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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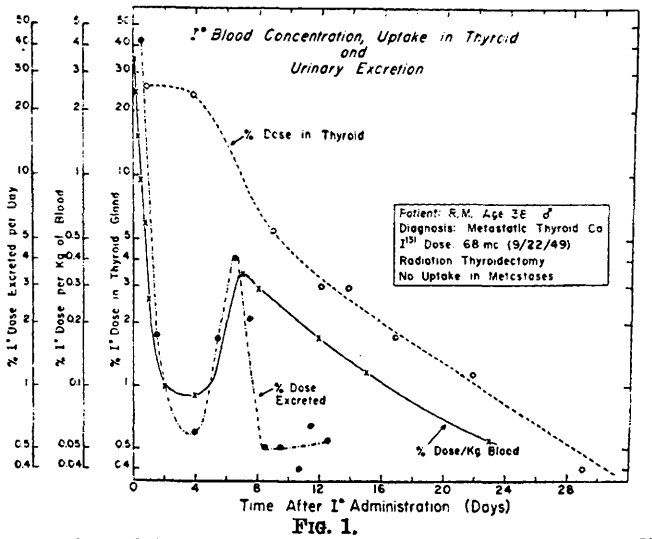

FIG. 1.

Demonstration of irradiation produced rise (IPR) in blood radioiodine concentration for patient receiving thyroidectomizing I^{131} dose. Note rise in blood I* concentration and urinary excretion occurring simultaneously with the sharp drop in radioiodine content of the thyroid gland.

concentration in the blood of patients with metastatic thyroid carcinoma who received large doses (50-200 mc) of radioiodine‡ during radiation thyroidectomy, during irradiation of metastatic thyroid carcinoma lesions in the course of radioiodine therapy, and after the cessation of I* uptake in both the non-neoplastic thyroid gland and the metastases. Weighed blood samples were taken at intervals of decreasing frequency after the oral administration of radioiodine, and their activity was determined by gamma ray counting. The per cent dose present per kilogram of blood was obtained by comparing the activity of the sample with that of an appropriate aliquot of the administered dose.

In the treatment of metastatic thyroid carcinoma, a thyroidectomy, surgical or radiation, is performed in order to induce or increase the function of the metastases, and hence their ability to localize radioiodine selectively(11). When the thyroidectomy is to be accomplished by internal irradiation, the patient is given a large dose of radioiodine. As the radioiodine is absorbed from the stomach, the blood I* concentration rises within a few hours to a maximum value. We find that a sharp drop in the radioiodine content of the thyroid gland occurs 4 to 8 days following ingestion of the isotope. A simultaneous rise in the blood I* concentration and in the urinary radioiodine excretion is observed. An illustrative case is shown in Fig. 1.

For reasons presented below we designate this secondary rise as the *irradiation produced rise* (IPR). Its magnitude is taken to be the ratio of the maximum observed blood I* concentration (% dose/kg) to the concentration immediately preceding the rise. Rises of less than 1.10 were not considered significant. The IPR's observed in this series have ranged from 1.12 to 3.90 (Table I).

High I* concentration in tissue will result in an intense local irradiation and hence considerable radiation trauma. We attribute the rise in blood and urinary I* concentration to the release of radioiodine from the disintegrating irradiated thyroid tissue. It is, therefore, not surprising that, in general, the IPR increases with the quantity of radioiodine retained by the thyroid. In our opinion, the

† S. M. Seidlin, Sixth Intern. Cong. of Radiology, July 23-29, 1950, London, England.

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TABLE I. Incidence of Secondary Rise in Blood I* Concentration (IPR) in Patients Receiving Therapeutic Doses of Radioiodine.

Group	Functional status of thyroid gland and metastases	No. of patients	No. of doses	Doses exhibiting IPR* No.	%	Avg IPR
A	Radiation thyroidectomy†	7	7	7	100	2.00
B	Low thyroid uptake‡ No demonstrable uptake in metastases	2	2	1	50	1.25
C	No demonstrable uptake in thyroid Uptake in metastases	13	33	8	24	1.35
D	No demonstrable uptake in thyroid No demonstrable uptake in metastases	4	4	0	0	—

* Only IPR $\geq$ 1.10 considered significant.
† Radioiodine uptake in thyroid $\geq$ 10% administered dose.
‡ Definite but slight I* uptake in thyroid, $<$ 10% of administered dose.

rise in the blood iodine concentration observed after administration of tracer doses of radioiodine to normals plays an insignificant role in the above-described phenomenon. We have also observed this IPR in totally thyroidectomized patients with functioning thyroid carcinoma metastases (Curve B.N., Fig. 2). As therapy proceeds, the quantity and the viability of functioning tissue decreases and along with it the magnitude of the IPR. The latter finally vanishes with the disappearance of the residual functioning tumor tissue (Curve S.W., Fig. 2). At this stage of therapy, the blood radioiodine concentration rapidly falls to very low values and there is no secondary rise.

