

They found hematocrit ratios of 0.85 for the blood of the body, and 0.7 for the minute blood vessels as compared with arterial hematocrits.

Furthermore, the hematocrits differ from organ to organ. Gibson *et al.*(6) found average hematocrit values in the small blood vessels of the dog ranging from 15% for the kidneys to 82% for the spleen. If similar differences hold true for the mouse, as they most certainly must, then estimates of whole blood volume values for a specific organ obtained with the help of hematocrits for venous blood (or arterial blood) must suffer from attendant errors.

Summary. The plasma and blood volumes of mice and of various mouse organs were determined by injecting mice with a protein iodinated with iodine containing tracer quantities of radioactive iodine, and determining the amount of radioactivity present in the various organs. The average plasma and blood volumes of the mice were found to be 6.7 ml and 12.7 ml per 100 g of body weight, respectively. The average plasma volume in ml per 100 g of wet tissue for the brain was 1.6; kidney, 19.1; liver, 20.2; lung, 23.9; small intestine, 5.0; spleen, 9.2; submaxillary gland, 5.9; testes, 3.4.

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Sex Differences in Weight-stimulating Effect of B₁₂ in Rats on Diets of Varying Composition.* (18084)

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In this laboratory as elsewhere(1) it has been observed that young rats depleted of B₁₂, and receiving either vitamin-free casein or soybean protein as the protein moiety of an adequate diet, show superior weight gains when given daily intramuscular injections of B₁₂. This has been noted in the case of both proteins fed at high and low levels. The greater gains were not accompanied by greater nitrogen retention(2).

In an effort to determine whether the source of the calories plays a role in the weight gains achieved with and without B₁₂, as indicated by the investigations on the growing mouse by Bosshardt, Paul, and Barnes(3), diets were fed that were high,

low or moderate in fat and/or carbohydrate content. The protein level was so adjusted that the percentage of calories from the protein was approximately the same in each ration.

Experimental procedure. The composition of the rations used is given in Table I. Twenty young rats of both sexes, 26 to 30 days old,

TABLE I. Composition of Rations Used.

	A %	B %	C %	D %
Casein (1)	40.	53.5	34.	34.
Salts #4 (2)	4.	4.	4.	4.
Primex (3)	12.	41.2	—	—
Cottonseed oil (4)	1.	1.	1.	1.
Maize dextrin (5)	42.7	—	60.7	10.
Dextrimaltose (6)	—	—	—	50.7
L-cystine	0.3	0.3	0.3	0.3

(1) Vit.-test casein, General Biochemicals.

(2) Hegsted-Mills, Elvehjem and Hart, *J.B.C.*, 1941, v138, 459.

(3) Hydrogenated cottonseed oil, Swift & Co.

(4) Wesson oil.

(5) Made from cornstarch, Corn Products Sales Co.

(6) Mead's Dextri-Maltose #2, Mead Johnson & Co.

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2. Chow, B. F. and Barrows, L. *Fed. Proc.*, (*Am. Inst. Nutr.*), 1950, v9, 354.

3. Bosshardt, D. K., Paul, W. J., and Barnes, R. H., *J. Nutr.*, 1950, v40, 595.

The following vitamin supplements* were added to all rations:

Dissolved in cottonseed oil and added to 100 g ration	
Percormorph oil (Mead Johnson & Co.)	1 drop
α -tocopherol	10 mg
Menadione	1.5 "
Added to 100 g ration	
Thiamine	.3 mg
Riboflavin	.5 "
Pyridoxine	.5 "
Ca. pantothenate	3.0 "
Niacin	5.0 "
Biotin	.015 "
Folic acid	.03 "
Inositol	15.0 "
<i>p</i> -aminobenzoic acid	25.0 "
Choline chloride	125.0 "

* All of the vitamins used were provided by Merek and Co.

were placed on each ration. In order to obtain animals with reduced stores of B₁₂ the young rats used were the offspring of adults from our stock colony which had been placed on a B₁₂-deficient soybean diet at the time of mating. The females were maintained on this ration during pregnancy and lactation. The young had access to the ration until placed on the experimental diets. The animals were allowed to eat *ad libitum*. Food consumption records were kept. Half of the animals on each ration received 0.5 mcg B₁₂[†] subcutaneously three times a week. The animals were weighed weekly and were kept in individual metal cages the floors of which were sufficiently elevated to prevent coprophagy.

