THE EFFECTS OF SODIUM SALICYLATE ON THYROID FUNCTION IN HEAT-STRESSED CHICKENS

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INTRODUCTION

Birds subjected to high environmental temperatures exhibit numerous adverse effects which include: decrease in body weight, decrease in feed consumption, increase in body temperature, decrease in egg production and decrease in thyroid activity. Of these adverse effects, it appears probable that the increase in body temperature and decrease in thyroid activity are primary changes which are responsible for the decrease in body weight, decrease in feed consumption and decrease in egg production. It has been shown in mammals and birds that there exists a reciprocal relationship between environmental temperature (and to a lesser extent, body temperature) and thyroid activity. Although thyroid activity has been shown to decrease in birds at high environmental temperature, the mechanism by which this decrease is brought about is not entirely clear.

Maintenance of a constant body temperature in birds, when the environmental temperature varies, depends on a balance between the heat produced and the heat lost. The thyroid gland plays an important role in regulating heat production and basal metabolic rate in birds as in mammals by controlling the rate of oxidation in the tissue cells. Variation in the secretion of thyroxine by the thyroid results in an alteration of heat produced by an animal and as a result, the temperature-regulating mechanisms are stimulated to alter heat loss and thus maintain a constant body temperature.

In an effort to reduce the adverse effects of high ambient temperatures in birds, various experimental approaches have been attempted. Turner, et al., (1945, 1946) controlled thyroid activity near normal levels

in laying hens exposed to the high temperature of a summer season by feeding thyroprotein which resulted in continued egg production during the summer on a more normal level as contrasted with the decrease in egg production noted for control birds. No change in body weight or of feed consumed was observed in the thyroprotein-fed birds. In contrast to these results, Mohamed (1953) observed a decrease in egg production in hyperthermic hens given thyroprotein. It appears that feeding thyroprotein to heat-stressed birds is not the complete answer for reducing the adverse effects of a decrease in body weight, feed consumption, and egg production which result when birds are exposed to high ambient environmental temperature.

Various substances other than thyroprotein have been given to hyperthermic birds in an effort to reduce the adverse effects of high environmental temperatures. Tranquilizers, such as chlorpromazine and reserpine, have been reported to depress body temperature and have possible beneficial effects on egg production, growth and feed efficiency in hyperthermic birds (Burger, Van Matre, and Lorenz, 1957a, 1957b). Reserpine has been shown by Premachandra and Turner (1960) to depress thyroxine secretion rate when large doses were injected into pigeons and adult chickens. They suggested that depression of thyroid activity by feeding high levels of reserpine was secondary to depression of food intake. Heywang (1959) found that low levels of antibiotics and arsonilic acid fed to laying chickens during hot weather improved egg production but had little effect on increasing body weight.

The thermoregulatory mechanisms which operate in birds to increase heat loss when the environmental temperature rises seem to become ineffective when the air temperature is greater than 90° F., since above this

ambient temperature the body temperature of birds increases .5 to 1.5° F. (Heywang, 1938; Wilson, 1948). Assuming that the adverse effects in birds exposed to high environmental temperatures are due to an increase in body temperature, then if the febrile condition in birds could be reduced, perhaps the body weight, feed consumption, etc., would approach values for normal birds. Antipyretics have been used extensively in mammals for reducing fever to normal and near normal levels, but no data are available in the literature concerning the use of antipyretics in febrile birds.

This experiment was designed primarily to observe the effects of a chronically administered antipyretic, sodium salicylate, on thyroid function, body temperature, body weight, and feed consumption in birds rendered hyperthermic by subjecting them to an elevated ambient temperature.

LITERATURE REVIEW

The Regulation of Body Temperature in Homeothermic Animals

The relative constancy of body temperature in a homeothermic animal depends on the proper balance of the heat lost and the heat produced by the organism. The ability of birds and mammals to integrate these two factors allows them to be more independent of their external environment than are poikilothermic animals.

Barbour (1921) recognized that water occupies a unique position in the regulation of body temperature. Water, as a mobile constituent of living organisms, ranks above most liquids for use in temperature equalization and regulation because of three qualities: high specific heat, high heat of vaporization, and high thermal conductivity. This investigator indicates that vasomotor shifts, physical regulatory mechanisms, result in a distribution of liquid between the blood and intercellular fluid that may terminate in a dissipation or conservation of heat. A large variation in environmental temperature requires an alteration in heat production. That water shifting mechanisms are important in maintaining or promoting a constant body temperature has been shown by Bass and Henschel (1956) who observed that hemodilution was one of the earliest responses of the body fluids to heat stress.

Barbour and Prince (1914) demonstrated the existence of a thermoregulatory center in the region of the corpus striatum of the rabbit. They found that when this region was heated by perfusing the area with warm water, there was a decrease in metabolic processes (decrease in CO_2

output and O_2 uptake) as well as a decrease in body temperature; cooling this region produced opposite effects. They felt, therefore, that stimulation of this region by changes in the temperature of blood in either direction would favor adjustments in heat dissipation and heat production. The existence of a thermoregulatory center for maintaining a constant body temperature was further strengthened by Martin (1930) who observed that the removal of the cerebral hemispheres and corpora striata in a homeothermic animal would not destroy that animal's ability to regulate body temperature. In that same species of animal, a section made between the optic chiasma and corpora quadragemina rendered that animal poikilothermic.

Evidence that the thermoregulatory centers for maintaining a constant body temperature are located in the diencephalon was given by Keller and Hare (1931a) who made transections in the midbrains of cats and noted that sweating and panting were not obtained or rarely observed, although the rectal temperatures rose to 43-44° C. In the same year, work by Keller and Hare (1931b) demonstrated that the chief central mechanism controlling body temperature was located in the hypothalamus. This was demonstrated by a section made in the hypothalamus that would leave it unattached to the remainder of the diencephalon; when this section was complete, the ability of the animal to maintain a constant body temperature was lost.

The question of which part of the hypothalamus serves as a "thermostat" in regulating body temperature was partly answered by the work of Teague and Ranson (1936). These investigators using normal cats and cats with hypothalamic lesions (lesions included optic chiasma, supraoptic portion of the hypothalamus, dorsomedial and ventromedial hypothalamic nuclei)

were placed in an environment with a temperature range of 102° to 104° F. Normal cats showed a rise in rectal temperature, increase in respiration and later panting, cutaneous vasodilatation, and sweating on the feet. Cats with hypothalamic lesions began to pant at a higher rectal temperature than the unoperated cats and some of these operated animals did not exhibit an increase in respiration or sweating on the feet. Additional evidence for the above results was obtained by Guerra and Brobeck (1944) who made lesions in the anterior and anterolateral hypothalamus of monkeys. When these primates were placed in a hot room (40° C.), the operated monkeys showed a small increase in respiration but no increase in sweat excretion; however, unoperated monkeys when placed in a warm environment exhibited an increase in respiration and sweat excretion. Reichlin (1960) localized a temperature-regulating center near the pre-optic area which when destroyed, produced fever in the rat. The centers localized by the above investigators appear to be centers in the hypothalamus that regulate heat loss rather than heat-conservation centers.

Pickering (1958) considered the hypothalamus to be the central coordinating mechanism for body temperature or as he described it "the central receptor." The hypothalamus consists of possibly two thermotaxic centers, a heat-dissipating center, which has been demonstrated by many investigators, and a heat-conserving center which has not been as well verified. This investigator stated that there are three effector mechanisms in man to regulate body temperature. These mechanisms are shivering, cutaneous vasoactivity, and sweating. In other mammals, polypnea and piloerection are additional effector mechanisms to regulate body temperature. These effector mechanisms require the integrity of the central nervous system up to and including much of the hypothalamus. They are activated chiefly

by "the central receptor," the hypothalamus, and to a lesser extent by the reflex stimulation of the cutaneous receptors. The central receptor in the hypothalamus may be activated by an afferent volley from the cutaneous receptors in the skin or by changes of about $\pm$ .2° C. in the temperature of the blood bathing the hypothalamus. Pickering (1958) provided some evidence for the latter statement by an experiment in which he immersed a limb in a water bath at 37° C. and arrested the circulation of that limb; no change in blood flow was noted in the opposite limb. When circulation was restored, vasodilatation occurred in the opposite limb. A cold bath, however, produced vasoconstriction in the opposite limb regardless of circulatory arrest to the cold exposed limb. This vasoconstriction occurred reflexly from the cutaneous receptors of the skin. Although this is a stimulus that man does not frequently encounter, the changes in vasomotor tone observed by Pickering (1958) may be due to any strong sensory stimulus. That thermoregulatory centers in the hypothalamus are partly activated by receptors in the skin and that these receptors differ from those serving sensation was shown by Cooper and Kerslake (1953). These investigators observed that radiant heating of the limbs of men produced vasodilatation that was independent of the warmed blood. They are of the opinion that vasodilatation of limbs occurred due to a response mediated by afferent nervous impulses from a heated area. Cooper and Kerslake (1953) examined patients that had undergone bilateral lumbar sympathectomy and observed an abolition or reduction of the normal nervous reflex vasodilator response in limbs other than the limb being heated.

The concept of the mechanism regulating temperature in man is summed up by Pickering as follows: "Small deviations in central body temperature are opposed by corresponding deviations in cutaneous vasomotor tone.

Larger deviations upward and downward are opposed respectively by sweating and by shivering. The effector mechanisms are activated chiefly and persistently by central receptors, less importantly and intermittently by cutaneous receptors. Coordination and integration takes place within the central nervous system, probably in the hypothalamus or below."

Because birds are homeothermic, an increase in body temperature due to a high ambient temperature is opposed probably by vasodilatation and hemodilution. Panting, a type of breathing where the rate is rapid and the depth of breathing is shallow, serves to oppose a rise in body temperature in birds. Randall (1943) found that panting in birds was due to an increase in body temperature. He showed that warmed blood probably acted on the hypothalamus, which initiated impulses to inaugurate panting.

Although a large amount of research has been performed concerning temperature regulation in homeothermic animals, much remains to be done regarding the control of body temperature by the thermoregulatory centers in the hypothalamus, peripheral regulation of temperature, and the function of the thyroid gland in regulating body temperature.

