SHORT REPORTS

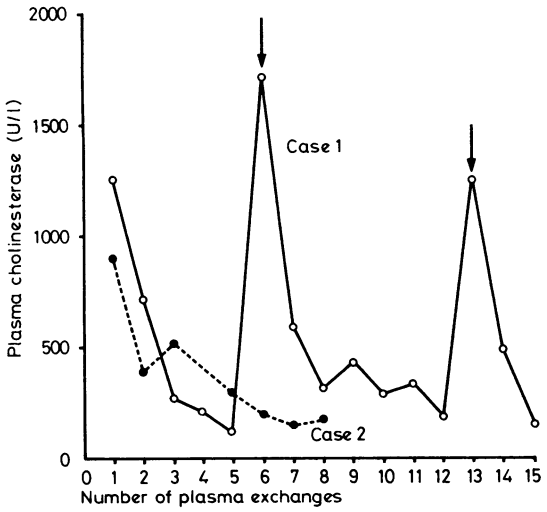
Progressive depletion of plasma cholinesterase during daily plasma exchange

Suxamethonium is used extensively in anaesthesia and intensive care to facilitate rapid endotracheal intubation. It is hydrolysed by the plasma enzyme cholinesterase, and the duration of action of the drug is thought to be prolonged when the enzyme concentration is less than 20% of normal.[1] Since a single four-litre plasma exchange removed 64% of the plasma cholinesterase,[2] we have examined the effects of daily plasma exchanges on the circulating cholinesterase concentration.

Patients, methods, and results

Two patients who received daily plasma exchanges for the treatment of Goodpasture's syndrome (15 days) and Wegener's granulomatosis (8 days) were studied. Four-litre exchanges were undertaken with a Haemonetic Model 30 blood processor and the plasma replaced with plasma protein fraction (PPF). Venous blood was collected at the end of each exchange for determining the plasma cholinesterase concentrations.[2]

The figure shows that repeated daily plasma exchanges progressively decreased the cholinesterase value to that of the infused PPF (100-200 U/l). The increases in cholinesterase concentration observed in case 1 after exchanges 6 and 13 were associated with the administration of whole blood together with PPF to replace the plasma removed.



Effect of daily plasma exchanges on plasma cholinesterase concentration.

Comment

Regular plasma exchanges carried out at intervals of one to four weeks are an accepted and safe form of treatment for diseases such as the paraproteinaemias and hypercholesterolaemia. Intensive daily exchange has been introduced recently as part of the treatment of fulminating antibody-mediated and immune-complex diseases. There is little information available about the effects of this regimen on blood constituents other than a decrease in immunoglobulins and clotting factors together with a moderate defibrinogenation.[3] Healthy donors undergoing daily plasma exchanges of only 1 litre for five days showed a mean decrease in total protein concentration of 18·4 g/dl.

We have shown that daily plasma exchange caused virtually complete removal of circulating cholinesterase in patients who started treatment with the low values of 1267 and 844 U/l (normal mean concentration 3637 U/l (SE of mean ±226), n=22). We recommend that drugs metabolised by cholinesterase, such as suxamethonium and procaine-like esters, should not be used in patients undergoing intensive daily plasma exchange so that their duration of action is not grossly prolonged.

We thank Professor D K Peters for permission to study the patients.

[1] Vickers, M D, Wood-Smith, F G, and Stewart, H C, *Drugs in Anaesthetic Practice*, 5th edn. London, Butterworths, 1978.
[2] Wood, G J, and Hall, G M, *British Journal of Anaesthesia*, 1978, **50**, 945.
[3] Pinching, A J, *British Journal of Anaesthesia*, 1979, **51**, 21.
[4] Kliman, A, *et al*, *Blood*, 1964, **23**, 647.

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Occupational handling of chemicals preceding Hodgkin's disease in men

In 1976 Olin[1] reported an increased death rate from Hodgkin's disease (HD) among Swedish chemistry graduates. We report an unduly high prevalence of occupations characterised by the handling of chemicals in men with HD.

Material, methods, and results

From tables describing the occupations of the working population of Sweden[2] we selected occupations indicating a high degree of exposure to chemicals (see table).

