora; vag., vagina; p, perineum. C, Male type; gp, glans penis; pr, prepuce; r, raphe; s, scrotum.

(Figs. 48, 49). These parovarium tubules are all atrophic structures of but little importance. The ovary is the important organ formed from the wolffian body in the female.

In the **male** the wolffian tubules and wolffian duct contribute the impor-tant system of excretory tubes represented by the vas deferens and the epi-

didymis, while the muellerian duct is atrophic, its ends alone remaining. Its outer end forms the "hydatid of Morgagni," closely connected with the epididymis, and its inner end forms the "sinus pocularis," or "uterus masculinus," opening into the prostatic portion of the urethra.

External Genitals (Fig. 1037). "Until the ninth or tenth weeks the external genitals afford no positive information as to sex"—they are indifferent. They then begin to differentiate and "usually by the end of the third month the external sexual organs are characteristic beyond doubt." Up to the sixth week the external openings of the intestine and of the urinary apparatus are received within a common cloacal recess whose rectourogenital orifice is surmounted by a small conical elevation, the "genital tubercle." The lower and posterior surface of the genital tubercle is divided by a furrow—the "genital groove"—bounded by thickened edges called the "genital folds." Gradually a septum develops, separating the rectal opening from the genitourinary opening. The "genital tubercle" forms the **clitoris** and the "genital folds" form the **labia.**

The **vestibule** is formed by the cloaca or common opening of the intestinal tract and urinary tract in the early embryo. The **perineum,** developing, separates the rectum from this common vestibule. And the septum (hymen) closing the end of the rudimentary vagina (fused muellerian ducts) breaks, allowing the vagina to open into the vestibule. This opening through the septum varies much in size, shape, and situation, giving the various forms of opening found in the hymen. It is usually small, and roughly crescentic in shape.

The **vagina** is formed by the fusion of the lower portions of the two muellerian ducts and the absorption of the longitudinal septum between the cavities. The **uterus** is formed by the fusion of the middle portions of the two muellerian ducts and the absorption of the septum between the cavities. The **fallopian** tube of each side is formed by the upper portion of the muellerian duct of that side. The **ovary** of each side is formed from a portion of the wolffian body of that side. The **parovarium** consists of the "transverse tubules," which are formed from the wolffian body, and the "head tube," which is formed from the wolffian duct. The **paroophoron,** lying in the broad ligament near the parovarium, is the atrophic remains of the lower segment of the wolffian body.

ANOMALIES OF DEVELOPMENT

The more common anomalies of development are as follows:

1. A septum is found between the vaginal cavity and the urogenital sinus, constituting **imperforate hymen** (Figs. 1038, 1039).

2. More rarely, perfect canalization does not take place in the fused muellerian cords (each of which develops a central canal and becomes a muellerian duct), resulting in a closed place at some point in the canal, giving **atresia of vagina** (Fig. 1040) or atresia of cervix. In very rare cases all of the lower fused cords fail to canalize, causing **absence of vagina** (Fig. 1047).

3. The septum between the two fused muellerian ducts may persist all the way to the hymen, in which case there exists **double vagina** (Figs. 1048, 1049).

4. The vagina may open into the urethra instead of into the urogenital vestibule. This gives the anomaly shown in Figs. 1050 to 1053.

5. The septum may persist into the uterine portion of the muellerian tract, forming a uterus septus.

6. The middle portions of the muellerian ducts may fail to fuse, giving a double uterus (uterus didelphys).

7. They may fuse only imperfectly, giving a uterus with rudimentary horns. There may be either two well-marked horns (uterus bicornis), or a fairly well-developed uterus with one rudimentary horn, as shown in the illustrations.

8. The wolffian duct may persist in some extent, giving a duct lying alongside the vagina called Gaertner's duct (Figs. 48, 49). This may extend all the way along the vagina and open near the hymen, or there may be only
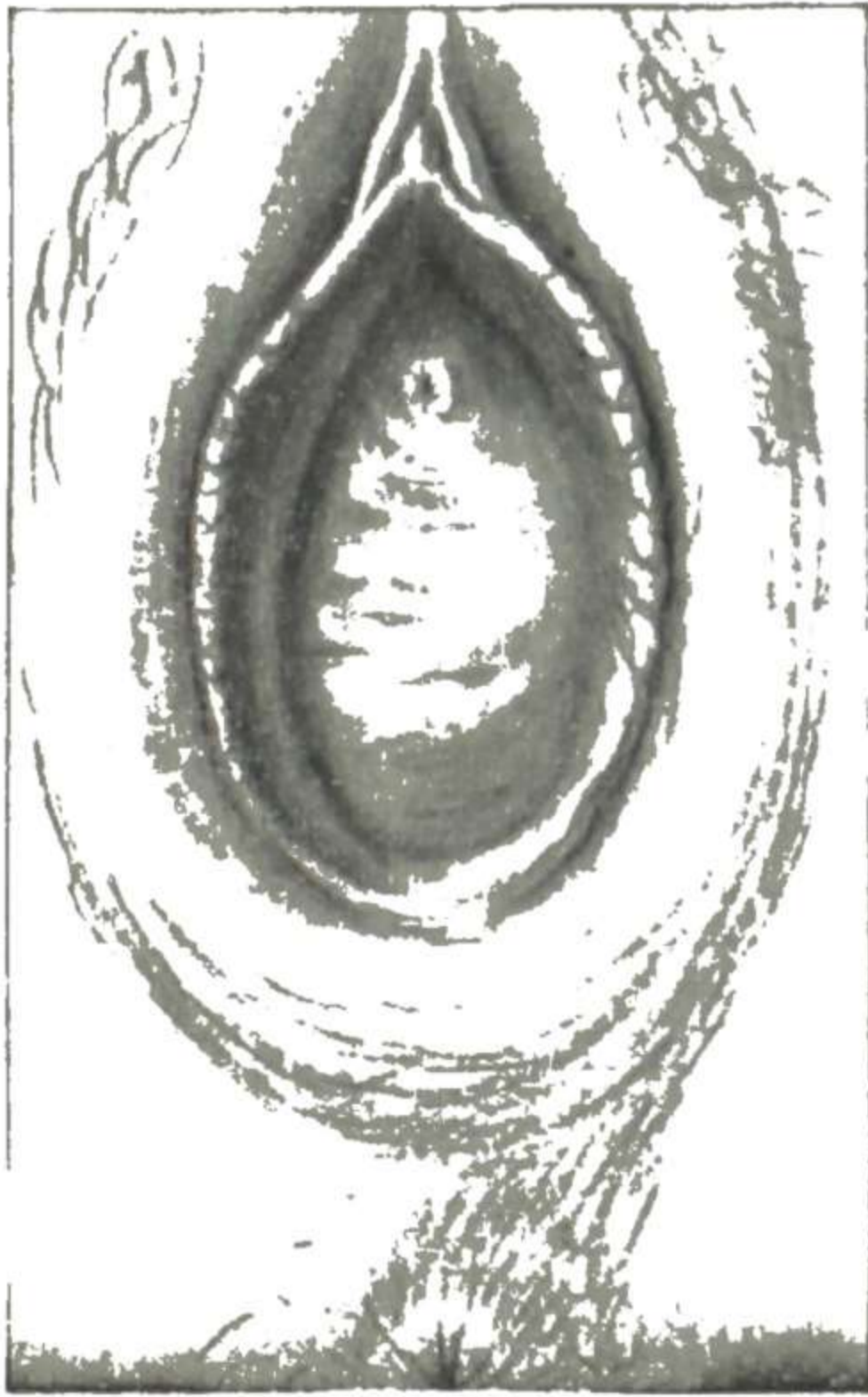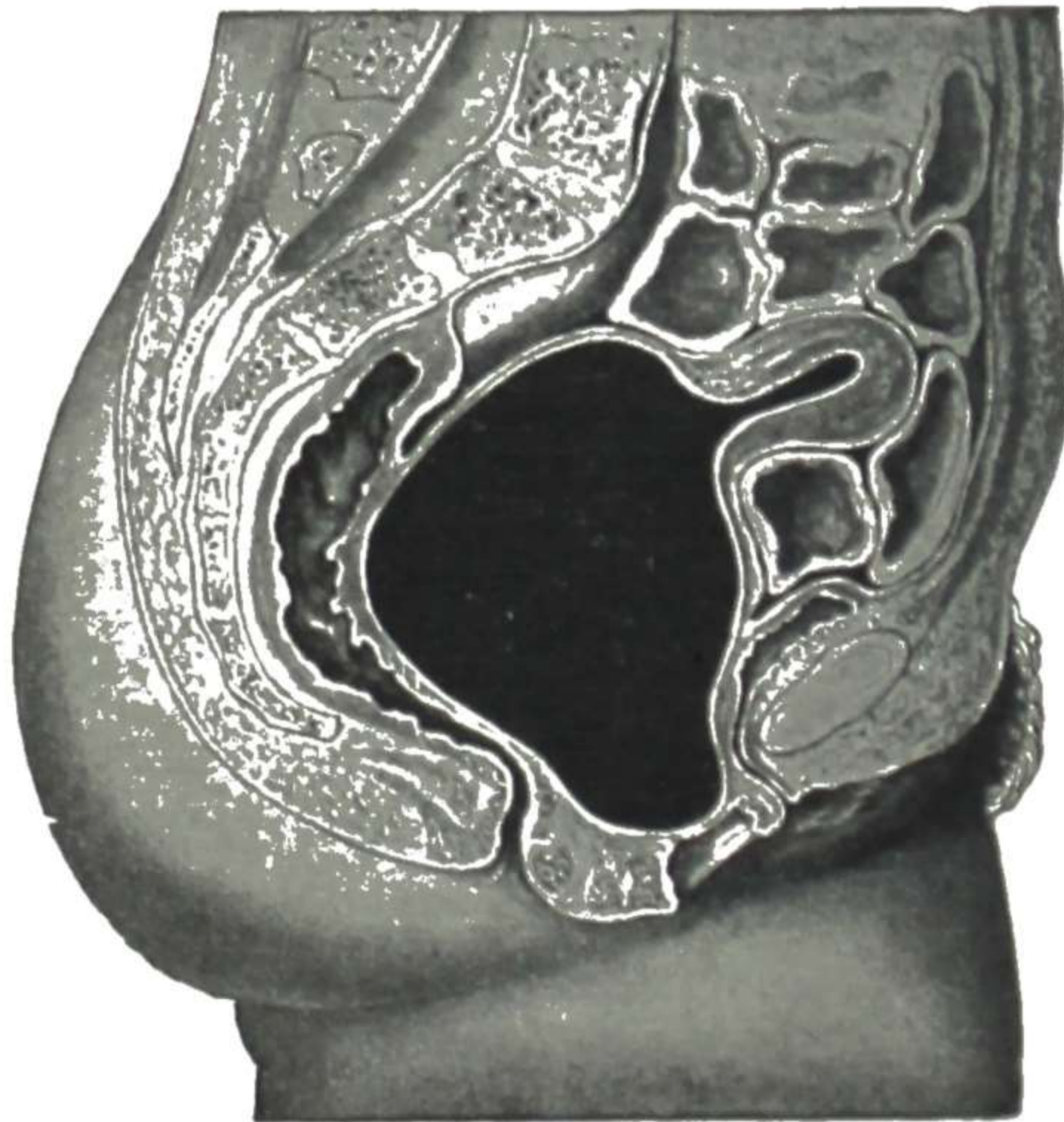

Fig. 1038.

Fig. 1039.

Fig 1038.—Imperforate hymen. There is no vaginal opening, the urethra being the only opening present in the vestibule. (Montgomery—*Practical Gynecology.*)

Fig. 1039.—Hematocolpos, which may result from imperforate hymen or from atresia at the lower portion of the vagina. The menstrual blood has not yet distended the uterus. (Montgomery—*Practical Gynecology.*)

remnants of the tube here and there. These remnants sometimes develop so as to form small vaginal cysts. Such cysts are situated in the vaginal wall along the course of the atrophic wolffian duct. This duct extends through a portion of the uterine wall, and a uterine tumor may arise from it.

The above mentioned are the principal gross developmental anomalies ordinarily met with. There are many other rarer anomalies, of which lack of space prevents mention. These vary in each organ all the way from slight modification to complete absence. The **ovary** is probably the least frequently affected by anomalies, and yet, as rare as they are, they have produced many surprises in abdominal work, especially in the cases of pregnancy following the supposed complete removal of both ovaries. This means, of course, that some ovarian tissue remains, and it is usually said to be a "third ovary."

While the development of three normal ovaries is not impossible, the condition present in the cases under consideration is, as a rule, "lobulation" of the ovary of one or both sides, and not the presence of a complete third ovary. The lobulated ovary may show only a marked constriction, or it may be divided into two or three or many separate lobules, with considerable space between various lobules. Bovée mentions a case of his in which the ovary of each side was represented simply by numerous small particles of ovarian tissue scattered over a large area of the posterior surface of the broad ligament, and resembling verrucal excrescences. It is evident that in such a case some outlying nodules of ovarian tissue would almost certainly be missed, especially if obscured by an inflammatory exudate.

The malformations most commonly requiring treatment are:

Imperforate Hymen.   Vagina Opens Into Urethra.
Atresia of Vagina.   Malformations of Uterus.
Double Vagina.   Pseudohermaphroditism.

Imperforate Hymen

If the time-honored supposition that the hymen is simply the remains of the septum between the embryonic vagina and the sinus urogenitalis is true, then imperforate hymen means the failure of this septum to break down. If, on the other hand, the hymen represents another structure formed by active circular proliferation just back of the septum area, then imperforate hymen or occluded hymen is the result of excessive proliferation and coalescence, instead of failure to break down. Taussig has investigated this subject embryologically and in two articles presents substantial points in favor of the proliferation theory.

Imperforate or occluded hymen causes no disturbance until puberty. After puberty there is a collection of menstrual blood back of the imperforate hymen (Fig. 1039). This gradually increases in amount and distends the vagina. If the obstruction is not relieved, there is gradual dilation of the uterus and even of the fallopian tubes, forming a cystic mass, the content of which is blood and the walls of which are formed by the vagina and uterus.

The **symptoms** are characteristic. At the age of puberty no menstruation appears, but about every four weeks the patient feels ill, with pain in the lower abdomen and the usual disturbances accompanying menstruation. The mother supposes that the girl is going to menstruate, but there is no flow. This is repeated month after month. As the collection of blood increases, the pain and disturbance become more marked, the patient's health begins to suffer, and a tender mass appears in the lower abdomen. Finally the patient becomes so sick that the physician makes a local examination. He finds that there is no vaginal opening, but instead there is a fluctuating mass occupying the position of the vagina and uterus (Fig. 1039).

The **treatment** is crucial incision of the distended hymen, and, if the membrane is thick, excision of the most of it. The cavity above should be washed out with normal saline solution and then packed with sterile gauze. Great care is necessary to prevent infection. The decomposing blood that

necessarily remains along the walls of the cavity favors the rapid growth of pus germs, and, though the operation is a simple one, patients have died from it, or rather from the infection following.

Tompkins reported a series of five cases of imperforate hymen with hematocolpos and collected 113 from the literature, and presented a study of diagnosis and treatment.

Atresia of Vagina, Absence of Vagina

The method of origin of this malforation has been explained. The condition may vary all the way from a thin septum blocking the canal to complete absence of the canal. The external genitals may be normal.

The serious conditions which may result from simple atresia of the vagina, and the importance of early investigation of symptoms, such as amenorrhea and slight recurring abdominal pains, are demonstrated in the following case of ours:

Miss D., aged twenty-three years, was referred for operation for pelvic tumor. Examination showed a tender mass filling the central pelvis and a mass on each side extending into the lower abdomen. The upper limits could not be outlined on account of the deep location and the tenderness. The patient had a temperature of 104° F. and was in a serious condition. On vaginal examination an obstruction was found just inside the vaginal opening, and there was a bloody discharge mixed with pus. The history was somewhat uncertain and there were other factors that made diagnosis of intrapelvic conditions difficult, but facts were eventually established to warrant a diagnosis of the following sequence of events.

The patient had atresia of the vagina near the outlet, as indicated in Fig. 1040. After puberty there was a slow accumulation of menstrual blood back of the obstruction, as indicated in Figs. 1041 to 1044. There had been no menstruation. She had had abdominal pains off and on, and on going over the matter she thought they had been worse about once a month for several months past. Apparently they were never very severe.

About a month previous to her admission to the hospital a slight bloody discharge appeared. Apparently the pressure of the accumulating blood had gradually stretched the thin membrane occluding the vagina so much so as to cause a small opening through which came the slight bloody flow, as shown in Fig. 1045. This flow continued for a week or so and then the patient became suddenly very ill, with high fever.

Bacteria eventually propagated in this bloody culture medium, followed up the stream into the mass of old blood, and then multiplied rapidly, forming an abscess involving the distended vagina and uterus and tubes, as indicated in Fig. 1046.

The plan of treatment was to drain from below. This might prove sufficient, and the anesthesia and vaginal work would permit deeper examination for confirming or disproving the diagnosis made. There was of course the possibility that the diagnosis was erroneous and that the large masses above were tumors, with degeneration or suppuration or twisted pedicle. The vaginal drainage improved conditions temporarily and the information obtained tended to confirm the diagnosis of genital tract distended with blood and infected.

In three days the temperature became high again, there was no diminution in the size of the lateral masses, and it was evident that abdominal operation was necessary in spite of the danger it involved. At the abdominal operation the tubes were found enormously distended, pushing up the sigmoid and the cecum. The distended tubes and uterus were removed and extensive drainage was established. Examination of the distended tubal specimens showed them filled with a mixture of pus and old blood. The patient had a stormy time, but eventually recovered.

On making the vaginal **examination,** an obstruction is met with at some point in the vagina. If there is a collection of menstrual blood back of the septum, fluctuation may be detected. Digital examination per rectum will give some

idea of the extent of the atresia and the amount of blood behind it. If the patient is well past the age of puberty, and there is no fluid above the atresia, the probability is that the uterus is anomalous, so much so that menstruation could not come on even though the obstruction in the vagina were removed. So, before undertaking an operation for making a vaginal canal, rectoabdominal examination, under anesthesia if necessary, should be made to establish the size, shape, and probable development of the uterus. In cases of apparent absence of the uterus, rectovesical examination may be of assistance in locating a small nodule in the situation of the uterus.

The **treatment** depends on the circumstances of the case. If only a thin septum is present it should be treated practically the same as an imperforate hymen—i.e., incised, to let out the blood, and then partially or wholly excised. If a considerable proportion or the whole of the vaginal canal is missing (Fig. 1047) the treatment requires extended operative measures according to the special conditions present. It may be necessary to build up a whole new vagina. The details of this operative work are considered in the authors' *Operative Gynecology*.
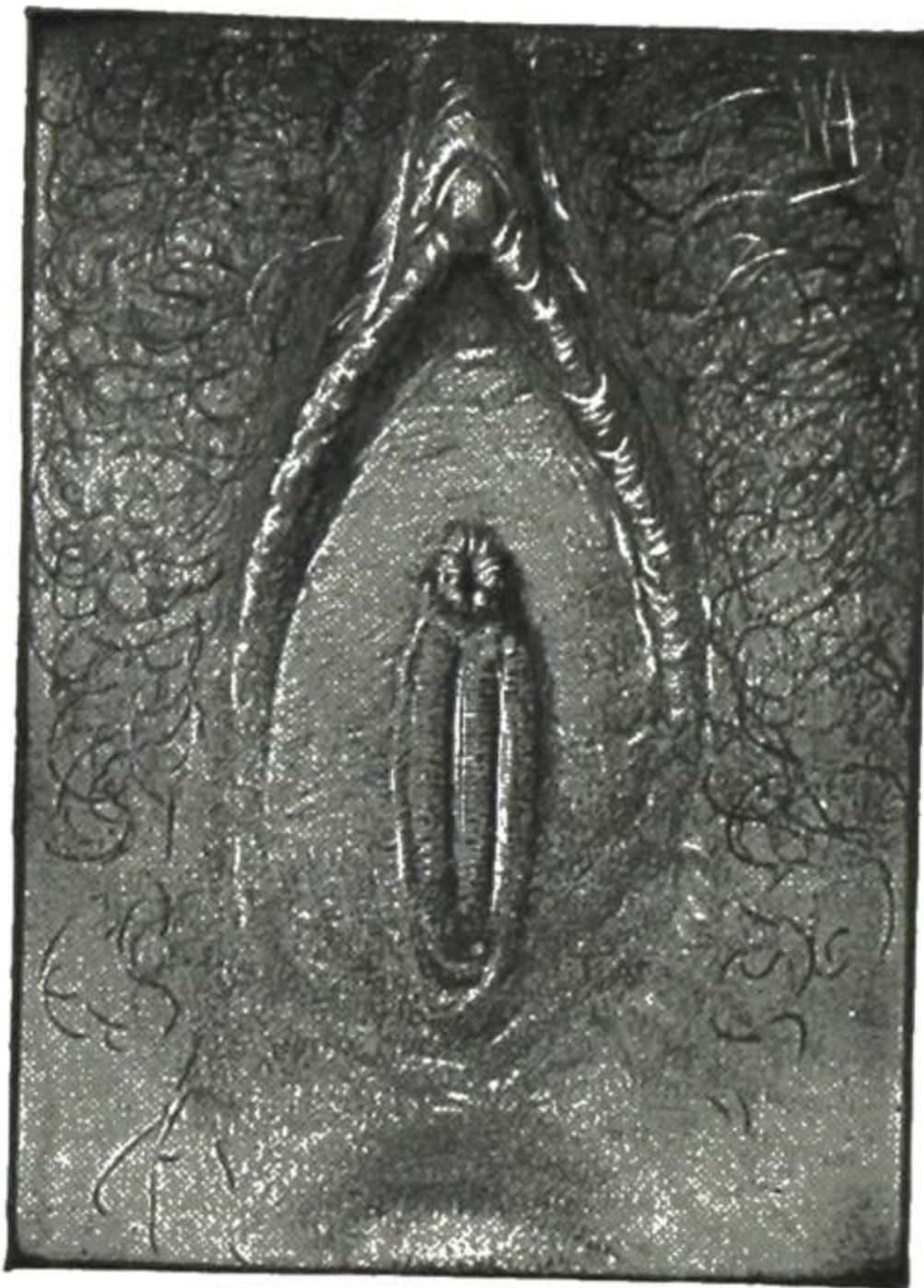

Fig. 1047.—The appearance of the external genitals in a case of absence of the vagina. (Kelly— *Operative Gynecology*.)

Acquired Atresia.—A considerable proportion of the cases of marked stenosis of the vagina, amounting almost to atresia, are acquired. Such a condition may result from injuries in childhood or inflammation, particularly the gonorrheal vaginitis of childhood and severe inflammations following the exanthemas. Congenital syphilis also may cause it, following severe ulceration. In later life, scar tissue resulting from injuries in labor is the most frequent cause of narrowings in the canal and bands and constrictions and distortions. Other causes in the adult are syphilitic ulceration, injuries, and severe destructive inflammations. A pessary left in the vagina for several years may lead to such a result. In rare cases even complete atresia may result from some one of these causes. The atrophic vaginitis or "adhesive vaginitis" of old age (senile vaginitis) leads to adhesion of the walls of the vagina and stenosis and partial obliteration of the canal. The treatment for acquired stenosis or atresia of the vagina is practically the same as for the con-

Fig. 1040.   Fig. 1041.   Fig. 1042.

Fig. 1040.—Indicating the Location of the Vaginal Atresia in the case described in the text.

Figs. 1041 and 1042.—After puberty there began an accumulation of menstrual blood, which distended the vagina and later the uterus.
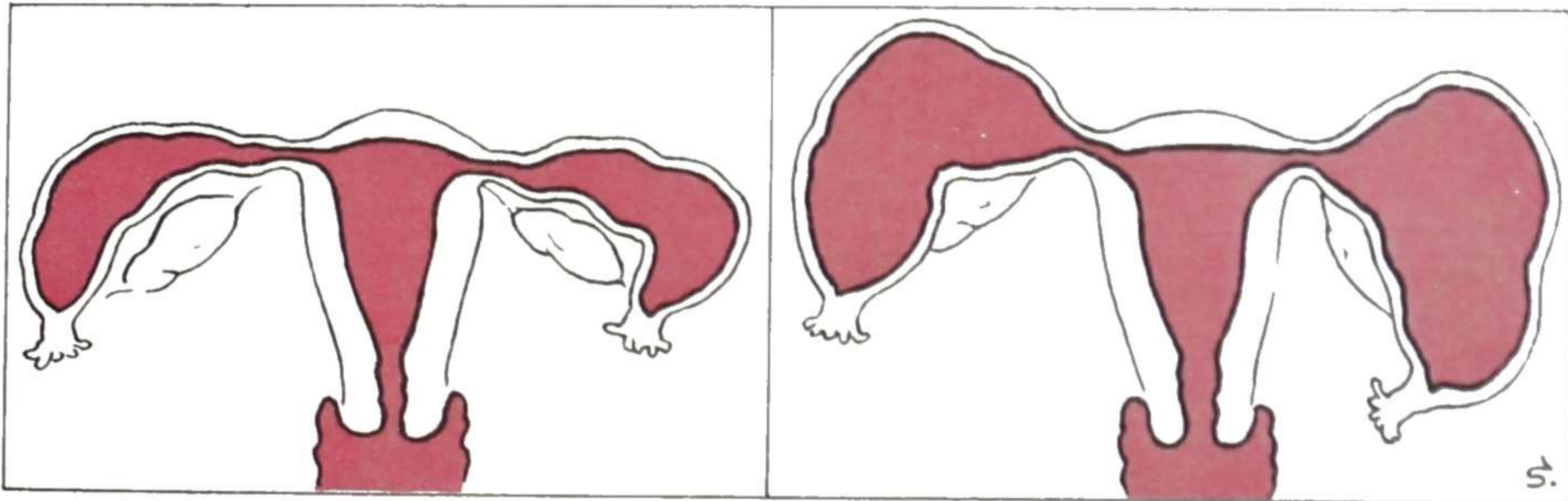

Fig. 1043.   Fig. 1044.

