PATHOLOGY OF EXPERIMENTAL HYPOTHYROIDISM IN GOATS

By

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THESIS

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DECLARATION

I hereby declare that this thesis entitled PATHOLOGY OF EXPERIMENTAL HYPOTHYROIDISM IN GOATS is a bonafide record of research work done by me during the course of research and that the thesis has not previously formed the basis for the award to me of any degree, diploma, associateship, fellowship, or other similar title of any other University or Society.

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C E R T I F I C A T E

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF ILLUSTRATIONS

INTRODUCTION

INTRODUCTION

The thyroid gland is unique among the endocrine glands in that its product thyroxin containing 70-80% of total body iodine significantly influences every organ in the body. It has been well established that iodine and thyroid functions are closely related and want of a little iodine could adversely affect the growth and production of the animal.

The existence of endemic goiter in man and animals due to absolute or relative deficiency of iodine has been well recognised since long. Kelly and Snedden (1960) while discussing the geographical distribution of endemic goiter in Asia have demarcated certain regions in India as endemic zones of goiter and this includes coastal areas in Kerala. It is also known that endemicity of goiter parallels iodine deficient soil zones. The iodine content of soil varies with geochemistry of the land and climatic conditions. In heavy rainfall areas the loss of iodine due to leaching of surface soil is a common occurrence. Besides this, addition of synthetic nitrogenous fertilisers containing no iodine induces iodine deficiency in soil. In a state like Kerala, with heavy rainfall and with the present trend of using abundant quantities of nitrogenous fertilisers, there is bound to have iodine deficiency in soil and its consequent effect on animal health. In certain coastal parts of Kerala particularly Quilon and Chavara the presence of monozite sand has also been considered to induce a hypothyroid state by chronic

radiation effect. The role of goitrogenic substances, widely distributed in nature, cannot also be overlooked in precipitating a hypothyroid state in the animal population. Therefore, it is justifiable to surmise that iodine deficiency does exist in Kerala, although no authentic reports have appeared on this subject. Therefore, there is need to make detailed investigations on this problem to delineate the influence of sub-clinical hypothyroid state on the health and growth of animals. Recognition of the existence of sub-clinical hypothyroid state in the animal population causing lowered production and increased susceptibility to infection is of paramount importance for adoption of suitable preventive measures to reduce losses due to lowered production and mortality in animal production programmes.

There has been no detailed investigations on this important problem of thyroid pathology in India as a whole and Kerala in particular. Although goiter as a problem in goats in certain parts of India was recognised as early as 1935, so far no systematic investigations have been undertaken on this. Against this background an experimental model of controlled hypothyroid state was induced in goats, using different dose regimes of thiourea with the objective of studying the sequence of pathological changes in different stages of hypothyroid state and its influence on the animal health. The results obtained have been presented and discussed.

Chapter–II

REVIEW OF LITERATURE

REVIEW OF LITERATURE

1. Historical Resume

Diseases of the thyroid have been recognised for many centuries back. Endemic goiter was described as early as the 14th century, but the sporadic form was not recognised until the beginning of the 20th century. King (1836) recognised thyroid as an organ of internal secretion. The relationship between the thyroid and various body functions was studied by experimental thyroidectomy (Cooper, 1836). Kocher (1883) reported that the changes in myxoedema corresponded with the effects of thyroidectomy. Baumann (1895-1896) indicated the association of iodine with the working of the thyroid. He also reported high concentration of iodine in the thyroid gland. Kendall (1915) isolated thyroxin from the thyroid gland. Smith and Smith (1922) first demonstrated that thyroid activity was regulated by pituitary hormone. Harington and Barger (1927) identified the chemical structure of thyroxin. Kimbal (1937) noted the association of hypoidism and endemic goiter. Hoskins (1949) proposed the theory of homeostatic feed back mechanism. Gross and Pitt-Rivers (1952) identified triiodothyronine (T_3) in human plasma. Thyroglobulin was classed as a glycoprotein and most of the carbohydrate was found accounted by glucosamine and mannose (Gottschalk and Ada, 1956).

The chemical characteristic of purified thyroglobulin have been discussed (Rall et al. 1964; Edelhoch and Rall, 1964).

2. Thyroid Pituitary Relationship

The activity of the thyroid gland is controlled by thyroid stimulating hormone (TSH) secreted by basophil cells of anterior pituitary gland which in turn is mediated through hypothalamus. Pituitary TSH secretion is in turn governed by a system of feed back control on the product of the target gland, thyroxin. Adams (1958) and McKenzie (1958) discovered thyroid stimulating factor (TSF) in serum. Its action on thyroid is long standing and disappear from blood slower than thyroid releasing factor (TRF). The iodine level in the blood and thyroid also affect the control mechanism. Purves (1964) reported that TSH is only a stimulating factor and not essential for secretion of hormone. The secretion of TSH by the pituitary is dependent upon the levels of unbound or free iodine in the blood. Pituitary and certain regions of hypothalamus respond to increased thyroxin level by depressing TSH release. Release of TSH is also influenced by TRF produced in hypothalamus and it stimulates pituitary to release TSH when levels of free thyroxin (T_f) are low (Kaneko, 1970). TSH has a number of effects on thyroid gland. Due to the action of TSH, the gland increases in size, the follicular cell height increases and there is loss of colloid (Kaneko, 1970). TSH hormone stimulates the accumulation of iodide, its organic synthesis and release of

thyroxin (Jubb and Kennedy, 1970). The response of thyroid to TSH is also influenced by the level of stable iodine intake. When the level of stable iodine intake is low there is an increase in the number and size of cell and in uptake and release of iodine. It is the result of increased level of TSH in circulation. Iodine also enhances the hydrolysis of thyroglobulin, thus liberating thyroxin from the gland.

3. Thyroid Hormone Synthesis

The iodinated thyroglobulin within the colloid of thyroid follicle represents the stored hormone. The active protease within the thyroid gland cleaves the iodinated amino acid from thyroglobulin (De Robertis, 1941). Wollman and Wodinsky (1955) indicated that the thyroglobulin is formed in the colloid rather than in the epithelial cells of the thyroid. Thyroglobulin has a molecular weight of about 6,60,000 (Edelhoch, 1960). The thyroglobulin is a polypeptide, made up of about 5650 amino acid residues, of which about 125 are tyrosyl units (Edelhoch and Rall, 1964). Bush (1969) reported that T_3 forms are in greater proportion of total hormone. Normally thyroglobulin contains not more than five tetraiodothyronine (T_4) residues per molecule. There are three major steps in the synthesis of thyroxin. The first step is the concentration of iodide by the gland from blood; this iodide is enzymatically oxidised to iodine. Then the iodine combines with the protein thyroglobulin and the synthesis of thyroxin commences (Tong, 1971).

4. Functions of Thyroid Hormone

The best known action of thyroid hormone is their ability to stimulate oxygen consumption for normal growth and development. The thyroid hormone regulates the rate of energy turn over in vital organs and this helps in maintaining normal body homeostatic mechanism. It exerts influence on the development of hair and pigmentation in animals (Berman, 1960). In conjunction with other hormones it exerts control by its action at cellular level over growth and development of young animal, temperature regulation, intermediary metabolism and reproduction (Bush, 1969). There is a close link between the catecholamines and peripheral effects of thyroid hormones (Jubb and Kennedy, 1970). Thyroxin is also essential for attaining maximal growth and in the absence of thyroid hormone the effect of growth hormone is greatly reduced. It is also involved in the production of ribonucleic acid and mitochondrial activity and cytoplasmic protein synthesis. It is again noted that thyroxin is essential for full translation of genetic message into ribonucleic acid and ribosomal synthesis of protein (Barker, 1971). In addition, many metabolic processes are accelerated such as protein breakdown, carbohydrate and lipid turnover and calcium metabolism. Nervous function at all level is influenced by thyroid; exchange of water and salts between cell andbody fluids, spontaneous electrical activity, threshold of sensitivity to a variety of stimuli, reflex time motor behaviours

(Gorbman and Bern, 1974). Anderson and Harness (1975) observed that for every unit increase in body weight there was a 69 unit increase in thyroid hormone secretion rate.

5. Thyroid Pathology

The thyroid gland exhibits a variety of diseases and a larger spectrum of gross and microscopical pathological changes. Thyroid diseases capable of producing clinical signs can be classified (Bush, 1969) as

1. Goiter
2. Hypothyroidism
3. Hyperthyroidism
4. Thyroiditis or
5. Thyroid neoplasia.

6. Goiter

The term goiter is defined as a non-inflammatory, non-neoplastic enlargement of thyroid gland. Cohrs (1966) classified the goiter on the basis of morphology.

1. Atoxic goiter, which include most sporadic form.
2. Goiter with functional change which may be
   a) athyroid or hypothyroid goiter
   b) hyperthyroid goiter.

There are generally two types of goiter,

1. Non-Toxic goiter, which produce normal amount of hormone (simple goiter) or less than normal amount of hormone (hypothyroid).

2. Toxic goiter, which is characterised by the excessive production of hormone (hyperthyroid) (Kaneko, 1970).

Smith et al. (1972) classified goiter on the morphological basis into four patterns.

1. Colloid goiter
2. Hyperplastic goiter
3. Nodular goiter
4. Exophthalmic goiter.

Endemic goiter.

This is the most common condition occurring to some degree in almost every country of the world. The co-existence of endemic goiter and cretinism was recognised in the mid 16th century and a concrete description of cretinism in Switzerland was made in the early 17th century. The geographic distribution of this condition has been well studied. In view of the occurrence of the disease, the terms endemic and sporadic atoxic goiter are often used. An endemic goiter area has been defined as one in which more than 10% of the population show clinical signs of thyroid enlargement. In endemic goiter an absolute or relative deficiency of iodine is the main factor. Besides this many environmental and some host factors also play a role. Stott et al. (1930-31) pointed out the association between high goiter rates and the dolomitic lime in India. Levine et al. (1933) reported that elemental iodine and inorganic iodine themselves in large doses has goitrogenic properties. Murray et al. (1948) indicated that there is a relationship between the distribution of goiter and calcium concentration

of drinking water in England. Several antithyroid substances have been isolated from plants and fodders responsible for endemic goiter. Greer (1950) made a comprehensive review of those which have been reported goitrogenic to experimental animals and discussed their importance. In addition to these factors genetic constitution play a role especially in regions where endemic goiter has existed for generations (Roche and Lissitzky, 1960). Cold climate also indirectly influences the prevalence of endemic goiter in regions of border line iodine supply as a result of increased demand for thyroid hormone (Scrimshaw, 1964). Suzuki et al. (1965) reported endemic goiter in Japan due to excessive iodine intake.

6.2. Colloid goiter.

Colloid goiter is regarded as an involutionary phase of hyperplastic goiter (Follis, 1959). The gland in this case is diffusely enlarged and the cut surface is translucent. Microscopically there is an increase in size of follicles and sometime they coalese to form cysts. All follicles are filled with deeply staining colloid (Jubb and Kennedy, 1970).

6.3. Parenchymatous goiter.

In parenchymatous goiter, the parenchyma is increased by the formation of new epithelial cells. There is development of solid masses and cords of cells which are broken up into solid or hollow follicles by ingrowth of stroma. They contain little or no colloid. The epithelial cells are tall and cylindrical (Cohrs, 1966).

6.4. Nodular goiter.

It is frequently seen in old animals. The characteristic feature is development of well defined nodules in one or both thyroid lobes. The nodules are clearly demarcated from rest of the thyroid tissue. The histological appearance of nodular goiter usually varied from nodule to nodule. Many follicles are greatly distended with colloid. Others are small and devoid of colloid. In simplest form, the epithelial cell is inactive and colloid is deeply stained. Focal hyperplasia of lining cells of follicles which are thrown into lumen may be noticed in some nodules. Retrogressive changes are common in nodular goiter (Smith et al. 1972).

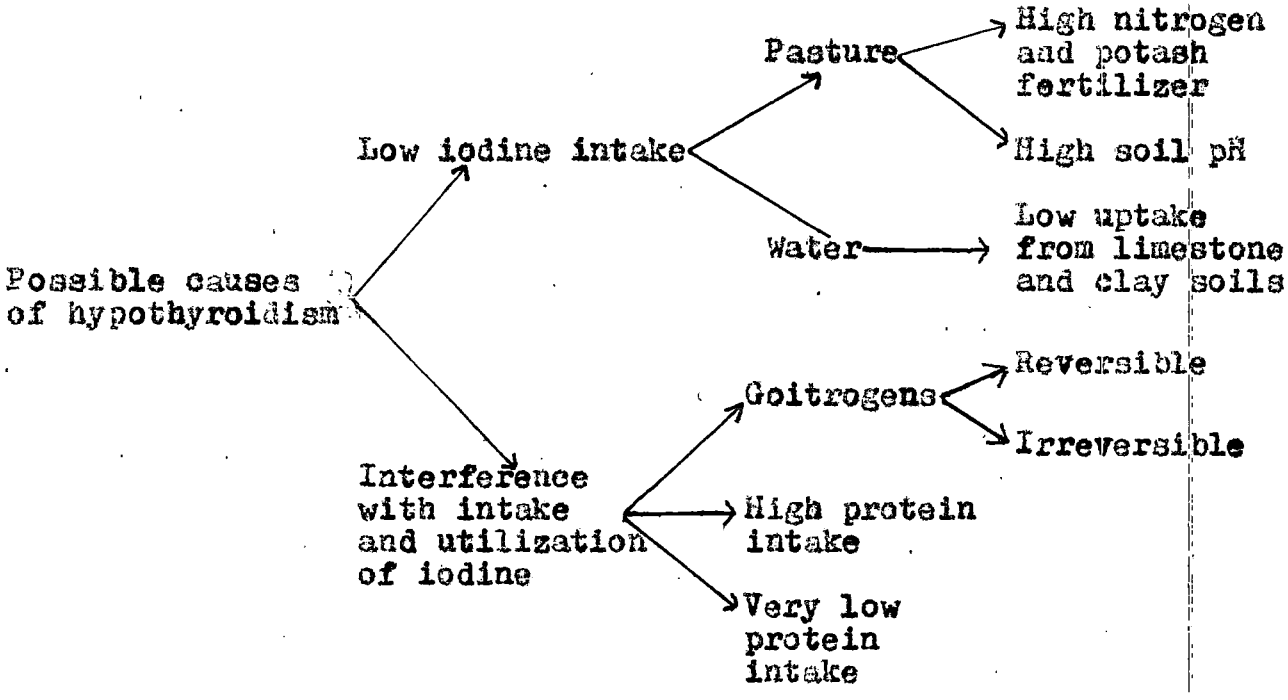
7. Hypothyroidism

If the thyroid glands fail to secrete enough thyroid hormone for the body needs the condition of hypothyroidism develops. There is reduction in total daily outputs and plasma concentration of T_3 and T_4. The known causes of hypothyroidism in animals are iodine deficiency and goitrogens present in nature. Genetic factors also play a role in regions where endemic goiter has existed for generations. Incidence of hypothyroid condition by chronic radiation effect also has been described. Ruminant hypothyroidism mainly occurs in areas of endemic goiter region (Hojer, 1931). Jubb and Kennedy (1970) reported that in domestic animals hypothyroidism is generally associated with congenital goiter of new born. Goats appear particularly susceptible to

both development of congenital goiter and associated effect of hypothyroidism (Mason and Wilkinson, 1973). They classified hypothyroidism into following categories, of which the last five categories were associated with enlargement of thyroid.

1. Primary hypothyroidism due to lack of functioning thyroid.
2. Secondary hypothyroidism due to pituitary insufficiency.
3. Hypothyroidism due to an extreme degree of iodine deficiency.
4. Hypothyroidism due to goitrogens.
5. Hypothyroidism due to dyshormonogenesis.
6. Hypothyroidism due to autoimmune thyroiditis.
7. Hypothyroidism due to neoplasia.

Wilson (1975) illustrated the mode of development of hypothyroidism in ruminants.



Ferguson et al. (1956) reported that hypothyroidism is more severe in young growing animals than in mature adults due to an interference in overall development. Calderbank (1958) reported cases of infertility associated with iodine deficiency. He also pointed out that high producing animals and breeds were particularly susceptible to deficiency of iodine. Calderbank (1963) pointed out that there is a close association between thyroid and gonadal function and mentioned about the loss of libido in males and sub-oestrum in females. Hypothyroidism is generally characterised by lowering of body temperature, increased sensitivity to low environmental temperature and retardation of growth rate (Wallach, 1965). Jubb and Kennedy (1970) observed that gestation is significantly prolonged in hypothyroidism in domestic animals. New born goats show myxoedema, alopecia and high mortality rate. Underwood (1971) indicated that reproductive failure is a common outstanding feature of iodine deficiency. The essential feature of hypothyroidism is an abnormally low basal metabolic rate. Disinclination to vigorous movement is also observed often. In the young retardation of growth with regard to total stature and sexual development are common findings. Elevated cholesterol level in blood serum is usual (Smith et al. (1972). Wilson (1975) summarised the effect of hypothyroidism in ruminants. They are

1. Retention of placenta,
2. Infertility,
3. Lowered milk production and low milk butter fat content,

4. Lowered resistance to infection,
5. Increased susceptibility to ketosis and
6. It is also usually associated with late abortion, still birth and weak offsprings.

8. Aetiology of Hypothyroidism

8.1. Iodine deficiency.

It is generally accepted that iodine deficiency in the environment is the main cause of simple hypothyroidism (Southcott, 1945 and Bush, 1969). Factors influencing the iodine content of soil have been surveyed (Goldschmidt, 1954). The iodine requirements are also influenced by the composition of diet as a whole (Scott et al. 1961). Calderbank (1963) suggested that there may be little or no correlation between the iodine content of soil and pasture growing in it; it will depend upon the prevailing wind, the amount of precipitation and the nature and reaction of soil. The geologic and climatic history of the land determines the distribution of iodine in soil and water supplies to some extent. The effect of heavy rain is also a determining factor (Scrimshaw, 1964). Besides this some micro-elements may also influence sensitivity to iodine (Blokhina, 1970). Wilson (1975) indicated that high protein intake will interfere with utilization of iodine.

8.2. Goitrogens.

Another important cause for hypothyroidism in animals is the presence of so called goitrogens in the feed stuffs. The

presence of goitrogens in many plants and forages have been well documented in literature. There are two main types of goitrogens (Calderbank, 1963). A thiocyanate type which inhibit thyroidal uptake of iodine and this blocking effect can be overcome by simultaneous administration of iodine. A thiouracil type which interferes with organic binding of iodine in the thyroid and this effect can be reversed by administration of thyroxin.

Greer et al. (1966) showed that thiocyanate was about 25 times as potent as nitrate in inhibiting thyroid function. There are two basic types of goitrogens, those like thiocyanate known as anionic goitrogens and those like thiouracil known as organic goitrogens. Anionic goitrogens are represented by thiocyanates and nitrates (Catt, 1970).

8.3. Natural goitrogens.

Sharpless et al. (1939) demonstrated the goitrogenic action of Soya bean flour meal in rats by producing enlarged thyroid. Kennedy and Purves (1941) produced goiter in rats fed with Brassica seeds. They observed hyperplasia of thyroid glands and the weight of the glands were found to be increased by 300 times. Rapid proliferative changes occurred in second and third week after treatment.

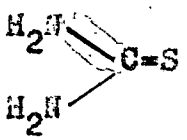
Examination of pituitary showed a rapid increase in basophil cells and this was associated with hyalination and vacuolisation and formation of 'signet ring' cells. There was also simultaneous

loss of acidophil cells in rats treated with Brassica seed diet (Griesbach, 1941). All the halogens, if present in excess are capable of displacing iodine causing iodine deficiency and fluoride has been reported as one of the factors responsible for goiter in Punjab (Wilson, 1941). Arsenic can act as a positive goitrogenic substance in nontoxic amounts. At 0.02% level in the diet in rats, the effect was decrease in growth, increase in thyroid weight and decrease in iodine concentration of the thyroid gland (Sharpless and Metzger, 1941). Sharpless et al. (1943) demonstrated experimentally that in rats goiter could be produced by calcium chloride in the presence of Vitamin D. A marked increase in the follicular colloid and decrease of follicular epithelium were observed in sheep and goats fed with Cauliflower leaves (Spisni and Garavaglia, 1954). Butler et al. (1957) observed a decrease in total iodine content of thyroid and also inhibition of the conversion of inorganic iodine to organically bound iodine in sheep fed with Whiteclover. A heavy diet of kale to pregnant ewes caused high incidence of goiter and hypothyroid in new born lambs (Sinclair and Andrews, 1958). Goitrogenic action of perennial grass has been reported (Setchell et al. 1960). A high incidence of goiter was observed in new born lambs of ewes and sheep grazing on pasture dominated by whiteclover (George et al. 1966). Thyroid glands were heavier than normal and showed severe hyperplasia of the lining epithelial cells of the follicles and complete absence of colloid in lambs which had grazed rape

(Russel, 1967). Blood and Henderson (1968) reported simple goiter and hypothyroidism in ruminants fed with Brassica seeds and brussel sprints.

8.4. Chemical Goitrogens.

Thiourea and allied compounds have frequently been employed as experimental goitrogens in animals to suppress thyroid activity.



Thiourea

Kennedy (1942) observed enlarged thyroids in rats treated with thiourea. The glands were three to four times heavier than normal and almost completely devoid of colloid. Pituitary showed an increase in basophil cells and loss of acidophil cells. Baumann and Marine (1945) noted a decrease in adrenal size among rats fed with thiouracil. Jones et al. (1946) produced typical hyperplasia of thyroid glands in rats fed with thiouracil. They observed resorbtion of foetus in these animals and indicated that thyroid hormone is necessary for full utilization of oestrogen or progesterone. Jones (1946) observed hypertrophy of thyroid gland, congestion of vessels and depletion of colloid in rats treated with repeated doses of thousand milligrams per kg body weight of thiourea. Zarrow and Money (1949) reported involution of adrenal cortex in rats treated with thiouracil. The involution of adrenal cortex after thiouracil treatment was both

morphological and physiological in nature. Sellers and Ferguson (1949) observed exophthalmus in rats treated with thiouracil.

