THE RESPONSE OF ADULT DOGS
AND ENGLISH BULL DOG PUPPIES
TO THYROID STIMULATION

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THE RESPONSE OF ADULT DOGS AND ENGLISH BULL DOG PUPPIES TO THYROID STIMULATION

By

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INTRODUCTION

The prime object of this research was to form a more perfect foundation for the use of thyroid products upon the dog. In the past, the dog has been used for a research animal from which to base studies upon other species. Although these past studies throw some light upon the status of the thyroid in the dog, they leave many questions unanswered.

With the increasing prosperity of the country and the consequent increase of the dog population, it becomes of increasing importance to perfect its medical therapy. The veterinary profession is complimented by the fact that more dogs are living beyond the stage of distemper and other puppyhood diseases. With this development, comes the problem of geriatrics, for the longer the period of residence of man's best friend, the greater his master's attachment becomes. There is good evidence that in man and animal, endocrines will lengthen life and prolong useful existence. With the senile decline of metabolism, come many of the "old age ills" such as loss of activity and reproduction. Accordingly, this is an attempt to form a basis for thyroid therapy in the dog.

Another phase of the work was to determine the effect of exogenous thyroid upon the growth rate of puppies. If this technic can be perfected, not only will growth be more efficient, but the pup will be sturdy at a time when he needs his strength to fight off the scourges of puppyhood. The period in which he would be susceptible to puppy diseases would be shortened.

The practicability of thyroid medication is increasing with the advent of standardized products. Desiccated thyroid U. S. P. XII is prepared from animals edible to man and standarized to the iodine content by chemical assay. The iodine content must be from .17 to .23% (U. S. P. Convention 1942). A less expensive preparation, Protamone (commercial name of the product supplied by Cerophyl Laboratories), is a synthetic iodinated protein. It is prepared by a controlled process whereby casein is iodinated in a buffered medium at a set temperature for a set period of time. The resulting compound is purified and dried (Reineke 1942). The advantages of this compound, other than its low cost, are that a greater standardization of the actual thyroxine content is to be had because of the controlled manufacture. The thyroxine content of natural thyroid materials depends somewhat upon the physiological state of the animal, and the iodine content is but a relative figure. The potency of Protamone has been shown to be several times that of desiccated thyroid.

PART I

REVIEW OF THE LITERATURE

Physiology of the Thyroid Gland

Under normal physiological conditions, the thyroid gland is the only organ having the endocrine action attributed to thyroxine. Recently it has been demonstrated by the use of thyroidectomized rats that injections of elemental iodine will produce a result similar to thyroxine injections. Elemental iodine has the power to form a thyroactive compound in the organism (Dvoskin 1947). Whether iodides share this ability is questionable but studies with radioactive iodine in thyroidectomized rats were believed to indicate thyroxine and diiodotyrosine formation in the liver and intestines (Morton, et al. 1943). Thyroidectomized rats are noted to grow better if given an iodine supplement which fact supports the theory of the extrathyroidal formation of thyroactive compounds (Chapman 1941). The thyroid gland surpasses all other tissues in its ability to fix circulating iodides. This ability is regulated to a large extent by the concentration of thyrotropic hormone (Hamilton and Soley 1940; Leblond and Sue 1941). The evidence is that the iodine is first united with tyrosine to form diiodotyrosine and this in turn forms thyroxine. This reaction probably takes place in the colloid space (Mann, et al. 1942). These reactions probably take place while the amino acid is still attached to the protein molecule, and the resulting molecule is termed thyroglobulin (Salter 1944). There has been some question as to the relative activities of l- and d-thyroxine. It is generally conceded that d-thyroxine has little or no activity while l-thyroxine accounts for practically all of the thyroid action. The thyroid gland normally produces l-thyroxine (Reineke 1945). Very little effect has been reported for diiodotyrosine except for one worker who used the questionable criterion of its maintaining the health of thyroidectomized dogs (Condorelli 1937).

Since the molecule of thyroglobulin has a molecular weight of about 700,000, it seems questionable that this entire molecule is able to enter the blood stream and then permeate the cells of the organism. The logical conclusion is that it is broken down at least to smaller fragments before making its physiologic circuit (Salter 1944). Attempts to identify thyroglobulin in circulating blood by highly effective precipitation methods have been negative (Stellar and Olken 1940).

By the use of studies with radioactive iodine, it was found that protein-bound iodine followed the pattern one might expect from the thyroid gland secretion. That is, the plasma protein bound iodine rose upon injections of thyrotropin and fell upon hypophysectomy (Chaikoff, et al. 1947). Chemical analysis of the circulating plasma iodine indicates that it is thyroxine (Taurog and Chaikoff 1947). The blood iodine content of dogs is very low, 0 to 8 micrograms percent, and is but little affected by enviromental temperature (Riggs 1942). In the human, the protein-bound plasma iodine is a definite indication of the basal heat production. The basal heat production is said to equal 52.3 log. (I)-0.8 calories/sq. meter/hour. The ratio is valid even after lugolization and thyroidectomy (Lowenstein, et al. 1944). It has been demonstrated that the thyroid hormone is able to permeate all the cells of the body and is even able to pass through the placenta and affect the fetus (Cunningham 1941).

Both thyroxine and thyroglobulin have effects orally and when given parenterally, but it has been noted that thyrotropin will produce a more rapid rise in metabolism than if thyroxine were given. This would indicate that the hormone of the thyroid possesses the calorigenic activity and that the thyroxine must undergo some alteration before becoming active. It was noted <u>in vitro</u>, that thyroxine was inactive upon tissues in saline solutions but exerted its influence part of the time in serum media. This may indicate that the thyroxine needs to form a protein linkage to become effective (Canzanelli, et al. 1939).

The thyroid hormone is generally classed as a catylyst rather than an enzyme because of the absence of effect upon dead or moribund cells. The hormone increases the metabolism of the cell by increasing its oxidative processes. Metabolism is able to take place in the complete absence of the thyroid hormone but at a rate of 10 to 50% below normal, depending upon the species in question. The presence of excessive amounts of thyroid hormone can only raise the metabolic rate to a physiological limit of 50 to 100% above normal (Canzanelli, et al. 1939). In lower species not possessing a thyroid gland, the effects of thyroid extracts are somewhat erratic. Usually the action is of a catabolic nature. It is of interest to note that the higher types of plants and animals show more of a beneficial response whereas in the lower types, the response is of an untoward and varied nature (Schneider 1939).

The thyroid hormone increases the activity of cell enzymes which are usually of the oxidative type. In young dogs fed .6 gm. of desiccated thyroid/kg. body weight/day for 3 to 6 weeks, the respiration was increased. The respiration of the liver, heart, and nerves was increased an average of 25% while the respiration of the thyroid gland was decreased 30% (Gerard and McIntyre 1932). Hyperthyroid animals' brain tissue was observed to oxidize glycogen, glucose, fructose, glycerolphosphate, lactate, and succinate at four times the normal rate; the rate of oxidation of glycine, methyl glyoxal, and pyruvate was unchanged. This would indicate that the thyroid hormone increases the activity of the specific dehydrogenases concerned with the oxidation of glucose and its metabolic relatives (Cohen and Gerard 1937). Hyperthyroidism hastened the oxidation of d-amino acids of cells of rat liver and kidneys. The enzyme, d-amino acid oxidase was increased (Klein 1939). The oxygen consumption of hyperthyroid rats' liver, kidney, diaphram, and heart was reported to be increased. These workers reported no increase in the respiration of the spleen, brain, and testes (Gordon and Heming 1944). Thyroid-treated dogs have the ability to synthesize amino acids from pyruvic acid and ammonia *in vitro* faster than control (Zitowskaya 1939).

Inasmuch as vitamins form a part of many tissue enzymes, one might expect that the vitamin requirements are increased in hyperthyroidism. The cocarboxylase content is lower in hyperthyroid animals and falls more rapidly. Extra amounts of thiamine have been shown to protect hyperthyroid rats from weight losses (Peters and Rossiter 1939). Hyperthyroid dogs on a yeast free diet developed anorexia in 17 days while anorexia develops in 32 days in normal dogs. Both thiamine and riboflavin had to be added to the diet of hyperthyroid dogs to prevent anorexia and a fall in weight (Drill and Shaffer 1942). In further studies on dogs rendered hyperthroid by .4 gm. to .6 gm of desiccated thyroid per kg. of body weight the pulse rose to 150 to 160 beats/minute. When yeast was removed from these dogs' diet while they were still receiving thyroid, their pulse dropped to below 100 beats/minute in 30 to 60 days. The rectal temperature of these dogs rose .5 degree while removal of yeast in the diet caused to drop back to normal. The yeast in the diet protected these dogs from a loss in weight (Drill and Hays 1942). More studies of hyperthyroid dogs revealed a blood cholesterol varying within normal limits while the serum phosphatase rose above normal. This rise could be inhibited by a high yeast diet. The serum phosphatase rose after bromsulphalein was retained indicating that the excess thyroid hormone caused liver damage.(Drill and Shaffer 1943). The requirements for vitamins A, B complex, and C are shown to be increased in hyperthyroidism. Vitamin D requirements are probably increased while vitamin E requirements are not affected in hyperthyroidism (Drill 1943).

The thyroid hormone plays an integral part in protein, carbohydrate, fat, vitamin, and mineral metabolism. By heavy feeding of fresh thyroid to dogs, it has been demonstrated that there is an increased protein breakdown and a fall in body weight (Schöndorff 1897). Thyroxine injection results in glyconeogenesis from protein in rats (Soskin 1941). In hypophysectomized dogs, thyroxine injections maintained a normal blood sugar during fasting (Soskin, et al. 1939). Thyroid hormone will also deplete the glycogen stores by glucose oxidation (Althausen 1940). In thyroidectomized dogs, the blood cholesterol, both free and esterified, phospholipids, and total fatty acids rose after thyroidectomy. The cholesterol was 27 to 380% of normal within a short period of time (Chaikoff, et al. 1941). Later work demonstrated that the rise of blood lipids depended upon the nutritional state of the dog. The high blood lipids could be reduced by reducing the caloric intake (Entenman, et al. 1942). The high blood cholesterol resulting from thyroidectomy in dogs could also be prevented by hypophyseotomy (Thompson and Long 1941). Both thyroidectomy and hypophyseotomy in dogs resulted in fatty livers, while thyroidectomy alone did not (Chaikoff, et al. 1943).

The minerals most affected by the thyroid hormone are calcium and phosphorus. Prolonged hyperthyroidism in humans results in osteoporosis and an increased calcium and phosphorus excretion through the kidney and the feces. The extent of mineral excretion was not correlated with the rise in metabolism. Myxedema in humans results in subnormal excretion of calcium and phosphorus (Aub, et al. 1929). Further studies revealed a negative calcium and phosphorus balance in humans (Hansman 1938). In dogs, 1 gm./kg. body weight/day of desiccated thyroid induced hyperthyroidism within three days and excretion of calcium began in the urine (Logan, et al. 1942). Small doses of desiccated thyroid in thyroidectomized dogs lowered calcium excretion and caused an increased intake of calcium. In these studies, small doses of desiccated thyroid restored a positive calcium and phosphorus balance, which effect lasted for some time after the discontinuance of dosage (Breitbarth 1940).

The thyroid hormone increases the activity of the kidney, generally to lower its threshold. Thyroxine treatment in normal dogs resulted in increased clearance of creatinine, glucose, and diodrast. This result was theorized to be due to a combination of the following, 1. Opening of previously inactive nephrons, 2. Increased functional activity of tubular tissue, 3. Hypertrophy of existing tubules and 4. Possibly an influence on the rate of transfer by effects on the activity or the concentration of adenosinetriphosphate (Eiler, et al. 1944). Thyroid feeding to normal dogs and dogs having diabetes insipidus resulted in increased glomerular filtration. Urea clearance was also raised (Hare, et al. 1944). Hyperthyroid dogs have been shown to excrete calcium through the kidney (Logan, et al 1942).

The absorptive powers of the intestine are increased by the thyroid hormone. The increased absorption of carbohydrates is theorized to be due chiefly to a stimulation of phosphorylation (Althauser 1940). Although thyroidectomy in the dog did not decrease jejunal secretion while the metabolism dropped to 85% of normal, thyroxine doses of 1 to 1½ mg/kg. body weight/day to normal dogs resulted in increases of metabolism of 13 to 16% and 27 to 51% respectively with increases of jejunal secretion on both dosages. The increased secretion remained some time after the cessation of the dosage (Fink 1944).

The metabolism of nerve cells is increased with resulting speeding of reaction time and cerebration (Salter 1940). Studies by the Warburg technic indicate the respiration of hyperthyroid brain cells to be 30% above normal (Cohen and Gerard 1937). The administration of .4 gm. of desiccated thyroid/kg. body weight/day for one week to normal dogs, reduced the shock time of intestinal manipulation from negative results even on long periods of manipulation, to 15 to 20 minutes when the intestines were handled (Schachter and

Huntington 1940).

The thyroid hormone results in increased function of the circulatory system such as increasing blood volume, and increasing the rate and strength of heart contractions. Accoring to McIntyre (1931) a dose of .3 gm. dried thyroid/kg. body weight/day given to dogs for 7 to 8 weeks resulted in weight loss and tachycardia. Denervating the heart protected the dogs from heart flutter and death. The animals lost weight on this dosage. A dose of .6 gm./kg body weight/day in the dogs with denervated hearts resulted in weight losses, tachycardia, and temperature elevation. The pulse rate was proportional to the metabolism in 2 dogs. The results are as follows.

Calories/24 hours	Pulse Rate
400	70
450	60
600-800	100
500-700	100-110

Electrocardiogram studies in sheep showed a diminished heart rate and amplitude of the t wave when the sheep were thyroidectomized (Mullick, et al. 1948). Human studies revealed a relationship of metabolism to pulse in children but this relationship was lost as the person aged (Sutliff and Holt 1925). A drop from 140 - 150 to 90 was reported in a number of human cases treated for hyperthyroidism when the metabolism dropped back to normal (Starr, et al. 1924). In human medical practice, this correlation is not of too great value because of the great variability of the pulse and the lack of a complete correlation (Means and Aub 1925).

The sexual apparatus is affected to some extent by the thyroid hormone. There are other functions of the thyroid hormone than in the development of the gonads. A male Jersey was thyroidectomized at 4 months of age and developed myxedema symptoms in 60 days. There was an absence of sex libido but semen extracted by ampulla manipulation produced pregnancy. A dose of 25 gms. desiccated thyroid restored him to normal behavior and sex libido (Peterson, et al, 1941). Similar results were obtained from thyroidectomized cows. Thyroidectomy resulted in abortion in some cases. Ovulation occurred without estrus symptoms and pregnancy was produced by artificial insemination. Thyrotherapy increased milk secretion and produced normal estrus (Spielman, et al. 1945).

The rate of thyroid secretion depends on several factors. Seasonal rhythm has been demonstrated in chicks (Reineke and Turner 1945). The thyroid secretion rate has been shown to be lessened by high environmental temperature in mice (Butt 1949). Hybrid chicks have a higher thyroid secretion rate than pure bred (Mixner and Upp 1947).

The secretion rate is regulated internally by reciprocal relations between the thyroid gland and anterior pituitary, and action of iodine containing compounds upon the thyroid gland itself. Lack of thyroid hormone will result in increased production of thyrotropin by the anterior pituitary while excess thyroid hormone will decrease the thyroid hormone (Leblond and Mann 1942). The oxygen consumption of the thyroid gland is increased by thyrotropin while this effect is nullified *in vitro* by the addition of thyroglobulin. Thus an excess of thyroid hormone would inhibit the thyroid by direct action (Galli-Mainini 1941). Inorganic iodides also inhibit the thyroid gland (Morton, et al. 1944).

The action of the thyroid hormone may be regulated in other ways than by regulation of its production and the physiological limits of the tissue. In guinea pigs, the response to thyroproteins varied as the logarithm of the dosage (Reineke and Turner 1942). Repeated injections of thyroglobulin into rabbits failed to cause a rise in metabolism upon subsequent injections. The worker postulated that antibodies may have been formed to the thyroglobulin (Lerman 1942). Dogs given thyroid preparations, by injection and orally, were stated to form substances in the isobutyl alcohol and acetone extracts of the urine which prevented the action of the thyroid hormone in rats so as to lower the metabolism of the rat (Keeser 1938). In a study made on the various organs of the pig, ox, and man, it was found that the paraxanthine content of the tissue was proportional to its iodine content. Paraxanthine was demonstrated to inhibit the action of thyroxine on the frog heart. The thyroid gland was found to be the highest in antithyroid activity by the paraxanthine determination. The thyroids from humans with toxic goiters were found to be somewhat lower than normal (Carter and Jenkins 1944). This hypothesis is borne out in studies with myxedematous and euthyroid humans. The euthyroid individuals were able to tolerate several times their own thyroid secretion rate of desiccated thyroid without showing a rise in metabolic rate while myxedematous persons gave a marked response in metabolic rate to much smaller amounts of desiccated thyroid (Winkler, et al. 1942). Blood iodine levels and metabolism studies on normal, thyroidectomized and thiourea or thiouracil-treated dogs indicate that the thyroxine destroying properties are not concentrated in the thyroid gland in the dog but are shared by other tissues. Doses of .38 gm. of desiccated thyroid per day caused a small increase in the metabolic rate and a slight increase of the blood iodine. A dose of .77 gm. of desiccated thyroid per day caused similar results with a small loss of body weight. In three to four weeks the blood iodine and metabolism fell back to normal. There was no difference in blood iodine levels in the normal, thyroidectomized and goitrogen-treated dogs. In none of the dogs could the metabolism be raised much above normal. Intravenous injections of 2 mg. of thyroxine for 13 to 27 days produced similar results to oral feeding of desiccated thyroid (Danowski, et al. 1946). Radioactive tracer studies in the rat indicate that large doses of thyroxine are detoxified in the liver and secreted in the bile (Leblond 1949).

Thyroidectomy of Adult Dogs

The early workers were unaware of the parathyroid function, and thus the thyroidectomy symptoms they recorded were mostly those of hypoparathyroidism. Even so, one of the earliest workers noticed that part of the thyroidectomy symptoms in dogs could be overcome by transplanting thyroid glands into them (Schiff 1884). Further attempts at thyroid replacement therapy to thyroidectomized dogs were also clouded by the parathyroid syndrome. Oral administration of fresh thyroid, various thyroid extracts, and an iodinated casein of doubtful potency yielded negative results because the dogs died of tetany. Death usually occurred too early for any myxedematous symptoms to occur. The description is accurate enough to show that the thyroid preparations used, probably aggravated the tetany symptoms (Wormser 1897).

The muscle fiber metabolism of thyroidectomized puppies was 24.2 to 24.8% below normal. Additions of 2 to 4 mg. of thyroxine caused the metabolism to be increased to a ceiling of 50% above normal in some after a period of 8 to 12 days on dosage. The increase was not uniform (Dye 1933). Another author reports that thyroidectomy resulted in a drop of .03 to .5 degrees C or an average of .3 degrees C in body temperature, some decrease in metabolic rate, a decrease in heart weight and heart rate, and an increase in body weight due to fat storage (Binswanger 1936). When female dogs were thyroidectomized, the blood iodine was reported to be relatively unaffected because the iodine concentrated in the ovaries (Perkin and Brown 1938). Thyroidectomy was reported not to decrease the jejunal secretion of adult dogs (Fink 1944). The dog may normally depend upon the thyroid to a lesser degree because the metabolism does not fall to the same extent as in man, and the severe myxedema syndrome was reported to be absent (Danowski 1946).

Studies with Radioactive Iodine

Radioactive iodine studies have revealed that the thyroid gland picks up iodides from the blood stream at a much greater rate than any other tissue. When large enough quantities of iodides were injected, they were found to a great extent in the urine (Hertz, et al. 1938). In previously untreated humans, 50% of the injected iodide is regularily bound (Chapman and Evans 1946). After thyroidectomy, the iodine content of the body normally drops, especially in organs such as the pituitary, adrenals, and ovaries which are otherwise high in iodine (Sturm and Buchholtz 1928). The concentrating action of the thyroid gland may be made use of to test the completeness of thyroidectomy when one uses radioactive iodine and a Geiger-Müller counter (Reinhardt 1942). Dogs' thyroids which had been perfused with iodides one to two weeks previously were prone to assimilate more (Sturm 1930). In humans, the lowest tracer dose of radioactive iodide will yield the greatest percent uptake (Hertz, et al. 1942). The thyroid shows the greatest ability to fix iodides when there is lack of iodine in the diet (Leblond and Mann 1942).

A study using five dogs from 8 to 10 kg. body weight showed a turnover rate of 50 to 100 micrograms of protein-bound iodine in 24 hours. The turnover time was judged to be 4 to 7.5 hours. These studies would indicate that the dog normally secretes 24 to 240 micrograms of thyroxine per day (Taurog, et al. 1947).

Canine Metabolism Determinations

In an early experiment, the dog was used to determine the caloric value of different foods. In this work, Rubner (1894) was able to get close correlation of the caloric intake and the direct and indirect metabolism determinations. Measurements by an indirect method, revealed a marked increase in the metabolic rate upon exposure to cold in dogs (Morgulis 1924). Adrenaline has been demonstrated to raise the basal metabolic rate of dogs. The determinations were made by an indirect method (Boothby and Sandiford 1923). Later work, by the use of a mask type respirometer, gave a host of normal basal values. The metabolism of dogs was demonstrated to be affected by fasting, mange or other skin irritations, and respiratory infections (Kunde 1922; Kunde and Steinhaus 1926). A review of much of the previous results of metabolism determinations on dogs has been compiled and graphed by Brody and Proctor (1932). A wealth of data has been recently obtained on the normal metabolic rate of dogs under light anesthesia. A mask type respirometer was used (Galvao 1946).

The use of anesthetics to produce quiescence in dogs prior to basal metabolism determinations does not vary the result to a great degree. Barbiturates in general produce prompt, dreamless sleep. Anesthetic dosages produce little disturbance of function. The body temperature is slightly lowered while the pulse is quickened (Sollman 1943). Hypnotic doses of Amytal, Barbital Sodium, Dial, Ipral, Neonal, and Phenobarbital produce a 4 to 10% decrease in the metabolic rate of humans (Anderson, et al. 1930). Intravenous anesthesia of humans with Amytal produces only a slight fall in metabolism (Zerfas, et al. 1929). Light anethesia with amytal permits normal labor and uterine contractions in humans (Robbins 1929).

Intraperitoneal injections of 50 to 60 mg./kg. body weight of amytal in the dog to produce deep narcosis, resulted in little change of the respiratory quotient and calories produced. The metabolism usually decreased less than 10% even when the body temperature fell as much as 2 to 3 degrees (Deuel, et al. 1926).

The metabolism remains within normal variability. Anesthesia in goats with Pentobarbital Sodium produces no disturbance of milk secretion (Reineke 1941). The same drug in calves lowered the metabolic rate about 10% (Mukerji 1948). The use of Dial (Ciba Pharmaceutical Co.) at the rate of 0.30 to 0.40 cc. intraperitonealy after previous injection of 10 mg. morphine subcutaneously, resulted in no significant change of metabolic rate in trained dogs which were also run without anesthesia (Galvao 1946). A small drop, approximating 10%, is found in dogs under light anesthesia with Pentobarbital Sodium (Schirmer 1948).

The expression of the metabolic rate of dogs in the past has been varied and problematical. An accurate means of expressing it in terms of surface area would be satisfactory if there were a reliable means of surface area determination in the dog. Meeh's formula for surface area has been much revised especially in humans. Some time ago, the surface area of humans was determined quite accurately by paper molds and a formula devised for calculating it from the individual's height and weight (DuBois and DuBois 1914; 1916). No such formulation has been devised for the dog which is valid for all breeds. Paper mold determinations have lead to a formula using weight, length, and state of nutrition (Cowgill and Drabkin 1927).

Since the formulations vary somewhat from each other on the same dog, a power of the body weight would seem to be the ideal method of expression of metabolism. Meeh's formula involves a constant multiplied by the 2/3 power of the body weight. Lusk reports the 0.60 power of the body weight to give fairly constant values when related to caloric output in young dogs (Lusk 1928). Galvao derived a formula of Calories per hour equal 2.00 $W^{0.90}$, when the weight is given in kg. for metabolism values obtained on dogs under tropical conditions. He discusses the possibility of the warmer climate making the metabolic rate less dependent upon the surface area. Brody, compiling records on all species, arrived at the constant figure of 70.5 calories/24 hours/kg. body weight to the .73 power. This, he also expressed as the .734 power (Brody 1945). In the light of his exhaustive survey, the specific metabolism expressed by Brody, that is the caloric output expressed as a function of the body weight in kg. to the 0.73 power, seems the best way to express metabolic results in this type of research.

