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RADIOACTIVE-IODINE CONCENTRATION IN THYROID GLANDS OF NEWBORN INFANTS

Richard E. Ogborn, M.D., Ronald E. Waggener, M.D., and Eugene VanHove, M.D.

Radioisotope Service, Veterans Administration Hospital, Omaha, and the Department of Radiology, University of Nebraska College of Medicine

THE ACCUMULATED evidence as presented in the world literature behooves the clinician to establish a diagnosis of athyroidism or congenital hypothyroidism as soon after birth as possible. If treatment for this condition is started later than the fourth to sixth month irreparable damage has occurred.

In the historical search for a practical, accurate method of determining thyroid function in infancy many clinical laboratory tests and roentgenologic examinations have been devised to aid the physician. Among the most commonly used laboratory tests are: concentration in the blood of protein-bound iodine (PBI), inorganic iodine, cholesterol and its ester. These tests have undesirable features for routine use in newborn infants, such as the requirement of large amounts of blood or the normal variation from the mean is so great that it overlaps the pathologic ranges. Measurement of basal metabolism is naturally very impractical. Although radiographic evidence of bone change assists physicians in diagnosis, a reliable practical laboratory method is needed. In recent years numerous variations of basic radioactive iodine (I^{131}) tests have been performed on children of older age groups.[1-7] However, an extensive review of the literature has revealed only two studies of thyroid function using I^{131} in newborn infants. The first study[8] reported was with seven normal newborn boys, 2 and 3 days old. The 24-hour I^{131} thyroid uptake ranged from 46 to 97% of the injected dose (mean 69.7%); the summary states, "The I^{131} uptake by the thyroid of seven normal infants has been demonstrated to lie within the range of values which would be found in hyperthyroid adults." The second study[9] was carried out with 65 premature infants, ranging in weight from 990 to 2,481 gm, and five full-term infants (2,522 to 2,694 gm) delivered by cesarean section. The age range at the time of testing was from 1 to 63 days old. The 24-hour I^{131} thyroid uptake ranged from 7 to 61% (mean 32.4%). These results were considered to be within the limits of normal as recorded in studies of adults. On the basis of this evidence it was assumed that the thyroid gland in premature and full-term infants functions similar to that of adults. The data and conclusions from these two previous studies are at variance.

The objection to the administration of radioactivity to normal newborn infants must be considered. Martmer *et al.*[9] consider the gamma exposure of a 5 μc dose "negligible" and the total beta dose "insignificant." Van Middlesworth[8] reports that a dose of 1 μc of I^{131} in a thyroid gland weighing 2.4 gm produces a maximal total radiation of 60 r (rep) or 144 gm − r (gm) × roentgen equivalent physical. He states, "A gastrointestinal x-ray series with fluoroscopy in an infant results in an exposure to at least 20 r or 3,600 gm − r."

In the present series the total integrated dose to the thyroid gland of a newborn (estimated weight 2.0 gm) was 214 rads if the total 5 μc of I^{131} was taken up by the thyroid gland and had a biologic half-life of 6 days. The calculations were based on the formulas of Quimby *et al.*[10] This calculated dose to the thyroid gland might be compared to the dose received by an infant in

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ADDRESS: (R.E.O.) V.A. Hospital, 4101 Woolworth, Omaha 5, Nebraska.

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an ordinary abdominal x-ray examination. Assuming a conservative 20 × 20 cm field (100 KV; hvl = 1 al; 0.027 r/ma − sec), the total dose received would be 4,285 gm − r.

Any active cardiovascular center will do complete roentgenographic and fluoroscopic studies on children suspected of heart disease. The radiation dose received by such children is higher than with a single abdominal examination but the danger from irradiation is believed to be acceptable and is rarely questioned as a diagnostic aid.

A calculated risk is taken in performance of any irradiation examination, but the potential benefits may outweigh any hypothetical dangers whenever such an examination is indicated.

The purpose of this paper is to present the results obtained in a study of the uptake of I^{131} by thyroid glands in normal newborn infants. The method of Martmer *et al.*[9] has been closely adhered to and modified only when necessary.

