THE EFFECTS OF PROLONGED INCREASED IODINE FEEDING[1]

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The effects of adding supplemental iodine to the diet of man and of animals has long been a matter of controversy. As a result its advisability has been questioned. Consequently we welcomed a recent opportunity to investigate this problem.[2]

A valuable herd of high milk-producing Brown Swiss dairy cows in New York State had been fed a relatively high iodine supplement for a period of approximately three years. Extra iodine had been given as potassium iodide, in fish meal and in kelp, and as forage crops grown on soil fertilized by iodine-containing substances. Since in the past a number of studies on the effects of iodine feeding have been conducted upon an empirical basis, it seemed of importance to us actually to determine the amount of iodine consumed daily, also the daily excretion of iodine in the urine, feces and milk. In addition the blood iodine was determined.

One of us, (O. E.), has directed the feeding of several large herds of dairy cows in the states of Ohio, New York and Pennsylvania for the past twenty years. Following the work of von Fellenberg, iodine was added to the diets about 1915. These early iodine feeding experiments were of necessity carried on empirically. Adequate micromethods were not available. Since that time suitable methods for determining the iodine content of the blood, milk, ingesta and excreta have been developed (25). These are now being applied.

A preliminary report of the results of this investigation has already been made (28).

HISTORICAL

The basic facts concerning iodine in nutrition have recently been reviewed in a valuable monograph by Orr and Leitch (1).

Subsequent to the historic French experiment (1), Rilliet

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described toxic symptoms which follow overdosage with iodine. He even denounced the procedure before the French Academy of Medicine. His arguments are still quoted by those hostile to supplementary iodine feeding. However, even before 1860 there were sporadic objectors. In this day of better scientific appreciation and understanding of the importance of minerals in the processes of life there are still those who censure adding iodine to the diet. The significance of minerals in nutrition has been effectively discussed recently by Sheldon (4).

As early as 1831 Boussingault collected data from the goitrous regions of the Andes which pointed to a close relationship between iodine and thyroid disease (1). Thirty-nine years after the discovery of elemental iodine by Courtois, Chatin began his extensive studies on the existence of iodine in nature (2). While his work was recognized, its importance was not fully appreciated at the time. In fact, contemporary chemists were unable to duplicate his findings. Modern advances in microchemistry have enabled scientists and clinicians, as well as chemists, to confirm the observations of these pioneers (3). The original deductions concerning the significance of iodine in biology and in pathology are now better understood, and more knowledge is being added (3, 4).

After preceding failures Baumann (5) succeeded in demonstrating the presence of a considerable quantity of iodine in the thyroid gland. This was in 1895. The thyroid hormone, *thyroxine*, was subsequently isolated, analyzed and synthesized (6, 7). Assay shows it to contain 65 per cent iodine. Recent investigations have further established the relation of iodine to goiter in man (8). The significance of adequate iodine in nutrition as a preventive to goiter is appreciated (4, 9). Adding iodine to the diet of pregnant women is recognized as a significant precaution (10, 11, 12). It would thus appear to be established that to function normally the thyroid gland should have an adequate supply of iodine.

Thus the ground that was lost from 1860 to 1895 has been rapidly regained. Progress in the understanding of iodine metabolism has greatly accelerated during the past decade. With further perfection of the microchemical methods now in use and with their application to determine the minute amounts of iodine occurring in nature, significant developments are certain to ensue.

LITERATURE

Lombroso (13) suggested that in districts where cretinism was common iodine should be added to the diets of animals as well as to those of goitrous individuals.

Several European workers have noted that increasing the iodine in the diet of dairy cows and of goats has increased the iodine content of the milk from these animals (14, 15, 16, 17, 18, 19). Karns in this country has made a similar observation (20). None of these investigators has mentioned any deleterious effects resulting from augmenting the iodine in the diet of their experimental animals. The quantitative studies reported have been done on laboratory animals or upon isolated animals. In no instance has a large number of animals been studied on the more scientific basis. Extensive work has been done on milking goats.

Scharrer found that larger quantities of iodine in the diet of goats increased the milk yield (17). Stiner reports specific instances of having increased the milk yield from 8 to 10 per cent by administering suitable amounts of iodine to cows in recognized iodine deficient areas (21). Hanzlik (22) observed that rats having a diet rich in iodine maintained a better general condition than those not having such a diet. In some of the animals there was an increase in weight and growth. This increase was variable. In his study he also used sulphocyanate, bromide, arsenic, thallium and manganese as controls. These salts brought deleterious results. Arsenic and thallium caused fatalities. Welch and others found that hairlessness in new-born pigs was preventable by giving the pregnant sow food to which appropriate quantities of iodine had been added (23, 24).

