A British Medical Association Lecture ON MENSTRUATION AND IRREGULAR UTERINE HAEMORRHAGE OF OVARIAN ORIGIN.*

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It is, at first sight, a somewhat remarkable fact that, if we except such gross pathology as the tumours and the abnormal conditions arising from pregnancy, we are still largely ignorant of the causation of the commonest gynaecological symptom—namely, irregular uterine bleeding. On the other hand, it is not surprising that in the past our etiology has rested on a crude basis of pathology when we remember that our understanding of the physiological counterpart of these bleeding discharges—namely, menstruation—has itself been so incomplete. Within recent years a large amount of research has been directed to the elucidation of the physiology of the sex cycle, of which menstruation forms one essential phase, and in respect of some of the cardinal questions we are now in possession of a body of positive fact. It is to these new data, and the bearing they are certain to have on our clinical problems, that I now wish to invite your attention.

PHYSIOLOGY OF THE SEX CYCLE.

One of the most significant results of recent research is the establishment of the fact that, both in its inception and in its maintenance, the sex cycle of the ovaries and the accessory organs is dependent upon the anterior part of the pituitary body. The work of Cushing and others had for many years indicated some such association by directing attention to the failure of sex development found in some pituitary disorders. After extirpation of the hypophysis the sex glands of young animals remain infantile, and the secondary sexual characters fail to develop. Conversely, by injecting immature animals with extracts of the anterior pituitary obtained from either similar or foreign species, Evans¹ and others have shown that the ovaries become activated with the establishment of the sex cycle of the adult animal. The pituitary has no such action on the uterus and the accessory organs except through the medium of the ovary; it is impotent in castrated animals. Ovaries from immature animals transplanted into sexually mature animals become active, with the exhibition of follicular activity, ovulation, and the formation of corpora lutea, because they come under the influence of the adult pituitary. It is thus apparent that the sex apparatus functions only when and whilst it is under this pituitary activation. The exact nature of this impulse has not been thoroughly worked out. It is unquestionably hormonal, but whether there are one or two or more ingredients with different effects is uncertain. Some workers support one single influence, whilst others believe that there is one hormone that controls oestrus and ovulation and another which controls the corpus luteum.

The sex cycle throughout the mammalian kingdom exhibits the same general characters. Let us first consider the lower orders. In them, during the first phase of the cycle, the follicles in the ovary mature, and this is correlated with an activation of the uterus, vagina, and other accessory organs, which in the lower orders consists of "coming on heat" or *pro-oestrus*. This phase is succeeded by *oestrus*, during which alone coitus is possible, and it is at this time that the ripe follicles shed their ova either spontaneously, as in the dog, the mouse, etc., or only after coitus, as in the rabbit, the cat, and the ferret. Oestrus is succeeded by the rapid growth of the corpus luteum from the cells of the wall of the follicle or follicles that have ovulated. This is correlated with an increase in the size of the uterus and a progressive thickening of the endometrium, caused by a great growth in and activity of the glands and a vascularization of the stroma. At the end of this phase,

unless pregnancy intervenes, the corpus luteum degenerates and the hyperplastic mucosa of the uterus recovers its more quiescent characters in preparation for the commencement of a new cycle. There are thus three main phases in the cycle: (1) the pre-ovulation or pro-oestrus, (2) the ovulation or oestrus, and (3) the post-ovulation or luteal. In some animals—for example, the horse and the sheep—such cycles succeed one another without intermission during the breeding season (the polyoestrous condition), whilst in other animals—for example, the dog—there is only one such cycle during each breeding season (the monoestrous condition), followed by a prolonged period of quiescence in ovaries and accessory organs (anoestrus). When ovulation is followed by pregnancy the corpus luteum and the correlated growth in the uterus and other organs, instead of retrogressing as they do in the infertile cycle, continue in a condition of progressive development. In some animals—for example, the dog, the rabbit, and the ferret—after ovulation without fertilization the corpus luteum continues to grow for a considerable time, and this is associated with such active changes in the uterus and mammary glands as to suggest a condition of pregnancy. To this prolonged luteal phase in a non-fertile cycle the term "pseudo-pregnancy" is given (Marshall²).

