THE CONDITION OF THE BLOOD IN TWO CASES OF PERNICIOUS ANÆMIA.

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HAVING had an opportunity of examining the blood in two cases of pernicious anæmia for a period extending over several months—from the time that the condition was diagnosed till within a short time of death, I have drawn up a table of the more important numerical alterations in the corpuscular elements of the blood.

A mere glance at this very clearly shows the temporary improvement which may take place in this disease, and also the relapses and ultimate failure of all treatment.

The patients were: A., a man, aged 32, in comfortable circumstances; and C., a woman, aged 42, living in poor surroundings. In both the disease came on very gradually, with progressive weakness without any determinable cause. In neither was there the slightest evidence of any malignant or organic disease, nor was there any emaciation, although there was in each some loss of weight from time to time.

Both presented the typical signs and symptoms of the disease. The lemon-yellow complexion, the breathlessness on the slightest exertion, the palpitation and at times marked tendency to syncope were present in both at one or other stage of the disease. In both there was occasionally slight elevation of temperature, and once or twice muttering delirium. Abdominal disturbances, particularly abdominal distension and diarrhoea, were not infrequently the cause of much distress.

One thing was very noticeable, that the state of the blood was found to coincide with this physical condition. When they were feeling worse, when weakness, buzzing, or swimming in the head, palpitation or faintness were more pronounced, the number of red corpuscles and the amount of hæmoglobin were almost invariably diminished.

The following tables show the number of the red and white blood corpuscles, the amount of hæmoglobin, the percentage of the leucocytes and nucleated red blood cells. The enumeration of the corpuscles was made with a Thoma-Zeiss hæmocytometer and Toison's diluting fluid. The amount of hæmoglobin was determined by von Fleischl's hæmometer. As the amount of hæmoglobin was exceedingly low, I have found it much more accurate to use double the amount of blood and then take half the resulting percentage.

The colour index was determined by dividing the percentage of hæmoglobin by the percentage of the red corpuscles present. As Fleischl's hæmometer gives rather a low reading, that is, the amount of hæmoglobin in health being usually found to be 90 per cent. instead of 100 per cent., I have in one column estimated the corrected colour index.

The percentage of the different forms of leucocytes was estimated by making a differential count of the white blood corpuscles in dry films stained with eosin and hæmatoxylin or eosin and methylene blue.

I may here mention that exceedingly few marrow cells or myelocytes were seen, and on no occasion did I find an eosinophile marrow cell. The nucleated red blood corpuscles were counted in the dry stained films, and it was noted how many of these were met with whilst counting 1,500 leucocytes. The absolute number of the nucleated red corpuscles per c.mm. cannot be determined with the hæmocytometer, and therefore the figures given are calculated relatively from the number of white blood corpuscles. I have not classified separately the very small nucleated red corpuscles, or microblasts, as these were only present in very small numbers, and I have therefore included them under the normoblasts.

At the end of the first case I have added the number of corpuscles and the percentage of leucocytes found in normal blood. The treatment adopted in both cases was similar. Arsenic and red bone marrow were given for a considerable time. The former was gradually increased in quantity till gastric symptoms occurred. It seemed as if the arsenic at times did more harm than good, and it was therefore discontinued for some time. The red bone marrow was given in the raw state (it would appear that it is extremely difficult to obtain the red bone marrow from butchers), in capsules, and

as the glycerine extract. Iron was from time to time also tried.

On account of the abdominal distension, various intestinal antiseptics—especially β naphthol and salicylate of bismuth—were given. The patients were kept at absolute rest, the woman in bed, whilst the man was often taken out in the fresh air whilst lying on a stretcher carriage.

In neither case could I attribute the temporary improvement to any one line of treatment, although I consider that the arsenic was chiefly instrumental in at first improving the condition of Case A. I made cultures from the blood of both cases on glycerine agar and blood serum, but with no very definite results, and in order to eliminate the possibility of there being any intestinal parasites I examined the fæces for ova, but with negative results.

Case of A., a man, aged 32.

Date.	Red Blood Corpuscles.	White Blood Corpuscles.	Hæmoglobin.	Colour Index.	Corrected Colour Index.
Oct. 11, 1897	1,642,500	5,092	37	1.12	1.25
" 29, "	3,152,083	3,395	58	0.92	1.31
Nov. 13, "	4,075,000	3,395	72	0.88	0.98
April 12, 1898	2,221,875	4,125	35	0.78	0.87
May 28, "	1,388,750	3,621	27	0.99	1.08
June 8, "	1,412,500	3,600	25	0.87	0.98
" 17, "	1,047,500	4,371	25 per cent.	1.19	1.32
" 29, "	943,750	2,541	17½	0.93	1.03
July 11, "	677,083	6,485	14	1.03	1.15
" 22, "	772,656	4,838	15 per cent.	0.97	1.07
" 29, "	970,312	10,695	20 per cent.	1.03	1.14
Aug. 5, "	1,070,312	3,157	28	1.30	1.45
" 12, "	1,176,562	1,920	23	0.97	1.04
" 25, "	818,750	1,700	18	1.10	1.22
Sept. 1, "	812,500	2,850	20	1.23	1.36
" 8, "	1,081,250	2,953	23	1.06	1.18
Normal blood	5,000,000	8-9,000	90 per cent. Fleischl	0.90	1.00

Percentage of Leucocytes.

