

**THE USE OF LUTEUM EXTRACT IN THE TREATMENT OF  
MENSTRUAL DISORDERS.\***

BY

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WHEN one essays to present a dissertation, no matter how brief, on the topic of corpus luteum therapy, it is at least assumed that he possesses some special knowledge of the subject, which, in all probability, is the result of extensive observation or investigation. In this instance, however, such is not the case. I have incorporated herewith little of scientific value or true originality.

A discussion of the time-worn text-book subjects of amenorrhea, dysmenorrhea and other phases of altered menstrual flow, and a consideration of the relation of these symptoms to certain underlying pelvic or constitutional conditions, would be decidedly bore-some, hence it is my intention only to offer, in an epitomized form,

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a few case histories embracing the result of personal experience with the use of luteum extract, combined with a small amount of comment as to the indications for its administration and the limits of its action.

To the corpus luteum is attributed a twofold action: First, of preventing the formation of an excess of scar tissue in the ovary, following follicular rupture and ovular expulsion; and, second, of subsequently elaborating an internal secretion.

As a result of an extensive series of experiments, it has become a well-established fact that this internal secretion exercises an important influence upon the sexual cycle, such as causing the phenomenon of menstruation, controlling the nutrition of the uterus and, if pregnancy occurs, probably aiding in the attachment of the ovum to the wall of the uterus by causing the endometrial changes which characterize the decidua. It seems also to influence the physical development of the woman and bears a distinct relationship to the other body glands of internal secretion, thereby aiding in the maintenance of normal metabolism.

Some years ago, acting upon the assumption that the ovary harbored this action, an immense amount of interest was taken in the possibility of successfully treating with ovarian extract, certain gynecologic disorders which could be theoretically attributed to hyposecretion of this organ. Little benefit was gained, however, in these cases for the obvious reason that we now know that the ovary, as a whole, did not furnish this active principle.

Following the valuable demonstration of Fraenkel and Loeb, enhanced by the reports from such men as Burnam, Kelly, McDonald and others, the corpus luteum extract supplanted the ovarian extract in therapeutic use and now we are well agreed as to its efficacy where there are certain given indications.

Its chief field of usefulness seems to be, (1) in the treatment of functional amenorrhea, (2) the neuroses of the natural, artificial and premature menopause and (3) in those cases which come under the head of the so-called "ovarian deficiency" type, occurring during menstrual life.

In this last class, dysmenorrhea should be especially included. In my own private practice I have observed, in a truly extraordinary manner, the cure or relief of many such cases through the medium of this type of organotherapy. My best results, however, have been gained in the administration of corpus luteum for the relief of the severe nervous symptoms attendant upon the menopause of both the physiological and artificial varieties and the functional amenorrhea of young women.



As illustrative of the action of corpus luteum in functional amenorrhea, I have two cases of interest which I should like to describe briefly: The first case is that of a young school girl, aged fifteen, who consulted me in November, 1914. She had first menstruated two years before this time. Six months had elapsed before the next period appeared. She menstruated but three times in the following year and when I first saw her, the history given was of amenorrhea for a period of nearly four months. Her weight was 196 pounds, and she had gained in weight rapidly during this time. She was very nervous, irritable and depressed. She had given up school because "it worried her so much." The appetite was good, but she complained of much disturbance of digestion. I commenced treatment by giving her luteum in the dose of 10 grains, three times a day. Three weeks later she menstruated normally. At this time I added thyroid extract in the dosage of five 2-grain tablets a day. She has continued the use of these two extracts up to the present time, with but one short intermission and a slight decrease in the dosage of the luteum extract. When last seen, on the second of this month, after having returned from a stay in the country for the summer, she weighed 167 pounds, a loss of 29 pounds, and has menstruated regularly every five weeks since the treatment was begun. There is absolute cessation of the nervous and digestive symptoms.

