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# FATE OF THE IODINE RADIOISOTOPES IN THE HUMAN AND ESTIMATION OF THE RADIATION EXPOSURE

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C.E.N., Mol, Belgium<br>(Received 2 January 1964; in revised form 27 May 1964)<br>Abstract—Fate of the iodine isotopes and resulting organ exposures have been studied using<br>the four-compartment model proposed by BROWNELL to acco clement.

Mathematical equations have bccn establishcd for this model from biological data acccpted in the human. They have been used to calculate the amounts of iodine-131 in the thyroid and in the remaining body as <sup>a</sup> function of timc in case of a single or a chronic contamination; in this latter case three phases have been considered: rise, cquilibrium and dccrease aftcr rcmoval of the contaminating source. The importance of the daily stable iodine intake from the food has been emphasizcd.

Some of these theoretical results have been checked by experiments on eight volunteers. Calculations have been extended to nine other iodine isotopes in order to determine the exposure doses of the thyroid and the remaining body for <sup>a</sup> single or <sup>a</sup> chronic contamination; maximum permissible concentrations in water and in air have also bcen computed.

maximum permissible concentrations in water and in air have also been computed.<br>It appears that some I.C.R.P. recommendations for maximum permissible body burden must be rcviscd.

#### **1. INTRODUCTION**

THE study of the fate of the iodine isotopes in the human body and of the resulting radiation doses dclivcrcd to the thyroid gland, is of prime importance for nuclear health problcms.

Indccd, one of the first consequcnces of a reactor accident can be the rclease of great amounts of <sup>131</sup>I in the atmosphere with the contamination of the neighbouring population by inhalation or by ingestion of contaminated food (in particular, the milk). This hazard has bcen illustrated by the Windscalc incident of 10 October 1957.<sup>(1)</sup> The high volatility of molccular iodinc is responsible for the casy dispersion of the compound and prevents its retention by ordinary filters.

 $\vert$ 

During the numerous nuclear bomb tests performed in 1961 and 1962, one of us (J. C.) found <sup>131</sup>I in the atmospheric fall-out and in the milk by  $\gamma$ -spectrometry. Identical observations were made at several stations in Europe<sup>(2)</sup> and in U.S.A. Morcover scvcral iodine radio-

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isotopes  $(^{129}I, ^{131}I, ...)$  are found during the reprocessing of irradiated nuclear fucls.<sup>(3)</sup>

The dcvclopment of the diagnostic and therapeutic uses of sevcral iodinc radioisotopes  $(125I, 131I, 132I, 133I)$  must also be considered hcrc; contamination may rcsult in radioisotopc laboratories and in production arcas owing to the high volatility of many iodine compounds. Such contaminations have been frequcntly obscrvcd in sevcral centres whcrc radioiodines are produced.<sup>(4)</sup>

The high radiotoxicity of iodinc is cxplaincd by the retention of a great fraction of the ingested or inhalcd radionuclide in the thyroid, <sup>a</sup> small organ of about <sup>20</sup> <sup>g</sup> in the adult human. This local concentration makes the thyroid the critical organ.

In order to calculate the dose dclivcrcd to the thyroid in case of a single as wcll as of a chronic absorption of radioiodine, it is necessary to know the metabolism of the clcment iodinc.

### **2. BIOLOGICAL DATA**

It can be found in recent textbooks $(5)$  that about <sup>85</sup> per cent of the body total iodine is

#### FATE OF THE IODINE RADIOISOTOPES IN THE HUMAN



#### FIG. 1

localized in the thyroid, i.e. 8 mg for a normal thyroid and 9-9.5 mg for the whole body.

The body iodine is divided between several compounds, chemically different, forming distinct pools with particular turnover rates. When radioiodine finds its way into the organism, there is no global homogenization; the specific radioactivities remain different in the various pools and the ratios of these activities are dependent on the periods of the radionuclide and a few other parameters. A simple scheme of the iodine metabolism, which is sufficient for the discussion on the tissue exposure after contamination by the radioisotopes of this element, has been published by BROWNELL;<sup>(6)</sup> three distinct pools, also identified as "spaces", are considered: iodide, thyroid iodine and extra-thyroidal organic iodine  $(Fig. 1)$ .

(A) The iodide space has 25 l.; it is divided into two compartments  $V_1$  and  $V_2$ . Iodide from the food penetrates in  $V_1$ ; it is also in this compartment that the thyroid and the kidneys take up iodine. The barrier between  $V_1$  and  $V<sub>a</sub>$  can be demonstrated with radioactive iodide: the homogenization in  $V_1$  is more rapid than the diffusion towards  $V_2$ .

Extrapolation at time O of experimental semi-logarithmic curves obtained after i.v.

injection of <sup>131</sup>I and plotting of the plasma radioactivities vs. time, enabled BROWNELL to calculate for  $V_1$  a mean volume of 71. This value, which exceeds the plasma volume, will be called "volume of immediate homogenization" hereafter.

The iodide biological half-life is very short so that the plasma concentration changes rapidly: relatively liigh after a meal, it falls quickly. In the calculations however, we shall use a mean concentration which is merely dependent on the daily iodine intake from the food,

(B) The thyroidal iodine is chemically polymorphous although it is mostly in the thyroglobulin. In the normal human, the decrease of the radioiodine (after correction for the radioactive decay) caught by the thyroid follows, after a few days, an exponential function and the hormone secreted by the gland has the same specific radioactivity as the thyroidal iodine.<sup>(7)</sup> It seems that, in normal adults, the 8 mg of thyroidal iodine behave as if they were in a single pool.\*

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<sup>\*</sup> Many investigators think that the active thyroidal iodine pool is more restricted; this would not have great influence on our results except in the case of long-lived iodine radioisotopes such as  $125$   $\Gamma$ .

