sodium in particular, two alternative possibilities should be considered. First, it may be assumed that all aspects of tubular function actually are impaired. In this event the renal tubular cells might tend to reabsorb additional quantities of sodium as the load is increased, but would be prevented from doing so because of the impairment of function. The resultant effect would be the constant T_{Na} which was observed. The second possibility is that only certain discrete enzyme systems are inhibited and that the sodium reabsorptive mechanism is spared, thereby allowing T_{Na} to remain constant, while Tm_{PAH} or Tm_G are significantly reduced. Credence is lent to this possibility by the fact that Tm_{PAH} appears to be much more markedly affected than is Tm_G, indicating that the various transport systems are not all altered to the same extent. At present, we cannot say which of these alternatives is the correct one.

Summary. 1. When the plasma sodium concentration is progressively elevated in dogs by the administration of hypertonic saline, the rate of renal tubular reabsorption of sodium remains constant in those experiments where the glomerular filtration rate is not significantly affected. If the filtration rate increases or decreases in response to the hypertonic saline, the rate of sodium transport deviates in the same direction. Therefore, in experiments where the sodium level is elevated for a period of one hour or less, any alteration in the rate of sodium transport is dependent upon the concomitant change in filtration rate. 2. Hypertonic saline exerts a profoundly depressant effect upon the PAH Tm, and a significant but less marked influence upon the glucose Tm. This depression is believed to be nonspecific in nature and contra-indicates the use of these determinations as an index of effective tubular mass in experiments in which variations in sodium concentration are involved.

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A Protective Role of Pyridoxin Against the Toxic Effects of P^{32}.* (19422)

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In a continuation of our study on the effects of internal radiation by P^{32} as related to various dietary factors(1,2), the role of pyridoxin has now been investigated. After

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whole body irradiation of mice with mid-lethal doses of X-rays, large amounts of pyridoxin prolonged the survival, but did not improve the anemia and leukopenia(3). In the present experiments when pyridoxin was added to a pyridoxin deficient diet with a low protein content, no change in the survival of mice injected with P^{32} was detectable. On the other hand, a marked degree of protection by the vitamin became apparent when the deficiency was made more severe by the administration of a pyridoxin analog (desoxypyridoxin)(4), or by diets which presumably increase the requirements for pyridoxin (high protein diets(5) with added cystine or methionine(6)).

Experimental. Two basal diets were employed, one with a 5% casein content (Diet 34(1)), the other with a higher protein level (Diet 41, containing: Casein 30 p.p. 100, dextrin 29.5, sucrose 29.5, Crisco 4, cod liver oil 1, Ruffex 2, salt mixture (U.S.P. No. 2) 4). A mixture of B vitamins(2) from which pyridoxin had been omitted, was incorporated in the diets. Six series of experiments were made on a total of 558 male albino mice, placed under experimental conditions which have been described(1,2). In each series of experiments the animals were distributed in 4 groups: *a, b, c,* and *d*. All 4 groups received the same diet and the same supplements, except that pyridoxin HCl (1 mg/100 g of diet unless otherwise indicated) was added to the diet of groups *b* and *d* only. After 3 to 10 days on the experimental diet, the mice of groups *a* and *b* were injected intraperitoneally with a solution of radioactive $Na_2HP^{32}O_4$ (5 or 6 μc/g) and kept under observation for 42 more days. Groups *c* and *d* were used as controls and observed for the same length of time. The criteria previously used as an indication of the toxic effects of the isotope(1,2) were applied also to the results of the present experiments, except that in computing the average length of survival, a survival of 42 days was ascribed to the mice still alive at the end of the experiment.

Results. In the experiments of Series I (Table I) supplementation of the low protein diet with pyridoxin did not alter the survival of the mice injected with P^{32}. The controls maintained on the pyridoxin-deficient diet and not injected with the isotope grew fairly well and did not show skin lesions, thus confirming previous indications(7) that, unlike the rat, the mouse on a moderately low protein diet does not develop typical symptoms of pyridoxin deficiency. In the experiments of Series II, III and IV (Table II) in which the low protein diet contained desoxypyridoxin, survival figures were higher in the groups injected with P^{32} and receiving pyridoxin, in addition to the anti-vitamin. Similar differences between the groups receiving or not re-

TABLE I. Survival of Mice Injected with P^{32} (6 μc/g) and Maintained on a Low Protein Diet (Diet 34).*

Groups of mice	Pyridoxin in diet	No. of mice	Survivors 21st day, %	Avg length of survival, days†
I a	—	24	67	32 ± 2.8
b	+	15	67	30 ± 2.5
c‡	—	12	100	42
d‡	+	12	100	42

* Time of 50% deaths was >42 days for all 4 groups.

† Values preceded by ± are the stand. errors of the means.

‡ Control groups not injected with P^{32}.

TABLE II. Survival of Mice Injected with P^{32} (5 μc/g) and Maintained on a Low Protein Diet (Diet 34) with Added Desoxypyridoxin.

Groups of mice		Pyridoxin in diet*	No. of mice	Time of 50% deaths, days	Survivors 21st day, %	Avg length of survival,† days
II§	a	—	46	13	15	16 ± 1.4
	b	+	46	>42	74	34 ± 1.9
	c‡	—	39	>42	87	38 ± 1.5
	d‡	+	13	>42	100	42
III‖	a	—	30	14	20	20 ± 2
	b	+	27	>42	59	30 ± 1.8
	c‡	—	26	41	93	36 ± 1.5
VI¶	a	—	18	15	22	22 ± 2.6
	b	+	18	>42	78	36 ± 2.5
	c‡	—	24	>42	92	39 ± 1.4
	d‡	+	12	>42	100	42

* 2 mg/100 g of diet, then 1 mg/100 g when desoxypyridoxin was omitted from diet.

