

THE BLOOD PICTURE IN SCURVY, WITH PARTICULAR REFERENCE TO THE PLATELET.

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It is now generally accepted that in those pathological conditions which are accompanied by a diminution in the number of blood platelets a tendency to haemorrhage is almost always observed.

Already in 1910 Duke,¹ from the analysis of a large number of platelet estimations in different clinical conditions, arrived at the following conclusions: (1) When the platelet count descends below the level of 60,000 per c.mm. there is an abnormal tendency to bleed; (2) if the count falls below 10,000 this tendency is always present; and (3) when below 1,000 it is present in its most severe form. The production of experimental purpura in animals (Ledingham,² 1914) by means of an anti-platelet serum, and following on this the observation that anti-platelet serums alone of the antiblood-element serums were capable of producing this pathological picture (Ledingham and Bedson, 1915³), completed the chain of evidence.

In scurvy we have another clinical condition in which haemorrhage is a constant feature. The bleeding from the gums and the subperiosteal haemorrhages over the tibiae, the "black eye," these are all characteristic signs met with in the acute stages of the disease. In experimental scurvy in the guinea-pig the haemorrhages are sometimes so numerous as to recall vividly the picture produced in these animals by means of an anti-platelet serum. The question, therefore, naturally arose as to whether or not the platelets were reduced in numbers in the acute stages of scurvy. On searching through the literature the observations made on this point were found to be extremely scanty.

S. Wassermann⁴ (1918), in a communication on the blood picture in scurvy as it occurs in man, remarks that the blood platelets are reduced in number in the acute stage, and increased in convalescence. Kirch⁵ (1919) gives the findings in two cases, the platelet counts being 280,000 and 14,000 per cubic millimetre, corroborating the observations of Wassermann. However, no details of the technique used by these two workers in the counting of platelets is given, so that it is more or less impossible to judge of the accuracy of their observations. Furthermore, in the two cases of Kirch's, bleeding times of 3 and 2.7 minutes respectively are given, which makes his platelet counts even more difficult to accept. Hess⁶ (1914), in a communication on infantile scurvy, states that the platelet count is normal and that the haemorrhages are most probably due to a decreased capillary resistance. In view of these contradictory findings it was decided to work out the picture in scurvy experimentally produced in guinea-pigs, paying particular attention to the platelet count.

Technique.

In the counting of red cells and leucocytes, and in making the differential leucocyte count, the usual tech-

nique was employed. The haemoglobin estimations were made by means of Haldane's modification of Gowers's haemoglobinometer. The number of platelets was estimated by the following method:

The skin (of the ear in most cases) is cleaned up with ether, and on the clean surface is deposited a large drop of diluent (the diluent employed consisted of 1 per cent. aqueous solution of brilliant cresyl blue 1 part, 2 per cent. sodium citrate in normal saline 6 parts). The skin is then stabbed, through the drop of diluent, by means of a sharp needle. The blood thus oozes directly into the diluent, which prevents clumping of the platelets, and at the same time stains them blue. With a platinum loop of convenient size some of the diluted blood is transferred to a slide and carefully covered with a cover-slip. The amount of blood taken should be sufficient to spread out evenly between the slide and cover-slip without causing the latter to float. The preparation is ringed with vaseline. The number of platelets and red cells is then counted in several fields of the preparation (Leitz 7, ocular 3), and the ratio of platelets to red cells determined. Having already determined the number of red cells per cubic millimetre, the actual number of platelets is readily arrived at.

Experimental Data.

A series of four guinea-pigs was put on a diet of bran, oats, and water only (no green food or autoclaved milk), it

TABLE I.

