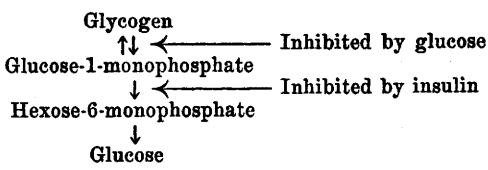

Summary. Insulin inhibits glycogenolysis in the liver, and reinforces the inhibitory effect of added dextrose.

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Influence of Vitamin A upon Urea Clearance in the Rat.*

R. C. HERRIN. (Introduced by W. J. Meek.)

From the Department of Physiology, University of Wisconsin Medical School.

The study of the effect of vitamin A upon renal excretion was extended to the rat because the diet could be made of simpler materials and avitaminosis A of a more severe degree could be studied economically.

Procedure. A high protein diet was used in order to make the physiological strain on the kidneys greater. It was composed of casein 56, lard 20, starch 16, yeast 5 and Wesson's salt mixture 3. For the first 100 days of the experiment the casein was extracted with ether but as this left appreciable amounts of vitamin A the casein thereafter was dry heated for 2 weeks in the autoclave by passing steam at 15 pounds pressure through the outer jacket of the autoclave. This prolonged heating has been used for many years to free casein of vitamin A. The rats were exposed to light from a quartz Hg vapor lamp to furnish vitamin D. The rats weighed 30 to 40 g when placed on the experimental diet.

The technic of Farr and Smadel[1] with modifications was used in making the urea clearance determinations. The rats were handled for training before being used for clearance study. They were placed in the urine collection cages without a preliminary withdrawal of food. After a urine collection period of 350 to over 600 minutes, blood was drawn from the tail, then the urine was collected for another period of approximately the same length. The same blood

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1 Farr, Lee E., and Smadel, Joseph E., *Am. J. Physiol.*, 1936, **116**, 349.

TABLE I.
Urea Clearances in Rats in Avitaminosis A.

Rat No.	Date	Urea excreted, per min, mg	Blood urea mg per 100 cc	Surface area in M^2	Urea clearance per M^2 of body surface
2	6-24-37	.293	61.4	.0284	16.8
		.241			13.8
	7-14	.242	39.5		21.6
		.245			21.8
	7-22	.179	67.0		9.5
	7-24 dead				
9	6-1	.265	51.7	.0254	20.2
		.318			24.2
	7-14	.296	68.8		17.0
		.218			12.5
	7-21	.180	213.5		3.4
		.162	114.6		5.6
	7-23	.135	114.6		4.6
	7-27 "				
6	5-26	.139	33.4	.0215	19.4
	6-1	.208	103.3		9.3
	6-6	.186	88.7		9.7
	6-25 "				
1	6-24	.218	92.9	.0267	8.8
		.174			6.7
4	7-14	.160	80.2	.0230	10.5
		.192			8.7
	7-21 "				
12	5-26	.260	34.2	.0262	29.1
	6-27	.438	29.5		55.4
	6-28	.080	29.5		18.5
	6-28 "				
13	5-19	.025	33.3	.0248	3.0
	7-21	.253	56.5		19.2
	7-21 "				
14	6-1	.205	49.0	.0257	16.4
		.323			25.7
	6-5	.231	52.1		17.3
		.254			18.9
	7-27	.236	73.8		12.5
	7-28 "				

concentration of urea was used in calculating the clearances for the two periods. In most cases the first period gave a higher clearance than the second. The former represents a post-prandial clearance and the latter, one of a post-absorptive state. Urine flow was maintained by administering 0.2% NaCl by stomach tube at the rate of 1.0 cc per hour during the period of urine collection.

Blood urea was determined by the micro-manometric method,

TABLE II.
Influence of Carotene upon Urea Clearance in Rats.

Rat No.	Diet	Date	Urea excreted, per min, mg	Blood urea mg per 100 cc	Surface area in M^2	Urea clearance per M^2 of body surface
3	Basal	7-23-37	.386	100.4	.0268	14.3
			.250			9.7
	" + carotene	7-24				
		8-10	.461	56.8		30.3
			.333			21.9
5	"	6-24	.226	54.9	.0287	14.4
			.313			19.9
	" + carotene	7-24				
		8-11	.313	60.3		18.1
			.264			15.3
10	"	6-24	.408	66.3	.0249	24.7
			.277			16.8
		6-28	.524	60.2		19.6
		7-23	.237	44.6		21.3
			.143			12.9
	" + carotene	7-26				
		8-10	.429	42.7		35.6
			.336			31.6
11	"	6-1	.212	73.5	.0259	11.1
			.330			17.4
		6-5	.242	149.8		6.2
			.384			9.9
		6-27	.472	75.2		24.3
			.454			23.3
	" + carotene	7-6				
		8-10	.360	56.0		24.8
			.341			23.6
18	"	7-20	.427	75.6	.0296	19.1
			.331			14.8
		7-23	.327	63.9		17.3
			.237			12.5
	" + carotene	7-24				
		8-10	.485	72.9		22.5
			.384			18.3
20	"	7-14	.361	50.0	.0273	26.7
			.334			24.5
		7-21	.240	85.2		10.3
			.188			8.1
		7-23	.209	53.8		14.3
			.145			9.8
	" + carotene	7-28				
		8-11	.347	55.3		23.0
			.233			15.5
21	"	7-14	.260	52.2	.0253	19.6
			.204			8.3
		7-20	.326	91.5		14.0
			.224			9.7
		7-23	.280	76.4		14.4
			.249			12.5
	" + carotene	7-28				
		8-10	.544	55.1		39.0
			.352			25.3

using urease.[2] The urine urea was determined by the urease, manometric method.[2]

