THE MANAGEMENT OF FUNCTIONAL MENSTRUAL DISORDERS

E. PERRY MCCULLAGH, M.D.

The majority of menstrual disorders are due to some derangement in the function of the ovaries. This may be due to factors which influence the general health or to more specific factors which alter the production of the hormones of the ovaries in one of several ways, i.e., (a) by affecting them directly, (b) by affecting their chief governing agent, the pituitary gland, or (c) through other endocrine glands, notably the thyroid or adrenal glands. In this paper, we shall deal with treatment of menstrual disorders chiefly from an endocrine point of view. The physiology of menstruation will be summarized briefly. We shall then examine the available hormonal and nonhormonal remedies, and discuss the application of these agents to menstrual disorders of known or presumed endocrine origin and to some of uncertain etiology.

PHYSIOLOGY

Sex is determined primarily by the gene, but the development of the sexual apparatus is dependent to a large degree upon the hormones elaborated by the sex cells. No new structures are formed in the body by the action of hormones, maleness and femaleness depending upon the degree of differentiation of structures already laid down. Male sex hormone acting prior to the time of sex differentiation causes development of sex organs of male character while female sex hormone (estrin) acting before the time of differentiation causes these structures to assume the female characteristics and is necessary for the maintenance of normal structure and function.

Estrin is elaborated chiefly by the graafian follicles and exists in several forms. Which of these forms is most important in normal body economy is not known. Estrus is a cyclic heightening of sexual excitement commonly known as "heat" or "rut" which has been studied in rodents and has formed the basis for most of our knowledge of the physiology of estrin. The estrous cycle has been divided into several parts. In dioestrum or the resting phase the ovaries are quiescent, the uterus is lined with low columnar epithelium, the vagina is lined by a thin layer of flat epithelial cells, and the vaginal smear contains many leucocytes. In proestrum, the follicle is seen to grow, the endometrium becomes deeper, and the vaginal mucosa becomes stratified. In full estrus, the follicle has reached the height of its growth, and it ruptures, freeing

the ovum. The endometrium has become deeper and the glands larger, but they retain a simple test-tube-like structure; the cornified cells of the vaginal mucosa are cast off, and the vaginal smear shows only large, clear, non-nucleated cells. In the rodent, no corpus luteum is formed in the absence of pregnancy, and the changes described above regress through metestrum to dioestrum.

Thus far, the changes which occur in the rat and mouse are comparable to the changes which take place in the human from the beginning of the growth of the follicle at the time of the menses up to the time of the bursting of the follicle at the mid-menstrual period. In rodents, the occurrence of pregnancy is the signal for the formation and maintenance of a corpus luteum, whereas in the human, the corpus normally occurs and is maintained for a time after ovulation. Those changes which are present in the genital tract of the rodent after fertilization of the ovum occur as the result of a hormone known as progestin which arises from the corpus luteum. It causes a great thickening of the endometrium, the surface of which is thrown into deep folds in preparation for the nidation of the fertilized ovum. The glands of the endometrium become tortuous, dip deeply into the uterine structure, and take on the appearance of actively secreting glands. This is the progestational endometrium and is comparable to the type which normally forms in the human during the latter half of the menstrual cycle.

The growth of the graafian follicle and the production of estrin is dependent upon the elaboration of an anterior pituitary hormone commonly called prolan-A, and according to current belief, the occurrence of a corpus luteum with its production of progestin depends upon the elaboration of a second sex hormone from the anterior lobe of the pituitary which is known as prolan-B.

