general practitioners and their neighbouring community pharmacists.

More pharmacists should be recruited into the pharmaceutical industry, the report recommends, not only because of the breadth of their training but because their membership of a professional body (Pharmaceutical Society of Great Britain) "imposes a duty on them to maintain standards which can be of great assistance to the firm that employs them." The report mentions advertising and marketing of products as particular aspects of their work where such standards would be important.

The developments in the practice of pharmacy recommended in the report can take place only if there are radical changes in undergraduate and postgraduate education. While the undergraduate course should continue to be strongly science based, the report recommends, science must be relevant to the practice of pharmacy today and not be constrained by the traditional organisation of the subject into pharmaceutics, pharmaceutical chemistry, and pharmacology. Time must be found in the course for increased teaching of those aspects of pathology, therapeutics, and social and behavioural sciences which are relevant to the students' future professional tasks. There seems to be an anomaly in the report on the question of provision within the undergraduate course for contact with the public, patients, and doctors. Though it appears to recognise that students in most schools (Bradford University alone incorporates two six month periods of practical experience within a four year sandwich course) have little or no contact with the "real world of pharmacy," that many teachers are not pharmacists, and that there is widespread concern that learning and practice are insufficiently integrated, it does not recommend that the course should be increased to four years in all schools in order to provide time for practical experience and contact with patient and public. This is a pity, for pharmacy is the only registrable health professional qualification that does not include such experience in its undergraduate course, and young graduate pharmacists may experience great difficulty in communicating with the public and with colleagues in other professions in their preregistration year.

Test of competence

A controversial recommendation which perhaps follows from this is that there should be a test of competence at the end of the preregistration year, whose emphasis should be on practical work and oral skills, and that this should be followed by further "continuing assessment of practice, the ability to pass which should, in due course be made a condition of continued registration." This has already attracted criticism from at least one pharmacist, who points out that other members of the "health team" such as nurses, dentists, and doctors are not subjected to "such blatant lack of confidence."[5] The Pharmaceutical Society of Great Britain should rethink its policy on undergraduate practical experience which could, as Bradford University has already shown, be accommodated in a four year course acceptable for registration.

The responsibility for most of the recommendations made in the report will rest on the Pharmaceutical Society of Great Britain, and this is recognised by the committee of inquiry, which has drawn attention to the need for the society to define more clearly—and then to enforce—standards of acceptable conduct in community pharmacy.

The Nuffield report points the way forward to our pharmaceutical colleagues, but medicine cannot avoid being caught up in the wake of the resulting changes. As drugs become more complex in their actions and interactions so prescribing doctors will become increasingly dependent on colleagues in clinical pharmacology and pharmacy to advise on their best use, and because departments of clinical pharmacology are all too few and far between pharmacists will be the source of such advice for most hospital doctors and general practitioners. Finally, it is inconceivable that continuing assessment of practice could be adopted by one health profession without demands for it to be mandatory on all, and our own colleges and representative bodies will be watching closely to see how pharmacy responds to this recommendation.

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Treatment of type II diabetes

The logical treatment of type II non-insulin-dependent diabetes is hampered by our lack of knowledge of its aetiology and pathogenesis.

Recent evidence suggests that some insulin deficiency coexists with insulin resistance.[1 2] The interplay between the two defects—or whether one is primary—remains unclear. These uncertainties make for difficulties in assessing the mechanism and appropriateness of standard treatments, and as a result the approach is largely pragmatic. Treatment seems simple: dietary manipulation and if this fails oral hypoglycaemic agents[3]; and some patients eventually become treated with insulin but are not, by current classification,[4] insulin dependent.

In recent years this line of treatment has been subject to variation with changes in evidence and fashion. In 1970 publication of the University Group Diabetes Program study of tolbutamide and phenformin showing increased cardiovascular mortality with both drugs led in the United States but not in Europe to a dramatic move away from the use of oral hypoglycaemic agents.[5] The refutation and repudiation of these findings only partly reversed this trend.[6] The long term results of the British prospective study of treatment in maturity onset diabetes should clarify this issue. In the mean time large centres treating diabetic patients can point to many examples of people spared treatment with insulin by the judicious use of oral agents.

