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upon the neural systems, even though control of its concentration in the blood is sometimes of critical importance to survival. However, its very close relative, carbon dioxide, is well known for its influence upon such neuro-muscular systems as those involved in breathing. Thus, it seems likely that carbon dioxide is one of the variables involved with the N-System, while carbon monoxide is not.

Although a detailed description is beyond the scope of this paper, it can be shown that the N-System, acting through the intermediary of the neural networks, achieves an effective, though rather crude, feedback control of these special physiological variables. Learning, then, is the result of these interactions, although in a way it is only a by-product.

Finally, let us consider the problem of chronic conflict. In our theory, chronic conflict can be defined as the situation when two higher feedback systems send different output signals into the *same* subordinate feedback system. Stress or inefficient operation occurs then because each of the higher order systems is driven to its limits because it treats the other higher system as a disturbing variable. We feel that this definition of chronic conflict can be applied in the analysis of psychopathology.

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VALUES FOR THYROID UPTAKE OF I^{131} AND PROTEIN-BOUND IODINE IN "NORMAL" INDIVIDUALS FROM BIRTH TO TWENTY YEARS[1]

JOHN E. KEARNS, M.D. and HERBERT F. PHILIPSBORN, JR., M.D.

Introduction

IN 1938 Hertz (5), using radioactive iodine, studied thyroid function in rabbits and humans. Since then an abundance of data on this subject have been published. However, there still exists scant data concerning thyroid uptake of I^{131} and values for protein-bound iodine among individuals demonstrated to be euthyroid. Some data referable to thyroid function of "normal" persons have been derived through studies concerned with abnormal thyroid function (4). The most systematic study of thyroid function using I^{131} in growing individuals was conducted by Oliner (7).

Thyroid uptake studies with I^{131} measure the ability of the thyroid gland to gather iodide. Protein-bound iodine expresses a distribution of "hormonal" iodine in the blood. These determinations offer evidence of thyroid function. Data gathered from studies of I^{131} and protein-bound iodine permit comparison of thyroid activity among large numbers of known euthyroid individuals.

Material and Method

All persons studied were free from organic disease and were "normal." The majority of subjects were well known in a routine pediatric practice. Some of the older individuals were healthy undergraduates at the Evanston Hospital School of Nursing. All of the persons demonstrated skeletal maturation consistent with their chronological age (3). Protein-bound iodine values were determined and unusually high or low values were repeated for verification and checked with butanol extractable iodine studies (1). Observations of thyroid uptake of I^{131} were carried out by using 25 microcuries of radioactive material in children up to the age of 6 years and 50 microcuries of radioactive material in older individuals. Gamma studies were made in a routine manner at 24-hour intervals.

Data

Results of this study are presented in Charts and Graphs (figs. 1-3) with accompanying legends. Values for thyroid uptake of I^{131} and protein-bound iodine in euthyroid individuals, from birth to 20 years, are shown in Figure 1C through 2D. Values of protein-bound iodine from 10 pregnant women, beyond the age of 20 years and at term, are available for comparison with the protein-bound iodine values from the cord blood of their infants (fig. 1B). Other data (fig. 1D) show increased values for thyroid uptake of I^{131} in the very young infant as opposed to lower values obtained during childhood and adolescence.

Our results are not in agreement with those of others (2, 6) who have reported butanol extractable iodine and the protein-bound iodine of infants' venous blood at birth as similar to that of their mothers at term. Our data demonstrate a distinct rise in the protein-bound iodine level of infants during their first few days of life.

