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A NUTRITIONAL EVALUATION OF IODINE IN THE DIET OF SOWS (*SUS DOMESTICUS*)

By

Jeffrey Paul Erickson

A DISSERTATION

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ABSTRACT

A NUTRITIONAL EVALUATION OF IODINE IN THE DIET OF SOWS (*SUS DOMESTICUS*)

By

Jeffrey Paul Erickson

Twenty-eight crossbred and purebred sows and gilts were allotted to four groups with attempts to equalize groups for the effects of parity, breed and body weight. Each group was then randomly assigned to receive a basal corn-soybean meal diet adequately fortified with all required vitamins and minerals with the exception of iodine (I) and supplemented with one of the following four levels of I supplied as pentacalcium orthoperiodate: 0, .2, 2 and 20 ppm. These levels were judged to be 0, 1, 10 and 100 times the sows's dietary I requirement. Sows were started on their respective diets after breeding and continued through gestation, lactation and postlactation rebreeding and were slaughtered 30 days after rebreeding. Total and live pigs born per litter, pigs weaned per litter, pig birth weights (g) and 21-day pig weights (g) from sows receiving 0, .2, 2 and 20 ppm of I diets, respectively, were: 11.6, 11.4, 9.9, 1,221 and 4,585; 7.3, 7.2, 6.8, 1,348 and 6,631; 9.4, 9.4, 9.0, 1,418 and 5,814; 5.4, 4.3, 3.8, 1,196 and 6,373. Sows receiving the .2 ppm

of I diet tended to gain the most weight during gestation. There was no significant difference in sow lactation weight change due to dietary I level. Hemoglobin level of sows on the 20 ppm I diet was depressed at the end of lactation. Colostrum I and Cu increased with increasing levels of iodine, while Zn, Mg and Fe peaked at the 2 ppm iodine level. Two-week milk Ca, Mg and Fe values were highest from sows in the 20 ppm iodine group; Cu was highest from 0 ppm iodine group. Weaning milk samples from sows in the 20 ppm iodine group contained more Cu, Zn and Fe. Baby pig, 24-hour, and weaning hemoglobin values decreased with increasing levels of iodine. Baby pig, 24-hour, serum Ca remained constant across treatments; Mg, Fe and Zn increased with increasing dietary iodine. Two-week serum Ca and Mg were lowest in the 0 ppm iodine group. Serum P, Fe and Zn values were similar across treatments; high dietary iodine depressed serum Cu levels. At weaning, serum P, Mg and Cu were similar across treatments; Mg and Zn values were lowest from pigs in the 20 ppm iodine group and serum Ca was lowest from the 0 ppm iodine group. One pig from each litter was killed at birth and another at four weeks of age and organs weighed and prepared for histopathological observations. Relative organ weights were similar across treatments. However, thyroid weights were elevated in sows receiving the lowest and highest iodine levels and in their newborn pigs. Organs examined grossly and histopathologically were described as normal. However, larger thyroid

follicle cells were found in sows and offspring in the 0 and 20 ppm iodine groups.

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A Nutritional Evaluation of Iodine in the Diet of Sows (*Sus domesticus*)

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TO MOM AND DAD,

AND ESPECIALLY ANNIE

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INTRODUCTION

Earliest indirect references to iodine deficiency in humans and animals were documented by the Chinese circa 1600 B.C. However, it was not until 1819 that physician Coindet concluded that the response to treatment for goiter (enlargement of the neck) with burnt sponges was due to its iodine content. Since then, his remedy of iodine salts for preventing iodine deficiency goiter has been used successfully. The natural occurrences of iodine were investigated by the French botanist Chatin 26 years later. In 1876, he described the incidences of goiter with areas deficient in environmental iodine. In 1957, Gilbert with more geographically precise information depicted the goitrous regions of the world.

The scientific discovery of the thyroid's role in body metabolism and its direct relationship with performance and carcass merit initiated massive research efforts during the 1940's and 1950's. Investigations to manipulate the thyroid's activity began in Germany. However, most research endeavors in this field must be attributed to Dr. E. P. Reineke at Michigan State College. Currently, trends in consumer purchasing of retail cuts

of beef, pork and poultry have curtailed the use of feed additives that affect the actions of the thyroid gland.

The incorporation of iodinated compounds into diets of lactating dairy cows in order to enhance milk production was also evaluated. After numerous research investigations, it was generally recognized that iodinated compounds were not the solution to increased milk production.

Iodine toxicity has been induced in several species by feeding very high concentrations of iodine (Highman, Webster and Rice, 1955; Correa and Welsh, 1960; Ammerman et al., 1964; Taylor et al., 1964; Arrington et al., 1965). Even though there exist species variations in dose response, only in dairy cows have iodine toxicity signs been reported in practical livestock production (McCauley, Johnson and Alhadji, 1972; Wallace, 1975).

Documentation of endemic goiter in livestock in the U.S. as a result of the lack of dietary iodine was reported by Hart and Steenbock (1918), Kalkus (1920) and Welch (1928). Later Andrews et al. (1948) found that the offspring of sows which had not received a supplementary source of iodine displayed hyperplasia of the follicular epithelium of the thyroid gland. In the growing pig, Sihombing et al. (1974) reported iodine deficiency signs similar to those found by researchers during the 1920's, when diets were not supplemented with iodine. Andrews et al. (1948) suggested the iodine requirement to be .35 ppm. Underwood (1966) estimated it to be .05 to .10 ppm.

The experiment presented in this dissertation was conducted to determine the effect of dietary iodine levels of 0, 1, 10 and 100 times the suggested requirement of gilts and sows and their progeny on the following parameters:

1. reproduction performance
2. growth performance of progeny
3. colostrum and milk mineral composition
4. serum mineral composition
5. gross and histopathological observations
6. serum thyroxine concentrations
7. total tissue iodine concentrations of sows

REVIEW OF LITERATURE

A. Iodine, Its Occurrence

1. Iodine Geochemistry. The element iodine exists in a biocycle as a result of its physical states, solid and gaseous. After originating from igneous rocks of the earth's crust and molten rock below the crust, years of weathering release iodine into the soil. It then washes into the streams and rivers and concentrates in the oceans. Iodine is sublimated from the ocean, attaches to dust particles, and is redeposited on the land by precipitation (Goldschmidt, 1954; Rankama and Sahama, 1955). Even though this cycle has been continuing for tens of thousands of years, there exist vast land masses deficient in iodine, as evidenced by goiter in both humans and livestock (Stott, 1933; Walker, 1933; Gilbert, 1957; Blokhina, 1969; Ewy et al., 1972; Anonymous, 1975). Beeson (1958) hypothesized this to be associated with geographical location of certain land masses and oceans. Quantifying his hypothesis, he estimated that iodine is redeposited on the Atlantic Coastal Plain and the Great Lakes Region at rates of 22 to 50 and 0.7 mg/acre/year, respectively. England, which is encircled by ocean, is estimated to accumulate iodine at the rate of 3.0 g/acre/year from precipitation plus 25.6

mg/acre/year from sea spray (Chilean Iodine Educational Bureau, 1956). This substantiates the hypothesis of depletion and selective repletion of iodine.

Bleyer, Schwaibold and Harder (1933), Goldschmidt (1954), and Kubota and Allaway (1972) concluded that the iodine deficient areas are a result of the Pleistocene glaciation. After collecting underground water samples, Bleyer et al. (1933) found that the glacial movements forming tertiary, brown and black Jurassic, Rhaetian and shell limestone yield water containing less iodine than waters from non-glaciated Jurassic red marl and sandstone. Thus, older soils had considerably more time to accumulate iodine than young glaciated areas. Convincing data were obtained when limestone and sandstone were compared; the younger limestone contained 1.179 ppm iodine while the sandstone contained 1.743 ppm iodine (Chilean Iodine Educational Bureau, 1956). Therefore, a combination of glaciation and the distance of land areas from oceans may be responsible for regions of endemic goiter.

A third factor that may contribute to the endemic goiter is plants. The relationship between plants and the geochemistry of iodine was investigated by Shacklette and Cuthbert (1967). They found that the iodine content of vegetables and native plants grown at the same location on glaciated and driftless soils was 6.5 and 6.8 ppm for vegetables and 5.2 and 4.5 ppm for native plants, respectively. These data were suggested to be confounded, because the authors indicated that soils may have been of the same

ages. These same authors conducted another study with ferns, trees and vegetables grown on soil originating from either carbonate (young) or siliceous (old) rocks. The soils contained 4.4 and 4.7 ppm of iodine, respectively. These findings indicate that parent rocks forming soils may have less influence on iodine content in soils than previously thouqht. Therefore, plants in some way accumulate atmospheric iodine. If this is true, the iodine variation in the soils is due to the humification of such plants. Other possible factors associated with improving soil iodine content are the absorption of iodine by clay colloids and cultivation of soils. On the other hand, depletion of soil iodine has occurred when crops are removed, preventing humification. If excessive alkalinity persists resulting in breakdown of humus, excessive levels of iron and manganese in soils may act as catalysts releasing iodine (Newton and Toth, 1951; Chilean Iodine Educational Bureau, 1956; Shacklette and Cuthbert, 1967; Whitehead, 1975). Therefore, the biocycle of iodine should also include plants, particularly those located close to oceans, since they concentrate higher levels of iodine than those in land.

2. Iodine in Plants. In order to verify the influence of plants on iodine geochemistry, Shacklette and Cuthbert (1967) studied two plants, an air plant (*Tillandsia usneides*) and a tuber. The former, a class of Spanish air moss, has no roots and supports itself by intricate branching

on telephone wires, dead or living trees. It was concluded that all of its nutritive properties, including iodine, were from the atmosphere. By establishing the iodine content in potatoes and soil in which they are grown, these authors theoretically determined that atmospheric iodine was the primary source of iodine available to the plant and concluded that iodine's entrance was through the leaves. Hence, iodine accumulation by plants from both the atmosphere and soils (Goldschmidt, 1954) would increase iodine content in soils through humification.

The iodine content in plants is dependent upon geographical location and evolution. Marine plants, brown and red algae, contain the highest concentration of iodine of all plants with 2488.8 and 382.5 ppm, respectively (Shacklette and Cuthbert, 1967). Their environment, the ocean, contains the highest concentrations of iodine, and this appears to be reflected in their iodine content. Apparently, these algae have morphologically and physiologically adapted to their environment. Flowering plants found in the oceans have been found to contain 52.5 ppm of iodine. Even though they survive in the same vicinity as the algae, their lower concentration of iodine has been attributed to the later evolutionary development. Both algae are said to have evolved since the Paleozoic Period, much earlier than the Mesozoic era of the Cretaceous Period when the marine flowering plants evolved (Shacklette and Cuthbert, 1967). Newton and Toth (1951) and Shacklette and

Cuthbert (1967) analyzed terrestrial plants for their iodine concentration. In comparing the content of iodine in terrestrial and marine flowering plants, 2.7 to 6.9 versus 52.5 ppm, these differences would support this theory of relative age and location.

3. Fertilization Effects on Plant Iodine Accumulation. McHargue et al. (1935) found that iodine application to soil would improve plant iodine content. Newton and Toth (1952) increased the iodine content in buckwheat through iodine fertilization practices. Whitehead (1975) concluded that the source of iodine and its retention in plants varies with soil types. Elemental iodine, iodate or iodide were added at 20 mg/kg of sandy loam soil, in which perennial ryegrass was planted. Elemental iodine was taken up and retained more readily. On the other hand, when either organic matter or chalk (lime) was added to sandy loam treated with a source of iodine, iodine accumulation and retention were depressed. The lime and/or elemental iodine treatments yielded the greatest iodine concentration in the ryegrasses. In this study, iodine fertilization did not improve yield of the herbage. Ranne (1974) in Russia reported humus rich soils which were abundantly fertilized with nitrogen improved the iodine content in the grasses. On the other hand, heavy application of nitrogen, phosphorus and potassium on pastures grown on soil considered high in mineral content did not significantly improve pasture iodine content. Orchard-grass pastures fertilized with

nitrogen ranged from 0.1 to 0.7 ppm iodine (Horn, Reid and Jung, 1974). They concluded that the seasonal variation irrespective of fertilization was the reason for the variability. Alderman and Jones (1967) conducted a similar study on grasses grown on the West Coast of Wales. Fertilizing pastures with 181.4 kg of sulfate of ammonia/acre reduced the average iodine content from .41 to .27 ppm, again related to variety and season of the year. Contrary to these results, application of Chilean nitrate of soda as a source of nitrogen fertilizer improved the iodine content of pastures and crops. This was associated with the large quantity of iodine present in this fertilizer (Chilean Iodine Educational Board, 1952). Since there is such diversity in environments and plant varieties, and their interactions, application of fertilizers cannot be relied upon to minimize endemic goiter. Transportation of Chilean fertilizer would also be uneconomical.

4. Sources of Dietary Iodine. Chatin's early studies (1853) indicated that the iodine content in drinking water varied, as influenced by soil and rock composition. Later work by Bleyer et al. (1933) and Walker (1933) confirmed Chatin's early work, by showing that variations in the iodine content in water were contiguous with its geological strata. Underwood's (1977) most recent review of iodine in water compared iodine concentrations in various regions of the world. In summary, goiter is prevalent in areas where the water is low in iodine and not found in areas

where the water contains high concentrations of iodine. However, von Fellenberg (1926) showed that the daily intake of iodine from drinking water was less than 10 percent of the total iodine intake in both iodine deficient and non-deficient regions. Therefore, water is insignificant as a source of iodine to meet the nutrient requirement. Stott (1933) indicated that the additive effect of excess calcium in drinking water, derived from limestone areas, produced the endemic goiter of the United Provinces. Taylor (1954) and Sampson and Putzki (1952) reported later that high doses of calcium can increase the iodine requirement.

The content of iodine varies among foods, which is associated with their areas of production. The edible portions of ocean fish and shellfish were found to contain 300 to 3000 ppb iodine, whereas fresh water fish contained approximately 20 to 40 ppb of iodine on a fresh basis (Chilean Iodine Educational Bureau, 1952). Dicotyledonous and monocotyledonous garden vegetables contained 6.9 and 6.3 ppm iodine (on a dry basis), respectively (Shacklette and Cuthbert, 1967). Vought and London (1964) analyzed meat, eggs, dairy products, vegetables, breads and cereals, and fruits and found their iodine content to be 260, 260, 130, 320, 100 and 40 ppb on a wet basis, respectively. These are mean values from products that are produced under normal conditions. Under certain circumstances these values will differ, as discussed in earlier sections.

The sources of nutrients used in formulating diets for livestock and fowl fluctuate in their iodine contents.

Hemken et al. (1971) analyzed hays from Illinois and Maryland. Midwestern hays contained less iodine than those from the Atlantic coast, .62 to 1.02 and 1.31 to 2.54 ppm iodine, respectively. Grass pastures in Wales ranged from .200 to .310 ppm iodine (Alderman and Jones, 1967). Researchers associated with the Chilean Iodine Educational Bureau (1952) reported that processed feed ingredients, oil seed meals, cereal grains, and milling by-products contain less iodine than roughage products. It appears that processing of feedstuffs reduces the iodine content. Hamilton and Miniski (1973) found that refined white sugar contained 1 ppb of iodine and Barbados brown sugar analyzed 30 ppb iodine. Even though animal by-products, which contain relatively high concentration of iodine, are used in diets of livestock and fowl, they should not be relied upon as the sole source of iodine because of limited quantities used in ration formulation.

In commercial feeds, iodine supplementation for livestock has become a common practice due to the low iodine content of farm feeds. Methods of iodine supplementation include the incorporation of iodine into mineral mixes, concentrates and salt. Iodine is commonly supplemented in the form of potassium iodide, calcium iodate, sodium iodate, cuprous iodide, diiododithymol, 3,5-diiodosalicylic acid, pentacalcium orthoperiodate (PCOP) or ethylenediamine dihydriodide (EDDI). The different forms of iodine do not have the same physical stability or nutritional value. Shuman and Townsend (1963) showed that potassium iodide and calcium

iodate volatilized from the surface of salt blocks, when placed out of doors, whereas diiodosalicylic acid was only 20% available and did not prevent iodine deficiency in the offspring of cattle and sheep.

In a later study of Aschbacher (1968), potassium iodate and diiodosalicylic acid containing .007% iodine were fed separately in combination with salt *ad libitum* to ewes. Iodine deficiency was found only in newborn lambs whose dams consumed diiodosalicylic acid. When Sprague-Dawley rats were fed 265 µg of iodine from diiodosalicylic acid/kg of diet, iodine deficiency signs were not present (Mittler and Benham, 1954). Aschbacher and Feil (1968) found that cows had less ability to remove iodine atoms from diiodosalicylic acid. Mittler and Benham (1954) also compared cuprous iodide and diiododithymol to potassium iodide. Supplying 265 µg of iodine/kg of diet, each source provided sufficient amounts of iodine to the thyroids. However, only cuprous iodide competed well with potassium iodide in availability. Miller et al. (1968) evaluated three other sources of iodine, calcium iodate, sodium iodide and pentacalcium orthoperiodate, as sources of iodine for the pregnant dairy cow and her fetus. Their findings indicated that all sources protect against iodine deficiency.

