

monthly exacerbations. These continuous pains were getting on her nerves to such an extent as to cause her to lose twenty pounds in weight, and become a semi-invalid. Always with these periodical pains she could feel a tumor over the left ovary, tender on pressure, which tumor would disappear with subsidence of pains.

Present Status. A beautiful, well-formed female, weighing 120 pounds, showed on examination well developed mammae, hair in axillae, and over pubis and genitalia. A manual examination of the abdomen showed nothing abnormal until by deep pressure with hand under left kidney showed considerable depression. A tentative diagnosis of congenital absence of left kidney was made. Palpation over left ovary elicited nothing special beyond slight tenderness on deep pressure. An ocular inspection of the genitalia showed well developed external organs, and a normally situated meatus; but no semblance of a vagina other than the merest depression. I was unable with one hand above the pubis, and one finger in the rectum to find any vestige of vagina or uterus. In fact a sound in the bladder felt to my finger in the rectum as if only a thin membrane intervened. However, my finger in the rectum felt a fixed semi-solid, smooth mass. The contour of the tumor gave me no clue as to its identity.

I suggested an explanatory laparotomy which was readily accepted by the patient, as she said she wanted relief of the pain which was annoying her continually. On October 23, 1911, I opened the abdomen through the median line. There was not the least vestige of a vagina, or uterus, the ovaries and tubes were attached to either side of the pelvis by a short reduplication of peritoneum. The tumor in the pelvis proved to be a congenitally displaced left kidney. The right kidney was present in its normal position. I removed the left ovary and tube and left the corresponding organs on the right side intact.

The patient recovered from the operation satisfactorily with relief from her distressing pains and much improved in her general health, except that she occasionally complains of smothering spells and a lump in her throat—globus hystericus.

Medical Progress.

PROGRESS IN GYNECOLOGY.

GYNECOLOGY AND NEUROLOGY.—ARTIFICIAL VAGINA.—MENSTRUATION.—INTERNAL SECRETIONS.

(Concluded from page 815.)

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Two hundred and fifty cases were examined, no attention being paid to the form of gynecological disease present. The coagulation time before, during and after menstruation was respectively 4.67 minutes, 4.72 minutes and 4.73 minutes. They were thus able to distinguish no effect of menstruation on the coagulation of the body-blood, a result in accord with the findings of most of the previous investigators. In a series of normal young women the figures were as follows: 4.53 minutes before, 4.63 minutes during and 4.64 minutes after menstruation.

In a series of women examined at various periods of time after the menopause, it was found that the coagulation time did not differ perceptibly from that of women before the menopause: 4.69 minutes before and 4.57 minutes after. The interval which had elapsed since the menopause and the nature of the disease present seem to have no effect on the blood coagulation time. In the cases in which the ovaries were removed there was no distinguishable variation from normal and the blood immediately after operation clotted in the same time as one year later. In a small series of normal pregnant and puerperal women the blood was found to be unchanged from that in the none-pregnant condition.

The conclusions of Adler,¹⁴ however, do not agree with those of Keller. He finds that in series of cases of genital hypoplasia, cases after the menopause, cases from which the ovaries had been removed and in castrated animals there was an increase of coagulation time of from thirty to fifty-five seconds. The coagulation time by the method employed by Adler was about two and a half minutes. This suggests two questions: (a) how is this delay of coagulation to be explained? (b) in what elements of the ovary does this regulating function lie? Adler is able to find no direct evidence that the delayed coagulation is due to increased calcium retention from decreased ovarian secretion. But this may be the case, and such an explanation is suggested by the beneficial effect of the removal of the ovaries as well as by the administration of adrenalin in osteomalacia. The exact interrelations of the ductless glands are, however, by no means clear, and various antagonistic actions reported by some investigators are denied by others. The literature is briefly reviewed.

In many patients in whom there are symptoms of ovarian cessation or insufficiency there is manifested a heightened susceptibility to adrenalin in small doses, which is to be attributed to increased sympathetic tonus. It may last for years after the removal of the ovaries. In the treatment of the symptoms of the menopause, as flushings, sweatings and so forth, calcium lactate has been used with notable results.

