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A STUDY OF THE UPTAKE OF IODINE (I-131) BY THE THYROID OF PREMATURE INFANTS

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THE USE of I-131 to measure the state of thyroid activity in the adult is one of the accepted methods of studying thyroid function. A review of the literature reveals a lack of data concerning the status of thyroid activity in premature infants.

A few studies have been reported concerning children and recently Van Middlesworth[1] reported a series of 7 normal full-term newborn infants who were studied to determine the uptake of I-131. In this study 1 microcurie (μc.) of I-131 was given by injection into the gluteus maximus muscle. Twenty-four hours after injection he reports 61 to 97 per cent of the I-131 had been taken up by the thyroid. In his comment he states, "Such data together with reports of high protein-bound iodine levels in infants of the same age suggest the newborn infant may experience a period of physiological hyperthyroidism. This could result from several mechanisms, i.e.,

(a) Increased sensitivity of the thyroid to thyrotropic hormone,

(b) Increased production of thyrotropic hormone, or

(c) Complex alteration of endocrine balance.

"Because several explanations are possible, no therapeutic indications should be drawn from these data until specific experiments have demonstrated the usefulness of possible therapy."

The estimation of protein-bound iodine and butanol-extractable iodine in premature infants presents some difficulty because of the amount of blood required for analysis.

In order to determine the range of uptake of I-131 among premature infants in the newborn period, a study was begun July 1, 1954, through the joint effort of the members of the Pediatric Division and the Radioisotope Laboratory at Harper Hospital.

PROCEDURE AND METHODS

The baby is given a tracer dose of 5 μc.* of I-131 in 0.5 ml. of water solution at 8:00 A.M., on an empty stomach if possible. The water solution contains a trace quantity of potassium salicylate as a stabilizing agent. It is pure but not specifically sterilized or autoclaved. If the baby is intubated, the dose is injected through the tube and washed through with sufficient water, sugar-water or formula. If the baby can swallow in the normal manner, the dose is injected into the mouth from a sterilized syringe and washed down with water or formula. Sterilized equipment is used throughout, and the actual administration is done by the nurse in charge. (A standard test dose exactly the same size and concentration is likewise injected into a polyethylene phantom representing the baby's neck.)

Twenty-four hours later the concentration of I-131 in the thyroid gland is determined.

* Using an average mass of 1 gm. and a thickness of 0.5 mm. for the thyroid of a premature infant with Glasser's calculations for a 5 μc. dose, the gamma exposure is negligible. The beta exposure, assuming a total absorption, 880 beta roentgen, would be serious. The range of the particular beta particle in question is 1.3 mm. and using a half thickness of the gland of 0.5 mm. maximum, an actual maximum absorption of 60 per cent and a half life of 7 days, the total beta dosage would be 4.7 roentgens delivered at the exponential rate of 10 per cent per day. This figure is considered insignificant, being less than the equivalent of 3 exposures for x-ray films over a 30-day period. The iodine content of 5 μc. of I-131 is 4×10^{-11} gm.

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Two types of counters are used. The first is a scintillation counter mounted on a cart. This instrument is a self-contained unit which includes a constant potential transformer, the scintillation counter and a count-rate meter which reads directly in percentage. Half of the cart is covered with a sheet of solid lucite. On it in an eccentric position is a small saddle formed of lucite. This is exactly centered over the 1.9 × 1.9 cm. crystal of the scintillation counter which is set in a vertical position 13 cm. below the point the baby's thyroid will occupy, assuming normal anatomical position with the child's neck on the saddle. The crystal is covered by a 2 mm. lead filter.

The percentage rate meter is standardized first for zero and then for 100 per cent using the polyethylene phantom. A count is also performed on the phantom with the standard Geiger-Mueller counter and the background radiation is observed.

The phantom representing the baby's neck is made of polyethylene, 51 mm. in diameter and 75 mm. in length. The cavity represe the thyroid is at the mid-point on one the center of the cavity is 8 mm. below the face and is 5 mm. in diameter and 6 mm. It is closed with a tapered seal on the end a threaded piece of polyethylene so that scattering mass is uniform throughout. phantom was designed with the aid of William Brosius and is a representation of neck of a normal baby, both anatomically in terms of density and scattering mass.