The next case is of a similar nature: A young married woman, aged nineteen, consulted me concerning arrangements for her confinement which she anticipated in another month's time. She gave a history of amenorrhea for eight months; during this time she was "sure she felt the motion of the child." On casual inspection she certainly looked the part of a pregnant woman; but upon examination she was found to possess a small infantile uterus and a hypoplastic condition of the genitals. An enormous deposition of fat was evident, especially on the abdomen and in the breasts. The hemoglobin about 70 per cent. She was drowsy, asthenic, at times exceedingly nervous, and has experienced violent attacks of tachycardia on several occasions. Bland's mass by mouth and iron citrate by injection, *plus* corpus luteum (30 grains a day) was prescribed. Her general and nervous condition gradually improved and menstruation appeared shortly thereafter. I saw this patient regularly for four months. During this period she menstruated four times with fairly normal intervals. I have had no opportunity to see her since.

In these two cases we have conditions of distinct similarity. While it is evident and granted that there was ovarian insufficiency present in both instances, one must consider diminished pituitary

function in the second. Here were present the various symptoms which would point to probable hypopituitarism with the resulting progressive general obesity associated with atrophic changes in the genitalia. No doubt, too, there was abnormal secretion of the thyroid which would explain the nervous symptoms. As Bandler states it, "if there is a diminution of the ovarian and thyroid activity and the ovarian activity is so diminished that a relative degree of thyroid hypersecretion exists, we have, in addition to the increase in weight, an excitable condition due to this thyroid hypersecretion."

There is no doubt that some cases of obesity with amenorrhea are due to ovarian inactivity; some are due to diminished thyroid function; many are of the so-called hypophysis type and, in all probability, many are due to an involvement which includes failure of function in more than one of these glands; as is illustrated in the cases just mentioned.

In the neuroses of the surgical and natural menopause, as I have said before, the corpus luteum therapy plays a most important part. The nervous, digestive and circulatory disturbances of the climacteric may be frequently controlled by its use. Likewise its efficiency in controlling similar symptoms, following hysterectomy and oophorectomy, has been repeatedly demonstrated. I consider it a necessary adjunct to the treatment of such cases.

Two years ago I removed the right tube and ovary from a woman in whom a ruptured tubal pregnancy on the opposite side had occurred a year and a half previously and, at which time a salpingectomy and oophorectomy was done on the left side. Shortly after my operation she experienced all the extreme and disagreeable symptoms of the climacteric to such an intense degree that her work, as a dressmaker, was greatly interfered with. No relief was obtained until she began the use of corpus luteum. Thirty grains a day soon brought about complete cessation of the symptoms. She still continues the use of the product in decreased dosage and can dispense with its ingestion for considerable intervals of time without experiencing any immediate return of discomfort.

In the treatment of those patients who, during their menstrual life, show severe nervous phenomena such as irritability, malaise and depression, accompanied by headache and scanty menstruation, corpus luteum is obviously indicated. It is really astonishing to see how quickly there is a change for the better. How often, too, do we see patients who suffer with dysmenorrhea, presenting this same train of symptoms, indicative of insufficient ovarian function.



This brings me to the subject of dysmenorrhea. I do want to make mention of my small experience with this condition in relation to my experience with corpus luteum extract as the remedial agent. The results gained by corpus luteum therapy, as applied to dysmenorrhea, have been far from remarkable, although the reports of some observers show its undisputed value, when utilized in those cases where functional ovarian deficiency is present. I have used it with varied results, but the recital of two cases of dysmenorrhea, in which absolute relief was obtained through its use, should have some weight in the consideration of this subject.

The first case was that of a married woman, aet. thirty-two, who had suffered intense pain at her periods ever since menstruation made its appearance. She had never been pregnant. The flow was normal in amount and occurred at regular intervals. I used every method known to me to relieve the condition. I confess that I often resorted to morphine. She experienced this pain only on the first day of the flow. She had an acutely anteflexed uterus with apparent cervical stenosis. I performed a dilatation and posterior division of the cervix, but no relief followed. I tried corpus luteum, giving her one 5-grain tablet three times a day; increasing to two 5-grain tablets three times a day, a week or ten days preceding the period. At first no appreciable relief was observed, but, subsequently, she menstruated almost painlessly. This was in the Spring of 1913. I have since received word from this patient, stating that she still uses the corpus luteum tablets, and that she has no pain at the time of menstruation. Relief after seventeen years suffering!

I have a parallel case in a woman, aged thirty, a semi-invalid, who is thin and poorly nourished. Her menstruation was regular but scanty, and she had always suffered much pain on the first day of menstruation. The pelvic organs are seemingly normal. Fifteen to thirty grains of lutein extract a day has relieved the pain almost entirely, increased the flow and bettered her general condition. These are but two of a dozen such cases which I have in mind, but they are sufficient to illustrate my point.

