THE IODINE CONTENT OF FOODS, MANURES AND ANIMAL PRODUCTS IN RELATION TO THE PROPHYLAXIS OF ENDEMIC GOITRE IN NEW ZEALAND.

STUDIES FROM THE UNIVERSITY OF OTAGO, NEW ZEALAND.

BY C. E. HERCUS AND K. C. ROBERTS.

(With 8 Charts.)

CONTENTS.

I. INTRODUCTION.

IN a previous study from this University the incidence of Endemic Goitre in New Zealand and its relation to the soil-iodine was discussed (Hercus, Benson and Carter, 1925). Preliminary data were given as to the iodine content of certain types of vegetables grown in soils of widely varying iodine content.

The present contribution is a continuation of the study of the iodine content of various foodstuffs, and also relates to other closely allied aspects of the subject. Thus a comparative study is made of the iodine content of certain typical food products obtained from endemic and non-endemic districts, and the average daily iodine intake in such districts is determined. Opportunity is also taken to study the seasonal variation in the iodine content of certain vegetables and animal food products, the findings indicating that a seasonal cycle occurs in both kingdoms. The important practical question of the effect of cooking on the iodine content of the food is investigated.

Throughout the research the problem of supplying the iodine deficiency in the food of the districts where goitre is prevalent has been kept constantly in view. The iodine content of various manures and the influence of soils treated with iodine-rich manures on the iodine content of vegetables grown thereon has been studied, as has the possibility of supplying an increased quantity of iodine in certain foods for animals. At the same time, the iodine content of the various commercial salts used in New Zealand has been determined in the hope of finding a salt which naturally contains sufficient iodine for prophylactic purposes.

In the light of these findings a further discussion on the subject of Goitre Prophylaxis is submitted. Brief mention is made of some preliminary work on the correlation of iodine intake with iodine excretion in human milk and urine, and on the iodine content of bacteria grown in an iodine-rich medium.

We have to acknowledge a liberal grant from the New Zealand Department of Health which has enabled one of us (K. C. R.) to devote his whole time for a period of twenty months to the analytical work of this research.

Dr Lilian Storms, of the Home Science Department of this University, and her assistants, have been of the greatest assistance to us in supplying accurate data with regard to diets, in collecting and sending 24-hour diet portions for analysis, in undertaking experimental feeding work on rats, and in assisting generally in the work. Our thanks are due also to Miss Thomson of the Home Science Department, who for some months has been assisting in the analytical work.

We are also indebted to Mr A. F. Hercus, of Auckland, Mr Roberts, of Taranaki, Mr Stafford, of Canterbury, and Mr Blackie, of Otago, for their co-operation in sending us for a period of twelve months regular monthly specimens of food products from their respective districts. Dr Baker McClaglan has also assisted us in this matter by enlisting the interest of teachers in the various districts visited by her in the goitre survey, who have sent in the various specimens referred to in Chapter III.

To our colleagues, Dr Carmalt Jones and Dr A. M. Drennan, we are indebted respectively for help in proof reading and in supplying histological data with regard to animal thyroids.

II. THE ANALYTICAL METHOD.

Throughout these investigations, the iodine analyses have been made by means of the method elaborated by Th. V. Fellenberg in 1923 and modified by him in 1924. Constant application of the method has led to the introduction of several minor improvements and modifications of the original technique. An outline of the procedure ultimately adopted is given here.

https://doi.org/10.1017/S0022172400008925 Published online by Cambridge University Press

A representative sample of the material to be examined is incinerated carefully in the presence of iodine-free alkali. Stirring is often necessary to ensure thorough penetration of the alkali through the material. The quantity necessary depends upon the nature of the specimen; thus for some waters 200 to 300 c.c. are required, for some vegetables 100 grm., whereas 0·01 grm. is sufficient for thyroid tissue. After incineration the residue is taken up with water, evaporated to dryness, and again incinerated until any glowing of the carbon residue has ceased. The amount of heat necessary to carry out the incineration without at the same time incurring loss of iodine can only be determined by constant practice.

The residue is next washed quantitatively on to a filter with water. Fellenberg recommends that at this stage the charcoal residue should be burnt, taken up with water and added to the filtrate, but it has been found that this step may be omitted without any detectable loss of iodine and with a considerable saving of time. The filtrate is now evaporated to a paste and extracted three times with 95 per cent. alcohol. The alcohol removes the potassium iodide and leaves behind the bulk of the other inorganic material. The extract is evaporated to dryness in a platinum basin, the greatest care being taken to secure complete incineration without at any time raising the basin to a red heat. The alcohol extraction and the incineration are now repeated. By this time the residue has become very small. A third extraction may be necessary, but as a rule the residue can now be taken up with 0·36 c.c. of water, 0·30 c.c. of which is transferred from the platinum basin to a calibrated "shaking-out" tube. One-fifth must be added to results obtained to allow for 0·06 c.c. of solution, which remains in the final basin.

The iodine is now liberated by the addition of one or two drops of a solution of sodium nitrite in $3N$ sulphuric acid. The latter solution was made up as required in 1 c.c. quantities, a small grain of sodium nitrite being added.

The liberated iodine is then extracted with an observed volume of chloroform, which experience shows should not be less than 0·02 c.c., and estimated colorimetrically. If the small globules of chloroform do not coalesce it may be necessary to centrifuge. The colorimetric standardisation is done by comparing the colour of the unknown solution with that of a suitable standard solution of potassium iodide contained in a tube similar to the "shaking-out" tube and likewise calibrated at 0·3 c.c. It has been found that the most expeditious procedure is to make up a standard colour approximately identical with the colour of the unknown chloroform solution, and then dilute either the standard or the unknown until the colours are identical. The total amount of iodine present in the unknown can then be calculated. Although the standard chosen must be adapted to the amount of iodine in the specimen, it was found that the most accurate comparison is obtained with 0·2 to 0·33 millionths of a gram of iodine dissolved in every 0·01 c.c. of chloroform, or, more briefly, with a 0·2 to 0·33 microgram colour. On account of the slow oxidation of the free iodine by the nitrosulphuric acid and of the widely differing amounts of iodine involved, fresh standards were prepared for practically every determination. Errors due to the distribution of iodine between water and chloroform and to the slight extent to which chloroform dissolves in water are minimised by taking equal volumes of the standard and the unknown solutions, and by making the volumes of chloroform in the two cases as nearly equal as possible.

It has been found that the comparison of the unknown solution with the standard is best made by suspending globules of chloroform of equal volume from the menisci in the two tubes, and viewing these side by side by diffuse transmitted light (*e.g.* with a sheet of filter-paper between the light and the tubes). By this means it is possible to estimate with considerable accuracy less than $0{\cdot}5\gamma$ of iodine (γ's = millionths of a gram).

It will be obvious to the chemist that even with months of practice, a result accurate within 10 per cent. cannot always be assured, and therefore duplicated analyses should be made whenever time permits or whenever loss of iodine by volatilisation of potassium iodide during the difficult combustion stage is suspected. Furthermore, it should be borne in mind that results always tend to be too low rather than too high, particularly if the solution to be extracted with chloroform has a slight yellowish colour. For this reason it is advisable, after deciding that the two colours are identical, to add more chloroform to the unknown solution and make another comparison. Occasionally a specimen is met with, the complete combustion of which below a red heat presents exceptional difficulty. In such a case the only course open is to make the best possible approximation.

In each of the following cases, the procedure adopted differs from that described by Fellenberg, and also from that detailed above, and is therefore described more fully.

Soils. A few drops of saturated potassium carbonate solution, and water as required, are ground up with ½–2 grm. of the soil, weighed out in a nickel basin, and the whole carefully incinerated. The residue is then taken up with water, filtered, evaporated to dryness, incinerated, and extracted with alcohol, etc., as above.

Eggs. For aqueous fatty foods such as milk, Fellenberg describes a method for the isolation and saponification of the fat prior to combustion. This is done in order to avoid loss of iodine. But it was found in the case of eggs that isolation of the fat was difficult and not necessary. The procedure adopted is as follows: To 25 or 50 grm. of beaten egg is added one-tenth its weight of iodine-free potassium hydroxide, and about one-half its weight of alcohol. On warming, the fat is quickly saponified without being first isolated, and the combustion then proceeded with in the usual way.

Thyroids. In the present investigation, the work on thyroid substance has required an expeditious method giving good comparative results. Fellenberg's method of macerating a large piece of thyroid with water, and taking an aliquot part of the resulting fluid has therefore been departed from. 0·01 to 0·02 grm. of fresh thyroid tissue is weighed out in a platinum basin, a drop of saturated potassium carbonate solution added, the thyroid disintegrated with a glass or agate pestle, incinerated, extracted, with 95 per cent. alcohol, and the extract transferred to a second basin whence the iodine is estimated as described above.

The above description of the method deals, of course, mainly with the modifications introduced in connection with the present work. For fuller details of the procedure, preparation of reagents, etc., reference must be made to the original papers.

Attention is drawn to the fact that the specimens analysed fall naturally into three groups, distinguished by the very different orders of their iodine contents. Accordingly, three different modes of expression of the iodine content have been adopted, viz.:

(*a*) Iodine in micrograms (γ's) per kilogram (or per litre) of specimen, *i.e.* parts per 1000 million (10^9)—used for foodstuffs and urines. Urines may also, when the necessary data are available, be expressed in γ's secreted per 24 hours.

(*b*) Iodine in parts per 10 million (10^7) of specimen—for soils and manures.

(*c*) Iodine in milligrams per gram of fresh specimen (*i.e.* parts per 10^3)—for thyroids.

III. THE IODINE CONTENT OF FOODSTUFFS.

1. GENERAL SURVEY.

In the accompanying table are given the iodine contents of a considerable number of foodstuffs, classified according to the main groups into which they fall, viz. cereals, root vegetables, leafy vegetables, fruit, animal foods, and sundries. Except where otherwise stated, only the edible portion (E.P.) of specimens has been analysed. The figures represent γ's (millionths of a gram) of iodine per kilogram of fresh material (per litre for liquids), *i.e.* parts per 1000 million. On the whole, they follow very closely those given by Fellenberg (1923, 1924) in similar tables.

The figures speak for themselves. Attention may, however, be drawn to the following points:

A. Edible seaweed, fish, eggs, wholemeal products, leafy vegetables, and milk in that order are seen to be the foodstuffs which are naturally richest in iodine, while fruits, root vegetables (E.P.), and the great majority of drinking waters are very low. The relationship of iodine in water to the geological structure was discussed in a previous paper (Hercus, Benson and Carter, 1925), and it was there shown how the water-supply in a region low in iodine might have its origin in iodine-rich country and so supply the deficiency in a given locality.