PROCEDURE

The newborn infant is given approximately 5 μc of I^{131} by injection through a gastric tube 3 hours after the last feeding. Immediately following this, two injections of 2 ml of sterile 0.9% saline solution from the same syringe are washed through the tube. The tube is then removed and saved for counting residual activity. Sterilized equipment is used throughout, and the administration is done by the same person every time. Twenty-four hours later the concentration of I^{131} in the thyroid gland is determined by recording the disintegrations by means of a scintillation counter through a countrate meter.* The standard reference for the test dose is prepared by putting 1 ml of the previous calculated I^{131} solution into a polyethylene phantom representing the baby's neck (to be described).

On a solid sheet of plasti-glass covering a small cart is an eccentrically placed plasti-glass saddle positioned exactly over the 1½ × 1 in. crystal of the scintillation counter which is set in a vertical position 13 cm below the point the baby's thyroid will occupy. The crystal is covered with a 2-mm lead filter. The phantom is made of polyethylene, 51 mm in diameter by 75 mm in length. The cavity representing the thyroid is at the mid-point on one side, the center of the cavity is 8 mm below the surface and is 5 mm in diameter by 6 mm long. It is closed with a threaded piece of polyethylene so that the scattering mass is uniform throughout. The design of the phantom is similar to the one used by Martmer *et al.*[9] in the study of newborns, and is a representation of the neck of a normal baby, both anatomically and in terms of density and scattering mass.

This phantom represents the amount of radioactive substance in 1 ml of the test solution at any time as the I^{131} undergoes physical decay.

Prior to making a determination of the uptake in an infant, the percentage ratemeter is standardized for zero, 100% and for high voltage. To make a determination of the radioactivity in the thyroid gland it is necessary to hold the infant in a prone position with the neck over the saddle and read the counts per minute directly from the ratemeter. A correct reading of less than 2% probable error is assured with this instrument while holding the infant in this position for 1 minute. By this arrangement the infant is comfortable, can breathe without difficulty and can be held as long as necessary with no possibility of injury. Following this, one of the infant's thighs is held over the saddle for 1 minute and the counts per minute recorded. Then readings are taken of the room background radiation and of the standard (phantom placed on the saddle). Before another infant is placed on the table, the entire table top and the saddle are cleaned with 70% alcohol.

The following formula was used to determine the percentage of I^{131} uptake by the thyroid in this series of newborn infants:

$$\frac{(A-B)-(D-B)\times 100\%}{(C-B)-(E-B)\times F} = \%\ \text{uptake}$$

A—Counts per minute (count/min) over neck
B—Count/min (background)
C—Count/min (standard)
D—Count/min (thigh)
E—Count/min (tube and syringe)
F—Milliters of standard injected

SUBJECTS

The normal character of the subjects was determined by an accurate prenatal history

* Precision Ratemeter from Tracerlab Inc.

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obtained for each infant studied, in regard to weeks of gestation, parity of the mother, abnormalities of the pregnancy, and medications the mother received prior to delivery. The period of delivery was investigated in regard to duration of labor, type of delivery, and condition of the infant at birth. The past history of the mother was reviewed in regard to previous illnesses, operations, and prescribed or proprietary medicines. The family history was also obtained in regard to familial diseases and health of the immediate family. The length, weight, sex, race, and age of the infant at the time of the determination of the thyroid I^{131} uptake and physical condition of the infant were also recorded.

Twenty-eight infants from the nursery at the hospital of the University of Nebraska College of Medicine were studied.

RESULTS

The data are presented in Table I. Sixteen males and 12 females were studied ranging in age from 72 to 180 hours and whose weight ranged from 2,600 to 4,663 gm. Two of the infants (Cases 1 and 3) were excluded from the analysis of this series because the mothers had taken iodine or magnesium compounds until the time of delivery. The mean of the age range is approximately 90 hours.

The extremes of I^{131} uptake by the thyroid gland are from 6.3 to 36.4%. The mean uptake of these 26 cases is 20.3%. The standard deviation is 8.5%. Fourteen of the cases (54%) are within one standard deviation of the mean; all of the cases are within two standard deviations of the mean.

An analysis of the data to show the effect of weight and sex is presented in Table II. The distribution of cases by per cent of uptake is shown in Figure 1.

