iron-storage disease, malignant disease, and a history of neck surgery or irradiation. Bone biopsy was not performed in either case because of the absence of any biochemical or radiological evidence of osteomalacia. Our first case is the oldest known patient to present with this disorder, the oldest described elsewhere being an 80-year-old man who presented with confusion.[4]

Little is known about parathyroid function in the elderly, but we suggest that these cases might represent extreme examples of an age-related decline in parathyroid function. The clinical features of hypocalcaemia are less dramatic in the elderly[5] and may easily be ascribed to irremediable causes, such as cerebrovascular disease. We therefore recommend that hypocalcaemia, which is disabling but remediable, should be more often sought in elderly patients, particularly those presenting with confusional states or epilepsy.

We wish to thank G H Beastall, of Glasgow Royal Infirmary, and S R Abbott, of the Regional Hormone Laboratory, Edinburgh, for the parathyroid estimations.

[1] Spinner, M W, Blizzard, R M, and Childs, B, *Journal of Clinical Endocrinology and Metabolism*, 1968, **28**, 795.
[2] Blizzard, R M, Chee, D, and Davis, W, *Clinical and Experimental Immunology*, 1966, **1**, 119.
[3] Nusynowitz, M L, Frame, B, and Kolb, F O, *Medicine*, 1976, **55**, 105.
[4] Eraut, D, *British Medical Journal*, 1974, **1**, 429.
[5] Philipson, B, *et al*, *Acta Medica Scandinavica*, 1978, **203**, 223.

(*Accepted 20 March 1979*)

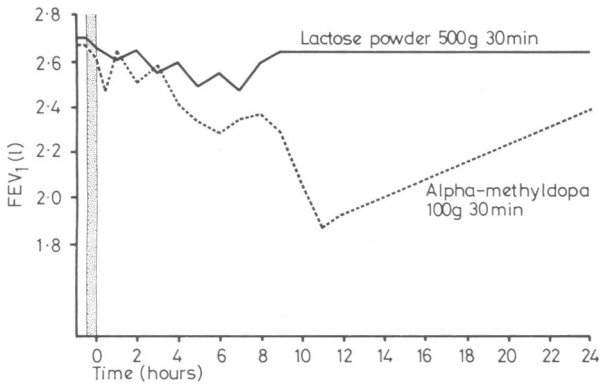
Division of Clinical Medicine, Southern General Hospital, Glasgow G51 4TF
K GRAHAM, MB, CHB, senior house officer
Victoria Geriatric Unit, Glasgow G42 9TY
B O WILLIAMS, MB, MRCP, consultant physician in geriatric medicine
Royal Victoria Hospital, Edinburgh EH4 2DN
M J ROWE, MD, MRCP, senior registrar in geriatric medicine (present appointment: consultant geriatrician, St Martin's Hospital, Bath)

Bronchial asthma due to alpha-methyldopa

Asthma from inhaling alpha-methyldopa powder was demonstrated by occupational type bronchial provocation testing in a woman who was handling the powder in a drug factory.

Case report

A 27-year-old woman started work in 1973 as an analytical chemist in a factory making methyldopa tablets. Two to three months later she developed blockage of the nose and repeated sneezing at work, which improved after three weeks. Her symptoms appeared intermittently with increasing frequency. She noted that they seemed to occur when methyldopa powder was present in the room. Six months before her referral to hospital she developed exercise-induced asthma. This was better when away from work on holiday.



Non-immediate asthmatic reaction resulting from 30 minutes' exposure to alpha-methyldopa dust, maximal at 11 hours. Recovery incomplete 22 hours later.

She was non-atopic and a prick test for sensitivity to alpha-methyldopa was negative. She had no serum precipitins to the drug and both direct and indirect Coombs tests were negative. She was admitted to hospital in May 1978.

Provocation tests were done in a ventilated sealed chamber measuring 6 cubic metres. She was exposed to methyldopa by pouring 100 g of powder between two trays for 30 minutes. After this challenge FEV_1 and FVC were measured with a dry wedge spirometer (Vitalograph) every five minutes for 30 minutes, then every 10 minutes for 30 minutes, and thereafter every hour for 12 hours. Control readings were made in the same way on a separate day after tipping dried lactose powder for 30 minutes. A fall in FEV_1 of 15% or more after challenge compared with lactose control was regarded as a significant bronchial reaction. Bronchial reactivity to histamine acid phosphate nebulised for 30 seconds up to a final concentration of 32 mg/ml was also measured on a separate day. Nine hours after exposure to alpha-methyldopa powder the patient complained of nasal stuffiness and sneezing, and 11 hours after she complained of tightness in the chest and wheezing. Her FEV_1 fell by 30% from 2·66 l to 1·85 l maximal at 11 hours (figure). There was no such asthmatic reaction to lactose control or to histamine.

