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ON

RECENT ADVANCES IN THE PHYSIOLOGY OF MENSTRUATION.*

BY

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In many countries, particularly France and America, there is grave danger of gynaecology becoming merged in general surgery. Emil Novak, who is fighting a magnificent battle for the autonomy of gynaecology, says, that so long as gynaecology is regarded as embracing also a knowledge of the special anatomy, physiology, and pathology of the female reproductive organs, it will constitute an effective breakwater against the invasion of general surgery. No gynaecologist to-day can consider himself thoroughly equipped unless he is well grounded in these fundamentals. This is particularly true of the physiological aspect, which to-day represents the growing edge of our specialty. It is for this reason that I have chosen as my theme a consideration of the many problems connected with the human menstrual cycle.

Ever since Knaeur, by his transplantation experiments in 1899, showed that the ovarian influence responsible for menstruation is exerted through the blood stream and not through the nervous system, the problem of menstruation has been the subject of extensive investigation. Within the past ten or twelve years the amount of experimental work that has been done on the internal secretions of the ovaries has been stupendous, and, although the results arrived at by different observers have been at times conflicting, none the less, in spite of disagreements here and there, a number of most interesting conclusions have been arrived at in accordance with the strictest rules of inductive logic. In order that we may appreciate the problems connected with menstruation, let me epitomize Novak's classical description of the sequence of events in the menstrual cycle.

The discharge of the ovum from the follicle occurs in the intermenstrual period, most probably about the fourteenth day of the cycle. To be sure, it may occur earlier or later than this date. As the ovum passes down to the uterus, the mucous membrane of the latter prepares for its reception. This preparation begins immediately after the preceding menstruation, for there is a gradual hypertrophic change from this time up to the beginning of the next period. At first this is very gradual, so that at the time the ovum is discharged from the ovary the endometrium is only slightly thicker and its glands are only moderately tortuous, with no sign as yet of secretory activity or decidual change. This phase of the menstrual cycle is called the interval or follicular phase. After the rupture of the Graafian follicle, the gland epithelium begins to show signs of secretory activity, though these are not pronounced until, perhaps, five or six days before the next period. This is the pre-menstrual phase. At the peak of the pre-menstrual phase decidua-like cells appear, which divide the endometrium into the superficial compact and the deep spongy layers.

These facts in regard to the menstrual process are well established. When, however, we come to spell out the proper significance of the facts described we are faced with one of the most fascinating yet difficult problems in physiology.

When I speak of the number of interesting findings that have been arrived at in regard to the internal secretions of the ovary I want to make it clear that, with the notable exception of the brilliant piece of histological work carried out by Novak and Wilfred Shaw on the human subject, these findings are largely the fruit of animal experimentation. Now unless the menstrual cycle resembles in its essentials the sexual cycle in the lower animals, we must be very cautious in trans-

ferring the results of animal experimentation to the interpretation of human phenomena.

What are the essential features of the sexual cycle in the lower animals?

During anoestrus, or the period of sexual tranquillity, the uterus is inactive, its glands are small and contracted, and the mucous membrane is anaemic. The ovaries, too, are inactive. With the advent of pro-oestrus or "coming on heat," there is a ripening of the follicles in the ovary. Coincidentally with follicular activity, there is a gradual development of the endometrium. The glands, also, show evidence of secretory activity, and the mucous membrane is hyperaemic and succulent.

Pro-oestrus is followed by oestrus, during which, as a rule, ovulation takes place (in some species only after copulation) accompanied by further changes usually of a retrogressive character in the accessory organs. It is at this period only, in the lower animals, that the female will receive the male. Should fertilization not take place, the period of oestrus is immediately followed by pseudo-pregnancy. The essential feature of this stage is the presence of a menstrual decidua which is a miniature representation of the decidua of true pregnancy.