METHODS

The quantitative method which we have used for determining the iodine (25) is here summarized. It is the result of adapting modern technic, apparatus and procedures to the principles as developed by von Fellenberg (3). It is carried out in from five to six hours. In careful and experienced hands it is about as accurate and dependable as the micromethod for the determination of the non-protein nitrogen of the blood.

The material to be analyzed is measured or weighed into a nickel crucible and mixed with an adequate amount of potassium hydroxide. This base binds the iodine and facilitates hydrolysis of the organic matter. After ashing completely the content of the crucible, at a carefully controlled optimum temperature, the water soluble salts are extracted. This extract is evaporated to dryness. The soluble salts are then extracted with 95% ethyl alcohol. The alcohol is evaporated. The remaining dry film containing the iodine salts is dissolved in water. The pH is adjusted to about 4. The iodides present are oxidized to iodates with chlorine water. The excess chlorine is boiled off. A crystal of potassium iodide is then added and the quantitatively liberated elemental iodine is titrated with one thousandth (0.001) normal sodium thiosulphate using starch as an indicator. An especially constructed microburet is recommended for this titration (26).

The food intake was measured by experienced attendants. Since the cows were allowed to drink water at will, from the regular stable fountains, it was impossible to make more than an estimate of the water intake.

Aliquot parts of representative food samples were analyzed. All analyses were made upon the wet basis. The milk, urine, and feces were collected over a period of 24 hours. Attendants were stationed with the cows for the entire 24-hour period. They collected and measured accurately the separate amounts from each cow. Blood was drawn in the usual manner at the end of the 24-hour period.

It is only in unusually efficient dairies that complete records of the milk and butter fat production are routinely kept over a long period of time. For this particular herd a nearly complete record for the years 1932 and 1933 was available.

The clinical condition of the herd was frequently inspected. Evaluation of the clinical results was based upon objective findings. The criteria considered in judging the effects of the prolonged increased iodine feeding were: (1) milk production; (2) general health of the herd; (3) fertility of the cows; and (4) the condition of the calves.

RESULTS

The results obtained are best presented in tabular form.

The iodine content of the foods ingested by the cows, over a continuous 24-hour period, is presented in Table 1. The "grain-mix," to which potassium iodide was added directly, obviously reveals the highest iodine content. The variation of intake, Table 5, is wide. This is due to the fact that the high milk-producing cows were fed greater amounts of the more concentrated foods. The iodine ingested in the water and roughage is minimal in comparison. The iodine obtained from foraging, from salt, and from other uncontrollable sources is indeterminate. The actual iodine ingested when the cows were also foraging is doubtless in excess of that shown in the table.

TABLE I

IODINE INGESTED

Source	Iodine Mg. %	Kg. Fed Daily	Mg. Iodine Fed Daily
"Grain Mix"	2.006	2.721 to 9.071	54.59 to 181.98
Alfalfa Hay	0.0326	11.339	3.70
Carrots	0.0099	9.072	0.90
Steamed Feed	0.0508	9.072	4.91
Ensilage	0.0391	10.886	4.26
Water	0.00071	45.359	0.33

Total intake ranged from 68.7 to 196.1 mg. daily

Table II presents a summary of the iodine eliminated in the milk, urine and feces. These figures present the variation of the actual amount of iodine eliminated. The loss closely parallels the intake for each individual cow, Table V. Since the intake is variable a general average has no particular significance.

TABLE II

IODINE EXCRETED

Origin	Output	Iodine Mcgm. %	Mg. Iodine
Urine	10.1 to 18.6 L	269 to 1005	34.6 to 130.0
Feces	9.1 to 29.5 Kg.	140 to 468	15.2 to 71.5
Milk	7.7 to 27.5 L.	15.7 to 181.9	1.5 to 19.5

Total iodine output ranged from 51.7 to 163.4 Mg. daily.

Table III presents a summary of the daily milk production of these cows. Of the 17 cows on which data are available, 13 showed an increase in daily milk production for the year. The average increase was 9.1 pounds. Four of the cows showed a decrease during this period. One of these, No. 59, had been milked constantly over a period of one year and three months subsequent to calving. This cow had an average daily milk production for the month, eleven pounds lower than it was the year before. The other three showed a smaller decrease for the period. The average for the four cows is 7.3 pounds.