Patients—We examined the case records of all men aged 20-65 years (median 36) diagnosed and treated for HD during 1973-8 at this department and recorded their occupations at diagnosis, ages, and histological classifications. We thus studied 88 patients.

Controls—Control patients comprised three groups. In group A the case records of 100 consecutive men aged 20-65 years (median 43) with non-malignant disorders treated at the department of internal medicine in 1977 were examined and occupations recorded. In group B the case records of 100 consecutive men aged 20-65 years (median 39) treated at the department of allergology in 1977 were examined in the same way. In group C the occupations of 32 men in the same age group (median 52) with chronic leukaemias (10 with chronic lymphocytic and 22 with chronic myeloid leukaemia) seen during 1969-77 at the department of internal medicine were recorded. The recording of occupation was similar in all departments. Because only men aged 20-65 years were included in the study an occupation was obtained for all the patients and controls.

Of the 88 men with HD, 17 (19%) had occupations indicating that they handled chemicals (table). The corresponding figures in the two control groups with non-malignant disorders (A and B) were 2% and 3% respectively. This difference between the patients with HD and each of the control groups was significant (P=0·0001 and 0·0002; Fisher's exact probability test). Of the men with chronic leukaemias (group C), one (3%) had an occupation indicating handling of chemicals. This was also significantly different from the patients with HD (P=0·02). In Sweden in 1976[2] about 64 000 out of 2·2 million working men (2·9%) had occupations listed in the table.

Only two out of 35 patients (6%) aged 20-30 years were occupationally exposed to chemicals, compared with eight out of 31 (26%) aged 31-50 years. The corresponding proportion for the patients aged over 50 years was seven out of 22 (32%). Histological classification did not differ significantly between the exposed and unexposed patients.

Comment

Of the men with HD, which was diagnosed between 20 and 65 years of age, about 20% had occupations indicating that they handled chemicals. In the three control groups the corresponding figure was only 2-3%, which agrees well with the prevalence (2·9%) of such

Numbers of patients with occupations indicating high degree of exposure to chemicals in 88 men with Hodgkin's disease (HD) and three control groups. (See text for description of controls)

	Patients with HD (n = 88)	Control groups A (n = 100)	B (n = 100)	C (n = 32)
Chemists	2		1	1
Painters and sprayers	5	1	1	
Glass and pottery workers	5			
Chemical processing workers	1			
Rubber product workers	2			
Plastics workers	1		1	
Photographic laboratory workers	1	1		

occupations in the working male population in Sweden. The results therefore suggest that exposure to some chemical agents may be important for the development of HD.

Interestingly, occupational exposure was uncommon in the patients with HD aged 20-30 years, whereas among the older patients 26-32% were occupationally handling chemicals. The incidence curve of HD is bimodal, with one peak between 20 and 30 years of age and a second increase beginning about the age of 35 years. This may be due to differences in aetiology between various age groups.[3] Our results indicate that occupational exposure to chemical oncogenic agents may be of some importance for the development of HD in men aged over 30, whereas other aetiological factors may be more important in the younger age groups.

We emphasise that occupational titles obtained from case records will give only crude and insufficient information on occupational hazards. Despite this shortcoming, our finding of occupational exposure to chemicals in about 20% of adult men with HD means that efforts should be made to define environmental hazards that may be important in the development of HD. Such studies are in progress at our department.

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[1] Olin, R, *Lancet*, 1976, **2**, 916.
[2] *Statistical Abstract of Sweden 1976*, vol 63. Stockholm, National Central Bureau of Statistics, 1976.
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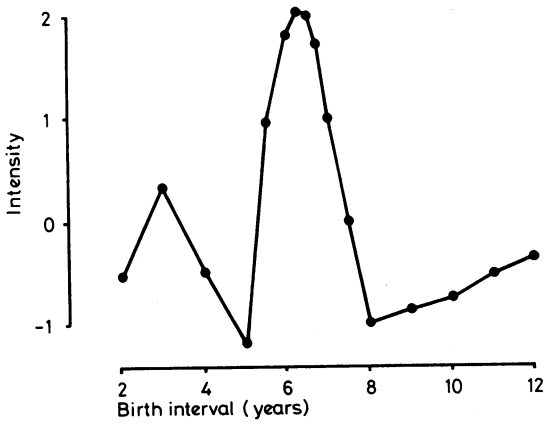
Who wants to sit on the GMC?

