THE SCIENCE COMMITTEE OF THE British Medical Association.

REPORT CXII.

OBSERVATIONS ON THE PHYSIOLOGY OF THE FEMALE GENITAL ORGANS.

BY
W. BLAIR BELL, and PANTLAND HICK,
M.D., B.S.LOND., M.B., B.S.LOND.,
ASSISTANT GYNAECOLOGICAL SURGEON, ROYAL INFIRMARY, LIVERPOOL. MEDICAL REGISTRAR, ROYAL INFIRMARY, LIVERPOOL.

II.—MENSTRUATION.*

OUR work on menstruation has for the most part been taken up with investigations into the relationship existing between this function and the calcium metabolism, and we have used in our deductions facts and observations which we demonstrated in connexion with the general calcium metabolism—alluded to in Paper I—as well as those which we now present as the result of our experi-

Fig. 1.—Systemic blood of hens—calcium indices.

mental and histological researches into the physiology of the function itself.

As one of us (W. B. B.) has already stated, the idea of some such relationship existing was engendered by morphological considerations in regard to certain egg-laying species, especially birds, which excrete lime salts in large quantities during this process from the calcium chamber, or lower part of the oviduct.

It has been asked why we used birds in these experiments. The answer seems so obvious that we are afraid we may have mistaken the point of the inquiry. Hens were used because we presume that no one will deny that they do excrete calcium in this way, and we thought that if we could prove certain histological and experimental analogies between the oviducts of hens when laying and human and other mammalian uteri when menstruating, we should have done all that could be reasonably required to prove the hypothesis we had set forth—apart from further evidence, of a more clinical nature, we are prepared to offer.†

* Based upon a paper read by W. Blair Bell before the Gynaecological Section of the Royal Society of Medicine, July 9th, 1908, "Menstruation and its Relationship to the Calcium Metabolism."

† We may call attention also to the fact that the lowest known mammal (*Monotreme*), the ornithorhynchus, lays calcium-coated eggs. If any one can furnish us with a female specimen of this rare creature we shall be extremely pleased.

First of all, then, we examined the systemic blood of three hens on consecutive days for about a week. We stipulated that one at least should be a non-layer for a control, but otherwise we were unaware of the eggs laid until the experiment was completed, although, of course, our charts soon gave us an inkling of what was happening.

From the charts which illustrate the results obtained it will be seen that the first, or control hen, showed practically no changes in the calcium index from day to day. The second hen, laying every other day, showed a marked drop after laying an egg, with a big rise the next day in preparation for the laying of an egg on the alternate day. The third hen was very interesting. An egg was laid on the first day and the index was low. This index remained low for several days, consequently no egg was laid, but finally the index rose and remained so high that an egg was laid on every day during the rest of the observation. The calcium content may have dropped for a short time after the laying of the egg, but the fall was of such short duration that it was not observed—a rapid rise, or maintained high index, being necessary for daily egg laying.

We should like to hazard the suggestion here that the well-known vaso-dilatation which occurs in the combs and wattles of laying hens is due to the drop in the calcium content of the blood whereby a sort of chilblain condition is produced.

Fig. 2.—Systemic blood calcium indices during vicarious menstruation.

Now these experiments are very important, and we think that the result was only what one would be reasonably led to expect if the matter were considered at all.

It has been stated by Dr. Amand Routh when discussing the paper of one of us,† that he "could not see the force of the charts showing the variations of the lime in the blood of the hen which laid eggs on alternate days, for the lime for any particular egg was required not on the day before it was laid, but several days before; and many eggs were in the process of development all the time." Now we cannot see where an explanation is required. Surely a comparison between Chart 2 and Chart 3 (Fig. 1) makes matters quite clear. If the hen is to lay every day, it must maintain a high index, with at most a drop for a few hours. If it cannot do this, it will only lay when it has the requisite high blood content which in Chart 2 occurred on alternate days. In these experiments the eggs were, as is usual, laid in the morning, and the blood estimated in the afternoon. Further, in reference to the statement that many eggs are in the process of development at the same time, we would point out that this is only true of the ovum and yolk sac, and that only one egg receives the further coverings of albumin and

shell at one time, these processes being completed in a few hours.