B. *Wholemeal products* contain much more iodine than the corresponding refined products such as white flour and polished rice. The single results given for wheat and brown bread are exceptionally low, the specimens having come from localities where the soil-iodine is low. The influence of the use of iodised salt is noteworthy.

https://doi.org/10.1017/S0022172400008925 Published online by Cambridge University Press

Table I.

Specimen	Iodine content parts per 10^9
Cereals and Cereal Products	
White bread	2
White bread (made with iodised salt)	32
Brown bread (from Canterbury wheat low in iodine)	12
Brown bread (made with iodised salt)	55
Flour (white)	3
Oatmeal	30
Oto	61
Rice (polished)	<8
Wheat (Australian)	14
Wheatmeal	44
Root Vegetables	
Beetroot (without skin)	3
Beetroot (with skin)	15
Carrot (without skin; mean of 12)	10
Carrot (with skin; mean of 2) ...	19
Carrot (artificial manure)	2500
Kumara (Maori Sweet Potato) ...	3
Marrow	6
Mangold (unmanured)	4
Mangold (artificial manure) ...	5000
Onion	11
Parsnip (without skin; stable manure)	12
Parsnip (with skin; stable manure)	53
Parsnip (with skin; unmanured) ...	18
Potato (without skin)	10
Potato (with skin)	22
Turnip (manured), root with skin	16
Turnip (manured), leaf	92
Turnip (unmanured), without skin	6
Turnip (unmanured), with skin ...	16
Yam	6
Leafy Vegetables	
Asparagus	17
Beans (Scarlet Runner)	18
Cabbage (unmanured; mean of 3)	17
Cabbage (manured)	200
Celery (stalks)	17
Leek (mean of 2)	18
Lettuce (unmanured; mean of 8)...	17
Lettuce (manured)...	130
Lucerne (autumn)	28
Silver-beet (mean of 20)	27
Spinach (autumn)	48
Sow thistle (Rauriki)	32
Average for root vegetables without skin and unmanured ...	7
Average for root vegetables with skin and unmanured	18
Average for leafy vegetables, unmanured	24

Specimen	Iodine content parts per 10^9
Fruits. Fresh	
Apple (whole fruit)...	6
Apple (without peel and core) ...	4·5
Bananas	5
Grapes	7
Lemons	3
Oranges	2
Pears (whole fruit)...	4
Tomato	8
Fruits. Dried	
Apricots	22
Figs	12
Prunes	10
Raisins	32
Animal Foods	
Fish (fresh)	
Groper	72
Oysters	880
Fresh-water trout	24
Tidal-water trout	50
Whitebait (*Galaxias attenuatis*)	96
Fish (tinned)	
Pilchards (mean of 2)	320
Salmon (British Columbia; sea-run)	750
Sardines	360
Others	
Bacon (medium fat)	15
Beef (mean of 18)	13
Butter	12
Cheese	31
Eggs (mean of 38)	94
Glaxo (dried milk)	96
Cow's milk (mean of 39) ...	20
Human milk (mean of 18) ...	32
Mutton	10
Rabbit	6
Sundries	
Casein (thrice extracted with alcohol)	72
Grass (mean of 36)	58
Hay (mean of 4)	124
Honey	18
Jam	12
Marmalade	10
Marmite	<15
Seaweed (Carrageen)	48,000
Sugar	0
Water, 12 samples (minimum) ...	<1
Water, 12 samples (maximum) ...	17
Wine (mean of 2)	5

C. The high results for *tinned fish* must be due to the inclusion of thyroid tissue, liver, or roe, all of which, according to Fellenberg (1923), contain large quantities of iodine, and which are not included in the edible portion of the fresh fish analysed.

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D. *Vegetables. Leafy vegetables* are seen to be distinctly better than *root vegetables*, while in the case of turnips the leafy tops are shown to be better than the roots. No doubt this distinction is quite general. *Grass* (and hence hay) is surprisingly rich in iodine, a fact which may account, at least in part (see B), for the lower incidence of goitre among animals than among human beings. Both in fruit and in root vegetables the skin is shown to have a higher iodine content than the flesh, while the important influence of *manures* on the iodine content of vegetable growth is also indicated. This influence will be discussed in greater detail in a subsequent chapter. It is to be noted that a few of the results obtained in the spring for both lettuce and grass have been omitted in calculating the mean results given in Table I. This was considered necessary, as the incineration of the spring samples of these plants was at times extremely difficult, owing to the presence in the plant at this season of organic matter which apparently would not burn below a red heat. Iodine was therefore apt to be lost by volatilisation of potassium iodide, and the results were correspondingly unreliable. The lucerne and spinach samples are marked "autumn" because at that period the iodine content of vegetable growth reaches a maximum (see Chart I), and therefore the single results given for these plants are not truly representative.

E. As is to be expected, the figures for dried foods are consistently higher than those for the corresponding fresh foods. (See glaxo and milk, bacon and fresh meat, dried fruits and fresh fruits.)

F. The difference between cow's milk and human milk is only apparent, being due to the fact that the figures for cow's milk do not include any for colostrum, while 50 per cent. of the results for human milk represent analyses of samples collected immediately after parturition, when the iodine content is abnormally high (see p. 75).

G. The high result for cheese relative to that for butter is apparently due to the inclusion in the former of casein (*q.v.*). In this connection it is interesting to note that casein has been used by some previous investigators as a standard iodine-free material (see Hunter, 1910).

2. Comparison of Iodine Contents of Foodstuffs in Goitrous and Non-Goitrous Districts.

Existing data on this point are due to Fellenberg (1924) and to McClendon and Hathaway (1924). Preliminary work by the present authors was referred to in a previous paper (Hercus, Benson and Carter, 1925). During the present work, all foodstuffs analysed have been correlated as carefully as possible with the soils on which they were produced, or, failing that, with the district in which they were grown. It is therefore possible to make an accurate analysis of a considerable number of results, and thus to place beyond dispute the fact that the soil iodine is reflected in the various foods produced thereon.

It is to be regretted that only one analysis of lettuce from a non-goitrous area, and one (an autumn sample) of silver-beet from a goitrous area has been

Table II.

Specimen	Non-Goitrous: No. of specimens analysed	Non-Goitrous: Iodine in γ's per kilogram (average)	Goitrous: No. of specimens analysed	Goitrous: Iodine in γ's per kilogram (average)
Carrot	7	9·5	4	7·7
Grass	17	64	13	47
Lettuce	1	24	8	12
Silver-beet (autumn)	6	32	1	24
Beef	8	16	10	9·5
Eggs	18	137	20	56
Cow's milk	18	25	21	15
Human milk	4	43	14	28

made. Only those results which were obviously anomalous (see asterisked figures in Table V) have been omitted in arriving at the above averages, so that, with the exception of the two cases mentioned, the table gives a true picture, based on results obtained during a twelve-month period, of the differences between the iodine contents of foods produced in goitrous and non-goitrous areas. In all cases the differentiation is seen to be well marked.

Corroborative evidence, if any were required, is provided by the following more detailed table, in which exact correlation of soil with food-iodine, and of food-iodine with the time of year, has been obtained.

Table III.

Specimen	Frankton (Nov.)	Whangarei (Nov.)	Levin (1) (Sept.)	Levin (2) (Sept.)	Hampden (Nov.)	Waipawa (Nov.—Dec.)	Wairoa (Nov.—Dec.)	Gisborne (Nov.—Dec.)
Soil/10^7	264	200	130	36	35	33	15	7
Milk/10^9	10*	12*	—	19	—	5	12	7
Egg/10^9	384	240	480	180	—	20	—	23
Grass/10^9	72	48	77	32	24	—	—	—
Root veg./10^9	9	19	—	6	—	—	—	—

* November minimum (see Chart IV).

Data providing further confirmation of the fact that vegetable-iodine is dependent on soil-iodine have been obtained by transplanting a root of silver-beet from Taranaki (soil-iodine 160) to Roslyn (soil-iodine 18) and observing the change in iodine content.

Result. Taranaki (April 1925) Iodine = 36γ per kgrm.
Roslyn (March 1926) Iodine = 24γ per kgrm.

3. Determination of Daily Iodine Intake through Food in Goitrous and Non-Goitrous Districts.

It is now proposed to consider the results incorporated in Tables I and II with a view to determining the average daily intake of iodine in goitrous and non-goitrous areas respectively. The determination of the normal physiological intake is shown in the accompanying table (Table IV), which is compiled from data supplied by the Home Science Department of Otago University, and represents diets used in its residential establishment. The figures arrived at from a consideration of these data will therefore represent very accurately the iodine intake from a normal diet in the two types of district.

Table IV. *Determination of iodine intake per person per day.*

	Fortnight May 2nd–15th (45 people)					Fortnight June 13th–26th (40 people)				
		I_2 intake calc. for typical non-goitrous area		I_2 intake calc. for typical goitrous area			I_2 intake calc. for typical non-goitrous area		I_2 intake calc. for typica goitrous area	
Food	Weight in kgrm.	I_2 in γ's per kgrm.	Total I_2 in γ's	I_2 in γ's per kgrm.	Total I_2 in γ's	Weight in kgrm.	I_2 in γ's per kgrm.	Total I_2 in γ's	I_2 in γ's per kgrm.	Total I_2 in γ's
Meat	102	16	1630	9·5	970	96	16	1540	9·5	910
Fresh sea fish	11·8	72	850	72	850	21·4	72	1540	72	1540
Tinned fish	4·6	500	2300	500	2300	0·91	500	450	500	450
Oysters	0·18	880	1580	880	1580	0·68	880	600	880	600
White carbohydrates	76	3	230	2	150	67	3	200	2	130
Brown carbohydrates	77	40	3080	20	1550	62	40	2480	20	1240
Milk	350	25	8750	15	5250	350	25	8750	15	5250
Fats	47	5	230	3	140	37·5	5	190	3	110
Eggs	14·1	137	1930	56	790	13·2	137	1810	56	740
Fresh fruit	91	5	450	3	270	86	5	430	3	260
Dried fruit	12	20	240	12	140	11	18	200	12	130
Root vegetables	164	9	1480	6	980	177	9	1590	6	1060
Leafy vegetables	44·5	27	1200	20	890	64	27	1730	20	1280
Water	630 (estim.)	2	1260	1	630	560 (estim.)	2	1120	1	560
Sundries	28	3	80	2	60	24	3	70	2	50
Total iodine intake in food	—	—	25290	—	16550	—	—	22700	—	14310
Whence iodine intake per person per day	—	—	40·1 γ	—	26·3 γ	—	—	40·5 γ	—	25·6 γ

Mean non-goitrous iodine intake per person per day = 40·3γ

Mean goitrous ,, ,, ,, ,, = 25·95γ

Mean difference between goitrous and non-goitrous = 14·35γ

It is interesting to note that the three mean values here arrived at are very similar to those given by Fellenberg (1923). In one or two minor instances, the figures for iodine contents of the foods have been estimated from rather incomplete data, or from data previously existing, but in the main they are the mean results obtained during the present investigation, for the edible portions of a considerable number of specimens of each of the different foods (see Tables I and III).