What makes an individual ambitious for power? Is it inborn or is it forced on us by environmental circumstances?

An unusual opportunity to examine the question arose recently in that mind-numbing list of 150 doctors wishing to represent England on the General Medical Council. It arrived on a hot afternoon, and the natural reflex to throw this bundle of paper away was inhibited first by inertia and then by a nagging curiosity. Who were these people who wished to assert themselves in Hallam Street, and what distinguished them from the rest of us—those meek and apathetic doctors whom they expected to vote for them?

The least demanding epidemiological approach was to examine the one quantitative variable they presented: their year of birth. It was at once apparent that this was no ordinary distribution: throughout the range from 1911 to 1952 periods of three or four years with many candidates were followed by two to three years with very few in a remarkably regular pattern. That one of the more vociferous representatives of a national organisation should have been born in a peak year when the year of birth of one of us two years later was in a quiescent trough was enough to clinch the matter. A more formal statistical approach seemed necessary, however, to convince the sceptical.

The data were examined by spectral analysis of the serial correlations between birth frequencies for intervals of 1, 2, 3, ... years. The serial correlations showed an undulatory pattern with peaks corresponding to about six-year intervals, and the cyclicity was confirmed by the peak in the periodogram (figure).



Periodogram showing cyclicity of birth data on GMC candidates. The intensity is a Fourier transform of serial correlation coefficients.

We offer this observation as the basis for a PhD thesis on the cyclical nature of medical aspirations. What happens in a regular six- or seven-year cycle to account for recurrent crops of politicians? Many comets have a periodicity of between six and seven years, but the data suggest a more gradual ebb and flow of influence, and there may be the basis here for making astrology respectable.

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Pindolol and pulmonary fibrosis

Of the beta-blocking agents used in clinical medicine practolol has been especially associated with adverse reactions. A lupus-like syndrome, ocular and skin disease, sclerosing peritonitis, deafness, nephrotic syndrome, joint effusion, pleural effusion, pulmonary fibrosis,[1] and pleural fibrosis[2] have been described. We present a patient who developed pulmonary fibrosis during treatment with a related beta-blocker, pindolol.

Case report

A 55-year-old man, a lecture-room projectionist, who smoked 15-20 cigarettes daily presented in December 1978 with a three-month history of progressive exertional dyspnoea and non-productive cough. He had been treated with pindolol for seven years for essential hypertension. His pulse rate was 82/min and his blood pressure 150/90 mm Hg. He had tachypnoea, respiratory crepitations in both mid and lower zones, but no finger clubbing. Dressing and walking 20-30 metres briskly on level ground induced dyspnoea. Chest radiographs showed small irregular opacities throughout both lung fields without pleural abnormality. A chest radiograph four years previously had been normal. Results of laboratory investigations included: erythrocyte sedimentation rate 40 mm in 1 h; haemoglobin concentration 14·9 g/dl; leucocyte count $6{\cdot}8 \times 10^9$/l with normal differential count; and no rheumatoid or antinuclear factors found. Forced expiratory volume in one second was 73% of predicted and forced vital capacity 63% of predicted. Total lung capacity was 70% of predicted, single breath carbon monoxide transfer factor 65% of predicted, and the ratio of transfer factor to effective alveolar volume 93% of predicted.

At thoracotomy the pleural surface of the left lung appeared granular and the lung substance felt rubbery. A wedge-shaped biopsy specimen from the posterior aspect of the left upper lobe showed patchy changes on microscopy (figure). In some areas closely packed sheets of desquamated cells filled alveoli and were within small airways, many containing PAS-reactive material (resistant to earlier diastase digestion). Alveolar septa were patchily thickened by fibrous tissue and there were varying amounts of cuboidal change, atypia, and syncytial arrangements of alveolar lining cells. Inflammatory changes were mild to moderate with an infiltrate of mononuclear cells in the fibrous tissue and the walls of the damaged bronchioles. The walls of some small pulmonary arteries showed mild thickening. There was