

1936

Dysmenorrhea with special reference to etiology

Howard W. Granden
University of Nebraska Medical Center

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SENIOR THESIS
DYSMENORRHEA
WITH SPECIAL REFERENCE TO
ETIOLOGY

Howard W. Granden

UNIVERSITY OF NEBRASKA
COLLEGE OF MEDICINE
OMAHA, NEBRASKA

APRIL 17, 1936

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DYSMENORRHEA

INTRODUCTION

Dysmenorrhea is not a disease. It is in reality only a symptom of some underlying pelvic or constitutional disturbance. There was a time when all pelvic pains accompanying the menstrual period were called dysmenorrhea. In the past few years two types of dysmenorrhea have been recognized: (1) the primary or essential; and (2) the secondary or acquired type. The primary type occurs without demonstrable pathology while the secondary or acquired type may be caused by ovarian tumors, uterine myomas, endometriosis, uterine displacements or other pelvic lesions.

The cause and treatment of the primary type of dysmenorrhea, has been one of the most important unsolved problems in gynecology. Much human suffering, chronic invalidism, ill health, neurosis, as well as expenditure of money and loss of time has resulted from this condition. The associated menstrual pain usually begins a day or so before the onset of the menstrual period, is of a colicky and spasmodic nature and may last for a day or so during the actual menstrual flow. It occurs most frequently in young unmarried women and in married nullipara.

- (7) According to Doderlein (7) American girls are subject to condition in greater number than European girls. The explanation of this is somewhat problematical, as many of our working girls came from Europe, where they enjoyed good health. Perhaps in a way this greater prevalence may be explained on the basis that our country was the pioneer in giving to women

employment in professional as well as along business lines which causes greater responsibilities and more concentration of mind and application of duties with total disregard for the weaknesses and disabilities which are more common to womanhood.

Dysmenorrhea as many other diseases has been referred to as a disease of theories. The difficulty lies in the fact that most of these theories are unproven. Some difficulties arise at times in separating theories from facts. Although theories are useful for progress, to accept them as facts before they are proven is often misleading.

It is the purpose of this paper to discuss the incidence of this condition as it occurs in various types of women in different modes of life. An effort has been made to present and clarify the many existing theories as we find them today. An effort has also been made to correlate these theories with physiological functions and facts. It is necessary for one to have the physiology of normal menstruation in mind, before making an attempt at an analysis and clarification of the many theories and hypothesis which have been put forth to explain the causation of dysmenorrhea.

DYSMENORRHEA

INCIDENCE

In this condition it has been difficult to gather accurate information as to the frequency of its occurrence and because of this there has been marked differences in opinion by various investigators. There have been several sets of statistics presented, collected from the office practices of various physicians, from colleges and from numerous industries.

There has been many variations in the use of the term dysmenorrhea. Many women complain of the slightest pains occurring during the menstrual period, which may be sufficient to incapacitate them. Other women have not complained although they have suffered severe pain at this time. When one takes into consideration these two extremes and the many variations occurring between them, it is seen a large source of error may be present. On the other hand, there is at times marked differences in the opinions of the various investigators, in their interpretation of pain and in their writings these various interpretations may be another source of considerable error.

In recording statistics, and in their interpretation it will be realized another great source of error may arise, namely, the group of women from whom the statistics have been made. In realizing the occurrence among the so called leisure class-in these women dysmenorrhea may be a common symptom, because of self pity and using it as a means to escape unpleasant duties and obligations. In the working girls, there is apt

to be a smaller amount of occurrence reported because of fear of dismissal from employment or that it would entail a loss of time and earnings by the absence of a few days which they might have to miss during this period. It would seem more conceivable that the more accurate results would be those reported from women in colleges because of the above reasons. Here again some difficulty may be experienced during an interview because of shyness and self consciousness in certain girls.

Much interest has been shown in this phase of the subject by various commercial institutions, such as those investigations as are carried out in factories, offices, department stores and other concerns employing large numbers of women. This has been done to decrease the amount of lost time and better the efficiency of their women employees at this period. This interest has been of great value to the medical profession.

(12) Lakeman (12) has recently sent out one thousand questionnaires, which were distributed among employed women in five electrical outfitting factories and in two textile mills. Three hundred and sixty five questionnaires were returned with satisfactory replies. Of the three hundred and sixty five girls, 327 or 89.6 per cent stated they had pain at some time and in some degree, of these 176 had pain at some time and in some degree during the period always and 156 reported pain occasionally.

In age, 146 were under 21 and 218 were over 21 years of

age. A division of the replies by age groups failed to show any significant difference between the older and the younger women.

In regard to marital status, 261 were not married and 23 were widowed or divorced. The conclusions of most investigators is that marital status seems to have little or no bearing on the presence or absence of pain.

Attempts have been made to learn whether the menstrual pain was affected by customary habits or to physical activity and to positions assumed while at work. In various questionnaires, no significant difference has been brought out in the replies given by these women who stated that they sat or stood continuously and of those who stated that they moved about during the working day.

(12)
(4) In contrast to the occurrence of 89.6 per cent of these industrial girls as reported by Lakeman (12), Clow (4) an English physician has questioned 2,050 healthy girl students, which ranged in ages from 12 to 22 years, over a period of five years. She reported 22 per cent as stating they had menstrual pain either slight, sub-acute or disabling. It is of interest to note that amongst the first 734 girls in her study which were questioned a much higher rate 46.7 per cent was found, than among those questioned during the latter part of the five year period. In two of her later groups, the number reporting pain were only 10.8 per cent and 5.6 per cent respectively. She attributed this marked decrease to the fact that the school regime was changed during the interval in such a way that during the later years, practically all the students carried on

the same physical activities during the menstrual period as they did at other times.