We will now deal with some facts and experiments which are of themselves just as convincing in regard to animals and the human subject. Having got the idea

tively, in that the content dropped to one-sixth of the previous amount.

It is not easy to obtain the chart of an absolutely normal menstrual cycle. We hardly remember seeing a woman who was without a single symptom at this period; but

Fig. 3.—Systemic blood calcium indices during menstruation, with hystero-epilepsy.

Fig. 4.—Systemic blood calcium indices during normal menstruation.

in regard to the existence of some connexion between the calcium metabolism and the female genital organs it of course at once struck us how easy it was to explain on this theory the fact that menstruation is nearly always in abeyance during lactation, for we know what an important and physiologically predominant ingredient of milk calcium is. It was easy to understand, too, why menstruation should frequently be absent in the debilitated, since we had already observed the important part the calcium salts play in the repair of diseased structures,² and that this form of amenorrhoea is invariably cured by the administration of lime salts; and why this function only commences when the economy has lime salts to spare from the constructive claims of the body.

To come to the actual observations on women. First, in regard to the systemic blood. There is always a very marked drop in the calcium content just before the menstrual bleeding commences. Often this drop is preceded by a marked rise (compare Reference³). The accompanying chart (Fig. 2) illustrates both of these points. It is the chart of a girl who is subject to haematemesis each menstrual period—a true case of coincident vicarious haemorrhage. We had her in hospital some time under observation.

The next chart (Fig. 3) illustrates the systemic blood content in another class of case. The patient was suffering from minor hystero-epilepsy, due to calcium deficiency, and was completely cured by the judicious administration of calcium lactate. Her premenstrual index was low. With the onset of bleeding, which only lasted for twenty-four hours, there was a marked drop. Though not so apparent as in the last case, it is almost as great rela-

tively, in that the content dropped to one-sixth of the previous amount. It is not easy to obtain the chart of an absolutely normal menstrual cycle. We hardly remember seeing a woman who was without a single symptom at this period; but

the third chart (Fig. 4) illustrates what we consider to be as normal a chart as it is possible to obtain from the human subject. In this one sees a slight rise followed by a drop—in some cases one sees two or even three abortive attempts, as it were—a further rise follows, then a big drop occurs with the onset of menstruation and any attendant symptoms the woman may periodically suffer from. In this case the patient suffered from pain and vomiting. As has been already pointed out elsewhere, it

is important that the blood should be taken for the estimation of calcium at the same time each day.³ There is, then, a marked drop in the systemic blood calcium content of the human subject, which is most marked just before the bleeding occurs. In the same way, the formation of an egg leads to a depletion in the systemic blood of birds; and in considering this we were next led to examine the excretion of the uterus during menstruation.

At the very commencement of menstruation the discharge is largely composed of leucocytes, and this local leucocytosis, which usually precedes the actual bleeding, is extremely interesting. For an examination of the discharge at this period by the method for calcium estimation mentioned shows that there are not only a

large number of free crystals, but also a far larger number precipitated within the white corpuscles themselves (Fig. 5). This was so surprising to us that we should have hesitated to give credence to what we saw, or thought we saw, or to have drawn deductions therefrom, had not other more authoritative observers than ourselves kindly examined the specimens and agreed with us. Professor J. E. S. Moore informs us that in some of the

Fig. 5.—(x420.) Menstrual discharge, first day; leucocytosis.

lower forms of life excretion is carried out by means of leucocytes which may come to the surface and be thrown out, or even go back after discharging their contents.