The assumption has been made in compiling the above table that all the naturally occurring iodine is consumed. It will be shown subsequently (section 5 of this chapter, p. 65) that when leafy vegetables are boiled, a good deal of the contained iodine goes into the cooking water. Hence, unless this water is used, *e.g.* in the making of soups and stews, this amount of iodine is lost. In all other cooking processes investigated the loss of iodine is found to be negligible, so that the making of this assumption does not materially affect the final result.

Another assumption made in the above table is that a given district is entirely self-supporting in the matter of food supply. Although this assumption would not be warranted in the large centres of population of the Old World, nor indeed in the larger towns of New Zealand, it can be accepted as practically true in country districts. Even with this assumption, the general significance of the above mean figures remains unaltered.

One further comment seems necessary. Sea fish has been included in the diet of a goitrous area. The iodine thus supplied bulks so largely in the total —and is also, of course, independent of the soil iodine—that the mean value given for the iodine intake of a goitrous district would be appreciably reduced by the omission of this item. Such an item, indeed, included in an otherwise goitrous diet, might easily raise its iodine content above that necessary to secure immunity. The elimination of fish even from an otherwise iodine-rich diet will make an appreciable difference in the average daily iodine intake in a non-goitrous district. Also it is noteworthy that, although New Zealand is an island, fish is by no means a general, far less a staple, item of diet, even in coastal towns. It has therefore been thought worth while to recalculate the above mean values for typical goitrous and non-goitrous iodine intakes, omitting fish altogether, and replacing it by the same amount of meat. The mean results are then as follows:

Mean non-goitrous iodine intake per person per day	= 34·85γ
Mean goitrous ,, ,, ,, ,,	= 20·15γ
Mean difference between goitrous and non-goitrous	= 14·70γ

Naturally the mean difference is not altered to any great extent.

The mean results here set forth show almost perfect agreement with those calculated by Fellenberg (1923) from much less complete data.

The effect of eliminating, or reducing appreciably, the amount of any other item in the diet such as milk, brown carbohydrates, or eggs, even though it will be in part compensated, is obvious. Thus a glance at Table IV shows that milk contributes about one-third of the total iodine in the diet, and its influence in this respect will thus be of paramount importance.

4. Seasonal Variations in Iodine Content of Foods.

Bourcet, in an admirable study on the iodine content of foodstuffs, records the fact that eggs are rich in iodine, and that their iodine content varies with the season of the year, being richest in summer. Fellenberg (1923) mentions the possibility of a seasonal variation taking place in the iodine content of milk. Seidel and Fenger (1913) show that a seasonal variation occurs in the iodine content of the thyroid in various animals.

It was decided to investigate this matter more closely over a wider range of foodstuffs, and to this end arrangements were made for a monthly supply of specimens over a twelve-month period from widely separated districts. People willing to help us in this matter were readily found, with the result that during a complete year from May, 1925, to May, 1926, monthly supplies of milk, meat, eggs, grass and vegetables arrived regularly from private gardens in Auckland and Taranaki (non-goitrous) and from farms on the Canterbury

https://doi.org/10.1017/S0022172400008925 Published online by Cambridge University Press

and Taieri Plains (goitrous). Each supplier was allotted a definite week in each month in which to forward specimens, an undue accumulation of material for analysis being thus avoided. As a result of this arrangement, it has been possible not only to study the question of seasonal variation, but also to make an accurate comparison of the iodine contents of locally grown foodstuffs in typical goitrous and non-goitrous regions. The results have already been considered from the latter point of view.

Table V.

	District	Goitre index %	Unmanured soils parts $I_2/10^7$	Water parts $I_2/10^9$	Months in which specimens gathered	Iodine in parts per 1000 million: Grass	Silver-beet	Milk	Eggs	Beef
Non-goitrous	Taranaki				May	—	36	19	96	—
					June	—	32	29	72	21
			192		July	75	32	17	72	19
					Aug.	33	12*	60	120	10*
					Sept.	38	24	95	64	18
		4		2	Oct.	—	24	72	160	12
					Nov.	48	40	8	288	—
					Dec.	16*	15	10	—	18
			160		Jan.	—	—	—	—	—
					Feb.	48	—	8	88	16
					March	48	24	9	—	19
					April	60	—	24	115	21
	Auckland				May	72	—	—	76	—
					June	104	32	19	64	—
					July	72	40	14	72	—
					Aug.	43	24	18	38*	—
					Sept.	58	14	14	60	—
		4	90	6	Oct.	43	16	16	—	—
					Nov.	40	24	—	50	—
					Dec.	—	—	—	—	—
					Jan.	—	—	—	—	—
					Feb.	84	25	16	64	—
					March	150	—	18	—	—
					April	—	—	12	—	—
Goitrous	Canterbury				May	—	—	14	116*	12
					June	300*	—	12	58	—
			15		July	86	—	15	72*	150*
					Aug.	1000*	260*	16	96*	120*
					Sept.	64	—	25	50	48*
		60		1·6	Oct.	54	—	9	56	24*
					Nov.	480*	—	—	—	60*
					Dec.	—	—	—	—	—
					Jan.	480*	—	24	48	800*
			18		Feb.	—	—	—	—	—
					March	—	—	—	—	—
					April	—	—	—	—	—
	Taieri				May	—	—	15	43	9
					June	71	—	28	41	6
					July	86	—	40	49	7
					Aug.	41	—	14	32	8
					Sept.	8	—	12	24	11
		30	24	4·8	Oct.	32	—	—	32	12
					Nov.	24	—	—	54	10
					Dec.	—	—	—	—	—
					Jan.	48	—	13	67	—
					Feb.	42	—	12	72	13
					March	32	—	17	70	10
					April	—	—	12	60	—

* Anomalous figures.

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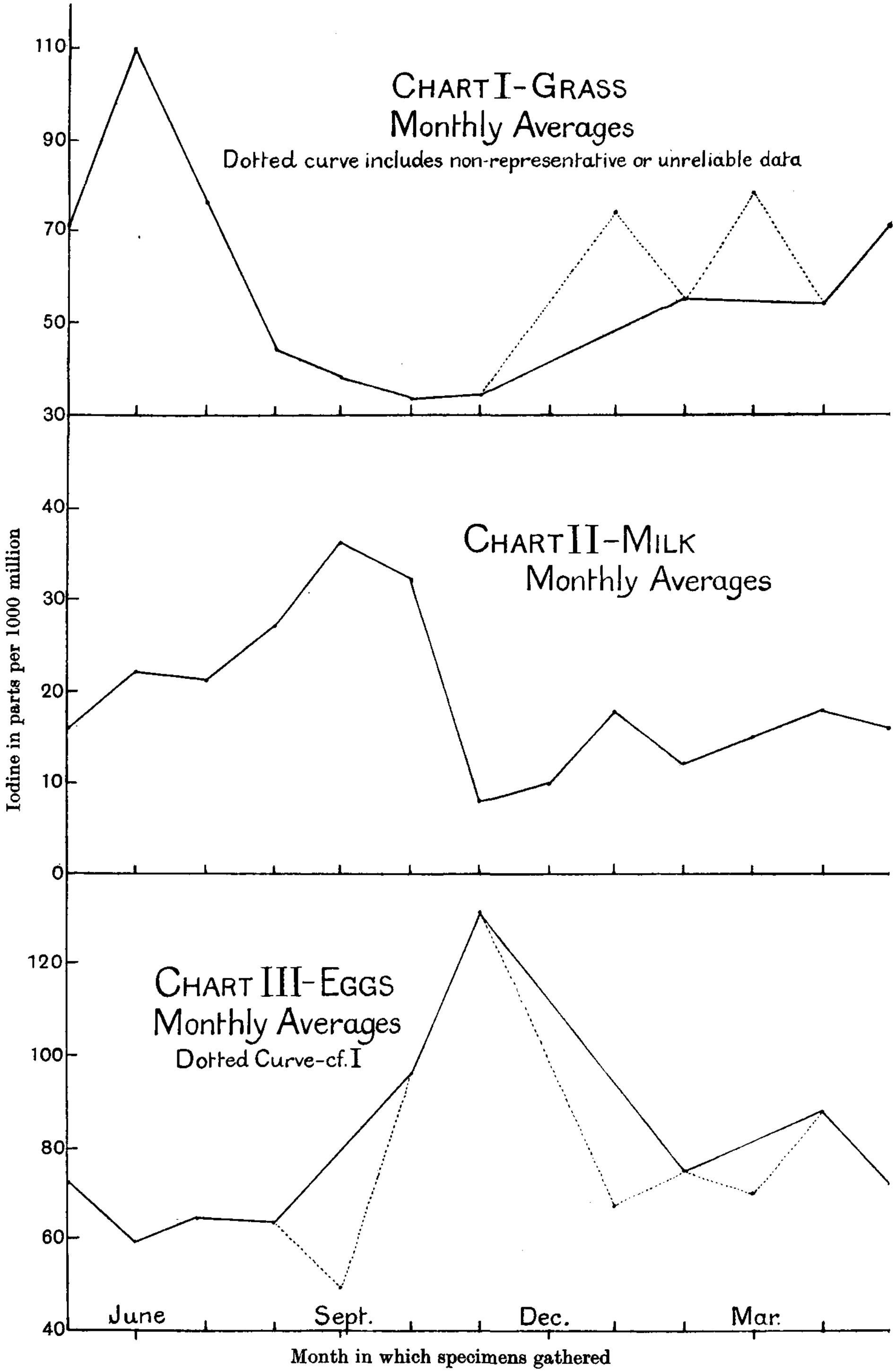
As was to be expected, a certain amount of inconvenience was met with in pursuing this line of work, owing to the difficulty of getting regular supplies exactly fulfilling our requirements from these widely scattered places. Also, it has not always been possible to obtain specimens of certain of the foods all the year round. But in spite of these facts and of the resulting rather numerous gaps in the accompanying table (Table V), even a casual inspection of the figures reveals a number of interesting facts regarding the seasonal variation under consideration, and justifies the making of certain generalisations.

These facts are brought out in a striking manner by the accompanying charts, which, together with the other results incorporated in the table, will now be discussed at some length.

Anomalous figures are marked with an asterisk, and are of two kinds —those presumably due to defective analyses, and those due to specimens which are obviously not representative of the district from which they come. All asterisked figures are omitted in plotting the charts and in calculating averages. The number of anomalies in the Canterbury figures is extraordinary, and consequently these figures, with the exception of those for milk, are of no value from our present point of view. But they are of considerable interest, nevertheless, in that the specimens which they represent were supplied by an agricultural college where artificial manures are widely used.