Maqsood (1951) reported tubular degeneration and interstitial cell degeneration of testis of rabbits and rams fed with thiouracil. D'Angelo et al. (1951) reported thyroid hyperplasia in guinea pigs treated with propyl thiouracil. Histological changes were uniformly evident after 15 to 18 days treatment and were characterised by increased vascularity and increase in height of acinar epithelial cells. Colloid resorbtion was a consistent feature. The microscopic changes in prolonged dosing with propyl thiouracil were colloid resorption and high vascularity. The follicular epithelial cells assumed cordlike formation. Hall (1952) reported a reduction in serum calcium level in thiouracil fed rams. However, serum vitamin A level in treated and untreated groups were the same. Swanson and Boatman (1953) reported symptoms of hypothyroidism in two young and one old dairy bulls after treating with thiouracil. The weight of thyroid glands in treated animals were twice the weight of normal. Histologically the follicles were filled with colloid and lined by low cuboidal epithelial cells. There was an increase in dead and abnormal spermatozoa as well as a reduction in motility, viability and concentration of semen. Prolonged administration of thiouracil to rats exhibited microscopical and macroscopical changes of late fibro lymphoid stage of struma fibrosa (Clausen, 1954). In addition to the thyroid hyperplasia Durlach et al. (1954[b]) observed an increase in liver weight in guinea pigs treated with thiouracil

at varying levels. Harkness et al.(1954) studied the effect of oral administration of thiouracil on collagen content of thyroid of rats. During the treatment an increase in weight and collagen content of thyroid glands were noticed.

Eshkol et al. (1956) observed 33% increase in total liver weight in thiourea treated rats. A decline in liver catalase activity and concomitant increase in urinary uric acid, allantoin phosphate and urinary volume were observed before the antithyroidal action of drug. In propyl thiouracil treated rats Goldberg et al. (1957) observed large thyroid glands with tall columnar cells, numerous mitotic figures, scanty colloid, papillary infoldings and increased vascularity. In the pituitary hyperplasia and hypertrophy of beta cells with characteristic granulation and vacuolation and complete absence of granulated alpha cells were observed. Lascelles and Setchell (1959) fed methyl thiouracil at a dosage of 0.5, 1.5 and 4.5 g daily to six Merino sheep after conception. The offsprings of the three survived sheep had goiter and retardation of ossification centres. The thyroid iodine concentration in treated lambs were decreased. A reduction in protein-bound iodine (PBI) and increase in cholesterol value were also noticed. Follis (1959) produced colloid goiter in hamster by thiouracil administration. Extensive thyroid hyperplasia and loss of colloid accompanied by an increase in vascularity were noticed in the first week after thiouracil administration. When thiourea was removed from diet, the follicles filled up with

colloid and epithelial cells became flattened, but some had residual springs projecting into the colloid when compared to normal. Most of the follicles were larger in size. McCarthy et al. (1959) reported adrenal atrophy among rats fed with goitrogens, thiouracil and tapzole. In addition to adrenal atrophy among thiouracil fed rats, Lazo-Wasem (1960) observed thyroid and pituitary hypertrophy with a concomitant reduction in adrenocorticotrophic hormone (ACTH) titer.

Mayberry and Astwood (1961) ascribed the mode of action of thiourea and related compounds to inhibition of the formation of iodotyrosine and their coupling to form iodothyronine. They also diminish the inorganic iodide content of thyroid and has a slight inhibitory effect on iodide pump (Danowski, 1962).

8.5. Dyshormonogenesis.

The occurrence of congenital goiter due to an inherited defect in the biosynthesis of thyroid hormone leading to increase in production of TSH which in turn causes hyperplasia of thyroid gland have been described in sheep (Falconer, 1966; Rac et al. 1968 and Mayo and Mulhearn, 1969).

Falconer (1966) reported high PBI concentration of serum from these goitrous animals but hormonal iodine was low in serum compared with that of normal. The concentration of TSH was also significantly higher in goitrous sheep. Rac et al. (1968) made a study on congenital goiter in Merino sheep. Enlargement of thyroid glands in affected animals was nearly 25 times more than the

control. Histologically the glands were classified into two distinct types. In the first type there was hyperplasia with infolding of cuboidal epithelium into vesical lumina as well as formation of many vesicles. In second type the epithelial cells were arranged in alveolar pattern resembling a solid adenoma histologically. Epithelial cells of this type had abundant cytoplasm and subnuclear vacuolation. There was significant increase in cholesterol value in one group of affected sheep. The PBI values were also higher in goitrous animals. In congenital goiter in sheep Mayo and Mulhearn (1969) observed oedematous ear and transverse folds of skin over nasal bones. The carpal joints were also swollen and forelegs were bowed either inward or outward, resulting in oblique plantar surface of hooves. The thyroid glands were also enlarged.

3.6. Surgical Thyroidectomy.

Hypothyroidism also can be caused by complete or partial destruction of thyroid tissue. Marston and Peirce (1952) observed a reduction in growth rate and metabolic rate in thyroidectomised Merino sheep. Zeckwer et al. (1935) reported degranulation of acidophil cells after thyroidectomy in rats. Silberg and Silberg (1940) indicated a delay in endochondral ossification in thyroidectomised immature guinea pigs. He also observed an accelerated sclerosis of the cartilagenous ground substance and inhibition of the complete differentiation of columnar cartilage cells into hypertrophic cartilage cells. Contopoulos et al. (1958)

reported that after thyroidectomy, the pituitary target organ atrophied and the plasma contained only decreased amount of somatotrophic hormone (STH). Anterior pituitary contained decreased amounts of TSH, interstitial cell stimulating hormone and growth hormone. After thyroidectomy the acidophil cells underwent extreme granulation and concomitant increase in number, accompanied by enlargement and vacuolation of cell cytoplasm. Solomon and Greep (1959) reported a significant decrease in the acidophil cells in thyroidectomised rats. Yatvin et al. (1964) noticed a decrease in liver weight and protein desoxyribonucleic acid ratio in thyroidectomised rats. Brooks et al. (1964) reported a reduction in gonadal and gonadotrophic hormone in thyroidectomised young ewes. Belonje (1967) reported an increase in plasma globulin and sedimentation rate of red cells in thyroparathyroidectomised Merino ram. In thyroidectomised goats there was reduction in phosphorus accretion into long bones and endogenous excretion of phosphorus. This was accompanied by hypophosphatemia (Symonds, 1969, 1970).

8.7. Radio Thyroidectomy.

Radio thyroidectomy also result in the development of clinical signs and pathological lesions of hypothyroidism. Goldberg and Chaikoff (1950, 1951) produced an early state of hypothyroidism in rats injecting various doses of I^{131} in rats. They observed hypertrophy and hyperplasia of basophil cells accompanied by degranulation of acidophil cells. Lewis (1956) noticed a dropping of PBI from 6.7 to 0.8 microgram per centage in a Jersey bull after

subcutaneous injection of carrier free I^{131}. Thyroid adenomas, fibroma and fibro sarcoma were produced in sheep following daily administration of I^{131} at varying levels (Bustad, et al. 1957, Marks and Bustad 1963) and interfollicular fibrosis, oedema and arterial damages were also reported (Marks et al. 1957). Potter et al. (1960) developed papillary and follicular carcinoma in rats by single injection of I^{131}. Ayoub (1968) reported damage of thyroid gland and reduction in the rate of uptake of radio active iodine by thyroid and its release into blood plasma in goats on administration of radio iodine.

9. Natural Incidence of Goiter in Sheep and Goats

The incidence of goiter and hypothyroidism have been reported by several workers in goats and sheep. Love (1942) observed changes in thyroid glands of four new born kids. He noticed alopecia in two cases out of four cases of parenchymatous goiter in still born kids. Mcintosh (1943) reported that new born lambs are weak and the wool growth is poor with focal areas of denudation. Southcott (1945) reported congenital goiter in lambs. The lambs were weak or born dead. Histologically follicles were depleted of colloid and were filled with finger like processes of the lining epithelium. The epithelial cells were low cuboidal or columnar type. Baumann (1948) described goiter in new born kids. In six cases partial or complete hairlessness and myxoedema were noticed. There were three cases of colloid goiter, two of parenchymatous goiter and four mixed type. Andrews et al. (1948)

noticed hyperplasia of thyroid epithelium and depletion of colloid in the thyroid glands of new born lambs from dams which were fed a diet not supplemented with iodised salt in Indiana.

Jovanovic et al. (1953) investigated on the incidence of goiter in goats, sheep, cattle, pigs and horses in Serbia. The incidence of goiter in animals was found to parallel with that in human population. They also observed large number of animals with goiter. Otomatus (1954) made an investigation on the incidence of goiter in sheep in Japan. He recorded congenital goiter in 25 per cent of new born lambs. In adults he documented an incidence of 33%. The gestation period of goitrous sheep was much larger than that was observed in normal sheep. The new born lambs affected with goiter were weak and majority died within few hours. He observed various forms of enlargement of thyroid glands and described them as circular goiter, horse shoe form, cannon headed form and war fan form. Some of the glands showed cysts in the central part of the cut surface. Histologically the lesions were typical struma parenchymatosa in new born lambs. Pantic and Jovanovic (1955) investigated on the nature and incidence of goiter in domestic animals. The diffuse colloid type of goiter was commonest in sheep and goats. The parenchymatous goiter was observed in goats only. Isolated cases of nodular goiter and cyst adenoma were encountered only in sheep.

Setchell et al. (1960) reported neonatal mortality in lambs associated with thyroid enlargement. He noticed that the affected lambs had gone weak and lethargic and were bearing coarser coat.

Histologically the glands showed varying degrees of colloid goiter. A number of glands showed microscopic cysts filled with watery fluid. Growth (1962) reported hypothyroidism in sheep. He observed adverse affect on wool growth and increased incidence of alopecia and still born lambs and kids. Watson et al. (1962) observed increased size and weight of the thyroid glands and decrease in the iodine content of the glands in congenital goitrous Doorset Horn lambs. There was pronounced hyperplasia of thyroid epithelial cells in these animals. Wallach (1965) reported goitrogenic hypothyroidism in feeder lambs. In the lambs he observed low basal metabolic rate, retardation of growth rate and increased sensitivity to low environmental temperature. There was significant enlargement of the glands and the enlarged thyroids were palpable. Tall columnar epithelial cells were seen lining the acini. The acini contained scanty colloid and papillary structures were seen protruding into the acini. George et al. (1966) conducted histopathological study of thyroid glands of dead lambs in order to assess the incidence of goiter. He observed parenchymatous and transitional parenchymatous goiter in the affected glands of lambs. The follicles were devoid of colloid but showed large cystic spaces.

10. Incidence of Goiter and Hypothyroidism in Sheep and Goats in India

Reports on the incidence of endocrine disorders in domestic animals in India are only few. So far the endocrine system has not been subjected to detailed pathological investigation in this country. However, a few reports have appeared on thyroid disorders in goats and sheep from India.

Lall (1952) reported congenital goiter in three kids with enlarged thyroid and alopecia. Histologically thyroid glands showed hyperplasia of lining cells of the follicles. These hyperplastic cells were thrown into papillary folds into the lumen. The colloid was scanty and feebly stained. In pituitary, the acidophils were few in number and there was an increase in basophil cells. The seminiferous tubules were found immature. Dutt and Kehar (1959) made a study on 1000 thyroid glands collected from Bareilly slaughter house, in order to assess the incidence of goiter in goats and sheep. The incidence of goiter was more common in goats, particularly in female goats, whilst not a single case of goiter was observed in sheep. In all 10% of the goats were found to be goitrous. Clinical and sub-clinical cases were also observed in goats. The goiter met with in goats were of the parenchymatous type. The thyroid glands in these animals were grossly enlarged. Histologically acini contained little colloid and were lined by tall columnar epithelial cells and this projected into the lumen of follicles. Blood vessels were very congested.

Dutt and Vasudeva (1963) described a case of hypothyroidism in a ram. The animal showed clinical signs like loss of weight, irregular appetite and intermittent diarrhoea. At autopsy the thyroid glands were found to be cystic and slightly enlarged. Histologically the follicles adjacent to the cyst had atrophied and were lined with low cuboidal epithelial cells. Most of the atrophied acini were devoid of colloid. Seminiferous tubules of the testis were atrophied and in some of the tubules multinucleate giant cells were observed. Pituitary glands showed cords of hypertrophied epithelial cells arranged as finger like processes in focal areas. Hyperplasia of Basophils was also evident.

Roy et al. (1964) conducted a comparative study of thyroid glands of 25 human and 50 goats, collected from severely endemic area in the Himalayan goiter belt. The thyroid glands of goats in endemic region were large, pale and hyperplastic with intense lobular hyperplasia. Grossly visible well circumscribed greyish white multiple nodules were noticed in human thyroids. There was extreme reduction of organic iodine content of thyroids in endemic area. Microscopically the epithelial cells were tall columnar type and they were thrown into papillary foldings. Follicles contained little or no colloid. The thyroid glands of human beings showed intense epithelial and stromal hyperplasia and nodular proliferation at focal points.

Rajkumar (1970) reported enlarged thyroid glands in 16 Barbari kids out of 29 in a Government Farm in Uttar Pradesh.

In his random survey study in village flock, taking gross enlargement of the thyroid gland as a criteria for diagnosis of goiter he recorded an incidence of 0.54%, 7.02% and 16.67% in local goats, Barbari x local and Alpine x local goats respectively.

MATERIALS AND METHODS

MATERIALS AND METHODS

1. Design of Experiment

Twelve cross-bred clinically healthy kids consisting of six males and six females of the age group between 3-4 months were randomly selected from the University Goat Farm, Mannuthy for the study. It was specifically ensured that kids were not having Jonhe's disease or coccidiosis. The experimental animals were housed separately in pens under hygienic conditions. The experimental animals were maintained on concentrates and green jacktree leaves. Water was given ad libitum. The animals were divided into two groups; consisting of a control group of four animals and experimental group of eight animals. The experimental group of animals were divided into four sub-groups. Each sub-group consisted of one male and one female. The control group consisted of two males and two females. Experimental hypothyroidism was induced by oral feeding of Thiourea (Glaxo Laboratories (India) Limited). Thiourea was daily administered orally mixing with jaggery as bolus at different dose levels and the details are presented in table 1. Experimental animals were either allowed to die or were sacrificed. Two of the control animals (one male and one female) were sacrificed on 42nd day after commencement of the experiment when the last animal of the 2nd group died. The other two animals in the control group were sacrificed when the animals in the fourth group were sacrificed.

Table 1. Details of sex, breed, experimental group, body weight, age, dosage and total consumption of thiourea and fate of animals in experimental hypothyroidism.

Sl. No.	Sex	Breed	Group	Body weight (kg)	Age (months)	Daily dosage (mg)/kg body weight	Total daily consumption (g)	Fate
1	Male	Cross	I	6.500	3.5	250	1.625	Died
2	Female	Cross		6.000	3.5	250	1.500	Died
3	Male	Cross	II	4.000	3.0	200	0.800	Died
4	Female	Cross		5.000	3.0	200	1.000	Died
5	Male	Cross	III	9.000	4.0	150	1.350	Died
6	Female	Cross		9.500	4.0	150	1.425	Died
7	Male	Cross	IV	7.250	3.5	100	0.725	Sacrificed
8	Female	Cross		10.000	4.0	100	1.000	Sacrificed
9	Male	Cross	Control	7.250	3.5			Sacrificed
10	Male	Cross		11.500	4.0			Sacrificed
11	Female	Cross		3.600	3.0			Sacrificed
12	Female	Cross		8.500	4.0			Sacrificed

Haemogram, bodyweight, plasma protein, serum cholesterol and protein-bound iodine (PBI) values of all animals were recorded before commencement of the experiment. Subsequently haemogram, body weight, plasma protein, serum cholesterol and PBI were estimated at fortnightly intervals. Development of clinical symptoms, if any, were observed and recorded daily.

The study covered the following aspects:-

1. Weight gain and growth rate.
2. Observation of clinical symptoms.
3. Haemogram values.
4. Estimation of total protein content in blood plasma.
5. Estimation of serum cholesterol.
6. Determination of PBI.
7. Gross pathology.
8. Histopathological and histochemical changes in organ systems.

2. Techniques

Weight gain and growth rate.

All the experimental and control group of animals were weighed at the commencement of the experiment and thereafter at fortnightly intervals.

Collection of blood samples for laboratory estimation.

Blood samples for analysis were collected using reagent grade Ethylenediaminotetra-acetic acid (disodium salt) (EDTA) as

anticoagulant. EDTA at the rate of ten mg for every ten ml of blood was employed as anticoagulant. Every time five ml of blood was drawn from the jugular vein for haematological studies with aseptic precautions. Five ml of blood was also collected separately in sterile test tube, without adding anti-coagulants. The blood was allowed to clot and then serum was separated by centrifugation for estimation of serum cholesterol and PBI values.

Erythrocyte sedimentation rate.

The technique of Wintrobe and Landsberg (1935) was followed.

Packed cell volume.

The method described by Wintrobe (1961) was adopted.

Haemoglobin.

The method of Miale (1967) for the determination of haemoglobin was modified in this estimation. The cyanmethemoglobin was prepared as detailed by Miale (1967), but the final readings were taken in Erma Haemo Photometer as against Spectronic 20.

Erythrocyte count.

Erythrocyte counts were made following the technique of Schalm (1965).

Leucocyte count.

Leucocytes were enumerated by the method described by Schalm (1965).

Differential count.

The technique of Schalm (1965) was adopted.

Erythrocyte Indices.

Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin (MCH) and Mean Corpuscular Haemoglobin Concentration (MCHC) were calculated from erythrocyte count, packed cell volume and haemoglobin content of blood (Benjamin, 1964).

$$\text{Mean Corpuscular Volume in cubic microns} = \frac{\text{Volume of packed erythrocyte} \times 10}{\text{Erythrocytes in millions per c.mm.}}$$

$$\text{Mean Corpuscular Haemoglobin in micro micrograms} = \frac{\text{Haemoglobin in grams per 100 ml} \times 10}{\text{Erythrocytes in millions per c.mm.}}$$

$$\text{Mean Corpuscular Haemoglobin Concentration in percentage} = \frac{\text{Haemoglobin in grams per 100 ml}}{\text{Haematocrit reading}} \times 100$$

Total protein content in blood plasma.

The Biuret assay method of Inchiosa (1964) was adopted for the estimation of total protein content in blood plasma.

Serum Cholesterol.

Serum cholesterol was estimated employing the method of Zak (1957) (Appendix I).

Protein-bound iodine.

The protein-bound iodine (PBI) in serum was estimated by the modified method of Barker et al. (1951) (Appendix II).

The kids which were dead/sacrificed were subjected to detailed autopsy. For autopsy the method advocated by FAO/SIDA (1963) was followed. Endocrine glands (thyroid, pituitary and adrenal) were dissected and loose fat and fascia were removed and they were

weighed. The glands were then incised and examined for gross lesions. Appropriate samples of tissues from all organs were collected in 10% formal-saline for histopathological examination. Tissues were processed by routine paraffin embedding technique (Armed Forces of Institute of Pathology, 1968). Paraffin sections cut at five to eight u thickness were stained routinely with Haemotoxylin and Eosin method of Harris described by Disbrey and Rack (1970). Reticulin stain (James, 1967) also was employed for sections of thyroid. Wherever necessary Periodic Acid Schiff (PAS) for thyroid, Heath's method for pituitary, Gomori's method for adrenal chromaffin, Alcian Blue method for mucosubstances, Van Giesons and Verhoeff's stain as detailed by Armed Forces of Institute of Pathology (1968) were employed. Frozen sections of appropriate samples of tissues were taken and stained with Sudan III for the demonstration of fat (Armed Forces of Institute of Pathology, 1968).

RESULTS

R E S U L T S

1. Clinical Findings

Symptoms.

Group I.

This group consisted of one male and one female kid. They were given 250 mg of thiourea daily by oral administration. These animals were active and clinically normal for the first fortnight. Subsequently the animals appeared dull and weak and remained isolated from other animals. The hair coat presented a rough appearance. Moderate oedema was noticed on the face and lower part of the hind and fore limbs (Fig. 1). The animals often carried their head in a drooping position. They had a tendency to lie down always and gait was unsteady during movement. The female and the male animal died on the 22nd and 25th day respectively after the commencement of feeding thiourea.

Group II.

One male and one female kid which constituted this group were orally dosed with 200 mg of thiourea daily. No clinical symptoms were observed during the first three weeks. Thereafter the condition of these animals slowly deteriorated. Oedema of moderate degree was noticed on the face and eye lids. The animals were not active and the appetite was also reduced. The condition of the animals worsened and two days before death the animals were in prostrated condition. The male and female kids died on 23rd and 42nd day respectively.

Group III.

The two animals in this group were given thiourea at a dose level of 150 mg daily by oral route. The animals showed progressive weakness and stunted growth from the third week onwards. The female kid always pressed its head on the wall. Oedema on the face below the eyes and in the lower portion of the limbs were also observed. The animals were reluctant to move from one place to another and there was reduction in the intake of feed. The animal held its neck stretched and was recumbent a day prior to its death. It died 32 days after commencing the treatment. The male animal showed no other clinical symptoms except stunted growth and died on the 68th day.

Group IV.

This group was given 100 mg thiourea daily by oral administration. Stunted growth and weakness were evident in the animals by three weeks after feeding thiourea. Subcutaneous oedema of moderate degree on the face and eye lids was also noticed (Fig. 2). The carpal joints were moderately and diffusely swollen and the animals stood in an abducted position (Fig. 3). The kids were not very active and feed consumption was considerably reduced. The hair coat was rough. Watery discharge from eyes was noticed in the female kid. The animals were sacrificed after 90 days of observation to study histopathological changes.

Weight gain and loss.

The data on weight gain and loss during the experimental period are given in Fig. 4.

Group I.

During the first fortnight there was a sharp reduction of weight (1 kg) in the female and there was only slight reduction in the male. Subsequently during the experimental period both the male and female showed progressive reduction in weight.