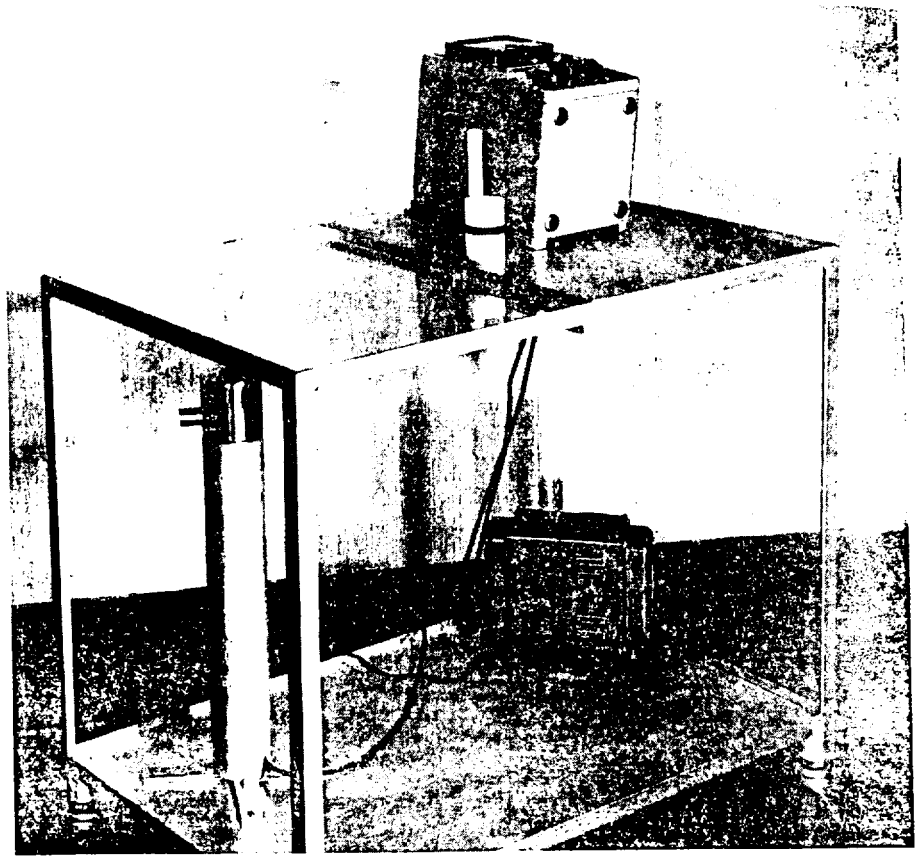

FIG. 1. Scintillation counter for premature infant. (Devised by Drs. Kenneth E. and Henrietta H. Corrigan.)

This phantom, containing 100 per cent do represents the "absolute normal" and as t radioactive substance undergoes physical d cay in the phantom it continues to repres 100 per cent regardless of the time interv which may elapse. (Example, if the actu count on the infant is performed at 20 hour 24 hours, 34 hours or 48 hours, it is only nece sary to count the phantom at the same tim in order to know exactly how much 100 p cent of the dose would count at that tim interval.)

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To take a reading on the scintillation counter it is necessary only to lay the infant face down on the plastic sheet with the neck in the proper position and read percentage directly off the count-rate meter. To assure a correct reading the child is maintained in position for 60 to 90 seconds. The design of the equipment has undergone several changes but is now very satisfactory. In the position described, the infant is comfortable, can breathe, can be held as long as necessary with no possibility of injury and reproducible results are obtained.

The second instrument is a Geiger-Mueller counter which is used to check the results obtained by the scintillation counter. This is the final instrument used for diagnostic purposes. It includes an electronic computer system which operates very rapidly and gives intensities in terms of counts per minute. From this percentage, concentration can be calculated. Scanning is done with the Geiger-Mueller counter to assure that the thyroid, if present, is in a normal anatomical position and to determine the presence or absence of aberrant tissue. A fixed distance count at 5 cm. is performed. The area covered by a thyroid of the size found in a premature infant is small enough to make the 5 cm. distance entirely satisfactory and the geometry completely reproducible. The use of the 2 types of counters provides a double check on the results obtained.