Vegetable Growth. So many factors are active in influencing vegetable growth, *e.g.* the slope, and the general aspect of the ground, whether northerly or southerly, the amount of shade, the degree of warmth and the amount of rainfall from week to week, etc., that it is not to be expected that the twelve-monthly sets of results for either grass or silver-beet will give a smooth curve. Furthermore, the kind of grass, and the portion of the leaves analysed (young or old), will also act as disturbing factors. But nevertheless, Charts I, IV, V and VI show definitely that the iodine content of vegetable matter reaches a maximum in late autumn and winter (the period of minimum growth) and thereafter falls away rapidly, the spring growth racing ahead of the absorption of iodine by the plant. The parallelism between the curve for Auckland silver-beet (Chart V) and that for the monthly averages for grass (Chart I) is remarkable, extending even to the flattening of the curve noticeable between December and May. The well-nigh smooth curve obtained in the case of the Auckland silver-beet is no doubt due to the equable climate of the island whence the specimens were obtained.

In order to eliminate some of the disturbing factors noted above, an additional series of observations on grass was made, the grass analysed being very carefully correlated with the soil on which it was grown, being in fact always collected from the same spot, and also collected with a view to getting a truly representative specimen each month. The result is shown in Chart VI, which is practically a smooth curve up to the gap bridged by the dotted line, and again beyond that, and shows the winter maximum and spring minimum mentioned above. The hiatus in the curve between January and February is



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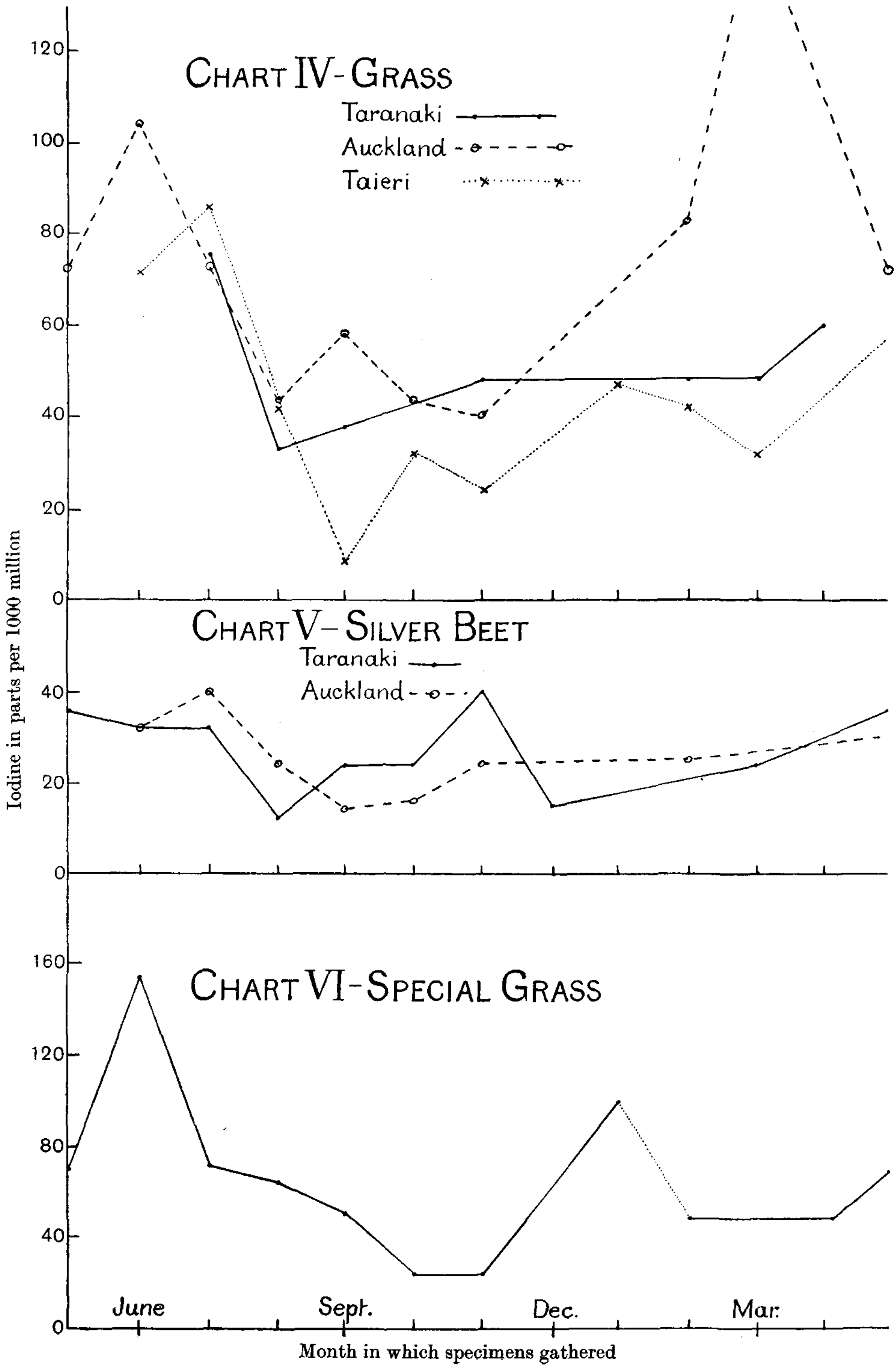

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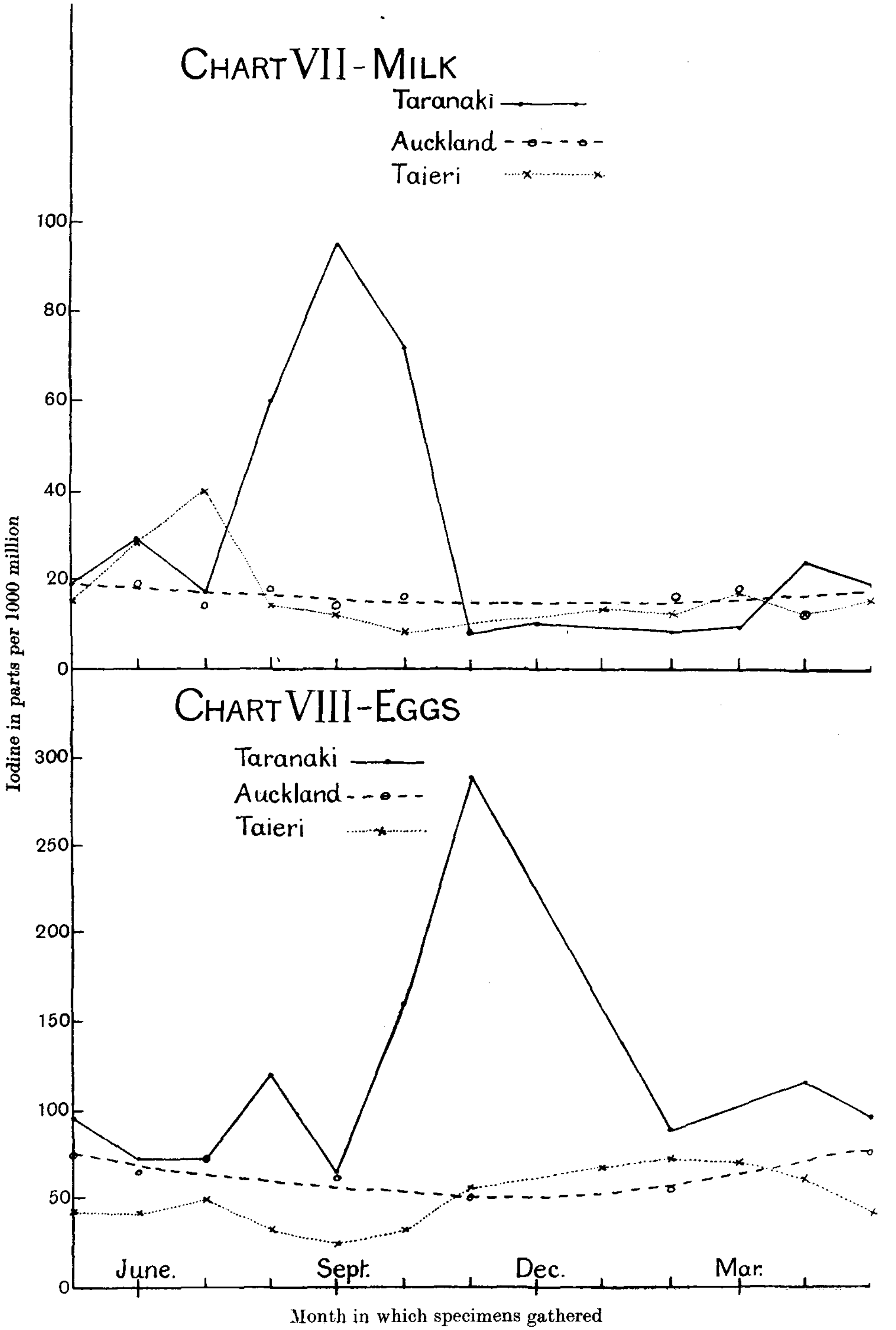

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explained by the fact that the grass was cut close during this interval, and a period of rapid growth similar to that of spring resulted, thus affording an interesting check on the accuracy of the observations.

Milk. In this case also the existence of a seasonal variation in the iodine content has been demonstrated (see Charts II and VII). Taranaki and Taieri both show distinct maxima in the spring. In this case, however, it has been observed that the variation is only indirectly associated with the season, the occurrence of a maximum really synchronising with the calving period. The interesting fact that increased iodine excretion in milk is definitely associated with the early stages of lactation is discussed later (pp. 74, 75). The maximum is followed by a distinct minimum, a finding which suggests that a period of high iodine excretion is followed by a period of recovery in which the iodine excretion falls very low. It will be noticed both here and also in the case of eggs (Chart VIII) that the Taranaki products show much greater maxima than do those of the goitrous Taieri district, presumably owing to the larger iodine reservoir existing in the soil in the former case. The secondary maxima in the monthly average curves for milk and eggs (Charts II and III) have no significance.

The Auckland results (represented by a smooth curve, Chart VII) are anomalous. This is doubtless due to the fact that the cow whose milk was being examined did not calve during this period.

NOTE. By analysing fat and skim portions of milk separately each month, it has been shown that the iodine content of the fat does *not* vary with the season, as Fellenberg (1923) suspected might be the case. No explanation is apparent of the observed variation, which is considerable and quite irregular. Probably, therefore, it depends upon chance factors, or it may be a fixed characteristic for the individual cow.