In our series, the blood of 21 patients was studied for 5 or more days following administration of 46 therapeutic doses of radioiodine. Table I shows the incidence of secondary rises in blood I* concentration. A definite correlation is shown between the frequency and magnitude of the IPR and the functional level of thyroid tissue, neoplastic or non-neoplastic, present in the body. Since we have not found a secondary rise in blood I* concentration in the absence of functioning thyroid tissue, the occurrence of such a rise in a totally thyroidectomized patient might be considered evidence of viable functioning thyroid carcinoma metastases. It is apparent that for the usual cases, where there is Geiger counter or radioautographic evidence of uptake in the metastases, the IPR is merely an additional diagnostic aid. Similar methods for detection of metastases in other types of tumors might be developed should radioactive substances with specific affinity for these tumors be discovered.

Summary. Four to 8 days after ingestion of therapeutic doses of radioiodine (50-200 mc) by patients with metastatic thyroid carcinoma, a rise occurs in blood radioiodine concentration which we attribute to irradiation damage to the thyroid gland or thyroid

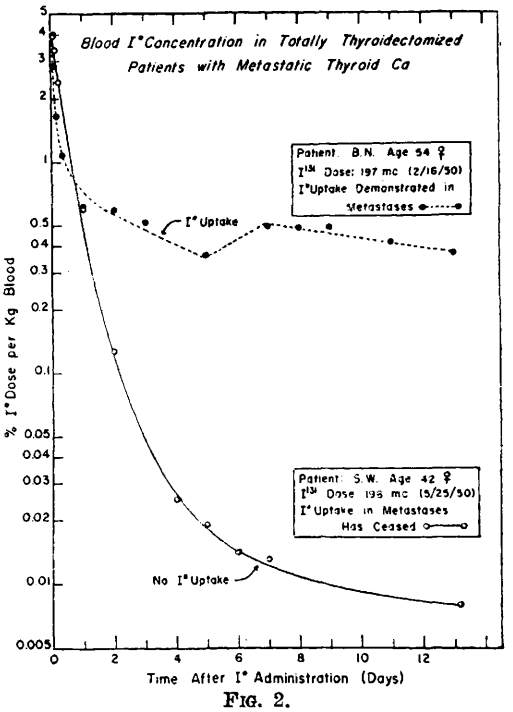

FIG. 2.

Dependence of IPR and I* blood level on function of thyroid metastases. The higher level and the IPR are observed in the patient (B.N.) having radioiodine uptake in metastases.

tumor tissue. This increase we have termed the irradiation produced rise. In a series of patients the magnitude of the IPR in general has been found to increase during radiation thyroidectomy with the quantity of radioiodine retained by the thyroid. In a given patient the magnitude and incidence of the IPR decrease with successive doses as functioning thyroid tissue is progressively destroyed. Finally, when there is no longer any functioning tissue, as demonstrated by absence of I* uptake, the blood radioiodine concentration rapidly falls to very low levels and there is no IPR.

The blood of 21 patients, in various stages of therapy, was studied. For all of 7 radiation thyroidectomy doses, significant IPR's were found; in thyroidectomized patients with functioning metastases, IPR's were demonstrated in 8 of 33 doses. However, no such rise in blood iodine concentration was observed following four doses to thyroidectomized patients lacking demonstrable I* uptake. Since no such rise is found in the absence of functioning thyroid tissue, either neoplastic or non-neoplastic, the occurrence of an IPR in a thyroidectomized patient may, therefore, be considered evidence of the existence of viable functioning thyroid carcinoma metastases.

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Changes with Age in Amino Acid Composition of Arterial Elastin.* (18604)

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During a study of human arteriosclerosis it became evident that changes in the media of the aorta preceded the formation of intimal plaques(1,2). In particular, the elastic tissue of the tunica media, free of minerals in youth, became heavily calcified in adult and aging individuals.

Elasto-calcinosis, as the process of calcification of arterial elastic tissue has been termed recently(1), is accompanied by a number of alterations in the morphologic appearance and tinctorial reactions of elastic fibers. In the light of these differences, we have initiated a program to compare the chemical properties of young and old elastic fibers. The changes with age in the amino acid composition of human arterial elastin are now being reported.

Experimental. Analytical procedures. Elastin was prepared from human aortas (aortic elastin) and pulmonary arteries (pulmonary elastin) and calcium determinations were made on ashed samples by methods which have been described previously(3). The nitrogen contents were determined and the amino acid distributions were made by microbiological and paper chromatographic methods, the details of which have also been given previously(4). Several phosphate determinations on the ash from elastin gave a molar Ca:P ratio of approximately 3:2. For purposes of calculation it was, therefore, assumed

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