Technical Papers

Sublethal Total Body Irradiation and I^{131} Metabolism in the Rat Thyroid

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Histological examination of thyroids taken at autopsy from burros exposed to high levels of total body irradiation invariably has revealed a microfollicular gland with colloid depletion and tall acinar epithelium, indicative of extreme hyperthyroidism. In apparent agreement with these observations, Evans *et al.* (*1*) reported that 500–1000 r of total body x-irradiation caused an increase in the uptake of I^{131} by rat thyroids. However, Botkin *et al.* (*2*) found a progressive decrease in thyroid and serum protein-bound I^{131} to subnormal levels following a small initial increase in rats subjected to 1000 r of x-irradiation.

Consequently, it became of interest to study the I^{131} metabolism in the thyroids of rats exposed to total body irradiation, with particular reference to sublethal levels. Further, it was thought worth while to determine the relative amounts of I^{131} present in the protein-bound and thyroxine fractions as an index of the rate of thyroid hormone formation.

Groups of approximately 100 mature male Sprague-Dawley rats (150–200 g) were subjected to 333 and 665 r of gamma rays from Co^{60} on a special large animal exposure field (*3*) and to 500 r of x-rays from a General Electric Maximar[1] x-ray machine. The Co^{60} gamma rays were of 1.25 Mev mean energy shielded for the absorption of beta particles and a 40 cm minimum target distance. The x-rays were 250 kvp, with 1.0 mm of aluminum and 0.5 mm copper filtration and a target distance of 50 cm. The rate of administration for both x-rays and Co^{60} gamma rays was at approximately 34.5 r/min. The animals were kept in ventilated lucite boxes and exposed dorsally to the x-rays and bilaterally to the gamma rays. Feed (Rockland) and water were given ad libitum. All experimental groups were compared with nonirradiated controls.

I^{131} was injected intraperitoneally (100 μc/rat) at periods of 1, 7, and 30 days following irradiation. In order to follow the rate of formation of thyroid hormone, 6–10 irradiated rats and 4–6 controls were sacrificed at intervals of 1, 7, and 24 hr after administration of I^{131}.

Of each thyroid removed at the time of sacrifice, one lobe was placed in 10% formalin for histological study and the other lobe pooled with similar samples from the same group. The pooled thyroids were macerated and aliquot portions taken for the determination of total, protein-bound, and thyroxine I^{131}. Protein-bound and thyroxine fractions were obtained by the method of Taurog and Chaikoff (*4*). All measurements were made by direct solution counting with a shielded G-M tube. Blood samples were taken by cardiac puncture and treated in a similar manner.

A response was observed only in the thyroids removed from rats one day after exposure to 665 r of Co^{60} or 500 r of x-rays. At the 7- and 30-day periods the thyroid I^{131} levels of the irradiated rats were the same as those in the controls. At no sacrifice period did the serum I^{131} levels of the irradiated and control rats differ. No response could be detected in the rats exposed to 333 r of Co^{60}.

TABLE 1.

Hours after I^{131} injection	Total I^{131}	Protein-bound	Thyroxine	Total I^{131}	Protein-bound	Thyroxine
	665 r—Co^{60}			Control		
1	11.3	8.5	2.4	10.8	8.4	2.9
7	36.5	29.8	9.3	23.8	13.3	6.0
24	45.3	28.9	14.1	20.7	12.5	6.3
	500 r—X-ray			Control		
1	19.9	9.8	2.1	7.7	4.6	1.4
7	38.9	26.6	6.4	21.7	—	6.0
24	119.	56.8	22.0	30.4	18.2	7.0

In Table 1 comparative values are presented for the uptake and binding of I^{131} by the thyroids of rats 1 day after 665 r of gamma and 500 r of x-irradiation. These values are expressed as a percentage of the injected I^{131} per 100 mg of fresh thyroid tissue. The thyroids of rats receiving Co^{60} irradiation accumulated about twice as much as the controls, and the thyroids of the x-irradiated rats showed a fourfold increase over the controls. Moreover, the I^{131} in the protein-bound and thyroxine fractions increased concomitantly with the total I^{131} in both groups of irradiated rats, indicating that there was no impairment in the mechanism of thyroid hormone synthesis.

These results are consistent with the concept that the stimulus to the thyroid is indirect and not caused by the radiations per se. This concept is further sus-

[1] Through the courtesy of Herbert D. Kerman, Medical Division, Oak Ridge Institute of Nuclear Studies (present address: University of Louisville, Louisville, Kentucky).

tained by the fact that the burro thyroids mentioned above resemble those responding to large amounts of thyrotrophic hormone but showed no signs of radiation damage.

The report of Evans *et al.* (*1*) in which shielded thyroids of total body x-irradiated rats had an increased I^{131} uptake is of course much stronger evidence of the indirect effect of ionizing radiations upon that organ. It does not, however, eliminate the possibility of a direct effect upon the release of thyroid-stimulating hormone by the anterior pituitary.