Eggs. Here again (Charts III and VIII) evidence is provided of the existence of a seasonal variation in the iodine content, the maximum now occurring in the summer. It is interesting to note that the maximum for Taieri (goitrous) eggs is just equal to the minimum for Taranaki (non-goitrous) eggs. Also the maximum for the former is deferred for two or three months, corresponding to the lateness of the season several hundred miles further south. The Taieri curve is practically smooth. The Auckland results are again seen to be anomalous, no maximum being shown. This is probably due to the fact that the specimens were obtained from an island situated within the Waitemata Harbour. Islands thus situated within harbours are well known to possess a remarkably equable climate, and under such conditions it is scarcely to be expected that the seasonal variation would be clearly defined.

Beef. In this case no variation has been detected. This might have been anticipated, as the thyroid gland acts as a kind of buffer between the flesh of an animal and the iodine of its food supply, thus tending to keep the iodine content of the flesh constant.

5. EFFECT OF COOKING.

The figures given in Table I represent the total iodine found in the raw foodstuffs examined. Some of this may of course be lost during cooking, and, when that is the case, the figure in the table does not indicate the amount of iodine in the foodstuff actually consumed by human beings. The point has therefore been investigated in a number of cases, and it will be seen that practically all loss can be avoided. A consideration of vegetables revealed the following interesting relationships:

Spinach. Raw	48γ iodine per kgrm.
Boiled	18γ iodine per kgrm.
Iodine content of water in which spinach boiled equivalent to	29γ iodine per kgrm. of original spinach
Total	47γ iodine per kgrm.

The boiling was prolonged for about an hour, and it is evident that no loss of iodine by volatilisation occurred during this time. Hence it may be safely assumed that when the cooking water is used for making soups and stews, all the naturally occurring iodine of green vegetables is ultimately ingested.

Carrot (without skin). Raw ...	18γ iodine per kgrm.
After being peeled, cut up, and boiled for 1 hour ...	14·4γ iodine per kgrm. of original specimen

From these results we may safely make the generalisation that green vegetables lose a much greater proportion of their iodine in the boiling process than do root vegetables, and that the water in the former case will therefore be more valuable from this point of view. Presumably the case will be the same with all the soluble mineral constituents of vegetable matter. This finding suggests that in the cooking of green vegetables a minimum of water should be used.

Bread. It might be anticiptated that little or no iodine is lost in the baking process. That this is so has been shown by analysing brown bread made both with ordinary salt and with iodised salt containing 1 part of potassium iodide per 250,000 of salt, and comparing observed and calculated values thus:

With ordinary salt	Iodine = 12γ	per kgrm.
With iodised salt	Iodine = 55γ	,,
∴ Iodine added	= 43γ	,,
But iodine added by calculation	= 42γ	,,

A similar result was obtained for white bread.

Oysters. Oysters have also been shown to lose no iodine when cooked.

Edible seaweed. 25–30 grm. of carrageen of iodine content 48,000γ per kilogram were soaked in water overnight, the water decanted, and the seaweed then boiled in milk and filtered. The filtrate solidifies to an edible jelly. The water, solid residue, and jelly were analysed as follows:

Water in which seaweed soaked	Iodine =	nil
Residue contained		330γ iodine
Jelly contained		1000γ iodine
Total ...		1330γ iodine

But the calculated original iodine content was $1200–1400\gamma$ iodine, *i.e.* only a small proportion of the total iodine is not consumed.

6. Salt as a Source of Iodine Supply.

In Table VI are given the iodine contents of a number of salt specimens, representative in the main of the different grades and brands of salt most widely used in New Zealand.

Table VI.

Specimen	Iodine content
Random specimen of table salt (? W. American littoral)	4 per 10^9
"Castle" salt (solar salt, W. Australia)	0
"Black Horse" table salt (Liverpool)	0
Cerebos salt	0
Cooking salt (Liverpool)	0
Fijian salt (marine)	20 per 10^9
"Red" rock salt	0
"Grey" rock salt	10 per 10^9
Salt lick (mean of three)	1700 per 10^9
Another salt lick	9000 per 10^9
Salt mixture for rat diet (no iodide added)	150 per 10^9
Iodised salt used at local orphanage (experimental)	25 KI per 250,000
"Pyramid" iodised salt (use not permitted in New Zealand) ...	47·5 ,, ,,
"Windsor" iodised salt (max. amt. permitted by New Zealand regs.)	1 ,, ,,
"Cerebos" iodised salt	0·4 ,, ,,
"Salodine" iodised salt (Liverpool)	0·25 ,, ,,

The figures for iodised salts are given in parts of potassium iodide (KI) per 250,000 for the sake of comparison with the amount allowed by the New Zealand Public Health Regulations, viz. 1 part potassium iodide per 250,000 of salt.

It is seen that, with the single exception of the specially prepared salt mixture, which is not an article of commerce, and is not used for human consumption, all the grades of non-iodised salt commonly in use in New Zealand are excessively low in iodine. Even the rock salts, which are used for stock, and which are popularly supposed to contain appreciable amounts of iodine, contain far too little to be of use prophylactically. In previous work, however (Hercus, Benson and Carter, 1925), a rock salt was analysed which contained as much as 1400 parts of iodine per 10^9. It would not seem possible, therefore, to ensure a steady supply of iodine to stock through the medium of crude salt; but work to be discussed in Chapter IV indicates that this could probably be satisfactorily accomplished by the general use of iodine-rich artificial manures. Salt licks, although those given in the table are rich in iodine, occur too erratically to be depended on in this connection.

7. TOBACCO SMOKE AS A POSSIBLE SOURCE OF IODINE INTAKE.

An investigation of tobacco smoke as a possible source of iodine intake has been made. Fellenberg (1923) made a similar series of experiments on cigars, but in the present instance pipe tobacco and cigarettes were used, since these are more widely used in New Zealand.

Results.

(*a*) "Clarence" cigarettes contain 0·40γ iodine per cigarette.
A number were smoked, and the residues analysed, thus:

Ash contains	0·18γ iodine per cigarette.
Butts contain	0·10γ iodine ,,
Total residues	0·28γ iodine ,,

∴ 0·12γ iodine per cigarette is volatilised.

(*b*) "Edgeworth" tobacco contains 0·24γ iodine per grm.
Ash from same contains 0·21γ iodine per grm. of original tobacco.

∴ 0·03γ iodine per grm. of tobacco is volatilised.

In both cases the amount volatilised, even if all inhaled and completely absorbed, which of course is not the case, would be insufficient to exert a lowering influence on goitre incidence, even among moderately heavy smokers.

Other results.	"Yankee Doodle" tobacco	0·35γ iodine per grm.
	New Zealand tobacco (medium)	0·40γ iodine per grm.

SUMMARY OF CHAPTER III.

1. The chief foods may be placed in order of merit as regards their iodine contents as follows (figures represent γ's per kilogram): Edible seaweed (48,000), oysters (880), tinned fish (500), eggs (94), sea fish (72), wholemeal products (50), green vegetables (24), milk (20), meat (12), root vegetables (7), fruit (5), white carbohydrates (2).

2. The correlation of food iodine with soil iodine has been established in the case of carrots, grass, lettuce, silver-beet, beef, eggs, and milk, whence it may be assumed that the correlation is quite general.

3. Consideration of the results set forth in sections 1 and 2 in conjunction with reliable data concerning typical New Zealand diets has enabled us to calculate the difference between iodine intake in average goitrous and non-goitrous areas. This was found to be 14·35γ per person per day, a figure which agrees remarkably well with those previously arrived at by Chatin (1851) and Fellenberg (1924).

4. Definite evidence has been obtained of a seasonal variation in the iodine content of grass, silver-beet, milk and eggs, the maxima occurring at different periods of the year in the different cases.

5. Cooking processes, with one or two exceptions, are found to have no appreciable effect on the iodine content of foods. Leafy vegetables lose about

5–2

two-thirds of their iodine when boiled, but the lost iodine is found in the cooking water, which may be used for soups, etc.

6. All the ordinary brands of table and cooking salt on the market are shown to be practically iodine-free. Even the rock salts analysed do not contain appreciable quantities of iodine.

7. Tobacco, even in the case of moderately heavy smokers, is shown to be negligible as a source of iodine supply.

IV. MANURES AND THEIR INFLUENCE ON THE IODINE CONTENT OF SOILS AND OF PLANT LIFE.

Work on the iodine content of manures has been discussed by Fellenberg (1923, 1924), and was also mentioned in a previous paper (Hercus, Benson and Carter, 1925). The nature of the influence of manures on the iodine content of plants was indicated in the same paper (p. 382) and in Table I of the present paper. It may be argued that the observed effect is too great to be due to the relatively small amounts of iodine added to the soil in the form of manure, but it is hoped that this apparent inconsistency will be removed in the following discussion.

In the first place, it has been observed that the use of stable manure containing 10–20 parts of iodine per 10^7, in a soil naturally poor in iodine, yields a plant with an iodine content comparable with that of one grown on a soil containing 100–200 parts of iodine per 10^7. This would appear to indicate that the iodine, even of organic manures, is practically all available as plant food, while that of soils is largely insoluble. The ready absorption of inorganic iodides by plants has been shown previously (Hercus, Benson and Carter, 1925). This inference has led, during the course of the present work, to numerous attempts to determine the relative proportions of water-soluble and water-insoluble iodine compounds in soil. But these attempts have always failed, owing to the colloidal nature of soils in general. The adsorption consequent upon this colloidal character renders the two types of iodine indistinguishable by laboratory means, though the plant mechanism is able to take up the adsorbed water-soluble compounds. It must be remembered that the plant will probably be able also to absorb certain insoluble organic iodides, in which case the above separation, even if achieved, would not indicate the amount of iodine in the soil available as plant food. The same considerations apply to manures such as guano, where the iodine is almost certainly available as plant food, though it has not been possible to demonstrate its solubility in water.

Other points to be borne in mind when considering the magnitude of the observed effect of manures on the iodine content of vegetable growth are that the manure is practically all within reach of the roots of the plant, and that, furthermore, the manure exerts a tonic action in stimulating root growth, thus increasing the power of the plant to take up soluble matter from the soil. The possibility of soluble constituents of the manure being dissolved out by percolating water before the roots have time to act is discussed later.

The experimental work on this question of manures and their influence falls under three heads:

1. General survey of iodine contents of manures.

2. Experiments to determine the relative adsorptive powers of different types of soil.

3. Experimental plots.

1. GENERAL SURVEY OF IODINE CONTENT OF MANURES.

A fairly complete survey of the artificial manures in commonest use in New Zealand with respect to their iodine contents has been made. The results are set forth in the following table:

Table VII.

