ly like those of PEGA (+S) and PE. The blood pressure responses to epinephrine were unchanged by the prior administration of any of these materials.

Discussion. The combination of glucose with β-phenylethylamine appears to change the qualitative toxicity of PE relatively little. However, quantitatively, the combination does appear to delay the onset of toxicity effects, and in the case of the levorotatory compound, PEGA (−15), molar toxicity is actually decreased. The blood pressure studies tend to confirm that PEGA (−15) is less active and more prolonged in its action than PE or PEGA (+8).

The quantitative change in activity that occurs in PEGA (−15) may be contrasted with the results of Swanson *et al.*(2). These workers in a study of the effect of optically active isomers of acids in combination with sympathomimetic amines, concluded that the configuration of the acid did influence the activity of optically active amine salts but did not influence the activity of optically inactive PE. While the degree of dissociation (ionization) of the amine salt as contrasted with the relatively undissociable covalent linkage of the glucosamine is great the glucosyl group does not act in the same manner as simple nitrogen substituents. Bovet(3) reports that all N-substituted PE derivatives in which the substituent was ethyl or larger were sympatholytic; none of the present materials is sympatholytic.

Summary. The glucosyl derivatives of β-phenylethylamine have been synthesized and compared with β-phenylethylamine with respect to toxicity and pressor effects. The levorotatory β-phenylethyl glucosamine is less toxic and more prolonged in its action than β-phenylethylamine or the dextrorotatory glucosamine.

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Distribution of P^{32} in Tissues of Normal Animals.* (19959)

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Many investigators are using radioactive phosphorus in biological studies but there is very little recent data available on the distribution of P^{32} in the various tissues. The most extensive investigations available up to the present time deal with the use of radioactive phosphorus in connection with the phospholipid metabolism, which was summarized by Chaikoff(1). As a preliminary study in connection with the effect of selenium poisoning on phosphorus metabolism we have investigated the distribution of P^{31} and P^{32} in the tissues of normal animals. In this review we would like to report our findings. Detailed studies on liver, kidney, spleen, heart, and brain will be given in subsequent reports.

Methods. Normal adult Sprague-Dawley male and female rats were used as experimental animals and injected intraperitoneally with 2.6684×10^8 counts per minute of P^{32}. The P^{32} (H_3PO_4) was received from Oak Ridge in weak HCl solution which contained 0.024 mg P per millicurie and was neutralized with NaOH before injection. Animals were sacrificed under nembutal anesthesia at 1, 2, and 12 hours after the administration of the isotope. The results are the average of 5 or

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TABLE I.
Distribution of P^{31} and P^{32} in the Tissues of Normal Animals at Various Time Intervals.

Organ	1 hr			2 hr			12 hr		
	P^{31}, mg %	P^{32},* g %	S.A.† × 10^4	P^{31}, mg %	P^{32}, g %	S.A. × 10^4	P^{31}, mg %	P^{32}, g %	S.A. × 10^4
Brain	309.6	.2	3.43	320.1	.3	5.25	299.3	.09	8.33
Heart	206.4	.33	87.44	199	.39	104.55	205.3	.19	42.15
Lung	259.3	.39	41.81	260.3	.70	82.24	264.8	.37	39.41
Liver	325.5	1.50	148.9	319	1.86	171.14	325	.99	84.72
Spleen	294.4	.48	50.38	299.2	.52	67.55	294	.50	52.60
Kidney	282.4	.94	114.28	287	1.27	130.5	290.8	.58	51.42
Stomach	197	.37	48.01	189.3	.52	78.13	185.2	.32	47.46
Small intestine	212.5	.55	65.86	201.3	.83	118.26	201.5	.42	53.79
Large intestine	178.8	.38	60.14	185	.71	108.99	181.2	.28	41
Uterus	184	.24	54.78	187.8	.70	108.66	193.4	.64	94.43
Testicle	193.9	.05	22.6				180.6	.09	42.1
Muscle	199.3	.14	14.32	201.4	.22	37.32	197.2	.17	22.52
Serum	7.5	.9	280.85	8.7	1.6	409.32	9.8	.03	88.31

