phenylbutazone, and the mechanism of interaction with warfarin is also similar. Azapropazone displaces warfarin from protein binding sites and also alters the renal clearance of R and S isomers of warfarin.^{4,5} Other non-steroidal anti-inflammatory drugs are less hazardous because they do not interfere with renal clearance of isomers of warfarin.

Azapropazone is absolutely contraindicated in patients taking warfarin. This potentially hazardous interaction should be highlighted further in both the data sheet¹ and the *British National Formulary*.⁶

- 1 Association of the British Pharmaceutical Industry. *ABPI data sheet compendium 1990-1991*. London: Datapharm, 1991:1378-9.
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- 6 British Medical Association, Royal Pharmaceutical Society of Great Britain. *British national formulary No 20*. London: BMA and Pharmaceutical Press, 1990:320-3.

Allergy to spiramycin during prophylactic treatment of fetal toxoplasmosis

Drs L S OSTLERE, J A A LANGTRY, and R C D STAUGHTON (Westminster Hospital, London SW1P 2AP) write: A 38 year old primigravida who was 29 weeks pregnant was admitted with a three week history of an erythematous pruritic rash. This had initially affected her hands and spread to her trunk and limbs. Eight weeks before she had been started on spiramycin 1.5 g twice daily for a positive maternal IgM titre indicating toxoplasma infection, which may have occurred up to one year before conception. Fetal blood sampling for toxoplasma antibody was negative and ultrasonography had shown no abnormality. She had a history of atopic eczema and was taking other drugs. On examination she had a widespread maculopapular rash sparing the umbilicus and forming erythematous plaques. There was no vesiculation or pustulation. The fundal height was consistent with 29 weeks' gestation. She was not feverish, and general examination was normal.

The white cell count was $11.7 \times 10^9/l$ (normal range 4-11) with eosinophils $2.8 \times 10^9/l$ (0-0.4 $\times 10^9/l$). She had a raised γ -glutamyltransferase concentration of 82 U/l (5-55) and the other liver enzymes were normal. A skin biopsy showed focal spongiosis and occasional parakeratosis. There was dermal oedema with a moderately severe perivascular infiltrate of chronic inflammatory cells, eosinophils, nuclear dust, and occasional extravasated red cells. Results of direct immunofluorescence of affected skin were negative.

She was initially treated with beclomethasone dipropionate 0.025% (Propaderm) ointment and emollient wet wraps to good effect but relapsed when the topical steroids were stopped. Because of the temporal relation to starting spiramycin treatment, eosinophilia, raised γ -glutamyltransferase concentration, and negative results of direct immunofluorescence, the rash was thought to have been caused by allergy to spiramycin. The risk of continuing spiramycin was considered greater than the possible benefits and the drug was stopped. Over the next two weeks the pruritus and rash resolved and remained clear. Her eosinophil count fell to $0.1 \times 10^9/l$ and γ -glutamyltransferase concentration settled within the normal range. She delivered a healthy girl at 37 weeks' gestation. Her skin remained clear and at 6 weeks her daughter had normal ophthalmological findings.

Toxoplasmosis is a worldwide infection of humans and animals caused by the protozoan *Toxoplasma gondii*. During pregnancy toxoplasma may cause fetal infection, with potentially serious

effects.¹ Spiramycin, one of the group of macrolide antibiotics, is thought to reduce the risk of fetal toxoplasmosis by more than half in toxoplasma infection during pregnancy.² It has been in clinical use for 15 years with little serious associated toxicity.³ In the United Kingdom it is available only on a named patient basis and is used to treat toxoplasmosis and cryptosporidiosis. In other European countries it is used with similar indications to those for erythromycin. The incidence of drug rash is approximately 1% (J G Bainbridge, personal communication), the most common being a transient erythema, and one case of allergic vasculitis has been reported.⁴ Other side effects include gastrointestinal upset and increased activity of liver enzymes.

France has had a national prevention programme for congenital toxoplasmosis since 1976. It includes mandatory serological screening of all pregnant women with monthly follow up tests if results are negative and treatment with spiramycin when acute infection is diagnosed. In the United Kingdom the prevention of congenital toxoplasmosis has received considerable attention in the mass media and the requests for antenatal screening have increased.⁵ Spiramycin is now recommended as first line treatment in pregnancy when maternal toxoplasma infection is proved or strongly suspected.⁶ It is increasingly important to recognise the side effects of spiramycin.

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- 3 Descoters J, Vial T, Delattre D, Evreux JC. Spiramycin: safety in man. *J Antimicrob Chemother* 1988;suppl B:207-10.
- 4 Galland MC, Rodor F, Jouglard J. Spiramycin allergic vasculitis: first report. *Therapie* 1987;42:227-9.
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Lung and skin hypersensitivity to 5-aminosalicylic acid

Drs V LE GROS, H SAVEUSE, G LESUR (Hôpital Ambroise Paré, 92104 Boulogne Cedex, France) and N BRION (Centre Hospitalier de Versailles, 78157 Le Chesnay Cedex, France) write: 5-aminosalicylic acid (5-ASA) is a half active component of sulphasalazine and has been used alone in the treatment of ulcerative colitis.¹ Sulphapyridine, a half inactive component, is held responsible for most side effects of sulphasalazine, including sulphasalazine induced lung diseases.^{2,3} We report a case of lung and skin hypersensitivity to 5-ASA. Neither the French adverse effect drug system nor the drug company have received previous reports of this.