Adler also tested the effect of aqueous ovarian extracts and ovarian tissue juices, obtained by pressure, *in vitro* and *in vivo*. In the former there was a distinct retardation of the blood coagulation with the ovarian extract. Isolated corpus luteum juice had no such effect. In experiments on animals it was found that the aqueous extracts and tissue juices were highly toxic. Modifying the dose, it was possible to produce changes in the internal genitalia, especially the uterus, which resemble the appearances of natural rut, only much more intense hyperemia and secretion. The significance of these phenomena and others which he describes is not clear. The whole subject is so complicated that clear cut conclusions are hard to draw. Perhaps on the cessation of function of a single organ, as for

example the ovary, changes are produced in the whole organism, through the effect of complementary glands, which appear to have nothing to do with the genital glands (coagulation of the blood, calcium content of the blood, tone of the sympathetic nervous system). Thus conditions which are now attributed to anomalies of the ovarian function may possibly be made manifest through the ovary only secondarily, but are due properly to anatomical or functional disturbances of the other glands of internal secretion. The ovary is the center for the genital system, a center which, however, does not originate but transmits impulses arising in some other part of the system of ductless glands. Perhaps some amenorrheas and bleedings are to be explained in this way.

Sufficient experience has been reported to establish the position of the secretion of the hypophysis as a distinctly valuable adjuvant in obstetrics, in increasing the force and frequency of the uterine contractions. Lehmann¹⁵ administered the extract in some form to a series of patients with various forms of gynecological disease in which the chief symptom was uterine bleeding. The cases included myomata, endometritis, bleeding at the climacteric, menorrhagias in young and adult women in whom no organic disease could be detected, retroflexion and subinvolution. The immediate effect was in general satisfactory and in some cases beneficial results at the next menstrual period also seemed to be present. Premenstrual pruritus and herpes were promptly relieved. The effect of the extract of the hypophysis is at least fourfold, (a) increasing the effect of the ovarian hormone, (b) elevating blood-pressure, (c) contracting smooth muscle of bladder and intestine as well as uterus, and (d) increasing the strength of the rhythmic uterine contractions, apparently quite distinct from (c). These considerations give some insight into the classes of cases in which it might be useful. The series of cases studied is too short to be more than suggestive for further work. The method employed was preferably hypodermic injection into the muscle of the gluteal region. Rarely was there complaint of pain; once faintness followed.

Aschner¹⁶ reports an experimental study of the hypophysis based on operations on animals. After extirpation of the hypophysis in the first three months of life, marked diminution of the interstitial glands of the ovary is evident in about six weeks after operation. There is apparently an increase in these glands later, but there is marked retardation of the development of the follicles of the ovary, the ovary itself being smaller than normal and in an infantile condition. Signs of rut appear but much later than normal, and instead of finding several ruptured follicles or corpora lutea in each ovary (normal), only one was found in the animals operated on. In no case did an animal from which the hypophysis had been removed become pregnant. The other genital organs besides the

uterus remain in an infantile state, but the changes are by no means like those of castration atrophy. In adult animals removal of the hypophysis is followed by only slight regressive changes; the extensive changes noted by several operators who use the intracranial method are due to injury of the adjacent brain tissue and are not found after the oral method. In adult animals with preservation of the hypophysis but with injury of the brain, there were actually more regressive changes in the genitalia than after simple removal of the hypophysis. Abortion followed removal of the hypophysis promptly in two or three days, care being taken to avoid shock by using a two-stage operation.

Under physiological conditions the hypophysis undergoes its greatest functional and morphological changes in pregnancy. Whether there occur during puberty and menstruation hyperemic changes analogous to those in the liver and thyroid has not yet been determined. Under pathological conditions the relation between hypophysis and ovary is shown, after castration, in the increase in size of the hypophysis, changes in the skeletal growth and tendency to adiposity. Similar relations exist in gigantism and acromegaly and the first symptom of the latter condition may be impotence, sterility or amenorrhea. It must not be forgotten, however, that many of the symptoms which appear with hypophysis disease in connection with other brain disease are not to be attributed to the hypophysis alone but may be due to the brain changes which co-exist.

