time as possibly injurious, although there is no conclusive evidence of harmful results following such treatments.

Karnaky has advocated using acidulated sugar in the vagina combined with occasional douches of dilute acetic acid. Little states that he has treated thirty-nine cases of gonorrheal vaginitis in this way, with the number of days required to effect a cure averaging 98.5. At present the number of our own cases in which this method of treatment was used is too limited to report. Sugar tablets must be inserted into the vagina two or three times a day. In our experience the vaginal secretions are not acid if measured some hours after the sugar tablets are dissolved. We have had but little experience with sulfanamides and wait with interest to learn what value it may have in the treatment of gonorrheal vaginitis.

Until recently the treatment of senile or postmenopausal vaginitis has been most unsatisfactory. After cessation of the secretion of estrogen following the menopause or castration, the vaginal mucosa reverts to the thin, ill-developed structure of childhood. The secretions are no longer acid and the mucosa becomes odorless again easily infected. When infected, such patients complain of burning, itching or pain in the vagina, and coitus may be painful or impossible. The appearance of the vaginal walls as described by Davis and others is characteristic. In 1935 Davis reported remarkable success in treating these cases with amniotin subcutaneously. In the majority of his cases he administered 100 r units of amniotin hypodermically three times a week. The average duration of the treatments was six weeks. Vaginal suppositories alone did not give satisfactory results. Usually complete symptomatic relief was afforded in about ten days. Biopsies taken at intervals during treatment showed the development of the vaginal mucosa in appearance exactly similar to that of a woman during the years of menstrual life. The vaginal secretions also became acid. Davis states that ordinarily the treatment of such patients should be continued for from six to eight weeks, for if any infection or inflammation remains the symptoms will return soon after it is stopped. In any event, when treatment is stopped the vaginal mucosa reverts to that of the childhood type, and if the factors that were responsible for the original infection are again encountered reinfection will follow.

Others have confirmed Davis’s observations. Jacoby and Rabbiner, for instance, report like results in twenty-five cases.

In our own experience, results have been good when the condition treated was a typical senile vaginitis. Vulvar leukoplakia has not been benefited. We have had two cases, one after removal of the ovaries and one following intra-uterine irradiation, in which the shrunken vagina became so dry and sensitive that intercourse was impossible. In both instances treatment with emmenin was effective in relieving the situation. It is probable that, as well as building up the vaginal mucosa, secretion from the cervix and Bartholin’s glands was restored.

Five years ago the treatment of vaginitis in children and in women at the menopause was anything but satisfactory. These newer methods of today are yielding gratifying results.

**CONCLUSION**

We have had better results with the use of estrogen suppositories than with hypodermic treatments with estrogen preparations.

52 Trumbull Street.

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**THE ENDOCRINE TREATMENT OF MENOPAUSAL PHENOMENA**

J. P. PRATT, M.D.

AND

W. L. THOMAS, M.D.

DETROIT

The menopause is an event which has attracted wide attention among the public as well as among members of the medical profession. A variety of symptoms have been attributed to the critical change in a woman’s life. A sharp distinction between the physiologic and the pathologic manifestations during this epoch of life has rarely been made. A causal relation between the symptoms exhibited and the physical changes in the body have been frequently assumed but seldom established. Numerous procedures and materials have been advocated for relief or cure, but proof of their specific efficiency is usually lacking. In recent years, special attention has been directed to endocrine preparations as therapeutic agents for relief of menopausal symptoms. In the present study of endocrine therapy, control observations have been used.

**MATERIALS**

The materials selected for study of the menopause may be divided into capsules and compressed tablets for oral administration, and sterile ampules of oil for hypodermic injection. The capsules, which were identical in appearance, contained theelol, phenobarbital or lactose. The compressed tablets, which were identical in appearance, contained either theelol or lactose. The ampules contained either oil alone or theelol in oil. For identification, the preparations were given a code number, which was changed frequently to keep the one prescribing them ignorant of the nature of his prescription. One of us changed the code number from time to time without informing the one who administered the preparations. Before the preparation of the unknowns was completed, eleven patients were treated with phenobarbital and six with bromides. With these seventeen exceptions, the agent prescribed was unknown until final observation was recorded.