Results. As was expected, the animals receiving the B₁₂ injections averaged greater weight gains than did their littermates not receiving the vitamin. After 28 days on the diet the greatest average gain in males was made by those on ration A. In the females those on the high carbohydrate diets, C and D, averaged the greatest gains. The differences between the average weight gains made by these animals and those on the same diets without B₁₂ were considerably greater than those of the males on the same rations. (Table II).

The females on the high carbohydrate diets (C) that were not given B₁₂, gained less than those not receiving the vitamin on the

TABLE II. Average Gain in Body Weight.

Diets	After 28 days on diets				After 63 days on diets			
	Females		Males		Females		Males	
	B ₁₂	No B ₁₂	B ₁₂	No B ₁₂	B ₁₂	No B ₁₂	B ₁₂	No B ₁₂
Low carbohydrate	86 ± 1.8(5) *	75 ± 5.3(6)	106 ± 8.9(5)	91 ± 11 (3)	143 ± 2.7(7)	143 ± 7.2(5)	218 ± 12.1(3)	205 ± 9.8(5)
—high fat								
Medium carbohydrate	89 ± 3.8(7)	78 ± 5.4(5)	124 ± 8.7(3)	101 ± 8.1(5)	154 ± 4.2(7)	139 ± 4.0(5)	253 ± 8.1(3)	242 ± 8.1(5)
—medium fat								
High carbohydrate	87 ± 4.9(7)	56 ± 9.8(5)	112 ± 5.8(3)	95 ± 11.5(4)	155 ± 5.7(7)	108 ± 16.5(5)	246 ± 11.0(3)	212 ± 11.5(4)
(dextrin)—low fat								
High carbohydrate	96 ± 5.3(6)	70 ± 2.7(6)	103 ± 7.0(4)	83 ± 7.0(4)	170 ± 12.0(6)	139 ± 3.7(6)	228 ± 23.0(4)	206 ± 7.5(4)
(dextri maltose)								
—low fat								

* Average gain in wt is expressed in g with stand. error of the mean. Number in parentheses indicates number of animals used.

† Rubramin—E. R. Squibb and Sons.

TABLE III. Average Grams of Protein Consumed per Gram Body Weight Gained.

Diets	After 28 days on diets				After 63 days on diets			
	Females		Males		Females		Males	
	B ₁₂	No B ₁₂	B ₁₂	No B ₁₂	B ₁₂	No B ₁₂	B ₁₂	No B ₁₂
Low carbohydrate —high fat	.94(5)*	.95(6)*	.83(5)	.79(3)	1.40(5)	1.33(6)	1.08(5)	1.10(3)
Medium carbohydrate —medium fat	1.03(7)	.97(5)	.88(3)	.82(5)	1.50(7)	1.43(5)	1.11(3)	1.12(5)
High carbohydrate (dextrin)—low fat	.99(7)	1.16(5)	.79(3)	.78(4)	1.47(7)	1.49(5)	1.10(3)	1.16(4)
High carbohydrate (dextrin maltose) —low fat	.91(6)	1.17(6)	.87(4)	.84(4)	1.33(6)	1.40(6)	1.11(4)	1.09(4)

* Figure in parentheses indicates number of animals used.

diets of moderate and high fat content. In the males, on the other hand, this difference was not so marked. The effect of B₁₂ on weight gain was not as striking among the females on the moderate and high fat diets (A and B) as among those on the two diets high in carbohydrate (C and D). The averages of weight gains made by the females receiving B₁₂ varied from 86 g on B to 96 g on D. Among males receiving B₁₂ the gains varied from 103 g on D to 124 g on A. On diet D, high carbohydrate, the weight-stimulating effect of B₁₂ is least marked in males and most marked in females whereas on ration A, moderate carbohydrate and moderate fat, the reverse is true. Among females not receiving B₁₂ the differences in weight gains between those on the high carbohydrate diets and those on the moderate and high fat diets were somewhat greater than the differences between the average gains of those females receiving B₁₂ and those not receiving the vitamin on the moderate and high fat diets. From this it appears that in young, growing, female rats, fed diets high in carbohydrate, B₁₂ exerts a greater effect on weight gain than it does on littermate males on the same diets. This suggests that B₁₂ is involved in the conversion of carbohydrate into fat. Since females in general have a higher percentage of fat in proportion to total body weight than do males it might be expected that greater weight gains would result in them than in males upon the administration of a factor concerned with the conversion of carbohydrate into fat.