B. Historical Overview of Iodine and the Thyroid Gland

Early Chinese documents from 1600 B.C. disclosed a disorder consisting of an enlarged neck, now termed goiter. First treatments for the swelling were conducted by the

Greeks with oral administrations of burnt kelp or sponges and sheep thyroid glands. Coindet, a French physician, established in 1819 that alleviation of the swelling was due to the iodine content in the sponges. In 1656, Wharton named the gland, thyroid, derived from the Greek term, *tiros*, because of its anatomical shield-like appearance. He proposed its functions to be: warming the cartilage of the trachea; rendering a smoother voice by lubricating the larynx; adding beauty to the female neck; and taking certain superfluous fluids emanating from the recurrent nerve. Throughout the 19th century the relationship of various physical disorders and the thyroid began to evolve. Flajani (1802), Parry (18185), von Basedow (1840) and Graves (1842) concluded that sweating, tremor, tachycardia and exophthalmos and goiter were a result of an overactive thyroid. In 1874, Gull associated reduced activity or hypothyroidism to extensive deposits of mucin under the skin, myxedema, linking it to cretinism, a disease characterized by dwarfism and mental retardation in young children. A prominent area of enlarged necks was observed in Switzerland. Independently, physicians Kocher and the Reverdins in 1883 performed successful thyroidectomies. However, several months postoperatively myxedema became evident. The utilization of extracts of sheep thyroid gland alleviated these symptoms, concluding that the thyroid secreted a material that would normally protect against signs of insufficiency. Between 1850 and 1876, the French botanist Chatin determined the natural occurrence of iodine in the

air, water, soil and foods from various localities. Chatin associated the incidence of goiter with areas deficient in environmental iodine. The establishment of iodine action and its relationship to body function began in 1895 by Bauman. He established that iodine was normally concentrated in the thyroid and found that the thyroid iodine concentration was reduced in endemic goiter. By 1899, Oswald found that thyroglobin was the principal storage form of iodine in the thyroid gland. Kendall (1914) isolated a hormone secreted from the thyroid, described the structure and named it "thyroxine", which contains a high concentration of iodine. Thyroxine was synthetically produced in 1927 by Harington and Barger, which resulted in correcting its previous biochemical structure described by Kendall. It was 25 years before the second hormone secreted by the thyroid, triiodothyronine, was unveiled. This task was accomplished by Gross and Pitt-Rivers in 1952. The work of P. E. Smith in 1927 led to the discoveries of the controlling mechanism of the pituitary on the thyroid (Salter, 1940; Frieden and Lipner, 1971; Underwood, 1971; Church and Pond, 1976; Goodman and van Middlesworth, 1974).

C. Iodine Metabolism

1. Absorption and Excretion. Iodine is primarily absorbed in the inorganic form, iodide, the major form of iodine in most foods, with a small amount absorbed as iodinated amino acids (Swanson, Miller and Cragle, 1965; Pike and Brown, 1975). Other forms are subsequently

reduced to iodide prior to their absorption (Cohn, 1932; Alexander et al., 1967; Barau, Cragle and Miller, 1964). Although absorption of iodine occurs throughout the gastrointestinal tract, the most prominent sites of absorption are the duodenum in monogastric animals and the rumen in ruminants (Pipes, Bauman and Turner, 1962; Barau et al., 1964; Cragle, 1973).

Routes of iodine excretion include: urine, milk, feces and perspiration. Fecal iodine is derived from thyroxine (T_4) which has been inactivated by conjugation through the phenolic hydroxyl group with glucuronic acid in the liver and excreted subsequently into the bile (Gross and Leblond, 1947; Taurog, Briggs and Chaikoff, 1951). A portion of this iodine can be degradated to iodide and reabsorbed across the gastrointestinal tract (Keating and Albert, 1949; Barau et al., 1964; Harrison et al., 1965; Alexander et al., 1967). In the ruminant, the abomasum is the major site of endogenous secretion, reentering the circulatory iodide into the digestive tract (Barau et al., 1964; Miller et al., 1971; Cragle, 1973). Hormonal iodide is also deiodinated by the kidney, excreting iodine into the urine, or recirculated to the thyroid. Generally, urine contains a larger portion of iodine than does the feces (Aschbacher, Miller and Feil, 1963).

The iodine in milk is iodide that has been actively transported from the plasma to the milk (Porter, Tong and Chaikoff, 1959). It is in an unbound form in milk of ruminants, whereas it is bound in the milk of some monogastric

animals (van Middlesworth, 1956; Lengemann and Swanson, 1957; Brown-Grant and Galton, 1958). Hormonal bound iodine, thyroxine, has been found in milk of rats, but not in physiologically effective doses (Porter et al., 1959). Reineke and Turner (1944) discovered that the ruminant's mammary gland is impermeable to thyroxine. The quantity of iodine secreted in milk, as well as in the urine, can be influenced by both physiological and environmental factors. In both cattle and goats during lactation, increased consumption of dietary iodine markedly increases the level of iodine in milk as well as in urine (Reineke, 1961; Lengemann, 1963, 1965; Hemken et al., 1972). Falconer's (1963) work with sheep indicates that the mammary gland is three times as efficient as the thyroid in removing iodide from the circulatory system. However, in cases where iodide intake is low, the mammary gland appears to have reduced ability to remove blood iodide, therefore retaining iodide for thyroid use (Flamboe and Reineke, 1959; Swanson, 1972). Lengemann, Swanson and Monroe (1957) noted seasonal differences could vary cattle milk iodide content by 20%. The rise in output was noted April through July. Phase of lactation also influences the level of iodine excreted by the mammary gland. Lewis and Ralston (1951) analyzed colostrum and milk samples from the same cows. Colostrum contained the highest concentration of iodine and the iodine content decreased with later phases of production. Lactating women show a similar trend, but once true milk is produced the iodine content remains constant (Salter, 1950).

2. Biosynthesis of Iodine Containing Hormones. Iodide is actively transported from the plasma and concentrated in the thyroid gland by an "iodide pump", which derives its energy from oxidative metabolism (Wolff, 1964). Inhibition of the iodide transport system occurs by antithyroid agents of the perchlorate and thiocyanate type (Wyngaarden, Wright and Ways, 1952). The iodide present in the thyroid gland is oxidized to elemental iodine or to some similar reactive form prior to being incorporated into an organic combination by a peroxidase (Taurog, 1970). At the junction of the follicular cell and lumen, under the control of iodide peroxidase and tyrosine iodinase, iodine combines with the tyrosine residue in the thyroglobulin molecule forming 3-monoiodotyrosine and 3,5-diiodotyrosine (DeGroot and Watson, 1962; Taurog, 1970). This iodination process can be blocked by anti-thyroid substances of the thiouracil type, such as allylthiourea (a compound present in mustard), 5-vinyl-2-thiooxazolidone (a compound present in yellow turnips), a sulfaguanidine and 2-mercaptoimmidazole (Frieden and Lipner, 1971). The final stages of synthesis require the joining of two diiodotyrosine (DIT) molecules forming a molecule of T_4 or a monoiodotyrosine (MIT) with dioodotyrosine, forming triiodothyronine (T_3). Both compounds are found and stored as a component of thyroglobulin, which needs to be degraded, allowing for the release of two iodoamino acids in a ratio favoring T_4 by 10- to 20-fold (Nagataki et al., 1972; Chopora et al., 1973).

> The secretory process requires that thyroglobulin be engulfed by pseudopods thrown out into the follicular lumen to resorb the thyroglobulin into vesicles that fuse with lysosomes. Lysosomal protease breaks thyroglobulin down into amino acids, T_4, T_3, MIT, and DIT. T_4 and T_3 are released from the cell. DIT and MIT are deiodinated to free tyrosine and iodide, both of which are recycled back to iodinated thyroglobulin. (Goodman and Van Middlesworth, 1974)

The activity of the thyroid gland is regulated by hormones. The hypothalamus secretes thyrotropin releasing factor (TRF) which reaches the adenohypophysis through the portal vessels in the pituitary stalk. The TRF stimulates the $beta_2$ cells of the adenohypophysis causing the release of thyroid stimulating hormone (TSH) into the blood stream. The TSH triggers the release in the thyroid gland of T_4 and T_3, which are bound to thyroglobulin. In the plasma, T_4 and T_3 are bound to a molecule composed of T_4-binding globulin, a prealbumin, and albumin (protein bound iodine). T_4 and T_3 are dispersed in the tissue when tissue concentrations are less than 10^{-8} M. As the plasma concentration of T_4 and T_3 increases, the release of TRF and TSH is inhibited (Gordon et al., 1952; Frieden and Lipner, 1971).

In a hypothyroid state, as a consequence of consuming goitrogenic substances, there is a blockage of hormone formation, but uniodinated thyroglobulin is still produced. When the T_4 concentration in the blood becomes depressed, TSH secretion is increased resulting in the formation of uniodinated thyroglobulin and growth of thyroid cells. Hyperthyroidism, as a result of excessive intake of iodide, inhibits the release of previously formed T_4 from the gland.

In the circulatory system four-fifths of the extra-thyroidal body pool of T_3 is derived from peripheral mono-deiodination of T_4 (Braverman, Ingbar and Sterling, 1970). The turnover rate appears to be six to seven days for T_4 and one day for T_3 (Nicoloff et al., 1972).

D. Peripheral Tissue Effects of Thyroid Hormones

The effects of the thyroid hormones are manifested throughout the body and at no particular target tissues. Their action may require several days before being noticed.

1. Calorigenesis. Magnus-Levy in 1895 first described the relationship between the thyroid and oxygen consumption or basal metabolic rate (BMR); hyperthyroidism increased the oxidative metabolism in animals. Later investigators found that the heart, liver, kidney, skeletal muscle, pancreas, salivary glands, epidermis and anterior pituitary increase in oxygen consumption when animals are in a hyper-thyroid state. Bernal and Refetoff (1977) reviewed the mechanism of thyroid hormone action in calorigenesis in animals. Classically, increased BMR, in animals considered to be in a hyperthyroid condition, was attributed to the uncoupling of oxidative phosphorylation. However, to induce this uncoupling in normal animals, dosage levels of T_4 required would be far above that physiologically secreted. Intracellularly, thyroid hormones have been found to increase metabolic activity of the mitochondria, as well as their size and number (Gustafsson et al., 1965; Buchanan, Primack and Tapley, 1971; Gross, 1971). Their data strongly

suggest the calorigenic response to thyroid hormones is modulated at the mitochondria. More recent work by Edelman and Ismail-Beige (1974) with ouabain and its inhibitory effect on Na^+-K^+ dependent ATPase and its association with the sodium pump suggests that the thyroid hormones exert their calorigenic effect by increasing the activity of this enzyme. They administered T_3 and found that the rise in the enzyme activity paralleled the rise in the oxygen consumption. Other suggested modes of regulating calorigenesis include control of activity of glycerol-phosphate dehydrogenase in the cytochrome system and lipolysis and adenyl cyclase activity in the adipose tissue. The latter three mechanisms have been found to have minimal influence on enhancing BMR in response to thyroid hormone stimulation (Bernal and Refetoff, 1977).

2. Lipid and Carbohydrate Metabolism. Iodinated casein fed to livestock induces hyperthyroidism and results in less subcutaneous fat. This is a result of the thyroid hormone's ability to synthesize, mobilize and degrade lipids, thereby creating an overall decrease of their storage and blood concentration. This is evident by the reduced serum cholesterol levels, once used as a diagnostic tool for indicating thyroid dysfunction, and by its increased fecal loss and conversion to bile acids (Friedman, Byers and Rosenman, 1952; Miettinen, 1968). Glucose catabolism is also accelerated by thyroid hormone (Goodman and van Middlesworth, 1974).

3. Protein Metabolism. Thyroid hormone produces a biphasic response in growth. Humans in a hypothyroid state have depressed synthesis and degradation of protein (Crisipell, Parsun and Hollifield, 1956). After administration of the hormone, net protein synthesis increases with a decrease in nitrogen excretion. When rats were thyroidectomized, an injection of T_3 increased liver RNA and protein synthesis (Tata and Widnell, 1963, 1966). In hypothyroid animals, deposition of mucoprotein in subcutaneous and extracellular spaces is also related to abnormal nitrogen metabolism. The osmotically active mucoprotein retains water, as evident in myxedematous individuals (Goodman and van Middlesworth, 1974). Overactivity of the thyroid gland or excessive doses of thyroid hormone results in a net catabolism of protein (Rall, Robbins and Lewallen, 1964). Another diagnostic tool once used in evaluating thyroid status is the amount of creatine in the urine. High levels of thyroid hormone increase the blood creatine as a result of muscle breakdown, followed by increased creatine in the urine. Negative nitrogen balance coincides with increased urine creatine (Bernal and Refetoff, 1977).

4. Vitamin Metabolism. Increased metabolic activity as influenced by thyroid hormone would create a demand for a larger quantity of coenzymes and their vitamin precursors because of decreasing concentrations. In an iodine deficiency situation where there would be depressed hormone secretory activity, carotene could not be converted to

vitamin A, the precursor of retinol, the pigment responsible for prevention of night blindness (Walton, Campbell and Tonks, 1965). Slingerland and Sullivan (1968) found that thiamin deficiency inhibits the biosynthesis of thyroid hormone. In a riboflavin deficiency state, peripheral degradation of thyroid hormone is inhibited (Galton and Ingbar, 1965).

5. Reproductive Organs and Development

a. Males. The physiological maturation of the gonads in all male species requires secretions of the thyroid hormones. Maqsood (1952) has suggested that the thyroid hormones regulate the maturation of the gonads, which is achieved by regulating the sensitivity of the gonads to the gonadotrophic hormones (Maqsood, 1952). In the mature male, variations exist across species as to the necessity of the thyroid hormone.

Most laboratory animals exhibited no differences as to mating behavior, number of conceptions or number of offspring produced when thyroidectomized males were mated with females with intact thyroids (Jones, Delfs and Foote, 1946; Bruce and Solviter, 1957). However, male rabbits showed evidence of depressed libido and spermatogenesis; these signs were relieved by small doses of T_4 (Maqsood, 1951). Man expressed similar symptoms when in a hypothyroid state (Lawerence, 1936). A decline in libido and deterioration of semen quality have been found in both bulls and stallions. Cases of mild hypothyroidism in rams have been found to be associated with poor semen quality and seasonal

variation (Underwood, 1977). Therefore, the role of the thyroid glands in mature males used for breeding purposes is a necessity.

b. Females. The thyroid hormones induce physiological maturation of the ovaries by sensitizing the gonadotrophins (Maqsood, 1951). Typically, the mature female laboratory animal exhibits irregular and lengthened estrous cycles when thyroid activity is suppressed (Krohn and White, 1950; Bruce and Sloviter, 1957; Hoar, Goy and Young, 1957). Thyroidectomized guinea pigs were found to have reduced follicle numbers without affecting corpora lutea. Gillman and Gilbert (1953) removed the thyroid gland from baboons, which led to cessation of the estrous cycle or noticeable irregularities. Brody and Frankenback (1942) and Speilman et al. (1945) thyroidectomized dairy cattle and found that physical estrus signs were not exhibited. By partial destruction of the thyroid gland with ^{131}I in dairy cattle, Miller and Swanson (1969) did not adversely affect reproductive performance, but did in fact create "silent heat." Canadian workers improved the conception rate of repeat-breeders by feeding an organic iodine preparation 8 to 12 days prior to the onset of estrus (McDonald, McKay and Thompson, 1961). Moberg (1961), in Finland, improved first service conception in dairy cattle using iodine supplementation (62.2% for controls versus 69.1% for iodine treatment). Lucas, Brunstad and Fowler (1955) found that estrous cycles in sows and gilts were not affected by induced hypothyroidism.

Prolonged gestation intervals were noted in laboratory animals if they were in a thyroid deficiency condition prior to and during gestation (Nelson and Tobin, 1937; Folley, Watson and Amoroso, 1942; Chu, 1944; Krohn and White, 1950; Hoar, Goy and Young, 1957; Krohn, 1951). Hoar et al. (1957) and Chu (1944) attributed this to an effect on parturition, which Bruce and Sloviter (1957) claim to be associated with a slight decrease in litter size. This could be a result of resorption of feti, which was found by Jones et al. (1946) when thiouracil was used to induce a hypothyroid state in rats. Although the lengthening of gestation of cattle has not been noted, abortions, resorptions, stillbirths or weak calves have been associated with iodine deficiency (Allcroft, Scanell and Hignett, 1954).

c. Fetal Thyroid. Iodine accumulation in the fetal calf begins between the 75th and 118th day after conception, with its greatest accumulation occurring prior to birth (Koneff et al., 1949). In fetal lambs the uptake of iodine commences about the 50th day of gestation (Barnes et al., 1957). Thus, the thyroid activity of the fetus begins approximately after the first trimester of gestation. Therefore, iodine is passed from the maternal blood to that of the fetus. In rabbits, fetal iodine levels have been found to be several times more concentrated than in the doe (Hall and Myant, 1956). The ability of the fetal thyroid to synthesize and secrete thyroid hormones again depends

upon species. The passage of maternal thyroid hormones is considered to increase with gestation (Hall and Myant, 1956; Myant, 1958). However, the permeability is limited to free maternal thyroxine and not that which is bound (Osorio and Myant, 1960). Therefore, thyroidal dysfunction in the fetus may exhibit thyroid deficiency. Miller and Swanson (1967) studied the transfer and concentration of iodine in the postpartum cow and her fetus. Iodine concentration in the blood of the fetus was five times greater than that of the dam. Amniotic fluid contained more iodine than fetal plasma, whereas the content values of iodine in chorionic fluid were midway between maternal and fetal plasma. It was also concluded that the high fetal iodine level was a result of no excretory pathway for iodine in the fetal calf.

E. Alterations in Thyroid Activity

1. Goitrogens. An enlargement of the thyroid gland has been associated with the consumption of particular feedstuffs and/or feed additives by inhibiting the synthesis of the thyroid hormones produced in the thyroid gland. McCarrison (1933) found that native Indian diets containing soybeans produced goiters in rats. In 1939, scientists at Michigan's Henry Ford Hospital fed a battery of unprocessed soybean flour diets to rats (Sharpless, Pearsons and Prato, 1939). Goiter became evident after several weeks on the test diets. Sharpless et al. (1939) found that by exposing the diets to either ether extraction, autoclaving at 20 psi

for 20 minutes, or steam treatment using iodine-free water resulted in reduction of goitrogenic activity associated with the unprocessed soybean flour. Kentucky researchers compared soya protein to casein in balanced diets for starting pigs supplemented with 0.0 or .2 ppm iodine (Sihombing et al., 1974). Thyroid glands were excised; those pigs fed soya based diets had significantly ($P<.01$) heavier thyroid glands. Maryland researchers fed 16 lactating dairy cows corn silage, as the only forage, plus a 24% crude protein concentrate mix made from either soybean meal or cottonseed meal plus urea (Hemken et al., 1971). Silage to concentrate ratios were 6:1 and 3:2. These diets were fed 90 days prior to parturition. Calf thyroid weights were significantly ($P<.05$) heavier for those calves whose dams consumed either of the soybean meal concentrate ratios. Miller, Lyke and Byrne (1972) fed free choice hay supplemented with either 2.7 kg of soybean meal or cottonseed meal daily to 200 kg calves. Their data indicated that both meals inhibited iodine absorption from the gastrointestinal tract. Beck (1958) fed soy flour to rats and concluded that soy protein interferes with normal reabsorption of organic iodine, but not the absorption of inorganic iodine. Therefore, the increased fecal loss of iodine would reduce iodine supply, which would result in a hypothyroid condition, if additional iodine were not supplied in the diet.