* % of the administered dose recovered/g tissue.
† Specific activity = c/m/mg/P. The figures listed are to be multiplied by 10^4 to obtain the specific activity.

more rats in each time interval studied. The weighed tissues were divided in two parts and duplicate tissues were ashed with 10N H_2SO_4 and HNO_3 and cleared with a few drops of 30% hydrogen peroxide. The ashed tissues were diluted to volume and aliquots were used for the determination of the total phosphorus and the radioactive phosphorus. The blood was obtained by cardiac puncture and serum and cells were separated by centrifugation. The protein from the serum was precipitated with 10 percent trichloroacetic acid and the results presented are the acid-soluble phosphate of the serum. The total phosphorus was determined according to the method of Fiske and Subbarow(2). The activity of P^{32} was measured on dried aliquot of the sample in a Geiger-Muller counter. All samples were corrected for decay and the values reported are in terms of the activity at the time of injection. The specific activity is defined as the c/m/mg P.

Results. It appears from the data presented in Table I that the radiophosphorus uptake and the specific activity of the various organs show considerable variation. It is apparent that a considerable amount of the inorganic phosphate entered into the tissues at the end of the first hour. The optimum uptake in the tissues was reached at the end of the second hour. The rapid turnover rate of phosphorus in the serum is indicated by the study of the specific activity of the serum at 1, 2, and 12 hours. The specific activity at the end of the first hour was 280.85 x 10^4 and increased to 409.32 x 10^4 at the end of the second hour but at the end of 12 hours it decreased to 88.31 x 10^4. It is quite evident from the data that the phosphorus from the serum is rapidly transferred to the various tissues of the body.

According to some investigators the difference in the uptake and turnover rate of phosphorus in the tissues is related to the permeability of the tissue cells to phosphorus. Lungsgaard(3) studied the rate of rejuvenation of phosphorus compounds in the liver using radioactive phosphorus and from his studies concluded that there is a rapid rate of rejuvenation of the acid-labile phosphoric esters and penetration of the phosphate ion into the liver cell. We have obtained similar results in our studies on the phosphorylated ester in liver which will be reported in a future publication. Our present data are based on the radioactive phosphorus uptake and specific activity of the total liver, which contains many phosphorylated compounds which are rejuvenated at various rates. However, on the total tissue basis the liver utilized the largest amount of radioactive phosphorus among all the organs studied.

The different anatomical parts of the gastrointestinal tract showed considerable variation as to the uptake and specific activity of radiophosphorus. The small intestine with its

highly selective absorption contained the highest percentage of P^{32} and the highest specific activity followed by the large intestine and stomach. It appears that the uptake of phosphates by the gastrointestinal tract is directly related to the physiological function of the segment of this organ.

Although the brain and liver have approximately the same amount of organic phosphates. the liver contained almost eight times as much radioactive phosphorus per unit weight and time as the brain. The extent which phosphorus is taken up by the cells appears to depend on not only the total amount of phosphorus present in the tissues but on the permeability of cells to the phosphate ion. The brain seems to be almost a closed system with regard to the interchange of phosphorus with the body fluids.

The specific activity and the gram % uptake in the heart is much higher than in the skeletal muscle. However, the heart was not perfused and the difference may be due to the presence of residual blood within the organ. The permeability of muscle cells to inorganic phosphate is low according to the earlier investigators. Hevesy and Rebbe(4) showed that the phosphate penetrates the skeletal muscle cells very slowly and concluded from their studies that the specific activity of the total tissue inorganic phosphate, which includes both the extracellular and intracellular components, is not the true indication of the specific activity of the inorganic phosphate within the cell. Kalckar *et al.*(5) by using perfusion technic studied the rate of penetration and the rate of rejuvenation of organic phospho compounds of skeletal muscle and liver. They have estimated that the rate of penetration of phosphate in muscle was approximately one gamma of P per minute per g of muscle. However, as in our data, when the results are based on the total tissue uptake and the specific activity without regard to the intracellular and extracellular phosphorus the rate of turnover of phosphorus in the skeletal muscle is very low.