Comment

Similar asthmatic reactions have been described in other pharmaceutical industry workers after inhaling the powders of piperazine dihydrochloride[1]; ampicillin, benzyl penicillin, and 6-aminopenicillanic acid[2]; spiramycin[3]; glycyl compounds; fenfluoramine[4]; and clam's liver extract used in cancer chemotherapy.[5] Asthma has also resulted from the ingestion of tetracycline in a sensitive subject. We were unable to demonstrate antibodies to alpha methyldopa in our patient, but she alone of those working with the drug developed rhinitis and asthma. These started after several months' exposure without symptoms, suggesting that they were allergic reactions. Since the diagnosis was made she has avoided exposure to alpha-methyldopa, with complete remission of symptoms.

[1] Pepys, J, Pickering, C A C, and London, H W G, *Clinical Allergy*, 1972, **2**, 189.
[2] Davies, R J, Hendrick, D J, and Pepys, J, *Clinical Allergy*, 1974, **4**, 227.
[3] Davies, R J, and Pepys, J, *Clinical Allergy*, 1975, **1**, 99.
[4] Burge, P S, personal communication.
[5] Karlin, J M, Abstract 216 American Academy of Allergy 35th Annual Meeting, 1979.

(*Accepted 4 April 1979*)

Brompton Hospital and Cardiothoracic Institute, London SW3 6HP
M G HARRIES, MB, MRCP, lecturer
A NEWMAN TAYLOR, MB, MRCP, consultant physician
Health and Safety Executive, Employment Medical Advisory Service, London EC4A 4BA
JUNE WOODEN, SRN, OHNC, employment nursing adviser
A MACAUSLAN, MB, BCHIR, employment medical adviser

Reversible haemolytic anaemia after levodopa-carbidopa

A positive direct Coombs test and rarely autoimmune haemolytic anaemia (AIHA) are well-known complications of methyldopa treatment, particularly when given at higher dosage.[1] Patients taking levodopa may also have a positive Coombs test, and a few have developed AIHA.[2] The positive Coombs test is due to a warm-reacting IgG autoantibody with rhesus specificity indistinguishable from that seen in idiopathic AIHA but becoming weak or negative within a few weeks after stopping the drug. In one case of AIHA[3] Parkinsonian disability became so severe after stopping levodopa that after two weeks it was reinstated, though at one-sixth the previous dose by using the dopa-decarboxylase inhibitor combination levodopa-benserazide (Madopar). The Coombs test remained positive but haemolysis did not recur. The following case, however, which was originally described by Barat *et al*,[4] shows for the first time that severe AIHA may develop with combination chemotherapy.

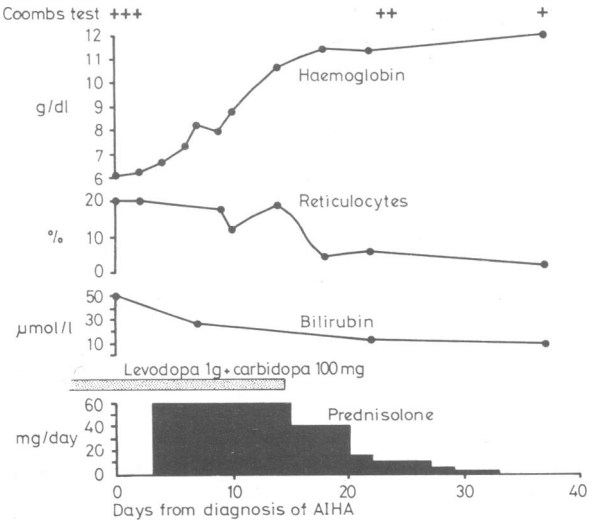
Case report

In 1969 a 65-year-old Frenchman developed Parkinson's disease. Levodopa was prescribed in 1974, the dose gradually being increased to 6 g daily. The

next year this was changed to combination chemotherapy with levodopa 1 g and carbidopa 100 mg daily (Sinemet). He remained well for a year but then became tired and pale. On admission to the Royal Free Hospital, London, he was anaemic and mildly jaundiced with no hepatosplenomegaly, no lymphadenopathy, and a clear chest radiograph. There was akinesia but no rigidity or tremor.

Results of investigations were: haemoglobin concentration 6·3 g/dl; reticulocytes 20%; nucleated red cells to white blood cells 5:100; white cell count 9×10^9/l (9000/mm³); platelet count 310×10^9/l; serum bilirubin concentration, total 50 μmol/l (2·9 mg/100 ml), conjugated 19 μmol/l (1·1 mg/100 ml); liver enzymes normal; serum folate concentration 9 μg/l; antinuclear antibody titre 10; serology for syphilis negative; direct Coombs test strongly positive. The red cells reacted strongly with antihuman IgG. The eluate and serum showed anti-e specificity, titre 64, against rr cells at 37°C. There was also a cold antibody, titre 8, against adult and cord red cells at 18°C, unreactive above 30°C. Bone marrow aspirate showed increased erythropoiesis.

The haemolysis was controlled with prednisolone. Levodopa-carbidopa was stopped and the prednisolone tailed off without relapse (figure). The Coombs test became less strongly positive. Parkinsonian akinesia worsened, so bromocriptine was begun. The patient then returned to France, where some weeks later levodopa-carbidopa was reinstituted. The direct Coombs test became strongly positive with the same specificity as before, and the haemolytic anaemia shortly recurred. Haemolysis was again suppressed with steroids but levodopa-carbidopa was continued and the Coombs test remained positive.