Figs. 1043 and 1044.—The Retained Blood Extended into the Tubes. Peritoneal irritation sealed the outer ends of the tubes, and the accumulating blood caused more and more distention.
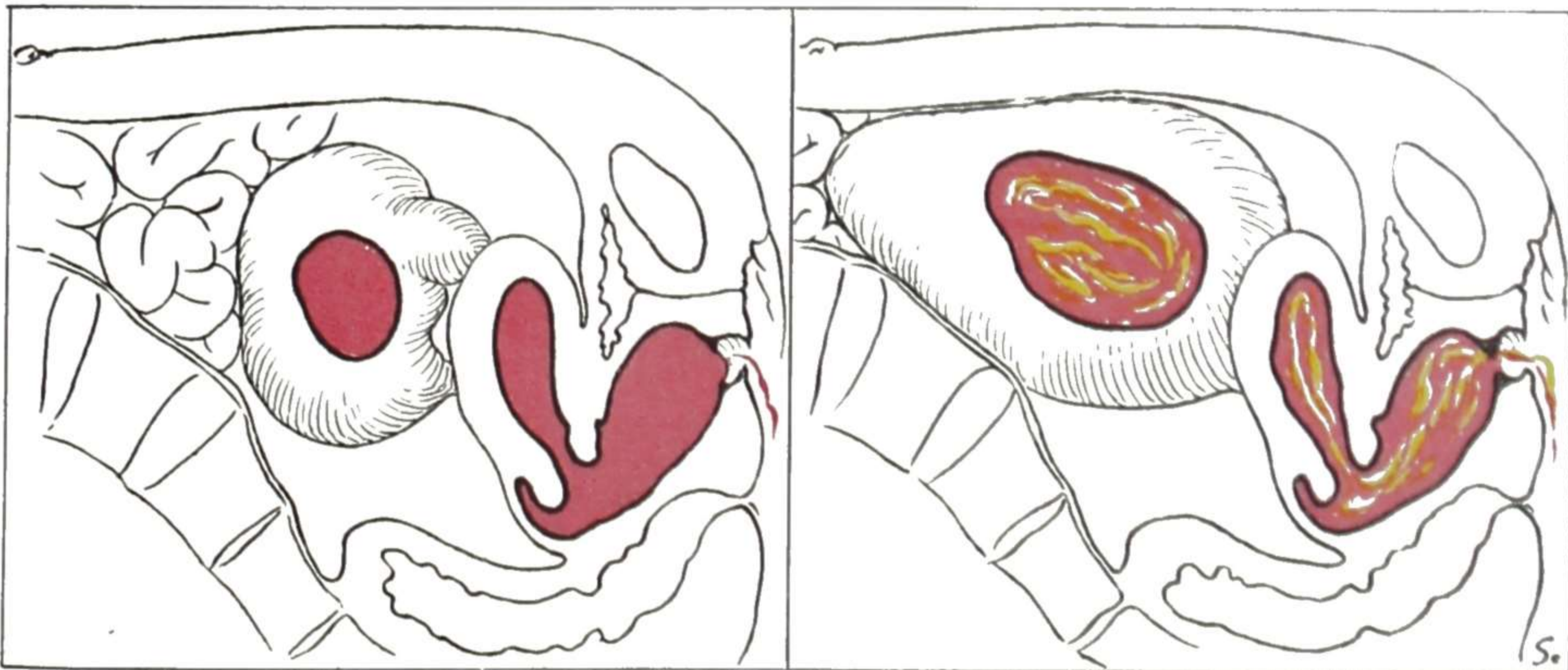

Fig. 1045.   Fig. 1046.

Fig. 1045.—These Blood-filled Masses in the Pelvis and Lower Abdomen had enlarged so gradually that they were not noticed, there being no acute symptoms leading to examination. Finally the vaginal distention thinned the abnormal septum to such an extent that a small opening occurred, and through this there was some leakage of the retained blood.

Fig. 1046.—Along this line of culture medium, inflammatory bacteria propagated into the vagina and then throughout the disintegrating blood mass. There was then rapid enlargement of the tubal masses, marked pain, high fever, sepsis, and the patient passed at once into a desperate condition—with the diagnosis obscure, until worked out as here shown.

genital. The acquired form, however, is, when extensive, likely to be more difficult of satisfactory treatment on account of the large amount of scar tissue in the vicinity.

Double Vagina

This consists usually simply in a longitudinal septum dividing the vagina into two canals (septate vagina). The vagina with entirely separate walls is a much rarer condition. The longitudinal septum is the persisting fused wall of the two muellerian ducts, as already pointed out. It may extend the whole length of the vagina, giving two openings at the vestibule, and half the cervix in each upper end (Figs. 1048, 1049). On the other hand, it may consist simply in a septum extending part way. Even when the septum extends the full length of the vagina, one canal is usually so much smaller than the other and placed so far to one side that it does not interfere with coitus or pregnancy.
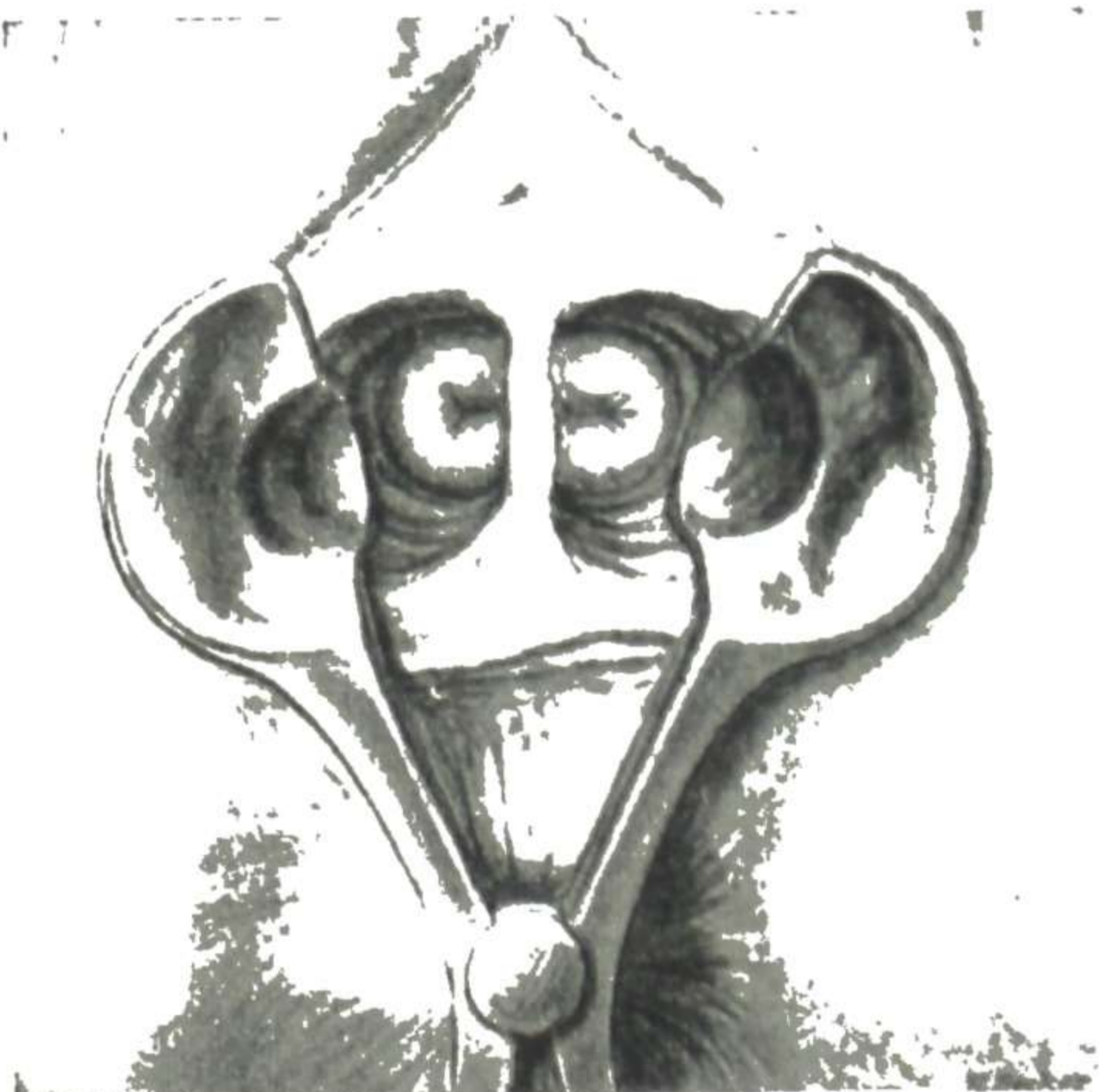

Fig 1048.

Fig. 1049.

Fig. 1048.—The appearance of the external genitals in a case of double vagina. (Kelly—Operative Gynecology.)

Fig. 1049.—Same case as Fig. 1048, with speculum introduced, exposing the two vaginal canals and the half cervix at the top of each. (Kelly—Operative Gynecology.)

In fact the opening of one canal may be so flattened out at the side of an apparently normal vaginal opening that it is not noticeable except on very close inspection. In such a case, however, when the slit beside the vaginal opening is noticed, further examination may reveal a rudimentary canal of considerable size, sometimes almost as large as the patulous one. At the upper part of each vagina is one-half of the cervix. When labor takes place in a case of double vaginal canal, the septum is likely to be torn, partially or completely, converting the two canals into one. Portions of the septum may remain as a partial septum at the upper part of the vagina or as irregular bands and tags.

The senior author recalls one case of septate vagina and uterus seen in the first pregnancy. The patient passed through labor without particular incident, except that the cervix (half cervix) was very slow in dilating. The lower part of the vaginal septum near the vaginal entrance was torn, but the greater part remained and seemed to occasion no trouble. Later, the patient returned to the

hospital with gonorrhea affecting the vaginal and uterine cavity of each side. Still later, the author was obliged to curette both uterine cavities.

The treatment of double vagina is simple. If the septum is causing any obstruction or disturbance, it is divided or, better still, largely excised, so that the two vaginal canals are converted into one.

Vagina Opens Into Urethra

When examination reveals no vaginal opening at the vestibule, that does not necessarily mean no vagina. There may be a fairly well-developed vagina opening into the urethra.
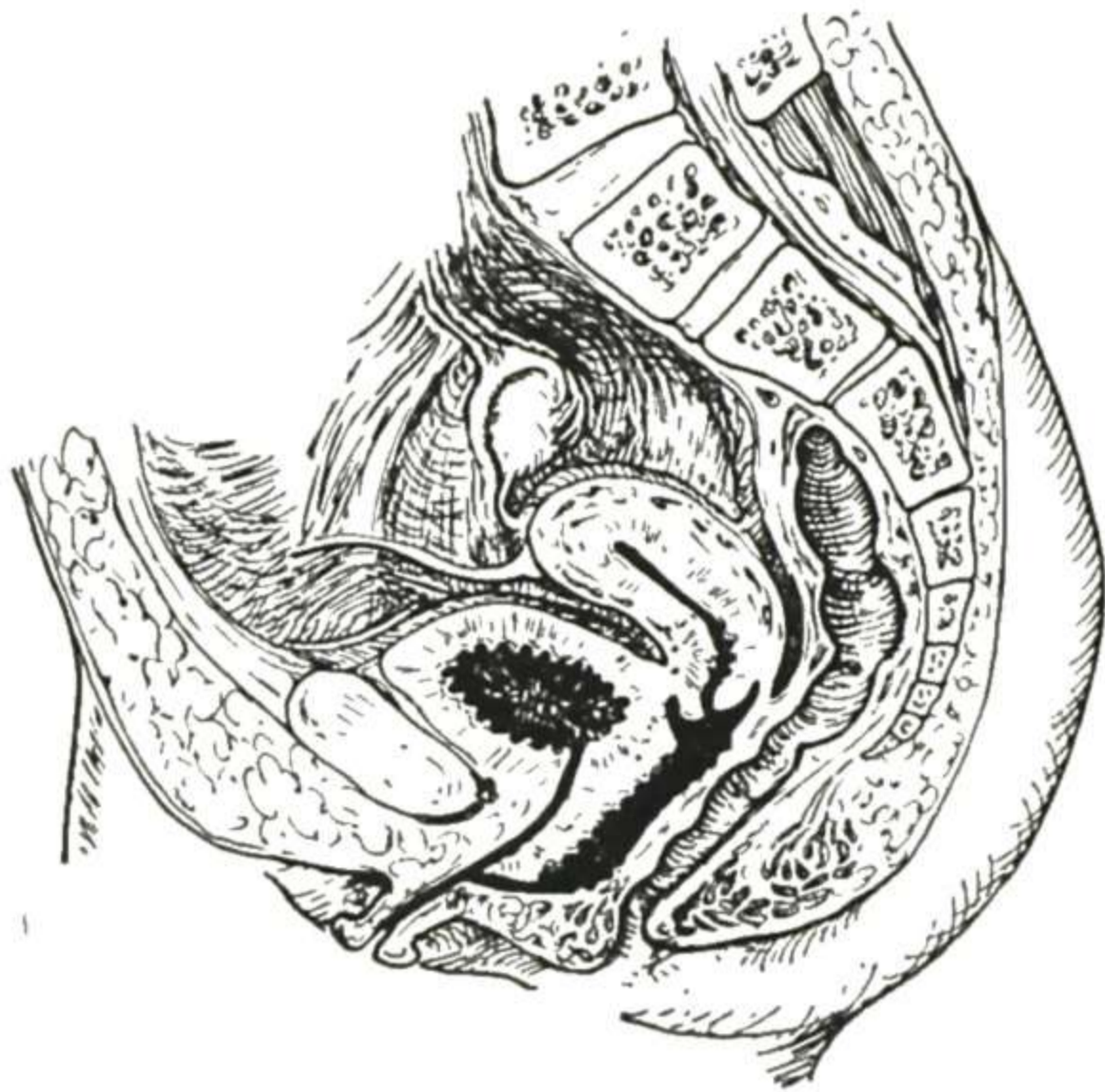

Fig. 1050.

Fig. 1051.

Fig. 1052.

Fig. 1053.

Olive Soule Fischer 1940
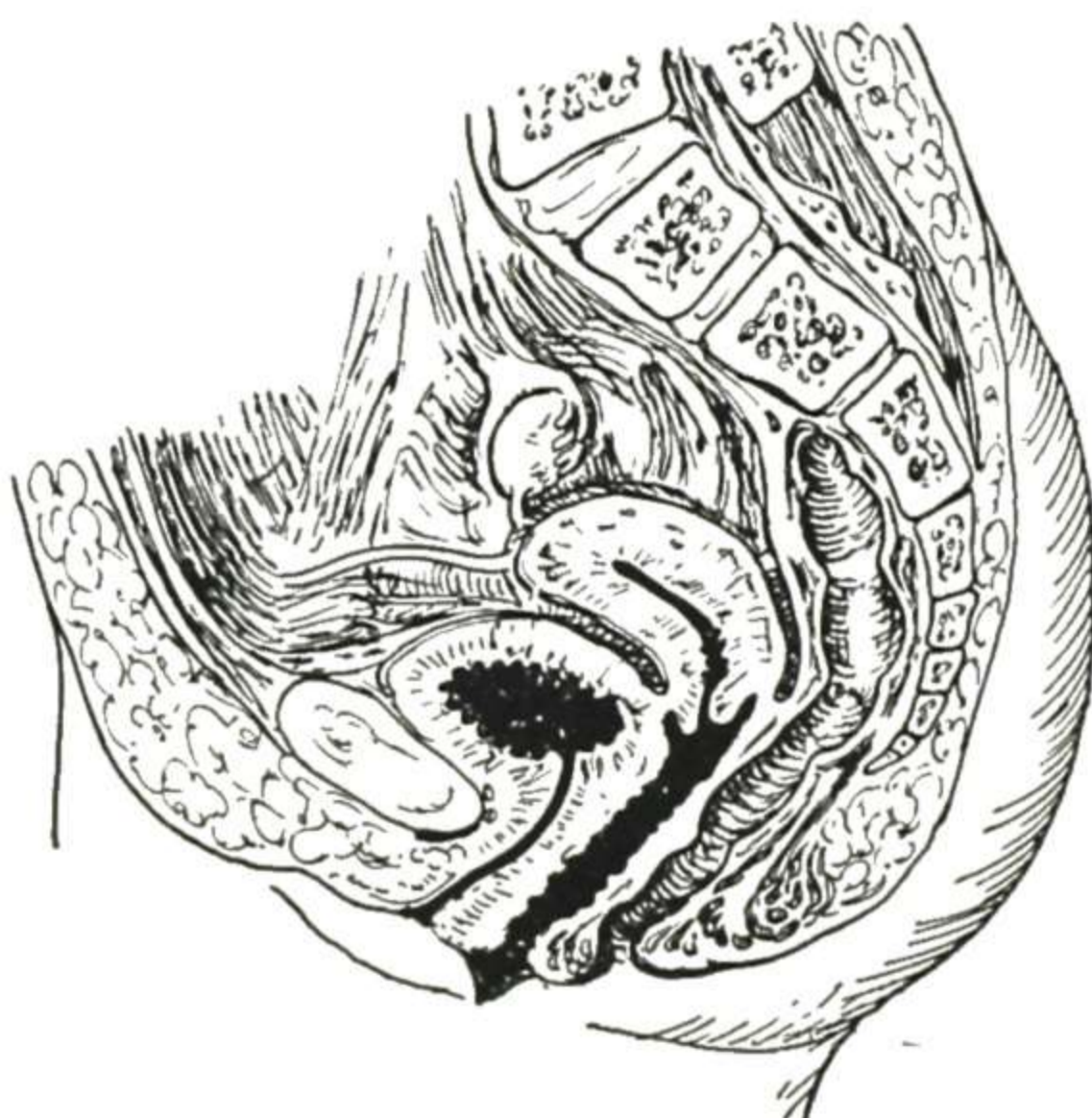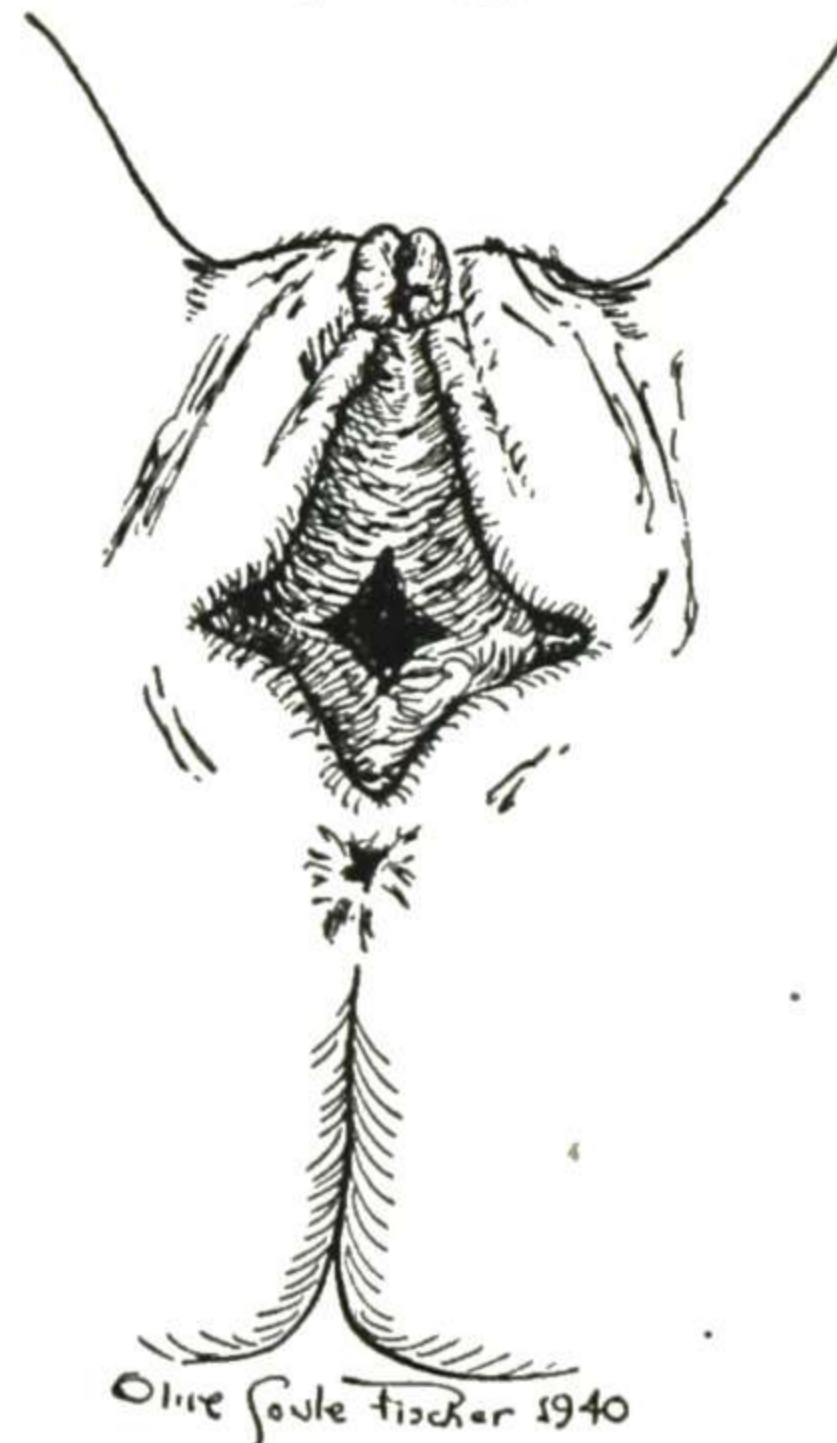
Fig. 1050.—A malformation consisting of a vagina which opened into the urethra instead of into the vestibule.

Fig. 1051.—Result of operation for opening the vagina into the vestibule and closing the opening into the urethra. (Barrows and Block—*Am. J. Obst. & Gynec.*)

Fig. 1052.—Result of further operation to enlarge the vestibular opening of the vagina.

Fig. 1053.—Front view, indicating the site of the enlarged opening and the appearance of the abnormal clitoris. (Barrows and Block—*Am. J. Obst. & Gynec.*)

Barrows and Block report such a case, in which the patient menstruated through the urethra. The condition is shown in Fig. 1050. Operation consisted of opening the vagina into the vestibule and repairing the urethra, as shown in Fig. 1051. In spite of dilatation treatments some stenosis persisted at the vaginal opening, and this was overcome by incisions, as indicated in Figs. 1052 and 1053.

Eldon reported a somewhat similar case. Young discussed this anomaly at length in his book on genital abnormalities, hermaphroditism and related adrenal diseases, and shows the cystoscopic appearance of the opening into the urethra, and also the cystoscopic appearance of the vaginal wall and cervix. The size of the anomalous vagina may be demonstrated by injection of opaque material.
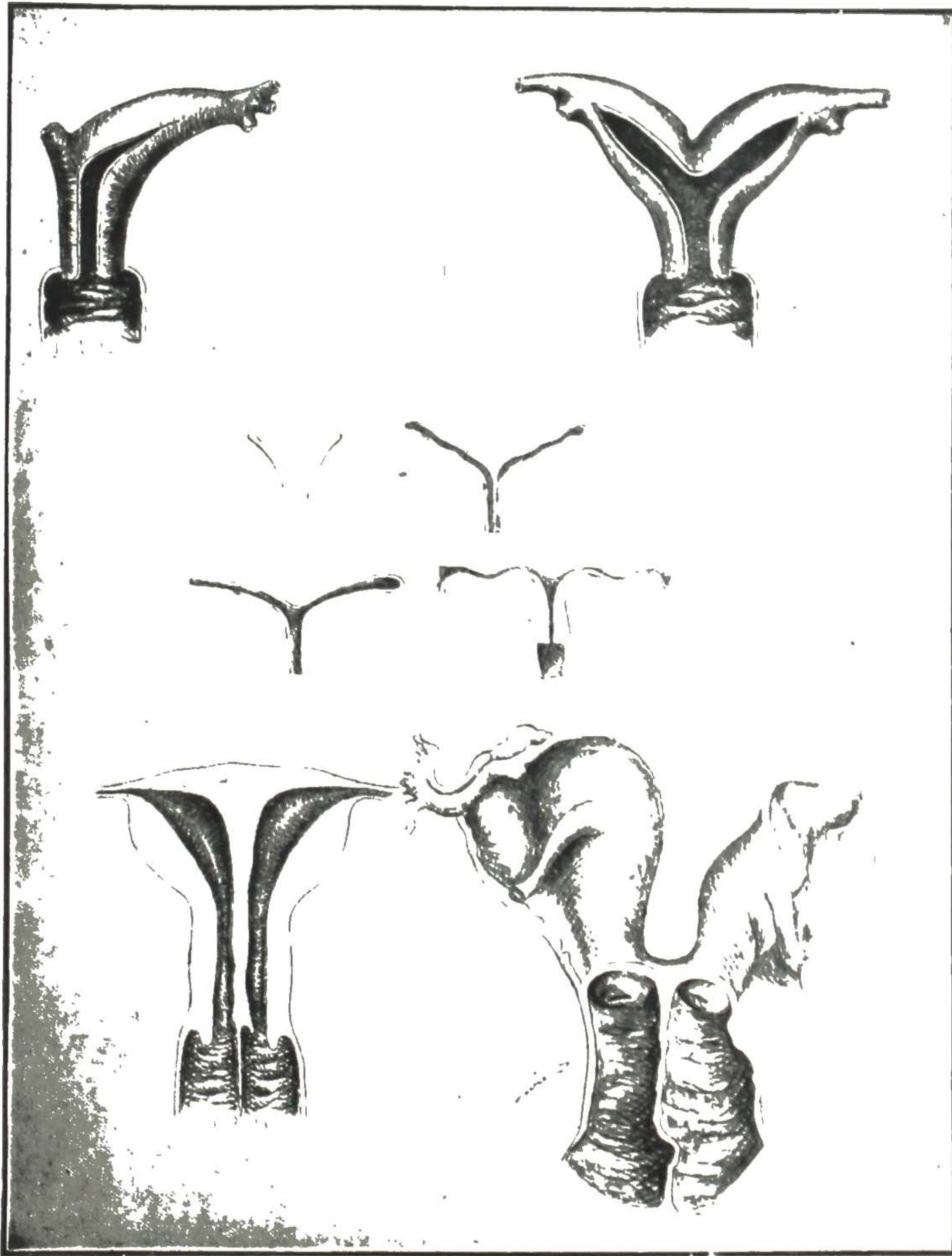
Fig. 1054.—Diagrammatic representation of the development and malformations of the uterus. *1.* Showing the different stages in the union of the muellerian ducts to form the uterus, vagina, and fallopian tubes. *2.* Uterus unicornis. *3.* Uterus bicornis. *4.* Uterus septus. *5.* Uterus duplex. (Gilliam—*Practical Gynecology.*)

Malformations of the Uterus

The formation of the uterus by the union of two tubes and certain malformations that may result are indicated diagrammatically in Fig. 1054. Cases of uterine malformation are illustrated in Figs. 1055 to 1059.