| Date. 1921. | Weight Grams | Red Cells. | Leucocytes. | Platelets. | Remarks. |
|--------------------------|--------------|------------|-------------|------------|--------------------------|
| GUINEA-PIG B. 41. | | | | | |
| Jan. 24 ... | — | 4,864,000 | 5,600 | 600,000 | |
| " 27* ... | 295 | 5,168,000 | 4,000 | 781,000 | |
| " 31 ... | 320 | 5,920,000 | 6,600 | 883,000 | |
| Feb. 3 ... | 350 | 6,496,000 | 8,200 | 713,000 | |
| " 7 ... | 280 | 7,888,000 | 5,000 | 1,655,000 | Not lively; coat rough. |
| " 10 ... | 270 | 6,566,000 | 4,400 | 1,042,000 | Unchanged. |
| " 14 ... | 280 | 6,896,000 | 4,000 | 1,275,000 | " |
| " 17 ... | 225 | 5,536,000 | 4,600 | 748,000 | " |
| " 19 ... | 210 | — | — | — | In moribund state. |
| GUINEA-PIG B. 42. | | | | | |
| Jan. 24 ... | — | 5,470,000 | 7,000 | 821,000 | |
| " 27* ... | 325 | 6,066,000 | 11,200 | 797,000 | |
| " 31 ... | 310 | 6,928,000 | 10,200 | 1,300,000 | |
| Feb. 3 ... | 330 | 6,896,000 | 9,400 | 1,300,000 | |
| " 7 ... | 270 | 7,584,000 | 6,400 | 1,547,000 | |
| " 10 ... | 290 | 6,272,000 | 12,800 | 896,000 | |
| " 14 ... | 300 | 6,480,000 | 11,600 | 841,000 | |
| " 17 ... | 260 | 5,021,000 | 9,000 | 913,000 | Quiet; out of condition. |
| " 19 ... | 270 | 5,472,000 | 6,400 | 781,000 | |
| " 21 ... | 260 | 5,536,000 | 6,000 | 779,000 | Looks ill. |
| " 22 ... | 250 | 5,341,000 | — | 785,000 | Unchanged. |
| " 23 ... | 210 | 4,960,000 | — | 82,000 | |
| " 24 ... | 220 | — | — | — | In dying condition. |
| GUINEA-PIG B. 43. | | | | | |
| Jan. 24 ... | — | 5,766,000 | 10,600 | 784,000 | |
| " 27* ... | 280 | 5,152,000 | 5,000 | 792,000 | |
| " 31 ... | 300 | 7,986,000 | 6,600 | 1,477,000 | |
| Feb. 3 ... | 320 | 6,361,000 | 7,200 | 936,000 | |
| " 7 ... | 260 | 7,072,000 | 4,800 | 1,102,000 | |
| " 10 ... | 300 | 5,808,000 | 6,200 | 735,000 | |
| " 14 ... | 270 | 5,504,000 | 6,000 | 797,000 | |
| " 17 ... | 225 | 6,016,000 | 4,800 | 761,000 | Quiet; out of condition. |
| " 19 ... | 200 | 4,848,000 | 7,200 | 673,000 | Very ill. |
| " 20 ... | — | — | — | — | Died during night. |
| GUINEA-PIG B. 44. | | | | | |
| Jan. 24 ... | — | 5,680,000 | 8,000 | 800,000 | |
| " 27* ... | 430 | 6,144,000 | 6,000 | 739,000 | |
| " 31 ... | 410 | 6,864,000 | 4,300 | 1,183,000 | |
| Feb. 3 ... | 410 | 6,624,000 | 11,000 | 973,000 | |
| " 7 ... | 340 | 8,000,000 | 5,400 | 754,000 | |
| " 10 ... | 390 | 5,968,000 | 7,000 | 575,000 | |
| " 14 ... | 360 | 6,352,000 | 4,600 | 907,000 | |
| " 17 ... | 325 | 5,648,000 | 3,600 | 910,000 | Looks ill. |
| " 19 ... | 300 | 6,208,000 | 6,000 | 886,000 | Unchanged. |
| " 21 ... | 270 | 5,200,000 | 6,800 | 675,000 | Very ill. |
| " 22 ... | — | — | — | — | Died 10 a.m. |

* Put on diet of bran, oats, and water *ad lib.*

Differential Leucocyte Count.—This showed fluctuations such as might be met with in normal animals—no constant or striking change. No lymphocytosis, relative or absolute, was noted.

Post mortem Findings.—Guinea-pig B. 41: Some swelling of costo-cartilaginous junctions; small haemorrhages in intestines; suprarenals congested, small haemorrhages. Guinea-pig B. 42: Small haemorrhages in gums; swelling of costo-cartilaginous junctions; large intestine shows one or two haemorrhages (¼ in. in diameter); haemorrhages in thigh muscles. Guinea-pig B. 43: Swelling of costo-cartilaginous junctions well marked; haemorrhages in both large and small intestine; suprarenals show some petechial haemorrhages. Guinea-pig B. 44: Swelling of costo-cartilaginous junctions; small haemorrhages in intestines.

having been shown that such a diet produces acute scurvy with death in the guinea-pig in about three weeks' time (H. Chick, E. M. Hume, and R. F. Skelton⁷). Blood estimations were made before the commencement of the experiment and at intervals of three to four days during its course.

These guinea-pigs lived for periods ranging from twenty-six to thirty-one days on the scurvy diet, and also show an appreciable loss in weight, roughly one-third of their original weight. *Post-mortem* the findings characteristic of scurvy were noted, though it must be admitted that these were not as severe as they usually are. The teeth were loose, there was some "beading" of the junction of the costal cartilages with the true ribs. Both small and large intestine showed some small haemorrhages, and the suprarenals were congested and showed some small petechial haemorrhages. The bone marrow of the femur was of the red active type.

As regards the blood picture, no change of an outstanding character has occurred. The red cells are apparently increased in what we might term the "prescurvy" period, dropping again to normal count at death. The platelets show the same increase and subsequent decrease. Even shortly before their death, when the animals were very weak, the platelets were normal in number. The total and differential leucocyte counts show nothing worthy of note. These findings, it must be admitted, were somewhat unexpected, as a drop in the platelet count was confidently anticipated. However, about this time, through the kindness of my colleague, Dr. Harden, I was able to make some platelet counts on monkeys suffering from experimental scurvy, which bore out the results obtained in the guinea-pig.

