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THE EFFECTS OF ESTROGEN
ON THE CHICK THYROID

Thesis for the Degree of M. S.
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David Irving Epstein
1950

This is to certify that the
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The Effects of Estrogen
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David I. Epstein

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of the requirements for

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Lester F. Wolthick

Major professor

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THE EFFECTS OF ESTROGEN ON THE CHICK THYROID

By

DAVID IRVING EPSTEIN

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DEDICATION

The writer affectionately dedicates this work to the memory of his beloved parents, Benjamin and Sema Irma Epstein, who continue to be a constant source of inspiration to their son. His greatest ambition is to accomplish all the great things of which they had thought him capable. It is his fervent wish that this work is a step in that direction.

ACKNOWLEDGEMENTS

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INTRODUCTION

It has been shown by Andrews and Schnetzler (1946), Muhrer (1947), McMillan et al. (1947), and many other workers, that feeding thiourea or its derivatives will increase the fat content of many domesticated animals including swine and fowl. The goitrogens depress thyroid activity which causes a decrease in the metabolic rate, which, in turn, is associated with the deposition of fat.

It has also been shown that feeding natural or synthetic estrogens may cause fat deposition in birds. Lorenz (1943 and 1945), Thayer et al. (1945), Glazener and Jull (1946), Thayer and Davis (1948), Davis and Thayer (1948), and Quisenberry and Krueger (1948), to name but a few, have obtained relatively good deposition of abdominal fat. However, Sykes et al. (1945) did not get as pronounced results as did any of the above investigators. Neither did Davidson et al. (1946), studying the administration of synthetic estrogens to turkeys. They found an increase in plasma fat but usually a decrease in abdominal fat. The best fat depositions in birds have been obtained in the Oklahoma and California experiments. Large deposits of abdominal fat in turkeys were obtained when the birds were reared out-of-doors in areas with rather warm mean temperatures (Davis and Thayer, ibid.). In contrast, turkeys reared out-of-doors in the northern portion of Michigan with much colder mean

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temperatures did not show the increase in abdominal fat with estrogen (Davidson et al., 1946). Apparently a difference in climate may have something to do with the laying down of fat. One immediately suspects the thyroid gland. If thiouracil, which depresses the thyroid, also induces fat deposition, a relative thyroid stimulation induced by a colder environment might prevent the fattening effect of estrogen. Unpublished data (Wolterink, Davidson and Epstein) on turkey hens at the end their first laying period indicate that the thyroid activity, per unit body weight, of these birds during the cold spring months is as great as that found in young chicks. Similar results were found by Blakely et al. (1949) in five-week-old poults. Whether or not climate, per se, is responsible for the decreased fattening results in turkeys is unknown. It becomes desirable, however, to reinvestigate the effect of estrogen administration under different conditions of thyroid activity.

The existing literature is primarily concerned with the effects of thyroidectomy or thyroid administration on the hypophysis, the gonads themselves, or the hypophyseal-gonadal axis. However, the consequences of different thyroid status on effects produced by the secretions of the ovary have been studied by Fleischmann (1946) in the chick. He showed that the inhibiting effect of thyroxine is confined to the metabolic changes induced by estrogen, whereas the morphological structural changes

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brought about by estrogen on secondary sex characters are not effected. His work demonstrated that thyroxine was able to neutralize the ability of the estrogen to increase serum calcium, inorganic phosphate, protein phosphate and cholesterol, yet it does not inhibit the growth of the oviduct induced by estrogen.

This is an extension of the earlier work of Van Horn (1933) and Meyer and Wertz (1938) who hypothesized that excess thyroxine may, by increasing metabolism, cause a more rapid elimination of estrogen from the body. Meyer and Wertz showed that in rats, with a dose level of thyroxine small enough to barely decrease the body weight in five days, the threshold for estrogen was raised, e.g., it required more estrogen to induce an estrus-type vaginal smear than was required in the normal intact animal. The technique of thyroxine inhibition of estrogen-induced estrus-type vaginal smear in the thyroidectomized rat has been used by Barker et al. (1950) in studying thyroxine analogues.

The effects of estrogen administration on the hypophyseal-thyroidal axis is not as well understood. Meyer et al. (1930), Leonard (1933), Severinghaus (1934), and Wolfe and Chadwick (1936) showed that estrogen injection into rats caused either a decrease in the gonad-stimulating potency of the anterior pituitary or that the basophil cells were degranulated by the estrogen. Since thyrotrophin is secreted by the basophils (Griesbach and

and Purves, 1945), it would seem logical to assume that the estrogen would depress the secretion of that hormone. In assaying for the thyrotrophic hormone, Meites and Turner (1948) actually found such a decrease in the amount of that hormone in the pituitary of estrogen-treated rabbits. The precise effect of estrogen on the pituitary cytology as affected by thyroidectomy has been studied most recently by Baker and Everett (1947). Their results are somewhat inconclusive due to incomplete removal of thyroid remnants and to the short time following thyroidectomy in which the thyroid effects might have become apparent. It is sufficient to point out that the precise effects are not only controversial, but apparently depend upon a combination of the effects of estrogen dose levels and total time of administration. Baker and Everett do conclude that "the stimulating effect of estrogen on the hypophysis is not mediated through the thyroid gland."

The present experiments were designed to determine whether or not exogenous estrogen administered to intact immature chicks with relatively nonfunctional gonads would alter thyroid secretion rate. In securing these data, information was also obtained on the effect of thyroxine administration on the estrogen-induced slowing of the iodine turnover time in the thyroids of thiouracil-treated animals.

- 1. The first step in the process of the scientific method is to ask a question.
The question is the starting point of the scientific method. It is a question that the scientist wants to answer. The question is usually based on an observation or a problem that the scientist has encountered. The question is usually a "how" or "why" question. For example, a scientist might ask, "How does the rate of photosynthesis change with light intensity?" or "Why do some plants grow faster than others?"
- 2. The second step is to do background research.
Before the scientist can ask a question, they need to know what is already known about the topic. This is done by reading books, articles, and other sources of information. The scientist also needs to know what methods have been used to study the topic. This helps the scientist to design their experiment and to interpret their results.
- 3. The third step is to form a hypothesis.
A hypothesis is a statement that the scientist believes to be true. It is a prediction of what the results of the experiment will be. The hypothesis is usually based on the background research. For example, a scientist might hypothesize, "If light intensity increases, then the rate of photosynthesis will also increase."
- 4. The fourth step is to design an experiment.
The experiment is a test of the hypothesis. It is a series of steps that the scientist follows to collect data. The experiment is designed to test the hypothesis by changing one variable (the independent variable) and measuring the effect on another variable (the dependent variable). For example, in the experiment on photosynthesis, the independent variable would be light intensity and the dependent variable would be the rate of photosynthesis.
- 5. The fifth step is to collect data.
The scientist collects data by performing the experiment. They record the results of the experiment in a table or graph. The data is then used to test the hypothesis.
- 6. The sixth step is to analyze the data.
The scientist analyzes the data to see if it supports the hypothesis. They look for patterns in the data and compare the results to the hypothesis. If the data supports the hypothesis, the scientist can conclude that the hypothesis is true. If the data does not support the hypothesis, the scientist may need to revise the hypothesis and repeat the experiment.
- 7. The seventh step is to draw a conclusion.
The scientist draws a conclusion based on the results of the experiment. They state whether the hypothesis was supported or not and explain why. The conclusion is the final step in the scientific method.

EXPERIMENTAL PROCEDURE

In this work we conducted seven experiments. In Exp. 1, 2 and 7 we used Rhode Island Reds, while in the intervening ones we used Barred Rocks. All chicks were pullorum-tested and came from a hatchery in Southern Michigan at the age of one day. The birds were caged in a commercial chick battery, and were fed ad libitum. All groups contained both males and females.

All chicks were started on an Arcady Chick Ration* for the two weeks after hatching prior to the beginning of the experiments. They were then leg-banded and weighed to the nearest gram. Groups as nearly equal as possible in average weights were set up, and the experiments were continued for two weeks.