The pineal body has not received much attention though it has been known for some time that the epiphysis is not simply a rudimentary organ as was formerly thought. The technical difficulties in the way of direct experiment on the pineal gland are considerable. Biach and Hülles¹⁷ undertook an indirect method, namely, removing the sexual glands of young animals and later studying the pineal glands. The results were uniform, a diminution in the number of the characteristic cells in the glands and an atrophy of the cells themselves. The clinical picture of disordered pineal function is not always clear, although the diagnosis of pineal tumor has been made from the symptom complex of abnormal longitudinal growth and premature sexual development of both primary and secondary sexual characteristics. The reconciliation of the experimental findings with all the clinical facts is not easy, for both atrophy and hypertrophy of the genital organs have been found with pineal affections. However, the effects of the removal of the sexual glands, causing atrophy of the epiphysis and hypertrophy of the hypophysis, seem to indicate a certain antagonism of these two organs.

A critical study of the alleged causes of uterine bleeding, apart from malignant new growths, shows how little foundation there is for the claims for endometritis, erosions, polyps and even certain forms of myoma to considerable

etiological significance. The ovary, too, has received attention and chronic oöphoritis with increase in connective tissue, sclerosis of the walls of the vessels and thickening of the albuginea, has been held responsible. But there is lacking this fundamental knowledge, namely, the relation between the anatomical structure and the function of the organ, knowledge particularly difficult of attainment in the case of a gland of internal secretion. We know in a general way that the uterus and the bleeding from it are under the control of the ovary, for the bleeding stops or does not appear if the function of the ovary is absent. It is not possible, however, to artificially stimulate the ovary to oversecretion, cause increased uterine bleeding and study the changes in the oversecreting ovary. In the absence of exact knowledge it is unscientific to hold "small cystic degeneration of the ovaries" responsible for uterine bleeding, as is so frequently done. An indirect way by which light may be thrown on the subject is the condition of the blood and the circulation, which Schickele¹⁸ has studied with care and at some length.

Schickele had previously observed that both *in vitro* and *in vivo* tissue juices and extracts from the ovary and uterus exert a retarding influence on blood-coagulation. These experiments were repeated and the results confirmed. The material used had been removed at operation and the histories of the patients could be studied. In those cases in which no abnormal bleeding had occurred, the influence of the ovaries was more marked than that of the uterus. In the cases in which severe menstrual bleedings had occurred, the effect of the uterine extract was more prominent than that of the ovarian. The mucous membrane of the uterus was more effective than the myometrium; and myoma less effective than uterus. This retarding effect found in young women was not found in women who were beyond the menopause, or if present was markedly less. If the tissue juices or the extracts were injected intravenously the blood-pressure was lowered, due to a peripheral dilatation. This property of lowering the blood-pressure seemed to be common to the whole ovary, to the corpus luteum alone and to the tubes and the uterus in about the same degree. The follicular fluid was inert in regard to blood pressure and blood coagulation. Previous or simultaneous injection of pituitrin or adrenalin prevents the effect of the tissue juices, and conversely the tissue juices prevent or markedly diminish the effect of adrenalin or pituitrin. The menstrual blood also has an inhibitory action on blood clotting.

Menstruation, then, may be explained as follows: The substances which cause menstruation are produced in the ovary, because if the ovary is removed menstruation does not occur. They enter the circulating blood and accumulate in the uterus. As they accumulate they cause dilatation of the vessels especially in the endometrium. At a certain point of dilatation

serum escapes from the vessels and the premenstrual congestion and edema are present. When this has reached a maximum the non-coagulable blood and exuded fluid escape into the uterine cavity. The bleeding ceases when the substances which produced the dilatation of the vessels and the non-coagulability of the blood have disappeared from the endometrium. While this is by no means an explanation of all the functions of the ovary, it agrees with many of the well known facts of menstruation and pregnancy.

In experiments on castrated animals injections of ovarian extract produced distinct signs of heat. Clinically, in several cases hyperemia of the external genitalia was produced, and cases of kraurosis vulvae were completely relieved of symptoms after several injections, while the local hyperemic changes were in marked contrast to the previous atrophy of the skin.

The old theory that menstruation is a purifying process receives confirmation from this experimental work. The substances which, arising in the ovary and accumulating in the uterus, prepare the endometrium for the nidation of the ovum, become useless and superfluous if impregnation does not take place, and are, therefore, thrown out of the body, to be replaced as time goes on by new accumulations. The non-clotting of the blood in the placental circulation in all its stages is of vital importance to the fetus, and placental blood does actually contain substances which prevent or retard clotting.