EXPERIMENTAL PROCEDURE AND EFFECTS

General Procedure for Metabolism Determinations

Temperature: A certified clinical thermometer was used in all cases to ascertain body temperature, and inserted approximately 3 inches in the rectum, and allowed to remain at least two minutes. The thermometer was shaken down immediately after reading. The temperature was taken before anesthesia, and before the animal became excited. Occasional readings taken after the metabolism determination did not show any depression of temperature during the time involved.

Pulse: An accurate watch was used for 30 seconds, or longer if the pulse tended to be irregular. It was taken from the median artery.

Body Weights: The weight of the operator, holding the dog, was taken on a Toledo non spring scales, and then the weight of the operator alone was subtracted. Weights were taken preceding metabolism runs, and after the animal had been without food for at least 12 hours, thus tending to show a more correct weight.

Basal Metabolic Rate: The dogs were fasted for 12 hours before the tests were made, but were given free access to water. Weights were always taken at the same time of night. After ascertaining pulse, body temperature, and time, Sodium Pentobarbital solution was administered intravenously until a light anesthesia was produced. The Sodium Pentobarbital solution consisted of an aqueous solution of 10% pure ethyl alcohol by volume containing 3% Sodium pentobarbital. The degree of anesthesia was that point at which the pupil of the eye barely contracted and the dog did not resist pressure around the nose. This would indicate whether he would tolerate the fixation of a mask. At this point of anesthesia, the dogs still possessed digital reflexes and reacted to noise and handling. The dog was then allowed to rest for 20 to 30 minutes in order to assure a level rate of metabolism.

In order to correct for atmospheric pressure, a Central Scientific Company mercury barometer was used. The temperature was taken from the water in the metabolism apparatus by a centigrade thermometer for at least five minutes. The caloric factor per liter of oxygen consumed for a dog on a mixed diet is known to be approximately 4.825 by comparison with direct calorimetry (Lusk 1928). The aqueous vapor saturation was assumed to be constant at 80%. As a further check on barometric pressure, another reading was taken after the last dog had been run.

The respirometer was of the Benedict-Roth type and used Wilson's soda lime to absorb the CO_2. This was changed about every 90 runs. A smaller bell was used on dogs to get a greater slope. The ratio was a 1 mm. rise for every 12.6 cc. of O_2 used. The machine was tested before each run by placing a 30 gm. weight on the bell and it was observed if the bell fell over a period of 5 minutes. This was repeated with the mask clamped off, and the valve to it open.

The oxygen used was thus calculated as calories per hour when the dogs were run for at least 6 minutes, or as long as was needed to get a steady slope for a six-minute period.

To convert to a constant figure somewhat in relation to surface area, the specific metabolism was computed as cal./hr./kg.$^{.73}$ (Brody 1945).

Food: Throughout the experiment, the food used was Dickinson's Dog Food given *ad libitum*., manufactured by Albert Dickinson Company, Chicago, Illinois.

Analysis:

Crude protein, not less than		25.0%
Crude fat, not less than		4.0%
Crude Fibre not over		3.5%
Carbohydrate	) not less	
	) than	44.0%
Nitrogen Free extract	)	

This diet was fed *ad libitum* throughout the experiments except for 12 hours previous to the metabolism determinations, at which time the dogs were kept off feed.

Trials with Protamone on Intact Dogs

Procedure: After normal values had been ascertained by at least three consecutive metabolism determinations, the dogs were divided into three groups and placed on Protamone. Group I was given a dosage of 2 mg./kg. for 30 days and then given 12 mg./kg. for 19 additional days. Group II was given a dosage of 4 mg./kg. for 30 days and then given 20 mg./kg. for 19 additional days. Group III was given a dosage of 8 mg./kg.for 30 days and then given 28 mg./kg. for 19 additional days. The dosage of exogenous thyroid was given in capsule form daily.

Effects: Group I included dogs 1, 2, 5A, and 28, Group II included dogs 3, 4, and 27, and Group III included dogs 25, 26, 5B, and 24. These dogs were of several breeds, both sexes, and adults. (table I)

On the lower dosages administered for the first 30 days to all the groups, no apparent symptoms were observed. Although it was impossible to keep food records, the amount consumed may be said to have risen.

As to general appearance, only two dogs appeared to be affected. Dog 5A in group I showed increased vigor and a more luxuriant hair coat than he had previously. Previous to the trial, this dog was somewhat lethargic and had a ragged coat Dog 26 in group III became overexcitable and had an intermittent diarrhoea. His movements may be described as lacking the intelligence normally expected.

On the higher dosages administered for 19 additional days, symptoms of hyperthyroidism began to appear. Food consumption was increased. Differences were not evident by groups, but more by breeds. Dogs 1, 3, 24, and 25, all Cocker-Pointer crosses, were more tense and exhibited a strained expression about the face. Dogs 5B and 27, both Cockers, showed no evident effect. Dog 5A showed no effect on lower dosage. In the Collies, dog 28 showed no effects, dogs 2 and 4 showed some hyperexcitability, and dog 26 became more excitable, with a persistant diarrhoea. Alopecia and a rough coat developed on dog 26. This was due in part to his rubbing against the cage. His facial features assumed those of an older dog.

The values such as Cal./hr/kg.$^{.73}$, body weight, pulse rate, and body temperature did not come to equilibrium during the trial.

Group I, on the lower dosage of Protamone, 2 mg./kg./day, showed a drop of metabolism to 75.8% of normal on the 8th day and then rose to 111.5% of normal on the 17th day. At the end of 30 days it was practically normal again. (tables II and V) The body weight rose to about 110% of normal by the 11th day and remained there (table VIII). The pulse rate rose with the metabolism but remained somewhat higher. It did not show a depression such as the metabolic rate had (table XI). The body temperature remained slightly, but probably not significantly, above normal (table XIV).

Group I, on the higher dosage of Protamone, 12 mg./kg./day showed a rise of metabolism to 131.4% of normal on the 19th day after the start of the higher dosage (tables II and V). The body weight showed an irregular rise (table VIII). The pulse rate and body temperature rose but not to the extent of the metabolic rate (tables VIII and XI). The average metabolism of this is compared with that of two other groups in Fig. 1.

Group II, on the lower dosage of Protamone, 4mg./kg./day, also showed a preliminary drop in metabolism. The metabolism fell to 74.0% of normal on the 8th day, and then rose to 112.9% of normal on the 17th day. At the end of 30 days, it was practically normal again (tables III and VI). The body weight rose to about 106% of normal by the 8th day and remained there (table IX). The pulse rate showed irregular rises above normal (table XII). The body temperature was from 100.1 to 100.8% of normal (table XV).

Group II, on the higher dosage of Protamone, 20mg./kg./day showed little change in metabolism. It fell to 91.4% of normal on the 12th day after the start of the dosage but was about normal on the 19th day (tables II and VI). The body weight rose to 111.3% of normal by the 19th day after the start of the dosage (table IX). The pulse rate was markedly increased 125.2 to 124.7% of normal (table XII). The body temperature was also high, 100.5 to 101.2% of normal (table XV).

Group III, on the lower dosage of Protamone, 8mg./kg./day showed the preliminary drop in metabolism which occurred on the 5th day, when it was 85.2% of normal. The drop was partially repaired by the 8th day. The maximum rise was on the 17th day when the metabolism was 114.3% of normal. After that it dropped back toward normal (tables IV and VII). The body weight rose to about 110% of normal by the 11th day and remained there (table X). The pulse rate was irregular but always above normal (table XIII). The body temperature was 100.0 to 101.3% of normal (table XVI).

Group III, on the higher dosage of Protamone, 28mg./kg./day, showed little change in energy metabolism (tables IV and VII). The body weight rose to 116% of normal (table X). The pulse rate was 120.4 to 119.1% of normal (table XIII). The body temperature was 100.6 to 100.8% of normal (table XVI).

The metabolic response of the intact dogs depended to a large extent upon the breed. The breeds were distributed fairly evenly throughout the groups. The Cocker-Pointer crosses, dogs 1, 3A, 24, 25, showed the least response except that they all showed the characteristic drop in metabolism on the 8th day following the initiation of dosage. They never rose a great deal above normal on any dosage (tables II to VII).

The Collies, dogs 2, 4, and 26 showed a greater response than the Cocker-pointers. Dog 28 was a Collie but of another litter. The Collies showed the drop in metabolism on the 8th day and by the 17th day it rose to its maximum. All were headed downward by the 30th day but 2 and 26 were still about 120% of normal. On the higher dosage, dog 2 rose markedly while the others were relatively unaffected (tables II to VII).

Of the rest, the response was variable. Dogs 28, a Collie; and 27 and 5B Cockers showed the drop about the 8th day but failed to show a marked rise in metabolism on any dosage. Dog 5A, an old dog of doubtful ancestry, failed to show a drop in the metabolic rate and was 102.8 to 132.4% above normal on 2mg./kg./day of Protamone and 125.6 to 132.6% of normal on 12mg./kg./day of Protamone (tables II to VII).

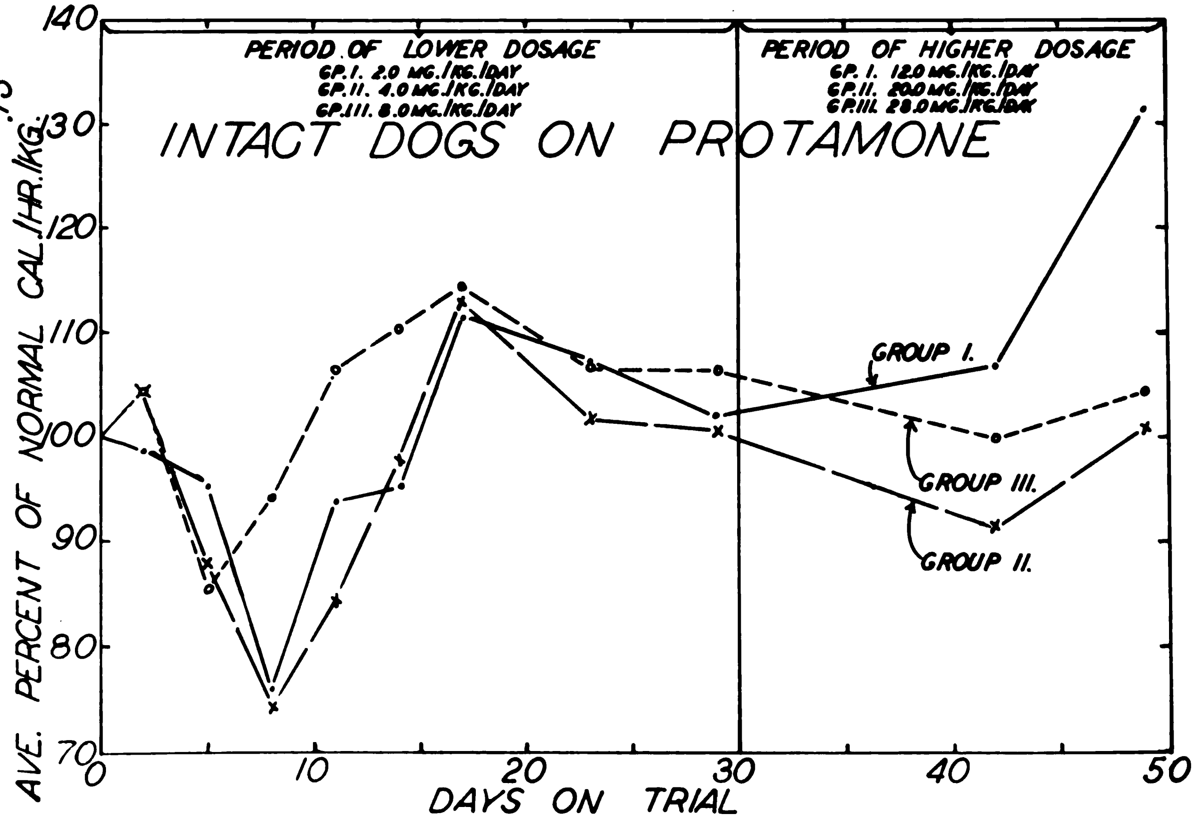

Figure 1

The effects of Protamone on the metabolic rate of three groups of intact dogs.

	1st 30 days	last 19 days
Group I	2.0 mg./kg./day	12.0 mg./kg./day
Group II	4.0 mg./kg./day	20.0 mg./kg./day
Group III	8.0 mg./kg./day	28.0 mg./kg./day

Trials with Desiccated Thyroid on Intact Dogs

Procedure: Two mature dogs were used in this study, Number 6 was an aged mongrel weighing about 9 kg. and about 7 years of age. The muzzle hairs were graying. Number 29 was a 5 year old, male, Scotch Terrier weighing about 8 kg. Number 6 was given 4 mg. per kg. of body weight and number 29 was given 2 mg. per kg. of body weight. The trial was continued 28 days.

Effects: There were no visible effects upon the dogs' behavior or appetite in any stage of the trial. The metabolism followed the same trend as that observed with the intact dogs given Protamone. The values obtained at the seventh day after the start of the trial were 67 to 70% of previous normal. The following values were close to previous normal and did not go much above or below normal (tables XVII and XVIII). The body temperature did not deviate much from normal and may have risen very slightly above normal (table XXI). The body weight of the dogs declined slightly on experiment (table XIX). The pulse of the dogs showed a rise some 20 to 30% above normal (table XX). The above effects are summarized in Fig. 2.

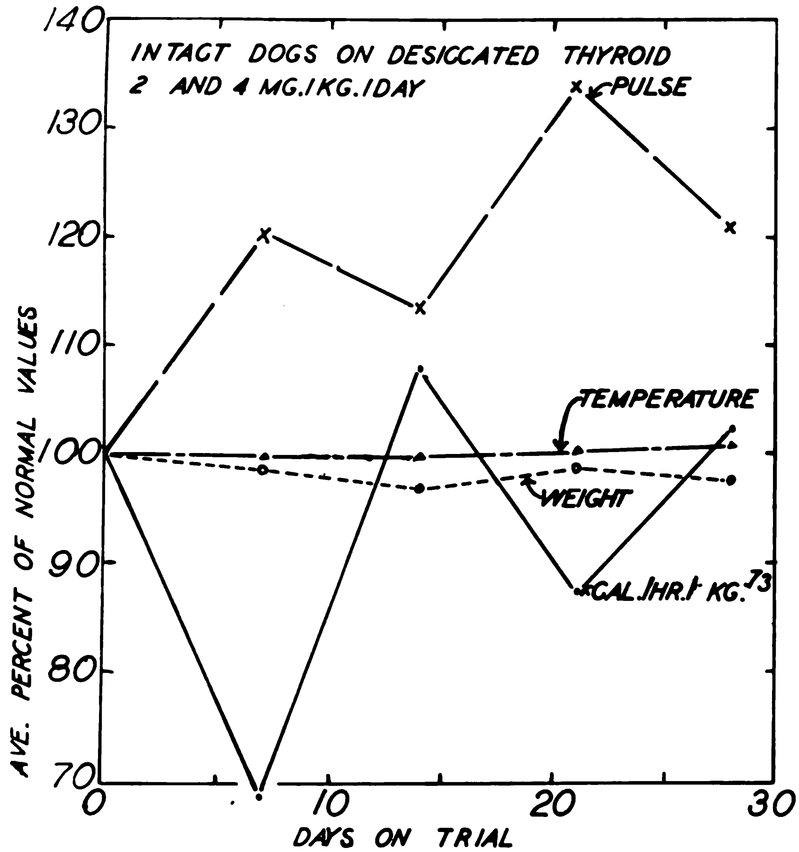

Figure 2

The effect upon metabolism, body weight, pulse rate, and body temperature of intact dogs receiving Desiccated Thyroid at the rate of 2 to 4 mg./kg./day for 28 days.

Long Time Trial with Protamone on Intact English Bull Dog Bitches

Procedure: Three adult English Bull Dog bitches were included in the trial. Number 1 was 3½ years old and had whelped a litter of 4, 2 of which had survived. She whelped 58 days previous to trial and weaned the pups 7 days previous to the beginning of trial. At the start of trial, she was gaunt, especially in the flanks, and shedding excessively. Number 2 was 2 years old and had whelped a litter of 8, 5 of which survived. She whelped 45 days previous to trial and was on trial the last 5 days before weaning. Number 3 was 1 year old and a maiden.

Dogs number 1 and 3 were put on 2 grams of Protamone per 100 lbs. of dry matter and number 2 was allowed to remain as a control.

The diet was fed once daily in the following proportions:

6 oz. Condensed Milk (75% water)

8 oz. Canned dog food (74% water)

8 oz. Dry meal

The meal was ground "Gropup" and supplied by the Kellogg Co., of Battle Creek, Michigan. Its guaranteed analysis was as follows:

Protein (Minimum)	22.5%
Fat (Minimum)	3.5%
Fiber (Maximum)	4.0%
Moisture (Maximum	8.0%

Nitrogen Free Extract (Minimum)	50.0%
Ash (Maximum)	9.0%
Potassium iodide was in the meal at	.00037%

The canned dog food was "Pard", marketed by Swift & Co. of Chicago, Illinois. Its guaranteed analysis was as follows:

Protein (Minimum)	10.5%
Fat (Minimum)	2.5%
Nitrogen Free Extract (Minimum)	9.0%
Fibre (Maximum)	1.0%
Ash (Maximum)	3.0%
Moisture (Maximum)	74.0%
Calcium (Maximum)	.65%
(Minimum)	.45%
Phosphorus (Minimum)	.30%
Salt (Maximum)	.75%
.50% iodized salt	

The diet was deemed adequate and the Protamone mixed in the meal in a proportion so that there was 2 grams of Protamone per 100 lbs. of dry matter fed. The amount fed, was the amount the dogs would clean up in 20 minutes.

The weights of the dogs were taken in the afternoon and the dogs were fed in the morning.

Effects: No evidences of changes were seen in Dog 2, the control, and dog 3 on Protamone. Dog 1 recovered from her poor condition by filling in at the flanks in the first three weeks. Her hair coat assumed a sheen and the shedding stopped during this period. The weight records of all the dogs revealed no marked difference between the control and the treated dogs (table XII).

For the first 48 days of the trial, the treated dogs received an average of 36.0 mg./day of Protamone. This would be about 2.0 mg./kg./day. For the last 100 days of the trial, the treated dogs received an average of 32.6 mg./day of Protamone. This would be about 1.7 mg./kg./day.

The radioactive iodine studies showed no definite depression of the thyroid gland activity (pg. 48).

The dogs all came into estrus normally while on trial.

Thyroidectomy

Procedure: The object was the complete removal of all the thyroid tissue, leaving as much parathyroid tissue as possible. In all cases, the two lateral parathyroids were left.

The operative procedure was done under sodium pentobarbital anesthesia and performed aseptically. A midline incision was made from the region of the thyroid carilage for about two inches posteriorly. The ribbon muscles ventral to the trachea were separated by blunt dissection. The thyroid was found on either side as an almond-shaped, reddish-brown gland, near the angle of the jaw and adjacent to the carotid sheath. The carotid artery could be palpated in this area, thus aiding in location. The vessels inferior to the gland were ligated with catgut and the gland dissected out, leaving vessel attachments. The lateral parathyroid was located as a pink, oval structure on the lateral surface of the thyroid. By use of a sharp, pointed scissors and small hemostat this was dissected free from the thyroid and its blood supply also was dissected free from the thyroid until it was possible to ligate the superior thyroid vessels without including those of the parathyroid. The superior vessels were ligated and the thyroid removed. This was repeated with the other thyroid. In some instances the parathyroid was high on the thyroid and it was impossible to remove it and its blood supply without including some thyroid tissue. In this event, the parathyroid was dissected free and inserted into the muscular tissue.

The ribbon muscles were sutured with catgut and, after sulfa-urea application, the skin was sutured with nylon. The dermal sutures were removed on the fifth day. The procedure of surgery is outlined by Markowitz (1937). Anatomy of the region is outlined by Sisson (1938).

No symptoms indicative of injury to the recurrent laryngeal nerves were observed.

Thyroid Weights:

Dog No.	Wt. left Gland	Wt. rt. Gland	Thyroid wt. as Per Cent of Body Wt.	Remarks
1	.6249	.4470	.00812	Group I: Protamone 2mg./kg. 10/19-11/19 12mg./kg. 11/20-12/16
2	.4447	.5245	.00740	
5A	.4170	.4953	.01049	
28	.4446	.4751	.00578	
3	.2105	.2943	.00407	Group II: Protamone 4mg./kg. 10/19-11/19 20mg./kg. 11/20-12/16
4	.2485	.2440	.00291	
27	.2000	.3684	.00458	
25	.3227	.3900	.00532	Group III: Protamone 8mg./kg. 10/19-11/19 28mg./kg. 11/20-12/16
26	.6604	.5567	.00665	
5B	.3117	.3549	.00580	
24	.3988	.4332	.00527	

The only evident difference seen here is that the dogs in Groups II and III had smaller thyroids, indicating that the Protamone had more depressing effects upon thyroid activities in higher dosages. There was no control group of the same breeds, so a further comparison would be of little value. Groups II and III had thyroids of almost the same size.

Individual Surgery Reports and Aftercare: The Calcium Gluconate used was a 10% aqueous solution with 10% dextrose and given intravenously and intraperitoneally (McClean 1942). The Parathyroid Extract (description of dogs, table I) was U. S. P., 1 cc. equaling 100 units (Albright 1942).

Group I

Number 1 was thyroidectomized 12/8/48 with a rather difficult dissection of the parathyroids. However, both were left intact. Three days later some tetany developed, alleviated by calcium gluconate. Moderate tetany developed for two days afterwards and was treated as before with the addition of .1 cc parathyroid extract intramuscularly and calcium chloride in the drinking water. There was no recurrence of tetany and recovery followed.

Number 2 was thyroidectomized 12/9/48 with an easy dissection of the parathyroids leaving both of them intact. On the third day there was some twitching which ceased upon calcium gluconate injection. The procedure was repeated on the fourth day. Calcium chloride was included in the drinking water. On the 14th and 15th day, tetany occurred and was treated by calcium gluconate injection. However, the dog died in coma on the 15th day.

Number 5A was thyroidectomized 12/9/48 with a difficult dissection of the parathyroids. Both the parathyroids were dissected free and replaced in muscle. There were no symptoms of tetany following the surgery.

Number 28 was thyroidectomized 12/9/48 with an easy dissection of the parathyroids leaving both of them intact. There were no symptoms of tetany following the surgery.

Group II

Number 3 was thyroidectomized 12/8/48 with a difficult dissection of the parathyroids. Both parathyroids were dissected free and replaced in muscle. Tetany occurred 3 days afterwards and was treated with calcium gluconate. Less severe tetany occurred the 4th and 5th day and was treated with calcium gluconate and .1 cc injections of parathyroid extract. Calcium chloride was put in the drinking water. Tetany occurred intermittently under treatment until the 18th day when the dog died in coma.

Number 4 was thyroidectomized 12/9/49 with a rather difficult dissection of the parathyroids. One gland was left intact while the other was dissected out and replaced and inserted into muscle. Tetany occurred on the 3rd day, was worse on the 4th and the dog died on the 5th day despite treatment with calcium gluconate and .1 cc parathyroid extract.

Number 27 was thyroidectomized 12/9/48 with an easy dissection of the parathyroids leaving both glands intact. There were no symptoms of tatany following the surgery.

Group III

Number 24 was thyroidectomized 12/8/48 with a difficult dissection of the parathyroids. However, both were left intact. Violent tetany occurred on the 3rd day. Calcium gluconate injections alleviated the convulsions but they reoccurred on the 5th day and were followed by death.

Number 25 was thyroidectomized 12/8/48 with a difficult dissection of the parathyroids. However, both were left intact. Severe convulsions occurred on the 3rd, 4th, and 5th days but were alleviated by injection of calcium gluconate and .1cc parathyroid extract. Severe tetany recurred on the 7th day, followed by coma and death despite calcium gluconate injections.

Number 26 was thyroidectomized 12/9/48 with a fairly difficult dissection of the parathyroids. One gland was left intact while the other was dissected free and reinserted into the muscle. Twitching occurred on the 2nd day and continued through the 5th under treatment with calcium gluconate and .1cc parathyroid extract. Intermittant periods of twitching occurred for 18 days and were treated with calcium gluconate injections and calcium chloride in the drinking water. Recovery followed.

Number 5B was thyroidectomized 12/9/49 with an easy dissection of the parathyroids leaving both glands intact. Slight twitching occurred on the 3rd and 4th days which was alleviated by calcium gluconate injections. On the 6th day, sudden tetany occurred, however, followed by coma and death.