**METHOD**

Two hundred consecutive menopausal cases were studied over a period of several months. Only 100 of the subjects returned often enough to justify tabulation. A complete clinical record was written, including history, physical examination and routine laboratory tests of blood and urine. By means of a special form, the presence or absence of most of the symptoms from the Department of Obstetrics and Gynecology, Henry Ford Hospital. The capsules and oil preparations were furnished by Parke, Davis & Co. The compressed tablets were furnished by Ayerst, McKenna and Harrison, Ltd.

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commonly attributed to the menopause was tabulated. Environmental and emotional states varied so greatly that they did not lend themselves readily to tabulation; therefore, individual records were made. The symptoms investigated were taken from the current medical literature, which suggests that these symptoms belong to the menopause. Our observations failed to confirm this relationship in many instances; e.g., arthritis and hypertension. The list included changes in the menstrual cycle, hot flushes, headache, languor, vertigo, palpitation, insomnia, digestive disturbances, paresthesia, neuralgia, arthritis, weight change, trend toward masculinity, impairment of memory, emotional instability, depression, melancholia, extreme irritability, agitation, apprehension, delirium and suicidal tendency.

After voluntary statements were accepted, leading questions were asked, to complete the record. Physical examination included observation on weight change, fat distribution, genital involution, blood pressure change, pulse rate, evidence of arthritis and signs of masculinity. Laboratory tests included bio-assay of the urine in only a few instances and are therefore not reported. Geist has recently called attention to the lack of correlation between excretion of hormones and menopausal symptoms.

### Results

<table>
<thead>
<tr>
<th>Drug</th>
<th>No. of Complete Cases</th>
<th>Relief</th>
<th>Improved or Doubtful Relief</th>
<th>Partially Relieved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unknown</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thecol</td>
<td>14</td>
<td>8</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Phencarbolatil</td>
<td>21</td>
<td>12</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Lactone</td>
<td>83</td>
<td>23</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Emetin</td>
<td>8</td>
<td>3</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Theolin in oil</td>
<td>10</td>
<td>5</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Phenolol</td>
<td>7</td>
<td>4</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Known</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phencarbolatil</td>
<td>11</td>
<td>10</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Bromide mixture</td>
<td>6</td>
<td>4</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Totals</td>
<td>100</td>
<td>57</td>
<td>18</td>
<td>15</td>
</tr>
</tbody>
</table>

Concurrent diseases and conditions which were not menopausal were treated as indicated.

All patients were sufficiently intelligent and informed to be aware of the popularly accepted relationship between failing ovarian function and menopausal symptoms. When treatment was prescribed, the patient inferred that she was receiving some ovarian preparation. Since the nature of the preparation was unknown at the time it was prescribed, the observer was unable to correct the patient's assumption.

The dosage was varied according to the severity of symptoms and the response obtained. One or two capsules or tablets were given from one to three times a day. Injections were given daily for a period of from five to ten days. After varying intervals, the injections were repeated as indicated by the results obtained. The total amount of thecolol given to a single patient in the course of treatment varied from 2 to 5 mg. The total amount of thecinol varied from 12,000 to 96,000 international units (1.2 to 9.6 mg.). No untoward effect was noted in any instance.

Patients who did not return regularly for observation were not included in the final tabulation of results. This excluded many who were entirely relieved by the first course of treatment and therefore failed to return. Those who had few or no symptoms besides cessation of menstruation were also excluded.

Many different personality types were encountered, but the patients were not classified according to this criterion. The psychotic patients were observed by a psychiatrist. These patients were retained in the hospital not less than three months. Not one of this group was improved.

The use of a placebo is by no means new. Practically every physician of experience has used it at one time or another. It has rarely been used, however, as a check to determine the value of hormone therapy in the human being. A similar experience was recently reported by Aschner and Buch Casamor in treating gonadal dysfunction in the male. Satisfactory results were obtained in males when no hormones were used if the patient believed that he was receiving gonadotropic stimulating therapy.

### Comment

The term menopause has been used with the generally accepted broad interpretation. Etymologically it means merely a physiologic cessation of menstruation. The climacteric, or critical age, signifies a period of life characterized by a complexity of phenomena, the most conspicuous of which is the cessation of menstruation. No term accurately distinguishes between physiologic and pathologic processes. The menopause, though loosely used, is popular among the public as well as the medical profession to express the concept of the period of transition in a woman's life from the reproductive period to senility.

