

no change in dimensions at end systole—so that the ejection fraction is decreased or little changed.

The origin of symptoms in these patients is less clear than in patients with acute heart failure. The classic teaching has been challenged by recent research.^{6,9} The feeling of breathlessness appears to be independent of changes in left atrial pressure as estimated from the pulmonary capillary wedge pressure. No correlation exists between the wedge pressure at rest or during maximal exercise and maximal oxygen consumption reached at the end of symptom limited exercise.^{7,9} The symptom which terminates exercise depends on the type of exercise performed despite the peak wedge pressure being the same.⁹ Rapid forms of exercise tend to result in breathlessness, whereas slower, prolonged forms of exercise come to an end because of fatigue.⁹ Furthermore, long term drug studies show that an improvement in exercise capacity is often but not invariably associated with an improvement in exercise haemodynamics and a fall in pulmonary capillary wedge pressure.¹⁰ Short term, vasodilator and inotropic agents almost always improve the haemodynamic indices and lower the pulmonary capillary wedge pressure but usually they do not increase exercise capacity either immediately or long term.¹¹⁻¹³ In one study amrinone given acutely to patients with severe heart failure did increase exercise capacity and peak oxygen consumption—but the pulmonary capillary wedge pressure also increased, indicating that a high pulmonary capillary wedge pressure had not been the factor initially limiting exercise.¹⁴

The postulated link between a raised left atrial pressure and breathlessness in chronic heart failure is also weakened by the lack of any obvious physiological mechanism. Juxta-pulmonary capillary receptors ("J" receptors) may be activated by stiffening of the lungs, as may occur with accumulation of interstitial fluid, and this causes tachypnoea and the feeling of breathlessness.¹⁵ Decreased lung compliance does not, however, correlate with the degree of dyspnoea^{16,17} and patients with left ventricular dysfunction develop only small increases in pulmonary blood volume and pulmonary extravascular fluid.¹⁸

An alternative explanation relates to the many and complex metabolic changes during exercise.⁹ The blood flow through skeletal muscles is reduced in patients with heart failure.¹⁹ A metabolic acidosis develops during rapid forms of exercise, and this may stimulate peripheral chemoreceptors and contribute to the hyperventilatory response and the feeling of breathlessness.⁹

In patients limited by fatigue several studies have suggested that the cause is an inadequate oxygen supply to skeletal muscle.^{19,20} During maximum exercise the oxygen content of blood in the femoral vein is negligible.²¹ Wilson *et al* showed that patients with chronic heart failure developed fatigue when the underperfusion of muscle reached a critical level and concluded that maximal exercise capacity of patients with heart failure was due to an impaired nutritive flow to the skeletal muscle.¹⁹ The mechanism may be an intracellular acidosis, accumulation of lactate, or depletion of phosphocreatinine.²² Persistent changes in the function of skeletal muscle also occur in chronic heart failure and may contribute to exercise limitation in these patients.²³

What these research findings show, then, is that the limitation of exercise and the feelings of breathlessness or fatigue in patients with chronic heart failure have multifactorial mechanisms. Their symptoms should not be related solely to an altered haemodynamic response to exercise. Which symptom is limiting in an individual patient will depend on the different mechanisms influencing neural and

metabolic signals from exercising muscle and the response of more central receptors.

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The Nuffield report: a signpost for pharmacy

Two years ago we reported the setting up of the Nuffield Foundation Pharmacy Inquiry and discussed some of the problems facing our pharmaceutical colleagues in the various branches of their profession.¹ The report of the committee of inquiry, on which there were three medical members, has now been published and, as we forecast, its conclusions and recommendations are far reaching.² The face of pharmacy will change appreciably over the next decade if they are put into effect, and they will have an impact on other health professions, including medicine.

The general tone of the report is positive and optimistic,

reflecting the view expressed by the committee's chairman, Sir Kenneth Clucas: "the pharmacy profession has a distinctive and indispensable contribution to make to health care that is capable of still further development." It is with this "further development" that the report is concerned.