(13) Meredith (13) writes of a physician who examined a large number of college girls and found that about 75 per cent had dysmenorrhea quite regularly ten years ago. However, in more recent times out of 749 girls only 17 per cent were troubled at all by pain at the menstrual period, and only about half of these regularly. She believed this to be due to an improved attitude in the minds of the girls toward the menstrual functions. For the most part they considered it as they should, a normal function, one which should not give them pain and it was not considered to be a period of invalidism. A second reason given for this improvement was thought to be the girls were now indulging in a greater degree of general activity during the period.

(24) Van Duyne (24) has made an interesting report covering a twenty-four year period at Goucher College, in which 3072 women were questioned. In the period from 1900-1907, it was found that 62.6 per cent of the women suffered no symptoms, 30.3 per cent had slight dysmenorrhea and 7.1 per cent had severe dysmenorrhea. The next period covered the years 1917-1923, 74 per cent of the women of this period had no symptoms, 3 per cent had severe dysmenorrhea and 23 per cent suffered slight symptoms. From 1923 to 1924 it was found 86.6 per cent of the women were free from symptoms, 13.1 per cent of the women suffered slight symptoms and .03 per cent suffered with severe symptoms.

(14) In 1927 Miller (14) reported 47 per cent of 785 college

girls examined by him suffered with dysmenorrhea, however only 17 per cent suffered severe symptoms. In 1932

(3) Boynton (3) at the University of Minnesota made a survey of the menstrual histories of 2282 girls, finding dysmenorrhea present in 20.38 per cent, while 10.34 per cent were irregular with their periods.

(23) Sturgis (23) in her investigation of 2077 working girls in department stores found only 14.7 per cent having pain at the menstrual period. This low incidence compares favorably with those reports of college women. Riving in his observations at the home office of the Metropolitan Life Insurance Company has found 7,390 women employes suffering with dysmenorrhea and a resulting loss of 1151 days time in this group.

From these observations, the incidence is seemingly somewhat higher in industrial women than in the college women. Because of this several questions have been raised by recent authors on the subject. Some of these have been, is it that the industrial girls have not had the opportunity, or perhaps the desire, for the physically active life as the girls in colleges to carry on during as between the periods? Or is it that a higher standard of general hygienic living prevails among the students? Or is it the prevailing mental attitude, an assumption that the days of menstrual flow are days of expected invalidism?

These questions and many others still await a definite answer, but the swing of the pendulum among the younger physicians and others is toward more freedom in activity by

girls and women during the recurring periods than was recognized as safe or wise a generation ago.

DYSMENORRHEA

PHYSIOLOGY

In order to gain a more complete knowledge of the causation of dysmenorrhea, and to better understand the more recent theories concerning this, it is of great importance to first review the knowledge of the normal menstrual flow and some of the endocrine factors connected with it.

The ovaries, with their formation of ova are the essential organs of reproduction. Primordial follicles are found in the stroma of the ovary from birth onward. At the stage of puberty some of these develop into mature Graafian Follicles, and from these ova are extruded into the peritoneal cavity and enter the Fallopian tube. Also at this stage of puberty there are changes in the accessory reproductive organs such as the vagina, uterus, tubes and mammary glands. These increase in size and become mature with the acquisition of secondary female characteristics.

At this stage of development the menstrual cycle usually begins, and recurs as an average, at monthly intervals until the menopause. The primordial ova and follicles mature and move toward the surface of the ovary and the endometrium of the uterus gradually increases in thickness, the blood and lymph spaces become filled and the glands increase in size, and become tortuous and branching. The Graafian follicle then ruptures and this liberates the ovum, and from this site the corpus luteum begins to develop. At this stage there is greater turgescence of the endometrium with a hyperplasia and tortuosity of its glands. Mucous goblet cells are

also found in the endometrium, and these are filled with their secretion. The stroma cells of the uterus undergo decidual changes also at this time. The small round cells are transformed into a triangular or a polyhedral type of epitheloid cells, which are rich in glycogen and are called the decidual cells. The menstrual flow then is ready to begin, providing the egg cell has not been fertilized.

Along with these changes, other factors also enter into the picture, which occur simultaneously with them. The follicular cells of the Graafian follicles, and possibly other portions of the ovarian tissue undergo changes. The granulosa layer is gradually vascularized and the granulosa cells undergo considerable proliferation and lipoids are deposited in them. In this liquor folliculi is produced which contains a sex hormone variously called oestrin, theelin, estrogen, folliculin, menoforn or progynon. This hormone is a crystalline compound, having the chemical formula, $C_{18}H_{22}O_2$ and is described as a keto-hydroxyoestrin. It has been isolated not only from the liquor folliculi of the Graafian follicle but also from pregnancy urine, placenta and amniotic fluid. The Graafian follicle then bursts, liberating the ovum. If the ovum is not fertilized, the corpus luteum passes through regressive changes, the cells of the granulosa and the luteinic cells of the theca gradually disappears, and the corpus albicans with its rich connective tissue is formed in its place. The corpus leuteum can develop even if the follicle fails to burst.

Theelin increases progressively in the blood during the

post- and pre- menstrual periods and when it is sufficiently concentrated, it is thought to bring about certain changes. There is thought to be caused an increased growth of the accessory genital organs, such as the uterus and tubes, as well as changes in the vaginal and uterine epithelium which includes morphological and functional changes in the glands of the endometrium and increased vascularizations of these structures. Theelin is also thought to cause contractions of the uterus and a growth of the secretory ducts and nipple of the mammary glands.