The average age of women in this series at the time of observation was 45.6 years. The average age at the onset of the symptoms was 43.5 years. Eleven of the patients had an artificial menopause. The average time that elapsed between the operation and the onset of the first symptoms of the artificial menopause was ten weeks. In general, the symptoms of the artificial menopause were more severe than were those of the natural menopause.

Hot flushes are such a constant symptom of the menopause that no patients are included in this series who did not have this symptom. The frequency and duration of the flushes were recorded but showed rather wide variation. In general, they are a good indicator of the severity of the condition. Some of the patients are more impressed by the sweats than by the flushes. The degree of relief from the flushes and the sweats is the best single indicator of the amount of improvement obtained. For the sake of accuracy in estimating results it is unfortunate that the best criterion is subjective.

Languor was the second most frequent symptom noted in this series. There is no satisfactory measure of the degree of languor besides the impression of the individual experiencing it. Other contributing factors than the menopause were frequently responsible for languor. Among these may be mentioned anemia, hypothyroidism and emotional disturbance.

Different observers agree that approximately 85 per cent of women pass through the menopause without interrupting their daily routine. The 100 cases presented here belong to the remaining 15 per cent, since only those women were included who came for treatment of symptoms of the menopause.

The menopause is a conspicuous event in the life of most women. Environmental changes are frequent and often profoundly influence the life of the individual.

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2. Aschner, Rerta, and Buch Casamor, A.: Zur Klinik des Späte

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DISCUSSION ON ENDOCRINE PRODUCTS

These changes are too diverse to permit detailed discussion here. The tabulation of results gives no indication of the importance of this factor. In every instance, however, the environment was given careful consideration.

It is realized that 100 cases is a small number from which to draw conclusions. They are sufficient, however, to establish a trend. The method was chosen because it was one means of controlling observations. Medical literature contains an abundance of impressionistic书写 without controls.

It is interesting to note in the tabulation of results that, regardless of the form of therapy, the majority of patients were relieved or improved. Furthermore, there is only a slight difference indicated for the different agents used.

The question arises whether those who failed to obtain relief would have been benefited by larger doses of theelin or longer periods of treatment. One of the patients in whom treatment failed received more theelin than any other patient. She was subjected to one environmental shock after another. During a three months vacation, however, she was living under ideal circumstances and remained symptom free, although she received no therapy at all. When she returned to the city, the unfavorable environment was again encountered and all her symptoms returned. She resented strongly the necessity of an artificial menopause. She was a highly sensitive woman who responded excessively to ordinary environmental stimuli.

The other failures are still under observation. They are being studied intensively to see whether they represent a group in which the symptoms of ovarian failure predominate. Other factors are being eliminated in an attempt to isolate ovarian deficiency as a primary cause.

One of the patients presenting the menopausal syndrome was seen by a psychiatrist ten years before. She presented identical symptoms on the two occasions. At the time of the first visit she was menstruating regularly and showed no signs of genital involution. The diagnosis at that time was anxiety neurosis. When seen ten years later for the same symptoms, she had ceased to menstruate and showed genital involution. The diagnosis was menopausal syndrome. In both instances she obtained striking relief from sedation. The frequent resemblance of menopausal symptoms to the symptoms of anxiety neurosis cannot be overlooked.

Life is a continuous process. During the reproductive period there is a gradual waning of ovarian function. The transition from the reproductive period to senility is physiologic and gradual. It is not a crisis. The transformation involves the body as a whole, though the change in the ovaries and the organs under their direct control is most conspicuous. In the majority of instances, it is illogical to assume that substitution for failing ovarian secretion will alter the whole body and arrest the natural aging process.

The symptoms occurring at the time of the menopause are complex. Many diseases and pathologic states may be concurrent with the menopause. Is the menopause an entity? Inclusive consideration of all menopausal symptoms really involves a large part of the field of medicine.

CONCLUSIONS

1. The symptoms attributed to the menopause are so diverse that it seems unreasonable to consider that all of them are due to ovarian failure alone.

2. The menopause is a term used loosely to indicate the physiologic transition in the life of a woman from the reproductive period to senility.

3. Pathologic conditions occurring at the time of the menopause should be distinguished from physiologic states.

4. Estimation of the merits of any form of therapy for the menopause should be based on the relief of pathologic symptoms and not on changes in physiologic states.