In general terms the sequence of events obtaining in the cycle of the lower animals is repeated in man and monkeys, but there are some striking differences which have led to some difficulty in identification. Here the cycle is polyoestrous, occupying about a lunar month, and there is no period of anoestrus. The ovarian cycle corresponds with that present in lower animals, consisting of a pre-ovulation phase of maturation succeeded by ovulation, which, in the primates, occurs any time between about the tenth and fourteenth days after the commencement of menstruation. From this stage follows the phase of luteal growth, during which the endometrium undergoes active changes involving the glands, the stroma, and the vessels. The most noteworthy distinction between the cycle of man and the primates and that of the lower animals is found in the characteristic monthly blood loss from the uterus which succeeds the stage of luteal growth, and which is associated with disintegration and shedding of a great part of the premenstrually overgrown mucosa. In man and monkeys this bleeding occurs each lunar month, and lasts for from three to five days. From this time the corpus luteum undergoes rapid degenerative changes.

The Significance of Menstruation.

It has commonly been believed that menstruation in man and monkeys is caused by a degeneration of the endometrium consequent upon the withdrawal of the luteal hormone, and that it is therefore timed by the declension in the corpus luteum known to occur at this stage. It has been suggested that the blood loss corresponds to the extravasation into the uterine mucosa known to occur at the end of a pseudo-pregnancy in some lower animals—for example, the dog (Marshall²). In favour of this conception there are several strong arguments. (1) It is established that for the premenstrual growth of the mucous membrane the corpus luteum is essential and, therefore, its degeneration must result in arrest of this growth activation. (2) Extirpation of the corpus luteum or the ovary containing it precipitates a menstrual flow usually within forty-eight hours. This has been established by many experiments both in man and in monkeys. (3) Conversely, it is known that pregnancy, when menstruation is in abeyance, is associated with continued growth of the corpus luteum. (4) In some animals—and there is some evidence of a similar nature in regard to woman—abnormal persistence of an active corpus luteum leads to arrest of the sex cycle. Taken together, these facts are in harmony with the view that menstruation is the culmination of the phase beginning with ovulation and ending with the luteal stage of the development of the follicle, and that, therefore, the timing of the event is registered by the timing of the follicular cycle.

This conception of menstruation has been finally invalidated by the observations of Corner,⁴ Hartman,⁵ Van Herwerden,⁶ and others that in monkeys menstruation can occur regularly when there is no follicular cycle taking place in the ovaries—that is, when there is no

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ovulation and no formation of corpus luteum. Moreover, in such animals there is no premenstrual growth in the endometrium. Further, this type of "non-follicular" menstruation occurs in healthy monkeys living in the wild state, and it is therefore not abnormal. There is evidence that a similar phenomenon can occur in women. It demonstrates that the menstrual cycle is to be considered as dependent upon some cyclic changes other than those of the follicle, and which are for this purpose more basic and essential. We may express it shortly by saying that there is a primary cycle with menstruation as one of its phases on which there is superimposed and accurately registered the secondary cycle of the follicle. These observations are in keeping with the findings of Parkes⁷ that, after ablation of the entire follicular apparatus of the mouse by means of α rays, the oestrous cycle nevertheless continues. Further, as Hartman⁸ has pointed out, several observers have shown the existence of abortive cycles in the anoestrous period of animals progressing towards oestrus, but before this—that is, the period of ovulation—has been actually reached (rat, dog, ferret). Moreover, Zondek⁹ has shown that after feeding mice with thallium the follicular cycle continues but the uterine cycle is arrested. He attributes these results to the suspension of the oestrus-producing hormone of the ovary. These considerations imply the necessity for a reorientation of our outlook both in regard to the factors underlying menstruation and the interpretation of some of the experimental data upon which the primacy of the luteal relationship was based. We have seen that experimental removal of the corpus luteum precipitates menstruation. At the same time, there is evidence, both in man and in monkeys, that destruction of the maturing follicle, even before ovulation, causes uterine bleeding (Beckwith Whitehouse,¹⁰ Hartman), so that it is not the fact of luteinization of the follicle that determines the effect of its extirpation. So far, we have no means of assessing the essential significance of these experiments. We may hazard the conjecture that they imply a sensitiveness of the basic rhythm to any traumatic assault inflicted on any part of the follicular or more purely reproductive apparatus of the ovary. This and cognate questions are of considerable interest to us as clinicians because of their possible bearing on the common irregularity in the menstrual cycle which we find in disease.

