Blood oxygen and carbon dioxide pressures during three admissions. Results are given under days after admission in each month

Pressure (kPa)	Month of admission											
	March				July				December			
	0	2	6	12	0	2	4	8	0	2	4	8
Oxygen	5·4	5·7	7·1	10·0	4·5	7·3	7·2	8·3	6·0	7·3	7·0	8·8
Carbon dioxide ..	8·7	8·8	6·7	6·0	9·6	9·7	7·1	5·1	9·3	7·9	5·6	5·6

Conversion: SI to traditional units—1 kPa ≈ 7·5 mm Hg.

Results of other investigations were: haemoglobin concentration 16·5 g/dl; packed cell volume 0·65 (65%); and peak expiratory flow rate (PEFR) 60 l/min (predicted value 535 l/min). A chest radiograph showed enlargement of the heart, and an electrocardiogram showed right axis deviation, right ventricular hypertrophy, and biatrial enlargement. Results of echocardiography showed that the right ventricular cavity was dilated; there was good left ventricular function, a normal mitral valve, and a small pericardial effusion. Cardiac catheterisation gave the following results: pulmonary artery pressure 80/50 mm Hg; mean right atrial pressure 22 mm Hg; and right ventricular pressure 80/20 mm Hg.

The table shows the severe hypoxia and hypercapnoea on each of his three presentations after further chlorine inhalation. After treatment on each occasion with diuretics, bronchodilators, digoxin, and oxygen he improved and his PEFR rose from 60 l/min to 200 l/min. Other tests at his best in hospital showed a forced expiratory volume in litres of 1·1 l (predicted value 4·8 l).

During the months in which he was no longer inhaling chlorine gas his heart size returned to normal and diuretics were stopped.

Comment

Vim and Ajax contain trichlorocyanuric acid, sodium carbonate, and sodium tripolyphosphate. When mixed with water chlorine is released and hypochlorite is formed in solution; hypochlorite reacts with protein to release chloramine, a respiratory tract irritant.

Acute exposure to high concentrations of chlorine results in headache, dyspnoea, coughing, lacrimation, and later the development of pulmonary oedema.[2] In patients studied soon after exposure, airways obstruction and hypoxaemia due to ventilation perfusion imbalance have been shown.[2] The pathological findings in fatal cases of acute chlorine poisoning include congestion of the tracheal mucosa, sloughing of the alveolar walls, and pulmonary oedema.[3] In workers chronically exposed to concentrations of chlorine of under one part per million no appreciable ventilatory impairment has been shown.[4]

This case is unusual because the patient repeatedly inhaled chlorine for the pleasant effect he claimed to experience. He has developed pulmonary hypertension for which we have found no other cause, and although the physical signs improve after stopping chlorine inhalation they recur immediately his behaviour relapses.

I thank Dr A M Holmes for her advice and her permission to report this case.

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Hope Hospital, Salford M6 8HD
P RAFFERTY, MB, CHB, senior house officer

Psychiatric morbidity and physical toxicity associated with adjuvant chemotherapy after mastectomy

Doubt has been cast on claims that adjuvant combination chemotherapy causes little physical toxicity and psychiatric morbidity in patients with breast cancer (Bush H *et al*, unpublished observations).[1 2] This prompted us to compare the psychiatric morbidity in women treated with a combination of cyclophosphamide, methotrexate, and 5-fluorouracil (CMF) with that found in patients given melphalan or no further treatment. We also examined the relation between this morbidity and physical toxicity.

Patients, methods, and results

Half the weeks in a 24-month period were randomly selected. Women admitted in these weeks were included in the trial if their axillary lymph nodes were found at mastectomy to have been invaded by breast cancer (63 women), and they were randomised to receive CMF, melphalan, or no treatment (control subjects).

Trained interviewers administered the present-state examination shortly after surgery and three months and 12 to 18 months later to determine the incidence of psychiatric morbidity.[3] They used a four-point scale (none to severe) to rate any physical toxicity, as did the clinicians following up these patients. Of the 63 patients, 59 completed all assessments.

Psychiatric morbidity—Of the 26 patients treated with CMF, 20 experienced an anxiety state compared with four of the 15 given melphalan and nine of the 18 control subjects (table). Depressive illness occurred more often in patients given CMF (20 patients) than in the melphalan group (five patients) or control group (nine patients). Fourteen of the 20 patients given CMF who had a satisfactory sex life before mastectomy subsequently experienced a severe loss of interest compared with three of the eight patients given melphalan and five of the 10 control subjects. Twenty-one patients treated with CMF developed psychiatric morbidity during follow-up. Fewer patients given melphalan (five) and fewer control subjects (nine) did so.