The fact that dysmenorrhea is oftentimes amenable to this therapy allows for some interesting theorization as to its exact mode of action. The ovarian secretion is responsible for menstruation. That is a well-proven fact. We also know that the result of this action is a periodic hyperemia of the uterus, and thickening of the endometrium followed by diapedesis of erythrocytes, rupture

of dilated capillaries and the formation of small hematmata; this is again followed by rupture of the subepithelial hematmata and exfoliation of small portions of the uterine mucosa. Yet this description does not fully cover the action of the ovarian internal secretion. To illustrate, let us take an analogy from the alimentary system. Inasmuch as we know that the hormone of the duodenum, called secretin, passes through the blood stream to the pancreas and there stimulates the acinar cells to pour out their enzymes, so it is quite possible to believe that the ovarian secretion acts as a hormone in the uterus. In addition to acting as a vasodilator of the uterine capillaries, it has perhaps a further selective action in exciting or stimulating an intracellular or autolytic enzyme in the endometrium, which so softens and digests the histological elements of this tissue that the physiological phenomena, previously described (namely, diapedesis, rupture of hematmata and exfoliation of mucous membrane) are made possible and easy, thereby constituting normal menstruation.

Such a theory as this furnishes for me an attractive explanation of some cases of dysmenorrhea of the so-called congestive or membranous type; for, where the ovarian hormone is altered or lessened, it may fail to excite in sufficient amount the uterine autolytic enzyme with the result that the endometrium, lacking its proper preparation and softening, acts as a barrier to an easy escape of blood; the congested membrane either remains to form a foreign body and set up uterine spasm, or becomes detached in the comparatively large portions that are characteristic of membranous dysmenorrhea. For this reason, I put forward the suggestion that the cases most suitable for the administration of corpus luteum are those which are characterized by excessive first-day pain, with scanty discharge, suggestive of an intense unrelieved congestion, usually followed later by a free flow and immediate relief of pain.

From my little experience, I am certain that there are cases of dysmenorrhea in which the main causal factor is deficient action of the natural corpus luteum. I am not carried away with the idea that the therapy of corpus luteum is a "cure-all" in any sense of the word; on the other hand, the cases which may be traced to ovarian deficiency are probably in the distinct minority. One must not allow himself to be so impressed with the etiological value of some one factor in the cause of disease, that he forgets, or becomes indifferent, to other factors of equal importance.

Surgery is necessarily indicated in those cases where we find pelvic pathological conditions or anatomical abnormalities, which



we are wont to consider as the probable causes of dismenorrhea. Too often, however, do we resort to operation and, consequently, too often are we disappointed in the results, because the defect is not surgical but glandular. Again more often than one would think, is organotherapy indicated in conjunction with surgical intervention.

There are some serious drawbacks to the use of corpus luteum. It generally has to be used routinely or continuously to obtain and to maintain results. Its cost hinders its more frequent administration. Its action is not immediate, it is cumulative; for that reason patients, and we ourselves, too often discard its use after a short trial, if it has been unproductive of good results.

As regards its dosage, I find that from 15 to 30 grains a day, seldom more, is sufficient in any case. Its prolonged administration has not brought about any untoward symptoms in my cases; with, perhaps, the possible exception of slight gastric disturbance in one or two instances.

The subject of organotherapy, in its present experimental state, is rather involved and indefinite, and while it is sometimes difficult to recognize and identify the cases which would be benefitted by corpus luteum, yet when there is a possibility of "ovarian deficiency" being an etiological factor in any gynecological disorder, we owe it to the patient to make use of this remedial agency, for its value is well determined.

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#### DISCUSSION.

DR. D. TOD GILLIAM, Columbus, Ohio.—I have only one or two remarks to make. The first statement made by the essayist is admirable and one which should teach us a good deal. There is one feature he has not mentioned, and which as I believe is very important, namely, you must give it for its physiological effects. Until you see evidences of diminished blood pressure. I do not think you have got to the point where you ought to stop. I have had experience with the luteum extract, both favorable and unfavorable, and in the revision of my work on gynecology I have given it a kind of black-eye; nevertheless, I have had some elegant results from it, especially when carried to its physiological effects and maintained for a while.

