and cardiac catecholamine release, so lessening myocardial oxygen demand, reducing the overdraft, and improving true efficiency. After treatment with a beta-blocker the left ventricle beats more slowly; diastolic coronary perfusion time is increased; and the velocity of contraction is reduced. Unfortunately, slowing the heart rate will reduce minute output if the stroke volume fails to increase. In the patient who has had an infarct and is sick or deteriorating IABP combines the virtues of the three different classes of drug by aiding delivery of blood to the tissues, improving coronary perfusion, and reducing myocardial oxygen demand.[10-14] No single drug or combination of drugs fulfils all three objectives.

IABP should, then, reduce final infarct size provided pumping is started as soon as possible after the onset of symptoms of infarction. It is no good starting IABP after cardiogenic shock has developed, for by this time usually too many myocardial cells have died to permit survival.[9] Furthermore, ischaemic but still viable myocardial cells will not contract, even though they can still recover if their blood supply is enhanced. If after 48 hours of IABP the patient with an infarct is still dependent on it, then the prognosis becomes extremely grave. One possibility under discussion at present is the use of IABP to help the patient through surgery for emergency coronary artery bypass grafting, so revascularising the ischaemic halo surrounding an infarct, but this procedure carries the hazard of possible haemorrhagic infarction of the already necrotic territory.

The value of IABP in helping a high-risk patient through cardiac surgery or in tiding him through a period of unsatisfactory low output postoperatively is much more generally agreed. Reversible myocardial cell injury is an unwelcome but still partially unavoidable concomitant of open heart surgery, and while this left ventricular disability is temporary it may tip the balance against survival in a minority of patients.

In common with the totally artificial heart, left ventricular bypass pumps have failed to graduate into clinical use because their development has been hampered by problems of thromboembolism or bleeding associated with the necessary anticoagulant regimen as well as with destruction of blood cells by the pump. In a recent article Bernstein *et al* have described a new compact centrifugal blood pump system for temporary left ventricular bypass.[15] No thoracotomy is required, access to the left ventricle being obtained through a thin-walled flexible non-kinking cannula, whose tip is introduced into an extrathoracic artery and then advanced retrogradely into the left ventricle. The outflow cannula of the pump is inserted into another artery, and the pump is then allowed to propel blood from the cavity of the left ventricle to the external artery. Though still in the research stage, this mechanical means of temporary whole or partial left ventricular bypass represents a further advance towards a system which can be applied with relative ease and safety.

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Antibiotic treatment in kidneys of unequal function

The bacteria most often found in urinary tract infections originate in the rectum or on the surface of the perineum and enter the urinary tract through the urethra. Once in the bladder, they multiply in the urine (which is a good culture medium) and may then ascend the urinary tract to infect the kidneys. In some cases this ascending infection may be helped by the presence of vesicoureteric reflux. Haematogenous infections of the kidney are rare. This concept of how most urinary tract infections arise is now generally agreed, and it has resulted in a consensus on the principles of management: elimination of bacteria from the urine in the bladder by the use of antibiotics achieving high concentrations in the urine; the maintenance of a high urine flow; and frequent emptying of the bladder. Few would argue with this approach when lower urinary tract infections are being treated, and then tissue levels of antibiotics are probably unimportant, so that use may be made of urinary antiseptics such as nitrofurantoin and nalidixic acid, which achieve high urine concentrations but low tissue levels.

When, on the other hand, there is evidence of infection of the kidney itself with systemic signs of infection and kidney pain or tenderness, there are attendant risks of Gram-negative bacteraemia or septicaemia. Antibiotic treatment should then be directed to the eradication of bacteria from the kidney by using antibiotics which achieve effective levels in the tissues as well as in the urine.[1] Nitrofurantoin and nalidixic acid are inappropriate in these cases, and antibiotics such as the penicillins, the cephalosporins, and the aminoglycosides should be used. Nevertheless, in treating relapsing infections (in which it is implied that organisms persist in the kidney tissue) Williams *et al*[2] found no evidence that ampicillin was any better than nitrofurantoin.

The dosage of antibiotics may have to be adjusted in patients with renal failure so that effective serum levels are achieved without causing accumulation of the drug, which could lead to toxic effects. In addition, adequate concentrations must be achieved in the urine. Nitrofurantoin is contraindicated in renal failure because inadequate urine concentrations are achieved[3] and more importantly because of the dangers of toxic effects (particularly polyneuropathy) which occur in patients with renal failure.[4 5]

Sullivan *et al*[6] have recently studied the urinary concentrations of nitrofurantoin, sulfamethizole, and cephalexin in patients with unequally functioning pyelonephritic kidneys and in monkeys with experimentally induced unilateral pyelonephritis. In all patients the blood urea nitrogen and serum creatinine concentrations were normal. They found that nitrofurantoin in the usual recommended dosage did not reach minimum inhibitory concentrations in the urine of those kidneys with a unilateral creatinine clearance of less than 20 ml per minute. Sulfamethizole and cephalexin, however, both achieved peak urinary concentrations greater than the minimum inhibitory concentration at the lowest studied

unilateral creatinine clearances of 4 and 11 ml per minute respectively.

