irradiation of inoperable salivary gland tumors: results of an RTOG-MRC cooperative randomised study. *Int J Radiat Oncol Biol Phys* 1988;15:1085-90.

3 Catterall M. "Controlled" clinical trials in neutron therapy. *Int J Radiat Oncol Biol Phys* 1987;13:1961-5.

4 Powers WE, Maughan RC. The cyclotron saga continues. *Br Med J* 1990;300:192. (20 January.)

Drug Points

Red man syndrome associated with amphotericin B

Dr MICHAEL E ELLIS (Monsall Hospital, Manchester M10 8WR) and Mr WILLIAM THARPE (King Faisal Specialist Hospital and Research Centre, Riyadh 11211, Saudi Arabia) write: We report a case of red man syndrome associated with amphotericin B.

An 18 year old Saudi man was treated with daunorubicin and cytarabine for acute myeloid leukaemia. Ensuing febrile neutropenia ($0.4 \times 10^9/l$) did not respond to intravenous piperacillin, gentamicin, metronidazole, and vancomycin so amphotericin B was added to cover the possibility of cryptic fungal infection. A test dose of 1 mg of amphotericin B was infused over two hours. Forty five minutes into the infusion an intense confluent blanching erythema appeared on the hands, soles, face, and neck and less so on the trunk. The hands became oedematous. A bounding sinus tachycardia (113 beats/min) developed with a blood pressure of 115/54 mm Hg. At the same time he was receiving intravenous vancomycin over one hour. Red man syndrome associated with vancomycin was diagnosed; amphotericin B and vancomycin were discontinued; intravenous diphenhydramine 25 mg with intravenous hydrocortisone 100 mg was administered; and the rash and swelling disappeared within four hours. On the next day vancomycin was withheld and a 1 mg test dose of amphotericin B repeated after premedication with diphenhydramine and hydrocortisone. The rash and swelling appeared as before. Once again the rash settled within two hours after the amphotericin B infusion was discontinued. Intravenous vancomycin was subsequently restarted with no incident, confirming that amphotericin B and not vancomycin had been responsible for the cutaneous reaction.

Common side effects of amphotericin B include fever, chills, and nephrotoxicity; a rash (maculopapular and truncal) has been reported only once,¹ and allergic reactions are rare.² This led to our wrongly blaming the vancomycin.³ This report indicates that a similar reaction can occur with amphotericin B. The Committee on Safety of Medicines has had 20 reports of rash occurring in association with the use of amphotericin B over a recent 17 year period, but red man syndrome was not mentioned. Amphotericin B is the antimycotic of choice for systemic fungal infections, and its increasing use may yield further cases of red man syndrome.

1 Lorber B, Cutler C, Barry WE. Allergic rash due to amphotericin B. *Ann Intern Med* 1976;84:54.

2 Bennett JE. Chemotherapy of systemic mycoses. *N Engl J Med* 1974;290:30-1.

3 Garrelts JC, Peterie JD. Vancomycin and "red man's syndrome." *N Engl J Med* 1985;312:245.

Pseudoporphyria due to Dyazide in a patient with vitiligo

Dr RICHARD J MOTLEY (Department of Dermatology, University Hospital of Wales, Cardiff CF4 4XW) writes: A 65 year old man presented with a 12 month history of skin fragility and blistering confined to areas of longstanding vitiligo on the dorsum of the hands and fingers (figure). The condition started within one month of his

UNIVERSITY HOSPITAL OF WALES

starting Dyazide, one tablet a day, for hypertension, and resolved four months after its discontinuation. The patient was otherwise well and receiving no other medication. Immunofluorescence antibody studies of the skin were negative and investigations of his porphyrin metabolism were normal. Pseudoporphyria has not been previously reported with Dyazide, which is a combination of triamterene and hydrochlorothiazide, but a similar case was reported after naproxen treatment in a woman with vitiligo.¹ The distribution of these lesions suggests that sunlight may predispose to the development of this reaction. The patient now receives bendroflumazide (5 mg/day) and there has been no further evidence of skin fragility.

1 Burns DA. Naproxen pseudoporphyria in a patient with vitiligo. *Clin Exp Dermatol* 1987;12:296-7.

Lobular panniculitis associated with ciprofloxacin

Drs E RODRÍGUEZ, J A MARTÍNEZ, M TORRES, A NUBIOLA, and J BUGES (Hospital de L'Esperit Sant, 08923 Barcelona, Spain) write: Ciprofloxacin, a new fluoroquinolone antibacterial agent, has recently been implicated in causing an erythematous papular rash due to vasculitis.¹ We present a case of lobular panniculitis occurring after ciprofloxacin treatment.