Years of clinical use have not clarified the mechanism of action of sulphonylureas. At first their administration raises the concentration of insulin in the blood, but in the long term this is not the means to a hypoglycaemic effect. Eventually the blood glucose concentration is reduced despite the insulin concentrations returning to pretreatment levels.[7 8] This finding has led us to the concept of an extrapancreatic mechanism of action. The data are compatible with an enhancement of the secretion of insulin in response to

stimulation by glucose, but there is also evidence that sulphonylureas have an effect on peripheral insulin resistance. The numbers of insulin receptors in peripheral tissues are increased by treatment with the sulphonylureas thus enhancing the action of insulin.[9 10] Yet this appears to be only part of the story since the action of insulin after binding has been shown to be improved.[11 12]

Of more practical importance than How? is Which? The sulphonylureas seem to share a common mechanism of action, the second generation ones being distinguished from the first generation by a simple increase in potency. Claims for a third generation of sulphonylureas, with effects on abnormalities in other systems, should be treated with scepticism, since many haematological abnormalities are corrected by control of hyperglycaemia.[13] Others of the more recent sulphonylureas are marketed on the basis of their safety in liver disease (the drug is metabolised in the kidney) or in renal disease (it is metabolised in the liver). Safety is equated with less hypoglycaemia—which remains the only side effect of real importance. Such claims are difficult to assess—in that context the safest drug would be one with little or no hypoglycaemic effect.

There is no "best buy" in sulphonylureas. Efficacy, potency, convenience of dose, incidence of side effects, and cost will be weighed differently by physicians. Though the division into first and second generation drugs may be of little value, the distinction between short acting and long acting is useful. Manufacturers have clouded this issue by quoting half life figures for the drug; this bears little relation to the half life of the hypoglycaemic effect. For convenience of dosage a long acting sulphonylurea should be used in patients under the age of 65 with normal renal function. In those with declining renal function and those who may be forgetful about food or who depend on external sources for their meals a short acting drug is safer. Clearly, then, as patients grow older they may need to be switched from a long to a short acting sulphonylurea, and general practitioners interested in looking after this particular group of patients should recognise this need. Common sense decrees that experience is best gained with one drug from each category. In our clinic tolbutamide and glibenclamide are dominant (despite brief flirtations with other drugs) and we believe that any new sulphonylurea will need to have proved advantages over the current tried and tested choices.

Two further practical points deserve mention. The first is the relation between the minimum and maximum doses. Treatment should be started with the minimum dose—which often produces a reassuring fall in the blood glucose concentration and an alleviation of symptoms. When control deteriorates again is it worth working up to a maximum dose? Dose response relations suggest that it is not (I Peacock, MD thesis, University of Cambridge, 1985). Doubts on this score, suggestions that only a short time is bought by an increase in dose, and the observation that the technique of insulin treatment is best learnt by the patients while they retain their manual dexterity have tended to lead towards earlier treatment with insulin. Recognising when treatment with sulphonylureas has failed is an important part of the management of non-insulin-dependent patients.

Secondly, though drug interactions are of less clinical concern than the textbook lists may imply, a lack of awareness of these possibilities is inexcusable.[14] Alcohol is a major concern—not through its interaction with chlorpropamide to cause embarrassing flushing but because the consumption of alcohol by a patient with alcoholic liver disease who is taking a sulphonylurea provides other mechanisms for hypoglycaemia.

While sulphonylureas dominate the oral hypoglycaemic market, metformin remains appropriate for overweight patients with poor dietary compliance. It has a less potent hypoglycaemic effect than the sulphonylureas,[15] there is a small risk of lactic acidosis, and its ability to cause diarrhoea is the cause of many unnecessary large bowel investigations. Yet in hyperglycaemic overweight patients sulphonylureas or insulin may cause further undesirable weight gain, and metformin has a better record.[16]

The combination of metformin with a sulphonylurea is of more dubious value. Often this regimen has been used to avoid insulin treatment at all costs but in practice, though insulin may not improve control, it may be preferred by the consumer.[17]

Oral hypoglycaemic agents will, then, correct symptoms and provide adequate control of hyperglycaemia for many patients but the physician's approach should be flexible. He or she should recognise that patients often benefit from a change in sulphonylurea with advancing years and control of the blood glucose may best be achieved not by increasing doses or by combinations of sulphonylureas and metformin but by a readiness to institute and subsequently reconsider insulin treatment.

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Akathisia—or not sitting

The term akathisia (not to sit) was coined by Haškovec at the beginning of this century to describe a psychological condition characterised by the patient's inability to sit still. Though Haškovec related akathisia to hysteria, later it