(C) The  $1200 \mu g$  of *cxtra-thyroidal* organic *iodine* (mostly thyroxine and triiodothyronine) arc in a spacc of 251. Thcsc compounds arc partially cxcrctcd in the fcccs; this pathway, which is quantitatively not very well known, will be ignored in this study. The catabolism of the thyroidal hormones yiclds iodide which is rccyclcd.

(D) For our purposc the wholc system can be supposed in a dynamic equilibrium. It is then obvious that:

The amount of iodide that enters the body (from the food) is equal to the amount excreted (mostly in the urine). This amount is not the same in different countries and depends on the dict; it is about  $150 \mu g$  per day in Boston,  $U.S.A.$ <sup>(7)</sup> but seems to be lower in western Europe: about 75  $\mu$ g pcr day<sup>(8, 9)</sup> (see also later).

The daily iodide uptake of the thyroid from the "volume of immcdiatc homogcnization" is equal to the amount of hormonal iodine sccreted; an cquivalent quantity of the extra-thyroidal organic iodine is catabolized to iodidc which diffuses back into the iodidc spacc. The daily turnover is about 70  $\mu$ g of iodine in the normal adult; the thyroid adapts the lcvcl of its plasma clearance in order to take this amount of iodidc daily whatcvcr the plasma concentration. However, when a huge dose of iodide is administcrcd (l00 mg for instance), it is likcly that the absolutc thyroidal intakc is larger although it would never exceed a few mg, i.e. <sup>a</sup> very small percentage of the given dose;<sup>(10,11)</sup> afterwards, the saturated gland will not take anything from a new feeding of iodidc which will be completcly cxcretcd by the kidncys.

#### 3. MATHEMATICAL ANALYSIS OF THE **METABOLISM**

The metabolism, summarized in Fig. I, can be analyzed mathematically in ordcr to know the fatc and distribution of radioactive iodinc that would pcnetrate accidentally into the body.

To set the equations, the mechanisms of diffusion between  $V_1$  and  $V_2$ , of transfers  $V_1 \rightarrow V_3$ ,  $V_3 \rightarrow V_4$ ,  $\dot{V}_4 \rightarrow V_2$ , and of kidney excretion, will be measurcd by the "clearance" values:  $k_g$ ,  $\dots$ ,  $k_g$ , whose dimensions are 1.1/hr;

thcsc coefficients are the volumes (fractions of  $V_1$ ....,  $V_4$ ) whose iodine is cleared per unit timc by the proccss involved.

#### 3.1. *Aute contamination by an iodine isotope having <sup>a</sup> radioactivity constant <sup>R</sup>*

The specific activities  $A_1 \ldots A_4$  in the diflcrent spaccs are givcn by the following system of differential cquations:

$$
\frac{dA_1}{dt} = -\left(\frac{k_2}{V_1} + \frac{k_3}{V_1} + \frac{k_4}{V_1} + \lambda\right) A_1 + \frac{k_2}{V_1} A_2
$$
\n
$$
\frac{dA_2}{dt} = \frac{k_2}{V_2} A_1 - \left(\frac{k_2}{V_2} + \lambda\right) A_2 + \frac{k_6}{V_2} A_4
$$
\n
$$
\frac{dA_3}{dt} = \frac{k_3}{V_3} A_1 - \left(\frac{k_5}{V_3} + \lambda\right) A_3
$$
\n
$$
\frac{dA_3}{dt} = \frac{k_5}{V_3} A_3 - \left(\frac{k_6}{V_4} + \lambda\right) A_4 \tag{1}
$$

with the following initial conditions:  
for 
$$
t = 0
$$
:  $A_1 = a/V_1$   
 $A_2 = A_3 = A_4 = 0$ 

The solution was obtaincd *by* a digital computer using thc following numcrical data  $(B_{\text{ROWNELL}}^{(6)}$  and RIGGs<sup>(7)</sup>.)

- $V_1$  Volume of the immediate homogenization compartment <sup>7</sup> 1.
- *V..* Volume of the diffusion compartmcnt - 18 1.
- $V<sub>1</sub>$  Thyroid gland volume  $2 \cdot 10^{-2}$  l.
- , Extra-thyroidal organic iodine volume 25 1.
- 25 l.<br>*k*<sub>2</sub> Diffusion constant between  $V_1$  and  $V_2$ <br>from BROWNELL's data = 14 l./hr<sup>\*</sup> **from BROWNELL's data = 14 1./hr<sup>\*</sup>**<br>*k<sub>3</sub>* Kidncy clearance = 2 1./hr
- 

\* **IlRoWNELL has isolatcd the proccs.s of diffusion** between  $V_1$  and  $V_2$  from the rest of the metabolism so that the specific radioactivity  $A_I$  is governed by the following cquation:

<sup>2</sup> *Im* **BROWSEL's data** = 14 1./l  
\n<sup>3</sup> *Kidney clearance* = 2 1./hr  
\n**BoxWELL has isolated the process of**  
\n**convWELL has isolated the process of**  
\n<sup>4</sup> *u q q for the rest of the m*  
\nat the specific radioactivity *A*<sub>1</sub> is gov-  
\nallowing equation:  
\n
$$
A_{\rm I}(t) = C_{\rm I} + C_{\rm 2} \exp\left(-\frac{0.693 \cdot t}{T}\right)
$$
\nwhere  $T = \frac{0.693}{k_2} \cdot \frac{V_{\rm I} V_{\rm 2}}{V_{\rm I} + V_{\rm 2}}$ 

Experimentally, BROWNELL got a mean value:  $T = 0.25$  hr; hence  $k_0 = 14$  l./hr.

 $k_A$ ,  $k_B$ ,  $k_B$ , when the metabolism is at equilibrium,  $k = dV/dt = (dQ/dt) \cdot (1/C)$  where  $dQ$ is the amount of iodine transferred during the time  $dt$ , and  $C$  is the concentration of stable iodinc in the compartment from which the iodine is taken.