Discussion

The physiological basis for increased thyroid uptake of I^{131} and the increased quantities of protein-bound iodine present in the infant soon after birth are as yet unexplained. Profound physiological changes occur when the umbilical cord is severed. The fetus becomes a nonparasitic one. Such a fundamental change requires adjustments by respiratory, cardiovascular, gastrointestinal, musculoskeletal and other systems. The thermoregulatory system, intimately associated

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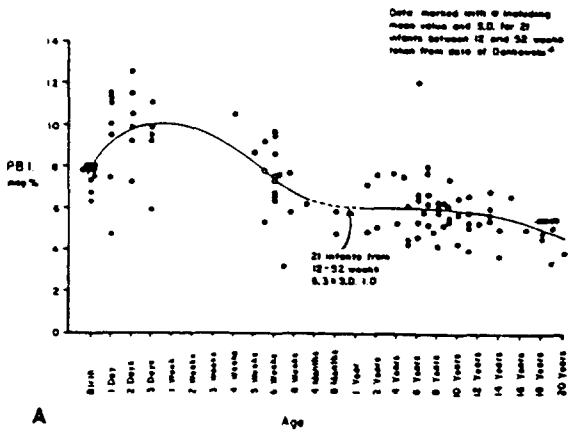

GROUP I – Mothers at Term and their Infants

Mother	Age	P.B.I. at Delivery	Newborn	Sex	P.B.I. Cord Blood	Wt (lbs)
De	26	8.7	De	F	8.0	9^{3}
He	26	7.0	He	F	7.3	7^{3}
Ki	23	7.5	Ki	M	7.8	7^{3}
Me	34	7.9	Me	M	7.8	7^{14}
Pe	21	7.8	Pe	M	7.8	8^{3}
Ra	25	7.1	Ra	F	7.8	8^{3}
Sn	26	12.2	Sn	F	6.3	7^{9}
Sw	32	10.5	Sw	F	8.0	7^{3}
Te	31	5.0	Te	M	6.7	7^{9}
Wa	39	7.5	Wa	M	8.0	7^{9}

B

GROUP II - Newborn Infants

Name	Sex	Age	I^{131}	PBI	BMR	Bone Age
He	M	4 hours	100%	7.5	-	Newborn
Ra	F	1 day	88%	7.4	-	Newborn
Tr	M	1 day	96%	4.7	-	Newborn
Cr	M	1 day	100%	11.3	-	Newborn
Ba	F	1 day	66%	10.0	-	1 month
Za	F	1 day	99%	9.5	-	3 months
Ale	M	1 day	74%	11.0	-	Newborn
So	M	1 day	56%	11.5	-	Newborn
St	F	2 days	72%	10.5	-	Newborn
Bu	M	2 days	37%	12.5	-	1-2 months
Ne	F	2 days	76%	11.5	-	Newborn
Va	F	2 days	100%	9.2	-	Newborn
Ma	F	2 days	69%	7.2	-	1-2 months
Ti	F	2 days	30%	9.9	-	Newborn
Pa	F	3 days	65%	11.0	-	1-2 months
Ja	M	3 days	90%	9.5	-	Newborn
Ba	M	3 days	58%	5.9	-	Newborn
Ma	F	3 days	73%	9.9	-	Newborn
Fr	F	3 days	75%	9.3	-	Newborn

C

Average Infant
2 days old
I^{131} - 75% (30% - 100%)
PBI - 9.4 (4.7 - 11.5)
Bone Age - Newborn

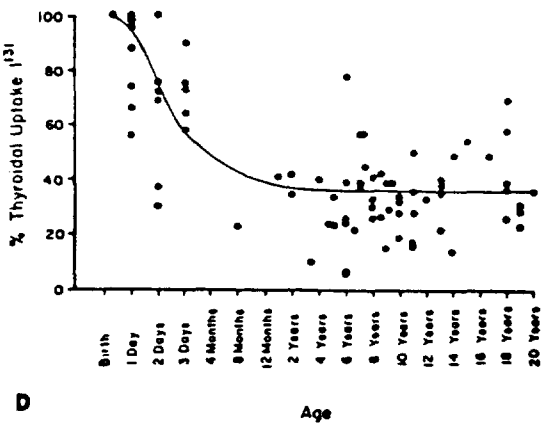

Fig. 1. A, Scatter graph and curve show values of protein-bound iodine in "normal" individuals from birth through 20 years. B, Values for protein-bound iodine from "normal" mothers and infants at time of birth. C, Values of uptake of I^{131} and protein-bound iodine from "normal" infants: 4 hours to 3 days old. D, Uptake of I^{131} by thyroid gland in "normal" individuals from birth through 20 years.

