uric acids were estimated in male in-patients who were given frusemide without regard to their particular disorder except that they required diuretic therapy. Similarly, control values were estimated on patients not receiving frusemide. The results were as shown in Fig. 1.

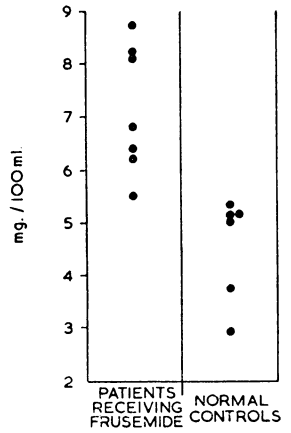

FIG. 1

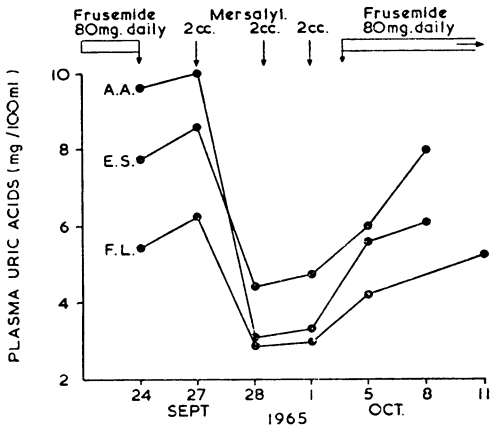

FIG. 2

FIG. 1.—Levels of plasma uric acids estimated in patients receiving frusemide and in normal controls. FIG. 2.—Fluctuations in plasma uric acid levels related to administration of frusemide or mersalyl to three male patients.

The patients tended to show high levels of plasma uric acid while on frusemide, three out of seven being above the gouty threshold of 7 mg./100 ml.; in these three no signs of gout were observed. Uric acid levels were estimated in three men who had been given frusemide either on admission or previously. The drug was then stopped for 10 days, and three doses of mersalyl 2 ml. given during this time. Plasma uric acids were again estimated. Finally the patients were given frusemide again and repeat estimations done. The results are set out in Fig. 2.

COMMENT

The case reported here emphasizes the need for care in prescribing diuretic therapy in gouty subjects who require this treatment for unrelated conditions. The figures from the pilot scheme show that the plasma uric acid levels were high while patients received frusemide, fell with mersalyl, and rose again on frusemide. Kerr and Robson (1965), following Schaefer (1964) and Wölfer *et al.* (1964), reiterated that there is a slight rise in plasma uric acid with long-term oral therapy. From this limited pilot study of patients who were in the ward as standard emergency admissions it might be inferred that the rise in uric acid is higher than previously suggested, and precipitation of gout by frusemide in susceptible persons is a real possibility.

I am grateful to Dr. J. R. Robson, biochemist, and his staff for biochemical estimations, and to Professor I. G. W. Hill and Dr. K. G. Lowe for helpful advice and comments.

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Myasthenia Gravis in Identical Twins

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Only one instance has been reported of myasthenia occurring in identical twins. Levin (1949) cites Dr. M. N. Walsh who had seen twin girls with myasthenia, but these cases were not described in detail. It is important to record a further twin pair with myasthenia in which monozygosity has been established beyond doubt, particularly as there is uncertainty about the importance of a genetic factor in myasthenia gravis.

CASE 1

A married woman, a 23-year-old half-caste Rarotongan (see Fig.), was admitted to Auckland Public Hospital in August 1962 complaining of weakness in her legs on exertion. Double vision, drooping eyelids, difficulty in swallowing, and a fading voice had been present, all intermittently, for about six months. Examination revealed bilateral partial ptosis, slight generalized weakness of upper and lower limbs, and pathological muscle fatigability. Reflexes were brisk and normal. There were no other neurological abnormalities. She had a palpable thyroid gland, estimated at 30 g., but no clinical evidence of thyrotoxicosis. She was given edrophonium chloride, 10 mg. intravenously, with complete but temporary reversal of ptosis and restoration of normal muscle power.

Haemoglobin, white blood count, and differential count were normal, as were the sedimentation rate, serum proteins, and electrophoresis. ^{131}I uptake at four hours was 14%. A radiograph of the chest was normal, special views failing to show thymic enlargement.

The patient was given pyridostigmine bromide, 60 mg. nine times daily, with considerable benefit. Over the next six months she improved and her tablets were reduced to four a day. She was able to go dancing.