The equilibrium implies that the kidney daily excretion is equal to the daily intake from the food  $(X \mu g)$  so that the concentration of stable iodine in the volume of immcdiate homogenization must be

on must be  

$$
C_1 = \frac{X}{2 \times 24} \mu \text{g/l}.
$$

With a daily transfer of 70  $\mu$ g of iodine through the thyroid and the extra-thyroidal organic iodine space, one ealculates:

$$
k_4 = \text{thyroidal intake} = \frac{140}{X} 1./\text{hr}
$$

 $k_5 =$  hormone secretion =  $7.3 \cdot 10^{-6}$  l./hr

$$
k_6 = \text{ hormone catalogism} = 6.1 \cdot 10^{-2} \cdot 1./\text{hr}
$$

The  $X \mu$ g intake of iodine from the food is likcly to vary much with the dict and the geographical localization; that is the reason why we kept it as a parameter with values ranging from 50 to 300  $\mu$ g/day.

The calculations were first done for <sup>131</sup>I which happens to be the most common contaminant and bccause its 8-day half-life  $(\lambda =$  $3.587 \cdot 10^{-3}$  hr<sup>-1</sup>) makes it more dangerous than its short-lived isotopes such as  $^{128}$ I,  $^{132}$ I,  $133$  $\text{I}$ ,  $\ldots$ 

The numerical data for the radioactivities obtained from equations (1) have been plotted on graphs. The activity in the thyroid,  $Q_3(t) = A_3(t) \cdot V_3$  is given by Figs. 2 and 3. The curves clearly show that the fraction of the radioiodine caught by the thyroid is greater when the diet contains less iodine.

The thyroidal uptake (obtained after correction for the radioactive dccay) is maximal betwccn 24 and 48 hr, and reaches 50 per cent of this maximum within about <sup>5</sup> hr (Table 1); this is in agreement with experimental results known for <sup>a</sup> long timc. The maximum of radioactivity in the thyroid is also found from <sup>24</sup> to <sup>48</sup> hrafter the contamination; this is only becausc ofthe rclativcly long physical half-life



Fics. <sup>2</sup> and 3. Thcoretical thyroidal activitics in per cent of the absorbed quantity of iodine-13I after <sup>a</sup> single contamination (at time *O)* for various intakes of stable iodine.

	Uptake	1317	Uptake	131 <sub>T</sub>	Uptake	131 <sub>T</sub>
$\boldsymbol{X}$	$($ %)	$(\mu c)$	$($ %)	(nc)	$( \% )$	(nc)
$(\mu$ g)	After 5 hr		After 24 hr		After 48 hr	
50	36.6	0.36	56.9	0.52	57.3	0.48
75	27.0	0.26	46.3	0.42	47.5	0.40
100	21.3	0.21	38.9	0.36	40.5	0.34
150	14.8	0.14	29.3	0.27	31.2	0.26
300	7.9	0.078	16.8	0.15	18.4	0.16

Table 1. Thyroidal uptake as a function of the stable iodine intake  $(X)$  from food.<br>Thyroidal activities 5, 24 and 48 hr after a single absorption of 1 µc of <sup>131</sup>I Thyroidal activities 5, 24 and 48 hr after a single absorbtion of  $1 \text{ }$  HC of  $131$ 

of  $^{131}I$ ; with isotopes of shorter physical periods, the maxima arc rcachcd much carlicr (sec Table 5).

Aftcrwards, the radioactivity in the thyroid dccrcases with an effective period of about 7.5 days rcsulting from the 8-day physical pcriod and an "apparent"<sup>\*</sup> biological period which varies betwcen <sup>95</sup> and <sup>160</sup> days depending on the magnitude of the recycling which is linked to the sizc of the iodine intakc from the food. One calculates indeed, between the fourteenth and the fifticth day, "apparent" biological half-livcs of:



The radioactivity in the rcmaining body (i.e. body without thyroid) is given by the sum  $A_1(t)V_1 + A_2(t)V_2 + A_4(t)V_4$  and represented in Fig. 4. There is a very rapid decrease due to the kidncy excretion and the thyroid uptakc so that, at the forty-eighth hr, only 1-2 pcr cent of the absorbcd radioactivity rcmains in the iodide pool. After 4 days, a rise of the radioactivity is observed in the rcmaining body owing to the secrction, by the thyroid, of hormones labelled with <sup>131</sup>I; this phenomenon has a maximal amplitude at about the tcnth day after the contamination. Afterwards that

• This biological half-lifc considcrcd by the health physicist characterizes the dccrcasc of radio**activityof the organ when the correction for the** physical decay has been made. It is different from that studicd by the physiologist who must correct **also for any recycling.**

radioactivity decrcases following the progressive decrease of the thyroid radioiodine.

#### 3.2. *Chronic contamination*

This situation is considcrcd for the calculation of the maximum pcrmissiblc lcvcls of contamination in the drinking water and in the air.

Let us assume a chronic contamination of *"a"* pc/hr. This case is mathcmatically dcscribed by the system of differential equations<br>(1); it is only necessary to add the term<br> $(+a/V_1)$  to the right hand side of the first<br>equation. (1); it is only necessary to add the term<br> $(+a/V_1)$  to the right hand side of the first equation.