To Allen and Doisy of America we are indebted for the experimental proof that a hormone from the fluid of the growing Graafian follicle is responsible for the oestrous cycle in the lower animals. This hormone is called oestrin, or the oestrus-producing hormone.

To Corner, Allen, Parkes¹ and others we are indebted for the experimental proof that a special hormone manufactured by the luteal tissue of the corpus luteum is responsible for pseudo-pregnancy. Oestrin, or the oestrus-producing hormone, even though it may produce actual bleedings in castrated monkeys, is unable, however, to produce the pre-gravid endometrium. As relevant to the problem of human menstruation let me indicate a few interesting variations in the sexual cycle of the lower animals.

In a bitch at the height of pro-oestrus, haemorrhage appears externally. At the end of pseudo-pregnancy in the same animal haemorrhage occurs into the endometrium of the uterus, but does not appear externally. From the point of view of the oestrous cycle animals fall into two well-defined groups:

(a) The species in which the sexual season is associated with but one complete oestrous cycle—the monoestrous type.

(b) The species in which there is a recurrence of short oestrous cycles throughout the sexual season—the polyestrous type.

In the lower animals, therefore, there are two distinct cycles, which come quite close to each other—the sexual or oestrous cycle and the reproductive cycle or the phase of pseudo-pregnancy. When we study the human menstrual cycle in the light of the sexual cycle in the lower animals we are at once struck by the fact that among the higher animals, like man and the monkey, the sexual cycle seems to have disappeared altogether, or if there are vestiges of it left they are difficult to decipher. It is this consideration that has led many clinicians to the view that the human menstrual cycle has only one phase—the reproductive phase or the phase of pseudo-pregnancy—and that the oestrous phase or cycle is completely missed out in the sequence of events that take place between one menstrual period and another. The pre-menstrual phase of the human menstrual cycle is, according to this view, designed to facilitate the implantation of the embryo, and thus corresponds to the luteal or pseudo-pregnant phase of lower mammals. Menstruation, therefore, represents the abortion of an unwanted decidua.

There is a good deal of evidence in support of this view so admirably put by Professor R. W. Johnstone in a paper published this year.² The pre-menstrual phase, like the pseudo-pregnant phase in the lower animals, begins after ovulation, and the breakdown of the endometrium, or menstruation, coincides with degenerative changes in the corpora lutea. Degeneration of pseudo-pregnant congestion, sometimes accompanied by bleeding, has been described in the rabbit by Hammond,³ in the dog by Gerlinger,⁴ and in the sow by Corner.⁵ X-ray sterilization

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stops the menstrual cycle in the human subject, whereas in the lower mammals such treatment blots out the luteal phase but not the follicular or oestrous phase. In spite of the plausibility of this view, it seems to me to conflict with the following well-established facts:

(a) That some humans and many monkeys have been known to menstruate without previous ovulation, and, therefore, without the presence of a pseudo-pregnant phase.

(b) That in the bitch bleeding takes place at the height of pro-oestrus as well as at the end of pseudo-pregnancy.

(c) Allen's⁶ induction of menstruation in the monkey and Whitehouse's⁷ induction in the human by the destruction of ripe Graafian follicles.

(d) Allen's induction of menstruation by the injection into ovariectomized monkeys of the oestrus-producing hormone.

From a consideration of these facts many experimentalists have been driven to Heape's original view that menstruation is identical with the pro-oestrous haemorrhage which takes place in such animals as the bitch, and that the menstrual decidua, which is the offspring of the activity of the corpus luteum, plays no part whatever in human menstruation. This view has been very clearly expressed by Carl G. Hartman.⁸