Hypothetical changes in the internal secretion of the ovary account for many of the anomalies of menstruation in which there is found no organic disease even of the endometrium, but changes in the tonus of the sympathetic system causing dilatation of the blood vessels must also be taken into account. There are many purely functional anomalies of menstruation which, if left alone, tend to correct themselves. Besides the frank disturbances in the onset and course of menstruation there occur slight departures from a perfectly regular menstrual flow. The more carefully the question is gone into, the more frequently slight variations are found, depending on some functional cause quite apart from any local disease.

Keeping in mind these conceptions of the cause of uterine bleeding, certain diseases of the uterus and their symptoms may be considered. Endometritis, once a well recognized and important clinical entity, has lost its prominent place, for in the majority of the cases so diagnosed there is no inflammation of the endometrium. The symptoms of uterine discharge and excessive menstruation, as well as the histological changes in the endometrium, may be accounted for on the basis of overfunction of the ovary. The immediate but not permanent relief given by curettage is explained by the removal with the curette of that part of the organ in which are accumulated the substances which prevent blood clotting and thus give rise to excessive

bleeding. When the endometrium regenerates the symptoms recur. The bleedings with "chronic metritis," certain forms of myoma and polyps have a similar explanation; but naturally it is not the ovary alone which is concerned, the whole nervous system and the other glands of internal secretion probably have their part. Following castration and at the climacteric the substances from the ovary which cause lowering of blood pressure disappear. Through the continued function of the other glands of internal secretion which are antagonistic in action, the blood pressure rises and there is produced a heightened tonus of the sympathetic system also, from which the symptoms of the menopause arise.

Schickele presents his conclusions, not as final, but merely as an attempt at a new interpretation. The accepted teaching in regard to normal and pathological bleeding from the uterus does not meet scientific demands and the time has come for us to readjust our views to now well known facts.

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Book Reviews.

Symptoms and Their Interpretation. By JAMES MACKENZIE, M.D., LL.D., Aberdeen and Edinburgh. Second edition. New York: Paul B. Hoeber, Publisher. 1912.

The appearance of the second edition of the book testifies to the cordial reception it has had. It is a certain relief in these days of much book-making to have an author approach his subject

from a somewhat new standpoint. This Dr. Mackenzie has succeeded in doing by his method of discussing symptoms and their significance. We commended this book before and have no reason to change the opinion then expressed although, as the author states in his preface there may be some difference of opinion as to visceral pain, this in no way militates against the general usefulness of the book and in fact rather enhances it. The subject matter is well arranged and the type large.

Fifth Scientific Report on the Investigations of the Imperial Cancer Research Fund. Under the Direction of the Royal College of Physicians of London and the Royal College of Surgeons of England. By DR. E. F. BASHFORD, General Superintendent of Research and Director of the Laboratory. Published by the Authority of the Executive Committee. London: Taylor and Francis. 1912.

This fifth scientific report of the British Imperial Cancer Research Fund represents the investigations carried out during the first half of the current year. It is "concerned with the nature of the resistance which may be artificially produced to the inoculation of cancer and the bearing of the results on the biology of the tumor cell." It consists of four papers, by Drs. Russell, Woglom, DaFano, and Higuchi. The third of these "is a somewhat abridged translation of a paper which has already appeared in German." The three others are new contributions to the knowledge of the subject. Together they afford "additional evidence that tumor or normal tissue produces immunity only when it is derived from the same species of animal as that on which the test is made, and that the immunity produced by these substances is of the same nature." The report is illustrated by numerous beautiful plain and colored micrographic plates, and forms a further valuable addition to the literature of this momentous subject.

Public Health Chemistry and Bacteriology. By DAVID MCKAIL, M.D. (Glasg.), D.P.H. (Camb.), F.R.F.P.S.G. New York: William Wood and Company. 1912.

This book by a Scotch doctor is based on the author's notes compiled in preparing lectures and demonstrations for his class. It is intended as a handbook for candidates for the doctorate of public health. Though not illustrated, and its preface modestly disclaiming originality, it shows, nevertheless, the personality of its writer; and has thereby a quality rare in modern scientific text-books of any sort, in that it stimulates the student's imagination. The appendices on British regulations for the diploma in public health, and on preservatives in milk and cream, are of little concern to American readers, but that on bovine and human types of tubercle bacilli is important.