The general plan was to set up a conventional thyroid secretion rate assay by the method of Mixner, Reineke and Turner (1944). One half of the chicks were placed on a normal ration and assayed. The other half was usually given estrogen in the feed. Due to limited space, it was not possible to use as many thyroxine dosage groups as might have been desirable. The exact conditions for each experiment may be noted from the tables. In addition, the turnover of radio-iodine (I 131) was used as a check on the thyroid activity in the last four experiments.

At the end of the assay period, the animals were sacrificed and their weights and sex recorded. Gonads, combs and thyroids were removed and weighed on a Roller

* Arcady Milling Company, Chicago, Illinois.

Smith balance to the nearest tenth of a milligram. Organ weights were expressed both in actual weight and as weight per hundred grams of body weight.

The thyroids of the animals receiving radio-active iodine were placed on copper discs and dried. They were then counted with a thin mica end window Geiger-Muller counter.

Unless otherwise stated, thiouracil was administered in the feed at a dose level of 0.1%. This dose level proved to be too low to completely suppress thyroid activity. However, it is the dose level employed by Mixner et al. (1944) and Schultze and Turner (1945).

Thyroxine solutions were prepared from crystalline thyroxine isolated by Dr. E. P. Reineke from iodinated casein. These were injected subcutaneously in the indicated doses daily for the two weeks of the experimental period.

The synthetic estrogen used, 3,4-dianisylhexene-3*, was injected in a corn oil suspension in the first two experiments. In the rest of the experiments it was given in the feed at a dose level of 0.01%.

Radio-active iodine (I 131) was obtained from Oak Ridge in a weak bisulphite medium. In experiment #3 it was given to the chicks in the drinking water. However, in the succeeding experiments approximately 0.2 of a micro-curie was injected subcutaneously.

* The dimethyl ether of stilbesterol, Breon.

Turnover times for the output of iodine for the thyroid glands are the times in which the radio-iodine content has been reduced to one half its value from the start of the period. These were computed from counts obtained at twenty-four hours and a later time (between forty-eight and seventy hours) after the injection of the radio-active tracer. An exponential rate of loss is assumed. The method is essentially that derived by Keating and Albert (1949).

RESULTS

Effect of Estrogen on Thyroid Size

Table 1 summarizes data obtained in six experiments in which a low estrogen dosage rate was employed. The average thyroid size of normal four-week-old Rhode Island Red chicks was 9.5 ± 0.4 milligrams per hundred grams body weight. In comparable chicks given estrogen the thyroid weight averaged 10.2 ± 0.2 milligrams per hundred grams body weight. The difference between the two groups was not significant.

In Barred Rocks of the same age, the control thyroids averaged 6.6 ± 0.1 milligrams per hundred grams body weight, while the thyroids of the estrogen-treated birds averaged 6.0 ± 0.1 . Estrogen treatment in Barred Rocks evidently decreased the average thyroid weights of the groups used in these experiments when the weighted average was computed from individual group averages. However, the actual difference in weights was only about ten per cent, and there ~~was~~ no significant difference in any of the groups from which the over-all average was computed. Thus, the effect of this estrogen dose level in reducing thyroid weights in Barred Rocks was probably of little importance. If real, the difference would indicate that estrogen slightly depressed thyrotrophin secretion by the pituitary.

Table 1 also lists the ^{thyroid} weights of similar animals receiving radio-iodine. In Exp. 7 with Rhode Island Reds no significant difference in thyroid size was produced by the amount of radio-iodine injected. In Exp. 3 (Barred Rocks), radio-iodine apparently decreased thyroid size, whereas in Exp. 5 (Barred Rocks) radio-iodine apparently increased thyroid size. No significant difference was noted in either Exp. 4 or 6. From the weighted means of all the experiments with Barred Rocks, it is impossible to conclude that radio-iodine treatment had any effect on the thyroid weights.

We will now discuss the effect of estrogen administration on thyroid size in birds which received thiouracil in the assay procedure. Results for groups which received 0.5 gamma of thyroxine per day will be omitted. As reported by Schultze and Turner (1945), a low dose of thyroxine in a thyroid assay gives a very low thyroid weight, a result which has been observed by numerous other investigators. Since the cause of this phenomenon is obscure, data in which this effect plays a part cannot be discussed profitably at the present time. Data for this dose level may be found, however, in the appendix and wherever the thyroid weight itself is not critical to the discussion.

Although there is considerable variation between experiments in the average thyroid weights of groups on

the same thyroxine dose level, the average thyroid weight of all groups on the same dose level shows a very interesting picture. The average of the thyroid weights in Exp. 4, 5 and 6 (Barred Rocks) for the chicks at a one gamma thyroxine dose level is 28.5 ± 1.4 milligrams thyroid per hundred grams body weight for the estrogen-treated birds as compared with 28.9 ± 1.1 milligrams thyroid per hundred grams body weight for the controls. This indicates that estrogen seems to have no effect on the thyroid weight when one gamma of thyroxine is given simultaneously with the thiouracil. However, when one gives two gamma of thyroxine, a different picture results. The controls (i.e., groups receiving 0.1% thiouracil plus two gamma of thyroxine per day) average 30.0 ± 1.2 milligrams thyroid per hundred grams body weight as compared with 18.8 ± 1.4 milligrams per hundred grams body weight for similar groups receiving estrogen. This reduction in thyroid size might indicate that at this level of thyroxine dosage, the administration of estrogen may have reduced the thyrotrophin secretion of the pituitary (either by stimulating the output of thyroxine from the thyroid and thus depressing pituitary thyrotrophin secretion indirectly or by direct depression of the pituitary output of thyrotrophin). If estrogen had no effect on thyrotrophin secretion, the reduced thyroid size could be accounted for only if the sensitivity of the thyroid to an unchanged thyrotrophin output was decreased.

We have only one group of animals with which to compare the thyroid weights from chicks receiving four gamma of thyroxine. As in the animals receiving two gamma of thyroxine, the control thyroids were larger than the ones treated with estrogen, 16.1 ± 1.9 as compared with 11.2 ± 1.0 milligrams per hundred grams body weight. This again indicates the possibility of mechanisms similar to those mentioned above.

Whether or not thyrotrophin secretion was effected by the conditions imposed in these treatments was not determined directly. As will be shown subsequently, a direct check on the thyroid output of radio-iodine did indicate that in the smaller thyroids (produced by estrogen), the turnover rate of iodine was increased. Thus, a more rapid thyroid activity may have resulted in a reduced thyrotrophin secretion which, in turn, may have been reflected in the reduced thyroid size.

TABLE 1

EFFECT OF ESTROGEN AND RADIO-IODINE ON THE THYROID SIZE OF NORMAL CHICKS

EXP. NO.	BIRDS*	ESTROGEN DOSE	THYROID WEIGHTS (MILLIGRAMS PER HUNDRED GRAMS BODY WEIGHT)		
I. RHODE ISLAND REDS			CONTROLS	<u>ESTROGEN-TREATED</u> <u>RADIO-IODINE TREATED</u>	
2.	19-14-00	5 ug/day (injection)	10.5±2.3#	11.2±1.1	--
7.	8-5-6	0.01% (feed)	7.2±0.6	7.5±0.8	6.6±1.0
		AVE.	9.5±0.4	10.2±0.2	
II. BARRED ROCKS					
3.	12-12-13	0.01%** (feed)	5.7±0.3	5.4±0.6	4.3±0.6
4.	10-8-8	0.01%	9.2±1.7	6.9±0.7	11.3±2.3
5.	11-7-6	0.01%	5.9±0.6	6.4±0.5	9.8±1.4
6.	17-14-12	0.01%	6.2±0.4	5.8±0.4	5.5±0.2
		AVE.	6.6±0.1	6.0±0.1	6.9±0.2

* First number is N for Controls; second is for Estrogen-treated; third is for Iodine-treated.

** In this Experiment the Estrogen was reduced from 0.01% after the first week to 0.005% for the second.

Standard Error of the Mean.