Manure	I_2 in parts per 10^7	Manure	I_2 in parts per 10^7
Bonedust and blood	14	Special grain manure No. 1	36
Guano (Walpole Islands)	264	Special grain manure No. 2	48
Ephos (Egyptian phosphate)	12	Special rape manure	45
Nauru/ocean phosphate	11	Special turnip manure	18
Nauru/ocean phosphate super.	22	Seaweed	480
Superphosphate (36–38 % sol.)	22	Ammonium sulphate	0
Superphosphate (40–42 % sol.)	25	Kainit	0
Superphosphate (44–46 % sol.)	33	Potash salts	0
Basic slag	0	Sodium nitrate	600

Sodium nitrate (Chilean), seaweed, and Walpole Island guano are thus seen to be by far the most iodine-rich of the manures commonly used. A preliminary treatment of the sodium nitrate with sodium bisulphite in acid solution is necessary (Fellenberg, II. p. 121) in order to reduce the iodate present (about 70 per cent. of the total iodine is present in this form) to iodide before proceeding with the ordinary estimation.

Simple calculations based on the use of 1 cwt. of manure per acre (the amount used in the standard official tests) reveal that this amount of Chilean nitrate would add approximately 3,100,000γ of iodine per acre to the soil. Similarly, 1 cwt. of Walpole Island guano would add about 1,300,000γ of iodine per acre. On the other hand, it is readily shown that an average crop of wheat (40 bushels per acre), grown on a naturally iodine-rich soil and containing, therefore, about 50γ of iodine per kilogram, would contain only 54,000γ of iodine per acre. Hence in view of the considerations advanced elsewhere regarding the tonic action of manures in promoting root growth, and the power of soils to adsorb added iodine, it is quite feasible that the use of iodine-rich manures should result in increasing the iodine contents of the foods grown thereon tenfold. Furthermore, such a reflection of iodine added in manures has been experimentally proved (see section 3 of this chapter). In occasional cases, *e.g.* by a liberal use of Chilean nitrate, by the use of large quantities of seaweed, or by uneven distribution of the manure, the iodine content might even be increased a hundredfold, as has several times been observed during the present investigation.

Looked at in another way, the distribution of (say) 1,000,000γ of iodine uniformly through a 2-inch surface layer of soil would result in increasing the iodine content of this soil only by about 0·1 part per 10^7. But it must be remembered that in farming operations, the manure is concentrated in drills which may be several inches apart, and that, furthermore, the manure is not mixed into the soil before the seed is added in the same drills. The young plant will therefore be able to absorb all the iodine from a considerable amount of manure.

2. Adsorptive Powers of Different Types of Soil.

The procedure adopted in this investigation was as follows: Typical specimens of loam, clay, and sand were obtained, and the iodine contents of the dried specimens determined. To 200 grm. each of the specimens were then added 200 c.c. of a solution containing 0·13 grm. of potassium iodide per litre; *i.e.* 1000 parts of iodine per 10^7 were added to each specimen. After being mixed thoroughly and allowed to stand overnight, the specimens were dried slowly. They were then transferred to fine muslin bags and suspended in three upright vessels, through each of which a steady current of six litres of water per hour was allowed to pass for one week. At the end of the week the samples were removed, dried, and analysed with very interesting results. In order to make certain that the washing had been uniform throughout the specimens, analyses were made of both the inner and outer portions of the contents of each muslin bag. Results:

Table VIII.

	Parts of I_2 per 10^7		
	Loam	Clay	Sand
Originally	36	38	0
After treatment with KI ...	1036	1038	1000
After washing—inner portion	168	50	0
After washing—outer portion	180	48	0

Loam is thus seen to retain a large percentage of the added iodine, even after the above-described washing action. Clay, under the same conditions, retains a small amount, but sand, as might be anticipated, retains none. The relationship shown to exist between the adsorptive powers of loam and clay is interesting in that clay is a standard example of a colloidal material, and might therefore be expected to retain a good deal of the added iodine. Loam, however, is also colloidal and while the clay colloid is "suspensoid," consisting of discrete particles, the loam colloids are partly "emulsoids" of much greater viscosity, and are therefore less easily washed and retain more adsorbed iodine.

If further proof were needed of the ability of manured soils to retain added iodine and hence to supply it to plants in even the wettest climates, it is provided by the analyses of manured soils, which show distinctly higher iodine contents than the adjoining unmanured soils, even at considerable periods after the addition of the manure, thus:

Lincoln—Unmanured	12, 18	Manured	24, 28
Taieri— ,,	24	,,	48
Hampden— ,,	34	,,	44

These figures do not include results for soils to which potassium iodide solution has been added for experimental purposes (see next section).

Vegetables grown on the manured soils were found to contain several times the normal amount of iodine. Thus for Hampden were found:

Grass (manured) 144 parts per 10^9
Grass (unmanured) 30 parts per 10^9

It is clear that plant life is a considerable drain on the iodine reservoir of the soil, but there are also periods of rest and of at least partial recovery by the return to the soil of the iodine contained in decaying vegetable matter. The surface layer would thus be enriched, particularly in the case of manured soils, and so account for the considerable differences observed in the iodine contents of manured and unmanured soils.

3. EXPERIMENTAL PLOTS.

Lettuces and turnips have been grown on three experimental plots to each of which had previously been added a small amount (0·2 grm., 1 grm., and 5 grm. respectively) of potassium iodide per square yard. Although the individual conditions for each plot, such as slope of the ground, amount of direct sunlight received, etc., have made it impossible that the plants should reflect accurately the different amounts of iodine in the three plots, it may nevertheless be claimed that in all cases the vegetables showed much higher iodine contents than corresponding ones grown in a control plot. All the results represent spring growth (minimum iodine content—see Chart I).

Table IX.

Plot	KI/sq. yd.	Soil I_2 per 10^7	Type of growth	Lettuces Young	Lettuces 6 wks. later	Turnips Young	Turnips 6 wks. later
Control	0	18	Normal	14	16	—	6
A	0·2 grm.	50	Stunted	—	20	0	48
B	1 ,,	84	Normal	180	60	360	30
C	5 ,,	56	Lank and pale	60	25	12	84

In two other plots, the effect of adding iodine-rich manure to the soil in the proportion of 1 cwt. per acre has been investigated as follows: To one plot, 1 square yard in area, were added 10 grm. of Chilean nitrate. The second plot was kept as a control. The manure was distributed evenly in drills in the first plot and turnips grown in both. Unfortunately, the planting was done late in the autumn, and so growth has been very slow. It was therefore necessary to analyse the leafy tops only of very immature plants which had been in the ground all the winter. Even so, the results give definite evidence of the reflection of the iodine added to the soil in the manure used. Thus:

Plot manured with nitrate. Iodine content of turnip tops = 40γ per kgrm.
Control plot. Iodine content of turnip tops = 28γ per kgrm.

Conclusion. This work on the establishment of the relationship between added soil iodine and the iodine content of plants is of particular interest in that it indicates that the use of iodine-rich manures will ensure a regular supply of iodine to stock in goitrous districts.

Summary of Chapter IV.

1. Manures in descending order of their iodine contents are as follows (figures in parts per 10^7): Chilean nitrate (600), seaweed (480), guano (264), superphosphate (30), blood and bone (14), natural phosphates (12), others negligible. Calculations based on these and on other figures show to what extent manures may be expected to influence the iodine content of crops.

2. Loam is shown to have great power to retain soluble iodides during prolonged washing. This power was less in clay, and in sand was nil. This is of obvious importance in considering fertilisers as a factor in increasing the iodine supply to stock through the medium of their food.

3. The power of plants to combine in their tissues iodine added to the soil in the form of potassium iodide and also in manures has been demonstrated in experimental plots, thus indicating a feasible way of supplying iodine regularly to stock in endemic areas.

V. STUDIES ON CERTAIN ASPECTS OF IODINE METABOLISM IN THE ANIMAL BODY.

1. Correlation of Iodine Intake with Excretion in Urine.

A very thorough investigation of the excretion of iodine through the various possible avenues (Fellenberg, 1924) has indicated that the majority is excreted in the urine, and that, furthermore, the iodine excretion in urine may be regarded, without serious error, as an index of the total iodine excretion at a given time. On the basis of this observation, iodine excretion in urine has been adopted in the subsequent investigations as an index of the total excretion.

A similar relationship to that between goitre incidence, soil iodine, and the iodine content of foods has been demonstrated in the excretion of iodine in urine, a striking difference being observed between specimens obtained from goitrous and non-goitrous subjects.

Table X.

Type	No. of specimens analysed	Range of iodine contents in γ's per litre	Mean result in γ's per litre
Goitrous	27	5– 75	25
Non-goitrous	35	11–384	49

The "non-goitrous" figures include results for urine specimens from non-goitrous subjects resident in an otherwise goitrous area. Furthermore, the results were obtained from specimens obtained at all seasons of the year from varying age groups, and from both males and females. In the latter case specimens have been included from girls at puberty and from women during pregnancy and the *post partum* period. The very marked influence of certain of these factors on the iodine excretion in urine will be discussed in subsequent paragraphs. The inclusion of all results influenced by such disturbing factors considerably increases the significance of the above mean results.

As often as possible, analysis was made of an aliquot part of a 24-hour sample of urine, and the excretion per 24 hours thus calculated. But for the sake of uniformity, and because in many cases the requisite data were not available, all results have been expressed in γ's per litre in compiling the above table.

The effect of iodine taken medicinally, even in very small doses, on the iodine excretion in urine is manifest and calls for no comment: it is illustrated in the following two cases:

(*a*) Toxic goitre. Receiving 100,000γ iodine per day; excretion in urine = 15,000γ per day.

(*b*) Toxic goitre. Receiving 30,000γ iodine per day; excretion in urine = 2150γ per day.

A more intensive study of the correlation of iodine intake through food with iodine excretion in urine was made in a local women's college. This was undertaken in order to corroborate Fellenberg's evidence on this point, but incidentally it has led to an interesting observation regarding the periodicity of iodine metabolism in the human body. The procedure was as follows: In September–October, the iodine content of the diet in the college was observed daily for a fortnight, and 24-hour specimens of urine collected from a number of students at the end of both the first and second weeks. The surprising observation was made that the excretion at this time (spring) was in the majority of cases considerably greater than the intake. It was then realised that Fellenberg's figures, showing a very definite dependence of the amount of iodine excreted on the amount ingested, had been obtained in the autumn. A set of observations similar to those made in the spring was therefore made in March–April (autumn), when, as was anticipated, the iodine excretion was found to be of the same order as the intake, which was approximately 30γ per day. Results:

Table XI.

	Spring: Excretion in γ's per day		Autumn: Excretion in γ's per day	
Subject	1st week	2nd week	1st week	2nd week
1	15	25	20	22
2*	34	60	54	75
3	11	192	13	17
4	192	384	45	25
5	60	100	165†	15
6	50	—	—	—
7*	50	36	—	—

* Goitrous subjects. † Meal of tinned salmon on previous day (see Table I).