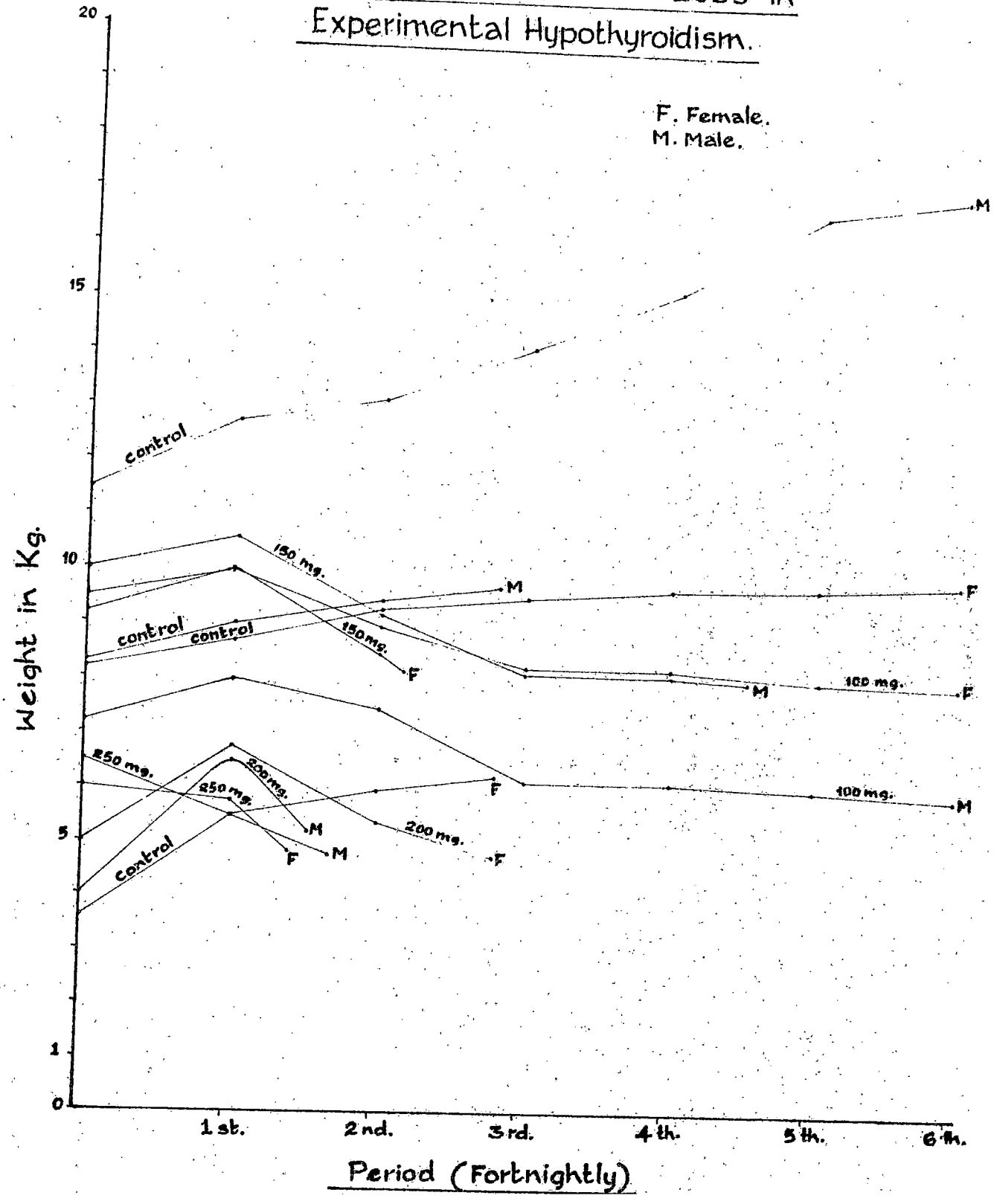
Group II.

In the first fortnight an increase in body weight was observed in both sexes. In the male the weight gain was nearly 2.5 kg, but in the female this was only 1.7 kg. After the first fortnight there was reduction of body weight in experimental animals. The body weight of the male kid at the time of death was higher than the initial body weight, but it was 0.7 kg less than the weight recorded in the first fortnight. In the second fortnight the female kid weighed more than its initial weight. However, there was a reduction of 0.7 kg in live weight when compared to the weight recorded during the first fortnight. The animal continued to loose weight and at the time of death the live weight was lower than the initial weight.

Group III.

Both the animals in this group recorded an increase of

Fig. 4. Weight Gain and Loss in Experimental Hypothyroidism.

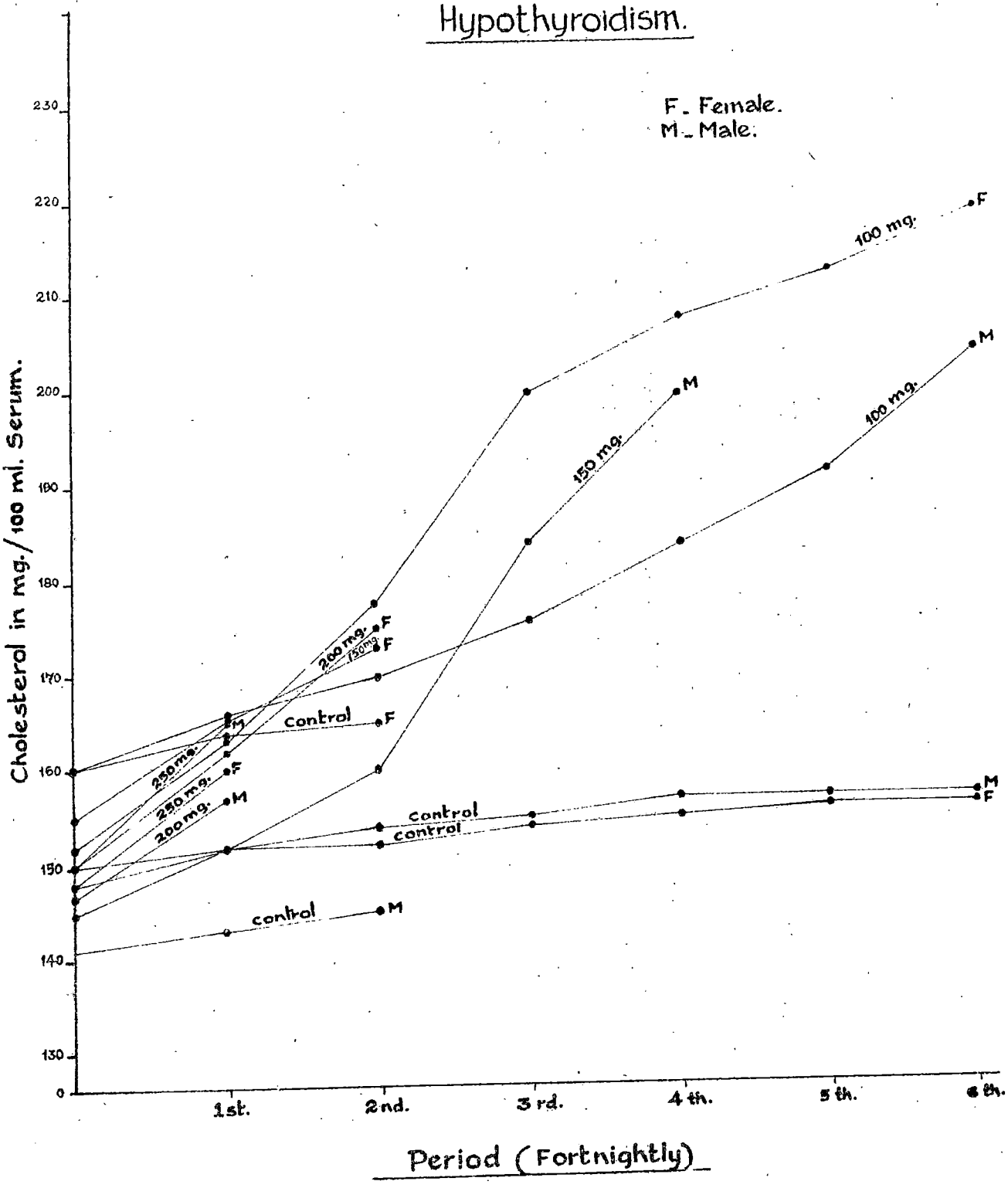


nearly 1.5 kg body weight in the first fortnight. A reduction of body weight of 1.5 kg was observed in the second fortnight in the female kid. Progressive reduction in weight continued till its death. A reduction of 0.6 kg was noticed in the second fortnight in the male animal. Subsequently there was neither gain nor loss of weight till its death. The body weight of both the animals at the time of death was lower than the initial body weight.

Group IV.

In this group also a moderate increase of 0.8 kg body weight was noticed in the first fortnight in both sexes. In the second fortnight both the male and female kids recorded a reduction in body weight of 1 kg and 1.5 kg respectively. There was sharp reduction of body weight in both the kids at the third fortnight. The body weight remained unchanged at the fourth fortnight. However, there was a reduction of 0.2 kg and 0.1 kg at the fifth fortnight in the female and male respectively. Afterwards the weight of the female remained unchanged till its destruction. However, the male showed a reduction of 0.1 kg at the sixth fortnight. The body weight of this experimental group of kids at the time of destruction was lower than the initial body weight. The total loss of body weight in both sexes was 1.1 kg and 1.2 kg respectively during the experimental period.

Fig_5. Serum Cholesterol Level in Experimental Hypothyroidism.



In contrast to the loss of body weight in all the experimental group of animals, a progressive but gradual increase in body weight was observed in the control group of animals during the course of the experimental period.

Serum cholesterol level.

The data on serum cholesterol level of the animals during the experimental period are given in Fig. 5.

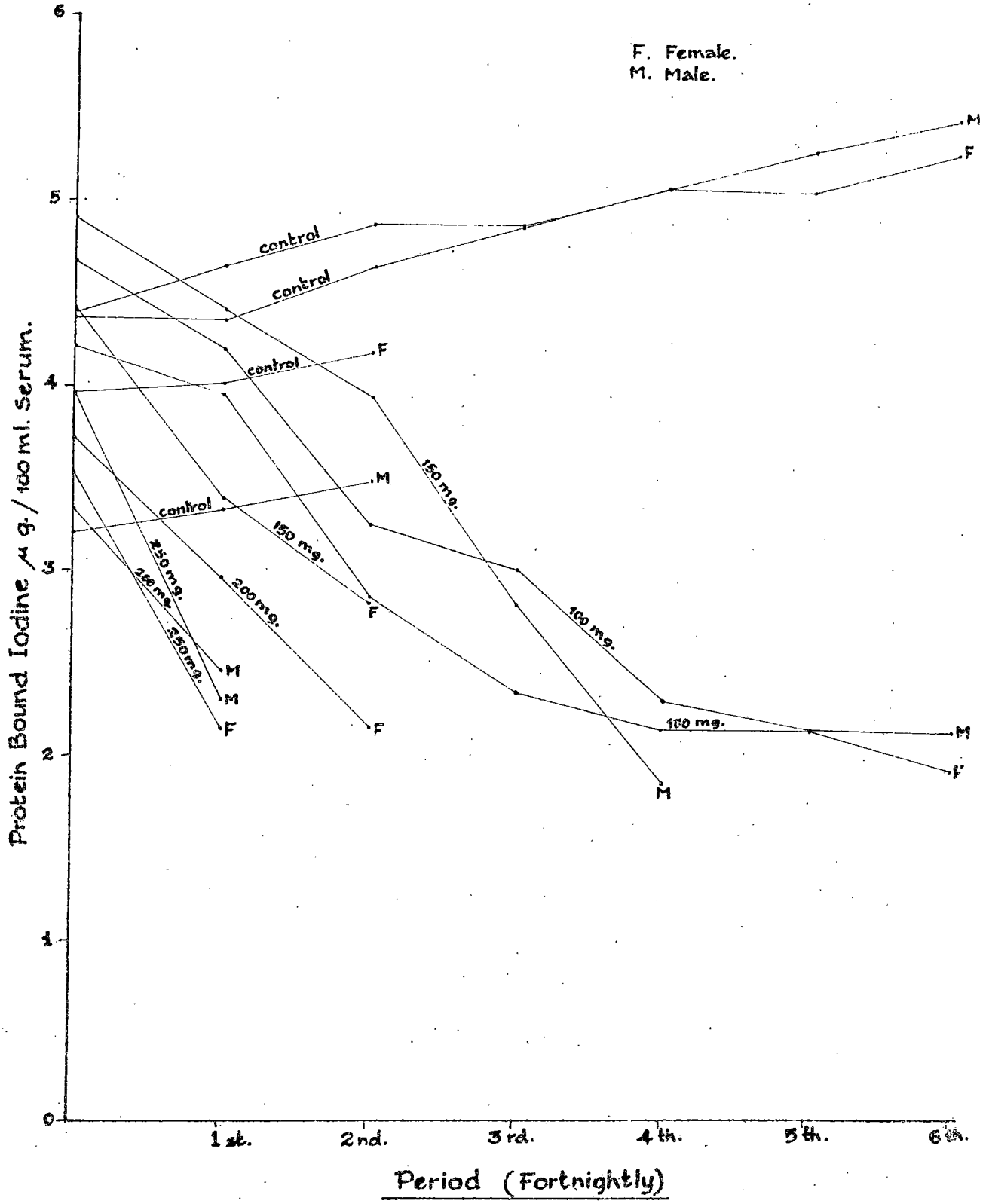
In all the animals dosed with thiourea a moderate increase in the serum cholesterol level was observed when compared to the control group of animals. However, highest increase in the level of serum cholesterol was observed in the fourth group and lowest increase was recorded in the first group of animals. Increase in the serum cholesterol level was more pronounced in the female kids except in the first group.

Serum protein-bound iodine (PBI) level.

The data on serum PBI level are presented in Fig. 6.

There was significant decrease of serum PBI level in all the animals dosed with thiourea. But a marked steep fall in serum PBI level was observed in the first and second group of experimental animals. However, reduction of serum PBI in the third and fourth group of experimental animals was gradual. Lowest PBI values were recorded in the third and fourth group of animals. The reduction of PBI values were more in the females in all groups.

Fig. 6. Protein Bound Iodine Level in Experimental Hypothyroidism.



Total blood plasma protein.

The data on total blood plasma protein are given in table 2.

There was slight increase in the plasma protein values of all the experimental animals dosed with thiourea when compared to the control group of animals. Increase in total plasma protein was slightly higher in the third and fourth group of animals when compared to the first and second group of animals.

Haemogram.

The haemogram of experimental animals are presented in tables 3-7.

There was no significant variation from the normal in any of the animals except in the fourth group of experimental animals. Animals in this group showed moderate anaemia characterised by reduction in RBC, PCV and Hb. It was a macrocytic hypochromic type of anaemia.

2. Autopsy Findings

Group I.

The animal carcases were very much emaciated. There was gelatinisation of subcutaneous tissue. Subcutaneous oedema of the facial region was evident. Hydropericardium of moderate degree was observed. There was hypertrophy and slight dilatation of the left ventricle. The thyroid glands were slightly enlarged

and dark brown in colour. Adrenal glands were moderately enlarged. The muscles were moist and atrophic and the entire muscle fat was gelatinised.

Group II.

The carcases were poor in condition. There was gelatinous infiltration in the subcutaneous tissue of the fore limbs, neck and thigh regions. The pericardial cavity contained nearly 90 ml of turbid fluid. There was hypertrophy and dilatation of the left ventricle. The thyroid glands of the female were pale and moderately enlarged while in the male the glands were slightly enlarged and dark brown in colour.

Group III.

The carcases were emaciated. In the female kid the skin was dry and hair coat was rough and matted. In both the animals subcutaneous tissue was uniformly oedematous and gelatinisation of subcutaneous fat in the neck, hind and fore limbs was observed. There was moderate dilatation of the left ventricle. Gelatinisation of the coronary and renal fat was evident. The thyroid glands were slightly enlarged in the female. Enlargement of the thyroid glands was more pronounced in the male kid. In the female the liver was moderately enlarged, pale, fatty and the borders were rounded. The adrenal glands were slightly enlarged.

Group IV.

Carcases were emaciated. The hair coat was rough and

lustreless. There was moderate diffuse subcutaneous oedema and gelatinous infiltration on the face and lower part of the hind limbs. The thyroid glands were greatly enlarged, elongated and pale in appearance. The adrenal glands were also slightly enlarged.

There was no other gross lesion in other organs in any of the experimental animals. The control group of animals did not show any gross abnormality in any of the organs.

The relative weight of the endocrine glands (Thyroid, Pituitary and adrenal).

The relative weight of the endocrine glands are presented in Fig. 7.

Maximum increase in the relative weight of the thyroid gland was observed in the group of animals dosed with 100 mg of thiourea (Fig. 8). Animals in this group were under experimental observation for longest period. Increase in weight was more pronounced in the female kids in all the group except in the 250 mg and 150 mg group.

Kids in the 200 mg group recorded highest increase in the relative weight of the adrenal gland while the increase was lowest in the 100 mg group. Generally increase in the adrenal weight was more pronounced in the females.

Maximum increase in the relative weight of the pituitary gland was also observed in the group of animals dosed with 200 mg and 100 mg of thiourea. Increase in weight was more pronounced in the female kids in the group except in the 250 mg and 100 mg group.

Fig. 7. Relative Weight of Endocrine Glands (Thyroid, Adrenal And Pituitary) in Experimental Hypothyroidism.

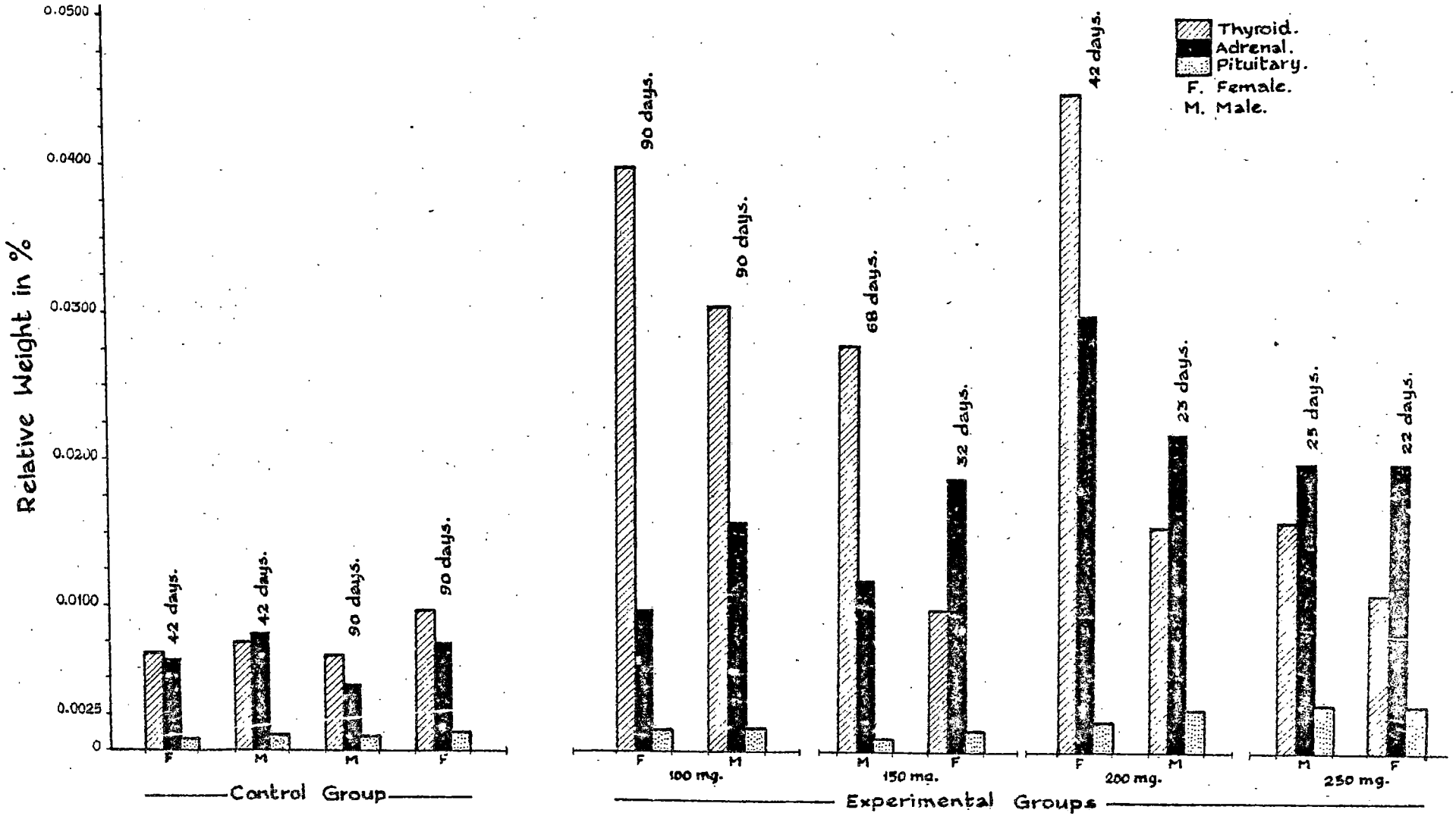


Table 2. Total blood plasma protein level in grams per 100 ml of blood plasma in experimental hypothyroidism.

Sl. No.	Sex	Group	Before experiment	First fortnight	Second fortnight	Third fortnight	Fourth fortnight	Fifth fortnight	Sixth fortnight
1	Female	Group I	7.10	7.30	-	-	-	-	-
2	Male		7.20	7.32	-	-	-	-	-
3	Female	Group II	8.25	8.42	8.51	-	-	-	-
4	Male		7.25	7.40	-	-	-	-	-
5	Female	Group III	7.25	8.10	8.48	-	-	-	-
6	Male		8.20	8.90	8.90	9.10	9.20	-	-
7	Female	Group IV	8.40	8.40	8.90	9.20	9.50	9.70	10.10
8	Male		8.80	9.00	9.00	9.40	9.80	10.20	10.40
9	Female	Control	8.10	8.20	8.20	-	-	-	-
10	Male		7.40	7.50	7.70	-	-	-	-
11	Female		8.10	8.10	8.20	8.30	8.50	8.60	8.60
12	Male		8.80	8.80	8.90	9.10	9.10	9.20	9.20

Table 3(a). Haemogram of Group I--female.

Parameters	Before experiment	First fortnight	Second fortnight	Third fortnight	Fourth fortnight	Fifth fortnight	Sixth fortnight
RBC mill/cmm	12.40	12.30	-	-	-	-	-
Haemoglobin (Hb) g/100 ml	8.20	8.10	-	-	-	-	-
ESR mm/hr	Nil	Nil	-	-	-	-	-
PCV %	30	29	-	-	-	-	-
MCV cm	24.20	23.60	-	-	-	-	-
MCH µµg	6.60	6.50	-	-	-	-	-
MCHC %	27.30	27.90	-	-	-	-	-
Leucocytes No./cmm	9150	9125	-	-	-	-	-
Differential count							
Lymphocytes	58	60	-	-	-	-	-
Neutrophils	39	38	-	-	-	-	-
Monocytes	-	-	-	-	-	-	-
Eosinophils	3	2	-	-	-	-	-
Basophils	-	-	-	-	-	-	-

Table 3(b). Haemogram of Group I--male.

Parameters	Before experiment	First fortnight	Second fortnight	Third fortnight	Fourth fortnight	Fifth fortnight	Sixth fortnight
RBC mill/cmm	12.32	12.10	-	-	-	-	-
Hb g/100 ml	7.60	7.40	-	-	-	-	-
ESR mm/hr	Nil	Nil	-	-	-	-	-
PCV %	30	31	-	-	-	-	-
MCV cμ	24.30	24.40	-	-	-	-	-
MCH μμg	6.10	6.10	-	-	-	-	-
MCHC %	25.30	25.20	-	-	-	-	-
Leucocytes No./cmm	11050	11135	-	-	-	-	-
Differential count							
Lymphocytes	62	58	-	-	-	-	-
Neutrophils	35	38	-	-	-	-	-
Monocytes	-	-	-	-	-	-	-
Eosinophils	3	4	-	-	-	-	-
Basophils	-	-	-	-	-	-	-

Table 4(a). Haemogram of Group II--female.

