lessen the importance attached to local patronage.

Money was discussed, and though there was no doubt how strongly the R.B. felt on this score it refused to risk jeopardizing negotiations by making an immediate inquiry into the financing of the N.H.S. a condition of further discussion on administration. Armed therefore with the R.B.'s decisions, the profession's negotiators are ready to meet the Secretary of State on 9 June.

The second major topic the R.B. considered was medical education and the Todd report. Bearing in mind the interest in this subject of other expert bodies such as universities, the royal colleges, and medical schools, it contented itself with setting out broad guide-lines only. Its members approached their task from their knowledge of the practical results of medical education.

In the absence of adequate facilities and money for postgraduate training and any clear reason at present for specialist registration—Britain has the general practitioner to say who is a specialist—the R.B. was in no doubt that statutory registration would be premature. Remembering also last year's attempt to introduce it over the profession's head, and fearing as its consequence the emergence of two grades of doctor, it voted overwhelmingly that the time when a doctor would be regarded legally as fit to practise should be on full registration; and, while accepting the desirability of continuing education, rejected all suggestion that this should be compulsory or rigidly programmed. It wanted programmes to be flexible enough to allow doctors to move from one branch of medicine to another.

The mood of the meeting was that the G.M.C. is likely to have little if any role in any period of education. Since the publication of the Todd report the colleges and faculties have revised and expanded their programmes of specialist training and their examinations; little more would be needed for them to maintain indicative registers. Perhaps the most difficult question is how to provide the right encouragement for further education. Doctors accept its value, and no doubt many will wish to avail themselves of the opportunities for it—when they come. But by the time doctors are fully registered they have already undergone a long period of education and training and many of them will have acquired family responsibilities. So it is only fair that at the end of yet more training there should be some tangible benefit for the effort and sacrifice involved. In the hospital field the spur to self-improvement is clear enough, for generally speaking the best posts go to the best trained. But for general practitioners the incentive is less obvious. True the principle of indicative vocational registration has been accepted, but it was made plain that the purpose of such registration must be solely indicative. Thus it would still be possible for a doctor to become a principal in general practice without any further vocational training beyond that of having served an apprenticeship. For some people this may be the best way, and it is certainly well sanctioned by tradition. But will being on an indicative register—and the esteem flowing from it—prove incentive enough? Before leaving its discussion of Todd the R.B. gave its support for the suggested Central Council for Postgraduate Medical Education and Training, though making it plain that this body must be independent of government control and advisory only. It also voted for a separate council for Wales (a Scottish one is already being formed). Under the central councils there are to be a series of regional committees to act locally.

The R.B.'s final task was to consider the Council's progress report of its negotiations on the G.M.C.'s composition and the annual retention fee. After hearing that a working party from the universities, royal colleges, and the B.M.A. would be meeting shortly and taking evidence from the G.M.C., the R.B. endorsed its earlier advice. It is recommended that in the present financial year doctors (other than those claiming exemption) should pay a contribution of £2 when they receive the demand from the G.M.C. for a retention fee. They should not complete the banker's order. The £2 is simply to help the G.M.C. through its present financial crisis. The R.B. turned down decisively a motion to refuse any money until the G.M.C.'s structure and functions have been agreed by the profession. In doing this it made plain that its purpose is to reshape, not wreck, the General Medical Council.

Drug Intoxication in Renal Failure

Drugs which depend wholly or in part upon renal excretion for their elimination from the body accumulate if given in standard dosage to patients with impaired renal function. At p. 394 of this issue, Professor G. Richet and his colleagues draw attention to a variety of neuropsychiatric disturbances in patients with chronic renal failure attributable to intoxication by drugs. Provided the dosage is suitably modified, however, there are few drugs which cannot be given with relative safety, even to patients with negligible renal function. If the relationship between plasma half-life of a drug and renal function is known a dosage schedule can be drawn up.

The antibiotics are probably the group of drugs to which most attention has been given in this respect, and even those with high potential toxicity, such as the aminoglycosides, are now used freely in the management of patients with end-stage renal failure.

Overdosage with the cardiac glycosides presents even greater hazards. Some 80% of an intravenous dose of tritiated digoxin is recovered from the urine in normal subjects. Its mean plasma half-life is prolonged from a normal value of 33 hours to 83 hours in advanced renal failure; and there is a linear correlation between the renal clearance of tritiated digoxin and that of endogenous creatinine with a ratio between the two clearances close to unity. A simple method based on the kinetics of tritiated digoxin for determining the dosage of digoxin in renal failure has been proposed by R. W. Jelliffe.

The appropriate loading dose, which does not depend on renal function and which is usually between 0.75 and 1.5 mg. (or more for the control of atrial fibrillation), is given in divided dosage at intervals of 4 to 5 hours until the desired therapeutic effect is obtained or signs of toxicity appear. The total amount administered as the loading dose represents the body digoxin stores required for full digitalization of that patient. The maintenance dose is then calculated as a percentage of the loading dose. Patients with normal renal function lose about 21% of their body stores of digoxin in

1 Kunin, C. M., and Finland, M., Archives of Internal Medicine, 1959, 104, 1030.
3 Doherty, J. E., Perkins, W. H., and Wilson, M. C., American Journal of Medicine, 1964, 37, 536.
4 Bloom, P. M., and Nelp, W. B., American Journal of the Medical Sciences, 1966, 251, 133.
5 Jelliffe, R. W., Annals of Internal Medicine, 1968, 69, 703.
the urine each 24 hours, while extra-renal losses account for about 14%. Thus the daily maintenance dose for a patient with a creatinine clearance of 120 ml./min. is 35% of the loading dose, and for a patient with a creatinine clearance of zero (anuria) it is 14%. Between these extremes the dosage is directly proportional to the creatinine clearance.

