red cell volume of 3.10 cc/100 g body weight was produced in these animals as compared to the average of 2.38 cc/100 g body weight for normal controls at this same age.

The average total red cell volumes for the 2 groups of normal controls differ slightly; however, when significance tests were applied, this difference was shown not to be significant.

The adrenal weights were measured in the animals autopsied at 206 days of age. As can be seen from the table, these weights are directly related to the red cell volume data. The untreated hypophysectomized rats had an average adrenal weight of 11.5 mg (2 adrenals). In the hypophysectomized rats treated with ACTH the adrenal weights gave the same average (57 mg) as did the normal controls. The normal rats treated with ACTH showed an increase in adrenal weight with an average of 116 mg.

These data are interesting in view of the fact that Sundstroem(10) found, along with the well known polycythemia, greatly increased adrenal weights present in rats placed in an atmosphere of reduced oxygen tension.

Conclusions. 1. Administration of ACTH prevents the decrease in the total circulating red cell volume which is normally found in hypophysectomized rats. 2. Administration of ACTH for 116 days to normal rats elevates the total circulating red cell volume to approximately 1.3 times that of the normal untreated controls.

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P^{32} Localization in the Intestine. (18602)

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Radioautographic and histochemical observations have been made on sections of frozen-dried rat and mouse intestine containing P^{32}. The tissue sections were prepared and mounted and radioautographs were made using procedures reported previously(1,2). These procedures are designed toward qualitative and quantitative preservation and retention at the original sites of tissue constituents. The radioautographs of rat and mouse duodenum and small intestine have shown a more striking concentration and localization pattern with P^{32} than has been observed for other soft tissues. This localization occurs in the glands of the mucosa with the greater concentration at the more basal groups of cells (Fig. 1).

Studies of the solubility of localized P^{32} in frozen-dried sections of rat intestine have been reported(3). The localized P^{32} exhibits the same general solubilities as the background P^{32} in other regions of the tissue, indicating a similar chemical form. The P^{32} is not in phospholipid form as it does not dissolve in organic solvents; other solubility tests have indicated the presence of free phosphate ions and at least a partial protein linkage. The use of formalin or Bouin's solution as a fixative results in a radioautograph showing the same general type of localization pattern, but of diminished intensity as compared to the results with frozen dried tissues. This would be expected on the basis of solubility data.

Observations made at varying time intervals from isotope administration to killing the animal have shown that the typical localization pattern is present in the intestine at 30

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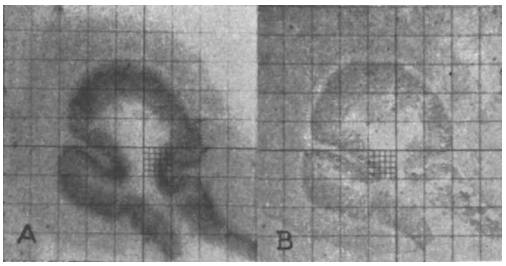

FIG. 1a. Radioautograph of rat intestine prepared from an approx. 2 μ tissue section. The tissue was mounted on a cover glass which was clamped so that it faced the emulsion of a contrast lantern slide. Direct contact of the tissue with the emulsion was prevented by placing "spacers" which consisted of strips of tantalum foil approx. 5 μ in thickness around the tissue section. The tissue and emulsion surfaces were therefore separated by a distance of approx. 3 μ. Isopentane at —160 to —195°C, paraffin, and xylol were the only reagents which came into contact with the tissue previous to the radioautographic exposure. 237 μc of carrier free P^{32} were administered subcutaneously to a 65 g rat for a $3\frac{1}{2}$ hr time interval. A 16-day exposure was used which was started 9 days following the isotope injection.