TABLE II.—Platelet Count of Monkeys suffering from Scurvy.

| Date. | Red Cells. | Platelets. | Platelet Ratio. | Remarks. |
|-------------------------------|------------|------------|-----------------|---|
| MONKEY I. Feb. 24, 1921 | 4,208,000 | 576,000 | 7.3 | Gums fungating; some bleeding. Teeth loose. Avoids use of hind legs (subperiosteal haemorrhages). Pallor of face. |
| Mar. 8, 1921 | 4,352,000 | 800,000 | 5.5 | Condition more severe. Proptosis of right eye. |
| MONKEY II. Feb. 24, 1921 | 5,737,000 | 735,000 | 7.8 | Condition not so acute as in Monkey I. Few haemorrhages to be seen in gums. |
| MONKEY III.* Feb. 26, 1921 | 4,560,000 | 600,000 | 7.6 | |

* Monkey III was the normal control animal.

Both these monkeys, though showing the typical picture of acute scurvy, gave more or less normal platelet counts. In Monkey I, in which the condition was the most acute, the red cells show a slight drop, whilst in Monkey II the red count is above that obtained in the normal control. Wassermann, in the paper already referred to, states that the red cells are sometimes slightly below the normal number, whilst in other cases a high red count up to seven millions is obtained. It is difficult to understand why an increase in the number of red cells should be met with in this disease, unless it is due to a diminution in the total volume of the blood. If this were so, the normal total leucocyte counts noted in the case of the scorbutic guinea-pigs would in reality represent a leucopenia.

In conclusion, the observations made in the case of two infants might be of interest, as pointing to a practical application of these experimental findings, and at the same time further supporting the contention that the platelets are not affected in scurvy. It is through the kindness of Dr. D. H. Paterson, of the Children's Hospital, Great Ormond Street, that I have had access to this material and am able now to publish these figures. They are tabulated below (see Table III).

In both these cases a diagnosis of scurvy had been made, though it must be admitted that in case R. E. there was some doubt as to the correctness of this view. When, however, the additional evidence afforded by the platelet count was available it was at once seen that the two cases were essentially deficient. In R. E. the platelet count was

TABLE III.

| Case. | Age. | Bleeding Time. | Red Cells. | Platelets. | Plate Ratio. | Blood Smear. |
|-------|-------|----------------|------------|------------|--------------|--|
| R. E. | 1½ | ++ | 3,248,000 | 60,000 | 53.3 | Nucleated red cells. Polychromatophilia. Anisocytosis. |
| F. S. | 10/12 | Normal | 4,000,000 | 560,000 | 6.8 | Nothing abnormal seen. |

Note.—R. E. had haemorrhages (skin) scattered all over the body; bleeding from mucous surfaces; subperiosteal haemorrhages (tibiae); a bruise 1 in. in diameter over the right eye. F. S. had bleeding from the gums, subperiosteal haemorrhages, and proptosis of both eyes.

found to be very low, and this fact, taken in conjunction with the low red count and evidence of a bone marrow reaction, confirmed the doubts felt as to the original diagnosis of scurvy, and it was changed to one of purpura haemorrhagica. The second case, F. S., in which there was little doubt as to the true condition, gave a normal platelet count and a red count slightly below the normal. The subsequent history of these cases bore out the revised diagnosis. Both children received antiscorbutic treatment. R. E. died in the course of a few days, with *post-mortem* findings in keeping with the diagnosis of purpura haemorrhagica, whereas F. S. made a rapid recovery.

Conclusions.

1. In scurvy produced experimentally in guinea-pigs and monkeys and in one human case the platelets were found to be normal in number. It is possible that very transient fluctuations in the platelet count occur in scurvy, and that it is during this period of platelet deficiency that the haemorrhages occur. It is hardly conceivable, however, that in making a comparatively large number of platelet observations such fluctuations should have been completely overlooked. Demmer⁸ cites a case of purpura haemorrhagica in which fluctuations in the platelet count, preceding the outburst of haemorrhages, occurred in a most regular manner.

2. The red cells in some cases showed an increase in number, this condition coinciding with a "prescurvy" or incipient scurvy stage. In the acute stages of the disease, particularly where haemorrhages were numerous, the number of red cells fell to slightly below the normal.

3. No variations in the total and differential leucocyte count were observed.

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CHRONIC DUODENAL ILEUS.

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I VENTURE to bring before a meeting of pathologists some observations on a condition which I believe to be a pathological entity, but which in the *post-mortem* room may readily escape notice unless definitely looked for. We are all probably familiar with the findings in a case of death from acute gastro-mesenteric ileus, in which enormous distension of the stomach and duodenum is found, the distension ending, as a rule, opposite where the superior mesenteric vessels cross the duodenum. Such cases, although usually occurring after an abdominal operation, and most frequently after operation on the biliary tract, occur also independent of any operation.

In a long series of examinations of the duodenum in the *post-mortem* room in search of diverticula I was struck by certain cases where a greatly dilated and congested duodenum was found, the dilatation extending as far as the crossing of the superior mesenteric vessels. In the histories of these cases no significant symptoms were