The corpus luteum also forms a hormone known as the lutein hormone, progestin or corporin. Various actions have been described to this hormone such as "complementary to", "antagonistic to" or "competitive with" those of theelin. It is thought to cause the formation of the decidua and sensitize the endometrium, so that an implantation and formation of the placenta can take place providing the ovum has been fertilized. It is thought that progestin completes the premenstrual changes which have been induced by theelin. Progestin also is supposed to render the uterine muscle refractory to the action of theelin and causes the uterus to be in a quiescent stage. It is also thought to directly or indirectly inhibit both ovulation and uterine bleeding.

The secretion of these estrogenic substances, theelin and progestin, and the production of the Graafian follicles are controlled by a gonadotrophic hormone of the anterior (30) pituitary lobes. Zondek (30) refers to this endocrine as the "motor of the ovaries".

Anterior pituitary transplants have been found to lead to growth of follicles and precocious sexual development. After a removal of the anterior pituitary lobes, the ovarian follicles have been found to fail to develop and those with cavities to undergo atresia, the uterus and vagina undergo atrophy and the menstrual changes to continue. The giving of suitable anterior pituitary extract counter- (27) acts these deficiencies. According to Wiggers (27) opinion is somewhat divided, as to whether there is a single gonadotrophic hormone of the anterior pituitary lobes, which is responsible for the maturation of follicles, ovulation and subsequent formation of the corpus luteum - or whether there are two separate factors concerned with ovulation and luteinization.

In correlation these various phases occurring in the menstrual cycle, it is thought following the menstrual flow, the gonadotrophic hormone of the anterior pituitary lobe stimulates the production of theelin in the Graafian follicle, which is instrumental in bringing about the repair of the uterine mucosa, in gradually increasing the vascularity and the growth of the uterine glands. This also causes contractions of the uterus and changes in the mammary glands. About the fifteenth day following the onset of the menstrual flow, the ova is extruded and with this there is an escape of liquor folliculi containing the theelin. Progestin is then formed, progressively increasing in amounts along with the reparative processes of the uterine mucosa in anticipation of the fertilized ova. This causes the formation of the decidua so

that implantation may take place and is antagonistic to theelin in inhibiting the uterine contractions and ovulation. If fertilization does not take place, these changes progress until about the twenty-eighth day following the onset of the menstrual flow, and the menstrual flow begins again, thus completing the cycle. In this connection Zondek (30) (30) states, "It can hardly be doubted that proliferation of the mucous membrane, menstruation, and the changes in the follicular apparatus are not only concurrent processes but are hormonally related."

For the functional cycle, it is thus seen that both the oestrin or theelin and the corpus luteum hormone, progesterin are required. The first causing a proliferation of the uterine mucosa and the second, transforms its proliferative into the secretory state.

DYSMENORRHEA

ETIOLOGY

Although dysmenorrhea has been known and recognized for a long period of years, and the study of this condition has caused much time and effort to be spent, nevertheless we are still very much in the dark as to the exact etiology of the condition. A number of theories have been advanced to explain the causation of the pain associated with the menstrual period in a great many women.

Dysmenorrhea may be roughly divided into two large classes or types: (1) Essential or intrinsic dysmenorrhea, by which reference is made to pain which is due to some inherent abnormality in the structure of the organs of menstruation or in the physiological processes connected with that function. (2) The second group may be termed extrinsic dysmenorrhea, denoting the menstrual pain which results from the presence of acquired pathological lesions in, or in the neighborhood of the pelvic organs. The pathology of this type may include : infections, neoplasms, displacements, traumata and subinvolution which may lead to an increased menstrual flow with the formation of large clots in the uterus which interfere with the normal force and rhythm of uterine muscular contraction, or by the production of adhesions to the ovary or fibrosis in the uterus, which will prevent the rupture of the Graafian follicles and swelling of the engorged uterus.

These lesions, may therefore give rise to menstrual pain. The treatment consists of the cure of the obvious lesion pre-

sent. Since the etiology of this type of dysmenorrhea is fairly well known, it will not be necessary to further discuss this type in this paper.

One of the oldest theories as to the etiology of primary or intrinsic dysmenorrhea is mechanical obstruction of the menstrual blood due to blocking of the cervical canal. The idea of mechanical obstruction of this type dates back (18) to 1832, when Mackintosh (cited after Novak and Reynolds)(18) reported twenty seven cases in which relief was obtained by a dilatation of the uterine canal. The explanation was that the dilatation had relieved some form of obstruction which might be present. This view was accepted generally and for many years it became one of the methods of treatment of this condition. It was further strengthened by the endorsement it received from such authors as Marion Sims and Sir J. V. (21) Simpson. Sims (21) has made the statement "there can be no dysmenorrhea, properly speaking, if the canal of the neck of the uterus be straight and wide enough to permit a free passage of the menstrual blood". Many of the early leaders of gynecology in this country have held to this theory.

Although many authors and textbooks still attribute this condition to mechanical causes, nevertheless it is being replaced by other theories, one of which is that of hypoplasia. The main argument in favor of this theory is that a certain number of cases are relieved by dilatation of the cervix. However the majority seem to be relieved only temporarily.

As this view has declined, the theory of hypoplasia has gradually gained foothold. It is believed by some that a

hypoplasia of the pelvic organs is present, particularly, (2) the uterus, which causes dysmenorrhea. Blair Bell (2) and others have linked the two factors of obstruction and hypoplasia together, believing that antiflexion is in itself an evidence of hypoplasia and that it in turn gives rise to obstructive dysmenorrhea.

The following local causes are thought to cause dysmenorrhea:

A. Morphological anomalies.

1. Underdevelopment of the uterus.

- (a) Underdevelopment of uterus of normal shape.
- (b) Underdeveloped uterus with or without underdeveloped ovaries with a conical cervix and pin hole external os, or an hypertrophied cervix.
- (c) Underdeveloped uterus with acute flexion.