Oils from the processing of soybeans, cottonseed and corn were compared with fats from chickens, beef and swine

and butter on thyroid pathology in rats (Kaunitz and Johnson, 1967). Each lipid was added individually at a rate of 20% to iodine deficient-purified diets and fed for 600 days. Thyroid glands were excised and weighed. Those fed vegetable oil diets had significantly ($P<.01$) heavier thyroids.

Sampson and Putzki (1952) suggested that diets high in calcium may produce goiter, if the level of iodine was not increased. Taylor (1954) fed diets containing 2% calcium carbonate and produced goiter in rats. He proposed that depressed iodine absorption from the intestine was not the reason. It has also been proposed that high calcium, as well as arsenic, fluoride, cobalt and sodium chloride in diets, increase the urinary excretion of iodine, or interfere with the uptake of iodine by the thyroid (Schutte, 1964; Underwood, 1966).

Nitrogen fertilization has numerically depressed the iodine content in forages and increased the nitrate content of forages. Ingestion of nitrate by rats increased their iodine requirement (Bloomfield et al., 1964). In a more practical situation, Smith et al. (1964) made corn silage from corn plots fertilized with one of the following: 670 lb of ammonium nitrate/acre; 670 lb of ammonium nitrate plus 400 lb of P_2O_5/acre (53%); or no fertilizer. When fed to feedlot cattle, performance was not influenced by either nitrate or soil factors.

The inability to utilize iodine at the level of the thyroid gland has been associated with consumption of particular plants by livestock. These plants all contain thiol

groups which are indicative of their goitrogenicity. Progoitrin, a compound present in the *Brassica* family, i.e., cabbage and rutabagas, prevents the formation of hormones and results in goiter. This can be overcome by feeding supplemental iodine. The presence of cyanogenetic glucosides in white clover (*Trifolium repens*) and flax seed converts HCN into thiocyanate in their tissues. After ingestion thiocyanate inhibits the selective concentration of iodine by the thyroid. Cruciferous plants also contain thioglycosides, which inhibit the iodination of tyrosine (Bachelard and Trikojus, 1960; Frieden and Lipner, 1971; Underwood, 1977).

2. Induced Hypothyroidism - Its Influence on Livestock and Fowl Production. Since the late 1930's the expanding knowledge of the physiological functions associated with the thyroid gland and thyroxine has stimulated extensive livestock and fowl production investigations to help meet the growing demand for efficient food production. Attempts were made to control this gland's function by the following methods: 1) thyroidectomy and 2) feeding compounds to reduce its activity (hypothyroidism).

The concept behind suppression of its secretory activity was to reduce the basal metabolic rate and thus the animal's activity would become lessened. It was hoped that this would make more efficient use of ingested net energy for fat deposition as well as bone and muscle development (Blaxter et al., 1949).

The isolation of the thioureylene radical from plants considered to possess goitrogenic activity by Astwood in 1943 resulted in the development of synthetic goitrogens such as thiouracil and thiourea. Thiouracil and thiourea produced hypothyroidism; however, thiourea was found to be toxic (Schultz and Turner, 1945).

a. Cattle and Sheep. Hypothyroidism induced by complete removal of the thyroid gland in both young and old ruminants resulted in growth depression, especially for the young growing ruminant (Simpson, 1924; Reineke and Turner, 1941; Spielman et al., 1945). However, partial removal of the gland created sporadic growth responses as a result of regeneration of thyroid tissue (Bullard and Andrews, 1943). The economic feasibility of adding thiouracil to diets, rather than thyroidectomizing to control production, was studied by Beeson et al. (1947) with yearling steers. Feeding 2.0 and 4.0 g/head/day increased daily gains; the 2.0, 4.0 and 6.0 g/head/day levels tended to improve dressing percent, as well as the degree of finish above the unsupplemented control group. Andrews et al. (1947) fed .18, .33 or .54 g of thiouracil/head/day to lambs, which slightly improved gains; feed efficiency increased with increasing increments of thiouracil. Carcass quality was improved only at levels of .18 and .33 g/head/day. In a second study, when feeding 1.15 g of thiouracil/lamb/day, both gain and feed consumption were depressed (Andrews et al., 1947). By feeding .21 or .39 g

of thiouracil/head/day to 70 lb Rambouillets, performance and carcass quality were not affected (Barrick et al., 1949).

The use of synthetic goitrogens for productive functions in ruminants is of little significance; its value may be applicable only when more subcutaneous fat is desired, a characteristic that has been almost eliminated as a result of demands of today's consumer of beef and lamb.

b. Swine. Lard-type hogs were in demand by consumers during the pre- and post-World War II era. Zorn and Bruggeman (1939) successfully increased adiposity of swine by removing their thyroids. This being economically unfeasible, Muhrer and Hogan (1945) initiated the first experiments with swine utilizing thiouracil to increase fatness. Thiouracil-fed hogs had improved gains and feed efficiency, 2.1 versus 1.4 lb and 3.10 versus 4.82 lb, respectively. Unfortunately, the thiouracil-fed pigs were shorter, wider and fatter than controls. In present-day markets, this is considered an inferior type of hog. van Der Noot, Reece and Skelly (1947), using free-choice rations treated with .25% thiouracil, found that pigs consumed 27.5% less feed per 100 lb of gain, and required a shorter period for that gain than did the control-fed pigs. Later studies (Van Der Noot, Reece and Skelly, 1948; Terrill et al., 1949; Willman, Asdell and Loosli, 1949) confirmed the thiouracil feed efficiency response, but were unable to

substantiate earlier claims of increased gains. Michigan researchers (1947) fed .15% thiouracil for 41 days prior to slaughter to crossbreds, Chester White and Yorkshire pigs (McMillen et al., 1947). They reported feed required per unit gain was reduced, 8.4, 13.8 and 18.8%, respectively, even though the daily gain was reduced slightly in each case. Carcass data failed to reveal any significant differences between experimental and control pigs. The improved feed efficiency reported was suggested to be a result of lowered heat production, because animals metabolize the same amount of food (Bratzler, Barnes and Swift, 1948). In conjunction with the previous statement, .15% of thiouracil fed during the last 4 weeks prior to slaughter is preferable because of reduced gains and reduced skeletal growth (Hale et al., 1948). At the level recommended by Hale et al. (1948), Terrill and co-workers (1950) also found depressed skeletal development with no differences in carcass measurements. Sixteen years later, Topel and Merkel (1966) investigated two other synthetic goitrogenic compounds, tapozole and methyluracil. Neither of these compounds appeared to influence carcass quality. Pearson et al. (1966) conducted a 2 x 2 factorial, 0.00 versus 0.15% thiouracil supplementation to diets and 4C versus 27C continual environmental temperature, using growing swine. At the 4C temperature, average daily gain was significantly ($P<.01$) greater for control-fed pigs; at 27C gains were similar. Feed efficiency was similar at both temperatures.

c. Fowl. Depressed growth is found in young birds when synthetic goitrogens are consumed. Kempster and Turner (1945) included .2% thiouracil in broiler rations for 10 weeks. Depression in growth, as well as feed efficiency, were noted. When thiouracil (.025%) was added to chick diets, feed efficiency was improved with a longer lighting program (Andrews and Schnetzler, 1946). The incorporation of thiouracil into these diets did increase fat deposition and carcass grade. Feeding .1 and .2% thiouracil during the first 10 weeks of life, Glazner and Jull (1946) found the typical depression in growth as well as poor quality carcasses. Reineke et al. (1946), incorporating thiouracil into turkey rations, increased fat deposition, 42 and 21% in males and females, respectively. Blakely and Anderson (1948) also increased carcass fat deposition in young growing turkeys, but reduced economy of gains. The incorporation of thiouracil in diets of fowl appears to be only beneficial for fat deposition.

3. Induced Hyperthyroidism - Its Influence on Livestock and Fowl Production. Induced hyperactivity of the thyroid gland was successfully achieved using a non-thyroidal derivative, iodinated casein, by Ludwig and von Mutzenbecher in 1936 (in Blaxter et al., 1949). Reineke and Turner (1942, 1946) improved Ludwig's and von Mutzenbecher's iodination process, resulting in a more biologically active iodinated casein. Successful iodination of serum albumin

(Muss, 1941), egg albumin and soya bean protein (Reineke and Turner, 1942), and whole blood protein (Pitt-Rivers and Randall, 1945) followed shortly after. Commercially prepared iodinated protein is referred to as a thyroprotein.

a. Cattle and Sheep. The creation of a hyperactive state in animals was hypothesized to accelerate growth. Braude (1947) indicated that such a physiological state would increase the metabolism process, thereby consuming more feed, resulting in faster growth. Dinussen, Andrews and Beeson (1948), pursuing this idea, fed .5 g of iodinated casein to 500-pound Hereford heifer calves for 185 days, finding no improvement in growth. Millen, Nevens and Gardner (1948) found improved growth when cattle were fed 1.3 g of iodinated casein/100 pounds of body weight. However, they found that cattle lost weight when it was fed at 4 g/100 lb of body weight. Recently, Boling et al. (1973) fed 367 Protamone, a commercially prepared thyroprotein compound, in the diet to yearling steers for 180 days or 84 days. As predicted earlier by Braude (1947), feed intake significantly ($P<.05$) improved in either treatment; from the 85th to the 180th day of the trial, feed utilization was significantly ($P<.05$) improved compared to untreated control or continuous feeding; the cattle on the 84 day treatment gained significantly ($P<.01$) faster than other cattle. Carcass grade was not affected by treatments; however, treatment groups had significantly ($P<.05$) smaller longissimus areas. Ely, Boling and Deweese (1976) fed

thyroprotein at the rates of .00, .04, .08, and .12% in diets fed *ad libitum* to 27 kg lambs. Daily gains were depressed with treatments .23, .16, .18 and .16 kg/day, respectively. Using 33 kg lambs, the same authors fed 0.0, 1.2 and 1.6 g of thyroprotein/head/day for 30 days. Feed intake was depressed and gains were significantly ($P<.05$) lower on the high thyroprotein diets.

b. Dairy Cows. The pioneering work in thyroid hormones and their influence on milk yield was conducted by Hertoghe in 1897. Renewed interest in the relationship between the thyroid gland and lactation was initiated by Graham (1934a,b). He found that thyroid gland preparations or injections of thyroxine improved milk and fat yields of cows. Successful stimulation of lactation using a synthetic product, iodinated casein, was achieved by Reineke (1942). These findings have been reconfirmed by Jack and Bechdel (1935), Folley and White (1936), Blaxter et al. (1949), Thomas (1953) and Thomas et al. (1957). Feeding thyroprotein for the entire lactation did not achieve its expectations based on short term studies. Thomas and Moore (1953) used fat corrected milk (FCM) values as the appropriate indicator for milk production and found no improvement in production with addition of thyroprotein to rations. In a later study, Thomas et al. (1957) established that 60 day feedings of thyroprotein were ineffective in increasing total production. Throughout two successive lactations, Swanson (1954) fed thyroprotein to dairy cows for an average

of 174 and 202 days; milk production for thyroprotein-treated cows was 10,278 and 9,975 lb, respectively; control cows produced 10,320 and 9,971 lb of milk, respectively. A long term study involving 3,565 lactations indicated that iodinated casein or L-thyroxine reduced milk yield, 110 and 159 lb, as a result of treatment during the first and second lactations, but increased production, 245 to 409 pounds, for the third and subsequent lactations (Leech and Bailey, 1953). Swanson (1954) successfully prevented the rapid decline in milk production, associated with thyroprotein feeding in earlier studies, by feeding thyroprotein for 10 to 14 weeks and withdrawing the hormone over 15 days. Thomas et al. (1957) concluded that withdrawing thyroprotein over 0, 10, 20, and 30 day periods did not inhibit the rapid decline in production. In three successive lactations, Thomas and Moore (1953) found a gradual depression in FCM production, 9,272, 9,012 and 8,355 lb, respectively, when thyroprotein was fed. FCM production in untreated cows improved, 9,675, 10,090 and 11,491, respectively. A more comprehensive study comparing the effect of thyroprotein versus no treatment, based on milk fat content, was conducted by Leech and Bailey (1953). After a 305 day lactation, weighted mean fat percentage of 914 treated cows and 899 control cows was 3.74 and 3.76, respectively.

Since thyroprotein increases basal metabolic rate, Thomas and Moore (1953) compared the efficiency of converting TDN into milk for cows fed thyroprotein or not fed

thyroprotein. After 300 days of feeding, thyroprotein did not influence efficiency when body weight was disregarded. In his 1957 study, Thomas found that 60 day feedings of thyroprotein did not impair conversion of TDN to milk efficiency.

c. Swine. The feeding of iodinated protein to induce hyperthyroidism in growing pigs was first recorded by Reineke and McMillen at Michigan State College in 1946. Improved gains and slight improvements in efficiency of weanling Berkshire pigs were noted when iodinated casein was added to the ration at .005 to .006%. Two years later Reineke added iodinated casein at the rate of .012% of the ration and fed these diets for 98 days, then changed to a ration containing .006% iodinated casein and fed for 14 more days. Pigs gained 27 lb more than the untreated controls. An 84 day performance study with Duroc pigs fed rations containing either .0000, .0044 or .0088% iodinated casein was conducted by Purdue researchers. Pigs gained significantly ($P<.05$) more weight with 10% improvement in feed efficiency only on rations containing .0088% iodinated casein. Longer carcasses and heavier bellies and picnic shoulders were also noted at the level of iodinated casein (Beeson et al., 1947b). The following year, Purdue researchers suggested that a 40 pound pig required .0132% iodinated casein in the ration to significantly improve gains and carcass quality (Perry, Beeson and Andrews, 1948).

The idea of feeding thyroprotein routinely to lactating sows was an attempt to increase the sow's milk production and decrease pig mortality and increase gains in baby pigs. Lucas, Brunstad and Fowler (1958) fed three groups of 15 Palouse gilts, one group receiving .15% thiouracil, another group receiving .0123% thyroprotein in the basal ration, and third group serving as a control. One-third of each group was slaughtered 12 to 24 hours after the second estrus, one-third slaughtered 25 days post-breeding and the remainder allowed to farrow. Ovulation rate, fertilization rate, embryonic mortality during the first 25 days of gestation, number of normal embryos at 25 days post coitum, or number of pigs born alive were not significantly different. Numerical differences of pigs born were considerably different among gilts fed thiouracil (3.25), those fed thyroprotein (7.33) and control (8.67), respectively. Length of gestation was 10 days longer for gilts being fed thiouracil. Pigs born from these gilts were lighter than those in the thyroprotein treatment group, 2.27 lb/pig versus 2.90 lb/pig, respectively. Recently, Iowa workers fed 32 sows, beginning the day after parturition, 220 ppm of thyroprotein/day (Aherne and Speer, 1974). Adjusting litter size to 8 pigs on day three postpartum and estimating milk yield on days 5, 12 and 21 of lactation, researchers confirmed significantly ($P<.05$) improved weight gains from birth to three weeks of age of pigs on sows fed thyroprotein. However, significant ($P<.01$) reduction in litter size and weight loss of these

sows was noted. Michigan State University (Hitchcock (1973) reported in 1973 the effect of three levels of thyroprotein feeding, 0, 150 and 200 g/ton of feed. Treatments commenced the day of lactation and results were expressed per pig nursed. Milk yield decreased with the addition of thyroprotein to rations. Offspring of sows on the highest treatment level gained faster. Significant ($P<.05$) losses of body weight were found as in the Iowa State University study (Aherne and Speer, 1974).

d. Fowl. Investigations in feeding iodinated casein to poultry were to enhance growth rate of meat strains of fowl and increase egg production in layers. Crew and Huxley (1923) found a depression in growth of maturing birds with thyroid feeding. In 1944, Turner, Irwin and Reineke depressed growth rate and decreased subcutaneous fat when they incorporated .1% iodinated casein to growing birds. Feeding as little as 10 g/100 lb of feed, Wheeler, Hoffman and Graham (1948) improved body weight gains in male Rhode Island Reds, but not in females. In another study, Quisenberry and Krueger (1948) fed iodinated casein to New Hampshire and White Plymouth Rock baby chicks until six weeks of age. Gains and feed efficiency were improved. Turner et al. (1945) evaluated iodinated casein in diets of laying hens. At 10 g/100 lb of feed, yearly egg production was 40.6% versus 22.6% for control diet fed hens. Turner et al. (1945) fed 10 g of iodinated protein to Rhode Island Reds in the pullet phase

of growth. Egg production was substantially greater than in the control birds, but only during the hot weather. This is a period when egg production normally declines (Brody, Funk and Kempster, 1938). Variations exist in response to iodinated protein feeding. Schultz and Turner (1945) demonstrated this by feeding White Plymouth Rocks iodinated casein and increased egg production was maintained during the year.

F. Iodine Toxicity

1. Laboratory Animals. Ammerman et al. (1964) studied the reproductive parameters of rats as influenced by high levels of dietary iodine. In their first trial, 10 female rats were fed either 0 or 2,500 ppm of iodine as potassium iodide beginning 12 days prior to cohabitation with males, and continuing until pups were weaned. High levels of iodine reduced the number of pups born per litter, 10 versus 8.8. Four dams on the high iodine treatment died within 48 hours after parturition; the one surviving female had only three live pups. The survival of the unsupplemented group was 90%. In the second trial, graded levels of potassium iodide, supplying from 500 to 2,000 ppm of iodine to gestating rats, resulted in an increase in pup mortality with increasing levels of potassium iodide. Postmortem examination revealed that dead pups had no milk present in their stomachs, nor was there milk present in the mammary gland of their dams. However,

mammary gland development was normal. Kon and Cowie (1961) suggested that the thyroid gland is not essential for milk secretion, but that in its absence the intensity and duration of secretion are reduced. These studies by Ammerman et al. (1964) indicated that there was no obvious effect of high iodine intake on ovulation rate, implantation rate, development of normal feti or length of gestation. The fertility of male rats fed 2,500 ppm of iodine as potassium iodide from birth to 200 days of age appeared to be unimpaired (Ammerman et al., 1964). Arrington et al. (1965) fed rats potassium iodide to supply up to 2,500 ppm of iodine during gestation. Survival rate was only 10% with addition of 2,500 ppm of iodine; those surviving weighed significantly ($P<.05$) less than controls. The influence of high levels of dietary iodine during gestation of rats was similar to the findings of Ammerman et al. (1964). The study by Arrington et al. (1965) also included rabbits and hamsters. Rabbits fed a minimum of 250 ppm of iodine as potassium iodide beginning 2 days prior to parturition had young that were born normal size but died shortly thereafter. This was attributed to their reluctance to nurse, even though milk was present in the mammary gland of their dams. Feeding 2,500 ppm of iodine as potassium iodide to hamsters 12 days prior to parturition and during lactation did not affect the number of offspring produced nor alter their postpartum survival rate. Taylor et al. (1964) fed late gestational rats and rabbits potassium iodide at 250 and 1,000 ppm of iodine,

respectively. Ninety-three percent of the pups and 94% of the newborn rabbits did not survive. There was a complete inhibition of lactation in postpartum female rats and partial inhibition in does. Excess iodine intake, 119 mg/day, when fed to rats for 9 months failed to produce myxedema or inhibition of organic binding of iodine by the thyroid (Correa and Welsh, 1960). Histologically, enlargement of the thyroid gland was attributed to accumulation of excessive colloid. However, hyperplasia of the epithelium was not present. The excessive colloid content caused the fusion of several follicles, resulting in an enlarged thyroid (Correa and Welsh, 1960).