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The spring anomalies could not be traced to the addition of iodine-rich foods to the diet, to the taking of iodine or iodides medicinally, nor yet to the possible disturbing factor of menstruation. The results therefore suggest that there is a seasonal periodicity in the functioning of the thyroid gland, part of the year being a time of storage, while the other part is a time of increased output. This observation fits in very well with the marked seasonal variation in the iodine content of various animal thyroids observed by Seidel and Fenger (1913), who showed that the minimum occurred in the spring. The periods of maximum excretion and minimum storage are thus seen to coincide. A seasonal variation of the magnitude indicated by the above results is rendered all the more feasible by the fact that the increased amounts of iodine observed in the spring urines are such that the thyroid could stand the extra drain thus put upon it without approaching exhaustion. In fact, the total storage (normally 40 mg.) would only be reduced by one-half if the extra demand (say 200γ per day) were maintained for over six months. From these findings one might reasonably expect that in endemic areas goitre would first manifest itself in the spring-time, and that the progressive enlargement of the thyroid would be more marked at this season of the year.

A further line of work suggested by the above figures, which has not yet been followed up, is the making of a periodical examination of urines from goitrous subjects.

2. Relationship between Iodine Excretion in Human Urine and Milk during Lactation.

In a previous paper (Hercus, Benson and Carter, p. 392) emphasis was laid on the importance of the effect of congenital influences on goitre in infancy. It was pointed out that iodine supplied to a pregnant woman was readily stored in the foetal thyroid after the sixth month, it thus being possible to compensate the natural deficiency in a goitrous area. In the normal course of events, as soon as a child is born, it becomes entirely dependent on the mother's milk for its iodine supply, and it was therefore thought worth while to make an examination of human milk from this point of view. Table XII shows that the iodine content of the milk of the goitrous woman is definitely lower than that of the non-goitrous.

Systematic investigations have revealed a very interesting relationship between the iodine excreted in urine and in milk, viz. that, during the first week or ten days after childbirth, the iodine content of the milk per litre is distinctly higher than that of the urine, while by the third month the ratio is inverted, the bulk of the iodine being then excreted in the urine. It must be borne in mind that more milk is secreted as lactation proceeds, but the increase in output is not sufficiently great to compensate for the falling-off in iodine content and thus to keep the amount of iodine excreted in the milk constant.

This observation agrees in a remarkable way with that of the seasonal variation in the iodine content of cow's milk (see p. 64, where it was pointed

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out that the occurrence of a maximum synchronised with the calving period). Results:

Table XII.

	Non-Goitrous						Goitrous			
	A		B		C		D		E	
	Urine	Milk	Urine	Milk	Urine	Milk	Urine	Milk	Urine	Milk
1	24	80	31*	15	22	30	192*	16	10	24
2	—	36	14	15	23	16	19	7	21	12
3	60	25	—	—	—	—	—	—	—	—
4	—	16	—	—	—	—	—	—	—	—

* Specimens apparently contaminated.

A 1, at parturition; 2, 4 weeks later; 3, 8 weeks later; 4, 5 months later.
B 1, 4th day of puerperium; 2, 12 weeks later.
C 1, 10th day of puerperium; 2, 6 weeks later.
D 1, 7th day of puerperium; 2, 12 weeks later.
E 1, early in lactation; 2, 10 weeks later.

The need for more complete data in this connection is clear. But the results here given are sufficient to show that, although the natural iodine deficiency in goitrous areas is in part compensated in an infant's natural food during the puerperium, yet the iodine supply in such areas becomes deficient within a few weeks. In view of the unbroken history of deficient iodine supply *in utero*, in infancy, and also in childhood when the organism becomes dependent on the food products of a district poor in iodine, it is scarcely to be wondered at that in certain parts of New Zealand over 30 per cent. of children have palpable goitres when they enter school at the age of five years.

3. EFFECT ON ANIMAL PRODUCTS OF ADDING POTASSIUM IODIDE TO THE DIET.

The reflection in the animal organism of what we may term the animal's "iodine environment" is strikingly shown by the following analyses of different types of fish-flesh:

Sea fish (groper) ... ... Iodine = 72γ per kgrm.
Tidal-water fish (trout caught 3 miles from the sea) Iodine = 50γ ,,
Fresh-water fish (trout caught 100 miles from the sea) Iodine = 24γ ,,

Cf. iodine content of sea water, which is 19γ per litre, and that of fresh water, which is only rarely observed to rise above $2-4\gamma$ per litre.

Whether iodine added to the diet in the form of potassium iodide will be similarly reflected in the animal organism is another problem. It is also one of great importance, in that our justification for advocating the use of potassium iodide in goitre prophylaxis (see Chapter VI) depends upon whether or not iodine administered in this form becomes incorporated, in organic combination, in the various products of the animal organism. Marine and Rogoff (1916) have shown that iodine injected intravenously in the form of potassium iodide is absorbed by the thyroid. The work now to be described has demonstrated that a similar reflection of iodine added to the diet in the form of potassium iodide takes place in eggs, milk and the thyroid gland. Hence the use of the

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less economical and more troublesome method of prophylaxis involving the supply of organic iodine becomes unnecessary.

Experiments with Poultry. To the water supplied daily to half a dozen hens was added in the form of potassium iodide the equivalent of several thousand micrograms of iodine per bird. This treatment was continued for a month, and the eggs analysed at intervals for seven weeks as follows:

Jan. 21st.	Iodine content of eggs	44γ	per kgrm.
Jan. 22nd.	Began treatment.		
Feb. 4th.	Iodine content of eggs	8800γ	,,
Feb. 18th.	Discontinued treatment.		
Feb. 19th.	Iodine content of eggs	7500γ	,,
Mar. 12th.	Iodine content of eggs	140γ	,,

The high result obtaining as long as three weeks after the discontinuance of treatment in itself amounts to a proof that the extra iodine so appearing has been first brought into organic combination. This follows because potassium iodide itself is so extremely soluble that it would not remain in the system as such for so long.

The maximum secretion per hen per day (assuming one egg per hen per day) is approximately 400γ, which is only a small percentage of the total iodine supplied.

Experiments with a Cow. A similar procedure was adopted to that outlined above, but in this case considerably less iodine was given, the effect having been so marked in the previous instance. About 10,000γ a day were given to a cow for fourteen days.

Results.

Initial iodine content of milk	20γ	per litre
Iodine content after one week	24γ	,,
,, ,, ,, two weeks	50γ	,,
,, ,, four weeks after discontinuing treatment	29γ	,,

The effect, though less marked than in the case of eggs, is quite definite and is particularly interesting in view of the fact that various workers claim that the addition of such items as fat, sugar, salt, calcium and phosphorus to the diet does *not* affect the composition of the milk (see Lane-Claypon, *Milk and its Hygienic Relationships*).

Experiments on Rats. Though we have not as yet observed a definitely pathological thyroid in experimentally treated rats (but see Animal Thyroids, next section), the influence of the addition of traces of potassium iodide to the diet on the iodine content of the thyroid gland is remarkable. Thus:

Thyroids of rats fed on white bread and milk (low iodine diet) contained 0·03 mg. iodine per gram of fresh gland. A number of these rats were isolated, and after ten days on the same diet to which was added 200γ of iodine per day in the form of potassium iodide solution, a rat of this batch was killed and its thyroid analysed and found to contain 0·57 mg. iodine per gram, an increase of nearly twenty times, thus showing that iodine supplied as potassium iodide is readily stored in the thyroid as thyroxin. These rats have now been put back on to the original iodine-poor diet, and the weight, iodine content and histology of their thyroids will be observed at intervals during the next few months with a view to finding whether any histological change occurs when the iodine store becomes exhausted.

4. SUNDRIES.

Bacterial action. Work on the power of bacteria to absorb iodine is important in that goitre sometimes appears to be due to a removal of a portion of the available iodine supply by intestinal bacteria. Unfortunately, our observations on this point are rather meagre, but such as we have are of a negative character. Thus no iodine was detected in 0·1 grm. of dried *B. coli* grown on an agar containing as much as 200γ of iodine per kilogram. The agar was very faintly alkaline (pH 7·6–7·8). Fellenberg (1924) claims to have shown that iodine set free in acid and alkaline solutions by atmospheric oxidation is absorbed by bacteria. If this is so, our result would appear to indicate that the amount of iodine involved is so small as to be without significance from the point of view of the available iodine supply of human beings. We obtained a similar result with streptococci, 0·4 grm. of which, grown in 1200 c.c. of broth, containing 60γ of iodine per litre, showed no detectable iodine after thorough washing with saline and distilled water.

Pituitrin. Ugo Pardi (1916) states that pituitary extract injected intramuscularly exerts a non-specific action in stimulating excretion of the thyroid colloid. In confirmation of other workers, we have shown that the iodine content of pituitrin is very low (2γ were found in one ampoule). This is of interest because pituitary extract may take the place of thyroxin in the therapeutic treatment of goitre and might therefore be reasonably expected to contain iodine as a constituent. But such is obviously not the case, and its therapeutic action is apparently connected with the inter-relation of the internal secretions and not dependent on the presence of iodine.

Animal Thyroids.

Seasonal Variation. It has been shown elsewhere (p. 74) that the period of maximum excretion of iodine in urine then commented on coincides with the period of minimum storage of iodine in the thyroid observed by Seidell and Fenger in the spring. Our own rather meagre results on the seasonal variation of the iodine content of animal thyroids indicate a maximum in the spring. But this apparent contradiction is doubtless due to the fact that New Zealand stock is frequently fed in the late winter and early spring months on root crops, which are often grown on iodine-rich manures. This apparently more than compensates for the depletion occurring naturally at this time.

Results. Mean iodine contents of histologically normal fresh sheep thyroids obtained in the following months:

July	1·0 mg. per grm.	
September	1·9	,,
November	0·9	,,
February	0·8	,,

The investigation was not pursued beyond this stage owing to pressure of more important work.

Evidences of Goitre in Animals. Hayden, Wenner and Rucker have shown that the size of white rats' thyroids may be doubled by feeding them on a diet deficient in iodine. We have also found that the thyroids of animals fed on deficient iodine show enlargements up to three times the normal size. Histologically, such glands were, with one exception, not found to be definitely pathological, being in the main of the simple colloid type of enlargement. In one or two cases a marked degree of hyperphasia was also shown, the gland thus being of the actively secreting type.

The one exception was a wild rabbit, bred in the very goitrous region of the Clutha Valley, whose thyroid was twice the normal size, showed marked hyperphasia, and was becoming atrophied and fibrosed.

The thyroids of white rats fed for some months on a diet of white bread and a little milk were also twice the normal size, and in one case consisted partly of a congested hyperplastic area, and partly of a group of very large acini filled with dense colloid mixed with cells.

