

positive results, whereas negative skin tests were obtained again with Solu-Medrone and Solu-Cortef and also with methylprednisolone sodium succinate, methylprednisolone sodium acetate, hydrocortisone sodium succinate, prednisolone, prednisone, triamcinolone, dexamethasone, cortisone acetate, and the diluent solution. Passive transfer of the positive reactions were negative on three recipients, though the patient's positive skin test to Bermuda grass was passively transferable to each of the recipients. Serial measurements during two intravenous challenges which provoked anaphylaxis showed no significant change in six components of the complement system or fibrinogen.

The interesting inconsistency between the results of the intravenous challenges and the skin tests is that the succinate salts of the steroid produced symptoms on challenge but only methylprednisolone or hydrocortisone alone gave positive skin tests. Mendelson *et al.* suggest that small structural changes in the molecule produced by succinylation or acetylation may have been responsible for the negative skin tests.

<sup>1</sup> Mendelson, L. M., Meltzer, E. O., and Hamburger, R. N., *Journal of Allergy and Clinical Immunology*, 1974, 54, 125.

<sup>2</sup> Schorr, W. F., *Journal of the American Medical Association*, 1968, 204, 859.

<sup>3</sup> Kahn, G., Aldrate, J. A., and Ryan, S. C., *Annals of Allergy*, 1971, 29, 480.

## Outmoded Barbiturates

How can drugs be changed back into words that mean something in our culture? Dr. Victor Parsons, of King's College Hospital, asked the question at a seminar on the uses and abuses of hypnotics and sedatives organized by the British Medical Association's Board of Science and Education and held at B.M.A. House, London, last week. Neither the six speakers nor the audience of about 80 had the answer. But there was general agreement that the prescribing of barbiturates came in for special criticism as being now outmoded for most purposes by the benzodiazepines.

The relentless increase over the years in the number of drugs prescribed in general practice was discussed by Dr. Peter A. Parish, of the University College of Swansea. This increase has occurred despite a constant relation between the numbers of general practitioners and the size of the population. Doctors were using more drugs in treatment, he said, not seeing more patients. In fact the number of consultations per doctor had decreased while the number of prescriptions had increased. The proportion of prescriptions for psychotropic drugs in the total had remained constant for some years, so the prescriptions for them had also increased. Dr. Parsons suggested what is probably a good reason for this. Nowadays, he said, there were very few symptoms for which no drug gave relief. But what, asked Dr. Parish, is responsible and rational prescribing? By responsible he was suggesting some kind of "peer review," to use a fashionable term for discussion among colleagues of how they should prescribe and in what circumstances. And rational prescribing, he pointed out, cannot be separated from social values. The future would have to compromise between chemical change and social change.

This has certainly always been man's lot. Alcohol and opium have given solace since primeval times—and brought new ills with them. Likewise the side effects of the psychotropic drugs occupied several speakers. Professor Roy Spector, of Guy's Hospital, discussed some of them. They all caused dependence, he said, as well as unnatural sleep and hangover, and were

potentiated by alcohol. More specific ill effects included depression of respiration, production of gastric lesions, and enzyme induction in the liver. Dr. Alan Richens, of St. Bartholomew's Hospital, who followed him, also stressed the poor quality of the sleep that hypnotics have been shown to give and the serious consequences for patients from hepatic enzyme induction. Among drugs causing the last the barbiturates are prominent, and among drugs affected by this mechanism are the oral contraceptives. These can be rendered ineffectual, so that pregnancy results in a patient on a hypnotic.

The hazards of barbiturates in acute overdosage were stressed by several speakers, and Dr. Richard Fox, of Severalls Hospital, Colchester, added the weight of his opinion to the general view that the prescribing of them should be greatly restricted. They should be replaced, he considered, by the benzodiazepines. Dr. Frank Wells, of Ipswich, who did so much to persuade the profession to prescribe amphetamines rationally<sup>1</sup>—and in consequence very rarely—likewise advocated the gradual replacement of barbiturates by benzodiazepines in those relatively few patients in his practice taking hypnotic drugs. He and his colleagues at Ipswich had decided, he said, not to prescribe barbiturates at all to anyone under 18 or to anyone unknown to the prescribing doctor. They had achieved a 65% reduction in the prescribing of barbiturates, and this had been offset by only a 35% increase in the prescribing of non-barbiturate hypnotics.

Doctors have been uneasy for some years about the large quantities of barbiturates being prescribed but until now have not felt confident that better alternatives exist.<sup>2</sup> Now sufficient experience of the benzodiazepines has accumulated to suggest that in the balance between benefit and risk they have the advantage over barbiturates. This is not to say they are harmless. In fact they share all the disadvantages of the older hypnotics, including dependence, unnatural sleep, hangover, and hepatic enzyme induction. But in general the risks associated with them are lower and in acute overdose they are safer. Whether prescribed in small doses to palliate anxiety by day or in larger doses to induce sleep at night they have now proved themselves to be an improvement, on balance, over the barbiturates.

Introducing the speakers at the beginning of the day, the chairman of the seminar, Dr. Ronald Gibson, of Winchester, made an observation which is so much taken for granted that it excited little attention. Prescribing, he said, is dominated by lack of time. What this means is that the doctor's most important gift to the patient, the relief of suffering, is impaired because he has not time to practise his profession as well as he is capable of doing. The realities of this indictment only occasionally came to the surface during the seminar, notably when someone asked why doctors laugh when alternatives to drugs are suggested for sleeplessness—for instance, a hot milk drink, a book, television, or sex. He might have added reasonable exercise in the day, abstinence from coffee at night, and abstemious eating and drinking. For the fact is that the majority of the millions of pills being prescribed for anxiety and insomnia are being handed over on what is largely self-diagnosis by patients who believe they have a legal right to order their treatment from their doctor, a belief that doctors have too little time and perhaps too little confidence to argue about. It is this situation rather than the niceties of pharmacology that need much more serious attention if the misuse of hypnotics as a whole is to be rectified.

<sup>1</sup> Wells, F. O., *British Medical Journal*, 1970, 2, 361.

<sup>2</sup> *British Medical Journal*, 1971, 1, 188.