FIG. **4. Thcorctical activities in the remaining** body (body without thyroid) in per cent of the absorbed quantity of iodinc-131 aflcr <sup>a</sup> single **contamination (at time** *O)* **for various intakes** ofstable iodinc.

						the thyroid $(g_3)$ and the extra-tayroidal organic tourne $(g_4)$ for a chronic contamination of $\iota$ pcfur	
$X(\mu g)$	50	75	100	150	300	500	1000
	HC	$\mu$ <sub>C</sub>	нс	$\mu$ C	ПC	нc	ПC
ų,	1.46	1.80	2.13	2.34	2.76	2.96	3.15
Q.	3.77	4.63	5.24	6.01	7.07	7.55	8.01
Q,	8.97	7.36	6.25	4.79	2.82	1.82	0.96
Total	14.2	13.8	13.6	13.1	12.6	12.3	12.1
Q <sub>3</sub>	1.48	122	103	79.0	46.9	30.0	16.0

*Table* 2. *Amonnts* of <sup>131</sup>I in the volume of immediate homogenization  $(Q_1)$ , the diffusion volume  $(Q_2)$ , *the thyroid*  $(Q_2)$  *and the extra-thyroidal organic iodine*  $(Q_1)$  *for a chronic contamination* of 1 *µ*c/*hr* 

The study of the cvolution of the body contamination by the isotope can be dividcd into thrcc phases:

(a) the bcginning of the contamination with a progressive approach to the equilibrium. The initial conditions arc then<br>  $A_1 = A_2 = A_3 = A_4 = 0$  for  $t = 0$ 

$$
A_1 = A_2 = A_3 = A_4 = 0 \text{ for } t = 0;
$$

(b) the cquilibrium is reachcd. The differentials are equal to zero. There remains a system of <sup>4</sup> cquations with <sup>4</sup> unknowns which is casy to solve;

(c) the decreasc of the contamination after



FIG. 5. Chronic contamination resulting from the absorption of  $1 \mu c$  of iodine-131 per hour **starting at time** *O.* **Thcoretical activitics in** thyroid and rcmaining body for various intakcs of stable iodine.

 $A_1$   $\cdots$  which exist in equilibrium in the various spaces considered. The analysis of the latter situation enables one to calculatc the irradiation dose that the pcrson will still rcccive in spite of

the suppression of the absorption of radioiodine.<br>(a) *Beginning of the contamination*. A chronic (a) Beginning of the contamination. A chronic contamination by the absorption of  $l \mu c/hr$  of <sup>131</sup>I has been considered. The results given by the digital computer arc reprcscnted in Fig. 5.

The radioaetivity concentratcd by the thyroid increases with time to reach 50 and 90 per cent of the cquilibrium value after <sup>8</sup> and <sup>25</sup> days rcspectivcly. The important corrclation between this activity and the iodine daily intakc from the food is particularly obvious.

On the other band, the aetivity in the remaining body reaches its equilibrium much more quickly: <sup>50</sup> per cent of the maximum is attained in lcss than <sup>I</sup> day; the subsequcnt variations arc duc mostly to the sccretion of radioactive thyroidal hormones.

(b) *Equilibrimn.* 'The solution of thc cquation describing the situation can be found in Table 2.

It can be seen that the amount of <sup>131</sup>I in the thyroid is very dependent on the intakc of stable iodine from the food; by contrast, the total activity in the remaining body is about constant in spitc of the variations in the distribution of this radioiodinc bctwecn the scvcral compartments according to the amount of stable iodinc in the diet. Consequently the ratio betwcen the thyroidal activity and that of the rcmaining body, is variable: for <sup>a</sup> man rcceiving daily 150  $\mu$ g of iodine from this dict, this ratio is 86/14, a rcsult very similar to that given by the literature for the stable iodinc: 85/15, (11)

(c) *Suppression ofthe source of contamination.* The results reported in Fig. <sup>G</sup> show that the activity in the thyroid diminishes with the



**Fra. 6. Interruption at time** *<sup>O</sup>* **of <sup>a</sup> chronic contamination of <sup>I</sup>** *<sup>c</sup>* **of iodine-II per hour. Theoretical activities in thyroid and remaining body for various intakes ofstable iodine.**

previously found efîective half-life of about *ï.5* days; there arc only slight variations depending on the stable iodine dict as in the case of the acute contamination.

The activity in the remaining body decreases in two phases: the first one is bound to the rapid climination of the iodide fraction from the volumes  $V_1$  and  $V_2$ ; the second to the slower disappearance of the organic iodine that is being continually secrcted by the thyroid.

#### 4. EXPERIMENTAL

Experiments have been carried out on cight male adults in order to check the validity of the hypotheses used in the present work for the calculation of irradiation doses. These people, fasting for more than 12 hr, ingested  $0.5 \mu c$ of carrier-free  $^{131}I$  as NaI in a solution of  $10^{-3}$  $M \cdot Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>$ . The radioactivity assays on the thyroid and on the remaining body wcre startcd <sup>1</sup> hr latcr and pursued at intervals, during <sup>40</sup> days. The urines were collectcd during the first days in ordcr to have a complcte picture of the mctabolism and to dctcrminc the cfficiencies of counting for <sup>131</sup>I in the thyroid or the remaining body for cach individual. \*

#### 4.1. *Apparats and methods*

The determinations of <sup>131</sup>I in the thyroid were performed with a NaI crystal of  $5 \times 5$  cm shielded with 2 cm of lead, and which was placed at 6 cm from the thyroid in a reproducible way by mcans of <sup>a</sup> lucite block in contact with the neck. The  $\gamma$ -spectrum was recordcd with <sup>a</sup> 256-channel analyzcr and the activity was obtained by the determination of the peak area at 364 keV and by comparison with a thyroid phantom; this phantom consists of two 10-ml flat vials containing a  $131$ standard solution placed at 0.5 cm depth within <sup>a</sup> cylinder full of water simulating the neck.

The radioactivity of the remaining body was measured, also by y-spectrometry, in a whole body counter.<sup>(12)</sup> The incidence of the thyroid radioactivity however was cancelled by a shield of 15-mm lead placed in front of the neck of the patient. The calculation of the activity in the body used the counting efficiency established previously by means of phantoms simulating the human body and fillcd with radioactive solution of known activity.

The urine assays were carricd out with <sup>a</sup> NaI crystal of  $5 \times 5$  cm surrounded by 10 cm of lead.<sup>(13)</sup>

The sums of the activities in the thyroid, the remaining body and the urine were compared with the amount of <sup>131</sup>I ingested in order to have a permanent check of the efficiencies utilizcd in the calculations.