On the other hand, a sheep thyroid weighing 32 grm., as against the normal 10–12 grm., showed only the typical colloid structure associated with a normal gland.

In all these cases the iodine content of the gland in milligrams per gram was abnormally low.

A characteristic feature of animals in general, and in particular of wild animals, seems to be that they are capable of remaining non-goitrous on a much lower iodine intake than is man. Thus the iodine contents of perfectly normal sheep thyroids were found to range from 0·28 to 2·9 mg. per gram of fresh gland, while the extreme range observed in the case of human beings was from 0·4 to 1·5 mg. per gram. Normal sized rat and rabbit thyroids were observed with iodine contents of 0·07 and 0·16 mg. per gram respectively. In considering these figures it is necessary to bear in mind that the ratio of the weight of the thyroid to the total body weight is probably very different in different animals.

Chemical figures obtained by one of us (K. C. R.) concerning the distribution of iodine in the various portions of pathological human thyroids will be correlated with histological findings and published elsewhere.

SUMMARY OF CHAPTER V.

1. A classification of the results of analyses of urine samples collected during a twelve-monthly period from all classes of people reveals a well-defined relationship between goitre incidence and iodine excretion in urine. The iodine excreted in urine does not accurately reflect the iodine ingested throughout the year, as is shown by the occurrence of anomalous results in the spring. The results obtained point to a periodic variation in the function of the thyroid gland.

2. Observations of urine and milk samples from both goitrous and non-goitrous women show that the iodine content of milk falls off as lactation proceeds, being initially much higher than that in urine. The iodine in urine shows a corresponding increase as lactation proceeds.

3. Small amounts of potassium iodide added to the diet of hens, cows, and rats are reflected in eggs, milk and thyroid respectively, thus showing the ability of the animal organism to incorporate iodine administered in this form in organic combination—an important point in connection with the method of prophylaxis suggested later.

4. No appreciable absorption of iodine by *B. coli* and streptococci from weakly alkaline media takes place, even though the media contain relatively large proportions of iodine.

The iodine content of pituitrin is not comparable with that of the related thyroid hormone.

Various animals are shown to live on a lower iodine intake than man without becoming goitrous. Evidence of goitre in sheep, rabbits, and rats has nevertheless been obtained.

VI. RECOMMENDATIONS REGARDING PROPHYLAXIS.

In a previous contribution (Hercus, Benson and Carter, 1925) results were given regarding the administration of small doses of iodine to school children with a view to preventing the development of endemic goitre. The procedure was criticised both on account of the irregular manner in which the iodine was supplied to the thyroid gland, and of the relatively excessive dosage adopted. Objection was also raised to the inadequacy of a scheme of prophylaxis limited to one section of the population of a goitrous district. The scheme of goitre prophylaxis adopted in Switzerland in which the necessary amount of iodine is added to the salt of the country was recommended as being at once more comprehensive, including as it does the whole population, and more physiological. Favourable results were reported of a limited trial of this method over a period of eighteen months. On the basis of Fellenberg's work (1923), a tentative recommendation was made that all salt used for human consumption in endemic areas should contain one part of potassium iodide in 200,000 parts of salt. Meantime the above-mentioned studies were undertaken to determine the actual deficiency in iodine in goitrous districts, and the average daily consumption of salt per head, so that the extent to which the salt should be iodised could be accurately established.

In Chapter III it has been shown that the daily ingestion of iodine in the food supply of a non-goitrous area is 34·85γ, whereas in a goitrous area it is 20·15γ, a difference of 14·70γ. Corroborative evidence was supplied by comparing the iodine excretion in the urine in such districts, and finding the average in the non-goitrous to be 49γ, in the goitrous 25γ. The average daily consumption of salt from all sources has been ascertained to be approximately 6 grm. It is evident, therefore, that if our previous recommendation that all salt be iodised so as to contain one part of potassium iodide in 200,000, which is approximately equivalent to one part of iodine in 250,000 be adopted, the iodine intake will be augmented daily by 24γ, which is ample for requirements.

If such a measure was adopted throughout the country, and considering the widespread incidence of goitre this would appear to be the most effective course, the dweller in the endemic area would have the daily iodine supply increased to 44γ, an amount a trifle greater than the normal intake in a non-endemic area, where the daily supply would be raised to 59γ. Fellenberg (1924, VI) has shown that the normal intake in some districts in Switzerland particularly rich in iodine is even greater than this. Hotz (1922) has shown that the daily intake must reach 700γ before any of the harmful effects of iodine on a pathological thyroid need be anticipated, so that it would appear that a reasonably safe margin is provided.

There have been several references in recent medical literature, particularly in that of the United States of America, to the dangers surrounding the indiscriminate use of iodine in the prophylaxis and treatment of goitre. Numerous cases of hyperthyroidism induced by the use of iodine are cited. Kocher (1910) drew attention to the fact that iodine acting in large dosage could convert a simple into a toxic goitre, and there are few physicians accustomed to the treatment of simple goitre with iodine who have not had personal experience of this complication. Whereas the normal thyroid can be subjected to enormous doses of iodine with no ill effect, as has been amply demonstrated in the liberal use of iodides in the treatment of syphilis and other conditions, the pathological gland, particularly in adult life, is frequently highly sensitive to it. The relatively large surface of thyroid tissue takes up the iodine, excess of thyroxin is elaborated and symptoms of hyperthyroidism may arise. Fortunately, as work with school-children shows, the enlarged thyroid of the child and the adolescent is tolerant to large doses of iodine, the iodine in excess of requirements being promptly excreted.

This boomerang action of iodine was recognised and provided for by the Swiss Goitre Commission (1924) when in advocating the universal iodising of the salt they limited the strength to 1 in 250,000, and stressed at the same time the need of prohibiting the sale of anti-goitrous remedies. In America, however, little attention has evidently been given to the dangers attending the universal use of relatively large doses of iodine, or to the actual requirements of the body for iodine. Hartsock (1926) cites sixteen male cases and twenty-three female cases of hyperthyroidism produced by the use of iodised salt within a period of six months in the Cleveland Clinic in the State of Michigan. He states that in May, 1924, Michigan adopted a state law that all salt sold in the State should contain "*a certain amount*" of iodine, but the actual amount is not stated, although the frequent appearance of iodine rashes is commented on. As a result of these findings the author proceeds to condemn the universal use of iodised salt in a goitrous community. The salt in Michigan is apparently iodised to the extent of 1 part in 5000, which is calculated to supply 300 mg. a year to the gland. As the normal requirement of the gland is about 10·4 mg. a year, and the total storage capacity of the normal adult gland does not exceed 25 mg., it is not to be wondered at that ill effects are being experienced. The remedy would appear not to lie in abandoning the iodising of salt, but in reducing the quantity of iodine to more reasonable proportions. In this connection we are of the opinion that methods of treatment, as well as of prophylaxis of goitre, require revision, in the direction of thinking of iodine in terms of micrograms. Although our results show that it is possible to supply the iodine deficiency in goitrous areas by means of the use of iodine-rich manures, or the more extensive use of sea foods and other iodine-rich foods or the giving of inorganic iodides to animals such as cows and fowls, these methods of control are so dependent on educational propaganda and are so relatively difficult and costly in application that we have no hesitation in definitely advising the universal addition to all salt intended for human consumption in New Zealand of potassium iodide in the strength of 1 in 250,000 or 0·0004 per cent., thus supplementing the iodine intake of all persons by 0·024 mg. per day or 8·76 mg. (0·135 grains) a year, an infinitesimal quantity not comparable to the amount of other inorganic salts the addition of which to common salt is permitted, viz. magnesium carbonate 1 per cent., calcium sulphate 1·4 per cent., calcium and magnesium chlorides 0·5 per cent.

Whether this measure, which seems to be a commonsense one, is adopted or not, the public of goitrous regions should be warned that the indiscriminate use of iodine for the treatment of goitre is a dangerous procedure, and at the same time the Public Health authorities should take steps to discourage, if they are unable to prohibit, the sale of patent anti-goitre remedies, rich, as they invariably are, in iodine.

VII. GENERAL SUMMARY.

The correlation of high goitre incidence in New Zealand with low soil iodine having been established previously, the distribution of iodine in its relationship to the goitre problem is further considered in this study. The method of analysis used throughout has been that of Th. V. Fellenberg, with certain minor modifications. The findings are summarised as follows:

1. In a general survey of the iodine content of foodstuffs in New Zealand, it has been shown that the foods richest in iodine, arranged in descending order

of iodine content, are edible seaweed, sea fish, eggs, wholemeal cereal products, leafy vegetables and milk. Refined cereal products, root vegetables, and fruits are shown to be of low iodine content. Dried foods contain more iodine than the corresponding fresh foods.

2. A comparative study of the iodine content of foodstuffs from goitrous and non-goitrous districts establishes the fact that the soil-iodine is accurately reflected in the food-iodine.

3. The difference in the daily iodine intake in the food supply of typical goitrous and non-goitrous districts is calculated to be 14·35 micrograms.

4. The iodine content of certain vegetables and animal foods is shown to present a well-marked seasonal variation. The maximum iodine content of vegetable matter is reached in the late autumn and winter when growth is at a minimum. In the case of eggs the maximum is reached in summer, in milk in the spring. In the latter case calving and lactation are shown to be disturbing factors of importance.

5. Cooking is shown to have little effect on the reduction of the iodine content of root vegetables, seaweed, fish and bread, but to reduce the content of green vegetables by about two-thirds.

6. Commercial salt is shown to be an unreliable source of iodine supply, the majority being practically iodine-free.

7. Tobacco smoke is a negligible source of iodine supply.

8. The iodine content of the artificial manures commonly used in New Zealand is determined, and their probable effect on the content of crops is calculated.

9. The iodine adsorptive powers of different types of soils is estimated experimentally. Loam is shown to have marked retentive powers for soluble iodides. In clay the retention is less and in sand nil.

10. Experimental studies on the influence of iodine-rich manures on plant life are presented.

11. A well-defined relationship is shown to exist between goitre incidence and iodine excretion in the urine.

12. The iodine content of human milk in the goitrous woman is shown to be lower than in the non-goitrous, and a relationship is shown to exist between the amount of iodine excreted in the urine and milk during lactation.

13. The flesh of fish is shown to vary in iodine content according to its "iodine environment."

14. Small amounts of potassium iodide added to the diet of various animals is shown to increase the iodine content of the thyroid glands and of the food products.

15. Certain intestinal bacteria are studied in regard to their power of absorbing iodine from an alkaline medium rich in iodine with negative results.

16. Certain data with regard to the iodine content of the thyroid glands of various animals are submitted which suggest that certain animals can live on a lower iodine threshold than man without developing goitre.

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(*MS. received for publication* 11. XI. 1926.—Ed.)