Comment

Apart from its use in the diagnosis of some forms of leukaemia and in following the progression of malignant diseases⁴ bone marrow is largely ignored by cytogeneticists today. Using the above method, we obtained well-spread metaphases. The use of a Polaroid camera attachment meant that the diagnosis could be confirmed within minutes. The object was to offer only a classical orcein diagnosis. Banding can be performed on bone marrow metaphases but this takes longer.

The availability of rapid chromosome analysis was particularly helpful in the following two cases. With the indications for an early exchange transfusion in case 5 knowledge that the infant was triploid, invariably a lethal condition, justified no medical intervention. The infant died aged 17 h. In case 2 the confirmation of Down's syndrome by rapid chromosome analysis helped during the discussions with the parents on operation for the duodenal atresia. In this case, as in two other reports,^{1,2} a decision was made not to operate and the baby died at 3 days.

Patients 7, 9, 10, and 12 had Down's syndrome where a confident diagnosis could not be made clinically. When the diagnosis is in doubt, particularly when the uncertainty of Down's syndrome is causing the parents appreciable anxiety, a bone marrow aspiration is indicated. Where the features of an uncomplicated case of Down's syndrome are sufficiently obvious for confident diagnosis, full discussion with the parents need not await the results of the chromosome analysis, usually available by 52 hours after peripheral blood culture.

Thus we have found rapid cytogenetic diagnosis on marrow aspirate of selected infants valuable in both the immediate management of the patient and the support of the parents. It is important to set strict criteria for its use as the technique is time consuming and necessitates the attendance of staff outside usual laboratory hours.

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Ventilatory function in Parkinson's disease

It is not easy to measure the response to treatment in Parkinson's disease because of the difficulty in eliminating a subjective element from the appraisal of voluntary movements, rigidity, or manipulative tasks. The need for a simple, objective test to follow improvement during treatment led us to consider ventilatory function tests. Some 87% of patients with the disease have impaired ventilatory function,¹ which appears to relate to the severity of the disease² rather than to underlying lung disease.³

Methods and results

Twelve patients (seven men and five women), diagnosed by two of the authors, agreed to serial measurement of ventilatory function over three weeks. Their age was 74-91 (mean 82), and, despite partial or severe disablement (ten were unable to walk without help), they were alert and co-operative, and had no evidence of other neurological disease or lung disease. They were treated with a preparation of levodopa and benserazide (Madopar), and were familiarised with the tests before any formal recordings were made. Forced expiratory volume (FEV₁), forced vital capacity (FVC), and peak expiratory flow rate (PEFR) were measured by a Vitalograph and

a Wright peak flow meter. Treatment was supervised by clinical appraisal of response by a doctor who did not know the results of pulmonary function tests. Seven other patients, aged 64-83, showing no evidence of Parkinson's disease, agreed to act as a control group by having serial ventilatory function tests for a similar period.

In two of the treated cases the initial peak expiratory flow rate was unrecordable; although they showed a significant improvement, they were excluded from statistical analysis. Nine of the remaining ten patients showed an improvement in FEV₁, FVC, and PEFR after one week's treatment and a smaller but still significant improvement occurred in the second week, corresponding with an independent appraisal of clinical improvement on levodopa treatment. Four patients continued ventilatory function tests for longer, and each showed a consistent improvement of lesser degree. The patient who did not respond to the treatment by lung function tests, showed no clinical improvement either. This failure of response was evident from the ventilatory function tests after one week. In contrast to the response of the patients, the controls showed no significant change in FEV₁, FVC, or PEFR over the three weeks.

Comment

Very little is known about ventilatory function in old people, as it is difficult to be certain that they are free from lung disease and that they are producing a maximum ventilatory effort. FEV₁, FVC, and PEFR were higher in controls than patients but lower than expected. Within one week of starting treatment the patients' values improved commensurate with the degree of clinical improvement while the control group's values remained unchanged (figure). Old people

Serial results of FEV₁, FVC, FEV₁/FVC%, and PEFR before and during two weeks' treatment in patients with Parkinson's disease (closed circles) and in control subjects (open circles). The vertical bars represent SE of mean.

need encouragement to produce a maximum ventilatory effort and they seemed to find the Wright peak flow meter easier to use than a spirometer. Changes in PEFR paralleled those in FEV and FVC but produced better separation of individual values on serial measurement. Thus serial measurement of PEFR provides a simple, objective method of monitoring the effects of treatment of Parkinson's disease during the early stages when the results of other clinical tests are more difficult to assess.

The ventilatory defect in Parkinson's disease appears to be due to rigidity and weakness of respiratory muscles which are ameliorated by treatment in the same way as those of skeletal muscles elsewhere. While our methods cannot rule out central depression of respiration as a mechanism, there is no evidence elsewhere to support this concept, while there is abundant support for rigidity in skeletal muscle. The results of other studies have suggested that airways obstruction may be present in Parkinson's disease² due to increased parasympathetic tone, but the constancy of FEV₁/FVC% throughout our treatment fails to support that concept. A diminished elastic recoil of the lung due to aging probably accounts for the low FEV₁/

FVC% in all our subjects.⁴ Fortunately, the ventilatory impairment is of little clinical importance but it offers the clinician an objective assessment of progress: the absence of any improvement in the first week makes it unlikely that treatment is effective, thereby saving time and allowing exploration of alternative therapeutic approaches.