Results. Table I shows the urea clearances on rats as they develop avitaminosis A. The latest clearance was taken a few days before death. All clearances are expressed in cc of whole blood/min per square meter of body surface

In 9 rats the urea clearance, a few days before death or before vitamin A administration began, had decreased 21 to 72% of the normal level. In Rats 1 and 4 a normal clearance was not obtained but the clearances obtained a few days before terminus were about half of the normals in the other rats. Rats 2, 12 (Table I) and 11 (Table II) showed a very great increase in urea clearance when they neared terminus, just as we have observed in young dogs.[3] The clearance of Rat 5 was the only exception, in that it remained within normal limits in avitaminosis A. The urine of rats displaying extreme avitaminosis A showed very little deviation from normal. Occasionally a trace of albumin was found and a few red and white cells. There was nothing to indicate renal damage. Histological sections of the kidneys showed no significant deviation from the normal, which observation confirms Wolbach and Howe.[4] Table II shows the effect of carotene upon urea clearance in avitaminosis A.

Avitaminosis A in 14 of 15 rats resulted in a marked decrease in urea clearance at some time in the course of the deficiency. In those not treated with carotene the percentage of decrease ranged from 23 to 77. Farr and Smadel[1] found that the average urea clearance in their normal rats was 10.9 cc. The average normal of the rats used in this study was 19.3 cc. This greater value is probably due to the high protein content of our diet. Notwithstanding the high protein diet, in 7 rats the clearance was less than 11 cc in avitaminosis A. Rats 11 (Table II) and 12 (Table I) showed a very great increase in urea clearance when they neared terminus, just as we have observed in young dogs.[3]

Administration of carotene equivalent to 100 units of vitamin A daily in 5 of 7 rats (Table II) resulted in a 30 to 170% increase in urea clearance. Rat 11, which did not seem to respond to carotene had had a very great elevation just prior to the addition of carotene. The second exception was Rat 5, whose clearance had not shown a very great fall in avitaminosis A. The range of clearance after

2 Peters, John P., and Van Slyke, Donald D., *Quantitative Clinical Chemistry*, Vol. II, The Williams and Wilkins Company, pp. 376, 360.

3 Herrin, R. C., and Nicholes, H. J., *Am. J. Physiol.*, 1939, **125**, 786.

4 Wolbach, S. Burt, and Howe, Percy R., *J. Exp. Med.*, 1925, **42**, 753.

carotene, varied from 15.5 to 39 with 4 rats having clearances above 21.

Summary. Vitamin A in the diet affects the magnitude of urea clearance in the rat. In avitaminosis A there is a 23 to 77% decrease in urea clearance. Urine examination and histological sections of the kidney showed no marked morphological alteration. It is a functional deficiency.

Administration of carotene in 5 of 7 rats resulted in a 30 to 170% increase in urea clearance above the level in avitaminosis A.

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The Potential Produced by Cardiac Muscle. A General and a Particular Solution.

ROBERT H. BAYLEY. (Introduced by R. Ashman.)

From the Department of Medicine, School of Medicine, Louisiana State University, New Orleans.

Let us consider a mass of cardiac muscle immersed in an extensive homogeneous volume conductor. The value of the potential at a point in the conductor, produced by any given distribution of depolarization or repolarization may be obtained theoretically in the following way:

Let v_2 denote the particular region or volume of the muscle mass which is undergoing depolarization at a given instant. Let us choose any point O as the origin of a rectangular coördinate system X, Y, Z. Let $(X_2\ Y_2, Z_2)$ be any convenient point within the region v_2. Let dv_2 be an element of volume of v_2 at the point (X_2, Y_2, Z_2). Let the magnitude of the vector $\mathbf{\emptyset}$ represent the intensity of depolarization of the element dv_2, and let the direction of $\mathbf{\emptyset}$ be that of a line drawn from the effective negative toward the effective positive ionic charge within the element dv_2. The vector quantity $\mathbf{\emptyset} dv_2$ is then the electric moment of depolarization.

Let us choose next any other (fixed) point (X_1, Y_1, Z_1) within the volume conductor, in the vicinity of the muscle mass, at which it is desired to know the value of the potential V due to the distribution of depolarization v_2. Let $\mathbf{r}_1$ and $\mathbf{r}_2$ be radius vectors drawn from O to the points (X_1, Y_1, Z_1) and (X_2, Y_2, Z_2) respectively. Let $\mathbf{r}$ be a vector drawn from the latter to the former point so that $\mathbf{r} = \mathbf{r}_1 - \mathbf{r}_2$. Since the elementary potential dV at (X_1, Y_1, Z_1) due