<u>Dogs Previously Untreated</u>: All of these dogs were used in the Studies with Protamone and Desiccated Thyroid in Thyroidectomized Dogs together with dogs 1 and 27 from the Studies of Protamone on Intact Dogs (Described in table XXXII).

Number 2 was thyroidectomized 12/13/48 with a difficult dissection of the parathyroids. One gland was left intact and the other dissected free and reinserted into the muscle. There were no symptoms of tetany following the surgery.

Number 3 was thyroidectomized 12/13/48 with an easy dissection of the parathyroids leaving both glands intact. There were no symptoms of tetany following the surgery.

Number 4 was thyroidectomized 12/3/48 with a rather difficult dissection of the parathyroids. One gland was left intact and the other dissected free and reinserted into the muscle. There were no symptoms of tetany following the surgery.

Number 24 was thyroidectomized 12/13/48 with an easy dissection of the parathyroids leaving both glands intact. There were no symptoms of tetany following the surgery.

Number 25 was thyroidectomized 12/13/48 with an easy dissection of the parathyroids. Both glands were left intact. There were no symptoms of tetany following the surgery.

Tetany Effects:

	Group I	Group II	Group III	Previously Untreated
Number of dogs in the group	4	3	4	5
Number of dogs developing tetany	2	2	4	0
Average days for tetany to develop	3	3	2.8	-
Number which succumbed	1	2	3	0
Number which survived	3	1	1	5

Group I received 2 mg. Protamone/kg./day for 30 days followed by 12 mg. Protamone/kg./day for 19 days.

Group II received 4 mg. Protamone/kg./day for 30 days followed by 20 mg. Protamone/kg./day for 19 days.

Group III received 8 mg. Protamone/kg./day for 30 days followed by 28 mg. Protamone/kg./day for 19 days.

The previously untreated group had no previous dosage of exogenous thyroid.

The effects of the surgery were to remove two of the four parathyroid glands and injure, or completely sever in some cases, the blood supply to the two remaining. The surgery was all performed by the author and thus differences in technic would be negligible. The extent of damage to the parathyroid's blood supply was not the determining factor in the development of tetany from hypoparathyroidism. For example, dog number 5A had his parathyroids reinserted and developed no tetany. The greater the previous dosage of Protamone, the quicker the development of tetany, the greater the fatality, the less survival, and the greater the number developing tetany. None of the dogs previously untreated developed tetany while all of the dogs on the highest dosage of Protamone developed tetany.

Effects of Thyroidectomy: Normal values were obtained from only those dogs which had been on previous Protamone studies and thus the comparisons with the normal runs were complicated by the effects of the protamone. Values were obtained from dogs number 1, 5, 26, 27 and 28. These dogs were formerly on

Protamone (tables II to XVI). In the case of dogs number 5 and 28 no drop could be seen in calories per hour per body weight, pulse rate, and body temperature. The body weight of both dogs was seen to change but little (tables XXIII to XXVII). In both of these dogs, radioactivity tests showed a retaining power for the I* and thus may be assumed to have had some thyroid function left (pg. 45). They also showed no other symptoms of thyroidectomy. For these reasons they were omitted from this phase of the study.

TABLE OF THYROIDECTOMY EFFECTS
(Compiled from tables XIII to XVII) Dogs 1, 26 and 27

	Normal	Average after Thyroidectomy	% of Normal
Cal./hr./kg.$^{.73}$	4.714	3.402	72.2
*Body weight (kg.)	13.0	15.2	117.0
Pulse rate/min.	86.8	72.6	83.8
Body temperature (degrees F.)	100.0	99.5	99.5

*The body weight was 113.1% of normal at the time of thyroidectomy.

Dogs number 1, 26 and 27 were seen to react within 35 to 40 days after the thyroidectomy by a marked fall in specific metabolism of nearly 30% while the body weight rose slightly. The pulse made a less sizable drop than the specific metabolism. The body temperature dropped an average of 0.5 degrees F.

Other effects of thyroidectomy on the above dogs were a general lethargy, and loss of appetite. They showed little inclination to play or romp as had been their previous custom. There was a slight but perceptible edema of the lower portions of the body such as the brisket and legs. One Cocker (#27) showed edema of the face. Less pentobarbital was needed to produce light anesthesia. Other dogs for which no pre-thyroidectomy determinations had been made showed similar symptoms of edema and lethargy. The progressive decline in metabolism and pulse rate with increasing time after thyroidectomy is shown clearly in Fig. 3

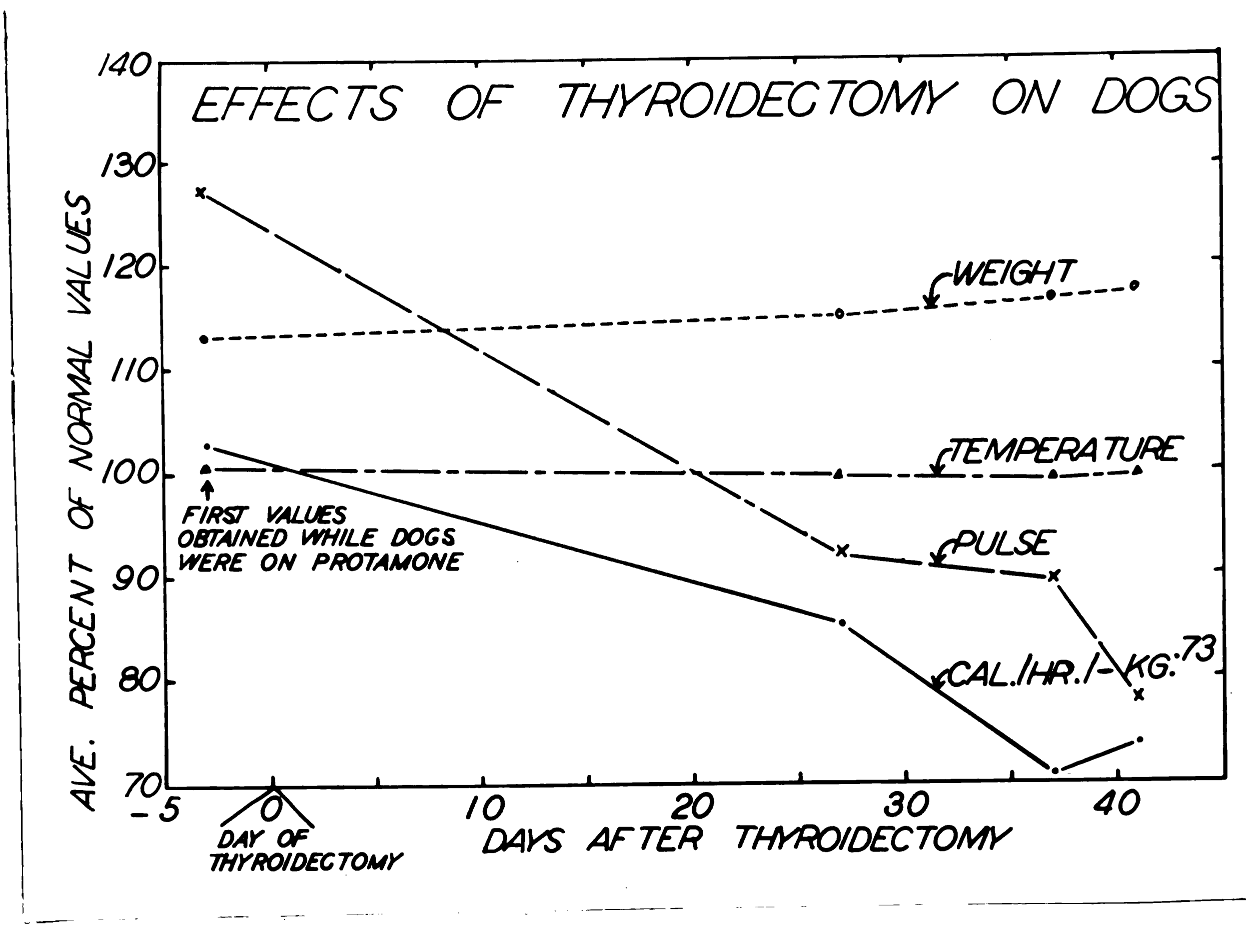

Figure 3

The effects of thyroidectomy on the metabolism, body weight, pulse rate, and body temperature. The first values obtained were gotten on the last day that they received Protamone. The normal values were obtained previous to the Protamone trial.

I*131 Determinations on Thyroidectomized Dogs

Procedure: The procedure was essentially that of Reinhardt to determine the completeness of the thyroidectomy and determine if there was any remaining thyroid tissue (Reinhardt 1942) (dogs described tables I and XXXII).

Five cc. of a solution of I*131 (1000 counts per minute per cc.) was injected into the dogs' radial veins. Counts over this area 2 minutes after injection revealed no foci of activity, thus verifying completeness of injection. Counts were obtained by a Geiger-Muller counter, over the regions of the kidney, extremities, body, heart, and thyroid. Besides the thyroidectomized dogs, a new dog from the pound was included as a control.

Results of I*131 Injection on a Normal Dog: Counts after injection of I* in a normal dog. Figures are in counts per minute on the Geiger-Muller counter. The dog's weight was 10.5kg.

Time	Extremities	Thyroid	Kidney	Heart
5 min.	** ---	** ---	350	** ---
10 min.	** ---	250	300	250
20 min.	** ---	250	300	250
$1\frac{1}{2}$ hr.	** ---	300	300	200
$3\frac{1}{2}$ hr.	50	250	200	100
8 hr.	25	350	100	50
24 hrs.	50	900	100	** ---
6 days	50-60	800-900	50-60	50-60
13 days	15-20	350-450	0	0
19 days	0-5	150	0	0

** no determination made

<u>Results of I*131 Injection on Thyroidectomized Dogs</u>:

Counts after injection of I* into thyroidectomized dogs. Figures are in counts per minute on the Geiger-Muller counter. The dogs are described in table XXXI. Ext. - extremities; Thy. - thyroid region; K. - kidney region; H. - heart region. *Body weight in kg.

Dog No.	Wt.*	24 hrs. Ext.	24 hrs. Thy.	24 hrs. K.	24 hrs. H.	53 hrs. Ext.	53 hrs. Thy.	53 hrs. K.	53 hrs. H.
1	12.3	5-10	5-10	25	5-10	0-5	0-5	0-5	0-5
2	9.6	35	35	50	60	0-5	0-5	25	10
3	9.7	30-35	35	260	100	0-25	5-15	5	15
4	8.7	20-35	15-25	160	35	15	15	25	20
5	8.9	40	90a	120	120	25	50-80a	80	50
24	19.3	30	20-25	160	25	5-10	0-10	25	10-15
25	12.9	35	35-40	310	35	15	5-15	15	15-20
26	18.7	25-30	25-30	50	20-25	10-20	10	30	20
27	13.8	40	30-35	60	35	10	10	10	10
28	15.5	25	25-30	110	30	5-15	5-15	100	15

a- mostly in the thymus region

The rapid disappearance of the I*131 from the thyroidectomized dogs was in marked contrast to the normal. In none of the dogs except number 5 was there any high incidence of count over the thyroid region in relation to the extremities and in this individual it was in the region of the thymus. The high initial count over the heart and kidneys would indicate circulating iodide rather than thyroxine. However, number 28 retained a high count especially over the kidney region.

Autopsy of Dogs with Indications of Thyroid Function: Inasmuch as both 5 and 28 had retaining powers for the I*131, it would indicate that they had some thyroid function left. Their metabolic rate had not dropped from the normal rate, (table XIV). Accordingly, they were sacrificed and autopsied 65 hours after injection of I*131.

Autopsy of Number 5

No thyroid tissue was found in the region of the removed thyroid. Both parathyroids were found functioning. The counts were as follows on the Geiger-Muller counter:

Body and extremities	20
Thymus	40-50
Liver	80
Kidney	20
Spleen	80
Aorta region	20-80 (80 where the aorta passes through the diaphram)

Autopsy of Number 28

No thyroid tissue was found in the region of the removed thyroid. Both parathyroids were found functioning. The counts were as follows on the Geiger-Muller counter:

Body and Extremities	10
Thymus	15
Liver	20
Kidney	20
Spleen	20
Aorta region	15-20
Adrenal	60

The retention of iodine would indicate some thyroid activity.

I*131 Determinations on Intact Dogs

Procedure: It was the objective to determine the effect of feeding exogenous thyroid materials on the function of the thyroid gland.

The dogs used were the English Bull Dog bitches on the long time trial on Protamone, dogs I, II, and III (pg 32); the intact dogs on desiccated thyroid, dogs 6 and 29 (pg 30); and the English Bull Dog Puppies on the growth experiment with Protamone (pg.80).

A solution of I*131 was injected into the radial vein and counts were taken over the area two minutes later to determine the completeness of injection. The solution used contained other iodides than the I*131. The English Bull Dog puppies and dogs 6 and 29 were injected with 2 cc of a solution of I*131 (1000 counts per minute per cc.) while the English Bull Dog bitches were injected with 4 cc. of the same solution. Counts were obtained over the thyroid region and the extremities. t values were calculated after the thyroid gland had picked up its maximum count (1 hr.) by the following formula: t equals $\frac{\text{counts per minute/body weight}}{\text{counts per minute injected}}$

Results of I*131 Injection on Intact English Bull Dog Bitches: The amount of iodine picked up by the thyroid gland of dog II (control) was slightly lower than in dogs I and III. The regression of the logs. of the t values was y equals .009177x -2.9249 for dogs I and III and y equals .005139x - 3.1035 for dog I. This would indicate a greater thyroid turnover of iodine in the treated dogs. The greater pickup of I* would indicate greater thyroid gland activity in the treated dogs.

<u>Results of I*131 Injection on Intact Dogs Receiving Desiccated Thyroid</u>: Both dogs were receiving desiccated thyroid for 28 days previous to the I*131 injection; number 6 at the rate of 4 mg./kg./day and number 29 at the rate of 2 mg./kg./day (described pg. 30). The counts picked up by the thyroid gland were low in relation to the extremity counts. The regression equation of the logs. of the t values was y equals .007252x-2.6295, indicating a low thyroid turnover of iodine (table XXIX) in these dogs. The small pickup of iodine by the thyroid would indicate low thyroid activity.

<u>Results of I*131 Injection on Intact English Bull Dog Puppies</u>: These dogs were in two groups, the control group consisting of dogs number 1, 3, 5, and 6, and the group receiving Protamone at the rate of 4 gm./100 lbs. dry matter for 48 days consisting of dogs number 2, 4, and 7 (described pg. 80). The uptake of iodine by the thyroid gland was slightly greater in the control group. However, the regression equation of the logs. of the t values was y equals .01003x-2.6488 for the control group and y equals .01131x-2.8194 for the group receiving Protamone. This would indicate the thyroid turnover rate of iodine was similar in both groups (tables XXX and XXXI). There was a lowered pickup of iodine by the thyroid glands of the Protamone group. Results of all I* determinations are summarized in Fig. 4.

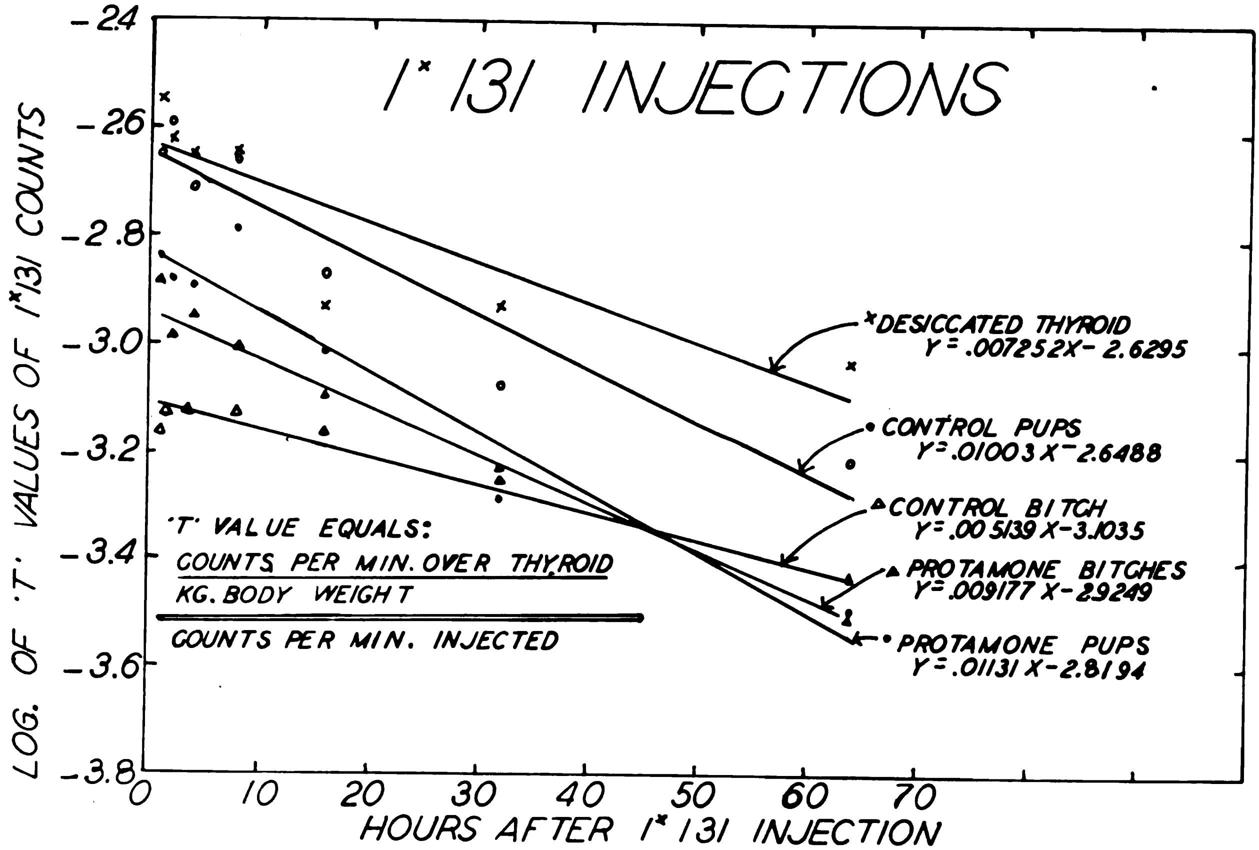

Figure 4

The log. of the t values of the thyroid counts at various times after the I*131 injection. The regression lines were calculated by the method of least squares.

Trials with Protamone and Desiccated Thyroid on Thyroidectomized Dogs

Procedure: The general procedure for obtaining the metabolism, pulse rate, body weight, body temperature and the feeding schedules was identical with that described previously (pg 21). The dosage of exogenous thyroid was given in capsule form once daily. Aftertwo runs were completed at the thyroidectomy level, dosage was initiated for for the Protamone group at 0.5 mg./kg. and continued for 14 days; on the 15th day it was increased to 1.0 mg./kg. The dosage was then increased to 2 mg./kg and continued for 14 days. The desiccated thyroid group received desiccated thyroid containing 0.3% Iodine and supplied by Parke, Davis & Co. of Detroit, Michigan. The initial dosage of 2 mg./kg. was continued for 14 days. The dosage was then 4 mg./kg. for 22 days, and finally increased to 8 mg./kg. for the last 14 days.

Effects: The Protamone group included dogs 1, 3 and 4. The desiccated thyroid group included dogs 2, 24, 25 and 27. These dogs were adults of both sexes (tableXXXI).

At the beginning of the trial, all of the above dogs showed the thyroidectomy symptoms of lethargy, poor appetite, and edema. On the sixth day following the initiation of dosage, there was a lessening in the extent of edema in numbers 1, 3, 4, and 24. These dogs appeared to be more lively although the difference was still not clear-cut. By the thirteenth day after the start of dosage, the evidence of edema was gone in all the dogs. At this time, numbers 1, 2, 3, and 4 appeared lively while numbers 24, 25, and 27 were still sluggish. By the 20th day after the onset of the low dosage or after the dogs had been on the medium dosage for 6 days, all were lively and no differentiation was possible. No further changes in behavior were evident in the dogs throughout the remainder of the experiment.

On the 11th day, dog number 2 came into estrus. Symptoms of this were observed four days prior to this. She remained in estrus for five days.

Lower Dosage of Protamone and Desiccated Thyroid on Thyroidectomized Dogs. (Compiled from tables XXXII to XLII)

Dogs 1, 3, and 4 on Protamone 0.5mg./kg./day

Dogs 2, 24, 25 and 27 on Desiccated Thyroid 2mg./kg./day

	Average % of Thyroidectomy Level on Dosage of Protamone	Average % of Thyroidectomy Level on Dosage of Desiccated Thyroid
Cal./hr./kg.$^{.73}$	107.7	105.0
Body Weight	103.1	103.2
Pulse Rate	99.8	106.7
Body Temperature	99.9	100.3

Medium Dosage of Protamone and Desiccated Thyroid on Thyroidectomized Dogs. (Compiled from tables XXXII to XLII).

Dogs 1, 3, and 4 on Protamone 1.0 mg./kg./day

Dogs 2, 24, 25, and 27 on Desiccated Thyroid 4 mg./kg./day

	Average % of Thyroidectomy Level on Dosage of Protamone	Average % of Thyroidectomy Level on Dosage of Desiccated Thyroid
Cal./hr./kg.$^{.73}$	140.8	122.2
Body Weight	106.1	105.6
Pulse Rate	95.3	109.4
Body Temperature	100.0	100.4

Higher Dosage of Protamone and Desiccated Thyroid on Thyroidectomized Dogs. (Compiled from tables XXXII to XLII).

Dogs 1, 3, and 4 on Protamone 2.0 mg./kg./day

Dogs 2, 24, 25, and 27 on desiccated thyroid 8 mg./kg./day

	Average % of Thyroidectomy Level on Dosage of Protamone	Average % of Thyroidectomy Level on Dosage of Desiccated Thyroid
Cal./hr./kg.$^{.73}$	132.2	131.3
Body Weight	109.0	107.1
Pulse Rate	104.2	115.0
Body Temperature	100.0	100.7

The lower dosages of Protamone (0.5 mg./kg./day) and desiccated thyroid (2.0 mg./kg./day) resulted in small, approximately equal rise in metabolism and body weight in both groups. The pulse rate and body temperature were little if any affected except that the pulse rate in the desiccated thyroid group was raised moderately. (Figs. 5, 6, and 7).

The medium dosages of Protamone (1.0 mg./kg./day) and desiccated thyroid (4.0 mg./kg./day) resulted in a marked rise in metabolism in both groups with the Protamone group higher and probably up to the normal rate. The weight rise in both groups was equal. Pulse and temperature were slightly higher in the desiccated thyroid group.

The higher dosages of Protamone (2.0 mg./kg./day) and desiccated thyroid (8.0 mg./kg./day) resulted in a slight decline of metabolism in the Protamone group and a rise of this value in the desiccated thyroid group up to the value of the Protamone group. The rise in body weights was nearly equal between groups. The pulse and body temperature were slightly higher in the desiccated thyroid group.