In the final report, the percentage as recorded by the scintillation counter is noted, the percentage retention as recorded by the standard Geiger-Mueller counter is noted, and if any anatomical or other variation occurs, this is also reported. All of the standards are checked at the end of the procedure.

RESULTS

Sixty-five premature infants ranging in weight from 991 gm. to 2481 gm. and 5 full-term infants delivered by cesarean section weighing 2522 gm. to 2694 gm. were given 5 μc. of I-131 either orally or by means of a polyethylene tube. Twenty-four hours later the uptake of I-131 by the thyroid was measured using both the Geiger-Mueller counter and the scintillation counter as previously described.

Table I presents the sex, age, birth

TABLE I

UPTAKE OF I-131 BY THE THYROID OF PREMATURE INFANTS

Sex	Case	Age (days)	Birth Weight (gm.)	Uptake I-131 (%) Scintillation Counter	Uptake I-131 (%) Geiger-Mueller Counter
		1000–1500 gm. Group			
F	1	39	991	37	37
M	2	63	1007	7	3
F	3	10	1007	37	37
F	4	20	1021	42	40
M	5	43	1048	28	24
F	6	42	1191	24	26
F	7	10	1191	19	15
M	8	16	1239	20	19
M	9	16	1290	17	11
F	10	26	1361	24	29
F	11	10	1416	26	29
		1500–2000 gm. Group			
M	12	8	1501	23	27
F	13	11	1511	26	25
M	14	13	1544	17	14
M	15	5	1580	26	20
M	16	11	1601	32	29
F	17	56	1631	22	20
F	18	4	1671	60	63
M	19	22	1701	29	30
F	20	5	1771	61	62
M	21	5	1814	24	20
F	22	2	1814	46	45
M	23	3	1814	18	15
F	24	18	1842	20	27
F	25	20	1871	20	21
M	26	8	1892	31	20
F	27	7	1892	18	12
F	28	9	1928	23	31
F	29	7	1928	15	12
M	30	7	1955	46	—
F	31	8	1955	10	13
F	32	12	1988	16	13
		2000–2500 gm. Group			
M	33	5	2041	39	31
F	34	4	2068	43	43
F	35	5	2068	49	51
M	36	5	2098	34	22
F	37	6	2098	23	31
M	38	6	2098	24	22
M	39	15	2111	29	24
F	40	5	2127	22	—
M	41	7	2141	51	48
M	42	7	2155	28	17
F	43	9	2155	21	20
M	44	3	2182	52	55

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TABLE I—(*Continued*)

Sex	*Case*	*Age (days)*	*Birth Weight (gm.)*	*Uptake I-131 (%)*	
				Scintillation Counter	*Geiger-Mueller Counter*
M	45	8	2211	19	19
M	46	11	2268	60	62
F	47	7	2268	9	6
M	48	7	2268	20	12
M	49	6	2268	24	20
F	50	6	2311	41	33
M	51	6	2352	34	26
M	52	7	2352	28	17
M	53	7	2368	15	16
F	54	6	2381	28	—
M	55	4	2381	47	44
M	56	5	2381	19	14
F	57	6	2395	36	24
F	58	4	2409	30	21
F	59	4	2409	34	30
F	60	4	2409	44	40
M	61	4	2409	23	25
F	62	6	2438	51	42
M	63	5	2465	35	24
F	64	3	2465	34	34
M	65	5	2481	29	29
			2500–3000 gm. Group		
F	66	2	2522	30	28
M	67	5	2551	37	37
F	68	6	2565	45	42
M	69	8	2629	30	21
M	70	9	2694	25	25

weight, as well as the percentage uptake as recorded by the scintillation counter and the Geiger-Mueller counter.

The distribution of cases by weight and sex is outlined in Table II.