The radioactive phosphate administered in inorganic form is readily incorporated into the kidney. The rate of appearance and disappearance based on the percent uptake and specific activity of P^{32} in this tissue appears to be similar to that of liver but the magnitude is at a lower level. Perlman *et al.*(6) measured the deposition of phospholipid in the kidney after a single injection of P^{32} and found that the deposition and disappearance of the labeled phospholipid was slower in the kidney than in the liver and intestine.

The P^{32} distribution and specific activity in the spleen showed very little change at the time intervals studied.

The specific activity and gram % uptake of P^{32} in the lung showed an increase at the end of the second hour and at the end of 12 hours there was considerable decrease indicating a high turnover rate in this organ.

The male and female sex organs showed considerable variation as to uptake and specific activity. The uterus showed a higher percent uptake than the testicle. This would indicate that the rate of phosphorus metabolism in the testicle is very low.

In comparing the distribution of alkaline phosphatase in the various tissues as was reported by Kabat and Furth(7) with the differences in the uptake of the radioactive phosphorus in the tissues studied we have found it of special interest that tissues which contain large amounts of alkaline phosphatase have a higher specific activity and higher percent of P^{32} uptake than tissues which are low in alkaline phosphatase. Whether there is any correlation between these two factors it is difficult to state since the function of alkaline phosphatase in many tissues is not clearly understood.

Summary. The distribution and the specific activity of P^{32} in the various organs of normal animals was studied at 1, 2, and 12 hours after intraperitoneal administration of the isotope. The P^{32} was rapidly taken up by the serum and distributed in the various organs. It appears that the distribution of P^{32} was not directly related to the amount of phosphorus present in the tissue but depended on the permeability of the cells to the phosphate ion.

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Comparison of Eosinophil and Circulating 17-Hydroxycorticosteroid Responses to Epinephrine and ACTH.* (19960)

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Since relatively pure adrenocorticotropin (ACTH) has become available, the eosinophil response test has emerged as a commonly used and simple method of assessing adrenocortical function. The usual response to the injection of ACTH, Compound E, Compound F. epinephrine or insulin, and to non-specific stress stimuli is characterized by a reduction in the number of circulating eosinophils(1). This eosinopenic response to the administration of ACTH has been used as a major criterion indicating an intact adrenal cortex, with the absence of eosinopenia interpreted as indicating adrenal cortical insufficiency. It has been assumed that in order to elicit an eosinopenic response to epinephrine or non-specific stress stimuli an intact anterior pituitary and adrenal cortex must be present. The postulation has been advanced that these stimuli act through the hypothalamus upon the anterior pituitary causing release of ACTH, which in turn stimulates the adrenal cortex to secrete its hormones(2). The hormones secreted by the adrenal cortex which are generally believed to effect the eosinopenia are the 17-hydroxycorticosteroids(3-7). However, because epinephrine eosinopenia occasionally has been induced in states of impaired function or absence of the adrenal cortex(1,8) the validity of this assumption has been questioned.

Recent development of methods allowing direct measurement of circulating adrenal hormones provides a technic permitting a more definitive evaluation of the relationship between eosinophil and adrenal steroid responses to a stimulating agent. In the present study the circulating plasma concentration of 17-hydroxycorticosteroids has been measured and the effects of ACTH or epinephrine injection on the levels of these steroids and of eosinophils have been compared in children. It should be emphasized that the influence of specific disorders on the type of adrenal response is of secondary interest only, and that the point of primary concern is the comparison of the responses of circulating eosinophils and 17-hydroxycorticosteroids.

Methods. Healthy children and children with various disorders have been used in this study. Responses of eosinophils and 17-hydroxycorticosteroids to the injection of .01 mg/K of epinephrine hydrochloride or 25 I.U. ACTH were studied. Eosinophils were determined by the method of Randolph(9) and circulating plasma 17-hydroxycorticosteroids by Nelson and Samuels' modification(10) of their method for whole blood(11). Total eosinophil counts were done at 0, 1, 2 and 4 hours. The minimum value obtained, expressed as per cent decrease from the control value, is used in the data of the tables. The circulating plasma 17-hydroxycorticosteroid values were obtained at 0 and 2 hours, because

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