The Effects of High Environmental Temperature on Thyroid Activity in the Bird

Birds exposed to an environmental temperature above 80° F. and especially above 90° F. exhibit a rise in body temperature (Wilson, 1948). This rise in environmental temperature results in a decrease of feed consumption and a decrease in body weight (Hutson, Joiner and Carmon, 1957). In addition to the adverse effects observed in body weight due to high temperatures, a decrease in thyroid weight and a decrease in thyroxine secretion rate in birds have also been observed. Hoffman and Shaffner (1950) observed that the thyroid weights of developing chick embryos were

modified by varying the incubator temperature. They found that the thyroids of chicks from eggs incubated at 96.8° F. were larger when compared to thyroid weights of chicks that were incubated at 102.2° F. and that these smaller thyroids showed histological evidence of reduced activity. Hutson, Joiner, and Carmon (1957) observed smaller thyroid glands from groups of 3 different breeds of domestic fowl grown to ten weeks of age at air temperatures of 90° F. Birds grown in a variable normal environment had significantly larger body and thyroid weights. Conner, Menje and Oto (1958) found smaller body and thyroid weights at environmental temperatures of 95° F. and 100° F., and significant adrenal enlargement at 100° F. in a "small thyroid" bred line of New Hampshire chicks.

The effects of high environmental temperature on thyroid secretion rate in young birds has been investigated recently by Heninger, Newcomer, and Thayer (1960). They subjected lots of chicks to environmental temperatures of 75° F., 95° F., and 105° F. for a two week growing period and measured the thyroid secretion rate using the method of Dempsey and Astwood (1943). The thyroid secretion rate was decreased as the environmental temperature increased in these chicks.

The above investigations produced evidence that high environmental temperatures act in some manner on the thyroid to decrease its size and activity. A partial explanation for this response may be the TSH-thyroxine "feed-back" mechanism of control over the thyroid (Brown-Grant, 1957). An increase or a decrease in circulating thyroxine acts via the anterior pituitary, which responds with a decrease or an increase in thyrotropin (TSH) output respectively.

A decrease in the environmental temperature brings about an increase in thyroid function by an augmentation in the utilization of thyroxine by

the peripheral tissues (Rand, Riggs, and Talbot, 1952; Leblond and Eartly, 1952). This results in a decrease of circulating thyroxine and subsequent stimulation of the anterior pituitary to increase TSH output. The reverse would probably be true for a rise in environmental temperature resulting in an inhibition of the anterior pituitary to decrease TSH output although there are no experimental data to support this statement.

Additional factors that possibly affect a control of thyroid secretion at various temperatures include a direct effect of environmental temperature on the binding of TSH to the thyroid gland. Heninger, Newcomer, and Thayer (1960) stated that when the environmental temperature increased to the point where it produced a rise in the body temperature of the animal, there was reduced affinity of TSH for its thyroid receptor site and a resultant decreased thyroid hormone secretion.

The Effects of Sodium Salicylate on Thyroid Activity

In febrile animals, sodium salicylate may be used as an antipyretic in reducing body temperature to near normal levels. In afebrile animals, sodium salicylate appears to have a metabolic stimulating action. This was shown by Denis and Means (1916) who gave euthyroid men as much as 6.6 grams of sodium salicylate per day and noted an increase in the excretion of nitrogen, phosphorus, and uric acid with one male exhibiting an increase in metabolic rate. Cochran (1953) observed an increase in consumption of oxygen and a slight increase in the excretion of carbon dioxide in human subjects given both oral and intravenous injections of sodium salicylate. That salicylates affect the metabolic rate has been verified by Sproull (1954), Reid (1957), and Smith (1959). By treating liver slices in vitro with a therapeutic dose of sodium salicylate and measuring oxygen consumption

in a Warburg respirometer, Sproull (1954) observed that sodium salicylate caused an increase in oxygen consumption. He concluded that sodium salicylate produces its metabolic stimulating effects at the cellular level.

In contrast to the previous work, recent investigation revealed no metabolic increase in rats given therapeutic doses of sodium salicylate. Gemmill, King, and Browning (1960) gave rats exogenous 3,5,3′-triiodothyronine and observed an increase in metabolism, pulse rate and rectal temperature in these animals. These changes were not observed in a second group of rats receiving a specific dose of sodium salicylate. When these two compounds were injected together into a group of rats there resulted a rise in basal metabolism comparable to the effects of injecting triiodothyronine alone. Furthermore, hypermetabolic rats were produced with exogenous triiodothyronine and then given sodium salicylate; sodium salicylate produced a fall in pulse rate and rectal temperature to normal limits, but did not affect the high basal metabolic rate.

It appears that there is some question as to the metabolic stimulating action of sodium salicylate in euthyroid animals. Alexander and Johnson (1956) noticed that sodium salicylate had a thyroxine-like effect in hypothyroid animals. These investigators gave hypothyroid patients eight grams of aspirin daily. An increase in oxygen consumption, decrease in serum cholesterol, and a decrease in hemodilution were noted in these patients. Improvement of cerebral retardation was not observed in these aspirin-treated patients, while thyroid extracts did bring about an improvement in activation of cerebral responses. Since sodium salicylate has been shown by most investigators to act as a metabolic stimulant in both normal and hypothyroid humans, what effect does therapeutic doses of sodium salicylate have on thyroid function?

This question was investigated recently by Austin, et al., (1958) who found that sodium salicylate depressed thyroid function in man. A total of six to eight grams of sodium salicylate was given orally once a day for 8 to 10 weeks to male euthyroid patients. Uptake of radioiodide by the thyroid and thyroid clearance of radioiodide was reduced in each patient during chronic salicylate administration. The salicylate level in the serum of such patients was not high enough to interfere with the incorporation and organification of I^{131} by rat thyroid slices, hence it was concluded that acute salicylate administration did not reduce the T/S ratio in the rat. The conclusion drawn by Austin, et al., (1958) was that the salicylate administration depressed thyroid function through the pituitary or higher centers by a reduction in thyrotropin release.

Wolff and Austin (1958) investigated the effect of salicylates on some thyrotropin-dependent functions of the thyroid gland in humans and rats. Salicylates appeared to inhibit thyrotropin release from the anterior pituitary since exogenous thyrotropin given to salicylate-treated patients caused them to respond with an increase in I^{131} uptake, an elevation of the serum protein bound iodine, and an accelerated rate of release of I^{131} from the thyroid. Salicylate treatment led to a partial inhibition of goitrogenesis in propylthiouracil treated rats. Radioactive salicylic acid was used to investigate localization of the drug in rat tissues, particularly the anterior pituitary, hypothalamus and higher nerve centers. A relatively high concentration of radioactivity was noted in the anterior pituitary when compared to the brain, but the visceral organs showed a similar degree of concentration when compared to the anterior pituitary.

The administration of sodium salicylate to mammals accelerated the disappearance of protein bound iodine (PBI) from the circulation. Austin,

et al., (1958) and Wolff and Austin (1958) believed the fall in the level of PBI, due to chronic salicylate administration, involves two principal components: the more important one which appears to be essentially a depression of thyroxine release due to a decrease in thyrotropic hormone production; and a second component due to an increased rate of peripheral utilization of thyroxine.

Both dinitrophenol (DNP) and sodium salicylate have a metabolic stimulating effect and depress PBI and thyroid function. An investigation made by Goldberg, Wolff and Greep (1955) as to the antithyroid action of DNP revealed that the fall of PBI following the administration of DNP may be due to the combined effect of these three mechanisms: (a) impairment of thyroid hormone synthesis, (b) depression of the rate of release of thyroid hormone into the circulation by the thyroid gland and (c) acceleration of the rate of disappearance of circulating thyroid hormone from the plasma. A later investigation made by Goldberg, Wolff, and Greep (1957) supported the mechanism that DNP impairs thyroid hormone synthesis by acting on the anterior pituitary to prevent the release of TSH. Both DNP and sodium salicylate appear to depress PBI in the intact animal by blocking or preventing the release of TSH from the anterior pituitary gland.

Good, Hetzel and Opit (1960) using thyroxine-maintained thyroidectomized rats observed that sodium salicylate would significantly depress the PBI level in these rats. Since the PBI level depended entirely on an exogenous supply of thyroxine, its fall should be due to increased peripheral utilization of thyroxine. These investigators believe that the increased peripheral utilization of thyroxine may be due to the metabolic degradation of thyroxine since salicylate is a metabolic stimulant, or it may be due to the simple displacement of thyroxine from PBI by sodium salicylate.

Christensen (1960) observed that sodium salicylate in vitro displaced thyroxine from the receptor site of the thyroxine binding plasma protein. He postulated that this displacement of thyroxine from the plasma protein resulted in an increase of free thyroxine in the blood plasma which acted on the anterior pituitary to inhibit the release of TSH.

The mechanism whereby PBI is depressed by sodium salicylate in the intact mammal is obviously a complex one and requires further investigation. The effect of sodium salicylate in birds has not been investigated and therefore, the effects of sodium salicylate on PBI levels in birds cannot be given.

The results of an investigation made by Alexander and Johnson (1958) did not agree with the theory that salicylates in a normal animal is an antithyroid agent. They observed that in euthyroid humans, chronic aspirin administration did not influence uptake of I^{131} by the thyroid or excretion of I^{131} in the urine.

The Antipyretic Action of Sodium Salicylate and Acetylsalicylic Acid

Sodium salicylate, acetylsalicylic acid, salicylamide, aminopyrine, and acetanilid are a few of the drugs used as antipyretics (Goodman and Gilman, 1955). When compared on a weight basis, sodium salicylate and acetylsalicylic acid are not as effective as a fever reducing substance as aminopyrine and acetanilid; however, the mechanism whereby these compounds reduce fever is the same for all of these drugs.

Some of the earlier work on the antipyretic mechanism of the salicylates was carried out by Barbour and Devenis (1919). They gave one gram of acetylsalicylic acid to normal adult patients and to febrile

patients who were directed to remain at rest for the remainder of the experiment. Heat production in these patients was estimated by determination of carbon dioxide excretion; heat elimination was estimated from the changes in rectal temperature. They noted that this dose of aspirin increased the excretion of carbon dioxide in normal patients which indicated an increase in heat production; however, no significant changes in body temperature was noted in the normal patients. Febrile patients after receiving one gram of acetylsalicylic acid showed a decrease of the high body temperature toward the normal limits and no significant increase in carbon dioxide excretion. Barbour and Herrmann (1921) injected sodium salicylate subcutaneously into febrile dogs and observed a decrease in rectal temperature that approached normal value. They also noted that there was an increase in blood glucose concentration and possibly creatine or creatinine, and a decrease in hemoglobin content in the blood. They felt that sodium salicylate acted to reduce febrile conditions by increasing blood volume. Hemodilution presents a greater volume of blood for the removal of heat at the cellular tissues and radiation of a larger amount of this heat to the external environment at the peripheral tissues. Guerra and Barbour (1943) gave febrile monkeys an oral therapeutic dose of aspirin. They observed an increase in sweat excretion, compared to normal controls, in monkeys made febrile by an injected pyrogenic agent and in monkeys exposed to a high environmental temperature; however, only those monkeys made febrile by pyrogenic agents exhibited a decline in body temperature. The decline in body temperature was about .15° C. each ten minutes after administration of the aspirin until the body temperature was only .4° C. higher than normal body temperature. On the basis of this work, it appears that aspirin is effective as an antipyretic in monkeys made febrile by a pyrogenic agent,

but not in febrile monkeys due to high environmental temperature. Buller, Miyo, and Carr (1957) injected subcutaneously a peptone solution into normal rats which caused fever within 4 hours in these rats. Acetylsalicylic acid was given to different groups of febrile rats in doses of 100, 200, 250 or 300 mg. acetylsalicylic acid per kg. body weight. The three higher doses of acetylsalicylic acid reduced the peptone-induced fever to approximately the normal body temperature of the control rats. No explanation as to the antipyretic action of acetylsalicylic acid was given by these investigators, only the doses that were effective as an antipyretic were given in the work.