The explanation of menstrual bleeding is less satisfactory. The following is the most commonly accepted theory at the present time: It is known that estrin in the human arises from both follicle and corpus luteum. It is generally accepted that estrin exerts a depressing effect upon the production of sex hormones by the pituitary gland. Therefore, after the follicle and the corpus luteum have produced a relatively large amount of estrin, the activity of the pituitary is said to become depressed, which in turn causes a disappearance of the corpus luteum, a loss of its power of maintenance of the endometrium with consequent sloughing and hemorrhage. Such an explanation is not entirely satisfactory for several reasons, one of which is that blood may be seen

prior to menstruation among the endometrial interstices without obvious associated evidence of endometrial disintegration. Also, the experiments of Werner and Collier[1] appear to indicate that cyclic menstrual bleeding may occur in castrated women who are treated with estrin alone. During pregnancy, maintenance of the corpus luteum results in growth of the endometrium and formation of the decidua. Other ovarian hormones probably exist but they will not be discussed here.

When the above knowledge of the physiology of menstruation is applied, we see that a marked underproduction of ovarian sex hormones before puberty results in profound underdevelopment of uterus, tubes, vagina, secondary sex glands, secondary sex characteristics, and amenorrhea. A mild prepuberal hypo-pituitarism and hypo-ovarianism could cause development of the follicle without its proper maturation and thus a lack of corpora lutea. This in turn would cause underproduction of progestin, lack of maturation and improper overgrowth of the endometrium, with consequent amenorrhea, irregular menses or in the case of sloughing, functional menorrhagia. In early pregnancy, a lack of prolan-B is considered in some instances to be responsible for the improper maintenance of the decidua which results in bleeding or abortion.

Underproduction of estrin which occurs after the menses have been established may result in hypomenorrhea or amenorrhea together with a tendency to atrophy of those parts which are dependent on estrin for their maintenance, the degree of atrophy depending upon the degree of reduction in the supply of the substance. Other associated metabolic changes also take place. Prepuberal hyperovarianism results in too early menarche and development of sexual characteristics and may be associated clinically with evidence of masculinization and those signs which at times accompany adrenal tumors.

Hyperfunction of the pituitary gland may lead to overstimulation of the ovaries and the so-called hyperhormonal amenorrhea. Clinically, one sees many complex multi-glandular pictures which are related to this condition. Overproduction of prolan may be the result of a compensatory mechanism caused by ovarian hypofunction such as that which follows surgical castration or the menopause.

Available Therapeutic Agents

A. Hormones

Pituitary Hormones: No discussion of the proposed differences between gonad-stimulating hormones of pregnancy urine and those from the pituitary is necessary here. Some pregnancy urine extracts which are in common clinical use are antuitrin-S (Parke-Davis), Fol-

lutein (Squibb), and A. P. L. (Ayerst, McKenna & Harrison). Regardless of the physiology which is involved, it should be borne in mind that from a clinical standpoint these substances generally are more effective in reducing the menstrual flow than in increasing it.

Pituitary sex hormone which is made from horse pituitaries is now available under the name of prephysin (Chappel Bros.) and it is standardized to have proportionately more follicle-stimulating than luteinizing effect. It is for this reason that it has been proposed for the treatment of sterility.

Pituitrin or other posterior lobe extracts are occasionally useful in the management of acute menorrhagia.

Ovarian Hormones: Urine from pregnant women also is the chief source of supply of estrin for therapeutic use, although Amniotin (Squibb) is made from amniotic fluid and Emmenin (Ayerst, McKenna & Harrison) is made from placenta. Popular forms of estrin for hypodermic use are Theelin-in-oil (1,000 and 2,000 international units in 1 cc. ampules) (Parke-Davis), Amniotin (Squibb) in 500 units in 10 cc. vials, Progynon (Schering) in 1 cc. ampules, 125 international units per cc., and Progynon-B (Schering) in ampules of 2,500, 10,000, and 50,000 units' strength, Folliculin-Menformon available through H. H. Beissner & Co., New York (1,000 units per cc.).

Theelol (Parke-Davis), Amniotin, Progynon, Emmenin and Menformon are available for oral administration.