DISCUSSION

Man[11] reported a series of children 6 weeks to 16 years of age, in which the serum PBI (as determined by the permanganate acid ashing method) was shown to have a normal range from 4.0 to 8.0 µg/100 ml. In nine cretins (3 months to 12 years of age)

TABLE I

UPTAKE OF I^{131} BY THE THYROID OF NEWBORN INFANTS

Sex	*Case*	*Age (hours)*	*Birth Weight (gm)*	*Uptake I^{131} (%)*
M	1	129	2,625	7.0*
M	2	128	3,568	19.5
F	3	122	3,111	2.3*
F	4	110	2,655	18.0
F	5	180	4,105	17.2
F	6	90	4,663	30.9
F	7	88	2,677	14.3
M	8	97	4,220	12.6
M	9	94	3,133	29.0
F	10	84	3,388	26.1
M	11	100	3,211	36.4
F	12	90	2,963	6.3
M	13	85	3,325	8.9
F	14	100	4,225	30.2
F	15	100	2,655	13.7
M	16	96	3,899	20.0
F	17	95	3,147	23.9
F	18	96	2,600	11.3
M	19	98	3,628	26.4
F	20	86	3,490	22.2
M	21	84	3,059	35.4
M	22	100	3,610	19.4
M	23	94	3,752	9.3
M	24	98	3,289	29.7
M	25	82	3,515	28.2
M	26	88	3,514	16.5
M	27	101	3,591	11.1
M	28	72	3,159	11.1

* Mothers of these infants had medication known to alter thyroid function.

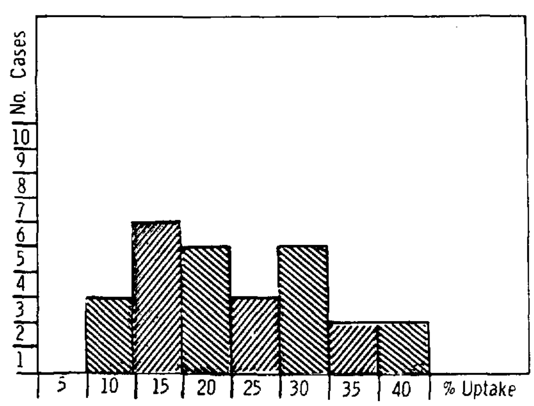

FIG. 1. Cases grouped by percentage uptake of I^{131} 24 hours following administration.

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TABLE II
DISTRIBUTION OF CASES BY SEX AND WEIGHT WITH RANGE OF I^{131} UPTAKE

Weight (gm)	Male No.	Male Range (%)	Female No.	Female Range (%)
2,600–3,000	0		5	6.3–18
3,001–3,500	6	8.9–36.4	3	22.7–26.1
3,501–4,000	8	9.3–28.2	0	
4,001–4,663	1	12.6	3	17.2–30.9

all values were below 2 μg/100 ml. Because, at the time, the test required 25 ml of blood, normals were not determined in this series. Similar results have been reported[12-14] in severe hypothyroidism. Kessel and Politzer[15] studied the PBI levels in blood of mothers and their infants at birth. Thirty-three cases were included in this study with a view of establishing a normal pattern. In six cases (all males) the PBI level was higher in the infants' cord blood than in the mothers' blood (3.0 to 11.6 μg/100 ml). In 21 of the mothers and in 21 of the infants, the PBI level was between the accepted normal range of 3.5 to 8.0 μg/100 ml. In only one mother and four infants the level was below 3.5 μg/100 ml. In 11 mothers and eight infants the level was over 8.0 μg/100 ml. The determinations in the infants were performed on samples of the cord blood.

Danowski *et al.*[16] studied 110 infants ranging up to 1 year of age, who were in good health and developing normally. The PBI concentrations were analyzed in duplicate by the method of Barker. All of these infants had been born at term following an uncomplicated pregnancy. The results revealed that at birth the level of PBI in the blood was the same as the mother's and then it rapidly increased to its peak from 1 to 4 days—mean 12.9 μg/100 ml, and then slowly decreased the remainder of the first year. In reviewing the findings of these authors, it would seem that the serum PBI would serve to distinguish hypothyroid infants from normals. However, there appear to be discrepancies in comparative normal ranges; and in Danowski's[16] work the age of testing is a very important criterion.

Inorganic iodine in blood, as a test of thyroid function, has been shown by others[17] to have a wide normal variance (4 to 32.0 μg/100 ml). Decreased or absent thyroid function reduces the inorganic iodine in serum to the range of 36 to 70% of normal, thus many of the blood levels of inorganic iodine in athyreotic children are in the range of normal.