The antipyretic action of acetylsalicylic acid and sodium salicylate is thought to be due to an increase in heat loss from the organism rather than a decrease in heat production (Barbour, 1921). This increase in heat loss is thought to be due to (a) a greater dissipation of body heat through cutaneous vasodilatation (b) an increase of blood sugar resulting in hemodilution which may account for the decrease in hyperthermia (Barbour and Herrmann, 1921) (c) a tendency of antipyretics to reduce urine flow and contribute toward hemodilution (Barbour and Herrmann, 1921) and (d) an increase in the rate of sweat secretion in febrile primates given sodium salicylate (Guerra and Barbour, 1943). Antipyretics do not appear to reduce the body temperature of normal animals nor do they appear to reduce the hyperthermic condition of animals exposed to a high environmental temperature.

MATERIALS AND METHODS

The effects of feeding sodium salicylate to birds exposed to high environmental temperatures were observed in two groups of White Leghorn cockerels during a growing period of approximately 20 days. At the beginning of the experiment, the two groups of one-day old chicks were individually weighed, tagged for identification, and randomly assigned to a designated lot.

A converted Buckeye, forced draft, insulated incubator was used to maintain heat-exposed lots within each group at the desired environmental temperature of 105° F. Individual lots were placed in cages which measured 38 x 28 x 9 inches and were constructed of wire mesh to enable adequate circulation of air and permit equality of temperature. The cages were arranged in the incubator so that all lots received approximately the same amount of light and heat. Circulation of air was accomplished by means of an 18 inch fan situated near the center of the incubator. Two 100 watt electric light bulbs situated on two opposite walls were kept burning 24 hours daily during the growing period. Relative humidity was not controlled.

All the chicks that were to be heat-stressed were placed in the Buckeye incubator at the beginning of each experiment. The initial temperature of the incubator was 100° F. During the four day "adjustment" period for the chicks, the temperature inside the incubator was raised approximately 1° F. daily until 105° F. $\pm$ 1° F. was reached. For the duration of the experiment, the high ambient temperature was kept at 105° F. $\pm$ 1° F. The normal control lots were exposed to normal fluctuation in temperature which occurred in a

well-ventilated brick building during periods when the outside temperature varied no more than between 60° F. to 90° F.

Twice a week at the same relative time of day, the body temperatures were taken with a glass rectal thermometer (maximum reading of 110° F.) and recorded. Since the body temperature of chicks is stable and is about the same as that of a mature chicken at 7 to 10 days of age (Lamoreux and Hutt, 1939), the body temperatures of these chicks were not taken until they were one week old.

Broiler ration EX-54 (Table I), as recommended by the Poultry Department of Oklahoma State University, was fed throughout the experimental period.

TABLE I

OKLAHOMA STATE UNIVERSITY BROILER RATION, EX-54

	Percent
Marco B-75 (fat)	7
Ground Yellow Corn	49
Pulverized Oats	3
Alfalfa meal (17%)	2
Fish Meal (60%)	12
Soybean Meal (44%)	14.5
Meat and Bone Scraps (50%)	2
Dried Brewer's Yeast	2
Dried Whey	2
Dried Fish Solubles	2
Dried Butyl Solubles	2
Di-calcium Phosphate (20% Phosphorus)	1.5
Trace Mineral Mix	0.05
Salt	0.5
**VC-55 (Vitamin Mix Concentrate)	0.5
d,l Methionine	0.05

**VC-55 (per pound of ration)

Vitamin A	4,000 USP
Vitamin D_3	2,000 USP
Riboflavin	3 mg.
Pantothenic Acid	4 mg.
Niacin	20 mg.
Choline	300 mg.
Vitamin B_{12}	3 ugm.
Procaine Penicillin	2 mg.
Menadione	3 mg.

Water and feed were available at all times and feed consumption per lot was recorded daily. In calculating feed consumption, no correction was made for the slight unavoidable wastage of feed by the chicks. Whenever a chick died within any of the lots, the total remaining feed in that lot was weighed and a notation made of the amount of feed consumed up to that point by that particular number of chicks within that lot. The feed consumption thereafter was based on one less than the original number of birds. No correction for feed consumed was made when deaths occurred during the first two days of the experiment since during this time the amount eaten by each bird was relatively small.

The purpose of the study made on the first group was an attempt to select the optimal percent of sodium salicylate in the ration that would perhaps reduce the hyperthermic condition in the heat-stressed birds to near normal levels. Three different doses of sodium salicylate were given to three of the four heat-exposed lots in Group I. (Table II).

TABLE II

TREATMENTS USED IN GROUP I

Lot No.	Concentration of Sodium Salicylate in Ration		Environmental Temperature
I	(None)	Heat-Stressed Control	105° F.
II	.1%		105° F.
III	.25%		105° F.
IV	.5%		105° F.
V	(None)	Normal Control	65° - 90° F.*

*Estimated from weather reports.

At the termination of the experimental work on Group I, a comparison was made of the three lots receiving various doses of sodium salicylate. The amount of sodium salicylate in the diet of the lot producing the greatest antipyretic action and change in thyroid activity was used for the experimental work in Group II.

The purpose of the second group was to repeat the observations made in the first group by giving the dose of sodium salicylate that gave the most favorable results in Group I. Also a lot was introduced into this group which was non-heat-stressed and received sodium salicylate in its diet. The purpose of including this lot was to obtain information concerning the effect, if any, of sodium salicylate on thyroid function in birds not subjected to heat stress. The birds of this group were divided into four lots of fifteen birds each and treated as seen in Table III.

TABLE III

TREATMENTS USED IN GROUP II

Lot No.	Concentration of Sodium Salicylate in Ration	Environmental Temperature
I	(None) Heat-Stressed Control	105° F.
II	.5%	65° - 90° F.*
III	.5%	105° F.
IV	(None) Normal Control	65° - 90° F.*

*Estimated from weather reports.

Thyroid activity was estimated in both Group I and Group II as the percent uptake of radioiodide by the thyroids. This assay was made at the end of the growing period from five birds randomly drawn from each lot in Group I and Group II (Lot II birds were not used any further in the

experiment because this lot showed no significant decrease in the elevated body temperature when compared to Lot I).

These birds were injected intraperitoneally with 0.2 ml. water containing 5 microcuries of NaI^{131}. One hour later the birds were killed by decapitation and the thyroid glands were removed and weighed on a Roller-Smith torsion spring balance. Using a well-type scintillation counter, relative counting was performed on the thyroids from each bird and the data were expressed as the uptake of radioiodide by the thyroids as a percentage of the amount of radioiodide injected.

The thyroid/plasma (T/P) ratio of iodide, an additional measurement of thyroid function, was performed on the birds in Group II. The purpose of adding this additional criterion was to investigate the possibility of sodium salicylate affecting the ability of the thyroid gland to concentrate circulating iodide. Thiourea, an agent that inhibits the organification of iodide in the thyroid, was injected into 5 birds from each lot one hour before injection of 5 microcuries of NaI^{131}. Using the method of Vanderlaan and Vanderlaan (1947), the thyroid/plasma radioiodide concentrating ratio was then calculated for each of the five birds from the four lots.

In order to observe if the effects of high environmental temperature and sodium salicylate had indirectly decreased thyrotropin release by stimulating the release of ACTH (Brown-Grant, 1956; Hetzel and Hine, 1951), the weights of the adrenal glands and the bursae of Fabricius were used as criteria for stress in these chicks. That the bursa of Fabricius may be used as an indication of chronic stress in these immature chicks has been shown by Newcomer and Connally (1960). At the conclusion of the growing period of each group, eight to ten birds from each lot were selected at random, sacrified by decapitation, and the adrenal glands and the bursae were

disected clean, weighed on a Roller-Smith torsion spring balance and these weights recorded.

At the end of the growing period prior to estimating thyroid activity, all birds in each lot from each group were weighed individually and these body weights were also recorded.

RESULTS

Group I

In order to determine a level of sodium salicylate that would be effective in decreasing body temperature of birds subjected to a high ambient temperature of 105° F. three lots of chicks were fed graded doses of sodium salicylate: .1%, .25%, and .5% (Table II). These lots were compared with a heat-stressed control lot (Lot I) and a normal control lot (Lot V). Comparison between these lots as to body temperature, thyroid activity, adrenal gland weight, bursae weight and body weight were made (Table IV).

An analysis of variance was calculated on the mean body temperature of the chicks from each of the five lots in order to see if the treatment effects had significantly changed the means and if so, by utilizing Tukey's Test to find where these mean differences might lie among the five lots. The latter method of analysis revealed at the .05 level of significance that Lots I and II had greater mean body temperatures than the other 3 lots. Lots III and IV had greater mean body temperatures ($P < .05$) than Lot V. No significant mean difference in body temperatures was noted between Lots I and II or between Lots III and IV. Because .5% sodium salicylate in the diet of Lot II was apparently ineffective as an antipyretic, this lot was discarded at this point and thyroid weight and activity studies were not made.

All of the lots subjected to the high environmental temperature showed a decrease in thyroid weight (mg. percent) and thyroid activity (uptake of

radioiodide). A statistical analysis of the mean differences between lots revealed significance at the .05 level, with Lot V having a greater mean thyroid weight and also a greater mean uptake of radioiodide than Lots I and III. Lot V did not have a significantly larger mean thyroid weight when compared with Lot IV, but in comparing the mean differences of I^{131} uptake, Lot V had a significantly ($P < .05$) larger mean value than Lot IV. Lot IV had a larger mean value of thyroid weight than Lots I and III, but the mean difference between these lots was not significant; however, Lot IV at .05 level had a significantly larger mean uptake of radioiodide than Lots I and III.

The effects of 105° F. environmental temperature on body weights of Lot I and Lot V are found in Table IV. A statistical analysis of the mean differences between the two lots revealed significance at the .05 level, with Lot V having a significantly ($P < .05$) larger mean body weight than Lot I, Lot III, or Lot IV. By comparing Lots III and IV to Lot I, it appeared that .25% sodium salicylate in the diet of Lot III did not affect the mean body weight because there is no statistical difference between this lot and the heat-stressed control lot. Lot IV had a mean body weight that was significantly ($P < .05$) less than the mean body weight of all the remaining lots. Feed efficiency was essentially the same for all four lots with the exception of Lot IV, which had a feed efficiency of .39 units higher than the heat-stressed control lot (Table VI).