Table III presents the distribution of cases by percentage of uptake of I-131 at 24 hours following either oral administration or by means of a polyethylene tube in the stomach. In 3 cases data concerning the percentage uptake using the Geiger-Mueller counter was not obtained.

TABLE II

DISTRIBUTION OF CASES BY SEX AND WEIGHT

Weight (gm.)	*Male*	*Female*	*Totals*
Up to 1500	4	7	11
1501 to 2000	9	12	21
2001 to 2500	19	14	33
Over 2500	3	2	5
Totals	35	35	70

Using the Geiger-Mueller counter as the standard, the variations in percentage uptake as recorded by the scintillation counter were: 10 cases identical counts; 8 cases ± 1 per cent; 9 cases ± 2 per cent; 13 cases ± 3 per cent; 6 cases ± 4 per cent; 2 cases ± 5 per cent; 3 cases ± 6 per cent. Of the cases where the variation amounted to between 7 and 12 per cent, 10 occurred during the first 3 months when modifications in the technique of the scintillation counter were being made. The remaining 6 instances are believed to be due to technical problems which have been largely overcome through experience with the method. At present using the technique outlined the variation between the 2 methods of counting is less than 5 per cent.

Table IV presents the results of the first 3 months of the study. During this period some difficulty was experienced in standardizing the technique of the scintillation counter which is apparent when the per

TABLE III

CASES GROUPED BY PERCENTAGE UPTAKE OF 5 μc. OF I-131, 24 HOURS FOLLOWING ADMINISTRATION ORALLY OR THROUGH A POLYETHYLENE TUBE

% Uptake	*0–9*	*10–19*	*20–29*	*30–39*	*40–49*	*50–59*	*60 plus*	*Total Cases*
Geiger-Mueller Counter	2	15	27	11	7	2	3	67*
Scintillation Counter	2	11	27	16	8	3	3	70

* Data concerning 3 cases are not available.

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TABLE IV

PRELIMINARY RESULTS DURING FIRST THREE MONTHS OF STUDY

Sex	Case	Age (days)	Birth Weight (gm.)	Uptake I-131 (%)	
				Scintillation Counter	Geiger-Mueller Counter
F	4	20	1021	42	40
F	10	26	1361	24	29
F	25	20	1871	20	21
M	26	8	1892	31	20
M	39	15	2111	29	24
M	42	7	2155	28	17
M	44	3	2182	52	55
M	48	7	2268	20	12
F	50	6	2311	41	33
M	51	6	2352	34	26
M	52	7	2352	28	17
F	57	6	2395	36	24
F	62	6	2438	51	42
M	63	5	2465	35	24
F	68	6	2565	45	42
M	69	8	2629	30	21

ntage uptake recorded by the scintillation counter is compared with the results obtained by using the Geiger-Mueller counter.

In 10 of the 17 cases studied the uptake I-131 at 24 hours measured by the scintillation counter was 8 to 12 per cent greater than the uptake recorded by the Geiger-Mueller counter.

In the 53 additional cases studied a variation of more than 6 per cent between the percentage uptake as recorded by the 2 methods occurred only 6 times.

As experience in the use of the scintillation technique has increased the incidence of wide variations between the 2 methods of counting has decreased.

DISCUSSION

This study was undertaken when a search of the literature failed to reveal any information concerning the uptake of I-131 in premature infants and only 1 article concerning full-term infants.

While the use of iodized salt has reduced the incidence of colloid goiter in the Great Lakes region, hypothyroidism in infants and young children still constitutes a problem. The indiscriminate use of iodine preparations and thyroid extract is also fairly extensive.

Clinical evidence of hypothyroidism in small infants is frequently meager so that a method of confirming such a diagnosis could be very useful.

Determination of protein-bound iodine and serum cholesterol require more blood than is feasible to withdraw from small prematures in many cases. Bone-age in this age group is not a reliable index of thyroid function.

Determination of the percentage uptake of I-131 by the thyroid 24 hours following administration was selected as the simplest radioactive iodine method for the appraisal of thyroid function which could be used in the age group under consideration.