A 67 year old woman with diffuse bronchiectasis, who had been treated for seven years with theophylline, prednisone, salbutamol, and beclomethasone, showed an increase in her usual cough and purulent expectoration. Sputum culture grew *Pseudomonas aeruginosa*, and oral ciprofloxacin 750 mg twice daily was prescribed. Four days later the patient had a rash on all her limbs. Physical examination showed a temperature of 38.5°C and many erythematous nodules in both legs, thighs, and forearms, which were painful on finger pressure. No other physical sign of systemic disease was found.

The red and white cell counts, hepatic and renal function, and values for plasma proteins, serum electrolytes, calcium, phosphate, creatine kinase, aldolase, amylase, antinuclear antibody, and complement were all normal or negative. Erythrocyte sedimentation rate was 80 mm in the first hour. The level of circulating immune complexes by Clq system inhibition was 20% (normal <15%). Skin biopsy showed a fragment of fat nodular tissue with fat necrosis and lymphocyte infiltrate with

preservation of vascular and septal areas, all of which were typical of lobular panniculitis.² The fever and rash disappeared 10 days after ciprofloxacin was stopped.

Skin disturbances after ciprofloxacin administration occur in 0.7-2.2% of cases and have been described as nettle rash, pruritus, photosensitivity, and skin oedema.³ We suggest that lobular panniculitis should be added to the list.

1 Choe U, Rothschild BN, Laitman L. Ciprofloxacin-induced vasculitis. *N Engl J Med* 1989;320:257-8.

2 Bondi EE, Latarus GS. Panniculitis. In: Fitzpatrick TB, Eisen AS, Wolff K, Freedberg IM, Austen KF, eds. *Dermatology in general medicine*. New York: McGraw-Hill, 1987:1131-48.

3 Harkin H. Adverse effects of the fluoroquinolones. *Rev Infect Dis* 1988;10(suppl 1):S258-61.

Reversible hyperpigmentation associated with high dose hydroxyurea

DRS G MAJUMDAR, S E HEARD, and N G P SLATER (Department of Haematology, St Thomas's Hospital, London SE1 7EH) write: We recently treated two patients suffering from chronic granulocytic leukaemia in accelerated phase with high dose hydroxyurea, both of whom developed hyperpigmentation during treatment.

Case 1—A 61 year old man of African origin was treated for four years with intermittent busulphan during the chronic phase of the disease. In the accelerated phase he was initially treated with subcutaneous cytarabine 10 mg/m² daily for two weeks with no response. High dose hydroxyurea, 9 g/day for two days a week, was started on 23 May 1989. He showed partial response after a week and the dose was increased to 9 g/day for five days a week. Hyperpigmentation over the palmar creases and the forehead was noted on 16 June. Over the next two weeks the hyperpigmentation increased in both extent and depth and also affected the buccal mucosa. After six weeks' treatment he developed blastic transformation with thrombocytopenia and died of a cerebrovascular accident in August. Necropsy was not performed.

Case 2—A 47 year old man of African origin was diagnosed in the blastic phase and was initially treated with mitozantrone, cytarabine, and etoposide. He went into chronic phase after two such courses and was left without any cytotoxic or other drugs. Three months later he developed accelerated phase leukaemia. On 18 April 1989 he was started on hydroxyurea 9 g/day for two days a week, which was increased to four days a week after two weeks' treatment. Hyperpigmentation, most prominent over the forehead and palmar creases, was noted on 16 June, four weeks after the start of high dose hydroxyurea. He returned to chronic phase on 15 August, and the dose of hydroxyurea was reduced to 1.5 g/day given continuously. Over the next few weeks his hyperpigmentation regressed slowly and by 10 October, eight weeks after reduction of the dose, the level of pigmentation returned to normal.

Hydroxyurea has been reported to cause hyperpigmentation only after prolonged use in patients with psoriasis, concentrated in the affected areas.¹ In some patients hyperpigmentation was transient and disappeared even when hydroxyurea was continued. Lichen planus has been reported in patients with chronic myelogenous leukaemia after prolonged treatment with hydroxyurea.² We have not found any reports of reversible hyperpigmentation developing over a short period. Neither the Committee on Safety of Medicines nor the manufacturer has had any such report. The dose used in these two patients was higher than the usual dose of 1-3 g/day. Hyperpigmentation in our patients may have been related to the use of this high dose.

1 Dahl MGC, Comaish JS. Long-term effects of hydroxyurea in psoriasis. *Br Med J* 1972;iv:585-7.

2 Kennedy BJ, Smith LR, Goltz RW. Skin changes secondary to hydroxyurea therapy. *Arch Dermatol* 1975;111:183-7.