of 740 mm. Blood sugar determinations were made by standard procedures, Folin and Wu.[4]

The experimental dogs were subjected to an environmental temperature of approximately 29 degrees higher than the controls. The average rectal temperature of the control animals was 101.4 degrees. As a result of the higher environmental temperature the rectal temperature of the experimental animals increased from approximately 101 to 105 degrees. However, the results, Table I, show that there were no significant differences between the blood sugar values of the control and the experimental animals following the administration of either glucose or starch. In both control and experimental animals the blood sugar level was more sustained when larger amounts of carbohydrate were given.

The fasting blood sugar level of the experimental dogs, which was determined after 1½ hours of heat treatment, showed no difference from the normal fasting level. This is in agreement with the observations of Flinn and Scott[3] and Weyl,[2] that increased temperature is without effect on the blood sugar content.

Summary. These findings indicate that exposure to high environmental temperature does not influence the digestion and absorption of carbohydrate in the dog, as far as the blood sugar content is concerned. Moreover, no relation is apparent between the blood sugar level and increased environmental temperature.

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Effect of Hepatic Injury on Vitamin C Excretion in Fasting Dogs.*

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Fasting dogs normally excrete a urinary substance that appears to be identical with Vitamin C. This substance reduces 2:6 dichlorphenol indophenol and gives the color reaction used in the estimation of the vitamin. Moreover, it was established in these investigations that the reducing substance further resembles vitamin

[4] Folin, O., and Wu, H., *J. Biol. Chem.*, 1920, **41**, 367.

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C in that it is not precipitated by mercuric acetate and is destroyed by incubation with the pressed juice of cauliflower. Dogs given a normal laboratory diet excreted increased amounts of substances that reduced the indophenol, but most of these could be removed from the urine by precipitation with mercuric acetate. After the dogs had been put on a fast, the excretion of reducing substance decreased over a period of about 4 days and thereafter the elimination remained constant throughout the period of fasting which usually was from 21 to 30 days.

The biological identity of the reducing substance excreted by the fasting dog has not been established, but Musulin, Tully, Longenecker and King[1] have shown that the reducing substance excreted in the urine by rats has antiscorbutic properties.

Experimental. Female dogs were fasted for a preliminary control period of about 10 days and for the duration of the experiment but were allowed free access to drinking water. The animals were kept in metabolism cages permitting quantitative collection of all urine in dark colored bottles containing acetic acid. At the end of each 24-hour period the dogs were catheterized.

Hepatic injury was induced by 3 different methods. One method was the induction of deep chloroform anesthesia by inhalation for one hour, and another was the administration of carbon tetrachloride by stomach tube.

In the third type experiment, various substances were administered in an investigation of their effects on urinary metabolism. Shortly following the administration of a hexane extract of oat oil the dog developed deep jaundice and evidence of severe hepatic injury. This animal had been studied repeatedly over a period of 4 years. During all the periods of study up to the onset of the hepatic damage the urinary metabolism had remained constant and all evidence of liver involvement had been lacking. While the causative agent is still being investigated the results were so striking that their inclusion in this report is justified. Histological study of the liver tissue showed an advanced atrophy of hepatic cells and an early increase in connective tissue.

Observations. The data observed in representative experiments on the effects of chloroform and carbon tetrachloride are shown in Table I. Chloroform inhalation induced definite increase in the excretion of both urinary nitrogen and vitamin C.

The effect of carbon tetrachloride was not uniform. In some experiments the excretion of the vitamin was increased, but in others

[1] Musulin, R. R., Tully, R. H., 3d, Longenecker, H. E., and King, G. G., *J. Biol. Chem.*, 1939, **129**, 437.

TABLE I.
Effect of Chloroform Anesthesia and of Carbon Tetrachloride.

Day of fast	Daily urinary exeretion: Total N, g	Daily urinary exeretion: Vitamin C, mg	Gmelin test	Remarks
33	2.52	26	0	
34	2.38	26	0	
35	3.98	56	+	Chloroform anesthesia one hr
36	3.27	28	+	
37	2.75	18	±	
8	1.99	36	0	
9	1.99	32	0	
10	2.26	26	0	14 cc C Cl_4 *per os.*
11	2.87	12	+	
12	2.51	8	+	
16	1.78	4	0	
17	1.68	4	0	
18	2.02	13	+	10 cc C Cl_4 *per os.*
19	2.75	11	+	
20	2.27	9	±	

the excretion was unaffected for the first day or two and then was decreased for several days.

Table II shows the data observed in severe hepatic injury. For comparison, observations made during a normal period are included. The data show that during the period of liver damage the vitamin C and creatine outputs were unusually large, the excretion of urea and creatinine was decreased, the urinary ammonia was abnormally high despite absence of infection, and an impaired ability to deaminize amino acids was demonstrated by the high output of amino nitrogen after administration of protein hydrolysate.

TABLE II.
Effect of Advanced Hepatic Injury on Daily Urinary Output.

Day of fast	Total N, g	Urea N, g	NH_4 N, mg	Amino N, mg	Creatinin, mg	Creatin, mg	Vit. C, mg
			Control Period, December, 1938.				
15	1.65	1.04	78	32	101	55	42
16*	2.10	1.26	73	26	135	45	30
17	1.54	1.12	84	18	109	29	32
			Period of Hepatic Injury, March, 1939.				
21	1.27	0.61	450	39	88	80	220
22†	1.99	0.77	450	366	89	94	176
23	1.40	0.57	390	36	98	86	270
24	1.25	0.56	420	40	81	100	260
25	1.25	0.59	460	67	83	101	280

*Given Protein Hydrolysate (0.67 g N) *per os.*
† " " " (1.0 g N) " "

Gmelin Test was strongly positive on all urinary samples during period of hepatic injury, and always negative during control period.

The observations suggest that in the dog the liver plays an important part in the metabolism of vitamin C. The changes in the output of the vitamin seen after induction of hepatic injury are much larger than the normal daily variations or those observed after the administration of a wide variety of substances studied as possible precursors of vitamin C, such as proteins, amino acids, carbohydrates and various vegetable and animal oils. It is likely the increase in vitamin C output following chloroform anesthesia was in part due to asphyxia and subsequent depletion of tissue glycogen.

The function of the liver that is concerned with vitamin C metabolism is not known, but the investigations on shivering and iodoacetate reported in an accompanying paper[2] suggest that the glycogenetic function is the one involved.

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Effect of Shivering, Iodoacetate, and Epinephrine on Vitamin C and Creatine Excretion in Fasting Dogs.*

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In a previous report[1] the excretion of vitamin C by the fasting dog was discussed, and it was shown that hepatic injury can increase the urinary output of the vitamin. In the following experiments, the effect of severe shivering, epinephrine, and iodoacetate on the excretion of various urinary substances was investigated.

Experimental. The technic was similar to that described previously.[1]

Shivering was induced by anesthetizing the animals with intravenous nembutal and then placing them in a refrigerator at 12°C. In most instances the body temperature fell to around 31°C. Although additional nembutal kept the animals in an unconscious state, severe and almost constant shivering occurred.

2 Milhorat, A. T., Hardy, J. D., Bartels, W. E., and Toscani, V., PROC. SOC. EXP. BIOL. AND MED., 1940, **45**, 397.

* Aided by a grant from the National Foundation for Infantile Paralysis, Inc.

1 Milhorat, A. T., Bartels, W., and Toscani, V., PROC. SOC. EXP. BIOL. AND MED., 1940, **45**, 394.