FIG. 1b. Feulgen stained tissue section which corresponds to the radioautograph shown in *a*. The dark areas which show the most intense reaction are in the basal mucosal layers, the positive reaction being located in the nuclei of the cells.

believe that this evidence identifies the P^{32} with that which is being incorporated into newly formed desoxyribose nucleic acid molecules in the rapidly dividing mucosal cells. However, from a quantitative standpoint, chemical analyses(4) have shown that the P^{32} incorporated into newly formed nucleic acid is only a minor fraction of the total intestinal P^{32} uptake. The radioautographs show that the major fraction of the P^{32} present in the intestine is distributed in the regions of high nucleic acid content. This suggests that localization of P^{32} in other chemical form (probably inorganic) occurs previous to or associated with the nucleic acid synthesis.

Other histochemical tests, on the other hand, have shown that the P^{32} localization does not correspond in position with the sites of high phosphatase concentration (Fig. 2a, b, c); and therefore that reactions involving this enzyme are not involved in the functional concentration of P^{32}.

This observed high local concentration of

FIG. 2a. Radioautograph of frozen-dried rat intestine. The tissue, in the process of preparation, was exposed only to Isopentane at —160 to —195°C, paraffin, and xylol. 500 μc were administered subcutaneously to a 120 g rat for a 4-hr time interval. A 9-day exposure to contrast lantern slide was started 10 days following isotope injection.

FIG. 2b. A routine hematoxylin and eosin stain of a tissue section which corresponds to the radioautograph shown in *a*.

FIG. 2c. Alkaline phosphatase (Gomori) reaction on a tissue section which corresponds to those shown in *a* and *b*. The sites of high phosphatase concentration are shown as darkened areas. Note these areas do not correspond in orientation to those of P^{32} localization shown in *a*.

minutes, 2, 4, 8, 24, and 48 hours. Some of the rat and mouse intestine sections were stained with the Feulgen reagent following radioautographic exposure. The pattern of localization of P^{32} in the radioautograph was found to correspond exactly with the pattern of localization of desoxyribose nucleic acid in the Feulgen stained sections (Fig. 1a, b). We

P^{32} associated with the high rate of nucleic acid turnover in the intestine is of particular importance in relation to the administration of P^{32} during various types of treatment and diagnostic procedures (for polycythemia, leu-

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kemia, tumors, etc.), and should be considered as a potential radiation hazard in these procedures.

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Irradiation Produced Rise in Blood Radioiodine Concentration Following Ingested Therapeutic Dose for Metastatic Thyroid Carcinoma.* (18603)

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In the study of physiological and pathological processes using radioactive substances, a clear differentiation must be made between the effects of tracer and therapeutic doses. While tracer doses have only a negligibly destructive effect upon living tissue, in therapeutic doses one deliberately administers a sufficient quantity of the isotope to produce tissue damage in selected areas.

In this paper we are concerned with the delayed rise in the blood radioiodine, usually occurring 4 to 8 days after ingestion of a therapeutic dose, and which we attribute to irradiation damage to the thyroid gland or thyroid tumor tissue. This rise is apart from the initial rise due to absorption of the isotope into the blood stream and a subsequent increase from 1 to 3 days later found in tracer studies by Pochin(1,2) and other investigators(3-5) and which they ascribe to the release of labeled thyroxine from the thyroid gland in the course of iodine metabolism of euthyroid and hyperthyroid individuals. McConahey, Keating and Power(6) have studied the effect of tracer and therapeutic doses of radioiodine for periods from 1 to 7 days. There is no reference in their paper to the rise in blood I* concentration reported here. They state that "one may be justified in assuming that the results (with therapeutic doses) observed correspond at least qualitatively to physiologic conditions." However, Marinelli, Trunnell and their associates(7,8) have occasionally observed transient hyperthyroidism with a rise in protein bound plasma iodine after administration of therapeutic doses of I^{131} to metastatic thyroid carcinoma patients. Marinelli and Hill(9) attribute this to "the release of thyroid hormone by functional cancer tissue under irradiation." This explanation is supported by the study on rats by Feller *et al.*(10), who have reported a drop in the stable iodine content of the thyroid and a rise in plasma protein bound iodine following intraperitoneal injection of massive I^{131} doses.

As was recently reported by one of us,† we have determined the pattern of radioiodine

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