The nature of the cyclic variation in hormonal activity that determines the sequential events in the sex cycle, including menstruation, has been the topic of speculation. By some a continued production of the hormone by the ovary has been predicated and the cyclic manifestations attributed to rhythmic variations in responsiveness on the part of the uterus and other accessory sex organs. It has more commonly been held that the cyclic variations are determined by variations in hormonal content, which represent either alterations in the ovarian output under pituitary influences or a rise and fall in a threshold mechanism (Frank¹¹). In this connexion the experiments of Pratt and Allen¹² and of Zondek¹³ are suggestive. The former investigators working with castrated monkeys, and the latter in an ovariectomized woman, produced menstruation by the abrupt stoppage of repeated injections of the oestrus-producing hormone of the ovary. Frank, moreover, has found a sharp rise in the female sex hormone in the circulating blood (as tested quantitatively by its capacity to produce oestrus in castrated mice) seven days before menstruation, and that this continues during the premenstrual phase, to stop suddenly with the onset of the flow. The available data are thus in harmony with the view that menstruation is dependent upon the removal from the circulation of an oestrogenic hormone which, during the premenstrual phase, has been responsible for an activation of the uterus.

Menstruation a Function of Implantation.

We have seen that it is impossible to explain the bleeding phase of the cycle in man and monkeys on the basis of an analogy with the phenomenon of pseudo-pregnancy in lower animals. The analogy breaks down from the unequivocal finding that, whereas the corpus luteum is essential for pseudo-pregnancy, it is not necessary for menstruation.

An attempt has been made by some observers to identify menstruation with the genital haemorrhage which in some animals occurs during pro-oestrus. Thus, in the dog, during the phase of maturation of the ovarian follicles and even into the period of ovulation itself (oestrus), there is a bleeding discharge from the mucous membrane, which may continue for as long as a week. Against this conjectured analogy between menstruation and such pro-oestrous bleeding, however, there is the very strong argument that in the primates ovulation typically takes place between ten and fourteen days after the onset of menstruation, and that there is therefore an interval of from six to ten days between the cessation of the bleeding and ovulation. It may thus be contended that, so far from throwing light on the inner meaning of menstruation, such attempted analogies as I have mentioned serve rather to emphasize the biological uniqueness of the form this phase of the cycle assumes in man and monkeys. Many years ago (1911) I¹³ pointed to the fact that this phase of bleeding into and from the mucous membrane of the uterus is found in those organisms (man and monkeys) in which, at the corresponding phase of the fertile cycle, placentation is accomplished by a free extravasation of blood in the same regions. I further showed that a personal study of two early human ova, the description of which I¹³ have published elsewhere, and of tubal pregnancy, provided conclusive proof that the young trophoblast obtains its blood supply by provoking a wide gaping of the maternal vessels and a free extravasation of blood. These conclusions, it was pointed out, were supported by the descriptions given for other early ova. There was, moreover, clear evidence that these striking tissue changes are produced by a chorionic hormone which acts by eliciting a vascular and tissue response similar to that present in the pre-bleeding phase of menstruation. It was contended that these observations alone satisfactorily explain (1) the peculiar structural properties of the endometrium which is adapted to respond in this specific way to the hormone, and (2) the biological significance of the bleeding phase in man and monkeys and its time relation to ovulation. I have expressed the relationship between menstruation and implantation somewhat figuratively by saying that the endometrium bleeds in anticipation just as it bleeds with realization.

Within recent times Hartman⁵ and Corner have directed attention anew to these interesting biological questions. Corner,¹⁴ in a very clear statement of the position, says:

"My conjecture is thus that in order to provide for the highly specialized embryonic implantation of primates, with its opening of the maternal blood vessels into the intervillous spaces, the endometrial process is carried so far as even to cause bleeding into the tissues during the last days of the interval, at the time during which the early embryo is to be implanted. The action of the embryo alters the latter part of the process so as to inhibit or limit the haemorrhage; but if no embryo be present to utilize the extravasation, then the blood escapes into the uterine lumen and externally visible bleeding occurs. Such a hypothesis seems to render the menstrual process something more than a pathological wastage, and also suggests a reason for its total absence in species which have less specialized forms of implantation."