5. Equally good results may be obtained by many agents used empirically.

6. Substitution therapy should be reserved for those cases in which the pathologic symptoms can be demonstrated to be due to ovarian failure.

7. The method used in this study offers one means of selecting cases probably due to ovarian failure.

2799 West Grand Boulevard.

ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. FRANK, GOLDBERGER, SALMON AND FELSHIN, DR. BURCH, MCCLELLAN, SIMPSON, JOHNSON AND ELLISON, DR. LITTMENBERGER, DRS. LEWIS AND ADLER AND DR. PRATT AND THOMAS

Dr. Emil Novak, Baltimore: The paper by Dr. Frank and his co-workers emphasized again that physicians are still floundering in the treatment of amenorrhea. The groups which they described on the basis of hormonal studies are not unlike those which can be demonstrated by serial endometrial biopsy. For example, in amenorrhea one may find a persistently scanty and atrophic endometrium or one which exhibits an essential hypertrophic cycle (except for the bleeding phase), or one may find a typical hyperplasia, this last corresponding to the polymorphic hyperplasia described by Zondick. In the same way, endometrial studies show that excessive menstruation can occur from almost any type of endometrium. Most characteristically one finds some degree of hyperplasia, but often the endometrium is of a normal interval type or even quite atrophic. Even a secretory endometrium may be seen in certain types of functional bleeding. The papers we have heard today illustrate the usual inadequacy of blood and urine hormone studies in pointing the way toward successful treatment. Valuable as such studies are from a scientific standpoint, they are not readily practical in the vast majority of cases, and I believe that in the present state of our knowledge endometrial studies will often furnish just as valuable information of ovarian function, and far more simply. I do not like the use of the term ovarian deficiency by Dr. Burch and his co-workers in the explanation of functional bleeding. Ovarian substance, or hypophysio-ovarian imbalance, would seem to be the underlying factor in these quantitative menstrual disorders, whether in the direction of excess or deficiency. It should not be forgotten that typical hyperplasia per se has nothing to do with uterine bleeding. It represents simply a maximum effect on the particular endometrium of a growth hormone, estrogen, which exerts a special growth effect on genital mucous membrane. But bleeding does not necessarily parallel this growth effect, for the bleeding "spill" may occur at almost any level. All physicians have seen cases of marked hyperplasia associated with long continued amenorrhea. Dr. Burch states that the degree of endometrial change corresponds to the severity of the bleeding, an observation which does not agree with mine. The thyroid type of either menstrual deficiency or excess offers the best results in treatment, but unfortunately it constitutes only a small proportion of all cases. I agree with Drs. Pratt and Thomas, and this could be stated almost a priori, that many symptoms are unjustifiably attributed to the menopause. They include in the symptoms studied in this group of cases such indefinite manifestations as languor, digestive symptoms, impairment of memory and many others of this very subjective group. Dr. Frank, formerly almost an organotherapeutic nihilist, has shown how adequate estrogenic therapy in menopausal cases brings...
about disappearance of gonadotropic substances in the urine, with corresponding improvement in the patient's symptoms.

Dr. Elmer L. Serafinihaus, Madison, Wis.: The discussion of Drs. Lewis and Adler shows how a physiologic mechanism can be used for a pharmacologic purpose. They applied estrogen not as a specific therapy, which is the usual goal of hormone therapy, but to facilitate healing in an infection. There is excellent agreement among the different clinics trying this therapy, which is a real contribution to the cure of vaginitis. This concept of the pharmacologic use of a physiologic process explains many results with thyroid hormone therapy, but not all.
DISCUSSION ON ENDOCRINE PRODUCTS

