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ARTICLES

EFFECT OF COBALT-IRON THERAPY ON THYROID FUNCTION*

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Several reports in the clinical pediatric literature have associated the appearance of hypothyroidism and goiter with the coincident administration of cobalt.[1-5] Thorough studies, however, have failed to demonstrate any effect of cobalt on thyroid function in children[6], in pregnant women or in animals.[7] The assumption that cobalt is a goitrogen has not been confirmed by the facts so far available and the appearence of thyroid dysfunction during cobalt administration has been variously ascribed to chance association,[7] to possible congenital goiter,[8] to impurity in the cobalt used, to the detoxifying action of simultaneously administered iron or to rare idiosyncrasy.[4]

We have used cobalt-iron therapy in over 500 infants and children with excellent hemopoietic results, and like others,[6-10] we have not seen clinical symptoms of any thyroid dysfunction. This is true even though some of our patients showed evidence of mild hypothyroidism prior to treatment.

This report represents data obtained in a group of children who were being treated for anemia with cobalt-iron therapy.*** Appropriate tests for thyroid function were carried out before and at the and of treatment. Results do not substantiate the assumption that cobalt has either goitrogenic or anti-thyroid action.

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*** Roncovite Drops and Roncovite Elixir were used in this study. These were supplied through the courtesy of Lloyd Brothers, Inc., Cincinnati, Ohio.

Material and Methods

The patients used in this study were from the Driscoll Foundation Children's Hospital, Corpus Christi, Texas. They ranged in age from 1 to 5 years. 12 showed some degree of anemia while 3 healthy, non-anemic children were included for purposes of comparison.

Thyroid function studies were carried out at the beginning and at the end of the study. Protein-bound iodine determinations were done by a modification of an alkaline-incineration method as described by Barker, Humphrey and Scoley.[11] Blood cholesterol was determined by Sackett's modification of the Bloor method.[12] Radioiodine uptake was determined by means of a scintillation counter 24 hours after the administration of 5 to 10 microcuries of I^{131}.

Hemoglobin determinations were done by the photo-electric method, erythrocyte counts were performed with certified equipment.

Seven patients (1,2,3,4,6,7,9) received 40 mg. of cobaltous chloride and 750 mg. of ferrous sulfate per day. This dosage of cobaltous chloride represents the administration of 10 mg. of elemental cobalt daily.

Six patients (5,8,10,13,14,15) received 15 mg. of cobaltous chloride and 750 mg. of ferrous sulfate per day. One patient (11) received 75 mg. of ferrous sulfate per day without cobalt and one patient (12) received no medication.

Treatment of these patients was continued for periods of six to twelve weeks. Patients were observed frequently for clinical signs of hypothyroidism or goiter development.

Results

Results of the thyroid function studies are shown in table 1. The pre-treatment values are slightly lower than the "normals" reported by Danowski et al[13] and Oliner et al.[14] The hemopoetic response obtained during therapy is shown in table 2. The appearance of relatively high cholesterol values, low protein-bound iodine and low iodine uptake in patients 1 to 12 prior to treatment is of interest.

No significant changes in the thyroid function tests were seen as a result of treatment. Patients 1,6,7, and 9 showed very low values for iodine uptake and protein-bound iodine prior to therapy. Upon completion of treatment, iodine uptake was slightly increased in all 4 cases but no significant changes were seen in other function studies. It is interesting to note that all 4 of these patients showed a rather striking response in terms of hemoglobin increase.

TABLE 1

RESULTS OF THYROID FUNCTION STUDIES IN PATIENTS RECEIVING COBALT — IRON THERAPY

Case No.	Duration of Therapy (wks.)	P.B.I. (mcg%)		Cholesterol (mg %)		I^{131} uptake (%)	
		Pre-therapy	Post-therapy	Pre-therapy	Post-therapy	Pre-therapy	Post-therapy
1	8	0.6	1.2	27	40	4	16
2	8	3.6	3.2	180	216	21	18
3	11	2.1	1.8	196	210	20	22
4	6	5.2	4.6	216	216	24	15
5	10	3.6	2.8	168	192	31	16
6	12	1.6	2.3	190	198	13	18
7	10	1.9	1.6	210	196	10	16
8	9	2.2	1.8	182	142	12	8
9	11	0.6	1.3	166	210	18	22
10	12	3.6	2.8	256	222	20	15
11	9[1]	5.3	4.4	268	210	28	23
12	8[2]	4.3	4.3	168	162	25	21
13	8[3]	3.2	3.8	246	210	12	10
14	8[3]	4.1	4.4	230	238	26	28
15	8[3]	5.1	5.6	242	220	14	18

[1] Received iron only.
[2] Received no medication.
[3] Normal healthy children given cobalt-iron.

No signs of clinical hypothyroidism or thyroid enlargement were observed in any of the patients treated. All individuals seemed to become more active and to show an improved state of well-being as their anemia was corrected.

