Excess Iodide Ingestion and Thyroid Function in Chicks* (33323)

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In certain susceptible humans, goiters develop when iodide intake is excessive. Patients with Graves' disease and some patients with Hashimoto's thyroiditis are also susceptible to iodide in that thyroxine synthesis is inhibited at high serum iodide levels. Most animals are resistant to the goitrogenic effect of iodides. The chick has been reported by Wheeler and Hoffmann (1) to be an exception in that goiters developed with high dietary levels of iodide. In studying the acute effects of iodide on protein-bound ^{131}I and ratios of monoiodotyrosine to diiodotyrosine in the thyroid, Pitt-Rivers (2) found a less pronounced effect in the chick than in the rat, which does not develop iodide goiter. Because Wheeler and Hoffmann's observation (1) has not been confirmed and because an animal model for thyroid iodide sensitivity in man is needed, we tried to confirm the goitrogenic effects of iodides in birds and to delineate the point at which inhibition of thyroxine biosynthesis occurs.

Materials and Methods. One-day-old White Leghorn, Rhode Island Red, White Rock, and Viking Meat Bird (Lead Breast cockerel x White Rock dam) chicks were fed a commercially available "chick starter" feed (containing 3.5 mg iodide/kg of feed), given unadulterated water, and housed in electrically heated brooders. These chicks served as controls, while chicks of similar breeds in similar-sized groups were given various concentrations of KI in their drinking water. At intervals over the period of observation, groups of chicks were killed with ether, body weight was determined, and thyroidectomy was performed. The thyroids were weighed immediately on an analytical balance.

Another group of Rhode Island Red chicks was given 35 μCi of ^{131}I intraperitoneally at 2 days of age. Twenty-four hours later, thyroid uptake of ^{131}I was determined by external counting. At that time, 29 chicks were continued on unadulterated water and 25 chicks were given water containing 0.5% (w/v) KI. Both groups received the same feed. In five chicks in the control group and five in the iodide group, ^{131}I activity in the thyroid was measured daily by external counting for 10 days. From the remaining chicks in the control group, four were killed and thyroidectomized at 24 hours after ^{131}I injection and then four more every 24 hr for 5 days. The same was done from the iodide group beginning at 24 hours after start of iodide treatment and continuing for 4 additional days.

The excised thyroids were analyzed as previously described (3). A protease from *Streptomyces griseus* (pronase) was used for a 2-hr hydrolysis. The digests were chromatographed in an ascending manner in one solvent system, *n*-butanol-ethanol-0.5 *N* NH_4OH (5:1:2). The chromatographed strips were counted in an automatic scanner with a 4π beta detector and integrator.

The effect of varying the dose of stable iodide on the thyroid uptake of radioiodide was determined in White Leghorn chicks. At 2 weeks after hatching, eight chicks were given 6.9 μCi of ^{131}I subcutaneously with varying amounts of stable iodide (0.1, 0.5, 1.0, and 20.0 mg of KI to two chicks each). At 24 hr, the thyroids were removed and counted in a well counter for 10 to 20 min.

Thyroid function was assessed also by measurement of oxygen consumption and by measurement of the serum level of total (4) and free (5) thyroxine in the control and iodide-treated chicks.

Results. The iodide-treated chicks did not grow as well as the chicks serving as controls. As shown in Table I, goiter was not observed in any of the breeds of chicks treated

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TABLE I. Effect of KI on Thyroid Weight of Various Breeds of Chicks.

Breed	No.	KI in H_2O, % (w/v)	At termination of experiment: Age (days)	Body wt. (g)	Days on KI	Thyroid wt. (mg/100 g)[a]
White Leghorn	24	0	37	632	0	6.3 ± 0.4
	23	0.1	37	565	36	7.9 ± 0.6
Viking Meat Bird	36	0	40	770	0	6.6 ± 0.3
	36	0.2[b] / 0.5	40	404	39	6.3 ± 0.3
Rhode Island Red	12	0	73	1,159	0	8.7 ± 0.8
	12	0.5	73	742	44	8.5 ± 0.9
White Rock	4	0	180	2,119	0	9.0 ± 3.1
	4	0.5	180	1,723	154	7.5 ± 2.7

[a] In terms of body weight, mean ± SE.
[b] For 14 days at 0.2% and remainder at 0.5%.

with the various levels of iodide in the drinking water. The thyroid weights of White Rock chicks treated for about 6 months with 0.5% KI in the drinking water were not significantly different from the thyroid weights of the control chicks. Periodically, sections of the excised thyroids were prepared for histologic study and no difference in thyroid histology was noted between glands from treated and control chicks.