DR. J. HENRY CARSTENS, Detroit, Michigan.—The very modest paper which Dr. Leighton has read is a help to us in showing some of the things that we can do to assist these peculiar cases, but there is this thing about it: The patient to whom he gave this extract was relieved for ten days, showing that we must keep on dosing them all the time. If the gentleman in some of these cases will introduce a silver stem pessary, about which I have spoken time and again, and I am sorry I have to hammer this in, he will not only develop



the uterus, he will not only keep it open and prevent spasmodic dysmenorrhea, but he will stimulate the growth and development of the uterus, which is generally an infantile uterus more or less, and he will also stimulate the growth and development of the ovaries, and as a result the patient will have plenty corpus luteum secretion and a supply of ovarian secretion, and if she should wear a stem pessary for six months she will be absolutely cured without medicine because she will then have normal pelvic organs. •

DR. ARTHUR THOMAS JONES, Providence, Rhode Island.—With reference to organotherapy, I think the profession is divided into two classes. As a rule, one class loses its head over organotherapy and believes everything can be cured by organic extracts. The other class is that group who would not give organic extracts if they knew they were going to get a good result. They will not take it up; they never have tried it. I believe these extracts are of value, and particularly the corpus luteum extract. I have had considerable experience with the use of lutein tablets, particularly in cases of surgical menopause. I have always used the tablet of Hynson, Wescott & Co. We are too inclined to say, "oh, well, we do not have many cases where the artificial menopause is troublesome," and we dismiss it with very little thought, but we do occasionally have a case in which the symptoms are very distressing. I recall one case in particular in a young woman upon whom I did a hysterectomy and had to sacrifice both ovaries that were badly diseased. The symptoms in that case were particularly distressing and the girl was almost driven to suicide. The doctors in the country were talking about sending her to a sanitarium for treatment. After two weeks use of the luteum extract that girl's mental condition cleared up, and she resumed her work in one of the jewelry factories, was perfectly comfortable and well so far as mental symptoms were concerned.

I have had any number of cases in which there were flashes of heat or bad perspiring spells, and I have found that the luteum extract will control these very nicely. We ought to give this a trial, particularly those who are doing surgery and have to sacrifice both ovaries. You will give your patients great relief. In cases of amenorrhea the results are pleasing; you will likewise get good results in cases of deficient menstruation, and in a short time they are having good normal menstrual periods in many cases.

DR. O. H. ELBRECHT, St. Louis, Missouri.—I want to call attention to one thing in connection with these tablets which I have been using for six years or more. I am not here to advertise any particular manufacturing firm, but this is true of corpus luteum as was brought out in the doctor's paper. At first, we were using simply the desiccated ovarian extract, commonly called the ovarian extract, which has been proven to be practically inert. The next step was the beef extract put out by a certain pharmaceutical company. At that time I had several cases on hand and I told this firm I would be glad to use their product if it proved efficacious. They furnished it to me, but having very little faith in it, I gave it to these patients



*ad libitum* with no results. I am free to say, however, that the tablets of Hynson and Westcott, which are made from the corpus luteum of the pregnant sow are an efficient product. I have also had failures as well as good results. Where there is no hyposecretion you have got to feel your way in using so harmless a method. But just as the essayist has reported, I succeeded in bringing about menstruation in a young girl who had missed menstruating for over a year. In that instance I used twelve 5-grain tablets each day. The only objection to it is the fact that it costs considerable money. I think these tablets are worth something like \$2.50 per bottle, and as soon as you get into giving large doses the patient will complain of the price of the treatment. There is no question but that form of luteum is excellent, and if you cannot give it in the prescribed doses and continue it, you might just as well prescribe something else. Unless you prescribe the luteum made from the pregnant sow you will not get results. The Hynson and Westcott tablets, recommended highly by Burnham and Kelly, are efficient, but higher in price. Parke, Davis and Company are following that plan and if you want to use tablets or capsules you can prescribe them, but they admit that their ovarian extract is not as successful as the other.