The term for the menopause, castration, and partial castration. This is an accepted fact. These symptoms are not due to failure of ovarian function per se; they are initiated by ovarian failure. Failure of ovarian function disturbs the pituitary gland, while the influence over some of the other internal secretions. This secondary disturbance causes imbalance of the two divisions of the autonomic nervous system and these combined factors produce the characteristic symptoms complained of by castrates and menopausal women. The duration of the menopause in some women is from three to six months; in others the duration may be five or six years. If a woman whose glandular-autonomic stabilization will require five years is treated for three months with relief of her symptoms, it can be expected that she will have a recurrence of her symptoms at a later time, and treatment must be reintroduced from time to time until they cease to recur. Some women have mild to severe psychotic symptoms at the climacteric, and if they are sufficiently severe the condition has been termed involutonal menarche. Drs. Pratt and Thomas stated that they had kept some of these psychotic women in the hospital under treatment for as long as three months without relief. We treated forty women having involutonal menarche (menopausal psychosis) at the St. Louis Sanitarium and at Missouri State Hospital No. 4. Twenty were given injections of theelin and twenty were given physiologic solution of sodium chloride. The results were muscularily as controls. Six months' treatment was decided on arbitrarily. Within six months, 66 per cent of the theelin treated women had recovered, and those who were given physiologic solution of sodium chloride were not improved. We then treated the controls with theelin and had approximately 66 per cent recovery that group. I cannot agree with Dr. Pratt that estrogenic hormones do not help these women or that such treatment is only psychic.

Dr. Charles W. Dunn, Philadelphia: An unmentioned group of endocrine disorders, the adrenal cortical hyperplasias or tumors, are concerned in all the presentations except that of Drs. Dunn and Adler. In the adrenogenital syndrome—and in basophilia the ovarian disorder accounts for the hypo-ovarian syndrome as defined by Dr. Sevringhaus. Dr. Broster of London performs partial adrenalectomy in cases of adrenocortical hyperplasia, with good results in restoring menstrual function. In his cases, preoperatively, the menstrual picture varied; some had amenorrhea, others hypermenorrhea and others increased menses. Adult cases of this type show early onset of menses and menorrhagia, at 16 to 18 years of age, diminishing or abrupt cessation of menses, onset of hypertrichosis and frequently hypertension. Sterility and the hypo-ovarian syndrome are also part of adrenal cortical hyperfunction. Dr. Novak and Wernick pointed out that group dealing with multiducernent disturbances. Crookes states that the pituitary pathology of basophilia (pituitary basophilic adenoma, carcinoma of adrenal cortex or thymus and arhennoblastoma of the ovary) is a hyaline cytoplasmic change and loss of basophilic granules in the basophil cells, the presumed somunit of the gonadotropic fraction. Although reputed to be a hyperfunctional basophilic reaction, pathologically and clinically a subovarian state results. In such adrenal cortical disorders, Grossman believes that the pituitary changes initiate the ovarian hyperactivity, and in some manner stimulate the androgenic zone, which is a destructive cell area lying beneath the adrenal cortex. He believes that adrenal cortical carcinoma does not produce basophilia. This view is supported by authentic cases and one recently reported by Ullman. Patients presenting hypertrichosis, moderate hypertension and a history of sterility were treated with progesterone and pregnancy occurred. Patients simulating the Cushing type became pregnant while amenorrheic, confirming Dr. Frank's observation. As early as one month after pregnancy, patients have developed an acute clinical condition with pituitary-adrenal origin; this brings forth Grossman's belief that puberty and pregnancy often gliarosis and an androgenic layer. In treating these cases I have to administer higher dosage of estradiol benzoate than given by Dr. Frank and his co-workers. If dosage is low the symptoms are relieved but the menses are not influenced. Higher dosage not alone relieves the symptoms but also induces uterine bleeding in the amenorrheic cases.

Dr. Jacob Hoffman, Philadelphia: At the Endocrine Clinic of the Jefferson Hospital we have had the opportunity of studying more than 800 cases of functional menstrual disorders, sterility and symptomatic menopause. Endometrial biopsy as the usual occlusion test we have sometimes used were used in the evaluation of these cases. An analysis of our observations reveals that these patients fall into two main groups. In one the disorder is purely functional, is capable of spontaneous correction and is amenable to therapy; in the other the condition is expression of constitutional inferiority or a deep-seated endocrinopathy and is very resistant to any form of therapy. We have employed both general medical measures and organotherapy. Controls were used in whom the sex hormone preparations were employed. Our experience shows that the commercial preparations are only of limited sphere of usefulness. This is not surprising, for the gonadotropic substances have not been shown to exert a stimulating effect on the human ovary, while the ovarian sex hormones, though capable of stimulating the accessory genitalia, cannot activate the ovary itself. An indirect effect of these substances by way of the anterior hypophysis has been demonstrated in the laboratory animals but not in man. The use of estrogenic preparations for the relief of menopausal symptoms has been hailed as an outstanding example of the value of sex hormone therapy. We have employed organotherapy, consisting of hypodermic injections of saline solution together with sedatives and found the former less effective, although large doses have been administered over a long period of time. I am therefore wholly in accord with the observations of Dr. Pratt and his co-workers. Whether the hypogonadal climacteric involves not merely a withdrawal of estrogen but also a general endocrine upheaval as well as structural alterations throughout the organism incident to the approaching senium, the beneficial effects of estrogen may well be questioned. Medical treatment voids the hazards but the long-term results. General hygienic measures, correction of nutritional faults and the correction or elimination of all constitutional depressive states, supplemented by thyroid extract where indicated, will favorably affect the organism as a whole and with it the gonads. Reduction of weight in the obese and an increase in weight in the thin asthenic type is often sufficient to regulate the menstrual rhythm and raise the level of fertility.