An analysis of variance was performed on the adrenal weights (mg. percent) between each lot. The analysis revealed no statistical significance ($P < .05$) between the means of all lots. Lot V had a larger mean bursa of Fabricius (mg. percent) ($P < .05$) than Lots I, III, and IV. There was no significant mean difference in bursae weights between Lots I, III, and IV.

TABLE IV

EFFECTS OF SODIUM SALICYLATE IN HEAT-STRESSED CHICKS ON BODY WEIGHT, BODY TEMPERATURE, THYROID ACTIVITY, ADRENAL GLAND WEIGHT AND BURSA OF FABRICIUS WEIGHT IN GROUP I

Lots	Treatment	Body Weight (gm.)	Body Temperature Degrees F.	Thyroid Weight (mg.%)	% Uptake Radio-iodide	Adrenal Weight (mg.%)	Bursa Weight (mg.%)
I	Heat-Stressed Control	161.58 ± 19.22	107.77 (1) ± .452	2.98 ± .747	1.55 ± .578	14.68 ± 2.84	202.01 ± 84.50
II	Heat-Stressed .1% Na Salicylate	145.49 ± 19.35	107.80 (1) ± .580				
III	Heat-Stressed .25% Na Salicylate	169.79 (4) ± 19.52	107.24 (2) ± .428	2.94 ± .567	1.97 ± .607	12.44 ± 1.40	264.32 ± 75.67
IV	Heat-Stressed .5% Na Salicylate	133.62 ± 24.02	107.07 (2) ± .368	3.69 ± .605	3.47 (3) ± 368	13.10 ± 2.62	242.81 ± 79.67
V	Normal Control	274.91 (1) ± 24.62	106.67 ± .295	5.06 (3) ± 1.17	5.14 (1) ± 1.170	11.79 ± 2.12	540.99 (1) ± 124.97

1. Significantly greater ($P < .05$) than all lots.
2. Significantly greater ($P < .05$) than Normal Control lot.
3. Significantly greater ($P < .05$) than Lots I and III.
4. Significantly greater ($P < .05$) than Lots II and IV.

Group II

In order to duplicate the findings of Group I at the effective antipyretic level of sodium salicylate, and to determine the effects of this level of sodium salicylate on birds at "normal" environmental temperatures, the experimental design followed in Group I was repeated (Table V). An additional parameter, the thyroid/plasma ratio of iodide which is a measurement of thyroid function, was added.

Group II consisted of Lot I which was the heat-stressed control lot, Lot III which was exposed to high environmental temperatures and received .5% sodium salicylate, and Lots II and IV which were exposed to normal environmental temperatures with Lot II receiving .5% sodium salicylate in its ration. An analysis of variance on the mean body temperatures between lots revealed significance ($P < .05$) among the means. Tukey's test was used to locate these significant differences between the mean body temperatures of each lot. Lot I had a significantly higher mean body temperature ($P < .05$) than the remaining three lots. Lot III had a higher mean body temperature ($P < .05$) than Lots II and IV. No significant mean differences in body temperatures were noted between Lots II and IV.

A statistical analysis of the mean thyroid weight and thyroid activity between the lots in Group II disclosed significance among the means ($P < .05$). Using Tukey's test to locate these differences, it was found that Lot II had a significantly ($P < .05$) greater mean thyroid weight (mg. percent) and a larger mean value for uptake of radioiodide than Lots I, III, and IV. The normal control lot, Lot IV, had a significantly ($P < .05$) greater mean thyroid weight than Lots I and III, and a significantly larger mean value for the uptake of radioiodide than the heat-stressed control lot, Lot I. Lot II

had a significantly ($P<.05$) larger mean T/P ratio than Lots I and III. No significant difference for the T/P ratio was found between Lots II and IV, Lots I and IV, or Lots II and IV. No significant difference between Lots III and IV for the uptake of radioiodide was found for Group II.

The mean body weight of each lot in Group II was similar to the results obtained in Group I. The normal control lot, Lot IV, had a significantly ($P<.05$) larger mean body weight than all the remaining lots in Group II. The non-heat-stressed lot, which received .5% sodium salicylate in its diet had a significantly ($P<.05$) larger mean body weight than the two heat-stressed lots. The heat-stressed lot receiving .5% sodium salicylate again had a mean body weight that was less than the heat-stressed normal control lot, but the difference in mean body weights between the two lots was not significant. Feed efficiency again was approximately the same for all lots (Table VI).

The group of young chicks did not exhibit a significant ($P<.05$) difference between the mean adrenal weights in the lots of Group II. As in Group I, the normal control lot, Lot IV, had the smallest mean adrenal weight (mg. percent) and the heat-stressed control lot, Lot I, had the largest mean adrenal weight. Lot I had a large standard deviation $\pm$ 6.37 about the mean adrenal weights which may be due to experimental error. Lots II and IV had a significantly ($P<.05$) larger mean bursa of Fabricius weight than did Lots I and III. No significant difference between the mean bursae weights was noted between Lots II and IV and Lots I and III.

TABLE V

EFFECTS OF SODIUM SALICYLATE IN HEAT-STRESSED CHICKS ON BODY WEIGHT, BODY TEMPERATURE, THYROID ACTIVITY, ADRENAL GLAND WEIGHT AND BURSA OF FABRICIUS WEIGHT IN GROUP II

Lots	Treatment	Body Weight (gm.)	Body Temperature Degrees F.	Thyroid Weight (mg.%)	% Uptake Radio-iodide	T/P Ratio	Adrenal Weight (mg.%)	Bursa Weight (mg.%)
I	Heat-Stressed Control	161.05 ± 14.43	108.12 (1) ± .291	2.38 ± .577	1.27 ± .459	43.33 ± 20.00	14.79 ± 6.37	324.19 ± 102.44
II	Non-Heat-Stressed .5% Na Salicylate	224.14 (3) ± 17.56	107.26 ± .345	4.65 (1) ± .534	3.43 (1) ± .370	113.67 (3) ± 47.59	13.20 ± 2.61	582.02 (3) ± 205.80
III	Heat-Stressed .5% Na Salicylate	148.40 ± 18.81	107.71 (2) ± .358	2.45 ± .641	1.93 ± .501	50.38 ± 24.31	14.31 ± 3.08	266.30 ± 56.50
IV	Normal Control	246.59 (1) ± 14.80	107.40 ± .239	3.88 (3) ± .608	2.22 (4) ± .436	84.95 ± 30.08	12.57 ± 1.43	560.32 (3) ± 147.85

1. Significantly greater ($P < .05$) than all lots.
2. Significantly greater ($P < .05$) than Lots II and IV.
3. Significantly greater ($P < .05$) than Lots I and III.
4. Significantly greater ($P < .05$) than Lot I.

TABLE VI

SUMMARY OF WEIGHT GAINS AND FEED CONSUMPTION
OF THE TREATED AND NON-TREATED LOTS

Group I

Lots	Treatment	Average Weight Gain in 21 Days (gms./Chick)	Average Feed Cons. in 21 Days (gms./Chick)	Feed Efficiency Feed Cons./ Wt. Gain
I	Heat-Stressed Control	122.33	254.52	2.08
II	Heat-Stressed .1% Na Salicylate	105.06	229.95	2.18
III	Heat-Stressed .25% Na Salicylate	131.15	270.92	2.06
IV	Heat-Stressed .5% Na Salicylate	95.83	247.30	2.58
V	Normal Control	234.65	454.15	1.93

Group II*

I	Heat-Stressed Control	114.00	237.40	2.08
II	Non-Heat-Stressed .5% Na Salicylate	176.30	324.61	1.84
III	Heat-Stressed .5% Na Salicylate	100.48	226.45	2.25
IV	Normal Control	200.89	398.12	1.98

*Length of Growing Period-20 days.

DISCUSSION

The Effects of Sodium Salicylate as an Antipyretic on Heat-Stressed Birds

Homeothermic animals, mammals and birds, are those animals which maintain a reasonably constant body temperature that is relatively independent of changes in the environmental temperature. To maintain an almost constant body temperature when the environmental temperature is changing requires a delicate balance between the heat produced by an animal and the heat lost by that animal. If, for example, the amount of heat produced increases and the dissipation of heat is not proportionally increased, a rise of body temperature will follow. Conversely, when the environmental temperature is increased to approximately the normal body temperature of an animal, the elimination of heat from an animal's body must be increased and heat production decreased in order for the body temperature to remain constant. The radiation of heat from an environment of high temperature to the cutaneous tissues of the chick may bring about a response which results in an increase of heat lost by the chick. This response, resulting in an increase of heat dissipation, may be initiated due to either or both the warming of blood in the cutaneous vessels or to a stimulation of the thermal receptors in the skin. Warmed blood or neural impulses received from the thermal receptors may act on the heat loss center of the hypothalamus and stimulate the heat loss center to reduce body temperature. The environmental temperature may continue to increase until the homeostatic mechanisms concerned with

temperature regulation become ineffective and the body temperature will rise. This statement is supported by the observations made in this work on the heat-stressed lots of Group I (Table IV) and Group II (Table V). These lots were exposed to an environmental temperature of 105° F. ± 1° F. which is near the normal body temperature of adult birds (106° F.) (Lamoreux, 1939). All of the heat-stressed lots exhibited, at this environmental temperature, a statistically significant elevation of the mean body temperature when compared to the normal control lot.

Heat is regularly lost from the mammal's body in the following ways (Fulton, 1955):

a. radiation, conduction and convection

b. vaporization of water from the skin and respiratory passage

c. excretion of feces and urine

The heat lost by the excretion of feces and urine amounts to very little of the total heat lost and may be disregarded. Since the temperature gradient between the atmosphere and the tissues of the birds in this experiment was very slight, presumably very little heat was lost by radiation, conduction, or convection. Birds do not possess sweat glands hence much of the body heat under these experimental conditions must be dissipated by vaporization of water from the respiratory passages. Symptoms of panting begin to appear in birds when the body temperature increases .1 to .4° F. due to fever or an increase in environmental temperature (Randall and Hiestand, 1939). These investigators stated that panting begins at a certain critical internal temperature which varies with individual birds and that once panting is inaugurated, acceleration is roughly proportional to body temperature. In this experiment, all birds that were subjected to high environmental temperatures panted, but no observations were made as to the rate of panting in these chicks.

