the locality of Hook Norton must be about 60 μ 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 μ 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 μ g. compared with 60 μ 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.

Thanks are due to the Education and Health Authorities, Oxfordshire County Council, and the Oxford City Borough Council for facilities for examinations in schools. Help in obtaining samples of water and of milk was given by the following: in Oxfordshire, the County Milk Production Officers, the Water Engineer, Banbury, and the Geological Survey; in Essex, the county milk production officer, the Stock Farm Livestock Research Station, and the county medical officer of health; in Glamorgan, the M.R.C. Pneumoconiosis Research Unit. We are indebted to Professor H. A. Krebs, to Professor Margaret Murray, and to Dr. W. R. Trotter for advice; and to the Nitrate Corporation of Chile and the Rockefeller Foundation for financial support.

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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

much greater at a low fluid intake than on high fluid intake—probably the reason for improvement during the earlier hospital admission.

Quinidine was then totally withdrawn and there had been no further symptoms of muscle weakness up to December, 1957, when the patient was last seen. To date the frequency of attacks of paroxysmal tachycardia has not caused anxiety.

The Table shows the results of fatigue testing on some muscle groups five days after quinidine had been withdrawn and on the fifth day after full dosage had been resumed. There was no detectable change in vital capacity.

Results of Fatigue Testing

Test	Following Withdrawal of Quinidine		5 Days After 9 gr. (0.6 g.) of Quinidine Daily Recommended	
	Possible Frequency Prevented	Frequency Before Further Repetition of Test	Weakness Before Repetition of Test	
Standing on one leg from sitting on 12-in. (30-cm.) stool	Right	6. Left	3	Both legs together only
Biceps lift 1½ lb. (680 g.)	24.	19	Right	2. Left 4
Rise on one toe (i.e., action calf)	14.	14	4.	4
Triceps lift—1½ lb. (680 g.)	11.	7	5.	5
Deltoid to full elevation—½ lb. (113 g.)	20.	20	Not at all	

Discussion

The mechanism of action of quinidine in the above case is not clear, but there are some reported studies which would suggest possible modes of action. One possibility is that quinidine acts at the motor end-plate by interfering with the acetylcholine mechanism. This may correlate with the recognized potentiating effect of quinine in myasthenia gravis.

Another possible mechanism which has received much attention recently is the effect of quinidine on ionic transfers across the cell membrane (Holland, 1957; Kärki *et al.*, 1957). It seems that quinidine, at concentrations comparable to those which might be expected in the above case, greatly inhibits both sodium and potassium shifts across the cell membrane. This applies both in restoration of a distributed normal equilibrium and also in the ionic shifts associated with depolarization, such as by acetylcholine. Presumably if these effects are pressed to a sufficient extent it will not be possible to disturb the ionic balance rapidly, as is required in muscle action, and paralysis will therefore occur.

However, if this explanation holds for quinidine action on cardiac muscle in arrhythmias, it is remarkable that the effect noticed in this case is so unusual considering the repetition rate of skeletal muscle action (5–10 per second even at minimal activity) compared with the cardiac rate.

If the mechanism of action is by disturbance of the balance between intracellular and extracellular electrolytes associated with a raised intracellular sodium level, this may be comparable to the mechanism described by Conn *et al.* (1957) in periodic paralysis. The distribution of weakness in the case described has a closer similarity to this disease than it has to myasthenia gravis.

The ability of quinine to suppress muscle cramp may have a similar explanation to the mechanism of paralysis in the case described.

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Medical Memorandum

Allergic Primary Pulmonary Aspergillosis and Schönlein-Henoch Purpura

Pulmonary aspergillosis is a clinical classification which at times has been loosely applied to lung disease where the fungus has been recovered in the sputum. However, the presence of aspergillus in the sputum alone may be of little significance in arriving at a diagnosis (Moolten, 1938; Van Ordstrand, 1940; Donaldson *et al.*, 1942; Coe, 1945; Delikat, 1955), for such fungus may originate in the nasal sinuses. A certain diagnosis can be established only with the recovery of aspergillus in secretion trapped at bronchoscopy (Stevenson and Reid, 1957) or tissue biopsy (Hiddlestone *et al.*, 1954) or at necropsy. A further complication lies in the ambiguous use of the term "pulmonary aspergillosis" in cases where the fungus is a harmless commensal leading a saprophytic existence in a lung already damaged by bronchiectasis, tuberculosis, bronchial carcinoma, or pneumoconiosis (Heppleston and Gloyne, 1949). In this connexion massive doses of antibiotics are stated to predispose to the growth of such fungi (Abbott *et al.*, 1952; Darke *et al.*, 1957). The term pulmonary aspergillosis should therefore be exclusively reserved for conditions where the fungus is primarily responsible for the patient's ill-health. Many such authenticated cases are to be found (Hetherington, 1943; Gerstl *et al.*, 1948; Hertzog *et al.*, 1949; Hinson *et al.*, 1952; Hiddlestone *et al.*, 1954), and at least four distinct varieties of primary pulmonary aspergillosis are described: (1) mycetoma or granuloma, (2) septicaemia (Just, 1931), (3) broncho-pneumonia, and (4) allergic.

The following case history demonstrates the bizarre clinical pattern exhibited by a boy who suffered from the allergic type of pulmonary aspergillosis.

CASE REPORT

The patient, a boy aged 15½, had been well until the age of 4 years, when he developed bronchial spasm. Minor attacks of a similar nature occurred intermittently until he was 12, when after a minor haemoptysis and wheezing his chest was x-rayed but failed to show any radiological abnormality. He remained in good health until 15 years of age, when he began to lose weight, felt fatigued, and was slightly short of breath on exertion. About this time he began to expectorate up to a quarter of a cupful of thick green sputum which contained yellow-brown hard plugs that could be crushed to the consistency of toothpaste. He visited a mass miniature radiography unit and was found to have bilateral shadowing in both lung fields.

In view of his symptoms and the radiological shadows he was admitted to hospital. On examination he was found to be non-toxic and almost afebrile apart from occasional spikes of temperature (99° F.—37.2° C.). A series of 25 sputa were negative for acid-fast bacilli on direct examination and culture, though eosinophils were repeatedly found in large numbers. His Mantoux test 1:100 was only faintly positive, and a haemogram showed a persistent eosinophilia of 16–22%. Intradermal tests for allergens were negative apart from a faint response to mixed pollens. His maximum voluntary ventilation was 35 litres a minute. Throughout his three months in hospital the radiological shadows migrated to every zone of his lung fields—clearing and recrudescing in a dramatic fashion. Pulmonary eosinophilia was diagnosed, antispasmodics and prednisolone were given, and he was discharged in good health.