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THE EXPERIMENTAL PRODUCTION OF ANÆMIA IN DOGS.

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In the course of some investigations into the etiology of different forms of anæmia I made two experiments on dogs, which it may be of interest to give in detail, as the condition produced presented some features resembling chlorotic anæmia, and some differing from it materially. My endeavour was to induce in the dogs a morbid state similar to chlorosis, in one of them by bleeding, and in the other by feeding on a diet containing insufficient iron, two factors which, I am convinced, play a very important part in the causation of chlorosis in the human subject.

Experiment 1.—A dog, weighing 11½ kilogs., was repeatedly bled from a vein in the leg, and observations were regularly made on the condition of the blood by means of Gowers' hæmoglobinometer and hæmacytometer. Such a dog should have, approximately, about 1000 c.c. blood, and in 3 weeks 687 c.c. were withdrawn, and then it was left to recover without any treatment. During the whole time it was fed daily on 200 grms. oatmeal, 1 pint of milk, and salt—a diet which is sufficient to maintain a dog in good health, and which contained about 8 mgrms. of iron. It occasionally got, in addition, scraps of bone and meat, so that the daily ingestion of iron would probably be from 8 to 10 mgrms.

On each day the corpuscles and hæmoglobin were estimated *before* the animal was bled, and 108 and 8,000,000 were taken as the normal quantities of hæmoglobin and red corpuscles respectively, in estimating the richness in hæmoglobin of the individual corpuscles.

On February 20 the dog was killed with chloroform. All the organs were healthy, and there was no fatty degeneration. The liver gave no staining with ammonium sulphide, and on estimating the iron in it only 0·015 grms. Fe. per 100 parts dried was found. The spleen gave a greyish-green colour, with ammonium sulphide; the bone marrow was very red to the naked eye, but no microscopic examination was made.

The details of the blood-condition are given in the following table:—

Date.	Per cent. Hb.	Red Corpuscles.	Hb. Value of each Corpuscle.	Bled to	Remarks.
Oct. 24	108	8,000,000	1·0	30 c.c.	
,, 25	108	8,000,000	1·0	85 ,,	
,, 29	94	6,980,000	1·0	92 ,,	Corpuscles well formed.
,, 31	84	5,740,000	1·06	40 ,,	
Nov. 1	78	6,300,000	0·92	130 ,,	Corpuscles well formed, a good many microcytes; sp. gr. of serum, 1·012.
,, 3	68	6,280,000	0·80	70 ,,	
,, 7	60	5,400,000	0·82	120 ,,	Sp. gr. of blood, 1·041; of serum, 1·022.
,, 12	50	5,640,000	0·65	120 ,,	Sp. gr. of blood, 1·038; of serum, 1·024.
				687 c.c.	
,, 16	48	5,280,000	0·66		
,, 21	48	5,500,000	0·62		Slight poikilocytosis.
,, 28	52	6,020,000	0·64		Corpuscles very pale, many somewhat misshapen, and a few nucleated.
Dec. 6	52	6,300,000	0·61		
,, 13	52	7,800,000	0·50		
,, 20	54	8,700,000	0·46		
,, 28	62	9,200,000	0·50		
Jan. 3	72	10,000,000	0·52		
,, 17	90	11,200,000	0·60		
,, 30	98	10,400,000	0·69		
Feb. 20	104	10,320,000	0·74		

On looking over the experiment, it will be observed that the red corpuscles and hæmoglobin diminished at first in equal proportions, but in a very short time the deficiency in hæmoglobin became much the more marked, and after the last bleeding, when both were at their lowest ebb, the hæmoglobin had sunk to less than half its original amount, while the corpuscles had fallen only about one-third. In one month the corpuscles had returned to their original number, the hæmoglobin having by this time gained only 4 per cent., and three months elapsed before the latter had returned even approximately to its original amount. There was some poikilocytosis with a good many microcytes, and the blood serum was little altered in specific gravity, although the specific gravity of the blood fell considerably, thus indicating that the deficiency was in the corpuscles. The hæmoglobin value of the individual corpuscle also became very low.