### 4.2. *Results*

For each patient, the curves of <sup>131</sup>I activities in the thyroid and in the remaining body have bcen plottcd as a function of timc. In Fig. <sup>7</sup> arc the examples of the graphs given by:

(a) an indiviclual whose iodinc metabolism appears to be normal; very similar rcsults were obtained with six other people;

(b) a patient whose thyroidal uptakc is accclcrated; the <sup>131</sup>I also leaves the thyroid quicker. There is a remarkable increase of the remaining body radioactivity due to the sccrction of the labcllcd thyroidal hormones.

The maximum radioactivity is reached in the thyroid after about <sup>24</sup> hr in normal people; it has a mean value of  $0.21 \mu c$  in the seven cases considered for a single ingestion of

These data gave the opportunity to check the validity of the phantoms used afterwards.



Fic. 7. Expcrimcntal data. Activities in thyroid and remaining body in pcr cent of the amount and remaining body in per cent of the amount of iodine-131 given at time  $O$ .

 $0.5 \text{ }\mu\text{c}$  of  $^{131}$ . The individual results are scattcred betwccn 0.16 and 0.26 *µc.*

#### 5. DISCUSSION. COMPARISON BETWEEN EXPERIMENTAL AND THEORETICAL DATA

The experimental curves are quite similar to those prcviously calculatcd (compare Figs. 2, 4 and 7). Table <sup>I</sup> howevcr shows that the agreement is good for the uptakc by the thyroid only if the stable iodinc brought by the food is about 75  $\mu$ g/day.

In order to know the daily intestinal absorption which, at equilibrium, is approximatcly equal to the daily excretion by the kidneys, an assay of the stable iodine in the urine has becn carried out by activation analysis.<sup>(14)</sup>

Samples of 10 ml of urine in polycthylene bottles werc irradiatcd for 15 min in a flux of  $1.2 \times 10^{12}$  neutrons/sec· cm<sup>2</sup> in the BR-1 nuclcar reactor. <sup>A</sup> chemical scparation was nccessary bccausc of the great amounts of other elements, particularly chlorine, which arc highly activatcd. 0.5 g of iodide was added as a carrier to the irradiated solution; the iodide was oxidized by HNO<sub>2</sub> to iodine which was extracted with CCI<sub>4</sub>. The organic solution was washed several times with an aqueous solution of NaCl, before the measurement of the <sup>128</sup>I

radioactivity by y-spectrometry on the 455-keV<br>photoclectric peak. A chemical assay of  $I_2$  in<br>the CCl, solution gave the vield of extraction photoelectric peak. A chemical assay of  $I_2$  in the CCI, solution gave the yield of extraction so that a suitable correction could be applied.

During the 24 hr following the ingestion of 131I, the seven normal males used in this work excreted in the urine:

79, 51, 78, 140, 340, 60, 58 µg of iodine.

These persons had been asked not to eat anything known to contain much iodine (such as sea food) during the <sup>3</sup> days preccding the as sea food) during the 3 days preceding the exception of the  $340 \mu g$ experiment. With the exception of the  $340 \mu$ g<br>value—which concerned an individual usually value—which concerned an individual usually<br>very fond of sea food—the mean value of the iodine intake was 78  $\mu$ g/day.

Other runs were made at 10-day intervals over a period of <sup>2</sup> months on two subjccts in order to see the possible variations of this iodine intake:

L: 53, 57, 48, 40, 42, 42,  $\mu$ g for 24 hr S: 120, 84, 121, 37, 50, 79, *µg* for 24 hr

It is obvious that the iodine content of the urine of <sup>L</sup> is very constant around an average of 47  $\mu$ g/day. For S, the two highest results were coincident with the ingestion of mussels during the cxpcrimcntal pcriod.

It thus seems that, for people living around the Bclgian Nuclcar Centre at Mol, the daily iodinc intake is between 50 and 100  $\mu$ g. With this rcsult, the agreement between experimental and thcorctical curve is suflicient to validate Brownell's mode! of iodinc metabolism for the purposc of this study.

#### 6. EXPOSURE DOSES RESULTING FROM ABSORPTION OF AN IODINE RADIO-ISOTOPE

The equations used for <sup>131</sup>I have also been applicd to other iodinc isotopes in order to calculate the permissible burdens for workers calculate the permissible burdens for workers<br>contaminated with these radionuclides.

The solution of the system of equations (1) The solution of the system of equations (1)<br>gives the activities in the thyroid  $A_3V_3$ , and in<br>the remaining body  $A_1V_1 + A_2V_2 + A_3V_4V_4$ . The<br>exposure doe for an exten is given by

exposure dose for an organ is given by  
\n
$$
R = \int_0^{T} \frac{q f_2 dt \cdot 3.7 \cdot 10^4 \cdot 1.6 \cdot 10^{-6} \epsilon}{100 \cdot m}
$$
 (2)

where:  $q =$  total activity in the whole body;  $f_0 = \begin{cases} 100 \cdot m & \text{(1)} \\ 0 & \text{(2)} \\ 0 & \text{(4)} \end{cases}$  in the whole body;<br>  $f_1 = \begin{cases} 100 \cdot m & \text{(5)} \\ 0 & \text{(6)} \end{cases}$  to that in the whole body:  $f_2$  = ratio of the activity in the organ<br>to that in the whole body;

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	Burden $(\mu c)$	Burden $(\mu c)$			
Isotope	in thyroid	ın body	Isotope	in thyroid	in body
$^{131}I(1)$	148	14	1297	5710	896
(2)	103	14	130 <sub>T</sub>	5.3	5.1
(3)	47	13	132 <sub>T</sub>	0.50	2.1
125 <sub>1</sub>	570	80	133 <sub>1</sub>	9.4	5.9
126f	165	21	134 <sub>1</sub>	0.33	3.0
128 <sub>l</sub>	0.034	0.52	135 J	7.0	12

Table 3. Radioactivities in thyroid and remaining body for a chronic absorption of  $1$  pc/hr. In the case of  $131$  the stable iodine daily intake is considered at three levels-50  $\mu$ g (1), 100  $\mu$ g (2) and 300  $\mu$ g (3). For the other isotopes, it is fixed at 100  $\mu$ g/day.