Now that methods are available for the measurement of digoxin in plasma, the reliability of this scheme of dosage can be checked. Though there is no close relationship between the concentration of digoxin in the plasma and in the myocardium, and it is probably the latter which determines therapeutic effect, high plasma concentrations have been shown to be associated with clinical toxicity. The plasma concentration, however, is not the only determinant of toxicity. In uraemia the biochemical disturbance, especially change in the level of plasma potassium, influences the effect of the cardiac glycosides. Too rapid reduction of the plasma level of potassium by peritoneal or haemodialysis (neither of which removes significant quantities of digoxin) or as a result of diuresis may precipitate fatal toxicity in the digitalized patient.

### Anxiety and Investigations

To a large extent the pain and anxiety of surgical operations can be removed by suitable drug therapy, including general anaesthesia. There are, however, many diagnostic and therapeutic procedures which, though not painful in themselves, are extremely uncomfortable or frightening for the patient. Notable amongst these are procedures in the x-ray department or prolonged conservative dentistry. General anaesthesia will remove all these difficulties, but it is associated with its own risks. There is a place, therefore, for a drug or combination of drugs which will adequately sedate the patient yet produce no depression of respiration or hypotension.

Diazepam is being increasingly used for such manoeuvres. It has been shown that when given intravenously in doses of 0.15 mg./kg. body weight (about 10 mg. for an average 70 kg. man) it can produce profound tranquillization within two minutes. This dose does not necessarily produce sleep, but it usually leads to adequate sedation with only a small reduction in systolic blood pressure and minimal changes in ventilation.

The injection may prove painful, so it should be given slowly into a large vein. Larger doses (1-0 mg./kg. body weight) have been used for cardiac catheterization in children, and when combined with light premedication and local infiltration an effect of profound sleep has been produced, but the airway has remained protected.

In the lower dose range very few side-effects have been observed. The commonest complications are dizziness and vertigo. When large doses are used over a prolonged period ataxia, dysarthria, rashes, and hypotension have been observed. A recent report suggests that diazepam may potentiate non-depolarizing muscle relaxants. At present, with the limited number of reports available, it seems that intravenous diazepam offers a safe and effective method of producing tranquillity and sedation. When combined with local anaesthesia it can lead to very satisfactory conditions for surgery or investigational procedures without depression of respiration or the circulation.

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### Evening at the Royal Society

Scientific research is apt to be unforeseeably expensive, acrimoniously competitive, and when not actually alarming in its results at least a bit remote from ordinary needs. That it can also be great fun is the aspect of it most in evidence at the Royal Society’s conversazioni. Last week guests to one of these enjoyable evenings at Carlton House Terrace could appreciate too that research can bring or clearly promise un-doubted benefits to mankind.

 Appropriately enough the exhibits began with one for babies. Mr. J. E. Lewin, of the National Institute for Medical Research, showed a pneumatic mattress on which a premature baby can lie in an incubator. If the baby’s breathing stops, the pulsation of air in the mattress ceases, and that operates an electric signal which sounds an alarm. A nurse can thus go to the baby’s aid within a few seconds of the arrest of breathing.

 From the division of virology at the same institute Dr. G. C. Schild and colleagues showed that even influenza viruses are not immune to exotic mating behaviour. Hybrids can be produced in the laboratory that possess antigens from both parents. It seems possible, therefore, that the antigenic variants which arise in nature to attack man every few years may be hybrids between human and animal strains. The counterattack by antibiotics is gradually getting under way, as an exhibit from Glasgow University showed. Dr. E. A. C. Follett and colleagues, of the Institute of Virology there, displayed some remarkable electron-photomicrographs of vaccinia virus being prevented from developing by rifampicin. But this research is still at an exploratory rather than a therapeutic stage.

 As well as mirroring the soul the human eye is remarkable for the direct view it gives of the blood vessels. An astonishingly magnified view of these, with the blood flow shown up by a dye, was the subject of a joint exhibit by Professor J. D. McGee, F.R.S., and colleagues, of Imperial College, and Professor C. T. Dollery, of the Royal Postgraduate Medical School. By electronic intensification of the optical image from a patient’s eye it was possible to examine cinematically and several thousand times enlarged the flow of blood through the capillary bed of the eye in health and disease. The effects of diabetes and other diseases on the retinal capillaries can thus be studied afield. Meanwhile the exploration of insulin by Professor Dorothy Hodgkin, O.M., F.R.S., and her collaborators goes on. Dr. T. L. Blundell and colleagues at Oxford combined with Drs. S. Howell and D. Lindsey, of Sussex University, to illustrate the molecular structure of insulin and the manner in which this protein may be packed in the granules of the pancreas that contain it.

 The “sweet Thames” of Spenser has been running ever