Although it is true that bleeding takes place in the bitch at the height of pro-oestrus, it is just as true that bleeding also takes place at the end of pseudo-pregnancy, not only in the bitch, but also in the rabbit and sow. Again, Heape's view cannot be reconciled with the well-known fact that menstruation in the human is invariably followed by degeneration of the corpus luteum or its surgical removal. We are led, therefore, to the view originally held by Marshall that in the human pro-oestrous development and the phase of pseudo-pregnancy coincide. On this view menstruation represents both pseudo-pregnant and pro-oestrous degeneration, telescoped, so to speak, into one. I am quite prepared to believe that the two cycles—the sexual and the reproductive—are originally and essentially separate. I would even submit that the monoestrous cycle is prior to the polyoestrous cycle. As animals become domesticated, and begin to live under more sheltered conditions, and as the chances of sexual congress become correspondingly less, the polyoestrous begins to replace the monoestrous cycle as the more certain method of fertilization. No sooner is one cycle finished than another begins. Nature enters upon a fresh adventure, in the hope that she will be more successful the next time. Now in the human subject, on account of evolutionary forces which we need not stop to consider, as the discharge of the ovum which originally took place, probably, at the height of pre-oestrus or commencing oestrus, began to take place on the slope, so to speak, Nature decreed that the sooner the bridal suite was prepared for the reception of the ovum after its discharge the better for the race. In this way, the pseudo-pregnant phase, instead of being a post-oestrous development, became fused with pro-oestrus. To my mind this theory is the most convincing that has yet been propounded. It harmonizes, not only with the workings of natural selection, but it *keeps strictly within the facts*.

Now this view of the pre-menstrual stage of the human menstrual cycle must soften to some extent the antagonism between the oestrus-producing hormone and the special hormone of the corpus luteum. In the lower animals experiments have proved that not only is the special hormone of the corpus luteum exclusively responsible for the development of the menstrual decidua and the sensitization of the uterus for the implantation of the embryo, but it also effectively inhibits the oestrous cycle and, therefore, ovulation. Now in the human menstrual cycle, although we are driven on clinical grounds to admit that the corpus luteum inhibits ovulation (for during the whole of pregnancy there is no ovulation), at the same time, if Marshall's view of menstruation is correct, we shall have to admit that the oestrus-producing hormone plays an essential part in the construction of the pre-menstrual phase of the human menstrual cycle, and that during the pre-menstrual phase both hormones instead of being

antagonistic are complementary to each other. In the human subject during the pre-menstrual phase, therefore, the oestrus-producing hormone takes on, probably, a hyperaemizing and secretory function; the hormone of the corpus luteum produces, of course, the menstrual decidua.

I have already referred to the interesting fact that the oestrous cycle in the lower animals is not prevented by the total ablation of the follicular apparatus, which can easily be done by suitable doses of α rays. More interesting still is the occurrence of follicular maturation without oestrus. This result has been very ingeniously produced by Zondek,⁹ who by feeding thallium to mice was able to suppress all cyclic changes in the uterus and vagina. The production of the oestrus-producing hormone was, in other words, inhibited, but nevertheless the ovarian cycle or the ripening of the follicles with the formation of corpora lutea was unaffected. From these interesting experimental facts we must infer that the production of the oestrus-producing hormone does not depend upon the maturation of the Graafian follicles, and, conversely, the maturation of the follicle does not depend upon the production of oestrin. All this work paves the way for the reception of the view that the cyclic structures of the ovary as well as the production of its internal secretions or hormones is regulated by outside influences.

The production of premature oestrus, with marked follicular ripening, by the transplantation of the anterior lobe of the pituitary gland into immature rats proves that the oestrus-producing hormone as well as the follicle ripening depends upon a hormone manufactured by the anterior lobe of the pituitary gland.