Date.	Multi-nucleated.	Lymphocytes.	Large Uninucleated.	Eosinophile.
Oct. 11, 1897	47	44	5	7
" 29, "	59	31	5	5
Nov. 13, "	48	40	4	8
April 12, 1898	45	48	3	4
May 28, "	34	53	6	7
June 8, "	40	54	3	3
" 17, "	44	50	3	3
" 29, "	52	42	3	3
July 11, "	57	37	2	4
" 22, "	34	56	3	7
" 29, "	44	47	5	4
Aug. 5, "	41	49	3	7
" 12, "	31	64	3	2
" 25, "	48	45	3	4
Sept. 1, "	59	36	3	2
" 8, "	56	30	2	12
Normal blood	65-70	25	3-6	2

Nucleated Red Blood Corpuscles.

	Proportion to Leucocytes.	Number per c.mm.	Normoblasts.	Megalo-blasts.
Oct. 11, 1897	74 in 1,500	251	24	50
" 29, "	0	0	0	0
Nov. 13, "	0	0	0	0
April 12, 1893	105 in 1,500	288	30	75
May 28, "	55 in 1,500	132	20	35
June 8, "	35 in 1,500	84	5	30
" 17, "	22 in 1,500	64	0	22
" 29, "	60 in 1,500	101	25	35
July 11, "	60 in 1,500	259	21	39
" 22, "	74 in 1,500	238	22	52
" 29, "	915 in 1,500	6,523	164	75½
Aug. 5, "	525 in 1,500	1,204	120	405
" 12, "	97 in 1,500	124	37	60
" 25, "	25 in 1,500	28	2	23
Sept. 1, "	146 in 1,500	277	34	112
" 8, "	60 in 1,500	118	15	45
Normal blood	0	0	0	0

Case of C., a woman, aged 42.

Date.	Red Blood Corpuscles.	White Blood Corpuscles.	Hæmoglobin.	Colour Index.	Corrected Colour Index.
April 24, 1897	914,583	1,944	15 per cent.	0.82	0.91
May 1, "	705,147	2,919	15.0	1.06	1.18
" 8, "	666,666	2,801	14	1.05	1.16
" 17, "	1,201,755	3,961	24 per cent.	1.00	1.11
" 22, "	1,485,833	3,060	30 per cent.	1.01	1.12
" 29, "	2,077,500	4,752	37.5	0.90	1.00
June 12, "	3,670,000	7,300	53 per cent.	0.72	0.80
" 26, "	3,581,250	5,873	53	0.76	0.85
July 10, "	4,400,000	9,166	50 per cent.	0.57	0.63
April 13, 1898	1,205,000	3,565	20 per cent.	0.83	0.92
" 27, "	920,833	3,216	20 per cent.	1.08	1.20
May 11, "	1,320,000	3,100	30	1.13	1.26
July 2, "	632,777	3,475	15 per cent.	1.19	1.32
" 20, "	673,437	3,577	12.5	0.94	1.03
" 28, "	866,250	4,227	15 per cent.	0.93	1.03
Aug. 6, "	651,136	2,738	14	1.07	1.19
Sept. 2, "	2,983,333	6,111	50	0.84	0.93
" 23, "	3,912,500	5,818	58	0.74	0.82
Oct. 14, "	2,525,000	5,092	35 per cent.	0.69	0.77

Percentage of Leucocytes.

Date.	Multi-nucleated.	Lymphocytes.	Large Uninucleated.	Eosinophile.
April 24, 1897	51.8	45.8	1.5	0.9
May 1, "	46.3	51.3	1.5	0.7
" 8, "	51.0	44.0	3.0	2.0
" 17, "	46.4	51.9	1.5	1.1
" 22, "	48.0	48.0	2.0	2.0
" 29, "	34.0	57.0	7.0	2.0
June 12, "	57.0	31.0	6.0	6.0
" 26, "	60.0	35.0	4.0	1.0
July 10, "	50.0	40.0	5.0	5.0
April 13, 1898	50.0	46.0	2.0	2.0
" 27, "	62.0	34.0	2.0	2.0
May 11, "	51.0	42.0	4.0	3.0
July 2, "	41.0	55.0	2.0	2.0
" 20, "	37.0	59.0	4.0	0.1
" 28, "	60.0	38.0	1.0	1.0
Aug. 6, "	43.0	53.0	3.0	1.0
Sept. 2, "	49.0	41.0	7.5	2.5
" 23, "	50.0	47.0	2.0	1.0
Oct. 14, "	53.0	43.0	2.5	1.5

Nucleated Red Blood Corpuscles.