- $\varepsilon$  = the energy effectively spent in the organ:  $\varepsilon = \sum E$ F (RBE)n
- $m =$  mass of the organ;
- $T =$  integration time = 13 weeks in this case.

The maximal dose rate exposures adopted are those recommended by the ICRP Committee II:(15)

8 rem during a 13-week period for the thyroid,

1.3 rem during a 13-week period for the whole body.

The energies effectively absorbed by the organ have been taken in Table 5a of ICRP for <sup>131</sup>I; they have been computed for isotopes 125, 128 and 130 following equations  $(25)$ - $(30)$ of ICRP. The following figures were obtained:

 $125$ I:  $\Sigma$  EF(RBE)n = 0.085 MeV (body) 0.031 McV (thyroid)  $128I$ :  $\Sigma$  EF(RBE)n = 0.86 MeV (body) 0.81 MeV (thyroid)  $^{130}I$ :  $\Sigma$  EF(RBE)n = 1.68 MeV (body) 0.49 MeV (thyroid)

#### 6.1. Chronic contamination

This case is considered by ICRP to establish the maximal permissible burdens. We have recalculated these levels for the thyroid which is always the critical organ, and also for the remaining body.

It appears useful to distinguish between the remaining body (without thyroid) and the whole body because the radioactivity localized in the thyroid does not irradiate the remaining body to any appreciable extent. Moreover, at the equilibrium, the amount of radio-iodine in the thyroid is usually much greater than the amount in the remaining body which is then only exposed to this latter small part of the total radioactivity (Table 3).

From the maximal burdens admitted in the organ<sup>\*</sup> and calculated with equation (2), the maximal permissible concentrations in water and air for 40 or 168 hr exposure per week can be computed.

Indeed

$$
MPC_{water} = \frac{MPB^x}{Q_{acc}^x \cdot C_m}
$$

where  $MPB^r =$  the maximal permissible burden in organ  $x$  ( $\mu$ c),

 $Q_{\text{acc}}^x$  = activity accumulated in the organ resulting from a chronic contamination of  $1 \mu c/hr$ ,

 $C_m$  = mean water intake in 1./hr.

When the contamination comes from the air, it is assumed that only 75 per cent of the inhaled activity is transferred to the blood, so that

$$
\text{MPC}_{\text{air}} = \frac{\text{MPB}^x}{Q_{\text{acc}}^x \cdot 0.75 \, G_m}
$$

The calculated data are shown in Table 4.

#### 6.2. Acute contamination

In the not infrequent event of a unique aecidental contamination, the maximal permissible burden of the radionuclide in the body is usually much higher than what is allowed in

\* It might be that the thyroid is not the critical organ for the very short-lived iodine isotope.