A point of vital importance is the fact that if the test animals are previously castrated all oestrous phenomena are absent. This indicates that the anterior pituitary produces its effects only through the agency of the ovary. It is to be regarded as the sexual motor of the ovary, so to speak. How is this experimental result to be reconciled with the findings of Evans¹⁰ that large amounts of a saline extract of the anterior pituitary of the ox, when injected daily into the normal rat, resulted in the disappearance of the oestrous cycle and the inhibition of ovulation? This suppression of oestrus and ovulation was found to be associated with remarkable changes in the ovary. All Graafian follicles which had reached the size at which the antrum appears had undergone luteinization—that is, had formed corpora lutea atretica without the intermediate act of ovulation. How can the same hormone produce such diametrically opposed results? In a recent paper Evans and Simpson state that they have been able to demonstrate two distinct hormones in the anterior pituitary, the one having an oestrus- and maturity-producing effect, the other having a luteinizing and oestrus-inhibiting effect. The luteinizing hormone, they say, cannot easily escape from the tissue fragments when transplantation methods are used, but is readily liberated by the method of extraction. Wiesner has also described the separability of these two hormones by different methods of preparation of the extracts. The oestrus- and maturity-producing hormone he calls "alpha," and the luteinizing hormone he calls "beta." He has also shown that if alpha and beta hormones are administered simultaneously, ovulation does not take place; we must logically conclude, therefore, that the beta hormone of the pituitary gland is only active during the stage of pregnancy or pseudo-pregnancy.

In deference to the principle that entities should not be multiplied beyond necessity an attempt has recently been made to identify the beta or luteinizing hormone with the growth hormone of the pituitary gland. It is true that in Evans's and Long's intraperitoneal injections of beef pituitary experimental gigantism was produced as well as the stimulation of the production of the luteal tissue in the ovaries. By the administration of a special extract from the placental tissue Wiesner and Crew have produced all the effects of the so-called beta hormone of the pituitary gland without experimental gigantism. They have, in other words, separated the beta hormone of the pituitary gland from the growth hormone.

Let me now epitomize the human menstrual cycle in terms of the most up-to-date endocrinology.

The alpha hormone of the pituitary gland stimulates the ripening of the follicles and leads to ovulation, while, *at the same time*, it activates the oestrus-producing hormone which produces the gradual development of the endometrium, which is characteristic of the interval phase of the menstrual cycle. The oestrus-producing hormone, combined with the luteinic hormone of the corpus luteum which has been activated by the beta hormone of the pituitary gland, produces the full series of changes which constitute the pre-menstrual phase of the human menstrual cycle. The degeneration of the corpus luteum is followed by decidual necrosis or menstruation. That the withdrawal of the **hormonic support** of the corpus luteum which is indicated by its degeneration or retrogression is an essential factor in the production of menstruation is a conclusion difficult to resist. That it is the only essential factor is a question we may well ask without being able to give any confident or dogmatic reply. The degeneration of the corpus luteum is brought about by the withdrawal of the protective influence of the beta hormone of the pituitary gland. Should the ovum become fertilized the trophoblastic cells of the latter prevents degeneration of the corpus luteum by stimulating the production of a further supply of beta hormone from the pituitary gland, and so the pregravid endometrium, instead of necrosing, undergoes further development, while the corpus luteum develops into the corpus luteum of pregnancy.

As I have already stated, Professor Whitehouse, by excising the growing Graafian follicle in the human, has produced menstrual bleedings during the interval phase of the menstrual cycle. In order to harmonize the mechanism of bleeding at this stage with normal menstruation which occurs at the end of the pre-menstrual phase, as well as the oestrus-producing hormone, he postulated the existence of another hormone in the Graafian follicle—a hormone identical in every respect with the luteinic hormone of the corpus luteum. It is the withdrawal of the uplifting influence of this hormone that causes menstrual bleeding. Now if a second hormone is necessary to explain the mechanism of bleeding that occurs during the interval phase of the menstrual cycle, then it cannot be identified with the special hormone of the corpus luteum, for the latter hormone is specific in its action. It is the only hormone that produces a decidual reaction, and there is no evidence of decidual reaction during the interval phase of the menstrual cycle.

