

In several cases a material increase in metabolism was obtained when the amount of the feeding was increased over the amount given before a preceding observation. Feedings of 10 per cent lactose and also dextrose solutions were given in several cases, particularly the first three days after birth and in most instances were as effective in increasing heat production as breast milk.

279 (2511)

Regeneration of hemoglobin and diet factors in prolonged, severe experimental anemia.

By G. H. WHIPPLE and F. S. ROBSCHEIT-ROBBINS.

[*From the Department of Pathology, School of Medicine and Dentistry, University of Rochester, Rochester, N. Y.*]

Our earlier observations were made upon dogs rendered anemic by two or three large hemorrhages. Following this sharp reduction of blood hemoglobin from about 120 per cent to approximately 60 per cent, we observed the curve of blood hemoglobin regeneration as it returned to a normal level. It was easy to show that under these conditions a maximal hemoglobin regeneration was induced by certain diets—for example, liver and meat feeding. Many other diet factors were almost inert and certain drugs (iron and arsenic) were inert in this type of experiment.

The data given in this paper are derived from experiments on dogs under very different anemic conditions but the methods used are similar to those described in recent papers.¹ The *anemia level* is maintained as near a constant level as possible by frequent bleedings. The number and amount of bleedings are determined by the hemoglobin, hematocrit and plasma volume figures. Under such conditions the animal is lively, active and healthy but with a constant hemoglobin level of 40 to 50 per cent. We assume, therefore, a constant and maximal stimulus to blood hemoglobin

¹ Whipple, G. H., Hooper, C. W., and Robscheit, F. S., *Am. J. Physiol.*, 1920, liii, 2, 151.

production. Such conditions should test the potential hemoglobin factors in any given diet.

A great deal of experimental work was needed to devise a basal bread ration which should be a complete food, palatable to the dogs yet producing the *minimal hemoglobin regeneration*. The bread which we are using at present meets these requirements and dogs can be maintained on this diet alone for months in good health. This bread is made in the laboratory and consists of the following ingredients: Wheat flour (bread) 12,000 gm., potato starch 6,000 gm., wheat bran 2,000 gm., sugar 4,000 gm., salt mixture (McCollum and Simmonds, minus iron citrate) 120 gm., cod liver oil 2,000 cc., canned tomato 2,000 gm., yeast (baker's cake) 454 gm., water 7,500 cc.

A glance at the sample tables (A and B) shows two standard experiments in condensed form. All these meat foods are boiled in water and hashed before feeding. The diet list favorable for hemoglobin production in this type of experiment is headed by liver and kidney. Beef heart muscle is more favorable than beef skeletal muscle. Salmon muscle is practically inert and has a minimal influence on hemoglobin construction in the body. Egg yolk is quite favorable, much more so than egg white which, however, is not inert. Red cells or hemoglobin given by mouth or hypodermically are distinctly favorable for hemoglobin production. It is a bit surprising that brains exert a favorable influence on hemoglobin production. Pancreas and thymus feeding have little if any effect on hemoglobin regeneration. Fresh tripe boiled has a slightly favorable effect on hemoglobin production but a very interesting influence upon the blood plasma which shows a great increase.

Under the conditions of these long continued experiments we note that iron (Blaud pills) has a distinctly favorable influence on hemoglobin production. Arsenic (sodium cacodylate), however, is quite inert. Ox or pig bile is likewise inert and the pigments if absorbed are not used in hemoglobin construction.

It will be noted that the bread feeding often causes no hemoglobin regeneration over and above the *maintenance factor* which is always present and presumably constant. Some dogs may give as much as 5 gm. of hemoglobin surplus a week on the standard bread ration. There are likewise individual variations in reaction to standard diet factors—for example, beef muscle. This question cannot be discussed at this time for lack of space.

TABLE A.

Dog No. 19-104.

Diet periods 1 week each	Food consumption per cent	Weight		Hemoglob. removed bleeding	Blood Hemoglob. 100 % = 13.8 gm.	Plasma vol.	Remarks
		Loss lbs.	Gain lbs.				
Standard bread 350 gm.	28	1.9	—	0	57	576	
Standard bread 350 gm.	56	0.9	—	0	56	730	22.8 lbs.
Liver 400 gm.	100	—	0.9	10.9	86	672	
Liver 400 gm.	100	0.3	—	69.3	66	618	23.4 lbs.
Standard bread 350 gm.	56	0.9	—	27.9	54	640	Liver carry over
Standard bread 350 gm.	69	0.1	—	0	48	632	22.3 lbs.
Whole red cells 10 gm. + bread 350 gm.	95	—	1.7	0	61	689	
Whole red cells 10 gm. + bread 350 gm.	93	—	0.5	13.9	43	753	
Whole red cells 10 gm. + bread 350 gm.	100	—	0.2	0	47	772	
Whole red cells 10 gm. + bread 350 gm.	100	—	1.0	12.9	43	706	25.6 lbs.
Hemoglob. intrap. 12 gm. + bread 350 gm.	98	—	0.4	0	51	694	Daily perit. inj. ave. 2 gm.
Hemoglob. intrap. 34 gm. + bread 350 gm.	68	0.4	—	29.0	44	752	Daily perit. inj. ave. 5 gm.
Standard bread 350 gm.	66	0.8	—	15.1	42	718	Slight carry over
Standard bread 350 gm.	61	0.5	—	0	46	650	24.3 lbs.
Standard bread 350 gm.	60	1.0	—	0	48	662	
Standard bread 350 gm.	45	0.9	—	13.2	42	616	24.3 lbs.
Canned salmon 200 gm. + bread 300 gm.	94	—	2.6	0	42	744	
Canned salmon 200 gm. + bread 300 gm.	85	—	0.1	0	38	732	25.0
Canned salmon 200 gm. + bread 300 gm.	38	0.4	—	0	36	814	Increased plasma volume
Beef heart 300 gm. + bread 200 gm.	88	—	2.4	0	49	723	
Beef heart 300 gm. + bread 200 gm.	98	—	0.4	17.9	49	776	27.4 lbs.
Standard bread 350 gm.	22	3.9	—	0	53	638	23.6 lbs.
Egg albumin 150 gm. + bread 250 gm.	29	1.6	—	11.5	38	625	22.0 lbs.
Liver 100 gm. + bread 250 gm.	100	—	2.3	0	52	606	
Liver 100 gm. + bread 250 gm.	100	0.1	—	28.5	53	646	24.3 lbs.
Standard bread 350 gm.	81	1.3	—	15.2	37	606	
Standard bread 350 gm.	14	2.0	—	0	36	544	21.0 lbs.