In January 1964 she began to deteriorate, and six months later she was taking 18 tablets a day. She had constant diplopia and had become exceedingly weak. She was readmitted to hospital for thymectomy. Haemoglobin, white blood count, sedimentation rate, and serum proteins were again normal. ^{131}I uptake was normal, but protein-bound ^{127}I was 9.9 μg./100 ml. Thymectomy was performed in August 1964. A diffusely enlarged thymus gland was removed weighing 87 g. Histological examination of the

specimen showed diffuse hyperplasia with occasional lymphoid follicles.

In the four months after thymectomy the patient did not improve, and in December she was taking 24 tablets of pyridostigmine bromide a day. Over this period she had sweated very easily, becoming very irritable, and developed slight proptosis. The right lobe of her thyroid gland had enlarged. A soft bruit was audible over the gland. A sleeping pulse was 120/min. Investigations confirmed the fact that the patient was thyrotoxic. The protein-bound ^{127}I was 16.4 μg./100 ml., the ^{131}I uptake at four hours 87%, and at 48 hours 91%. Serum potassium was 4.3 mEq/l. She was treated with carbimazole, 10 mg. eight-hourly, and after one month she appeared very much better. In the last few months she has continued to improve, she can get about the house and is able occasionally to go to town.

Case 2

The unmarried twin (see Fig.) of Case 1 was well until June 1964, when she developed a fading voice and intermittent difficulty in swallowing. In October 1964 she had rubella, and with this developed marked dysarthria and dysphagia. She complained of double vision, heavy eyelids, and general muscle weakness. Pathological fatigability was present in limb muscles. A clinical diagnosis of myasthenia gravis was made; it was confirmed by the administration of 10 mg. of edrophonium chloride intravenously, which temporarily restored her to normal. She was given pyridostigmine bromide with significant improvement in her symptoms. She has remained well on eight tablets a day. Haemoglobin, white blood count, differential count, and sedimentation rate were normal, as were serum proteins and electrophoresis. The protein-bound ^{127}I was 7.1 μg./100 ml., the ^{131}I uptake and serum protein-bound ^{131}I at 48 hours were normal. A triiodothyronine suppression test for latent thyrotoxicosis (Johnson *et al.*, 1959) was normal.

The twins. Case 1 (right) has developed thyrotoxicosis.

Proof of Monozygosity.—Blood groups were ABO, MNSs, Rh, Fy, P, Hp, and Sec; total finger ridge count and atd angles from palm prints were estimated. On the basis of these observations, calculations carried out by Dr. A. M. O. Veale showed that the probability of the twins being monozygous was 97.83%. Confirmation of this was achieved when full-thickness exchange skin grafts were successfully transplanted from each twin to the other.

Family History.—The twins were born in Atutake, Cook Islands, Oceania, and spent their infancy and childhood there. They have lived in New Zealand for five years, but in different cities until a year ago. They have 13 siblings, four of whom died in infancy. No other members of the family show manifestations of myasthenia, and there is no family history of this disease. There is no known consanguinity in the last three generations.

Comment

The occurrence of myasthenia gravis in identical twins brings up the question of a genetic factor in this condition. There are occasional reports of familial aggregates of myasthenia gravis; the most recent review of the literature is that of Celesia (1965), who was able to find 54 cases occurring in 22 families. The myasthenia was limited to one generation in 17 families and two generations in four families. There are no reports of three generations being affected. Affected cousins have been described by Osserman (1958) and Bowman (1948). Osserman has also described a family with consanguinity in the parents of two affected siblings. A maternal male cousin of this family was also affected. Familial aggregations of myasthenia gravis continue to be reported but the occurrence of these is rare, and Kurland and Alter (1961) have suggested that there is insufficient evidence to propose that genetic factors are significant in the aetiology of myasthenia. Twin studies to date have been inconclusive. There have been five reported instances including Walsh's case. Wilson and Stoner (1944) mention identical twins, one developing myasthenia, the other unaffected; Alter and Talbert (1960) describe a 6-year-old negro boy with myasthenia whose unaffected identical twin showed a normal response to curare. Osserman (1958) and MacKay (1951) have also reported cases, but these have been non-identical twins and only one has been affected. These, if anything, argue against a significant genetic factor.

In the patients here reported no evaluation of the possibility of a chance association of the disease has been attempted; it is, however, unlikely, and it is considered much more probable that a genetic factor would account for the occurrence of myasthenia gravis, an uncommon disease, in identical twins within the span of two years.

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