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3 August 1962

Minimal Dosage of Iodide Required To Suppress Uptake of Iodine-131 by Normal Thyroid

Abstract. Sodium iodide was given in increasing doses to mentally defective children with normal thyroid function. Maximal suppression of iodine-131 uptake was achieved with 1500 to 2000 micrograms of iodide per square meter of body surface per day, but quickly rebounded when iodide was discontinued. This minimal effective dose is important if countermeasures against fallout are employed.

The release of radioactivity into the atmosphere from nuclear explosions in the recent past has created an acute awareness of the problem of human protection from such radiation. Radioactive iodine (I^{131}) is one of the principal contaminants in fallout (*1*). Government health agencies and others have considered several countermeasures for reducing the hazard of such radiation in humans. One of the most practical methods considered has been the suppression of thyroid function to prevent the retention by the thyroid of radioactive iodine regardless of the route by which it gains entrance into the blood stream. The use of iodide added to milk or other vehicles is obviously a first line of defense, but to employ this as a prophylactic measure it is desirable to know the minimal effective daily dosage of iodide. Surprisingly, a search of the literature as well as consultation with the subcommittee on countermeasures of the National Advisory Committee on Radiation (*2*) revealed the stark fact that the minimal effective oral dose of iodide for suppression of radioactive iodine uptake by the normal thyroid was unknown.

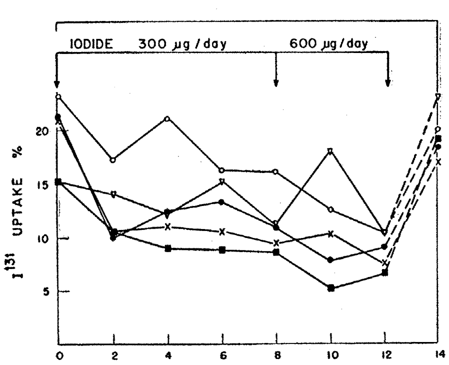

Fig. 1. Iodine-131 uptake by the thyroids of 2-year-old children given sodium iodide, 300 μg/day over an 8-week period, followed by 4 weeks of 600 μg daily, and the uptakes 2 weeks after discontinuation of iodide.

It is the purpose of this paper to present data acquired from observations on children, which define this minimal effective dosage of iodide required to suppress the avidity of the normal thyroid for radioactive iodine, and the time required to achieve such suppression.

The studies were carried out between 14 December 1961 and 14 April 1962 on children at the Wrentham (Massachusetts) State School, which is a hospital for long-term care of mentally defective children. We chose this population of children because it was desirable to secure children living under constant conditions of environment, diet, and iodide uptake. Their salt supply was found to be free of iodine.

The children were selected in three age groups (see Table 1) for study only if their thyroid function was normal clinically, and as judged by protein-bound iodine and radioactive iodine uptake (I^{131} uptake). None of the children had an enlarged thyroid. Iodide was administered orally as sodium iodide in aqueous solution, pipetted from a stock solution.

The effect of a single dose of 1500 $\mu g/m^2$ of iodide was studied on a separate group of seven children to see how soon one can get suppression of I^{131} uptake. Table 1 shows the age groups studied and the doses of iodide administered daily.

The protein-bound iodine was determined at the beginning and end of the experiment in all children. Twenty-four-hour urinary excretion of iodide was measured in eight children at the beginning and end of the observations. Measurements of 24-hour I^{131} uptakes were done before the administration of iodide and repeated every 2 weeks during iodide administration until either the uptakes decreased to approximately 5 percent or until there was no demonstrable change in successive uptakes.

Table 1. Number of children in each age group and their daily dose of iodide.

Sub-group	Dose (μg)	Children (No.) Group I (1–3 yr)	Group II (4–6 yr)	Group III (9–11 yr)
A	100	5	5	4
B	300	5	5	5
C	600	5	10	5
D	1000	5	4	5

The iodide was then discontinued and one or more measurements of I^{131} uptakes were made during subsequent weeks. In subgroup B of groups I and II, when the I^{131} uptake had become stabilized on 300 μg of iodide daily, the dose was increased to 600 μg daily before discontinuation.

The tracer doses of 1 μc of I^{131} were given orally. Standard and patient background counts were done before each tracer, and corrections were made in the calculations.

The mean protein-bound iodine was 5.5 μg per 100 ml before and 5.9 μg per 100 ml after iodide administration; the corresponding values for total iodine were 6.4 and 7.4 μg per 100 ml. At the end of the investigation 24-hour urinary excretion of iodine was considerably increased from the pretreatment mean value of 176 μg, depending upon the dose of iodide given.

The I^{131} uptakes by the thyroids of 2-year-old children given 300 μg of iodide daily are shown in Fig. 1. The maximum change occurred at 2 weeks with some further fall during the next 2 to 4 weeks when the uptakes levelled

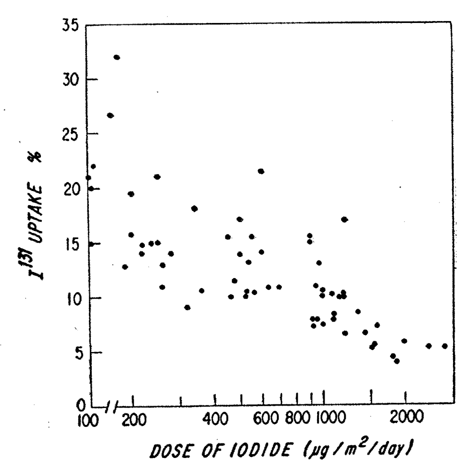

Fig. 2. Each dot represents from the ordinate the uptake of radioactive iodine by one child at the end of 2 weeks administration of iodide. The abscissa gives the dose in micrograms of iodide per square meter of body surface per day.