Highman, Webster and Rice (1955) injected intraperitoneally 100 mg/kg sodium iodide to study iodine toxicity in mice. These injections resulted in extensive necrosis of renal convoluted tubules, adrenal cortical lipid depletion, severe fatty changes in liver and kidney, and occasionally fatty changes in the myocardium. Increasing the dosage to 500 mg of 3 to 6% potassium iodate/kg, or oral administration of sodium iodate, resulted in degeneration of gastric parietal cells and animals dying within 48 hours. In a third study, 115 to 142 mg/kg potassium iodate was injected intraperitoneally to mice; severe retinal degeneration was observed. This was also found in rabbits and guinea pigs. Webster, Stohlman and Highman (1966) found similar results in dogs fed 200 mg potassium iodide/kg. They also noted fatty infiltration of the viscera and

necrotic lesions in the liver, kidney and mucosa of the gastrointestinal tract.

2. Cattle. When Newton et al. (1974) fed up to 200 ppm iodine as calcium iodide to calves, they found that high dietary iodine depressed gains. Coughing and profuse nasal discharge were also noted. Significant ($P<.05$) depression in serum calcium and blood hemoglobin concentration were found in calves fed 200 ppm iodine as calcium iodide. Based on depressed blood hemoglobin concentrations, it was concluded that high dietary iodine depressed liver iron stores (Newton et al., 1974). Serum iodine levels increased with dietary iodine intake, but did not influence the level of circulating hormonal iodine in approximately 75% of the animals. Postmortem examination of these calves showed heavier adrenals and degeneration of the gastrointestinal tract. Miller and Swanson (1973) fed lactating dairy cows up to 50 ppm iodine as potassium iodide, sodium iodate or EDDI; no signs of toxicity were evident. Field reports in dairy herds having iodine toxicity were described by Wallace (1975) as follows:

> loss of milk production, chronic low-grade fevers, nasal and lacrimal discharge, coughing and development of lameness and over-grown hooves, serum iodine levels were elevated, necropsy findings of thyroid hypertrophy and adrenocortical hyperplasia.

It was calculated that these cattle were being fed 10 times (107 mg daily) the iodine requirement. McCauley et al. (1972) described similar signs in market weight steers. These investigators also found severe bronchopneumonia

with extensive chronic lung damage, prolapsed rectums and death. In another field observation in which 680 to 1,700 mg/day of EDDI had been consumed, the following were found in dairy animals: decreased appetite, diarrhea, metritis, retained placenta, reabsorbed feti, stillborn calves, and poor response to fight infections (McCauley et al., 1972).

3. Swine. Young pigs showed depressed performance when fed 4 ppm (40 times the requirement) of iodine as potassium iodide (Frape et al., 1958). In a more recent study, Newton and Clawson (1974) found no depression of performance of growing pigs when fed 400 ppm (4000 times the requirement) of iodine as calcium iodate. However, they did observe increased serum iodine levels and thyroid gland weights. When the level of dietary iodine was increased to 800 or 1,600 ppm, there was depressed growth rate, feed intake, hemoglobin level and liver iron concentration. Also, lesions in the cornea were detected. Oral or parenteral administration of iron improved performance of swine and their hemoglobin levels (Newton and Clawson, 1974). The effect of excessive iodide on sows was evaluated by feeding up to 2,500 ppm dietary iodine as sodium or potassium iodide during the final 30 days of gestation. Litter size, weight, survival and growth during lactation were not significantly reduced as compared to the control group (Arrington et al., 1965). This confirms earlier work where 220 ppm dietary iodine was fed as potassium iodide during gestation and lactation without producing any observed

toxicity signs (Hart and Steenbock, 1918). Weiser and Zaitschek (1933) did not observe adverse effects from feeding 50 mg iodine daily during gestation and 83 mg daily during lactation as 2% iodized calcium carbonate.

4. Fowl. Arrington and co-workers (1967) fed five levels of iodine as potassium iodide, 0 to 500 ppm, to sexually mature pullets and hens that had completed one year of laying. Egg production decreased as the level of iodine increased. Even though hens with high iodine intake stopped laying eggs, they did not molt. However, eggs were present in the isthmus of the egg tract. When these birds were returned to the control diet, egg production returned to normal. Although there was no effect on egg fertility, hatching was delayed, percent hatchability decreased, and embryonic death increased. Feeding potassium iodide at the rate of 312 to 5,000 mg of iodine/kg of diet to mature Leghorn hens resulted in early embryonic death and delayed or reduced hatching, but did not affect egg fertility (Perderno, Harms and Arrington, 1966). Wheeler and Hoffman (1949) reported enlarged thyroids in hens that were fed 8.8 ppm dietary iodide.

G. Iodine Deficiency in Swine

The characteristic signs of iodine deficiency in swine are thickened skin and subcutaneous edema. Because of the subcutaneous edema, an enlarged thyroid gland is not externally evident. However, on necropsy the gland is enlarged and hemorrhagic. The offspring of iodine deficient

sows are born almost hairless with wrinkled skin and most die within a few hours of birth (Hart and Steenbock, 1918; Kalkus, 1920). The marginally deficient sow tends to give rise to weak offspring. Andrews et al. (1948) examined the thyroid glands of piglets nursing sows not supplemented with iodine. There was a high incidence of hyperplasia of the follicular epithelium of the thyroid gland. Iodine content of the thyroid glands was significantly correlated with the height of the thyroid epithelium ($r = -.525$) and the thyroid weight ($r = -.350$). Sihombing et al. (1974) showed that when pigs were fed iodine deficient diets, the plasma protein bound iodine levels were reduced. The syndrome of iodine deficiency in growing pigs has been reported as:

> long bones appear shorter, a stunted chubby appearance, reluctance to move in standing position; lethargic; a rough, coarse hair, wrinkled skin; brown exudate and severe myxedema.
> (Sihombing et al., 1974)

H. Iodine Requirements of Swine

Hart and Steenbock (1918) in Wisconsin, Kalkus (1920) in Washington, and Welch (1928) in Montana established that the Northwestern and Great Lakes regions of the United States are areas with a high incidence of hypothyroidism in swine. This is due to the low iodine content of feed ingredients produced in these regions. Andrews et al. (1948) prevented all signs of iodine deficiency of growing and adult swine by adding 0.5% stabilized salt containing 0.007% iodine (0.35 ppm iodine in diet) to the diet.

Frape et al. (1958) found that 0.005 ppm dietary iodine was adequate for young, growing swine. Underwood (1966) estimated that the dietary iodine requirements of swine range from 0.05 to 0.1 ppm. Considerations for increasing the iodine intake as a result of consumption of particular compounds as previously described should be made. Cromwell, Sihombing and Hays (1975) found that swine diets formulated with soybean meal must be supplemented with .086 to .132 ppm of iodine in order to prevent goiter. The N.R.C. (1973) iodine requirement for swine has been estimated to be 0.2 ppm.

EXPERIMENTAL PROCEDURES

A. Introduction

A long term experiment was conducted to determine the effect of deficient and excess levels of dietary iodine on various nutritional, physiological and pathological parameters of gilts, sows and their offspring. These parameters were evaluated throughout breeding, gestation and lactation for two parities. The animals were from the purebred and crossbred herds of the Michigan State University Swine Research Farm, where this experiment was conducted.

B. Experiment

1. Breeding Herd. Twenty-eight gilts and sows, which were Yorkshire, Hampshire or Yorkshire X Hampshire, were allotted to four dietary treatment groups. An attempt was made to equalize for the effects of parity, breed, age of sow or gilt, and boar to which they were bred. Groups were randomly assigned to one of four treatments. Basal corn-soybean meal gestation and lactation diets (Table 1) adequately fortified with all required vitamins and minerals (N.R.C., 1973) with the exception of iodine were fed. These diets were supplemented with one of the following levels

Table 1. Composition of basal gestation and lactation diets

Ingredient	Internat'l. Ref. No.	Percent Gestation	Percent Lactation
Gd. shelled corn	4-02-915	84.50	74.00
Soybean meal, 48%	5-04-112	11.50	22.00
Defluorinated phosphate, (6)	6-01-780	1.25	.75
Calcium carbonate comm. mn 38% Co, (6)	6-01-067	.75	1.25
Salt, plain white		.50	.50
Low Iodine -vitamin- trace mineral premix[a]		.50	.50
Iodine premix[b]		.50	.50
Selenium premix[c]		.50	.50
		100.00	100.00

[a]See Appendix, Table A-1.

[b]See Appendix, Table A-2.

[c]Selenium premix contains 20 mg Se per kg as sodium selenite.

of iodine supplied as pentacalcium orthoperiodate:[1] 0.0, .2, 2.0 and 20.0 ppm. According to the 1973 N.R.C. requirements, these levels were 0, 1, 10 and 100 times the sow's iodine requirement, as indicated in Table 2. The study was initiated approximately 10 days post-breeding. Gestation diets (Table 1) were fed at the rate of 1.8 kg per day until farrowing; lactation diets (Table 1), with the respective iodine levels, were begun the day after farrowing and fed at an average rate of 5.5 kg daily. Twenty-four hours post-weaning, gestation diets with respective iodine levels were resumed at the rate of 1.8 kg per day. Barren gilts and sows were maintained on their respective

Table 2. Iodine treatments

Treatment No.	Iodine conc. ppm	Multiple of estimated requirement
1	0.0	0
2	0.2	1
3	2.0	10
4	20.0	100

gestation diets during this experiment. The study was continued with the same sows, including the barren females, on their respective iodine treatment. However, only three

[1]Morton Salt Company, Woodstock, IL.

females on the 0.0 and .2 ppm iodine treatment groups were maintained in the experiment for a second gestation and lactation. Water (containing .002 µg iodine/ml) was offered *ad libitum* during all experiments.

The sows and gilts were double mated by hand and tested for leptospirosis and brucellosis. All were found to be free of these bacterial pathogens which can cause reproductive failure. Pregnancy checks utilizing the Scanaprobe[1] and visual appraisal were made approximately 30 days post-breeding. Attempts were made to rebreed those individuals that appeared to be "open."

During gestation, sows and gilts were tethered and crated, respectively, in a completely enclosed, slotted floor, environmentally controlled building. Three days prior to farrowing they were moved into crates in a farrowing facility. Each treatment group was stratified as illustrated in Figures 1 and 2 to decrease the possibility of inhalation of volatile iodine.

Bodyweights were taken on all sows and gilts approximately 10, 50 and 90 days after initiation of the study. Sows were weighed at 24 hours, 2 weeks and 4 weeks (weaning) postpartum.

Blood was collected from the anterior vena cava at 50 and 90 days of gestation, farrowing and weaning. It was immediately deposited in acid washed centrifuge tubes with and without heparin. Hemoglobin, hematocrit, erythrocyte

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[1]Ithco, Ithaca, NY.

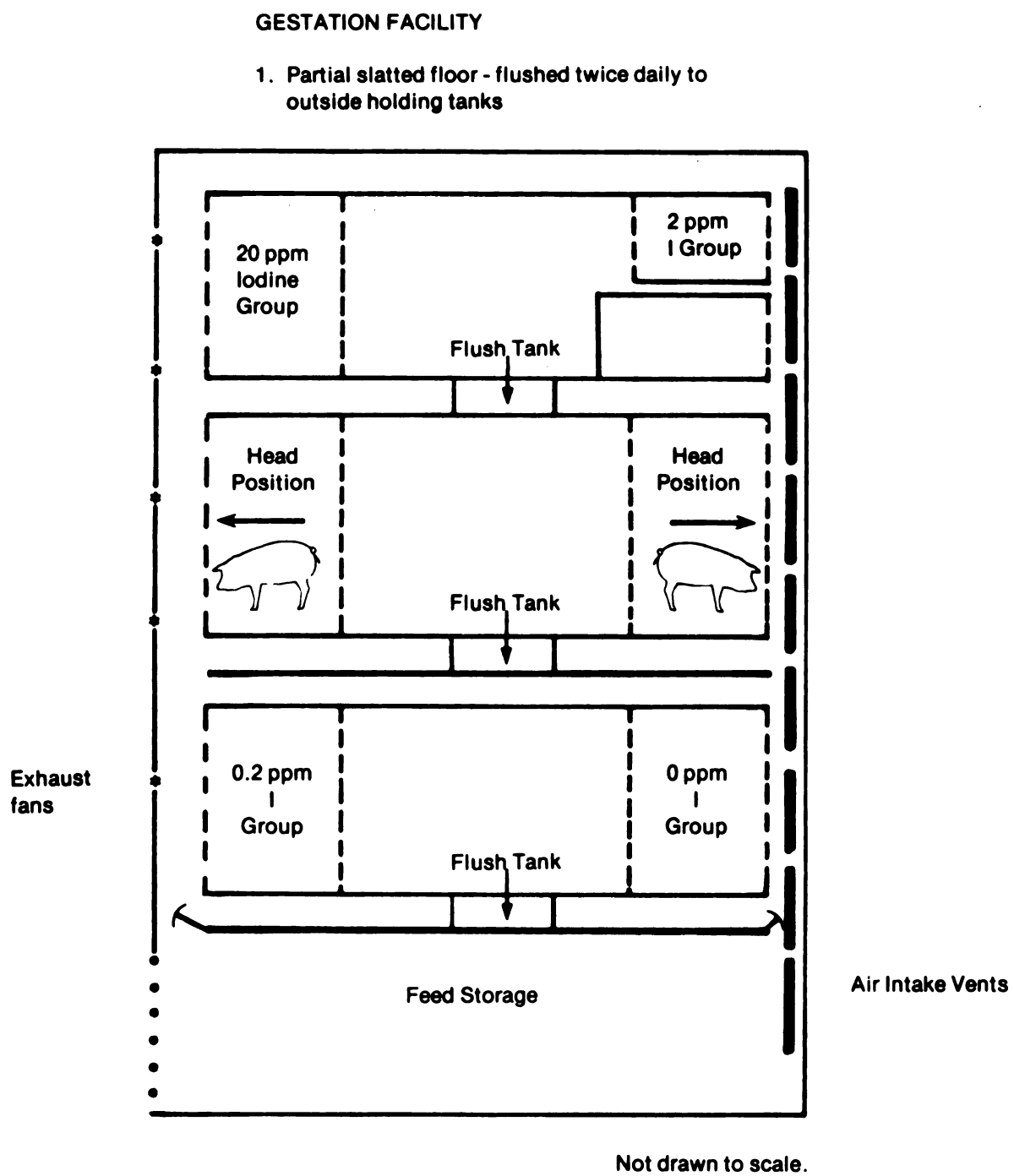

Figure 1. Treatment locations in gestation facility.

FARROWING FACILITY

1. Partial slatted floor with holding pit.
2. Full slatted floor with holding pit outside.

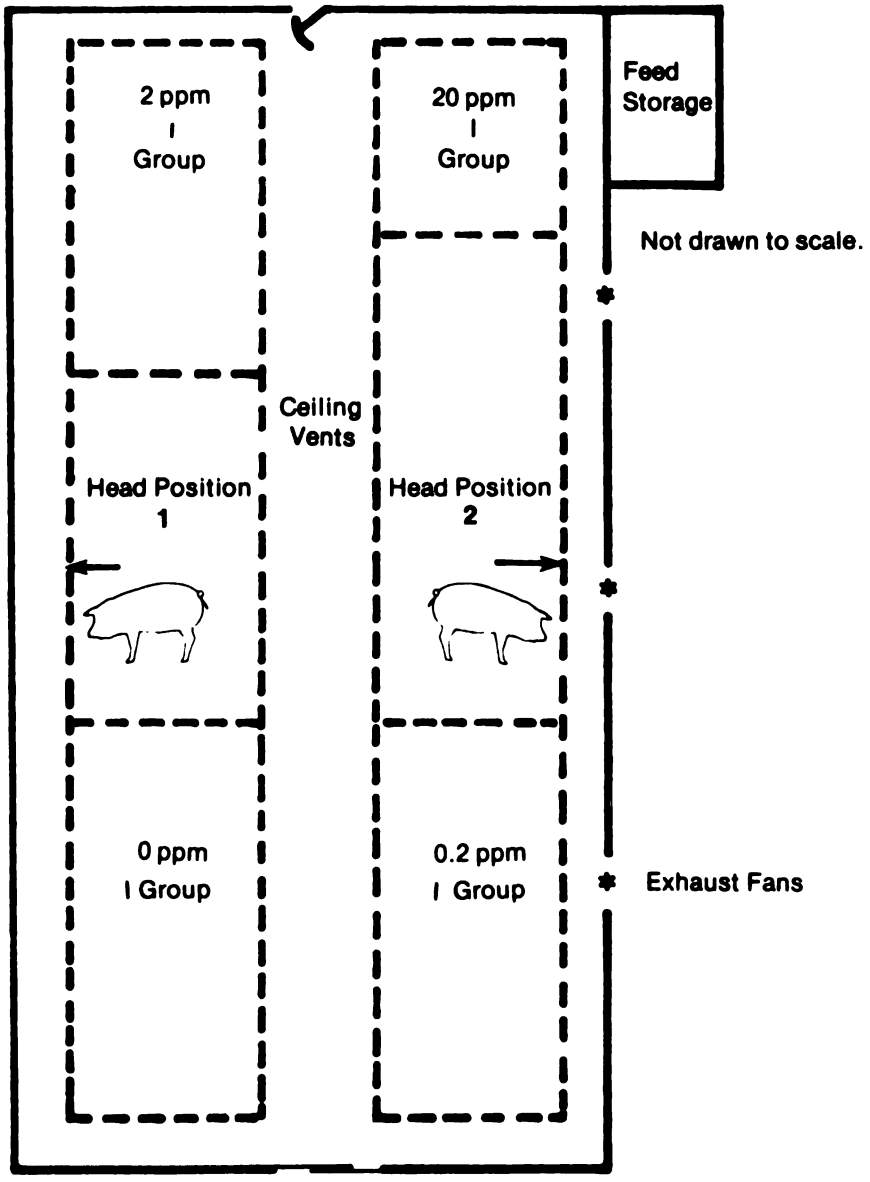

Figure 2. Treatment locations in farrowing facility.

and leukocyte determinations were made on the heparinized whole blood. Non-heparinized blood samples were allowed to clot and retract at room temperature (approximately 21C). Serum was collected by centrifugation and stored at -20C until thyroxine analysis was made.