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TABLE 2

EFFECT OF ESTROGEN ON THYROID WEIGHT OF CHICKS RECEIVING THIOURACIL AND THYROXINE

EXP. NO. BIRDS*	ESTROGEN DOSE	THYROXINE DOSE	THYROID WEIGHT (MILLIGRAMS PER HUNDRED GRAMS BODY WEIGHT)	NON-ESTROGEN BIRDS ESTROGEN-TREATED BIRDS
I. RHODE ISLAND REDS				
2. 15-00	none	2ug/day	39.8±2.5 #	
13-00	none	4ug/day	18.1±2.9	
7. 6-6	0.01% (feed)	1ug/day	28.6±4.1	25.9±6.4
6-6	0.01% "	2ug/day	36.6±6.0	19.8±3.4
5-6	0.01% "	4ug/day	12.0±1.1	10.1±1.6
II. BARRED ROCKS				
3. 12-12	0.01% " reduced to 0.005% after a week	none	21.3±0.1	27.1±4.2
6-4	"	thyroprotein**	2.3±0.2	1.5±0.4
4. 8-6	0.01% (feed)	1ug/day	32.3±3.9	20.7±7.5
8-5	0.01% "	2ug/day	23.2±4.3	21.4±3.8
5. 6-5	0.01% "	1ug/day	29.4±8.1	34.8±5.2
6-8	0.01% "	2ug/day	29.0±3.6	19.6±1.6

* First number is for Controls; second is for Estrogen-treated.

** Thyroprotein in feed 0.52% for first week; reduced to 0.16% for the second.

Standard Error of the Mean.

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TABLE 2 (CONTINUED)

EXP.	NO. BIRDS*	ESTROGEN DOSE	THYROXINE DOSE	THYROID WEIGHT	(MILLIGRAMS PER HUNDRED GRAMS BODY WEIGHT)	
					NON-ESTROGEN BIRDS	ESTROGEN-TREATED BIRDS
6.	14-13	0.01% (feed)	1ug/day	25.1 $\pm$ 2.1 #		30.0 $\pm$ 3.2
	12-13	0.01% "	2ug/day	37.8 $\pm$ 4.6		15.3 $\pm$ 1.1
	14-15	0.01% "	4ug/day	16.1 $\pm$ 1.9		11.2 $\pm$ 1.0

* First number is for Controls; second is for Estrogen-treated.
Standard Error of the Mean.

The Effect of Estrogen on the Uptake of Radio-Iodine by the Thyroid Gland

In normal chicks, estrogen had no effect on the uptake of the administered radio-iodine (Table 3).

In the groups on thiouracil and graded thyroxine levels, estrogen did modify radio-iodine uptake. Exp. 4,5 and 6 were run on Barred Rocks, while Exp. 7 was on R. I. Reds. When one gamma of thyroxine was used it was found that the thyroids of the R. I. Reds receiving estrogen picked up more iodine than did their controls, whereas in two of the three experiments run on Barred Rocks the control thyroids accumulated more radio-iodine at twenty-four hours.

When two and four gamma of thyroxine were given to the thiouracil-treated groups, both breeds showed a greater uptake of radio-iodine with estrogen administration. Apparently in Barred Rocks estrogen increases iodine uptake by the thiouracil-treated thyroid only when a dose of thyroxine above one gamma is administered. These results indicate that estrogen administered to thiouracil-treated chicks produces an effect on uptake opposite to its effect on thyroid size. Thus, despite the decrease in thyroid weight produced by estrogen (Table 2), the synthetic female hormone produced an actual increase in iodine uptake. If estrogen first decreased thyrotrophin secretion, it is difficult to see how iodine uptake could have been increased

subsequently. On the other hand, if estrogen first stimulated the thyroid, reduced thyrotrophin secretion by the anterior pituitary would normally follow.

TABLE 3

EFFECT OF ESTROGEN AND RADIO-IODINE ON RADIO-IODINE UPTAKE BY THE THYROID GLANDS OF NORMAL BIRDS*

EXP.	IODINE counts/sec/mgm	ESTROGEN thyroid weight
4.	0.769±0.505 #	0.341±0.451
5.	10.670±2.00	9.07 ± 1.21
6.	3.024±0.404	3.187±0.347
7.	0.977±0.162	0.782±0.143

* The number of birds in each group may be seen in Table 1.

Standard Error of the Mean.

TABLE 4

EFFECT OF ESTROGEN AND RADIO-IODINE ON RADIO-IODINE UPTAKE BY THE THYROID GLANDS

OF BIRDS RECEIVING THIOURACIL AND THYROXINE

EXP.	THYROXINE DOSE*	NON-ESTROGEN BIRDS counts/second	ESTROGEN-TREATED BIRDS milligram thyroid weight
4.	1.0 gamma	0.045	0.118
	2.0 gamma	no data	0.128
5.	1.0 gamma	0.540 $\pm$ 0.13 #	0.271 $\pm$ 0.118
	2.0 gamma	0.514 $\pm$ 0.47	no data
6.	1.0 gamma	0.277 $\pm$ 0.010	0.140 $\pm$ 0.063
	2.0 gamma	0.056 $\pm$ 0.002	1.391 $\pm$ 0.340
	4.0 gamma	0.421 $\pm$ 0.196	1.060 $\pm$ 0.814
7.	1.0 gamma	0.030 $\pm$ 0.018	0.174 $\pm$ 0.089
	2.0 gamma	0.086 $\pm$ 0.004	0.256 $\pm$ 0.134
	4.0 gamma	0.043 $\pm$ 0.017	0.085 $\pm$ 0.030

* Injected subcut. daily.

Standard Error of the Mean.

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The Effect of Estrogen on Turnover Time of Radio-Iodine
in the Thyroid

Table 5 shows the effect of the administration of the dimethyl ether of stilbesterol on the turnover time of radio-iodine in the thyroids of normal chicks. In Exp. 4, 5 and 6 (Barred Rocks) the groups receiving estrogen require from fifteen to more than 370 hours longer for half of the thyroid iodine to be discharged than do their normal controls. This indicates that in the dose level employed here, estrogen causes a depression of the thyroid iodine turnover in intact animals.

Exp. 7 employed R. I. Reds. In this experiment the control birds had an infinite turnover time. That is, in forty-eight hours no iodine loss from the thyroid occurred. There was no apparent reason for these presumably normal birds having completely inactive thyroids. The estrogen-treated group in this experiment had a turnover time of 75.3 ± 5.8 hours. In view of the aberrant control values, the effect of estrogen cannot be determined in this case.

When the chicks were placed under the influence of thiouracil, the thyroxine dose level again seemed to determine what the estrogen effect would be. When a low dose of exogenous thyroxine was administered to chicks receiving thiouracil and estrogen, turnover time for the radio-iodine was longer than in their non-estrogen-treated controls. This was true for the 0.5 and 1.0 gamma level of thyroxine. However, when 2.0 and 4.0 gamma of thyroxine were administered,

the iodine turnover times in the thyroids of the chicks receiving estrogen were shorter than those in non-estrogen-treated birds.

It is apparent that in hypothyroid animals (i.e., in birds whose thyroids have been depressed by thiouracil and in which the exogenous/^{thyroxine} dose level is low) estrogen depresses the thyroid gland. However, in an animal on a higher dose of thyroxine (a relatively hyperthyroid animal) the estrogen seems to stimulate thyroidal turnover.

If the thiouracil were completely blocking the synthesis of thyroxine, the data would suggest that in this case exogenous estrogen acts primarily on the turnover of the inorganic iodine which is returning to the blood stream. This might or might not be under direct pituitary control. However, the dose of thiouracil used (0.1% in the feed) apparently did not completely suppress thyroxine secretion in the two week period of these experiments. This is shown by the effect of thyroxine on the thiouracil but non-estrogen-treated birds (Table 6). The greatest slowing of iodine turnover occurred only when extra thyroxine was administered. In the presence of estrogen, the additional thyroxine-induced slowing was, in fact, reversed.