Lots III and IV in Group I (Table IV) which received .25% and .5% sodium salicylate in their diet, had a significant decrease in their mean body temperature when compared to the heat-stressed control lot. Lot III in Group II (Table V) which was exposed to 105° F. and received .5% sodium salicylate in its diet, had a significantly lower body temperature than the heat-stressed control lot. Lot II in Group II (Table V) which received .5% sodium salicylate and was exposed to normal environmental temperatures, did not have a significantly lower body temperature than the normal control lot. This is in good agreement with Barbour and Devenis (1919) and Guerra and Barbour (1943), who found that acetylsalicylic acid depressed the elevated body temperature of febrile primates to near normal or normal levels; however, this antipyretic would not decrease the normal body temperature to subnormal levels.

The specific means by which sodium salicylate acts as an antipyretic in hyperthermic birds is unknown. One of the earliest hypothesis for its effect in mammals was put forth by Barbour and Herrmann (1921) who observed that in salicylate-treated dogs there was a dilution of blood which favors a reduction in body temperature by affording a greater volume for radiation of heat from the body's periphery. In dogs, as in birds, very little heat is lost by sweating; instead, excess heat is lost by panting.

Sodium salicylate may have increased the dissipation of heat from these hyperthermic birds by stimulating the panting center in the midbrain to produce a greater increase in panting rate. Indirect evidence for this action comes from the work of Randall and Hiestand (1939) who gave birds a respiratory stimulant, lobeline, and noticed that this drug had the following effects:

1. a decrease in panting threshold; i. e., an earlier onset of panting at a lower body temperature

2. a greater increase in panting rate in relation to internal temperature

3. a greater maximal panting rate

They concluded that lobeline increased the efficiency of the temperature regulating mechanism of the chicken, although its action was of a short duration. Sodium salicylate also is a respiratory stimulant in large doses (Sproull, 1954). This antipyretic, however, stimulates respiration by a reflex stimulation of the respiratory center while the action of lobeline is analogous to that of nicotine wherein respiratory stimulation is caused chiefly by stimulating the carotid body chemoreceptors and thus reflexly increasing respiratory rate and depth (Liljestrand, 1951). The hypothesis that sodium salicylate stimulates an increase in panting rate and thereby increases heat loss, lacks direct evidence in the literature to support it. Although panting was observed in the birds in this experiment, no observation was made as to the rate of respiration or of panting.

Sodium salicylate may exert its antipyretic action through the heat loss center in the anterior hypothalamus. Evidence for this statement comes from the work of Guerra and Brobeck (1944) who produced lesions in the anterior and anterolateral hypothalamus of monkeys and noticed marked temperature lability. Acetylsalicylic acid given to non-operated febrile monkeys produced excessive sweat excretion, but in operated febrile monkeys no increase in sweat excretion was noted.

Some excess heat may have been lost from these salicylate-treated heat-stressed birds by a greater increase in peripheral vasodilatation resulting in a considerable loss of heat by radiation, conduction and convection. Due to a slight temperature gradient between the bird and

the heat-stressing environmental atmosphere, only a small amount of heat could be lost by cutaneous vasodilatation in this experiment.

To summarize, the reduction in body temperature obtained in these experiments could have resulted from one or a combination of: hydremia, vasodilatation or an increase in the panting rate. Sodium salicylate is not only an antipyretic but in large doses, it is a metabolic stimulant in mammals, (Cochran, 1953; Sproull, 1954; and Reid, 1957) and consequently produces an increase in heat production. It appears that if sodium salicylate acted as an antipyretic in this experiment, the increase in the dissipation of excess heat was greater than the increase in heat production due to the metabolic stimulating action of sodium salicylate, so that a general decrease in body temperature was the net result.

The Effect of Temperature on Thyroid Weight and Function

The adverse effects of high environmental temperatures and high body temperature on thyroid weight and function are noted in Table IV and Table V. All heat-stressed birds not given salicylate had significantly smaller thyroid weights (mg. percent) than the normal controls as well as significantly smaller uptake of radioiodide by the thyroids. An additional measurement of thyroid function was made in Group II (Table V) namely, the thyroid/plasma ratio of iodide. As in Group I, the heat-stressed control lot, Lot I of Group II, had a significantly smaller thyroid gland and a significant decrease in thyroid function when compared to the non-heat-stressed lots. This decrease in size of the thyroid due to high environmental temperature is in agreement with the work of Hoffman and Shaffner (1950) and Joiner and Hutson (1957). The decrease in thyroid function in birds due to high environmental temperature agrees

with the seasonal variation in thyroid secretion rate noticed by Reineke and Turner (1945) and the decrease in secretion rate of birds exposed to 95° F. and 105° F. when compared to the thyroid secretion rate at 75° F. which was observed by Heninger, Newcomer and Thayer (1960).

The explanation for the decrease in thyroid activity due to the effects of heat has not been fully resolved and several factors probably affect it. Chief among these may be the "feed back" hypothesis (Brown-Grant, 1957) between the thyroid and anterior pituitary. Decreased peripheral utilization of the thyroid hormone due to the decreased need for heat production in heat-stressed birds results in an excess of thyroid hormone. Thyroid hormone then acts upon the anterior pituitary to suppress the release of TSH and a corresponding decrease in thyroid function is the net result. Evidence for this hypothesis comes from the work of Rand, Riggs, and Talbot (1952) who confirmed the increased utilization of thyroid hormone in cold-exposed rats.

The hypothalamus appears to modulate the activity of the pituitary-thyroid system by influencing the production and release of TSH by the pituitary. Evidence for this statement comes from the facts that:

1. Anatomical interruption of the hypothalamohypophyseal system profoundly alters the secretion of TSH (Barrnett and Greep, 1951).
2. Anterior hypothalamic lesions in the rat result in a decrease of TSH release from the anterior pituitary (Greer, 1951; Florsheim, 1958; D'Angelo, 1958).
3. Electrical stimulation of the supraopticohypophyseal tract causes a discharge of TSH from the anterior pituitary gland (Campbell, George and Harris, 1960).

The level of circulating thyroxine does not appear to regulate the secretion of TSH from the anterior pituitary indirectly through the hypothalamus. D'Angelo (1958), using rats with anterior hypothalamic lesions, found that TSH release was suppressed by exogenous thyroxine while Reichlin (1960), using rats with hypothalamic lesions, observed an inhibition of I^{131} release from the thyroid with exogenous thyroxine. Both investigators agree that the primary action of thyroxine is on the adenohypophysis rather than the hypothalamus and that the anterior pituitary-thyroid servomechanism is consequently not under neural control. Since the hypothalamus is not acted upon by thyroxine to regulate thyroid function, the hypothalamus is not controlled by changes in the peripheral utilization of thyroxine due to changes in environmental temperature.

Since the hypothalamus exerts a governing influence on body temperature and is one of the factors involved in regulating thyroid function, it is believed that thyroid function is indirectly controlled by the thermoregulatory centers in the hypothalamus. Evidence for the control of the release of TSH by the thermoregulatory centers came from the work of Knigge and Bierman (1958) who found that the rate of release of organic I^{131} in the normal hamster was accelerated by the exposure to cold. This response was blocked by bilateral hypothalamic lesion in the median eminence, by reserpine, and by hypophysectomy. This work by Knigge and Bierman (1958) was supported by von Euler and Holmgren (1956) who grafted anterior pituitary tissue into a rabbits eye and noted that the intact hypothalamus hypophyseal portal vessels and neural tracts were not a necessary condition for feed back control of thyroxine levels in the blood, but when these animals were exposed to cold, little change in thyroid secretion was noted in these grafted animals as compared to an increase of thyroid secretion in intact animals. Reichlin (1960) located a heat loss center in the

hypothalamus of the rat, near the pre-optic area and the TSH-releasing center was located between the paraventricular nucleus and the median eminence. Histologic evidence indicated that although these areas were distinct in their functions, they partially overlapped anatomically. The conclusion reached by this investigator was that this general area serves to integrate short term heat loss, heat conservation, and heat mobilization reactions with long term metabolic control by the pituitary-thyroid axis. The theory that the thermoregulatory centers in the hypothalamus regulate thyroid activity has not received general support from all the investigators in this field. Barrnett and Greep (1951) sectioned the pituitary stalk and prevented the hypophyseal-portal vessels from regenerating and noted that the thyroids were atrophic indicating a subnormal release of TSH; however, on exposure to cold there was an increase in TSH secretion by the anterior pituitary. Essentially the same results were obtained by Van Beugen and Van der Werff ten Bosch (1960) who produced hypothalamic lesions in rats which resulted in a decreased release rate of radioiodide from the thyroids in operated rats exposed to 4° C. and 22° C. although the cold induced an accelerated release of radioiodide that was proportional to that accelerated release found in the normal controls. They believed that this demonstrated that the effect of cold upon thyroid function was not mediated by the anterior hypothalamus. These investigations which were made supporting the theory that the thermoregulatory centers in the hypothalamus partially regulate thyroid activity and the investigations made that did not support this theory were similar in operation but produced different results. This may be partially explained on the basis of an investigation made by Florsheim (1958) who demonstrated that lesions produced near the thyrotropin center in the hypothalamus interferred with the hypophyseal TSH production, however, lesions

produced in the thyrotropin center were the most effective in blocking the hypertrophy response of the thyroid to goitrogens. He also stated that there appeared to be great differences in the control of thyroid function in various species. On the basis of the preceding work, it appears that more investigation is required concerning the control of thyroid function by the thermoregulatory centers in the hypothalamus during changes in environmental temperature.

The adrenal cortex may cause a depression of thyroid activity in animals subjected to acute exposure to cold, which acts as a "general stress" (Brown-Grant, 1956). Since heat could be a form of acute stress to these chicks, thyroid activity may be depressed by adrenal cortex activation. That the adrenal cortex has been activated is seen by the effects of heat on the weights of the adrenal gland and on the bursa of Fabricius in Groups I and II. Each of the heat-stressed lots in Groups I and II had an average adrenal gland weight that was not significantly different from the adrenal gland weights of the normal control lot. This indicates that on the basis of adrenal gland weights alone, these birds were not subjected to heat-stressing conditions; however, adrenal gland weight is not a satisfactory indication of stress in birds. Newcomer and Connally (1960) injected immature birds with repeated doses of ACTH and subjected immature birds to stress. They observed no statistically significant difference in adrenal gland weights between these birds and non-treated birds. However, they observed in these birds that the decrease in size of the bursa of Fabricius may be used as a criterion of adrenal cortical stimulation by repeated injection of ACTH or repeated application of stressors. Examination of the average weights of the bursae of all the heat-stressed lots in this work revealed significantly smaller bursae when compared to the

normal control lots. This evidence indicated that the birds were stressed by the heat and that the adrenal cortex was activated to release a greater amount of adrenal steroids which stimulated involution of the bursa of Fabricius and subsequently depressed thyroid function. Sodium salicylate did not appear to have any stressing action in the chicks because there was no significant difference in the weight of the bursa of Fabricius between lots receiving sodium salicylate and those lots not receiving the substance at the same environmental temperature.