This report further strengthens the case against the use of nitrofurantoin in patients with upper urinary tract infections, particularly where there is an appreciable disparity in function between the two kidneys, even though overall renal function may be normal. Fortunately other antibiotics—including the penicillins, cephalosporins, aminoglycorides, and sulphonamides—do appear in the urine in adequate concentration in the presence of overall renal failure,[7-9] and Sullivan *et al* found adequate urine concentrations of cephalexin and sulfamethizole in unilateral renal failure.

Clearly, then, the use of nitrofurantoin should be restricted to the treatment of lower urinary tract infections in patients with normal renal function. In complicated urinary tract infections where there is an abnormality of the urinary tract—anatomical or due to calculi—repeated courses of antibiotic treatment may be necessary, and these can result in the emergence of highly resistant strains. In these circumstances antibiotic treament can be regarded only as a palliative second-best to the appropriate corrective surgery.[10]

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Laboratory proficiency

Soaring costs and tightening purse strings prompt reappraisal of many aspects of the NHS. Laboratories cannot escape this scrutiny, and increasingly they are being asked whether they give value for money. An answer requires assessment both of the laboratory's performance and its contribution to patient care. The data issued from laboratories range from the purely numerical, as exemplified by most clinical chemistry reports, to the diagnostic opinions of histopathologists; and the quality of these data is one measure of a laboratory's performance.

Quality control may be both internal and external. At present much of the emphasis has been on analysing simulated specimens. The production, stability, and transport of these specimens present problems peculiar to the discipline concerned, and, not surprisingly, more is known about comparative performance in clinical chemistry than, say, in virology. Most clinical chemistry laboratories are aware of the precision (or imprecision) of their assays (the analytical variation occurring when the same sample is analysed many times), whereas they are less certain of the accuracy (how near to the true value of the measured constituent they are)—for usually what is available is only a consensus value of the constituent rather than its true value. The national scheme, operating from Birmingham[1] and financed by the Department of Health, has limitations, since relatively few of the substances assayed for clinical purposes are covered; and, while the largest commercial scheme, used internationally, incorporates many constituents, it still omits others of importance. As a result additional specialised schemes have been set up, such as that for digoxin.

Predictably, the various schemes have shown how variable performance can be and have alerted some laboratories to their inadequate standards. Variations due to methodological differences have been allowed for by analysing the data according to the method used. Some methods have proved to be more precise than others, and some methods show a steady bias in terms of the consensus value. These voluntary and anonymous schemes raise the question of what action, and by whom, can or should be taken against the few persistently poor laboratories—which may not necessarily be in the NHS. Within the USA there has been a growth of interest in standardising methods and investigation especially into definitive,[2] reference, and routine methods, the routine methods being standard practicable laboratory procedures which can be related to the other two.

However important this work, it must be seen in perspective. To what extent need laboratory variation be reduced, when one considers that biological variation is much greater than experimental variation? Too little regard is paid to variables such as age, sex, activity, and drug effects: we have little knowledge of how to make adequate allowance for such variations in our reference ranges. Indeed, one may question whether the attack on experimental variation—which is so costly in terms of the control materials (figures such as one-sixth to one-quarter of the laboratory budget for consumables have been quoted) and manpower—is the most beneficial approach.

Poor laboratory performance may also be due to bad environmental conditions, poor instrumentation, or faulty reagents. Though it is relatively easy to test chemical reagents, the variation within individual batches of bacteriological culture media may be remarkable,[3] accounting for failure to isolate an organism from a quality control or patient specimen. Furthermore, laboratory performance should also be measured in terms other than production of a so-called correct answer on a given specimen. The right specimen (or part of specimen for histopathology) must be taken and transported under appropriate conditions; the results must be correctly reported and returned to the right place at a time relevant to the patient's condition; and they must be properly interpreted in the light of both laboratory and clinical information. How are these factors to be measured? Should one ask also whether the laboratory should have been asked to perform the tests at all?

Particularly difficult to assess objectively are histopathological opinions. Circulating specially prepared slides, or the assessment by panels of random samples taken from one individual's own specimens, is at best a slow educative process which is unlikely to help directly the individual patient. Such procedures may improve professional standards, but are they a true measure of professional competence? Quality control may, perhaps, be moving into the field of medical audit, and who is the arbiter? "Through autopsy he [the morbid anatomist] is also the conscience of the hospital."[4] "Did I say so?" replied he coolly; "to be sure if I said so, it was so."[5]

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