Septate Uterus, Double Uterus.—The malformation may consist simply of a partial or complete septum in an otherwise normal uterus (uterus septate)

or of a rudimentary horn with a nearly normal uterus or of a uterus with a body divided into two horns (uterus bicornis) or of a double uterus, with the body and cervix of one side separate from the body and cervix of the other side (uterus didelphys) or of a "unicorn uterus"—i.e., uterus made up of muellerian duct of one side only, the other being absent or nearly so. The most severe grades of deformity are very rare, though they are to be thought of in the diagnosis in puzzling cases. A septum in an otherwise normal uterus
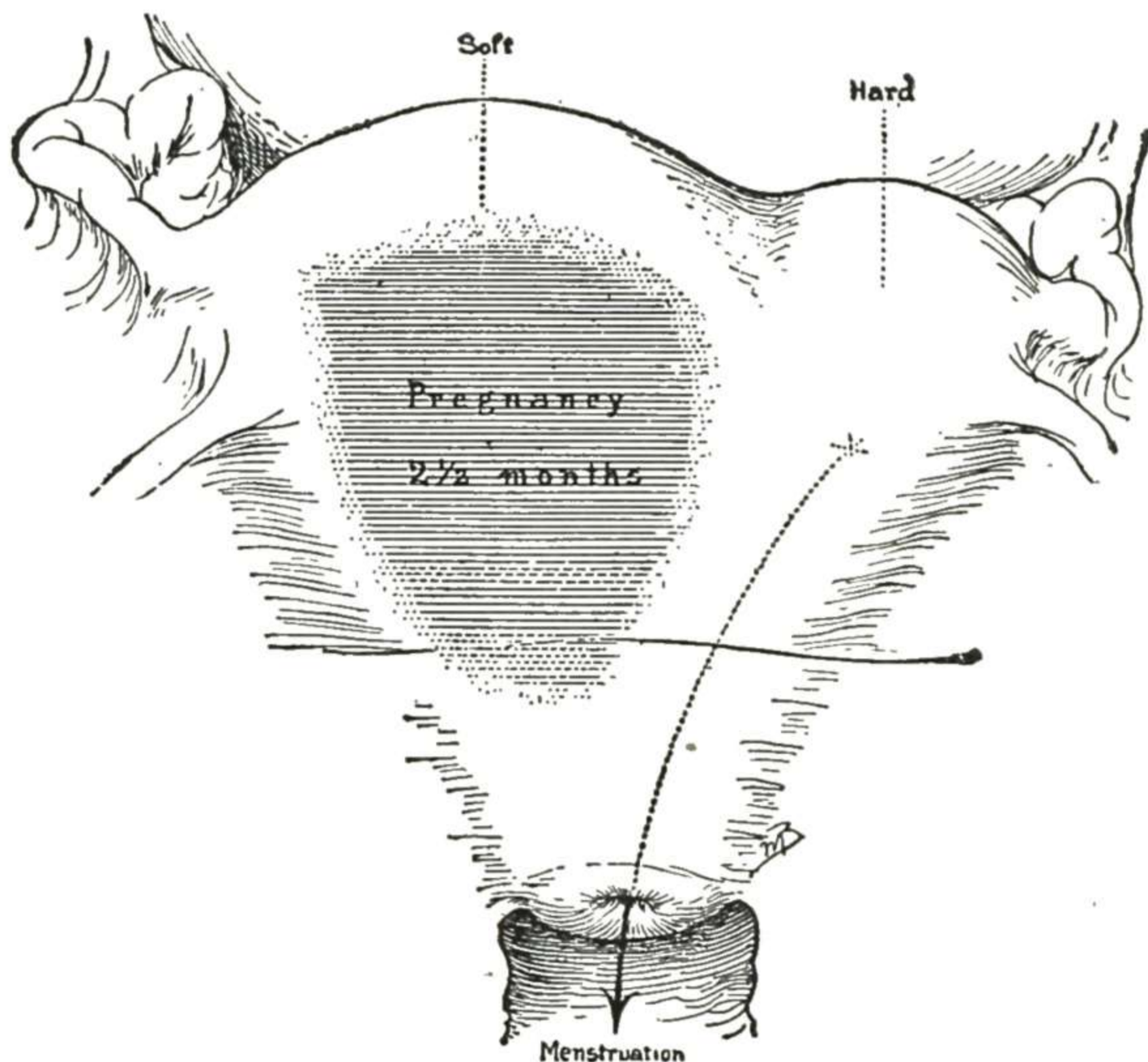
Fig. 1055.—Pregnancy in the right half of a septate uterus. (Kelly—*Operative Gynecology.*)
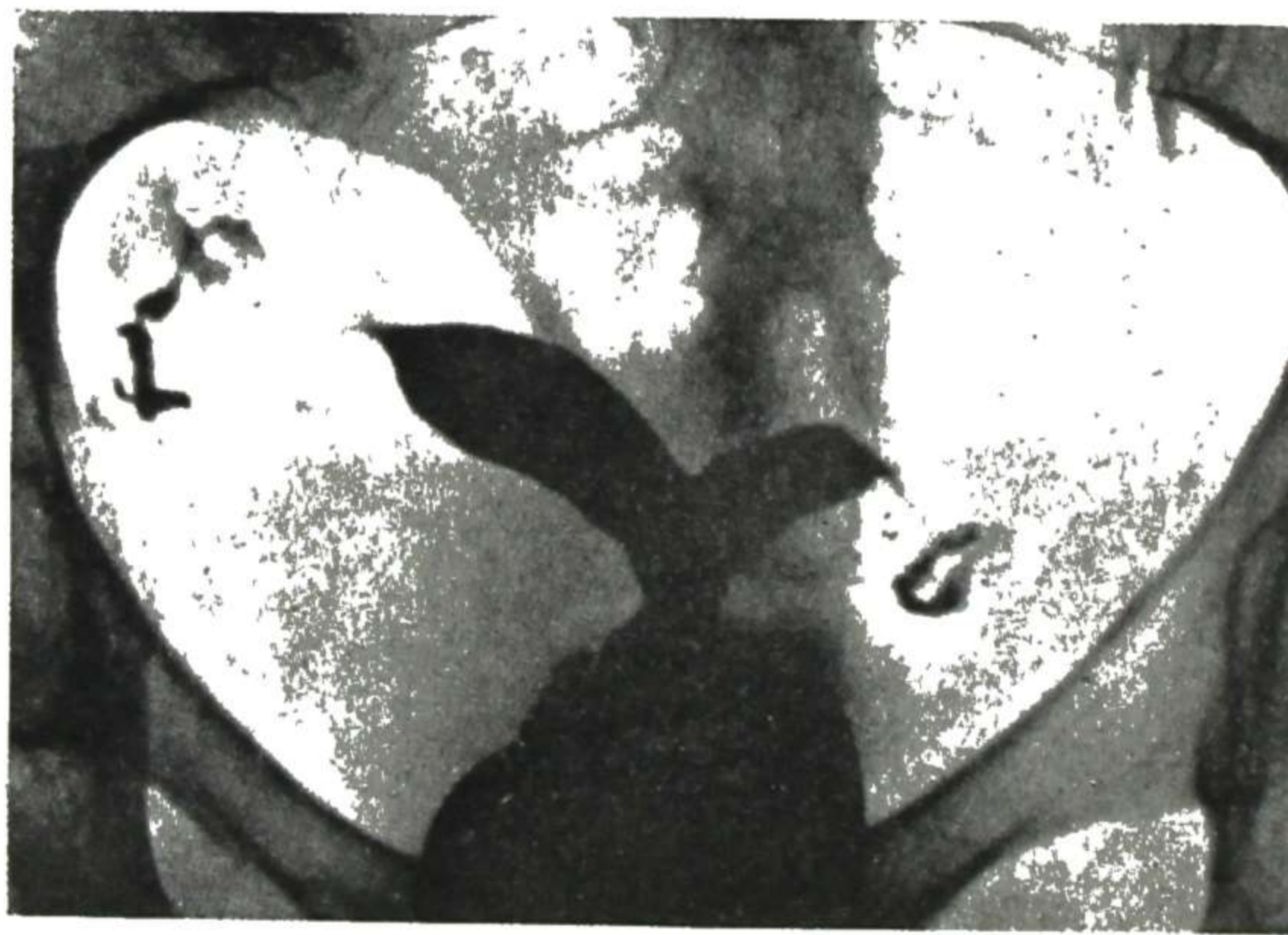
Fig. 1056.—Lipiodol x-ray of bicornate uterus six weeks after removal of septum. (Luikart—*Am. J. Obst. & Gynec.*)

is discovered only by intrauterine manipulation, such as curettement or the introduction of the hand after labor for the removal of adherent placenta or for other reasons.

No treatment for double uterus is required ordinarily, with the exception of the precaution, when curetting the uterus, to be certain that both cavities are clear. It is appreciated, of course, that in this connection, and also in double uterus, pregnancy may take place in each of the two cavities, and at different times, producing various surprising results.

Shelly reported a case of septate uterus, with adenocarcinoma in one side and a pedunculated polyp in the other, and remarked:

If the curette had gone into the right cavity instead of the left the uterine polyp would have been removed and might well have been considered to be the sole cause of the bleeding. Had this happened, the opportunity for early removal of the adenocarcinoma of the uterus might have been lost, unless there was considerable continued bleeding after discharge from the hospital. When the pieces of adenocarcinoma were obtained with the curette, no additional curetting was done. Had the polyp been removed first, of course, a thorough curettage would have followed. But it is possible to see how the curette might have gone into only one cavity of the uterus.
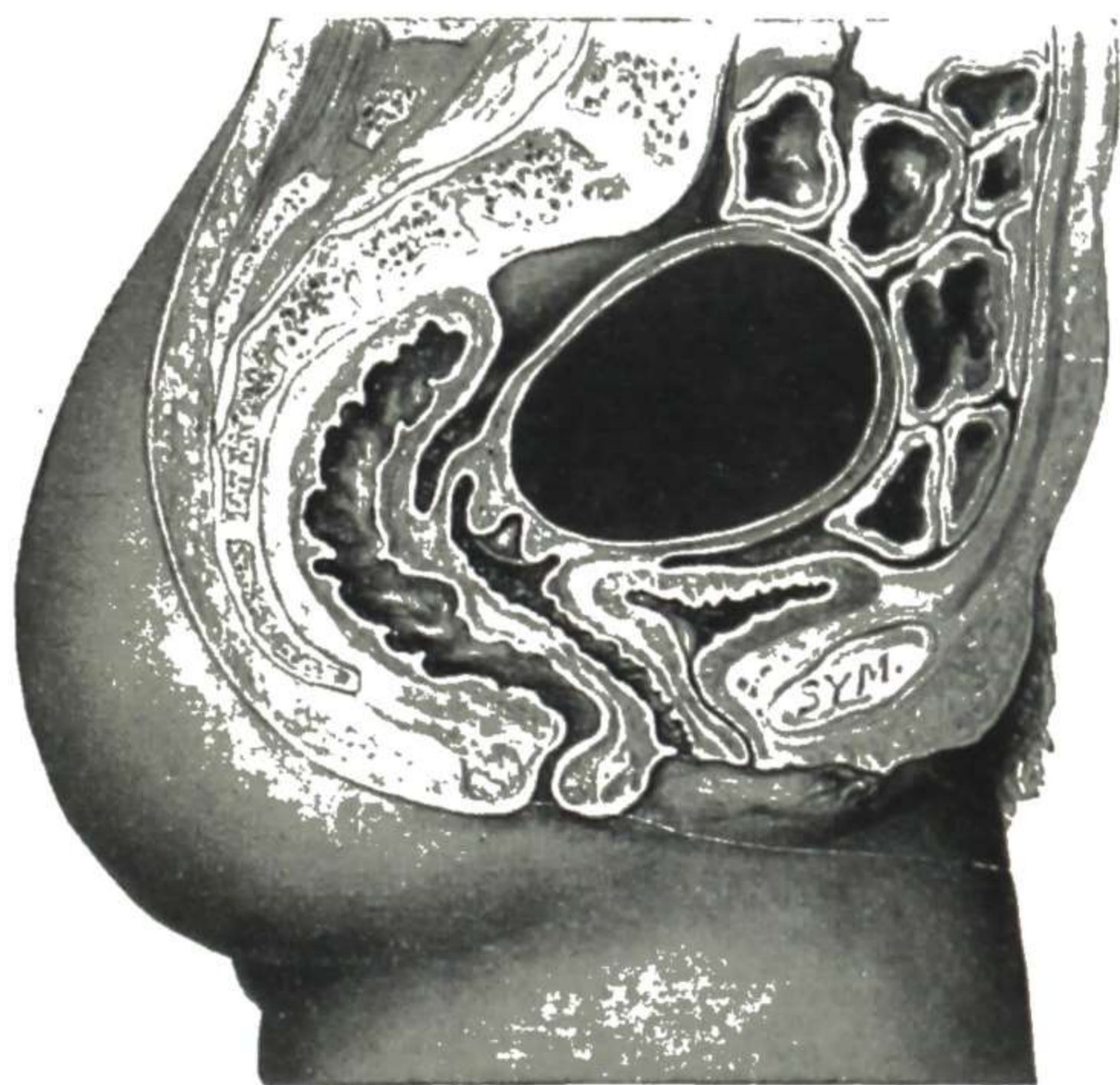
Fig. 1057.   Fig. 1058.

Fig. 1057.—Uterus distended with menstrual blood (hematometra) due to atresia of the cervix. (Montgomery—*Practical Gynecology.*)

Fig. 1058.—Double uterus with atresia in one side. (Montgomery—*Practical Gynecology.*)

If the septum in a uterus gives trouble, it may be removed. Luikart reported such a case, the septum being associated with a bicornate condition of the uterus. Fig. 1056 shows the outline of the cavity after removal of the septum. This method of outlining by opaque injection and x-ray may be employed for diagnosis in uncertain cases.

There may be also atresia at the lower part of a uterus, or of part of a malformed uterus, with a collection of menstrual blood in the cavity (hematometra), as shown in Figs. 1057 and 1058.

Rudimentary Horn.—The uterine malformation of most practical interest is that of a rudimentary horn with an otherwise nearly normal uterus. This is not so very infrequent and many are the diagnostic difficulties that result therefrom. Such a rudimentary horn extends outward from the main body of the uterus, and receives at its outer extremity the attachment of the fallopian tube and round ligament of that side. The point of attachment of the round ligament is, in some cases, the only decisive gross evidence as to whether the mass in question is an enlarged fallopian tube or a rudimentary horn of the uterus. The cavity of the rudimentary horn may be complete, extending

all the way from the fallopian tube to the main cavity of the uterus, or it may be only partial, being absent at some part, or the cavity may be entirely absent, the horn existing merely as a musculofibrous cord connecting the fallopian tube and round ligament with the uterus. Most of the trouble resulting from a rudimentary horn comes from infection in it or pregnancy in it (Fig. 1059).

The **symptoms** and **differential diagnosis** and **treatment** are the same as for similar affections of the fallopian tube, with the following special points:

1. The mass is usually connected to the uterus by a much broader attachment.

2. There is more enlargement of the uterus and distortion of its cavity.

3. The mass may become much larger without rupture if pregnant or without adhesions if inflammatory.
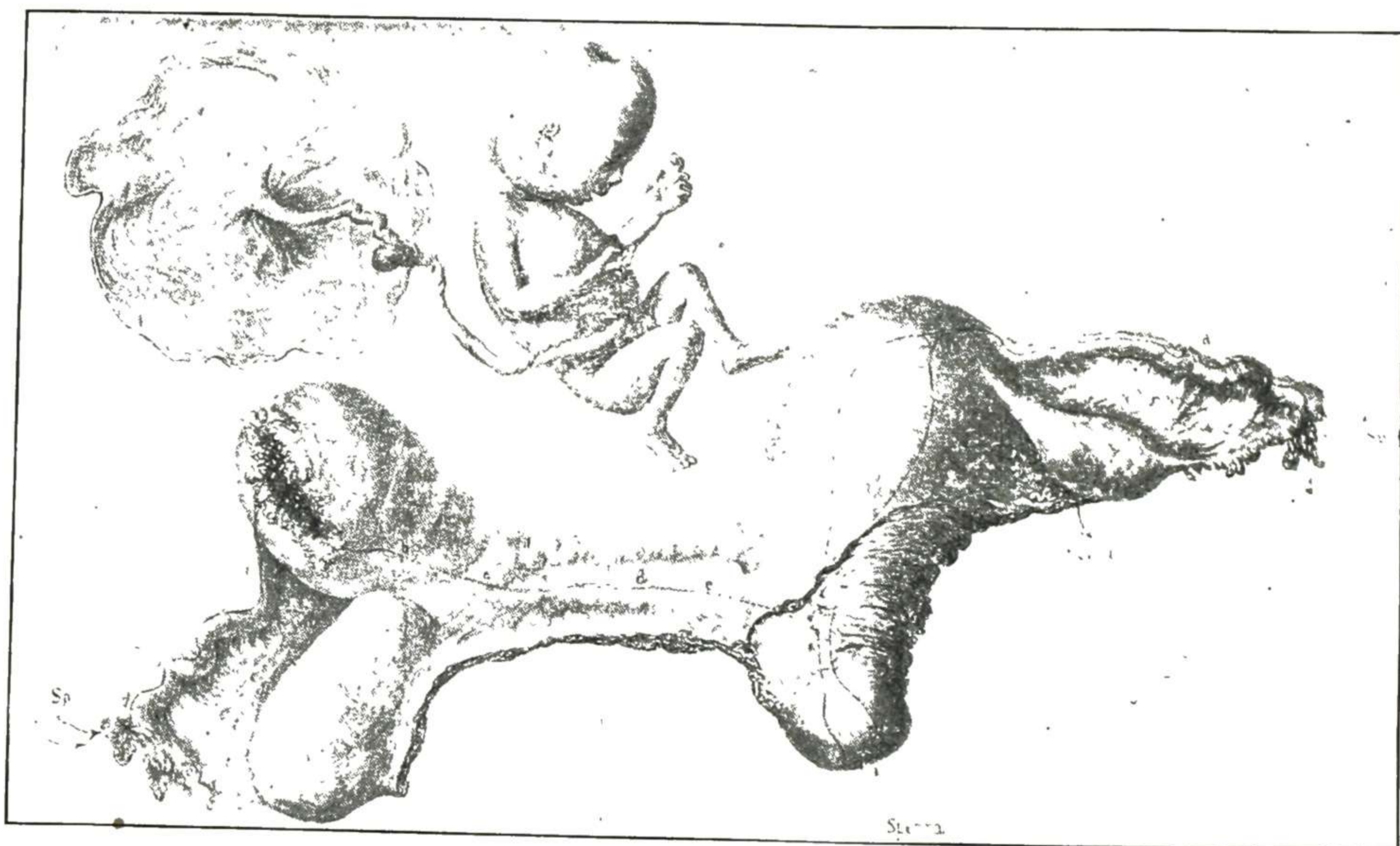
Fig. 1059.—Pregnancy in a rudimentary horn of the uterus. As there is no communicating cavity between the uterine cavity and site of the pregnancy in the rudimentary horn, the spermatozoa evidently came by way of the opposite tube, as indicated by the small arrows. (Kelly— *Operative Gynecology.*)

4. There may be a communication with the main uterine cavity. In most cases the condition is not thought of until found during the course of an operation for what was supposed to be some one of the more common affections. Even when thought of, a diagnosis is rarely possible (except in an examination under anesthesia), for it produces the symptoms and signs of more common conditions, and the trouble is naturally supposed to be some one of these more common affections. In some cases, however, there are anomalous symptoms or signs that make diagnosis difficult and doubtful, and arouse suspicion of this malformation. Sometimes there is decided resemblance to a fibroid. The senior author recalls one such case. The symptoms and signs were anomalous and puzzling. He made a diagnosis of probable fibroid with complications. Operation revealed a rudimentary uterine horn, with the remains of an early pregnancy in it. There was no fibroid.

Pseudohermaphroditism

A true **hermaphrodite** is, according to Ahlfeld's definition, "an individual with functionating active glands of both sexes, provided with excretory ducts." No such case has been reported in which the diagnosis has been fully accepted, though there is considerable dispute among authorities concerning some. Several cases have been recorded in which, among other anomalies, there were glands that on microscopic examination presented some of the characteristics of both ovary and testicle. But that condition does not constitute a double set of glands and excretory ducts.
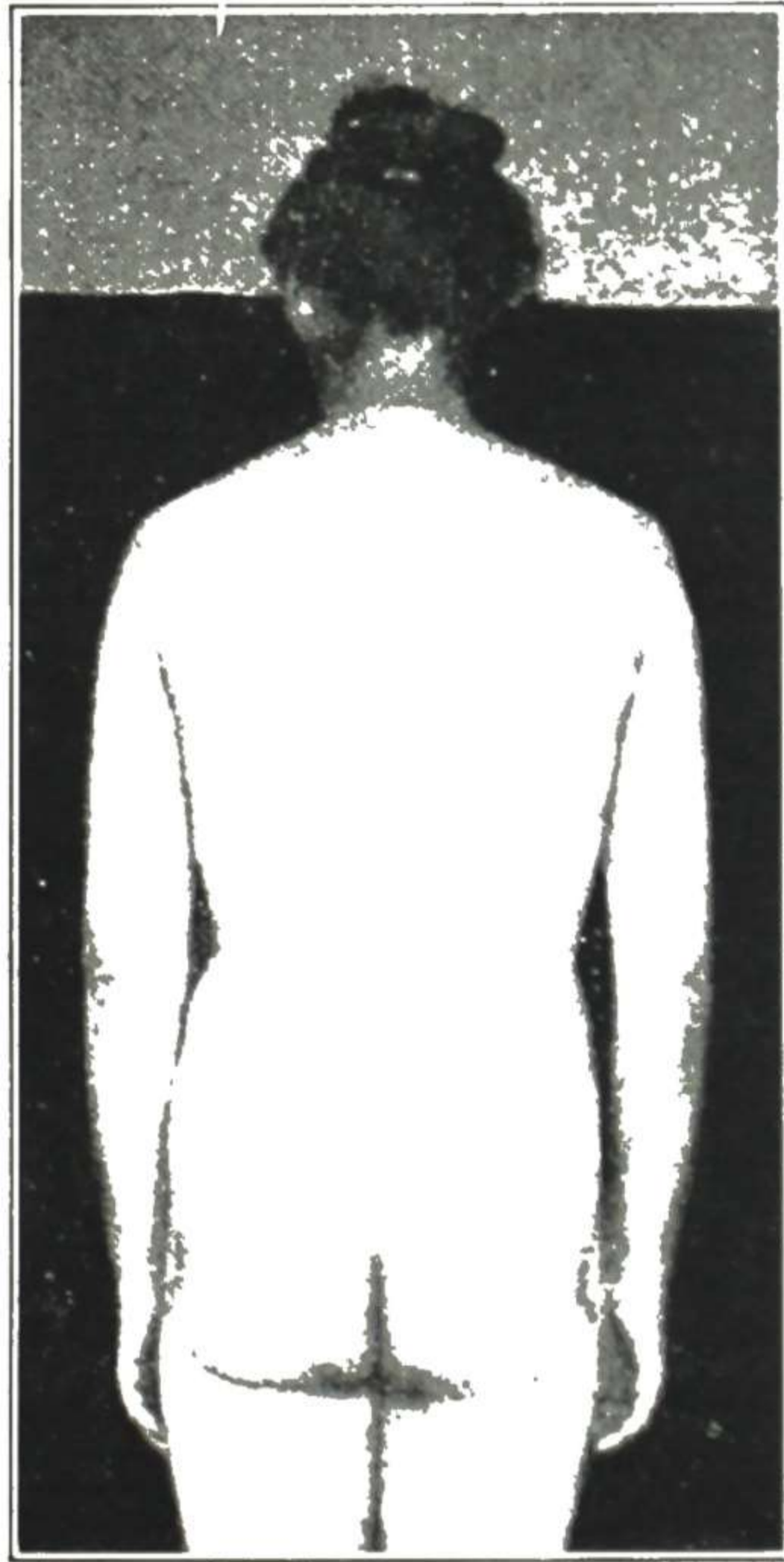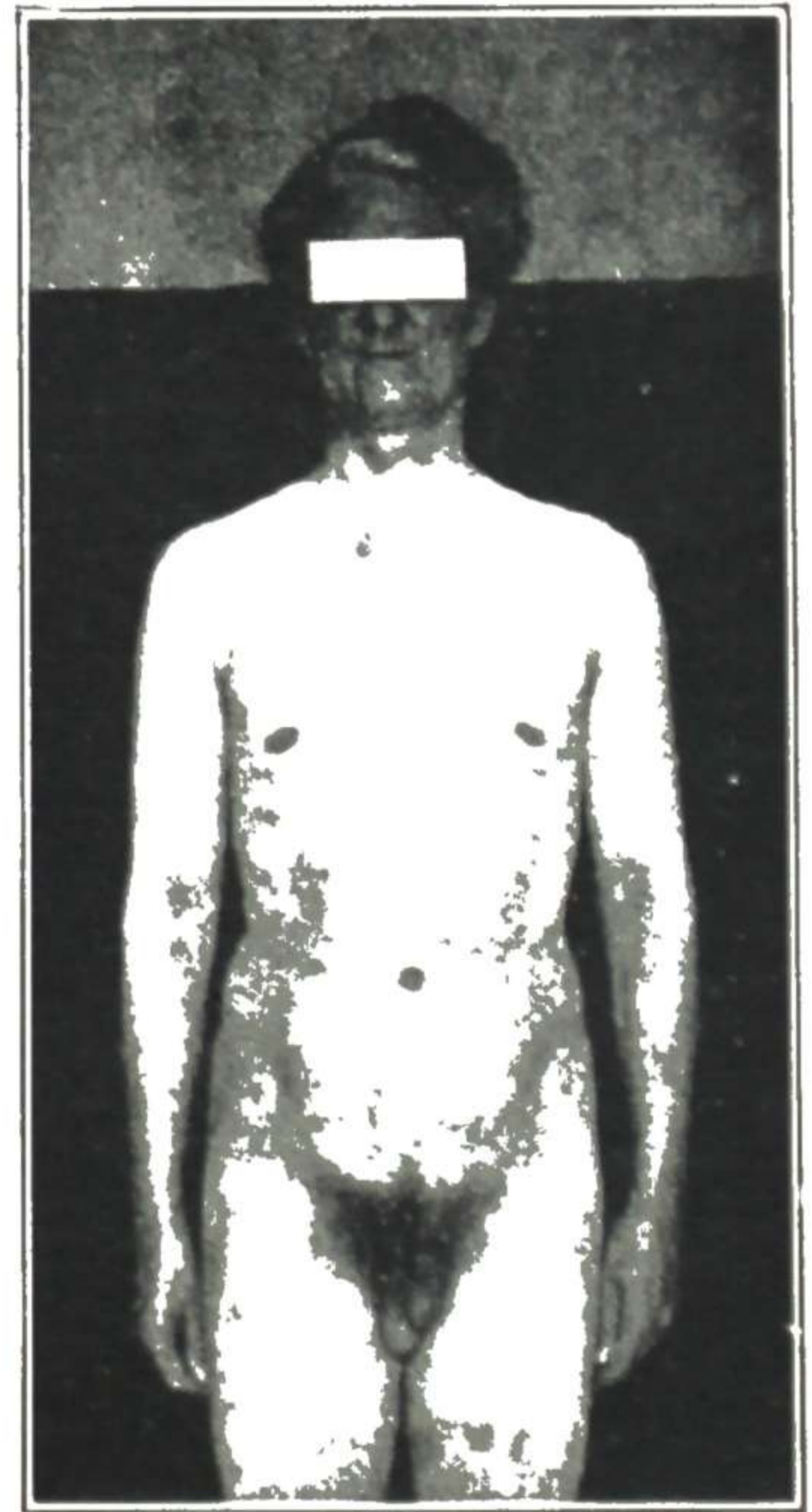
Fig. 1060. Fig. 1061. Fig. 1062.

Figs. 1060 to 1062.—A pseudohermaphrodite. Fig. 1060, As the patient appeared on coming to the author's office for examination. Fig. 1061, Back view, showing the male type of body. Notice the broad shoulders and narrow pelvis. Fig. 1062, Front view, showing the male type of breasts. Notice that the upper limit of the pubic hair is horizontal, as in the female. Otherwise the external genitals present the typical appearance of hypospadias in the male. The divided scrotum and contained testicles hang down almost as in the normal male, though the rudimentary penis is hidden.

A **pseudohermaphrodite** is an individual of one sex presenting some of the local characteristics of the other sex. Many such cases have been recorded and not a few of them have presented a most difficult problem in regard to the diagnosis of sex. Neugebauer was able to collect 942 cases of pseudohermaphroditism. In at least 41 of the pseudohermaphrodites the true sex was positively determined only after abdominal section, though in only four cases was the operation undertaken specifically for diagnostic purposes. Numerous cases are recorded in which the individual dressed and lived for many years as a man or as a woman, and then ascertained that the real sex was the opposite one. The most celebrated case, perhaps, is that of Carl Hohmann, a masculine pseudohermaphrodite, who from infancy to the age of forty-six years

was considered a female and lived as such. The true sex being then ascertained, he assumed male attire and married as a man. The space available is not sufficient to permit the subject of pseudohermaphroditism to be taken up in an extended way. It is sufficient to mention some of the more practical points.