The "hormonic machinery" by which, with embedding of the ovum, widespread bleeding into the mucosa is accomplished necessarily demands some localization of the process after the ovum's needs are complete. Otherwise the hormone soaking through the tissues and reaching the distant areas of the sensitized mucosa via the blood stream must provoke extensive and disastrous bleeding. In my early work I suggested that we might see in the decidua the method by which this generalized inhibitory mechanism is expressed, and I pointed out that such a view has the advantage of accounting for the universal distribution of the decidua (reflexa, serotina, and vera), an explanation obviously lacking in the orthodox view that it is laid down to protect the maternal tissues against the inroads of the trophoblast. This conception, which contains a germ of truth, arose at a time when the opening up of the maternal tissues was erroneously believed to be accomplished by a phagocytic action of the chorionic cells. I have shown that in tubal pregnancy we sometimes discover a striking demonstration of the role thus attributed to the decidua in that the only areas of the tubal wall protected against this

hormonal dissolution are those areas which can exhibit an effective decidual response—that is, the mucosa. The existence of a decidua in the uterus in such cases can be similarly explained. This conception of the antihormonal function of the decidua necessarily, in view of recent work, involves a restatement of the role of the corpus luteum. The work of Loeb and others has shown that it is this body that confers upon the endometrium its deciduability, and this, taken in conjunction with the above considerations, enables us to formulate more exactly the part which it is known to play as an essential pregnancy organ.

The Placental Hormones.

Many observers have shown that hormones with properties similar, on the one hand, to the oestrus-producing hormone of the ovary, and, on the other, to that of the anterior pituitary, can be isolated in considerable amount from the human placenta. There is a good deal of evidence that these hormones are directly elaborated in the organ, and are not, as has been suggested, merely transferred there for storage. Whilst the large scale on which they are manufactured by the placenta would seem to leave no doubt that they subserve some important pregnancy functions, the exact nature of these functions remains a mystery. I have indicated above how in the early phase of placentation there is recognizable evidence of the hormonal activity of the trophoblast. It is now well known that the secretion of the hormone similar to that of the anterior pituitary in the urine of a pregnant woman forms the basis for the very sensitive Zondek-Aschheim test for pregnancy. The urine is injected into immature mice, and the activation and luteinization of the ovarian follicles constitute a positive result.

PATHOLOGICAL UTERINE HAEMORRHAGE.

The impetus which the new discoveries have given to the study of sex physiology has expressed itself also in a renewed study of the pathology of the sex process. At the same time, the uncertainty still surrounding the basic factors of function imposes a limit on the extent to which we can appeal to physiology for aid in our clinical problems. For this reason it is natural that, whilst the development of our pathological studies has necessitated much restatement of fact, in regard to the essential causative agencies we are still largely ignorant. We have seen that the physiological function of menstruation is under the hormonal regulation of (1) the anterior pituitary and (2) the ovary, which by a co-ordinated mechanism operate on (3) the uterus. Not unmindful of the fact that diseased processes may, and not infrequently must, influence this tripartite mechanism from without, we may profitably pass under review the ways in which each member of it may contribute to the production of irregular or excessive uterine bleeding.

The Anterior Pituitary and Irregular Uterine Haemorrhage.

On this question there are few data. It is reasonably certain that dystrophia adiposo-genitalis (Fröhlich's syndrome), with its arrested sex functioning and amenorrhoea, is determined by hypofunction of the anterior pituitary. On the other hand, except perhaps in the case of acromegaly, where there is commonly an initial menorrhagia, we have no direct evidence of the part played by the pituitary in producing excessive bleeding. At the same time, the primary part which it is now recognized to play in the control of the ovary will make it necessary for us in the future to bring it increasingly under scrutiny in all ovarian dysfunction associated with irregular bleeding. It is, in the meantime, legitimate to conclude that in many instances the well-known influence of mental excitement or shock on menstruation may arise from a sympathetic disturbance transmuted in the pituitary into an endocrinal stimulus to the ovary. Hence, for example, we may imagine an explanation of the frequency with which menstruation starts prematurely in the patient faced by the ordeal of the examination room. On the basis that uterine haemorrhage of obscure origin may be controlled from the pituitary, Hofbauer¹⁵ and others have employed x-radiation of the region of the sella turcica.