Sodium salicylate administration in mammals has been shown to reduce ascorbic acid significantly from the adrenal cortex (Hetzel and Hine, 1951). Salicylate appeared to reduce ascorbic acid by acting through the hypothalamus which caused the release of ACTH. Stephenson (1959) observed a decrease in the size of the thymus in immature rats with the administration of .29% to .58% sodium salicylate in the diet. He observed this involution of the thymus in both normal and adrenalectomized rats with salicylate administration, and concluded that the action of the sodium salicylate was directly upon the thymus. In mammals, sodium salicylate appears to possess glucocorticoid activity and acts directly on the thymus gland to bring about a reduction in size. From this present experiment, it appears that sodium salicylate does not have a glucocorticoid effect in birds. This is supported by the insignificant difference in bursal weights between Lots II and IV in Group II.

The Effect of Sodium Salicylate on Thyroid Function in Birds

Chronic administration of sodium salicylate to mammals resulted in a reduction of thyroid function which was probably due to the action of sodium salicylate on the anterior pituitary or on the hypothalamus

(Wolff and Austin, 1958). Examination of the thyroid weight and function in the lots of birds receiving sodium salicylate in Groups I and II (Tables IV and V) revealed that sodium salicylate appeared to have either no effect on thyroid function or to increase thyroid function in birds. The thyroid function in heat-stressed birds receiving .25% sodium salicylate was not significantly different from the heat-stressed control lot. In Group I (Table IV) heat-stressed birds which received .5% sodium salicylate had a significantly greater mean uptake of radioiodide than Lots I and III, but in Group II (Table V) the lot of heat-stressed chicks receiving .5% sodium salicylate did not have significantly greater uptake of radioiodide compared to the heat-stressed control lot. Although the non-heat-stressed birds receiving .5% sodium salicylate had a significantly greater mean thyroid weight and uptake of radioiodide than the normal control lot, the thyroid/plasma ratio of radioiodide was not significantly different between the two lots.

That sodium salicylate could have such contrasting effects on thyroid activity in mammals and birds seems rather improbable and some possible explanation should be made for the differences in thyroid response to sodium salicylate in mammals as compared to the results obtained in this work in chicks.

In mammals, the administration of sodium salicylate and dinitrophenol led to a reduction of thyroid function with an observed acceleration in the disappearance of protein bound iodine (PBI) from the circulation. This decrease of PBI in the circulation was not in accordance with the expected increase in thyroid activity (Christensen, 1960 and Goldberg, Wolff, and Greep, 1957). Christensen (1960) believed that salicylates compete with thyroxine for the receptor sites of plasma proteins and subsequently caused

a rise in free serum thyroxine levels which then inhibit thyroid function by the feed-back mechanism. Mellen and Hardy (1957) pointed out that the blood PBI in chickens and ducks was consistently and characteristically much lower than the PBI in mammals. High ambient temperatures did not produce a significant decrease in PBI levels; however, the thyroid secretion rate was reduced. The PBI in mammals in contrast to birds may be used as a reliable and valuable criterion of thyroid activity. This statement agrees with the work of Goldberg (1954) who observed a decrease in PBI and thyroid function in rats with elevated body temperature. If Christensen's hypothesis is correct, that sodium salicylate given to mammals is an anti-thyroid substance because of its action on PBI, then in fowls because the PBI is not a good criterion of thyroid activity, perhaps sodium salicylate would have little antagonistic effect on thyroid activity. This assumption agrees with the observations made in this work that sodium salicylate appears either to have no effect or a stimulating effect on thyroid activity in chicks. The effects of sodium salicylate on the PBI in birds has not been investigated and some investigators feel that in mammals sodium salicylate inhibits thyroid function directly through the anterior pituitary or higher neural centers.

An increase in thyroid activity in birds receiving sodium salicylate might be due to the significant decrease in the average body temperature of the heat-stressed antipyretic-treated birds. If the body temperature of heat-stressed animals is elevated, it has been shown that thyroid activity will be reduced (Goldberg, Wolff, and Greep, 1957). Assuming that this elevated body temperature could be reduced with certain antipyretics to normal or near normal levels, then the thyroid activity should increase to near normal activity. This hypothesis indicates that sodium salicylate

does not directly influence thyroid activity but, by its antipyretic action in reducing hyperthermic body temperature to near normal levels, the thyroid function would increase. The following data derived from the present work do not adequately support this hypothesis:

(1) Heat-stressed birds which received .25% sodium salicylate did not exhibit any increase in thyroid function or body weight although the antipyretic significantly reduced the average body temperature of the lot to near normal levels.

(2) Heat-stressed birds in Group II which received .5% sodium salicylate did not have a significant increase in thyroid activity when compared to the heat-stressed controls, although, again this lot of birds had a significantly lower body temperature than the heat-stressed control lot.

(3) Non-heat-stressed chicks in Group II which received .5% sodium salicylate had a significant increase in thyroid weight and uptake of radioiodide when compared to the normal control, but no significant difference was noted between the thyroid/plasma ratio in Lots II and IV. No significant differences in the average body temperature of these non-heat-stressed lots were noted; however, the Group II non-heat-stressed chicks were exposed to a variable summer temperature that ranged from a high of 97° F. to a low of 65° F. with an average relative humidity of 85%* for the 20 day growing period. These birds were exposed to a relatively high environmental temperature and the normal control lot in Group II had an average body temperature that was .8° F. higher than the normal control lot in Group I.

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*Taken from the late June and early July weather reports in the Tulsa Tribune.

The Effect of Temperature and Sodium Salicylate on Body Weight and Feed Consumption

Chickens exposed to high environmental temperature exhibit a decrease in feed consumption and a decrease in body weight (Heninger, Newcomer and Thayer, 1960). Results obtained in this work also support this statement since all the chicks exposed to 105° F. environmental temperature had a decrease in the feed consumed (Table VI) during the growing period and a significant ($P < .05$) decrease in the body weight recorded at the termination of the experiment (Tables IV and V).

The explanation for the decrease in feed consumed by these hyperthermic chicks was given by Brobeck (1960) in a review of the relation between feed ingested and body temperature. This reveiw points out that "the major concern of a body under conditions of thermal stress is to react in such a way as to reduce the stress. Because feed is a source of heat production, the organism dictates the reduction of feed consumption with increasing body temperature so as to reduce heat production." The decline in the gain of body weight in these chicks was probably due to the reduction of feed consumption in these heat-stressed animals.

Examination of the lots receiving .5% sodium salicylate in their diet, showed a consistent decrease in body weight and feed consumption when compared with the heat-stressed controls. The body weight for Lot IV (Table IV) was significantly less ($P < .05$) than the final body weight observed in the remaining heat-stressed lots. In Group II, final body weight for those heat-stressed chicks receiving .5% sodium salicylate was less than the heat-stressed control lot, but this was not significant. Chicks receiving .5% sodium salicylate and exposed to normal environmental temperatures exhibited a decrease in feed consumption and a decrease in body

weight which was significantly less ($P < .05$) than the final body weight observed in the normal control lot. It appears that chronic administration of sodium salicylate had an adverse effect on the gain in body weight in young chicks. This statement is supported by the work of Austin, et al., (1958) who observed a decrease in nitrogen retention in humans receiving 6 - 8 gms. sodium salicylate daily for 32 days. These subjects experienced a negative nitrogen balance and a weight loss of 5 to 12 pounds. Cochran (1953) gave humans sodium salicylate intravenously, which resulted in a decrease in respiratory quotient. This indicates that more protein and fats were being oxidized than before sodium salicylate administration.

This decrease in body weight of the chicks receiving .5% sodium salicylate may be explained partially on the basis that therapeutic doses of sodium salicylate cause a negative nitrogen balance and a decrease in body weight; however, sodium salicylate will also produce an increase in blood glucose (Barbour and Herrmann, 1921) due to its glycogenolytic action (Sproull, 1954). This increase in blood glucose may give these chicks a feeling of "satiety" and a subsequent decrease of feed intake.

SUMMARY AND CONCLUSIONS

Sodium salicylate was fed in the diet at levels of .1%, .25%, and .5% to immature chickens subjected to an ambient temperature of 105° F. Those chicks receiving .25% sodium salicylate exhibited a statistical decrease in body temperature, while chicks receiving .5% sodium salicylate exhibited a significant decrease in body temperature and an increase in thyroid function as compared to the heat-stressed control chicks. Sodium salicylate did not significantly decrease the body temperature of cockerels given .5% sodium salicylate and exposed to normal environmental temperatures. There was a statistical significant increase in uptake of radioiodide by the thyroids in these chicks but not in the thyroid/plasma ratio when compared to normal control birds (no salicylate, normal environmental temperature). Chicks receiving large doses of sodium salicylate had a consistently smaller gain in body weight when compared to the normal controls.

This experiment indicates that in contrast to the situation in mammals where sodium salicylate inhibits thyroid function, sodium salicylate in cockerels either does not affect thyroid function or stimulates thyroid function. The action whereby sodium salicylate stimulates thyroid function could be due to the significant decrease in body temperature noted in hyperthermic cockerels receiving a large amount of sodium salicylate in their diet. However, cockerels exposed to normal environmental temperatures and receiving the same amount of salicylate, had more active thyroids than did the normal control group of cockerels. No explanation

can be given for the differences in thyroidal response to sodium salicylate noted in birds as compared to mammals, but it appears according to this experiment that sodium salicylate does not depress thyroidal activity because at no time during the course of the experiment was this observed in the cockerels receiving sodium salicylate.

Sodium salicylate did not stimulate the adrenal cortex to release adrenal steroids, since significant involution of the bursa of Fabricius did not occur in cockerels receiving sodium salicylate. Cockerels receiving .5% sodium salicylate exhibited a decrease in body weight in spite of the fact that the body temperature of the chicks was significantly less than the heat-stressed controls.