Sows were injected intramuscularly with 30 IU of oxytocin;[1] nipples were cleaned using an alcohol-soaked piece of cheesecloth. Colostrum and milk samples (2 and 4 weeks) were collected and stored at -20C until calcium, phorphorus, magnesium, iron, zinc, copper, and iodine (total) analyses were made.

2. Offspring. The offspring of the treatment sows remained with their dams for 4 weeks, during which time they had access to her diet. Baby pigs were earnotched, weighed and bled at 1 day of age. Blood was collected from the anterior vena cava at 24 hours, 2 and 4 weeks of age. Blood was prepared for analyses as described previously. Hemoglobin and hematocrit determinations were made. Serum was collected and stored at -20C for thyroxine, calcium, phosphorus, magnesium, copper, zinc, and iron determinations. At 3 days of age the following procedures were performed: tails docked, navels trimmed and needle teeth clipped, intramuscular injections of iron-dextran[2] given (providing 150 mg of elemental iron) and an antibiotic

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[1]Haver-Lockhart Laboratories, Shawnee, KS.

[2]Chromalloy, Animal Health Div., Omaha, NE.

drench (providing 17.5 mg of neomycin sulfate) given.[1] At 3 weeks of age, male pigs were castrated. Throughout this experiment, 70% ethanol instead of tincture of iodine was used as the antiseptic.

3. Pathology. Gilts, sows and offspring were observed for clinical signs of iodine deficiency and toxicity throughout the study. Microscopic examinations of organs were made following an intravenous injection of sodium pentobarbital to anesthetize the newborn or weaned pigs prior to exsanguination. Thyroid, heart, liver, kidney, adrenals and spleen were obtained from one sacrificed newborn and weaned pig per litter. Organs were blotted dry and weighed. Tissue slices, approximately 5 mm thick, were obtained from the same location of each organ across all treatments and ages. Organ slices were fixed in a buffered neutral formalin solution[2] and submitted for histopathological examination.

A minimum of 3 sows per treatment group were sacrificed 30 days after post-lactation rebreeding. The same organs and preparation procedures utilized for histopathological examination for pigs were used to assess the effect of various iodine levels on sows' organs. The remaining

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[1]Anchor Laboratories, Inc., Div. of Philips Roxane, Inc., St. Joseph, MO.

[2]Buffered neutral formalin was prepared as follows: 100 ml formalin (37% formaldehyde), 900 ml deionized distilled water, 4 g sodium phosphate (monobasic) and 6.5 g sodium phosphate (dibasic, anhydrous).

portions of the organs and a sample of the trapezius muscle were then placed in polyethylene bags and stored at -20C for iodine (total) analyses. Reproductive tracts were removed and examined for feti.

C. Analytical Methods

1. Hematology

a. Hemoglobin. The method of Crosby et al. (1954) was used for hemoglobin determination. Two microliters of heparinized whole blood was delivered from Sahli hemoglobin pipette into 5 ml Drabkins solution.[1] Complete mixing of the solution and blood on a vortexing apparatus followed by a 10 minute reaction period at room temperature resulted in the formation of the stable pigment, cyanmethemoglobin. The optical density of cyanmethemoglobin was measured on a Stasar II spectrophotometer.[2] The concentration of hemoglobin was calculated as follows: (OD 540) x (Std hemoglobin factor of Drabkins solution) = hemoglobin concentration in g/100 ml.

b. Hematocrit. Hematocrit was determined according to the method of McGovern et al. (1955). A 20 µl microcapillary tube was filled with heparinized blood

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[1]Drabkins solution was prepared by dissolving 1 g sodium bicarbonate ($NaHCO_3$), 0.05 g potassium cyanide (KCN) and 0.2 g potassium ferricyanide ($K_3Fe\ CN_6$) in deionized distilled water and diluting it to 1 liter.

[2]Gilford Instrument Laboratories, Inc., Oberlin, OH.

and sealed by melting the glass with a Bunsen burner gas flame. The tube was then placed in the hematocrit centrifuge[1] and spun at 10,000 rpm for 5 minutes. At the conclusion of the centrifugation, the hematocrit was read with the values expressed as a percentage of whole blood.

c. Leukocytes. Heparinized whole blood was drawn into a "zero error" Hellige pipette and diluted 1:20 with a 2% acetic acid solution. This allowed for lysis of non-nucleated erythrocytes. Pipettes were then placed on a mixing apparatus and mixed for 2 minutes. Discarding 50% of the pipette contents, the pipette tip was placed to the edge of a hemacytometer with Neubauer ruling, allowing the fluid to flow under a National Bureau of Standards certified cover glass by capillary action. Using a microscope[2] with a 16 mm lens and a 10X ocular, the leukocytes formed in the 4 primary squares were counted and multiplied by 50 to obtain the number of cells per mm^3 of blood. This procedure was repeated using the remainder of blood-acetic acid mixture in the pipette and the average was recorded.

d. Erythrocytes. Following the preceding procedure for leukocyte determinations, heparinized whole blood was diluted 1:200 with .85% physiologic saline solution.

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[1]International Hematocrit, Centrifuge, International Equipment Co., Boston, MA.

[2]American Optical, Spencer, MA.

The center primary squares of the hemacytometer, as viewed through the high dry power lens of the microscope, was used for erythrocyte count. The erythrocyte count per mm^3 was calculated as follows:

> 10,000 x total number of erythrocytes in 5 groups of 16 squares.

2. Thyroxine Assay. Thyroxine (T_4), the principal product of thyroid biosynthesis and the major circulatory thyroid hormone, was determined from serum of sows and their offspring at the previously described intervals. The double antibody radioimmunoassay technique, which utilizes the principle of competitive binding, quantifies the intact thyroxine molecule without interference by substances as found when the protein-bound iodine (PBI) technique is used. Thyroxine concentrations were determined using commercial radioimmunoassay reagents.[1] The following procedure was used. Twenty-five microliters of serum plus 200 µl diluent[2] were added to 12 x 75 mm disposable glass tubes[3] in duplicate using a high speed micropipetter[4] and mixed on a vortexing apparatus. To diluted serum samples, 100 µl of ANS (8-anilino-1-naphthalene-sulfonic acid) was added and vortexed. To the samples, 100 µl of the first antibody

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[1]Radioassay System Laboratories, Inc., Carson, CA.

[2]One percent normal rabbit serum in phosphate buffer, pH 7.6, containing 0.01 M EDTA.

[3]Scientific Products, McGraw Park, IL

[4]Micromedic Systems, Inc., Niles, IL.

was formed. Radioactive labeled ^{125}I-T_4 was pipetted and vortexed followed by 1.5 hour incubation period in a 37C water bath during which time swine T_4 is displaced by ^{125}I-T_4. After incubation, second antibody, 100 µl, was pipetted into these test tubes and vortexed. After 24 hours of incubation at 4C, a first and second antibody complex is formed. Samples were centrifuged[1] at 2,500 rpm for 30 minutes. Supernatant was decanted. The remaining labeled precipitate in the test tubes was counted using a gamma counter.[2] Each sample was counted for 10 minutes or 4,000 counts. The quantity of T_4 present in swine serum samples was determined by the ratio of bound ^{125}I-T_4 to the first antibody. Percent bound ^{125}I-T_4 was then read directly off a graph of the standard curve for each assay to determine ng T_4 per ml of serum.

D. Chemical Analyses

1. Colostrum and Milk Minerals. Colostrum and milk samples were thawed at room temperature, followed by vigorous shaking for 2 minutes, by hand, to reestablish dispersion of nutrients throughout samples. Five milliliter samples of either colostrum or milk were pipetted into preweighed acid washed 250 ml Phillips beakers. Total contents and beaker weights were taken. To each beaker, 20 ml of

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[1]Ivan Sorvall, Inc., Newton, CN.

[2]Searle Analytic, Inc., Southfield, MI.

concentrated (12 N) nitric acid and 7 ml of 70% perchloric acid were added and the samples were placed on hot plates for digestion. When the solution was almost completely evaporated and clear, digestion was considered to be complete. Samples were allowed to cool at room temperature. Samples were brought to a constant weight of 10 g using deionized distilled water. Subsamples of these solutions were taken and prepared for mineral analyses. Samples for calcium and magnesium determinations were diluted 1:10 with deionized distilled water and treated 1:2 with 10,000 ppm strontium chloride solution. Iron and copper required no dilution. Samples for zinc analysis were diluted 1:3 with deionized distilled water. Using artificially prepared serum as standards,[1] calcium, magnesium, iron, zinc and copper concentrations were determined with the aid of an atomic absorption spectrophotometer[2] at the following wavelengths: 422.7, 285.2, 248.3, 213.0 and 327.7 nm, respectively. Samples for phosphorus determination required a 1:19 dilution with deionized distilled water followed by analysis according to Gormorri (1942) modification of the

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[1]Artificial serum standards were prepared to contain the following:

Std. 1: 2000 ppm Na, 100 ppm K, 1.0 ppm Cu, 0.5 ppm Zn, 50 ppm Ca, 20 ppm Mg, 25 ppm P, and 1.0 ppm Fe.
Std. 2: 3000 ppm Na, 200 ppm K, 1.5 ppm Cu, 1.0 ppm Zn, 100 ppm Ca, 40 ppm Mg, 50 ppm P, and 2.0 ppm Fe.
Std. 3: 4000 ppm Na, 300 ppm K, 2.0 ppm Cu, 1.5 ppm Zn, 150 ppm Ca, 60 ppm Mg, 75 ppm P, and 3.0 ppm Fe.

[2]Instrumentation Laboratory, Inc., Lexington, MA.

Fiske-SubbaRow method (1946). These samples were treated with molybdate-sulfuric acid (MS) solution and Elon (p-methyl-amino-phenol sulfate) solution at levels 1:5:.5, respectively. Samples were incubated at room temperature for 45 minutes, and phosphorus concentrations were determined colorimetrically with the aid of a Stasar II spectrophotometer at a wavelength of 700 nm.

2. Serum Minerals. Serum samples were thawed at room temperature. Equal volumes of serum from each pig, by litter, were pipetted into acid washed glass test tubes and stored at 20C for analyses. Serum used for calcium, phosphorus, magnesium, copper and zinc analyses were deproteinized in a 1:4 dilution with 12.5% trichloroacetic acid (TCA). Serum and TCA were mixed using a vortex apparatus and allowed to settle. This mixture was centrifuged for 15 minutes at 2,000 rpm.[2] The supernate was decanted and placed in acid washed test tubes. Strontium chloride was added to a measured amount of decanted serum to be analyzed for calcium and magnesium. The final concentration of strontium in the samples was 10,000 ppm in order to overcome phosphate interference. Phosphorus determinations were performed as previously described. Elemental iron was determined by the method of Olson and Hamilin

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[1]Damon/IEC Division, Newton Hts., MA.

(1969). Serum was first deproteinized with 20% TCA and followed by incubation at 90C for 15 minutes in a water bath. This mixture was then centrifuged at 2,000 rpm, decanted and the serum was read undiluted. Serum mineral concentrations were determined using the same instruments and wavelengths as mentioned earlier.

3. Total Iodine Determinations. Previously frozen colostrum and milk were thawed, mixed by vigorous shaking and weighed into 25 ml zirconium crucibles.[1] Samples were prepared in triplicate according to the procedure by Convey et al. (1977). Total iodine content of samples was determined using a Polarographic Analyzer-174A[2] with a Houston XY 2000 recorder.[2]

Frozen tissue samples were thinly sliced without thawing. Using a Polytron,[3] homogenates were prepared by blending slices 1:2 with carbonate buffer,[4] pH 11.3. Samples were immediately refrozen to -20C and stored for total iodine analyses. The analysis procedure used was the same as that previously mentioned.

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[1]Sargent-Welch Scientific Co., Detroit, MI.

[2]Princeton Applied Research, Princeton, NJ.

[3]Brinkmann Instruments, Westbury, NY.

[4]Prepared by mixing 21.3 g sodium carbonate to 1 liter of deionized distilled water.

E. Plots

The statistical program for social science (SPSS) sub-program PLOT was used in conjunction with CDC-6500 computer to plot and draw figures. Colostrum and milk iodine thyroxine levels were plotted on the ordinate. Dietary iodine treatments were indicated on the abscissa.

F. Statistical Analyses

The data were subjected to a one-way analysis of variance using the Unequal-1 format on a CDC-6500 computer at the Michigan State University Computer Laboratory. Level of significance of differences between means was determined using the Bonferroni t-statistics test (Miller, 1966).

RESULTS AND DISCUSSION

A. Influence of Dietary Iodine on Gilts and Sows

1. Reproductive and Mothering Performance. Results of the effect of dietary iodine levels on first parity reproductive and mothering ability are shown in Table 3. Thirty days postbreeding, one female in treatment 3 was diagnosed nonpregnant. At approximately 50 days of gestation, zero, one, two and two females from treatments 1, 2, 3 and 4, respectively, returned to estrus. Abortions were observed in two sows fed 20 ppm iodine within 20 days of parturition. It appears that supplemental iodine at 20 ppm level prevents full-term pregnancy. In contrast, the remaining sows in that treatment group had extended gestation phases of 3.5 days longer than the normal 114 days, and surpassed the range of 112 to 115 days (Kenneth, 1953; Catchpole, 1969). This extended phase may be a result of the level of iodine in the diet since Rathnasabapathy, Lasley and Mayer (1958) indicated that litter size, first pregnancy versus subsequent pregnancy, has little, if any, influence on the length of gestation. Weiser and Zaitscheck (1933) reported that feeding 50 mg of iodine daily during gestation neither altered the length of

Table 3. The effect of dietary iodine levels on sow productivity (parity 1)

Treatment	1	2	3	4
I conc., ppm	0.0	0.2	2.0	20.0
Sows bred	7	7	7	7
Sows open[a]				
30 days post-breeding	0	0	1	0
50 days post-breeding	0	1	2	2
90 days post-breeding	0	1	2	4
Sows farrowed	7	6	5	3
Length of gestation, days	114.0	114.8	114.0	117.5
Total pigs/litter	11.6	7.3	9.4	5.5
Live pigs/litter	11.4	7.2	9.4	4.3
Pigs weaned/litter	9.9	6.8	9.0	3.8
Rebred	6	4	6	4
Deceased[b]	0	1	0	1

[a]Cumulative number of sows returning to estrus.

[b]Sows deceased during experiment.

gestation nor induced late gestation abortions. Due to the lack of pertinent experimental protocol in the Weiser and Zaitscheck (1933) experiment, it is difficult to compare and contrast differences reported. When Arrington and associates (1965) fed sows 2,500 ppm of iodine during the last 30 days of gestation, no deleterious effects were produced. This may be due to an inadequate length of time or stage of gestation necessary to physiologically influence gestation.

Analyses of variances were not performed on litter size because of the insufficient number of sows per treatment (N.C.R. 42, 1976). Largest litter sizes, total pigs and live pigs per litter were farrowed from those sows consuming the unsupplemented iodine diet (Table 3). Twenty parts per million of iodine appeared to depress the number of pigs born per litter. Ammerman and associates (1964) found that high levels of dietary iodine depressed the number of rat pups born per litter. At the 20 ppm iodine level, a litter of stillborn pigs was farrowed. Similar observations have been reported for calves born to cows consuming 10 times their iodine requirement (McCauley et al., 1972). Sows in treatments 1 and 3 farrowed and weaned litters equal to or greater than national averages of 9.5 and 7.3 pigs per litter, respectively (Bauman, 1964; Schwab, 1976). Substantially fewer pigs were weaned per litter from sows in treatment 4 (3.8) as compared to treatments 1, 2 and 3 (9.9, 6.8 and 9.0, respectively). However, the

reduction in litter size, during lactation, in treatment 4 is similar to that of the other treatments.

Approximately 30 days postlactation rebreeding, pregnancy diagnoses indicated that six, four, six and four sows from treatment groups 1, 2, 3 and 4, respectively, were bred (Table 3). One sow each from treatment groups 2 and 4 died of causes unrelated to iodine nutrition.

Reproductive and mothering ability from the second parity data are presented in Table 4. Only sows fed the unsupplemented diet and the .2 ppm iodine diet were evaluated; the remaining sows were removed from the experiment. Of the three sows bred in each treatment group, one sow from the .2 ppm iodine treatment group returned to estrus during the second trimester of pregnancy. The level of iodine did not influence the length of gestation in either treatment. Sows consuming the unsupplemented iodine diets produced and raised larger litters than sows fed .2 ppm iodine. However, each treatment was substantially higher in offspring farrowed and raised than those reported by Bauman (1964) and Schwab (1976).

2. Hematology. Hemoglobin, hematocrit, red blood cell and white blood cell counts are summarized in Table 5. Dietary iodine level did not appear to depress hemoglobin or hematocrit levels except in the 20 ppm iodine treatment group at weaning, and this returned to an adequate concentration by 30 days postlactation rebreeding. Across treatments there were declines in hemoglobin and hematocrit

REPORT OF LABORATORY EXAMINATION

Veterinary Diagnostic Laboratories
Department of Pathology
Michigan State University
East Lansing, Michigan 48824

Case No. 153281
Clinic No. none given
Received November 19, 1976
Reported December 1, 1976

Veterinarian Dr. D. J. Ellis
MSU Veterinary Clinics

Owner MSU Swine Farm
(Erickson)

Specimen 1 pig, 110-1 **Breed** Hampshire X **Age** 2 yr. **Sex** F

PRIVILEGED INFORMATION - NOT FOR PUBLICATION

HISTORY:

This 2-year-old Hampshire crossbred sow was submitted to the laboratory for euthanasia and examination. The only history available was that of hemorrhagic urinations.

