all cereals, milk having been taken with all. Milk drinking at breakfast was a little less rare among patients with Crohn's disease, but it was still unusual.

Apart from the absence of an obvious common factor, the observed association of Crohn's disease with cornflake eating is so strong as to make it unlikely to be indirect. The weaker association of the other cereals with Crohn's disease may adequately be explained by the correlation of habits shown in table III. Wheat and bran eating would thus be linked with Crohn's disease secondarily through their association with cornflake eating. The association of porridge and of rice eating with cornflake eating, though significant, are not strong enough to bring these habits, too, into association with Crohn's disease.

If these findings should be confirmed on a wider scale and in other communities and populations, they would require a re-examination of the question of a dietary factor in Crohn's disease. Lewkonia and McConnell[3] cite the paucity of reports of affected spouses as evidence against the existence of such a factor. There is also evidence for a transmissible agent of viral size,[4] for which the cornflake would seem an improbable vehicle. Further, cornflakes are made from maize, which has long been a traditional foodstuff of several major populations. They have, however, the new property of being ready to eat, which makes it possible to eat them soon after waking when, as will be mentioned below, special digestive conditions obtain. This concept, which was the point of departure for this investigation, finds some support in the data of table V, though they fall short of significance. The absence among the patients of people who eat cornflakes not at breakfast but later, and their presence among the controls, show that the significant association is not simply with eating cornflakes but with doing so at breakfast.

From the data presented, and taking the prevalence of Crohn's disease as 30 per 100 000, one may estimate that the disease will be found in one of 1200 who have regularly eaten cornflakes since leaving school, and in one in 3000 of those who have occasionally done so. Susceptibility to Crohn's disease may thus be rare; some of it may be inherited and possibly racial,[3] and it may perhaps depend on abnormal immune responses.[5] A further factor, in the light of the present findings, may be the individually different readiness with which digestive secretion begins after waking. The "waking secretion"[6] of the stomach is sometimes immediate and rapid,[7] but in unpublished observations among other individuals I have found it to be sluggish or even undetectable. In subjects of the latter kind breakfast foods will not be exposed to gastric acid nor to pepsin, nor possibly to pancreatic enzymes; some part of such foods could thus reach the lower intestine unaltered. Further work would be necessary to show whether such a pattern of secretory behaviour is indeed associated with Crohn's disease.

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SIDE EFFECTS OF DRUGS

Chloroquine induced involuntary movements

Four cases of involuntary movements induced by amodiaquine were recently reported.[1] Chloroquine is similar to amodiaquine and both are used effectively in the treatment of malaria. Chloroquine has many well-recognised, minor side effects including transient headache, visual disturbances, gastrointestinal upset, and pruritus.[2] T wave changes in the electrocardiogram (without evidence of cardiovascular damage), visual symptoms, and mild skin eruptions[3] have been noted in patients given large doses of chloroquine over a period. Long-term chloroquine treatment also frequently causes retinopathy; while ototoxicity has been reported in a few cases.[4] No accounts exist, however, of involuntary movements after chloroquine. We report here five cases of chloroquine-induced involuntary movements.

Case reports

Case 1—A boy aged 12 presented with persistent protrusion of the tongue with fasciculation, excessive salivation, and difficulty in swallowing. The previous day he had been given an injection of chloroquine phosphate together with two tablets by mouth and had repeated the dose of tablets the next morning. There was no previous history of adverse reaction to chloroquine tablets, though he remembered having taken them before. He seemed well-adjusted, and it was assumed that the symptoms were induced by chloroquine. No other drug had been taken. Over the next 48 hours the symptoms receded under treatment with chlorpromazine. His parents were advised not to give him chloroquine again, but eight months later the boy was readmitted with the same symptoms having been given chloroquine sulphate tablets for an attack of malaria.

Case 2—A girl aged 16 was admitted to hospital one evening by the nurses. She had abdominal pain, nausea, fever, and poor appetite, and was given two tablets of chloroquine and two tablets of paracetamol. The next morning she was seen by the doctor, who diagnosed urinary tract infection. She was then given a triple dose of sulphonamide tablets and an injection of dipyrone. Later that afternoon she developed protrusion of the tongue, the neck was involuntarily pulled to one side, and her speech was slurred. These symptoms abated during the next 48 hours, though all treatment apart from chloroquine was continued.

Case 3—A civil servant aged 26 presented with paraesthesia of the right side of the face and neck. There was no previous history of fits. The previous day he had had a fever and had taken two tablets of chloroquine and two tablets of aspirin. On examination the neck was drawn to the right and there was fasciculation of the facial muscles. His blood pressure was 140/100 mm Hg and a diagnosis of stroke was considered. He was admitted to hospital and developed protrusion of the tongue that evening. No more chloroquine was given, and the symptoms abated during the next 36 hours on treatment with diphenhydramine and methocarbamol.

Case 4—A housewife aged 19 presented with typical symptoms of malaria —fever, headache, aches and pains, and palpitation. Chloroquine phosphate 4 ml intramuscularly, chloroquine tablets, two daily for four days, and aspirin two tablets three times daily were prescribed. Two days later she presented with twitching of the left side of the face and difficulty in keeping her eyes open. She could not open her mouth fully. She was made to lie down quietly and given chlorpromazine 25 mg intramuscularly. Two hours later she had recovered and was allowed home.