2. Gross malformations.

- (a) Divided states of the uterus, due to imperfect fusion of the Mullerian ducts.
- (b) Atresia of the cervix or vagina with a single or divided cavity.
- (c) Accessory occluded uterine cavities.

B. Physiological anomalies.

- (a) Intrauterine clotting of menstrual blood with the subsequent expulsion of blood casts of the uterine cavity.
- (b) Excessive exfoliation of the endometrium (membraneous form).

A discussion of these local causes will be made in order to bring out more clearly how they may be factors in the production of dysmenorrhea.

In regard to the group of cases in which there is an underdevelopment of the uterus, of normal function, with or

without an underdevelopment of the ovaries the following ideas were held.

There appears to have been a general impression among gynecologists in the past that an incomplete development of the uterus was most always associated with amenorrhea, although these cases have occurred with a normal flow or even a menorrhagia was present. Dysmenorrhea was usually present under these circumstances, however it did seem to occur more frequently when the menstrual flow was normal or excessive than when it was scanty.

- (2) Blair Bell (2), in studying the histories of many cases of conical type of cervix and those of a pin hole os uteri, noticed a great number of these cases did not complain of dysmenorrhea. In those cases in which dysmenorrhea was present, he concluded that it was primarily associated with a poor development of the body of the uterus. These two factors were found to be associated in many cases whose complaint was pain at the menstrual period.

In many cases in which there has been found to be a congenital hypertrophy of the cervix, it has also been discovered that the majority of these did not complain of dysmenorrhea, but symptoms were present more like those of a prolapse. In most of these cases the body of the uterus has been found to be normally developed and the lengthening of the cervix concerned the vaginal portion only. It was then thought, if there were an associated dysmenorrhea, that it might be due to the fact that the uterus was proportionately underdeveloped in regard to the development of the cer-

vix and pain would arise when the relatively smaller uterus would try to expel the menstrual flow through a long, hypertrophied cervix.

In some cases of antiflexion of the uterus it has been noticed that the uterus was underdeveloped and contained a large quantity of fibrous tissue. In these cases in which dysmenorrhea was found to be present it has been thought to be due to fibrosis and also to the interference with the normal peristaltic wave of contraction at the angle of flexion.

In displacements of the uterus, Holden, (cited by (18) Novak) (18) states, "that in 25 per cent of all cases of retroversions in nulliparous women there is an associated dysmenorrhea". These displacements have been thought to possibly be due to congenital displacements of the uterus. In regard to the development of the genital organs, two stages have been recognized, the fetal and puberty stage. It is thought that at these stages or between these stages, some anomaly may arise, possibly favored by posture of the child and other like factors.

Many cases of bicornate uterus have been reported and in a number of these dysmenorrhea has been found to be absent. If there is an associated dysmenorrhea, it is thought to be due to excessive menstruation with intra-uterine clotting of blood. If both horns are equally well developed in a bicornate uterus, or if the uterus is fully developed in a septate or cordiform type, dysmenorrhea is thought to be no more likely to present than under normal circumstances.

Nevertheless, if there be an underdevelopment in one or both halves of the uterus, it is thought that dysmenorrhea may be present. These ideas have been further stressed since many cases of malformation have been reported with the above findings.

In the group of congenital anomalies in which there is an atresia of the cervix and vagina with a single or divided cavity there occasionally occurs a severe type of dysmenorrhea. The formation of a small portion of the upper end of the vagina just below the cervix with a complete absence of the middle portion, is rare. However, in these circumstances the menstrual pain is as severe as in those cases of cervical atresia. It is thought to be due to an increased tension, produced in the enclosing tissues by the addition of menstrual secretions at regular intervals - this is also augmented by the contractile attempts of the uterine musculature in the presence of this resistance.

It is rather uncommon to find a congenital occlusion of the cervix with a functional uterus either alone or with total occlusion of the vagina. It is not so uncommon to find cases in which one horn of a bicornate uterus with an occluded cervical orifice has formed a hematometra. In these cases too, the dysmenorrhea may be of the most severe type.

One of the more common causes of hematocolpos is an occlusion of the vagina at the outlet. In these cases there has been noticed to be an associated menstrual pain in about 25 per cent of the cases. The presence of accessory uterine cavities in an otherwise normal uterus has not been

definitely established although a few cases of dysmenorrhea have been attributed to this anomaly.

Among the physiological anomalies which may cause dysmenorrhea, one has been thought to be that of intrauterine clotting of blood. It is thought not to be normal for menstrual blood to clot in the uterine cavity. However some authors hold an opposite view, as Whitehouse (cited after (2) Blair Bell) (2) who believes fibrin ferment is absent from the menstrual blood. This absence is thought to be due to an antithrombin or a thrombolytin which may be secreted from the mucosa. This view has been generally denied by most authors and the concensus of opinion is that normally there is no intrauterine clotting of menstrual blood.

In the clinical histories of patients suffering with dysmenorrhea which was thought to be due to the intrauterine clotting of blood, the evidence of cause and effect is generally fairly clear and complete. First, almost always there is a free menstrual flow if not a menorrhagia. Second, by careful investigation and questioning it can generally be found that the onset of dysmenorrhea coincided with the first passage of clots during menstruation.

The explanation of the phenomenon of intrauterine clotting is thought to be due to the prevention of formation of fibrin ferments, or the substance when formed is extracted or destroyed by some vital process in the endometrium as the blood passes through to reach the uterine cavity. Then if there be a menorrhagia with the passage of a large quantity of blood over a period of several days, or merely a sudden

gush during a few hours, much of the blood will escape too rapidly and there is not sufficient time for the endometrium to act upon it, as described above. In only those cases in which the blood is retained in the uterine cavity long enough to clot is dysmenorrhea apt to be present. The retention may be due in part to lack of tone in the uterine muscle. The process of expelling this large blood clot may be responsible for giving rise to considerable menstrual pain.