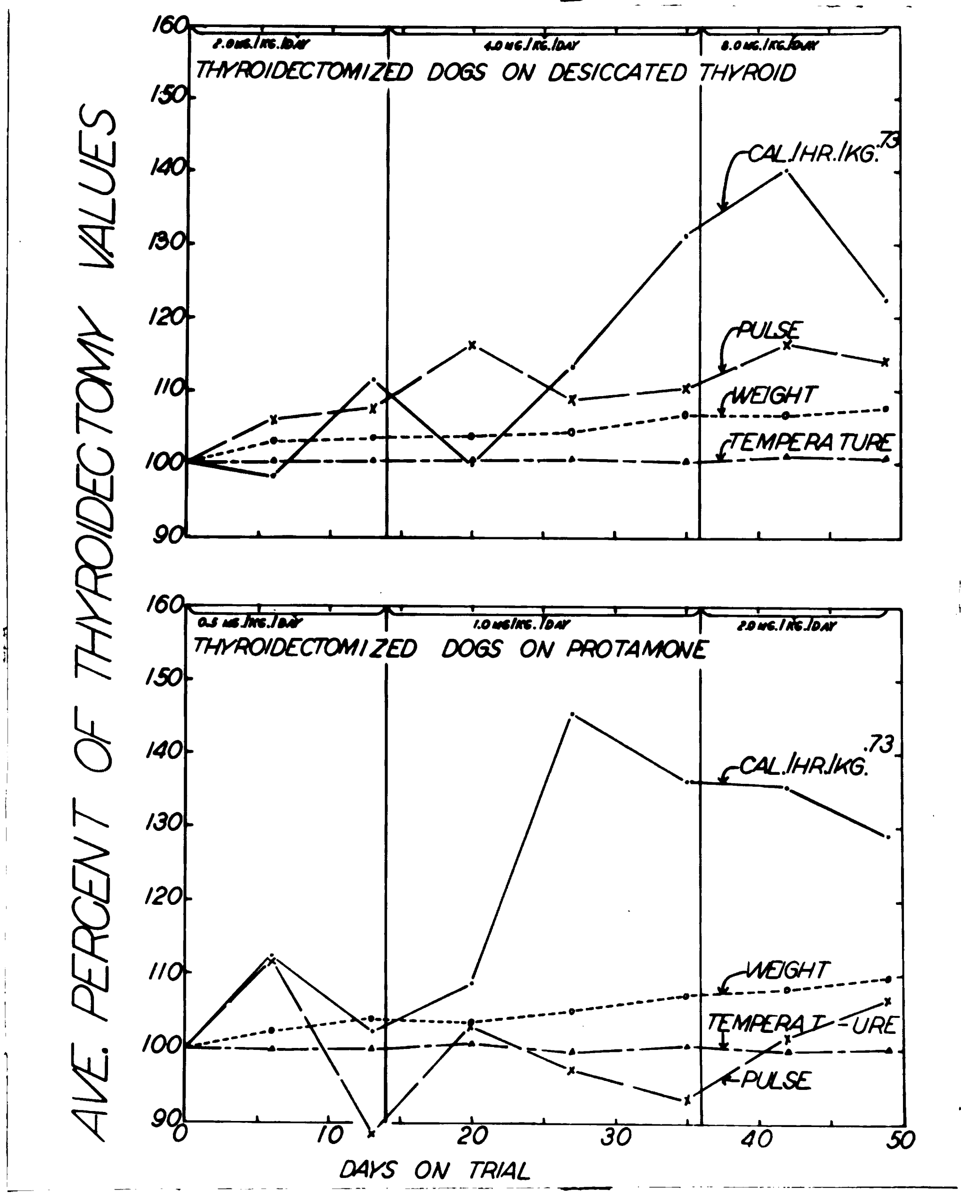

Figure 5

The effects on dogs' metabolism, body weight, pulse rate, and body temperature of Desiccated Thyroid (50% stronger than U. S. P.). The dosage was as follows:

1st	14 days	2 mg./kg./day
next	22 days	4 mg./kg./day
next	14 days	8 mg./kg./day

Figure 6

The effects on dogs' metabolism, body weight, pulse rate and body temperature of Protamone. The dosage was as follows:

1st	14 days	0.5 mg./kg./day
next	22 days	1.0 mg./kg./day
next	14 days	2.0 mg./kg./day

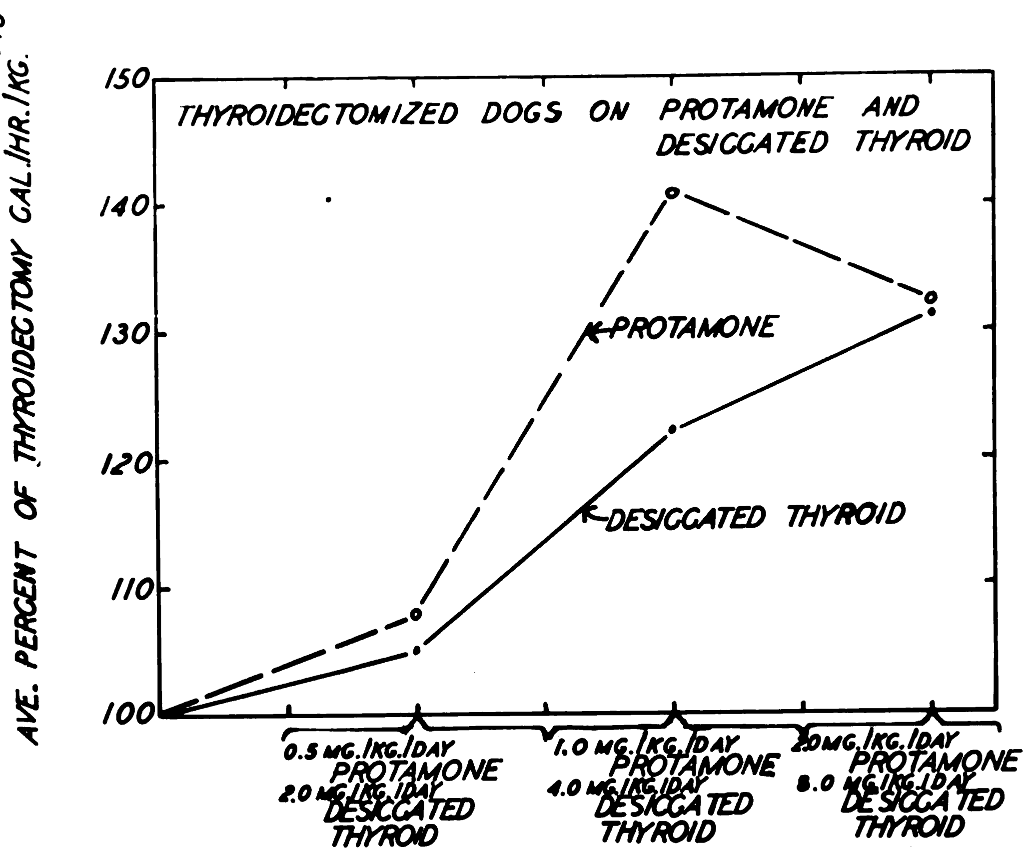

Figure 7

The effects on metabolism of dogs when given Protamone and Desiccated Thyroid in various dosages after the exogenous thyroid had time to become effective. 0.5, 1.0, and 2.0 mg./kg./day of Protamone was given while 2.0, 4.0, and 8.0 mg./kg./day of Desiccated Thyroid was given.

COMPARISONS OF POTENCY OF PROTAMONE AND DESICCATED THYROID

The Protamone was of lot P. A. 2-011 supplied by Cerophyl Laboratories. Isotope dilution values of the preparation gave 0.578% thyroxine while the butanol extraction of thyroxine-like compounds gave a value of 3.5% (Reineke, et al. 1949).

The desiccated thyroid was 50% stronger than U. S. P., containing 0.3% iodine, supplied by Parke Davis Co. Assuming that 25% of the iodine was thyroxine iodine, this would yield a value of 0.1147% thyroxine.

Thus, the Protamone by chemical methods of analysis would appear to be 5.04 times as potent as the desiccated thyroid.

The trials with Protamone and desiccated thyroid on the thyroidectomized dogs yielded a more accurate comparison of the two. The last two runs may be taken, when the dosage of both preparations was highest, the metabolism of the Protamone group was 132.2% of the thyroidectomy level while the metabolism of the desiccated thyroid group was 131.3% of the thyroidectomy level. Inasmuch as the dosage of Protamone was 2mg./kg./day while the dosage of desiccated thyroid was 8mg./kg./day, the Protamone would appear to be 4 times the strength of the desiccated thyroid. If, however, the 1 mg./kg./day of Protamone which raised the metabolism to 140.8% of thyroidectomy level, is compared with the 8 mg./kg./day dosage of Desiccated Thyroid which raised the metabolism to 131.3% of the thyroidectomy level, the Protamone would appear to be 8 times the strength of the desiccated thyroid.

Another method of comparison makes use of the .73 power of the body weight in kg. When the percentage rise above the thyroidectomy level of the Cal./hr./kg.$^{.73}$ is divided by the body weight in kg.$^{.73}$ a constant figure is obtained for all the thyroidectomized dogs on all dosages. This was averaged for each dosage for each group. Then these averages were added for each group and compared. By this comparison, the Protamone appeared 5.131 times as potent as the desiccated thyroid. This result agrees very closely with the ratio of 5.04 estimated from the thyroxine content of the Protamone, as estimated by the highly specific isotope dilution method, and the probable thyroxine content of the desiccated thyroid.

DISCUSSION

The normal metabolic rates of the dog as determined in this study were within the range reported in Brody's compilations (1932) and the work of Galvao (1946). A comparison of the caloric output in relation to the body weight is impossible from this number of dogs, but the body weight to the 0.73 power gave a figure which was in general agreement between weight ranges. The largest deviations from the average were seen in the smaller, more energetic breeds. The average cal./hr./kg.$^{.73}$ was generally above the figure of 2.937 given by Brody (1945) as universal for all species.

The body weight trends were generally in agreement with other workers. Evidently the vitamin B complex was in high enough concentration in the diet because the dogs did not lose weight when given exogenous thyroid. Weight loss has been reported in dogs rendered hyperthyroid only when the diet was yeast free (Drill and Hays 1942; Drill and Shaffer 1942) and in rats (Peters and Rossiter 1939). A transient fall in body weight for 3 to 4 weeks after which the normal weight was regained was reported in dogs receiving 2 mg. thyroxine daily and .77 gm. desiccated thyroid U. S. P. daily (Danowski, et al. 1946). This was in the vicinity of the largest dosage of exogenous thyroid used here. The two oldest dogs, on 2 and 4 mg./kg./day desiccated thyroid, showed a slight weight loss which may be attributable to their age. Heavy dosage of thyroid caused weight losses in dogs by nitrogen breakdown (Schörndorff 1897). A dose of .3 to .6gm./kg./day of desiccated thyroid in dogs caused a marked fall in body weight during 7 to 8 weeks in an experiment of another worker (McIntyre 1931).

Dott (1923) reports a similar weight fall on .07 mg./kg./day of desiccated thyroid. Ten gm. of fresh horse thyroid per day per dog caused severe losses in body weight (Moussu 1899). Undoubtedly, the caloric intake is a factor in the maintaince of body weight during hyperthyroidism.

The weight gain seen after thyroidectomy agrees with the general consensus of opinion which attributes the increase to more body fat and fluid, (Dott 1923).

The pulse rate could not be correlated to the metabolic rate. Perhaps the enzyme system of the heart did not have time to build up to the point where the thyroid hormone could act upon it to increase the rate of beat. The thiamine status of the dog has been reported to affect his pulse rate under hyperthyroidism. Dosage of .4 to .6 gm./kg./day of desiccated thyroid caused a rise in the pulse to 150 to 160 beats per minute within 6 to 8 days. When they were still receiving the exogenous thyroid and the yeast was removed from their diet, their pulse dropped to below 100 beats per minute (Drill and Hays 1942). In the present experiments, the pulse did not usually rise this high, probably because of the lower dosage used.

On the intact dogs receiving Protamone the pulse rose to a greater extent than the metabolic rate. The intact dogs on desiccated thyroid showed little if any rise above normal in the metabolic rate while the pulse rate rose considerably above normal. In the thyroidectomized dogs, the pulse rate of the group on Protamone did not rise appreciably while the metabolic rate rose to normal, and the pulse rate of the group on desiccated thyroid showed somewhat of a rise when the metabolism rose to normal. The lack of rise in the thyroidectomized groups may be attributed to the low caloric intake before the administration of exogenous thyroid began. The thyroidectomy pulse rate in this experiment ranged between 64 and 94 which is below normal for dogs. In the diagnosis of hypothyroidism, the pulse probably is not of paramount importance because of its large variability (Means and Aub 1925).

The difference between the response of the intact and thyroidectomized dogs to Protamone and desiccated thyroid is parallel to the findings of other workers working on thyroidectomized rats. In their work, iodinated protein raised the metabolism of the rats to normal without appreciably affecting the pulse rate while desiccated thyroid raised both the metabolic rate and the pulse rate. They attributed this to a cardiotropic factor in the natural thyroid gland (Meyer and Danow 1940). They reported the amount of the cardiotropic factor in the thyroid gland as being variable and dependent upon the physiological status of the gland and the amount of preiodination in the living animal before extraction of the desiccated thyroid (Meyer and Danow 1941; Meyer and Thompson 1940).

The body temperature followed the general trend expected of intact dogs on exogenous thyroid. The increase in body temperature of 0 to 1 degree F. is in agreement with the rise of .5 degree F. reported by Dott (1923) and Drill and Hays (1942). In the later work, the temperature rise could be prevented by removing yeast from the diet. The drop from normal of .5 degree F. after thyroidectomy is verified by other work (Dott 1923, Binswanger 1936). Exogenous thyroid did not raise the temperature back to normal in this experiment as reported by Dott (1923).

The behavior of the dogs was generally in agreement with the metabolic rate. Exogenous thyroid, in the dosages used upon intact dogs, caused little effect upon behavior in the lower range. Appetite was increased, confirming previous work (Moussu 1899). Hyperthyroid symptoms when the dogs were on the highest dosage are those generally described for other species. Hypothyroid symptoms of thyroidectomy were similar to those reported by several other workers (Dott 1923; Binswanger 1936). On the other hand, little effect on behavior was seen after thyroidectomy and goitrogenic drug administration of dogs by Danowski (1946) and Mayer (1947). ~~The slight edema~~ reported here, is not generally reported for dogs. However, thyroidectomy in dogs has been reported to cause high blood concentrations of cholesterol, phospholipids, and fatty acids which are associated with myxedema in humans (Chaikoff, et al. 1941; Entenman, et al. 1942; Thompson and Long 1941).

Replacement therapy corrected the hypothyroid symptoms as reported in most species. Early trials with iodocasein in dogs resulted in failure of the replacement because of the removal of the parathyroids and the doubtful potency of the compound (Wormser 1897). Recently, more potent iodocasein preparations have resulted in replacement therapy in several species (Brody and Frankenbach 1942; Reineke and Turner 1941). The percent drop in metabolism is greater than that reported by several other workers (Fink 1944; Danowski 1946).

Thyroidectomy and removal of part of the parathyroids resulted in tetany with resultant disturbance of the calcium metabolism. At the time of thyroidectomy, the dogs were not markedly above the normal level of metabolism. However, in hyperthyroid humans, it has been demonstrated that the degree of calcium excretion is much greater than the rise in the metabolic rate. In these persons, if the condition has existed long enough, osteoporosis occurs due to excessive secretion of calcium and phosphorus (Aub, et al. 1929). Similar results have been obtained in the dog (Logan, et al. 1942). Since the dogs in this experiment were thyroidectomized 2 to 3 days after Protamone was stopped, it is a logical assumption that some of the effects of excess thyroxine were still in force. Due to the removal of 2 of the parathyroid glands and trauma to the blood supply to the 2 remaining in the surgery, the dogs are consequently hypoparathyroid while there is excessive excretion of calcium under the influence of the excess thyroid hormone. Thus, under such conditions, one would expect the number of dogs undergoing tetany and death to be greater when the previous dosage of exogenous thyroid was greatest. Such was the case in this work, while none of the previously untreated dogs showed tetany effects.

The drop of metabolism on the 7th to 8th day of determinations with its rise back to or above normal on the 11th to 15th day in euthyroid dogs receiving exogenous thyroid is puzzling. It occurred in dosages of 2 mg./kg./day of desiccated thyroid to 8 mg./kg./day of Protamone representing 0.002294 to 0.04624 mg./kg./day of thyroxine, respectively. Such a drop has been reported in hyperthyroid humans given 2 grains of desiccated thyroid per day (Cavett et al. 1934). There has been some question as to whether the thyroxine is active alone or needs a particular protein linkage to exert its calorigenic effect (Canzanelli, et al. 1939). The thyroid hormone inhibits the anterior pituitary gland from secreting thyrotropin thus decreasing stimulation of the thyroid gland (Leblond and Mann 1942). Thyroglobulin will nullify the effect of thyrotropin on the thyroid gland itself (Galli-Mainini 1941). Inorganic iodides will inhibit the thyroid gland (Morton, et al. 1944), and will lower the metabolism in hyperthyroidism (Starr, et al. 1924). It seems conceivable that the exogenous thyroid temporarily upset the normal thyroid-anterior pituitary balance and was not able to act immediately itself because it lacked the proper linkage. It may also have inhibited the thyroid gland and thus had the same effect.

There is also evidence that the dog produces antimetabolites to thyroidal materials (Keeser 1938) and thus there might have been a temporary imbalance between the antimetabolite production and the action of the exogenous thyroid.

It is also known that iodinated protein in Protamone and desiccated thyroid is not entirely thyroxine, but compounds similar structurally to thyroxine are present also. Some of these compounds have been shown to have little thyroxine inhibiting action (Barker et al. 1949), but they may have the ability to depress the thyroid gland secretion through the anterior pituitary gland or act on the thyroid gland itself. There may be some that inhibit the thyroid hormone in the tissues. The destruction of the excess thyroid hormone may have taken place in the liver (Leblond 1949) out of balance with the normal rate of thyroxine destruction, because of the added impetus of the extra thyroid and thus destroyed all the animal's own thyroid hormone in addition to that given, thus causing the metabolic rate to be temporarily lowered.

The above described drop in metabolism did not occur in an intact dog with a low metabolic rate, 5A, and the thyroidectomized dogs, even though the dose of exogenous thyroid given was similar to those showing a drop. Work on euthyroid and myedematous humans has shown that the myedematous persons are more sensitive to exogenous thyroid, and that the metabolic rate of euthyroid humans was little affected by exogenous thyroid (Winkler, et al. 1942). The concentration of paraxanthine, an alleged thyroxine inhibiting substance, is highest in the thyroid gland (Carter and Jenkins 1944). It may be that the thyroid gland destroys the excess thyroid hormone and thus in the euthyroid, the excess thyroid hormone increases the thyroxine destroying action of the thyroid gland so that it destroys all of the normal secretion and the excess also for a short period of time.

The failure of the metabolism to increase as the logarithm of the dosage, and remain greatly above normal for a long period of time is of interest. The metabolism and blood iodine levels in thyroidectomized and euthyroid dogs given large doses of exogenous thyroid could not be raised much above normal, or for prolonged periods, in the work of Danowski (1946). Euthyroid humans are able to metabolize several times their own thyroid secretion rate without showing a rise in metabolism (Winkler, et al. 1942). Probably there were no antibodies produced, since the thyroid preparations were not given parenterally (Lerman 1942). The production of an antimetabolite by the dog (Keeser 1948) is a theory to be given some credence. The production of paraxanthine by the tissues of the dog to inhibit the action of the excess thyroid hormone may be the key to the situation (Carter and Jenkins, 1944). Probably the liver is able to metabolise excess thyroxine (Leblond 1949) after the dog's liver becomes adjusted to the situation. This is done in a delicate enough balance to center upon a level near the normal even under higher dosages of exogenous thyroid. The rise was in agreement with the rise on these dosages of exogenous thyroid reported by Fink (1944).

The therapeutic range of dosage of thyroid preparations may be termed as the amount which will replace the animal's own thyroid secretion rate. This amount of Protamone was 1 to 2 mg./kg./day and for desiccated thyroid was 4 to 8 mg./kg./day. Since the thyroidectomy resulted in a 27.8% fall in metabolism from the normal rate, the metabolism would have to rise to 138.5% of the thyroidectomy level to be back to normal. Inasmuch as the amount of the exogenous thyroid which was absorbed is not known, the thyroid secretion rate of the dog cannot be definitely determined from these data. However, it required 5.78 micrograms of thyroxine/kg./day, given orally in Protamone to replace the secretion rate and 4.588 to 9.176 micrograms/kg./day of thyroxine orally in desiccated thyroid to replace the thyroid secretion rate. This is within the range of the thyroid secretion rate of 24 to 240 micrograms thyroxine per day for the dog given by another worker on the basis of radioactive studies (Taurog, et al. 1947).

The differences in breed responses to exogenous thyroid in the intact animal may reflect differences in the ability of different breeds to metabolize excess thyroxine and also may be some indication of the animal's thyroid secretion rate. If cross breeding increases thyroid secretion rate of dogs, as it does in chicks (Mixner and Upp 1947), it might be theorized that the dog would have a higher metabolic rate, be closer to the threshold of response, and thus be more active in destroying the excess hormone. It may be seen in this work that the Cocker-pointer crossbreds were able to metabolise all the exogenous thyroid without showing an appreciable rise in metabolism. The Cockers were similar in response to these and it would seem that the Cocker is normally a relatively hyperthyroid individual.

The radioactivity studies with I*131 on the thyroidectomized dog succeeded in locating those dogs which had some thyroid function left. The determinations on the intact English Bull Dog bitches revealed no depression of the thyroid iodine turnover rate by the Protamone. Such results are not borne out by other work which points to depression of the thyroid secretion rate by exogenous thyroid. Indeed, even in this experiment the dogs receiving high dosages of Protamone exhibited small thyroid glands. It may be that the I*131 was retained in the ovaries (Perkin and Brown 1938) and thus disrupted the test. Small thyroid glands have been shown to pick up a higher concentration of iodine and thus perhaps size of the gland is not a determining factor (Hertz and Roberts 1941).

SUMMARY

1. The amount of Protamone needed to raise the cal./hr./kg.$^{.73}$ back to the normal level in thyroidectomized dogs was 1 mg./kg./day.

2. The amount of desiccated thyroid (containing 0.3% iodine) needed to raise the cal./hr./kg.$^{.73}$ back to the normal level in thyroidectomized dogs was 4 to 8 mg./kg./day.

3. Dosages well above the therapeutic dosage of Protamone were well tolerated by intact dogs, with no disturbances of behavior and little permanent rise in the metabolism, pulse, and body temperature. 2 mg./kg./day stronger desiccated thyroid resulted in no rise in metabolism above normal in 2 intact dogs.

4. Protamone caused an increase in body weight due to increased caloric intake.

5. Protamone caused no ill effects in a long time trial with intact English Bull Dog bitches when fed at the rate of 2 grams per 100 lbs. dry matter for a period of 148 days. It improved the condition of one of the dogs.

6. Metabolism determinations at the 7th to 8th day in intact dogs on 2 to 8 mg./kg./day of Protamone and 2 mg./kg./day of desiccated thyroid resulted in a drop to 67.2% and lesser amounts of the normal metabolism. This drop was repaired to or above normal in 10 to 15 days. The drop was not observed in thyroidectomized dogs given exogenous thyroid.

7. The thyroid secretion rate of the dog was roughly computed as 5.78 to 9.176 micrograms thyroxine/kg./day assuming that

the exogenous thyroxine was mostly assimilated.

8. By chemical analysis the strength of the Protamone was 5.04 times the potency of the desiccated thyroid, while by assay on thyroidectomized dogs, the Protamone was 4 to 8 times the potency of the stronger desiccated thyroid. The most logical ratio shows Protamone to be 5.13 times as potent as stronger desiccated thyroid.

9. I*131 injections located thyroid functions in thyroidectomized dogs.

10. I*131 injections failed to detect depression of thyroid iodine turnover rate in intact English Bull Dog Bitches fed Protamone at the rate of 2 mg. per 100 lbs. of dry matter for 87 days previous to the injection.

11. High dosages of Protamone given intact dogs for a period of time reduced the size of the thyroid glands.

12. The Protamone antagonized the action of the parathyroid gland, causing tetany in dogs thyroidectomized while still under the influence of the Protamone. The incidence of tetany was proportional to the previous dosage of Protamone.

13. Thyroidectomy resulted in a 27.8% drop in metabolism, a drop in the pulse to below 100, and a small drop in body temperature. Lethargy and slight edema resulted also.

14. Replacement with Protamone or desiccated thyroid alleviated the symptoms of thyroidectomy.

15. Desiccated thyroid caused greater responses on pulse rate than Protamone in both intact and thyroidectomized dogs.

16. Using the body weight to the .73 power as a base for computing the metabolism gave a fairly constant figure for comparison.

CONCLUSIONS

1. Both Protamone and desiccated thyroid can be used therapeutically in the following dosages, Protamone 1 to 2 mg./kg./day, Stronger Desiccated Thyroid (50% stronger than U. S. P.) 4 to 8 mg./kg./day and Desiccated Thyroid U. S. P. 6 to 12 mg./kg./day.

2. These dosages will produce no untoward effects even when used over prolonged periods of time.

3. The dog is able to metabolize large amounts of exogenous thyroid without dire effects upon his behavior, metabolism, weight, pulse, and body temperature.

4. Dogs receiving exogenous thyroid in moderate dosages will usually gain weight because they eat more.

5. Radioactive iodine determinations are of use in determining the completeness of thyroidectomy in the dog.

6. Thyroidectomy will result in symptoms of lethargy, fall in metabolism, lowering of pulse and body temperature, and decrease in body temperature.

7. There is a transient fall in the metabolic rate on the 7th to 8th day when a euthyroid dog is given exogenous thyroid, in small to medium dosages.

8. Excess exogenous thyroid will aggravate hypoparathyroidism in the dog and result in tetany if given in sufficient dosage.