When a child presents any anomaly of the genital organs, a most careful examination should be made and all the possibilities considered, in order to determine positively the real sex. Figs. 1060 to 1064 show a case in which a mistake in diagnosis of sex was made in infancy, and the individual who was really a male dressed and lived as a woman for forty years. Steps in the development of the external genitals are shown in Fig. 1037. Most of the pseudohermaphrodites are really males (have testicles in the abdomen or scrotum), the resemblance to the female external genitals being due to some form

Fig. 1063.
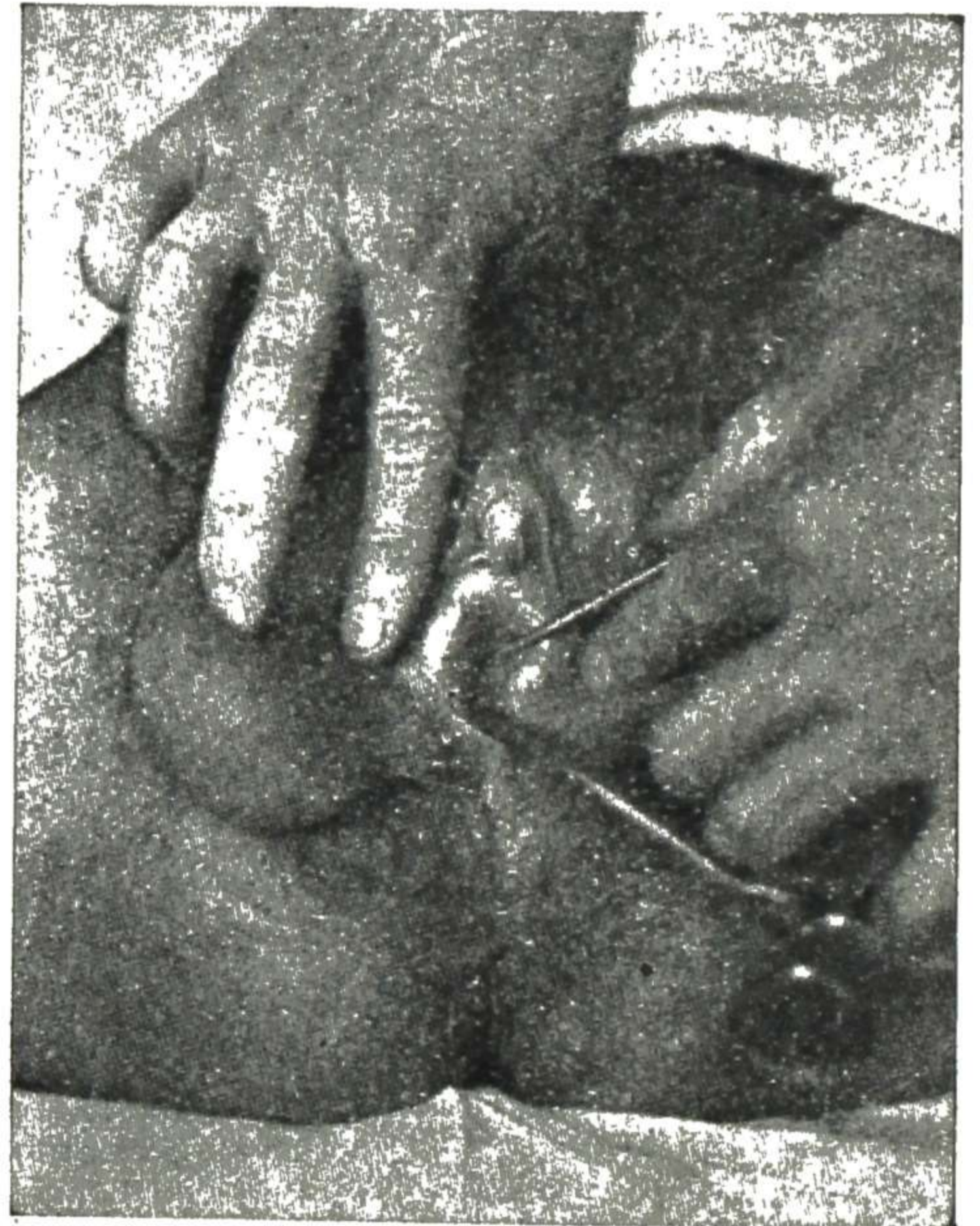
Fig. 1064.

Figs. 1063 and 1064.—External genitals of the individual in Fig. 1060. Fig. 1063, Showing the general appearance—the divided scrotum and contained testicles, the rudimentary penis and the urogenital vestibule. Fig. 1064, The urogenital vestibule has been spread open, a uterine sound has been introduced into the urethra, and a forceps into the sinus pocularis. The condition here is one of male hypospadias (as will be seen by referring to the explanatory drawings in Figs. 1065 and 1066) and yet this individual had dressed and lived as a woman for forty years.

of hypospadias accompanied with an abnormal opening or pocket that is mistaken for a vagina (Figs. 1065, 1066). The principal anomaly in female pseudohermaphrodites, that causes some resemblance to the male sexual organs, is hypertrophy of the clitoris, accompanied with adhesions of the labia minora or labia majora over the vaginal opening, or with imperforate hymen (Fig. 995), or with labial hernia, or hydrocele or other labial swelling covering the vestibule.

In some cases the positive determination of the sex is very difficult and may even be impossible except by abdominal section. The general rule in cases of doubt is to class the pseudohermaphrodite as a **male** until unmistakable evidence

of the opposite sex appears. This will avoid a mistake in a great majority of instances. In the case of four supposed female pseudohermaphrodites who were subjected to abdominal section, three of them proved to be males.

There are exceptional cases in which the sexual instincts of a patient do not correspond to the predominating type of sex organs present. Such a case presents a difficult problem in sex classification, and its solution can probably be best elucidated by detailing the handling of such a case. The patient came under the care of the senior author and the following quoted details are from his report of the case (see Reference List).

Fig. 1065.

Fig. 1066.

Fig. 1065.—Male pseudohermaphroditism. The appearance of the external genitals in marked hypospadias.

Fig. 1066.—A section explanatory of Fig. 1065. B, Bladder; R, rectum; P, penis with lower urethral wall absent; H, abnormal condition constituting hypospadias and requiring a careful examination to determine the sex of the child; X, sinus pocularis, enlarged and opening on perineum, and likely to be mistaken in the newborn for a vagina.

Malformations of the genital organs seldom impose any serious obstacle to the fundamental sex classification of the individual. In some cases abdominal operation is necessary to give definite information concerning the internal organs, but this usually clears the matter promptly. Even in the cases of mixed sex gland, that is, where one individual carries both ovarian tissue and testicular tissue, the sex determination is not difficult. All that is required is to preserve the gland tissue corresponding to the patient's preferences and instincts, and remove the other type. Occasionally, however, a case is encountered which is not covered by our usual methods of sex recognition and requires a much deeper consideration of what constitutes the real sex of an individual and how this primary sex may be modified or partly obscured by later pathologic developments. Such was the problem presented by the following case:

About the first of September, 1938, a young woman was sent to me for construction of a vagina. (Fig. 1067 shows the patient as she came for consultation.) She was twenty-eight years of age, and had never menstruated, though there had been some irregular bleeding when she was about twenty and again two years ago. On examination, I found the

genital organs identical with those of a male pseudohermaphrodite. (The conditions are shown diagrammatically in Figs. 1065 and 1066.) There was the small hypospadiac penis, and back of that a vestibule with two openings, the one in front being the urethra, and the one a little farther back, an enlarged sinus pocularis. The testicles were in the groins.

The general build was masculine, with narrow hips compared to the shoulders (Fig. 1068). There was marked hair growth, with masculine distribution. Also, the patient had a beard which required regular shaving. There was more breast tissue than is ordinarily found in the male (Fig. 1069). The left testicle was lower in the groin than the right, extending down into the upper part of the left labium majus (Fig. 1070).

When such conditions are present, the individual's inclinations and sexual desires ordinarily correspond with the male gonads, and in that case the classification as a male is correct. But in this case, the patient's instincts and preferences from childhood up, and the sexual desires and mental outlook of the present, were all strongly feminine.

Fig. 1067.—Another pseudohermaphrodite, as the patient appeared for examination.

This apparent sexual paradox made it necessary to determine if ovaries were present. Abdominal exploration was then carried out. This showed that there were no ovaries nor tubes nor uterus, the space between the bladder and rectum being entirely clear. With this operative revelation of no ovaries, the patient's earlier history became of special interest. During childhood there had been no departure from the ordinary activities of a girl. She went to the country school, got along very well with her studies, and associated with the other girls in their games. When not in school, she worked on the farm with the other children, doing her share of the heavy work. She always dressed and played as a girl. There were no tomboy inclinations, nor desire for boys' clothes nor amusements.

Pubic hair appeared at about fifteen years of age, but there was no menstruation. Sex desire towards men was noticed at age of eighteen or twenty. At about twenty, she had a slight pinkish discharge for three or four days. This was repeated four or five times, at intervals, she thinks, of about a month.
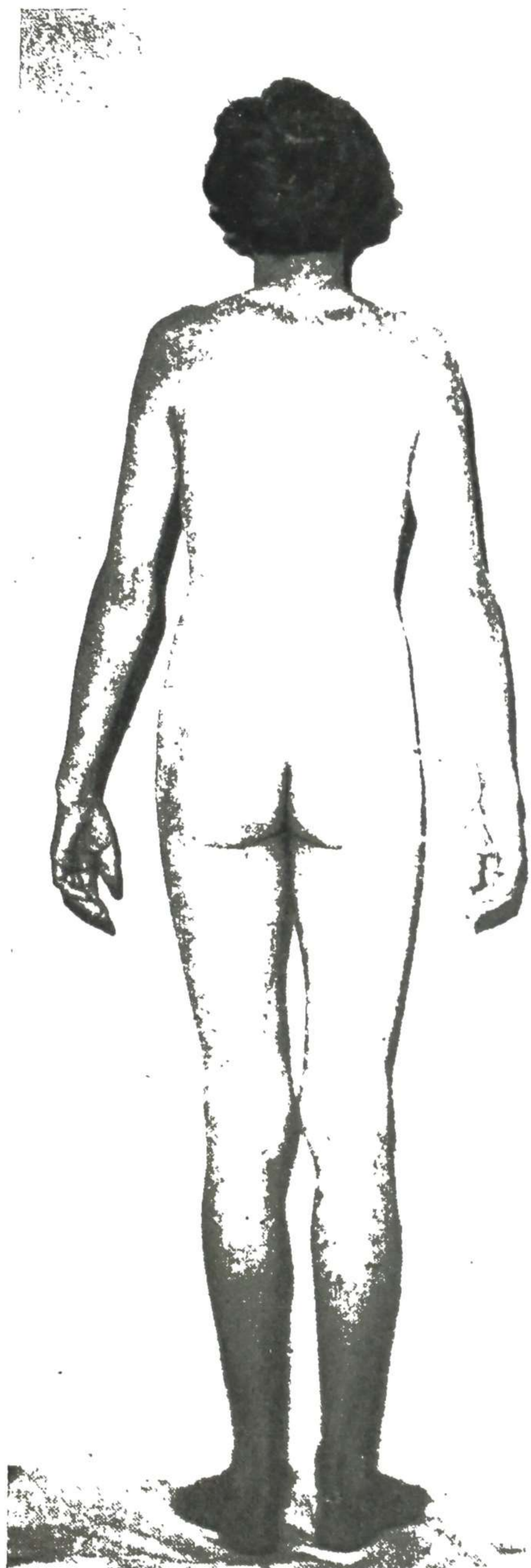
Fig. 1068.

Fig. 1069.

Fig. 1068.—Showing the male type of body form, with broad shoulders and narrow hips.
Fig. 1069.—There was more breast tissue than in the male.

There was no more bloody discharge until about two years ago, when sexual intercourse began. Immediately after the first coitus there was a very free bloody discharge, which stopped the next day. Two weeks later there was profuse flow for some days, and five weeks later another short flow, but not so free. The last two flows came spontaneously, without coitus. Since that time coitus has taken place frequently, without any bleeding or pain or other disturbance, except that the vagina is very short. Her sexual desires have always been toward men, never shifting to women.

Fig. 1070.—The external genitals, showing marked hair growth, a testicle in the left labium majus, an enlarged clitoris and the perineal opening leading into a short vagina (or an enlarged sinus pocularis).

Here, then, was a patient with strong feminine instincts, sexual desires, and general outlook on life, but with testicles and no ovary. What sex classification should be made of such an individual? That was the important and difficult problem which had to be worked out before anything could be done in the way of constructive surgery for the patient, because the type of surgical help required depended on whether the individual was to live as a man or as a woman.

If I followed the gonads and classified the patient as a male, I was directly opposed by the whole record of the individual's instincts, sexual desires and response, and the outlook into the future. If I followed the latter and classified the patient as a female, there was no ovarian tissue on which to rest the decision. A female with testicles and no ovary seemed paradoxical, and of doubtful authenticity. Still the patient had to be classified one way or the other. There was no neutral ground.

What are the dependable criteria for determining the primary sex of an individual? Of course, in this endocrine age, the gonads and their hormones occupy the center of the stage and are looked upon as the decisive factors in the sexual field. But are they? Such a case as this casts serious doubt on their fundamental importance in determining the primary sex personality. The gonad with its hormones may be an effect instead of a cause, as far as primary sex is concerned. Their influences are easily seen and may seem all-important, but there are other influences which enter into the building up of the instincts and directing forces. There is the whole nervous and mental system, which is as important a part of the individual as the gonads, and probably comes from just as strong genetic factors.

Wolf, of the University of Bern, holds that in the chromosomal arrangement and determination of primary sex an impress is made on the somatic cells which takes precedence over that on the gonadal elements, which develop later. In discussing such cases, he states that the somatic and psychic impress seems predominant and that, though hormones play a role in later structural developments, the sex of the somatic cells is decisive. Novak, in discussing his case mentioned later, states, "Such patients as I have described represent genetic females, in which gonadal reversal took place at a very early phase of development, with complete replacement of ovarian by testicular elements."

Reviewing then the two sets of phenomena which help in primary sex classification, we have in this case a personality with well-developed female instincts, preferences, sexual desires, and mental outlook, and on the other hand rudimentary male gonads and associated secondary developments. The testicles undoubtedly lack spermatozoa formation, and hence have stopped short of full development. The spermatic cords and prostate are still more rudimentary, being hardly appreciable in the abdominal exploration. The phallus is rudimentary, and resembles an hypertrophied clitoris as much as a hypospadiac penis. The canal in the perineum, which admits a finger for about an inch, may as well be considered a small vagina as an enlarged sinus pocularis. In such a case, of good development of instincts and mental make-up and poor development of physical structures, it seemed to me that the individual should be classed on the side of the well-developed set of phenomena. Hence, I felt that the patient should be considered as primarily and essentially a female, and that our advice and treatment should be directed accordingly.

Now, could any substantial support be found for thus classifying and treating as a female, a patient with testicles and no ovary? The decision was a serious matter, for on it rested the direction of the future life-activities of the individual. Also, the decision had to be made promptly, as the patient was recovering from the abdominal exploration and was about ready for the further surgical work required.

In the short time available, I found records of seven comparable cases, that is, of cases in which predominant female sex desires and preferences persisted in the presence of testicles without an ovary. Of course, there are many other reported cases of this type, but these seven cases had been handled in recent years, under the present fund of knowledge concerning endocrines and sex determination, and hence their handling was studied with particular interest.

In these seven cases, the absence of ovaries was confirmed by abdominal exploration in five, and seemed fairly certain in the other two. The testicles were removed in six cases, and in the other case they were shifted from the groin to inside the pelvis. The hypertrophied clitoris was removed in four cases. In all of the patients operation was followed by improved social and sexual adjustment and continuation of normal libido. The essential details of these reported cases applying to our problem, were briefly as follows:

Mishell (Case 1): Patient, aged 35, was of feminine build, but had never menstruated. She came for treatment for tender lumps in the groins. Examination showed double

inguinal hernia with a testicle in each. External genitals were normal, with vagina repre-sented by a small canal three inches long ending bluntly with no cervix.

Abdominal exploration showed no ovaries, tubes or uterus. The testicles were re-moved, and the hernias repaired. Improved adjustment. Patient returned to her work. Normal libido.

Mishell (Case 2): Sister of preceding patient, aged 23, feminine build, complained of tender lumps in groins. Abdominal exploration showed no ovaries, tubes, or uterus. Testicles were removed. Improved adjustment and patient continued with good health. Headache which had troubled her disappeared after the operation.

Mishell (Case 3): Sister of the preceding, aged 32, had lumps in the groins and had never menstruated. Examination showed the same conditions in this sister as in the other two. Feminine build, good breasts, no hirsutism, and instincts and feelings all feminine. The only thing special was that she became gray in childhood at the age of nine. The patient was well-adjusted, emotionally stable, had no complaint, and no operation was re-quired. This was one of the two cases in which the absence of ovaries was not confirmed by abdominal operation, but careful pelvic palpation along with the similarity to the other two sisters excluded ovaries with fair certainty.

Rubovitz: Patient, aged 39, masculine build, beard, testicles in groins, hypertrophied clitoris, short vagina, came complaining of severe libido and painful erections. The testes and the hypertrophied clitoris were removed, and the short vagina lengthened. There was improved adjustment and normal libido. The relief from the annoying erections was prob-ably due more to removal of the enlarged and hypersensitive clitoris than to removal of the testicles, for as pointed out later the removal of the testicles seems to exert no influence on the sexual desires and responses of these patients. This is the other case in which the absence of ovaries was not confirmed by abdominal operation. But by deep palpation and the use of pneumoperitoneum, it was felt that ovaries were excluded with fair certainty.

Wharton: Patient, aged 18, was of masculine build from the waist up and feminine build from the waist down. Had a beard. There were bilateral inguinal hernia, hypertrophied clitoris and short vagina. On this diagnosis, the troublesome hypertrophied clitoris was removed and the hernia operation begun. In the hernial sac a testicle was found. An incision on the other side showed another testicle. The incisions were then closed, and later it was explained to the patient that a serious mistake had been made in amputating the supposed enlarged clitoris, which was in fact a penis, and that she was not a female but a male with two testicles. But the patient took quite a different view of the situation. She stated that no mistake had been made in amputating the enlarged clitoris, that she knew she was a woman and that she intended to live as such, and insisted on removal of the testicles. The testicles were finally removed, and abdominal exploration showed no ovaries. Improved adjustment. Normal libido. The patient married and sexual intercourse was satisfactory on her part and also on the part of the husband, except that the vagina was short. It was lengthened later.

Young: Patient, aged 21, masculine build, but no beard. Lumps in the groin, no vagina. Patient was engaged to marry. Abdominal exploration showed no ovaries, tubes, or uterus. A vagina was constructed and the inguinal testes were put back in the pelvis instead of being removed. Improved adjustment. Normal libido.

Novak: Patient, aged 19, masculine build, beard, hypertrophied clitoris, short vagina. In this case pelvic palpation showed bodies in the position of the ovaries, and about that size. Abdominal operation showed these bodies to be testicles in the usual position of ovaries and with a rudimentary broad ligament, but no ovaries, tubes, or uterus. The ab-dominal testes and the hypertrophied clitoris were removed. Improved adjustment. Normal libido. The vagina is to be lengthened later.

Our Case (for comparison). Patient, aged 28, masculine build, beard, testicles in the groins, short vagina. Came for construction of vagina. Abdominal exploration showed no ovaries, tubes, or uterus.

It was clear then that those who had already struggled with the problem of the cases of this type had reached the same conclusion I had, namely, that the patient should be treated as a female. Some had reached this conclusion in the primary study of their pa-

tient, and others had been forced to it by later developments which confirmed and emphasized the predominance of the female element in the personality.

Having classified the patient as a female, with the right to live as such, the next step was to plan treatment to help as much as possible in that direction. The patient's two complaints were: first, the hair on the face which required frequent shaving and, second, the smallness of the vagina. So the two problems were to lessen the facial hair, by lessening the masculinity, and to lengthen the vagina. To accomplish these things, a combination treatment was planned consisting of (a) removal of the testicles, (b) administration of estrin preparations, and (c) stretching treatments for the short vagina.

Accordingly, I removed the testicles, doing the work under local anesthesia and checking each one with frozen section examination before removal, to exclude herniated ovary or ovotestis from removal. Later, Dr. Hobbs, in charge of the Laboratory, made a careful microscopic study of the testicles and there was no indication of ovarian tissue anywhere. As usual with retained testicles, there was no spermatozoa formation. At the preceding abdominal exploration, Dr. Sanford made a critical palpation of the kidney areas and could find no indication of adrenal tumor.

Systematic stretching treatments for the vagina are being employed. If sufficient lengthening cannot be secured in that way then operation is to be carried out. Estrin administration is being pushed with the double purpose of lessening the facial hair, by diminishing the masculinity, and of aiding the vaginal stretching by softening the pelvic tissues.

Various details discussed must be omitted here for lack of space, but it may be stated that in this case and in the reported cases the absence of ovaries and the presence of testicles seemed to exert little or no influence on the strong female desires and responses. Despite the hindering presence of testes and later the lack of sex glands altogether, the patient's feminine personality continued the even tenor of its way.

An important point in taking care of such a patient is to avoid terms or expressions which may disturb her psychologic balance by making her uncertain as to her sex. All records and explanations and reports should be made to conform to the correct primary sex, as worked out by careful study of the case. The patient is already disturbed by the malformation which she wishes corrected, but as a rule she has no thought that she may not be a woman, and it is strongly inadvisable to put her further adrift on the sea of uncertainty by branding her as a male according to the old superficial structural classification.

This patient married about a year later, and a recent report states they "are getting along fine."
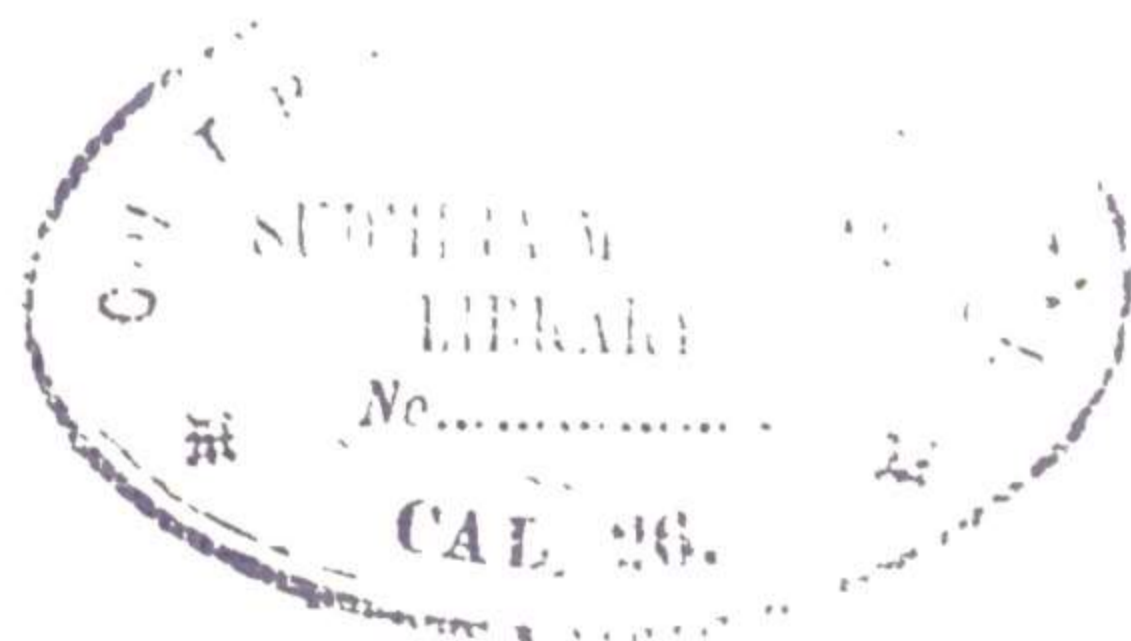
CHAPTER XIV

Disturbances of Function

MENSTRUAL DISTURBANCES

In taking up disturbances of function in this and the succeeding two chapters, we shall consider not only those disturbances which are designated as "functional" because no organic lesion is apparent, but also the disturbances of function due to various organic diseases—that is, all "disturbances of function," whether or not accompanied by evident organic disease. These conditions are, of course, only symptoms. They are not diseases and must not be taken to constitute a diagnosis. They are only indications of some disease, and the physician must determine the nature of that disease by further investigation.

In these three chapters the disturbances of function will be taken up in the following order:

Menstrual Disturbances
Sterility and Sexual Disturbances
Miscellaneous Disturbances (including those of the Climacteric)

MENSTRUAL DISTURBANCES

In considering disturbances of menstruation we shall take them up in order as follows:

Menorrhagia, Metrorrhagia, Irregular Menstruation, Precocious Menstruation, and Vicarious Menstruation.
Amenorrhea, Scanty Menstruation, and Suppression of Menstruation.
Painful Menstruation (Dysmenorrhea), Intermenstrual Pain.

MENORRHAGIA AND METRORRHAGIA

When a patient complains of uterine bleeding, it is often a question at first whether the bloody discharge is excessive menstruation or bleeding from some other cause. A considerable period of investigation and treatment may be needed to determine this point. The pelvic examination may not settle it, for even if no palpable lesion is found there may still be a small submucous myoma or other nonpalpable lesion. Consequently, in the diagnosis and treatment of these cases in the office and at the bedside, the start is made with the combined groups represented by the bleeding patient.

In taking care of such a patient, naturally treatment is given to stop the blood loss while investigating its cause. The response to treatment aids some-

what in further differential diagnosis, and in determining what additional therapeutic measures are required. It is apparent, then, that the practical handling of these patients comprises a treatment-investigation program which checks the blood loss and, step by step, differentiates the underlying cause so that curative measures may be instituted.

TREATMENT-INVESTIGATION PROGRAM

The first interview and examination will identify those patients with an obvious lesion sufficient to account for the bleeding. The treatment for such lesions will be found in the appropriate chapters. For handling patients with no obvious lesion, it is convenient to group them into classes representing different age-periods, as follows: 1. Infancy and childhood (ages one to ten). 2. Developmental period (ten to twenty). 3. Childbearing period (twenty to forty-five). 4. Involutional period (forty-five to sixty). 5. Senile period (beyond sixty).

Infancy and Childhood (Ages One to Ten)

The principal causes of bleeding in this age-period are endocrine disturbance from withdrawal of maternal estrin at birth, ovarian tumors exerting an endocrine influence (granulosa-cell tumors), pituitary or adrenal or pineal tumor, and rarely malignant growth in the vagina or ovary or uterus. Bleeding at birth or a few days thereafter, not due to birth injury, is caused by withdrawal of the maternal estrogenic hormone which the fetus has been receiving. This show of blood is of no clinical importance and requires no treatment.

From the general examination one can tell if the child belongs in the endocrine group of cases found in adrenal, ovarian, pituitary, and pineal tumors. The differential diagnostic points are given in Chapter II, and suggestions for the examination will be found under the details for the next age-period.

The treatment consists of general supportive measures while the underlying cause is being investigated. After the cause of the bleeding in that case is determined, treatment is given for that particular disease as outlined in the appropriate chapter. Vaginal bleeding in young girls which cannot be accounted for by some general blood dyscrasia or other evident lesion calls for a thorough investigation, because a pelvic tumor is the cause of the bleeding in a large proportion of the cases of this age-group. This investigation should include, when necessary, pelvic examination under anesthesia and curettage, with microscopic diagnosis of the tissue removed.

Developmental Period (Ten to Twenty)

This is the developmental age as far as the functions of the genital tract are concerned. The causes of bleeding in this age-period are endocrine disturbances, blood dyscrasias, inflammatory lesions, pregnancy complications, ovarian tumors, uterine myomas, and malignant disease—the relative frequency of occurrence being about in the order given.

The first step in the investigation-treatment program in these cases is to obtain in the history an accurate record of certain items of special importance in the differentiation, as follows:

History items of special importance.

    a. Menses—age of onset, regularity, duration, amount.

    b. Weight—loss or gain, with time involved.

    c. Hair—texture, distribution, premature graying, or undue falling out.

    d. Headaches—location, type, duration.

    e. Vision—glasses necessary, or other disturbance.

    f. Gastrointestinal symptoms.

    g. Nervous symptoms—irritability, depression, crying spells.

    h. General symptoms—Does patient tire easily? Is she sleepy most of the time? What are her habits of sleep, exercise, work about the home, study, recreation at home, vacation activities?