These considerations do not provide direct proof for the localization of the estrogen effect in a single locus in the thyroid gland itself. They are in line, however, with the hypothesis that there is at least some initial effect

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of estrogen in the thiouracil-treated birds in stimulating thyroxine output. Only in this case would it be logical to expect to get the observed depression of thyroid weight. If the initial effect of estrogen were to increase pituitary thyrotrophin secretion, the increased iodine turnover might be explained, but not the decreased thyroid weight. The third possibility, that estrogen reduced the thyroid sensitivity to thyrotrophin, should mean that both thyroid weight and iodine should be concurrently decreased. The observation is that although thyroid weight was decreased, iodine turnover was increased by estrogen in these thiouracil-treated birds.

We come to the tentative conclusion that in thiouracil-treated chicks, if sufficient exogenous thyroxine is administered, there is at least some direct stimulation of thyroxine output ^{by estrogen} regardless of whatever other effects the estrogen might have at other points in the thyroid-pituitary-gonadal axis. In normal birds, and in birds on thiouracil and low thyroxine dosages, estrogen depressed the iodine turnover with no evidence of change in thyroid size. The pituitary could not have been extensively involved, even secondarily, in the normal birds since even iodine uptake was unaffected.

The net result of these data is to emphasize the point that the effect of estrogen may be either to depress the thyroid or to stimulate it. Depression was observed in normal or relatively hypothyroid animals. Stimulation was

observed only where higher thyroxine levels were maintained. In the birds on these experiments, no evidence was found to indicate that the primary effect of estrogen was solely on the pituitary, although the pituitary was probably involved secondarily. It is always possible that estrogen administration produced minor effects by direct action on either the pituitary cytology (which was not studied) or on other points in the axis. Such effects, if present, were not large enough to result in changes demonstrable by the techniques used here.

TABLE 5

EFFECT OF ESTROGEN ON TURNOVER TIME OF RADIO-IODINE IN THE THYROIDS OF

NORMAL BIRDS

<u>EXP.</u>	<u>IODINE</u> <u>Hours</u>	<u>ESTROGEN</u> <u>Hours</u>
4.	52.7	426.5
5.	19.4±1.3 #	34.8±0.8
6.	79.2±1.9	124.7±3.3
7.	Infinite	75.3±5.8

Standard Error of the Mean

TABLE 6

EFFECT OF ESTROGEN ON TURNOVER TIME OF RADIO-IODINE IN THYROIDS OF BIRDS RECEIVINGTHIOURACIL AND THYROXINE

EXP.	THYROXINE DOSE	NON-ESTROGEN BIRDS		ESTROGEN-TREATED BIRDS	
		Hours		Hours	
4.	0.5 gamma)	(combined)	34.01	39.3	
	1.0 gamma)				
	2.0 gamma)				
5.	0.5 gamma	#	14.1±8.2	30.5±0.2	
	1.0 gamma				
	2.0 gamma				
6.	0.5 gamma		18.8±1.8	18.6±3.4	no data
	1.0 gamma				
	2.0 gamma				
7.	0.5 gamma		26.5±0.4	46.3±4.3	
	1.0 gamma				
	2.0 gamma				
	4.0 gamma		Infinite	18.2±5.5	
	1.0 gamma				
	2.0 gamma				
	4.0 gamma		21.0±86.1	308.0±36.6	
	1.0 gamma				
	2.0 gamma				
	4.0 gamma		18.2±55.2	24.9±63.3	
	1.0 gamma				
	2.0 gamma				
	4.0 gamma		148.0±17.5	47.5±16.9	
	1.0 gamma				
	2.0 gamma				

Standard Error of the Mean

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The Effect of Estrogen on the Daily Rate of Iodine Output
by the Thyroid

The data cited in the previous section may also be computed in terms of the daily output of iodine from the thyroid gland. This is conveniently expressed as per cent of the iodine or the thyroid ~~eliminated~~ in twenty-four hours per hundred grams of body weight. In the four experiments on normal birds (Table 7), the estrogen caused a decreased output as compared with the control groups. Thus, in the dose level administered, estrogen depressed the thyroid output of iodine.

In one case (Exp. 7, R. I. Reds) a net uptake, rather than an output, of iodine was found forty-eight hours after the injection of radio-iodine in the estrogen-treated birds as compared with 19.8% output for the normal controls. As reported previously, no apparent reason can be given for this aberrant result.

Again the rate of daily output is correlated with the thyroxine dose rates in the groups receiving thiouracil and thyroxine in addition to the estrogen (Table 8). In the thiouracil-treated birds receiving one ug of thyroxine per day, the daily output from the thyroid glands is less in the estrogen groups. Conversely, in the animals receiving 2.0 and 4.0 ug of thyroxine, the amount of iodine eliminated per twenty-four hours is increased by estrogen administration.

TABLE 7

EFFECT OF ESTROGEN ON THE IODINE TURNOVER RATE OF THE THYROID GLANDS PER 24 HOURS

EXP.	<u>OF NORMAL BIRDS</u>	
	TREATMENT	PER CENT IODINE ELIMINATED PER 24 HOURS
4.	IODINE CONTROL	27.5%
	ESTROGEN CONTROL	3.1%
5.	IODINE CONTROL	50.6%
	ESTROGEN CONTROL	38.1%
6.	IODINE CONTROL	18.9%
	ESTROGEN CONTROL	12.5%
7.	IODINE CONTROL	19.8%
	ESTROGEN CONTROL	accumulation

TABLE 8

EFFECT OF ESTROGEN ON THE IODINE TURNOVER RATE OF THE THYROID GLAND PER 24 HOURS OF

BIRDS RECEIVING THIOURACIL AND THYROXINE

EXP.	THYROXINE DOSE	NON-ESTROGEN BIRDS	ESTROGEN-TREATED BIRDS
4.	0.5 gamma) 1.0 gamma(2.0 gamma)	(combined) 38.7%	34.5%
5.	0.5 gamma 1.0 gamma 2.0 gamma	69.2% 57.2% 74.3%	42.0% 59.2% no data
6.	1.0 gamma 2.0 gamma 4.0 gamma	46.0% 17.4% accumulation	50.2% 42.8% 59.9%
7.	1.0 gamma 2.0 gamma 4.0 gamma	65.6% 59.9% 10.6%	5.3% 48.8% 29.5%

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Thyroid Secretion Rates as Calculated by the Method of
Mixner, Reineke and Turner (1944)

Computation of thyroid secretion rates involves plotting the thyroid weights of birds on thiouracil against the thyroxine dosage. Since the lower thyroxine dosages used in these experiments give aberrant thyroid weights (as mentioned above), the calculation of secretion rates had to be made on the basis of only the 2.0 and 4.0 ug thyroxine dose level. The data are, therefore, subject to considerable error. Nevertheless, the values so computed are listed in Table 9. They are in general agreement with those found by Boone et al. (1950). The data obtained show no clear evidence for any effect of estrogen on the thyroid secretion rate. In view of the rest of the data and the inadequacies in these direct assays, it seems impossible to credit these results for more than an estimate of the general level of thyroid secretion.

The average thyroid secretion rate was 2.1 gamma per day per hundred grams body weight. In view of this magnitude of thyroxine secretion rate, four gamma of exogenous thyroxine per day should definitely produce a hyperthyroid animal.

UNIT 1: THE HISTORY OF THE UNITED STATES

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TABLE 9

THYROID SECRETION RATES AS COMPUTED FROM THYROID WEIGHTS
PER HUNDRED GRAMS BODY WEIGHT

<u>EXP.</u>	<u>CONTROLS</u>	<u>ESTROGEN-TREATED BIRDS</u>
4.	1.8 ug/day	
5.		2.7 ug/day
6.	2.2 ug/day	
7.	1.9 ug/day	1.9 ug/day

Effect of Estrogen on Body Weights

In all of the groups under observation, both control and experimental, there seems to be no change in body weight when the animals are treated with estrogen (Tables 10 and 11). Thayer, Jaap and Penquite (1945) found an increase in the body weights of cocks on an estrogen diet, while Davidson et al. (1946) found that the weights of young turkeys was usually decreased by the administration of estrogen.