Uterine Haemorrhage of Ovarian Origin.

In a paper published in 1913, and entitled "Uterine haemorrhage of ovarian origin,"¹⁶ I directed attention (to quote from the paper) to

"those cases where excessive menstrual and an intermenstrual loss are present, and where on examination nothing abnormal or only some uterine enlargement is found. Such cases are very common. They are unceremoniously thrown into that lumber-room of classification—endometritis. As a sort of hit in the dark curettage is done. On microscopic examination there is no evidence of inflammation, but only an oedematous and haemorrhagic endometrium without, or more commonly with, an increase in the glandular elements. . . . Many cases of glandular increase are certainly pathological. But for them 'glandular endometritis' is a misnomer."

The views then expressed sprang from a conviction based upon an extensive study of the pelvic pathology in such "bleeders." This, characterized, as it typically was, by general uterine enlargement and endometrial thickening, partook rather of the nature of an exaggeration of the functional changes occurring during the normal cycle. The paper included a study of two typical cases where, in association with this pathology, there were haemorrhagic lesions in the corpus luteum of the ovary. I further emphasized that

"where there is found on examination nothing abnormal except some uterine enlargement, and where the mucosa is found to exhibit the appearance of so-called 'glandular endometritis,' an ovarian source should be suspected."

Subsequent experience has confirmed me in the views then expressed that, except in rare instances, the terms chronic endometritis, chronic metritis, and fibrosis uteri, as ordinarily employed for such cases, spring from a misreading of the essential pathology. A true histological picture of endometritis is rare, apart from an infected childbed or abortion, degenerating tumours in the interior of the uterus, and those other conditions, such as infection after operation, in which the history and pathology present more or less acute characters. Similarly, a true metritis I have never seen, except in the unequivocal presence of inflammation—for example, in an adhesive peritonitis in which uterus and infected appendages are involved in a contact infection. The investigations of Schroeder¹⁷ on metropathia haemorrhagica—the term which he has given to a common condition exhibiting, in association with irregular and excessive bleeding and a proliferative lesion in the uterine musculature and mucosa, characteristic ovarian changes—have directed attention to ovarian disease as a frequent factor in chronic bleeding disorders. Beckwith Whitehouse,¹⁸ in this country, has, in a series of communications, emphasized the same lesson, and has sought to explore the field of physiology for the solution of some of the problems in pathology. More recently Wilfred Shaw¹⁹ has published the most comprehensive attack on the subject that has so far appeared, consisting as it does of a combined clinical and pathological study of 200 consecutive cases of irregular uterine bleeding at St. Bartholomew's Hospital, excluding instances of malignancy, polypi, caruncles, erosions of the cervix, and senile vaginitis. Wilfred Shaw was able to divide the cases into different classes. (1) Of the total, 50, or about 25 per cent., fell into the category of metropathia haemorrhagica. In 50 per cent. of these there was a uniform thickening of the musculature of the uterus and, typically, the endometrium was thick and polypoidal and the glands were cystic and increased. The ovaries contained large unruptured, or recently ruptured, cystic follicles, and corpora lutea were rare. Cases occurred at any age from puberty till after the menopause, but the chief age incidence is 40 to 50. Frequently before the characteristic continuous haemorrhage there was a period of amenorrhoea of a duration of one month or more; 80 per cent. of the women were parous. Schroeder has explained the bleeding as being due to the absence of the inhibitory influence of a corpus luteum. (2) The second class, including 72, or 36 per cent., exhibited in association with excessive loss, a reduction of the menstrual cycle to two or three weeks. Examination of the ovaries showed a corresponding alteration in the cycle of ovulation. The chief age incidence again is between 40 and 50. Shaw attributes the menstrual abnormality and the uterine