Now this is probably an instance of what has been called pinocytosis.⁴ We have to thank Dr. R. J. M. Buchanan for calling our attention to this subject, which he did after one of us had stated elsewhere² that it was probable that the leucocytes absorbed the calcium in a fluid form, and carried it from the glands to the exterior, possibly preventing a free secretion of calcium compounds which might increase the coagulability of the blood *in utero*. We shall allude to this point again in a moment.

An examination for calcium salts in the menstrual discharge at a later period—third to fourth day—shows that there is still a marked excess as compared with the systemic blood; but the discharge is then sanguineous and contains the usual vaginal epithelial cells with but a few leucocytes, and it shows a marked tendency to clot (Fig. 6). Thus it will be seen that there is an excretion of calcium coincident with the fall in the blood of the calcium content.

Further, to prove these views we tied the uterine horns of rabbits and examined the contents. The fluid thus collected was found to be exceedingly rich in calcium—more so in the adult menstruating rabbit than in the virgin. In Fig. 7 is seen the fluid collected from a young

uteri of women and rabbits were next examined histologically.

We found, as others have done, that there is a marked activity in the glands at this time, with a diapedesis of leucocytes in the neighbourhood. In Fig. 9 is seen a section of the menstruating rabbit's uterus under a low

power. In Fig. 10 a gland from the same section is shown under a high power. It is a gland in a state of activity. Leucocytes are seen outside the gland, and in the process of making their way between the gland epithelium. To this we would call special attention. It will be noticed that they become elongated and flattened. They were recently observed and figured by Marshall and Jolly⁶ in this condition, but these observers concluded that these elongated cells were merely gland epithelial cells in an actively secreting condition. Ernst Holzbach⁸ also mentions the same cells, and comes to the same conclusion as Marshall and Jolly.

Lastly, it will be observed that there is a collection of leucocytes within the gland lumen, embedded in the secretion of the gland. We believe that these leucocytes then carry some calcium compound with them to the exterior. Apparently the columnar epithelium that lines the interior of the uterus plays the same part as that lining the glands, which are formed by a process of invagination from the surface.

In Fig. 11 the same thing is seen happening in a gland from a menstruating woman's uterus. We have not space

Fig. 6.—(×420.) Menstrual discharge, third day.

Fig. 7.—(×420.) Fluid from artificial hydrometra of young virgin rabbit.

Fig. 8.—(×420.) Fluid from hydrometra of menstruating rabbit.

non-menstruating virgin rabbit. Here one finds the calcium combined or mixed with mucin with which it is precipitated. In the older menstruating rabbit it exists in larger quantity, free, as well as with the mucin and leucocytes, as is seen in Fig. 8.

We may here mention that the secretion from the Fallopian tubes contains very little calcium in comparison with the quantity secreted by the uterus. We performed several experiments to test this point.

To complete the chain of evidence the menstruating

here to discuss the other points of histological interest, for they are many and somewhat controversial. But we cannot pass on without illustrating the histological analogies to be observed in the calcium chamber of the hen. In Fig. 12 is seen a section (low power) of the calcium-secreting chamber of a non-laying ("sitting") hen. In marked contrast with this is a section under the same power—shown in Fig. 13—of the calcium-secreting chamber of a laying hen. In the former the *rugae* or papillae are small, and the stroma underlying the epithelial

layer full of cells which have hardly any definite glandular formation (as is seen in Fig. 14). In the latter (Fig. 13)—from the laying hen—the *rugae* are large and there is a great regularity of actively-secreting glands, as will be seen in the high-power sections (Figs. 15, 16, and 17).

In Fig. 15 there are two points of interest to which we attach some comparative importance. At one spot is seen a rupture in the continuity of the epithelial surface, such as can be seen in one place in the menstruating rabbit's

considered in order to get on to *terra firma*, and into a region from which we can glean facts of importance from a clinical point of view. In the first place, let us briefly consider the periodicity of menstruation and its significance. From the very earliest times this periodicity has been the subject of much mystery, more speculation, and not a little unconscious humour. As a result the periodicity has been allowed to form the chief stumbling-block to a solution of the problem which has been so long *sub judice*.