Dr. Misch Casper, Louisville, Ky.: This symposium brings out some real advancement in endocrinology. Why do little girls have to have gonorrhea vaginitis? Is the first question. Why does any one have to have gonorrhea vaginitis? Why can't this humilitating and distressing disease be banished, when we have knowledge that such is the case. There is much known about the gonococcus and gonorrhea and there really exists something to offer in the way of care of this disease? The medical profession has been derelict in the handling of gonorrhea in the past; but I believe now there is an awakening, because of the way of treatment to get rid of gonorrhea. I am sure that Lewis and Adler, while not discussing gonorrhea generally, have no objection to using other means of treatment along with the endocrine treatment. The Elliott hot water treatment, hyperpyrexia, and later the sulfanilamide treatment have all proved effective in getting rid of gonorrhea.

Dr. Cecil Stricker, Cincinnati: I should like to ask Dr. Frank whether he has any fear or any evidence of malignant changes following massive doses of these hormones, and I should like to have an expression both from him and from some of the other authors.

Dr. Peter B. Salatch, New Orleans: I would like to ask Dr. Litzenberg whether the question of sterility in the male side of the picture was thoroughly studied.

Dr. Jean Paul Pratt, Detroit: I am grateful to the discussers for helping to emphasize some of the varied manifestations of the so-called menopause. Dr. Novak emphasized the therapeutic use of the estradiol as well as some hypogonadal symptoms. I agree in part that the hot flashes may be objective. For the most part, however, they are subjective. They seem to be such an important symptom of the menopause that we did not include cases as menopausal unless the women had hot flashes, because that seems to be the one symptom on which nearly every one agrees when they discuss menopause.
the number of flushes. We asked the patient to do the same, but we were confronted with an unscientific observer furnishing the information. Most observations of the menopause are unscientific. It is extremely difficult to set up any experiment that will hold with the care of controlled laboratory experiments. Dr. Sevringhaus terms the question "physiologic or pathologic states." Life is a continuous process. There is a period of rapid growth in childhood, a period of continued rapid growth in adolescence. Then there is a flattening of the curve during the reproductive period, following which the curve trends downward to senility. Somewhere along that curve occurs the first conspicuous event of the reproductive life; namely, the first menstruation. In the mind of the public the first menstruation is puberty, but physicians know that puberty extends over a long period. The same is true of the menopause. The public is firmly convinced that cessation of menstruation is the menopause, but physicians know differently. It is a very gradual change. The function of the ovaries trends downward for a period of several years. That is what I mean by a physiologic state. It is not a sudden change in the state of the ovaries. It is a gradual process which has been going on for years. The question of the use of large doses of estrogens has been very kindly answered by Dr. Hoffman. Dr. Werner insists on keeping the psychoses in the group of menopausal symptoms. I am sorry to give Dr. Werner some quarters furnished by a superintendent of a large institution for the insane, who told me that the expectancies of the psychoses of that type were no greater in relation to the menopause than they were at any other time in the individual's life, so that the justification for calling the psychosis menopausal is not borne out by statistics. We do not mean to imply that the menopause cannot be cured by the estrogenic hormones. Fortunately, they can cure, as well as almost anything else. It does not make so much difference in the large proportion of cases what agent is used.

We were discussing what particular pattern of evidence of ovarian failure and reserved estrogenic therapy for that particular group. The 85 per cent who go through the menopause without any particular disturbance keep most of the menopausal women from seeking medical aid, so we probably are dealing with only 15 per cent. Of that 15 per cent we found that 75 per cent were relieved by almost any form of therapy. Probably in the small group remaining it will be found that there is a definite need for some specific therapy.