Parameters	Before experiment	First fortnight	Second fortnight	Third fortnight	Fourth fortnight	Fifth fortnight	Sixth fortnight
RBC mill/cmm	10.86	10.95	9.70	-	-	-	-
Hb g/100 ml	8.20	8.40	7.20	-	-	-	-
ESR mm/hr	Nil	Nil	Nil	-	-	-	-
PCV %	30	30	28	-	-	-	-
MCV c μ	27.60	27.60	28.70	-	-	-	-
MCH $\mu\mu g$	7.50	7.50	7.40	-	-	-	-
MCHC %	27.30	28.20	25.70	-	-	-	-
Leucocytes No./cmm	12650	12315	12450	-	-	-	-
Differential count							
Lymphocytes	58	57	62	-	-	-	-
Neutrophils	39	38	36	-	-	-	-
Monocytes	1	-	-	-	-	-	-
Eosinophils	2	4	2	-	-	-	-
Basophils	-	1	-	-	-	-	-

Table 4(b). Haemogram of Group II--male.

Parameters	Before experiment	First fortnight	Second fortnight	Third fortnight	Fourth fortnight	Fifth fortnight	Sixth fortnight
RBC mill/cmm	12.86	12.93	-	-	-	-	-
Hb g/100 ml	8.40	9.10	-	-	-	-	-
ESR mm/hr	Nil	Nil	-	-	-	-	-
PCV %	30	31	-	-	-	-	-
MCV cμ	23.30	23.90	-	-	-	-	-
MCH $\mu\mu$g	7.40	7.90	-	-	-	-	-
MCHC %	28.00	29.30	-	-	-	-	-
Leucocytes No./cmm	9875	8750	-	-	-	-	-
Differential count							
Lymphocytes	60	57	-	-	-	-	-
Neutrophils	38	40	-	-	-	-	-
Monocytes	-	1	-	-	-	-	-
Eosinophils	2	2	-	-	-	-	-
Basophils	-	-	-	-	-	-	-

Table 5(a). Haemogram of Group III--female.

Parameters	Before experi-ment	First fort-night	Second fort-night	Third fort-night	Fourth fort-night	Fifth fort-night	Sixth fort-night
RBC mill/cmm	14.61	14.84	14.42	-	-	-	-
Hb g/100 ml	9.50	9.80	9.20	-	-	-	-
ESR mm/hr	Nil	Nil	Nil	-	-	-	-
PCV %	31	32	34	-	-	-	-
MCV c μ	21.30	21.50	23.50	-	-	-	-
MCH $\mu\mu$g	6.50	6.60	6.30	-	-	-	-
MCHC %	30.60	30.60	27.00	-	-	-	-
Leucocytes No./cmm	9850	9875	9425	-	-	-	-
Differential count							
Lymphocytes	54	60	64	-	-	-	-
Neutrophils	42	38	34	-	-	-	-
Monocytes	1	-	-	-	-	-	-
Eosinophils	3	2	1	-	-	-	-
Basophils	-	-	1	-	-	-	-

Table 5(b). Haemogram of Group III--male.

Parameters	Before experiment	First fortnight	Second fortnight	Third fortnight	Fourth fortnight	Fifth fortnight	Sixth fortnight
RBC mill/cmm	13.45	13.70	12.55	12.50	9.10	-	-
Hb g/100 ml	9.00	9.30	10.00	8.50	7.40	-	-
ESR mm/hr	Nil	Nil	Nil	Nil	Nil	-	-
PCV %	31	31	34	29	22	-	-
MCV Cμ	23.80	22.60	24.30	23.30	24.10	-	-
MCH $\mu\mu$g	6.60	6.70	7.30	6.80	8.20	-	-
MCHC %	29.00	30.00	29.40	29.30	32.70	-	-
Leucocytes No./cmm	9785	9750	9615	9675	9435	-	-
Differential count							
Lymphocytes	62	59	58	63	57	-	-
Neutrophils	35	37	42	34	42	-	-
Monocytes	1	-	-	2	1	-	-
Eosinophils	2	4	-	-	-	-	-
Basophils	-	-	-	1	-	-	-

Table 6(a). Haemogram of Group IV--female.

Parameters	Before experiment	First fortnight	Second fortnight	Third fortnight	Fourth fortnight	Fifth fortnight	Sixth fortnight
RBC mill/cmm	14.20	15.10	13.80	11.20	10.80	10.85	10.52
Hb g/100 ml	10.00	10.00	9.00	8.50	7.20	7.20	7.00
ESR mm/hr	Nil	Nil	Nil	Nil	Nil	Nil	Nil
PCV %	33	35	33	27	26	27	27
MCV $c\mu$	23.00	23.10	24.60	24.10	24.00	24.90	24.70
MCH $\mu\mu g$	7.00	6.60	6.10	7.70	6.60	6.60	6.60
MCHC %	29.50	28.50	27.20	31.40	27.60	26.60	25.90
Leucocytes No./cmm	12835	12674	11545	11525	11525	11545	12150
Differential count							
Lymphocytes	62	58	58	59	60	62	59
Neutrophils	37	38	41	39	40	37	40
Monocytes	1	-	-	2	-	-	1
Eosinophils	-	4	1	-	-	1	-
Basophils	-	-	-	-	-	-	-

Table 6(b). Haemogram of Group IV--male.

Parameters	Before experiment	First fortnight	Second fortnight	Third fortnight	Fourth fortnight	Fifth fortnight	Sixth fortnight
RBC mill/cmm	13.30	13.51	12.80	12.10	10.30	10.25	10.14
Hb g/100 ml	9.50	10.20	9.50	8.70	7.60	7.50	7.30
ESR mm/hr	Nil	Nil	Nil	Nil	Nil	Nil	Nil
PCV %	29	31	30	28	25	26	26
MCV c/μ	21.80	22.10	23.40	23.00	23.30	25.45	25.70
MCH μμg	7.10	7.50	7.40	7.20	7.30	7.40	7.20
MCHC %	29.50	28.50	27.20	31.40	27.60	26.60	25.90
Leucocytes No./cmm	10650	10345	9725	9725	10150	10450	10525
Differential count							
Lymphocytes	62	62	58	58	62	61	61
Neutrophils	37	33	39	39	37	39	38
Monocytes	-	2	3	-	1	-	-
Eosinophils	1	3	-	3	-	-	1
Basophils	-	-	-	-	-	-	-

Group 7(a). Haemogram of control group--female.

Parameters	Before experiment	First fortnight	Second fortnight	Third fortnight	Fourth fortnight	Fifth fortnight	Sixth fortnight
RBC mill/cmm	11.57	11.50	12.15	-	-	-	-
Hb g/100 ml	8.60	8.90	8.90	-	-	-	-
ESR mm/hr	Nil	Nil	Nil	-	-	-	-
PCV %	30	31	31	-	-	-	-
MCV $c\mu$	26.70	26.90	25.50	-	-	-	-
MCH $\mu\mu g$	7.40	7.40	7.30	-	-	-	-
MCHC %	28.60	27.70	28.70	-	-	-	-
Leucocytes No./cmm	9580	9715	9655	-	-	-	-
Differential count							
Lymphocytes	54	58	60	-	-	-	-
Neutrophils	43	39	37	-	-	-	-
Monocytes	-	-	-	-	-	-	-
Eosinophils	3	2	3	-	-	-	-
Basophils	-	1	-	-	-	-	-

Table 7(b). Haemogram of control group--male.

Parameters	Before experiment	First fortnight	Second fortnight	Third fortnight	Fourth fortnight	Fifth fortnight	Sixth fortnight
RBC mill/cmm	13.54	13.40	13.50	-	-	-	-
Hb g/100 ml	8.80	8.90	9.20	-	-	-	-
ESR mm/hr	Nil	Nil	Nil	-	-	-	-
PCV %	30	30	29	-	-	-	-
MCV Cμ	22.10	22.30	21.40	-	-	-	-
MCH $\mu\mu$g	6.50	6.60	6.80	-	-	-	-
MCHC %	29.30	29.60	31.70	-	-	-	-
Leucocytes No./cmm	9800	9550	9745	-	-	-	-
Differential count							
Lymphocytes	58	56	62	-	-	-	-
Neutrophils	40	42	35	-	-	-	-
Monocytes	1	-	-	-	-	-	-
Eosinophils	1	2	3	-	-	-	-
Basophils	-	-	-	-	-	-	-

Table 7(c). Haemogram of control group--female.

Parameters	Before experiment	First fortnight	Second fortnight	Third fortnight	Fourth fortnight	Fifth fortnight	Sixth fortnight
RBC mill/cmm	12.40	12.65	12.50	12.80	12.80	13.00	13.42
Hb g/100 ml	8.50	8.50	8.40	8.80	9.00	9.30	9.50
ESR mm/hr	Nil	Nil	Nil	Nil	Nil	Nil	Nil
PCV %	30	30	30	31	30	31	31
MCV Cμ	24.10	24.70	24.00	24.20	23.40	24.60	23.10
MCH $\mu\mu$g	6.10	6.70	6.70	6.80	7.00	7.10	7.10
MCHC %	28.30	28.30	28.00	28.30	30.00	30.00	30.60
Leucocytes No./cmm	11270	11175	11315	11245	11370	11255	11700
Differential count							
Lymphocytes	62	60	57	59	57	62	64
Neutrophils	37	40	41	40	41	36	34
Monocytes	1	-	-	-	-	1	2
Eosinophils	-	-	2	1	2	1	-
Basophils	-	-	-	-	-	-	-

Table 7(d). Haemogram of control group--male.

Parameters	Before experiment	First fortnight	Second fortnight	Third fortnight	Fourth fortnight	Fifth fortnight	Sixth fortnight
RBC mill/cmm	14.42	14.35	14.50	14.44	15.00	15.30	15.60
Hb g/100 ml	9.00	9.10	9.00	9.30	9.20	9.20	9.50
ESR mm/hr	Nil	Nil	Nil	Nil	Nil	Nil	Nil
PCV %	31	31	31	31	30	32	32
MCV cμ	22.10	22.20	21.30	21.50	20.00	20.90	20.50
MCH $\mu\mu$ g	6.20	6.20	6.20	6.40	6.10	6.00	6.00
MCHC %	29.00	29.20	29.00	30.00	30.00	28.70	29.60
Leucocytes No./cmm	9245	9540	9215	9715	9575	9410	9235
Differential count							
Lymphocytes	60	62	58	63	59	59	58
Neutrophils	37	36	40	36	39	41	39
Monocytes	1	-	2	-	-	-	-
Eosinophils	2	2	-	1	2	-	3
Basophils	-	-	-	-	-	-	-

3. Histopathology

Group I.

Thyroid.

There were numerous follicles of small size lined by prominent columnar epithelial cells when compared to the normal thyroid gland (Fig. 9, 10). The basally placed nucleus of the epithelial cells were hypertrophic. The cytoplasm of some of the cells showed vacuolar degeneration. The size of the lumen of the follicle was smaller and none of them contained colloid. Some of the follicles contained granular eosinophilic PAS negative material. The epithelial cells lining many of the follicles had desquamated and filled the follicles. Capillaries were severely engorged. In focal areas, in some of the follicles epithelial cells had undergone granular degeneration. The degenerated and desquamated epithelial cells were large and had eccentrically placed nucleus and abundant acidophilic cytoplasm. Interstitial oedema was also noticed.

Pituitary.

There was diffuse hyperplasia and hypertrophy of basophil cells. These cells had well defined borders and abundant cytoplasm with prominent granulation. Occasionally vacuolation of the cytoplasm was evident (Fig. 11). There was moderate engorgement of capillaries. The acidophils were hypertrophic and some of them showed degeneration and hyalinisation of the cytoplasm.

Adrenal.

Zona fasiculata was moderately enlarged and the cells were depleted of fat. There were scattered foci of haemorrhage and necrosis in the upper third of the fasiculata (Fig. 12). Focal areas of hyaline degeneration and necrosis was evident in the cortico-medullary junction. Medullary cells showed slight hyperplasia and vacuolation of the cytoplasm.

Ovary.

The ovaries were inactive. Only a few scattered primary follicles were seen in the cortex. There were only a few isolated developed secondary follicles. The stroma was very scanty and the germinal layer was only poorly developed. There were a few corpus albicans.

Uterus.

There was moderate submucosal and intermuscular oedema. The mucosal glands were inactive.

Testis.

There was moderate degree of interstitial oedema. The seminiferous tubules were smaller in size when compared to the normal tubules (Fig. 13). The seminiferous tubules were lined by single layer of spermatogonial cells. The tubules contained only a few inactive primary and secondary spermatocytes. Spermiogenesis was

completely absent (Fig. 14). None of the tubules contained sperms. There was no evidence of sertoli-cells. The interstitial cells were scattered and few in number.

Skin.

Moderate degree of hyperkeratosis of the stratum corneum was evident when compared to the normal skin (Fig. 15). There was slight diffuse oedema and scattered lymphoid infiltration in the subcutaneous tissue. Dermal collagenisation was appreciable. A few of the hair follicles showed degeneration and keratinisation (Fig. 16).

Heart.

There was slight interstitial oedema (Fig. 17). Focal areas of hyalinisation were seen in the myocardium.

Liver.

The hepatic cells were moderately hypertrophic. There was slight engorgement of the sinusoids. Fatty change, characterised by diffuse vacuolar degeneration of hepatic cells was evident (Fig. 18).

Aorta.

Intima was intact without evidence of any degenerative changes. There was fragmentation of elastic fibres and hyalinisation of muscle fibres. Sub intimal fatty deposition was noticed.

Brain.

Moderate degree of perivascular and perineuronal oedema was evident (Fig. 19). Venules were slightly engorged.

Group II.

Thyroid.

Histological picture was characterised by the presence of numerous micro-follicles (Fig. 20). There was hypertrophy of the lining epithelial cells of the follicles. Most of the follicles were lined by tall columnar epithelial cells with a basal nuclei. In some of the follicles lining cells were seen forming more than one layer thickness. The follicles were completely devoid of colloid (Fig. 21). Hypertrophied epithelial cells were seen filling many of the follicles. Some of the follicles showed degeneration and desquamation of epithelial cells. Cytoplasmic vacuolisation of epithelial cells was also noticed. Most of the follicles were filled with degenerated epithelial cells. Reticulin stain revealed collapse of the follicles in focal areas and fusion to form cystic spaces (Fig. 22). These cystic spaces were seen filled with degenerated and desquamated cells. Follicles contained PAS negative granular eosinophilic material. There was no evidence of colloid formation. Interstitial tissue showed hypercellularity and interstitial oedema. There was increased vascularity.

Pituitary.

Focal areas showed hyperplasia and hypertrophy of basophil cells (Fig. 23). The acidophils were enlarged; borders were irregular and poorly defined. In focal areas acidophils showed granular degeneration and vacuolisation of cytoplasm. Congestion of blood vessels was also observed.

Adrenal.

There were focal areas of congestion and haemorrhage in the zona fasiculata of the adrenal cortex (Fig. 24). Cells in this zone were devoid of fat. Sinusoids were moderately engorged. There was slight proliferation of the chromaffin cells of the medulla.

Ovary.

Only a few primary follicles were observed in the cortex. A few corpus albicans and graafian follicles were seen scattered in the cortex. There was moderate stromal oedema when compared to the normal ovary (Fig. 25, 26).

Uterus.

There was moderate submucosal and interstitial oedema when compared to the normal uterus (Fig. 27). The glands and interstitial tissue were inactive. Lining epithelium was low cuboidal type. Slight serosal oedema was evident (Fig. 28).

Testis.

Seminiferous tubules contained only a few primary and secondary spermatocytes. There was complete absence of spermatozoa and germ layer in some of the tubules. The lumen of the tubules contained only a net work of fibres and scattered round cells. There was also moderate interstitial oedema (Fig. 29).

Liver.

There was severe diffuse fatty change of hepatic cells. Sinusoids were slightly engorged (Fig. 30).

Skin.

There was slight but diffuse hyperkeratosis of the epidermal layer. Dermal layer showed moderate degree of oedema and diffuse round cell infiltration (Fig. 31, 32). Hair follicles had degenerated and they were plugged with dense masses of keratin. There was increased deposition of acid mucopolysaccharide (AMP) in the dermal tissue.

Heart.

Interstitial oedema of cardiac muscle fibres was evident. Muscle fibres showed focal areas of degeneration and hyalinisation. Extensive fatty degeneration of muscle fibres was observed (Fig. 33)

Aorta.

Intima was intact but there was lipid deposition on the sub-

intimal layer (Fig. 34). Elastic tissue stains revealed fragmentation of elastic fibres. There was hyalinisation of muscle fibres.

Brain.

Mild perivascular and perineuronal oedema was evident. There was also slight diffuse gliosis (Fig. 35).

Spleen.

Lymphoid follicles were few in number. Focal areas showed deposition of haemosiderin pigments.

Kidney.

Glomeruli were engorged with blood. Tubular epithelial cells showed granular degeneration and some of them had undergone vacuolar degeneration.

Group III.

Thyroid.

There was pronounced stromal oedema and interstitial tissue appeared thickened. Structural disorganisation of the follicles was evident. In certain areas there was no well defined follicles but there were only scattered dense dark staining nuclear material amidst a mass of homogenous basophilic granular material. The follicles were completely devoid of colloid and were filled with degenerated desquamated epithelial cells (Fig. 36). The follicle contents gave negative reaction with PAS. In certain areas collapse and fragmentation of follicular reticulin was evident

with reticulin stain. In most of the cells cytoplasm was scanty and if present it was basophilic. Focal areas showed collections of proliferating hyperchromatic blast cells. In the male kid well formed follicles were lined by columnar epithelial cells. Proliferative changes were not so pronounced as in the female.

Pituitary.

There was diffuse hyperplasia of basophil cells (Fig. 37). Vacuolisation of cytoplasm causing displacement of the nucleus was evident in some of the cells. Many of the acidophils had irregular cellular border and the cytoplasm had ballooned showing pronounced hyaline change (Fig. 38). Capillaries were moderately engorged.

Adrenal.

Adrenal capsule had moderately thickened. Diffuse hyperplasia of zona fasiculata was evident. Accessory cortical nodule formation characterised by clumps of zona fasiculata cells encapsulated by fibrous tissue was evident (Fig. 39). There was depletion of fat in zona fasiculata and sinusoids showed engorgement.

Ovary.

In the ovary very few primary follicles and few well developed graafian follicles were observed. There was numerous closely packed elongated spindle shaped stromal cells. The graafian follicles were small in size contained only little liquor folliculi. Cells in the theca interna and externa zones were very few.

Uterus.

The lining epithelial cells were low cuboidal type. Submucosal oedema was evident. A few small mucous glands and abundant stroma were evident in the mucosa.

Testis.

The seminiferous tubules were small in size and appeared collapsed. The size of the lumen was small. There was no evidence of sperms in any of the tubules and it was lined by a single layer of epithelial cells (Fig. 40). The tubules contained granular pink staining material and few desquamated epithelial cells. There was no evidence of spermiogenetic activity in the tubules. Moderate degree of interstitial oedema was evident. Interstitial cells were only few in number and cells were smaller in size with little amount of cytoplasm.

skin.

The epidermis was thrown into small papillary folds. There was hyperkeratinisation of epidermal layer (Fig. 41). In focal areas there was acanthosis and parakeratosis of the epidermal layer. The dermal layer was slightly thickened due to diffuse dermal oedema and increased deposition of AMP. A few small lymphocytes were seen scattered in the dermis. Many of the hair follicles had degenerated and the follicles were plugged with masses of pink staining keratin.

Liver.

Hepatic cells exhibited diffuse cytoplasmic vacuolisation.

This was fonfirmed as focal areas of fatty change by Sudan stain. Degenerative and necrotic areas were seen scattered in the parenchyma (Fig. 42).

Kidney.

Tubular epithelium showed degeneration and desquamation of epithelial cells. There was slight congestion of capillaries.

Heart.

The myocardium showed separation of strands of muscle fibres due to moderate interstitial oedema.

Aorta.

There was focal areas of hyalinieation of muscle fibres and fragmentation of elastic fibres (Fig. 43).

Spleen.

Spleen showed depletion of lymphoid follicles and slight haemosiderosis.

Brain.

There was slight perineuronal oedema. The cytoplasm showed many small vacuoles giving a spongy appearance to the tissue.

Group IV.

Thyroid.

The gland consisted of numerous microfollicles of varying

size. None of the follicles contained colloid material. The follicles were lined by tall columnar epithelial cells (Fig. 44). These cells had abundant acidophilic cytoplasm and basal nuclei. Some of the cells showed vacuolar degeneration of the cytoplasm. In occasional places more than one layer of lining cells of the follicles were evident and these were seen thrown into small papillary folds. The foldings projected into the lumen and filled the lumen. Many of the cells had degenerated and these areas appeared as homogenous pink staining material above the follicular basement membrane and below the cellular layer (Fig. 45). Many of the follicles contained masses of degenerated desquamated epithelial cells. Some of the follicles contained granular eosinophilic material which was PAS negative. Reticulin stain revealed collapse of reticulin in certain areas and duplication of reticulin fibres. The stroma appeared prominent due to moderate degree of collagenisation. Engorgement of capillaries was less in this group of animals. The reactive hyperplasia was more in the female kid.

Pituitary.

There was diffuse hyperplasia of basophil cells. Many of them had swollen and showed either granular degeneration or vacuolisation of the cytoplasm (Fig. 46). The acidophils were few in number and some of them showed degranulation and hyalinisation.

Adrenal.

Depletion of fat in zona fasiculata was observed (Fig. 47).

Ovary.

Germinal cells were inactive low cuboidal type. There were only few primordial follicles and few developing follicles in the ovary. The ovary was inactive, but contained a few corpus albicans.

Uterus.

There was moderate submucosal oedema. A few mucous glands seen in the submucosa were inactive.

Testis.

Seminiferous tubules showed no evidence of spermiogenesis. The small sized tubules were lined by a single layer of spermatogonia. There was no evidence of sperm in many of the tubules (Fig. 48). The tubules contained pink staining granular material. Interstitial fibrosis and oedema of moderate degree were observed. Interstitial cells were few in number but did not show any evidence of degeneration.

Skin.

The epidermal layer was thrown into small papillary folds. There was hyperkeratinisation of stratum corneum. In focal areas moderate degree of dyskeratosis and parakeratosis was also evident. Hair follicles were of small size and were seen filled with purplish staining masses of keratinised material. Dermal layer was

thickened due to oedema and deposition of AMP. There was also scattered round cell infiltration in the dermal tissue (Fig.49, 50).

Heart.