GROSS LESIONS:

Externally, the sow appeared in good general condition. Internal examination revealed the mucosal surface of the urinary bladder to be hemorrhagic and necrotic throughout. Both ureters were approximately 2 to 3 times larger than normal and displayed a hemorrhagic mucosa throughout the entire length. The wall of the ureter appeared thickened and fibrous. Both kidneys appeared normal both in size and shape. The uterus was gravid and contained 1 fetus. Approximately 25% of the mucosal surface of the uterus displayed hemorrhagic lesions. No other changes were noted. Examination of the nasal turbinates revealed no abnormalities.

LABORATORY FINDINGS:

Microbiologic examination: Kidney and lung - Very heavy growth of a slow-growing nonhemolytic *Streptococcus sp.* (not a viridans nor a fecal *Streptococcus*, light growth of nonhemolytic *E. coli*. Bladder - Very heavy growth of nonhemolytic streptococci, lighter growth of nonhemolytic *E. coli*. Intestine - Heavy growth of nonhemolytic streptococci and nonhemolytic *E. coli*, and a probable *Enterobacter*. The *E. coli* was sensitive to chloramphenicol, furaltadone, gentamicin, neomycin, nitrofurazone, and polymyxin B. The nonhemolytic streptococci were sensitive to ampicillin, chloramphenicol, furaltadone, nitrofurazone, and penicillin.

Histopathologic examination: Microscopically, the kidneys appeared congested and displayed some edema within the medulla and dilatation of the collecting tubules. Some mild changes were seen within a few

continued...

Pathologist

REPORT OF LABORATORY EXAMINATION

Veterinary Diagnostic Laboratories
Department of Pathology
Michigan State University
East Lansing, Michigan 48824

Case No. 153281 cont.

Clinic No. _____

Received _____

Reported _____

Veterinarian **Owner**

Specimen _____ **Breed** _____ **Age** _____ **Sex** _____

PRIVILEGED INFORMATION - NOT FOR PUBLICATION

of the glomeruli. Focal areas of hemorrhage and necrosis were present within the ureter walls along with complete sloughing and degeneration of the mucosal epithelium. Large bacterial colonies were also present within the lumen of the ureters along with a heavy infiltration of inflammatory cells within the ureter walls. The bladder wall was also edematous and displayed an inflammatory cell infiltration. Necrosis and epithelial cell death was evident throughout. The uterus was hyperemic with areas of edema and destruction of the epithelial lining. The lungs were congested and displayed widespread alveolar edema. All other tissues appeared relatively normal.

CONCLUSIONS:

Severe acute cystitis with an ascending ureteritis.

A. D. Hall
jf
cc: Dr. Ellis
Records
Dr.Hogberg
Pathology

7309-1000.0
7310-1500.0

A. D. Hall
Pathologist

O-7822

Table 4. The effect of dietary iodine levels on sow reproduction (parity 2)

Treatment	1	2
I conc., ppm	0.0	0.2
Sows bred	3	3
Sows open[a]		
30 days post-breeding	0	0
50 days post-breeding	0	1
90 days post-breeding	0	1
Sows farrowed	3	2
Length of gestation, days	114	114
Total pigs/litter	12.3	9.5
Live pigs/litter	11.7	8.5
Pigs weaned/litter	8.0	7.0

[a]Cumulative number of sows returning to estrus.

Table 5. The influence of dietary iodine levels on sow hemoglobin, hematocrit, and red blood cell and white blood cell counts

Treatment	1	2	3	4	
I conc., ppm	0.0	0.2	2.0	20.0	EMS
50 days of gestation					
Hb,[a] g/dl	14.43(5)[e]	14.13(5)	14.92(6)	14.22(5)	1.98
Hct.,[b] %	46.80(5)	44.96(5)	43.96(6)	42.10(5)	27.29
RBC,[c] $10^6/mm^3$	6.75(6)	6.84(5)	6.77(6)	7.02(4)	.72
WBC,[d] $10^3/mm^3$	11.77(5)	8.92(5)	9.68(6)	9.96(5)	1.22
90 days of gestation					
Hb, g/dl	13.24(7)	13.34(7)	13.98(5)	14.82(7)	1.76
Hct., %	35.93(7)	37.46(7)	37.76(5)	40.25(7)	16.91
RBC, $10^6/mm^3$	6.45(7)	6.57(7)	7.21(5)	7.03(7)	.95
WBC, $10^3/mm^3$	9.32(7)	8.97(7)	10.04(5)	11.84(7)	7.04
Farrowing					
Hb, g/dl	13.14(1)	10.09(4)	11.19(1)	10.21(3)	4.73
Hct., %	34.90(1)	28.62(4)	31.63(1)	30.25(2)	40.31

Table 5 (continued)

Treatment	1	2	3	4	
I conc., ppm	0.0	0.2	2.0	20.0	EMS
Weaning					
Hb, g/dl	11.27(5)	11.21(6)	11.30(4)	8.6(2)	3.32
Hct., %	32.50(5)	32.80(6)	32.23(4)	23.80(2)	17.43
30 days post-breeding					
Hb, g/dl	12.39(3)	13.23(3)	13.34(5)	14.41(5)	2.29
Hct., %	37.17(3)	39.00(3)	38.24(5)	40.48(4)	22.47

[a]Hemoglobin; [b]Hematocrit; [c]Red blood cells;

[d]White blood cells; [e]Number of observations in parentheses.

levels, which are typical physiological responses occurring during ongoing gestation and lactation (Miller et al., 1961). Red blood cell counts were similar across treatment levels and were within the normal range for swine (Miller et al., 1961). White blood cell count at 50 days of gestation was numerically higher for the unsupplemented group in comparison to the other three treatments. At 90 days of gestation the white blood cell count of the 20 ppm iodine fed swine was non-significantly higher than those of other treatments.

Serum thyroxine concentrations of sows during gestation, lactation and postlactation rebreeding are shown in Table 6. Thyroxine concentrations at 50 days of gestation were lowest for swine in treatment 4. Depressions in thyroxine concentrations at the first three intervals were more pronounced in treatments 1, 2 and 3. At weaning, values were similar across treatments, and lower than those recorded at the previous interval, except for the .2 ppm I group. Wung et al. (1977) have reported similar trends of reduced serum thyroxine during lactation in sows and attributes it to the demand for thyroxine by the mammary gland during lactation. Since thyroxine was undetectable in colostrum and milk samples in the study reported herein, the demand of the mammary gland may in fact be for the iodine attached to the thyroxine molecule. They also reported that the level is not influenced by the number of nursing pigs. This could be further substantiated by the data in Tables 3 and 6 in this manuscript.

Table 6. The influence of dietary iodine levels on sow serum thyroxine concentrations

Treatment	1	2	3	4	
I conc., ppm	0.0	0.2	2.0	20.0	EMS
	Serum Thyroxine, ng/ml				
Intervals					
50 days of gestation	43.4(7)[a]	47.9(7)	46.9(7)	36.8(7)	82.0
90 days of gestation	27.0(7)	33.5(7)	33.7(7)	35.7(6)	51.5
Farrowing	15.2(6)	16.8(4)	18.0(4)	27.5(2)	38.6
Weaning	13.5(7)	19.2(6)	16.2(5)	16.4(1)	25.1
30 days post-lactation rebreeding	---(0)	36.8(4)	40.4(5)	42.8(3)	49.6

[a]Number of observations in parentheses.

Figure 3 depicts the physiological response of thyroxine at particular intervals during the study. Treatments 2 and 3 maintained near identical serum thyroxine concentrations during the study. The unsupplemented iodine treatment group's serum thyroxine levels decreased as the study progressed. Since there were no serum thyroxine values recorded at the postlactation rebreeding interval for this group, there was a slight distortion of this particular curve. The thyroxine concentrations at the postlactation rebreeding interval are similar to those recorded at the 50 day interval. Overall, the physiological concave response curves of serum thyroxine indicate probable demands for fetal development and by the mammary gland at the onset and during lactation.

3. Gross pathology. Periodic observation of the experimental herd was maintained in order to detect possible symptoms related to iodine disorders. During both parities of the experiment, goiter was not visibly apparent, nor was it palpable. The characteristic signs of iodine deficiency in swine, as described by Hart and Steenbock (1918), Kalkus (1920) and Welch (1928), were not evident in the experimental herd. Gross pathological signs described for other livestock and laboratory animals fed diets considered to be deficient or toxic in their iodine content were not seen.

Sow weight changes during gestation, lactation and rebreeding are presented in Table 7. Significant

Figure 3. Effect of iodine intake and stage of production on sows' serum thyroxine concentration.

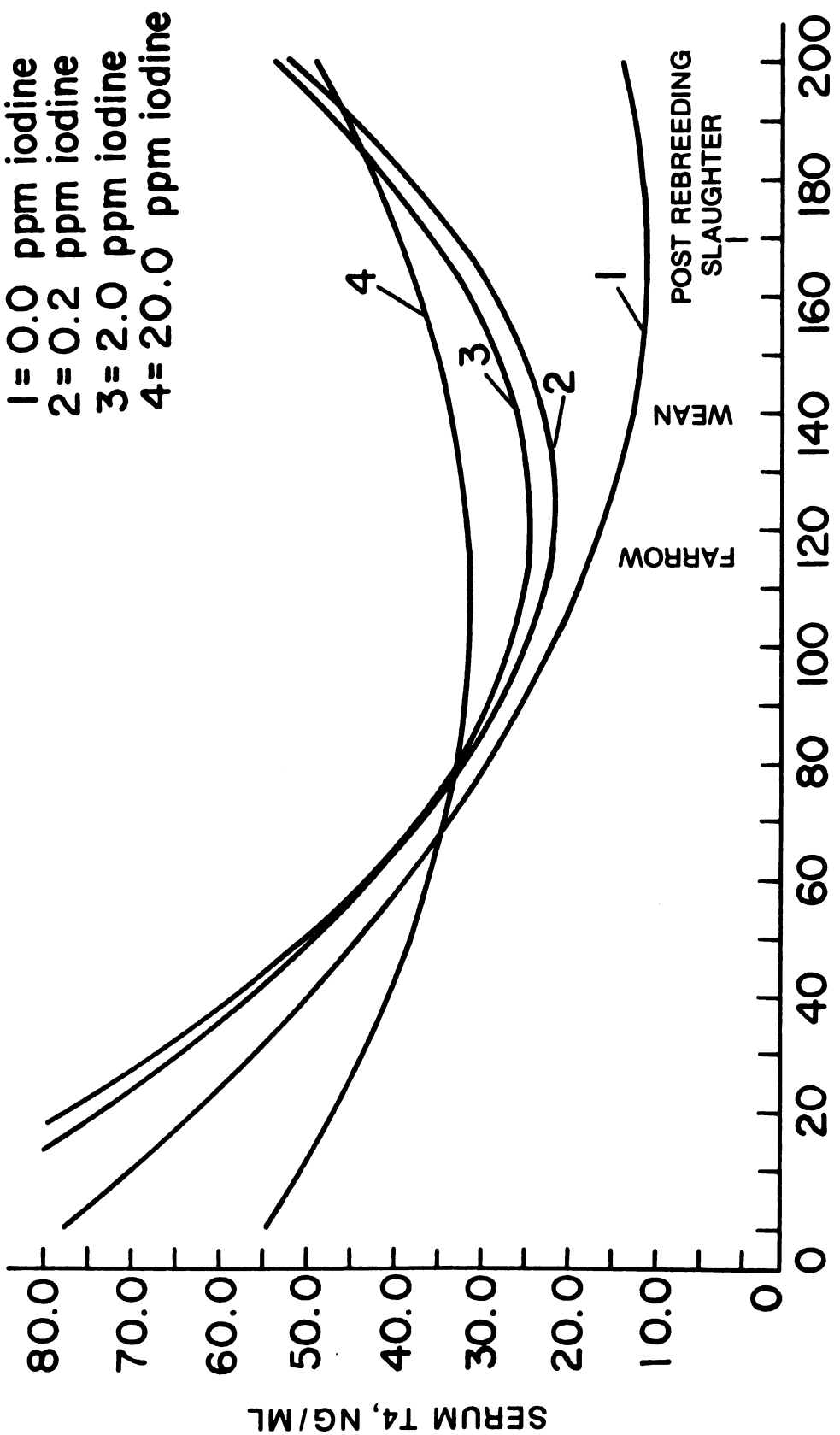
1= 0.0 ppm iodine
2= 0.2 ppm iodine
3= 2.0 ppm iodine
4= 20.0 ppm iodine
SERUM T4, NG/ML
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
20
40
60
80
100
120
140
160
180
200
DAYS
FARROW
WEAN
POST REBREEDING SLAUGHTER
1
2
3
4

Figure 3

Table 7. Sow body weight changes as influenced by dietary iodine

Treatment	1	2	3	4	
I conc., ppm	0.0	0.2	2.0	20.0	EMS
Weight, kg					
10 days gestation	166.4(7)[a]	167.5(7)	169.1(7)	170.9(7)	529.8
50 days gestation	183.6(7)	184.3(7)	185.0(7)	183.4(7)	437.8
Weight change, 10 to 50 days	17.2(7)	16.8(7)	15.9(7)	12.4(7)	84.0
90 days gestation	187.7(7)	189.5(7)	190.8(7)	186.4(7)	437.3
Weight change, 10 to 90 days	21.3(7)	21.9(7)	21.7(7)	15.4(7)	177.5
Farrow	191.2(7)	206.8(6)	198.8(5)	190.0(4)	366.3
Weight change, 10 days to farrow	24.8(7)	35.5(6)	33.4(5)	28.6(4)	142.2
Wean	197.8(7)	217.0(6)	203.7(5)	205.5(1)	239.4
Weight change, farrow to wean	6.6(7)	10.1(6)	4.8(5)	17.3(1)	65.3
30 days post-lactation rebreeding	168.5(3)	192.0(4)	201.9(5)	183.1(5)	180.6
Weight change weaning to 30 days post-lactation rebreeding	-20.8[b](3)	-21.4[b](3)	-0.3(3)	-19.1[b](1)	263.5

[a]Number of observations in parentheses.

[b]Significantly greater than least value ($P<.01$).

differences in body weight changes were not detected until postlactation rebreeding. Swine fed 20 ppm of iodine tended to gain less weight from 10 to 50 days and from 10 to 90 days of gestation than those in other treatment groups. Swine fed .2 and 2 ppm iodine diets tended to gain more weight between 10 days of gestation and farrowing than those fed 0 and 20 ppm of iodine. At the final interval, sows in treatments 1, 2 and 4 lost significantly ($P<.01$) more weight than those in treatment 3.

Salmon-Legagneur (1965) reported that nonpregnant sows gained less weight than those pregnant fed the same quantity of ration. Hence, less body weight gain in treatment 4 during gestation may be a result of sows and gilts that may have resorbed or aborted their feti. Hitchcock (1973) reported that high levels of thyroprotein in the lactation ration of sows resulted in substantial losses of weight. It is probable that the numerically heavier weight gains of sows in the 20 ppm iodine treatment group was due to the *ad libitum* feeding regime followed and with so few nursing pigs (Table 3).

4. Organ and Gland Weights. Actual and relative organ and gland weights of sows receiving different levels of dietary iodine are summarized in Table 8. Thyroid, adrenals, kidneys, liver and spleen were not significantly affected by dietary iodine. Sows in treatment 1 and those in treatments 3 and 4 had significantly ($P<.01$ and $P<.05$, respectively) heavier hearts than those in treatment 2.

Table 8. Actual and relative organ and gland weights of sows receiving different levels of dietary iodine

Treatment	1	2	3	4	
I conc., ppm	0.0	0.2	2.0	20.0	
No. of sows	3	4	7	4	EMS
Body wt., kg	168	192	190	182	239
Organs and Glands					
Thyroid, g	22.364(1)[a]	14.918(4)	19.227(6)	22.133(4)	29.268
% of body wt.	.013	.008	.010	.012	.000009
Heart, g	595.000[b]	490.750	550.286[c]	562.800[c]	5215.704
% of body wt.	.333[b]	.253	.290[c]	.310[c]	.001
Adrenals, g	7.541	8.512	8.716	10.829	4.749
% of body wt.	.004	.005	.005	.006	.000001
Kidneys, g	474.333	444.000	476.714	482.750	8222.775
% of body wt.	.282	.232	.251	.266	.022
Liver, kg	1.994	2.011	1.942	2.107	.066
% of body wt.	1.182	1.052	1.029	1.157	.021
Spleen, g	230.167	276.500	271.429	319.250	2864.688
% of body wt.	.137	.144	.144	.176	.00008

[a]Number of observations for thyroid glands in parentheses.
[b]P<.01.
[c]Significantly greater than least value (P<.05).

The relative weights of thyroids from sows in treatment groups 1 and 4 were numerically heavier than thyroids from treatment groups 2 and 3. The relative weights of kidneys and liver displayed similar trends to those of the thyroid. The relative weight of the adrenals and spleen tended to increase with the level of dietary iodine. Newton et al. (1974) found that 50 ppm of iodine substantially increased adrenal gland weight, which they associated with the stress affiliated with high dietary iodine. Earlier work by Gross (1962) indicated that enlargements of adrenal glands is a direct result of increased output of adrenocorticoid hormones, which would be increased under stress. Newton and Clawson (1974) found that increasing dietary iodine levels in growing pigs increased the weight of the thyroid gland. It is possible that non-significant relative thyroid weight differences across treatments were partially due to atmospheric iodine. Caurer (1933) reported that atmospheric iodine prevented signs of iodine deficiencies in humans when dietary iodine was very minimal. It is possible that non-significant relative thyroid differences across treatments may be due to sows' enhanced metabolic efficiency of nutrients during gestation. The iodine found in water and naturally presented in the diet, as well as that in the air, may have prevented iodine deficiency.