Examination items of special importance.

    a. Type of build—measurements symphysis to floor, symphysis to crown, span from finger tips to finger tips.

    b. Secondary sex characteristics—hair distribution and texture, breast development, vulvar hair growth and development of parts (labia, clitoris).

    c. Lean or fat. If fat, note distribution.

    d. Blood pressure and pulse.

    e. Findings in the abdominal, rectal, and rectoabdominal palpation.

Having obtained the items of information and recorded them for study, the physician is in a position to begin recognition of the general type of disturbance, which recognition will indicate the next step in the diagnostic-therapeutic program. The general groups to be considered in these bleeding patients of the developmental age, are (1) the blood dyscrasia cases, (2) the general disease groups, (3) the pelvic lesion groups, and (4) the endocrine cases.

1. Blood Dyscrasia Group. Uterine bleeding may be due to the condition of the blood without any local disease. It is surprising over how long a period patients will be given endocrine and other treatment before having a blood examination, which reveals the serious disease back of the symptomatic uterine bleeding. To mention this is sufficient to call attention to the importance of prompt investigation of the blood condition in bleeding cases, so that any serious disorder in the blood-making organs will be discovered early.

2. General Disease Group. Other serious general diseases, such as pulmonary, gastrointestinal, kidney, and cardiovascular, are to be eliminated, and in this age-group it is ordinarily advisable to make that elimination before subjecting the patient to vaginal examination.

3. Pelvic Lesion Group. The patient may have a uterine myoma or an ovarian cyst or one of the special tumors with endocrine influence (granulosa-cell tumor) or one of the rare malignant tumors of adolescence (teratoma, sarcoma). Any one of these conditions may cause sufficient disturbance to result in a bloody discharge.

Some differentiation information in this direction has been secured in the general examination, which in these patients should include careful abdominal palpation and rectal and rectoabdominal palpation. The latter will show if there is any mass of considerable size in the pelvic interior or any area with undue tenderness.

4. Endocrine Group. If there is no evidence placing the patient in one of the three groups above mentioned, we assume for the time being that she belongs to the endocrine group, and proceed accordingly.

Endocrine Cases.—The quantitative blood and urine tests for ovarian and pituitary hormones are still not decisive enough to be of practical value in directing therapy. The determinations which will probably eventually be helpful are the pregnanediol test for progestin, quantitative test for the various estrogens, especially estriol, and quantitative tests for pituitary A and B.

From a clinical standpoint the premenstrual endometrial biopsy is still the most accurate index of ovarian function. Recent studies indicate that not only can ovulation be determined, but also deficiency of the corpus luteum function is indicated by an incomplete premenstrual picture.

With functional bleeding all patterns are found, from a normal premenstrual endometrium to an anovulatory type of interval or hyperplastic endometrium. The majority of the cases with functional bleeding show an anovulatory type of endometrium or one in which the premenstrual changes are poorly defined, indicating that ovulation has occurred but that the resulting corpus luteum is defective or deficient in its output of progestin.

At present we are interested in what can be done for the bleeding patient with the knowledge we now possess.

Treatment.—Before starting on specific types of therapy it is well to mention several **general principles** controlling the order in which treatment methods should be used.

1. First in importance is the amount of flow. If this is excessive and the blood loss is marked, curettage will be the first step. After the bleeding is controlled then investigation may be carried out to determine treatment. (Fatal menstrual hemorrhage has been reported in young girls.)

2. The age of the patient is important. For instance, we prefer conservative treatment in young women, whereas in women over forty-five radiation may be the method of choice.

3. The economic status of the patient will arbitrarily limit the therapy to medicine which the patient is able to afford.

The **order of treatment** then in young girls and women in childbearing age will be about as follows, with variations as dictated by the above-mentioned conditions:

1. Regulation of *diet* as needed, with special attention to an adequate supply of vitamins. Vitamin C was found by Junghans to control capillary hemorrhage.

He treated 35 women suffering from menorrhagia with vitamin C, using 50 mg. doses intramuscularly twice daily. In 33 of these women the bleeding stopped in four to six days. He found this treatment valuable also in thrombopenic cases with uterine bleeding. Vitamin K has proved helpful in controlling bleeding in jaundiced cases and in hemorrhage in the newborn, and may later be found to be successful in other conditions. Calcium is necessary in the blood-clotting mechanism. It is supplied in milk, cheese, and dairy products. A high protein diet, with oral fibrogen or arrhenopectin, is used if the clotting time is found to be abnormally prolonged. Foods high in iron are needed to help replace that lost, and if enough cannot be taken in the diet additional iron should be given (as ferrous iron).

2. *Thyroid* therapy should be given when the basal metabolism indicates a need for it. The basal rate is not always accurate as a guide to therapy, but usually a grain of standard thyroid for a minus 10 of the basal rate will be adequate. If symptoms persist, the dose may be increased cautiously, using the patient's feelings and the pulse as a guide.

3. In atonic individuals the bleeding may be due to a lack of uterine tone, and these are the cases most frequently helped by *ergotrate*. The firm contraction of the uterus, by compressing the deeper circulation, diminishes the volume of blood flow through the uterus and thus the amount of blood loss.

4. *Snake Venom* has been used successfully in the treatment of functional bleeding by Goldberger and Peck.

They reported relief in 17 of 20 women treated, and state that the expense of therapy is considerably less than it is with hormone therapy. The venom has a direct effect on the walls of the small blood vessels, making them more resistant to bleeding. The improvement in these cases extended from 2 months to 4 years.

Method.—Moccasin venom in 1:3,000 dilution (prepared by the Lederle Laboratories) is used. Daily doses are given subcutaneously, starting with ½ c.c. and increasing to 1 c.c. by the third dose. If the bleeding is very profuse, 1 c.c. is given twice daily until the bleeding is controlled, then two to three times a week for three menstrual periods.

As much treatment as possible should be given during the first ten days, for patients develop a sensitization to the venom and must be desensitized before continuing therapy. Peck has been able to separate the antigen of the venom from the factor active in controlling bleeding so that the undesirable sensitization action is eliminated.

5. *Hormone Therapy.* Of the hormones used there are three main groups from which to choose.

A. Chorionic Gonadotropins, from pregnancy urine or pregnant mare's serum.

B. Anterior Lobe Extracts.

C. Sex Sterols—estrogens, progestin, androgens.

These will be discussed in the order named:

A. Chorionic Gonadotropins.—a. Pregnancy urine—antuitrin-S, follutein, korotrin, etc. The action of these hormones on the control of bleeding is still not clear. It was formerly thought to cause luteinization and ovulation but this has been disproved in the human by Hamblen and Geist and others. It is probable that the effect is due to a direct action on the uterine muscle or to an indirect one through destruction of persistent ovarian follicles. Good results have been reported by a number of men.

Method.—100 U. daily till bleeding is controlled, then 100 U. every other day, starting seven days prior to the expected flow. This is continued through several cycles, and then the treatment is discontinued to determine if the patient needs more therapy to control the flow. If so, it is given as needed.

b. Pregnant Mare's Serum—gonadogen, gonadin, anteron, etc. This preparation offers real hope of correcting the underlying cause in the anovulatory type of bleeding.

Davis and Koff were able to cause ovulation in normally ovulating women at any desired time in the cycle, though they were not able to duplicate this in women having nonovulatory cycles. There is considerable disagreement among workers at the present time as to the ability of this preparation to cause ovulation in nonovulatory cases, but its success in some proved cases of nonovulatory sterility suggests that it does cause ovulation in some cases.

Method.—Davis and Koff recommend intravenous administration. But many workers are now using 10 to 20 units of gonadogen intramuscularly daily from the fifth to the twelfth day, and then giving one intravenous dose of 20 to 40 units as the last dose. Treatment should be tried for several cycles and then a rest period given, so as to prevent the development of antihormones. The patient should always be tested for sensitivity to horse serum before giving pregnant mare's serum.

B. Anterior Lobe Extracts—prephysin, gynatrin, etc. Hisaw and Fevold used this preparation experimentally and found that it contained follicle-stimulating hormone. L. H. Sevringhaus has reported excellent clinical results in menorrhagia, and other endocrine disturbances.

Method.—The cyclic therapy is used the same as with the pregnant mare's serum, but it is not given as a rule intravenously. The dose is 50-100 units daily from the fifth to the twelfth day.

Mazer and Ravetz have reported excellent results in 14 out of a group of 18 cases of functional bleeding, using a combination of chorionic gonadotropin from human pregnancy urine and an extract from the anterior lobe of the pituitary. The latter seems to contain a synergist necessary for the action of the luteinizing hormone of pregnancy urine. This product will soon be available under the trade name of synapoidin (Parke, Davis).

C. Sex Sterols—(a) estrogens (estrone, estradiol, estriol, and the benzoated compounds, also stilbestrol), and (b) progestin (progesterone, pregneninonol or pranone). These two hormones are considered together, for it is by the combination of both, used in cyclic therapy, that control of bleeding is obtained.

Hamblen found that bleeding in anovulatory patients could be stopped in three days by daily doses of 10,000 to 20,000 I.U. of estrogen. On cessation of treatment, however, the bleeding would recur in three to ten days. Progestin given in the early phase of the cycle frequently caused the patient to start to bleed, and, if given during the menses it usually increased the flow.

When estrogen and progestin were used in the time relations as they act in a normal cycle Hamblen, in a series of 12 patients, obtained 45 normal cycles out of 46, and most of these patients continued for months with normal cycles after the treatment was stopped. Hamblen also obtained good results using estradiol, estriol, and pranone by mouth, but at present the dosages required make the expense of this treatment prohibitive.

Method.—The following cyclic therapy is used by Hamblen. First a cessation of bleeding is secured either by curettage or estrogen therapy as mentioned above. Starting one week after the cessation of the bleeding the patient receives 10,000 to 20,000 I.U. of estrogen daily for fourteen days, following which she is given 5 I.U. of progesterone daily for seven days or until the bleeding starts.

A less expensive oral therapy is now being tried at several medical centers using stilbestrol, but as yet it is too early to evaluate this work. Progestin alone, 5 mg. daily for several days before the period, is adequate in some cases of functional bleeding.

c. Male Sex Hormone or Androgens—testosterone propionate. The action of this hormone in controlling bleeding is thought by some to be an indirect one through the inhibition of the pituitary, while others, notably Sturges and Abarbanel, feel that the action is a direct one on the uterine muscle and on the muscle fibers constricting the coiled arterioles. The general action on the muscle inhibits rhythmic (estrin) contractions, thereby decreasing the volume of blood flowing to and through the uterus, and the local action stimulates the myometrial elements about the arterioles constricting them and thus helping to control the blood loss.

Method.—An initial dose of 10 to 25 mg. is given intramuscularly, and then the same dose is given subcutaneously for three or four days. The bleeding usually increases twenty-four hours before it stops.

Subsequent therapy depends upon the type of endometrium found. If premenstrual changes are present, then 10 to 30 mg. are given subcutaneously in divided doses over seven to ten days prior to the expected period. If a proliferative or hyperplastic endometrium is found, 50 to 100 mg. subcutaneously in divided doses are given over two to three weeks

preceding the period. Greenhill gives 25 to 50 mg. every other day in cases of severe bleeding, until it is controlled. Geist found that by mouth it was necessary to give 300 to 1,000 mg. male hormone to be effective.

There are reports in the literature of undesirable effects, such as hair growth on the lip, enlargement of the clitoris, deepening of the voice and other masculinizing effects, from the use of the androgens. Abarbanel found no masculinization in over 200 cases treated with the androgens.

6. *Curettage*, repeated as needed is a helpful therapeutic and diagnostic aid.

7. *Radiation.*—The cases treated by radiation are divided into two main groups (a) women past the childbearing period, in whom the purpose is to stop menstruation entirely, and (b) women in the childbearing age or young girls, in whom the purpose is to regulate the menstruation. In the latter group it is well to try endocrine treatment first before resorting to radiation, as the menses are occasionally stopped permanently even by small doses of radiation.

Method.—Pemberton in a series of 131 cases, 45 per cent under twenty years and the rest under forty years, obtained 78 per cent of cures using radium in doses of 200 to 500 mg. hr., most of the dosages being under 400 mg. hr. Keene and Payne secured excellent results, using dosages of 200 mg. hr. if under twenty years, 400 mg. hr. from twenty to thirty years, and 300 mg. hr. from thirty to forty years.

X-ray of the ovaries, and in some cases the pituitary, thyroid, and spleen, has been reported by a number of workers. Drips claims cures in 3 out of 4; Mazer, 35 of 44; Molinari and Vierhiller, 21 of 46; Kaplan, excellent results.

Radiation of an endocrine gland of such vital importance to the body as a whole as is the anterior lobe of the pituitary, has always seemed to us a rather risky thing to do. Hence we feel that x-ray of the pituitary should be reserved for cases which do not respond to other forms of therapy.

8. *Operation.*—In young women with bleeding severe enough to damage their health, hysterectomy is sometimes necessary. Repeated curettements, however, plus endocrine therapy should be used before resorting to this radical procedure.

Childbearing Period (Twenty to Forty-Five)

In this age-period bleeding is caused by conditions associated with pregnancy, inflammations in the pelvis, myomas, ovarian cysts, endocrine disturbances, blood dyscrasias, and pelvic malignancies. The relative frequency of these conditions in the childbearing period is about in the order here mentioned.

Pregnancy complications causing bleeding can all usually be determined by the history and examination. If there is still doubt, an Ashheim-Zondek test will ordinarily settle that point. Inflammatory lesions and the larger myomas and ovarian tumors are evident from the history and pelvic examination findings. In patients approaching the age of forty carcinoma of the uterus must always be considered, and if the bleeding does not respond promptly to treatment, there should be no delay in doing a therapeutic and diagnostic curettage.

In this period when the normal endocrine cycles have been fully established, the endocrine deviations are not so frequent as in the susceptible developmental period. Bleeding in the childbearing age is more likely to be due to some definite lesion in the genital tract or in some other system of the body. However, with the exclusion of lesions including pregnancy complications, endocrine dis-

turbance must be considered, and even with a lesion there may be associated endocrine factors. Consequently, this element must be kept in mind in all cases in which there is no other definite and sufficient cause for the bleeding. In the endocrine cases, a careful history will often show endocrine disturbances in the developmental period.

The treatment-investigation program for the handling of bleeding patients in the childbearing period is much the same as that for the developmental period, with certain obvious variations. Curettage may be employed more promptly for bleeding which tends to persist, taking care, however, not to curette for the irregular bleeding of tubal pregnancy and not to be deceived by the made-up story of the woman seeking a curettage for the purpose of abortion.

Involution Period (Forty-Five to Sixty)

In the bleeding cases of this age-group, pelvic malignancies come forward to the place of first importance. The malignancy may be in the form of carcinoma of the uterus or the ovaries. In regard to the uterus, carcinoma of the cervix is more frequent in the decade forty to fifty and carcinoma of the corpus in the decade fifty to sixty.

In this period of declining endocrine function, endocrine disturbances again become rather frequent, but serious ones leading to structural change are much less frequent than in the developmental period. Though granulosa cell tumors causing bleeding occasionally occur, most of the endocrine disturbances of this period are the minor nervous and circulatory discomforts constituting the common "menopause symptoms," which will be considered in Chapter XVI.

In the treatment of bleeding in the period of involution, curettage of the endometrium and conization of the cervix for chronic cervicitis are to be carried out promptly on account of the danger of carcinoma in those locations. If the microscopic examination of the curettings shows no malignancy, but only hyperplasia of the endometrium, the subsequent treatment differs somewhat according to the age of the patient. If still in the early forties with fairly regular menstruation, showing that ovulation is still going on, it is well to follow the curettage with hemostatic and endocrine treatment to control the bleeding tendency as in the childbearing period, so as to preserve the ovarian endocrine influence. If the patient is approaching the age of fifty, irradiation treatment (by radium or x-ray) should be given to stop the undue endometrial activity, as the persistence of it at that age may eventuate in endometrial carcinoma. The use of very large doses of estrogenic substances for the treatment of menopausal symptoms should be avoided after forty years of age.

Senile Period (Beyond Sixty)

Beyond sixty years of age, bleeding has about the same significance as it does in the latter part of the involution period. It is usually due to carcinoma of the endometrium or of the cervix uteri or of the ovaries. If no maligancy is found, the most probable cause is granulosa-cell tumor of the ovary. The bleeding here referred to is, of course, bleeding from the uterus. There may be some bloody vaginal discharge due to atrophic vaginitis or other simple inflammatory trouble, but that is easily recognized on the vaginal examination.

IRREGULAR MENSTRUATION

The menstrual flow may come too soon, the interval being only ten days or two weeks. Again the flow may not come soon enough, running overtime from one to two weeks. It is sometimes difficult to determine positively whether the irregular flow complained of is really menstruation or simply a bloody discharge from some disease of the vagina or uterus. Unless the bleeding resembles closely the menstrual flow in character and onset and duration, it should be regarded as a pathologic discharge, and an examination should be made to determine its cause, that proper treatment may be instituted.

PRECOCIOUS MENSTRUATION

Precocious menstruation is the appearance of menstruation at an early age. For genuine menstruation to take place, there must be considerable development of the genital organs, and this very rarely occurs before the age of ten, except in a patient with granulosa-cell tumor. A description of the clinical characteristics of these tumors with illustrative cases will be found in Chapter XII. Novak describes a constitutional type of precocious menstruation.

Great care is necessary, however, in establishing the fact of precocious menstruation in a given case. Every stain of blood does not mean menstruation. The blood may come from some inflamed or irritated area or ulcer, or growth on the vulva or in the vagina, uterus, rectum, or bladder. In infants a slight bloody uterine discharge occurs not infrequently within the first few days after birth, due to the withdrawal of the maternal estrin.

VICARIOUS MENSTRUATION

Vicarious menstruation is the discharge of blood from other parts of the body at the menstrual time. The uterine discharge may or may not be wholly or partially suppressed. The bleeding usually takes place from the nose or from some open sore, though it may come from almost any mucous surface, such as the lungs or stomach, or bladder, or rectum. Much more rarely some area of the cutaneous surface is affected, the axilla and the groin being the most frequent. At the affected site there appears an ecchymosis and later a distinct flow of bloody serum. The vicarious flow is likely to be irregular, appearing only at some menstrual periods. Allied closely to this is the monthly discharge of milk from the breasts sometimes observed.

Vicarious menstruation in any form is rare. Goffe records a very interesting case in which the vicarious discharge came alternately from the nose and the axilla, and seemed to be associated with periods of ungratified sexual desire. Vicarious menstruation is found principally in nervous women in whom there is imperfect development of the uterus or imperfect performance of its functions. The treatment consists in the correction of any pelvic disease present and endocrine treatment to regulate ovarian function.

Some of these cases of vicarious menstruation are probably due to metastatic bits of endometrial tissue which are transplants from a pelvic endometriosis.

ABSENCE OF MENSTRUATION (AMENORRHEA)

Amenorrhea is the absence of menstruation for one or more periods between puberty and menopause. This definition includes the absence of the menses during pregnancy and lactation. This is known as "physiologic amenorrhea."

Pregnancy must always be taken into consideration in a case of amenorrhea, and before the amenorrhea is attributed to any other cause, pregnancy must be excluded—by the circumstances of the case or by questioning the patient or by an examination.

Amenorrhea from other causes is found principally in girls and young women in whom the function of menstruation has not yet been completely established. The age of puberty, i.e., the beginning of menstruation—varies within normal limits considerably. Girls begin to menstruate, as a rule, at the age of twelve or thirteen or fourteen. The beginning of menstruation may be postponed until the age of sixteen or seventeen without disturbance. Usually, however, after the age of sixteen, and often before that, if the menstrual flow does not appear, there are disturbances that indicate some departure from normal health, and the patient may be said to have amenorrhea.

Amenorrhea is not a disease, but only a symptom. It may be an indication of any one of several entirely distinct conditions, just as a cough may be an indication of laryngitis or bronchitis, or pneumonia or tuberculosis. When a patient comes complaining that she does not menstruate, the first thing to do is to determine **why** she does not menstruate, i.e., what disease or condition lies back of this symptom.

In practice it is convenient, for purposes of diagnosis and treatment, to divide the cases of amenorrhea into two classes: one class (A) including those patients who have never menstruated, and the other class (B) including those who have.

A. WHEN THE PATIENT HAS NEVER MENSTRUATED

A mother brings her daughter, aged fifteen or sixteen or perhaps eighteen, to you, stating that the girl has never become unwell. The mother is anxious to know why the girl does not menstruate and, of course, what should be done for her.

There is a tendency on the part of physicians generally to treat this situation lightly and assure the mother that it is of no importance. The error of this advice is appreciated when, ten years later, the patient returns to know why she is unable to become pregnant and examination shows a very small, undeveloped uterus. If an investigation had been made when the mother first brought the girl to the doctor, the underlying cause of the amenorrhea might have been located and the uterus developed by proper treatment. After a uterus has remained small long past the normal time for development, the chance for improvement becomes much reduced.

When the patient has never menstruated, the absence of menstruation may be due (1) to some malformation, such as imperforate hymen or atresia of the vagina or imperfect development of the vagina, uterus, or ovaries, (2) to poor general health, usually with pronounced anemia, or (3) to endocrine dysfunction. The order given is the one preferable to use in the investigation-treatment program.

1. Malformation

Because of the possibility of there being some serious defect in the developmental processes, examination of the pelvic structures is indicated early in the investigation.

Obstruction in the genital canal gives rise to no symptoms until puberty is reached. At the age of thirteen or fourteen or later the patient begins to feel ill each month. At intervals of about four weeks she notices marked lassitude and loss of appetite, feels somewhat feverish and out of sorts, has pain in various parts of the body, more particularly in the back and lower abdomen. She complains just as a woman does when she is about to menstruate. Her mother thinks menstruation is coming, but no flow appears. After a few days the pain and other disturbing symptoms subside and she feels fairly well until the next month. After several months the pain and accompanying disturbances last longer—in fact, may become almost continuous—and the patient's general health begins to suffer. A swelling may appear in the lower abdomen or at the vaginal entrance.

Such a history makes a local examination imperative. In the local examination, if the condition be imperforate hymen, the vaginal entrance is found closed. There may be a bulging of the hymen due to the pressure of menstrual blood behind it. If the atresia is situated high in the vagina, the vaginal entrance is found open, but after the examining finger has been introduced for a short distance it meets an obstruction, consisting of a wall of tissue blocking the vagina. If there is a collection of menstrual blood behind the obstruction, fluctuation may be obtained. Digital examination by the rectum will give additional information as to the location and length of the vaginal atresia and as to the amount of menstrual fluid collected behind it. In long-standing cases the vagina and uterus and even the fallopian tubes may be distended with blood.

In cases of atresia of the vagina there are likely to be other malformations higher, and sometimes the uterus is entirely absent. If the patient is past the age of puberty and no collection of blood is found above the vaginal atresia, the strong probability is that the uterus and appendages are either absent or so poorly developed that menstruation would be impossible even though the vaginal obstruction were removed. Careful examination should be made to determine certainly whether or not the uterus is present.

In opening into the blood collection in a case of imperforate hymen, careful asepsis must be maintained, for the old blood is a culture medium for the rapid growth of any bacteria introduced, and if the collection extends to the uterus and tubes serious sepsis may result. The remedying of any defect greater than imperforate hymen requires special surgical work, the details of which are given in the authors' *Operative Gynecology.*

2. General Diseases

General diseases may cause amenorrhea by depressing the functional activity of the endocrine system or by affecting the general nutrition through vitamin deficiency or damage to the blood or organs, or by a combination of these effects. Chronic diseases, such as tuberculosis, malaria or syphilis, which

tend in one way or another to depress the vitality of the patient, may cause amenorrhea. Acute diseases, especially mumps, occasionally cause enough ovarian damage to produce amenorrhea.

The importance of nutrition in amenorrhea has long been recognized and all of our more recent knowledge on the relationship of vitamins to endocrine function has empha sized the need for a diet adequate in *vitamins, minerals* and *calories*. As mentioned in Chapter I, W. M. Allen demonstrated regressive changes in the pituitary and ovaries in undernourished animals fed on low calorie diets even though the vitamin contents of the diets were adequate. Clinically it is known that in the overweight patient endocrine func tion is sometimes restored to normal merely by bringing the weight down to normal by diet, this being especially true at puberty.

The same is true when undernourishment is corrected, and in patients who cannot be made to gain by diet alone *insulin* may be given before meals, as suggested by Thayer, to increase the appetite and aid in the absorption of the food given. Liegner, in two cases of long-standing amenorrhea in undernourished young women, initiated menstruation by insulin and high carbohydrate feedings plus intravenous glucose. Both cases had previ ously been given prolonged ovarian and pituitary therapy without success. At the start of the treatment he used twenty units of insulin three times a day and gave intravenous glucose every second day until the patients began to make consistent weight gains; then the therapy was continued with smaller doses of insulin and a high calorie diet until a normal weight was attained.

Simple anemia is frequently a factor in the causation of amenorrhea and, if pres ent, should be corrected by *iron* administration, preferably a product containing ferrous sulphate, trace of copper, and vitamin B complex.

3. Endocrine Dysfunction

If the amenorrhea cannot be accounted for by any of the above conditions, an endocrine investigation is indicated.

The basal metabolism test is usually the first step in the investigation unless there are definite signs or symptoms pointing to one of the endocrine glands as the cause. A lowered thyroid function is a frequent cause of amenorrhea, especially in girls from sixteen to twenty years old.

The thyroid dosage should be about one grain of desiccated thyroid daily to every minus ten of the basal metabolism, but this dosage can be raised or lowered according to the response to treatment. Usually the thyroid must be taken through the menstrual life of the patient, though occasionally we find a case in which it can be discontinued after some months of treatment.

If there is no improvement in the amenorrhea after some months of treat-ment, it usually means that the seat of the trouble is elsewhere and further investigation is needed.

The following is the plan of investigation for a patient with amenorrhea of probable endocrine origin.

1. In the history and physical examination, note especially the points indicative of endocrine disturbances, such as hair and fat distribution and development of secondary sex characteristics. The pelvic examination should rule out a tumor which may require removal (such as arrhenoblastoma), congenital defects, etc. Signs suggestive of basophilic adenoma of the pituitary or of hyperplasia of the adrenal cortex should be noted.

2. The usual special examinations include basal metabolism rate, x-ray of the sella turcica, sugar tolerance test, visual fields, and blood examinations.

3. The next step is to determine whether the patient is ovulating and, if so, the time of ovulation. The technique of Rubenstein, using vaginal smears plus the daily rectal temperature, should help to determine the important point of the day of ovulation. If the approximate time of ovulation is indicated by this curve, an endometrial biopsy two weeks later will decide the point.

4. If ovulation does not occur, it may be due to inadequate pituitary stimulation or it may be due to the inability of the ovary to respond to normal pituitary stimulation. In order to decide this point, the following test, suggested by Hamblen, is used. A dose of pregnant mare's serum is administered, using anteron (200 U.) or gonadogen (20 to 40 U.). This is given intramuscularly, after previous allergic study to rule out serum sensitivity. The dose is repeated daily for three or four weeks, during which time careful clinical observations are made, including a bimanual examination twice a week to evaluate alterations in the genital tract. In the pelvic examinations, special attention should be directed to the ovaries, and if cystic change occurs a rest period is allowed. Measurement of the uterine canal with the occasional endometrial biopsy will give accurate information on uterine and endometrial growth. The daily dosage should not be continued longer than three or four weeks at a time, because of the possibility of the ovaries becoming refractory due to antihormones or to lowered receptivity.