The myocardial fibres showed interstitial oedema (Fig. 51).

Liver.

Hepatic cells exhibited moderate diffuse fatty change. Sinusoids were moderately engorged (Fig. 52).

Kidney.

There was slight granular degeneration in tubular epithelial cells.

Spleen.

Slight haemosiderosis was evident.

Aorta.

Focal areas of hyalinisation in the tunica media was associated with fragmentation of elastic tissue (Fig. 53).

Brain.

There was little but appreciable perivascular and perineuronal oedema. Diffuse type of gliosis was also evident. Nerve cells showed small vacuoles in the cytoplasm giving a moth eaten appearance to the brain tissue (Fig. 54).

DISCUSSION

thickened due to oedema and deposition of AMP. There was also scattered round cell infiltration in the dermal tissue (Fig.49, 50).

Heart.

The myocardial fibres showed interstitial oedema (Fig. 51).

Liver.

Hepatic cells exhibited moderate diffuse fatty change. Sinusoids were moderately engorged (Fig. 52).

Kidney.

There was slight granular degeneration in tubular epithelial cells.

Spleen.

Slight haemosiderosis was evident.

Aorta.

Focal areas of hyalinisation in the tunica media was associated with fragmentation of elastic tissue (Fig. 53).

Brain.

There was little but appreciable perivascular and perineuronal oedema. Diffuse type of gliosis was also evident. Nerve cells showed small vacuoles in the cytoplasm giving a moth eaten appearance to the brain tissue (Fig. 54).

Chapter–V

DISCUSSION

DISCUSSION

Hypothyroidism of varying degree was produced experimentally in kids using thiourea as an experimental goitrogen. The study has yielded valuable informations on the manner in which kids are affected by hypothyroidism. Though it has been considered that incidence of goiter is high in goats no attempts seems to have been made to elucidate its nature by experimental studies. A perusal of the available literature did not reveal any reports on the pathological changes in goats in experimental hypothyroidism. Thiourea and related compounds have been used to induce experimental hypothyroidism in different species of animals. There has been no report on thiourea induced hypothyroidism in goats and this would appear to be the first report on this aspect in goats. In this study it has been possible to produce hypothyroidism of varying nature experimentally by feeding thiourea to kids. The observations made during the course of this investigation have clearly shown that thiourea could be used as an experimental goitrogen in goats without any side effects in the dose schedules adopted.

All the kids dosed with thiourea died except kids in the lowest dosage group. This observation indicates that the thyroxin deficiency was very acute with dosages upto 150 mg of thiourea per kg bodyweight leading to a thyroid crisis and death. Clinically, thyroid suppression by thiourea was evidenced by disturbance in growth and health. There was stunted growth and weight loss in

all groups of animals dosed with thiourea. Lombardi et al. (1962) did not observe any deleterious effect on the growth in dogs dosed with thiouracil. This was attributed to the fact that the metabolic processes in the dog are less dependent on the production of thyroid hormone. Significant clinico-pathological changes observed in this study indicate that goats are more dependent on thyroid hormone for their growth and development than dogs.

It is significant to observe that there was a sharp reduction in weight in the first fortnight itself in the first group of kids dosed with 250 mg of thiourea. The high dose of thiourea would have caused sudden suppression of thyroxin production causing lowered BMR, cellular growth and consequent weight loss. It is relevant to mention here that goitrogens have been found to retard growth rate in sheep (Lascelles and Setchell, 1959) and poultry (Singh et al. 1968). Retardation of growth in hypothyroidism has been attributed to defective synthesis of new protein by Metzger and Freinkel (1971). Kimberg (1971) has reported diminution of absorption of nutrients in human beings in the absence of thyroxin; this might also explain reduction in weight. It is interesting to observe that animals in all the groups except in the high dosage group recorded a gain in bodyweight during the first fortnight. This would suggest that there has been some anabolic effect at lower dose level causing gain in weight. The slow onset of hypothyroidism lowers the BMR and causes reduction in the catabolism of protein and utilisation of energy for body functions and this

perforce leads to a transient positive anabolic effect causing gain in weight. Thus it would appear that low doses of thiourea have transient beneficial effect in increasing bodyweight when given for shorter periods. It is relevant to mention here that in pigs thiourea in low doses has been used for fattening (Pearson et al. 1966). The observation made in this study therefore indicates that in goats also low doses of thiourea could be of use in fattening goats intended for slaughter.

Stunted growth characterised by reduction in weight gain and stature was a consistent feature in all the kids dosed with thiourea. Growth hormone in association with thyroxin has great influence on the growth of animals. Thyroxin is considered as a spark necessary for all metabolic processes to take place and necessarily in the absence of this hormone a retarded growth can be expected. There was reduction in the feed intake of animals dosed with thiourea and this might again be a cause of retardation in growth. Similar observation has been made in pigs dosed with thiourea (Pearson et al. 1966). Stunting in growth in experimental hypothyroidism has been reported in lambs, (Marston and Peirce, 1932) in rats (Green et al. 1974) and in spontaneous hypothyroidism (Smith et al. 1972).

The reduction in growth and weight was appreciable in experimental animals. It is important to mention here that clinical symptoms were not so pronounced and in the field conditions, hypothyroidism as the cause for the stunted growth and reduction in

weight might be overlooked. The common finding of poor growth and production of animals in Kerala should be viewed against this background. Reduction in growth rate of animals is a major problem in the field and although the reason for this condition may be varied, the observation noted in the present investigation points out the need to undertake a study to assess the role of hypothyroidism in stunted growth and production in animals in Kerala. It is more so in Kerala where the rains are heavy and the plants may be deficient in iodine. This type of investigation will go a long way in identifying and preventing hypothyroidism and this would help to improve the productive status of the animals.

Subcutaneous oedema of varying degree was observed in all groups of experimental animals. Histologically it was characterised by oedema and excess deposition of AMP in the dermal tissue. Reports have not appeared about such myxoedematous changes in goats although this is a common change in hypothyroid state in man. Wegelius (1971) has reported excessive deposition of AMP in the dermal tissue in human hypothyroidism. Reduction of rate of breakdown of mucoprotein in the absence of thyroxin with the unchanged rate of formation of mucoprotein has been explained as the reason for the accumulation of AMP in human myxoedema by Crispell and Wilson (1964).

The hair coat of the animals also showed changes. Clinically the coat was rough and matted. Histologically degeneration of hair follicles and hyperkeratosis were the characteristic features.

Although, destruction of hair follicles were seen, grossly there was no evidence of alopecia suggesting that changes were not advanced. If the animals were allowed to live long with low dose of thiourea, it might have lead to chronic hypothyroidism and alopecia. The epidermal layer was considered as an important target organ to the action of thyroxin by Freedberg (1971) and therefore significant pathological changes could be expected in the skin.

Few of the animals, besides being lethargic, weak and depressed showed a tendency to hold the head down and press the head against walls. Histological evidence of cereberal oedema in these animals would explain this clinical manifestation.

The serum cholesterol level, one of the clinico-pathological parameters studied, was significantly higher in all the animals dosed with thiourea. Increase in the serum cholesterol level has been reported in experimental hypothyroidism in sheep (Lascelles and Setchell, 1959; Belonje, 1967) and in chicken (Nangia et al. 1975). The increase in the serum cholesterol level was more pronounced in the group given low dose of thiourea for longer duration Increase in the serum cholesterol level has been observed as a more specific change in lipid metabolism by Peters and Man (1950) in human myxoedema. Fletcher and Myant (1958) indicated that in hypothyroid rats the hepatic synthesis and release of cholesterol from acetate is subnormal but the peripheral breakdown and biliary excretion is lowered and this they ascribed as the reason for in-

crease in the serum cholesterol level. Observations made on this parameter in this study suggest that serum cholesterol level could be used as a useful marker to detect sub-clinical cases of hypothyroidism in goats and could be used advantageously as one of the screening tests to detect hypothyroidism in the goat population in endemic areas.

Hypothyroid state in the animals dosed with thiourea was also associated with increase in total plasma protein level. Similar increase in plasma protein level and serum albumin has been reported in hypothyroidism in human beings (Lamberg and Grasbeck, 1955). An increase in plasma globulin in thyroidectomised Merino ram (Belonje, 1967) and in poultry (Nangia et al. 1975) has been reported. This increased level might have been due to defective utilisation of nutrients in the absence of thyroxin which causes accumulation of blood proteins. Crispell and Wilson (1964) have documented reduction in both anabolism and catabolism of protein, the latter being more reduced than anabolism of proteins in hypothyroidism. This would again account for the rise in plasma protein level.

The animals fed on thiourea to induce hypothyroidism showed a significant decrease in the PBI level in serum. This observation is in close agreement with the results of experimental hypothyroidism in sheep (Lascelles and Setchell, 1959), in bull (Lewis, 1956) and in spontaneous hypothyroidism in sheep (Watson et al. 1962). No comparable data is available in literature on

PBI values in goats in experimental hypothyroidism. From the observations made during the course of this investigation it is reasonable to conclude that the PBI values in conjunction with serum cholesterol level could be used as a reliable test to screen the existence of hypothyroid state in goats. These data will truly reflect the degree of hypothyroid status in the individual.

Thiourea inhibits the organification of iodide and iodination causing reduced synthesis and release of thyroid hormone (thyroxin) from the gland. Reduction in PBI level was very much pronounced in the high dose level group suggesting that thiourea in high doses has markedly suppressed iodination in the thyroid gland and had caused acute deficiency of thyroxin. A significant observation, worth noting is that females in all the groups showed much lower value than males. This is an observation which would support the view that females are more prone to develop hypothyroidism and are more susceptible to the action of antithyroid drugs (Russell, 1970).

The blood picture of experimental animals revealed a macrocytic hypochromic anaemia. Anaemia was apparent only in the longer duration treatment group suggesting that persistent thyroxin deficiency would lead on to anaemic state. Rivlin (1971) has observed that the most significant effect of hypothyroidism in man is the reduction of intestinal absorption of Vitamin B_{12}.

How far this would be applicable to ruminants has to be clarified by further detailed investigation. It is relevant to mention here that, Adamson and Finch (1966) have demonstrated decreased production of erythropoietin in hypothyroidism.

There was significant increase in the relative weight of the thyroid gland in all the kids dosed with thiourea. The increase being more pronounced in kids fed low doses of thiourea for longer duration. This observation shows that there has been reactive hyperplastic response in thyroid under the influence of thiourea. The increase in thyroid weight can be explained as a compensatory hyperplastic response mediated through pituitary under the influence of lowered thyroxin level. It is significant to observe that enlargement was progressive and there was correlation between the time interval, dosage and degree of enlargement. As the duration of experiment increased, increase in weight was also found to be more. This indicates that compensatory hyperplastic thyroid response has been mediated efficiently through pituitary. However, functionally it was not found to be compensated since the PBI values in the thiourea dosed kids were much lower when compared to the euthyroid control animals.

Although, there had been sufficient increase in the weight of the gland in experimental animals, the enlargement was not appreciable by palpation during clinical examination. This observation is pertinent and has to be stressed here since this

points to the fact that sub-clinical hypothyroidism could exist in animals without gross evidence of thyroid enlargement. Therefore, palpable thyroid enlargement, cannot be taken as a criterion for diagnosing sub-clinical hypothyroid state in animals. However, it should be observed that thyroid enlargement has been reported in experimental hypothyroidism in different species of animals (Kennedy, 1942; Jones et al. 1946; Harkness et al. 1954; Goldberg et al. 1957; Lascelles and Setchell, 1959; Lazo-Wasem, 1960) and in spontaneous hypothyroidism (Southcott, 1945; Lall, 1952; Dutt and Kehar, 1959).

There was significant increase in the relative weight of the adrenal glands in animals treated with high level of thiourea than lower dose level and longer duration. This observation is in contrast to the reports of atrophy of adrenal glands in laboratory animals and pigs dosed with thiouracil and allied compounds by Baumann and Marine (1945), Zarrow and Money (1949) and McCarthy et al. (1959). However, the present observation is in agreement with the findings of Durlach et al. (1954[a]) who have reported an increase in adrenal weight in guinea pigs dosed with propyl thiouracil. The animals with induced hypothyroid state with large doses of thiourea was under the influence of stress and this stress might have been responsible for the enlargement of the adrenal glands. Microscopic changes like depletion of fat, focal areas of haemorrhage, degeneration and necrosis of zona fasiculata seen in the adrenal glands of thiourea dosed kids are all histological features

seen in stress reaction in the adrenal gland, more specifically in an exhaustion stage (Symington, 1972). This would again justify the existence of stress in the thiourea dosed animals.

Consistently there was increase in the relative weight of the pituitary gland in all the thiourea dosed animals. Similar observations have been reported in experimental hypothyroidism in laboratory animals (Kennedy and Purves, 1941; Griesbach et al. 1941; Goldberg et al. 1957; Lazo-Wasem, 1960) and in spontaneous hypothyroidism in goats (Lall, 1952). The increase in the relative weight of the pituitary was much more in animals dosed with high levels of thiourea. This could be explained by the fact that high levels of thiourea interferes with organic binding of iodine and acute deficiency of thyroxin stimulates basophil cells and these undergo hypertrophy with concomitant increase in number in order to meet the increase demand for TSH.

All the kids dosed with thiourea were in poor condition and there was gelatinisation of body fat. This might have been due to reduced feed consumption and feed conversion in the absence of thyroxin. Russell (1943) indicated that most energy demand are being met from preformed lipid in hypothyroid rat. Therefore, gelatinisation of body fat might be due to utilisation of fat for body vital functions and energy requirement for the animal.

It is note worthy that all kids showed dilatation and hypertrophy of the left ventricle and animals in the high dosage group

showed moderate degree of hydropericardium. Similar findings have been reported in human beings in myxoedema (Zondek, 1918). Hydropericardium might have been due to pericardial effusion presumably resulting from increased capillary permeability. Cardiac hypertrophy and dilatation could be considered as a pathological change resulting from theeffort on the part of the heart to compensate the function in the face of reduced cardiac output and decreased velocity of blood flow in hypothyroidism.

Reactive hyperplasia was the characteristic histological picture observed in the thyroid gland. In a hypothyroid state this is an expected pathological change. This is a direct histological evidence which shows that thiourea has caused lowered thyroxin production and pituitary mediated compensatory thyroid hyperplasia. Thyroid hyperplasia has been reported in spontaneous hypothyroidism in sheep (Growth, 1962; Wallach, 1965; George et al. 1966), in goats (Lall, 1952; Dutt and Kehar, 1959; Roy et al. 1964) and in experimental hypothyroidism in laboratory animals (Jones, 1946; D'Angelo et al. 1951; Durlach et al. 1954; Goldberg et al. 1957). Hyperplastic response of the thyroid was more severe in the animals given low doses of thiourea, suggesting that the effect of TSH on the thyroid was continuous and long. This is also evidenced by marked increase in weight of glands in these animals. It was also observed that thyroid hyperplasia was more severe in females than in males in the 150 mg and 100 mg dosage group. Formation of new small sized follicles with hypertrophic one or

two layered tall columnar epithelial cells was the consistent histological feature in all the groups. However, vascular changes were very much pronounced in the high dosage group. This would appear to be a change occurring as a result of sudden depression of thyroxin production and severe stimulation by pituitary TSH. The most important histological observation was the complete absence of colloid in almost all the follicles of the thyroid. It was difficult to identify the tissue as thyroid on histological examination. This would suggest that, although there had been stimulation by TSH and hyperplasia of thyroid epithelium, there has been no synthesis of thyroglobulin due to the non-availability of iodine in the presence of thiourea. This would support the observation that thiourea has effectively blocked the thyroglobulin production and has lowered the PBI level. The unsuccessful severe hyperplastic reaction also resulted in degeneration and desquamation of many lining cells and the granular PAS negative material seen in the follicles might have been only the degenerated cells. Formation of new small follicles without having colloid would suggest that TSH stimulation was very severe and blocking of iodide and incorporation of iodine has been very effective. If the target gland stimulation has been low and continuous and if the animals had lived long that would have resulted in follicles with wellformed and multilayered epithelial cells. This was not observed in this study indicating that thyroid suppression was more or less acute with high dosage levels of thiourea. However, in the lowest dosage group

changes of this type were seen. Therefore, it is worthwhile to take up further study with still lower doses of thiourea. Proliferation of supporting tissue of the thyroid gland was reported by Roy et al. (1964) in hypothyroid goats in endemic area. This was observed in the thyroid glands of animals dosed with low levels of thiourea. The stromal reaction leading to fibrosis might also be a part of the response for the formation of new follicles under the influence of TSH. Increase in collagen content in the thyroid has been reported by Harkness et al. (1954) in rats after feeding thiouracil.

In the pituitary gland there was hypertrophy and hyperplasia of the basophils. Pituitary basophil hyperplasia is an observation which would support the conclusion that thyroid activity had been diminished by the administration of thiourea to the kids. With increasing thyroid dysfunction the initial hypertrophy of basophil cells with storage of granules was followed by the loss of granules in the cells of certain areas and finally complete degranulation and vacuolation of basophil cells. These have been described as "thyroidectomy cells" (Zeckwer et al. 1935). The cytoplasmic vacuolation might represent and exhaustion stage in the reactive hyperplastic process. These changes have been described in experimental hypothyroidism in dogs (Lippincott et al. 1957) and in rats (Goldberg and Chaikoff, 1951). The hypertrophy of basophil cells has also been reported in spontaneous hypothyroidism (Lall, 1952; Dutt and Vasudeva, 1963) in goat and sheep.

Vascular changes were very pronounced in the first two groups. The increased vascularity might have been a response to acute thyroxin deficiency mediated through hypothalamus to enhance the functional activity.

The acidophils showed degranulation and degeneration. This might be due to a feed back inhibition of the acidophils resulting from inefficient utilisation of growth hormone produced by the pituitary in the absence of thyroxin. In hypothyroidism, induced by thyroidectomy and goitrogens in laboratory animals similar histological changes in the pituitary acidophil cells have been described (Zeckwer et al. 1935; Goldberg et al. 1957; Contopoulos et al. 1958).

There was depletion of fat, focal haemorrhage, hyaline degeneration and necrosis in the zona fasiculata of adrenal gland. These are changes encountered in stress and this observation indicates that kids were under a stress in hypothyroid state. Slight medullary hyperplasia was encountered in the group of animals dosed with 150 mg of thiourea. Similar observation has been reported in experimental thyroidectomy in laboratory animals. (Gley, 1923).

Hepatic fatty change was a consistent histological change in all the kids. Chaikoff et al. (1948) have documented similar changes in dogs. They suggested that the fatty change occurring in experimental hypothyroidism in dogs was due to some interference

in the activity or use of lipotropic factors. They have also shown that lipotropic factors in the normal diet appears to be particularly influenced by the action of thyroid hormone.

The histologic picture of the heart was characterised by interstitial oedema, focal areas of degeneration, hyalinisation and fatty degeneration. Similar cardiopathology has been described in human myxoedema (Sobel and Braunwald, 1971). Fatty change in the myocardium can be expected because there was high cholesterol level in the blood. Similar myocardial fatty infiltration has been reported in hypothyroidism induced by thyroidectomy in dogs (Lippincott et al. 1957).

Degenerative changes in the aorta might have been initiated by hypercholesterolemia and general increase in blood lipids in circulation.

Hyperkeratosis, slight diffuse oedema and scattered lymphoid infiltration were the common histological lesions encountered in the skin. Similar changes have been reported in both natural and experimental hypothyroidism in dogs (Lippincott et al. 1957). However, no reports have appeared describing skin lesions in hypothyroidism in goats. Atrophy of the hair follicles and hyperkeratotic plugging of follicular opening as observed in this study have also been recorded in the skin in hypothyroid condition in dogs (Bush, 1969). The changes like acanthosis, parakeratosis and dyskeratosis were observed in animals dosed with 100 mg and 150 mg of thiourea. This is an indication of degenerative processes that

has taken place in the epidermis in the thyroxin deficient kids. This is an observation which is seen to develop in severe and prolonged hypothyroidism. This finding is in agreement with the observations of Bush (1969) in dogs in hypothyroidism. There was evidence of dermal collagenisation and deposition of AMP in kids, particularly in the low dosage groups. The latter is a pathognomonic picture in human myxoedema and it is significant to observe that in goats dermal changes have been almost similar to that seen in man though not pronounced as seen in human beings. Freedberg (1971) attributed increased dermal collagenisation in human myxoedema to decreased synthesis of collagen and decreased rate of its breakdown.

No significant pathological changes were seen in kidney and spleen. Bradley (1971) has observed that hypothyroidism is not usually associated with any serious defect in renal function in human beings.

The testis showed varying degree of degenerative changes in all the groups dosed with thiourea. This observation clearly reflects the importance of thyroxin in gonadal development. Similar changes have been reported in experimental hypothyroidism induced by thiouracil in ram and rabbits (Maqsood, 1951). Thyroxin has a priming effect on the action of hormones on cells and in the absence of thyroxin, the gonadotrophic hormone of the pituitary in particular, will not be functioning effectively and this might explain the degenerative changes in the testicular tissue. Brooke et al.(1964

have observed a reduction in gonadal and gonadotropic hormones in hypothyroidism induced by thyroidectomy in ewes. Besides this, lowered protein synthesis and BMR in hypothyroidism may also contribute to the development of degenerative changes in the gonads. It is relevant to mention here that studies on the influence of hypothyroidism on the reproductive organs in different species of animals have been varied (Werner, 1971). In this context it is pertinent to observe here that no reports have appeared describing changes in gonads of goats in experimental hypothyroidism. The finding of significant degenerative changes in the reproductive organs of both males and females in hypothyroid state in this study has great economic importance. It is only reasonable to assume that in the goat population in sub-clinical hypothyroid state, there is bound to have infertility problem in both males and females. The histological picture of pronounced degenerative changes in the reproductive organs of kids on lowest dose of thiourea draws attention to this direction. While the control animals had showed well developed seminiferous tubules with sperms, the seminiferous tubules of kids in the same age group dosed with thiourea showed complete aspermiogenesis and degeneration of tubules. Therefore, this study stresses the need for a detailed investigation into the thyroid pathology of animal population particularly of goats in Kerala, so as to evaluate the influence of hypothyroidism on the infertility problem in the State.

SUMMARY

SUMMARY

1. Employing thiourea at different dose levels, varying degree of hypothyroidism was induced in kids with the objective of studying sequence of olinico-pathological changes in different stages of hypothyroid state. So far no reports have appeared describing pathological changes in experimental hypothyroidism in goats.

2. Thiourea was found to be a useful experimental goitrogen at the dosage levels employed. Experimental model of hypothyroidism of varying severity was successfully induced in kids.

3. During the course of observation for a period of three months all the kids dosed with thiourea except those in the lowest dosage group died at varying intervals due to thyroxin deficiency. These animals were sacrificed after three months of observation.