TABLE 10

EFFECT OF ESTROGEN ON BODY WEIGHT OF NORMAL CHICKS

EXP.	NO. CHICKS	CONTROL Grams	ESTROGEN-TREATED BIRDS Grams	RADIO-IODINE-TREATED BIRDS Grams
1.	11	220.5±28.1*		
2.	19-14	236.1±9.8	187.1±21.8	
3.	12-12-13	308.3±10.7	294.1±18.1	330.5±9.9
4.	10-8-8	166.8±10.7	216.0±7.1	226.0±3.2
5.	11-7-6	224.4±6.7	228.9±14.2	188.3±17.9
6.	17-14-12	241.5±9.6	221.5±6.6	222.2±7.8
7.	8-5-6	240.4±12.0	244.1±5.0	215.7±10.2

* Standard Error of the Mean.

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TABLE 11

EFFECT OF ESTROGEN ON BODY WEIGHT OF CHICKS RECEIVING THIOURACIL AND THYROXINE

EXP.	NO. BIRDS*	ESTROGEN DOSE	THYROXINE DOSE	BODY WEIGHT IN GRAMS	
				CONTROLS	ESTROGEN-TREATED
<u>I. RHODE ISLAND REDS</u>					
1.	11	5 mg/inject daily	1 ug/day	none	195.6±28.0
2.	15-00	none	2 ug/day	223.6±11.1 #	
	13-00	none	4 ug/day	217.2±14.6	
7.	6-6	0.01% (feed)	1 ug/day	219.8±7.0	229.2±14.9
	6-6	0.01% "	2 ug/day	234.8±10.6	236.3±10.9
	5-6	0.01% "	4 ug/day	222.0±11.4	237.0±11.0
<u>II. BARRED ROCKS</u>					
3.	12-12	0.01% " reduced to 0.005% after a week	none	289.5±9.9	281.2±9.8
4.	6-4	"	thyroprotein**	237.2±11.9	175.5±23.8
	8-6 8-5	0.01% (feed) 0.01% "	1 ug/day 2 ug/day	202.0±9.0 204.0±10.6	202.3±5.7 179.2±9.0
5.	6-5 6-8	0.01% " 0.01% "	1 ug/day 2 ug/day	235.0±14.1 225.0±12.5	242.0±11.7 206.8±12.2

* First Number is for Controls; second is for Estrogen-treated.

** Thyroprotein in feed 0.32% for first week; reduced to 0.16% for the second.

Standard Error of the Mean.

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TABLE 11 (CONTINUED)

EXP.	NO. BIRDS*	ESTROGEN DOSE	THYROXINE DOSE	BODY WEIGHT IN GRAMS	
				<u>CONTROLS</u>	<u>ESTROGEN-TREATED</u>
6.	14-13	0.01% (feed)	1 ug/day	222.5±8.0#	220.6±6.7
	12-13	0.01% "	2 ug/day	242.4±11.9	235.3±10.5
	14-5	0.01% "	4 ug/day	221.6±8.8	215.9±7.8

* First Number is for Controls; second is for Estrogen-treated.

Standard Error of the Mean.

Effect of Estrogen on Comb Growth

Since the estrogen was administered to the chicks in the feed in the last five experiments, it was considered desirable to measure the growth of the combs in order to gain some indication of the oral effectiveness of the estrogen. In the normal chicks (Table 12), it will be noted, the estrogen caused a depression of the comb growth in all groups, as compared with the controls.

Radio-iodine had no effect on the comb growth of normal chicks as compared with normal controls not receiving the isotope.

On the whole, the estrogen caused a decrease in comb weight even when exogenous thyroxine was administered to the chicks on the thiouracil assay (Table 13). The administration of thiouracil did not potentiate the action of the estrogen. Conversely, the action of the estrogen on the comb weights was not modified at all by the administration of even four ug of thyroxine per day.

It is very interesting to note that while estrogen had no apparent effect on the pituitary as far as the thyrotrophic hormone was concerned, it did affect the pituitary gonadotrophin. This is evidenced by the decrease in comb growth with the administration of estrogen. Boas and Ludwig (1950) report that the effect of estrogen on comb growth is manifested through the action on the pituitary. On the basis of comb histology

in normal and hypophysectomized birds, they maintain that estrogen depresses the secretion of gonadotrophin and thereby causes a depression of comb size.

This indicates that in our experiments the estrogen is affecting the gonadotrophin but not the thyrotrophin, both presumably products of the same cells of the anterior pituitary.

Summary of Effects of Estrogen on the Chick

In order to facilitate reading and understanding of the discussion section of this paper, we are summarizing the results found in the experiments herein reported. This summary may be found in Table 14.

TABLE 12

EFFECT OF ESTROGEN ON COMB WEIGHTS IN NORMAL BIRDS

EXP.	NORMAL	ESTROGEN-TREATED	IODINE-CONTROL
	Milligrams per 100 Grams Body Weight		
2.	100.9±18.7 #	23.3±2.8	
3.	19.7±3.7	11.3±2.1	25.8±4.4
4.	29.1±4.2	16.2±2.3	25.5±4.6
5.	27.8±4.0	20.2±2.7	33.6±9.1
6.	37.4±5.9	15.8±0.9	28.9±5.9
7.	32.2±4.6	15.8±1.5	41.6±7.9

Standard Error of the Mean.

TABLE 13

EFFECT OF ESTROGEN ON COMB WEIGHTS OF BIRDS RECEIVING THIOURACIL AND

THYROXINE

EXP.	THYROXINE DOSE	NON-ESTROGEN BIRDS Milligrams per 100 Grams Body Weight	ESTROGEN-TREATED BIRDS Milligrams per 100 Grams Body Weight
3.	0.32% 1st week 0.16% 2nd week	14.1±2.0#	15.4±1.5
4.	0.5 gamma 1.0 gamma 2.0 gamma	25.1±12.5 15.8±2.4 19.5±5.0	17.0±3.6 10.4±2.0 16.8±2.4
5.	0.5 gamma 1.0 gamma 2.0 gamma	14.5±2.8 34.2±9.7 22.3±4.2	17.2±2.4 17.0±3.2 16.4±1.7
6.	1.0 gamma 2.0 gamma 4.0 gamma	16.6±2.0 24.7±5.5 19.2±2.4	18.0±1.7 16.0±1.3 15.5±1.2
7.	1.0 gamma 2.0 gamma 4.0 gamma	41.8±5.9 38.3±7.6 30.8±6.5	17.9±2.2 17.4±3.3 18.2±3.0

Standard Error of the Mean.

TABLE 14

SUMMARY OF THE EFFECTS OF ESTROGEN ON THE CHICK

1. ON THYROID SIZE

- a. Normal Animals - estrogen has no effect
- b. Thiouracil-treated Animals
 - (1) Low dose of thyroxine - estrogen has no effect
 - (2) Two and four gamma of thyroxine - estrogen depresses size of glands

2. ON UPTAKE OF RADIO-IODINE

- a. Normal Animals - estrogen has no effect
- b. Thiouracil-treated Animals
 - (1) Low dose of thyroxine - estrogen generally depresses uptake
 - (2) Two and four gamma of thyroxine - estrogen stimulates uptake

3. ON TURNOVER TIMES OF RADIO-IODINE

- a. Normal Animals - estrogen causes a longer turnover time (reduced daily output)
- b. Thiouracil-treated Animals
 - (1) Low dose of thyroxine - estrogen causes a longer turnover time (reduced daily output)
 - (2) Two and four gamma of thyroxine - estrogen causes a shorter turnover time (increased daily output)

4. ON COMB SIZE

In all cases estrogen depresses the size of the combs.

5. ON BODY WEIGHTS

In all cases estrogen has no effect on the body weights.