5. Histopathology. Histopathological examinations indicated that heart, liver, spleen, kidney and adrenal glands of all sacrificed sows were normal. In light of the elevated thyroid weights in the 0 and 20 ppm iodine treatment groups (Table 8), differences in thyroid follicle cell size might have been expected. There appeared to be a tendency toward larger follicles in the thyroid glands of sows consuming 20 ppm of iodine (Figures 4, 5 and 6). However, this finding was not consistent; some sows fed 20 ppm of iodine had follicle cell sizes similar to those of sows fed .2 and 2 ppm of iodine (Figures 4, 5 and 7). Viewed under 250 power, the epithelial lining of the thyroids (Figure 8) from some sows consuming 20 ppm of iodine was much thinner than the .2 ppm iodine group (Figure 9). Andrews et al. (1948) reported that the epithelial height of the follicle cell was less for growing pigs receiving iodine than those receiving no supplemental iodine. Even though epithelial cell heights differed in the study reported herein, nonconclusive evidence can be ascertained based on relative thyroid weights (Table 8), nor can serum thyroxine values (Table 4) substantiate iodine toxicity in sows fed 20 ppm iodine.

6. Tissue Iodine Concentration. The iodine contents of sow organs and tissues are summarized in Table 9. Sows fed 0 ppm of iodine had substantially less iodine in their thyroids than thyroids of sows in the other treatment groups. The concentration of iodine in the thyroids of

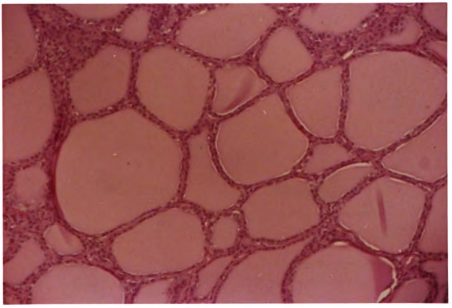

Figure 4. Photomicrograph of thyroid of sow consuming .2 ppm of iodine (100X).

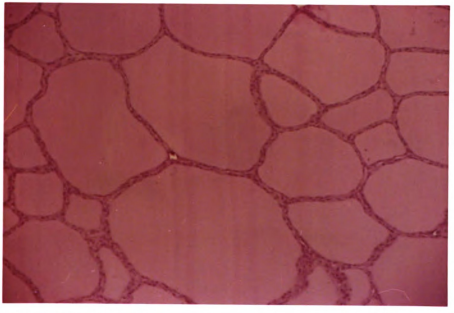

Figure 5. Photomicrograph of thyroid of sow consuming 2.0 ppm of iodine (100X).

Figure 6. Photomicrograph of thyroid of sow consuming 20.0 ppm of iodine (100X).

Figure 7. Photomicrograph of thyroid of sow consuming 20.0 ppm of iodine (100X).

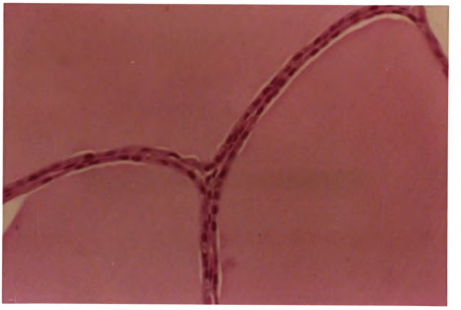

Figure 8. Photomicrograph of thyroid of sow consuming 20.0 ppm of iodine (250X).

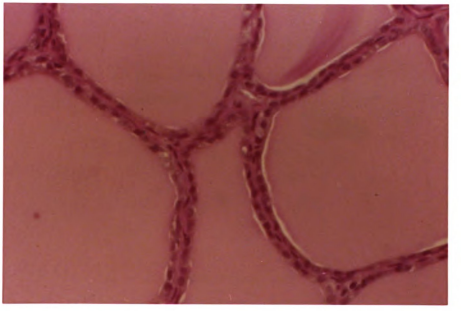

Figure 9. Photomicrograph of thyroid of sow consuming .2 ppm of iodine.

Table 9. Iodine concentrations in tissues and organs of sows fed varying levels of iodine (wet basis)

Treatment	1	2	3	4	
I conc., ppm	0.0	0.2	2.0	20.0	EMS
Iodine, ppm					
Thyroid	495.99(3)[a]	1611.30(5)	1688.60(4)	2889.60(5)	1333083.68
Heart	4.76(4)[b]	3.35(5)	1.26(5)	1.84(5)	2.73
Adrenals	13.35(1)	6.13(3)	4.21(3)	6.16(4)	11.22
Kidneys	4.47(4)	1.90(5)	4.71(6)	4.95(5)	8.72
Liver	.51(4)	2.42(5)	2.34(5)	1.174(5)	6.66
Spleen	19.91(4)	16.80(5)	4.29(5)	3.31(4)	440.92

[a]Number of observations in parentheses.

[b]Significantly greater than least value ($P<.05$).

the .2 and 2 ppm of iodine groups was essentially the same. The increased intake of iodine in treatment 4 resulted in a higher concentration of iodine in the thyroid glands. No significant differences were detected in the adrenal, kidney, liver, spleen and trapezius across treatments. Although there is considerable variation in iodine content in these glands and tissues, statistically significant differences were not found. This is due to the wide variation in iodine content of tissues within each treatment group. Significant differences were detected in the heart. Sows in the unsupplemented group contained a significantly ($P<.05$) higher level of iodine in heart tissue than those in treatment group 3.

7. Mineral Concentration of Colostrum and Milk. The influence of dietary iodine intake levels on colostrum and milk mineral concentrations is summarized in Table 10. The calcium (Ca) level in colostrum and milk was similar across treatments at the respective intervals and increased in concentrations with the duration of lactation. These values are nearly identical to those reported by Miller (1967). Colostrum phosphorus (P) concentrations were significantly ($P<.01$) greater from sows consuming .2 ppm of iodine than those fed 20 ppm of iodine, and significantly ($P<.05$) higher than those consuming .2 ppm of iodine. Even though significant differences were found, the range in colostrum P lies within the range reported by Miller (1967), Jylling (1959) and Travnicek (1960). Two and four

Table 10. The influence of dietary iodine levels on colostrum and milk mineral concentrations

Treatment	1	2	3	4	
I conc., ppm	0.0	0.2	2.0	20.0	EMS
Calcium, %					
Colostrum	.08(7)[a]	.10(5)	.08(5)	.06(2)	.0003
2-week	.21(6)	.20(6)	.21(5)	.22(2)	.0002
4-week	.24(7)	.24(5)	.25(5)	.26(1)	.0008
Phosphorus, %					
Colostrum	.12	.13[c,d]	.11	.10	.0001
2-week	.15	.14	.15	.15	.0002
4-week	.17	.17	.18	.18	.0009
Magnesium, %					
Colostrum	.016	.019	.020[b]	.019	.000003
2-week	.022	.024	.022	.025	.000007
4-week	.026	.029	.029	.029	.000015
Iron, ppm					
Colostrum	1.87	1.92	2.22	2.05	.085
2-week	1.48	1.23	1.44	1.59	.042
4-week	1.40	1.54	1.45	1.95	.126
Copper, ppm					
Colostrum	2.19	2.46	4.17[c]	3.72[b]	.492
2-week	1.37	1.25	1.24	1.19	.037
4-week	1.16(7)	1.31(4)	1.30(5)	1.65(1)	.025
Zinc, ppm					
Colostrum	7.55	8.61	14.52[e,f]	11.64[b,d]	1.577
2-week	5.68	6.04	5.66	5.48	.667
4-week	6.76	6.64	7.12	8.23	1.134

[a]Values in parentheses are number of observations evaluated.

[b]Significantly greater than least value ($P<.05$).

[c]($P<.01$).

[d]Significantly greater than least 2 values ($P<.05$).

[e]($P<.01$).

[f]Significantly greater than all other values ($P<.05$).

week mineral P levels were not influenced by dietary iodine. As lactation continued, the concentration of P also increased, following a similar trend as outlined by Miller (1967). Feeding 10 times the iodine requirement, 2 ppm of iodine, resulted in significantly ($P<.05$) more magnesium (Mg) present in colostrum than that from unsupplemented sows. The levels of Mg recorded to the hundredth of a percent by Miller (1967) and Guegen and Salmon-Legagneur (1959) are similar to those reported in Table 10. The addition of iodine to diets of gestating and lactating sows did not statistically influence the concentration of iron (Fe) in colostrum or milk. As lactation progressed, milk Fe declined in treatments 1 and 3, whereas the Fe content of milk from sows in treatments 2 and 4 increased from 2 to 4 weeks. Milk copper (Cu), like iron, a divalent cation, has been previously described as not being influenced by lactation dietary Cu level (Pond and Houpt, 1978). In the study reported herein the concentration of Cu in colostrum is significantly ($P<.01$) greater from sows consuming 2 ppm of iodine and significantly ($P<.05$) greater from sows fed 20 ppm of iodine than those consuming 0 ppm of iodine. At the two-week interval, milk Cu decreased with increasing levels of dietary iodine, while at four weeks this trend was reversed. Feeding 2 ppm of iodine to sows significantly ($P<.05$) enhanced zinc (Zn) concentrations in colostrum in comparison to other feeding levels of iodine. At that level, Zn concentrations were significantly ($P<.01$) superior to Zn colostrum concentrations from sows fed 0 and

.2 ppm of iodine. Colostrum Zn from the 20 ppm iodine fed sows was significantly ($P<.01$ and $P<.05$) greater compared to the Zn concentration from the 0 and .2 ppm, respectively, iodine treatment groups. At two and four week samplings, milk Zn levels were similar across treatments. Values reported are comparable to those reported by Miller (1967). It appears that feeding 2 ppm of iodine (10 times the requirement level) during gestation influences the concentration of Mg, Fe, Cu and Zn in colostrum.

Table 11 is a summary of the iodine content in colostrum and milk as influenced by dietary iodine level. Colostrum iodine levels were the same for 0 and .2 ppm of iodine treatment groups, increasing two-fold at the 2 ppm iodine level and peaking at the 20 ppm iodine level, which was significantly ($P<.01$) higher than all other treatment groups. Two weeks after parturition the 2 ppm treatment group's milk contained significantly ($P<.01$) more iodine than the .2 ppm iodine group and significantly ($P<.05$) greater than the 0 and .2 ppm iodine groups. The iodine content of milk from sows consuming 20 ppm of iodine was significantly ($P<.01$) higher than all other treatment groups. The four week milk measurements were significantly ($P<.01$) greater from sows consuming 2 ppm of iodine in their diets in comparison to those fed 0 and .2 ppm of iodine. Again, the concentration of iodine in milk from the 20 ppm iodine group was significantly ($P<.01$) higher than the other groups. Hemken et al. (1972) found a similar response in lactating dairy cows fed graded levels of

Table 11. The influence of supplemental dietary iodine level on sow colostrum and milk iodine level

Treatment	1	2	3	4	
I conc., ppm	0.0	0.2	2.0	20.0	EMS
			Iodine, µg/ml		
Interval					
Colostrum	.44(5)[a]	.45(6)	1.05(5)	4.09(3)[f]	.498
2-week	.81(7)	.47(5)	1.62(5)[c,d]	6.51(2)[f]	.307
4-week	.37(7)	.36(6)	.79(5)[e]	4.40(1)[f]	.035

[a]Values in parentheses are number of observations evaluated.

[b]Significantly greater than least value ($P<.05$).

[c]($P<.01$).

[d]Significantly greater than least 2 values ($P<.05$).

[e]($P<.01$).

[f]Significantly greater than all other values ($P<.01$).

dietary iodine. The concentration of iodine in milk peaked at two weeks; at four weeks, iodine concentrations decreased to levels similar to those recorded in colostrum. In contrast to human beings and dairy cattle, iodine concentrations were greatest in colostrum and decreased with ongoing lactation (Salter, 1950; Lewis and Ralston, 1951).

At each stage of lactation sow milk iodine values were linearly related to supplemental dietary iodine levels ($r = .99$) (Figure 10). Regression equations of milk iodine levels (y in mcg/ml) on supplementary dietary iodine levels (x in ppm) for initial, 2-week and 4-week milk samples were $y = .21X + .52$, $y = .29X + .74$ and $y = .12X + .38$, respectively.

B. Influence of Dietary Iodine on Baby Pigs

1. Performance. Data for body weight changes of baby pigs from the first parity are summarized in Table 12. Mean birth weights of pigs from sows fed either the iodine requirement or 10 times it, farrowed significantly ($P<.01$) heavier pigs than sows fed the unsupplemented diet. This may be a reflection of the large litter size farrowed by sows fed unsupplemented diets (Table 3). It has been suggested by Krider and Carroll (1971) that there exists an inverse relationship between litter size and mean pig weight. Hart and Steenbock (1918), Kalkus (1920) and Welch (1928) reported that offspring born to sows fed diets unsupplemented with iodine produced weak offspring. In the experiment reported herein, baby pigs were very

Figure 10. Influence of dietary iodine levels on colostrum and milk iodine (total) concentrations.

---------- farrow samples

—.—.—.—.—. 2-week samples

———————— wean samples

Table 12. Baby pig body weight changes as influenced by dietary iodine (parity 1)

Treatment	1	2	3	4	
I conc., ppm	0.0	0.2	2.0	20.0	EMS
Live pig birth weight, kg	1.189(62)[e]	1.420[b](36)	1.465[b](39)	1.419[b](12)	.067
2-week weight, kg	3.364(62)	4.403[b](36)	4.272[b](39)	4.877[b](12)	.868
Gain, kg birth to 2 weeks	2.174(62)	2.982[b](36)	2.807[b](39)	3.458[b](12)	.673
21-day adjustment weight, kg	4.585(62)	6.631[b](36)	5.814[a](39)	6.373[a](12)	.561
Weaning weight, kg	6.218(62)	8.605[d](36)	7.497[b](39)	8.046[b](12)	3.052
Gain, kg birth to weaning	5.028(62)	7.185[d](36)	6.032[b](39)	6.627[b](12)	2.775

[a]Significantly greater than least value ($P<.05$).

[b]($P<.01$).

[c]Significantly greater than least 2 values ($P<.05$).

[d]($P<.01$).

[e]Number of observations in parentheses.

mobile and aggressive to nurse, but at two weeks old, offspring in treatments 2, 3 and 4 weighed significantly ($P<.01$) more than those in treatment 1. A similar trend was found in body weight gain from birth to two weeks of age. Offspring in treatment 4 gained significantly ($P<.05$) more weight than offspring in treatments 1 and 3. This may be due to the fewer number of pigs per litter in treatment 4 than in treatments 1 and 3 (4.3 vs. 11.4 and 9.4, respectively). At the 20 ppm level iodine does not appear to interfere with lactation. Adjusted 21 day body weights were found to be significantly ($P<.01$) heavier for pigs fed the requirement level than the unsupplemented group. Offspring in treatments 3 and 4 were significantly ($P<.05$) heavier than the unsupplemented iodine treatment group. The mean weaning weights of pigs in treatment 2 were significantly ($P<.01$) heavier than those in treatments 1 and 3. Body weight gain from birth to weaning was significantly ($P<.01$) more for pigs in treatment 2 than those in treatments 1 and 3. Pigs in treatment 4 also gained significantly ($P<.01$) more weight than those in treatment 1. Reversal in the order of body weight gains between treatments 2 and 4 at the 2-week and weaning intervals may imply that high iodine levels may increase milk production initially, but cause a more rapid decline in milk production with ongoing lactation.

The second parity offspring weight changes are summarized in Table 13. Progeny from sows fed the iodine requirement, .2 ppm, weighed significantly ($P<.01$) more

Table 13. Baby pig body weight changes as influenced by dietary iodine (parity 2)

Treatment	1	2	
I conc., ppm	0.0	0.2	EMS
Live pig birth weight, kg	1.314(35)[a]	1.555[b](17)	.110
2-week weight, kg	3.088(16)	4.676[b](11)	.987
Gain, kg birth to 2 weeks	1.746	2.966[b]	.883
Weaning weight, kg	6.760(14)	7.835(12)	1.830
Gain, kg birth to weaning	5.447	6.138	1.489

[a]Number of observations in parentheses.

[b]Significantly greater than other treatment groups ($P < .01$).

at birth than those born to sows in the unsupplemented group. At each interval during the nursing phase, pigs in treatment 2 weighed significantly ($P<.01$) greater than treatment 1 pigs. Body weight gains were significantly ($P<.01$) larger for the iodine supplemented group from birth to two weeks. Overall body weight gains were greater for offspring in treatment 2. Only numerical differences in gain between the two treatment groups were noted for parity 2, in contrast to significant differences found in parity 1 (Table 12). This may be a result of similar litter sizes between the two treatment groups in parity 2, whereas litter sizes in parity 1 were considerably different. However, these differences in gain may be in response to dietary iodine level as reported in the classical investigations by Hart and Steenbock (1918), Welch (1928) and Kalkus (1920).

2. Hematology. Hemoglobin and hematocrit values for first parity offspring are summarized in Table 14. At birth hemoglobin values decreased with increasing levels of iodine. Hemoglobin values of pigs in treatment groups 2, 3 and 4 at the 2-week interval were significantly ($P<.01$) greater than those in the unsupplemented group. At weaning, hemoglobin values followed a similar trend as seen at birth. The depression in hemoglobin values at birth and weaning coincide with the depressed hemoglobin level and liver iron stores found by Newton and Clawson (1974) for growing pigs fed high levels of dietary iodine.

Table 14. The effect of dietary iodine levels on baby pigs' hemoglobin and hematocrit (parity 1)

Treatment	1	2	3	4	
I conc., ppm	0.0	0.2	2.0	20.0	EMS
Birth					
No. of pigs	74	45	46	17	
Hb,[a] g/dl	9.92	9.76	9.14	8.77	4.63
Hct,[b] %	28.74	29.05	27.62	28.89	28.18
2 weeks					
No. of pigs	57	35	36	10	
Hb, g/dl	9.95	11.21[d]	10.99[d]	11.60[d]	1.76
Hct, %	31.79	33.01	32.58	34.44[c]	8.73
Wean					
No. of pigs	57	36	37	11	
Hb, g/dl	10.32	10.32	10.03	9.97	1.80
Hct, %	31.39	31.57	31.25	31.23	13.82

[a]Hemoglobin.

[b]Hematocrit.

[c]Significantly greater than least value ($P<.05$).

[d]($P<.01$).

The significantly higher hemoglobin levels at two weeks for baby pigs in treatments 2, 3 and 4 can be associated with the repletion of liver iron stores, because of the iron dextran injections given three days after birth. Newton and Clawson (1974) found that oral or parenteral iron improved hemoglobin levels in growing pigs on high iodine diets. Hematocrit levels were similar across treatments at birth and weaning. Hematocrit, like the hemoglobin, exhibited significantly ($P<.05$) higher values for pigs in treatment group 4 at the 2-week interval.