The largest part of the report deals with community pharmacy, often known as general practice pharmacy. Their education and training equip pharmacists to play a "unique and vital role" in provision of health care in the community, but this is not being realised in practice. They spend ever less time personally dispensing prescriptions, and with the increasing introduction of computers into general practitioners' surgeries as well as into pharmacies their valuable function as "long stops" to refer back faulty scripts to the prescriber will also decrease. The report recommends that pharmacists and general medical practitioners should cooperate on a systematic basis to increase the effectiveness and reduce the costs of prescribing. This cooperation should include regular discussions on appropriate medication, drug interactions, and adverse drug effects. This recommendation has already received the support in principle of the Pharmaceutical Society of Great Britain, the British Medical Association, and the Royal College of General Practitioners. A more controversial recommendation is that a pilot study should be set up to explore the usefulness of adverse drug reaction reporting by community pharmacists. A recent report of the Adverse Reactions Working Party of the Committee on Safety of Medicines did not support this proposal, however, though Professor David Grahame-Smith, its chairman, was a member of the Nuffield Inquiry Committee.³ There is no valid reason why undesirable clinical events possibly associated with drug treatment should not be reported by pharmacists, who may well see the patient much earlier than does the doctor, and this recommendation should be implemented as soon as possible.

Advice from pharmacists

The report takes a cautious approach to the possible contribution of the community pharmacist in giving advice on symptoms. While welcoming the willingness of pharmacists to offer much advice, it emphasises the importance of proper education and training to perform that task, which must include the ability to decide when the inquirer should be recommended to seek medical advice. It is warmer, however, in its recommendations that pharmacists should give advice on taking medicines and on the use of devices, and that this advice should be concentrated on those groups who will most benefit from it, particularly the elderly. In fact it goes so far as to recommend that the elderly should be encouraged to register with a single pharmacy in which their medication records would be kept. The chronic sick and mentally handicapped are also specifically mentioned as being candidates for additional support and help from the pharmacist. His role should extend into the patient's home, the report suggests, not only for the domiciliary oxygen service, but also for help in providing and administering complex drug regimens, parenteral nutrition, and with patients with particular problems such as the seriously disabled or blind.

The report does not gloss over the fundamental problem of remuneration of the community pharmacist and its influence on his work. There is, it recognises, "a clash between the promotion of what is professional and the requirements of running a business." This obviously has implications for the

giving of advice already referred to, when a medicine may not be required and so no fee is forthcoming. The recruitment of pharmacists to health centres has also been affected by this conflict. It had been hoped that such centres would have provided good opportunities for doctors and pharmacists to work closely together, but this has generally not come about. This, says the report, is because the establishment of a pharmacy in a health centre does not represent new business but redistribution of business previously conducted by existing pharmacies in the centre's catchment area. The pharmacy in the centre is usually run by a consortium of existing pharmacy owners, who have to offset the loss of business in their own pharmacies by processing and dispensing the prescriptions at least cost. The report concludes unhappily that "as a result the service provided in some health centre pharmacies is worse than can be found elsewhere."

New pattern of payments

In order to remove, at least in part, this conflict between professional and commercial interests the report recommends that the basis of remuneration of community pharmacists should be changed so that the objectives set for the profession may be reinforced. In particular it suggests that payments under the NHS contract in respect of prescriptions dispensed should be reduced and separate payments made for other professional activities such as work done in collaboration with doctors, advice to patients, long term patient care, domiciliary activities, and health education.

Turning to clinical pharmacy the report rightly emphasises the importance of maintaining a flexible definition of its function in the context of local requirements in a particular hospital setting.⁴ It recommends, however, that clinical pharmacy should be practised in all hospitals, the clinical pharmacist being concerned in providing the clinician with information and advice on drug medication, in therapeutic drug monitoring, in reporting adverse drug reactions, and in clinical trials. To release more highly trained staff on to the wards for these functions and to "maximise scarce resources," all activities within the hospital pharmacy should be carried out by staff at the most junior level competent to perform it. This will often mean pharmacy technicians rather than graduate pharmacists. Clinical pharmacists should be appointed, together with doctors and nurses, to drug and therapeutics committees. Specialisation within clinical pharmacy should increase not only in the recognised functions of production, quality control, radiopharmacy, and drug information, but also in large individual clinical departments such as oncology, paediatrics, and psychiatry. Pharmacists in drug information, the report recommends, should remain in touch with work at ward level because "the provision of evaluated information requires in those giving it a recognition of the clinical context within which the information is to be used." There is more to the provision of drug information than the development of more complex databases, and the educational requirements of pharmacists aspiring to carry out this function need consideration not given in the report. Finally, the report recognises the difficulties that have arisen between medical and pharmacy staff within some hospitals because of misunderstanding about the nature of clinical pharmacy and welcomes the increasing cooperation between pharmacists and junior hospital doctors. This should lead in the future not only to better relations within hospitals, but also to closer cooperation between those doctors who become

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 pharmaceuticals, 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 agents³; 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