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# BRITISH MEDICAL JOURNAL

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*We may return unduly long letters to the author for shortening so that we can offer readers as wide a selection as possible. We receive so many letters each week that we have to omit some of them. Letters should be typed with double spacing between lines and must be signed personally by all their authors, who should include their degrees. Letters critical of a paper may be sent to the authors of the paper so that their reply may appear in the same issue.*

*Correspondents should present their references in the Vancouver style (see examples in these columns). In particular, the names and initials of all authors must be given unless there are more than six, when only the first three should be given, followed by et al; and the first and last page numbers of articles and chapters should be included.*

## Adverse reactions to new drugs

SIR,—Dr W H W Inman (26 February, p 719) defends loyally the yellow cards he left behind when he moved to Southampton to explore a different approach. His arguments for exonerating the yellow card failures to provide first alerts for lincomycin, clindamycin, stilboestrol, and aerosols are unconvincing in the light of the references cited, the relevant dates, and the delays to regulatory action. We agree about the three practolol reactions (and about subacute myelo-optic neuropathy, for which causality was unproved). Thus the yellow cards failed to provide first alerts for seven reactions to five drugs in table I all occurring after the start of the system in 1964. I have no evidence, however, that the yellow cards provided first alerts to any of the 48 other reactions to 56 drugs identified as important in tables II and III in part I (15 January, p 199). A number of these were also identified after 1964. Further detailed analysis of this unbiased list would provide a valid method for auditing the system in operation.

Dr Inman also refers to "hundreds of signals . . . and many serious problems quietly and efficiently attended to. . ." If none of these have been identified by any one of 20 doctors, including Dr Inman himself, as important (as defined) then it seems inescapable

that the yellow cards are better at identifying less important reactions and less effective at providing first alerts to the most serious reactions, which are usually very infrequent. This is precisely what might be predicted on general common sense grounds and on review of the yellow card files, in which there is a marked preponderance of reactions that are already known and very large numbers of minor reactions which have clogged up the system for reading and assessing the reports.

For the specific purpose of first alerting I proposed, when working at the Department of Health and Social Security, that it would be far more efficient to employ someone to read the published work and to base yellow peril letters to the medical profession and warnings in *Current Problems* on the first alerts and first verifications from the journals which have in the past almost always preceded the first regulatory warnings based on yellow card data. This is now happening and should yield a better return on the investment, particularly in terms of prompt alerting of the medical profession in the publications of the Committee on the Safety of Medicines.

Dr Inman made a number of important contributions to the DHSS, whose value was mainly dependent on his sound epidemiological

approach and his reliance on valid methods that have little or nothing to do with yellow cards. He is, in fact, to be congratulated on what he achieved in spite of the indisputable weaknesses of the system. Firstly, he conducted a number of formal verification studies using a case orientated approach along the lines proposed in my conclusions to the series (12 February, p 544). Secondly, he was careful to validate yellow card reports, using the part time medical officers employed by the DHSS. This important safeguard was not in operation recently. Thirdly, his work on the pill and thromboembolism included analysis of death certificates. Unlike the yellow cards these provide an unbiased data base suitable for case control studies. Fourthly, his work on the pill and myocardial infarction was critically dependent for its value on the analysis of dose response data. This is only applicable to a minority of adverse reaction problems and provides, as pointed out, one of the only ways of using for verification of suspected reactions a system that is fundamentally flawed in epidemiological terms.

On a general note the data available to the Committee on the Safety of Medicines, which form the basis of "serious problems quietly and efficiently attended to," are not usually