Presence or absence of psychiatric morbidity judged to require treatment in patients with breast cancer. Figures in parentheses give percentage of treatment group showing morbidity

Treatment group	Anxiety*		Depression†		Sexual problems‡		Overall morbidity§	
	+	−	+	−	+	−	+	−
Mastectomy alone	9 (50)	9	9 (32)	19	5 (50)	5	9 (50)	9
Mastectomy and melphalan	4 (27)	11	5 (33)	10	3 (38)	5	5 (33)	10
Mastectomy and CMF	20 (77)	6	20 (77)	6	14 (70)	6	21 (81)	5

Significance of difference between numbers of patients showing morbidity and numbers of patients not showing morbidity at: *$\chi^2 = 10{\cdot}1$, df = 2, $p < 0{\cdot}01$; †$\chi^2 = 8{\cdot}0$, df = 2, $p < 0{\cdot}02$; ‡$\chi^2 = 4{\cdot}4$, df = 2, NS; §$\chi^2 = 9{\cdot}9$, df = 2, $p < 0{\cdot}01$.
CMF = Cyclophosphamide, methotrexate, and 5-fluorouracil.

Physical toxicity—The clinicians and interviewers judged that 20 of the patients given CMF had experienced moderate or severe physical toxicity such as nausea or hair loss. Of these, 18 developed an anxiety state compared with two of the six patients with mild or minimal toxicity. The results for depressive illness were identical. Sexual problems occurred in 13 of the 15 patients with moderate or severe toxicity but in only two of the five patients who escaped it.

Disclosure of toxicity—The interviewers detected the toxicity in 18 of the 20 patients but the clinicians recognised it in only 12. Eight of these 12 reported the toxicity to a medical oncologist but not to the surgeons. Five of the eight patients who did not disclose toxicity failed to complete treatment compared with only two of the 12 who disclosed it.

Comment

Our sample is small, but our findings confirm a high incidence of psychiatric morbidity in patients given CMF and suggest that it is linked to physical toxicity.

The non-disclosure of toxicity is worrying, since it misleads clinicians about the consequences of treatment and results in poor compliance. It may explain the low toxicity reported in earlier studies. The greater honesty of patients with the medical oncologist may have reflected his skill in the use of cytotoxic drugs, his more detailed inquiry into toxicity, his sensitivity to cues given by the patients, and his greater awareness of barriers to communication.[4]

Unless the adverse effects of CMF are recognised and combated its potential benefit on survival will not be fully realised.

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University Department of Psychiatry, Withington and Christie Hospitals, Manchester 20
G P MAGUIRE, FRCPSYCH, senior lecturer
A TAIT, SRN, research nurse
M BROOKE, SRN, research nurse
C THOMAS, MRCPSYCH, senior registrar

University Department of Surgery
J M T HOWAT, FRCS, lecturer
R A SELLWOOD, FRCS, professor

Cancer Research Campaign, Department of Medical Oncology
H BUSH, PHD, MRCP, senior lecturer (now professor of oncology and director, Ontario Cancer Research and Teaching Foundation, Victoria Hospital, London, Ontario, Canada)

Dapsone-induced optic atrophy and motor neuropathy

Blindness is one of the most serious side effects of treatment with drugs. We report a case of a young man who became blind and developed weakness of the legs after inappropriate use of dapsone. This is the first report of optic atrophy in association with dapsone.

Case report

A 20-year-old healthy Sudanese man was convinced that a lipoma on his shoulder was a lepromatous nodule. To cure his "leprosy" he took dapsone 600 mg daily for 10 days. Eleven days later he was admitted to hospital with vomiting, dizziness, and blurred vision. He looked ill and had cyanotic mucous membranes. No other physical abnormalities were noted. Dapsone poisoning was diagnosed, though tests for methaemoglobinaemia were not done. His condition improved when he was treated with fluid replacement and ascorbic acid. Two days later he was completely well and was discharged. He was told not to take dapsone and reassured that he did not have leprosy.