off. An increase of dose to 600 μg daily brought about further suppression. Noteworthy is the rapidity and uniformity with which the uptakes went back to their original levels or higher when iodide was discontinued. Figure 1 is representative of the results obtained in the other children except that the degree of suppression achieved was in direct correlation with the dose of iodide and size of the child. This relation is shown graphically in Fig. 2, where the I^{131} uptake after the second week of iodide administration is represented on the ordinate. Each dot represents the response of one child. It is evident that the maximum suppression is achieved with a dose of iodide of from 1500 to 2000 $\mu g/m^2$ per day. On this dose the minimum uptake of about 5 percent was reached in 2 to 4 weeks, at which point the neck and thigh radioactivity counts were approximately the same and the neck-to-thigh ratio was 1. Even after these higher doses, as soon as the iodide was stopped, the uptakes rebounded to near pretreatment levels. Increasing the dose to over 2000 $\mu g/m^2$ per day did not increase either the rate or the degree of suppression.

When a single dose of 1500 $\mu g/m^2$ was given an hour before the tracer dose, the uptakes 24 hours later fell to about 50 percent of their control values. The dose of iodide used in these investigations did not cause any toxic effects.

The following correlation of ideas emerged from the data obtained in this study. First, it became apparent that the response with respect to suppression of uptake of radioactive iodine is related to the magnitude of the dose of stable iodide. In turn, this dose was related to the size of the individual regardless of age. For this reason, we employed the surface area of the body as an index of the thyroid mass. Perhaps in the normal population correlation with age might be possible, but in the group investigated age loses its significance since mentally defective children are usually physically retarded. It was found that the minimal effective dose of iodide required to suppress completely the uptake of radioactive iodine by the normal human thyroid was 1500 to 2000 $\mu g/m^2$ per day. Thus for the adult, the minimal effective daily dose of iodide becomes 3 to 4 mg and for children 1 to 2 mg. Suppression of uptake begins almost immediately after the oral administration of these larger doses and by 24 hours, a 50-percent reduction is achieved. Subsequently, there is a gradual decrease in uptake to a minimal value of 5 percent in 4 to 6 weeks.

There was no relation in most of the individuals between the degree of suppression and the radioactive iodine uptake before treatment.

A surprising finding was the rebound of uptake within a week after iodide administration was stopped. In some instances, these uptakes were even higher in subsequent weeks, and there is a suggestion that after very small doses of iodide (100 μg), the uptakes reached were higher than obtained before administration of iodide. This indicates the necessity for continued daily administration of iodide in adequate (1500 to 2000 $\mu g/m^2$) doses for the protection of individuals exposed to possible contamination with I^{131}.

Toxic effects of iodide from doses of this order of magnitude given over relatively short periods of time are extremely unlikely. We know from clinical experience (*3*) that toxic effects of iodide are not observed with doses of 100 mg of iodide per day given to children over a course of years. Iodide goiter has been observed (*4*) to occur only following daily doses of several hundred milligrams of iodide administered for years, a fact which indicates that it is desirable to have a ceiling on the doses used for prophylactic purposes (*5*).

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16 July 1962

Two Meteorites of Unusually Short Cosmic-Ray Exposure Age

Abstract. The chondrites Cold Bokkeveld and Farmington seem to have reached the earth less than 200,000 years after they left their parent body. Either these meteorites came from the moon, or, more probably, the collision life times of interplanetary objects are occasionally much shorter than has been assumed heretofore.

Eberhardt (*1*), Stauffer (*2*), and Zähringer (*3, 4*) have recently measured the noble-gas content of over 50 stony meteorites. A plot of the Ne^{21} produced by cosmic rays in these meteorites, corrected for any primordial Ne^{21} present, is shown in Fig. 1. If differences in shielding, which are not likely to exceed 30 percent, are neglected, the Ne^{21} content should be proportional to the period of time during which the meteorite was freely exposed to cosmic rays—that is, to the "cosmic-ray exposure age" of the meteorite. The production rate of Ne^{21} in chondrites has been variously estimated as 2.5, 4, and 5×10^{-9} cm^3 (STP)/g per million years (*1, 2, 5*). Taking the latter value, we can convert the Ne^{21} contents shown in Fig. 1 to the exposure ages indicated on the abscissa. These values are probably accurate to within a factor of two.

Two meteorites, Cold Bokkeveld and Farmington, have much lower Ne^{21} contents than any of the others. This may well indicate an exceptionally short exposure age, but since both meteorites are rather dark in color, an alternate explanation would be that they lost gas because of solar heating at perihelion (*6*). To decide between these alternatives, I measured the Al^{26} content of two samples of these meteorites, weighing 44 and 84.5 grams, respectively (*7*), by γ-γ coincidence spectrometry, using instruments and nondestructive techniques described previously (*8*).

If the true exposure age of these meteorites were long compared with the half-life of Al^{26} (740,000 years), then their Al^{26} content should approach the saturation value, N_∞, of about 54 disintegrations per minute per kilogram, which is typical of chondrites (*9*). (In the case of Cold Bokkeveld, only about 39 dpm/kg would be expected, owing to its lower Si and Al content.) For shorter exposure ages, on the other hand, a value lying somewhere on the growth curve in Fig. 2 would be expected, possibly as low as 15 to 20