FATE OF THE IODINE RADIOISOTOPES IN THE HUMAN

	Critical organ	MPB in organ	MPB in total body	$(MPC)_{\text{water}}$	$(MPC)_{\text{air}}$ for 40 hr week	$(MPC)_{water}$	$(MPC)_{\text{a1r}}$ for 168 hr week
	$(\mu c)$	$(\mu c)$	$(\mu c)$	$(\mu c/cm^3)$	$(\mu c/cm^3)$	$(\mu c/cm^3)$	$(\mu c/cm^3)$
131(1)	Thyroid	0.15	0.16	$3 \cdot 10^{-5}$	$5 \cdot 10^{-9}$	$1 \cdot 10^{-5}$	$2 \cdot 10^{-9}$
	Body	44	500	$1 \cdot 10^{-1}$	$1 \cdot 10^{-5}$	$3 \cdot 10^{-2}$	$5 \cdot 10^{-6}$
(2)	Thyroid	0.15	0.17	$4 \cdot 10^{-5}$	$6 \cdot 10^{-9}$	$2 \cdot 10^{-5}$	$2 \cdot 10^{-9}$
	Body	44	370	$1 \cdot 10^{-1}$	$2 \cdot 10^{-5}$	$4 \cdot 10^{-2}$	$5 \cdot 10^{-6}$
(3)	Thyroid	0.15	0.19	$1 \cdot 10^{-1}$	$1 \cdot 10^{-8}$	$4 \cdot 10^{-5}$	$5 \cdot 10^{-9}$
	Body	$4+$	210	$1 \cdot 10^{-1}$	$2 \cdot 10^{-5}$	$4 \cdot 10^{-2}$	$6 \cdot 10^{-6}$
$125$ $\mathbf{I}$	Thyroid	1.1	1.3	$6 \cdot 10^{-5}$	$9 \cdot 10^{-9}$	$2 \cdot 10^{-5}$	$3 \cdot 10^{-9}$
	Body	230	1900	$9 \cdot 10^{-2}$	$1 \cdot 10^{-5}$	$3 \cdot 10^{-2}$	$4 \cdot 10^{-6}$
126 <sub>I</sub>	Thyroid	0.21	0.24	$4 \cdot 10^{-5}$	$6 \cdot 10^{-9}$	$1 \cdot 10^{-5}$	$2 \cdot 10^{-9}$
	Body	85	770	$1 \cdot 10^{-1}$	$2 \cdot 10^{-5}$	$4 \cdot 10^{-2}$	$7 \cdot 10^{-6}$
128 <b>J</b>	Thyroid	0.042	0.68	$4 \cdot 10^{-2}$	$6 \cdot 10^{-6}$	$1 \cdot 10^{-2}$	$2 \cdot 10^{-6}$
	Body	23	24		$2 \cdot 10^{-1}$	$5 \cdot 10^{-1}$	$7 \cdot 10^{-5}$
129]	Thyroid	0.50	0.59	$3 \cdot 10^{-6}$	$4 \cdot 10^{-10}$	$1 \cdot 10^{-6}$	$1 \cdot 10^{-10}$
	Body	220	1600	$8 \cdot 10^{-3}$	$1 \cdot 10^{-6}$	$3 \cdot 10^{-3}$	$4 \cdot 10^{-7}$
1301	Thyroid	0.14	0.27	$8 \cdot 10^{-1}$	$1 \cdot 10^{-7}$	$3 \cdot 10^{-1}$	$4 \cdot 10^{-8}$
	Body	12	24	$7 \cdot 10^{-2}$	$1 \cdot 10^{-5}$	$2 \cdot 10^{-2}$	$4 \cdot 10^{-6}$
132 <sub>I</sub>	Thyroid	0.053	0.28	$3 \cdot 10^{-3}$	$5 \cdot 10^{-7}$	$1 \cdot 10^{-3}$	$2 \cdot 10^{-7}$
	Body	13	16	$2 \cdot 10^{-1}$	$3 \cdot 10^{-5}$	$6 \cdot 10^{-2}$	$9 \cdot 10^{-6}$
$133$ <sup>T</sup>	Thyroid	0.064	0.10	$2 \cdot 10^{-3}$	$3 \cdot 10^{-7}$	$7 \cdot 10^{-1}$	$1 \cdot 10^{-7}$
	Body	23	60	$1 \cdot 10^{-1}$	$2 \cdot 10^{-5}$	$4 \cdot 10^{-4}$	$6 \cdot 10^{-6}$
$131$ [	Thyroid	0.042	0.42	$4 \cdot 10^{-3}$	$6 \cdot 10^{-7}$	$1 \cdot 10^{-3}$	$2 \cdot 10^{-7}$
	Body	13	14	$1 \cdot 10^{-1}$	$2 \cdot 10^{-5}$	$5 \cdot 10^{-2}$	$7 \cdot 10^{-6}$
135 <sub>1</sub>	Thyroid	0.066	0.18	$3 \cdot 10^{-4}$	$4 \cdot 10^{-8}$	$1 \cdot 10^{-1}$	$2 \cdot 10^{-8}$
	Body	15	24	$4 \cdot 10^{-2}$	$6 \cdot 10^{-6}$	$1 \cdot 10^{-2}$	$2 \cdot 10^{-6}$

Table 4. Maximum permissible burden in critical organ and in total body and maximum permissible concentrations in water and air. In the case of iodine-131 the stable iodine daily intake is considered at three levels: 50  $\mu$ g (1), 100  $\mu$ g (2) and  $300 \mu g$  (3). For the other isotopes, it is fixed at 100  $\mu g$ /day

the case of a chronic contamination at equilibrium, because of a progressive decrease of the radioactivity due to the biological metabolism and the physical decay: the exposure dose must indeed be integrated over a period of 13 weeks.<sup>(16)</sup> The maximal permissible quantities computed from equation (2) for the radioiodines can be found in Table 5.

# COMPARISON OF THE RESULTS OF THIS<br>STUDY AND THE DATA USED BY IRCP<br>TO SPECIFY THE MAXIMUM PERMISSIBLE **LEVELS**

According to ICRP, the human body contains 40 mg of iodine, one-fifth of which is concentrated in the thyroid. This iodine forms a single pool in the thyroid and the remaining body, which is not divided by any chemical or physical barrier and which has a half-life of 138 days.

When a contamination with radioactive

iodine is considered, the effective half-life takes the place of the biological half-life in order to account for the radioactive decay. But as, for ICRP, iodinc is in a single pool, the homogenization is instantaneous and the distribution of the contaminating radioisotope between the thyroid and the remaining body must be precisely the same as that of the stable iodine:  $f_2 =$  thyroidal iodine/total iodine =  $0.2.$ The repartition of the radionuclide between the thyroid and the remaining body and the exposure doses for the tissues, in case of a single absorption, are computed in the following way:

thyroidal activity:  $q^{th} = qf_1f_2' \cdot \exp{-\lambda^{th} t}$ where  $q =$  absorbed radioactivity,

 $f_1 = 1$  = fraction of absorbed quantity passing in the blood,

 $f'_{\underline{i}} = 0.3$  = fraction from blood to organ,<br>  $\lambda$  = cffective time constant,

*Table* 5. *Acte contamination. Maximal pemissible absorption: resulting maximum burdens in thyroid, and time 11ccenmy lo reach thcse maxima*

Isotope of iodine	Maximum permissible intakc $(\mu c)$	Maximum permissible burden in in thyroid $(\mu c)$	Delay to reach burden (hr)
$^{131}I(1)$	2.2	1.2	30
(2)	3.2	1.1	36
(3)	7.0	1.1	48
1251	5.3	2.1	48
126 <sub>l</sub>	2.9	1.1	36
128 <sub>l</sub>	2700	73	0.4
1291	1.6	0.67	50
1301	29	5.0	8
1321	230	16	$\overline{2}$
1331	14	3.0	12
131 <sub>l</sub>	810	32	0.8
1351	620	78	5

In the calculations, a dose rate of 8 rem/13 weeks In the calculations, a dose rate of  $8 \text{ rem}/13$  weeks<br>has been admitted. In the case of  $^{131}I$  the stable **iodine daily intake is considered at three levels:** 50  $\mu$ g (1), 100  $\mu$ g (2) and 300  $\mu$ g (3). For the other isotopes, it is fixed at  $100 \mu g$  per day.