Fig. 9.—(×250.) Menstruating rabbit's uterus.

uterus (Fig. 9), and directly opposite to this is seen the secretion collected and infiltrated with leucocytes outside the mouth of a gland, a condition frequently seen in the menstruating uteri of women and rabbits, and, we suppose, in other mammals.

Fig. 16 shows an invagination forming a superficial gland in the calcium chamber through the epithelial cells of which leucocytes may be seen passing. Fig. 17 illus-

Fig. 10.—(×1200.) Menstruating rabbit's uterus showing glandular activity.

trates the vascularity and diapedesis which is seen in these *rugae* when actively engaged. Figs. 15 and 17 were taken from a hen while an egg was in the process of being coated with lime salts.

Since it has recently been established by Heape⁷ and others that the pro-oestrus stage of the "rut" in animals is really analogous to the human menstruation, these facts are of considerable importance, and we think sufficiently demonstrate the cause and effect we wish to emphasize.

There are, however, a few other points which must be

Fig. 11.—(×1200.) Menstruating woman's uterus showing glandular activity.

And yet after all there is no mystery, nor is there anything supernatural or obscure about what regularity there may be in the appearance of the catamenia. We have ceased to wonder at the rhythm of respiration and cardiac contraction—we now know that the basis of all the causative factors is founded upon chemical changes—anabolic and katabolic in nature—and that these changes themselves are entirely dependent for their regularity upon the

Fig. 12.—(×250.) Calcium-secreting chamber of a laying hen.

general metabolism in whole or in part. However little understood or insufficiently explained there is little doubt that other factors are merely correlated.

The periodicity of the menstrual function—of the "rut" and breeding in animals—is exactly on the same lines. Merely a question of whether or not certain necessary articles—among them calcium—are at the disposal of the organs concerned for excretion at certain times. To some extent Stevenson⁸ argued on the same lines in discussing his "menstrual wave" theory in very general terms. This

periodicity has really no immutable law of a fixed time, as one might be led to think by the way some authorities have written of it. It is subject to many influences, for the individual has first claim upon all ingredients necessary for herself before she has any to spare for excretion—that is, for supplying a fresh individual (her embryo) or for menstruation. These influences, apart from pregnancy,* are seasonal and climatic, dietetic and hygienic. How important they are can be gauged by the effect evolution

Fig. 13.—($\times 250$.) Calcium-secreting chamber of a laying hen.

has had, or even by the effect domestication has upon the habits of wild animals and civilization upon the human race.

The periodicity of the catamenia is, then, merely the result of a concomitant series of metabolic processes—such as are seen in other spheres of physiological activity—which may or may not allow of regular menstruation. We do not think we need go further into this point; it

Fig. 14.—($\times 1200$.) Tip of ruga from calcium chamber of non-laying hen.

seems to us to be very obvious, and if viewed in this light makes a strong argument for our ideas concerning this influence of the calcium salts in particular.

As already mentioned, we have come to the conclusion that the calcium metabolism is largely influenced by the

* The interesting fact, which has been overlooked or underestimated by most students of menstrual periodicity, of repeated oestrus (every fortnight in rabbits) in unimpregnated animals is surely comparable to the monthly menstruation of non-pregnant women. That this condition is not more frequently observed in animals is due to the promptness with which impregnation usually occurs.

secretions of the ductless glands, and it may be worth while, therefore, to mention briefly the part which these secretions may play in the economy of this function. In the first place, let us point out that clinically we have used the calcium salts with very good results in the following classes of cases:

1. *Amenorrhoea* from general debility of a chronic nature, but more especially that resulting from acute diseases, such as influenza, in which the exhibition of

Fig. 15.—($\times 1200$.) Rugae from calcium-secreting chamber of laying hen.

calcium (in doses of 30 grains of calcium lactate every other day) not only relieves the amenorrhoea but also the symptoms ("nervous headaches," etc.) associated with the debilitated state of the patient.