Thyroid Hormones: Desiccated thyroid or whole gland (the latter one-fifth the strength of the former) is still a very useful adjunct in the hormonal management of menstrual disorders. This is used alone or in addition to other forms of therapy. Small doses are usually quite as effective as large ones, except where the indications for thyroid are especially clear cut.

Insulin: According to recent reports, insulin occasionally may be a useful adjunct. I have observed a few cases of amenorrhea where sex hormone therapy has failed to produce clinical results alone but a good clinical response has been obtained following a short course of adrenal cortical hormone in the form of eschatin (Parke-Davis). The use of insulin and eschatin, however, must be very limited and at present is entirely empirical.

Progestin is not, so far as I am aware, available in a well standardized form for clinical use.

B. Non-Hormonal Agents

The general physical condition of the patient is of great importance. Menstrual disorders occasionally correct themselves after the weight of an obese patient has been reduced or after weight has been gained by a malnourished woman. The therapeutic value of exercise, fresh air and sunshine must not be overlooked. More specific nutritional factors, such as a relative deficiency in vitamins, especially in B and E, may need correction, as it is known that these substances influence the activity of the pituitary and ovary considerably. Vitamin B is easily supplied if the diet contains sufficient dark cereals, or yeast or yeast concentrates may be used. Fresh vegetables or wheat germ are excellent sources of vitamin E. That fright or anxiety may cause irregular menses or amenorrhea is common knowledge, and the psychic factor must be taken into consideration.

If anemia is present, the use of iron may be required. Simple microcytic anemia with or without achlorhydria will usually respond well to iron if it is administered in sufficiently large doses, sometimes 60 or even as high as 120 grains per day of Blaud's mass may be necessary. Liver or stomach therapy may be useful.

Infection in the pelvis requires treatment according to the indications of each individual case. Tuberculosis, syphilis or other general infections may require special care. Undulant fever causes amenorrhea not infrequently, and it sometimes is associated with signs of encephalitis, which usually is of a mild grade.

Radiation therapy is very useful in some cases. Sometimes from 10 to 25 per cent of an erythema dose to the pituitary will cure amenorrhea when other measures have failed to do so and even 60 or 70 per cent of an erythema dose to this gland appears to be entirely harmless. I still hesitate, however, to apply x-ray to the ovaries even in the so-called stimulating dosage unless all other measures have been given an adequate trial and have failed.

In my opinion, the application of radium to the uterine canal in small doses, from 800 to 1,400 milligram hours, is the treatment of choice where general measures have failed to control functional menorrhagia. By the use of this method, we avoid the outspoken castration effects which are produced by heavy doses of x-ray therapy and also avoid the constant risk which attends hysterectomy. In malignancy of the fundus uteri, hysterectomy undoubtedly is the treatment of choice.

Diagnosis and Treatment

In this discussion of the diagnosis of menstrual disorders, the matter will be examined chiefly from the point of view of etiology. I believe the fact that our diagnostic acumen in this field is inadequate, makes it

doubly important that we use all available means for making a correct diagnosis.

Many attempt to deduce what sort of ovarian dysfunction is present from an evaluation of the amount and character of the menstrual flow alone, and usually, a pelvic examination in itself yields no positive information. In all cases, therefore a painstaking history should be taken, a careful general examination and examination of the urine and blood should be made, and usually the basal metabolic rate should be estimated. The possible presence of a pituitary tumor should always be remembered, and roentgenograms of the skull should be made and visual field examination done when these examinations are indicated. When bio-assays for sex hormones are available, they often are very useful adjuncts.