The country physician faced with the problem of outlining endocrine therapy for a case of amenorrhea naturally feels a certain inadequacy because of his inability to obtain the various hormone tests required in certain cases. This, however, need not deter him in his efforts, for much can be done in many cases with the ordinary diagnostic and treatment procedures. The intelligent use of the means at hand will enable him to treat successfully the cases which can be thus handled, and to differentiate the more serious cases which require the extensive investigations and radical treatment measures available in the large medical centers.

Ovulating Patient.—When on endometrial biopsy it is found that there is a well-proliferated endometrium, indicating a full estrogenic response, a dose of 80 U. of gonadogen is given intravenously, and this is followed by daily doses of 500 to 2,000 U. of urinary gonadotropins daily for fourteen days. During this time the urinary sodium pregnanediol glycuronide is followed, and at the onset of any bleeding an endometrial biopsy is carried out to see if a progestational endometrium is present.

If secretory activity is present, it indicates that ovulation has occurred and that the ovary has passed through its biphasic cycle. When this result is obtained no further treatment is given for six weeks, but observations are continued. If spontaneous ovarian activity does not follow, the gonadotropic therapy should be repeated several times. If still there is no further menstruation, then replacement ovarian therapy is instituted.

Nonovulating Patient.—If no response is obtained by the above investigation plan, that means that the ovaries or the endometrium or both are seriously deficient in functional power. Such marked deficiency is due usually to defective development of the genital apparatus, either alone or as part of a general underdevelopment, and hence is found principally in the poorly developed girl in whom normal menstruation has never been established.

The treatment of such a condition presents a difficult problem, but for the hopeless outlook of former years we can now substitute a good chance of suc-

cessfully aiding development, thanks to the great increase in the knowledge of pelvic physiology and endocrinology due to the splendid work of investigators in these fields.

The many details in the treatment of such a condition, with the examination points and the adjustments and variations in time and dosage of medicines used, are best presented by following the actual treatment of such a patient step by step. The following typical case is instructively detailed by Hamblen in an article in *Endocrinology*.

G. R., a single colored girl, 17½ years of age, had not begun to menstruate and had shown signs of incomplete sexual maturation. On examination she presented a classical syndrome of juvenile hypoövarianism. Her span exceeded her height by 5 inches and her lower measurement exceeded the upper one by 6.5 inches. Hands and feet were large and slender with long tapering digits. Her weight was 105 lb. despite a height of 67.5 inches. Characteristic feminine padding was absent. There had been slight physiologic hyperplasia of the breasts. There was a slight growth of pubic hair. The external genitals were markedly hypoplastic. The vaginal cavity was approximately 1.5 inches in depth; the fornices were undeveloped; the walls were thin, smooth and relatively inelastic; vaginal discharge was scanty. The cervix was flush with the upper vaginal vault and, in its size and character, resembled an urethral meatus more than a cervix. A small, flat, triangular uterus without convexity of the fundal portion was identified. The entire uterus and cervix were estimated not to exceed 1.5 inches in greatest dimension. A sound could not be introduced because of the hypoplasia; therefore, no endometrial biopsy was possible. Ovaries could not be palpated, nor any adnexal structures identified.

The basal metabolic rate was −4 per cent. Roentgenologic studies showed the sella turcica to be normal, and studies of the ankle, knee, wrist and elbow showed ununited epiphyses. The osseous age was estimated to be approximately 15 years.

No treatment was given except that of injections of gonadotropes. The patient was given injections of 200 R.U. of a gonadotropic extract from the pituitary (gonadotropic factor) on Oct. 28 and 30 and on Nov. 2, 4, 6, 9, 13, and 16 the total dosage was 1,600 R.U.

Clinical observations, including bimanual pelvic examination and cytologic studies of the vaginal fluid, yielded no significant data, except that there was an increase in the leucocytes of the vaginal smears on Nov. 4 and 16.

At this point treatment with a serum gonadotrope was begun. Doses of 100 M.U. of this gonadotrope were given on Nov. 20, 23, 25, 27, and 30 and on Dec. 2, 4, 7, 11 and 14, making a total dosage of 1,000 M.U. Examination on Dec. 16 showed a definite increase in the size of the genitals and of the vagina. The cervix and uterus had increased sufficiently in size so that a regular uterine sound could be inserted. This procedure indicated a uterine depth of 2 inches. An endometrial biopsy was made and the tissue obtained showed upon microscopic examination a good estrogenic response. On bimanual pelvic examination, the left ovary was felt and judged to be somewhat cystic and about normal size.

Treatment was discontinued at this stage to avoid possibility of the development of a secondary refractivity to the therapeutic agent.

The patient reported back on Jan. 13 (after an interval of 4 weeks). There had been no menstruation. Slight regression of the effects of treatment had occurred. An additional series of treatments with antex was given as follows: doses of 200 M.U. were administered on Jan. 13, 15, 18, 20, 22, 25, 27, and 29 and Feb. 1, 3, 5, 8, 10, 12, 15, 17, and 22, the total dosage for the series being 3,400 M.U. On Feb. 3, both ovaries were felt on bimanual pelvic examination and they were estimated to be about one-half normal size. Studies of vaginal cytology showed nothing significant except a disappearance of leucocytes on Feb. 10 and 12. At the conclusion of the series of therapy on Feb. 24, sounding of the uterus showed it to be 2.5 inches in depth. An endometrial biopsy was made and examination of the tissue obtained showed a well-developed progestational endometrium. Bimanual examination indicated the left ovary to be about normal in size and to have a soft cystic feel. The

right ovary remained small. Treatment was discontinued at this point to await developments and to test the therapeutic value of the alterations produced.

On Feb. 26, the patient began her first menstrual period which continued until March 2, and which appeared normal in all respects. The patient returned for further observation on March 24. She had had no therapy since Feb. 22. She had had no further menstruation. Genital structures had shown no regressions since last examined. The uterus measured 2.75 inches in depth. An endometrial biopsy was made; the tissue obtained showed a normal estrogenic endometrium. No treatment was initiated; observations were continued.

On April 7, another biopsy of the endometrium was made. The endometrium at this time showed a well-differentiated progestational response. On April 8, the patient's second menstrual period began. It continued until April 11 and was normal in all respects. No further treatments were advised. Her last visit was on Aug. 18 when she reported regular menses each month since April. Her last period had begun Aug. 4 and had lasted six days. A general survey showed the following evidences of sexual maturation: an increase of weight to 115 lb. with fat localized in a typical feminine fashion; increased hypertrophy of breasts; increase in pelvic and axillary crines; continued hyperplasia of the genital structures; roentgenologic evidence that all epiphyses except those of the radius and ulna had closed; and ovaries, uterus, cervix and vagina appeared normal in size and character.

Occasionally, some general or local disease will cause this serious functional deficiency type of amenorrhea in an individual who has menstruated to some extent. Vesell reported the cure of amenorrhea of ten years' standing in a woman thirty-one years of age and married eleven years. The patient eventually became pregnant and was delivered of a normal child. Vesell used cyclic therapy with the urinary gonadotropic hormones alone.

More recently a combination of the urinary gonadotropin and the pituitary gonadotropin has been used in the treatment of amenorrhea by Mazer and Ravetz.

In their preliminary report on the use of this combination, called synapoidin, they were able to evoke one or more menstrual periods in 19 of 23 severely amenorrheic women, and in two of these the menses continued without further treatment. They warn against uncontrolled use of this very potent combination and state that they saw evidence of overstimulation of the ovaries in twenty of twenty-three patients who received small amounts preoperatively.

Though it is impossible to evaluate the results from the meager reports to date, this treatment seems to offer hope of success in therapy with the gonadotropes.

In patients who do not respond to the gonadotropic therapy, cyclic treatment with the sex sterols is indicated. Some idea of the dosage needed and the best time for administration can be obtained by the use of vaginal smears as suggested by Papanicolaou and Shorr. They classify the amenorrheas into three groups by vaginal smears as follows:

1. That characterized by the constant presence of the atrophic smear, a type which may be interpreted as indicative of virtual absence of ovarian activity. This group includes most ''primary'' and many ''secondary'' amenorrheas.

2. That showing smears which are from time to time quite constant for the individual and indicate some degree of subnormal but uniform ovarian activity. This group includes most of the ''secondary'' amenorrheas.

3. That showing irregular cyclic smear changes imitating those seen during the normal menstrual cycle but which are, however, insufficient to produce overt menstruation although they reflect periodic ovarian activity. This is the smallest group and includes some ''secondary'' amenorrheas and adolescents with delayed puberty.

The "atrophic" type of vaginal smear is illustrated under menopause disturbances in Chapter XVI, where is given also a comprehensive table describing the transitional forms, which indicate whether or not the patient is receiving effective treatment. Groups one and two seldom respond to gonadotropic therapy while the remaining group usually does respond.

Since detailed examinations for the hormones in the blood and urine are not generally available, a discussion of their use in directing treatment would be of little practical value and hence it is omitted. For articles dealing with this subject, see those by Frank, Goldberger, Salmon and Felshin on the causation and treatment of amenorrhea, by Tamis on the management of secondary amenorrhea of functional origin, and by Hamblen on the gynecic employment of equine gonadotropins.

Cyclic therapy with the sex sterols was suggested in the early days of endocrine therapy by Novak. It is of course a substitutional therapy, but in some cases, especially of the secondary type, the production of several artificial periods sometimes helps the patient to establish her own cyclic mechanism and carry on without further treatment.

The underlying principle in the treatment is an attempt to initiate the normal menstrual cycle by supplying the hormones concerned in their usual sequence.

Beginning with oral administration of theelin (0.24 mg.) or amniotin or emmenin, two or three times daily, and of the same preparation hypodermically, 10,000 U. dose daily, the treatment is continued for fourteen days. The hypodermics of the estrin are then discontinued, and the oral administration is continued. On the seventh day pelvic massage is started to aid ovulation. Cervical dilatation may help, but the definite danger of infection must be remembered and strict antiseptic precautions employed. Prephysin (100 U.) or gonadogen (40 U.) should be started on the fifth day and continued daily until the sixteenth day as an aid to ovulation.

After the fourteenth day, a good progestin preparation, such as proluton, should be given daily to help promote premenstrual changes in the endometrium. A urinary gonadotropin also may be given during this period. On the twenty-sixth day another dose of an estrin product is given, with the final dose of proluton, and all medication is stopped. The patient should show signs of menstruation in from two to four days. If no period occurs, it is probable that the treatment has not coincided with the optimum cycle of the hormones in the patient's blood.

Of course if we have no tests we do not know when the patient's blood contains the maximum amount of hormone and hence we cannot know just when to supplement with an additional amount of the proper hormones. Because of this unknown factor we must try different periods in the month, hoping that one of the series of treatments given will coincide with the optimum cycle of the patient. For this reason the next series of treatments should be started nine days after the last dose of medicine was given, so that this second series would be started five weeks after the first one. Each one is started nine days after the preceding one, and in this way there is a greater possibility of coinciding with the normal hormone cycle of the patient.

If the patient responds to this treatment, then an attempt is made to keep the periods coming until the patient is able to establish her own cycle. This is done by continuing the preparations given by mouth, using pranone, 5 to 10 mg. daily, for the corpus luteum product. The hypodermic medication should be used if needed to supplement the medicine given by mouth. Many patients will gradually improve, so that later the oral medication also may be discontinued. Thyroid, if needed, should always be given with the above outlined treatment.

Zondek, Rozin and Vesell reported causing bleeding in secondary amenorrhea by means of progesterone. They used 5 mg. daily for ten days, and bleeding occurred 60 to 72 hours after the last hormone injection. In primary amenorrhea, the endometrium was first primed with 20,000 I.B.U. of estradiol benzoate distributed over a four-day period, after which the ten-day course of progesterone was given. Several normal periods followed in some of the cases of amenorrhea, but there were no permanent results. In two of our cases we used progesterone with satisfactory temporary relief.

If the medication causes no flow or premonitory signs, then the question arises as to whether it is wise to continue treatments. It may be well to try another series in the spring and fall of the year, as an occasional patient is seen in whom the fundamental pulse of estrus resembles that seen in lower animals. We have had one patient who menstruated only twice a year—in the spring and in the fall.

If the endocrine make-up of the patient is entirely inadequate, it should be explained to her that the absence of menses has little deleterious effect on the general health. If the question of the possibility of pregnancy later arises, it can be stated that the condition does not entirely exclude the possibility of offspring, but that the chances for progeny are not good. A patient of ours became pregnant during a period of amenorrhea which lasted more than two years.

X-ray and radium are usually contraindicated in adolescent amenorrhea, because here we are dealing with immature ovaries which may be unduly sensitive to radiation. Mazer limits this type of treatment to patients aged seventeen or older.

An arrhenoblastoma of the ovary would be an indication for operative treatment as would hyperplasia of the adrenal cortex.

In a case of amenorrhea where the girl is engaged to be married, the question of the propriety of the marriage sometimes comes up, the parent or the patient desiring to know whether it would be right for her to marry when she has never menstruated. The answer is that the case should be thoroughly investigated according to the plan outlined, to determine whether or not there is any serious trouble that would interfere with childbearing (see page 809).

B. WHEN THE PATIENT HAS MENSTRUATED

When the patient has menstruated and later ceases, the amenorrhea may be due (1) to physiologic amenorrhea, (2) to some general condition, (3) to pelvic lesions or treatment, or (4) to endocrine dysfunction.

1. Physiologic Amenorrhea

Normal Pregnancy.—If the patient has previously been regular in menstruation, is in good health and has had an opportunity to become pregnant, the natural supposition is that she is pregnant, and until it is proved that she is not pregnant, nothing should be done that could in any way interfere with pregnancy.

The patient may assert positively that she is not pregnant, may even deny any possibility of pregnancy, but when after examination there is any suspicion in your mind, postpone all local treatment until after the next menstrual flow. If you doubt the patient's

honesty—that is, if you think she may return and tell you that she menstruated when in fact she did not—tell her that she must come during the flow, that you may determine the character of the flow. In this way you can establish certainly whether or not she really menstruates.

In this matter of the question of pregnancy it requires considerable judgment and tact, on the one hand, to detect the cases of pregnancy, and, on the other hand, to avoid wounding the feelings of innocent persons by ill-advised questions. Concerning the question of pregnancy, the cases may be divided into three classes. In the first class come the girls and unmarried women in whom, from the character of the trouble or from the known character of the patient and the examination findings, the possibility of pregnancy may be at once eliminated. These correspond very closely with the patients who have never menstruated and require the same treatment.

In the second class come the married women. If the diagnosis is still doubtful after examination, the patient is told that it is too early yet to be certain about it, and she is directed to come again after a month or six weeks. If the patient is anxious to know at once, an Aschheim-Zondek test may be made.

In the third class come the girls and unmarried women about whom you know but little—they may be all right or they may be all wrong; you simply do not know and hence must be cautious. In this class come also widows, divorced persons, women living apart from their husbands—all of whom, if pregnant, might wish to conceal the fact. Some of these patients are perfectly truthful with the physician, telling him their fears or leaving a clear opening for the asking of questions that would bring out the information. In other cases the patient gives the whole history of her case without any intimation of a misstep. Occasionally the patient tries deliberately to deceive the physician, hoping that in his examination or treatment something may be done that will bring about an abortion.

In such uncertain cases it is usually best for the physician to keep his thoughts to himself, and not to intimate any suspicion of pregnancy until some good evidence of it is found. Do not depend too much upon the history the patient gives. Just keep in mind that it may be all truth and it may be all falsehood. If after examination there is still doubt, an Aschheim-Zondek test will ordinarily be decisive in the matter. If this is negative, the prostigmine test should be tried. This consists in giving 1 c.c. of 1:4,000 prostigmine by hypodermic daily for three days. If the patient is not pregnant and has no marked endocrine disturbance, she will menstruate shortly after the last dose. To date this procedure has never been known to cause abortion.

In the exceptional cases where it is thought best not to suggest the possibility of pregnancy at the time of local examination, a specimen of urine may be requested on general principles, and the pregnancy test made. From three to four ounces of morning urine is satisfactory for the laboratory work. In this way the physician protects himself and at the same time gives the patient good treatment. If it turns out that no pregnancy is present, the patient need never know that pregnancy was suspected. On the other hand, if it turns out that pregnancy is present, nothing has been done that could possibly interfere with it.

Extrauterine Pregnancy.—The evidences of tubal pregnancy have already been given in Chapter XI. In the case of a doubtful pelvic mass the Aschheim-Zondek test may help in differentiation.

Lactation.—As a rule, a woman does not menstruate while nursing a baby. There are, however, many exceptions to this rule, especially after the first six months. Quite frequently a patient, while nursing her child, will begin to menstruate within five or six months after labor and occasionally within two or three months. This happens most frequently in those cases in which the mother has only enough milk to partly nourish the baby.

Beginning Menopause.—The age at which the menopause begins varies much in different persons. The average age is about forty-five, but it often begins somewhat earlier, in exceptional cases before forty. If the patient is past forty

and the menstrual flow has been getting gradually less for several months, the menopause is probably beginning. There are two separate phenomena that usually accompany the climacteric and that may aid in the diagnosis—the "hot flashes" with some irritability and other evidences of nervousness, and the tendency to increase in the subcutaneous fat deposit. Neither one of these is pathognomonic, but both of them occurring in a patient past forty, with menstruation gradually diminishing, make the diagnosis of the climacteric fairly certain.

2. General Conditions

Sudden mental shock will sometimes cause a very persistent amenorrhea in normally menstruating women. The mechanism of this is not understood but it may be due to an indirect adrenal effect on pelvic function. It is well known that psychoses usually upset menstrual function.

Acute and Chronic Diseases.—These have been discussed under primary amenorrhea.

Changes in Routine or in Climate.—A long journey (particularly on the ocean), change of residence from country to city or vice versa, extraordinary grief, joy, anxiety, or exciting work, study (as in preparing for examinations), taking up a new occupation, financial troubles, love affairs, and difficulties in home life. Any of these may cause an expected menstruation to be missed.

When the amenorrhea is apparently due to these causes, it is usually a sign of slight endocrine deficiency and as a rule is due to a mild hypothyroidism.

3. Pelvic Lesions or Treatment

The local diseases that may cause amenorrhea, independent of their general effect on the blood, are those diseases that affect the integrity of the endometrium (from which comes the menstrual blood) or that affect the integrity of the ovaries (from which comes the menstrual impulse).

Hyperinvolution of the Uterus.—The process of involution following pregnancy and labor may continue farther than normal, reducing the uterus below normal size and so modifying the endometrium as to interfere with menstruation. This is a rare condition, but must be kept in mind in considering a case of amenorrhea in a patient who has given birth to a child within a year or two.

In one of the authors' cases the patient was twenty-eight years of age. Three years before she had had a severe infection following the birth of her child, and there had been no menstruation since. Bimanual examination showed the uterus to be very small. On account of other trouble it was necessary to open the abdomen, and the opportunity of inspecting the internal genital organs was offered. Everything was atrophic—the uterus, ovaries, tubes, and round ligaments. The uterus was about half the normal size. Hyper-involution may occur also following simple curettage for chronic endometritis, though that is even more rare.

The treatment in such a case is to try to restore the functioning power of the uterus by active endocrine treatment.

Chronic Metritis.—Long-continued inflammation of the uterine wall may so disturb the blood supply to the endometrium as to interfere with its functions. The treatment is to attempt restoration of function by endocrine medication,

unless the troublesome symptoms from the chronic metritis and associated adnexal inflammation are so marked as to call for hysterectomy.

Dilatation and curettage may act as nutritional stimulants to poorly functioning uterus or ovaries, and Anspach recommends them in selected cases of persistent amenorrhea. Transplantation of tissue (endometrial or ovarian) may be employed in exceptional cases.

Solomons grafted some endometrium and a portion of ovary, obtained from a patient being operated upon for myomas of the uterus, into a twenty-eight-year-old patient who had been amenorrheic for three years. The amenorrhea had followed a pelvic operation complicated by mumps during the convalescence. The transplantation operation was followed by the reappearance of the menses in two months and the periods had recurred regularly at the time of the report, which was six years after the operation. He mentions that there were some adhesions about the remaining ovary which were freed at the time of the second operation, so this might possibly be a factor in the cure.

Hysterectomy.—The removal of the uterus ordinarily means cessation of menstruation. In certain cases of supravaginal hysterectomy for fibroids, sufficient of the lower part of the corpus uteri may be preserved to continue menstruation. Of course, such an operation constitutes only a partial amputation of the corpus uteri. The removal of the cervix uteri alone has practically no effect on menstruation.

Ovarian Disease.—With most ovarian diseases extensive enough to cause amenorrhea, the ovarian disease overshadows the amenorrhea in importance. There is, however, one exception, namely, thickening of the capsule of the ovaries. This may be sufficient to prevent ovulation and menstruation without otherwise troubling the patient. Operation by stripping off portions of the thickened capsule of each ovary is sometimes necessary. It is employed of course only after less radical measures have been thoroughly tried.

Bailey reported such operation on the ovaries in seventeen cases of secondary amenorrhea that had had previous endocrine therapy without result, and thirteen of these cases showed a successful result with the establishment of regular periods following operation. While recognizing the inadvisability of subjecting young women to laparotomy, he feels that it is justified in the following types of cases: (1) When endocrine therapy fails to establish regular periods. (2) When multiple cystic changes in the ovaries can be detected and endocrine therapy does not correct the condition. (3) When time itself does not rectify menstrual function one should not wait until all hope of help has passed. (4) When the psychic need for menstruation is important.

In rare instances the grafting procedure used by Solomons, previously mentioned, may be indicated.

Double Oophorectomy.—The complete removal of both ovaries (removal of all ovarian tissue in the pelvis) causes menstruation to cease, either at once or within a short time. In many cases, even with both ovaries badly damaged, enough ovarian tissue may be left to continue menstruation. In suitable cases this is the practice ordinarily followed. To secure the desired result, however, the ovarian tissue left must continue to functionate.

On the other hand, in exceptional cases, when both ovaries have supposedly been completely removed, the patient has continued to menstruate and has even become pregnant. That means, of course, that some ovarian tissue was left.

Some part of the normal-shaped ovaries may have been unwittingly left or there may have been lobulation of one ovary. Islands of ovarian tissue, from mal-formation of ovary, are occasionally found in the pelvis, either close to the nor-mal site of the ovary or at some distant part of the broad ligament.

The removal of one ovary has little or no effect on menstruation, provided the other continues to functionate. The removal of one or both fallopian tubes has no effect on menstruation.

Radiation.—X-ray treatment or radium treatment may stop menstruation temporarily or permanently.

4. Endocrine Dysfunction

Endocrine disturbance is an important cause of amenorrhea in patients who have menstruated as well as in those who have not. Imperfect functioning of the ovary or other endocrine gland is partly responsible for amenorrhea and scanty menstruation ordinarily attributed to poor general health, to acute general or local diseases, to obesity and to nervous impressions. It is wholly responsible in still other cases, and in these the endocrine treatment outlined under Pri-mary Amenorrhea should be followed through to restoration of function.

In these mature patients low-dosage x-ray therapy has proved remarkably successful in overcoming persistent amenorrhea and accompanying sterility. It must, of course, be administered by a skilled radiologist in conjunction with examination and advice of a gynecologist, for radiation is double-edged and can harm as well as benefit.

Several techniques are used and for details the reader is referred to the articles by Kaplan and by Mazer and Goldstein.

In 1943 Mazer and Greenberg gave the results of a long-time follow-up of their patients so treated. Reidenberg had reported on 136 of them treated be-tween 1927 and 1937. Of the amenorrheal 71 per cent and of the oligomenor-rheal 78 per cent were still menstruating at normal intervals. Eighty children were born to these women and no deleterious effects were observed in the chil-dren, some of whom are now of high-school age. In ninety later cases with a follow-up of nearly three years, sixty-five of the patients have continued to menstruate normally. Fifty-four were sterility cases in which the sterility had persisted in spite of organotherapy and other measures. Thirty of these conceived and twenty-eight carried to term, with healthy children, and the other two aborted early.

SCANTY MENSTRUATION

A diminution in the menstrual flow, or a too slight flow from the beginning of menstruation, is caused by the same condition that leads to absence of the menses (with the exception of those obstructive lesions that prevent the escape of any blood), and the treatment also is practically the same.

PAINFUL MENSTRUATION (DYSMENORRHEA)

Dysmenorrhea is one of the most frequent symptoms met with in gyne-cology and, in some cases, it is one of the most difficult to treat. Stone esti-mates that 35 per cent of all women complain of some pain with menses.

Among 1,400 women students at the University of California, Cunningham found that 50 per cent complained of *some* pain and 35 per cent complained of *severe* pain. The question of the degree of pain a patient has depends, of course, entirely upon her interpretation of a subjective symptom, and this fact makes the investigation and evaluation of treatment very difficult.

The subject can best be covered by discussing therapy, and referring under each kind of treatment to the theories or facts upon which the therapy is based.

The term dysmenorrhea includes all degrees of pain, from that causing slight inconvenience to severe pain confining the patient to bed and in some cases requiring the use of opiates. Wide variation in the individual threshold for pain determines to some extent the disability and, of course, this must be considered in planning treatment.

Since there is no single cause for dysmenorrhea, classification for treatment is difficult, for, though certain types can be classified on an etiologic basis, it is impossible, as will be explained later, to classify endocrine therapy on the basis of etiology. For convenience the following outline is used in the discussion of therapy.

1. Mental and physical hygiene.
2. Pelvic and extrapelvic lesions.
3. Allergic causes.
4. Neurogenic causes.
5. Mechanical causes.
6. Endocrine causes and therapy.
7. Premenstrual tension.

1. The importance of **mental** and **physical hygiene** has long been recognized. We all know of instances where dysmenorrhea has been consciously or subconsciously used as a shield to avoid an unpleasant situation. Many girls have been brought up to believe that one is supposed to be ill at the menstrual time. The very words used to describe the event, such as "unwell" and "sick time," certainly help to foster this false idea. An illustration of what can be done by hygienic instruction is shown in an article by Clow. She was able to reduce the incidence of dysmenorrhea in an English girls' school 70 per cent by having the girls take warm showers and moderate exercise during their periods, laxatives and diet as needed, and by explaining to them that menstruation is a normal function. For hypnosis, see Kroger and Freed (1943).

Faulty posture is considered an important cause of dysmenorrhea by Adams and he reported that he was able to relieve a number of cases by postural correction. In contradistinction to this, Miller, in observations on 302 college women over a four-year period concluded that posture is not a factor in dysmenorrhea.

2. The **pelvic lesions** most frequently causing dysmenorrhea are endometriosis and adenomyosis, ovarian cysts, pelvic inflammatory disease, and occasionally uterine displacements.

With endometriosis, the ectopic bits of endometrial tissue menstruate with each period, forming hematomas filled with the typical chocolate-colored material. Since there is no avenue of escape for the menstrual discharge, these

isolated glands become markedly distended with each period and the distention causes pain. The pain in this condition usually is most marked just before and during the period.

Payne in a series of 307 cases of endometriosis found that he was able to determine the onset of the pain in relation to the period in 92 patients. He gives the following table:

Premenstrual	18 per cent ⎫
Pre- and intramenstrual	25 per cent ⎬ 93 per cent
Intramenstrual	50 per cent ⎭
Intra- and postmenstrual	4+ per cent
Postmenstrual	1+ per cent
Intermenstrual	1− per cent

The pain is described as "boring or grinding" in character. In adenomyosis of the uterine wall the pain is usually most severe in the latter part of the period and for a day or so after the period.

In an attempt to determine the importance of the uterine position as a cause of dysmenorrhea Bell and Parsons made a study of the women students at the University of Michigan.