TABLE III

COMPARATIVE DAILY MILK PRODUCTION RECORD

Herd No.	November, 1932 Lbs. Milk	November, 1933 Lbs. Milk	Lbs. Gain	Lbs. Loss
32	43.6	53.7	10.1	....
1	29.6	20.1	....	9.5
8	19.7	29.9	10.2	....
14	24.7	38.4	13.7	....
13	20.5	48.2	27.7	....
52	32.9	43.8	10.9	....
59	40.8	29.8*	....	11.0
24	20.2	20.7	0.5	....
35	18.1	19.7	1.6	....
19	17.6	28.1	10.5	....
49	37.9	22.7	....	4.3
54	40.2	35.9	....	4.3
56	20.1	24.4	4.3	....
2	22.3	23.0	0.3	....
10	25.4	25.9	0.5	....
50	24.9	29.5	4.6	....

Average Increase in Production in 13 Cows, 9.1 lbs.
Average Decrease in Production in 4 Cows, 7.3 lbs.

*1 yr., 3 mo. after calving.

Cow 15 made the most outstanding improvement in milk production under this feeding regimen. Data are available on her as far back as 1929. In three years she increased both her milk and butter fat production approximately two and one-half times. Table IV presents this information in summary form from the official G. V. L. record.

Table V presents in summary form the relation between ingested and excreted iodine. The total iodine ingested and eliminated is given in milligrams.

The blood iodine of these animals on a high iodine diet is of particular interest. It is greatly increased. The first modern figure for the iodine content of bovine blood was obtained by Kendall and Richardson (27) as 13 micrograms per cent. In our own studies (25) made on blood from cattle killed at the abbatoir, the iodine content averaged 14 micrograms per cent. The normal human blood iodine is about 12 micrograms per cent (29). This figure has been obtained and confirmed by a large group of workers both in this country and abroad (29).

TABLE IV

Cow 15: 8 Years Old

1929

Average Daily Milk Production—25.0 lbs.
Total Milk Produced—9,139 lbs.
Average Percentage Butter Fat—4.9
Total Butter Fat Produced—447.7 lbs.

*1932**

Average Daily Milk Production—59.9 lbs.
Total Milk Produced—21,924.9 lbs.
Average Percentage Butter Fat—4.73
Total Butter Fat Produced—1,037.1 lbs.

*Official G. V. L. Record.

As shown in Table VI, the range in these twenty cows is from 35.9 to 78.1, averaging 54.9 micrograms per cent. The cows were thus living and reproducing with a blood iodine more than three times its normal level.

DISCUSSION

The value of adding iodine to the diet of dairy cows has been considered by many. Some have tested its effects. Unfortunately in most instances it has been necessary for those who favor the use of supplemental iodine in nutrition to make their experiments sporadically, and to base judgment of their results almost entirely upon objective clinical findings.

The native farmers of Normandy, two centuries ago, procured seaweed to feed their milking cows. They did this because they had discovered a more seemly appearance of the cows after having been fed seaweed. The existence of iodine in seaweed was then unknown. Hence their feeding seaweed was as empirical as the use of burnt sponge in the treatment of goiter. It was not until iodine had been used more or less

TABLE V

	Iodine Ingested							Iodine Excreted			
Herd No. of Cow	Grain Mix	Alfalfa Hay	Carrots	Wet Steamed Feed	Ensilage	Water	Total Iodine Ingested	Milk	Urine	Feces	Total Iodine Eliminated
							Mg.				Mg.
8	63.69	3.697	0.898	4.909	4.257	0.304	77.755	3.6	41.5	43.046	88.146
24	63.69	3.697	0.898	4.259	4.257	0.304	77.755	1.9	65.3	28.395	95.595
19	63.69	3.697	0.898	4.909	4.257	0.304	77.755	4.8	103.5	33.090	141.390
18	72.79	3.697	0.898	4.909	4.257	0.304	86.855	3.9	69.2	....	....
3	72.79	3.697	0.898	4.909	4.257	0.304	86.855	5.8	55.0	32.297	93.097
13	54.59	3.697	0.898	4.909	4.257	0.304	68.655	3.1	45.5	44.994	93.594
14	63.69	3.697	0.898	4.909	4.257	0.304	77.755	4.9	38.4	53.276	96.576
10	63.69	3.697	0.898	4.909	4.257	0.304	77.755	5.9	....	23.496	....
9	54.59	3.697	0.898	4.909	4.257	0.304	68.655	14.3	51.2	....	....
2	54.59	3.697	0.898	4.909	4.257	0.304	68.655	1.5	48.2	15.197	64.897
20	0.0	3.697	0.898	4.909	4.257	0.304	14.065	3.0	26.6	22.112	51.712
1	90.99	3.697	0.898	4.909	4.257	0.304	105.055	6.2	60.7	56.931	123.831
59	109.19	3.697	0.898	4.909	4.257	0.304	123.255	11.3	46.6	66.674	124.574
23	54.59	3.697	0.898	4.909	4.257	0.304	68.655	....	34.6	54.539	....
31	81.89	3.697	0.898	4.909	4.257	0.304	95.955	11.7	69.3	44.469	125.469
22	90.99	3.697	0.898	4.909	4.257	0.304	105.055	....	77.2	35.844	....
54	109.10	3.697	0.898	4.909	4.257	0.304	123.255	6.1	85.8	71.483	163.383
35	54.59	3.697	0.898	4.909	4.257	0.304	68.655	10.2	54.2	44.040	108.440
52	90.99	3.697	0.898	4.909	4.257	0.304	105.055	11.2	51.9	59.995	123.095
56	54.59	3.697	0.898	4.909	4.257	0.304	68.655	4.3	43.7	....	....
49	90.99	3.697	0.898	4.909	4.257	0.304	105.055	....	130.0	34.638	....
50	109.19	3.697	0.898	4.909	4.257	0.304	123.25	9.9	50.1	50.465	110.465
32	163.78	3.697	0.898	4.909	4.257	0.332	188.873	12.2	74.1	36.143	122.443
15	181.98	3.697	0.898	4.909	4.257	0.332	196.073	19.5	59.3	38.829	117.660