After 28 days on the diet, except among the females on the high carbohydrate diets, (C and D), there were no significant differences in grams of protein consumed per gram of weight gain between the animals receiving B₁₂ and those not receiving it. In every case on all the rations, both with and without B₁₂, the average amount of protein required per gram of weight gain was greater for females than for males. (Table III).

The data obtained after 63 days serve to extend those collected after the animals had been on the diets for 28 days. The trends are approximately the same at the end of the longer period as those noted for the first 28 days. (Table II). The most apparent difference between the results at the ends of the 2 periods is in the amount of protein required per gram of weight gain. After 63 days in both males and females, on all 4 rations, with and without B₁₂, the amount of protein required per gram of weight gain is markedly increased over that required during the first 28 days on the diets.

Summary. Comparison of the average weight gains made by young, growing rats (offspring of B₁₂-depleted animals) on diets of varying fat and carbohydrate content, with and without B₁₂, shows that subcutaneous administration of B₁₂ produces increased weight gains in both sexes on all four of the rations studied. It appears that when the calories are derived primarily from carbohydrate the vitamin exerts a greater effect on weight gain in young, growing, female rats than in their littermate males. The weight-

stimulating effect of B₁₂ is more marked in females on high carbohydrate diets than in littermate sisters on diets of like protein con-

tent but with the calories provided by fat or a mixture of fat and carbohydrate.

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Suppression of Vasomotor Reflexes in Man Following L-Hydrazinophthalazine (C-5968).^{*} (18085)

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A recent paper by Reubi(1) indicates that L-hydrazinophthalazine (C-5968), produces an increase in renal blood flow in hypertensive patients as well as a variable reduction in arterial pressure. Since no other hypotensive agent thus far studied possesses such properties(2) it seems of interest to attempt to localize further the site of action of C-5968 in man.

Method and results. L-hydrazinophthalazine was administered intravenously to 12 normotensive and 3 hypertensive patients in doses of 0.30 to 0.35 mg per kg. Sympathetic vasopressor responses, digital plethysmography, and skin temperature recordings were carried out according to methods previously described(3). Following intravenous injection of the phthalazine derivative all of the changes described below began to develop after 10 minutes, reached a maximum in 20 to 40 minutes, and then slowly receded over a period of several hours. The reduction in

systolic + diastolic
mean (————) arterial pres-
2

sure ranged from 0 to 24% (average 8.5%) in the normotensive subjects and from 0 to 23% (average 8.6%) in the hypertensive patients. In both groups the percentile reduction of diastolic pressure was greater than the percentile fall in systolic pressure. In all patients the visible precordial and carotid pulsations appeared more prominent and forceful. A moderate tachycardia appeared in all patients (pulse rate increase 4 to 32 beats per minute) except 2 of the hypertensive patients who developed bradycardia. Transient inversion of the T waves particularly in leads V2 to V5 frequently were observed in the electrocardiogram.

After C-5968 there usually occurred marked inhibition or abolition of the vasopressor "overshoot" following the Valsalva maneuver, the tiltback "overshoot" and the cold pressor response. Postural hypotension occurred frequently but not invariably. Significant changes in digital skin temperature were not observed in a room maintained at 70°F. However, in environmental temperatures of 75° and higher, flushing of the hands frequently was seen, and there was an increase in pulse volume of both fingers and toes. The reflex vasoconstrictor responses to "noxious" stimuli in the digits were significantly inhibited.

Preparation C-5968 in the dosages used in the present studies in man did not prevent or reverse the hypertension produced by commercial epinephrine infused intravenously at rates of 0.11 to 0.23 µg per kg per min. Also, the tachycardia produced by epinephrine was not prevented. However, in 3 of 3 patients studied when norepinephrine was

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