pathology to hyperactivity of the ovaries. (3) In a further class there were 27 cases, or 13.5 per cent., in which the essential clinical features consisted of an augmented blood loss associated with a lengthening of the cycle to thirty-five or forty-two days. In some the newly acquired spacing of the cycle became more or less regular, whilst with others the cycle was irregular, varying between three and six weeks. There was again evidence of an underlying ovarian aberration. (4) In 48 cases out of the total the etiology was obscure, and, whilst ovarian causes might be operative, this could not be established. (5) In only 13, or 6.5 per cent., was there histological evidence of endometritis, and in all except one the symptoms had not extended beyond two months. In none of Shaw's cases were there findings warranting an explanation based upon such conditions as chronic metritis and fibrosis uteri; and, further, it is stated that "there is no evidence to support the view that cases of irregular uterine haemorrhage are determined by subinvolution."

These investigations are of great importance, and, if confirmed, they will necessarily demand a complete re-orientation of our outlook in regard to this question, for they infer that, in the absence of a gross lesion in the uterus, chronic bleeding diseases, in a ratio of over 70 per cent., are associated with ovarian disorders. At the same time, the exclusion of a primary uterine factor and the invocation of an ovarian dysfunction do not explain the disease complex, for we are still left with the necessity of accounting for the ovarian disturbance. For this we must await the outcome of future research. In this connexion I²⁰ have elsewhere pointed to one such possible factor in the frequency with which chronic cervicitis is associated with menstrual arrhythmia and excessive loss. I have found such menstrual derangements in 82 out of a consecutive series of 124 cases—that is, 66 per cent. Other observers have referred to the same fact. Thus Masson and Parsons²¹ found that menstrual irregularity was the chief complaint in 25 per cent. of their cases of chronic cervicitis, although a larger number admitted deviations when specifically questioned. Jeff Miller²² and Behney²³ also refer to this relationship. In these cases there is no pelvic abnormality capable of accounting for the menstrual irregularity and excess, the examination revealing nothing more than some general uterine enlargement and some hyperplasia and proliferation of the endometrium—the conditions, that is, which we have seen to accompany ovarian disorders. Moreover, as I have shown, in a considerable number the menstrual disturbance clears up after treatment limited to the cervical condition. Behney has had a similar experience, obtaining cure of menorrhagia in 63 per cent. of his cases after cauterization of the cervix. For these reasons I have suggested that in some way which is at present obscure, perhaps via the rich sympathetic supply of this region, we may conclude that the cervical lesion leads to involvement of the ovarian function. There is evidence in the lower animals of an intimate nerve relationship between the cervix and the ovary. Thus, in the mouse, mechanical irritation of the cervix causes the prolongation of the luteal phase normally accomplished by coitus, and in the rabbit coitus, whether fertile or infertile, produces ovulation. It is likely that these phenomena, whilst originating in sympathetic impulses, are transformed by the pituitary into hormonal influences sent to the ovary, and it is conceivable that pathological impulses from the cervix may initiate through similar channels an aberration of ovarian function. I have shown that positive evidence of disease of the ovarian follicular system was found in two such cases in which the abdomen was opened for the purpose of hysterectomy.

Differential Diagnosis and Treatment of Irregular Haemorrhage of Ovarian Origin.

In many such cases the diagnosis can be made with approximate accuracy from a study of the clinical history combined with the absence of any gross pathology found on pelvic examination. The bulk of the cases occur in women between the ages of 40 and 50, however, when fibroids and cancer loom large as causes of haemorrhage, and to exclude these an exploration of the uterus is necessary. Cervical cancer, with its foul discharge and its

indurated, friable, and frequently excavated lesion, and its irregular, intermittent bleeding, is rarely a cause of difficulty. In corporeal or endocervical cancer, in small fibroid polypoidal growths and the chronic bleeding from placental fragments, exploration alone reveals the condition. The bleeding from threatened abortion may occasionally cause confusion, especially since, in such conditions as metropathia, the continued bleeding may be preceded by amenorrhoea. It would seem that some post-menopausal cases of bleeding are caused by ovarian "rejuvenescence," but, mindful of the frequency with which bleeding at this time connotes malignancy, cervical cancer should be suspected; with a healthy cervix, curettage, followed by microscopical examination of the material removed, is always necessary. In the last series, comprising a total of seventy-two consecutive cases of post-menopausal haemorrhage which I have had in hospital, there were sixteen cases in which no uterine pathology adequate to explain the condition was found, and, in a majority of such cases, ovarian factors may be postulated. In three there was a condition of simple cystadenoma of the ovary.