He returned three days later with blurred vision, generalised muscular pains, and difficulty in climbing stairs. He denied taking dapsone or any other drugs since discharge from hospital. Visual acuity was reduced in both eyes to counting fingers only. There was bilateral restriction of peripheral visual fields. Haemorrhages and exudates were present in both fundi, but the optic discs were normal. There were no other cranial nerve lesions. He had severe weakness in both legs and obvious foot drop on the left. Tendon reflexes were symmetrically decreased in the legs, but plantar reflexes were normal. There was no sensory deficit.

Results of laboratory tests on second admission were: haemoglobin concentration 14·8 g/dl, white blood cell count $5{\cdot}4 \times 10^9$/l (5400/mm^3), and erythrocyte sedimentation rate 3 mm in first h. No reticulocytes were seen and the red-cell sickling test gave a negative result. Results of cerebrospinal fluid examination and liver function tests were normal, as were fasting blood sugar concentration and concentrations of plasma urea and electrolytes.

Dapsone-induced motor neuropathy was diagnosed, and this drug was also considered as a cause of his blindness. A month after admission the visual loss persisted and both optic discs became pale, suggesting optic atrophy. Some of the exudates and haemorrhages, however, had cleared. Neither vision nor weakness showed any improvement during six months of follow-up.

Comment

The predominantly motor peripheral neuropathy, absence of sensory features, and clear drug history strongly incriminate dapsone. Dapsone-induced peripheral neuropathy is well recognised, though the mechanism is unknown and diagnosis is based largely on history and examination.[1] In common with some reported cases our patient has not shown improvement after stopping dapsone.[2]

Dapsone was stopped five days before the onset of blindness and weakness, though the dosage of dapsone was much higher than normal.

In our patient retinal haemorrhages and exudates were seen on the second admission. Pale optic discs suggesting optic atrophy developed gradually, without preceding optic neuritis or papillitis. Optic atrophy has not been reported in association with dapsone. Brain haemorrhages and thrombosed vessels, however, have been noted at necropsy in a fatal case of dapsone poisoning,[3] and peripheral gangrene has occurred after administration of high doses of dapsone.[4] We therefore suggest that a vascular process may have caused the optic atrophy.

The absence of cerebellar and long-tract signs, the development of optic atrophy without preceding optic neuritis, and the tropical environment make multiple sclerosis extremely unlikely. Repeated clinical and laboratory examinations have not detected parasitic or other infections.

We believe that dapsone should be included with disulfiram, chloroquine, and clioquinol[5] as a cause of peripheral nerve damage and optic atrophy, though the risk of optic atrophy may be related to large doses of dapsone.

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Department of Medicine, University of Khartoum, PO Box 102, Khartoum, Sudan
M HOMEIDA, MD, MRCP, lecturer in medicine and consultant physician
A BABIKR, MB, BS, medical registrar
T K DANESHMEND, MB, MRCP, visiting research assistant (now honorary medical registrar, University Department of Medicine, Bristol Royal Infirmary, Bristol BS2 8HW)

Rifampicin-associated pseudomembranous colitis

Pseudomembranous colitis has been associated with most antimicrobial agents except antituberculous drugs. Rifampicin may not be immune,[1] though the diagnostic criteria in the only case reported did not prove the involvement of *Clostridium difficile*. We report a further case of pseudomembranous colitis, apparently related to the administration of rifampicin.

Case report

A 60-year-old man, who had previously been given only phenoxymethylpenicillin, was admitted to hospital with tuberculous meningitis. He was treated with isoniazid, ethambutol, and streptomycin for one week and then with isoniazid, ethambutol, and rifampicin. After two weeks he was given nystatin, flucloxacillin, and gentamicin for one week for intercurrent infections and then dexamethasone 12 mg/day for one week, after which it was gradually withdrawn over about five weeks. Diarrhoea developed one week after nystatin, flucloxacillin, and gentamicin were stopped and soon after the initial dose of dexamethasone had been halved. The diarrhoea resolved after three days but recurred five weeks later, when dexamethasone was withdrawn. Pseudomembranous colitis was diagnosed and histologically confirmed after two weeks. Rifampicin was stopped, dexamethasone was restarted in low dosage, and he was given two one-week courses of vancomycin 2 g by mouth daily separated by one week, during which his diarrhoea returned. Sigmoidoscopic appearances were unchanged after one week but almost normal after two weeks. The diarrhoea settled within three weeks and did not return.