Is a second hormone, however, necessary to explain the induction of menstruation in the human by destruction of the ripe Graafian follicle, or for that matter, to explain the occurrence of normal menstruation in monkeys without previous ovulation? Surely Allen's induction of menstruation in the monkey by injection into the ovariectomized animal of the oestrus-producing hormone completely shatters Whitehouse's view. In Allen's experiments it is interesting to note that bleeding does not take place during the injection of the oestrus-producing hormone. The injections, in other words, may be continued indefinitely without producing bleedings. It is only when the injections cease after a certain quantity has been administered that bleeding takes place. From these considerations we must infer that actual bleeding is caused by the withdrawal of the protective influence of the oestrus-producing hormone.

Let me draw attention for a few moments to the most interesting and impressive characteristic of normal menstruation—I mean its remarkable periodicity. The traditional view of the "primacy of the ovum," so strongly advocated by Meyer, has been completely shattered by a number of recent experiments. According to the traditional view the ovum after its discharge from the Graafian follicle lives for a definite span, averaging about fourteen days. If not fertilized it dies at the close of this period, and its protective influence on the corpus luteum comes to an end with a consequent degeneration of this organ. The degeneration of the corpus luteum is followed by a dismantling of the menstrual decidual, which has been produced by the internal secretion of the corpus luteum.

There was never at any time any experimental proof that the ovum possessed any hormonal influence or that it had a definite life span of fourteen days. There were hypothetical characteristics that were invoked to explain the facts. In spite, however, of the plausibility of the theory, it must give way before certain facts that have been fairly well established. In my inaugural address to the Medical Society of University College, Dublin,¹¹ I questioned the validity of the primacy of the ovum on the following grounds:

(a) That in hyperaemic conditions of the ovary the menstrual cycle may be unduly prolonged, which means that either the life span of the ovum is not a fixed quantity or that the life of the corpus luteum depends upon other influences. (From animal experiments we now know that the life of the corpus luteum can be indefinitely prolonged by the continuous administration of the beta hormone of the pituitary gland.)

(b) That in many cases of salpingitis with completely occluded tubes the menstrual cycle continues normally.

Such pathological conditions do not, of course, eliminate the possibility of an hormonal influence from the ovum, even if it is lost in the peritoneal cavity. This factor can, however, be eliminated by allowing the ovum to enter the tube and then washing it out. This experiment has been done by a number of investigators, and even in the human subject by Allen and his associates, who first successfully removed human ova from the tube. In these cases, even though the ova were washed out, the sexual cycle was undisturbed. Lastly, the occurrence in monkeys of definite periodic bleeding with no sign of ovulation is conclusive proof that the periodicity of menstruation, at any rate, is not regulated by the ovum.

A recent publication by Wagner¹² ascribes to the corpus luteum the important role in the menstrual rhythm hitherto credited to the ovum. Wagner believes that the ovum can exert a distinct hormonal effect only in combination with other cells like the trophoblastic cells. The fertilized egg, for example, is like the corpus luteum an inhibitor of ovulation and menstruation. It is to the corpus luteum rather than to the ovum that Wagner ascribes a definite span of life. When this has been run and the structure retrogresses menstruation occurs. That, of course, is quite true, but the life span of the corpus luteum depends upon the hormonal influence of the beta hormone of the pituitary gland. Is the beta hormone of the pituitary gland, then, responsible for the menstrual rhythm? Now the beta hormone only becomes active after ovulation, which is stated to occur at about the fourteenth day of the cycle. It may occur at any time. Its variable occurrence, however, does not seem to upset the menstrual rhythm. Besides, the periodic appearance of the beta hormone demands the existence of a special mechanism whose nature, so far as I know, has not yet been ascertained. Instead, however, of looking at the end of the cycle let us look at the beginning of it. Perhaps the alpha hormone of the pituitary gland regulates the rhythm. No—because continued administration of the alpha hormone does not prolong the oestrous cycle. It cannot, therefore, change the date of menstruation. In my presidential address I stated that the menstrual rhythm seemed to depend upon no special mechanism. It was due, I thought, to the harmonious adjustment of many ductless glands, the disturbance of any one of which may disturb the periodicity of the cycle.