Average Iodine Ingested, 94.17 Mg.

TABLE VI

Blood Iodine in Micrograms Per Cent

Herd No. of Cow		Herd No. of Cow	
8	57.6	1	63.2
24	49.7	59	55.0
18	50.4	31	63.8
3	40.7	54	64.0
13	37.9	35	78.1
14	33.8	56	57.0
10	42.1	50	59.8
9	54.6	32	75.6
2	38.6	15	62.4
20	58.1	38	54.6

The range is from 33.8 to 78.1.
The average is 54.9 micrograms per cent.

extensively in the practice of medicine, and particularly in the treatment of goiter and of cretinism, that it was recommended for animals other than man. One of the earliest records of its use in the diet of animals is in 1859 (13).

Dairymen and veterinarians were slow to recognize the value of iodine as a dietary necessity. In fact many have been skeptical concerning its use, and have even suggested that iodine added to animal diets was likely to cause deleterious effects. The unfortunate experience of giving large amounts of iodine to French school children in 1860 is perhaps responsible for this attitude among those who have not studied the facts carefully.

Twenty years of experience in adding iodine to the food of dairy cows (O. E.) has yielded in no instance objective evidence of unfavorable effects directly or indirectly attributable to the extra iodine ingested. In fact, in those instances where an added iodine food regimen has been instituted, the milk production and the fertility of the cows have increased.

In this investigation, previous to the institution of the increased iodine regimen, still births, goitrous calves, and premature calves were noted. In one of the herds 75% of the cows were sterile or sporadically fertile. In 1933 85% of the cows of this herd were fertile. Some of them were descendants of the original sterile 75%.

Although in this particular study only 25 cows are included a similar increased iodine feeding regimen has been carried out over a period of from three to seventeen years on more than 500 dairy cows of various breeds throughout different localities in the Great Lakes region. In all instances the results have been distinctly beneficial. In these herds the evaluation of the results has been based upon objective clinical findings.

The general mineral content of the diet of these cows was increased at the same time as that of the iodine content. It is therefore important to state that the subsequent improvement is not necessarily due to the iodine alone. The addition of calcium, phosphorus, iron and magnesium was undoubtedly beneficial to the general health of these animals. However, in other studies carried out by one of us (O. E.) the addition of elements other than iodine did not produce so marked an improvement in the physical condition and reproduction of the cows. It has been observed that the fertility of the cows improved after the addition of iodine to their food. The quality of the calves has improved over that before the institution of the iodine feeding regimen.

This investigation was carried out under definite technical difficulties. No claim is made that it represents a true balance experiment. The travail of making an accurate balance study on patients under strict modern hospital management is beset with difficulties. Hence even to attempt such an approximation upon a herd of dairy cows required courage. The information in Tables I, II, V and VI is as reliable as that given in the average laboratory experiment. The striking increase in the iodine content of the blood and of the milk is significant.

The data which are presented represent a fairly accurate estimate of the increased iodine transport. They show a great increase in the iodine intake. They reveal also a corresponding increase in the elimination of iodine in the urine, feces, and milk. They demonstrate the consequent elevation of the blood iodine. As a whole they reveal clearly increased iodine feeding. Since this had been maintained for a period of three years, and since the clinical condition of the herd was excellent, we were unable to demonstrate any deleterious effects of prolonged increased iodine feeding to these cows.

CONCLUSION

This investigation demonstrates that adding increased amounts of iodine to the diet of dairy cows does not ordinarily produce deleterious effects on the physical condition, general health, milk production and reproduction of these animals. Iodine is apparently beneficial when fed in optimal amounts or, in this instance, even in amounts in excess of the normal requirement.

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