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APPENDICES

APPENDIX A

APPENDIX A

BODY WEIGHT AND WEIGHT GAINS - GROUP I

Lot #1				Lot # 2			
Bird No.	Weight on Arrival	Weight at 21 Days	Gain	Bird No.	Weight on Arrival	Weight at 21 Days	Gain
701	40.0	179.3	139.3	780	34.5	147.0	112.5
702	41.5	157.2	115.7	778	46.5	142.5	96.0
704	40.0	173.3	133.3	779	42.5	166.8	124.3
705	41.5	136.5	95.0	786	41.5	161.5	120.0
706	42.5	178.5	136.0	797	35.5	137.5	102.0
708	40.0	167.5	127.5	783	41.5	191.5	150.0
709	40.0	153.0	113.0	795	36.0	163.0	127.0
710	44.0	194.6	150.6	781	36.0	140.0	104.0
712	35.0	150.8	115.8	798	49.0	126.0	77.0
713	35.0	135.0	100.0	750	38.0	159.2	121.2
714	33.0	174.5	141.5	790	38.0	151.5	113.5
715	41.0	170.0	129.0	796	41.5	139.5	98.0
716	39.5	173.5	134.0	799	36.0	115.7	79.7
717	37.0	181.3	144.3	748	44.0	127.5	83.5
718	37.0	162.2	125.2	793	42.0	141.4	99.4
719	37.0	135.7	98.7	794	41.0	146.2	105.2
720	41.0	125.2	84.2	791	44.5	130.0	85.5
722	44.5	170.5	126.0	747	44.5	169.7	125.2
723	39.5	181.0	141.5	788	38.5	115.0	76.5
724	35.5	165.7	130.2	749	38.5	159.3	120.8
770	40.0	128.2	88.2	785	39.5	124.5	85.0
	824.5	3,393.3	2,569.0		849.0	3,055.3	2,206.3
Mean	39.26	161.58	122.33		40.42	145.49	105.06

Lot #III				Lot #IV			
Bird No.	Weight on Arrival	Weight at 21 Days	Gain	Bird No.	Weight on Arrival	Weight at 21 Days	Gain
725	43.0	173.7	130.7	727	39.0	154.0	115.0
726	38.0	172.0	134.0	741	38.0	138.0	100.0
728	34.0	140.0	106.0	752	36.0	129.0	93.0
729	36.0	162.0	126.0	753	35.5	106.3	70.8
730	39.0	167.1	128.1	754	41.5	151.7	110.2
732	39.5	162.0	122.5	756	36.0	111.3	75.3
734	39.0	164.2	125.2	757	34.8	125.4	90.6
735	43.0	163.3	120.3	758	40.0	146.5	106.5
736	35.5	165.3	129.8	759	36.0	146.5	110.5
738	41.0	183.3	142.3	760	37.0	135.3	98.3
739	36.0	147.5	111.5	761	37.5	114.5	77.0
740	38.0	228.8	190.8	762	39.0	163.8	124.8
742	38.5	160.4	121.9	763	37.5	124.5	87.0
743	38.5	163.5	125.0	764	39.0	52.3	13.3
744	40.5	159.8	119.3	766	38.0	155.8	117.8
745	36.5	151.4	115.1	767	35.0	160.5	125.5
746	41.5	203.3	161.8	768	36.0	120.8	84.8
775	37.5	157.8	120.3	769	40.0	139.5	99.5
787	36.5	188.5	152.0	772	40.0	144.5	104.5
914	41.5	182.0	140.5	915	40.0	145.0	105.0
				773	38.0	141.0	103.0
	773.0	3,395.9	2,623.1		754.8	2,806.2	2,012.4
Mean	38.65	169.79	131.15	Mean	37.74	133.62	95.83

Lot #V			
Bird No.	Weight on Arrival	Weight at 21 Days	Gain
901	38.0	306.8	268.8
902	40.0	277.5	237.5
904	35.5	247.0	211.5
905	40.0	247.0	207.0
906	39.0	275.5	236.5
907	41.0	294.0	253.0
909	41.0	276.0	235.0
910	38.5	258.0	219.5
911	45.0	293.4	248.4
912	36.5	265.7	229.2
913	35.0	294.5	259.5
916	36.5	265.5	229.0
917	38.0	272.0	234.0
918	34.5	269.0	234.5
919	40.5	286.5	246.0
920	40.0	280.5	240.5
922	36.5	193.0	156.5
923	41.0	316.8	275.8
924	35.5	269.8	234.3
925	37.0	273.5	236.5
	769.0	5,462.0	4,693.0
Mean	38.45	274.91	234.65

APPENDIX A

BODY WEIGHT AND WEIGHT GAINS - GROUP II

Lot #I				Lot #II			
Bird No.	Weight on Arrival	Weight at 20 Days	Gain	Bird No.	Weight on Arrival	Weight at 20 Days	Gain
708	52.5	131.4	78.9	720	47.5	218.7	171.2
711	46.5	165.2	118.7	738	52.0	242.0	190.0
726	45.5	165.9	120.4	740	54.0	229.2	175.2
747	47.0	163.3	116.3	743	46.0	208.5	162.5
749	47.5	140.7	93.2	767	46.0	227.5	181.5
769	47.0	146.7	99.7	779	48.5	250.9	202.4
771	46.5	176.3	129.5	780	48.0	205.4	157.4
778	50.0	160.2	110.2	781	48.5	256.2	207.7
783	45.0	165.5	120.5	790	46.0	206.2	160.2
785	43.0	162.0	119.0	794	50.5	218.2	167.7
791	50.5	179.3	128.8	796	50.5	239.6	189.1
792	46.5	173.3	126.8	915	42.0	207.7	165.7
799	44.5	157.3	112.8	919	42.5	203.8	161.3
902	46.5	144.3	97.8				
908	47.0	184.4	137.4				
	705.5	2,415.8	1,710.0		622.0	2,913.9	2,291.9
Mean	47.03	161.05	114.00	Mean	47.84	224.14	176.30

Lot #III				Lot #IV			
Bird No.	Weight on Arrival	Weight at 20 Days	Gain	Bird No.	Weight on Arrival	Weight at 20 Days	Gain
710	47.5	144.0	96.5	709	46.5	243.8	197.3
712	48.5	161.4	112.9	745	43.5	241.9	198.4
713	52.0	180.0	128.0	798	50.0	254.3	204.3
722	58.5	161.0	102.5	926	48.0	247.9	199.9
723	41.0	123.0	82.0	927	41.5	227.4	185.9
734	47.0	124.6	77.6	928	43.5	213.5	170.0
750	46.0	175.8	129.8	929	45.3	244.6	199.3
773	45.0	140.8	95.8	930	47.0	253.6	206.6
793	48.5	150.3	101.8	931	49.0	239.3	190.3
797	53.0	166.3	113.3	932	45.2	242.0	196.8
914	47.5	121.0	73.5	933	44.0	277.3	233.3
916	43.0	144.6	101.6	934	42.5	247.5	205.0
935	45.5	136.5	91.0	936	44.0	236.2	192.2
				937	48.0	269.2	221.2
				938	47.0	262.5	215.5
				939	46.2	244.5	198.3
	623.0	1,929.3	1,306.3		731.2	3,945.5	3,214.3
Mean	47.92	148.40	100.48	Mean	45.70	246.59	200.89

APPENDIX B

APPENDIX B

MEAN BODY TEMPERATURE - GROUP I

Lot #I		Lot #II		Lot #III		Lot #IV		Lot #V	
Bird No.	Mean Temperature	Bird No.	Mean Temperature	Bird No.	Mean Temperature	Bird No.	Mean Temperature	Bird No.	Mean Temperature
701	108.20	747	107.35	725	106.82	727	107.00	901	106.55
702	108.50	748	108.30	726	107.20	741	107.42	902	106.82
704	107.47	749	108.70	728	107.02	755	107.15	904	106.57
705	107.30	750	107.77	729	107.65	753	107.47	905	106.75
706	108.15	778	107.50	730	106.75	754	107.52	907	106.22
708	107.60	779	108.22	732	107.67	756	107.20	909	107.45
709	107.17	780	107.45	734	106.75	757	107.70	910	107.12
710	107.40	781	107.10	735	106.55	758	106.87	911	106.52
712	107.52	783	108.75	736	107.52	759	107.60	912	107.10
713	107.95	785	108.17	738	107.12	760	106.92	913	106.85
714	108.52	786	108.47	739	107.62	761	106.67	916	106.57
715	108.07	788	106.55	740	107.97	762	107.20	917	106.70
716	107.80	790	107.92	742	107.72	763	106.70	918	106.65
717	107.97	791	107.90	743	106.67	766	106.37	919	106.75
718	106.97	793	108.10	744	106.97	767	107.42	920	106.45
719	107.62	794	107.00	745	107.42	768	107.12	906	106.43
720	108.05	795	107.80	746	107.37	769	106.70	922	106.22
722	108.55	796	108.10	775	107.57	772	106.75	923	106.65
723	107.62	797	107.62	787	107.70	773	106.67	924	106.62
724	107.55	798	108.17	914	106.80	915	106.97	925	106.50
770	107.32	799	107.05						
	2,263.30		2,263.99		2,144.86		2,141.42		2,133.49
Mean	107.77		107.80		107.24		107.07		106.67

APPENDIX B

MEAN BODY TEMPERATURE - GROUP II

Lot #I		Lot #II		Lot #III		Lot #IV	
Bird No.	Mean Temperature	Bird No.	Mean Temperature	Bird No.	Mean Temperature	Bird No.	Mean Temperature
708	107.90	720	107.24	710	107.44	709	107.52
711	108.30	738	107.26	712	108.04	745	107.36
726	107.80	740	106.76	713	108.06	798	107.38
747	107.80	743	107.56	722	107.74	926	107.84
749	108.30	767	107.06	723	107.28	927	107.32
769	108.10	779	107.66	734	107.34	928	107.26
771	108.40	780	107.48	750	107.32	929	107.44
778	108.40	781	106.54	773	108.04	930	106.96
783	108.34	790	107.58	793	107.50	931	107.06
785	108.10	794	107.48	797	108.42	932	107.46
791	108.58	796	106.94	914	107.56	933	107.66
792	107.90	915	107.34	916	107.62	934	107.34
799	108.20	919	107.52	935	107.96	936	107.18
902	108.26					937	107.82
908	107.50					938	107.52
						939	107.38
	1,621.88		1,394.42		1,400.30		1,718.50
Mean	108.12		107.26		107.71		107.40

APPENDIX C

APPENDIX C

THYROID GLAND WEIGHT AND PERCENT UPTAKE RADIOIODIDE

GROUP I

Bird No.	Thyroid Weight (mg.)	Thyroid Weight (mg.%)	Thyroid Uptake (c/min.)	% Uptake* Radio-iodide	Bird No.	Thyroid Weight (mg.)	Thyroid Weight (mg.%)	Thyroid Uptake (c/min.)	% Uptake* Radio-iodide
Lot #I					Lot #III				
770	5.5	4.29	48,586	1.759	787	4.7	2.49	27,506	.996
724	4.2	2.53	22,812	.826	744	4.4	2.75	65,390	2.367
719	3.9	2.87	63,928	2.314	735	4.5	2.76	57,574	2.084
704	4.4	2.54	47,988	1.737	746	8.0	3.94	51,476	1.864
717	4.9	2.70	30,348	1.098	728	3.9	2.79	70,632	2.557
	22.9	14.93		7.734		25.5	14.73		9.868
Mean	4.58	2.98		1.546		5.10	2.94		1.973
Lot #IV					Lot #V				
758	5.9	4.03	105,489	3.820	901	16.0	5.21	114,384	4.142
754	5.7	3.76	71,362	2.584	913	15.9	5.39	172,870	6.260
768	3.2	2.65	80,746	2.924	904	13.9	5.63	172,682	6.254
752	5.0	3.88	107,586	3.895	917	8.3	3.05	103,356	3.742
772	6.0	4.15	114,414	4.143	911	17.7	6.03	147,082	5.326
	25.8	18.47		17.366		71.8	25.31		25.724
Mean	5.16	3.69		3.473		14.36	5.06		5.144

*This number obtained by dividing estimated dose I^{131} injected (2,761,500 c/min.) into thyroid uptake.

