

of all animals had remained constant or had begun to decline.

Thiamin added to the basal diet is shown to produce growth in accordance with the amounts administered. Five micrograms per day per animal is sufficient for maintenance of body weight but insufficient to allow growth over the test period. Subnormal weight increases take place when thiamin is given at levels of 5 to 10 μg per animal per day. Ten micrograms daily produced normal growth. All animals receiving thiamin maintained a healthy appearance during the experimental period. No distinction is made between sexes because growth rates of both sexes are the same over the range indicated in this experiment.

Rat controls grew normally when receiving 10 μg of thiamin per day each. Basal diet controls lost weight and showed characteristic symptoms of acute thiamin deficiency after 15-20 days on the basal diet. The diet was thus shown to be deficient in thiamin as judged by the response of both rats and mice receiving it.

Summary. The amount of thiamin required for growth of albino mice has been determined. Five micrograms per mouse per day was found to maintain body weight attained at the time of weaning. Ten micrograms per mouse per day is the minimal level for normal growth. Less than 5 μg per mouse per day results in loss of weight and eventual death.

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Toxicity of Potassium and Phosphate for Normal and Adrenalectomized Rats.

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Several investigators¹ have shown that the potassium ion has a greater toxicity for adrenalectomized animals than for normal animals, and have suggested that this increase in toxic effects of potassium might be due to the derangement of normal relationships between extra- and intracellular electrolytes that follows adrenalectomy. In such a condition one might also expect the phosphate ion to have an increased toxicity since phosphate is an important intracellular anion with metabolism closely related in some respects to that of potas-

¹ Fenn, W. O., *Physiol. Rev.*, 1940, **20**, 377.

sium. Such considerations stimulated the investigations here reported.

Experimental. Male rats from the stock of Sprague and Dawley, weighing 170 to 210 g, were used. They were fed Bills' modification of Steenbock's stock diet² a week and then both adrenals were removed under ether anesthesia. Food was withdrawn the third day after operation, and 24 hours later solutions containing potassium and/or phosphate were injected intraperitoneally. The toxicity of these solutions was judged by the amounts of potassium and/or phosphate which killed the animals in less than 24 hours. Three solutions were employed, containing respectively 0.5 molar concentrations of: A, potassium chloride; B, a mixture of one part KH_2PO_4 and 4 parts Na_2HPO_4 , of pH 7.4; C, a mixture of one part NaH_2PO_4 and 4 parts Na_2HPO_4 . Two dosages of each solution were employed: 1, an amount deemed just sufficient to kill all experimental animals, as determined in preliminary experiments; and 2, about three-fourths of this dose. The animals were left without food 24 hours after the injection. If they survived this period, feeding was resumed. Practically all animals that survived the injections 24 hours, the time limit of the test, lived 3 to 5 days longer. Normal control animals were injected in the same manner, after a 24-hour fast.

Results. The data listed in Table I indicate that on a molar basis the toxicity of the phosphate ion is approximately equal to that of potassium for normal and adrenalectomized rats. Differences in rates of absorption might explain the somewhat longer survival time of rats injected with phosphate, compared with the survival of rats injected with KCl. The lethal dose of both phosphate and potassium for adrenalectomized rats was about one-fourth their lethal dose for normal rats. The results found following injections of solution B, containing both potassium and phosphate, suggest accumulative effects.

Sodium chloride was similarly injected into adrenalectomized rats in amounts up to 10 mM per kilo, and double that amount into normal rats. None of these died, whereas 2.6 mM of sodium phosphate per kilo regularly killed adrenalectomized rats.

The effect of the preliminary administration of cortical extracts and of NaCl solution on the toxicity of phosphate in adrenalectomized rats also was studied in a few experiments. Seven adrenalectomized rats, following operation, were injected twice daily with 1 cc doses of cortical extract (Upjohn) up to the day of injection with

² Bills, C. E., Honeywell, E. M., and MacNair, W. A., *J. Biol. Chem.*, 1928, **76**, 251.

TABLE I.
Lethal Effects of Intraperitoneal Injections of Potassium and Phosphate in Normal and Adrenalectomized Rats.

Rats		Sol.*	Amts injected		Died within 24 hrs		
					No.	Survival time	
Preparation	No.		Potassium mM/kg	Phosphate mM/kg		Range, hr	Avg, hr
Normal	10	A	10	0	9	0.5- 4	1.9
	10	A	9	0	5	1 - 3	1.6
	10	B	2	10.3	8	3 -15	9.4
	10	B	1.75	9	3	6.5-23	17.1
	10	C	0	11	9	1.5-12	4.8
	10	C	0	9	2	3 - 5	4.0
Adrenalectomy	10	A	3	0	10	0.8-14	3.3
	10	A	2.5	0	7	1 -23	5.5
	10	B	0.5	2.6	10	2.5-10	5.4
	10	B	0.38	1.9	8	4.5-22	9.3
	10	C	0	2.6	10	3.5-23	14.0
	10	C	0	1.9	6	4.5-22	16.7

*Test solutions: 0.5 molar concentrations of A, KCl; B, 1 part KH_2PO_4 + 4 parts Na_2HPO_4 ; C, 1 part NaH_2PO_4 + 4 parts Na_2HPO_4 .

the phosphate solutions. Three rats received an amount of solution B containing 0.75 mM of K and 4 mM of P, and 4 rats received a dose containing 1 mM of K and 5.3 mM of P, all injected intraperitoneally. All animals survived the injections 5 to 7 days. Another group of 5 animals were given 1% NaCl solution as drinking fluid following adrenalectomy; when these were injected with a dose of solution B containing 0.6 mM of K and 3.3 mM of P, all survived for periods exceeding 24 hours.

The results suggest that the derangement of normal relationships between extra- and intracellular electrolytes that follows adrenalectomy involves both phosphate and potassium, the principal intracellular ions.

Summary. In adrenalectomized rats the toxicity of phosphate injected intraperitoneally is increased, and approximates that of potassium.