There is another form that has not been referred to which is given in hypodermic solution, which is in the experimental stage, and I would like to ask Dr. Schwarz to say something about that. But it strikes me, if we want to get active results by hypodermic administration why not use it that way. If it can be put up in sterile solution in acceptable form, why not use it in that manner? I have used it in the same form in the case of an obese woman, thirty-two years of age, allowing her to use it *ad libitum*, with no results.

DR. ORANGE G. PFAFF, Indianapolis, Indiana.—I dislike very much to advertise anybody's preparations, but I understood Dr. Elbrecht to say that the capsules of Parke, Davis and Company had proved in his hands inert. I do not know what changes they have made, but previous to the last six months I have used Parke, Davis and Company's corpus luteum capsules, and whether it was a coincident or otherwise, I have learned to think that we have found something of an ovarian stimulant or ovarian tonic, or whatever we may call it, because in a great many cases—at least in a number of cases—in my hands, especially in those young women attending boarding schools and who are in the developmental stage, with scanty and sometimes absent menstruation, I failed to get any results with the so-called emmenagogue list, but by using these capsules put up by Parke Davis and Company I have had quite a number of charming and delightful results in every way. Possibly they may be looked upon as coincidences, but I doubt it. I have also used the tablets and have had the good results spoken of. I think very frequently we get utter failures perhaps on account of not selecting cases properly, but I must say that I have had very good results from the use of these capsules.

DR. GORDON K. DICKINSON, Jersey City, New Jersey.—We are



still worshipping at the shrine of Lane and why not give the prostatic extract he speaks of.

DR. HUGO O. PANTZER, Indianapolis, Indiana.—It is only such a paper as Dr. Leighton has given us, reporting cases having had methodical treatment, that will bring order out of chaos. Perhaps nothing has been adduced in recent times that has been of more interest to the subject under discussion than the work during the last two years of Schroeder of the Rostock University. Both by animal experimentation and studies on the human to the fullest extent that this was possible, Schroeder, at last, has developed the scientific basis of menstruation. He shows conclusively that ovulation occurs at the fourteenth to the sixteenth day. Then the uterine mucosa takes on activity. The uterine mucosa, as is long known, desquamates from the first to the fourth day of the ordinary twenty-eight days' menstrual cycle. Then it regenerates itself and up to the sixteenth day is inactive. Under the influence of ovulation on the sixteenth day, the endometrium begins a secretory activity which in turn stimulates the corpus luteum formation, which completed on the twenty-eighth day, eventuates in desquamation and appearance of the monthly flow. To take up the cycle methodically, desquamation occurs the first to the fifth day, regeneration of mucosa from the fifth to the sixteenth day. Ovulation takes place on the fourteenth day, and secretion in the mucosa is established by the sixteenth day and the corpus luteum of menstruation begins its development, which matures at the close of the twenty-eighth day. This matter has pertinency here to the extent that the knowledge of this function would clearly indicate that the administration of the corpus luteum extract shall be with regard to the time and purpose of nature, namely, between the sixteenth and twenty-eighth day.

DR. LEIGHTON (closing the discussion).—I am very glad that my paper has elicited such a free discussion. With reference to the remarks made by Dr. Gilliam concerning blood pressure, I will say that I never had any untoward results such as a sudden drop in the blood pressure subsequent to the continuous use of the luteum extract. If it should drop 15 millimeters, it is time to discontinue giving the extract, but I have seen no such happening. The girl of whom I have spoken who had been under treatment since November, 1914, with the exception of one slight intermission, had no untoward symptoms whatsoever, and I have been careful to take the blood pressure at different times.

This therapy has its limitations, there can be no doubt about it. It is not a cure-all. There is one trouble, and that is, we do not use it enough! It is absolutely nontoxic. If we can get results with it, it is worth almost any price that it may cost. As one patient said to me, "if it should be \$15.00 a bottle I would want it." She was cured, and if we can get such results in patients who are otherwise unaided, it surely is worth it. One of the reasons why there have been so many failures is because it has not been used sufficiently. Some patients have used a hundred tablets and have then left off using them at a time when they were beginning to get results. I



have used the Hynson and Westcott product altogether, with one exception, and that in the case of the girl just mentioned, where I used Armour's tablets as well as thyroid extract. Undoubtedly the Hynson and Westcott tablets from the sow are the best. Burnam and Kelly have recommended very highly the use of these tablets.