Of the 840 women students 12 per cent complained of severe dysmenorrhea. Of the 12 per cent the uterus was retrodisplaced in 43 per cent, it was acutely anteflexed in 9 per cent, while in the remaining 48 per cent the uterus was in normal position. Twelve of the dysmenorrheic women required opiates for relief at the menstrual time, and, in these the uterus was retroflexed in seven, acutely anteflexed in one, and in normal position in the remaining four.

A trial of pessary treatment is helpful in determining whether in a given case the retrodisplacement is the factor causing the pain. If a pessary cannot be fitted, the knee-chest posture will relieve some cases.

Extra-pelvic lesions in which dysmenorrhea is occasionally a symptom are ureteral strictures and a chronic appendiceal irritation in a low-seated appendix. Hunner of Baltimore was the first to call our attention to ureteral strictures as a frequently overlooked cause of dysmenorrhea.

In 1928 one of us (R. J. C.) spent a day with Hunner going over the histories and x-rays of cases of this type. After seeing numerous cases in which the patient had had one or two operations for relief of the dysmenorrhea without result, and then to see these cases relieved after ureteral dilatation, was thoroughly convincing that this condition must be kept in mind in searching for a cause for pain in the obscure cases. In 1939 Sears reported 14 cases in which dilatation of the ureteral stricture cured the dysmenorrhea. Most of these patients had had operations either for chronic appendicitis or salpingitis.

In cases in which severe nausea and vomiting are associated with the dysmenorrhea a low-seated appendix which hangs down in the pelvis should be ruled out. We recall two such cases in particular in which simple removal of the appendix gave the patients complete relief. In one of these the appendix was so firmly attached to the ovary that a small wedge of ovarian tissue had to be taken in order to remove the appendix. Previous dilatation had not helped in this case.

3. The importance of **allergy** was first mentioned by Duke in his monograph on asthma and allergy. The first extensive series of cases, however, was reported by **D. R. Smith.**

He found that the three symptoms complained of most frequently were dysmenorrhea, mucous vaginal discharge, and irregular menses. The foods most frequently giving positive reactions were: wheat, eggs, milk, chocolate, fish, beef, pork, nuts, beans, peppers, cabbage, and cauliflower. The treatment consists of elimination diets and in cases where definite allergy was present, the results were strikingly good. The allergic factor was proved in some cases by a return of the pain after discontinuing the diet. The importance of keeping the allergic factor in mind in searching for a cause of dysmenorrhea in a given case is emphasized in a later article by D. R. Smith and Otto Schwarz. In the 26 cases reported by them 5 had had abdominal operations and 3 had had, in addition, dilatations without relief. The sensitivity of uterine muscle to the allergens has been known for years and the most satisfactory tissue for testing the relative potency of the various allergens is the uterine muscle of a guinea pig.

4. The **neurogenic factors** causing dysmenorrhea have been investigated by Kieffer. He found that stimulation of the internal os caused uterine contractions, cervical spasm, and pain. From his study he concluded that the cervix was a sphincter with its tone governed by a reflex arc through the lumbar cord and the cervical ganglia of Frankenhauser. Kieffer feels that the spasmodic pain experienced in cases of dysmenorrhea may be due to an abnormal state of the cervical ganglia. This theory has received support from the practical work of Blos and also of Kennedy.

The former cured 90 per cent of his dysmenorrheic patients by injecting the cervical ganglia with 70 per cent alcohol. The technique of this injection method is given by Davis who reports permanent results in six cases. She injects 1 c.c. of 85 per cent alcohol into the Frankenhauser ganglion under evipal anesthesia. She emphasizes that the procedure is not free from danger. Certain drugs are said to secure their results through their action on the nervous mechanism. Hundley, using benzedrine sulphate, reported complete relief in 61 per cent of 186 attacks, using one or two 10 mg. doses. Atropine, syntropin, mecholyl, and adrenalin have all been used with relief in some cases. Ainley obtained good results using a capsule containing aspirin 5 gr., phenacetine 3 gr., and propadrine hydrochloride ¾ gr. The use of calcium gluconate 60 gr. daily for two weeks before the period gave relief in 70 per cent of 49 cases in one series. The calcium lessens the irritability of the muscles and nerves.

In severe cases of dysmenorrhea of any type where all conservative measures have failed, relief can usually be obtained by resection of the presacral nerve as recommended by Cotte, Leriche, Wetherell, Behney, and others.

5. **Mechanical obstruction,** because of a pin-point opening, stricture, tight internal os, acute anteflexion, polyp or fibroid, is the cause of pain in some cases. The exact mechanism of the relief secured by dilatation is not known but two theories are advanced:

a. Relief of tension in the uterine cavity. It seems reasonable to assume that the increased tension from stenosis would tend to make the uterine contractions painful, as it does in the intestine and other hollow organs.

b. By the mechanical dilatation stimulating ovulation, as does an electric current in the canal. This seems opposed to the general assumption that nonovulatory menstruation is painless.

The diagnosis of the obstructive factor in the complex symptomatology is made from the abrupt onset of severe cramping pains just preceding the flow and their relief when the flow is well established, along with the usually associated small cervix and small cervical opening.

The technique of office dilatation consists in gently introducing graduated dilators past the internal os under antiseptic precautions, starting with a small size and advancing to the largest that can be easily introduced. The dilators are shown in Fig. 279. It is well to leave the last one in the dilated cervix for several minutes. In married women, the dilatation is carried out in the pre-ovulatory interval. E. L. Stone, in reviewing the various treatments for primary dysmenorrhea, concluded that his best results were obtained by dilatation.

If a patient obtains temporary relief by office dilatation, then it is probable that a more lasting result will be secured by thorough dilatation under anesthesia followed by the insertion of a hard rubber stem (Fig. 1071) or the soft thick-walled rubber-tube stem (Fig. 1072).
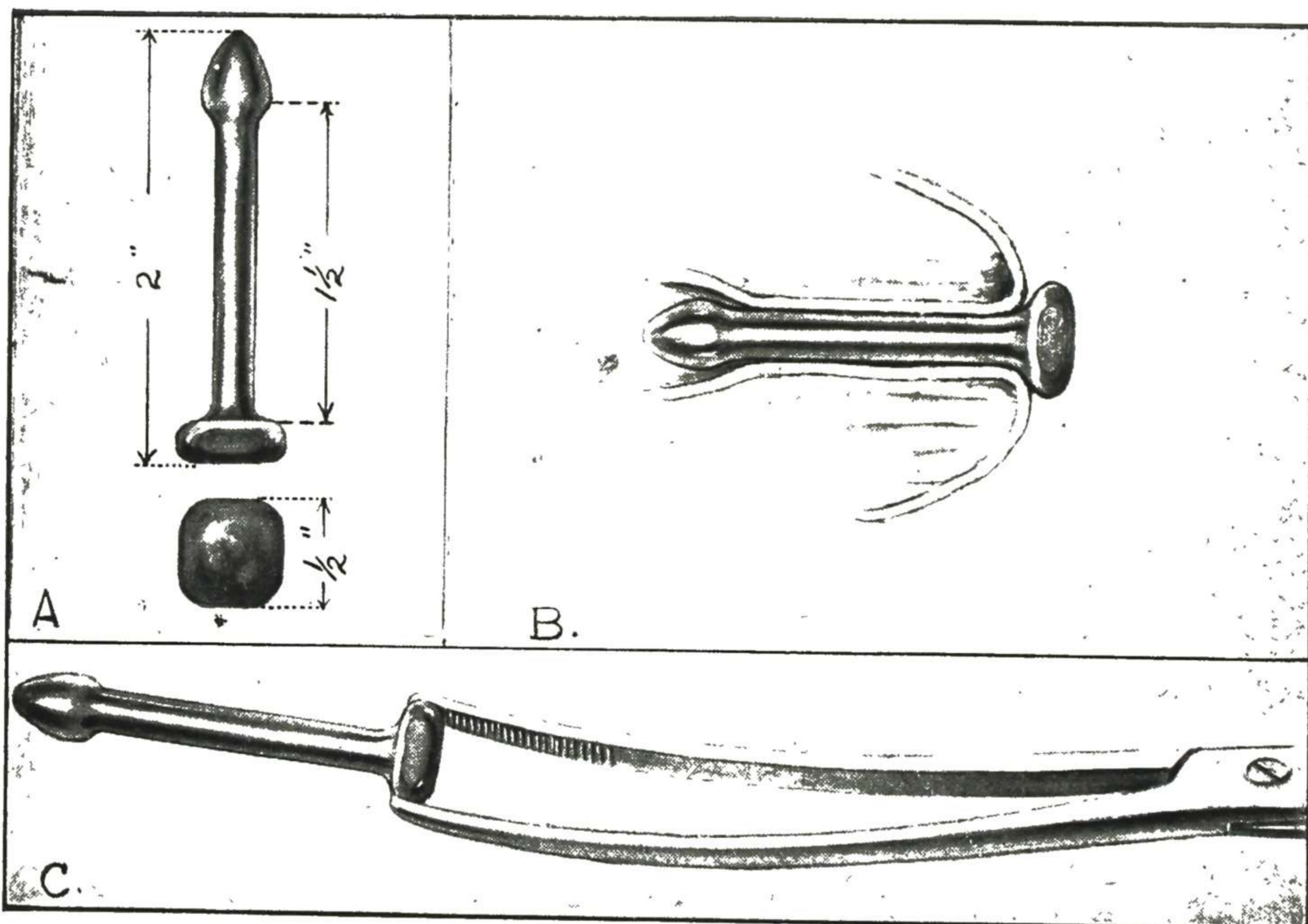

Fig. 1071.—Improved stem of hard rubber, for use in the cervix to maintain a good-sized canal after dilatation for stenosis. *A*, Dimensions of stem. *B*, Stem in place in dilated cervical canal. *C*, Showing the use of the flattened areas on the base, by which the stem may be grasped with a forceps for introduction or for removal. (Crossen and Crossen—*Operative Gynecology.*)

Various forms of metal, glass, and hard rubber stems have been employed for this purpose. The stem shown in Fig. 1071 is the most satisfactory of this type. The marked shoulder at the inner end usually keeps its place above the internal os, and the flattened areas at the outer end facilitate handling with forceps. However, the shaft of the hard-rubber stems, being only ¼ inch in diameter, does not maintain the wide dilation desired, and in many cases there is more or less recurrence of the stenosis. Consequently, in the severe cases with a very resistant internal os which contracts back to small as soon as the dilator is removed, we try to hold the wide opening gained by dilatation by using the larger rubber-tube stem.

Rubber-Tubing Stems.—In an endeavor to maintain the secured dilatation practically to the full extent for the first week or two, we employ thick-walled rubber tubing which fits the secured dilatation, instead of the regular hard rubber stem. Three sizes of pure gum rubber tubing are on hand for this purpose (Fig. 1072, *A*), the largest being ½ inch in diameter (outside measurement) about ⅛ inch wall thickness and ³⁄₁₆ inch hole, and

the other two $\frac{7}{16}$ inch and $\frac{3}{8}$ inch outside measurement, respectively. Pieces an inch and a half long are cut, and one end rounded to facilitate introduction. These are sterilized and kept ready for use in cases of dilatation for obstructive symptoms.

This rubber tubing with thick walls as specified has the advantages that (a) it is stiff enough to maintain practically the full dilatation secured, (b) the central opening allows escape of fluid and prevents back pressure during uterine contraction, which is a necessary provision when trying to maintain such wide dilatation, (c) the size may be selected to fit the extent of dilatation secured, and (d) rubber tubing is always at hand, as it may be easily secured in required sizes at small expense.

After securing the full dilatation which is safe in that case, the size of rubber tubing stem is selected to fit that dilatation. To facilitate removal it is well to pass a piece of strong braided silk through the wall of the tube well up from the end. A large Mayo needle threaded with the silk is passed inside the tube (Fig. 1072, B) and out through the wall. The two ends are then tied together to form a strong loop, as in Fig. 1072, C, which may be grasped for removing the tube. The tube is then dipped in A-G solution (1 per cent solution of neutral acriflavine in glycerin) for lubricating and antiseptic effect. After introduction well past the internal os, the tube is fastened in place by a suture through it and including the cervical wall (Fig. 1072, D). The large soft rubber stem should be left in place for a week. In a severe case, it is well to leave the stem in place in the uterus until after the next menstruation, if the patient can be kept under observation so that the stem may be removed should any symptoms of irritation develop.

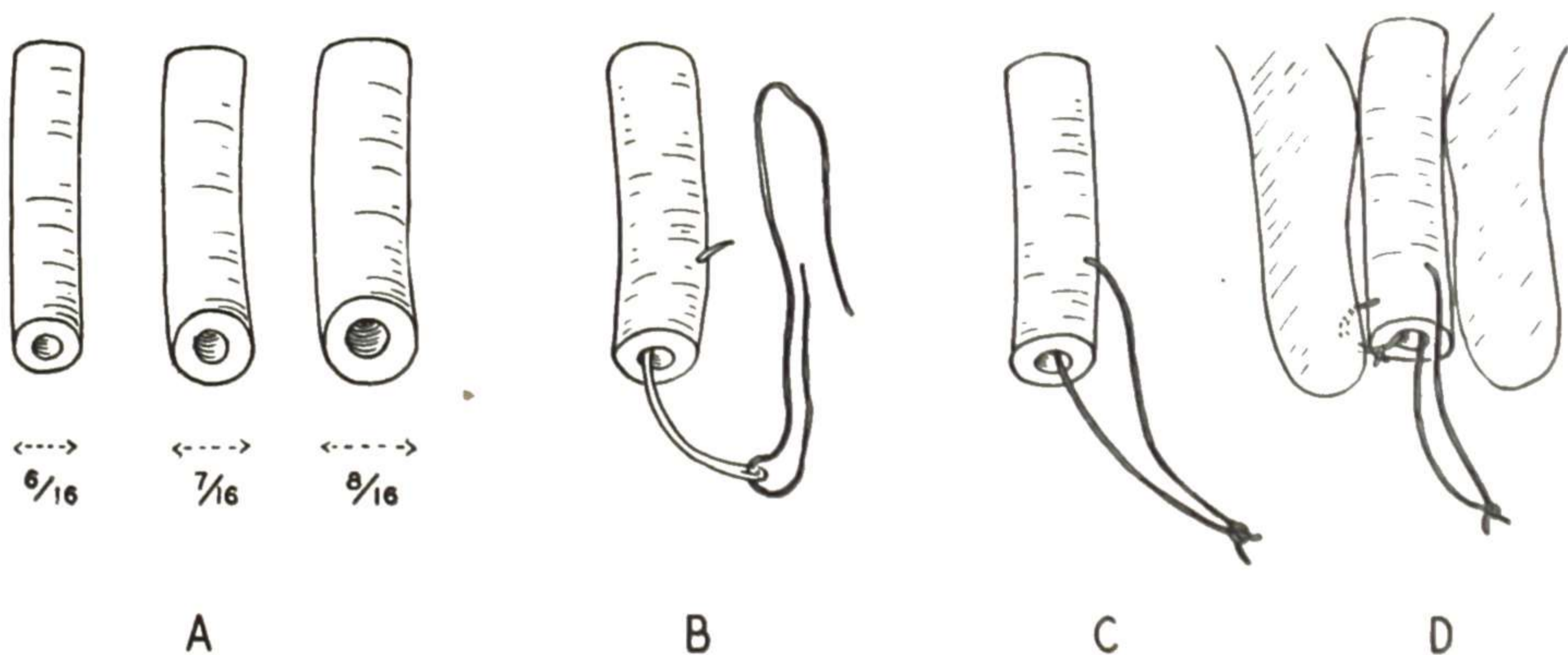**A**   **B**   **C**   **D**

Fig. 1072.—Rubber-tubing stems. A piece of thick-walled rubber tubing is used, instead of the usual hard-rubber stem, to maintain better widening of the internal os after dilatation for the obstructive factor in dysmenorrhea. A, Three sizes of rubber-tubing stems. They are 1½ inches long, with one end rounded to aid introduction. They are cut from three sizes of rubber tubing, the wall of each being about ⅛ inch thick and the width (outside measurement) being ⅜ inch, $\frac{7}{16}$ inch, and ½ inch respectively. The size is selected to fit the dilatation secured, so as to maintain that dilatation to the full extent as far as practicable.

When in place, the upper end of the stem should be well up past the internal os, and the lower end should be slightly *inside* the cervix, so as to avoid irritation of the vaginal wall. (Crossen and Crossen—*Operative Gynecology.*)

Thorough dilatation and curettage and stem give marked relief in most cases. It should be followed, of course, by treatment to overcome the other features in the case, namely, the endocrine disorder and the hypersensitive and hypercontractile uterine muscle. The duration of satisfactory widening of the canal is variable, usually continuing at least several months and sometimes several years or indefinitely. Though there is a tendency to return gradually toward the former condition, the narrowing of the canal seldom becomes as troublesome as before the dilatation.

In the exceptional cases in which the obstructive feature again becomes severe, relief from obstruction may be given by a special plastic operation on the cervix. This consists of splitting the cervix posteriorly and then sewing it in such a way as to maintain widening of the canal at the internal os. This operation, devised many years ago by Dudley, has proved effective in most of these exceptionally troublesome cases. The operation, how-

ever, must be carried out accurately, keeping in mind that the essential point is permanent enlargement of the internal os. The technical details of the operation are shown in Figs. 1073 to 1079. The steps of the operation are as follows:

a. The cervix is dilated thoroughly and the uterus curetted in the usual way.

b. The posterior lip of the cervix is then split longitudinally up to the vaginal vault, the incision being carefully continued internally up to and past the internal os. The constricting ring about the internal os should be divided sufficiently to admit a finger readily.
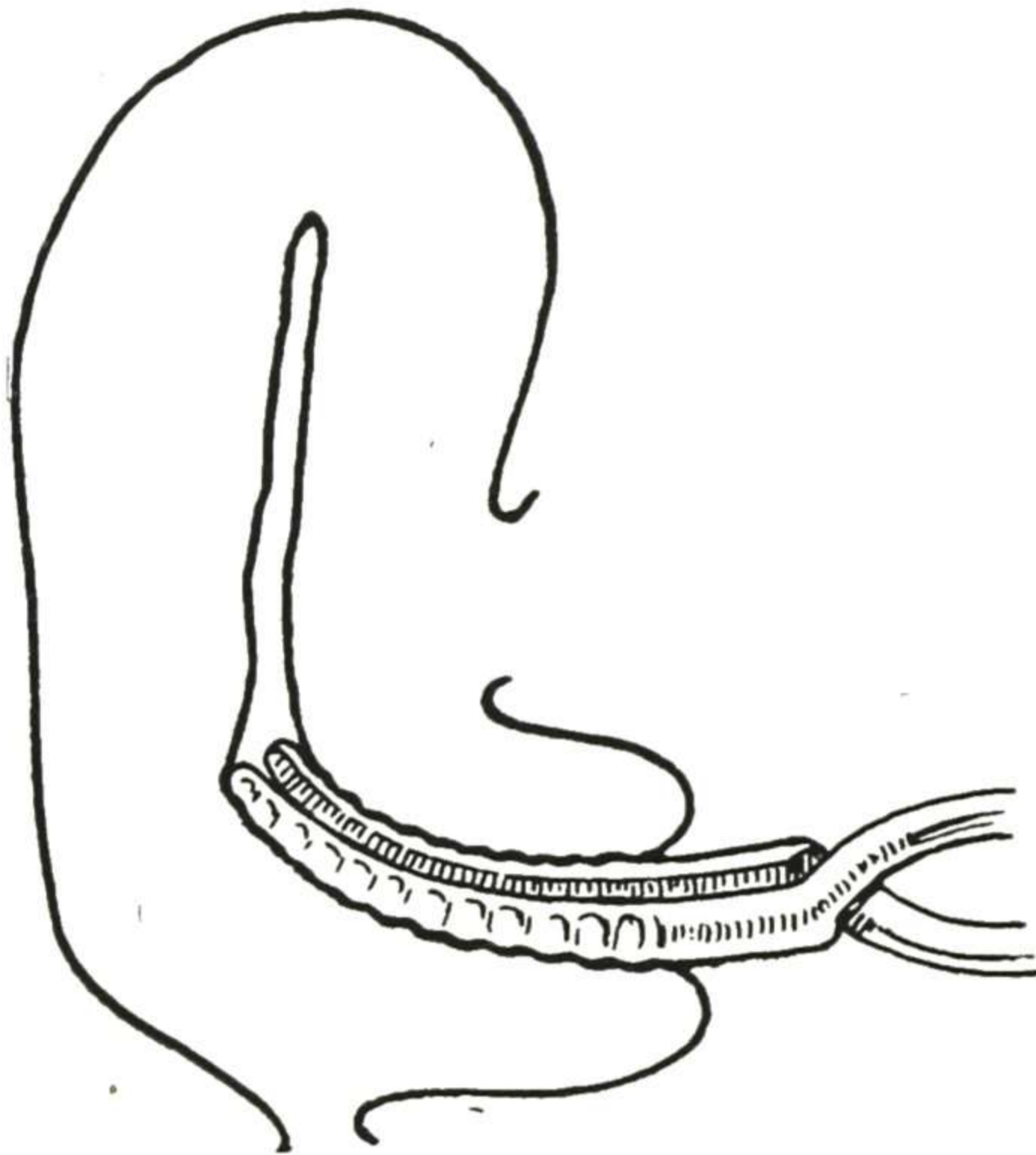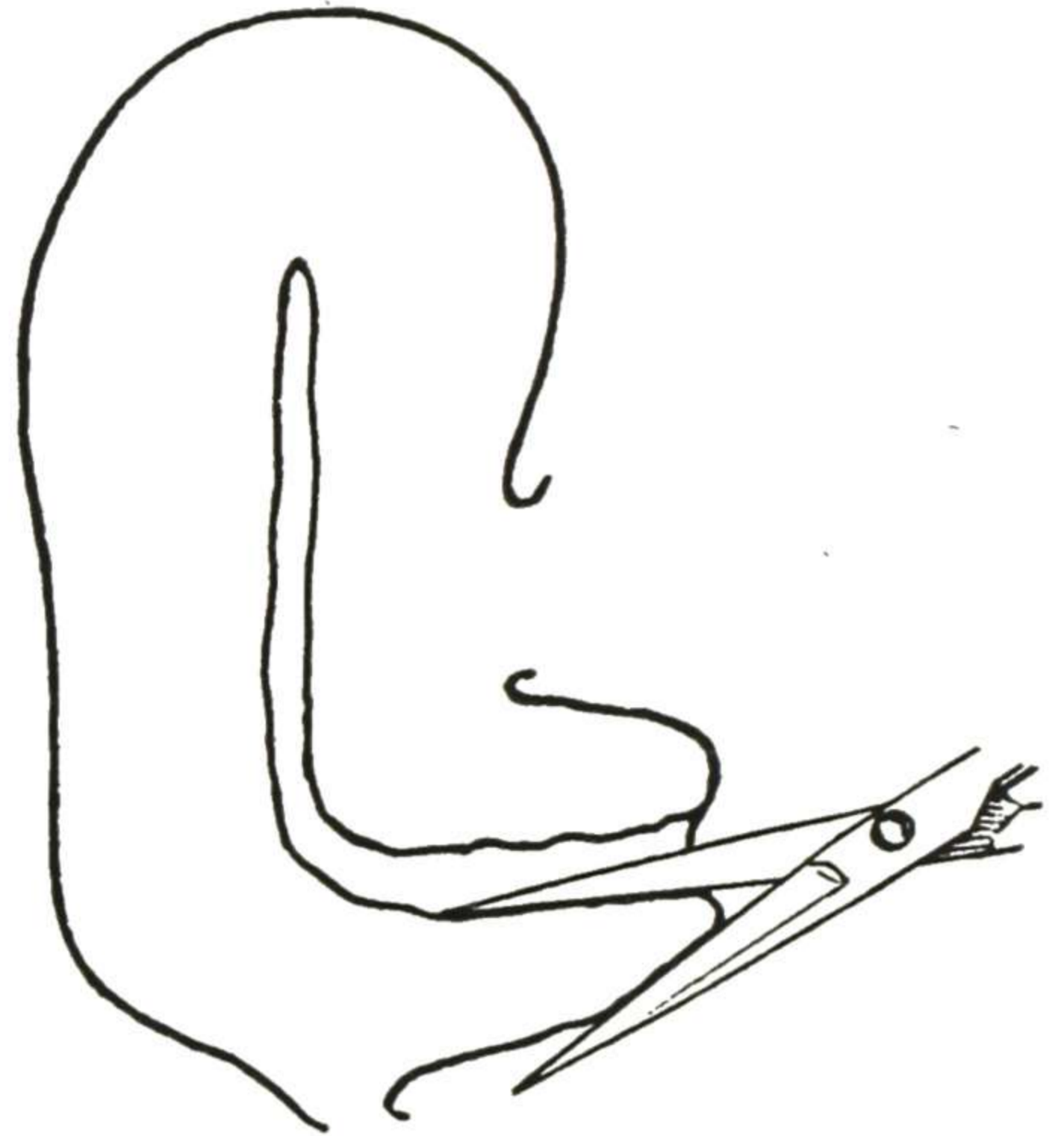
Fig. 1073.   Fig. 1074.

Fig. 1073.—Dilating the cervix, which is the first step in the operation of posterior division of the cervix.

