hormone is a major factor in sac maintenance. Animal 1399 (Table III) is of special interest, however, because the epididymis was removed from the sac on one side, and was left intact in the other; the empty sac weighed 0.0799 gm. while the other weighed 0.0982 gm. That the weight of the empty sac in unilaterally castrated animals is not due to a subminimal amount of testis hormone is suggested by the fact that seminal vesicles were entirely typical of those found in normal breeding males. It seems probable, or at least possible, that some of the decreased weight of sacs in both unilateral and bilateral castrates may be due to a decreased tonus of the cremasteric fibers, perhaps due to an absence of mechanical stress following testis removal.

It is concluded from these results that the ascent of the testes in adults of this species is not primarily due to scrotal failure, since the scrotum appears to be dependent on the testis. Perhaps the decrease in testis weight is the primary factor causing ascent, but the results of the present study do not prove that it is. The evidence suggests that testis hormone is responsible for maintenance of the sac. Decrease in the output of testis hormone, which has been previously found to closely follow testicular regression in normal males,[3] could account for the decrease in the weight of the sac. But the character of the functional sac is not entirely determined by testis hormone; mechanical stress produced by mere presence of the testis within the sac appears to be a factor in both development and maintenance of the fibro-muscular scrotal sac. Variation in the weight of the sac is caused by fluctuation in the amount of skeletal muscle. Whether this variation is due to hypertrophy or hyperplasia of muscle fibers is being investigated.

9337

Amino Acids (Natural and Synthetic) as Influencing Hemoglobin Production in Anemia.

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We wish to submit evidence that histidine and phenylalanine (both natural and synthetic forms) may under certain conditions exert a definite influence upon the regeneration of red cells and hemoglobin in standardized dogs made anemic by blood withdrawal. We have

been accumulating experimental data relating to the influence of various amino acids by mouth upon hemoglobin production and hope to publish a report in the near future.

Many of the dogs used had been under observation for more than 6 to 8 years continuously anemic and carefully standardized with liver, iron and other food factors. In these dogs upon the experimental regimen recently described[1] fluctuation of 10 gm. hemoglobin production per 2-week period may come within physiological limits but fluctuations of 20 gm. hemoglobin or over have significance. It will be noted in Tables I and II that an increase in hemoglobin output above the basal control levels associated with amino acid feeding may amount to 25-50 gm. hemoglobin per 2-week period. The standard salmon bread[1] was fed during all these diet periods and the amino acid added to the first portion of this diet to insure its prompt total consumption. Pure crystalline amino acids were used in these experiments.

TABLE I.
Histidine Dihydrochloride and Hemoglobin Production in Anemia.

Dog No.	Amino Acid by mouth	Daily dose fed	Hemoglobin Net Output per 2 wks.	Control Net Hemoglobin Output per 2 wks.		
				Iron 40 mg. daily-oral	Liver 300 gm. daily-oral	Basal bread ration alone
		gm.	gm.	gm.	gm.	gm.
27-236	l-natural	1	29	57	86	10
23-1	l "	1	34	46	107	14
27-238	l "	1	44	59	—	20
30-121	l "	2	0	46	87	30
29-326	l "	2	28	46	65	12
27-238	d-optical isomer	1	33	59	—	20

It has been believed by chemists and physiologists that the natural forms of the amino acids are much more active in protein metabolism than the optical isomers or the synthetic dl forms. The evidence relating to hemoglobin production (internal protein synthesis) indicates that in an emergency (anemia) the dog can use all forms of certain amino acids to increase the hemoglobin production.

Histidine (the natural or l form) obviously has an effect when given in one gm. doses per day for a 2-week period. The increase in hemoglobin production due to this amino acid (Table I) approximates ⅓ the increase due to liver feeding in control periods. A single experiment with histidine (the optical isomer or d form)

[1] Whipple, G. H., and Robscheit-Robbins, F. S., *Am. J. Physiol.*, 1936, **115**, 651.

shows a similar effect upon hemoglobin production and other experiments are in progress. The presence of this amino acid in these amounts added to the standard ration enables these standardized dogs to produce much more hemoglobin per week. The mechanism of this reaction is obscure but it may well be argued that this amino acid is of importance in the fabrication of the large globin molecule which makes up the bulk of the hemoglobin molecule. From other experiments with bile fistula dogs it appears that the anemic bile fistula dog can produce readily large amounts of the pyrrol nucleus.[2]

TABLE II.
Phenylalanine and Hemoglobin Production in Anemia.

Dog No.	Amino Acid by mouth	Daily dose fed	Hemoglobin Net Output per 2 wks.	Control Net Hemoglobin Output per 2 wks.		
				Iron 40 mg. daily-oral	Liver 300 gm. daily-oral	Basal bread ration alone
		gm.	gm.	gm.	gm.	gm.
29-326	l-natural	1	18	46	82	12
29-326	d-optical isomer	1	27	46	82	12
26-102	dl-synthetic	0.5	12	39	84	14
26-102	" "	1	25	39	84	10
30-116	" "	1	51	42	91	14
29-326	" "	1	36	46	82	12
23-1	" "	1	8	46	81	16
23-1	" "	2	11	46	81	16
27-238	" "	3	29	38	—	24

Table II shows that phenylalanine may give a response when fed as the d or l or dl form. Of the 7 experiments with the dl form we accept 3 as negative (below 20 gm.) and the other 4 as positive (25-51 gm. hemoglobin). It is at least possible that the amino acid may be more or less potent in any given period depending upon the store of amino acids or aggregates at hand in the liver or other body tissues. More experiments with the natural form of phenylalanine are in progress.

Dogs under these conditions show individual variations in their response to food factors or iron. For this reason we give for each dog its individual response to the 40 mg. daily dose of iron and a 300 gm. feeding of liver. On the average the response to this dose of iron is about 50 gm. hemoglobin and for liver about 95 gm. hemoglobin per 2 weeks. A dog which gives a high output of

[2] Hawkins, W. B., Sribhishaj, K., Robscheit-Robbins, F. S., and Whipple, G. H., *Am. J. Physiol.*, 1931, **96**, 463.

hemoglobin following a standard dose of liver or iron is apt to react above the average to other food factors. We speak of dogs as overactive or subnormal in their response with hemoglobin production.

It may be objected that amino acids added to a diet containing proteins of unknown amino acid make-up give a confused picture of no value. No such objections are made to experiments where iron or copper are added to various diets in anemia due to blood loss or deficient diets. Moreover the internal metabolism of proteins is almost limitless in its complexity and we are merely adding one factor to a host of others in even the simplest type of experiment. To illustrate, an anemic dog during a complete fast with no intake of food factors whatever will produce a considerable amount of new hemoglobin and if given some iron during a fast of 2 weeks will often produce more than 100 gm. of new hemoglobin. This must come from body protein and it has been shown that this new hemoglobin is in part related to the materials which otherwise would appear in the urine as waste products (urea and ammonia fraction).[3] This remarkable conservation of end products and exchange of materials within the body during a fast is an index of what the body can do and indicates the complexity of the internal protein metabolism related to hemoglobin production. The addition of an amino acid to this complex reaction may give a significant response which must be accepted as a fact even if the explanation is unpalatable.

9338 P

Transplantation of Gonads from Lethal to Normal Larvae in *Drosophila melanogaster.*

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Those lethal genes which allow the individual to develop up to a certain stage before death occurs are of particular interest in analyzing experimentally the problem of gene action during ontogeny.

[3] Daft, F. S., Robscheit-Robbins, F. S., and Whipple, G. H., *J. Biol. Chem.*, 1933, **103**, 495.

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