with thyroid activity, is triggered to new activity as the fetus leaves its controlled intra-uterine existence. We have as yet unpublished evidence that the newborn is relatively deficient in thyroxin-binding protein. By the third day of life, this protein factor is increasing. (This or any one of these factors may be responsible for the increased thyroid activity during the neonatal period.)

Small amounts of maternal thyroxin cross the placental membrane during pregnancy. With the onset of labor, this extra-fetal supply of thyroxin is abruptly withdrawn. The immediate post-birth condition of the infant should appear to be hypothyroid. Unexplained by such simple placental transfer are the increased values of I^{131} and the rise of protein-bound iodine occurring soon after birth.

We have been interested in the histology of the placenta as it is related to transplacental migration of certain blood components. The placental anatomy in lower orders of animals is such that the maternal-fetal circulation appears to be

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GROUP III - Children 8 Months - 5 Years

Name	Sex	Age	I^{131}	PBI	BMR	Ht (in)	Wt (lbs)	Bone Age
No	M	8mo	23%	4.8	–	–	22¾	6 mo
Sp	F	1½ yrs	41%	4.9	–	–	–	18 mo
Be	F	1½	–	7.1	–	–	–	18 mo
Wi	M	2	35%	5.1	–	–	–	–
Ne	M	2	42%	7.6	–	–	–	–
Wi	F	3½	10%	7.7	–	–	–	3½ yrs
Ti	M	4	40%	5.3	–	–	–	4 yrs
Ba	F	4½	24%	7.5	–	–	–	4½ yrs
Wi	M	5	–	4.5	–	–	–	–
Re	M	5	34%	4.3	+8%	46	43¾	3½ yrs
Pa	F	5	23%	6.1	+20%	46	40	5-5½ yrs

Average Child
3" years
I^{131}-30%(20%-42%)
PBI-5.9(4.3-7.7)

A

GROUP IV - Children 6-9 Years

Name	Sex	Age	I^{131}	PBI	BMR	Ht (in)	Wt (lbs)	Bone Age
Ru	F	6	78%	6.6	–	–	–	6 yrs
Pa	F	6	26%	5.3	–	63¾	34½	5½-6 yrs
Th	F	6	39%	4.6	–	–	–	6 yrs
Sa	M	6	25%	6.4	–	46¾	53	6 yrs
Al	M	6	6%	3.0	–	48	50	6 yrs
Wh	M	6½	22%	3.6	–	–	–	6½ yrs
Sc	M	7	57%	6.7	–	–	–	6 yrs
Ma	F	7	–	8.0	–	–	–	7 yrs
Be	F	7	39%	6.2	–	47	42	–
Ar	M	7	37%	5.2	–	–	–	–
My	F	7	57%	6.7	–	47	43	7 yrs
Bo	M	7½	46%	4.9	+1%	53¾	68¾	7½ yrs
Pa	F	8	26%	5.8	+3%	48¾	70¾	8½-9 yrs
Ne	M	8	41%	4.2	–	49	52	7 yrs
Al	M	8	30%	6.1	–	52	62	8 yrs
Eg	M	8	33%	6.3	–	50	73	8 yrs
Wa	M	8½	42%	6.3	–	–	70	8½ yrs
Ma	F	8½	26%	5.2	–	–	–	8 yrs
Ro	F	9	39%	6.1	–	50¾	67	9 yrs
Ta	M	9	15%	5.4	–	–	–	7½ yrs
Sr	M	9	39%	5.5	–	–	69	9 yrs
Da	M	9	29%	7.4	–	57	90	9 yrs