Resolution of haemolytic anaemia with initial steroid treatment and withdrawal of levodopa-carbidopa.
Conversion: SI to traditional units—Serum bilirubin: 1 μmol/l ≈ 0·06 mg/100 ml.

Comment

In this patient AIHA developed during treatment with levodopa-carbidopa and recurred on its reintroduction. The Coombs test was not performed before beginning treatment with levodopa. During the year that he was taking levodopa alone he had no clinical evidence of AIHA. The dopa-decarboxylase inhibitor reduces extracerebral breakdown of levodopa, so that lower dosage does not result in less exposure to the drug. While in one case[3] a similar regimen of combination chemotherapy reduced haemolysis, in the present patient severe haemolysis occurred.

I thank Dr C Symons for permission to report this case.

[1] Worlledge, S M, Carstairs, K C, and Dacie, J V, *Lancet*, 1966, **2**, 135.
[2] Gabor, E P, and Goldberg, L S, *Scandinavian Journal of Haematology*, 1973, **11**, 201.
[3] Lindstrom, F D, Leiden, G, and Engstrom, S, *Annals of Internal Medicine*, 1977, **86**, 298.
[4] Barat, M, *et al*, *Nouvelle Presse Médicale*, 1977, **6**, 2442.

(*Accepted 26 March 1979*)

Department of Medicine, Royal Free Hospital, London NW3 2QG
ROBERT M BERNSTEIN, MA, MRCP, medical registrar (present address: Department of Medicine, Hammersmith Hospital, London W12 0HS)

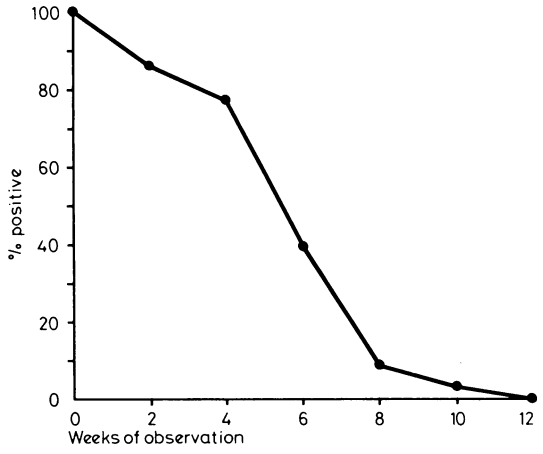
Pharyngeal neisseria gonorrhoeae: coloniser or pathogen?

During the past decade there has been increasing awareness of the prevalence of gonococcal pharyngeal infection.[1] The natural history of the condition is not clear. Most cases are asymptomatic and it is difficult to show a significant correlation between symptoms in the throat and the presence of *Neisseria gonorrhoeae*.[1] Gonococcal pharyngeal infection has been implicated as a risk factor for disseminated disease, and treatment-failure rates are higher for pharyngeal infection than for anogenital infection.[1] We have seen several patients with pharyngeal cultures positive for *N gonorrhoeae* who were refractory to treatment and became culture-negative over several weeks without invasive or local complications. We therefore decided to conduct a prospective study to try to elucidate the natural history of asymptomatic gonococcal pharyngeal infection.

Patients, methods, and results

During 1973-5, 12 men and six women were identified who had positive cultures of *N gonorrhoeae* from the pharynx and negative cultures from all other sites. All were asymptomatic, none had signs of pharyngitis, and none had taken antibiotics for 30 days. After giving informed consent the patients remained untreated and returned at two-week intervals for pharyngeal culture until negative cultures were obtained on two consecutive occasions. The patients were strongly advised against orogenital contact but mouth-to-mouth contact with their partners was not discouraged. The regular partners in nine cases returned with the study patient on each occasion for pharyngeal culture.

During the study period 17 of the 18 patients remained asymptomatic and free of complications. One patient developed pharyngitis after being followed up for seven weeks and a throat swab yielded β-haemolytic streptococci, group A, for which he was treated; *N gonorrhoeae* was not recovered. One patient was followed up for 10 weeks with positive cultures, but by the end of 12 weeks throat cultures from all 17 untreated patients were negative for *N gonorrhoeae* (see fig). Four patients had negative throat cultures at one visit then a positive culture two weeks later before their cultures became negative on two consecutive occasions. Pharyngeal cultures from the nine regular partners were repeatedly negative despite frequent mouth-to-mouth contact.



Proportion of 17 untreated patients with throat cultures positive for *N gonorrhoeae* during period of observation after initial positive culture.

Comment

A commonly accepted practice is to treat all patients with *N gonorrhoeae* isolated from the pharynx to prevent transmission and the development of complications. Although mouth-to-mouth transfer of the gonococcus may be a mode of transmission, no evidence of this has been found. Our results suggest that mouth-to-mouth transmission is an unlikely mode of spread of the gonococcus.

The lack of complications in our untreated patients contrasts with reports that pharyngeal gonorrhoea is a risk factor for disseminated disease.[1] The magnitude of this risk, however, is unknown. Factors that lead to pharyngeal colonisation rather than invasion are not understood. The position with the gonococcus may be analogous to