REVIEW OF THE LITERATURE ON THE RELATIONSHIP OF THE THYROID GLAND AND GROWTH

The m a n y aspects of the thyroid gland's role in growth and maturation have been studied in several ways. The first, and most natural method, was the removal of the gland in the infant animal and observation of the resulting syndrome. Replacement of the gland by feeding of thyroidal materials was the next logical step. The last, and more promising step, was the feeding of thyroid to intact animals to augment the normal growth and maturation processes.

Historical

The dog was one of the earliest animals to be used. An early French worker removed the thyroid of young dogs and noted tetany and death. Part of this syndrome can be attributed to the removal of the parathyroids. The observed myxedema could be somewhat alleviated by transplantation of thyroid glands into the operated dogs (Schiff 1884). Another French worker noted a cessation of growth when he thyroidectomized puppies. Using fresh horse thyroids, he fed litter mate puppies varying amounts and noted that on the lower dosage levels, the dogs matured more quickly but did not become any larger than their controls finally became. He claimed the dogs grew faster in weight, height, and length. When he fed higher dosages -- 10 gms. of fresh horse thyroid per kg. of body weight -- the dogs lost weight and died (Moussu 1899).

Exogenous thyroid also stimulates growth in other animals. The thyroid is the only endocrine which was shown to augment growth when fed orally to white rats (Schafer 1912). In thyroidectomized rabbits, the cretinism symptoms of small size, coarse coat, and lethargy could be partly overcome by feeding desiccated thyroid (Basinger 1915).

Relation with Anterior Pituitary Growth Hormone

Thyroxine has been shown to stimulate development of fibroblasts, periosteum, heart, lung, and other tissues (Schneider 1939). This stimulating action of the thyroid has no effect in the absence of the growth hormone of the anterior pituitary. This has been demonstrated in rats which were thyroidectomized and hypophysectomized. Growth hormone and thyroid gave the greatest growth response when administered together, while in the absence of the thyroid, the growth hormone only produced half as much growth; the rats administered thyroid alone showed no gain over the untreated, operated rats (Evans, et al.1939). By observations on the development of osteoid tissue of guinea pigs, thyroidectomy produced a lessening of development which is not as great as that produced by both thyroidectomy and hypophysectomy (Silberberg and Silberberg 1936). Hypophysectomized rats gave the optimum growth response when given both growth hormone and thyrotrophic hormone (Marx, et al. 1942). In rats, which were thyroidectomized on the day of birth, the body weight and skeletal growth were markedly increased over the untreated controls by the administration of growth hormone. The secondary ossification centers of the bone were not affected and the response did not depend on the time of starting the injections. The response was greatest in those rats which possessed thyroid fragments (Scow and Marx 1945). The above findings were not borne out by other work on rats thyroidectomized at birth in which no skeletal growth was noted in completely thyroidectomized animals given growth hormone (Salmon 1941). In humans, hypothyroidism resembles the picture of hypophysectomy inasmuch as radioactivity studies show that there is little iodine metabolism of the thyroid (Hamilton, et al. 1943).

Mechanism of Action

The general concept at the present time is that the thyroid hormone augments the action of the growth hormone. The growth hormone is mainly responsible for the proliferation of cells while the thyroid hormone increases the size of the cells.(Evans, et al. 1939; Salter 1940).

The first requirement for increased growth is that of nutrition. In ruminants, it has been demonstrated that raising the metabolism by thyroprotein administration causes an increase in appetite (Blaxter 1949). The jejunal secretion rate and peristalsis was increased in the dog by the administration of large amounts of desiccated thyroid (Fink 1944). This effect lasted for some time after the thyroid administration was terminated. Increased absorption of carbohydrates has been demonstrated in the hyperthyroid rat, chiefly due to an increase in phosphorylation (Althausen 1940). Thyroid-treated dogs' liver in vitro had the ability to synthesize amino acids from pyruvic acid and ammonia faster than normal (Zitowskaya 1939). Increase of d-amino oxidase in the rat liver has been observed under hyperthyroid conditions (Klein 1939). In growing animals, thyroid administration causes increased retention of nitrogen and anabolic protein activity. Excess thyroid will result in catabolic protein metabolism (Soskin 1941).

Bone metabolism has been used as a more concrete example of thyroid effects. By the use of radioactive phosphorus it has been shown that the greatest turnover of phosphorus occurs in the early growth stage when the thyroid secretion rate is the highest. In mice, it was impossible to demonstrate a significant increase of phosphorus turnover as a result of thyroxine administration (Falkenheim 1942). In dogs, the calcium-phosphorus balance was shown to be disturbed by thyroidectomy. This could be corrected by thyroid administration. The calcium excretion was lowered at the same time as the uptake of calcium was increased (Breitbarth 1940). Large amounts of thyroid hormone in the guinea pig, at first, caused slight hyperplasia, hypertrophy, and accelerated differentiation of the euhyaline cartilage of the epiphyseal line, ribs, joints, and vertebrae. Later, the replacement of the hypertrophied cartilage by bone was retarded and increased bone absorption by the osteoclast cells lead to osteoporosis and arthropathic rarefication of the cartilagenous covering of the joints (Silberberg and

Silberberg 1938). In mice, the growth and development of the epiphyseal cartilage is inhibited by castration. This effect may be counteracted by thyroxine. Thyroxine was demonstrated to cause ageing of the epiphseal cartilage and epiphyseo-diaphyseal union earlier (Silberberg and Silberberg 1947). In hypothyroid children, thyroid therapy was shown by radiographic studies to increase bone density and hasten epiphyseal union besides increasing the growth rate and mental alertness.(Finkler, et al. 1944). In newborn rats, the eruption of teeth was shown to be hastened by severe hyperthyroidism (Karnofsky and Cronkite 1939).

Species Results

All species of mammals studied have been demonstrated to need the thyroid gland for normal growth and maturation. Some species show a further increase in growth upon the administration of exogenous thyroid to the normal animal while other species do not. The amount of thyroid administered is thought by some to be necessarily above the animal's own secretion rate to produce results (Hurst and Turner 1947).

Mice, in general, show an increased growth rate when exogenous thyroid is given. Desiccated thyroid, at the rate of 1 mg. per day per mouse, increased the rate of growth but not the final weight attained (Robertson 1928). Similar results were obtained on white mice when .015 to .04 mg. of crystalline thyroxine was injected per day.

The treated mice showed a greater retention of nitrogen (Koger, et al. 1942). Later, similar effects were obtained by thyroprotein feeding at .15% to .60% of the ration, although the heavier dosages tended to depress growth (Koger, et al. 1943).

In guinea pigs and rabbits, thyroprotein in the ration had no effect upon growth in low dosages and depressed growth in higher dosages. In rats, there was little response (Koger and Turner 1943).

In chicks, a thyroprotein level of .1% to .2% in the ration, resulted in better gains on less feed per unit gain. The chicks showed a more mature type of feathering than the control (Parker 1943). Other workers reported similar findings in chicks fed low dosages of thyroprotein while higher dosages in the ration (113 gms per 100 lbs. of feed) resulted in depressed growth and a high mortality rate (Irwin, et al. 1943).

In humans, cretinism has been the main point of study. There is some evidence that this malady is hereditary (Lewis 1937). For dwarfism, thyroid therapy has been a valuable tool even in cases where there was no clearcut evidence of thyroid insufficiency (Webster 1939). There is some evidence from studies of thyrotoxic girls, that the excess thyroid will result in an unusually tall individual (Hertz and Galli-Mainini 1941).

In ruminants, thyroidectomy has resulted in premature cessation of growth when done on a young heifer (Brody and Frankenbach 1942) and in fattening when done on steers

(Andrews and Bullard 1940). In goats, a lethargic, undeveloped, dishfaced individual resulted from thyroidectomy. .5 to 1 gm. of thyroprotein daily served as replacement to produce normal growth (Reineke and Turner 1941).

There is somewhat of a breed difference in swine in the response to feeding of exogenous thyroid. The dosage of thyroprotein used ranged from 1.4 to 5.6 grams in 100 lbs. of feed. On the higher dosages, some ill effects were observed. The optimum dose seemed to be about 2.8 gms./100 lbs. of feed. Berkshires, Yorkshires, and Duroc Jerseys were noted to make greater and more economic gains, while Chester Whites showed no beneficial effects (Reineke, et al. 1948).

There is also some variation in the data reported from the dog. After the work previously cited for the dog, further studies were carried on under improved methods of surgery. Thyroidectomy resulted in a cessation of growth, subnormal temperature, adiposity, a scaley and course hair coat, and a reduction of 81% in femoral-epiphyseal activity. In normal mongrel dogs administered 0.07 gm. of desiccated thyroid per kg. of body weight, there was a slight elevation of body temperature, loss of body fat, and an increase of 28% in epiphyseal activity. No unnatural activity was reported. The gonads grew more quickly and the dogs matured at an earlier age but at a subnormal size (Dott 1923). Other workers (Dye and Maugham 1929) removed the thyroid glands of mongrel puppies at 5 to 6 weeks of age and reported dwarfing of most of the pups. The absolute diameter of the epiphyses of the bones was little if any diminished. The skull, mandibles, scapulae, vertebrae, and coxae were disproportioned. The cranial cavity was of less volume and the growth of bone from cartilage was greatly diminished. Subperiosteal or membrane bone was unaffected. The weight was also much reduced. Further work on mongrel dogs showed a somewhat less striking reduction of the growth impulse which may be due to a different strain. Most of the dogs thyroidectomized were dwarfed (Binswanger 1936). A goitrogenic drug, propylthiouracil, was used at the dose of 30 mg./kg. body weight per day and given in capsule form once per day to growing Beagle puppies (Mayer 1947). This was started at 33-40 days of age and continued through 6 to $8\frac{1}{2}$ months. There was no difference reported in the growth rate behavior, and only slight differences in the hematology. On autopsy, no differences were found in any of the endocrines except an enlargement of the thyroid. There was no difference in the degree of ossification or the appearance of the red bone marrow. There is some question as to whether goitrogenic drugs administered in the above manner will completely suppress the thyroid secretion. In Collies, the growth rate and efficiency of gain was increased by thyroprotein in the feed at the rate of 2 gms. and 4 gms. per 100 lbs. of dry feed (Brown and Smithcors 1948). The greatest growth and efficiency of gain was reported on 4 gms. per 100 lbs. of dry feed. In a similar experiment using Cocker-pointer cross-breds, and dosages of 2, 4, and 8 gms. of thyroprotein per 100 lbs of feed, no effect upon the growth rate and efficiency of gain was observed. Both the above types of dogs showed no difference in the rate of ossification of the epiphyseal cartilages of the humeral-radial-ulnar joint and carpal joints when demonstrated by X-ray plates.

EXPERIMENTAL PROCEDURE AND EFFECTS

Trials with Protamone on Intact English Bull Dog Puppies

Procedure: Seven English Bull Dog puppies were put on the trial at weaning. The control group consisted of four dogs, 1, 3, 5, and 6 while the protamone group consisted of three dogs, 2, 4, and 7. Dogs 1, 2, 3, and 4 were males and 5, 6, and 7 were females. Dogs 1 and 2 were littermates from a litter born 64 days previous to the start of the trial and weaned 15 days previous to the start of the trial. Dogs ~~2,~~ 3, 4, 5, and 6 & 7 were littermates and were born 53 days previous to the start of the trial and weaned 2 days previous to the start of the trial. Dog ~~2~~ 3 was placed on the same bitch as 1 and 2 and thus received more nourishment than his littermates and thus grew faster. All of the dogs were in good condition at the start of the trial. Their ancestry indicates that they were of a small type of English Bull Dog.

The diet throughout the experiment consisted of condensed milk, canned dog food, and dry meal. The milk contained 25% dry matter. The canned dog food was "Pard" marketed by Swift & Co. of Chicago, Illinois. Its guaranteed analysis was as follows:

Protein (Minimum)	10.5%
Fat (Minimum)	2.5%
Nitrogen Free Extract (Minimum)	9.0%
Fibre (Maximum)	1.0%
Ash (Maximum)	3.0%
Moisture (Maximum)	74.0%

Calcium (Maximum) .65%
(Minimum) .45%

Phosphorus (Minimum) .30%

Salt (Maximum) .75% - 50% iodized salt

The meal was ground "Gropup" supplied by the Kellogg Co. of Battle Creek, Michigan. Its guaranteed analysis was as follows:

Protein (Minimum)	22.5%
Fat (Minimum)	3.5%
Fiber (Maximum)	4.0%
Moisture (Maximum)	8.0%
Nitrogen Free Extract (Minimum)	50.0%
Ash (Maximum)	9.0%
Potassium iodide was in the meal at	.00037%

For the first 5 days on experiment the diet was given in the following ratio:

910 gm. canned dog food

740 gm. milk

400 gm. meal

For the next 28 days on experiment the diet was given in the following ratio:

1135 gm. canned dog food

1092 gm. milk

500 gm. meal

For the next 54 days on experiment the diet was given in the following ratio:

1135 gm. canned dog food

728 gm. milk

1800 gm. meal

For the remaining period of experiment the diet was in the following ratio:

1362 gm. canned dog food

2800 gm. meal

In the Protamone group, the Protamone was mixed with the meal so that it comprised 4 gm. per 100 lbs. of dry matter fed. The pups were fed three times daily for the first three months of experiment and then were fed twice daily for the remainder. They were given the amount which they would clean up in 30 minutes at a feeding. Each pup was also given 1/2 teaspoon of cod liver oil and 7 1/2 gms. di-calcium phosphate three times weekly throughout the trial. All pups were permanently innoculated for distemper between the 14th to the 24th day of trial by intradermal injections of distemper vaccine without any ill effects. The pups were treated, with no ill effects, for ascarids and hookworms with Oil of Chenopodium when they had been on experiment for 2 1/2 months. The infestation was mild.

Effects: The behavior of the Protamone group became more aggressive than that of the controls by the 2nd week on experiment although the difference was not marked until the 2nd month. By the second month of experiment, the Protamone group became more active than the controls and also showed some features that indicated greater mental alertness. For instance, pups naturally resent being weight, measured, and having their teeth examined; but the Control group continued to come to the side of the pen after the first pup had gone through the above procedure, while the Protamone pups observed the process taking place in the control group and retreated to a farther corner when motions were made in their direction. The Protamone pups were more aggressive in their play as determined by scratches on the author's knuckles. Toward the end of the experiment, the Protamone group succeeded in dislocating the partition between them and the controls, thus gaining entrance to the Control's pen, after which the Control group was thoroughly beaten and dispersed with several teeth puncture wounds. By the 2nd month of the experiment, the Protamone group was cleaning up its food at a markedly greater rate than the Control group.

Throughout the experiment, the hair coat of all the dogs was in good shape. The hair coat may have been slightly more shiny in the Protamone lot, but the effect was not marked. However, after the first month on experiment, the hair coat of the Protamone group was a great deal darker than that of the Controls although the dogs were all of the same shade at the start. This effect was present throughout the remainder of the experiment.

The general appearance of all the dogs at the beginning of the experiment was a lack of uniformity, as expected in normal puppies at their age. By the second month on trial, the Protamone group began to become more uniform than the Controls and began to assume a more mature appearance than the Controls. These effects became more pronounced during the remainder of the experiment. The Protamone group, by the 3rd month on trial, had more protruding lower jaws, more wrinkled faces, were wider chested and narrower in the flanks although the flanks were full, and generally showed the more rugged appearance of the adult English Bull Dog. By the 5th month of the trial, the Protamone group appeared to be about a month older than the Control group.(Figs. 8 and 9).

The rate of dentition did not appear to be appreciably affected by the administration of Protamone.

The body measurements showed a trend toward a more mature type of dog in the Protamone group. The measurements of the males of the Control group showed a greater flank girth than heart girth up until measurements taken on the 81st day after the start of trial (table XLV). The heart girth of the males of the Protamone group was greater than the flank girth on the 53rd day after the start of trial when the first measurements were taken (table XLVI). Toward the end of the trial, the ratio of the heart girth to flank girth became similar in the Control and Protamone groups. This ratio was not quite as pronounced in the females. In the Control females, the heart girth did not become greater than the flank girth until a period between measurements taken on the 81st to the 109th day after the start of the trial (table XLV). The female in the Protamone group evidenced a larger heart girth than flank girth when the first measurements were taken on the 53rd day after the start of the trial (table XLVI). Toward the end of the experiment, the heart girth to flank girth ratio was still greater in the Protamone group female, and the measurements were also greater.

Of the other body measurements, there was little difference in body lengths except that the female in the Protamone group was longer than the females in the control group by 3 inches (tables XLV and XLVI). The height appeared to be little affected except that the female in the Protamone group was generally 1 to 2 inches taller than the females in the control group (tables XLV and XLVI).

As to the body weight, the Protamone group finished the experiment heavier than the Control group. The Protamone males after 158 days on trial were 1.442 kg. heavier or 8.52% heavier than the males in the control group and the female in the Protamone group was 3.785 kg. heavier or 30.20% heavier than the females in the control group after 158 days on trial (tables XLIII and XLIV). The Protamone males did not become heavier than the controls until about the 60th day of trial. The Protamone female gradually became heavier than the controls after the start of trial, was about 1 1/2 kg. heavier than the controls after 40 days on trial, and by the 70th day on trial was 2 1/2 kg. heavier than the controls(Fig. 10).

The paired littermate males, #1 and #2, were least affected by exogenous thyroid, since their weights did not vary much during the course of the experiment. Dog #3, a male, had a head start in growth because of his being placed with another bitch and thus had better nourishment. His paired littermate on Protamone overtook his early lead by the 66th day on trial and finished 2.800 kg. heavier.

Soon after the trial started the weights on the Protamone group became more uniform than those of the Control group.

The food consumption and amounts of Protamone received and efficiency of gain are as follows:

Months on Trial	Amount of dry matter consumed (lbs.) Controls	Protamone	Efficiency of gain (kg.dry feed/kg. gain in body wt.) Controls	Protamone	Amount of Protamone received by Protamone Group (Based on average of weight at beginning and end of the month
1st	107.415	90.501	4.076	4.073	8.061 mg./kg./day
2nd	84.708	87.814	3.029	4.061	4.669 mg./kg./day
3rd	103.700	112.108	6.079	5.418	4.331 mg./kg./day
4th	124.439	112.108	7.308	6.700	3.476 mg./kg./day
5th	137.892	100.897	11.419	8.039	2.710 mg./kg./day
last 8 days	30.830	30.269	*negative	24.971	2.868 mg./kg./day
Gain (kg.)	46.148	43.117			
Total time	588.983	533.697			

21.348 gms. of Protamone were consumed in all.

After the first month, the efficiency of gain was greater in the control group, but by the third month, it was consistantly greater in the Protamone group. The efficiency of

* Weight lost during this period.

gain coincided with the rapid growth period and was naturally greater in the Protamone group.

Figure 8

Upper photo:

Control Group of English Bull Dog Puppies. Picture taken at the end of trial. Left to right are dogs 5(female), 1(male), 6(female), and 3(male).

Figure 9

Lower photo:

Protamone Group of English Bull Dog Puppies picture taken at the end of trial. Left to right are dogs 2(male), 4(male), and 7(female).

Notice the greater uniformity, the wider chested and more robust individual, the more adult type face, and the greater size.

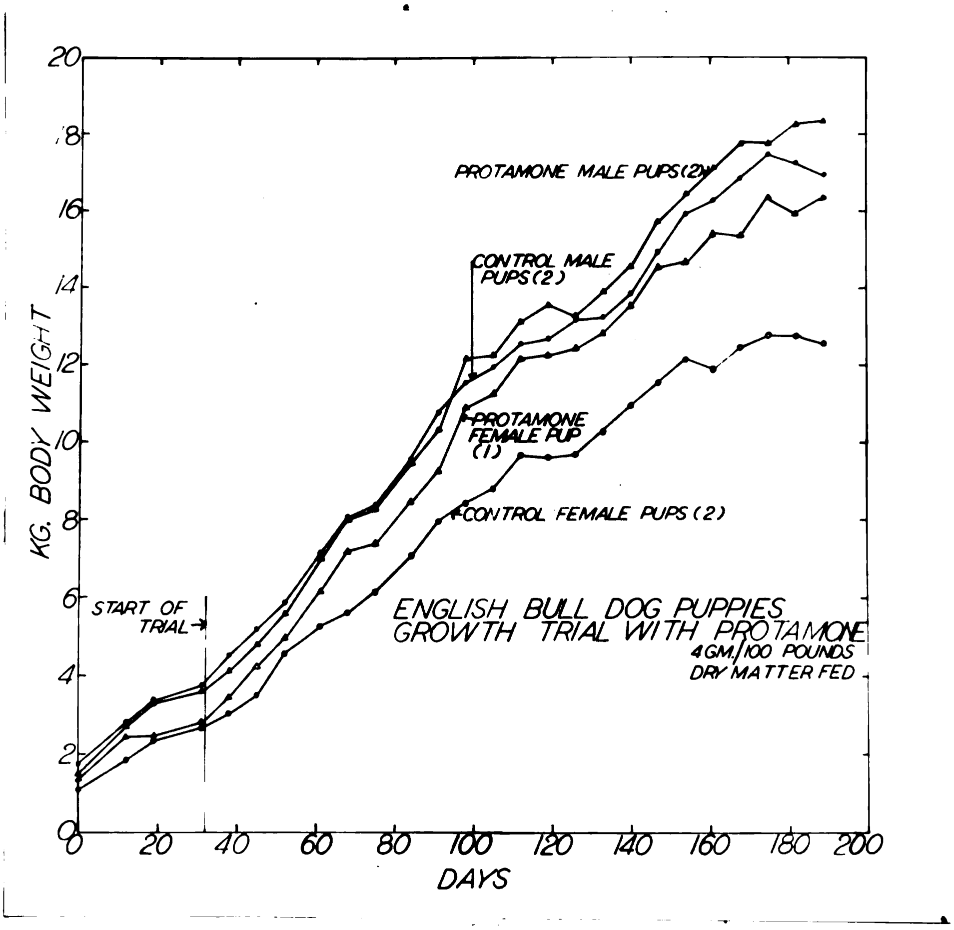

Figure 10

Growth curves of male and female Bull Dog Puppies in control and Protamone fed groups. Notice the marked difference between the female s when Protamone was given.

DISCUSSION

The effects of exogenous thyroid on the behavior are what one would expect if the species in question inclined to be hypothyroid. Such was indicated by the similarity of thyroid histology of the English Bull Dog to that of a breed of swine which responded well in growth to exogenous thyroid (Reineke, et al. 1948). Since cretinism is believe to be hereditary in humans (Lewis 1937), it is conceivable that such is the case in various breeds of dogs inasmuch as their origin is a history of inbreeding. Since the hypothyroid symptoms in humans include slow cerebration and dullness of the sensorium (Thompson 1942), it is logical that the use of exogenous thyroid would increase the mental alertness as seen here. The English Bull Dog, by appearance, suggests a hypothyroid individual.

Increased hair growth is to be expected in the hypothyroid individual upon the administration of exogenous thyroid. Such has been demonstrated in the mouse (Koger, et al. 1942). The darker hair coat in the Protamone group may be explained as the type of hair coat of a more mature individual. Such has been demonstrated in feather growth of chicks on exogenous thyroid (Parker 1943).

The more mature appearance of the Protamone group is similar to the results on chicks (Parker 1943; Irwin, et al. 1943) in dogs (Moussu 1899; Dott 1923), in humans (Webster 1939), in swine (Reineke, et al. 1948) and in goats (Reineke and Turner 1941).

The rate of dentition was not noticeably different between the groups because the dosage was probably not as great as in mice where the rate of dentition was increased (Karnofsky and Cronkite 1939).

The more mature type of appearance was also reflected in the body measurements inasmuch as in mature animals, the heart girth becomes greater than the flank girth. The increases of height and length were not as marked as Moussu (1899) reported on his dogs of a mongrel type. Perhaps the difference lies in the breed of dog used. Since the dosage was not unduly great, it did not cause a premature cessation of growth at a small size as reported by Dott (1923).

The weight records followed the expected trend of a species which benefits by exogenous thyroid in the growth period. The reason for the wider difference in gain in the females is a matter for speculation. The difference in response between the litters may reflect a strain difference comparable to the hereditary hypothyroidism reported in humans by Lewis (1937). The weight increase was generally of the nature of that reported in Collies on Protamone (Brown and Smithcors 1948) and in swine (Reineke, et al. 1948). It would be interesting to note if the final weight attained by the dogs in both groups would be equal as indicated by work on mice (Robertson 1928), and dogs (Moussu 1899); or if the final weight would be greater than the controls such as is reported in thyrotoxic girls (Hertz and Galli-Mainini 1941). If the English Bull Dog were a hereditary cretin, one would expect a larger than usual individual to be produced by exogenous thyroid as has been shown in humans (Webster 1939).