Case 5—A young nurse aged 23 had malaria and was given chloroquine phosphate 4 ml intramuscularly and two tablets of chloroquine. After three hours she complained of involuntary turning of the neck to one side. Later protrusion of the tongue and excessive salivation developed. She had used chloroquine in the past without any such reaction. She was known to be a timid person and the possibility of hysteria was raised. No further chloroquine was given, however, and during the next 48 hours the symptoms abated after treatment with diazepam and diphenhydramine. She was encouraged to take chloroquine again the next time she had malaria. Three months later an attack of malaria occurred and the side effects were repeated on taking two chloroquine tablets.

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Comment

Although other drugs could not always be excluded, in most of the cases reported here chloroquine appeared to be responsible for the involuntary movements. In a previous case of involuntary movements attributed to amodiaquine[1] the patient had also taken chloroquine, so either drug may have produced the side effects. Benztropine, which is well recognised in the treatment of Parkinsonian syndromes, was successfully used in this case,[1] although it was not available to us. We would recommend the same treatment for chloroquine-induced involuntary movements. Although chlorpromazine may produce extrapyramidal effects it was successful in controlling involuntary movements in one of our patients, who responded rapidly when the drug was given parenterally.

Normal therapeutic doses of chloroquine may induce involuntary movements whether it is given by mouth or by injection. Furthermore, some of the patients had taken chloroquine before without adverse reactions. In the past five years we have used chloroquine to treat over 25 000 patients with malaria, and these five patients are the only ones to develop this side effect. The incidence is less than 1/5000. It is also notable that all our patients were under the age of 30, which appeared to be the case in those reported previously,[1] though the ages were not always stated.

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Intramuscular iron and local oncogenesis

Seven cases of sarcomas arising in the area of a previous iron injection site have been reported in man.[1-3] We report here what seems to be another such case.

Case report

A 35-year-old White Caucasian woman (para 2+0) was referred to our outpatient clinic with a four-month history of pain and swelling in the left hip. Examination showed a large craggy mass in the left gluteal region. Biopsy of this mass showed a poorly differentiated spindle cell fibrosarcoma. There was no stainable iron present. The patient received radiotherapy to the tumour site.

Further questioning showed that 14 years earlier this patient had received a short course of intramuscular iron dextran (Imferon) after delivery of one of her children. Her haemoglobin concentration had been 9·4 g/dl at the time. She received one injection into the right gluteal muscles, after which she developed a mass in that area. The lesion resolved slowly over three weeks. The other four injections were therefore given into the left gluteal muscles. A few days after the end of this short course of injections the patient developed an itchy purpuric rash on her legs. More detailed information on the dose and frequency of the injections was not available as the case notes had been destroyed. The proprietary name was mentioned only in a discharge letter lodged in her general practitioner's records.

There was no history of other allergies or of any other intramuscular injections having been given to either buttock. The only other injections the patient could remember having received were childhood vaccinations into the deltoid muscle. The patient did not take any regular medication.

Comment

The carcinogenic risks of iron dextran were discussed in an editorial in the *British Medical Journal* in 1960.[4] Extensive animal studies had shown that sarcomas readily arose at the sites of large intramuscular iron injections, and this raised the possibility that sarcomas might arise at the sites of such injections in man. It was thought, however, that oncogenesis was local and dose-dependent,[5 6] and the product was not removed from the market.

The average interval between injection and the appearance of the neoplasm in the other seven cases reported in man was five years (range a few months to 13 years). In our case it was 14 years. Other unusual features, although they have been reported before,[7] were the development of swelling at the injection site and the occurrence of a rash after the iron dextran injections.

Sarcomas arising at the site of intramuscular iron injections are much rarer in man than in animals, possibly because of the different sizes of the muscles. The much larger human gluteal muscle may allow the iron to be dispersed to such an extent that the concentration necessary to trigger the induction mechanism is rarely achieved in humans. There may also be a long induction period in man. For this reason we think that it is important that this and all similar cases should be recorded.

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Guanidine treatment and impaired renal function in the Eaton-Lambert syndrome

The myasthenic-myopathic or Eaton-Lambert syndrome and its electrophysiological characteristics were described in 1956[1] and 1957.[2] The case reported here is unusual in that guanidine, which was essential for maintaining power,[3] seemed to produce renal impairment.

Case report

A 61-year-old White post office engineer weighing 72·6 kg suddenly developed diplopia and severe muscular weakness in March 1969. Examination by one of us (JM) six weeks later showed bilateral ptosis, diplopia, and variable muscle weakness. At worst he could not raise his arms to the horizontal nor rise from the squatting position; at best he could do both, albeit with effort. There was no wasting or fasciculation. Tendon reflexes were sluggish but became brisker after strong contraction of the muscles. Plantar responses were flexor, and sensation and co-ordination were normal. The blood pressure was 150/85 mm Hg with no abnormality in the cardiovascular or other systems. Edrophonium (Tensilon) 10 mg intravenously produced a very slight increase in power, much less than that expected in myasthenia gravis.

Investigation for carcinoma was negative; in particular a chest radiograph was normal and tomography showed no evidence of a mediastinal mass. Plasma urea was 4·1 mmol/l (25 mg/100 ml), and alkaline phosphatase was slightly raised at 121 IU/l (normal 12-65 IU/l). The muscle action potential in abductor digiti minimi in response to stimulation of the ulnar nerve was of low amplitude with a post-tetanic contraction potentiation of two and a half times the baseline value.

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