



Editorial

Is pharmacovigilance still a clinical science?

Karl Kimbel

Övelgönne 92C, D-22605 Hamburg, Germany

Accepted 1 September 1994

Louis Lewin, better known for his popular works on poisons, wrote the first book on Side Effects of Drugs (“Nebenwirkungen der Arzneimitiel”) in 1881. In the introduction to the 3rd edition (1899) he postulated: “As valuable as reports on side or after-effects of drugs *per se* may be, as much the practitioner may benefit from instructions as to how to avoid and treat such effects for his patients’ sake, the true educational impulse results solely from demonstrating the link between such phenomena and other biological facts. Where purely chemical effects are believed to be causal they should, if possible, be elucidated.” He knew what he was talking about, for he met with stiff resistance from some clinicians whose unthinking approach to drug therapy he openly criticized.

While research on the mechanisms of therapeutic actions or interactions are today pursued vigorously by experimental and clinical pharmacologists, the pharmacological, biochemical and immunological causes of adverse reactions are much less commonly studied. We still do not know *why* the practolol syndrome occurred, and even frequent pulmonary reactions to such widely prescribed drugs as the ACE inhibitors still await clarification. Quite apart from the apparent lack of scientific interest in such matters, there is rarely regulatory action obliging the manufacturer to sponsor such studies; it is not surprising that the funds for such studies are not forthcoming.

The differential diagnosis of an adverse drug event is not an administrative act but a recurrent medical problem, and one with which the general practitioner or the practising specialist are particularly likely to find themselves faced. Where faced with unusual symptomatology of a type falling outside his or her own discipline, the doctor can always seek the advice of a consultant in the field of medicine concerned. The possibility of finding a consultant with special knowledge of adverse effects as such is, however, much more limited; even in the most highly developed countries, specialists in adverse reaction studies are

few and far between. While the National Health Service in Great Britain provides an exception to the rule by employing close to a hundred clinically trained clinical pharmacologists, some of their colleagues in other countries, even those holding academic posts, tend to have little bedside experience, and are thus reluctant to participate in clinical decision making; some of them do not even consider pharmacovigilance to be part of clinical pharmacology.

This situation imposes an unusually heavy burden on physicians working in regulatory authorities. They are very much alone when decisions have to be taken on apparent shifts in the benefit/risk ratio of a drug, and when the need arises to provide proper information on such matters to the prescribing physician. Even worse, they may have to deal with such matters under considerable legal pressure. In most countries their workloads (and sometimes even their contracts of service) prevent them from accepting part-time clinical appointments or even doing their own research. As a result they risk drifting ever further away from the field of knowledge which they are supposed to apply in their work. A few do have (and many more wish that they had) an independent, multidisciplinary advisory board readily to hand.

These are real problems in regulation; one must hope that the new European Medicines Agency in London will find — or create — the scientific environment in which good regulatory medical work relating to drug safety is possible. But what are the real prospects of that happening? To date there has been only meagre support from Brussels for pharmacovigilance based on sound medical and scientific principles. The “Draft Guidelines for Marketing Authorization Holders on ongoing Pharmacovigilance Evaluation during the Post-marketing Period” issued by the Working Party on Pharmacovigilance of the European Union’s Committee for Proprietary Medicinal Products in December 1983 define the responsibilities of the group leader who carries responsibility for monitoring and risk–benefit evaluation as follows:

“(i) the establishment and maintenance of a system which ensures that information about all suspected adverse reactions which are reported to the personnel of the company and the medical representatives is collected at a single point within the company

(ii) the preparation for the competent authorities and the European Agency of the reports referred to in the Regulation and Directives and further detailed in the Guidelines”

The person responsible, however “ . . . if not medically qualified should report to, or have access to, a medically qualified person within the company.”

If even the European Community is convinced that a person responsible for pharmacovigilance at an important primary source of benefit/risk information

and assessment, i.e. a pharmaceutical company, does not need medical training, one begins to understand that professional organizations as well as universities consider pharmacovigilance as an administrative task not deserving of professional and scientific scrutiny. Some parts of industry seem only too ready to welcome this cost-saving, trouble-avoiding approach, and in doing so they risk allowing their public image to deteriorate further. Our scientific conscience should surely by now insist that the adverse effects of a drug deserve the same quality of scientific scrutiny as that accorded to beneficial effects.