The fact that thyroids of burros after lethal doses of radiation appeared to be receiving a much greater stimulus than the two- to fourfold increase measured in this study, plus the fact that none of the present rat thyroids showed histological evidence of stimulation, suggests that the extent of the thyroid response to total body irradiation is probably a function of the amount and/or rate of irradiation. The observation that there is a difference in the response of the thyroid to photons of different quality (i.e., that x-rays were more effective than Co^{60} gamma rays) agrees with lethal dose studies (*5*) and studies on skin (*6*) and lens of the eye (*7*) sensitivity.[2]

References

1. EVANS, T. C., CLARKE, G., and SOBEL, E. *Anat. Record* **99**, 577 (1949).
2. BOTKIN, A. L., *et al. Endocrinology* **50**, 550 (1952).
3. WILDING, J. L., SIMONS, C. S., and RUST, J. H. *Nucleonics* **10**, 36 (1952).
4. TAUROG, A., and CHAIKOFF, I. L. *J. Biol. Chem.* **163**, 323 (1946).
5. MCLEAN, F. C., RUST, J. H., and BUDY, A. M. *Military Surgeon* **112**, 174 (1953).
6. MACCOMB, W. S., and QUIMBY, E. H. *Radiology* **27**, 196 (1936).
7. ALTER, A. J., and LEINFELDER, P. J. *Arch. Ophthalmol. (Chicago)* **49**, 257 (1953).

[2] John J. Lane and Moyer Edwards assisted in the chemical procedures. Charles S. Simons, Oak Ridge Institute of Nuclear Studies, calculated the dose of Co^{60} gamma rays. This report is published with the approval of the director of the Experiment Station, University of Tennessee. The I^{131} was obtained from the Oak Ridge National Laboratory on allocation from the U:S. Atomic Energy Commission.

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The Salinity of the Ocean

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Many authors (*1–3*) have noticed that the relative amounts of water, nitrogen, and volatile halides of volcanic origin approximate the composition of such volatiles in the atmosphere and hydrosphere. This fact has been used as a basis for arguments that the ocean was formed by the steady surface accretion of water from volcanic sources (*3*).

If the ocean were formed by volcanic action continued for a long time, it might be possible that nitrogen and halide too were collecting in the atmosphere and ocean respectively during the time the ocean was forming.

TABLE 1.

Amount in metric ton-atoms $\times 10^{-14}$	
Halide in ocean	7.6
Nitrogen in atmosphere	2.8

Though the terrestrial concentration of nitrogen is low compared to cosmic abundance of the element (*4–6*) it is quite plentiful compared to the inert gases.

Urey (*7–9*) suggested that nitrogen could be retained on the earth to the extent it is, as a metal nitride or as an ammonium halide. Both compounds could be held within the earth's crust under non-equilibrium conditions. Because the ammonium halides dissolved in water hydrolyze somewhat, they form acidic solutions that can rapidly penetrate basic rock. Many metal ions hydrolize too, but most of them also deposit insoluble silicates or carbonates which would lower the permeation rate of the solutions through the basic rock mantle.

By the time the water solution which originally might have contained ammonium chloride had reached the earth's surface, the solution would have become more basic and would consist of soluble alkali or alkaline earth halides and some ammonia besides gaseous hydrogen and nitrogen. The amount of nitrogen and hydrogen relative to ammonia would depend on the temperatures the solutions encountered.

As the remaining ammonia can be decomposed photochemically, provided that hydrogen can escape from the earth's gravitational field (*9*), atmospheric nitrogen plus some organic material results if reducing gases such as methane are present. The halide will be found in the sea. The amounts of nitrogen in the atmosphere and the halide in the sea should correspond on the basis of this picture. The degree of agreement is shown in Table 1. The weight of nitrogen in the atmosphere was taken from the work of Humphreys (*10*). The amount of halide in the ocean from Sverdrup, Johnson, and Fleming (*11*).

Since the amount of nitrogen is low relative to halide, nitrogen either may have escaped from the atmosphere with the hydrogen (*9*) or there is another accumulation of nitrogen on the earth.

The only accumulations that would appear to be large enough to contain 4.8×10^{14} metric ton-atoms of nitrogen would be the deep sea deposits. Based on sedimentation rates, Kuenen (*12*) estimated that deep-sea deposits laid down from Cambrian time should be of the order of 3 kilometers deep when compacted. Such deposits covering almost three-quarters (*13, 14*) of the area of the globe would weigh 1.8×10^{18} metric tons, assuming the compacted density of the deposits comparable to sandstone.

The most complete analyses of nitrogen in deep sea deposits are those described by Bradley (*15*) for the Globigerina ooze. The mean values for 11 cores was $0.022\% \pm 0.0012$ nitrogen of weight of the sediment (of about 75% porosity). No perceptible variation of nitrogen percentage with depth except that