These postgraduate educational issues of the British Journal of Anaesthesia are intended to provide an authoritative and current review of selected topics of interest in anaesthesia and related disciplines. It is self-evident that the factual knowledge of adverse effects is of direct benefit to patient safety, but the fundamental concepts, which are so much more important for good clinical practice, are surprisingly complex. An overview of the subject needs to distinguish between at least four general categories: overdose effects, side actions, abnormal responses and drug interactions. An overdose can be either relative or absolute, but an important factor is the spread of sensitivity to the drug effect within the general population. This finite variability of response is relevant to the degree of predictability of an overdose effect. Side actions are usually more predictable than overdose effects as they accompany the major drug action and are only called side actions because the physician attempts either to minimize or to ignore their effects. It is, of course, only a proportion of these actions which need to be classified as adverse. In contrast to these first two categories, abnormal responses are characterized by their unpredictability and the rarity of the events. Finally, drug interactions have to come into a separate category because not only do they modulate separate drug actions, but also they can introduce hitherto new and unsuspected adverse effects.

In planning this postgraduate issue, the complexity of the subject was recognized and it was decided to group the adverse effects by considering those associated with principal drug groups, rather than combining the actions of different types of drugs on specific organ systems. In order to avoid the danger of the subdivisions degenerating into a catalogue of contraindications—which would duplicate material already published—the guest contributors were asked to consider the different drug effects in terms of both underlying principles and clinical relevance.

The true overall incidence of anaesthetic morbidity is unknown, but all would accept that anaesthetic drugs can be associated with iatrogenic injury if administered at high enough concentrations. This aspect of the problem is not necessarily synonymous with an overdose effect. For example, the adverse actions of local anaesthetics have been considered in terms of local and focal effects—both of which are associated with high concentrations of the agents—in contrast to systemic effects which are produced at low concentrations following absorption into the general circulation. One of the complications of adverse effects is that what is considered an acceptable physiological response in one set of circumstances becomes an adverse effect in another. This is the case with the respiratory depression associated with the opioids. During operation, far greater degrees of respiratory depression are compensated for by artificial ventilation, but it is the fact that these drugs continue to have subtle effects, or are administered during the postoperative period, that gives rise to the concern about adverse effects.

The distinctive feature of many of the drugs used in anaesthesia is the lack of specificity in their actions. One generalization is that a drug with non-specific multiple actions is more likely to have associated adverse effects. This is not, of course, true of all drugs, and the review of the neuromuscular blocking drugs concentrates on more specific adverse effects. Anaesthesia may involve polypharmacy, with many drugs being used as part of the anaesthetic regimen. For this reason a review of drug interactions seemed appropriate, since a knowledge of this subject must form an increasing part of the essential information for the modern anaesthetist.

Research on the adverse effects of general anaesthetics is proceeding intensively both in the laboratory and in the clinical field. Advances in these two areas do not necessarily go hand in hand. For example, in the case of nitrous oxide, there is a mass of biochemical data, but an absence of obvious adverse clinical effects. This apparent contradiction can only be resolved by more clinical
studies. On the other hand, the paper on the volatile agents brings out the opposite problem. The clinical evidence for and against anaesthetic-associated hepatitis has accumulated for many years, but we will be unlikely to be able to specify the predisposing factors more precisely until there have been advances in our understanding of the underlying biotransformation and immunological mechanisms.

Adverse effects of drugs is a topic which unites the theoretical, experimental and practical interests of anaesthetists. This is especially true in the case of the new i.v. agents; further clinical evaluation will be required for the recently released agents, particularly when they are administered by continuous infusions for prolonged sedation in intensive therapy units over periods of weeks. It is necessary to know the methods of investigation of allergic and hypersensitivity reactions in order to take up the challenge of learning more about these aspects of the drugs. Finally, the medical profession must be one of the few groups who have co-operated with such success in a prospective study of the potential adverse effects of anaesthetic environmental pollution. Some 11000 woman have been recruited into the anaesthetists’ 5-year epidemiological study which finished at the end of 1986. For these reasons this seems a particularly opportune time to review all the adverse effects of drugs used in anaesthesia.

What is needed in the future is for everyone to improve their reporting of the adverse effects of all drugs. In Britain the reporting system includes the use of a yellow card on which the details of all apparent reactions are notified to the Committee on Safety of Medicines. A possible modification, currently being considered, is the introduction of what has been called “the red card” specifically for acute adverse reactions. Such a system could be particularly relevant to anaesthetists, whose potential problems are somewhat different from those of other physicians.

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