All this is similar to the blood condition found in chlorosis, and if the experiment had been stopped sooner than it was, the impression would have been produced that a condition exactly similar to chlorosis had been induced in the dog. But the animal went on producing more red corpuscles, until at one point the number reached over 11 millions per cub. mm., a state of affairs never seen in chlorosis, where the corpuscles are frequently normal in number, but

more usually are deficient. The animal never developed heart murmurs or breathlessness, and throughout appeared to enjoy the best of health.

It has now been well established that, after bleeding, the red bone marrow of dogs hypertrophies and rapidly produces new corpuscles, and this accounts no doubt for the increase of corpuscles over the normal, and for the fact that they do not diminish rapidly in number as they have time to regenerate in the intervals between the bleedings. The hæmoglobin, however, is in a different position, as the reserve supply of iron in the liver and other organs is soon used up in making it, and the iron of the food (only about 8 mgrms. per day) is not sufficient for the greatly increased manufacture of red blood corpuscles. Hence the hæmoglobin returns very slowly to the normal, and the hæmoglobin value of each red disc remains extremely low, while it takes a very long time to re-establish the balance between corpuscles and hæmoglobin. After death the dog's liver contained much less than the usual amount of iron, showing the drain there had been upon it.

EXPERIMENT 2.—A dog, weighing 12½ kilogs., was fed on a diet of starch, lard, milk coagulum, and salts, from all of which the iron had been removed as completely as possible. It got as much of this as it cared to eat daily, which furnished it with 2 to 3 mgrms. of iron per diem. Previous to commencing this diet, it was fed for a fortnight on skim milk—a diet poor in iron—with the object ef exhausting the reserve iron in its liver and other organs. In calculating the hæmoglobin value of each corpuscle, 90 and 6,000,000 were taken as the normal value of the hæmoglobin and red corpuscles respectively.

Date.	Per cent. Hb.	Red Corpuscles.	Hb. value of each Corpuscle.	Remarks.
Jan. 10	90	6,000,000	1·0	Put on diet containing 2–3 mgrms. iron per day.
,, 21	80	6,000,000	0·88	
,, 28	74	6,800,000	0·72	
Feb. 12	66	6,250,000	0·70	
,, 25	64	6,800,000	0·62	Put on diet containing about 10 mgrms. iron per day — oatmeal milk and scraps.
March 4	65	6,500,000	0·66	
,, 11	68	6,500,000	0·69	
,, 22	70	6,400,000	0·72	
April 9	76	8,000,000	0·62	
May 3	76	8,000,000	0·62	

Dog killed. Its organs were found healthy. During the experiment the dog kept its weight and remained in good health.

During the 46 days the dog was fed on the diet poor in iron, the hæmoglobin had diminished about one-third, while the red corpuscles

had slightly increased in number, and afterwards continued to do so until the increase was very marked, namely, one-third of their original number. Except for this increase in the number of red discs the condition of the blood was similar to what is found in chlorosis.

It is evident that during the first part of the experiment the excretion of iron must have been greater than the ingestion, and that there was not enough iron in the dietary to furnish sufficient hæmoglobin for any new corpuscles formed. During the second stage more than enough iron was furnished, as the hæmoglobin increased in amount, but only very slowly, as it required 67 days for the hæmoglobin to rise from 64 to 76 per cent. on Gowers' scale. It is the invariable experience that in recovery from chlorosis the hæmoglobin increases much more slowly than the corpuscles, whether medicinal preparations of iron be given or not. In the human subject, in chlorosis, recovery takes place with extreme slowness, or more usually not at all,[1] when purely dietetic treatment is used owing to the very small amount of iron in ordinary dietaries; hence it is necessary to give iron in addition.

While clinical observation has led me to the conclusion that blood loss (usually during the menstrual periods) and insufficient iron in the dietary are the immediate causes of chlorosis, yet by these means the condition cannot be exactly simulated in dogs, as these animals immediately produce an excess of corpuscles as if to make up for the deficiency in hæmoglobin, and this we never find in cases of chlorosis. There must therefore be some cause or causes superadded in the human subject. As chlorosis occurs almost invariably during the years of growth, when an extra strain is thrown on all the functions of the body, which is often very inadequately met in many directions, it seems to me that this may limit the blood-making power as well as impair the digestion and general nutrition, so that these causes combine with those above mentioned to produce the pathological conditions of chlorosis.

[1] Cf. Stockman, "The Treatment of Chlorosis by Iron and some other Drugs," *Brit. Med. Journ.*, London, 1893, vol. i.