Average Child
7.5 years
I^{131}-34.3%(8%-78%)
PBI-6.2(4.2-12)

B

GROUP V - Children 10-14 Years

Name	Sex	Age	I^{131}	PBI	BMR	Ht (in)	Wt (lbs)	Bone Age
Pa	M	10	34%	4.3	+1%	59¾	82	10 yrs
Al	M	10	28%	6.9	+8%	58	73	10 yrs
Ar	M	10	19%	5.7	+4%	54	67	–
Ma	M	10	32%	–	+4%	53¾	79	–
Ba	M	11	38%	5.1	+2%	59¾	108	11 yrs
Al	M	11	16%	4.6	+7%	58¾	77¾	11 yrs
Sa	M	11	50%	5.3	+7%	56¾	94¾	11 yrs
Sc	M	11	17%	5.9	0%	53¾	60	9½ yrs
Lo	F	11	28%	4.0	+2%	63¾	103	–
Sr	M	12	33%	5.3	–	–	–	–
Co	F	13	38%	6.0	–	–	–	13 yrs
Al	M	13	22%	5.7	+4%	60¾	89	13 yrs
Ma	M	13	39%	6.0	+0%	60	108	13 yrs
Pa	M	13	40%	5.4	+1%	67¾	135	13 yrs
Al	M	14	14%	3.7	-4%	71¾	134	14 yrs
Ma	F	14	49%	5.0	+1%	60	112¾	–

Average Child
11.7 years
I^{131}-30.8%(14%-50%)
PBI-5.4(3.7-6.8)
BMR-(-1%-+10%)

C

GROUP VI-Adolescents 15-20 Years

Name	Sex	Age	I^{131}	PBI	BMR	Ht (in)	Wt (lbs)	Bone Age
Vo	M	15	54%	6.6	–	65	184	15 yrs
Du	F	16½	49%	5.0	-20%	62¾	130½	15 yrs
Si	F	18	26%	4.6	–	62½	121	–
Ch	F	18	37%	5.5	–	–	–	Young Adult
Br	F	18	39%	5.5	–	–	–	Young Adult
El	F	18	58%	5.5	–	–	–	Young Adult
Ni	F	18	69%	4.8	–	–	–	Young Adult
Fe	F	19	29%	5.1	-18%	67	130	Young Adult
Ri	F	19	23%	5.5	-9%	64¾	139½	Young Adult
Vo	F	19	31%	3.4	–	–	–	Young Adult
Co	F	19	–	5.5	-8%	–	–	Young Adult
Di	F	20	36%	3.9	-6%	68	126¾	Young Adult

Average Adolescent
18+ years
I^{131}-41%(23%-69%)
PBI-5.0(3.4-6.6)

D

Fig. 2. A, Values for uptake of I^{131} and protein-bound iodine in "normal" children: age 8 months through 5 years. B, Values for uptake of I^{131} and protein-bound iodine in "normal" children: age 6 through 9 years. C, Values for uptake of I^{131} and protein-bound iodine in "normal" children: age 10 through 14 years. D, Values for I^{131} and protein-bound iodine in "normal" adolescents: age 15 through 20 years.

considerably less intimate than that of primates. We feel that when maternal-fetal circulation becomes less intimate, differences in values between protein-bound iodine levels of mothers and their offspring should be observed. Values of protein-bound iodine among cows and calves were determined in an attempt to evaluate the transfer of thyroxin across the placental barrier. Values for protein-bound iodine from 6 registered Holstein calves between 2 days and 4 months of age have been compared with those of 6 pregnant, non-lactating, registered Holstein cows between 2 and 7 years of age (fig. 3).