2. *Menorrhagia* due to what are called "constitutional" conditions; that is to say, where there is no local pathological manifestation. We explain this paradoxical position in regard to amenorrhoea and menorrhagia in the

Fig. 16.—($\times 1200$.) Superficial gland in calcium chamber of laying hen.

following way: In the first class of cases there is not sufficient calcium at the disposal of the economy for menstruation, and in the second, that though there is enough for menstruation the blood content does not rise rapidly enough to stop the flow.

Now, it is a matter of common observation that, in young girls especially, the thyroid enlarges in the majority of cases just before the onset of menstruation—that is to say, when the blood calcium content is high. With the enlargement the onset of bleeding soon follows. Inci-

dentally, it may be mentioned that a similar enlargement of the gland occurs early in pregnancy, when the menstruation is suppressed, and before the fetus can utilize the amount of calcium at its disposal in the blood. We have also observed this thyroid enlargement in artificial menopause.

The function of the thyroid secretion in this respect is to stimulate calcium excretion, which may take place from the uterus, or, failing that, from the kidneys or by the bowel. In this way thyroid may be a valuable drug—indeed, it has often been so used—in amenorrhoea.

In the same way, we believe that the internal secretion of the ovary has the property of depleting the blood and tissues of calcium salts, and possibly a special action in stimulating excretion by way of the uterus.

We have in opposition to these the secretion of the adrenals, and probably that also of the pituitary gland. Both, as will be shown in a subsequent paper, act in a similar manner upon the uterus, especially when in the pregnant state. But, as regards their influence upon menstruation, the extract of these glands assists in the production of uterine contractions which are marked at that time, and also in other more obscure ways from their relationship to calcium metabolism in general, and in particular that of menstruation.

Fig. 17.—Vascularity and diapedesis in calcium chamber of laying hen.

Further, with regard to the secretion of the pituitary body—for we have at present little direct clinical evidence as to the adrenals—it has been shown that tumours of, and in the neighbourhood of, the pituitary gland cause amenorrhoea, and that cessation of the menses is one of the earliest symptoms of acromegaly.⁹ It has also been shown that sexual infantilism with an absence of menstruation is a general complication in early disease of the pituitary gland.¹⁰ An analysis of about 150 cases of acromegaly recently made confirmed the above statement regarding amenorrhoea, and also that lactation hastens the progress of the disease.¹¹

CONCLUSIONS.

1. That menstruation is a periodic function only in so far as the calcium metabolism is in harmony with this periodicity, and that the function is dependent upon the calcium metabolism in all its ramifications.

2. That the haemorrhage into the Graafian follicle may be coincidental, and is probably the result of the lowered coagulability of the blood or vasomotor changes; but that rupture of the follicle is in no way responsible for menstruation.

3. That the bleeding from the uterus, while due to the lowered coagulability of the blood in part, is also dependent on the local changes in the capillaries from which the diapedesis of leucocytes and corpuscles occurs; and, further, that these leucocytes are an active factor in the conveyance of calcium salts from the glands to the exterior.

4. That the uterine glands excrete calcium and mucin, and that therefore the uterus is a "menstrual organ."¹²

5. That there is a correlation between the ovaries and uterus in reference to menstruation, but that the ovary is probably no more predominant than other ductless glands in this respect.

6. That menstruation *per se* is not a necessary adjunct nor concomitant to fertility and reproduction.

REFERENCES.