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Acute renal failure due to polymyositis

Crush injury is a recognised cause of acute renal failure, histologically giving characteristic myoglobin casts in biopsy specimens. A similar syndrome can be precipitated by muscle damage associated with barbiturate overdose¹ and carbon monoxide poisoning.² We report a case of acute renal failure in which the renal biopsy specimen showed a typical "crush injury" appearance due to severe acute polymyositis.

Case report

A 56-year-old theatre technician was admitted with a ten-day history of increasing proximal muscle pain, tenderness, and weakness. He was afebrile but had dark urine and increasing oliguria. Investigations showed blood concentration of urea 34 mmol/l (205 mg/100 ml), creatinine 569 µmol/l (6.4 mg/100 ml), potassium 6.9 mmol(mEq)/l, creatinine phosphokinase 681 IU/l (normal 26-200 IU/l), and alanine transferase 1004 IU/l (normal range 0-40 IU/l). The blood concentration of urea rose to 77 mmol/l (464 mg/100 ml) with a creatinine of 1164 µmol/l (13.2 mg/100 ml) over the subsequent three days. An arteriovenous shunt was inserted and haemodialysis started. A specimen obtained by renal biopsy to determine the cause of his acute renal failure showed casts in tubules reminiscent of those seen in "crush injury." Electromyography showed irritability to needle provocation at rest with repetitive potentials and abundant fibrillation. During contraction there were many polyphasic and brief-duration potentials compatible with severe polymyositis. A muscle biopsy specimen of the vastus internus showed necrotic fibres undergoing phagocytosis and a perivascular infiltration of mononuclear cells and lymphocytes.

He was given prednisolone, 100 mg/day. He remained anuric for 10 days requiring repeated haemodialysis. Subsequently his renal function returned to normal. He continued to lose weight with weakness, wasting, and tenderness of the proximal muscles, and he lost 20 kg in weight in three weeks before improving. An electromyogram six weeks later while he was taking prednisolone 10 mg/day showed all muscles electrically silent at rest with no fibrillation activity. During contraction there were full interference patterns of motor unit potentials. A muscle biopsy specimen showed an obvious improvement with a few scattered atrophic fibres and no interstitial inflammation. In view of his occupation as a theatre technician, specimens of muscle were examined in vitro for sensitivity to halothane and other anaesthetic agents. No abnormality was detected.

When last seen his muscle bulk and power had returned to normal, as had his serum biochemical values. He was well and no longer receiving steroids. The results of investigations for autoimmune disorders, viral infection, and malignancy had been negative.

Discussion

Polymyositis is a disease of unknown aetiology. It presents as proximal, symmetrical muscle weakness with pain and tenderness. The urine is frequently dark red, due to myoglobin. Muscle biopsy

specimens show muscle fibre degeneration with a variable, often perivascular, inflammatory cell infiltrate. Electromyography shows spontaneous activity and myopathic changes³⁻⁵ and the serum creatinine phosphokinase concentration is raised. These features were all present in this patient, supporting a diagnosis of polymyositis. The disease may occur in association with connective tissue disorders, such as rheumatoid arthritis or dermatomyositis, carcinoma, and viral infections. There was no evidence of such conditions in this patient.

Treatment is with corticosteroids, initially prednisolone 30-100 mg/day, the dose depending on the severity of the disease, reducing to a maintenance dose of 5-15 mg/day, depending on the clinical response. This patient made a satisfactory and rapid response to treatment. With reduction and cessation of this there has been no evidence of any relapse and he remains asymptomatic.

This case is unusual in as much as the muscle lysis was produced by a polymyositis of unknown cause, severe enough to produce a "crush injury" type kidney with reversible acute renal failure.

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Long-term self-administered subcutaneous heparin in pregnancy

Antenatal thromboembolism is an important complication of pregnancy and a major cause of maternal death. Patients previously advised against pregnancy now present to the obstetrician with prosthetic heart valves or a history of major thromboembolism² and require anticoagulants throughout pregnancy. Oral anticoagulants may increase the perinatal mortality and are probably teratogenic.^{1 3} If their administration during the first trimester and the last three weeks is avoided the risks to the fetus can be reduced.² Heparin, which does not cross the placenta, is safer but the need for long-term parenteral treatment is a disadvantage. Self-administration of subcutaneous heparin is safe and effective,⁴ and we describe our experience.

Patients, methods, and results

Nineteen patients received subcutaneous heparin during 22 pregnancies. Thromboembolism occurred in 14 pregnancies and subcutaneous heparin was preceded by an intravenous heparin infusion (40 000 units daily). Eight patients with a history of thromboembolism started receiving prophylactic subcutaneous heparin after their first antenatal visit, around 12 weeks. One patient taking long-term warfarin was changed to heparin at six weeks' gestation. The patients were instructed to give their own injections in a manner similar to diabetics. The site of injection was left to the patient, the thigh being preferred to the abdomen. When they were considered competent and their dosage had been established, the patients were allowed home. The dose was monitored in most cases by the activated partial thromboplastin time (APTT). A result lower than the control was taken as an indication for increasing the dose. If the APTT result was comparable with or higher than the control the same dose was maintained. In a few patients antifactor Xa assay was performed and the dose altered to keep the level in the prophylactic range. Those patients breast-feeding were maintained on heparin for about six weeks post partum and those electing to bottle feed were changed on to warfarin.

The duration of treatment in the antenatal period ranged from two to 34 weeks. The total antenatal experience was 374 weeks (169 weeks in the