XXI. STUDIES IN ANAEMIA. II.

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COMPARISON OF METHODS OF PRODUCING AN ANAEMIA CHARACTERISED BY A LOW COLOUR INDEX.

MOST investigators of anaemia, in making observations on such points as basal metabolism, circulation rate and blood reaction, and also on such questions as the influence of iron, etc., on blood regeneration, have confined themselves to acute experimental anaemia produced by bleeding. Such an anaemia is at best a transitory phenomenon, the blood soon being regenerated either from a reserve of blood forming materials or from constituents of the diet. The production of a sub-acute anaemia by bleeding and feeding as described in Part I of this paper [1923] is a process so tedious and laborious that before proceeding further it seemed desirable to search for some easier method of producing a more permanent anaemia, and the expedient of breeding from females which had been kept on a diet poor in iron (bread and milk only) from the age of puberty till ten months was adopted. These rats showed practically no anaemia themselves, their colour index being about 0.52 as against the normal 0.56. Healthy males were used for breeding and the process was looked upon as a case where deficiency of some chemical substance in the mother caused a deficiency of the same substance in more marked degree in her offspring.

This was the course adopted by M. B. Schmidt in 1912. Schmidt [1912] found that if a diet of rice and milk were continued in growing mice they gradually became anaemic and were stunted in their growth. The offspring of such mice were studied through several generations throughout which the feeding was continuously "iron-free." If now iron were given to one of a litter of such stunted anaemic mice it quickly outgrew the others and acquired a high percentage of haemoglobin and a nearly normal blood count.

Attention may also be drawn to the work of Brinckmann [1921], who showed that after feeding young guinea-pigs on iron-poor food anaemia of chlorotic type ensues.

In view of our more intimate knowledge of the rat and his greater range of usefulness in experimental procedure it seemed desirable to repeat the experiments with these animals and to institute a comparison between the

ease of this process and the process adopted in Part I of this work for the production of anaemia and to compare the degree of chronicity of the anaemias produced.

Rats were bred from healthy fathers and from mothers which had been kept till ten months old on white bread and whole milk. The results of blood examination of the offspring at various ages are shown in Tables I, II and III. It will be seen that as compared with normal controls and with control rats from the same litters which had green stuff added to their diet they show when young a marked depression of the colour index of the corpuscle and that this shows a tendency to ameliorate naturally as the animals get older. Males recover faster than females.

Table I. *Showing blood condition in normal rats at ages 40 and 60 days.*

For adult rats see Table I, Part I.

Age: 40 days. Average weight: 92 g.				
Sex	Hb %	R.B.C. in millions per mm. ³	Colour index (human = 1)	Average colour index
M.	85	7.70	.55	.57
M.	78	6.33	.62	
M.	80.5	7.36	.55	
F.	85.5	7.87	.54	.56
F.	88	8.00	.55	
F.	93	8.10	.58	
Age: 60 days. Average weight: 104 g.				
M.	95	8.86	.54	.57
M.	85	7.54	.57	
M.	93	7.80	.60	
F.	95	8.74	.54	.57
F.	94	7.73	.61	
F.	89	7.67	.58	

RESULTS.

Young rats bred from mothers which had been kept on a diet of white bread and whole milk from puberty till ten months old showed a marked fall in the colour index of the corpuscle owing to the fact that the haemoglobin content of the blood had fallen while the number of corpuscles had risen. This is a phenomenon to which attention may be called. The anaemia was fairly chronic but tended to ameliorate naturally in time on a diet of white bread and whole milk. Its experimental production was easy compared with the method previously adopted in Part I. Control rats from the same litters fed on the same diet but with green stuff added showed a speedy recovery from the anaemic condition.

DISCUSSION.

Hartwell [1921, 1922] has reported work in which she shows that a diet of white bread and milk is adequate for nursing mother rats and indeed gives the best growth curves for sucklings. Sherman and Muhlfeld [1922] also regard a very similar diet of whole milk powder and ground whole wheat as

Table II. *Showing blood condition at various ages of rats bred from mothers ten months old, mothers and young having been kept on a diet of bread and milk.*

A. Females.				
Age in weeks	Hb %	R.B.C. in millions per mm. ³	Colour index (human = 1)	Average colour index
8	68.5	10.60	.33	.33
	68.5	10.22	.34	
	68.5	10.58	.33	
10	73	10.78	.34	.33
	73	11.82	.31	
	73	11.00	.33	
12	78	12.00	.33	.34
	78	11.42	.34	
	85	12.22	.35	
16	93	11.18	.42	.42
	88	10.70	.41	
	81	9.72	.42	
22	100	10.32	.48	.50
	105	10.40	.50	
	101	9.67	.52	
24	100	11.20	.45	.51
	117	11.02	.53	
	112	10.40	.54	
	107	10.52	.51	
	100	9.56	.52	
	110	10.60	.51	
B. Males.				
8	76	11.36	.34	.35
	61	9.60	.32	
	63	8.10	.39	
10	73	11.10	.33	.32
	73	11.20	.33	
	73	11.90	.31	
13	102	12.58	.41	.35
	61	9.14	.33	
	78	12.88	.30	
18	95	10.48	.45	.46
	95	10.05	.47	
	98	10.63	.46	
22	110	9.92	.55	.54
	105	9.58	.55	
	102	9.76	.52	

Table III. *Showing blood condition at various ages of control rats from the same litters which had been fed since weaning at four weeks old on green stuff in addition to bread and milk.*

Age in weeks	Hb %	R.B.C. in millions per mm. ³	Colour index (human = 1)	Average colour index
8	100	10.60	.47	.49
	95	9.30	.51	
	100	8.82	.56	
	96	10.34	.46	
	94	9.86	.48	
	91	9.56	.47	
10	104	10.10	.51	.48
	104	11.46	.46	
	107	11.60	.46	
13	102	9.42	.54	.54
	93	8.30	.56	
	100	9.65	.52	

adequate for the growth, reproduction, and successful suckling of the second generation. While these conclusions might be justified from the evidence of growth curves alone, yet the work reported in this paper shows that this cannot be interpreted as meaning that these diets are adequate for blood formation. While it is true that we do not know what the blood condition of Miss Hartwell's rats was like, and it may or may not have been abnormal even though growth was normal, the obvious difference between her rats and these was that her rats were bred of robust mothers, who presumably had given them at birth what these rats lacked and were unable to acquire from the poor diet on which they were fed. It would appear that growth curves alone over a limited period of time are not a sufficient test of the adequacy of a diet. An animal may exhibit a satisfactory growth curve and yet be flabby. Further it may have latent a diathesis which manifests itself as anaemia in its offspring.

CONCLUSION.

A simple method of producing a comparatively chronic anaemia characterised by a low colour index and by a tendency to natural cure is described.

REFERENCES.

- Brinckmann (1921). *Z. Kinderheilk*, **30**, 158-94.
Hartwell (1921). *Biochem. J.* **15**, 149.
— (1922). *Lancet*, i. 323.
Schmidt (1912). *Verh. deutsch. path. Gesellsch.* **15**, 91.
Scott (1923). *Biochem. J.* **17**, 157.
Sherman and Muhlfield (1922). *Proc. Soc. Exp. Biol. Med.* **19**, 76.