The effects of dietary iodine levels on second parity offspring hemoglobin and hematocrit levels are presented in Table 15. Hemoglobin levels at all three evaluation periods were similar across treatments. The trend of slightly elevated 2-week hemoglobin levels over those of birth and weaning is due to the iron dextran administration. Hematocrit values, like hemoglobin, were similar across treatments and not influenced by level of maternal dietary iodine.

Serum T_4 concentrations of offspring as influenced by dietary iodine levels are reported in Table 16. Thyroxine concentrations were similar across treatments at birth and at two weeks. Significant ($P<.01$ and $P<.05$) T_4 differences were detected in pigs at weaning consuming 2 and .2 ppm, respectively, of iodine in comparison to those in the 0 ppm iodine group (Figure 11).

Table 15. The effect of dietary iodine levels on baby pigs' hemoglobin and hematocrit (parity 2)

Treatment	1	2	
I conc., ppm	0.0	0.2	EMS
Birth			
No. of observations	32	9	
Hb,[a] g/dl	10.76	10.85	2.88
Hct,[b] %	33.72	33.17	28.45
2 weeks			
No. of observations	12	9	.59
Hb, g/dl	11.04	11.18	.59
Hct, %	36.28	35.33	5.70
Wean			
No. of observations	12	8	
Hb, g/dl	10.72	10.55	1.18
Hct, %	33.12	34.13	10.34

[a]Hemoglobin.

[b]Hematocrit.

Table 16. The influence of dietary iodine levels on baby pigs' serum thyroxine concentrations (parity 1)

Treatment	1	2	3	4	
I conc., ppm	0.0	0.2	2.0	20.0	EMS
		Serum Thyroxine, ng/ml			
Sampling Interval					
Birth	64.5(62)[a]	62.1(32)	72.5(39)	67.5(18)	293.4
2 weeks	49.7(61)	51.8(35)	53.3(38)	53.3(11)	135.07
Wean	37.4(58)	47.4[b](35)	48.6[c](34)	38.8(10)	147.1

[a]Number of observations in parentheses.

[b]Significantly greater than least value ($P<.05$).

[c]($P<.01$).

Figure 11. Effect of iodine intake on serum thyroxine levels of offspring.

---------- Farrow

—.—.—.—.—. 2-week

———————— Wean

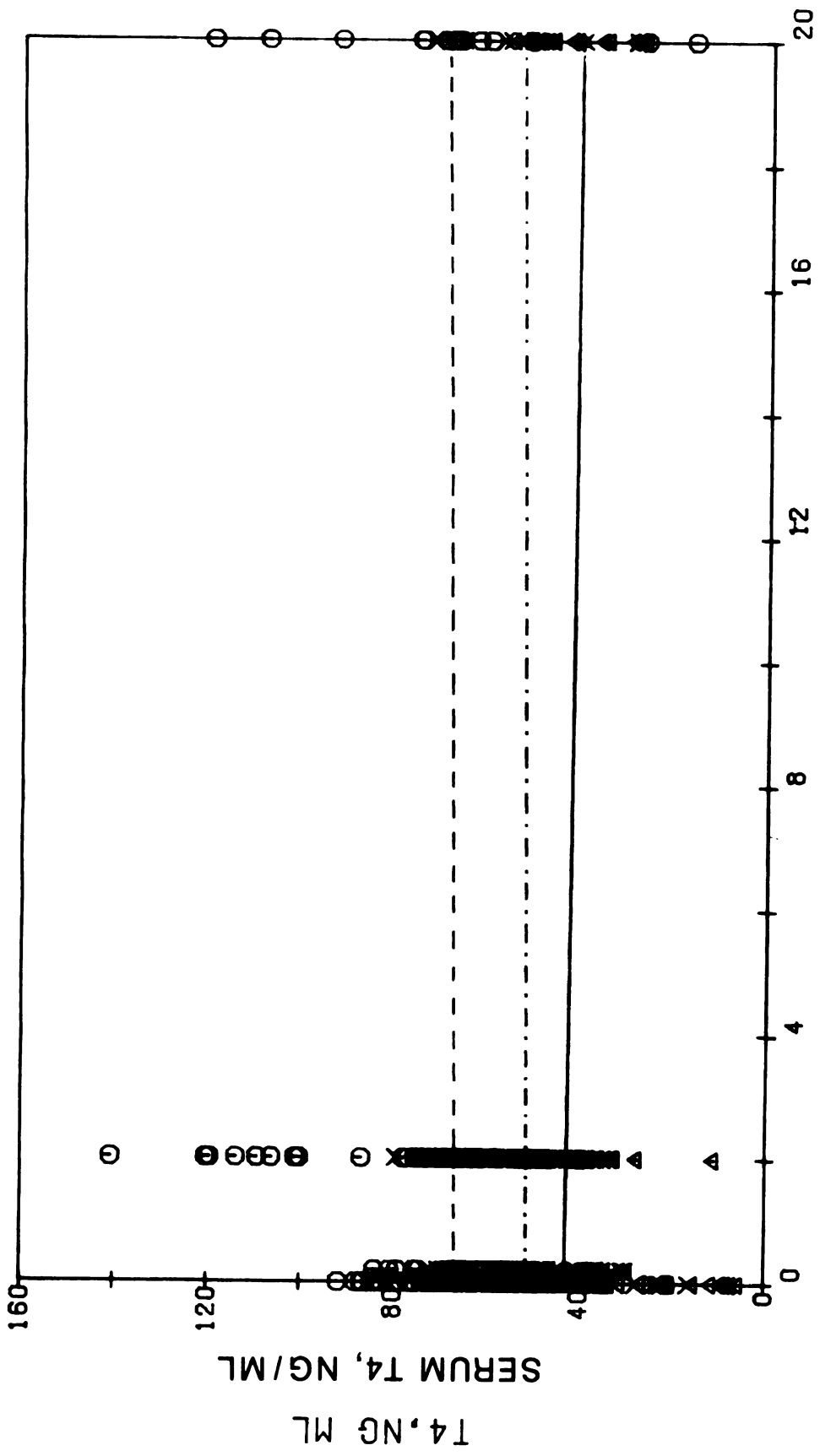
T4,NG ML
SERUM T4, NG/ML
160
120
80
40
0
0
4
8
12
16
20
PPM IODINE IN RATION

Figure 11

3. Gross Pathology. Newborn pigs, from either parity, born to sows and gilts that were fed no supplemental iodine displayed no gross pathological signs. This is in variance with the classical iodine deficiency signs described by Hart and Steenbock (1918), Kalkus (1920) and Welch (1928) and, more recently, by Sihombing et al. (1974) for growing pigs. During the nursing phase young pigs in the unsupplemented iodine groups in either parity appeared to possess the same characteristics as those in the supplemented groups. Goiter was neither observed nor palpable at any time during this study. The high level of iodine feeding to sows and gilts did not influence the appearance of their offspring either at birth or during the nursing phase.

4. Organ and Gland Weights. Actual and relative organ and gland weights of day-old swine are summarized in Table 17. The influence of maternal iodine intake did not significantly affect the actual or relative weights of organs and glands of baby pigs in parity 1. Numerically, relative weights of thyroid glands from baby pigs from the 0 ppm iodine and 20 ppm iodine groups were heavier than those in other treatments. Relative spleen weights displayed a similar trend. The control group, .2 ppm of iodine, had lighter weight hearts and adrenals. Relative weights of kidneys and liver were less for baby pigs in the 0 and 20 ppm iodine groups.

Table 17. Actual and relative organ and gland weights of day-old pigs as influenced by maternal dietary iodine levels (parity 1)

Treatment	1	2	3	4	
I conc., ppm	0.0	0.2	2.0	20.0	EMS
No. of pigs	7	6	5	4	
Body wt., kg	1.186	1.239	1.121	1.039	.062
Organs					
Thyroid, g	.256	.192	.223	.253	.005
% of body wt.	.022	.016	.020	.025	.00004
Heart, g	8.691	8.726	8.749	7.740	2.882
% of body wt.	.731	.726	.885	.771	.020
Adrenals, g	.351	.325	.333	.307	.005
% of body wt.	.030	.027	.031	.031	.00005
Kidneys, g	9.023	9.626	9.294	7.139	5.610
% of body wt.	.758	.792	.825	.670	.025
Liver, g	30.270	34.298	32.492	28.506	80.099
% of body wt.	2.545	2.775	2.884	2.652	.180
Spleen, g	1.195	1.133	1.039	1.108	.071
% of body wt.	.099	.094	.093	.111	.00003

The second parity actual and relative organ and gland weights of day-old swine are presented in Table 18. Relative weights of thyroid, heart, liver and spleen were numerically heavier for baby pigs born to sows fed diets unsupplemented with iodine, whereas adrenals and kidneys weighed less. Thyroid, heart, kidneys and spleen relative weights followed the same trend as found in parity 1 (Table 17).

The actual and relative organ and gland weights of weaned swine from parity 1 are presented in Table 19. Organ and gland weights were not significantly influenced by the level of dietary iodine. Relative thyroid weights increased slightly with the increasing level of dietary iodine. Heart, kidney, liver and adrenal glands from pigs in the control group weighed less than those from treatment groups. Liver and adrenals were heaviest for pigs in the 20 ppm of iodine treatment group. Spleens and kidneys weighed relatively more for pigs in the 2 ppm of iodine treatment.

The influence of iodine on weaned swine organs and gland weights, actual and relative, is presented in Table 20. The relative weights of the thyroid, heart, adrenals and spleen were numerically heavier for swine in the unsupplemented iodine group. The heart, adrenal and spleen weights show the same trend as in parity 1 (Table 19).

Table 18. Actual and relative organ and gland weights of day-old pigs as influenced by maternal dietary iodine levels (parity 2)

Treatment	1	2	
I conc., ppm	0.0	0.2	EMS
No. of pigs	3	2	
Body wt., kg	1.51	1.387	.019
Organs			
Thyroid, g	.223	.244	.004
% of body wt.	.020	.017	.00002
Heart, g	7.801	8.758	1.439
% of body wt.	.674	.632	.002
Adrenals, g	.231	.329	.005
% of body wt.	.020	.023	.00005
Kidneys, g	8.118	10.300	8.169
% of body wt.	.706	.731	.036
Liver, g	30.568	34.878	36.328
% of body wt.	2.640	2.512	.111
Spleen, g	1.111	.968	.058
% of body wt.	.098	.069	.00003

Table 19. Actual and relative organ and gland weights of weaned pigs as influenced by maternal dietary iodine levels (parity 1)

Treatment	1	2	3	4	
I conc., ppm	0.0	0.2	2.0	20.0	EMS
No. of pigs	7	5	6	3	
Body wt., kg	6.105	8.284	7.196	6.900	1.985
Organs					
Thyroid, g	.519	.781	.621	.695	.029
% of body wt.	.008	.009	.009	.010	.000003
Heart, g	34.435	41.342	39.539	35.377	48.061
% of body wt.	.563	.499	.559	.518	.002
Adrenals, g	.761	.680	.760	.757	.012
% of body wt.	.012	.008	.012	.013	.000009
Kidneys, g	30.396	38.387	39.314	33.678	46.470
% of body wt.	.500	.459	.560	.489	.004
Liver, g	147.358	191.820	174.479	198.708	2061.951
% of body wt.	2.410	2.293	2.416	2.841	.073
Spleen, g	10.652	13.855	13.629	10.402	14.252
% of body wt.	.176	.163	.190	.151	.001

Table 20. Actual and relative organ and gland weights of weaned pigs as influenced by maternal dietary iodine levels (parity 2)

Treatment	1	2	
I conc., ppm	0.0	0.2	EMS
No. of pigs	3	2	
Body wt., kg	5.585	6.630	.845
Organs			
Thyroid, g	.542	.552	.017
% of body wt.	.010	.008	.0000005
Heart, g	28.713	30.184	43.346
% of body wt.	.508	.455	.001
Adrenals, g	.773	.577	.064
% of body wt.	.014	.009	.000006
Kidneys, g	30.678	37.803	115.412
% of body wt.	.532	.570	.011
Liver, g	151.153	183.156	1505.281
% of body wt.	2.679	2.759	.089
Spleen, g	11.941	11.146	13.924
% of body wt.	.213	.168	.002

5. Histopathology.[1] Cross sections of organs and tissues from newborn and weaned pigs (four weeks) were examined for abnormalities that may have been due to dietary iodine. The heart, kidneys, adrenals and spleen showed no detectable differences in tissues across treatments. Even though the relative thyroid weights tended to be larger for pigs from the 0 and 20 ppm iodine groups than the .2 and 2 ppm iodine treatment groups, the degree of hypertrophy detected was only slight.

6. Mineral Concentration of Serum. The serum mineral concentration of offspring from birth to weaning as influenced by dietary iodine intake is presented in Table 21. Calcium values did not vary appreciably across treatment groups at birth, two weeks and weaning (four weeks), although the lowest mean values were recorded at birth. Inorganic phosphorus levels were similar across treatments at birth, two weeks and weaning. In contrast to birth and/or 24-hour inorganic phosphorus values reported by Ullrey et al. (1967), inorganic phosphorus values from the experiment reported herein are two-fold greater. Miller et al. (1964) have shown that serum inorganic phosphorus values are subject to dietary phosphorus intake. Therefore, high serum inorganic phosphorus values could be a reflection of the high phosphorus levels found in colostrum of sows in this experiment. Magnesium at each bleeding

[1]Examination was conducted and reported by Dr. S. D. Sleight, Department of Pathology, Michigan State University.

Table 21. Serum mineral concentrations of offspring in response to maternal dietary iodine levels

Treatment	1	2	3	4	
I conc., ppm	0.0	0.2	2.0	20.0	EMS
Calcium, mg/100 ml					
Birth	10.27(7)[a]	10.28(6)	10.10(4)	10.55(2)	.60
2-week	13.12(7)	15.12(6)	14.83(4)	15.25(2)	1.102
4-week	13.66(5)	14.92(6)	15.05(4)	14.30(2)	.888
Phosphorus, mg/100 ml					
Birth	10.61(7)	8.83(6)	9.48(4)	8.60(2)	1.698
2-week	10.29(7)	10.93(6)	10.55(4)	9.80(2)	.461
4-week	9.57(6)	9.78(6)	10.55(4)	8.90(2)	1.121
Magnesium, mg/100 ml					
Birth	2.23(7)	2.28(6)	2.30(4)	2.40(2)	.151
2-week	3.57(7)	3.82(6)	4.05(4)	4.20(2)	.130
4-week	3.12(5)	3.20(6)	3.35(4)	2.95(2)	.228
Iron, µg/100 ml					
Birth	70.4(6)	54.0(4)	83.7(2)	84.7(2)	170.701
2-week	170.1(7)	161.2(6)	136.5(4)	166.5(2)	1346.212
4-week	107.6(5)	87.5(6)	86.8(4)	94.0(2)	1598.881
Copper, µg/100 ml					
Birth	26.0(6)	24.0(4)	28.0(3)	19.0(2)	77.80
2-week	221.0(7)	216.0(6)	235.0(4)	201.0(2)	659.47
4-week	189.0(5)	188.0(6)	190.0(4)	190.0(2)	839.08
Zinc, µg/100 ml					
Birth	72.50(6)	80.50(5)	76.50(4)	84.50(2)	599.385
2-week	70.86(7)	70.08(6)	67.38(4)	72.75(2)	144.725
4-week	62.07(6)	75.72(6)	74.78(4)	52.30(2)	355.778

[a]Number of observations in parentheses.

interval displays a non-significant increase with the increasing concentration of iodine in the diet. Magnesium values peaked at the second week and declined at weaning. Copper values increased sharply from birth to two weeks irrespective of iodine treatment. Weaning interval copper values were slightly depressed in comparison to the 2-week values. Serum zinc decreased with age across all treatments. The addition of graded levels of iodine to diets of sows did not influence serum zinc values. Serum iron values increased two-fold from birth to two weeks, declining by nearly half at weaning. Such a trend is expected because of the administration of iron dextran at three days of age (Ullrey et al., 1967). There was no effect of maternal dietary iodine level on serum iron levels of offspring.

Significant differences were not detected across treatments at each sampling time for any of the serum mineral values. Serum mineral values were similar to those reported by Ullrey et al. (1967), if not otherwise stated.

CONCLUSIONS

1. Feeding sows 100 times their daily iodine requirement may induce resorption of feti and/or abortions, as well as reduce the number of pigs born per litter.

2. No supplemental iodine in corn-soybean meal diets of sows depresses birth weight of offspring and their body weight gain from birth to weaning. At this level, newborn and weaned pigs' hemoglobin values are depressed.

3. Relative thyroid weights were elevated in sows on 0 and 20 ppm of supplemental iodine levels and their newborn and weaned pigs. Relative heart weights of sows were elevated in the 0, 10 and 100 times the iodine requirement groups.

4. The level of iodine fed had no effect on the group pathology in histopathology of organs, except for the thyroid glands. Follicle cell size increases with increases in dietary iodine.

5. Colostrum and milk iodine increase linearly with I intake. Colostrum Cu and Zn concentrations increase with increasing dietary iodine, also.

6. Iodine concentration of the sows' thyroid increases with increasing dietary iodine.

7. Serum Ca, P, Mg, Fe, Zn and Cu concentrations of baby pigs are not influenced by maternal dietary iodine.

8. Serum thyroxine concentrations are depressed in sows fed diets unsupplemented with iodine, as are their offspring at weaning.

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APPENDIX

Table A-1. Low-iodine vitamin trace mineral premix used in gestation and lactation diets

Ingredient	Amount, g
Vitamin A[a]	2202.6
Vitamin D_3[b]	1475.8
Vitamin E[c]	400.9
Vitamin K[d]	44.1
Vitamin B_{12}[e]	3000.0
Riboflavin	88.1
Niacin	396.5
D-calcium pantothenate	176.2
Choline chloride	20000.0
$FeSO_4 \cdot 7H_2O$	5947.0
$CuSO_4 \cdot 5H_2O$	792.9
Zn O	1872.2
Mn O	1151.9
Ethoxyquin	5000.0
Finely ground corn	57451.5
	100.0 kg

[a] 30,000 IU/g.

[b] 3,000 IU/g.

[c] D-α-tocopheryl acetate.

[d] Menadione sodium bisulfite (2-methyl-1,4-naphthaquinone).

[e] Cyanocobalamin.