Dr. Jennings C. Litzenberg, Minneapolis: The question was asked whether anything had been done about the male studies. I was discussing one subject only, and that is the endocrine influence on the female. It goes without saying that every one of these patients was studied thoroughly from every other standpoint, which always should be done with every sterile couple before taking up the endocrine studies. The thorough study of the male as well as the female was made to study the case of sterility. One should not study individual sterility alone but should approach the question as pair sterility. Any one who attempts to treat sterility without studying the male as well as the female, of course, is not doing his duty.

Dr. Morris A. Goldberg, New York: In our bio-assay and treatment of amenorrhea, only functional cases of amenorrhea were studied. Cases in which there were severe endocrine disturbances were omitted. The animal response to extracts from human beings is not positive proof that the substances obtained are definite caustive factors in the production of symptoms in the human being. Our hormone bio-assays have shown that cases of amenorrhea fall into four groups: the acyclic type, the subthreshold type, the normal type and the polyhormonal type of Zondek. The presence of gonadotropic factors, or an absence of them, may be found in any of these groups. The response of the menopause patient to 30,000 rat units, as viewed objectively, consists in the disappearance of the gonadotropic factors from the urine, and the change in the vaginal smear. The patient is instructed how to prepare the smears, and when obtained they are sent to our laboratory, where they are stained with 1 per cent aceto-equivine. The change in the smear occurs corresponding to that in the rodent and consisting in the replacement of the leukocytes by small epithelial cells even to complete squamous cell metaplasia. These effects are definitely noticed in the menopause, and these cases of amenorrhea which respond in this way are taken of the functional amenorrhea group and placed in the menopause group. Dr. Novak stressed the use of serial endometrial biopsies. We have done this in several of our cases but as yet have not fully correlated the results obtained with our bio-assays. Another point that Dr. Novak made is that the uterus in our amenorrhea cases appears to be refractory to treatment with hormones. We agree with Dr. Sevringhaus that we do not as yet know whether or not the hormone assays are quantitatively and qualitatively the same. To Dr. Fall's question of the use of progesterin in addition to estrogen in the treatment of amenorrhea we can only say that, were it to be used, a definite change in the endometrial picture to one resembling more nearly the normal premenstrual endometrium would be obtained. Bleeding may take place, but the cost of treatment would be doubled, since approximately 35,000 rabbit units of progesterin is necessary. Besides, in the long run the patient would not be appreciably benefited because, in order to insure a continuation of the menstrual function, treatment would have to be prolonged. In answer to Dr. Striker, whose concern questions the fear of the use of large doses of estrogenic preparations, I may say that in adults we have never experienced any untoward effects or any changes suggesting malignancy. Bleeding, however, has been obtained. On the other hand, in prescribing gonadotropic substances, especially the newer products made from homin fixed in high concentrations, care must be exercised in their use because of the proteins present, to which many individuals may be sensitized. When these substances are used, we invariably test for sensitivity intradermally.

A NEW DIAGNOSTIC INTRADERMAL REACTION WITH BOWEL ANTIGEN

INDICATING THE PRESENCE OF THE VIRUS OF VENEREAL LYMPHOGRAVULMA IN THE INTESTINE AND DIFFERENTIATING COLITIS ASSOCIATED WITH THAT VIRUS

MOSES PAULSON, M.D.

WITH THE TECHNICAL ASSISTANCE OF BETTY KRAVETZ

Baltimore

Idiopathic or nonspecific ulcerative colitis is an involvement of the large intestine, regional or general, of unknown etiology, resulting in an exudate of, or feces containing, blood, mucin or pus, or all of these. There was reason to believe that in some cases colitis will or without a structure might be due to a virus. If this were proved, a virus as a factor in intestinal disease would come into being, and the classification idiopathic ulcerative colitis would be narrowed.

The first step in attempting to demonstrate colitis associated with virus rests, if not in the actual isolation, at least in the indication of the presence of such an agent directly from the region of suspected colonic involvement.

Patients with ulcerative colitis of indeterminate etiology were selected in whom the possible presence of a virus in the colon might be related to the colitis as suggested by their having a positive intradermal response to inactivated bubo pus due to the virus of

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