What is the explanation, however, of this nice adjustment? To answer that question I invited my auditors to look at the matter from the teleological point of view.

"Although," I said, "the monthly recurrence of menstruation is rather inconvenient for the individual, it is a beautiful piece of design from the point of view of the race. On account of the fact that in the higher animals sexual intercourse may take place at any time and that ovulation and insemination do not occur at the same time, a monthly recurrence of a pregravid endometrium is Nature's method of securing fertility among the higher animals. Why should only a certain amount of secretion be present at this particular time and at that particular place, in order that Nature's end may be achieved? These are teleological questions which, of course, we are entitled to ask. If we could but answer them all we should solve the mystery of life."

I am glad to see that Emil Novak¹³ in a recent paper agrees with my view of the periodicity of the human menstrual cycle. These are his words:

"In reference to Wagner's views on the primacy of the corpus luteum, provocative as Wagner's study is, it makes one wonder whether we are not chasing a will-o'-the-wisp, for beyond the corpus luteum looms the pituitary, and perhaps beyond the latter we shall have to fall back on some innate periodic human factor as elusive as the life principle itself."

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SUBACUTE COMBINED DEGENERATION OF THE CORD IN PRIMARY ANAEMIA OF THE FOWL:

ITS PATHOGENESIS AND THAT OF ASSOCIATED LESIONS.

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(With Special Plate.)

In a previous communication¹ subacute combined degeneration of the cord was described as occurring in fowls with primary or pernicious anaemia. This subject is of such importance to an understanding of pernicious anaemia and its nervous complications in the human being that the condition has been taken up again for more detailed discussion in the present paper.

During the past four years seven such cases have been recognized and observed in some detail. Their essential nature was first suspected when, post mortem, the milk-chocolate-coloured liver, small in size, was found present. This, indicative of the presence of haemosiderosis, is one of the most characteristic findings in primary anaemia of the fowl. A description of the cases in question will now be given.

CASE I.

Hen 104. White Leghorn, 1 year old, has been ill for some time, lying about on its side. When approached it tries to escape, but staggers and at once tumbles on to its side again; mentally it is quite alert. It died before any extended examination of its blood was made. The haemoglobin, however, was 60 per cent., while a blood film showed a fair degree of erythroblastosis.

Post mortem it was found to be very emaciated. Naked eye, no obvious lesion was seen except that the liver, spleen, and kidney were exceptionally small in size, and that the liver showed the "milk-chocolate" hue. The femur and tibia were filled with an abnormal marrow, which resembled blood in its colour and consistence; while the metatarsal bone was exceptional in that the fat there, instead of being pure yellow in colour, was of a reddish tint.

Microscopic examination disclosed a marked haemosiderosis in the liver, spleen, and kidney; in the latter, especially of the secreting tubules. The occurrence in this latter situation is to be emphasized because, in my experience, this has been found associated only with haemolytic conditions, and has not been observed to occur otherwise, as, for instance, in feeding experiments with large doses of iron salts. Its occurrence, together with the appearances in the liver and spleen, in cases like the present one, is regarded as strong evidence of a primary anaemic condition, existing behind the more obvious nervous implication.

The marrow showed the appearances one finds in a primary anaemia—namely, a haemocyto-blastic hyperplasia and entire absence of fat cells. The lower dorsal region and the lumbar enlargement of the spinal cord were treated by Marchi's method. Sections prepared from these situations showed in both, but especially in the dorsal region, degeneration of the white matter in the posterior and antero-lateral columns of the cord. There was no neuroglial proliferation or sclerosis.

CASE II.

Hen 105. White Leghorn, 1 year old, has been lying about for some time; quite alert, but shows a weakness of the right leg. Haemoglobin is 70 per cent. (normal for fowl); blood films show slight changes only, of the nature of anisocytosis; no erythroblasts seen.