Membraneous dysmenorrhea or excessive exfoliation of the endometrium is thought to be not a common cause of pain during the menstrual period. Many cases of this type are overlooked for the reason that a uniform cast of the endometrium is expected to be found. This is rarely the case for in the greater majority of patients a complete cast has never been obtained.

The cause of the condition is not known. Many women who menstruate normally differ greatly, in regard to the amount of denudation of the endometrium that occurs; and the effect produced in different women by the passage of an unusual amount of endometrium, which has become detached, varies considerably - some have severe pain during the process, others appear to suffer little or not at all. Not infrequently a membrane becomes rolled up, mixed with blood and is converted into a solid cast which causes considerable pain on expulsion.

The histological features of the cast of exfoliated endometrium are constant if the tissue is fixed before auto-

lytic changes have occurred. There is a well defined premenstrual decidual reaction of the stroma cells which especially near the surface lie in a medium of serous and sanguineous effusion. In most cases of excessive exfoliation there is a profuse menstrual flow and the blood being unable to break through the dense decidual barrier, the membrane is stripped off the deeper structures by the effusion behind it.

There are several ideas which have been put forth to explain the primary cause of this membranous dysmenorrhea.

- (18) Novak and Reynolds (18) believe it is due to a nutritive change. Lawrence believes it to be due to a pelvic inflammatory condition, following any one of the exanthemata near the age of puberty. The condition may be unilateral and involve the tube or ovary or both. Membranous dysmenorrhea has been seen in association with diabetes.
- (7) Doderlein (7) believes the discharge of the membranes is often only a symptom rather than a cause of dysmenorrhea, just as a membranous colitis is sometimes of a neuropathic or toxemia origin.

In the passage of years much work has been done by various authors in an attempt to either prove or disprove the value of these theories in offering an explanation for the cause of dysmenorrhea. Many of these ideas have been left aside, explaining only perhaps a minority of these cases. Many arguments have been advanced against the theory of mechanical obstruction in which antifixion of the uterus was thought to play such a large part.

(17) Those put forward by Novak (17) are:

(1) Cases have been reported in which antiflexion of the uterus has been found but no dysmenorrhea occurred.

(2) Many women have complained of menstrual pain in which there was no antiflexion and the uterus showed no gross abnormality.

(17)(3) Novak (17) has demonstrated that at the height of the menstrual pain, a probe could be passed into the uterine canal with no evidence of obstruction present.

(17)(4) Novak (17) has also observed that the rate of discharge of menstrual blood in normal women averages about 2/3 drop per minute and it is not believed that antiflexion could produce sufficient obstruction to interfere with the exit of such small amounts.

The chief arguments against the theory of hypoplasia are: that in those cases in which the uterus is markedly hypoplastic, as the so-called type uterus infantilis, there is often no menstrual pain, and on the other hand, primary dysmenorrhea has been found when the uterus was of normal size. The main evidence against the importance of the developmental factor lies in the fact that dysmenorrhea is often an acquired disorder. The history of the patient usually shows in a great many instances that after the onset of puberty, the patient menstruated for perhaps a long time, after which, menstrual pain made its appearance. This was found to be true in 42 per cent of a series of patients

(17) followed by Novak (17).

(1) Schultz, cited by Barry (1) believes the pain in the

hypoplastic uterus to be due to the failure of the uterine musculature to empty the uterine veins during the physiological hyperemia accompanying menstruation. This results in a nervous stasis with pressure on the uterine nerves.

Nervous theory -

There are some gynecologists as J. Novak and M. Harnik (16) in Germany, (cited by Novak (16)) who believe that all cases of primary dysmenorrhea are explainable on the basis that the psyche plays an important part in the production of the menstrual pain. Many other authors have since taken up this view and believe that a psychic trauma; of one sort or another is the primary cause for the first attack of dysmenorrhea. The recurrence of monthly attacks is the result of anxiety or fear thus subconsciously associated with the function.

The patients making up this type of cases are generally considered to be the robust, well developed girls with little or no displacement, and well developed genitalia. This type is thought to be found especially among people of better circumstances and girls possessed of an excitement or pleasure seeking mania, in which there is an inherited neurotic tendency. It is also believed that those cases in which the dysmenorrhea may be produced by a long repression of the sexual instinct may be also included in this class. In many cases it is known that at the age of puberty dysmenorrhea has not occurred. They, up to that time, apparently lead a fairly natural life and developed symmetrically. Later on, her mother's daily warnings and corrections, social convention-

alities, and her own studies induce her to repress her sexual instincts, which may be a contributing factor in the production of the dysmenorrhea.

Most observers agree that girls who seek to gratify their sexual feeling by conventional contact with the opposite sex, as in games, walks, drives and dancing, not speaking of those who practice illicit relations, are rarely affected by dysmenorrhea.

In this type it is also considered very important to decide whether the neurotic tendency is primary or secondary. It may be possible that with the nervous exhaustion, and recurrence of menstrual pain which is often severe with each menstrual period, that as time goes on reaction from this will eventually lead to a constant nervous irritation, and the patient becomes thoroughly neurotic, though the neurosis is not of a primary nature.

(16) Novak (16) in his article in 1930 has regarded this theory under three headings: hysterical, neurasthenic and neuralgic.

In those who have manifestations of the hysterical type it is thought that the diagnosis should be made with great care, and not in the absence of such other symptoms of hysteria as paresthesia and anesthesia, etc. There are many women of the hysterical type who complain of pains in the region of the ovary although no pathological lesions have been found to exist even after the most thorough examination. It is thought that many times a like situation may exist in which the hysterical type of woman may suffer with dysmenorrhea,

even though there are no abnormalities in the pelvic organs. These cases are seen perhaps more frequently in the young patients. The girl may be a victim of suggestion by a sincere but over anxious mother, by whom she is informed that pain during the menstrual period is to be expected. She is put to bed with a hot water bottle to await the arrival of the menstrual pain. If the girl is of an impressionable type, the pain is almost certain to materialize.