DISCUSSION

The earliest intimation of the interrelationship between the thyroid and the ovary seems to be the discovery by the Chinese - that women are more prone to goiter than men. Salter (1940) points out that the ratio of goiters ^{goiters in} in women to men decreases progressively as sex becomes less important in the life cycle, becoming equal between the sexes after the menopause. Much work has been done on the relationship of these two glands of internal secretion, but many of the results are of a very controversial nature.

Kunde et al. (1931) found that when estrin was administered to dogs for seventeen weeks, there was hyperplasia of the thyroid. Pincus and Werthessen (1933) found similar results in rats if the estrin were administered to rats for five to ten days, but they found involution of the thyroid if they administered the hormone for twenty or more days. Karp and Kostkiewicz (1933), working with rabbits, and Benazzi (1933), working with mice, found that folliculin caused an increase in thyroid size.

An increase in thyroid weight might indicate that the thyrotrophin secretion is either directly increased by estrogen or indirectly stimulated by decreasing the secretion of thyroxine. The possibility also exists that the estrogen directly increases the sensitivity of the

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thyroid to thyrotrophin. Conversely, a decrease in thyroid weight might indicate that the thyrotrophin is being depressed. Again this might be a direct action on the anterior pituitary, or it might be an indirect consequence of a primary thyroid depression. As reported in the introduction, most of the work on pituitary cytology indicates that estrogen causes degranulation of the basophil cells which produce the thyrotrophin. This cytologic picture is usually interpreted as being sufficient to indicate a depression of the secretion of that hormone, a result in agreement with the depression of pituitary thyrotrophin on direct assay as reported by Meites and Turner (ibid).

The increased thyroid weights induced by estrogen, as reported by the investigators cited above, are difficult to explain if thyrotrophin is reduced. If, on the other hand, estrogen first suppresses the thyroid output of thyroxine, as is suggested by the chick data reported herein, pituitary thyrotrophin should be increased and, given sufficient time, thyroid enlargement should result, as was reported by Kunde et al., Pincus and Werthessen, and Karp and Kostkiewicz (ibid.). Such enlargement was not observed in the chicks in these experiments, however.

The data from thiouracil-treated birds given two or four gamma of thyroxine indicated that estrogen does not always suppress thyroid turnover, but may, in fact, stimulate it if circulating thyroxine is present in sufficient

amounts. In that case estrogen should depress thyrotrophin as suggested by the evidence of pituitary cytology. In either event, the decisive factor, or factors, apparently lies in some combination of the ratio of estrogen to circulating thyroid hormone and the duration of treatments. Data from experiments set up with these points in mind are urgently needed.

If we were to base our conclusions solely on thyroid size, we should be forced to conclude that estrogen administration to normal and hypothyroid chicks has no effect on the thyroid gland. Also, estrogen administration to chicks made somewhat hyperthyroid by thyroxine increases thyroid activity.

Data obtained from the uptake and turnover of radio-iodine give a more sensitive criterion of thyroid activity. We found that in normal chicks estrogen had no effect on the twenty-four hour uptake of radio-iodine. Similar results were found in rats by Paschkis et al. (1948) at four hours after iodine administration. Since Morton et al. (1942) have shown that the uptake of iodine by the thyroid gland is controlled by thyrotrophin, we might readily assume that in our experiments, two weeks of estrogen administration had no effect on the secretion of thyrotrophin.

In chicks on the thiouracil assay, estrogen caused less radio-iodine to be taken up when a low dose of thyroxine was administered daily. This would indicate a depression of thyrotrophin secretion. Yet, it is difficult to see

how a decreased thyrotrophin secretion could have caused a decreased uptake of iodine and still not decrease the size of the thyroid gland, that is, in view of the observation of Keating et al. (1945) that thyrotrophin first influences thyroid weight and only later influences uptake of radio-iodine.

When two or four gamma of thyroxine were administered to the chicks on the thiouracil assay, estrogen stimulated the thyroid to take up more of the injected radio-iodine. If the stimulation were the result of increased pituitary thyrotrophin secretion, an increased size of the thyroid should have been observed. The data give no indication there was any direct effect of the estrogen on the secretion of thyrotrophin by the anterior pituitary (unless it be concurrently assumed, in disagreement with Keating et al., that under the influence of thyrotrophin altered radio-iodine uptake can occur without change in thyroid size).

Turning our attention to the turnover of radio-iodine, we find that estrogen increased the turnover time in normal chicks. This indicates that the estrogen is depressing the activity of the thyroid by decreasing the output of iodine. From the present data this is the first indication we have of any effect of estrogen on the thyroids of normal animals. We had no indication of this from the size of the glands, or from the uptake of radio-iodine. This must mean that, in normal chicks at least, estrogen depresses

the thyroid directly. If it did exert its effect through the pituitary, even secondarily, we should have expected to see some change in the size of the thyroid and in the uptake of radio-iodine. However, such was not observed.

In the chicks on the thiouracil assay, we find that when a low dose of thyroxine was administered, estrogen again depressed thyroidal activity, indicated by a longer turnover time in the estrogen-treated birds than in their controls. This depression was reflected in the decreased iodine uptake of these birds. However, we found no change in the size of their thyroids. If Keating and his co-workers are correct, this again indicates that thyrotrophin secretion could not have been extensively involved. They showed the differential effect of thyrotrophin on thyroid size as compared to radio-iodine uptake in three days. Surely, in the two weeks of our experiment, the thyroids of the chicks should have had enough time to react to altered thyrotrophin levels if such had been induced by estrogen. Therefore, since we found no change in the thyroid size and a decrease in the uptake of iodine, we must presume that there is no effect on the pituitary thyrotrophin. This is in direct contrast to the effect of estrogen on gonadotrophin. As pointed out earlier, the depression of comb size by estrogen is clear evidence of the depression of the secretion of gonadotrophin.

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The conclusions reached here add direct evidence for the thyroid-pituitary mechanisms in the modifications of those metabolic effects of estrogen cited by Fleischmann (1946). He found that the ability of the estrogen to increase serum calcium, inorganic phosphate, protein phosphate and cholesterol was neutralized by the administration of equal parts of thyroxine. It is thus apparent that the fattening of birds by estrogen must be profoundly influenced by the level of thyroid activity. The data of the present experiments directly demonstrate that estrogen can primarily alter thyroid activity.

SUMMARY AND CONCLUSIONS

1. Thiouracil administered orally as 0.1% of the feed did not completely suppress iodine turnover in the thyroid.

2. Estrogen had no effect on the thyroid size of normal chicks.

3. Radio-iodine injections (0.2 microcuries) had no effect on the size of the thyroid glands.

4. In chicks receiving thiouracil and one gamma of thyroxine a day, estrogen had no effect on the thyroid size.

5. In chicks receiving thiouracil and either two or four gamma of thyroxine per day, estrogen caused a decrease in the size of the thyroid glands.

6. In normal chicks, estrogen had no effect on the uptake of radio-iodine by the thyroid.

7. In chicks receiving thiouracil and one gamma of thyroxine per day, the Rhode Island Reds picked up more radio-iodine under the influence of estrogen than did their controls, while in the Barred Rocks the estrogen administration caused less iodine to be taken up.

In chicks receiving thiouracil and two or four gamma of thyroxine per day, estrogen caused a greater uptake of radio-iodine in both breeds.

8. Estrogen caused a depression of thyroxine turnover in normal animals.

9. When the chicks were placed under the influence of thiouracil, the thyroxine dose level seemed to determine what the estrogen effect would be. When a low dose of exogenous thyroxine was administered to chicks receiving thiouracil and estrogen, turnover time for the radio-iodine was longer in these birds than in the non-estrogen-treated controls. However, when two or four gamma of thyroxine were administered to comparable animals, the turnover time was shorter in the estrogen-treated animals than in their controls.

10. If sufficient exogenous thyroxine is administered, estrogen stimulates thyroxine output by a direct action on the thyroid gland. With low thyroxine levels, estrogen depresses iodine turnover by the thyroid gland.

11. Changes in pituitary thyrotrophin output, as nearly as can be determined from these data, were the secondary results of the alteration in the thyroid as induced by estrogen.