Fig. 1074.—The scissors in place for division of the posterior wall of the cervix. A strong pair of sharp scissors is most convenient for this division, though a knife may be used if preferred. The higher division is preferably made with a knife, as shown in the next illustration.
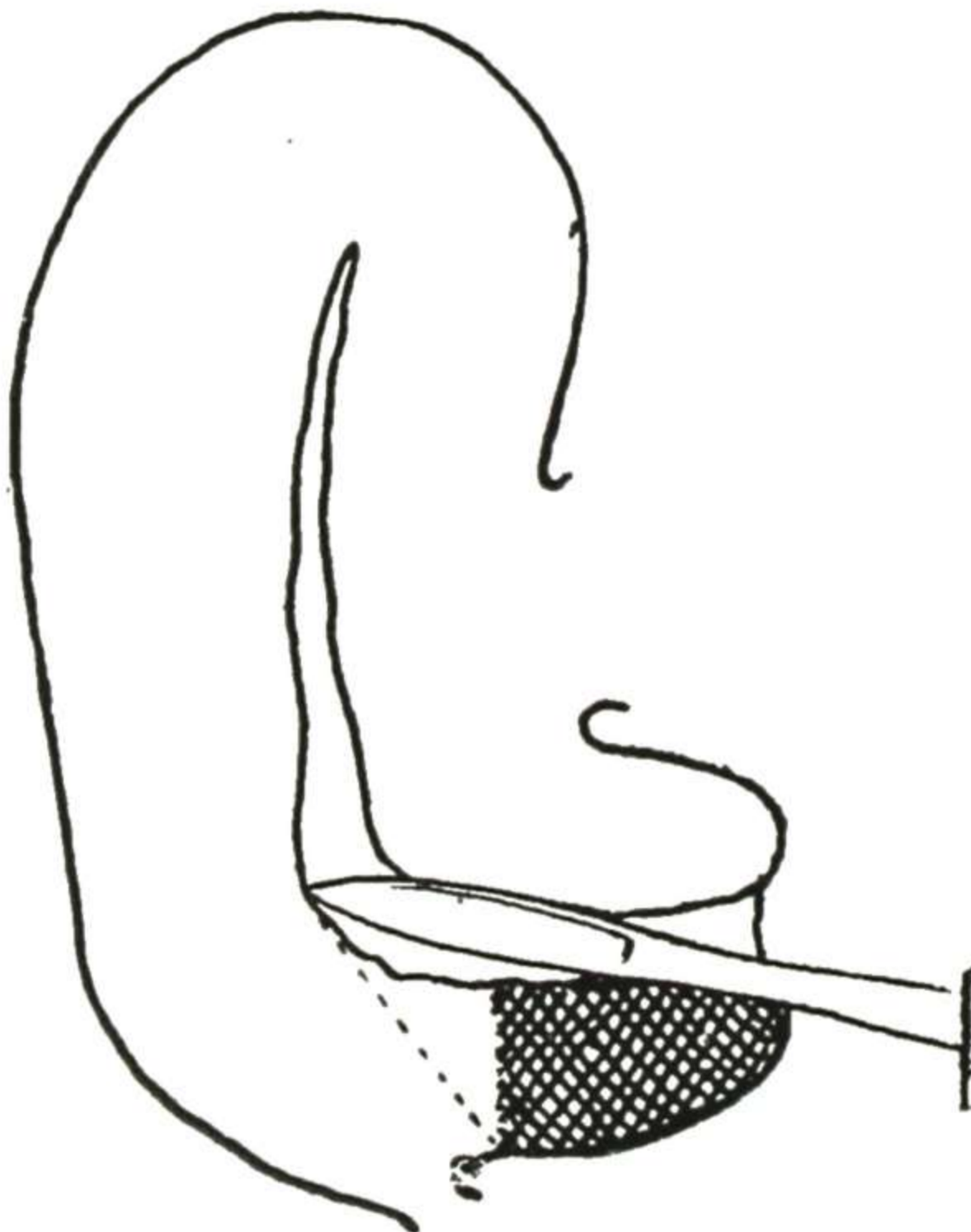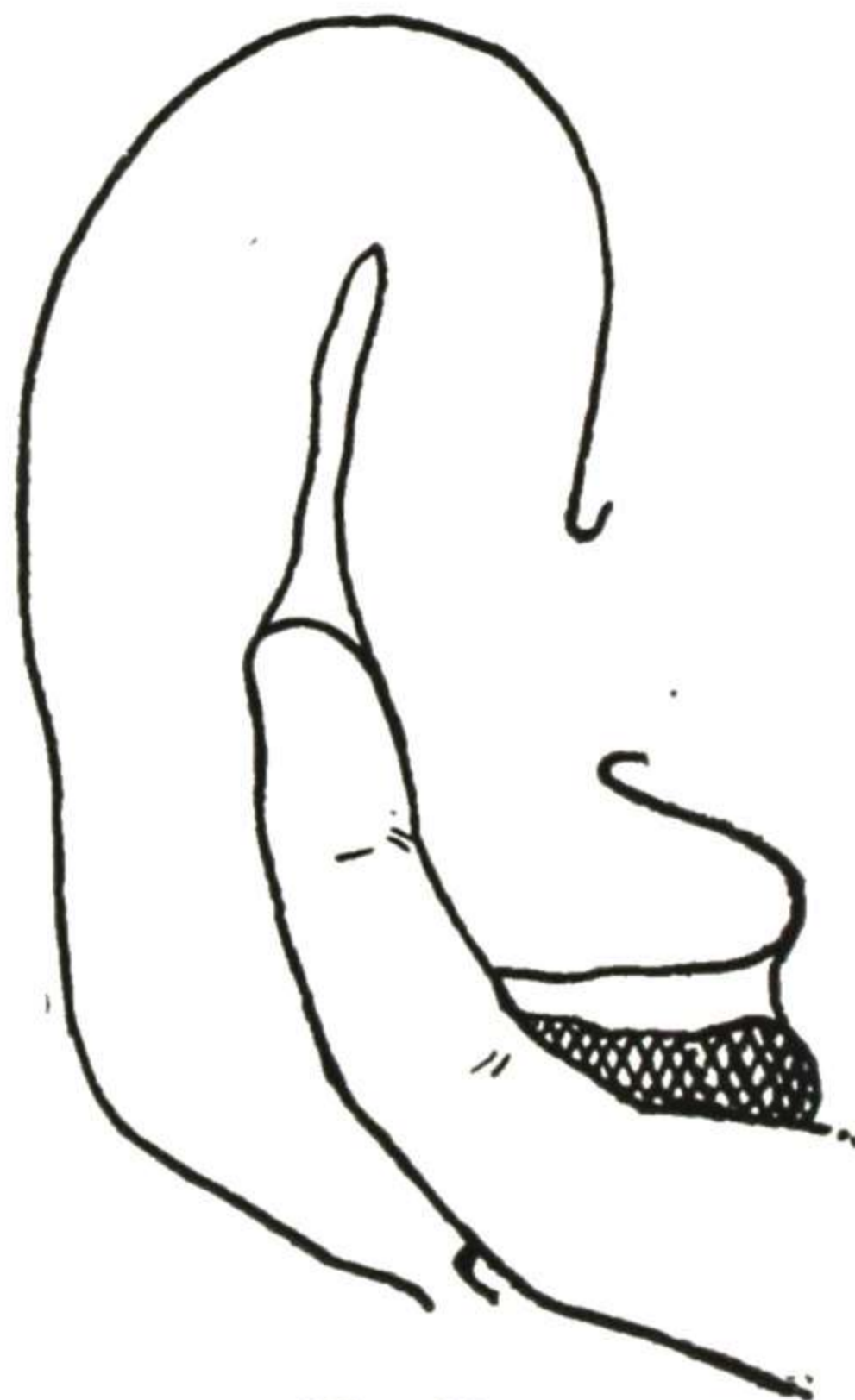
Fig. 1075.   Fig. 1076.

Fig. 1075.—Completing the division of the posterior wall up past the internal os. The dotted line indicates the limit of the necessary division. This division of tissue by the knife is made a little at a time under the guidance of the finger.

Fig. 1076.—The necessary division of tissue completed, permitting the finger to be passed up through the internal os. (Crossen and Crossen—*Operative Gynecology*.)

Care is necessary to avoid cutting too deeply into the uterine wall at this point, for, if the wall is cut through and the peritoneal cavity opened, there is danger of peritonitis. Ordinarily, there is no necessity for opening the peritoneal cavity. In some cases, however, the posterior peritoneal pouch comes very low or the internal os is situated unusually high. In either case, it may be advisable deliberately to open the peritoneal cul-de-sac in order to complete the operation properly. The division of the intravaginal portion of the cervix may be most conveniently made with long scissors (Fig. 1074). The careful division of the ring about the internal os is made with a bistoury under the guidance of the finger (Figs. 1075 and 1076).

c. A wedge of tissue is then cut out of each lip, as indicated by the dotted lines in Fig. 1077, so that each of the two cut edges will fold well on itself when the principal suture is tied.

d. A strong suture of chromic catgut or nonabsorbable material is then passed as shown by the main suture in Fig. 1078. This, when tied, folds the cut surface of each lip upon itself in such a way that the ends are brought into the angle of the wound (Fig. 1079), and this tends to hold apart permanently the divided tissues about the internal os. Before this main suture is tied, however, secondary sutures of catgut should be passed, as in Fig. 1078 at left, in sufficient numbers to close the lateral portions of the wound and prevent any hemorrhage. The main suture is then tied, and finally the secondary sutures.
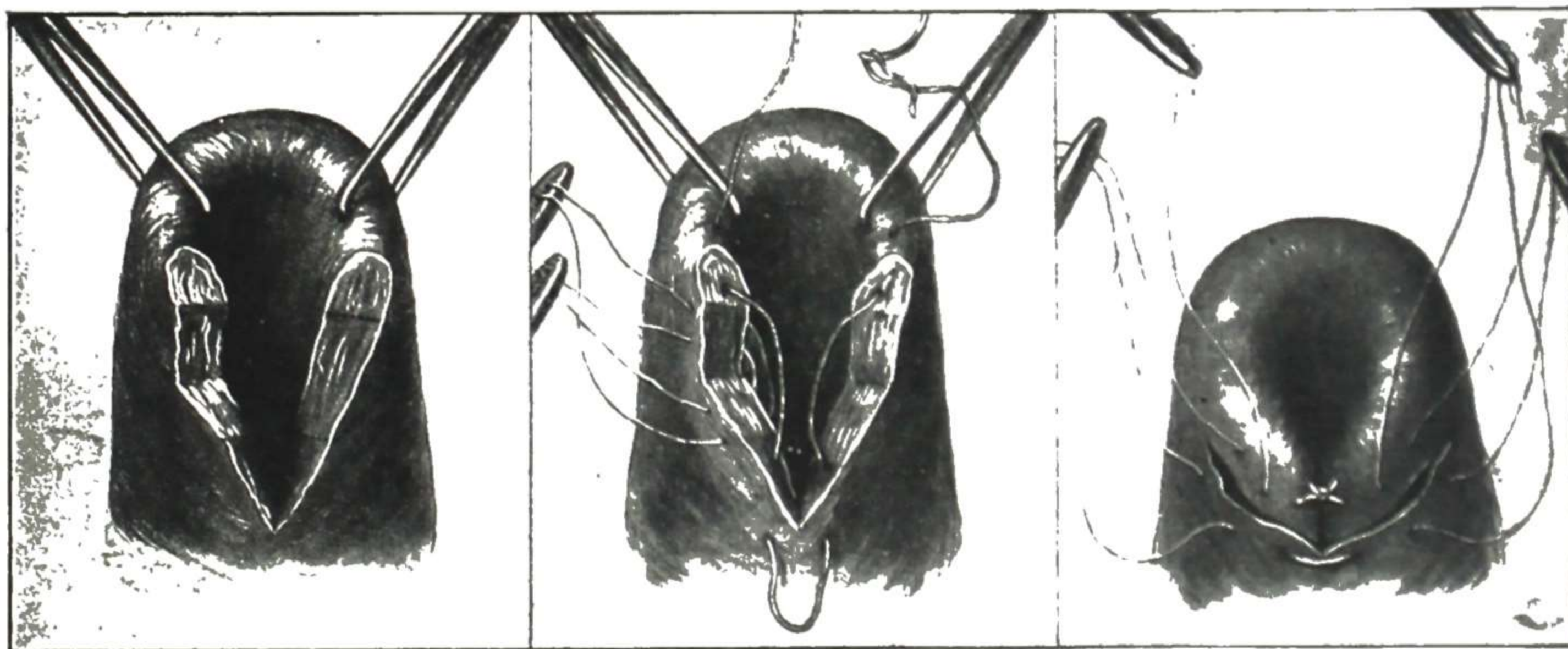

Fig. 1077.   Fig. 1078.   Fig. 1079.

Fig. 1077.—The posterior wall of the cervix divided. The wedge of tissue has been removed from one lip and the wedge to be removed from the other lip is shown in dotted outline.

Fig. 1078.—The sutures for closing the wound. The central approximation suture is in place, and also the lateral hemostatic sutures on one side.

Fig. 1079.—The central approximation suture tied, bringing tissue into the angle of the incision to keep the internal os open. (Crossen and Crossen—*Operative Gynecology.*)

It is important to pass the sutures deeply enough to catch the bulk of the divided tissue to prevent subsequent oozing. In one of our cases persistent oozing followed the operation and this increased after several hours to a flow of blood, which firm vaginal packing failed to stop and which affected the patient's pulse, and assumed serious proportions. The patient was placed in Sims' posture, all the packing removed, and two or three strong catgut sutures were placed deeply through the cervix in such a way as to constrict effectually all the tissue from which the bleeding might come. This was done without anesthesia and without disturbing the other sutures. It stopped the bleeding and the patient convalesced without further trouble.

e. In cases where the anterior lip of the cervix is very long it may be advisable to shorten it so as to allow the cervix better to assume its normal backward direction, instead of being again bent forward by pressure of the posterior vaginal wall. This is accomplished by excising the redundant portion of the anterior lip and closing the resulting raw surface by sutures passed transversely. This draws a good wedge of tissue into the angle between the cervix and corpus uteri and tends to push the cervix back toward its proper direction.

If the dysmenorrheic patient is engaged to be married soon, the examination under anesthesia with the dilatation and curettage should not ordinarily be carried out. Wait until several months after marriage before employing any local measures. In the meantime pregnancy may take place, and that will do more toward a permanent cure of the trouble than the most radical operative measure. The marked effect of pregnancy in these cases of dysmenorrhea is an additional indication that it is largely an endocrine and metabolic trouble. Pregnancy exercises a most profound influence upon the metabolism of the uterus and the ovaries. It has been argued that pregnancy and parturition produce the marked curative effect in these cases by overcoming the stenosis. Without doubt it does overcome the stenosis better than any other known measure, but, as has already been explained, the stenosis is only one feature of the trouble, and the removal of the stenosis alone does not always effect a cure.

We may confidently expect considerable relief from thorough dilatation and curettage in the great majority of the cases.

Wire stem pessaries, which are left in the canal for months, have been recommended. These may cause severe infection and abortion and for these reasons are considered too dangerous to use.

6. **Endocrine Causes** and **Therapy.**—Before discussing the hormones specifically concerned with pelvic physiology, it would be well to discuss two of the general metabolic hormones which have been found to relieve dysmenorrhea. These are thyroid and insulin.

Most of the *thyroid* cases with associated dysmenorrhea have a lowered metabolism and by administering thyroid alone, the pain frequently disappears. On the other hand, cases of interstitial thyrotoxicosis with an associated dysmenorrhea are occasionally cured when the thyrotoxicosis is treated and the overactive thyroid function corrected. Iodides and bromides are the drugs used, for example, potassium iodide 2 gr. and sodium bromide 12 gr. to the teaspoonful, and give a teaspoonful three times daily as needed.

It has long been known that there is a high incidence of dysmenorrhea among undernourished individuals. Quite by accident Altschul, while using *insulin* to treat a group of undernourished patients, found that the pain in dysmenorrheic patients was relieved. In order to determine whether the relief was due to the improvement of the malnutrition or to some unknown insulin effect he gave it to a series of normally nourished dysmenorrheic women and found that 10 of the 12 women treated were relieved.

Tedstrom and Wilson obtained relief of 80 per cent of dysmenorrhea patients by high carbohydrate feeding, suggesting that the underlying cause of the pain was hypoglycemia. Immediate relief occurred with intravenous glucose. They found that the same result was obtained in patients with normal blood sugar and hence concluded that the relief was due to the stimulating effect of the carbohydrate therapy on the pancreas causing it to secrete extra insulin.

Schrik obtained equally excellent results using 5 units of insulin before lunch daily, starting three to five days before the onset of the period and continuing through the period. The permanency of the relief had not been determined but some of the cases had had no pain for months after discontinuing the insulin.

In regard to **specific hormones,** as previously mentioned, treatments using the ovarian, testicular hormones, and the chorionic gonadotropins are based on

confusing, and in some cases diametrically opposed, *etiologic* bases. Hence it is best merely to outline some of the investigation in the physiology of the uterine muscle and then discuss therapy from an empiric standpoint.

The similarity of dysmenorrheic pains to labor pains or to those caused by a foreign body in the uterus led to the supposition that pain of functional dysmenorrhea was due to uterine contractions. Studies in normal uterine physiology by Reynolds, Novak, Wilson, Kurzrok, and others have shown that the contractions of the uterine muscle reach their maximum amplitude at the period time. They gradually diminish in amplitude in the post-menstrual period, reaching the minimum amplitude at the time of ovulation. In castrated animals uterine contractions disappear, but if the castrate is given estrogenic substances strong contractions occur. If, then, this is followed by progestin the contractions are markedly diminished. The same is true with the chorionic gonadotropins, due to the fact that in animals this hormone caused ovulation and hence corpus luteum formation and progesterone secretion.

Just as we all began to feel that at last the mysterious cause of endocrine dysmenorrhea had been settled, a contradicting article appeared last summer. Wilson and Kurzrok, using the intrauterine balloon method of testing dysmenorrheic women, found that there was no difference in the amplitude of uterine contractions in the normal and the dysmenorrheic women. This method, of course, is open to the criticism that any foreign body in the uterus will cause exaggerated contractions. They felt, however, that this factor could be ruled out as they waited to take their readings until the immediate stimulation caused by introduction of the balloon had worn off. These workers feel that functional dysmenorrhea must be regarded as a disorder in which the normal uterine contractions during the phase of maximum amplitude reach consciousness, and that the exact explanation for the reduction of the pain threshold is as yet unknown.

Another approach to the problem has been made by Phelps. He injected mature castrated does, having estrin-stimulated contractions, with the urine of normal, laboring and dysmenorrheic patients and recorded uterine contractions by the balloon method. He found that variations in contractions with urine of normal or parturient women were quite different from those caused by the urine of dysmenorrheic women, not only during the period but also between periods. He concluded that there was a marked imbalance in secretion of substances affecting uterine motility in dysmenorrheic patients.

In regard to blood levels, most workers find a high level in the majority of dysmenorrheic patients. Kotz and Parker, testing daily estrogen content in the blood and urine of 15 such patients, concluded that a high level of estrogenic substances is present in a majority of the cases of functional dysmenorrhea. The fact that the urine level is also high indicates to them that the high blood level is not due to faulty elimination of the estrogens by the kidney.

In regard to progesterone investigation, little has been done. Hamblen reported one case in which the urinary excretion of pregnanediol glucuronide was increased and the patient was relieved by estrogenic therapy. Cannon in a critical analysis of ''Modern Theories of Dysmenorrhea'' feels that membranous dysmenorrhea is due to ''overactivity of the corpus luteum, probably secondary to overactivity of the luteinizing hormone of the pituitary.'' On the other hand, in a series of endometrial biopsies done in dysmenorrheic patients, 64 per cent showed evidence of deficient corpus luteum activity. So the etiology remains uncertain.

Therapy will be discussed from an empiric standpoint. The interesting fact is that all of the treatments outlined give good results, which again warns that we must not forget the psychic factor.

Estrogenic Therapy.—The beneficial results obtained by estrogenic therapy have been explained in various ways.

Some think that the improved nutrition of the uterus is of importance, others that the pain is relieved because of the nutritive effect of the estrogens on the ganglia of Frankenhauser. Sturges and Albright feel that prevention of ovulation, indirectly by the

estrogenic inhibition of the pituitary, is the essential factor in the relief of the dysmenor-rhea. They relieved 25 cases of severe dysmenorrhea by estrogenic therapy and in each case they showed that ovulation had been prevented. The physicians who believe in this method of treatment now go so far as to claim that, if a patient had dysmenorrhea, it is proof that she is ovulating normally.

Stilbestrol is being tried in this condition with some success, but since its toxicity is still an unknown factor it should be used with caution.

Technique for estrogen.—10,000 I.U. of estradiol is given intramuscularly every three days for six doses. The first injection must be given on or before the sixth day of the cycle to make this therapy effective. This treatment is repeated over a period of a year. The permanency of the result is still unproved.

Corpus Luteum.—The corpus luteum hormone has been used on the theory that since it diminishes the amplitude of the uterine contractions it should allay the pain.

Novak and Reynolds, and Campbell and Hisaw have reported success with this hor-mone, and the latter recommend 5 mg. of progestin daily for five days prior to the menses. They state that the results lasted several months.

Novak originally recommended pregnancy urine on the theory that it caused ovulation in the human, which idea has since been disproved. The effect which is occasionally obtained with pregnancy urine is probably due to a direct action on the uterine muscle. In an article last year Novak advised giving 200-500 U. daily for a week before the period.

Testosterone.—In the past year there have been several articles in the na-tional journals on the treatment of dysmenorrhea with testosterone. The ration-ale of its use is based upon the fact that it has a dual action, one resembling the estrogenic effect and inhibiting ovulation, and the other, resembling a progester-one effect and reducing the amplitude of the uterine contractions.

If the testosterone is to be used subcutaneously 5 to 10 mg. are given on the fifth and eighth days prior to the period; if used percutaneously a preparation of 2 Gm. in sesame oil is massaged into the skin under each arm each night for ten days before the period. Abarbanel obtained excellent results with testosterone and had no trouble with masculinization effects. Patients of the masculine type should not receive the testosterone, as it has in some cases caused hair growth on the face, deepening of the voice, and other undesirable masculinization effects.

7. **Premenstrual Tension.**—Much has recently been written about premen-strual tension. The symptoms included under this term vary from headache, nausea, bloating, emotional disturbances with irritability and depression, to occasionally definite edema of various parts of the body. The cause of this distress is thought to be an excess of estrogen or a diminished amount of pro-gestin. Recently Greenhill and Freed have advanced the idea that premenstrual distress is the result of tissue edema caused by a retention of the sodium ion in various body tissues, under the influence of an increased level of sex steroids in the blood.

It is well known that estrogens, androgens and some of the sex steroids can cause retention of the sodium ion which in turn causes an increase in the extracellular fluid re-sulting in microscopic or gross edema, depending upon the amount of fluid retained. The

symptoms under this theory result from edema: the headache from edema of the brain, the nausea and bloating from edema of the gut, and other symptoms from other organs involved.

The therapy used in selected cases, some of which had gross edema with the periods, was uniformly successful. The patients were told to refrain from adding table salt to their food for two weeks prior to the menstrual period and to take ammonium chloride, 10 gr., three times a day. The salt-free diet cuts down the intake of the sodium ion and the ammonium ion of the ammonium chloride is changed to urea, resulting in an increase of the chloride ion which in turn unites with the sodium in the extracellular fluid, increasing the excretion of sodium chloride. Water is lost from the extracellular spaces with the excretion of the sodium ion.

MENSTRUAL HEADACHE

In a patient inclined to headache, the menstrual period is the favorite time for the most troublesome manifestation, as it is for many other disturbances of the nervous system. There is not space for a general differentiation of the various types of headache which may occur at the menstrual time. The disturbed salt balance has been mentioned, and it is advisable to call attention to another troublesome type, which has recently been elucidated with considerable relief to the patients so afflicted. This type is characterized by exostoses on the inner table of the skull in the frontal region (Fig. 310) with resulting pressure on the "silent area" of the brain.

This condition is of interest to gynecologists in that it is the cause of one of the severe types of menstrual headache (often with visual disturbances) and not infrequently there are other menstrual disturbances, such as excessive flow or amenorrhea. Another point of interest is that the pelvic and other symptoms closely resemble those ordinarily associated with certain cases of pituitary dysfunction, and this diagnosis is very likely to be made and the exostosis overlooked.

The details of this condition were worked out by Dr. Sherwood Moore, professor of Radiology, Washington University School of Medicine. He investigated very extensively these inner-table exostoses, the resulting clinical symptoms, and associated bodily changes, and has called attention to their importance in an article (see Reference List).

The symptoms listed by Moore as characteristic of this condition are: 1. Headaches, often disabling. Cranial tenderness with sometimes a feeling of pressure. 2. The obesity may be extreme and is of the rhizomelic type. 3. Visual disturbances of various types. 4. Easy fatigue and muscular weakness. 5. The breasts are usually larger and more pendulous than they are in women who do not have hyperostosis of the skull. 6. Hair growth on the chin is common. 7. Mental dullness, dizziness, depression, and poor memory. 8. Epileptiform-like seizures. 9. Cranial nerve disturbances. 10. Regional sensory and motor disturbances, tingling, numbness, transitory hemiplegias and hemiparesis.

One of the clinical features of diagnostic importance is the fat distribution just to the middle of the upper arm and to the middle of the thigh. This is shown in Fig. 311, which is a photographic study from Dr. Moore's collection. The sella turcica was normal.

We have had several patients with this disorder. Dr. Carr, of the Department of Neurology, has obtained complete recession of troublesome symptoms in some of them on a diet high in gelatin.

W. M. Hull found that in some allergic patients with severe menstrual headache the sella turcica was of the closed type, which would cause troublesome pressure from any swelling of the pituitary which might take place at that time. He advised estrogenic therapy preceding the period.

INTERMENSTRUAL PAIN AND SPOTTING

The interesting subject of pain occurring at a certain time every month in the intermenstrual period has received considerable attention from investigators, and the conclusion has been reached that it is not an indication of any particular lesion.

Malcolm Storer, who reported 20 cases of his own and 25 additional cases collected from literature, found that in 10 of the cases there was a marked increase in the leucorrhea at that time, indicating congestion of the uterus. There may be a slight bloody flow at this time. In the 45 cases reported by Storer the pain appeared with regularity in all cases, practically every month unless pregnancy was present. In 22 cases it appeared always at the same time (in most cases about two weeks) after the beginning of the last menstrual flow. In 13 cases there was a variation of two days, in 4 cases there was a variation of four days, and in 2 cases of irregular menstruation it would appear on a certain day before the menstruation. In 37 out of 41 cases the pain appeared from twelve to sixteen days after the beginning of the last menstruation and in 20 of them it began exactly on the fourteenth day. In 2 cases it came from the seventh to the tenth days, in 1 case on the seventeenth day, and in 2 cases on the eighteenth day. Observations like these well support the view now generally held that this periodically returning pain, often alternating in the right and left side from month to month, is actually caused by the enlarged graafian follicle at the time of ovulation. It seems plausible that under certain conditions this process might be associated with pain.

Endocrine disturbance is probably a large factor in the conditions which cause ovulation to be painful. This pain in the mid-interval ("Mittelschmerz"), often accompanied with a slight show of blood ("spotting"), is probably more common than we realize, for Papanicolaou found microscopic blood in about 25 per cent of women examined at the ovulation time. This, as well as the pain, is probably due to the temporary drop in estrin and inadequate progesterone secretion to prevent a little blood loss. As the progesterone and estrone levels increase with the maturing corpus luteum the bleeding and pain stop. This would indicate the administration of progesterone and estrone as the painful time approaches. Pelvic heat is a helpful adjunct to any other treatment during the pain.

Radiation has been used successfully, both x-ray and radium. In persistent cases Keene used 100-200 mg. hr. of radium and in so doing he obtained the double benefit of dilatation and mild radiation effect on the ovaries. The x-ray is given to the pituitary region and men using it claim excellent results. The pituitary has so many important functions and the effect of x-ray is so little understood that pituitary radiation should be reserved as a final measure.

MENSTRUAL PRURITUS

Menstrual itching and irritation about the vulvar and anal areas may be due (1) to congestive aggravation of some continuing skin lesion such as acne or eczema, (2) to herpes or fungus infection appearing at that time, (3) to allergic reaction to pad material or powder or soap or other article used locally, (4) to local reaction to special medicine or food, or (5) to allergic reaction of the patient to her own menstrual blood. Wilson (1943) presents an instructive review of this subject.

CHAPTER XV

Disturbances of Function

STERILITY AND SEXUAL DISTURBANCES

The disturbances belonging in this chapter will be taken up in the following order:

Sterility.
Contraception.
Sterilization.
Dyspareunia.
Sexual Frigidity.
Sexual Hyperesthesia.

STERILITY

The question of sterility is one of increasing importance, socially as well as medically. The estimates by different authorities of involuntary sterile marriages vary from one in ten to one in six. In recent years the heretofore underestimated male responsibility has been emphasized. This percentage ranges from 30 per cent in some series to 48 per cent in others. Only a small number of cases show a single lesion which can be held entirely responsible for the sterility. Usually there is a combination of lesions in the wife or husband or both, any one of which would probably not render the couple sterile; but their combined influence is enough to bring about that result. However, an occasional case presents two or more lesions, any one of which could cause sterility. The problem of therapy in such a case hinges on the question as to which lesion carries the chief responsibility for the sterile union. Endocrine disturbance and deficiencies in diet have been shown to be definite factors in certain cases. Absence of lytic power in the semen and abnormalities of the sperm have been found to be more important than heretofore realized.

It is the purpose here to give a comprehensive and systematic method of investigating and treating the sterile couple. On account of limited space only essential items can be considered, and the statements concerning these must be concise and limited to points of diagnostic or therapeutic importance.

Causes

In order to assist in determining the exact cause of the sterility in the various cases, it is well to consider what is necessary that a normal pregnancy may take place. It is necessary ordinarily (a) that healthy spermatozoa be deposited in the vagina, (b) that the spermatozoa remain healthy and pene-