	Proportion to Leucocytes.	Number per c.mm.	Normoblasts.	Megaloblasts.
April 24, 1897	29 in 1,500	38	11	18
May 1, "	23 in 1,500	45	16	7
" 8, "	15 in 1,500	28	6	9
" 17, "	5 in 1,500	13	5	0
" 22, "	52 in 1,500	106	52	0
" 29, "	1 in 1,500	3	1	0
June 12, "	0	0	0	0
" 26, "	0	0	0	0
July 10, "	0	0	0	0
April 13, 1898	9 in 1,500	21	2	7
" 27, "	2 in 1,500	4	2	2
May 11, "	20 in 1,500	41	5	15
July 2, "	9 in 1,500	21	1	8
" 20, "	23 in 1,500	56	10	13
" 28, "	2 in 1,500	5	2	0
Aug. 6, "	10 in 1,500	18	4	6
Sept. 2, "	2 in 1,500	8	2	0
" 23, "	0	0	0	0
Oct. 14, "	8 in 1,500	27	4	4

Both cases ended fatally—the man within seven days of the last blood count, and the woman within about five months of that period. As both died at their respective homes away from Bournemouth, there was no opportunity of having a post-mortem examination.

I will not describe here the various morphological alterations in the blood corpuscles, as these were quite typical of

pernicious anæmia, and I have elsewhere given a detailed account of the subject.¹ I may, however, mention that the more important features in both cases were: the great reduction in the number of red blood corpuscles, and in the amount of hæmoglobin, although the latter was seldom quite as great as the former; the marked alteration in the size and shape of the red cells, numerous poikilocytes, and the increase in the average diameter of the red blood corpuscles. Megalocytes were more frequent than microcytes, and nucleated red corpuscles were usually present. It will be noticed that the large nucleated red corpuscles or megaloblasts were usually more numerous than the normoblasts. There was no leucocytosis; but a relative lymphocytosis.

On examining the table of Case A, it will be seen that the number of red blood corpuscles increased enormously within the first month from October to November. The patient then returned home, feeling and looking very well, and one almost felt inclined to doubt the original diagnosis. Five months later he again came under observation, and from that time the up and down progress is very evident. The lowest count was on July 11th, 1898, when red cells were 677,000 per c.mm. and the hæmoglobin 14 per cent., yet at that period the nucleated red corpuscles were not so numerous as at several other periods.

On July 29th it will be noticed that the leucocytes are apparently increased. This, I think, is an error, as in counting with the tinted diluting solution many of the large nucleated red blood corpuscles took on the stain and were probably mistaken for white blood corpuscles. At this date the nucleated red corpuscles were more numerous than in any case of pernicious anæmia which I have seen. They were of all sizes, and in some there were two or three nuclei, whilst in others there were all the stages of a nuclear division. In dry-stained films these nucleated erythrocytes seemed quite as plentiful as the white blood corpuscles.

In the second case, C, it is interesting to notice that, although on May 8th, 1897, the red corpuscles fell to 666,666 per c.mm. and the hæmoglobin to 14 per cent., yet the woman went home on July 10th, two months later, with nearly 4½ million red corpuscles and 50 per cent. of hæmoglobin. She, however, came under observation on April 13th, 1898, when the red corpuscles were only just over 1 million and the hæmoglobin 23 per cent.

In both cases during the stage of greatest improvement, when in fact the number of the red blood corpuscles approached the normal, the red cells appeared very much like those seen in moderate cases of chlorosis, that is, they were distinctly pale in colour, and the colour index was low. There was, however, I think, this important difference, that the average size of the corpuscles appeared on careful examination somewhat larger than the normal, and not, as is usually the case in chlorosis, smaller.

Quite a noticeable and constant feature in both cases was the diminution in the absolute number of the white blood corpuscles. In malignant disease or hæmorrhage—the two most probable causes of intense anæmia—there would almost certainly be a distinct leucocytosis. The lymphocytes throughout were relatively increased, whilst the multi-nucleated or neutrophile cells were diminished. The eosinophile cells were in Case A always above the normal, reaching on one occasion 12 per cent.

With regard to the amount of hæmoglobin the lowest recorded in either case was 14 per cent. It is very instructive to notice that the colour index was nearly always high, but seldom higher than the normal, and that when improvement took place the increase in the number of red blood corpuscles was greater than the amount of hæmoglobin and a chlorotic condition of the blood—in which the colour index was below 1, the normal—was present. The highest corrected colour index was 1.45, the lowest 0.63, whilst the average in the case of the man A. was 1.13, in the woman—Case C—1.2.

From either chart it will be evident how difficult it would have been at one or two stages to make a diagnosis from one examination, and also the impossibility of giving a definite prognosis for the immediate future. Both cases might at one time have been regarded as cured.

REFERENCE.

- ¹ *The Blood; How to Examine and Diagnose its Diseases.* London J and A. Churchill.