12. The direct effect of estrogen on the pituitary or on the sensitivity of the thyroid to thyrotrophin could not be demonstrated from these data.

13. Estrogen was not observed to have any effect on body weight under these conditions of ad libitum feeding.

14. Comb weight was depressed by estrogen but not by radio-iodine in the normal birds.

15. The depression of comb weight induced by estrogen was not modified either by thiouracil or by exogenous thyroxine.

Since comb weight is controlled by pituitary gonadotrophin, no pronounced effect of thyroxine depression or excessive thyroxine on gonadotrophin secretion could be demonstrated from these data.

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1. The first part of the document discusses the importance of maintaining accurate records of all transactions and activities. It emphasizes that proper record-keeping is essential for transparency and accountability, particularly in financial matters. The text notes that without reliable records, it is difficult to track progress, identify trends, and make informed decisions.

2. The second part of the document outlines the various methods and tools used to collect and analyze data. It mentions the use of surveys, interviews, and focus groups to gather qualitative information, as well as the application of statistical software for quantitative analysis. The importance of ensuring the validity and reliability of the data is stressed throughout this section.

3. The third part of the document describes the process of interpreting the collected data and drawing meaningful conclusions. It highlights the need for a systematic approach to data analysis, including the identification of key variables and the use of appropriate statistical tests. The text also discusses the importance of considering external factors that may influence the results of the study.

4. The fourth part of the document provides a detailed overview of the findings of the study. It presents the results of the data analysis in a clear and concise manner, using tables and graphs to illustrate key points. The findings are discussed in the context of the research objectives and the existing literature on the topic.

5. The fifth part of the document discusses the implications of the study and offers recommendations for future research. It suggests that further investigation is needed to explore the underlying mechanisms of the observed phenomena and to test the generalizability of the findings. The text also provides practical advice for stakeholders based on the study's conclusions.

6. The final part of the document is a conclusion that summarizes the main points of the study and reiterates the significance of the findings. It expresses the hope that the research will contribute to a better understanding of the topic and inform future decision-making. The document concludes with a statement of appreciation for the support and assistance provided throughout the research process.

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APPENDIX

Complete data for each experiment are found on two successive pages. Body and organ weights are listed on the first page and radio-iodine data are listed on the second page. The headings on each page give the experiment number and the breed of the chicks used.

EXPERIMENT 1
RHODE ISLAND REDS

TREATMENT	NO. CHICKS	BODY WT. GRAMS	THYROID WT. MG/100 GM.	COMB WT. MG/100GM.	GONAD WT. MG/100GM.
Controls	7M 4F	220.5±28.1 #	8.1±0.8	No Data	No Data
0.1% Thiouracil 1.0 Microgram Thyroxine	7M 2F	194.0±26.9	35.9±6.0		
0.1% Thiouracil 1.0 Microgram Thyroxine 5.0 Milligrams Dianysilhexene (Estrogen)	4M 7F	195.6±28.0	47.4±1.7		
0.1% Thiouracil 1.0 Microgram Thyroxine 1 Milligram Testosterone Propionate	4M 2F	169.3±28.7	37.6±8.7		

Standard Error of the Mean

EXPERIMENT 2
RHODE ISLAND REDS

TREATMENT	NO. CHICKS	BODY WT. GRAMS	THYROID WT. MG/100 GM.	COMB WT. MG/100GM.	GONAD WT. MG/100GM.
Controls	12 M 7 F	236.1±9.8	10.5±2.3	100.9±18.7	No Data
5.0 Micrograms Estrogen*	5 M 9 F	187.1±21.8	11.2±1.1	23.3±2.8	
1.0 Milligrams Testosterone Propionate	7 M 10 F	200.5±10.4	11.1±0.6	744.6±46.5	
0.1% Thiouracil 2.0 Micrograms Thyroxine	9 M 6 F	223.6±11.1	39.8±2.5	49.6±6.7	
0.1% Thiouracil 4 Micrograms Thyroxine	6 M 7 F	217.2±14.6	18.1	60.8±6.8	

* Dianisylhexene

Standard Error of the Mean.

EXPERIMENT 3

BARRED ROCKS

TREATMENT	NO. CHICKS	BODY WT. GRAMS	THYROID WT. MG/100GM.	COMB WT. MG/100GM.	GONAD WT. MG/100GM.
Controls					
	2 M 10 F	308.3±10.7#	5.74±0.3	19.8±3.7	No Data
Iodine*	8 M 5 F	330.5±9.9	4.3±0.6	25.8±4.4	
Iodine ** Estrogen	3 M 9 F	294.1±18.1	5.4±0.6	11.3±2.1	
Iodine 0.2% Thiouracil	5 M 7 F	289.5±9.9	21.3±1.0	10.7±1.0	
Iodine 0.2% Thiouracil Estrogen	4 M 8 F	281.2±9.8	27.1±4.2	9.1±1.2	
Iodine 0.2% Thiouracil Thyropotein	3 M 4 F	237.2±11.9	2.3±0.2	14.1±2.0	
Iodine 0.2% Thiouracil Estrogen Thyropotein	1 M 3 F	175.5±23.8	1.5±0.4	15.4±1.5	

* Radioactive Iodine in Drinking Water for One Week

** Dianisylhexene in feed 0.01% for first week; then 0.005% second week

***Protomone in feed - 0.32% for first week; then 0.16% the second (0.32% too toxic)

Standard Error of the Mean

EXPERIMENT 4

BARRED ROCKS

TREATMENT	NO. CHICKS	BODY WT. GRAMS	THYROID WT. MG/100GM.	COMB WT. MG/100GM.	GONAD WT. MG/100GM.
Controls	5 M 5 F	166.8±10.7#	9.2±1.7	29.1±4.2	35.1±10.4
Estrogen	3 M 5 F	216.0±7.1	6.9±0.7	16.2±2.3	26.5±6.0
Iodine Control	5 M 3 F	226.0±3.2	11.3±2.3	25.5±4.6	46.6±7.7
0.1% Thiouracil Estrogen 0.5% Microgram Thyroxine	4 M 3 F	204.5±17.5	33.0±5.7	16.9±3.6	25.2±4.3
0.1% Thiouracil 0.5% Micrograms Thyroxine	2 M 5 F	180.0±14.6	22.6±9.7	25.1±12.5	46.9±11.4
0.1% Thiouracil Estrogen 1.0 Microgram Thyroxine	2 M 4 F	202.3±5.7	20.7±7.5	10.4±2.0	33.11±6.4
0.1% Thiouracil 1.0 Microgram Thyroxine	3 M 5 F	202.0±9.0	32.3±3.9	15.8±2.4	42.4±5.1
0.1% Thiouracil Estrogen 2.0 Micrograms Thyroxine	4 M 1 F	179.2±9.0	21.4±3.8	16.8±2.4	26.1±6.1
0.1% Thiouracil 2.0 Micrograms Thyroxine	3 M 5 F	204.0±10.6	23.2±4.3	19.5±5.0	42.2±3.3

* 0.01% Dianisylhexene in feed for two weeks.
Standard Error of the Mean.

EXPERIMENT 5

BARRED ROCKS

TREATMENT	NO. CHICKS	BODY WT. GRAMS	THYROID WT. MG/100GM.	COMB WT. MG/100GM.	GONAD WT. MG/100GM.
Controls	5 M 6 F	224.4±6.7#	5.9±0.6	27.8±3.9	32.3±4.4
1. Estrogen*	4 M 3 F	228.9±14.2	6.4±0.5	20.3±2.7	16.9±1.6
2. Iodine**	3 M 2 F	188.3±17.9	9.8±1.4	33.6±9.1	43.9±6.0
3. 0.1% Thiouracil Estrogen 0.5 Microgram Thyroxine	5 M 2 F	226.6±9.8	26.5±3.5	17.2±2.4	20.9±2.6
4. 0.1% Thiouracil 0.5 Microgram Thyroxine	2 M 5 F	215.1±6.7	35.4±5.4	14.5±1.3	33.9±3.6
5. 0.1% Thiouracil Estrogen 1.0 Microgram Thyroxine	3 M 2 F	242.0±11.7	34.8±5.2	16.9±3.2	20.2±2.9
6. 0.1% Thiouracil 1.0 Microgram Thyroxine	3 M 3 F	235.0±14.1	29.4±8.1	34.2±9.6	33.5±3.4
7. 0.1% Thiouracil Estrogen 2.0 Micrograms Thyroxine	4 M 4 F	206.8±12.2	19.6±1.6	16.4±1.7	20.6±1.7
8. 0.1% Thiouracil 2.0 Micrograms Thyroxine	4 M 2 F	225.0±12.5	29.0±3.6	22.3±4.2	26.9±3.6

* 0.01% Dizinylhexene in feed daily for two weeks

** All animals except normal controls on radio-active IODINE-131

Standard Error of the Mean.

