caused deaths. Since all three known mechanisms for drug-induced immune haemolysis (drug adsorption, "immune complex", autoantibody) have now been observed in cephalosporin-induced haemolytic anaemia, it is important that tests for drug-dependent antibodies are done on the patient’s serum in the presence of the drug (immune complex mechanism), and that the patient’s serum and an eluate from the red cells are tested with drug-coated red cells (drug-adsorption mechanism); drug independent antibodies should be evaluated with untreated red cells (to demonstrate autoantibodies).

American Red Cross Blood Services,
Los Angeles, CA 90006, USA

GEORGE GARRATTY

7. Shulman IA, Armit PA, McGee W, Garratty G. Cefazolin-induced immune hemolytic anemia due to antibodies reacting in vitro by more than one mechanism. Transfusion 1990; 30: 96-100.

Stevens-Johnson syndrome after fluconazole

SIR,—Fluconazole is a new triazole antifungal drug that has proved effective against deep-seated candidial infections in immunocompromised patients, and oropharyngeal candidiasis and cryptococcal meningitis in patients with AIDS.1,2 So far few serious side-effects of fluconazole have been reported. We describe a patient in whom Stevens-Johnson syndrome developed, probably because of fluconazole therapy.

A 30-year-old homosexual man was admitted because of high fever, diarrhea, vomiting, and a rash consisting of disseminated macular and maculopapular eruptions on the upper trunk. The oral mucous membrane showed erythema and several superficial ulcerations. Two weeks earlier 150 mg fluconazole daily had been prescribed for oral candidiasis and was taken until three days before admission. The patient proved HIV-positive (ELISA and western immunoblot). Because septicemia was suspected the patient received 120 mg gentamicin twice daily, 500 mg metronidazole thrice daily, and 1 g ampicillin four times daily. After two days, ampicillin was replaced by 1 g cefazidime thrice daily. On admission, fluconazole (100 mg daily) was reinstituted because of severe oral candidiasis. Within two days the skin lesions progressed to severe bullae covering the trunk and limbs. The mucous membranes were also severely affected. The clinical picture was consistent with Stevens-Johnson syndrome. The patient was severely ill with high fever and general malaise. Laboratory investigations showed raised hepatic enzyme and pancreatic amylase activities. Fluconazole was discontinued and within two days the general condition of the patient improved; the skin lesions did not progress further. Broad-spectrum antibiotics were discontinued two days after clinical improvement.

Up to now three cases of Stevens-Johnson syndrome during treatment with fluconazole have been reported.1,4 However, in all three patients the condition could not be attributed directly to fluconazole because other drugs, such as betalactam antibiotics, trimethoprim, sulphonamethoxazole, pyrimethamine, amphotericin B, zidovudine, sodium valproate, metoclopramide, and barbiturates, were also given. In our case we are convinced that Stevens-Johnson syndrome can be attributed to fluconazole because this was the only drug being used when the skin abnormalities first appeared. Moreover, the lesions improved after its discontinuation, whereas the antibiotics were still being given. Although this serious side-effect seems to be rare, we believe that fluconazole should be used with caution for conditions that can also be treated with topical, non-absorbable antifungal drugs.

M. J. E. GUSSENHOVEN
A. HAAK
J. D. R. PEEREBOOM-WYNIA

Department of Infectious Diseases, University Hospital, 2300 RC, Leiden, Netherlands

J. W. VAN’T WOUT


N-methylation of pyridines in Parkinson’s disease

SIR,—At low dose nicotinamide is rapidly metabolised to N-methyl-nicotinamide (NAM) and N'-methyl-2-pyridine as well as to nicotinic acid and nicotinamide N-oxide.1 N-methyl-NAM has structural similarities to the 1-methyl-4-phenylpyridinium ion (MPP+), which is the specific nigrostriatal, dopaminergic neurotoxin derived from 1-methyl-4-phenyl-1,2,3,6-tetra-hydropyridine (MPTP).2 We have studied NAM metabolism in patients with Parkinson’s or motoneuron disease and in controls to examine whether there were differences in N-methylation capacity in Parkinson’s disease. Patients were not receiving medication and were recruited sequentially at presentation.

After an 8 h overnight fast 50 mg of nicotinamide was given orally between 0700 and 0800 h. Urine was collected for 8 h. Urinary excretion of nicotinamide and certain of its metabolites was assayed by high performance liquid chromatography with ultraviolet detection.3 Excretion of NAM and its metabolites did not vary with age or sex in patients or controls. The table shows the 8 h urinary excretion of NAM and its metabolites. Total NAM excretion did not vary between the groups. Excretion of the oxidised N'-methyl-2-pyridone-5-carboxylic acid derivative was reduced in Parkinson’s disease and excretion of N'-methyl-nicotinamide was raised. No difference was found between controls and patients with motoneuron disease. The ratio of N'-methyl-2-pyridone to N'-methyl-nicotinamide excretion is consequently substantially disturbed in Parkinson’s disease.

N-methylation is carried out by the cytosolic N-methyltransferases that act on various substrates other than nicotinamide. Pyridine metabolites are thought to arise from initial hydroxylation of NADII.
of the pyridine ring by cytochrome P-450 or xanthine oxidase, followed by oxidation by aldehyde oxidase. Cytochrome P-450 activity in Parkinson's disease when tested with debrisoquine seems normal, but probing with phenytoin showed that there may be impairment in a few patients since reduced para-hydroxylation was seen. Our results might be explained by dysfunction of hydroxylation mediated by an isoenzyme of cytochrome P-450 or perhaps xanthine or aldehyde oxidases, leading to accumulation of the N'-methyl derivative. This may provide a basis for individual susceptibility to selective neuronal damage from pyridines, isoquinolines, or B-carbolines, whose N-methylated derivatives are known to be more toxic and more MPP+-like than the parent compounds.

Sandra Green
Steve Buttrum
HeLEN Malloy
Glyn StevEntOn
Stephen Sturman
Rosemary Waring
Hardy Pali
Adrian Williams

University Department of Neurology and School of Biochemistry
University of Birmingham
Edgbaston, Birmingham B15 2TH, UK