APPENDIX C

THYROID GLAND WEIGHT, PERCENT UPTAKE RADIOIODIDE AND T/P RATIO

GROUP II

Bird No.	Thyroid Weight (mg.)	Thyroid Weight (mg.%)	Thyroid Uptake (c./min.)	% Uptake* Radio-iodide	Plasma .1 ml. (c./min.)	Thyroid (c./min./ .1 gm.)	T/P Ratio
Lot #I							
708	3.0	2.28	50,942	1.869			
711	3.0	1.81	17,344	.636			
785	3.1	1.91	40,802	1.497			
799	3.0	1.90	29,184	1.071			
902	2.2	1.52	34,860	1.279			
747	4.7	2.87	6,548**		2,768	139,319	50.33
749	4.8	3.41	5,514		2,950	114,875	38.94
778	4.6	2.87	5,820		2,714	126,521	46.61
783	4.8	2.90	4,108		3,456	85,583	24.76
792	4.2	2.42	8,228		2,540	195,904	77.12
908	4.4	2.38	4,680		4,778	106,363	22.26
	41.8	26.27		6.352			260.02
Mean	3.80	2.38		1.270			43.33

*This number obtained by dividing estimated dose I^{131} injected (2,724,800 c./min.) into thyroid uptake.

**These chicks were given thiourea prior to the injection of I^{131}

Bird No.	Thyroid Weight (mg.)	Thyroid Weight (mg.%)	Thyroid Uptake (c./min.)	% Uptake* Radio-iodide	Plasma .1 ml. (c./min.)	Thyroid (c./min./ .1 gm.)	T/P Ratio
Lot #II							
740	8.2	3.57	100,268	3.679			
779	11.8	4.70	81,028	2.973			
780	10.0	4.86	91,280	3.349			
781	12.3	4.79	99,152	3.638			
794	9.6	4.39	83,108	3.050			
796	11.8	4.92	106,770	3.918			
720	9.6	4.39	25,610**		1,768	260,770	150.88
738	12.6	5.20	15,408		1,800	122,285	67.93
743	8.2	3.93	20,722		1,823	252,707	138.62
915	11.6	5.58	37,824		2,109	326,068	154.60
919	9.6	4.71	14,194		2,624	147,854	56.34
	125.1	55.79		20.607			568.37
Mean	10.42	4.65		3.434			113.67

* This number obtained by dividing estimated dose I^{131} injected (2,724,800 c./min.) into thyroid uptake.

**These chicks were given thiourea prior to the injection of I^{131}.

Bird No.	Thyroid Weight (mg.)	Thyroid Weight (mg.%)	Thyroid Uptake (c./min.)	% Uptake* Radio-iodide	Plasma .1 ml. (c./min.)	Thyroid (c./min./ .1 gm.)	T/P Ratio
Lot #III							
710	4.2	2.91	62,682	2.300			
713	3.8	2.11	52,916	1.942			
750	3.6	2.04	68,664	2.519			
793	3.2	2.12	59,346	2.177			
797	2.0	1.20	33,774	1.239			
935	3.2	2.34	38,984	1.430			
712	4.6	2.85	5,378**		2,056	116,913	56.86
722	3.8	2.36	4,350		3,074	114,473	37.23
723	3.6	2.92	7,472		2,170	207,555	95.64
773	5.2	3.69	6,226		3,132	119,730	38.22
914	2.4	1.98	2,946		2,610	122,750	47.03
916	4.2	2.90	3,426		2,984	81,571	27.33
	43.8	29.42		11.607			302.31
Mean	3.65	2.45		1.934			50.38

* This number obtained by dividing estimated dose I^{131} injected (2,724,800 c./min.) into thyroid uptake.

**These chicks were given thiourea prior to the injection of I^{131}.

Bird No.	Thyroid Weight (mg.)	Thyroid Weight (mg.%)	Thyroid Uptake (c./min.)	% Uptake* Radio-iodide	Plasma .1 ml. (c./min.)	Thyroid (c./min./ .1 gm.)	T/P Ratio
Lot #IV							
798	11.0	4.32	55,588	2.040			
933	10.8	3.89	64,396	2.363			
937	12.4	4.60	65,952	2.420			
938	8.2	3.12	42,606	1.563			
939	7.0	2.86	74,110	2.719			
709	8.4	3.44	14,094**		1,670	167,784	100.46
926	11.2	4.51	12,422		1,873	110,910	59.21
928	8.2	3.84	5,154		1,513	62,853	41.54
931	8.4	3.51	13,444		1,450	160,046	110.35
932	9.6	3.96	21,744		1,924	226,458	117.70
934	11.6	4.68	16,198		1,735	139,637	80.48
	106.8	42.73		11.105			509.74
Mean	9.70	3.88		2.22			84.95

* This number obtained by dividing estimated dose I^{131} injected (2,724,800 c./min.) into thyroid uptake.

**These chicks were given thiourea prior to the injection of I^{131}.

APPENDIX D

APPENDIX D

ADRENAL GLAND AND BURSA OF FABRICIUS WEIGHT

Group I					Group II				
Bird No.	Adrenal Weight (mg.)	Adrenal Weight (mg.%)	Bursa Weight (mg.)	Bursa Weight (mg.%)	Bird No.	Adrenal Weight (mg.)	Adrenal Weight (mg.%)	Bursa Weight (mg.)	Bursa Weight (mg.%)
Lot #I					Lot #I				
716	26.8	15.44	292.2	168.41	726	22.0	13.26	491.0	295.96
705	19.2	14.06	237.0	173.62	747	26.7	16.35	467.8	286.46
714	22.8	13.06	254.2	145.67	749	26.8	19.04	398.4	283.15
702	29.9	19.02	288.4	183.46	769	28.6	19.49	591.8	403.40
701	25.1	13.99	238.6	133.07	778	15.4	9.61	424.6	265.04
706	17.1	9.58	505.2	283.02	783	28.8	17.40	539.7	326.10
718	24.2	14.92	611.8	377.18	785	21.0	12.96	564.4	348.39
715	29.6	17.41	257.9	151.70	792	23.8	13.73	933.8	538.83
					908	20.8	11.27	314.2	170.39
	194.7	117.49	2,685.3	1,616.13		213.9	133.11	4,725.7	2,917.72
Mean	24.3	14.68	335.66	202.01	Mean	23.76	14.79	525.07	324.19
Lot #III					Lot #II				
732	18.4	11.35	447.0	275.92	720	26.8	11.92	1,745.0	797.89
729	17.8	10.98	234.6	144.81	738	27.8	11.48	1,010.6	417.60
725	26.2	15.08	409.6	235.80	743	26.6	12.75	1,213.6	582.07
742	18.8	11.72	463.8	289.15	767	36.2	15.91	1,390.6	611.25
736	23.8	14.39	599.8	362.85	781	21.2	8.27	1,006.3	392.62
775	21.0	13.30	388.0	214.19	790	30.6	14.83	1,993.8	966.92
730	21.9	13.10	376.1	225.07	915	31.4	15.11	926.8	446.22
739	14.2	9.62	541.0	366.77	919	31.4	15.40	900.0	441.60
	162.1	99.54	3,409.9	2,114.56		232.0	105.67	10,186.7	4,656.17
Mean	20.26	12.44	426.23	264.32	Mean	29.0	13.20	1,273.33	582.02

GROUP I					GROUP II				
Bird No.	Adrenal Weight (mg.)	Adrenal Weight (mg.%)	Bursa Weight (mg.)	Bursa Weight (mg.%)	Bird No.	Adrenal Weight (mg.)	Adrenal Weight (mg.%)	Bursa Weight (mg.)	Bursa Weight (mg.%)
Lot #IV					Lot #III				
757	17.6	14.03	303.8	242.26	712	19.7	12.20	488.2	302.47
741	17.4	12.60	225.2	163.18	722	28.2	17.51	397.1	220.61
755	22.4	14.37	401.8	257.89	723	20.2	16.42	309.4	251.54
727	13.9	9.02	178.0	115.58	736	18.6	15.92	343.8	275.93
762	18.6	11.35	318.2	194.26	773	11.6	8.23	351.0	249.28
756	19.0	17.07	361.8	325.06	793	24.3	16.16	506.8	337.19
761	12.6	11.00	371.9	324.80	914	18.8	15.53	394.4	325.95
753	16.4	15.42	339.6	319.47	916	18.2	12.58	242.2	167.49
	137.9	104.86	2,500.3	1,942.50		159.60	114.55	3,032.9	2,130.46
Mean	17.23	13.10	312.52	242.81	Mean	19.95	14.31	379.11	266.30
Lot #V					Lot #IV				
907	40.0	13.60	1,732.1	589.14	709	32.1	13.16	1,825.4	748.76
920	22.4	7.98	1,347.2	480.28	745	26.0	10.74	1,348.8	557.58
924	36.8	13.63	2,102.0	779.09	926	33.6	13.55	1,157.6	466.96
909	36.1	13.08	1,244.0	450.72	927	29.8	13.10	1,206.4	530.51
903	37.1	11.71	1,146.8	361.99	928	31.8	14.89	753.2	352.81
925	26.6	9.72	1,518.2	555.10	930	29.6	11.67	1,046.3	412.61
918	36.8	13.68	1,639.9	609.62	931	31.4	13.12	1,767.8	738.77
910	28.1	10.89	1,295.2	502.01	932	26.6	10.99	1,219.4	503.88
					934	30.4	12.28	1,260.6	509.33
					936	29.0	12.27	1,847.2	782.04
	263.9	94.29	12,025.4	4,327.95		300.3	125.77	13,432.7	5,603.25
Mean	32.98	11.79	1,503.1	540.99	Mean	30.03	12.57	1,343.29	560.32

VITA

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Candidate for the Degree of

Master of Science

Thesis: THE EFFECTS OF SODIUM SALICYLATE ON THYROID FUNCTION IN HEAT-STRESSED CHICKENS

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