In the neurasthenic type of patient, the manner of production of dysmenorrhea is thought to be somewhat different than in the hysterical type of patient. The former type was seemingly a result of such factors as heredity, environment, mode of life, etc. In this type there is thought to be a condition of general weakness or asthenia of the nervous system. There is a wide variety of symptoms which may be present and they may be referable to any part of the body. However, the chief symptoms are generally referable to the pelvic organs and dysmenorrhea is probably one of the most common of these. It has been found that with an improvement in the patients' general condition, the dysmenorrhea is generally relieved in this type.

A secondary neurasthenia is sometimes thought to occur, primarily caused by some underlying condition which is of a definite anatomic basis. The secondary neurasthenia generally occurs in the type of woman who is apparently normal and well developed, but whose nervous system is more unstable than the average. If there is a removal or cure of some definite pathological lesion of the pelvic organs she frequently is no more relieved of her dysmenorrhea than before.

This has been explained on the basis that the neurasthenia still persists and this must be corrected before the relief from the dysmenorrhea is obtained.

The third class of patients, those belonging to the neuralgic type, the dysmenorrhea is thought to be of a distinctly nervous origin. In these patients the complaint is usually of the nature of sharp shooting pains over one or both ovaries. These pains may occur at irregular intervals, not necessarily during the menstrual period and they may be noticed in the intermenstrual period. These pains are thought to be of the same nature or analagous to those seen in supra-orbital or intercostal neuralgia, however, neurologists have been unable to offer a plausible explanation for these pains. In former years the diagnosis of these cases was ovarian neuralgia or oophoralgia.

Although many gynecologists feel that this theory may explain some of the cases of dysmenorrhea, however, the greater majority believe that this theory will not explain (16) all cases. J. Novak and Harnik, (cited by Novak (16)) believe that all cases of essential dysmenorrhea are neurotic in origin and that a careful investigation will reveal that some psychic trauma, many times sexual in nature, forms the basis of the first attack. The recurrence of subsequent monthly attacks is a result of anxiety and fear, which is subconsciously associated with the menstrual function. They also believe that cure can be obtained by gaining the confidence of the patient and having her realize that her monthly attacks of pain result from a state of her subconscious re-

flexes rather than any disease of the pelvic organs. They report 168 cases treated by psychic reeducation. Seventy-one were completely relieved and eighty-nine were markedly improved.

Other investigators however, have found the psychotherapy treatment to be unreliable in many cases, although an explanation of the condition to the patient, allaying her fears and gaining the patients' confidence has done much toward obtaining successful results.

It has been thought that the time honored method of treatment of dilatation of the cervix might have an explanation of its effect as appeasing the psyche of the patient.

- (7) Doderlein (7) believes a hyperesthesia of the uterine mucosa serves as a basis for many cases of dysmenorrhea, while others are of the opinion that the dysmenorrhea is an exaggeration of the normal physiological uterine contractions which normally causes no pain in women of sound nervous temperaments. Gibbons (10) advanced a theory that dysmenorrhea was caused by some bio-chemical material circulating in the blood stream which acted upon a hyperesthetic mucous membrane of the uterus, and also possibly upon the nerve centers regulating the genital tract.

Since these ideas are based on a similar fact which will be presented, they will be discussed together. These are based on the fact, that in the region of the internal os and beyond, in a normal healthy women, disagreeable sensations are noted when the mucous membrane of this region

is touched with a uterine sound. However the patient can stand the examination very well. If, in those women who suffer dysmenorrhea, a probe is passed into this region it is found to be extremely painful contractions of the uterus. This has been noted in a number of instances.

- (10) Gibbons (10) attributed this condition to a hyperesthesia of the mucous membrane and in the region of the internal os, which was due primarily to some form of biochemical material which acted upon the mucous membrane and the genital nerve centers in this manner. He further believed that this material was due to a faulty secretion of the ovaries.

A form of dysmenorrhea of a special interest is the so called nasal dysmenorrhea, first described by Fleiss in 1893. Fleiss described genital spots in the nose consisting of erectile tissue situated on the anterior end of the inferior turbinate and on the tubercle of the nasal septum. According to Fleiss, these spots are swollen, congested and hypersensitive during menstruation. He distinguished two types of dysmenorrhea; one in which the pain disappeared with the appearance of the menstrual flow, the other in which the pain continued.

The first type he believed due to cervical stenosis, the second included numerous patients in whom cocainization of the genital spots caused immediate cessation of the menstrual pain. Permanent relief from nasal dysmenorrhea was often possible by cauterizing the genital spots with galvano cautery, electrolysis or trichloroacetic acid.

- (1) Schiff (cited by Barry (1)) later confirmed Fleiss's

observations and stated that 72 per cent of all types of dysmenorrhea yielded to this treatment.

This theory has had some supporters since then, however it has not been met with general acceptance. Many objections have likewise arisen to this theory. The main one being that this is merely the result of a suggestion made to patients of a hysterical type. It has been noticed according to (16) Novak (16) that cocainization of other mucous surfaces will have the same effect. He reports two cases in which relief from dysmenorrhea has been obtained by cocainization of spots on the cervix and in the rectum.