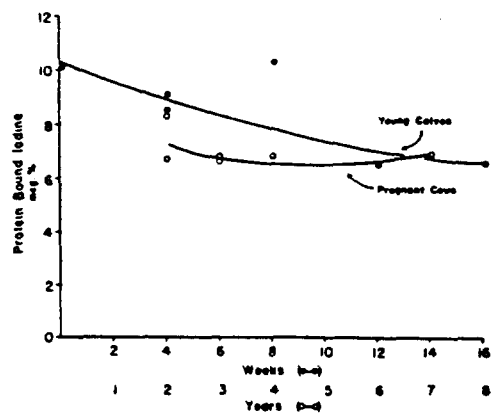

Fig. 3. Values for protein-bound iodine in registered Holstein pregnant cows and calves.

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Summary

1. Charts and graphs indicate values of thyroid uptake of I^{131} and values for protein-bound iodine. Serums were from 90 euthyroid individuals between birth and 20 years of age. In addition, protein-bound iodine values of 10 pregnant women at term, and beyond the age of 20 years, are available for comparison with their infants.
2. Increased thyroid activity in the neonatal period is described.
3. Graphs and charts demonstrate "normal values" of protein-bound iodine and thyroid uptake of I^{131} from birth to 20 years.
4. Physiological implications of increased thyroid activity soon after birth are discussed.
5. The role of placental histology in the transmigration of blood substances is discussed.

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THE EFFECT OF CORTISONE ADMINISTRATION UPON HUMAN AMNION GRAFTS IN HETEROLOGOUS HOSTS (RATS)[1]

MARSHALL S. SALKIN, M.D.,[2] EDWARD F. SCANLON, M.D., PAUL E. SCHULTZ, M.D.[2] and ROBERT L. BONUS, M.D.[3]

Introduction

IN order to facilitate study of the effects of cancer therapy upon human neoplasm, a series of control and cortisone treated rats were grafted with amnions taken from freshly delivered human placentas to determine the possibility of obtaining a bed upon which human tumor could be grafted more readily. Skin being the most difficult of all tissues to transplant (1), it was thought that perhaps a young, less antigenic tissue such as amnion would be more readily adapted to grafting procedures. As human tumors were to be studied, human amnion was used. On the basis of the results obtained by Toolan (2-5), in her studies with embryonic and tumor tissue transplants in cortisone-treated laboratory animals, it was decided to use this preparation in the experiment to depress the homograft reaction of the rat.

Materials and Methods

Placentas were obtained from the Obstetrical Department and were placed, under sterile conditions, in a normal saline solution containing a penicillin-streptomycin preparation. These were used within 12 hours of delivery. The amnions were separated from the chorions and then placed on a 3 by 1 inch clear glass slide with the interface side up. This procedure expedited smooth and accurate placement of the amnion graft, with the interface side down, by merely inverting the slide over the area to be grafted and holding one edge of the amnion against the rat's abdomen, proximal to the graft side as the slide was removed by pulling away from the graft site.

The experiment was divided into two series. In the first series, 12 adult male Wistar rats, weighing approximately 300 gm were used as host animals. The animals were anesthetized with ether and nembutal (0.1 to 0.2 cc intraperitoneally) and the abdomens shaved and prepared with Dial soap and water. An area 1 by 1½ cm was marked off on the rat's abdominal wall and the demarcated epidermis and dermis stripped off with scalpel and scissors, exposing muscularis and fascia. The prepared amnion graft was then applied and held in place with 5-0 dermalon sutures. The excess amnion was trimmed and the entire area was dusted with oxytetracycline powder. The graft was covered with a piece of nylon cut to size (originally ordinary gauze and telfa were used but discarded because of their adherence to the amnion graft) which, in turn, was covered by a 3 by 3 inch piece of gauze and the entire dressing held in place by 1½ inch adhesive tape around the animal's abdomen. (It was found that if this tape was too tightly drawn, it restricted abdominal respirations and death resulted.) Four rats acted as controls and received no further treatment except for wound examination approximately every 3 days for 15 days. At these times, the graft site was measured, the graft examined, the area redusted with oxytetracycline powder, and fresh dressings applied. The remaining 8 rats received 3-mg cortisone injections subcutaneously on the day of

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