4. Clinical findings revealed stunted growth and appreciable reduction in weight in all the kids dosed with thiourea. However, a gain in weight was recorded in the first fortnight in all the groups except in the highest dosage group. This observation indicates that thiourea in low doses for short periods could be used for fattening goats. Prolonged dosage resulted in progressive reduction in weight. It was concluded that reduction in weight is a constant feature in prolonged hypothyroidism.

5. Weakness, lethargy, depression, reduction in feed intake and subcutaneous oedema of varying degree were the important clinical features observed.

6. The hypothyroid kids had high blood cholesterol values and plasma protein levels when compared to euthyroid control kids. Hypercholesterolemia was significantly higher in females and in the lower dosage group which were under observation for longer periods.

7. A significant decrease in the serum PBI was consistently recorded in all groups of animals dosed with thiourea. Female kids in all the groups showed much lower levels of PBI than males. The results of the study indicate that estimation of serum cholesterol level and PBI values could be used as reliable markers for detecting hypothyroidism in the goat population.

8. There was no significant variation in the haemogram values of hypothyroid kids except in the 100 mg group. In this group haemogram revealed a macrocytic hypochromic type of anaemia.

9. An increase in the relative weight of thyroid was consistently observed. It was more marked in kids dosed with 100 mg of thiourea. The increase in the weight was found to be due to compensatory thyroid hyperplasia. However, thyroid enlargement was not palpable by gross examination. Therefore it was reasonable to conclude that palpable enlargement of the thyroid glands cannot be taken as a criterion to indicate hypothyroid state.

10. There was increase in the relative weight of the pituitary and adrenal glands in animals dosed with thiourea. This increase was more in animals fed thiourea at 200 and 250 mg levels. The pathogenesis of this condition has been discussed in detail.

11. Hydropericardium and left sided ventricular hypertrophy and dilatation of varying severity were observed in the hypothyroid kids. Histologically there was interstitial oedema and myocardial degeneration.

12. Histologically the thyroid gland exhibited varying degree of hyperplastic changes. Hyperplasia was characterised by formation of colloid depleted microfollicles. Lining cells were hypertrophic and concomitant degenerative changes were also observed. Thyroid hyperplasia was more pronounced in the female kids. Absence of colloid formation was considered as a definite indication of blocking of thyroxin formation by thiourea. Pathobiology of reactive thyroid hyperplasia has been discussed in detail.

13. Predominant histological picture in the pituitary was hypertrophy and hyperplasia of basophil cells. Degenerative changes were also seen in these cells. Acidophils showed degeneration, degranulation and hyalinisation.

14. Pathological changes in the adrenal glands were similar to that seen in stress reaction. It was therefore concluded that

kids dosed with thiourea particularly in the higher dosage group were in a state of stress.

15. Fatty change in the liver was a common histological change in all the groups. Histogenesis of the condition has been described and discussed.

16. Aorta revealed athero-sclerotic changes and the role of hypercholesterolemia in the pathogenesis of the lesion has been detailed.

17. Histological changes in the skin of hypothyroid kids were similar to that reported in human skin in myxoedema.

18. This study has clearly brought out significant pathological changes in the gonads. Gonadal degenerative changes both in males and females were found to be very significant in experimental groups. Aspermiogenesis was a characteristic histological finding in all the male kids dosed with thiourea. Importance of recognition of spontaneous hypothyroidism and the need to assess its influence on the fertility of animals have been stressed.

19. Pathoanatomical changes observed in this study have convincingly established the importance of recognising hypothyroid state in livestock for economical livestock production and the need for taking up further studies to assess the effect of hypothyroidism in animals.

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Fig. 1. Kid - Group I - Oedema of the face and lower part of hind limbs are evident.

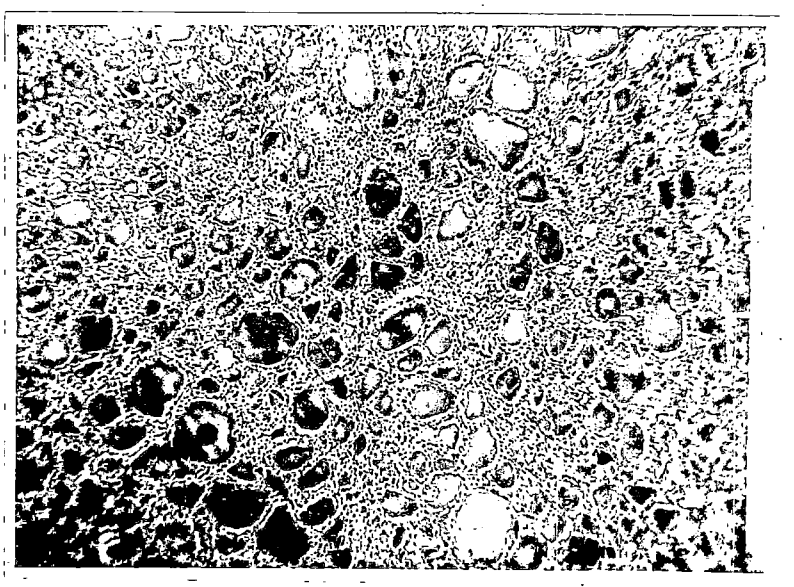
Fig. 2. Kid - Group IV - Showing oedema of the face and lower eye lid.

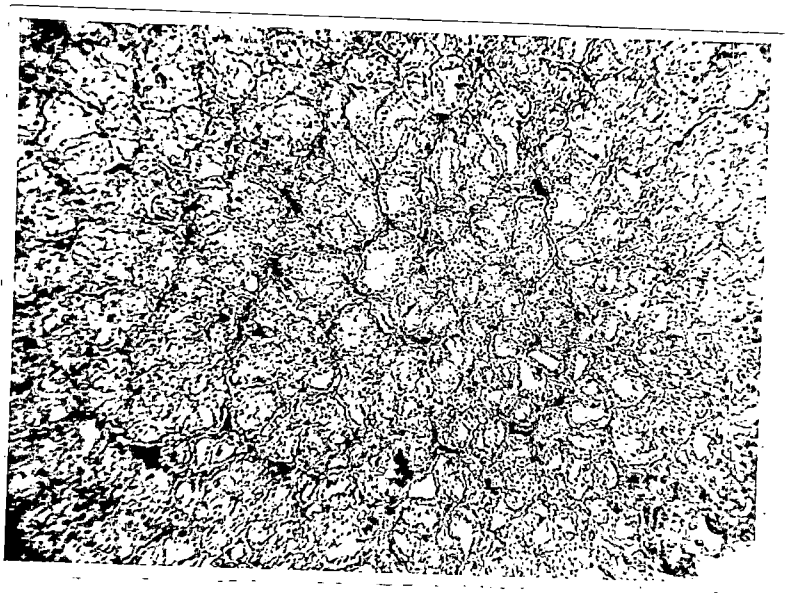
Fig. 3. Kid - Group IV - Kid standing in abducted position with swollen carpal joints.

Fig. 8. Thyroid - Enlarged thyroid glands of the kid in the Fourth Group. Glands from the kid in the control group are seen below.

Fig. 9. Thyroid - Control Group - Histology of the normal thyroid gland.

Fig. 10. Group I - Thyroid - Numerous small follicles are seen lined by tall columnar epithelial cells. Follicular lumen is small and is devoid of colloid. H & E x 100.





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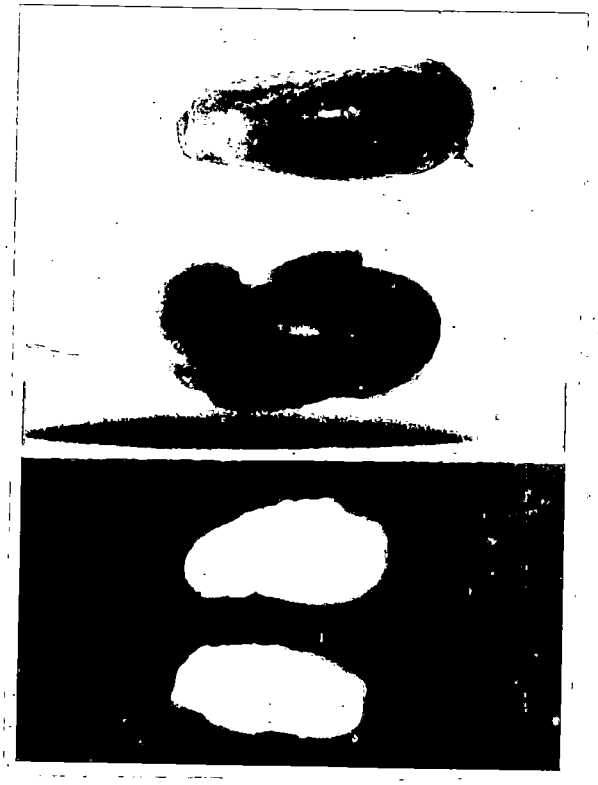
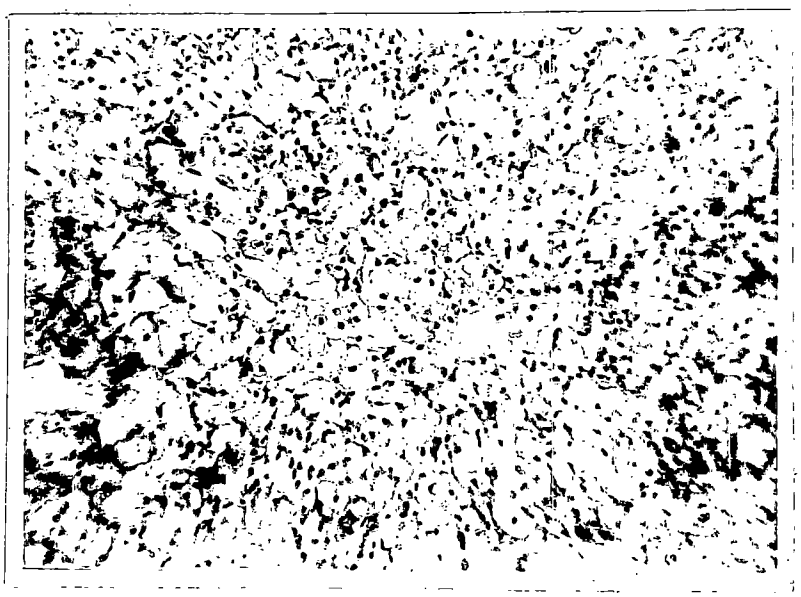


Fig. 11. Group I - Pituitary - Hypertrophy and hyperplasia of basophil cells. Vacuolar degeneration of hypertrophied basophil is evident. H & E x 200.

Fig. 12. Group I - Adrenal - Focal area of degeneration and necrosis in the zona fasiculata. The cells are devoid of fat. H & E x 100.



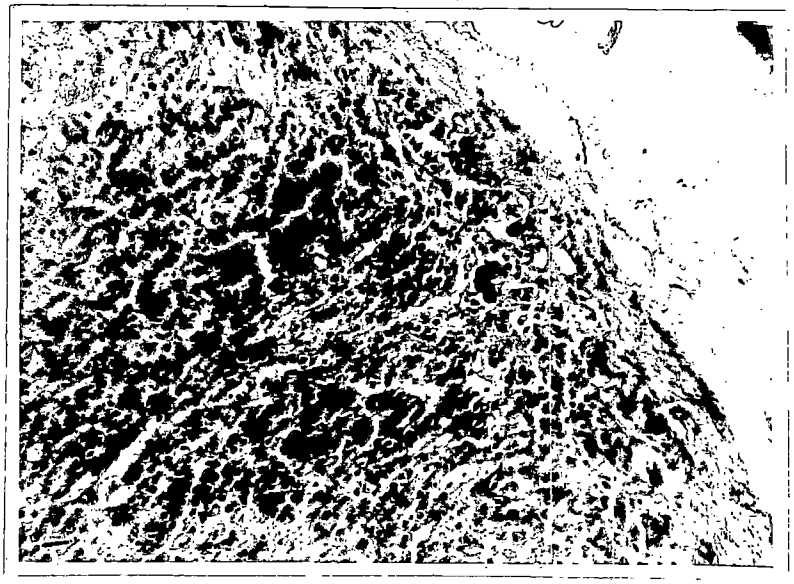


Fig. 13. Control Group - Testis - Normal histological features of testis. H & E x 100.

Fig. 14. Group I - Testis - Poorly developed seminiferous tubule and interstitial oedema. H & E x 100.

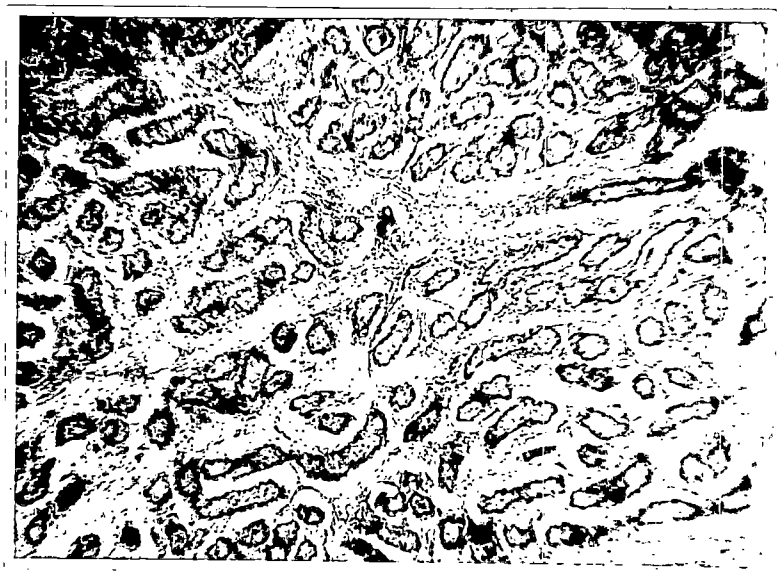
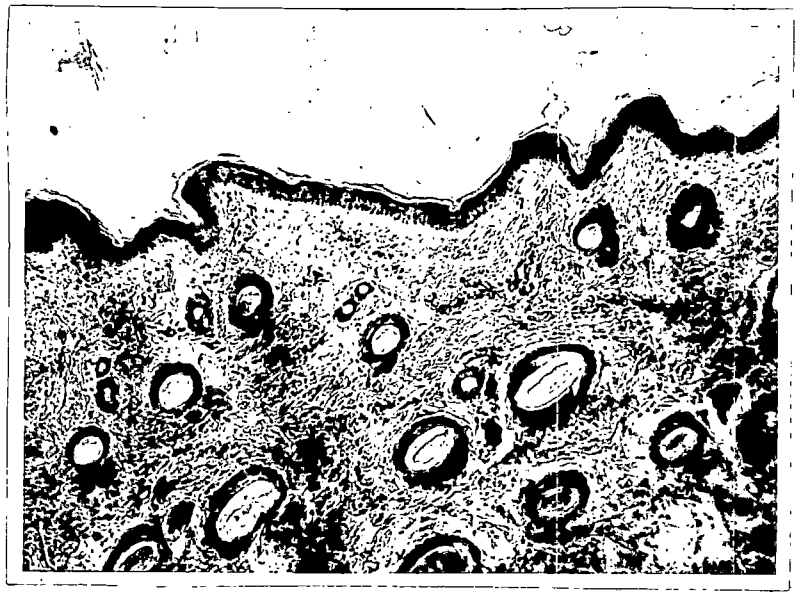


Fig. 15. Control Group - Skin - Normal histology of the skin. H & E x 100.

Fig. 16. Group I - Skin - Diffuse subcutaneous oedema and lymphoid infiltration. Moderate hyperkeratosis and collagenisation are also evident. H & E x 100.



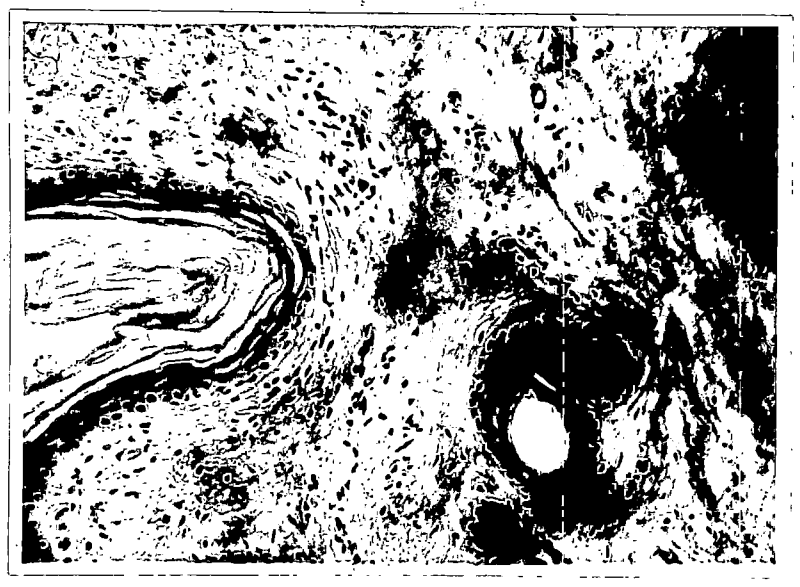
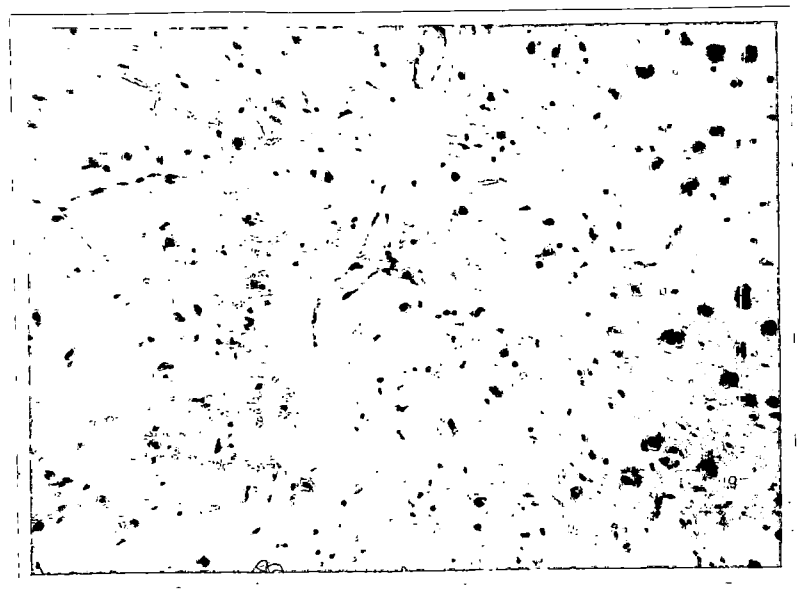


Fig. 17. Group I - Heart - Interstitial oedema and focal areas of hyalinisation. H & E x 200.

Fig. 18. Group I - Liver - Severe fatty change. H & E x 200.

Fig. 19. Group I - Brain - Cereberum - Perivascular and perineuronal oedema. Slight gliosis is also seen. H & E x 200.

Fig. 20. Group II - Thyroid - Showing numerous micro-follicles and epithelial hyperplasia. Follicles are devoid of colloid but contain granular degenerated material. H & E x 100.



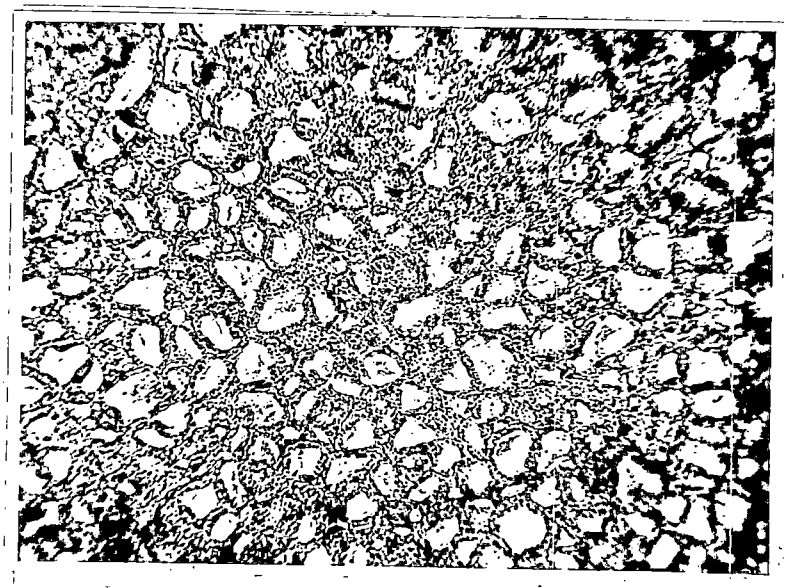
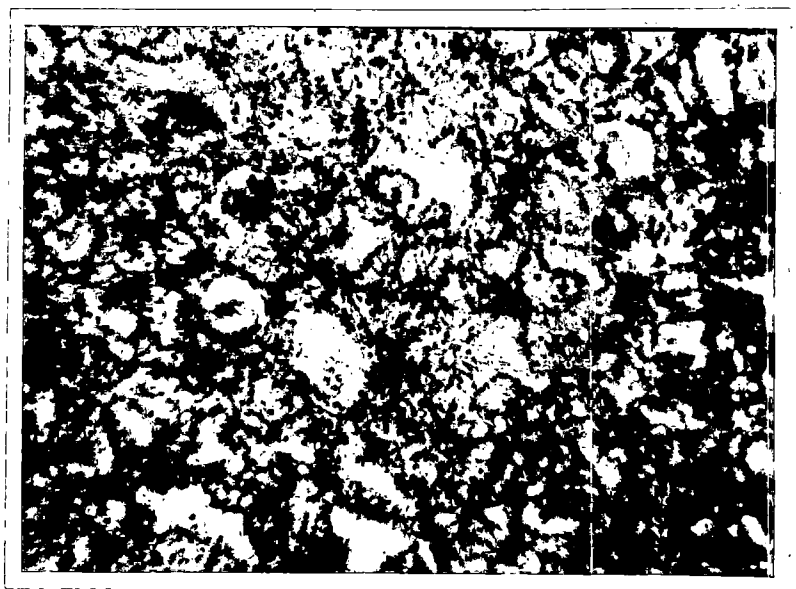


Fig. 21. Group II - Thyroid - Higher magnification. Showing colloid depleted follicles lined with prominent columnar epithelial cells. H & E x 200.

Fig. 22. Group II - Thyroid - Showing collapse of follicle and cystic space. Fragmented follicular reticulum are seen as spikes. Reticulin stain x 200.