Posture -

The study of posture and body mechanics in regard to their relationship in the production of dysmenorrhea, has been a subject of much interest and controversy for a period of years. N. F. Miller (15) probably has done as much work as any other observer on this phase of the subject. His studies covered a series of 302 college women over a period of four years. These women represented the average normal healthy college women. These women were closely questioned, examined and a classification of each individual type was made in regard to their posture and muscle tone. By means of silhouette photographs, a permanent record of their posture was kept each year. By following these records each year, he could demonstrate an improvement of posture in the individual. However, pain at the menstrual period seemed to be as frequent in those cases in which there was good posture as in those with poor posture. The average wo-

man who did not have dysmenorrhea seemed to be of the slightly taller build and with a more pronounced breast development.

The results of other observers have been similar to (15) those of Miller (15) and it would seem that correction of posture or poor posture exerted very little effect on the production of dysmenorrhea.

Allergy -

Several observers, have thought that allergy may be (6) a factor in the production of dysmenorrhea. Cooke (6) reported two cases in whom asthmatic coryza and urticaria were associated with cramp like pains in the lower abdomen. Duke has reported a case which was sensitive to certain foods and disturbances of menstruation was a part of the general reaction. This disturbance did not appear after the offending food was withdrawn.

(11) Kahn (11) reports a case in which he was desensitizing for hay fever with timothy grass extract and in about twenty minutes after the onset of the reaction, the patient experienced severe pains in the lower abdomen, simulating (26) labor pains. Walbott (26) reported a case in which the patient was sensitive to various animal hair and her attacks (22) were more severe at the menstrual period. Smith (22) reported 12 cases of essential dysmenorrhea in which the patients were found to be sensitive to various foods. All of these patients were free from symptoms in the intermenstrual period. When the offending foods were omitted one week before the expected date of the menstrual period, and

during the period, eight were found to be relieved from all pain and four were partially relieved.

That the uterus reacts to allergy and can be desensitized, has been proven by Dale, according to Dutta (9). Dale sensitized guinea pigs to various antigens, removed their uteri and thoroughly perfused them to remove all traces of blood and suspended them in Ringers solution. Various amounts of foreign protein were added to this solution. He found minute traces of the substances to which the animal was sensitized would cause an immediate contraction of the uterine muscle. He also demonstrated that the uterine strips could be desensitized with the specific antigen.

A connection between allergic conditions and malfunction of the endocrine glands has often been suggested.

It has been thought that factors operating in certain cases of allergy might depend upon the varying activity of the glands of internal secretion, since it has been often noticed that an association of allergic conditions is present with an increase or decrease in the function of the sex glands. Boys are noticed to improve at puberty, were as, in girls allergic attacks usually start at this time or become worse - and spontaneous improvement has been noted at the menopause. It is also found that allergic attacks as asthma, urticaria and migraine, either start or get worse at the menstrual period. There may be some alteration in the normal balance of the endocrine system connected with this.

The effect of pregnancy on allergic conditions is rather interesting. Usually the attacks either decrease or disappear

- (5) at this period. However, Collins (5) and others have reported cases in which asthmatic attacks occurred during pregnancy with more or less complete relief at other times.
- (28) Williamson (28) has reported 13 cases of pregnancy complicated with asthma and 14 cases with pollen sensitivity. In none of them did allergic attacks bring about a miscarriage or premature labor.

Many observers have thought the calcium content of the blood was lowered in certain allergic conditions and have recommended the use of calcium in its treatment. Recent investigators believe there is no alteration of the calcium content from the normal; however lately it has been suggested that calcium occurs in different forms in the blood, and the diminution or preponderance of one or another fraction may be conducive to allergic reaction.

It is fairly certain that the uterus is susceptible to allergic conditions and responds to it by contraction, and the blood calcium is increased during pregnancy and decreased during menstruation. It has already been mentioned that most of the cases of asthma are influenced during pregnancy and asthmatic attacks are often associated with menstruation. On these grounds it may be supposed that blood calcium may play some part in bringing about allergic attacks in women.

Mild infection of the genital tract is thought to induce allergic action, especially during the menstrual period. Bacterial infection is thought to act in three ways, (a) a phase of lowered resistance, activates a dormant allergic state (b) a definite sensitivity may develop to some allergen

due to the damaged state of the mucous membrane and (c) by reason of her allergy.

The calcium excretory function of the uterus is controlled by an ovarian hormone according to some authors and the action of adrenalin is possibly antagonistic to the ovarian secretions. There is a fall in blood pressure during the menstrual period which is slight, but more than can be accounted for by the loss of blood. For this reason it has been suggested that the adrenals may be inhibited during menstruation. Since most women at this period are in an over excitable state and an incident which will not affect her at other times, may upset her sympathetic and parasympathetic balance at this time, especially in one who is of a vagotonic type or one who has an allergic diathesis. It is thought that one of these may precipitate an attack of asthma, (9) urticaria, dysmenorrhea or migraine attack. Dutta (9) states, "We do not know the exact cause of the actual localization of the lesion, but it is likely that this will be at the site which has become oversensitive from some injury, inflammatory or mechanical condition."

(9) Dutta (9) has reported three cases. In one of these, the menstrual fluid was examined for eosinophils, and they were found to be present. This patient suffered from allergy and when she exposed herself to the offending agent just before the menstrual period, she had dysmenorrhea. The attack was relieved by adrenalin. The second case suffered from dysmenorrhea from the beginning of her menstrual life, which has always been associated with asthmatic attacks. The third

patient was found susceptible to a certain pollen and she would have dysmenorrhea on exposing herself to this pollen. She was cured by desensitization to that particular pollen.

Since the etiology of dysmenorrhea is still very obscure and allergic conditions are fairly common, it would seem that further investigation alone can decide whether it is a common or a rare cause of dysmenorrhea. It would seem very probable that this may be the cause in many obscure cases.

Hormonal theory.

The importance of endocrine dysfunction as a possible etiological factor in the production of dysmenorrhea and if it were associated with other more definite types of endocrine imbalance found elsewhere in the body, has been a subject of a great amount of discussion by many authors. Although a great amount of literature has been written, there is yet comparatively little known of this subject.