The Pituitary and Functional Menorrhagia

Physical examination usually yields no evidence of hypofunction of the pituitary when it is of the mild prepuberal type which is the presumed cause of functional menorrhagia. It has been my practice that young girls and women under 30 years of age whose pelves are normal should not be subjected to curettement of the uterus. Beyond this age, diagnostic curettage must be advised, if we are to avoid treating medically some cases of carcinoma of the fundus. If no evidence of neoplasm is evident and especially where endometrial hyperplasia is found, large doses of prolan should be administered. In general, in those cases in which less than the normal amount of endometrium is found, the response to such therapy is poor. Among such cases are examples of so-called anovular bleeding. More consistent results are to be expected near the menarche than near the menopause, although it is a remarkable fact that menorrhagia occurring at the menopause will in many instances respond well to such therapy, and this is true in spite of the fact that prolan assays usually show that the urine already contains a measurable excess of the substance.

Our personal experience with prolan therapy is limited almost entirely to antuitrin-S which has been used for this purpose for several years. The dose usually employed is from 1 to 2 cc. (100 to 200 units) daily for a period of from one to three months, but this period may be shortened if results are obtained earlier. If good results are not obtained in three months, further treatment will be useless in most cases. Occasionally, larger doses may be given at times when the bleeding is more severe. In rare instances, single doses as high as 5 cc. have been used without apparent harm. Severe hemorrhage may require other measures and for this purpose, ergot by mouth or by hypodermic may be efficacious as an emergency measure. Rest in bed and application

of cold to the lower abdomen may be useful. Curettage and packing may be required and sometimes in the beginning, massive doses of estrin alone or together with pituitrin will produce rapid effects, although of course, the continued use of estrin therapy is contraindicated under such circumstances. The results of prolan therapy in functional menorrhagia are generally excellent, and we have obtained satisfactory clinical results in over 80 per cent of selected cases. Usually, only one course of treatment is necessary, but it may be necessary to repeat the course in some cases.

The use of radium has been mentioned above.

Hypopituitarism: In more severe prepuberal pituitary failure, general evidences of disease of this gland may be present. One must keep in mind pituitary dwarfism of the microsomatic or Lorain-Levi type and Fröhlich's syndrome which are extreme disorders of this type, the latter probably being associated with hypothalamic damage. Pituitary failure may be evidenced not only by mild or definite dwarfism but by other signs, such as tapering of the fingers, spacing of the teeth, and unusually fine texture, dryness or hairlessness of the skin. Obesity of the cerebral type, polydipsia, polyuria, polyphagia, or somnolence may suggest hypothalamic damage. Evidences of hypogonadism may be present, such as late menarche, relative underdevelopment of the genitalia and secondary sex characteristics. Amenorrhea frequently is a symptom, as are hypomenorrhea and oligomenorrhea. In such instances, the presence of a pituitary tumor should be carefully ruled out, and the glucose tolerance may be altered sufficiently to be of diagnostic significance. A low basal metabolic rate and habitually low or absent urinary prolan are consistent with a diagnosis of pituitary disease. In such cases, assays almost invariably show a diminished amount of estrin.

In cases where a pituitary tumor is present, it should be treated by x-ray or surgery. The general health and disturbances in weight should be corrected, and if reducing diets are necessary, great care should be exercised that vitamin deficiencies or anemia are not produced.

In the treatment of hypopituitarism, prolan or prephysin may be used in small amounts such as one-half cc. three times weekly in addition to theelin or estrin in some other form. Estrin may be given in doses of 1,000 or 2,000 units daily hypodermically or in larger doses by mouth. Some workers are using progynon-B in doses as large as 10,000 units every third or fourth day for three weeks and Proluton (Schering) for a few doses during the fourth week. From one-half to two grains per day of thyroid (desiccated) are often prescribed as well.

The results of such treatment are not particularly encouraging. In the more severe cases, if menstrual bleeding occurs at all, it is usually not normal and may disappear entirely when the treatment is discon-

tinued. In the milder cases, good results often are obtained, and the menses may remain normal after cessation of these measures. I have seen cases of unquestionable pituitary disease in which measures similar to those mentioned above have been followed by reestablishment of the menses after five and eight years of amenorrhea respectively, but such results are not the rule. In not a few instances, there may be sufficient improvement in the general health and sense of well being to warrant the partial continuation of these measures, even though menstruation may not be resumed normally.

