re:ACTION December 1996 No.11

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 on all serious or unusual reactions to well-established drugs.

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.

No stamp is needed. If you would like a supply of pre-addressed and stamped yellow cards, please contact the above address.

ADDITIONS TO CLOSELY MONITORED DRUGS include

- **testosterone (Andropatch®)**
- **meloxicam (Mobic®)**
- **valsartan (Diovan®)**
- **stavudine (Zerit®)**
- **ritonavir (Norvir®)**
- **saquinavir (Invirase®)**
- **ACT-HIB® DTP**
- **pantoprazole (Protium®)**
- **penciclovir (Vectavir® Cold Sore Cream)**
- **olanzapine (Zyprexa®)**
- **lamivudine (Epivir®)**
- **indinavir (Crixivan®)**
- **riluzole (Rilutek®)**

We are keen to receive reports of all suspected reactions to all closely monitored drugs, and to vaccines and unlicensed herbal preparations.

RECENT REPORTS

Not certain, not severe, not noteworthy? Under-reporting of adverse drug reactions (*Brit. J. Clin. Pharmacol*. 1996; **42**: 423)

The mainstay of adverse drug reaction reporting in the United Kingdom is the Yellow Card Scheme, which has proved extremely valuable as an early warning system for possible drug safety issues. Yellow Cards have highlighted serious problems such as marrow dysplasia with mianserin, and hepatitis with amiodarone. In addition, the data for the comparative safety of non-steroidal anti-inflammatory drugs have stood up well when compared with data from more sophisticated analyses.

The scheme can only work if doctors are able to send in relevant reports. Unfortunately, under-reporting has always been a difficulty. A recent survey from a major teaching hospital in Oxford gives a clearer idea of the proportion of adverse reactions seen on the general medical wards and reported to the Committee on Safety of Medicines.

In a prospective survey, 1420 adverse reactions were collected from 20 695 consecutive admissions, a rate of 69 per 1000 admissions. Of these, 477 would have fulfilled the CSM's criteria for reporting, but only 30 yellow cards seem to have been sent, accounting for only 6.3 % of the identified 'reportable' reactions. There appear to be three reasons why doctors worry about reporting a reaction that they suspect: that they

have not proved the relationship between drug and reaction, though the CSM asks specifically for **suspected** adverse reactions; that the reaction is not severe enough, a problem that can be resolved by reporting all reactions severe enough to require hospital admission, and all reactions that are life-threatening; and that the reaction is well-known, even when severe - though failure to report reduces the chances of meaningful comparisons between different drugs.

We welcome reports of any suspected reactions to 'black triangle' drugs and vaccines, and any serious or unusually suspected reactions to older drugs.

The emperor's new coat... The risk of aspirin associated bleeding with different preparations (*Lancet* 1996; **348**: 1413)

Aspirin is now the mainstay of treatment for atheromatous cerebrovascular disease, coronary heart disease, and several other conditions that require long-term therapy. Even at doses of 300 milligrams per day or less, aspirin increases the risk of upper gastro-intestinal haemorrhage. A recent case-control study has examined whether the risks differed among plain, buffered and enteric-coated aspirin tablets

The cases were 550 patients admitted with a first upper GI bleed to hospitals in Massachusetts, demonstrated to have a peptic ulcer or gastritis; two controls from the same area of residence were matched with each case. The (corrected) relative risks for upper GI bleeding for those who took 325 milligrams of aspirin or less each day were: 2.6, 2.7 and 3.1 in those on plain, enteric-coated, and buffered aspirin.

Although numbers of events were small in all three groups, the authors concluded:
'Physicians should not assume that [enteric-coated or buffered] forms are less harmful to the gastrointestinal tract...'

We welcome reports of drug-induced gastrointestinal haemorrhage severe enough to cause admission; details of the formulation used will be helpful.

Not bleeding but clotting... Heparin-induced thrombocytopenia and thrombosis
(*New Engl. J. Med.* 1995; **332**: 1330)

Heparin anticoagulation occasionally induces thrombocytopenia. There are two distinct types of heparin-induced thrombocytopenia (HIT). In Type 1 HIT, the platelet count falls soon after heparin treatment is introduced. The total platelet count remains above 100×10^9 per litre, and there are no clinically important sequelae. The cause is thought to be a direct aggregatory action of heparin on platelets.

Type II HIT is an uncommon but life-threatening condition in which there is a marked fall in platelets that can be associated with arterial and venous thrombosis and embolism. It is caused by an antibody reaction to heparin + a platelet factor, and so occurs after some days of heparin treatment, except in previously sensitized patients.

Although low-molecular-weight heparins are not as immunogenic as unfractionated heparin, and therefore seem less likely to cause Type II HIT, they react with the antibodies formed, and so cannot be used once the condition is established.

Because the mortality is over 30% in reported series, urgent action is needed in patients where the diagnosis is suspected. Heparin should be stopped at once, and expert advice sought.

Heparin-induced thrombocytopenia with thrombosis is an example of a serious adverse drug reaction that can be confused with the condition for which treatment was initially given.

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