The treatment to be adopted in these conditions will be determined by various factors, of which age is the chief. The fact that we are progressing towards a rational pathology justifies the hope that we are within measurable distance of a scientific therapeutics directed towards the factors that disturb the ovarian function. Meanwhile, however, until we have this knowledge, the only alternative left to us in many cases consists of symptomatic treatment for the bleeding. It is my practice in women over 40 to carry out an exploratory curettage to establish a diagnosis. When malignancy is excluded, and as curettage is occasionally followed by cure, I discharge the patient with instructions to report if excessive bleeding returns. In this event she is sent to the radiologist for α -radiation of the ovaries and the production of an artificial menopause. In the hospital patient this involves three visits as an out-patient. Radium may be employed as an alternative. This is my routine practice also in younger women where the failure of other treatment precipitates the need for drastic measures. The employment of these means has, in my practice, led to the elimination of hysterectomy for such cases. The operating records no longer show, as in former days, the comparatively frequent tale of "hysterectomy for intractable haemorrhage," with its not inappreciable mortality, apart from the mental and physical distress associated with all major surgery. Suffering women have much reason for gratitude since the advent of radiation therapy beyond the relief it confers in the sphere of cancer treatment. In young women these conditions are frequently a source of great anxiety because, on the one hand, palliative measures are so commonly ineffective, and, on the other hand, the above drastic therapeutic measures constitute at this age so terrible an alternative. The haemorrhage of puberty and of girls in their teens, which probably is practically always hormonal in origin, sometimes reacts satisfactorily to curettage, general hygienic measures, the administration of calcium salts, etc. In such cases, and in women still in the reproductive period, we must necessarily postpone to the last moment any decision which is in its nature irrevocable, in the hope that time will bring relief. The commercial ovarian preparations of proved activity, such as sistomensin, agomensin, etc., may be tried, although I have not found the same response with such drugs in cases of haemorrhage as in dysmenorrhoea, in which the effects may be remarkable. Such therapy is, in the present state of our knowledge, necessarily largely empirical, and must remain so until our knowledge increases. In intractable cases α -radiation in minimum dosage may be cautiously tried in the hope that alleviation without sterilization may be accomplished. On this treatment some gynaecologists have reported favourably, although there is always attendant on it the spectre of overdosage, leading to permanent infertility. I have had better results with radium administered in minimal doses than with α rays.

In cases associated with cervicitis, in my experience the best treatment at all ages is the use of the cautery. The cervix is dilated to a degree sufficient to allow access

of the electric cautery to the internal os. Three linear incisions behind and three in front are made from internal to external os and over the catarrhal patch on the vaginal portion. The cautery sears through the mucosa into the subjacent fibro-muscular wall, and Nabothian follicles are individually punctured. In some cases a repetition of the process at the end of a month is required. After each application a plain warm water vaginal douche should be given daily for a week or ten days to act as a mechanical cleanser, and to facilitate the removal of the sloughs which sometimes form.

Pathological Haemorrhage of Uterine Origin.

It will have become apparent from the preceding remarks that recent advances in our knowledge have enabled us to lift bodily out of this category a large group of cases which were previously and erroneously considered as having a uterine cause for the irregular bleeding, and which are now to be regarded rather as ovarian aberration with secondary uterine change. This applies to a large number of these cases previously described under such headings as "fibrosis uteri," "chronic metritis," "chronic polypoidal endometritis," "chronic glandular endometritis," and "subinvolution." The discovery in cases of fibromyoma of ovarian changes similar to those found with the above conditions even raises the question as to whether the irregular bleeding found with these tumours may not, in reality, sometimes spring from this cause. Frank has even suggested that the tumour may derive its origin from localized overgrowth in the uterine wall, arising from ovarian hyperactivity.

SUMMARY.