Hyperfunction of the pituitary gland: So far as the growth hormone is concerned, hyperfunction of the pituitary gland is not a common finding in the early life in women, gigantism usually occurring in men. Hyperpituitarism of the type accompanying the so-called polyglandular disease or pituitary adrenal syndrome (Cushing's syndrome—pituitary basophilism) occurs in a mild form quite frequently. It is difficult, if not impossible, to differentiate this from the adreno-genital syndrome clinically. In outspoken cases, obesity is present which is confined chiefly to the trunk, head, and neck, and hirsutism, amenorrhea, purple striae atrophica, large breasts, polycythemia, mental dullness, excitability, tremor, tachycardia and sometimes elevated blood pressure and elevated basal metabolic rate are found also. In such cases, the Friedmann test frequently gives positive findings and peculiarly enough, there are no clinical evidences of hypo-ovarianism to be found except that there is amenorrhea; in spite of the high urinary prolan, urinary estrin usually is very low.

Mild cases of this sort are frequently encountered in young women who complain of scanty or irregular menses or amenorrhea. The patient is usually a healthy, robust type, alert and active. As a rule, the body is broad and thick, the breasts rather large, and there is a tendency to obesity. A distinct trend toward male deportment is often obvious. The polycythemia and purple striae are absent but mild hypertrichosis of the face and a tendency to male escutcheon of pubic hair are common. Positive Friedmann tests are commonly found and the urinary estrin is low. This type of patient may be benefited by estrin therapy but in my experience, this type represents the group which is most frequently helped by the administration of x-ray to the pituitary. From 10 to 25 per cent of an erythema dose may be all that is required, or the dose may be increased to 75 per cent or more in some cases if necessary. Severe cases will not respond well to roentgen therapy as a rule, but in many instances, the symptoms may be completely controlled by adrenal surgery which consists either of bilateral denervation or of partial adrenalectomy. The remarkable response after adrenal surgery which is seen in some such cases makes it quite clear that many of the symptoms are due to disturbances of the adrenal gland. Such improve-

ment may occur even when the syndrome is associated with a proven tumor of the anterior lobe of the pituitary. It should not be forgotten that a similar clinical picture may be associated with a definite adrenal tumor or a masculinizing tumor of the ovary (arrhenoblastoma).

Hyperpituitarism of a compensatory type may follow hypo-ovarianism at any time during the menstrual life of a woman or at the natural menopause. The external evidences of the excessive production of sex hormones may be scant or absent. Recurrent headaches of migrainous or non-migrainous character which occur prior to or at the time of menses or near the menopause may be found to be associated in some instances, as Kurzrok[2] has shown, with an excessive amount of prolan. Such headaches may at times be markedly benefited or eradicated by the use of estrin in relatively large doses—1,000 to 3,000 units per day. The control of such headaches may require a smaller dose throughout the month and an increase in dosage at or about the time when the headache is likely to occur.

Ovaries

Prepuberal Hypo-ovarianism: A marked degree of hypofunction of the ovaries which is of the prepuberal type and which is unaccompanied by any clinical evidence of pituitary disease is uncommon. When it occurs, one finds primary amenorrhea, infantile genitalia, absence of pubic and axillary hair, infantile breasts and nipples. The patient is usually tall and since the epiphyses of the long bones close late, the span may be several inches greater than the height. Sexual libido is slight or absent. In milder cases, there may be a delay in the menarche past the average normal time of 13½ years; the genitalia may be hypoplastic, the uterine canal measuring less than 7 cm. in length; the secondary sexual characteristics may be underdeveloped; and roentgenograms may show a distinct delay in epiphyseal closure. Such a slowing of epiphyseal growth occurs also in the hypothyroidism of childhood, in which case it almost invariably is associated with a distinct increase in the blood cholesterol. Large doses of estrin appear to be necessary in the treatment of most of these cases. We have used from 1,000 to 2,000 units per day for periods of many months. In addition to these measures, gonad-stimulating substances, such as antuitrin-S or prephysin in one-half or one cc. doses every second or third day may be used. If one attempts to increase the dose of estrin to a point where normal amounts of the substance can be obtained by assay from the urine, it will be found that doses as large as 10,000 units every second or third day may be necessary.

