THYROID ENLARGEMENT IN SCHOOL-CHILDREN OF NORTH OXFORDSHIRE

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It was shown in the report of the Goitre Subcommittee of the Medical Research Council (Murray, Ryle, Simpson, and Wilson, 1948) that although the incidence of endemic goitre in adults was decreasing in many areas there were other areas in this country in which the incidence of thyroid enlargement in children remained very much above normal. The enlarged thyroid gland in childhood and goitre in adults are the result of the body's efforts to maintain thyroid hormone production whenever dietary iodine is insufficient or when goitrogenic substances in foodstuffs prevent the utilization of iodine by the gland. Such enlargement is prevented by the administration of extra iodine. Genetic factors influencing the synthesis of thyroid hormone may also cause thyroid enlargement, but such conditions are rare. The enlarged gland in adolescence is often regarded as a normal physiological response because it diminishes and disappears at about the age of 20. There is no doubt, however, that, in regions where the incidence of enlarged thyroid gland in adolescents is high, goitres also occur more often in adults (Stocks, 1927).

Present Investigation

It was of interest, therefore, to be able to examine the thyroids of schoolchildren in North Oxfordshire, where it had been shown in the previous survey that the incidence of enlargement was much higher than normal (Murray *et al.*, 1948).

The area in question lies on a belt of limestones and marls extending through the county from Witney to Banbury. It is typical of many such areas in this country in that the amount of iodine in the soil and circulating water is low. For instance, our estimations show that the water drawn from the local wells contains from 0.6 to 3.9 μg . of iodine per litre; a level below 3 to 5 $\mu\text{g}/\text{l}$. is generally regarded as goitrogenic (McClendon and Williams, 1923). Owing to its high calcium content the water is hard, and such water is believed to interfere with the utilization of iodine (Taylor, 1958).

The thyroids of schoolchildren in the same schools in North Oxfordshire which were surveyed in 1944 have been examined for enlargement. The same method of examination and classification used previously has again been used (Murray *et al.*, 1948). The results showed a significant increase (26.9% to 40.4%) in the number of children with an enlarged thyroid gland. In several schools the areas from which the children were drawn had changed since 1944, and further inquiry was based on Hook Norton, where the supply area had not changed. It was found that the mean percentage incidence of visible enlargement of the thyroid gland amongst Hook Norton children had remained high, at 46% (formerly 38%). Amongst a

comparable group of Oxford City children the incidence was 6%—that is, near the normal limits for adolescence, which is about 3% (Murray *et al.*, 1948). Hook Norton residents (population 1,153) who had taken part in the 1944 village goitre survey were re-examined. Six persons who in 1944 had shown thyroid enlargement now had obvious goitre, one with nodules and the symptoms of toxic goitre (tachycardia, slight exophthalmos, and tremor). Five others who had persevered with the advised use of iodized salt were now free of thyroid enlargement. Two large cystic goitres were again noted in familial groups who had lived a "closed community" life; the photograph of one such case is shown above.

A large cystic goitre in a man who lived a "closed community" life.

Sources of Iodine

The main sources of iodine in the dietary, apart from sea fish, are milk, vegetables, and cereals (von Fellenberg, 1926). The iodine in drinking-water contributes to a lesser degree directly but influences the iodine content of locally grown farm produce (Remington, Culp, and von Kolnitz, 1929). Of the 100 to 150 μg . of iodine needed daily to maintain good health, about one-half to one-third may be derived from milk. Samples of milk from North Oxfordshire have therefore been compared with those from a known high iodine area in Essex, where the drinking-water of the cattle contained from 18 to 120 μg . of iodine per litre. Information from farmers included feeding plans for both summer and winter. There was no significant difference between the iodine contents of milks from the three areas, but there was a marked difference between the summer and winter samples. The amount of iodine present was lowest in summer, when little or no concentrates were fed. (Summer milk contained from 8 to 56 μg . of iodine per litre; mean 20 μg .; winter milk from 11 to 150 μg .; mean 60 μg .). In some cases when iodine supplements were fed to the cattle the iodine content of the milk was increased by a factor of twenty. An experiment on the effect of iodine-containing fertilizers on the iodine content of milk is at present in progress.