1. Menstruation can occur in the absence of ovulation and the corpus luteum, and it cannot, therefore, be interpreted in terms of an analogy with pseudo-pregnancy in lower animals, for which a luteal phase is necessary.
2. Further, its place in the cycle in relation to ovulation undermines the conjectural analogy between it and oestrous bleeding in lower animals.
3. These analogies can be further invalidated, and the essential meaning of its existence in man and monkeys explained by recognizing it as a function of the peculiarly haemorrhagic type of implantation of the ovum found in these higher animal forms. The bleeding of menstruation and the bleeding of implantation are homologous, in that they occupy the same place in the sex cycle, and the external bleeding expresses the escape of the unwanted "implantation blood" in an infertile or a non-ovulating cycle.
4. Many of the bleeding disorders erroneously attributed to such conditions as chronic glandular endometritis, chronic metritis, fibrosis uteri, etc., are in reality expressions of disturbances of unknown origin in the ovarian (or combined pituitary-ovarian?) regulation; and definite clinical entities with correlated structural changes in the ovary can be recognized.

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CONGENITAL DISLOCATION OF THE HIP.

LATE RESULTS OF TREATMENT BY MANIPULATION.*

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(With Special Plate.)

For the purposes of this communication an attempt has been made to examine clinically and by x rays 70 cases of congenital dislocation of the hip which were treated by me by manipulation at the Royal National Orthopaedic Hospital between the years 1903 and 1920. I have succeeded in examining, within the last two months, 25 of these cases, involving 32 joints. All surgeons in large cities have found a difficulty in tracing patients after a lapse of many years. Stephens' reports that he could examine and x-ray 7 patients only out of 185 treated in the Hospital for Ruptured and Crippled between 1891 and 1910.

The 25 cases comprised: 4 right unilateral (4 joints), 14 left unilateral (14 joints), and 7 bilateral (14 joints). The average period since reduction was upwards of fifteen years, and the average age of the patient at the time of reduction was upwards of 4½ years.

Method Employed.

During the earlier years the Lorenz method was employed, with its violent stretchings, its "hackings," and its leverage over a wedge. Gradually less violence and fewer stretchings were found sufficient for reduction, and traction with the fingers replaced the wedge. With few exceptions a short spica has been employed, fixing one hip only in unilateral cases. The first plaster has fixed the limb in the position of greatest stability, and as much as 120 degrees of flexion and 110 degrees of abduction have been employed. But these extreme positions have been maintained for the shortest possible period, and usually within four to six weeks of reduction fixation in the position of 90 degrees flexion, 70 degrees abduction, and 0 degree of rotation has been possible. This position has been retained until the end of the fixation period, and no attempt has been made to diminish this state of 90 degrees of flexion or 70 degrees of abduction. Exceptionally, a long spica including the foot has maintained the limb in the position of abduction and internal rotation. I have very rarely found the degree of anteversion sufficient to necessitate this position. The period of fixation has varied from less than a month in a 9-months-old child to as much as one and a half years when stability was unassured. A patten, usually 5 to 6 inches high, has allowed locomotion during the fixation period in unilateral cases. After removal of the plaster the child has been encouraged to kick about and perform active exercises in the supine position for three months. Standing has not been allowed until three months have elapsed from the end of the period of fixation. I am afraid in some cases this rule has been broken by parents, and the child has walked on its softened and decalcified neck, and that some of the changes in the neck are due to this. I consider this is the most important period of treatment, but in-patient treatment at this stage has been found impossible owing to pressure upon beds. Massage and passive movements have rarely been employed. A plaster bed, holding the limb in 90 degrees flexion and 70 degrees abduction, has been used at night until three years after the date of reduction. For three months after walking has commenced a patten 1½ inches high has been used on the sound leg to keep up the abduction on the affected side.

Clinical Results.

The clinical results of these 25 cases are as follows: bad 1, poor 2, good 13, perfect 9. Unfortunately there is no standard of criterion when we try to classify end-results in terms of function, and we are faced with many difficulties. There are two constant disabilities in the unreduced hip, however well it may function for locomotion—namely, shortening and limp. To arrive at the measure of shortening in unreduced hips, I used the opportunity,

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