The relationship of cholesterol and its esters in the blood to myxedema has been known for years, but as many studies have shown very little reliability can be associated with the cholesterol level in blood as a diagnostic test.[12,14,18,19]

It is well known that there is radiologic evidence of bone age retardation in hypothyroid states of infants and children. The radiologic signs were grouped and very adequately explained in a report by Astley.[20] He concluded that evidence of bone age retardation is a useful link in the chain of diagnostic evidence, but is not by itself of any great significance because there are many other causes that produce similar radiologic findings. For further information the reader is referred to excellent studies of roentgenological findings in infants and children with hypothyroidism..[12,19,21-23] These studies tend to confirm Astley's conclusions.

A need exists for an accurate harmless clinical test to aid physicians in establishing a diagnosis of congenital hypothyroidism in newborn infants.

In a review of the literature the various tests of thyroid function were found to present difficulties when applied to newborn infants; only two articles were found using I^{131} uptake technics. Their results and conclusions were in opposition to each other.[8,9] Therefore, it was felt necessary to investigate the I^{131} uptake method further and to attempt to determine a normal range of thyroid activity in the newborn.

Although our findings concur with those obtained by Martmer *et al.*,[9] we have not

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accumulated a series of abnormal patients. Theoretically it would appear that I^{131} uptake would be diagnostic only in those cases of hypothyroidism due to aplasia of the thyroid gland. At the moment there seems to be no single test which can be employed in the newborn period for accurate diagnosis of hypothyroidism.

CONCLUSIONS

The thyroid function of 28 newborn infants was studied by the uptake of I^{131} by the thyroid gland.

The range of I^{131} uptakes was from 6.3 to 36.4% with a mean of 20.3% (standard deviation is 8.5%). Fourteen of the cases were within one standard deviation of the mean and all cases were within two standard deviations.

In this study sex and weight were not found related to thyroid function.

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GROWING UP IN NEWCASTLE UPON TYNE: A Continuing Study of Health and Illness in Young Children within their Families, F. J. W. Miller, *et al.* New York, The Oxford University Press for the Nuffield Foundation, 1960, 369 pp., $5.75.

In order to appreciate this book one should be familiar with the volume on the same subject "A Thousand Families in Newcastle on Tyne." That told of all the children born in Newcastle in May and June of 1947 who were intimately observed by Sir James Spence and his collaborators. During the first year of these children's lives a complete record was kept of their illnesses and other significant observations.

This volume continues the intimate follow-up of the 847 children age 1 to 5 and their families. The book should be of interest to anyone responsible for the health of children. The pediatrician can find much of interest as Newcastle is comparable in many ways to cities of 300,000 people in this the United States. The growth, development and illness of these children is related to family and environmental circumstances. Despite lowered infant mortality the study shows there is still a large amount of childhood infectious illness. There is also a considerable residue of permanent disability found in the child under 5 ——mental deficiency, neurologic defects, poor vision, cerebral palsy and related problems. Disturbed behavior in children seems to be deeply rooted in the personalities of the parents and children and are not always easy to recognize. The authors point out that child health and disease are closely related to family environment. Although most families care for their children, many live in poor and overcrowded houses where parents themselves are beset with illnesses or instability. The authors feel some of the ways of improving the situation are education of parents, physicians, hospitals and others responsible for child health. Medical education can also be made more effective in forwarding concepts in family care.

The book is conveniently divided into sections with summaries. The first section deals with families and social and economic changes occurring over the 5-year period. Part two discusses the child's environment in medical care, housing and environment. Part three details illnesses; four makes an appraisal of child illness and the resulting defects on entering school. Part five gives statistical data and detailed techniques in a series of appendixes.

Despite pertinent and useful information about respiratory disease, accidents, developmental and behavioral problems, there is also considerable less essential information. Some information regarding socioeconomic factors in the families as well as detail of certain aspects of illness may not be of broad interest.

On the whole, the volume is interesting and should be of value to the pediatrician if he is willing to overlook the sometimes confusing differences between the British and the American medical and social scene. As these children are to be followed until age 15, the next volume covering their school years should be of interest also.

ROBERT W. DEISHER, M.D.

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