The daily intake of iodine in milk from farms in the Hook Norton area is at the most about 50 μg . a day in winter and considerably less in summer. Very little sea fish is readily available, and most of the vegetables are grown locally. Mains water has recently been supplied to Hook Norton village, and contains from 2 to 5.5 μg . of iodine per litre, depending on the mingling of the different sources from which it is derived. Some people continue to use local well water, which is very low in iodine (0.6 $\mu\text{g}/\text{l}$.) and often bacteriologically impure. Thus the iodine available in

the locality of Hook Norton must be about 60 $\mu\text{g.}$ daily in winter and less in summer. It is thus approaching the goitrogenic level, and this, coupled with the hardness of the drinking-water and its possible bacterial contamination (cf. McCarrison, 1913), is probably sufficient to explain the observed high incidence of thyroid enlargement. In Oxford City, where the incidence of enlarged glands is about normal, the water contains 4 $\mu\text{g.}$ of iodine per litre and the dietary is urban.

The Committee on Nutrition of the British Medical Association (1950) supported the recommendation of the Goitre Subcommittee of the Medical Research Council that the bulk of common salt in this country should be iodized by the addition of 1 part of potassium iodide or iodate to 10,000 parts of salt. All practical difficulties in the way of this, such as assay procedure, stabilization of packeted salt, dangers of overdose, have now been overcome. Experience in many parts of the world (McClure, 1934; Kimball, 1946) shows that this is the most practical method of goitre prophylaxis, and there is no reason to doubt that it would not be effective in rapidly reducing the high incidence of thyroid enlargement in schoolchildren of North Oxfordshire. Taylor (1958) in discussing the evolution of toxic goitre from simple nodular goitre has pointed out that the cost to this country of not using iodized salt must be immense if calculated in terms of the demands made on the medical services and by the loss of working-time.

Summary

A survey of thyroid enlargement in schoolchildren in North Oxfordshire has been made. The mean incidence of enlargement is 40% compared with 6% in Oxford City, and has increased from 27% since 1944.

The high incidence of thyroid enlargement is related to the low iodine content of the dietary and is possibly aggravated by the goitrogenic effects of hard water.

The iodine content of milk from farms in low and high iodine areas was found not to be significantly different. There was, however, a significant difference between winter and summer milk (20 $\mu\text{g.}$ compared with 60 $\mu\text{g./l.}$). The higher content of iodine in winter milk can be attributed to the feeding of winter supplements.

It is suggested that there is a strong case for the prophylactic administration of extra iodine, especially in low-iodine areas. This is best given in the form of iodized salt.

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QUINIDINE POISONING AS A CAUSE OF GENERALIZED MUSCLE WEAKNESS

BY

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As I have been unable to find any reported cases of muscle weakness following the therapeutic use of quinidine, the following record may be of interest.

Case History

A male child, born on February 19, 1952, was seen for the first time on August 28, 1957, with recurrence of intermittent generalized weakness. His weight was 41 lb. (18.6 kg.). His present illness had begun with weakness of the right leg, for which the parents sought medical advice on August 24. This weakness progressed during the next week to a generalized weakness not specifically isolated to any muscle group or having any particular central or peripheral distribution. There was no history or clinical evidence of an acute infection, and he was admitted to hospital for investigation as a possible case of poliomyelitis or polyneuritis. Investigations, which included lumbar puncture and virus cultures, were negative, and the child improved in hospital and was discharged apparently well but undiagnosed.

At home he reverted to his previous state, and the salient feature of the history at this stage was the day-to-day fluctuation in severity of paresis, varying from disinclination to move in bed, complete inability to stand, and requiring to be fed, on the one hand; to near normality on the other.

When first seen by me, on August 28, he had obvious generalized weakness, but not of great severity. His general appearance suggested a myasthenia gravis (although there was no ptosis). The weakness increased rapidly with fatigue testing of any muscle group.

There had been repeated attacks of paroxysmal tachycardia of distressing frequency and duration, for which no simple reflex inhibition had been found. Investigation had shown a diffuse cardiac enlargement of undetermined origin, and a Wolff-Parkinson-White syndrome was confirmed by electrocardiogram.

Digitalis, $\frac{1}{2}$ gr. (30 mg.), and quinidine, $1\frac{1}{2}$ gr. (0.1 g.), t.d.s. had failed to prevent attacks, but when the quinidine was increased to 3 gr. (0.2 g.) t.d.s., early in July, 1957, complete prevention of attacks was obtained. This dosage was maintained (with the exception of one week from July 10, when it was stopped during a minor illness) up to August 29, 1957 (including the whole of the period of in-patient investigation, mentioned above).

Quinidine was withdrawn on August 29, and improvement began within 24 hours, with complete recovery of muscle function in five days. When quinidine was recommenced, muscle weakness recurred, and was severe by the fifth day. Unfortunately it was not possible to do any biochemical tests. Of particular interest would have been blood quinidine levels and sodium and potassium biochemistry. It was noted, however, that weakness was