A 54 year old woman was admitted to hospital for fever and erythematous skin rash occurring five days after treatment with 5-ASA (mesalazine) was initiated for an acute episode of ulcerative colitis (250 mg oral doses three times a day). She had no history of intolerance to salicylates but 10 years previously had developed a skin rash after three weeks of treatment with sulphasalazine. A chest radiograph disclosed bilateral interstitial opacities. Lung function tests showed a carbon dioxide pulmonary diffusion capacity of 53% of the expected value. Bronchoalveolar lavage fluid contained 138×10^4 cells/ml with 63% macrophages, 1.5% eosinophils, 0.5% neutrophils, and 35% lymphocytes with a CD4/CD8 ratio of 0.95 (1.70 in blood). A blood test of basophil degranulation in presence of 5-ASA was positive at 60%. 5-ASA was given for 17 days. After drug withdrawal the fever abated within 24 hours, lung opacities disappeared within 10 days, and skin rash disappeared within three weeks. One month later, the lung diffusing capacity was at 86% of the expected value.

The diagnosis of hypersensitivity to 5-ASA was based on the absence of any other aetiology; a history of hypersensitivity to sulphasalazine; lymphocytosis and low CD4/CD8 ratio in bronchoalveolar lavage fluid; blood tests positive for basophil degranulation in the presence of 5-ASA; and rapid improvement after drug withdrawal. This case suggests that 5-ASA moiety of sulphasalazine may be the responsible agent in some cases of lung diseases induced by sulphasalazine.

- 1 Rachmilewitz D. Coated mesalazine (5-aminosalicylic acid) versus sulphasalazine in the treatment of active ulcerative colitis: a randomised trial. *BMJ* 1989;298:82-6.
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- 3 Thomas P, Seaton A, Edwards J. Respiratory disease due to sulphasalazine. *Clin Allergy* 1974;4:41-7.
- 4 Moseley RM, Barwick KW, Dobuler K, Deluca VA. Sulphasalazine-induced pulmonary disease. *Dig Dis Sci* 1985;30:901-4.

Catatonias in the allopurinol hypersensitivity syndrome

Drs C E COLLINS, D J B THOMAS, and J M GUMPEL (Mount Vernon Hospital, Northwood, Middlesex HA6 2RN) write: A 67 year old woman presented with a 24 hour history of vague affect, a widespread itchy maculopapular rash, and a temperature of 37.5°C. She was uncommunicative, staring into space; her elbows, hips, and knees were flexed and unyielding. Eight weeks previously she had suffered a "flare up" of her longstanding gout, which was being treated with indomethacin (Indocid R 75 mg thrice daily). At the time of admission her only medication was allopurinol 100 mg thrice daily, which she had started six weeks previously. Her urea concentration had been 12 mmol/l, serum urate concentration 609 mol/l, and haemoglobin concentration 104 g/l when she was first prescribed allopurinol.

The following investigations were abnormal after admission: erythrocyte sedimentation rate 133 mm in the first hour, urea concentration 29 mmol/l, creatinine concentration 391 mmol/l, haemoglobin concentration 96 g/l falling to 69 g/l three days later. There were atypical red cell antibodies with specificity for anti-D. Tests for smooth muscle antibodies, antinuclear factor, and double stranded DNA antibodies were negative. The patient was treated with intravenous hydrocortisone 200 mg six hourly for 48 hours, followed by oral prednisolone 40 mg daily for two weeks; the allopurinol was discontinued. The catatonias, rash, and temperature rapidly improved and the renal function returned to its previous level. The gouty arthritis was successfully treated with tiaprofenic acid, which is a uricosuric non-steroidal anti-inflammatory drug. The patient remained well without taking steroids.

The allopurinol hypersensitivity syndrome is a rare, life threatening complication that usually affects patients who are also being treated with diuretics, particularly patients with impaired renal function.^{1,2} Catatonias has not been described with this syndrome and its presence is difficult to explain. There was no previous psychiatric history in this patient, and allopurinol does not have any known neuroleptic activity.³ Whatever the aetiology of the catatonias in this patient, it seemed to be sensitive to steroids, improving within two hours and disappearing within 10 hours when intravenous hydrocortisone was given. Paradoxically, prednisolone was incriminated as a causative factor when catatonias developed in a patient with myeloma.⁴

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- 3 Fricchione GL. Neuroleptic catatonias and its relation to psychogenic catatonias. *Biol Psychiatry* 1985;20:304-13.
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