Here again in the severe cases, estrin therapy, even when large doses are used over long intervals, may yield only meagre results. Some growth of the vagina and uterus may be obtained and some increase in

body hair and size of the breasts may occur. The menses, however, usually do not occur, and if they do, complete normality is rarely obtained and cessation of treatment usually will be followed again by amenorrhea. In the milder cases, the periods may become normally established or hypomenorrhea may be definitely benefited.

Hypo-ovarianism of the late or secondary type is very common, occurring in mild or severe form after pelvic inflammation, surgery, radiation therapy or in association with the natural menopause. The emotional and nervous changes, including the sympathetic nervous changes with hot flashes are the most outspoken symptoms. In mild cases, hypomenorrhea is common but it may not occur. Assays may show a constant deficiency in urinary estrin, and clinical signs such as mild genital atrophy, breast atrophy, general weight gain, together with trochanteric and large anterior malleolar fat pads may be present without any very obvious abnormality in the amount of the menstrual flow.

Estrin therapy is most efficacious and gives its greatest symptomatic benefit in cases of secondary hypo-ovarianism especially at the menopause. Here adequate dosage will apparently eradicate the symptoms in approximately 95 per cent of the cases. However, it is difficult to explain why even large doses fail to give symptomatic relief in some cases. It has been our practice to begin the treatment by prescribing 1,000 or 2,000 units of estrin by hypodermic in the form of menformon or Theelin-in-oil which is taken daily or every second day for from ten to twenty doses. This method not only gives prompt relief and increases the confidence of the patient in most instances, but also indicates as soon as possible those cases in which oral therapy will be worth a trial if symptoms recur, since if large hypodermic doses fail, certainly small doses by mouth will be valueless. In the cases where estrin therapy fails to correct the symptoms, hyperpituitarism can often be detected by prolan assay, and it is possible that x-ray therapy to the pituitary has not been utilized sufficiently under such circumstances.

The melancholia which occurs at the menopause may be relieved by treatment with large doses of estrin for long periods. The persistence of such therapy will, I believe, give complete recovery in many instances.

Prepuberal ovarian hyperfunction (pubertas praecox) is quite an uncommon condition, but it is obvious when it occurs. This condition is the complete antithesis of prepuberal hypogonadism and in its presence all the genital and secondary sexual changes are premature and there may be abnormally early epiphyseal closure with dwarfism. Such an abnormality may be associated with hyperadrenalism or adrenal tumor, and in severe cases, adrenal exploration, denervation or partial extirpation of the gland must be considered.

Thyroid

Prepuberal or childhood hypothyroidism is a frequent cause of delayed menarche, or of irregular, scant or profuse menses. The diagnosis even in relatively severe cases is very frequently missed because in the mind of the physician, acquired hypothyroidism in children may not be clearly distinguished from cretinism. In childhood hypothyroidism, there is often nothing about the appearance of the patient to suggest the presence of the disease. Basal metabolic rate determinations are not dependable in childhood, although at the time of puberty or after puberty, they may be as useful as in the adult. The disorder should always be suspected where there has been abnormally slow growth, especially when late and irregular dentition has occurred. Coldness, lack of energy, edema, dry hair and nails and poor memory may be present. Roentgen evidence of delayed epiphyseal closure, together with a distinct hypercholesteremia are the most important diagnostic signs.