The conditions found, post mortem, and microscopically in the liver, spleen, and kidney, especially as regards haemosiderosis, and in the marrow, were as in hen 104. The cord in the dorsal and lumbar regions showed similar degenerative changes.

CASE III.

Hen 107. Light Sussex, 3 years old, paralysed in both legs and unable to stand. Haemoglobin is 70 per cent., red blood cells 2,000,000 per c.mm., while the blood films show nothing distinctively abnormal.

Post mortem, the conditions present were much as in the previous cases. This hen, however, was very fat. The femur and tibia were greatly sclerosed and thickened, resulting in a great diminution in the quantity of marrow. This was of a pale colour, and looked like dirty tallow.

Microscopically the liver, spleen, and kidney, especially as regards haemosiderosis, resembled previous cases. Here, however, the marrow was of a very fatty aplastic nature, there being very little evidence of any haematopoietic activity, and it was greatly reduced in quantity owing to the bone sclerosis.

The cord in the dorsal and lumbar regions was more markedly involved than in the previous cases. The same columns as previously were affected with the degenerative process. Fig. 1 shows the condition in the lumbar enlargement, degeneration being especially noticeable in the posterior columns.

CASE IV.

Hen 121. White Leghorn, 1 year old, unable to walk. When it tries to do so it tumbles over on to its side. Haemoglobin is 70 per cent., while the blood films show nothing abnormal. The conditions found post mortem were as usual. The omentum, however, contained a great quantity of fat; the fowl was not emaciated. The marrow in the femur and tibia was of a pale grey colour, and quite abnormal.

Microscopically the appearances in the liver, spleen, and kidney, especially as regards haemosiderosis, were as in previous cases. The marrow was aplastic and fatty, and showed very little active haematopoiesis. Very marked degenerative changes similar to those already described were found in the dorsal and lumbar regions of the cord.

CASE V.

Hen 122. White Leghorn, 1 year old, showed considerable weakness in the legs, but not so marked as some of the others. Haemoglobin was 60 per cent., while the blood films showed nothing markedly abnormal. Post mortem the usual conditions were found, including the milk-chocolate-coloured liver. There was great emaciation. The marrow in the femur and tibia was crimson and very fluid, resembling thin red-currant jelly.

Microscopically the liver, spleen, and kidney were as usual, the haemosiderotic condition being marked. The marrow showed great congestion of numerous blood sinuses, which had replaced the usual fat cells and functioning marrow tissue. The changes in the dorsal and lumbar cord were as in hen 121, only not so marked.

CASE VI.

Hen 223. White Leghorn, 1 year old, paralysed and unable to stand. The haemoglobin was 40 per cent., while the red blood cells numbered 845,000 per c.mm. Blood films showed marked erythroblastic changes.

Post mortem the conditions found were as in previous cases. This hen, however, was not emaciated. By this time one had come to appreciate the importance of the duodenum in relation to the excretion of iron in primary anaemia,² and the duodenal mucosa in this case was found to be deep rusty brown in colour. The femur and tibia were very markedly sclerosed, while the greatly diminished marrow was quite abnormal in appearance, being of a pale grey colour.

Microscopically the appearances in the liver, spleen, and kidney were as in the previous cases, including the haemosiderosis. The duodenal villi showed considerable iron pigment in their cores. The marrow was very definitely aplastic. The dorsal and lumbar cord showed the usual lesions.

CASE VII.

Hen 360. White Leghorn, 2 years old, can walk about and even run, but every now and then, without warning, it falls backwards and sits down. It lies in the house all day, and does not mingle with the other hens in the run. The haemoglobin was 70 per cent., and red blood cell count 2,100,000 per c.mm. Blood films showed nothing markedly abnormal.

The conditions found post mortem were as usual, including the typical liver appearances. The mucosa of the duodenum was slightly less brown than in hen 223. The femur and tibia showed