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An occasional bulletin from the West Midlands Centre for Adverse Drug Reactions Reporting

REPORTING TO CSM West Midlands

We welcome Yellow Card reports on all adverse reactions to new (–) drugs and vaccines, and on all serious or unusual reactions to well-established drugs. A serious reaction is one which is fatal, disabling, incapacitating, or which results in or prolongs hospitalization.

Yellow Cards can be found in the BNF, MIMS, the ABPI Datasheet Compendium, OTC Directory and in FP10 prescription pads. Further supplies can be obtained from CSM West Midlands.

Please send reports to

CSM West Midlands Freepost SW2991 BIRMINGHAM B18 7BR.

If you would like a supply of pre-addressed and stamped yellow cards, please contact the above address.

ADDTIONS TO CLOSELY MONITORED DRUGS include

– Sevoflurane®	sevoflurane	– Livostin®	levocabastine
– Betaferon®	interferon beta	– Nimbex®	cisatracurium
– Curatoderm®	tacalcitol	– Flomax®	tamsulosin
– Preservex®	aceclofenac		

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RECENT REPORTS

Coming out in a cold sweat...hypoglycaemia with pentamidine

The antiprotozoal drug pentamidine is second-line therapy for *Pneumocystis carinii* pneumonia in patients with AIDS, in whom this opportunistic infection is one of the most important causes of morbidity and mortality. The drug is excreted unchanged in the urine, and can be nephrotoxic, partly because of severe hypotensive reactions. It also causes hypoglycaemia by stimulating insulin release. About 30% of patients with AIDS given infusions of the drug become hypoglycaemic during therapy. The hypoglycaemia sometimes recurred or persisted for days after the drug was stopped. It is usually symptomatic, and can prove fatal. High drug dosages and significantly impaired renal function are important precipitants. Inhaled pentamidine can also cause hypoglycaemia. Because the drug damages the pancreatic B-cells, hyperglycaemia can follow pentamidine treatment, usually after several weeks or month, and sometimes in patients who have suffered from episodes of hypoglycaemia previously.

Pentamidine is a potentially toxic drug and it should only be administered by those experienced in its use.

A fall in Reye's...a success for drug regulation

(Hardie *et al*, *Archives of Diseases in Childhood* 1996; **74**: 400)

Reye's syndrome (RS, pronounced "Rye's" syndrome) is a rare but very nasty disease of children, originally described in 1963 as "encephalopathy and fatty degeneration of the viscera". The diagnosis is now made on the basis of an otherwise unexplained non-inflammatory encephalopathy in a child under 16 years old, with one or more of: characteristic fatty infiltration of the liver, a plasma ammonia more than 3 times normal, or hepatic transaminases more than 3 times normal.

The disease usually follows a trivial viral illness, especially influenza B or chickenpox. About 40% of affected children die. Epidemiological studies show that the risk is about 40 times higher in children given aspirin for their fever than who are not. In the United States, where suspicions about aspirin surfaced in the early 1980s, and a warning label was introduced in 1986, the number of cases of RS fell from 555 in 1980 to 25 in 1989. In Britain, since the introduction of label warnings in 1986 contra-indicating the use of aspirin in children below the age of 12, there has been a fall from 79 that year to a provisional 17 cases in 1994-5 (Dr Susan Hall, personal communication). The fall is even more striking if only those cases with "absolutely classical" RS are taken into account. Because of the concern arising from 3 cases of RS from 1991-93 the CSM/MCA reminded doctors in 1993 about the association between RS and aspirin (*Current Problems* 1993; **19**: 4).

RS is certainly rarer since the introduction of warnings on labels for aspirin contra-indicating its use in children under the age of 12 years. There is persuasive evidence that aspirin provokes RS, and that the warning has been effective in reducing the incidence of the disease.

A jaundiced view of co-amoxiclav...a cause of drug-induced hepatic dysfunction

(Thompson, *Med J Aust* 1995; **162**: 638)

Co-amoxiclav (Augmentin®) combines amoxycillin with the beta-lactamase inhibitor potassium clavulanate. The clavulanate prevents bacterial beta-lactamases from destroying the amoxycillin, and so extends the range of organisms sensitive to the amoxycillin. We have received 5 reports this year, and the CSM has received nearly 300 reports of hepatic dysfunction associated with co-amoxiclav, and has already noted this problem (*Current Problems* 1993; **19**: 2). Liver disorders are very rare when amoxycillin is given alone. The current BNF contains a CSM warning that cholestatic jaundice with co-amoxiclav can occur up to six weeks after treatment has stopped.

A recent retrospective case-control study has examined 34 cases of cholestatic jaundice related to co-amoxiclav treatment, compared with 136 control patients given co-amoxiclav, but not developing jaundice. Age was the most important risk factor for jaundice: the risk was 16 times greater in patients over the age of 55, compared with those under the age of 30. And men were 2 to 3 times more likely to suffer from jaundice than women.

The latest Australian Adverse Drug Reaction Bulletin (1996; **15**: 6) describes how the number of reports of adverse hepatic reactions with co-amoxiclav continue to rise, in parallel with drug sales. In total, there have been 309 cases, including 5 of patients dying from hepatic failure. In most cases, though, the cholestasis resolves in a few weeks.

The 'secondary' component of a combination drug can be an important cause of adverse reactions.

Please send any comments, questions or suggestions to: Dr R E Ferner, CSM West Midlands, City Hospital, Dudley Road, BIRMINGHAM B18 7BR