total body activity:

dy activity:  
\n
$$
q^{TH} = q(f_1 - f_1 f^{U}) \exp(-\lambda^{HT}t)
$$

where:  $f^U =$  fraction rapidly excreted in urine. But as ICRP supposes an instantaneous homogcnization, cven in the thyroid, and that thcre is no immcdiatc urinary cxcretion there is no immediate urinary exercise  $qf_1f^U$  (equations (41) and (42) of ICRP):

tions (41) and (42) of  

$$
q^{Th} = qf_1 \exp{-\lambda^{TB}t}
$$

Moreover, for ICRP,  $\lambda^{th} = \lambda^{T}$  so that, at any<br>moment:<br> $f_2 = \frac{q^{th}}{q} = \frac{q f_1 f_2'}{q f_1} = f_2'$ moment:

$$
f_2 = \frac{q^{th}}{q} = \frac{qf_1f_2'}{qf_1} = f_2'
$$

Thus a contradiction appears when ICRP uses<br>different values for  $f_2$  and  $f'_2$  (0.2 and 0.3).<br>In the case of a chronic contamination, the

In the case of a chronic contamination, the ratio of the body and thyroid radioactivities is obviously the samc as for an acutc contamination, i.e. the ratio of the amounts of stable iodine. Accepting a rate of exposure of 8 rem/13 wecks for the thyroid, ICRP calculates a maximum burden of  $0.15 \mu e^{-13}I$  in the thyroid and  $0.7 \mu c$ <sup>131</sup>I for the whole body.  $\overline{3}$ 

ln contradiction with thc abovc data uscd by ICRP, recent textbooks<sup>(5)</sup> put 85 per cent of the body iodine in the thyroid, i.e. 8 mg out of <sup>a</sup> total of 9-9.5 mg. Moreovcr this iodine forms several pools. The iodide in the plasma and in the diffusion volume is quickly removed by the kidneys and the thyroid; its biological half-lifc is only about <sup>6</sup> br. The organic iodine secreted by the thyroid has a longer half-life of 12 days<sup>(7)</sup> that is still much shorter than the 80-day half-life of the thyroidal iodine. A complete analysis of this metabolic sequence led us to propose  $0.17 \mu c$  as the maximal constant burden permissible for the whole body; this lcvcl of contamination corresponds to the prcscncc of 0.15 *µc* **in** the thyroid (this latter figure is obviously identical with that of ICRP).

The MPC for water and air that we have computed arc in bctter agreement with those of ICRP which utilizcs in the calculation only of ICRP which utilizes in the calculation only<br> $f_2' = 0.3$  referring directly to the critical<br>organ—thyroid, This value, likely derived<br>from alinical crudics unulel, is consistent with from clinical studies, would be consistent with a daily stable iodine intake of  $160 \mu$ g (adopting the other data of the prescnt papcr). With the mean intake of  $75 \mu$ g found in our small

sample of the Belgian population  

$$
f_2' = \frac{70}{70 + 78} = 0.47
$$

#### **CONCLUSIONS**

The concentration of the radioiodine in an organ of small sizc makcs **it** an important hazard for hcalth as dcmonstratcd by the values of the maximal permissible body burdens.

Becausc the activity ratio betwccn thyroid and body changes rapidly, it is neccssary to measure directly the radioactivity of the critical organ. For this purpose, wc use at the C.E.N. a cylindrical NaI crystal of  $5 \times 5$  cm shielded with 2 cm of lead; when it is localized at 6 cm from the thyroid, it is possible to dctcct lcss than  $0.002 \mu c$  of <sup>131</sup>I in the organ. Another sct-up with two NaI crystals of 7.5 cm diam.  $\times$ 5 cm ht. placed on each side of the neck enables to reach an even higher sensitivity:  $3 \times 10^{-5}$  $\mu$ c.  $^{(17)}$ 

The radioiodinc in the remaining body can be assessed with a total body counter. The ratio of the activities in thyroid and remaining



FIG. 8. Thyroid and rcmaining body activities **ratios after <sup>a</sup> single absorption of iodine-131 at time**  $O$  for various intakes of stable iodine.

body cnablcs one to dctcrminc the timc of contamination in Fig. 8 for <sup>131</sup>I.

Workers liable to be contaminated with the radioisotopcs of iodine must be frcqucntly checked. When the physician thinks that it is important to prevcnt the accumulation of radioiodinc in the thyroid by the administration of <sup>a</sup> carrier {Nal, lugol ...), this mcdication must be givcn in the vcry first hours following the accident. We believe however that a regular preventive administration of these drugs to workcrs frcquently in contact with radioiodines is not to be rccommcndcd; it could givc a false impression of security and be responsible for <sup>a</sup> relaxing of the ncccssary precautions in the working and near-by areas.<br>Moreover it is not impossible that the frequent Moreover it is not impossible that the frequent<br>intake of important doses of stable iodine for years can finally deteriorate the health of these people. Howcver workers with a dict rich in iodine are better protected than others.<sup>(18)</sup>

In the case of a chronic contamination *(or* a situation that can be considercd as such), when the worker is removed from the contaminated zone, it is important in the computation of the cumulatcd dose to take into account what the tissues will get before the radioisotopc is complctcly climinated. For <sup>1</sup> *µe* of radioiodine in the thyroid, this complementary dose for the organ will be:

for 
$$
^{125}
$$
1: 3.6 rem  
for  $^{126}$ I: 7.1 rem  
for  $^{129}$ I: 12.7 rem  
for  $^{131}$ I: 6.5 rem

It is worth mentioning that, for Euratom, the thyroid must not be considcrcd apart from the other internai organs, and the permissible dose rate ought not to excced 4 rem/ <sup>13</sup> wecks. If this point of view is adopted (as it is by the Bclgian rcgulations), ail the data in the Tables 4 and <sup>5</sup> must be divided by 2. Sorne authors think howevcr that the 1000 thyroid has a rather good radioresistance.  $(19)$ 

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