Before undertaking this study careful consideration was given to the possible danger of using I-131 in a 5 μc. dose for a premature infant. The matter was discussed by a group composed of the Director of Research, the Chief of the Radiology Department, the Director of the Radioisotope Laboratory, the Director of the Pathology Department and the Chief of the Pediatric Division. It was the consensus of opinion that a dose of 5 μc. of I-131 administered orally would not be harmful.

The range of uptake of I-131 measured by the Geiger-Mueller counter 24 hours following oral administration in older children using the technique outlined has been found to be 20 to 60 per cent. At the hypothyroid end of the scale values from 10 to 20 per cent have been found in both euthyroid and hypothyroid individuals, while at the opposite end there is likewise some overlapping in the range of 50 to 60 per cent.

This study of 65 premature infants and 5 infants weighing between 2500 and 2700 gm., delivered by cesarean section suggests that the activity of the thyroid in premature and full-term infants is within the range considered normal in older children and

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adults. It further suggests that individual infants who show evidence of possible hypo- or hyperfunction of the thyroid gland as measured by the uptake of I-131 should be further investigated to determine, if possible, the underlying cause of the variation from the normal uptake (Cases 2, 47, 18, 20, 46).

In Cases 2 and 47 there is a possibility that the mother was surreptitiously taking thyroid extract during the course of her pregnancy. Cases 18, 20, and 46 may possibly be instances of the unexplained fluctuations which occur from time to time in normal individuals, because these patients did not show any clinical evidence of hyperthyrodism and have developed in a normal manner.

SUMMARY

In a series of 65 premature infants weighing from 991 to 2481 gm. and 5 full-term infants from 2522 to 2694 gm., who were from 1 to 63 days old, the uptake of I-131 by the thyroid 24 hours following the administration of 5 μc. orally or by means of a polyethylene tube in the stomach, as measured by both a Geiger-Mueller counter and a scintillation counter, ranged from 10 to 60 per cent. In 2 cases with an uptake of less than 10 per cent and 3 cases bordering 60 per cent, technicalities and the possible surreptitious use of thyroid by the mother may account for the variation.

The range of uptake of I-131 as recorded in this series of infants is within the limits of normal as recorded in studies of children and adults using the Geiger-Mueller counter.

The difference in percentage uptake as recorded by the Geiger-Mueller counter and the scintillation counter, after acquiring experience with the equipment, was less than 5 per cent.

The technique, and the scintillation counter used, are described. I-131 administered orally or by a polyethylene tube in the stomach is well tolerated and in this series did not cause vomiting.

The activity of the thyroid gland in premature and full-term infants, as revealed by the uptake of I-131 24 hours following administration, is discussed and evidence presented that in such individuals the thyroid functions in a manner similar to that found in children and adults.

REFERENCES

1. Van Middlesworth, L.: Radioactive iodine uptake of normal newborn infants. Am. J. Dis. Child., 88:439, 1954.
2. Morgan, R. H., and Corrigan, K. E.: Handbook of Radiology. Chicago, Yr. Bk. Pub., 1955, p. 250.

SPANISH ABSTRACT

Estudio del Aprovechamiento del Iodo (I 131) Por la Tiroides de los Niños Prematuros

Los autores describen un método para determinar el aprovechamiento del I 131 a las 24 horas de administrar 5 microgramos de la substancia a niños prematuros, empleando la vía oral en tanto fuera posible y sonda de polietileno cuando fue necesario. Describen además el equipo que emplearon, constituido por un contador Geiger-Mueller y otro contador de cintilación especialmente planeado.

El estudio se hizo en forma seriada en 65 prematuros con peso variable de 991 a 2,481 gramos y en 5 niños a término con peso de 2,522 a 2,694 gramos, y edad de 1 a 63 días. El aprovechamiento del I 131 hecho por la glándula tiroides a las 24 horas de haberse administrado por vía oral o por el tubo de polietileno los 5 microgramos señalados, fue de 10 a 60% en los 65 casos, según se determinó tanto por el contador Geiger-Mueller como por el de cintilación. En dos casos las variaciones alcanzaron un aprovechamiento de menos del 10% y en 3 alrededor del 60%, explicables por razones técnicas y el uso posiblemente subrepticio del tiroides por la madre.