The increased efficiency of gain found in the Protamone group is what one would expect from previous work. Similar findings were reported by Brown and Smithcors (1948) in Collies and by Koger, et al. (1943) in mice. The faster gain in the Protamone group is probably the reason for the increased efficiency. Similar findings in swine have been reported (Reineke, et al. 1948).

Radioactivity studies with the pups on their 48th day of trial, indicated a lessened pickup of iodine by the thyroid glands of the Protamone group. The turnover rate of iodine in the thyroid was indicated to be similar in both groups. This is not in entire agreement with the opinion of Hurst and Turner (1947) that the amount of thyroid administered must be greater than the animal's own thyroid secretion rate to produce an effect. Such radioactive results would not be the case if the thyroid gland were completely suppressed. The lessening of the pickup of iodine may be explained (Galli-Mainini 1941) by a suppression of thyroid function by the exogenous thyroid.

SUMMARY

1. Protamone, at the dosage of 4 gm./100 lbs. of dry matter consumed resulted in increased growth and hastened maturity in Intact English Bull Dog Puppies started on trial at weaning. The effect was more marked in the females.

2. The hastened growth and maturity were judged by more mature appearance, measurements, and weight.

3. The disposition of the Protamone group was more alert and aggressive.

4. The efficiency of gains was generally greater in the Protamone group.

5. Radioactivity studies indicated a decreased pickup of iodine by the thyroids of the Protamone group; the turnover rate of iodine by the thyroid was similar in both groups.

CONCLUSIONS

English Bull Dog Puppies respond to exogenous thyroid by increased growth rate and greater alertness.

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APPENDIX

Table I

DESCRIPTION OF THE INTACT DOGS ON PROTAMONE

Group I

* Dog 1 was a female, 9 months old, Cocker-Pointer weighing 10.7 kg.

** Dog 2 was a male, 9 months old, Collie weighing 11.6 kg.

Dog 5A was a female, 5 years old mongrel resembling a Scottish Terrier weighing 8.0 kg.

Dog 28 was a male, 3 year old, Collie weighing 15.4 kg.

Group II

* Dog 3 was a female, 9 months old, Cocker-Pointer weighing 10.6 kg.

** Dog 4 was a male, 9 months old, Collie weighing 15.3 kg.

Dog 27 was a female, 3 years old, Cocker weighing 11.9 kg.

Group III

* Dog 24 was a male, 9 months old, Cocker-Pointer weighing 12.3 kg.

* Dog 25 was a female, 9 months old, Cocker-Pointer weighing 11.4 kg.

** Dog 26 was a male, 9 months old, Collie weighing 16.7 kg.

Dog 5B was a female, 5 years old, Cocker weighing 10.9 kg.

* Cocker-Pointer litter mates

** Collie litter mates

Records of the Effect of Thyroidectomy include dogs 1, 5, 26, 27 and 28.

Table II

RECORDS OF CALORIES PER HOUR OF INTACT DOGS ON PROTAMONE GROUP I

	Normal			10/19		2 mg./kg./day					11/18	12mg./kg./day	
Dog No.	10/10	10/14	10/17	10/21	10/24	10/27	10/30	11/2	11/5	11/11	11/17	11/29	12/6
#1	25.556	26.819	27.760	27.893	29.183	18.464	24.595	25.556	30.020	28.370	25.346	26.661	26.570
	Average normal cal./hr. 26.712												
	% normal cal./hr.			104.4	109.2	69.1	92.1	95.7	112.4	106.2	94.9	99.8	99.5
#2	29.591	27.361	29.121	26.803	33.312	19.550	27.027	31.743	37.394	37.372	37.480	36.428	59.849
	Average normal cal./hr. 27.358												
	% normal cal./hr.			97.8	121.8	71.4	98.6	111.6	136.7	136.6	137.0	133.2	218.8
#5A	17.486	15.170	15.276	18.050	16.520	20.093	23.243	18.831	21.594	20.459	20.493	21.118	23.081
	Average normal cal./hr. 15.977												
	% normal cal./hr.			113.0	103.4	125.8	145.5	117.9	135.2	128.0	128.3	132.2	144.5
# 28	40.890	39.010	38.647	36.910	24.230	21.722	28.649	30.936	38.974	37.372	35.592	35.108	45.088
	Average normal cal./hr. 39.516												
	% normal cal./hr			93.4	51.3	55.0	72.5	78.3	98.6	94.6	90.1	88.8	114.1
Ave. cal./hr.	28.381	27.090	27.701	27.414	25.811	19.957	25.878	26.766	31.996	30.893	29.728	29.829	38.647
Average % normal cal./hr.				102.2	99.0	80.3	102.2	102.0	120.7	116.4	112.6	113.5	144.2

Table III

RECORDS OF CALORIES PER HOUR OF INTACT DOGS ON PROTAMONE GROUP II

	Normal			10/19 2 mg./kg./day								11/18 12mg./kg./day	
Dog No.	10/10	10/14	10/17	10/21	10/24	10/27	10/30	11/2	11/5	11/11	11/17	11/29	12/6
#3	25.018	23.839	26.944	25.970	25.600	20.636	25.405	25.287	23.700	27.825	27.503	22.965	27.106
Average Normal cal./hr. 25.284													
% normal cal./hr.				102.7	102.7	81.6	100.5	100.0	93.7	104.2	99.8	81.8	94.2
#4	29.591	27.632	29.121	36.092	26.154	22.265	27.568	35.509	37.658	36.554	30.200	30.621	33.816
Average Normal cal./hr. 28.781													
% normal cal./hr.				125.4	90.9	77.4	95.8	123.4	130.8	127.0	104.9	106.4	117.5
#27	28.515	31.474	28.715	27.892	23.681	21.451	28.108	25.287	26.861	24.551	29.660	27.453	30.327
Average Normal cal./hr. 29.568													
% normal cal./hr.				94.3	80.1	72.5	95.1	85.5	90.8	83.0	100.3	92.8	102.6
Ave. cal./hr.	27.708	27.648	28.260	29.984	25.145	21.451	27.027	28.694	29.406	29.643	29.121	27.013	30.416
Average % Normal cal./hr.				107.5	90.7	77.2	97.1	103.0	105.1	106.7	104.7	96.7	109.1

Table IV

RECORDS OF CALORIES PER HOUR OF INTACT DOGS ON PROTAMONE GROUP III

	Normal			10/19 2 mg./kg./day								11/18 12mg./kg./day	
Dog No.	10/10	10/14	10/17	10/21	10/24	10/27	10/30	11/2	11/5	11/11	11/17	11/29	12/6
#25	31.743	27.632	27.760	31.720	25.600	23.895	29.459	29.591	30.811	32.462	32.357	27.717	28.985
	Average Normal cal./hr. 29.045												
	% normal cal./hr.			109.2	88.1	82.3	101.4	101.9	106.1	111.8	111.4	95.4	99.8
#26	34.433	37.930	33.050	36.912	25.603	50.776	48.649	41.428	58.725	50.193	44.491	45.403	47.235
	Average Normal cal./hr. 35.490												
	% normal cal./hr.			104.0	72.1	143.1	137.1	116.7	165.5	141.4	125.4	127.9	133.1
#5B	24.211	23.297	24.222	25.704	22.300	20.093	25.946	37.661	22.121	23.733	25.885	28.773	28.180
	Average Normal cal./hr. 23.910												
	% normal cal./hr.			107.5	93.3	84.0	108.5	157.6	92.5	99.2	108.3	120.3	117.9
#24	30.667	27.632	28.305	30.623	28.910	24.709	31.892	25.825	38.711	33.008	33.116	26.925	33.279
	Average Normal cal./hr. 28.868												
	% normal cal./hr.			106.1	100.1	85.6	110.5	89.4	134.1	114.3	114.9	93.3	115.3
Ave. cal./hr.	30.264	29.123	28.334	31.240	25.603	29.868	33.986	33.628	37.592	34.849	33.975	32.204	34.420
Average % Normal cal./hr.				106.7	88.4	98.8	114.4	116.4	124.6	116.7	115.0	109.2	116.5

Table V

RECORDS OF CALORIES/HOUR/BODY WEIGHT$^{.73}$ OF INTACT DOGS ON PROTAMONE GROUP I

	Normal			10/19	2 mg./kg./day								11/18	12mg./kg./day	
Dog No.	10/10	10/14	10/17		10/21	10/24	10/27	10/30	11/2	11/5	11/11	11/17		11/29	12/6
#1	4.560	4.659	4.698		4.631	4.876	3.009	3.892	4.044	4.723	4.489	3.963		4.345	4.040
	Average cal/hr/wt$^{.73}$ 4.639														
	% cal/hr/wt$^{.73}$				99.8	105.1	64.9	83.9	87.2	101.8	96.8	85.4		93.7	87.1
#2	4.974	4.515	4.718		4.241	5.301	3.076	4.226	4.908	5.719	5.715	5.964		5.609	9.153
	Average cal/hr/wt$^{.73}$ 4.736														
	% cal/hr/wt$^{.73}$				89.5	111.9	64.9	89.2	103.6	120.8	120.7	125.9		118.4	193.3
#5A	3.867	3.387	3.509		4.030	3.688	4.286	4.752	4.017	4.490	4.291	3.914		4.505	4.758
	Average cal/hr/wt$^{.73}$ 3.588														
	% cal/hr/wt$^{.73}$				112.3	102.8	119.4	132.4	112.0	125.1	119.6	109.1		125.6	132.6
#28	5.530	5.226	5.178		4.922	3.277	2.870	3.700	4.088	5.197	4.870	4.660		4.793	5.985
	Average cal/hr/wt$^{.73}$ 5.311														
	% cal/hr/wt$^{.73}$				92.7	61.7	54.0	69.7	77.0	97.8	91.7	87.7		88.7	112.7
Ave. cal/hr wt$^{.73}$	4.733	4.447	4.526		4.456	4.286	3.310	4.142	4.264	5.032	4.841	4.625		4.813	5.984
Average % cal/hr/wt$^{.73}$					98.6	95.4	75.8	93.8	95.0	111.4	107.2	102.0		106.6	131.4

Table VI

RECORDS OF CALORIES/HOUR/BODY WEIGHT$^{.73}$ OF INTACT DOGS ON PROTAMONE GROUP II

	Normal			10/19 4 mg./kg./day								11/29 20 mg./kg./day	
Dog No.	10/10	10/14	10/17	10/21	10/24	10/27	10/30	11/2	115	11/11	11/17	11/29	12/6
#3	4.694	4.228	4.808	4.511	4.418	3.537	3.281	4.279	4.723	4.769	4.566	3.743	4.313
	Average cal/hr/wt$^{.73}$ 4.577												
	% cal/hr/wt$^{.73}$			98.6	96.5	77.3	71.7	93.5	103.2	104.2	99.8	81.8	94.2
#4	4.079	3.772	3.957	4.790	3.471	2.864	3.561	4.528	5.719	4.703	3.972	3.922	4.293
	Average cal/hr/wt$^{.73}$ 3.936												
	% cal/hr/wt$^{.73}$			121.7	88.2	72.8	90.5	115.0	145.3	119.5	100.9	99.6	109.1
#27	4.647	5.162	4.768	4.574	3.859	3.496	4.395	4.097	4.378	3.931	4.865	4.503	4.826
	Average cal/hr/wt$^{.73}$ 4.859												
	% cal/hr/wt$^{.73}$			94.1	79.4	71.9	90.4	84.3	90.1	80.9	100.1	92.7	99.3
Ave. cal/hr/wt$^{.73}$	4.473	4.387	4.511	4.625	3.916	3.299	3.746	4.301	4.940	4.468	4.468	4.056	4.477
Average % cal/hr/wt$^{.73}$				104.8	88.0	74.0	84.2	97.6	112.9	101.5	100.3	91.4	100.9

Table VII

RECORDS OF CALORIES/HOUR/BODY WEIGHT^{73} OF INTACT DOGS ON PROTAMONE GROUP III

	Normal			10/19	8 mg./kg./day							11/18 28mg./kg./day	
Dog No.	10/10	10/14	10/17	10/21	10/24	10/27	10/30	11/2	11/5	11/11	11/17	11/29	12/6
#25	5.407	4.676	4.728	5.332	4.172	3.803	4.555	4.601	4.791	4.909	5.031	4.214	4.369
	Average cal/hr/wt^{73} 4.937												
	% cal/hr/wt^{73}			108.0	84.5	77.0	92.3	93.2	97.0	99.4	101.9	85.4	88.5
#26	4.487	5.035	4.252	4.607	3.236	6.475	5.985	5.097	7.121	6.215	5.509	5.398	5.673
	Average cal/hr/wt^{73} 4.644												
	% cal/hr/wt^{73}			99.2	69.7	139.4	128.9	109.8	153.3	133.8	118.6	116.2	122.2
#5B	4.233	4.157	4.353	4.558	3.874	3.468	4.336	6.585	3.792	4.042	4.496	5.065	4.737
	Average cal/hr/wt^{73} 4.248												
	% cal/hr/wt^{73}			107.3	91.2	81.6	102.1	155.0	89.3	95.2	105.8	119.2	111.5
#24	4.939	4.450	4.559	4.845	4.446	3.655	4.756	3.851	5.468	4.573	4.555	3.641	4.438
	Average cal/hr/wt^{73} 4.649												
	% cal/hr/wt^{73}			104.2	95.6	78.6	102.3	82.8	117.6	98.4	98.0	78.3	95.5
Ave. cal/hr/wt^{73}	4.766	4.579	4.473	4.836	3.932	3.398	4.908	5.034	5.793	4.935	4.898	4.580	4.804
Average % cal/hr/wt^{73}				104.7	85.2	94.2	106.4	110.2	114.3	106.7	106.1	99.8	104.4

Table VIII

RECORDS OF *BODY WEIGHT OF INTACT DOGS ON PROTAMONE GROUP I

*Weight in kg.

	Normal						10/19	2 mg./kg./day								11/18	12mg./kg./day	
Dog No.	10/2	10/6	10/8	10/10	10/14	10/17		10/21	10/24	10/27	10/30	11/2	11/5	11/11	11/17		11/29	12/6
#1	10.4	10.2	10.6	10.6	11.0	11.4		11.7	11.6	12.0	12.5	12.5	12.6	12.5	12.7		12.0	13.2
Normal average weight 10.7																		
% normal weight								109.3	108.4	112.1	116.8	116.8	117.8	116.8	118.7		112.1	123.4
#2	11.3	11.6	11.5	11.5	11.8	12.1		12.5	12.4	12.6	12.7	12.9	13.1	13.1	12.4		12.7	13.1
Normal average weight 11.6																		
% Normal weight								107.8	106.9	108.6	109.5	111.2	112.9	112.9	106.9		109.5	112.9
#5A	8.4	8.6	8.1	7.9	7.8	7.5		7.8	7.8	8.3	8.8	8.3	8.6	8.5	8.1		8.3	8.7
Normal average weight 8.0																		
% normal weight								97.5	97.5	103.8	110.0	103.8	107.5	106.2	101.2		103.8	108.8
#28	15.0	15.5	15.1	15.5	15.7	15.7		15.8	15.5	16.0	16.5	16.0	15.8	16.3	16.2		15.3	15.9
Normal average weight 15.4																		
% normal weight								102.6	100.6	103.9	107.1	103.9	102.6	105.8	105.2		99.4	103.2
Ave. of body wts.	11.3	11.5	11.3	11.4	11.6	11.7		12.0	11.8	12.2	12.6	12.4	12.5	12.6	12.4		12.1	12.7
Average % normal weight								104.3	103.4	107.1	110.8	106.9	110.2	110.4	108.0		106.2	112.1

Table IX

RECORDS OF *BODY WEIGHT OF INTACT DOGS ON PROTAMONE GROUP II

* Weight in Kg.

	Normal						10/19 4 mg./kg./day								11/18 20 mg./kg./day	
Dog No.	10/2	10/6	10/8	10/10	10/14	10/17	10/21	10/24	10/27	10/30	11/2	11/5	11/11	11/17	11/29	12/6
#3	10.4	10.6	10.5	9.9	10.7	10.6	11.0	11.1	11.2	12.4	11.4	11.6	11.2	11.7	12.0	12.4
Normal average weight 10.4																
% normal weight							105.8	106.7	107.7	119.2	109.6	111.5	107.7	112.5	115.4	119.2
#4	14.8	15.4	15.6	15.1	15.3	15.4	15.9	15.9	16.6	16.5	16.8	16.7	16.6	16.1	16.7	16.9
Normal average weight 15.3																
% normal weight							103.9	103.9	108.5	107.8	109.8	109.2	108.5	105.2	109.2	110.5
#27	12.1	12.2	12.0	11.9	11.7	11.5	11.9	12.0	12.0	12.7	12.1	12.0	12.3	11.9	11.9	12.4
Normal average weight 11.9																
% normal weight							100.0	100.8	100.8	106.7	101.7	100.8	103.4	100.0	100.0	111.3
Ave. Body wt.	12.4	12.7	12.7	12.3	12.6	12.5	12.9	13.0	13.3	13.9	13.4	13.4	13.4	13.2	13.5	13.9
Average % normal weight							103.2	103.8	105.7	111.2	107.0	107.2	106.5	105.9	108.2	111.3

Table X

RECORDS OF *BODY WEIGHT OF INTACT DOGS ON PROTAMONE GROUP III

* weight in kg.

	Normal						10/19	8 mg./kg./day								11/18	28 mg./kg./day	
Dog No.	10/2	10/6	10/8	10/10	10/14	10/17		10/21	10/24	10/27	10/30	11/2	11/5	11/11	11/17		11/29	12/6
#24	12.6	12.5	12.0	12.2	12.2	12.2		12.5	13.0	13.7	14.4	14.4	14.6	15.0	14.1		14.4	14.8
	Normal average weight 12.3																	
	% normal weight							101.6	105.7	111.4	117.1	117.1	118.7	122.0	123.6		126.0	128.4
#25	11.3	11.6	11.3	11.3	11.4	11.3		11.5	12.0	12.4	12.9	12.8	12.8	13.3	12.8		13.2	13.4
	Normal average weight 11.4																	
	% normal weight							100.8	105.2	108.7	113.1	112.3	112.3	116.7	112.3		115.8	117.5
#26	16.6	16.4	16.3	15.9	16.6	16.7		17.3	17.0	16.8	17.7	17.7	18.0	17.5	17.5		18.2	18.3
	Normal average weight 16.4																	
	% normal weight							105.5	103.6	102.4	107.9	107.9	109.8	106.7	106.7		111.0	111.6
#5B	10.9	11.0	11.0	10.9	10.6	10.5		10.7	11.0	11.1	11.6	10.9	11.2	11.3	11.0		10.8	11.5
	Normal average weight 10.8																	
	% normal weight							99.1	101.8	102.8	107.4	100.9	103.7	104.6	101.8		100.0	106.5
Ave. Body wt.	12.8	12.9	12.6	12.6	12.7	12.7		13.0	13.2	13.5	14.2	14.0	14.2	14.3	14.1		14.4	14.8
Average % normal weight								101.8	104.1	106.3	111.4	109.6	111.1	112.5	111.1		113.2	116.0

Table XI

RECORDS OF *PULSE OF INTACT DOGS ON PROTAMONE GROUP I

* pulse/min.

	Normal				10/19 2 mg./kg./day							11/18	12 mg./kg./day	
Dog Number	10/8	10/10	10/14	10/17	10/21	10/24	10/27	10/30	11/2	11/5	11/11	11/17	11/29	12/6
# 1	82	98	88	104	112	102	110	106	110	142	98	104	--	106
Average normal pulse 93.0														
% pulse normal					120.4	109.7	118.3	114.0	118.3	152.7	105.4	111.8	--	114.0
# 2	102	104	106	102	112	104	80	104	96	102	108	112	106	112
Average normal pulse 103.5														
% pulse normal					108.2	100.5	77.3	100.5	92.8	98.6	104.3	108.2	102.4	108.2
# 5A	74	74	80	70	78	84	80	96	74	100	104	80	92	80
Average normal pulse 74.5														
% pulse normal					104.7	112.8	107.4	128.9	99.3	134.2	139.6	107.4	123.5	107.4
#28	54	64	72	92	82	80	72	76	80	78	90	90	92	120
Average normal pulse 99.3														
% pulse normal					116.3	113.5	102.1	107.8	113.5	110.6	119.5	113.8	118.8	125.0
Ave. Pulse	78.0	85.0	86.5	92.0	96	92.5	85.5	95.5	90.0	105.5	100.0	96.5	96.7	104.5
Average % normal pulse					112.4	109.1	101.3	112.8	106.0	124.0	119.5	113.8	118.8	113.6

Table XII

RECORDS OF *PULSE OF INTACT DOGS ON PROTAMONE GROUP II

*pulse/min.

	Normal				10/19	4 mg./kg./day							11/18	20 mg./kg./day
Dog Number	10/8	10/10	10/14	10/17	10/21	10/24	10/27	10/30	11/2	11/5	11/11	11/17	11/29	12/6
# 3	98	86	82	98	102	96	96	96	126	94	100	112	120	118
Average normal pulse 91.0														
% pulse normal					112.1	105.5	105.5	105.5	138.5	103.3	109.9	123.0	131.9	129.7
# 4	85	108	116	104	102	118	112	102	120	118	124	108	120	116
Average normal pulse 103.2														
% pulse normal					98.8	114.3	108.5	98.8	116.3	114.3	120.2	104.7	116.3	112.4
# 27	104	74	94	92	102	84	84	140	140	86	102	106	110	120
Average normal pulse 91.0														
% pulse normal					112.1	92.3	92.3	153.8	153.8	94.5	112.1	116.5	127.5	131.9
Ave. pulse	95.7	89.3	97.3	98.0	102.0	99.3	97.3	112.7	128.7	99.3	108.7	108.7	118.7	118.0
Average % normal pulse					107.7	104.0	102.1	119.4	136.2	104.0	114.1	114.7	125.2	124.7

Table XIII

RECORDS OF *PULSE OF INTACT DOGS ON PROTAMONE GROUP III

* pulse/min

	Normal				10/19 8 mg./kg./day								11/18 28 mg./kg./day	
Dog Number	10/8	10/10	10/14	10/17	10/21	10/24	10/27	10/30	11/2	11/5	11/11	11/17	11/29	12/6
# 25	100	88	100	106	88	82	106	118	108	94	102	108	106	88
Average normal pulse 98.5														
% pulse normal					89.3	83.2	107.6	119.7	109.6	95.4	103.6	109.6	107.6	89.3
# 26	50	86	90	80	98	114	84	92	164	102	88	88	76	104
Average normal pulse 76.5														
% pulse normal					128.1	149.0	109.8	120.3	214.4	133.3	115.0	115.0	99.3	135.9
# 5B	100	100	100	102	106	108	120	136	140	120	142	100	142	132
Average normal pulse 100.5														
% pulse normal					105.5	107.5	119.4	135.3	139.3	119.4	141.3	99.5	141.3	131.3
# 24	86	102	86	86	104	130	102	100	112	100	110	100	120	108
Average normal pulse 90.0														
% pulse normal					115.6	144.4	113.3	111.1	124.4	111.1	122.2	111.1	133.3	120.0
Ave. pulse	84.0	94.0	94.0	93.5	99.0	108.5	103.0	111.5	131.0	104.0	110.5	99.0	111.0	108.0
Avex % normal pulse					109.6	121.0	112.5	121.6	146.9	114.8	120.5	108.8	120.4	119.1

Table XIV

RECORDS OF *BODY TEMPERATURE OF INTACT DOGS ON PROTAMONE GROUP I

* body temperature degrees F.