The effect of stable iodide on the thyroid uptake of ^{131}I at 24 hr in White Leghorn chicks is shown in Table II. The fraction of the ^{131}I collected was reduced by increasing quantities of stable iodide. On the basis of the fractions of ^{131}I retained by the glands at 24 hr, the quantity of ^{127}I collected (last column) was calculated. The fraction of ^{131}I in the gland was low in all instances but, with counting for long times, distinct differences could be discerned. When the log of dose of ^{127}I was plotted against the mean log of percentage thyroid uptake of ^{131}I, a straight line was formed with a correlation coefficient (r) of −0.996. When the individual thyroid uptakes were similarly plotted, r was −0.89. This lends some credence to the validity of the calculations of ^{127}I collected by the thyroid and suggests that a block in thyroid uptake of iodide did not occur with iodide doses sufficient to produce serum iodide levels of 0.5 mg/ml (on the basis of rapid distribution of the iodide in a volume equivalent to 20% of body weight).

TABLE II. Effect of Carrier (^{127}I) on Thyroid Uptake of ^{131}I in Chicks.[a]

Group no.[b]	Subcutaneous dose: KI (mg)	Subcutaneous dose: ^{131}I (μCi)	Thyroid uptake[c]: ^{131}I (% dose)	Thyroid uptake[c]: ^{127}I (μg)
1	0.1	6.9	0.59	0.59
2	0.5	6.9	0.18	0.89
3	1.0	6.9	0.11	1.11
4	20.0	6.9	0.019	3.73

[a] White Leghorn; mean body weight, 47 g.
[b] Two chicks per group.
[c] Mean.

When ^{131}I was given 24 hr prior to treatment with stable iodide, there was a difference in ^{131}I release between control and treated birds. The release of ^{131}I from the thyroid of Rhode Island Red chicks is shown in Fig. 1. The biologic half-life of ^{131}I in the thyroid of control birds was 4.1 days. In the iodide-treated chicks, the release suggested two rates, with the initial component representing a half-life of 2.2 days and the second, 5.4 days. However, a single straight line drawn to fit all the points defines a line that suggests a half-life similar to that in the control chicks.

The components of hydrolysates of thyroid of Rhode Island Red chicks in the 6 days after a dose of ^{131}I are shown in Table III. There was no detectable triiodothyronine

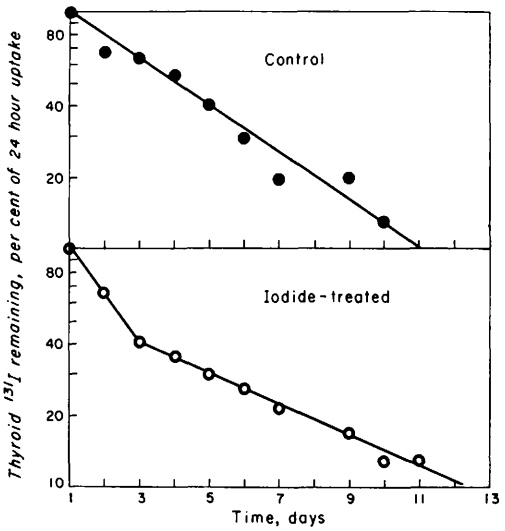

FIG. 1. Release of ^{131}I from thyroids of control and iodide-treated Rhode Island Red chicks. One hundred per cent level at day 1 represents 16.5 and 17.3% of administered dose of ^{131}I in control and treated groups respectively.

(T3) in any of the hydrolysates. This is different from the situation in rats (3) in which 2–5% of an injected dose of ^{131}I would be present at 24 hr as T3. Chicks fed a low-iodine diet for several days did not have a significant fraction of a dose of ^{131}I incorporated into T3. As seen also in the rat (3), the proportion of components in this type of experiment remained reasonably constant over the five days of observation during which time about 66% of the ^{131}I present at 24 hr was released from the gland. Similar findings for the iodide-treated chicks are shown in Table IV. There was no appreciable difference in monoiodotyrosine/diiodotyrosine ratio or in the proportion of ^{131}I activity in thyroxine (T4) with either the passage of time or when the control group was compared to the iodide-treated group.