- ¹ Menstruation and its Relationship to the Calcium Metabolism, W. Blair Bell, *Trans. Royal Soc. Med.*, July, 1908. ² Some Observations on the Physiological Importance of the Calcium Salts, W. Blair Bell, *Liverpool Med.-Chir. Journ.*, July, 1908. ³ Investigations on the Coagulation of the Blood during Menstruation, Birnbaum and Osten, *Archiv f. Gynaek.*, Band lxxx, Heft 2 (these investigators were unable to determine the causal factor). ⁴ Gabritschewsky, *Annal. de l'Institut Pasteur*, 1894, vol. viii, p. 673. ⁵ Marshall and Jolly. ⁶ Ernst Holzbach, *Zett. f. Geb. u. Gyn.*, Bd. lxi, Heft 3. ⁷ W. Heape, *Quart. Trans. Microscop. Soc.* ⁸ Stevenson, On the Menstrual Wave, *Amer. Journ. Obstet.*, vol. xv, 1882. ⁹ Axenfeld, *Neurolog. Centralbl.*, 1905, p. 608. ¹⁰ Harvey Cushing, *Journ. of Nervous and Mental Dis.*, 1906, xxxiii, 2, p. 292. ¹¹ Patellani, *Ann. d. Obstet. e. Gyn.*, 1907, March and April. ¹² Johnstone, The Menstrual Organ, *Brit. Gynaec. Journ.*, 1886, p. 292.

OBSERVATIONS ON PLEURAL PAINS AND ADHESIONS.

By JOHN T. MACLACHLAN, M.D.,

ASSISTANT PHYSICIAN, GLASGOW ROYAL INFIRMARY.

EVERY physician is called sooner or later to treat cases of phthisis pulmonalis, which, notwithstanding all the methods of treatment introduced since Koch announced his brilliant discovery of the tubercle bacillus in 1882, still remains one of the most deadly diseases known. The disease is undoubtedly curable in its early stage; but that stage is only too frequently allowed to slip past, ere the patient, his friends, and perhaps his medical adviser, realize the exact position of affairs.

Clinical observation warrants, I think, the conclusion that phthisis pulmonalis may begin in one of three ways: Firstly, as pleurisy; secondly, as bronchitis; and, thirdly, as a caseating pneumonia, or the deposition of tubercle in the substance of the lung with bronchopneumonia. The second and third modes of origin are well recognized, but the first is not sufficiently appreciated.

Patients often complain of shooting or darting pains in the chest long before tubular breathing or expectoration reveals the presence of serious mischief in the lungs. These darting pains are too often ascribed to what has been called pleurodynia or intercostal neuralgia, because no physical signs have been discovered to denote the presence of pleurisy. I assert, after four years' careful observation, that the so-called pleurodynias are in reality localized patches of pleurisy, and I infer that they are mostly, if not always, of tuberculous origin. These sharp pains in the chest come on suddenly, without reference to wind or weather. I do not wish to deny that rheumatism may attack the pectoralis major or the latissimus dorsi; but the pains I refer to are not, in my opinion, of a rheumatic nature.

Of 300 patients who came to the dispensary for advice, 50 complained of sharp pains in the chest. Their ages ranged chiefly from 20 to 40 years; although younger people and older people were not exempt. The pains were referred to certain well-defined regions, namely, where the lungs divide into their lobes, or the free margins of the lungs. Thus, the pains were often referred to the right nipple, either a little above it or below it; to the left border of the heart; frequently to the lower left axillary region, corresponding to the division between the upper and lower lobes of the left lung; and to points a little below the apex of each scapula.

The involved areas may be diagnosed by very delicate percussion, which may be called tactile percussion, as the sense of resistance is strongly appealed to. The ordinary stroke in percussion strikes through those areas of pleurisy patches and brings out lung resonance. The fingers of the left hand are placed flat on the chest. The tip of the middle finger of the right hand is the plessor, and it should not be raised above 1 or 2 in., and then brought down on the surface of the middle finger of the left hand. The percussing finger should be kept at an easy angle, and should move from the knuckle-joint, the wrist being kept steady. If this method of percussion be practised for several weeks or a few months, it will be