	Normal					10/19 2 mg./kg./day								11/18 12 mg./kg./day	
Dog No.	10/6	10/8	10/10	10/14	10/17	10/21	10/24	10/27	10/30	11/2	11/5	11/11	11/17	11/29	12/6
# 1	99.8	100.2	100.4	100.6	102.2	100.4	101.0	101.2	101.4	100.4	100.0	101.6	100.4	99.6	101.4
	Average normal temperature 100.6														
	% normal temperature					99.8	100.4	100.6	100.8	99.8	99.4	101.6	99.8	99.0	100.8
# 2	100.2	98.6	101.0	100.4	101.4	100.4	100.0	100.0	100.2	98.8	100.8	100.2	101.0	101.6	101.0
	Average normal temperature 100.3														
	% normal temperature					100.1	99.7	99.7	99.9	98.5	100.5	99.9	100.7	101.3	100.7
# 5A	99.4	97.6	100.6	99.6	99.4	99.4	98.0	99.4	100.8	99.4	100.4	100.5	101.9	100.3	101.7
	Average normal temperature 99.3														
	% normal temperature					100.1	98.7	100.1	101.5	100.1	101.1	101.2	102.6	101.0	102.4
# 28	98.8	100.6	98.4	99.6	99.0	100.4	99.6	100.6	100.2	100.4	100.8	99.6	100.8	100.6	100.4
	Average normal temperature 99.3														
	% normal temperature					101.1	100.3	101.3	100.9	101.1	101.5	100.3	101.5	101.3	101.1
Ave. body temp.	99.6	99.2	100.1	100.0	100.5	100.2	99.6	100.3	100.6	99.8	100.5	100.4	100.8	100.4	101.0
Average % normal temperature						100.3	99.8	100.4	100.8	99.9	100.4	100.8	101.2	100.6	101.2

Table XV

RECORDS OF *BODY TEMPERATURE OF INTACT DOGS ON PROTAMONE GROUP II

*body temperature degrees F.

	Normal					10/19	4 mg./kg./day								11/18	20 mg./kg./day	
Dog No.	10/6	10/8	10/10	10/14	10/17		10/21	10/24	10/27	10/30	11/2	11/5	11/11	11/17		11/29	12/6
#3	100.2	98.0	102.0	100.2	100.0		99.6	99.4	101.0	101.0	100.4	100.6	100.6	101.0		99.0	102.4
	Average normal temperature 100.1																
	% normal temperature						99.5	99.3	100.9	100.9	100.3	100.5	100.5	100.9		98.9	102.3
#4	99.4	98.6	100.4	100.0	100.0		100.2	101.8	100.4	100.6	100.6	100.4	102.1	100.9		102.3	100.9
	Average normal temperature 99.7																
	% normal temperature						100.5	102.1	100.7	100.9	100.9	100.7	102.4	101.2		102.6	101.2
#27	100.4	99.2	98.2	98.6	99.0		99.4	99.6	99.6	99.2	101.4	99.6	99.0	99.6		99.4	99.6
	Average normal temperature 99.1																
	% normal temperature						100.3	100.5	100.5	100.1	102.3	100.5	99.9	100.5		100.3	100.5
Ave. body temp.	100.0	98.6	100.2	99.6	99.7		99.7	100.3	100.3	100.3	100.8	100.2	100.5	100.4		100.1	100.9
Average % normal temperature							100.1	100.6	100.7	100.6	101.2	100.6	100.9	100.9		100.6	101.3

Table XVI

RECORDS OF *BODY TEMPERATURE OF INTACT DOGS ON PROTAMONE GROUP III

* body temperature degrees F.

	Normal					10/19	8 mg./kg./day							11/18	28 mg./kg./day	
Dog No.	10/6	10/8	10/10	10/14	10/17		10/21	10/24	10/27	10/30	11/2	11/5	11/11	11/17	11/29	12/6
# 25	97.2	100.4	99.8	99.2	99.2		101.0	98.6	99.6	100.6	99.6	100.8	100.4	103.0	99.4	99.0
Average normal temperature 99.2																
% normal temperature							101.8	99.4	100.4	101.4	100.4	101.6	101.2	103.8	100.2	98.8
# 26	101.4	101.0	99.4	100.0	99.6		102.8	103.2	100.2	99.4	99.4	100.4	101.0	99.0	101.4	101.6
Average normal temperature 100.3																
% normal temperature							102.5	102.9	99.9	99.1	99.1	100.1	100.7	98.7	101.1	101.3
# 5B	98.4	98.6	99.4	99.6	99.0		99.6	100.6	99.6	99.6	99.6	100.4	101.2	99.4	101.0	99.8
Average normal temperature 99.0																
% normal temperature							100.6	101.6	100.6	100.6	100.6	101.4	102.0	104.0	102.0	100.8
# 24	97.4	100.6	100.6	100.0	100.6		100.0	99.6	100.0	100.6	99.8	101.4	99.6	100.6	99.6	100.2
Average normal temperature 99.8																
% normal temperature							100.2	99.8	100.2	100.8	100.0	101.6	99.8	100.8	99.8	100.4
Ave. body temp.	98.6	100.2	99.8	99.7	99.6		100.8	100.5	99.8	100.0	99.6	100.8	100.6	100.5	100.4	100.2
Average % normal temperature							101.3	100.9	100.3	100.5	100.0	101.2	100.9	101.8	100.8	100.6

Table XVII

RECORDS OF CALORIES PER HOUR OF INTACT DOGS RECEIVING DESICCATED THYROID

		Period Previous to Dosage			Dose Period (# 6 received 4 mg./kg./day (# 29 received 2 mg./kg./day			
Dog Number		1/4	1/14	1/18	1/27	2/3	2/10	2/17
# 6	Cal./hr.	28.305	21.688	29.053	17.796	31.081	22.317	23.008
	% of normal cal./hr.				67.5	118.0	84.7	87.3
	Average normal cal./hr. 26.349							
# 29	Cal./hr.	31.571	28.114	38.199	22.110	30.270	28.849	37.145
	% of normal cal./hr.				67.8	92.8	88.4	113.8
	Average normal cal./hr. 32.628							
Average cal./hr.		29.938	24.901	33.626	19.953	30.676	25.583	30.076
Average % normal cal./hr.					67.6	105.4	86.6	100.6

Table XVIII

RECORDS OF CALORIES/HR./KG.$^{.73}$ OF INTACT DOGS RECEIVING DESICCATED THYROID

Dog Number		Period Previous to Dosage			Dose Period (# 6 received 4 mg./kg./day (# 29 received 2 mg./kg./day			
		1/4	1/14	1/18	1/27	2/3	2/10	2/17
# 6	cal/hr/kg$^{.73}$	5.647	4.362	5.843	3.551	6.302	4.519	4.704
	% of normal cal/hr/kg$^{.73}$				67.2	119.3	85.5	89.0
	Average normal cal/hr/kg$^{.73}$		5.284					
# 29	cal/hr/kg$^{.73}$	6.919	6.336	8.609	5.079	7.023	6.502	8.452
	% of normal cal/hr/kg$^{.73}$				69.7	96.4	89.2	116.0
	Average normal cal/hr/kg$^{.73}$		7.288					
Average cal./hr./kg.$^{.73}$		6.283	5.349	7.226	4.315	6.662	5.510	6.578
Average % normal cal/hr/kg$^{.73}$					68.4	107.8	87.4	102.5

Table XIX

RECORDS OF WEIGHTS* OF INTACT DOGS RECEIVING DESICCATED THYROID

*weight in kg.

(# 6 received 4 mg./kg./day
(#29 received 2 mg./kg./day

		Period Previous to Dosage			Dose Period			
Dog Number		1/4	1/14	1/18	1/27	2/3	2/10	2/17
# 6	Weight	9.1	9.0	9.0	9.1	8.9	8.9	8.8
	% of normal weight				101.1	98.9	98.9	97.8
	Average normal weight 9.0							
# 29	Weight	8.0	7.7	7.7	7.5	7.4	7.7	7.6
	% of normal weight				96.2	94.9	98.7	97.4
	Average normal weight 7.8							
Average weight		85	8.4	8.4	8.3	8.2	8.3	8.2
Average % normal weight					98.6	96.9	98.8	97.6

Table XX

RECORDS OF PULSE* OF INTACT DOGS RECEIVING DESICCATED THYROID

* pulse/minute

		Period Previous to Dosage			Dose Period (# 6 received 4 mg./kg./day (#29 received 2 mg./kg./day			
Dog Number		1/4	1/14	1/18	1/27	2/3	2/10	2/17
# 6	Pulse	106	114	104	130	108	160	128
	% normal pulse				120.4	100.0	148.1	118.5
	Average normal pulse 108.0							
# 29	Pulse	90	122	114	130	138	130	134
	% normal pulse				119.6	127.0	119.6	123.3
	Average normal pulse 108.7							
Average weight		98	118	109	130	123	145	131
Average % normal weight					120.0	113.5	133.8	120.9

Table XXI

RECORDS OF BODY TEMPERATURE* OF INTACT DOGS RECEIVING DESICCATED THYROID

*temperature in degrees F

		Period Previous to Dosage			Dose Period (#6 received 4 mg./kg./day; #29 received 2 mg./kg./day)			
Dog Number		1/4	1/14	1/18	1/27	2/3	2/10	2/17
# 6	Temperature	101.0	100.4	100.0	99.8	99.4	100.0	100.6
	% of normal temperature				99.3	98.9	99.5	100.1
	Average normal temperature 100.5							
# 29	Temperature	100.8	99.4	100.2	100.6	100.4	101.0	99.6
	% of normal temperature				100.5	100.3	100.9	99.5
	Average normal temperature 100.1							
Average temperature		100.9	99.9	100.1	100.2	99.9	100.5	100.1
Average % normal temperature					99.9	99.6	100.2	99.8

Table XXII

*BODY WEIGHT RECORDS IN A LONG TIME TRIAL WITH PROTAMONE ON INTACT ENGLISH BULL DOG BITCHES

* in kg.

** Dog II is the control

Date	Dog I	**Dog II	Dog III
11/25	15.100	—	13.000
11/29	15.778	16.977	13.119
12/2	16.170	18.410	13.190
12/9	16.519	18.440	13.426
12/18	16.810	19.090	14.318
1/4	17.080	19.553	14.055
1/11	16.645	19.759	14.950
1/24	15.400	18.430	13.820
2/7	17.115	20.010	14.900
8/21	16.290	19.525	13.740
3/7	16.730	19.680	14.550
3/21	15.960	19.160	13.965
4/4	16.020	18.680	14.300
4/18	15.780	18.935	14.545

Dogs I and II were fed Protamone at the rate of 2 gms./100 lbs. dry matter in the feed. Dog II was the control.

Table XXIII

EFFECTS OF THYROIDECTOMY UPON CAL./HR.*

* figures in cal./hr

Dog No.		Average Normal 10/10/48-10/17/48	12/6/48 Last run under Protamone	1/4/49	1/14/49	1/18/49
#1	Cal./hr.	26.712	26.570	20.684	17.136	18.024
	% of normal cal./hr.		99.5	77.4	64.2	67.5
Thyroidectomy 12/8/48						
#26	Cal./hr./	35.490	47.235	41.096	32.398	36.585
	% of normal cal./hr.		133.1	115.8	91.3	103.1
Thyroidectomy 12/9/48						
#27	Cal./hr.	29.568	30.327	26.400	24.098	22.597
	% of normal cal./hr.		102.6	89.3	81.5	76.4
Thyroidectomy 12/9/48						
Accessory thyroid indicated						
#5	Cal./hr.	15.977	23.081	21.773	20.349	29.860
	% of normal cal./hr.		144.5	136.3	127.4	186.9
Thyroidectomy 12/8/48						
Accessory thyroid indicated						
#28	Cal./hr.	39.516	45.088	40.007	38.020	--
	% of normal cal./hr.		114.1	101.2	96.2	--
Thyroidectomy 12/9/48						
Average cal./hr. with #5 and #28 omitted		30.590	34.711	29.393	24.544	25.735
Average % of normal cal./hr. with #5 and # 28 omitted			111.7	94.2	79.0	82.3

Average cal./hr. of 1/14/49 and 1/18/49 with # 5 and # 28 omitted 25.140

Average % of normal cal./hr. with #5 and #28 omitted 80.6

Table XXIV

EFFECTS OF THYROIDECTOMY UPON CAL./HR./KG.$^{.73}$

*figures in cal./hr./kg.$^{.73}$

Dog No.		Average Normal 10/10/48-10/17/48	12/6/48 Last run under Protamone	1/4/49	1/14/49	1/18/49
#1	Cal./hr./kg.$^{.73}$	4.639	4.040	3.312	2.744	2.836
	% of normal cal./hr./kg.$^{.73}$		87.1	71.4	59.2	61.1
Thyroidectomy 12/8/48						
#26	Cal./hr./kg.$^{.73}$	4.644	5.673	4.846	3.719	4.394
	% of normal cal./hr./kg.$^{.73}$		122.2	104.3	80.1	94.6
Thyroidectomy 12/9/48						
#27	Cal./hr./kg.$^{.73}$	4.859	4.826	3.886	4.529	3.192
	% of normal cal./hr./kg.$^{.73}$		99.3	80.0	72.6	65.7
Thyroidectomy 12/9/48						
Accessory thyroid indicated						
#5	Cal./hr./kg.$^{.73}$	3.588	4.758	4.415	4.126	6.054
	% of normal cal./hr./kg.$^{.73}$		132.6	123.0	115.0	168.7
Thyroidectomy 12/9/48						
Accessory thyroid indicated						
#28	Cal./hr./kg.$^{.73}$	5.311	5.985	5.411	5.001	--
	% of normal cal./hr./kg.$^{.73}$		112.7	101.9	94.2	--
Thyroidectomy 12/9/48						
Average cal./hr./kg.$^{.73}$ with #5 and #28 omitted		4.714	4.846	4.015	3.331	3.474
Average % of normal cal./hr./kg.$^{.73}$ with #5 and #28 omitted			102.9	85.2	70.6	73.8

Average cal./hr./kg.$^{.73}$ of 1/14/49 and 1/18/49 with #5 and #28 omitted 3.402

Average % of normal cal./hr./kg.$^{.73}$ with #5 and #28 omitted 72.2

Table XXV

EFFECTS OF THYROIDECTOMY UPON BODY WEIGHT*

* weights in kg.

Dog No.		Average Normal 10/10/48-10/17/48	12/6/48 Last run under Protamone	1/4/49	1/14/49	1/18/49
#1	Weight	10.7	13.2	12.3	12.3	12.6
	% of normal weight		123.4	115.0	115.0	117.8
Thyroidectomy 12/8/48						
#26	Weight	16.4	18.3	18.7	19.4	18.3
	% of normal weight		111.6	114.0	118.3	111.6
Thyroidectomy 12/9/48						
#27	Weight	11.9	12.4	13.8	13.9	14.6
	% of normal weight		104.2	116.0	116.8	122.7
Thyroidectomy 12/9/48						
Accessory thyroid indicated						
#5	Weight	8.0	8.7	8.9	8.9	8.9
	% of normal weight		108.8	111.2	111.2	111.2
Thyroidectomy 12/9/48						
Accessory thyroid indicated						
#28	Weight	15.4	15.9	15.5	16.1	15.6
	% of normal weight		103.2	100.6	104.5	101.3
Thyroidectomy 12/9/48						
Average weight with #5 and #28 omitted		13.0	14.6	14.9	15.2	15.2
Average % of normal weight with #5 and #28 omitted			113.1	115.0	116.7	117.4

Average weight of 1/14/49 and 1/18/49 with #5 and #28 omitted 15.2

Average % of normal weight of 1/14/49 and 1/18/49 with #5 and #28 omitted 117.0

Table XXVI

EFFECTS OF THYROIDECTOMY UPON PULSE*

*figures in pulse/minute

Dog No.		Average Normal 10/8/48-10/17/48	12/6/48 Last run under Protamone	1/4/49	1/14/49	1/18/49
#1	Pulse	93.0	106	78	94	72
	% of normal pulse		114.0	83.9	101.1	77.4
Thyroidectomy 12/8/48						
#26	Pulse	76.5	104	78	66	66
	% of normal pulse		135.9	102.0	86.3	86.3
Thyroidectomy 12/9/48						
#27	Pulse	91.0	120	82	74	64
	% of normal pulse		131.9	90.1	81.3	70.3
Thyroidectomy 12/9/48						
Accessory thyroid indicated						
# 5	Pulse	74.5	80	100	80	82
	% of normal pulse		107.4	134.2	107.4	110.1
Thyroidectomy 12/9/48						
Accessory thyroid indicated						
#28	Pulse	99.3	120	88	70	90
	% of normal pulse		120.8	88.6	70.5	90.6
Thyroidectomy 12/9/48						
Average pulse with #5 and #28 omitted		86.8	110.0	79.3	78.0	67.3
Average % of normal pulse with #% and #28 omitted			127.3	92.0	89.6	78.0

Average pulse of 1/14/49 and 1/18/49 with #5 and #28 omitted 72.6
Average % of pulse of 1/14/49 and 1/18/49 with #5 and #28 omitted 83.8

Table XXVII

EFFECTS OF THYROIDECTOMY UPON TEMPERATURE *

* temperature in degrees F.

Dog No.		Average Normal 10/6/48–10/17/48	12/6/48 Last run under Protamone	1/4/49	1/14/49	1/18/49
#1	Temperature	100.6	101.4	98.6	99.8	101.2
	% of normal temperature		100.8	98.0	99.2	100.6
Thyroidectomy 12/8/48						
#26	Temperature	100.3	101.6	100.6	99.4	98.8
	% of normal temperature		101.3	100.3	99.1	98.5
Thyroidectomy 12/9/48						
#27	Temperature	99.1	99.6	100.0	99.0	98.8
	% of normal temperature		100.5	100.9	99.9	99.7
Thyroidectomy 12/9/48						
Accessory thyroid indicated						
#5	Temperature	99.3	101.7	99.6	99.4	99.4
	% of normal temperature		102.4	100.3	100.1	100.1
Thyroidectomy 12/9/48						
Accessory thyroid indicated						
#28	Temperature	99.3	100.4	100.6	99.4	99.8
	% of normal temperature		101.1	101.3	100.1	100.5
Thyroidectomy 12/9/48						
Average temperature with #5 and #28 omitted		100.0	100.8	99.7	99.4	99.6
Average % of normal temperature with #5 and #28 omitted			100.9	99.7	99.4	99.6

Average temperature of 1/14/49 and 1/18/49 with #5 and #28 omitted 99.5
Average % of normal temperature of 1/14/49 and 1/18/49 with #5 and #28 omitted 99.5

Table XXVIII

RESULTS OF I*131 INJECTIONS OF INTACT ENGLISH BULL BITCHES

ON PROTAMONE

Figures are in counts per minute

I, II, III were injected with 4000 Ct./min.

Ext. = Extremities   Thy. = Thyroid region

Time	Dog-I-17.1 kg.		Control Dog-II-20.0 kg.		Dog-III-149 kg.	
	Ext.	Thy.	Ext.	Thy.	Ext.	Thy.
7.5 m.	25	45	30	40	45	60
15 m.	30	80	20	35	35	50
30 m.	35	85	30	70	30	85
1 hr.	55	100	25	55	40	85
2 hr.	45	80	40	60	35	55
4 hr.	30	75	40	60	20	70
8 hr.	40	60	50	60	45	65
16 hr.	30	40	35	55	35	60
32 hr.	20	25	15	45	25	50
64 hr.	15	15	10	30	10	25

Table XXVIII (cont.)

t values of the above and logs of same

Time	t	log	t	t	log of ave. I and III
1 hr.	.000687	-3.16304	.001462	.001176	-2.87976
2 hr.	.000750	-3.12494	.001169	.000922	-2.98047
4 hr.	.000750	-3.12494	.001096	.001174	-2.94500
8 hr.	.000750	-3.12494	.000876	.001090	-3.00745
16 hr.	.000687	-3.16304	.000585	.001006	-3.09909
32 hr.	.000562	-3.25026	.000345	.000838	-3.22768
64 hr.	.000375	-3.42597	.000219	.000414	-3.50031

Dogs I and III were on 2 gm. of Protamone per 100 lbs. dry matter, which amounted to 2.0 to 1.7 mg./kg./day.

Dog II was untreated.

The t value was calculated after the thyroid gland had picked up its maximum count (1 hr.) by the following formula:

$$t = \frac{\text{counts per minute/body weight}}{\text{counts per minute injected}}$$

The regression equation of the logs of the t values was obtained for Dogs I and III as y = .009177 x -2.9249 and for dog II as y = .005139 x 3.1035

Table XXIX

RESULTS OF I*131 INJECTIONS
OF INTACT DOGS ON DESICCATED THYROID

All dogs were injected with 2000 cts./min. Figures in counts/min.
#6 was receiving 4 mgm./kg./day for 28 days before tests
#29 was receiving 2 mgm./kg./day for 28 days before tests
Ext.-extremities, Thy.- thyroid region

Time	Cts. Ext.	Dog #6 - 8.8kg. Thy.	Cts. Ext.	Dog #29 - 7.6kg. Thy.
7.5 min.	20	35	30	30
15min.	15	15	25	25
30 min.	20	55	15	25
1 hr.	20	50	30	45
2 hr.	40	45	40	45
4 hr.	15	35	15	40
8 hr.	30	30	30	45
16 hr.	20	25	20	25
32 hr.	15	25	5	25
64 hr.	5	10	10	20

t values of the above and logs of same

Time	t	t	log. of average
1 hr.	.002841	.002860	-2.54516
2 hr.	.002056	.002860	-2.61942
4 hr.	.001888	.002631	-2.64589
8 hr.	.001704	.002860	-2.64168
16 hr.	.001420	.001644	-2.92474
32 hr.	.001420	.001644	-2.92474
64 hr.	.000568	.001315	-3.02595

The t value was calculated after the thyroid gland had picked up its maximum count (1 hr.) by the following formula.

$$t = \frac{\text{counts per minute/body weight}}{\text{counts per minute injected}}$$

The regression equation of the logs. of the t values was obtained for the above dogs and was y = .007252x - 2.6295.

Table XXX

RESULTS OF I*131 INJECTIONS
ON INTACT ENGLISH BULL DOG PUPPIES ON PROTAMONE

All injected with 2000 cts./min. Figures in counts/min.
This group had been fed 4 gram/100 lbs. dry matter for 4 months previous to the test. Ext. - extremities, Thy. - thyroid region

Time	Cts. Dog 2 - 12.8kg. Ext.	Thy.	Cts. Dog 4 -13.5kg. Ext.	Thy.	Cts. Dog 7 - 12.2kg. Ext.	Thy.
7.5 min	35	40	55	55	30	55
15 min.	40	40	55	50	30	40
30 min.	75	75	70	80	40	45
1 hr.	25	45	30	35	40	45
2 hr.	25	25	50	55	20	25
4 hr.	30	30	35	35	40	35
8 hr.	45	40	30	55	30	45
16 hr.	15.	20	20	30	20	25
32 hr.	5	15	0	15	5	10
64 hr.	0	5	0	10	5	10

t values of the above and logs of same

Time	t	t	t	log. of average
1 hr.	.001753	.001296	.001344	-2.83446
2 hr.	.000938	.002037	.001024	-2.87517
4 hr.	.001172	.001296	.001434	-2.88572
8 hr.	.001562	.002037	.001344	-2.78304
16 hr.	.000781	.001111	.001024	-3.01233
32 hr.	.000586	.000555	.000410	-3.28651
64 hr.	.000180	.000370	.000410	-3.49485

The t value was calculated after the thyroid gland had picked up its maximum count (1 hr.) by the following formula.

$$t = \frac{\text{counts per minute/body weight}}{\text{counts per minute injected}}$$

The regression equation of the logs. of the t values was determined to by y = .01131x - 2.8194.

Table XXXI

RESULTS OF I*131 INJECTIONS
ON INTACT, UNTREATED, ENGLISH BULL DOG PUPPIES

All injected with 2000 cts./min.
Ext. - extremities, Thy. - thyroid region

Time	Cts.Dog1-11.4kg.		Cts.Dog3-13.7kg.		Cts.Dog5-9.6kg.		Cts.Dog6-9.6kg.	
	Ext.	Thy.	Ext.	Thy.	Ext.	Thy.	Ext.	Thy.
7.5 min.	30	40	15	35	40	50	35	55
15 min.	40	50	30	40	40	55	40	45
30 min.	60	70	25	55	45	60	55	55
1 hr.	30	40	40	65	20	40	20	55
2 hr.	25	55	40	55	35	60	30	55
4 hr.	30	45	35	65	35	40	30	30
8 hr.	40	55	40	40	25	40	35	55
16 hr.	20	30	30	35	15	25	20	30
32 hr.	5	15	20	25	5	15	10	20
64 hr.	10	10	10	20	5	10	15	15

t values of the above and logs of same

Time	t	t	t	t	log of average
1 hr.	.001754	.002372	.002083	.002864	-2.64436
2 hr.	.002412	.002007	.003125	.002864	-2.58469
4 hr.	.001973	.002372	.002083	.001562	-2.70940
8 hr.	.002412	.001459	.002083	.002864	-2.65679
16 hr.	.001315	.001277	.001302	.001562	-2.86519
32 hr.	.000658	.000912	.000781	.001041	-3.07160
64 hr.	.000438	.000729	.000521	.000781	-3.20971

The t value was calculated after the thyroid gland had picked up its maximum count (1 hr.) by the following formula.

$$t = \frac{\text{counts per minute/body weight}}{\text{counts per minute injected}}$$

The regression equation of the logs. of the t values was determined to be $y = .010030x - 2.6488$.