In Table V, additional tests of thyroid function are shown for the two groups of chicks. The levels of serum total thyroxine were not different for the groups, but the values were much lower than normal values found in man (6). This probably reflects the fact that chickens do not have thyroxine-binding globulin (7). The levels of free thyroxine, expressed as a fraction of the total thyroxine, were equivalent in the two groups

TABLE III. Components of Hydrolysates of Thyroid from Chicks without Treatment.[a]

Time after ^{131}I (hr)	^{131}I activity in components of thyroid hydrolysates (%)[b]				
	MIT	DIT	T4	I	Origin
24	14 ± 3	64 ± 4	10 ± 3	2 ± 0.5	10 ± 1
48	15 ± 6	61 ±10	14 ± 6	2 ± 2	8 ± 1
72	19 ± 2	56 ± 4	11 ± 2	1 ± 1	13 ± 3
96	30 ± 5	47 ± 6	13 ± 7	1 ± 1	9 ± 1
120	11 ± 3	60 ± 6	17 ± 2	2 ± 1	10 ± 1
144	22 ± 5	53 ± 7	15 ± 5	1 ± 1	9 ± 2

[a] Rhode Island Red; ^{131}I given when chicks 1 day old.

[b] Mean ± SD; four animals per group.

TABLE IV. Components of Hydrolysates of Thyroid from Chicks Treated with 0.5% KI in Drinking Water.[a]

Treatment time (hr)	^{131}I activity in components of thyroid hydrolysates (%)[b]				
	MIT	DIT	T4	I	Origin
0[c]	14 ± 3	64 ± 4	10 ± 3	2 ± 0.5	10 ± 1
24	14 ± 4	65 ± 4	13 ± 4	1 ± 1	7 ± 1
48	24 ± 3	53 ± 4	12 ± 3	1 ± 1	10 ± 3
72	23 ± 5	54 ± 5	14 ± 2	1 ± 1	8 ± 3
96	14 ± 3	58 ± 3	18 ± 4	2 ± 1	8 ± 2
120	20 ± 4	57 ± 3	15 ± 5	1 ± 0.3	7 ± 1

[a] Rhode Island Red; ^{131}I given when chicks 1 day old.

[b] Mean ± SD; four animals per group.

[c] Equivalent to 24 hr after ^{131}I injection.

but about fourfold higher than seen in man (6). As a reflection of the foregoing situation, the calculated values for absolute level of free thyroxine in the chick are well within the normal range for man.

Discussion. We have been unable to confirm Wheeler and Hoffmann's report (1) of goiter production in chicks caused by feeding excess iodide. The thyroid weight of birds fed a "chick starter" diet was similar to that of birds treated with excess iodide for periods of up to six months. Additional thyroid-function tests confirmed the euthyroid state of iodide-treated chicks. When large doses of ^{127}I were given with ^{131}I, no block in uptake

TABLE V. Thyroid Function Tests in Control and Iodide-Treated Chicks.[a]

Test	Chicks	Mean body wt. (g)	Days on KI	Mean test value
O_2 consumption	2	1,139	0	144 ml/100 g
	2	658	60	145 ml/100 g
Serum total thyroxine	9	187	0	1.25 μg/100 ml
	10	115	14	1.33 μg/100 ml
Serum free thyroxine	9	187	0	0.191% of total or 2.39 ng/100 ml
	10	115	14	0.198% of total or 2.63 ng/100 ml

[a] KI, 0.5% in drinking water.

of ^{131}I by the thyroid was detected. When the thyroids were "prelabeled" with ^{131}I and iodides were administered in the drinking water for ten days, the release of ^{131}I was compatible with an initial blockade in thyroxine synthesis followed by a release of the blockade. The data are compatible with the concept of a Wolff-Chaikoff effect (8) in chicks but offer no conclusive proof of such.

The hydrolysates of thyroid glands showed ^{131}I activity of similar proportions in the components of both groups of chicks. The lack of derangement in the monoiodotyrosine/diiodotyrosine ratio or in the level of T4 offers further proof of the lack of significant inhibition of thyroxine synthesis or lease in iodide-treated chicks.

The data show that the chick, as are mammals (2), is resistant to the goitrogenic effect of excess iodide.

Summary. The effect of excess ioide in the drinking water on the thyroid function of chicks has been studied. There was no evidence of goiter production in four breeds of chicks fed up to 0.5% (w/v) KI in water for periods of up to six months. There was some evidence in acute experiments to suggest a temporary Wolff-Chaikoff effect with excess iodides. Components of thyroid hydrolysates were not different in iodide-treated chicks as compared to chicks not given excess iodide.

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