† Values preceded by ± are the stand. errors of the means.

‡ Control groups not inj. with P^{32}.

§ Desoxypyridoxin (5 mg/100 g diet) for 9 days.

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TABLE III. Survival of Mice Injected with P^{32} (5 μc/g) and Maintained on a High Protein Diet (Diet 41) with Added Cystine (Series V) or Methionine (Series VI).

Groups of mice	Pyridoxin in diet	No. of mice	Time of 50% deaths, days	Survivors 21st day, %	Avg length of survival,* days
V† a	—	23	18	22	21 ± 2.6
b	+	23	>42	83	36 ± 2.4
c‡	—	24	41	96	37 ± 1.4
d‡	+	19	>42	95	39 ± 1.3
VI§ a	—	28	15	28	21 ± 2
b	+	27	28	67	27 ± 2.4
c‡	—	24	>42	100	39 ± 1
d‡	+	23	>42	91	40 ± 1

* Values preceded by ± are the stand. errors of the means.
† Control groups not inj. with P^{32}.
‡ Cystine (.3 g/100 g diet) for 52 days.
§ Methionine (.5 g/100 g diet) for 47 days.

TABLE IV. Statistical Appraisal of the Protection by Pyridoxin Against P^{32} Toxicity.

		10% casein + desoxypyridoxin	30% casein + S-containing amino acids
No. of mice inj. with P^{32}		185	101
No. of survivors 21st day	*Chi*²	41	24
	P*	< .01	< .01
Avg length of survival	Diff. between adjusted means	11±1.12†	10±.98†
	t	9.9	10.2
	P*	< .01	< .01

* Probability for a chance occurrence.
† Stand. errors of the diff. between adjusted means.

ceiving pyridoxin are apparent (Table III) in the experiments with a high protein diet supplemented with cystine (Series V), or methionine (Series VI). In the pyridoxin deficient groups of all 5 Series of experiments acrodynia appeared early and often progressed to the almost complete loss of hair. Growth of these mice was also definitely impaired. For a statistical evaluation, the results of the experiments of Series II-IV, or Series V and VI, respectively, have been grouped together. The average values from the groups *a* and *b* were then adjusted on the basis of the data from the corresponding controls which did not receive the isotope (groups *c* and *d*). The significance of the differences between these adjusted means was then estimated, using the *Chi*² method for the number of survivors at the 21st day and the *t* test of significance for the average length of survival (Table IV).

Discussion. It is apparent that the administration of pyridoxin to mice which are actually deficient in pyridoxin exerts a significant protection against the injurious effect of P^{32}. This protection is of about the same degree as that observed previously with the combined administration of vitamin B_{12} and folic acid to mice, placed on sulfasuxidine-containing diets and injected with P^{32}(2). It is possible that both groups of findings may be due primarily to a beneficial effect on the recovery of the bone marrow, although evidence for a specific role of pyridoxin in erythropoiesis is somewhat equivocal and restricted to certain animal species (see, for instance(8)). On the other hand, atrophy of the thymus and lymphoid tissue accompanied by changes in the white blood cells is a striking and constant finding in acute pyridoxin deficiency(9). It is tempting to compare our present observations with others(10), suggesting that the integrity of large sections of the lymphatic system (as by lead-shielding the spleen during exposure to X radiation) increases the survival of the animals and hastens the regeneration of hemopoietic tissues.

Summary. Mice placed on pyridoxin-free diets were injected with a single dose of radioactive phosphate (5-6 μc/g). In the animals maintained on a low protein diet (in which symptoms of vitamin deficiency did not appear), the administration of pyridoxin did not affect the survival. On the contrary a marked protection by pyridoxin against the injurious effects of P^{32} was observed in experiments in which the vitamin deficiency had been made more severe by adding a pyridoxin analog (desoxypyridoxin) to the low protein diet, or by increasing the requirements for the vitamin (high protein diets with added cystine or methionine). In these experiments the differences between the groups receiving and those

not receiving pyridoxin were larger than the differences which might result from a simple additive effect of the internal radiation and vitamin deficiency.

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Effects of Some Metabolic Analogs on Growth of Mumps and Influenza Viruses in Tissue Cultures.* (19423)

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The inhibition of viral multiplication by various metabolic antagonists in tissue cultures has been studied by several investigators, using a number of viruses(1-4). Indeed, this technic is a promising avenue of approach for studying the growth requirements of many viruses. Using this method, certain vitamin, amino acid, and purine analogs were investigated to determine if they would inhibit effectively multiplication of mumps and influenza viruses in cultures of chick embryonic tissue without serious toxic effects on the host tissue.

Methods. Cultures of 9- to 11-day-old chick embryonic tissue were prepared, employing a method similar to that of Earle(5). Perforated cellophane discs cut to size were placed in the bottoms of 10 ml Erlenmeyer flasks which were then autoclaved. Using whole embryo tissue for the cultures to be inoculated with influenza virus, and amniotic membrane tissue for those cultures to be infected with mumps virus, the tissues were minced with scissors in Hanks's(6) balanced salt solution without added sodium bicarbonate. The tissue fragments were then planted in the flasks underneath the cellophane discs. Two ml of nutrient solution composed of 2 volumes of Hanks's solution with sodium bicarbonate and one volume of ox serum ultrafiltrate, to which the virus was added, were then placed into each flask. The viruses employed were strains of mumps and influenza (PR8) viruses which had been cultivated in the allantoic sacs of embryonated eggs. Incubation of the tissue cultures was at 36°C. After 24 hours the infected nutrient

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