Los límites de aprovechamiento del I 131 en esta serie están dentro de las cifras normales señaladas en estudios hechos en niños mayores y adultos, empleando también el aparato Geiger-Mueller. Las diferencias en el porcentaje de aprovechamiento según el registro de ambos aparatos, considerado después de que se hubiera adquirido experiencia con el equipo, fueron menores de 5%.

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Los autores describen el equipo empleado en el aparato de cintilación. El I 131 fue ben tolerado y no causó vómitos en esta serie, nto cuando se empleó la vía oral como la nda de polietileno introducida al estómago. Discuten la actividad tiroidea en prematuros niños nacidos a término, según los datos tenidos por el aprovechamiento del I 131, 4 horas después de su administración; adelantan la idea de que en ellos funciona la andula en forma similar a niños mayores.

INTERLINGUA ABSTRACT

Un Studio del Sorption de Iodo (I-131) per le Thyroide de Infantes Prematur

Es describite un methodo pro determinar le rption de I-131 24 horas post le administra-a de 5 μc a infantes prematur per via oral si ssibile o per un catheter polyethylenic si cesse. Le instrumentario includeva un con-tor Geiger-Mueller e un contator a scintilla-a de construction special. Iste ultime es cribite in detalio.

In un serie de 65 infantes prematur con os ab 991 g a 2481 g e cinque infantes scite a termino con pesos ab 2522 g a 2694 a etates de inter 1 e 63 dies, le sorption de 31 per le thyroide, mesurate per le contator iger-Mueller e le contator a scintillation 24 ras post le administration de 5 μc per via oral o per un tubo polyethylenic a in le stomacho, variava in 65 casos ab 10 a 60 pro cento. In 2 casos con un sorption de minus que 10 pro cento e in 3 casos con un sorption vicin a 60 pro cento, le valores obtenite se explica possibilemente per rationes technic o le uso surrepticie de extracto thyroide per le matre.

Le distribution del valores de sorption de I-131 obtenite in iste serie es intra le limites del norma registrate in studios con pueros e pueras de plus alte etates e con adultos per medio del contator Geiger-Mueller.

Le differentias del valores obtenite in le presente studio per medio de (1) le contator Geiger-Mueller e (2) le contator a scintillation esseva minus que 5 pro cento si tosto que nostre experientia con le apparatura habeva maturate.

Le apparatura usate in connexion con le contator a scintillation es describite. I-131 administrate oralmente e per tubo polyethylenic a in le stomacho es ben tolerate. In le presente serie illo causava nulle vomito.

Es discutite le activitate del glandula thyroide in infantes prematur e in infantes nascite a termino in tanto que illo se manifesta in le sorption de I-131 24 horas post le administration. Es presentate datos que indica que in tal individuos le glandula thyroide functiona in un maniera simile al maniera de su functionamento in infantes e juveniles de etates plus avantiate.

COMBINED ANTIBIOTIC THERAPY FOR THE SUPPRESSION OF RESISTANT VARIANTS IN URINARY INFECTION. H. Stern and S. D. Elek. (Brit. M. J., **4951**:1304, November 26, 1955.)

The use of pairs of antibiotics to suppress the emergence of resistant strains has been the subject of several investigations and has been particularly successful in tuberculosis. The authors investigated the effect on the coliform group of organisms, commonly the cause of urinary tract infections, of combinations of streptomycin with chloramphenicol or tetracycline. The testing was done *in vitro* and the technique is described. Streptomycin plus tetracycline and streptomycin plus chloramphenicol proved to be the most effective combinations for suppressing resistant variants while at the same time maintaining bactericidal activity. The latter feature is considered an important factor in the prevention of relapses in urinary tract infections. The investigations did not include a clinical trial of the value of these antibiotic combinations but the *in vitro* tests indicate that good results are to be expected in application in clinical practice.

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