TABLE B.

Dog No. 21-64

Diet periods 1 week each	Food consumption	Weight		Hemoglobin removed bleeding	Blood Hemoglobin, 100% = 13.8 gm.	Plasma vol.	Remarks
		Loss	Gain				
Standard bread 450 gm.	per cent 46	lbs. 2	lbs. —	gm. 14.0	per cent 40	cc. 818	
Standard bread 450 gm.	64	—	0.9	0	36	966	31.9 lbs.
Liver 450 gm.	100	0	0	0	80	866	
Liver 450 gm.	100	1	—	47.3	97	747	30.8 lbs.
Standard bread 450 gm.	67	—	0.9	26.6	59	906	
Standard bread 450 gm.	100	—	1.0	0	55	894	32.7 lbs.
3 Bland's pills + bread 450 gm.	89	0.4	—	0	80	826	
3 Bland's pills + bread 450 gm.	82	0.6	—	43.6	47	960	31.6 lbs.
Standard bread 450 gm.	85	0.5	—	0	63	959	31.1
Standard bread 450 gm.	49	1.3	—	18.3	44	934	Bleeding 1st day of 2nd wk.
Chloroform orally + bread 450 gm.	44	2.1	—	0	48	813	Chloroform 2 dos. 2 cc. ea.
Standard bread 450 gm.	55	—	0.1	0	43	816	27.8 lbs.
Liver 400 gm. + bread 300 gm.	96	—	4.6	20.6	46	952	
Liver 400 gm. + bread 300 gm.	100	—	1.7	28.3	45	1000	34.1 lbs.
Standard bread 450 gm.	90	1.0	—	0	57	956	
Standard bread 450 gm.	100	0.2	—	30.9	43	1000	32.9 lbs.
Sodium cacodylate sub. + bread 450 gm.	87	—	0.1	0	45	1017	1 cc. of 1 per cent sol. daily
Sodium cacodylate sub. + bread 450 gm.	88	0.6	—	0	46	967	32.4 lbs.
Beef kidney 400 gm. + bread 300 gm.	100	—	4.1	26.0	51	972	
Beef kidney 400 gm. + bread 300 gm.	100	—	1.4	35.1	56	849	37.9 lbs.
Standard bread 450 gm.	69	2.6	—	17.5	60	892	
Standard bread 450 gm.	87	—	0.5	15.5	58	866	35.8 lbs.
Egg yolk 85 gm. + bread 350 gm.	100	—	0.1	19.0	69	850	
Egg yolk 85 gm. + bread 350 gm.	100	—	0.3	44.4	47	818	35.9 lbs.
Standard bread 450 gm.	100	—	0.8	23.1	56	902	
Standard bread 450 gm.	72	1.8	—	15.5	40	888	35.2 lbs.
Egg albumin 150 gm. + bread 350 gm.	100	—	1.0	0	45	980	36.2 lbs.

Following a very favorable diet (for example, liver) we note a *storage* of potential material which, in the next week or two of unfavorable diet, will be responsible for the production of a considerable excess of hemoglobin. We may speak of this as a carry over due to storage of parent substances capable of manufacture into hemoglobin. It is probable from our feeding experiments that this substance is stored in the liver and kidney in considerable quantity. On a normal diet dogs always store in the body a considerable reserve of material which can be built into hemoglobin when the diet is changed to one unfavorable to hemoglobin production.

The importance of plasma volume determinations is evident from an examination of the tables and often an apparent increase in hemoglobin value is explained by the blood plasma volume decrease rather than by actual hemoglobin increase. Change in plasma volume with change of body weight due to favorable diet is illustrated. The complete experimental data will be published in the near future.

280 (2512)

The effect of potassium on the metabolism of surviving muscle tissue.

By FRED R. GRIFFITH, JR.*

[From the Laboratories of Physiology of the University of Buffalo, Buffalo, N. Y., and the Harvard Medical School, Boston, Mass.]

The following experiments were undertaken in order to determine whether the pronounced effect of potassium on the contractile process in skeletal and cardiac muscle is associated with changes of metabolism, as indicated by variations in the rate of acid production.

Isolated frog tissues were used in all the experiments and their "normal" rate of acid production was determined in Ringer's solution before treating them with potassium. The Ringer's

* Introduced by Wayne J. Atwell.