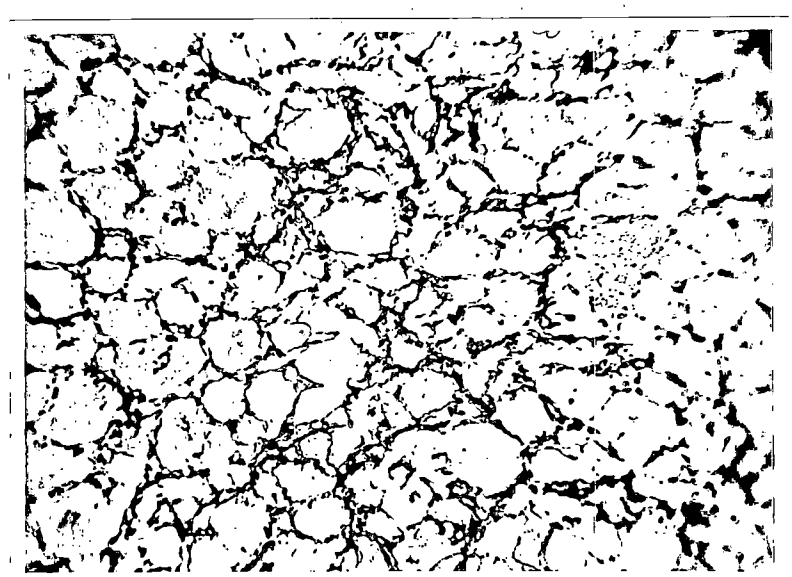
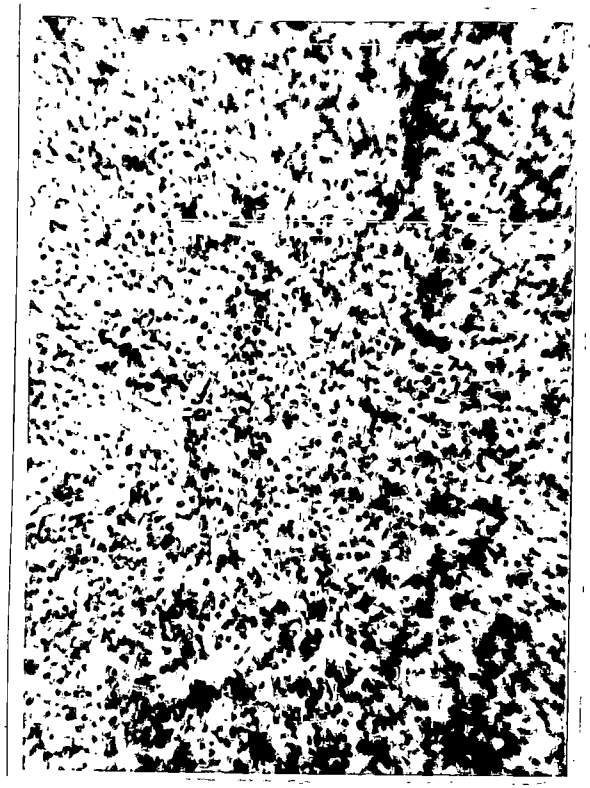


Fig. 23. Group II - Pituitary - Groups of dark staining hypertrophic basophils are evident. H & E x 200.

Fig. 24. Group II - Adrenal - Haemorrhage and depletion of fat in zona fasiculata. H & E x 100.



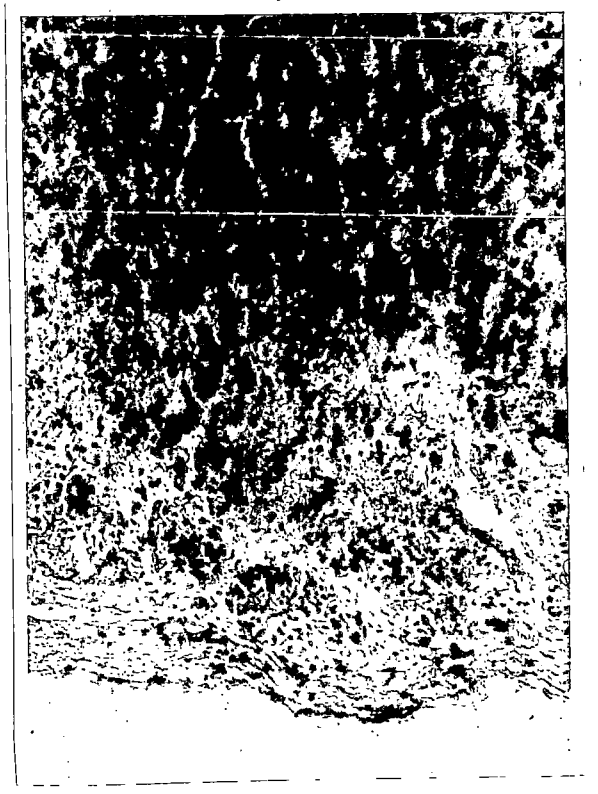
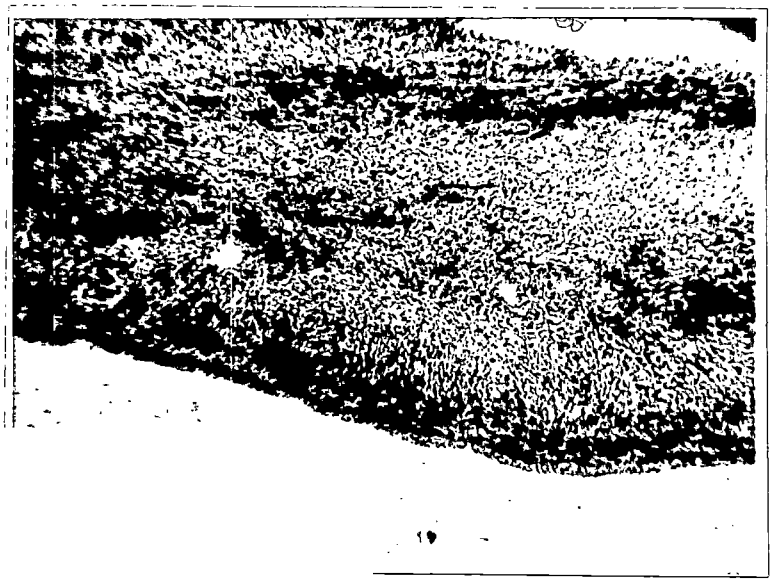


Fig. 25. Control Group - Ovary - Normal histological feature. H & E x 100.

Fig. 26. Group II - Ovary - Inactive ovary showing very few primordial follicles. Stromal oedema is also seen. H & E x 100.



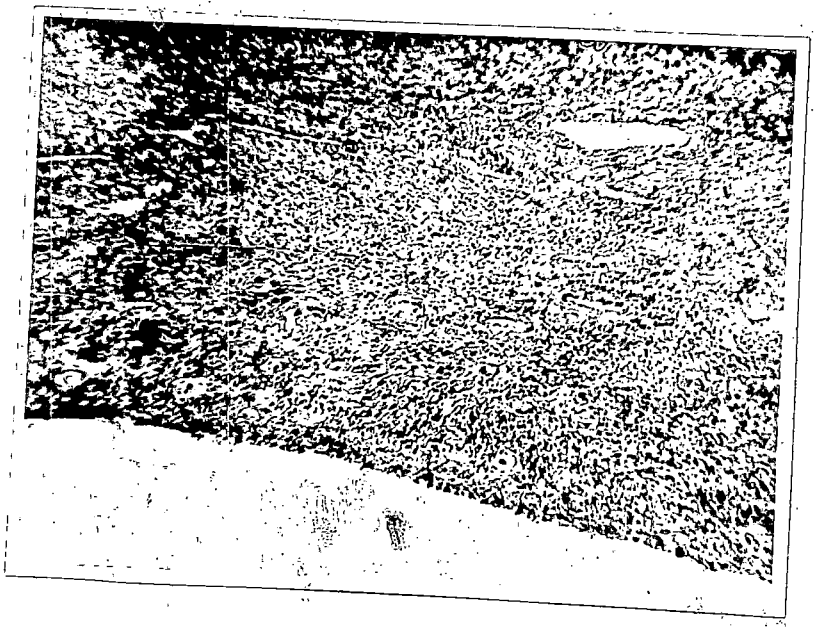


Fig. 27. Control Group - Uterus - Normal histological feature. H & E x 100.

Fig. 28. Group II - Uterus - Showing submucosal oedema and interstitial oedema. H & E x 100.

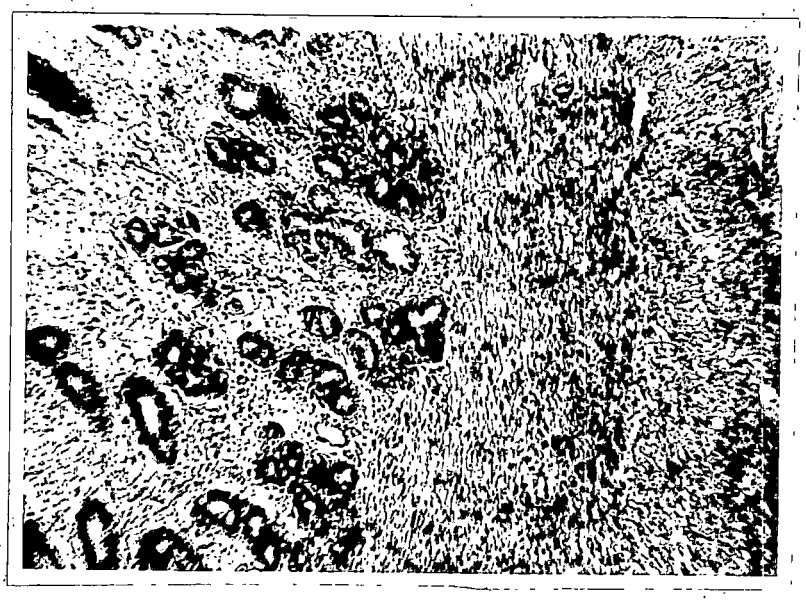
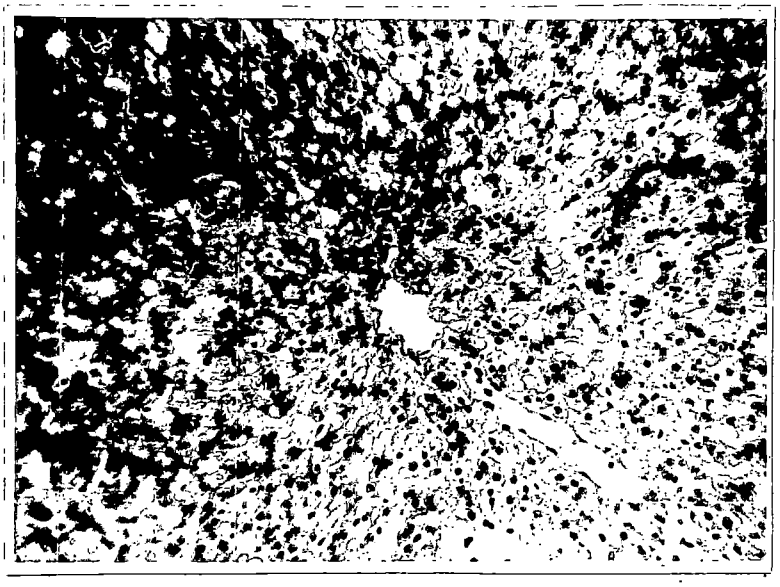


Fig. 29. Group II - Testis. Showing severe degenerative changes in the seminiferous tubules. There is complete aspermiogenesis. Spermatogonial cells are few. Interstitial oedema is moderate. H & E x 100.

Fig. 30. Group II - Liver - Fatty change. H & E x 200.



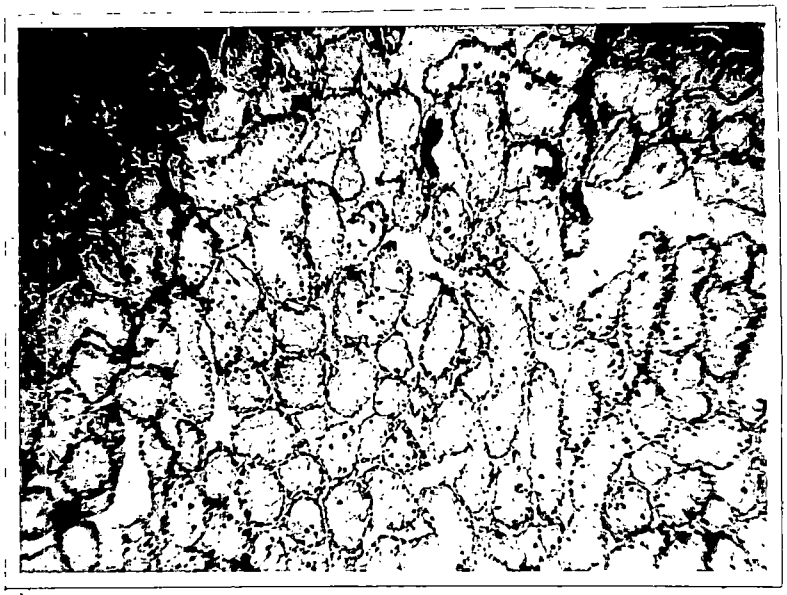


Fig. 31. Group II - Skin - Diffuse dermal oedema. The subcutaneous tissue is thickened due to oedema and deposition of AMP. Hyperkeratosis is also evident. H & E x 100.

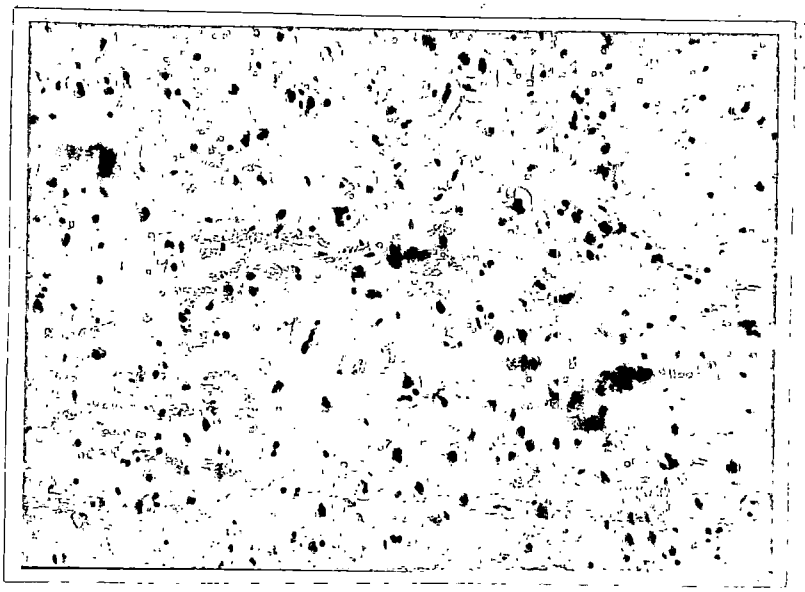
Fig. 32. Group II - Skin - Degenerated hair follicle filled with keratin. Dermis shows oedema and dense lymphoid infiltration. H & E x 200.

Fig. 33. Group II - Heart - Fatty change in cardiac muscle fibre. H & E x 200.

Fig. 34. Group II - Aorta - Deposition of lipid in subintimal layer and focal area of hyalinisation in tunica media. H & E x 100.

Fig. 35. Group II - Brain - Gliosis, perivascular and perineuronal oedema. H & E x 200.

Fig. 36. Group III - Thyroid - Follicles filled with degenerated and desquamated epithelial cells. None of them contain colloid. H & E x 200.



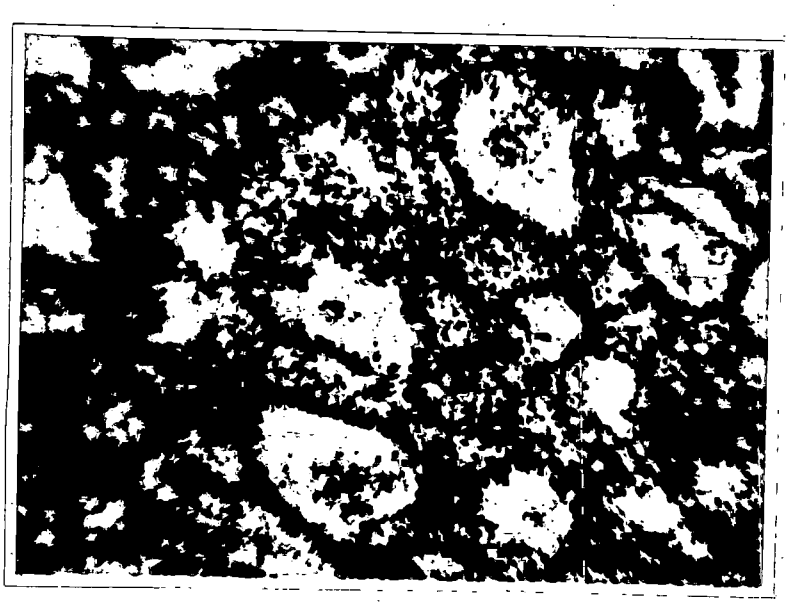


Fig. 37. Group III - Pituitary - Diffuse hyperplasia and vacuolation of cytoplasm of basophils. H & E x 200.

Fig. 38. Group III - Pituitary - Hyalinisation of acidophils. H & E x 800.

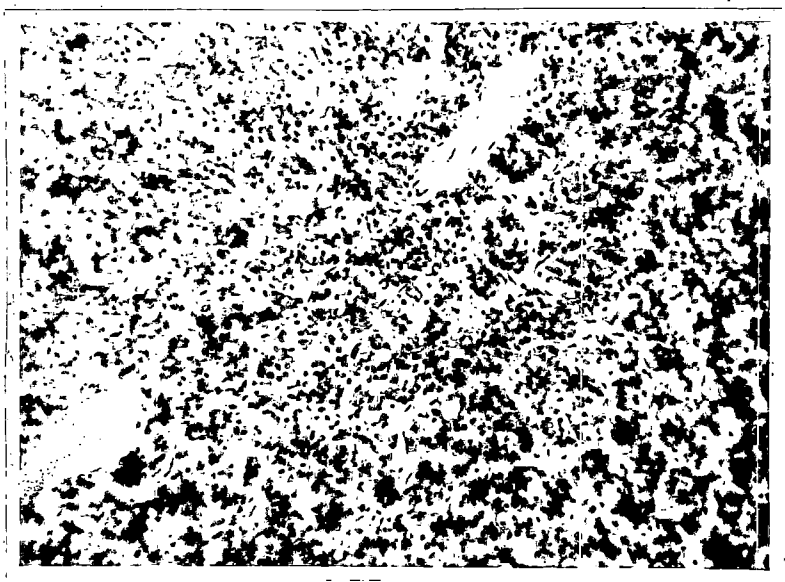


Fig. 39. Group III - Adrenal - Thickened capsule showing accessory cortical nodules. Cells in the zona fasiculata are devoid of fat. H & E x 100.

Fig. 40. Group III - Testis - Small sized seminiferous tubules showing no evidence of spermiogenesis. Lumen of the tubules contains granular material. H & E x 200.

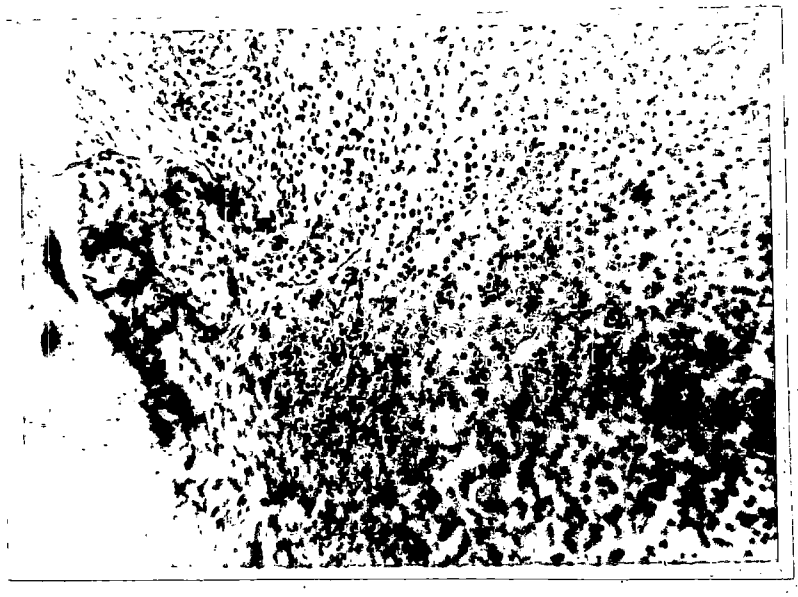


Fig. 41. Group III - Skin - Papillary folds in epidermis with hyperkeratosis and diffuse dermal oedema. Degeneration of hair follicles. H & E x 100.

Fig. 42. Group III - Liver - Fatty change, degeneration and necrosis of hepatic cells. H & E x 200.

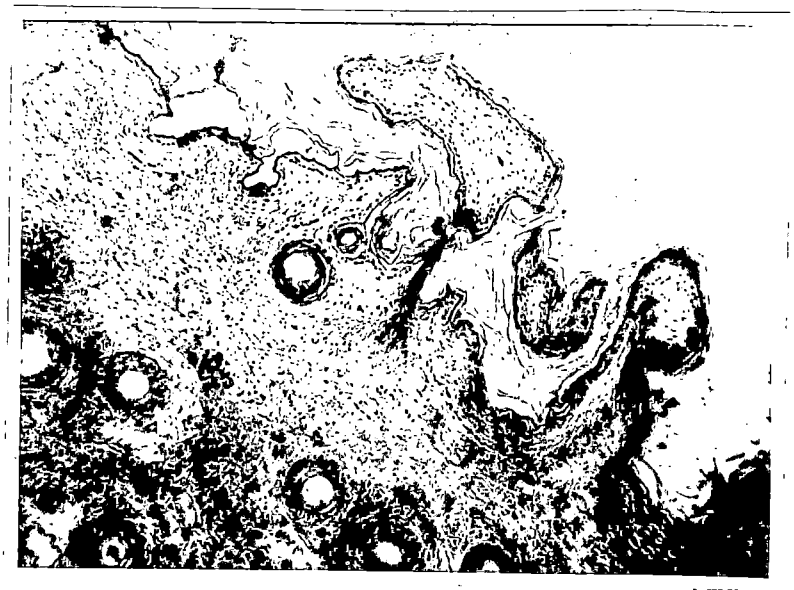


Fig. 43. Group III - Aorta - Focal areas of hyalinisation in the tunica media. H & E x 100.

Fig. 44. Group IV - Thyroid - Numerous small follicles are seen lined with more than one layer of epithelial cells. Follicles are devoid of colloid. H & E x 100.