The treatment is obvious—thyroid is forced to tolerance, but it must be remembered that the symptoms of thyroid overdose are not identical in childhood and adult life. One-half grain of the desiccated thyroid can usually be well tolerated at the beginning of treatment. Irritability, sleeplessness and headache appear as evidences of thyroid overdosage more frequently in children and adolescents than they do in adults.

Hypothyroidism in the adult is diagnosed easily enough as a rule if the possible presence of this condition is constantly kept in mind. A low basal metabolic rate of course in itself does not indicate the presence of hypothyroidism, and improvement in symptoms after the administration of thyroid does not prove the existence of the disorder. These distinctions, however, are somewhat academic and as a rule, thyroid medication is indicated when the metabolic rate is low. When the rate is low and the typical symptoms are present, a positive diagnosis can be made. Ordinarily, physical signs are wanting, and in cases of doubt, the laboratory test which is of greatest value aside from the determination of the basal metabolic rate, is the determination of the blood cholesterol which, when increased to over 250 mg. per hundred cubic centimeters is an important diagnostic aid. The common symptoms—lack of energy and endurance, dryness of the skin and hair and brittleness of the nails, mild edema, paresthesia of hands and feet, a tendency to coldness and relatively diminished memory, and often nervousness—are to be elicited by careful history. Treatment consists of the oral use of desiccated thyroid, one-half to three grains per day as a rule or from five to fifteen grains of whole gland. The clinical signs and symptoms usually are a better guide to therapy than the metabolic rate.

THE MANAGEMENT OF FUNCTIONAL MENSTRUAL DISORDERS

Dysmenorrhea

The etiology of dysmenorrhea is badly understood, and the various theories will not be discussed here. Menstrual pain may be aggravated by constipation, uterine displacements and other factors which increase pelvic congestion. Dilatation and curettage performed empirically where no cause is evident, probably do not give relief in more than 10 or 15 per cent of cases. Constipation should be overcome, and displacements should be corrected. If correction of a displacement by use of a pessary fails to relieve the pain, operation probably will fail also. Exercise is very important. Systematic postural and knee chest exercises or active regular outdoor exercise in young women in whom there is no obvious cause for pelvic pain will sometimes accomplish wonders.

There is a small but definite group of patients in which the dysmenorrhea seems to be due to hypo-ovarianism. The uterus is small and there may be functional sterility. Secondary sex characteristics may give additional suggestive evidence, and assays show low urinary estrin. In these cases, active estrin therapy alone or with prolan will usually give marked relief. Remarkable results are claimed for emmenin. X-ray therapy given in doses of from 10 to 15 per cent of an erythema dose on each of two or three occasions may help. The physiological cure of this type of menstrual pain of course is pregnancy.

If menstrual pain is very severe and especially if it begins before the menstrual flow and leaves abdominal soreness afterward, endometriosis is to be suspected. Even if the disease is localized within the ovary as in the case of a chocolate cyst, very severe pain may be present. Here removal of the affected part will bring relief. At times, fever and elevation of the white cell count may accompany pain from this condition. If the endometrial transplants are diffuse, there is no cure except to render them inactive by removing estrin from the body, either by radiation or by surgical castration.

An unusual type of menstrual pain (Mittleschmertz), which sometimes is associated regularly with bleeding, occurs directly between the normal menstrual periods. This phenomenon which probably is associated with ovulation, may be helped or cured by the use of prolan, and it may be necessary to repeat this regularly at the time the pain is due.

For the treatment of the attack of dysmenorrhea, there is nothing new to offer. Narcotics should not be used. Alcohol which frequently will give great relief must be prescribed with caution. Atropine in moderate doses given regularly for 24 hours preceding and during the attack is sometimes of considerable value. Apart from this, one may advise avoidance of sexual excitement just prior to the menses,

thorough evacuation of the bowel by cathartic or enema, hot sitz bath, rest, heat locally, and analgesics, such as amidopyrine or acetysalicylic acid or cibalgene (Ciba).

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