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GROUP	24 HOUR IODINE UPTAKE CTS./SEC./MG.	SUBSEQUENT IODINE RETENTION CTS./SEC./MG.	TIME INTERVAL	TURNOVER RATE CONSTANT k (hours ⁻¹)	TURNOVER TIME HOURS	DAILY OUTPUT %/24 HRS.
1.	9.070±1.210#	3.480±0.410	48 hours	0.01993±0.016	34.8±0.8	38.0
2.	10.670±2.000	1.920±0.250	"	0.03569±0.048	19.4±1.3	58.6
3.	0.040±0.120	0.135±0.010	"	0.02271±0.004	30.5±0.2	42.0
4.	0.794±0.460	0.075±0.040	"	0.04909±0.400	14.1±8.2	69.2
5.	0.271±0.118	0.045±0.002	"	0.03736±0.126	18.6±3.4	59.2
6.	0.540±0.130	0.099±0.005	"	0.03531±0.064	18.6±1.8	57.2
7.	No Data	0.089±0.030	"	No Data	No Data	No Data
8.	0.514±0.470	0.034±0.001	"	0.05653±0.667	12.3±11.8	74.3

Standard Error of the Mean

EXPERIMENT 6

BARRED ROCKS

TREATMENT	NO. CHICKS	BODY WT. GRAMS	THYROID WT. MG/100GM.	COMB WT. MG/100GM.	GONAD WT. MG/100GM.
Controls	11 M 6 F	241.5±9.6#	6.2±0.4	37.5±5.9	36.1±3.2
1. Estrogen*	8 M 6 F	221.5±6.6	5.8±0.3	15.8±0.9	17.4±2.0
2. Iodine**	4 M 8 F	222.2±7.8	5.5±0.2	28.9±5.9	29.6±1.4
3. 0.1% Thiouracil Estrogen 1.0 Microgram Thyroxine	6 M 7 F	220.6±6.7	30.0±3.2	17.9±1.2	20.5±2.0
4. 0.1% Thiouracil 1.0 Microgram Thyroxine	3 M 11 F	222.5±8.0	25.1±2.0	16.6±1.9	29.8±0.9
5. 0.1% Thiouracil Estrogen* 2.0 Micrograms Thyroxine	6 M 7 F	235.3±10.5	15.3±1.1	16.0±1.3	16.6±1.7
6. 0.1% Thiouracil 2.0 Micrograms Thyroxine	5 M 7 F	242.4±12.0	37.9±4.6	24.7±5.5	35.2±2.0
7. 0.1% Thiouracil Estrogen* 4.0 Micrograms Thyroxine	5 M 10 F	215.9±7.8	11.2±1.0	15.5±1.13	22.8±1.9
8. 0.1% Thiouracil 4.0 Micrograms Thyroxine	3 M 11 F	221.6±8.8	16.1±1.9	19.2±2.4	34.5±1.6

* Dianisylhexene - 0.01% in feed daily for two weeks

** All groups except control given radio-active IODINE—131

Standard Error of the Mean



GROUP	24 HOUR IODINE UPTAKE CTS./SEC./MG.	SUBSEQUENT IODINE RETENTION CTS./SEC./MG.	TIME INTERVAL	TURNOVER RATE CONSTANT k (hours ⁻¹)	TURNOVER TIME HOURS	DAILY OUTPUT %/24 HRS.
1.	3.187±0.404#	2.790±0.36	24 hours	0.00556±0.018	124.7±3.3	12.5
2.	3.024±0.404	2.429±0.160	25 "	0.00874±0.017	79.2±1.9	18.9
3.	0.140±0.063	0.095±0.020	26 "	0.01496±0.065	46.3±4.3	30.2
4.	0.277±0.010	0.112±0.019	27 "	0.02616±0.011	26.5±0.4	46.6
5.	1.391±0.340	0.572±0.110	29 "	0.02228±0.047	31.1±2.1	42.8
6.	0.056±0.002	0.044±0.011	30 "	0.00798±0.025	86.9±3.1	17.4
7.	1.060±0.814	0.223±0.033	41 "	0.03804±0.209	18.2±5.5	59.9
8.	0.421±0.196	0.624±0.084	43 "	---	Accumulation ---	---

Standard Error of the Mean.

EXPERIMENT 7
RHODE ISLAND REDS

TREATMENT	NO. CHICKS	BODY WT. GRAMS	THYROID WT. MG/100GM.	COMB WT. MG/100GM.	GONAD WT. MG/100GM.
Control	3 M 5 F	240.4±12.0	7.2±0.6	32.2±4.6	38.0±4.0
1. Estrogen*	1 M 4 F	244.1±5.0	7.5±0.8	15.8±1.5	32.4±5.3
2. Iodine**	4 M 2 F	215.7±10.2	6.6±1.0	41.6±7.9	32.5±7.5
3. 0.1% Thiouracil Estrogen 1.0 Microgram Thyroxine	4 M 2 F	229.2±14.9	26.0±6.4	17.9±2.2	24.8±5.1
4. 0.1% Thiouracil 1.0 Microgram Thyroxine	5 M 1 F	219.6±7.0	28.6±4.1	41.8±5.9	35.8±4.6
5. 0.1% Thiouracil Estrogen 2.0 Micrograms Thyroxine	3 M 3 F	236.3±10.9	19.8±3.8	17.4±3.3	27.4±5.5
6. 0.1% Thiouracil 2.0 Micrograms Thyroxine	4 M 2 F	234.8±10.6	36.6±5.9	38.3±7.6	38.7±6.7
7. 0.1% Thiouracil Estrogen 4.0 Micrograms Thyroxine	3 M 3 F	237.0±11.0	10.1±1.6	18.2±3.0	24.1±5.3
8. 0.1% Thiouracil 4.0 Micrograms Thyroxine	1 M 4 F	222.0±11.4	12.0±1.2	30.8±6.5	42.6±3.1

* Dianisylhexene - 0.01% in feed daily for two weeks

** All groups except normal controls received radio-active IODINE-131
Standard Error of the Mean

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GROUP	24 HOUR IODINE UPTAKE CTS./SEC./MG.	SUBSEQUENT IODINE RETENTION CTS./SEC./MG.	TIME INTERVAL	TURNOVER RATE CONSTANT k (hours ⁻¹)	TURNOVER TIME HOURS	DAILY OUTPUT %/24 HRS.
1.	0.782±0.143#	0.633±0.092	48 hours	0.00920±0.053	75.3±5.8	19.8
2.	0.977±0.162	1.170±0.102	48 "	---	Accumulation	---
3.	0.174±0.089	0.059±0.018	48 "	0.47000±1.752	307.9±36.6	5.3
4.	0.030±0.018	0.006±0.001	49 "	0.70330±4.040	21.0±86.1	65.6
5.	0.256±0.134	0.073±0.038	49 "	0.60000±2.940	24.9±63.3	48.8
6.	0.086±0.004	0.013±0.005	49 "	0.82100±2.569	18.2±55.2	59.9
7.	0.085±0.030	0.041±0.013	50 "	0.31700±0.780	47.5±16.9	29.5
8.	0.043±0.017	0.034±0.017	50 "	0.10182±0.805	148.0±17.5	10.6

Standard Error of the Mean.

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