Discussion

Results obtained in our study showed no evidence of antithyroid effect during cobalt-iron therapy. As has previously been pointed out, negative findings in even a large number of patients do not rule out the possibility of individual idiosyncrasy. It should be noted, however, that all but two of the several clinical reports which have connected goiter development with cobalt administration could well have been due to chance association. In the two exceptions, the investigators

TABLE 2

HEMATOLOGICAL AND GENERAL DATA
INFORMATION ON PATIENTS RECEIVING COBALT-IRON THERAPY

Case No.	Age		Body Weight (kg)		Dosage		Hemoglobin (Gm. %)		Erythrocytes (per cu. mm x 10⁶)	
	Yr.	Mo.	Pre-therapy	Post-therapy	Cobaltous Chloride mg./day	Ferrous Sulfate mg./day	Pre-therapy	Post-therapy	Pre-therapy	Post-therapy
1	2	2	12.5	13.9	40	75	7.5	12.0	4.7	5.5
2	1	1	8.3	9.9	40	75	5.0	11.0	3.1	4.5
3	2	4	9.6	11.4	40	75	5.5	12.0	2.8	4.1
4	1	6	9.4	11.2	40	75	4.8	11.5	3.9	4.4
5	4	10	16.1	16.5	45	750	6.5	11.0	3.2	4.5
6	1	11	11.9	13.7	40	75	5.5	11.5	3.1	4.7
7	2	0	11.2	12.9	40	75	7.5	12.0	4.2	5.1
8	3	0	12.6	12.9	45	750	8.0	13.0	3.3	4.1
9	1	4	7.6	8.2	40	75	9.0	11.5	3.9	5.2
10	4	0	16.9	17.8	45	750	9.0	11.5	4.1	5.2
11	2	6	11.2	11.7	--	75	6.5	9.5	4.5	4.0
12	1	11	11.4	11.9	--	--	9.0	10.5	4.3	4.3
13	4	11	16.9	20.3	45	750	10.5	12.5	4.2	5.6
14	3	0	15.3	16.9	45	750	11.5	13.0	4.7	5.4
15	1	6	11.1	12.8	45	750	11.0	12.5	3.9	4.8

were able to produce positive evidence either in a control case[5] or in *all* patients tested.[16]

This latter point is important. If cobalt induces antithyroid action in all patients as claimed by Kriss et al[5] and by Roche and Layrisse,[16] this effect cannot be one of individual susceptibility or idiosyncrasy. Lack of *any* effect in our study and in other carefully controlled investigations[6,7] would eliminate idiosyncrasy as a factor.

In our studies, a significant degree of thyroid hypofunction was indicated prior to treatment in several anemic children. It is recognized that the thyroid dysfunction might result from the anemia but it is also quite possible that, at least in some cases, the hypothyroid state played a role in the etiology of the anemia. These and other clinical observations[15] sugg st that unr cognized thyroid dysfunction may play a part in the etiology of anemia in infants and children more frequently than has generally been supposed.

In severe cases of this latter type, any exacerbation of the existing thyroid dysfunction would be improperly ascribed to the anti-anemia medicaments being administered. We regard this as a possible explanation of the contradictory data concerning the effect of cobalt on the thyroid gland. Further studies of the frequ ncy of thyroid dysfunction in anemic children would appear to be very desirable.

It should also be noted that the purity of commercially available cobalt chloride varies considerably and that at least one investigation has reported the presence of toxic impurity in lots of supposedly pure material.[17] We, therefore, obtained detailed analytical reports on the particular lots of cobalt chloride used in our study and found it to be essentially pure material. In the absence of a legal standard for medicinal cobalt chloride the pharmaceutical manufacturer has adopted standards which preclude the presence of significant amounts of arsenic, lead, heavy metals, and other possible toxic impurities. In this connection, it should be noted that the goitrogenic activity found in cobalt chloride by Kriss and co-workers[5] and by Roche and Layrisse[16] was obtained with cobalt chloride from other sources.

In conclusion, our studies indicate that cobalt has no anti-thyroid or goitrogenic action. Consideration of previous reports and of the facts presented makes it extremely unlikely that idiosyncrasy is a factor to be considered. In our opinion the appearance of goiter in anemic patients treated with cobalt can best be explained on the basis either of pre-existing thyroid pathology, as first suggested by Klinck,[8] or possibly on the basis of impurity in the cobalt used by some investigators.

Summary

We have studied the effect of a cobalt-iron preparation (Roncovite) on thyroid function in a group of anemic children.

Neither clinical experience nor laboratory findings in these patients suggest any anti-thyroid effect from cobalt chloride administration.

The findings of certain other investigators show a consistent reduction in thyroid function when cobalt is given. This tends to rule out idiosyncrasy as a factor in the purported goitrogenic action of cobalt.

Two possible explanations are presented. Exacerbation or progression of a pre-existing thyroid dysfunction could occur independently during cobalt treatment for anemia. The presence of toxic impurities in some cobalt preparations could be involved.

Pure cobalt chloride is not a goitrogen.

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