Table XXXII

DESCRIPTION OF THE THYROIDECTOMIZED DOGS
ON PROTAMONE AND DESICCATED THYROID

Protamone Group

Dog 1 was a female, 1-year-old, Cocker-Pointer weighing 12.6 kg. and was dog 1 in the intact dogs on Protamone

Dog 3 was a male, 1-year-old, Smooth Haired Fox Terrier weighing 9.9 kg.

Dog 4 was a female, 1-year-old, short haired, mongrel weighing 9.7 kg.

Desiccated Thyroid Group

Dog 2 was a female, 2-year-old, Smooth Haired Fox Terrier weighing 9.5 kg.

Dog 24 was a male, 1 1/2-year-old, Gordon Setter weighing 19.5 kg.

Dog 25 was male, 1-year-old, long haired mongrel weighing 13.3 kg.

Dog 27 was a female, 2-year-old, Cocker weighing 13.9 kg. and was dog 27 in the intact dogs on Protamone.

Table XXXIII

RECORDS OF CAL./HR. OF THYROIDECTOMIZED DOGS ON DESICCATED THYROID

Dog Number		Thyroidectomy Level		Desiccated Thyroid 2.0mg./kg./day		Desiccated Thyroid 4.0mg./kg./day			Desiccated Thyroid 8.0mg./kg./day	
		1/14	1/18	1/27	2/3	2/10	2/17	2/24	3/3	3/10
#2	Cal./hr.	11.781	13.989	13.212	14.595	9.798	11.088	17.176	15.585	15.135
	% of thyroidectomy cal./hr.			102.5	113.3	76.0	86.0	133.3	121.0	117.5
	Average of thyroidectomy cal./hr.			12.885						
#24	Cal./hr.	20.884	23.135	21.302	25.946	25.583	29.938	31.400	31.717	34.054
	% of thyroidectomy cal./hr.			96.8	117.9	116.2	136.0	142.7	144.1	154.7
	Average of thyroidectomy cal./hr.			22.010						
#25	Cal./hr.	28.917	25.018	26.425	31.351	26.672	35.759	35.426	49.489	29.730
	% of thyroidectomy cal./hr.			98.0	116.2	98.9	132.6	131.4	183.5	110.2
	Average of thyroidectomy cal./hr.			26.968						
#27	Cal./hr.	24.098	22.597	24.537	25.676	28.032	26.334	--	33.631	--
	% of thyroidectomy cal./hr.			105.1	110.0	120.1	112.8	--	144.0	--
	Average of thyroidectomy cal./hr.			23.348						
Average cal./hr.		21.420	21.185	21.369	24.392	22.521	25.780	28.001	32.606	26.306
		Average	21.302	Average	22.880		*Average	26.890	Average	29.456
Average % of thyroidectomy cal./hr.				100.6	114.4	102.8	116.8	135.8	148.2	127.5
				Average	107.5		*Average	126.3	Average	137.8

* 2/10 was not included in the average because the dogs had not had time to show an effect.

Table XXXIV

RECORDS OF CAL./HR./KG.$^{.73}$ OF THYROIDECTOMIZED DOGS ON DESICCATED THYROID

Dog Number	Thyroidectomy Level		Desiccated Thyroid 2.0mg./kg./day		Desiccated Thyroid 4.0mg./kg./day			Desiccated Thyroid 8.0mg./kg./day	
	1/14	1/18	1/27	2/3	2/10	2/17	2/24	3/3	3/10
#2 Cal./hr./kg.$^{.73}$	2.278	2.683	2.516	2.800	1.880	2.127	3.295	2.990	2.882
% of thyroidectomy cal./hr./kg.$^{.73}$			101.5	112.9	75.8	85.8	132.9	120.6	116.2
Average of thyroidectomy cal./hr./kg.$^{.73}$ 2.480									
#24 Cal./hr./kg.$^{.73}$	2.388	2.665	2.428	2.934	2.893	3.386	3.450	3.497	3.729
% of thyroidectomy cal./hr./kg.$^{.73}$			96.1	116.2	114.5	134.0	136.6	138.4	147.6
Average of thyroidectomy cal./hr./kg.$^{.73}$ 2.526									
#25 Cal./hr./kg.$^{.73}$	4.373	3.771	3.850	4.475	3.968	5.210	5.057	7.064	4.221
% of thyroidectomy cal./hr./kg.$^{.73}$			94.5	109.9	97.4	127.9	124.2	173.3	103.7
Average of thyroidectomy cal./hr./kg.$^{.73}$ 4.072									
#27 Cal./hr./kg.$^{.73}$	3.529	3.192	3.416	3.591	3.756	3.528	--	4.423	--
% of thyroidectomy cal./hr./kg.$^{.73}$			101.7	106.9	111.8	105.0	--	127.8	--
Average of thyroidectomy cal./hr./kg.$^{.73}$ 3.360									
Average cal./hr./kg.$^{.73}$	3.142	3.078	3.052	3.450	3.124	3.563	3.934	4.494	3.611
	Average	3.110	Average	3.251		*Average	3.748	Average	4.052
Average % of thyroidectomy cal./hr./kg.$^{.73}$			98.4	111.5	99.9	113.2	131.2	140.1	122.5
			Average	105.0		*Average	122.2	Average	131.3

* 2/10 was not included in the average because the dogs had not had time to show an effect.

Table XXXV

RECORDS OF *BODY WEIGHTS OF THYROIDECTOMIZED DOGS RECEIVING DESICCATED THYROID

*Body weight in kg.

Dog N Number		Thyroidectomy Level		Desiccated Thyroid 2.0mg./kg./day		Desiccated Thyroid 4.0mg./kg./day			Desiccated Thyroid 8.0mg./kg./day	
		1/14	1/18	1/27	2/3	2/10	2/17	2/24	3/3	3/10
#2	Weight	9.5	9.6	9.7	9.6	9.6	9.6	9.6	9.6	9.7
	% of thyroidectomy weight			101.6	100.5	100.5	100.5	100.5	100.5	101.6
	Average thyroidectomy weight 9.55									
#24	Weight	19.5	19.3	19.6	19.8	19.8	19.8	20.6	20.5	20.7
	% of thyroidectomy weight			101.0	102.1	102.1	102.1	106.2	105.7	106.7
	Average thyroidectomy weight 19.4									
#25	Weight	13.3	13.4	14.0	14.4	13.6	14.0	14.4	14.4	14.5
	% of thyroidectomy weight			104.9	107.1	101.9	104.9	107.1	107.1	108.6
	Average thyroidectomy weight 13.35									
#27	Weight	13.9	14.6	14.9	14.8	15.7	15.7	15.7	16.1	16.2
	% of thyroidectomy weight			104.6	103.8	110.2	110.2	110.2	113.0	113.7
	Average thyroidectomy weight 14.25									
Average weight		14.0	14.2	14.6	14.6	14.7	14.8	15.1	15.2	15.3
		Average	14.1	Average	14.6		*Average	15.0	Average	15.2
Average % of thyroidectomy weight				103.0	103.4	103.7	104.4	106.7	106.6	107.6
				Average	103.2		*Average	105.6	Average	107.1

* 2/10 was not included in the average because the dogs had not had time to show an effect.

Table XXXVI

RECORDS OF *PULSE OF THYROIDECTOMIZED DOGS RECEIVING DESICCATED THYROID

*Pulse/minute

		Thyroidectomy Level		Desiccated Thyroid 2.0mg./kg./day		Desiccated Thyroid 4.0mg./kg./day			Desiccated Thyroid 8.0mg./kg./day	
Dog Number		1/14	1/18	1/27	2/3	2/10	2/17	2/24	3/3	3/10
#2	Pulse	80	80	86	78	70	92	94	74	96
	% of thyroidectomy pulse			107.5	97.5	87.5	115.0	117.5	92.5	120.0
	Average thyroidectomy pulse 80.0									
#24	Pulse	76	74	60	74	80	60	62	92	80
	% of thyroidectomy pulse			80.0	98.7	106.7	80.0	82.7	122.7	106.7
	Average thyroidectomy pulse 75.0									
#25	Pulse	54	102	110	94	112	92	86	100	106
	% of thyroidectomy pulse			141.0	120.5	143.6	117.9	110.2	128.2	135.9
	Average thyroidectomy pulse 78.0									
#27	Pulse	74	64	66	78	88	84	90	84	64
	% of thyroidectomy pulse			95.6	113.0	127.5	121.7	130.4	121.7	92.8
	Average thyroidectomy pulse 69.0									
Average pulse		71	80	80.5	81.0	87.5	82.0	83.0	87.5	86.5
		Average	75.5	Average	80.8		*Average	82.5	Average	87.0
Average % of thyroidectomy pulse				106.0	107.4	116.3	108.6	110.2	116.3	113.8
				Average	106.7		*Average	109.4	Average	115.0

* 2/10 was not included in the average because the dogs hadnot had time to show an effect.

Table XXXVII

RECORDS OF *BODY TEMPERATURE OF THYROIDECTOMIZED DOGS RECEIVING DESICCATED THYROID

*Temperature in degrees F.

Dog Number		Thyroidectomy Level		Desiccated Thyroid 2.0mg./kg./day		Desiccated Thyroid 4.0mg./kg./day			Desiccated Thyroid 8.0mg./kg./day	
		1/14	1/18	1/27	2/3	2/10	2/17	2/24	3/3	3/10
#2	Temperature	100.0	99.4	99.8	99.6	100.8	100.0	100.4	100.8	100.0
	% of thyroidectomy temperature			100.1	99.9	101.1	100.3	100.7	101.1	100.3
	Average thyroidectomy temperature			99.7						
#24	Temperature	99.4	99.8	100.0	100.6	100.4	100.8	99.6	100.8	100.4
	% of thyroidectomy temperature			100.4	101.0	100.8	101.2	100.0	101.2	100.8
	Average thyroidectomy temperature			99.6						
#25	Temperature	98.4	98.8	99.2	99.4	99.4	99.6	99.2	99.6	99.8
	% of thyroidectomy temperature			99.6	99.8	99.8	100.0	99.6	100.0	100.2
	Average thyroidectomy temperature			99.6						
#27	Temperature	99.0	98.8	99.8	100.0	99.2	100.0	99.2	100.6	99.2
	% of thyroidectomy temperature			100.9	101.1	100.3	101.1	100.3	101.7	100.3
	Average thyroidectomy temperature			98.9						
Average temperature		99.2	99.2	99.7	99.9	100.0	100.1	99.6	100.4	99.8
		Average	99.2	Average	99.8		*Average	99.8	Average	100.1
Average % of thyroidectomy temperature				100.2	100.4	100.5	100.6	100.2	101.0	100.4
				Average	100.3		*Average	100.4	Average	100.7

* 2/10 was not included in the average because the dogs had not had time to show an effect.

Table XXXVIII

RECORDS OF CALORIES/HR. OF THYROIDECTOMIZED DOGS ON PROTAMONE

Dog Number		Thyroidectomy Level		Protamone 0.5mg./kg./day		Protamone 1.0mg./kg./day			Protamone 2.0mg./kg./day	
		1/14	1/18	1/27	2/3	2/10	2/17	2/24	3/3	3/10
#1	Cal./hr.	17.136	18.024	19.953	18.378	19.868	28.552	19.860	19.960	22.162
	% of thyroidectomy cal./hr.			113.5	104.5	113.0	162.4	113.0	113.5	126.1
	Average of thyroidectomy cal./hr. 17.580									
#3	Cal./hr.	19.278	24.480	28.851	23.784	21.773	31.601	29.253	34.724	27.568
	% of thyroidectomy cal./hr.			131.9	108.7	99.5	144.4	133.7	158.7	126.0
	Average of thyroidectomy cal./hr. 21.879									
#4	Cal./hr.	16.600	9.415	12.134	12.973	14.969	18.018	22.812	19.686	20.000
	% of thyroidectomy cal./hr.			93.3	99.7	115.1	138.5	175.4	151.3	153.8
	Average of thyroidectomy cal./hr. 13.008									
Average cal./hr		17.671	17.306	20.313	18.378	18.870	26.057	23.975	24.790	23.243
		Average	17.488	Average	19.346		*Average	25.016	Average	24.016
Average % of thyroidectomy cal./hr.				112.9	104.3	109.2	148.4	144.6	141.2	135.3
				Average	108.6		*Average	144.6	Average	138.2

* 2/10 was not included in the average because the dogs had not had time to show an effect.

Table XXXIX

RECORDS OF CAL./HR./KG.$^{.73}$ OF THYROIDECTOMIZED DOGS ON PROTAMONE

Dog Number		Thyroidectomy Level		Protamone 0.5mg./kg./day		Protamone 1.0mg./kg./day			Protamone 2.0mg./kg./day	
		1/14	1/18	1/27	2/3	2/10	2/17	2/24	3/3	3/10
#1	Cal./hr./kg.$^{.73}$	2.744	2.836	3.008	2.779	3.021	4.366	3.037	3.009	3.278
	% of thyroidectomy cal./hr./kg.$^{.73}$			107.6	99.4	108.1	156.2	108.6	107.6	117.3
	Average of thyroidectomy cal./hr./kg.$^{.73}$	2.795								
#3	Cal./hr./kg.$^{.73}$	3.617	4.430	5.184	4.187	3.833	5.526	5.081	5.952	4.634
	% of thyroidectomy cal./hr./kg.$^{.73}$			128.8	104.0	95.2	137.3	126.3	147.9	115.2
	Average of thyroidectomy cal./hr./kg.$^{.73}$	4.024								
#4	Cal./hr./kg.$^{.73}$	3.161	1.958	2.588	2.698	3.139	3.653	4.444	3.865	3.958
	% of thyroidectomy cal./hr./kg.$^{.73}$			101.1	105.4	122.6	142.7	173.6	151.0	154.6
	Average of thyroidectomy cal./hr./kg.$^{.73}$	2.560								
Average cal./hr./kg.$^{.73}$		3.174	3.075	3.593	3.221	3.331	4.515	4.187	4.275	3.957
		Average	3.124	Average	3.407		*Average	4.351	Average	4.116
Average % of thyroidectomy cal./hr./kg.$^{.73}$				112.5	102.9	108.6	145.4	136.2	135.5	129.0
				Average	107.7		*Average	140.8	Average	132.2

* 2/10 was not included in the average because the dogs had not had time to show an effect.

Table XL

RECORDS OF *BODY WEIGHTS OF THYROIDECTOMIZED DOGS ON PROTAMONE

Dog Number		Thyroidectomy Level 1/14	Thyroidectomy Level 1/18	Protamone 0.5mg./kg./day 1/27	Protamone 0.5mg./kg./day 2/3	Protamone 1.0mg./kg./day 2/10	Protamone 1.0mg./kg./day 2/17	Protamone 1.0mg./kg./day 2/24	Protamone 2.0mg./kg./day 3/3	Protamone 2.0mg./kg./day 3/10
#1	Weight	12.3	12.6	13.4	13.3	13.2	13.1	13.1	13.4	13.7
	% of thyroidectomy weight			107.6	106.8	106.0	105.2	105.2	107.6	110.0
	Average of thyroidectomy weight 12.45									
#3	Weight	9.9	10.4	10.5	10.8	10.8	10.9	11.0	11.2	11.5
	% of thyroidectomy weight			102.9	105.9	105.9	106.9	107.8	109.8	112.7
	Average of thyroidectomy weight 10.2									
#4	Weight	*8.7 (9.7)	8.6	8.3	8.6	8.5	8.9	9.4	9.3	9.2
	% of thyroidectomy weight			96.0	99.4	98.3	102.9	108.7	107.5	106.4
	Average of thyroidectomy weight 8.65									
Average weight		10.6	10.5	10.7	10.9	10.8	11.0	11.2	11.3	11.5
		Average	10.6	Average	10.8		*Average	11.1	Average	11.4
Average % of thyroidectomy weight				102.2	104.0	103.4	105.0	107.2	108.3	109.7
				Average	103.1		*Average	106.1	Average	109.0

* Weight in parenthesis is weight day before.

* 2/10 was not included in the average because the dogs had not had time to show an effect.

Table XLI

RECORDS OF *PULSE OF THYROIDECTOMIZED DOGS ON PROTAMONE

*pulse/minute

Dog Number		Thyroidectomy Level		Protamone 0.5mg./kg./day		Protamone 1.0mg./kg./day			Protamone 2.0mg./kg./day	
		1/14	1/18	1/27	2/3	2/10	2/17	2/24	3/3	3/10
#1	Pulse	94	72	88	78	70	84	64	74	92
	% of thyroidectomy pulse			106.0	94.0	84.3	101.2	77.1	89.2	110.8
	Average of thyroidectomy pulse 83.0									
#3	Pulse	54	68	76	44	68	54	60	68	64
	% of thyroidectomy pulse			124.6	72.1	111.5	88.5	98.4	111.5	104.9
	Average of thyroidectomy pulse 61.0									
#4	Pulse	80	96	92	86	100	90	92	92	92
	% of thyroidectomy pulse			104.5	97.7	113.6	102.3	104.5	104.5	104.5
	Average of thyroidectomy pulse 88.0									
Average pulse		76.0	78.7	85.3	69.3	79.3	76.0	72.0	78.0	82.7
		Average	77.4	Average	77.3		*Average	74.0	Average	80.4
Average % of thyroidectomy pulse				111.7	87.9	103.1	97.3	93.3	101.7	106.7
				Average	99.8		*Average	95.3	Average	104.2

* 2/10 was not included in the average because the dogs had not had time to show an effect.

Table XLII

RECORDS OF *BODY TEMPERATURE OF THYROIDECTOMIZED DOGS ON PROTAMONE

*Body temperature in degrees F

Dog Number		Thyroidectomy Leval		Protamone 0.5mg./kg./day		Protamone 1.0mg./kg./day			Protamone 2.0mg./kg./day	
		1/14	1/18	1/27	2/3	2/10	2/17	2/24	3/3	3/10
#1	Temperature	99.8	101.2	100.0	100.0	101.6	100.0	101.2	99.6	99.6
	% of thyroidectomy temperature			99.5	99.5	101.1	99.5	101.7	99.1	99.1
	Average of thyroidectomy temperature 100.5									
#3	Temperature	100.2	100.8	100.2	100.6	100.6	99.4	100.0	100.8	101.4
	% of thyroidectomy temperature			99.7	100.1	100.1	98.9	99.5	100.3	100.9
	Average of thyroidectomy temperature 100.5									
#4	Temperature	100.6	99.6	100.6	100.2	100.8	100.6	100.2	100.4	100.6
	% of thyroidectomy temperature			100.5	100.1	100.7	100.5	100.1	100.3	100.5
	Average of thyroidectomy temperature 100.1									
Average temperature		100.2	100.5	100.3	100.3	101.0	100.0	100.5	100.3	100.5
		Average	100.4	Average	100.3		*Average	100.3	Average	100.4
Average % of thyroidectomy temperature				99.9	99.9	100.6	99.6	100.4	99.9	100.2
				Average	99.9		*Average	100.0	Average	100.0

* 2/10 was not included in the average because the dogs had not had time to show an effect.

Table XLIII

RECORDS OF *BODY WEIGHTS OF ENGLISH BULL DOG PUPPIES
CONTROL GROUP

* body weight in kg.
Dogs 1 and 3 are males, dogs 5 and 6 are females.
Protamone Group started on trial 12/3/48

Date	Dog #1	Dog #3	Dog #5	Dog #6
11/1/48	1.984	1.503	1.134	1.049
11/13/48	3.232	2.353	1.843	1.843
11/20/48	2.800	3.900	2.440	2.200
12/2/48	2.980	4.475	2.737	2.570
12/9/48	3.664	5.327	2.913	3.115
12/16/48	4.100	6.170	3.372	3.600
12/23/48	4.850	6.792	4.270	4.740
1/1/49	5.840	8.380	5.200	5.300
1/8/49	6.985	9.102	5.475	5.730
1/15/49	7.560	9.170	6.100	6.140
1/24/49	8.820	10.263	7.130	6.965
1/31/49	10.050	11.460	8.100	7.800
2/7/49	10.995	12.065	8.265	8.560
2/14/49	10.985	12.860	8.710	8.855
2/21/49	11.430	13.698	9.645	9.638
2/28/49	11.815	13.565	9.415	9.775
3/7/49	12.005	14.370	9.645	9.710
3/14/49	12.380	14.035	10.170	10.405
3/21/49	12.940	14.755	11.045	10.880
3/28/49	14.590	15.330	11.593	11.450
4/4/49	15.220	16.600	12.300	11.970
4/11/49	15.530	17.040	12.145	11.620
4/18/49	16.200	17.515	12.955	11.950
4/25/49	16.830	18.100	13.415	12.105
5/2/49	16.330	18.170	13.185	12.320
5/9/49	16.010	17.830	13.100	11.970

Table XLIV

RECORDS OF *BODY WEIGHTS OF ENGLISH BULL DOG PUPPIES ON PROTAMONE

*body weight in kg.
Dogs 2 and 4 are males, dog 7 is a female.
Started on Protamone 4gm./100 lbs. of dry matter consumed 12/3/48

Date	Dog #2	Dog #4	Dog #7
11/1/48	1.899	1.106	1.361
11/13/48	3.260	2.268	2.410
11/20/48	4.100	2.440	2.450
12/2/48	4.855	2.273	2.800
12/9/48	5.247	2.950	3.424
12/16/48	5.760	3.800	4.200
12/23/48	6.585	4.550	4.960
1/1/49	7.520	6.360	6.130
1/8/49	8.235	7.800	7.145
1/15/49	8.650	7.845	7.365
1/24/49	9.650	9.255	8.440
1/31/49	10.290	10.310	9.220
2/7/49	12.015	12.355	10.875
2/14/49	11.755	12.740	11.260
2/21/49	12.800	13.465	12.165
2/28/49	13.030	14.100	12.290
3/7/49	12.620	13.940	12.435
3/14/49	13.310	14.505	12.805
3/21/49	13.810	15.275	13.530
3/28/49	15.140	16.341	14.545
4/4/49	15.370	17.530	14.675
4/11/49	15.655	18.555	15.405
4/18/49	16.205	19.285	15.365
4/25/49	16.060	19.460	16.340
5/2/49	16.475	20.080	15.940
5/9/49	16.095	20.630	16.320

Table XLV

RECORDS OF *BODY MEASUREMENTS OF ENGLISH BULL DOG PUPPIES, CONTROL GROUP

*Body measurements are in inches.
Dogs 1 and 3 are males, dogs 5 and 6 are females.
Protamone group started on trial 12/3/48
H-heart girth, F-flank girth, L-length from tailhead to nose, Ht-height at withers

	Dog #1				Dog #3				Dog #5				Dog #6			
Date	H	F	L	Ht	H	F	L	Ht	H	F	L	Ht	H	F	L	Ht
1/27/49	19	20	21	12	21	21	25	13	16	17	21	12	16	17	22	11
2/7/49	20	21	24	13	21	21	25	13½	17	19	23	13	18	17	22	12
2/21/49	20	18	24	13	22	20	26	15	18	18	24	13	18	18	24	12
3/7/49	20½	18	25	13½	22	20½	28	14½	19	19	26	12½	19½	18½	26	12½
3/21/49	22	20	27	14	23	21	30	14½	20	19	27	13	20	19	27½	12½
4/4/49	22	21	31	14	25	23½	28	15½	22	20	27½	14½	20½	20½	27	13½
4/18/49	23	22	30	14½	25	24	29	15½	21	20	29	14	20½	18	28	14
5/2/49	23	20	29	14½	24	21	30	15½	21	19	29	14½	21	19	29	14

RECORDS OF *BODY MEASUREMENTS OF ENGLISH BULL DOG PUPPIES ON PROTAMONE

*Body measurements are in inches.
Dogs 2 and 4 are males, dog 7 is a female.
Started on Protamone 4 gm./100 lbs. of dry matter consumed 12/3/48

	Dog #2				Dog #4				Dog #7			
Date	H	F	L	Ht	H	F	L	Ht	H	F	L	Ht
1/27/49	19	17	24	13	19	18	22	13	18	17	23	13
2/7/49	19	17	23	13	21	20	25	14	19½	19	23	14
2/21/49	20	19	25	13	21	19½	26	15	20	20	25	14
3/7/49	21	18	26	13½	22	19	28	14½	21	20	25	14
3/21/49	21	17	27	14	22	20	30	15½	21	17½	28	14
4/4/49	22	19	28	13½	23½	22	31	14½	22	19	28	15
4/18/49	23	20	29	15	25	22	33	15	23	19	29	15
5/2/49	22	20	29	14½	25	23	33	15½	23	20	29	15