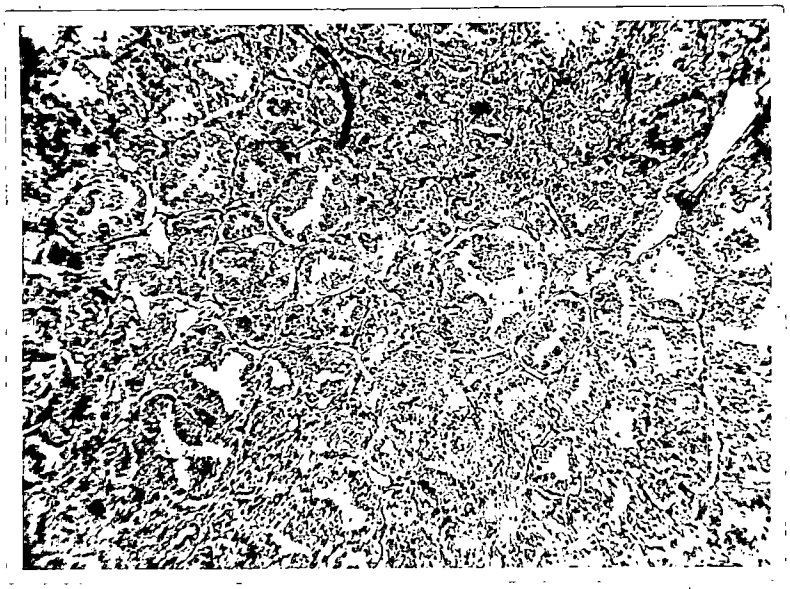


Fig. 45. Group IV - Thyroid - Showing hypertrophic and degenerated epithelial cells. Degenerated pink staining materials between follicular basement membrane and cellular layer is also evident. H & E x 400.

Fig. 46. Group IV - Pituitary - Severe degeneration and vacuolisation of the cytoplasm of the basophils. H & E x 200.

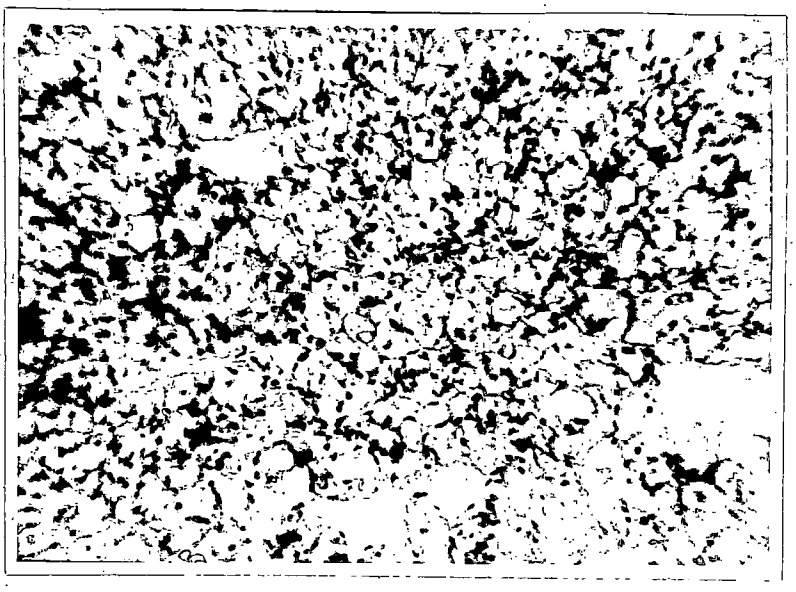
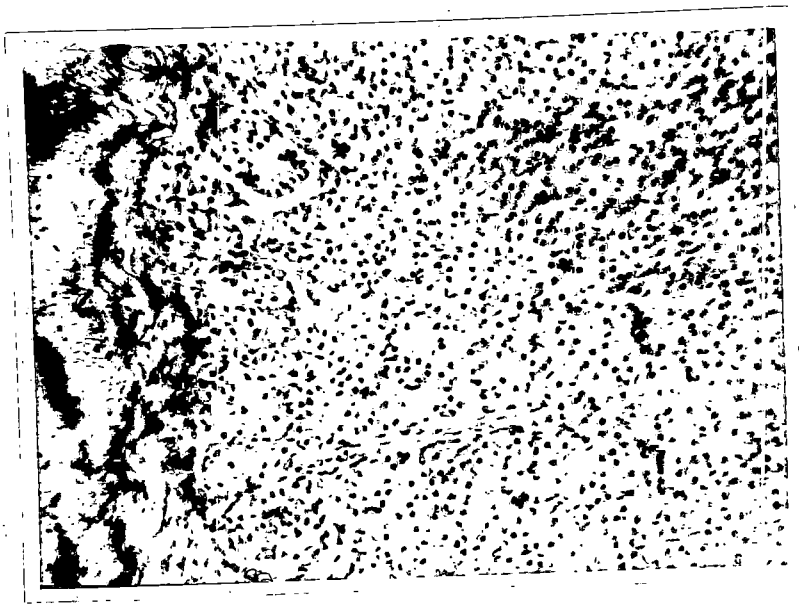


Fig. 47. Group IV - Adrenal - Depletion of fat in the zona fasiculata. H & E x 200.

Fig. 48. Group IV - Testis - Complete absence of spermiogenesis. Spermatogonial cells has completely degenerated. Only a few scattered cells are evident in the tubules. H & E x 100.



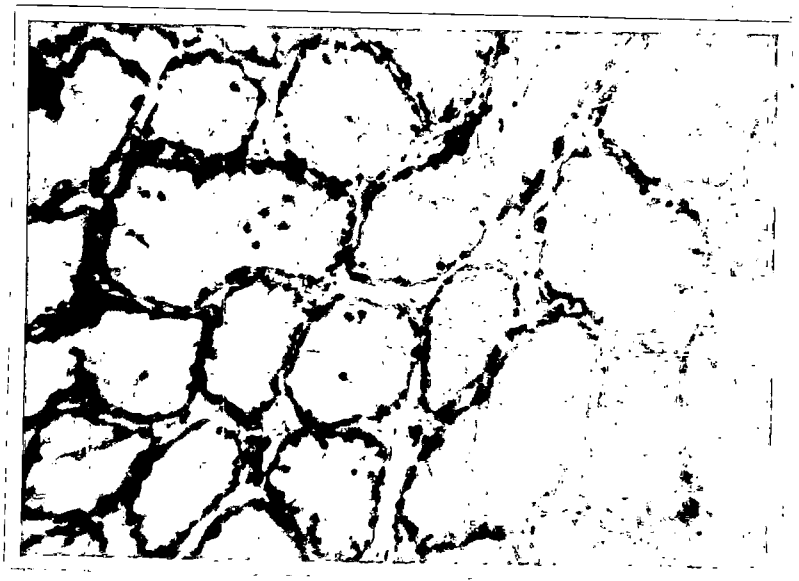


Fig. 49. Group IV - Skin - Acanthosis, hyperkeratosis, dyskeratosis are seen. Dermis shows oedema, collagenisation and cellular infiltration. H & E x 100.

Fig. 50. Group IV - Skin - Showing parakeratosis and acanthosis. Degenerated hair follicles are also seen. H & E x 200.

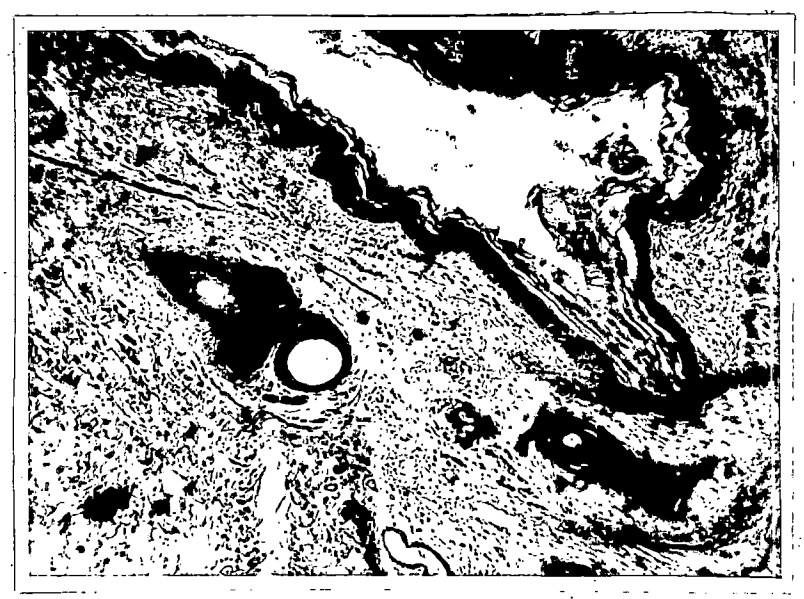
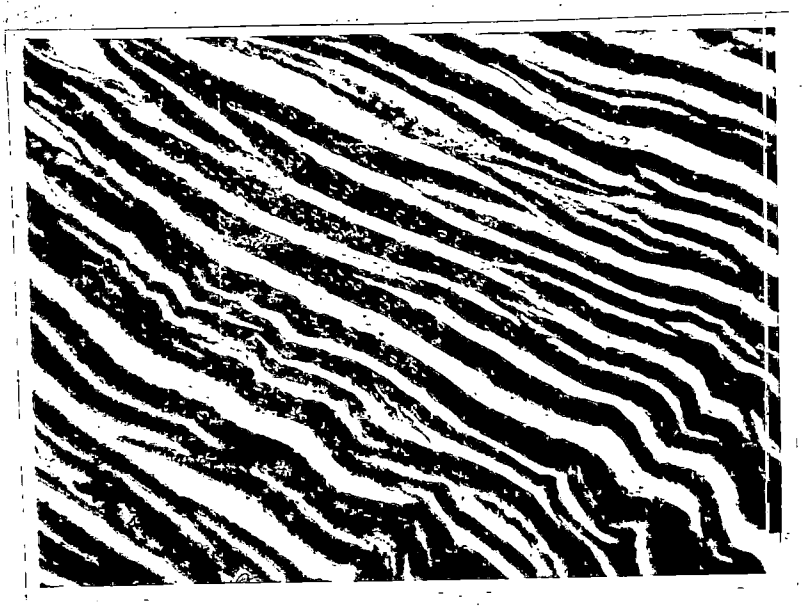


Fig. 51. Group IV - Heart - Myocardium showing interstitial oedema. H & E x 100.

Fig. 52. Group IV - Liver - Diffuse fatty change. H & E x 100.



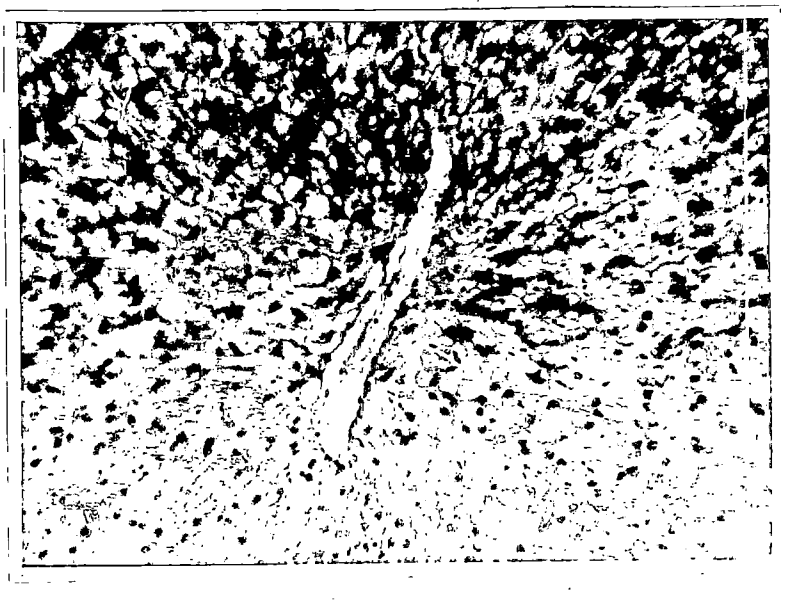
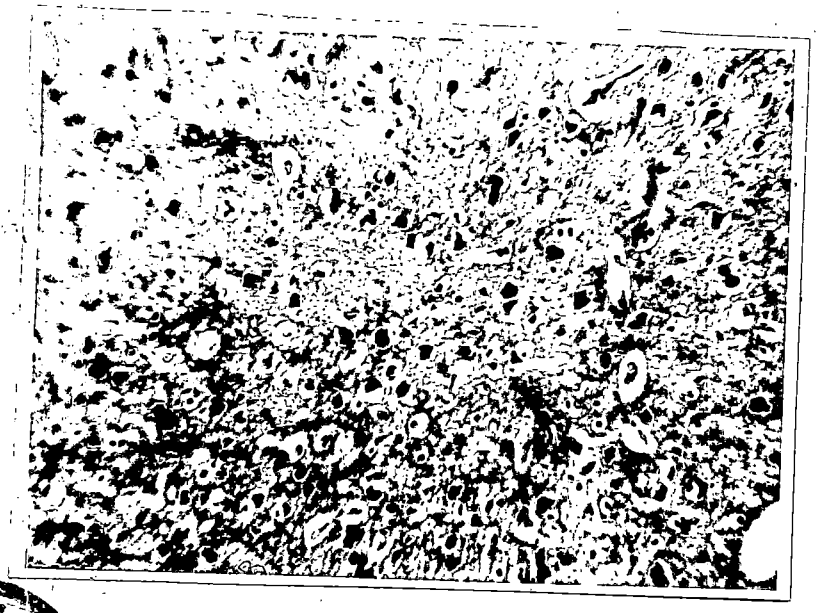


Fig. 53. Group IV - Aorta - Hyalinisation and fragmentation of elastic fibres in the tunica media. H & E x 200.

Fig. 54. Group IV - Brain - Perineuronal oedema and gliosis. Spongiosis is also evident. H & E x 200.



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APPENDIX

A P P E N D I X - I

Determination of total Serum Cholesterol

Total serum cholesterol level was estimated by the method of Zak (1957).

Principle.

A red colour is produced when an acetic acid solution of cholesterol is treated with ferric chloride and sulphuric acid. The colour produced is estimated colorimetrically.

Reagents.

(1) Stock ferric chloride solution:- 840 mg of ferric chloride was dissolved in glacial acetic acid, diluted to 100 ml with acetic acid and stored in a refrigerator.

(2) Ferric chloride precipitating reagent:- The stock ferric chloride solution was diluted 1 in 10 with glacial acetic acid.

(3) Ferric chloride blank:- 1.7 ml of the stock ferric chloride solution was diluted to 20 ml with glacial acetic acid.

(4) Cholesterol stock standard:- 100 mg of pure dry cholesterol was dissolved in 100 ml of glacial acetic acid and stored in the freezer.

(5) Working standard:- 2 ml of the cholesterol stock standard was mixed with 1.7 ml of stock ferric chloride solution and diluted to 20 ml with glacial acetic acid.

(6) Final standard:- This was always prepared just before use by mixing 2 ml of the working standard and 4 ml of the ferric chloride blank.

Procedure.

0.1 ml of the serum was added to 6 ml of the ferric chloride precipitating reagent, mixed and filtered through a dry Whatman No.42 filter paper and the filtrate collected in a dry test tube. 3 ml each of the filtrate, final standard and ferric chloride blank were taken in separate test tubes and 2 ml of concentrated sulphuric acid was added to each tube. Mixed by gentle shaking and allowed to cool. The readings were taken in a Klett-Summerson photoelectric colorimeter, using the blue filter and setting the instrument to zero with the blank.

Calculation.

$$\frac{\text{Reading of unknown}}{\text{Reading of standard}} \times \frac{0.1}{0.05} \times 100$$

= mg of total cholesterol in 100 ml serum, where 0.1 was the concentration of the standard and 0.05, the volume of serum used.

A P P E N D I X - II

Determination of Serum Protein-Bound Iodine (PBI)

The Protein-Bound Iodine (PBI) was estimated by the modified method of Barker et al.(1951).

Principle.

Serum proteins are precipitated with zinc hydroxide. The precipitate is washed and then ashed in a muffle furnace. The iodide is eluated from the ash with acid and determined spectrophotometrically by its catalytic effect on the rate of the reaction between the ceric ion and arsenious acid. Here the yellow ceric ion is converted to the colourless cerous ion.

Reagents.

(1) Water. Triple-distilled water.

(2) Zinc sulphate solution, 10% aqueous.

(3) Sodium hydroxide, 0.5 N solution.

Dissolve 20 g of sodium hydroxide in one liter of water.

(4) Sodium carbonate, 4 N solution.

Dissolve 212 g of anhydrous, reagent sodium carbonate and dilute to one liter.

(5) Hydrochloric acid, 2 N solution.

Add 200 ml of concentrated reagent hydrochloric acid to 500 to 600 ml of water, mix and dilute to one liter.

(6) Sulfuric acid, 7 N solution.

Add 196 ml concentrated reagent sulfuric acid to 500 to 600 ml of water, mix and dilute to one liter.

(7) Iodine stock solution.

Dissolve 130.8 mg reagent potassium iodide in water and dilute to one liter in volumetric flask. This solution contain 100 µg (gamma) of iodine per ml.

(8) Iodine intermediate solution.

Dilute 2 ml of stock solution to one liter in a volumetric flask. This solution contain 0.2 µg (gamma) of iodine per ml.

(9) Iodine working solution.

Prepare immediately before use.

a) Dilute 25 ml of the intermediate iodine solution to 100 ml in a volumetric flask. Mix and mark "0.05". This solution contains 0.05 µg (gamma) per ml.

b) Dilute 5 ml of the intermediate iodine solution to 100 ml in a volumetric flask. Mix and mark "0.01". This solution contains 0.01 µg (gamma) per ml.

(10) Ceric ammonium sulfate, 0.02 N solution.

Dissolve 12.65 g of ceric ammonium sulfate in 500 ml of water and 230 ml of 7 N sulfuric acid. When the solution is clear, dilute to one liter.

(11) Sodium arsenite, 0.1 N solution.

Dissolve 12.99 g of sodium arsenite in water and dilute to one liter.

(12) Reagent blank.

Prepare each day. Mix together 4 ml of 4 N sodium carbonate, 8 ml of water, 8 ml of 7 N sulfuric acid and 8 ml of 2 N hydrochloric acid.

Wave length 420 mu.

Procedure.

1) Precipitation and Washing of Plasma Proteins.

One ml serum is pipetted into each of two 15 x 125 mm Pyrex test tubes containing 7 ml water. One ml 10 percent zinc sulfate solution and 1 ml 0.5 N sodium hydroxide solution are added, and the contents mixed. The tubes are centrifuged at 2,500 rpm for 20 minutes. The supernatant is decanted and saved for the cross-contamination check. Three washings of the precipitate are carried out by the addition of 3 ml distilled water, resuspension, then addition of another 7 ml water, thorough mixing, centrifugation for 15 minutes at 2,500 rpm, and then decanting the supernatant after each washing.

2) Drying and Ashing of Precipitate.

One ml of 4 N sodium carbonate solution is added to the washed precipitate, which is then resuspended by thorough mixing. The tubes are placed in the oven, and the precipitate is thoroughly dried at 100°c for 12 to 18 hours, after which it is ashed in a muffle furnace at 625°c (± 25°) for 2½ hours and then allowed to cool.

3) Extracting iodide from the Ash.

Four ml of the mixed acid solution are added to each tube, the contents are mixed, and allowed to stand for 10 minutes. Three ml distilled water are added, the contents are mixed, and the tubes are centrifuged briefly to pack insoluble particles.

4) Determination of iodide.

A 3 ml aliquot of the supernatant iodide solution and 5 ml distilled water are added to each colorimeter cuvette. An 8 ml water blank, and three 5 ml iodine standards (0.01, 0.05 and 0.1 ug of iodine per ml) are set up in duplicate. The iodine standards are made upto volume of 8 ml by addition of 3 ml reagent blank solution. To each cuvette (water blank, standards and test sample) add 0.5 ml of 0.1 N sodium arsenite solution and mix. The cuvettes are placed in a water bath at 39°c (± 1°) for 10 minutes. One ml of similarly warmed ceric ammonium sulfate solution is added by using an Ostwald-Folin blow-out pipet to each cuvette in the water bath, at timed 30 second intervals. Beginning 20 minutes after the addition of the ceric ammonium sulfate solution, the absorbance is measured at timed intervals of 30 seconds.

5) Calculations.

The absorbance of the blank and of the standard iodine samples is plotted on semilog paper. Concentrations of iodine in the unknown are read from the graph and multiplied by 7/3, the correction factor for dilution.

PBI in µg/100 ml = 7/3 x 100 x µg Iodine per sample.

PATHOLOGY OF EXPERIMENTAL HYPOTHYROIDISM IN GOATS

BY
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ABSTRACT OF A THESIS
submitted in partial fulfilment of
the requirement for the degree

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Mannuthy - Trichur
1976

ABSTRACT

An experimental model of hypothyroid state was induced in kids, using different dose regimes of thiourea with the objective of studying sequence of clinico-pathological changes in different levels of hypothyroidism and its influence on the animal health and growth.

Twelve cross-bred clinically healthy kids of the age group between 3-4 months were employed for the study. The animals were randomly divided into a control group of four animals and experimental group of eight animals. Experimental hypothyroidism was induced by feeding thiourea at the dose levels of 100 g, 150 g, 200 g and 250 g per kg body weight. Haemogram, body weight, plasma proteins, serum cholesterol and PBI values were estimated at periodic intervals. The kids were subjected to detailed autopsy after death/sacrifice. Gross lesions were recorded and detailed histopathological examination of tissues was carried out employing special stains wherever necessary.

During the course of observation for a period of three months all the kids dosed with thiourea died at varying intervals except the kids in the lowest dosage group. There was stunting of growth and appreciable reduction in weight of the animals. Weakness, lethargy, depression, reduction in feed intake, subcutaneous oedema of varying degree were the important clinical features observed.

There was significant increase in blood cholesterol values and plasma protein levels in thiourea dosed kids. A significant reduction in serum PBI was also recorded. There was significant increase in the relative weight of thyroid, adrenal and pituitary glands of animals in the experimental group. Gelatinisation of subcutaneous fat and hypertrophy and dilatation of the left ventricle were common findings at autopsy. Histologically the thyroid glands exhibited varying degree of hyperplastic changes and depletion of colloid in the follicles. Hyperplasia and hypertrophy of lining epithelium was also observed. Predominant histological change in the pituitary was hyperplasia and hypertrophy of basophil cells and degenerative changes in the acidophils. Hepatic lipidosis was a common observation. Histological lesions in the skin were similar to that reported in human myxoedema. Adrenal glands showed hypertrophy, depletion of fat and focal areas of haemorrhage in the zona fasciculata. In all the hypothyroid kids, varying degrees of degenerative changes were observed in the gonads indicating that in hypothyroidism fertility will be seriously affected.