The close relationship of the pelvic organs to the endocrine glands makes this supposition possible, however the knowledge at present shows no characteristic indication that there is an association of dysmenorrhea with any of the recognized endocrine disturbances. Administration of thyroid, pituitary, ovarian and mammary extracts, have only too often ended in failure. However, recent work promises to throw some light upon the hormonal origin of primary dysmenorrhea. This has been largely brought about by experimental work. The investigations have been directed chiefly to a study of the cyclic influences concerned in uterine irritability.

Many authors in Germany have reported a considerable amount of work along this line and similar investigations have been (25) carried on in this country by Van Dyke and his co-workers (25), (8) Durrant and Rosenfeld (8), Novak and Reynolds (18), Reynolds (18) and Friedman (19) and others.

(20) Reynolds (20) has studied the uterine contractions of experimental animals in the unanesthetized state. This procedure has been quite an advantage because of the influence of practically all forms of anesthesia on uterine motility has made a considerable amount of error.

Through an abdominal incision in rabbits, a cut across the vagina was made below the cervix. The vaginal cuff was turned downward, and the cervical end was brought through the abdominal incision and sutured in situ. This created a uterine fistula. A small balloon was then placed in the uterus and connected to an air-water manometer and kymograph. By this method the action of drugs and hormones could be easily studied.

(20) Reynolds' (20) investigations have shown that the oestrous phase in the non-pregnant rabbit is associated with marked uterine activity, while the anoestrous phase is characterized by only feeble motility, if any at all.

If these observations are applied to the human, it may be said that uterine rhythmic contractions become increasingly more active as the Graafian follicle develops. When this follicle ruptures and there is corpus luteum formation, the uterine contractions are inhibited. Then during the last half of the menstrual cycle, the progestin phase, the uterine

muscle is fairly quiet. By substitutional therapy, with the follicular hormone, activity can be restored, which would indicate this hormone stimulates uterine activity. Castration produces complete quiescence of the uterine muscle. Experiments with other endocrine preparations seems to show that the follicular hormone alone possesses this property.

In castrated animals, the uterus has been stimulated to activity by the follicular hormone. The administration of the hormone derived from pregnancy urine, inhibits uterine motility, having an action similar to that of progestin. This observation has been noticed even in normal rabbits when the pregnancy urine has been given in such small amounts that it causes no ovarian change. From these facts it has been concluded that there is a direct action of the hormone of pregnancy urine on the uterine muscle. It has been found that the action of this pregnancy urine hormone is not specific to the rabbit, since it produces ovarian stimulation in the mouse, rat, guinea pig, ferret, monkey and other animals.

- (29) Knaus in Austria, (cited by Witherspoon (29)) has studied uterine motility in the human by a technique based on the responses to posterior pituitary extract (pituitrin) , exhibited by the uterine muscosa at different phases of the cycle. He found the uterus to react to stimulation by pituitrin in the first half of the menstrual cycle. After ovulation the uterus was found to be refractory to pituitrin and remained quiescent. This observer noticed a marked motility of the uterus in patients on the second day of menstruation and also on the fourteenth and eighteenth days of the cycle.

The pain in primary dysmenorrhea has been noticed to be characteristically of a spasmodic, colicky nature. It generally begins a day or two before the onset of the menstrual flow, which is theoretically the time when the lutein body begins to degenerate, and when the follicular hormone stimulation again becomes prominent. The height of the corpus luteum activity is several days before the onset of the menstrual flow, not at the time of flow. This can be found by excision of the corpus luteum, the menstrual flow generally begins 24 to 48 hours later.

The pain of primary dysmenorrhea is explained as being due to the taking away of the progestin influence which results in stimulating the uterus into marked contractions by the action of the follicular hormone. The uterus previously has been lying in a quiet state during the preceding ten to fourteen days.

This hormonal sequence probably occurs in all women, however there is relatively only a small number who are affected with dysmenorrhea. Two explanations have been offered to account for this. First, there is thought to be a heightened sensitivity to pain stimuli because of psychogenic or constitutional factors. Second, there may be a real endocrine imbalance which acts upon the uterine motility. It is not known whether this endocrine imbalance would be in the form of a quantitative factor, causing marked uterine contractions to result from the excessive secretion of large amounts of the follicular hormone over the progestin; or it may be of the nature of a chronological factor, in which the follicular

stimulation came on too abruptly and there is not a gradual stimulation after the withdrawal of the corpus luteum influence.

According to this theory, the aim in the treatment of this condition is either to counterbalance the excess of the follicular hormone by substituting additional corpus luteum influence, or to withdraw the corpus luteum influence slowly, so that the follicular hormone stimulation will not be precipitated, but will appear gradually.

DYSMENORRHEA

SUMMARY

Dysmenorrhea has been shown to be a fairly common complaint varying in severity, and causing much disability and loss of time at monthly intervals, in a great number of American women. It has not only been of great concern to patients and the medical profession, but to industrial companies as well.

As yet no specific cause has been assigned to this condition, although a great amount of time and money has been spent in its study. Many theories have been brought forth, however most of these do not seem to explain all cases. The more recent theories, those of allergy and the various hormones, especially the latter seems to throw a great deal more light on the subject than ever before. These theories in years to come will in all probabilities be changed in a great many of their details, as new knowledge is accumulated, however the basic ideas contained will stimulate much thought on the subject.

It may be that the causative factors cannot be ascribed to any one single cause, more probably, there will be several causative factors, each exerting its particular influence in the production of this condition. However, with the finding of this factor or factors, the etiology of dysmenorrhea will be placed on a more firm basis, in turn the treatment will be more effective and a problem of interest to many will be answered.

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