Surgeons and the specialist advisory committee in the specialty have recently discussed the work of paediatric surgeons and how the service should be organised. Their recommendations are for a regionally based service that encompasses three elements.

Firstly, the regional service should be specifically funded as such—just as, for example, neurosurgery. The surgeons should be responsible for most regional neonatal surgery and should work with obstetricians and neonatologists in managing pregnancies where the fetus may be malformed. Until now operations on fetuses have been largely experimental in the laboratory, but the lessons learnt may soon be incorporated into clinical work. The regional centres should be developing the necessary expertise.

Secondly, the regional centre should provide a referral service for patients with specialised problems. Most will be in the younger age groups and will be referred by paediatricians or surgical colleagues: the problems will include, for example, Hirschsprung's disease and abnormalities of the urinary tract leading to recurrent infection. Some of this service will be provided by the paediatric surgeons doing monthly clinics in district hospitals.

Thirdly, there must be a district service for routine surgery, particularly for children under 5. This would be provided by a general surgeon with a special interest and training in paediatric surgery. When a district hospital has four or more surgeons one should have such a special interest, and it is the policy of the Royal College of Surgeons to encourage such appointments. As well as being responsible for most of the children in surgical wards the surgeon with the special interest would provide advice to obstetricians, neonatologists, children's nurses, and administrators. His or her training would be gained either as a registrar or during a temporary six month or one year secondment to a children's surgical unit during higher surgical training.

MALCOLM H GOUGH

Consultant Surgeon,
John Radcliffe Hospital,
Oxford OX3 9DU

Time to scrap creatinine clearance?

The chemical pathologist R B Payne has recently argued that creatinine clearance should be scrapped and serum creatinine concentration used alone as a measure of renal function.[1] Creatinine clearance, he argues, is inaccurate because the urinary creatinine concentration is raised both by tubular secretion of creatinine[2] and by dietary meat,[3] giving falsely raised clearances. (Surprisingly he does not mention the inaccuracies of urine collection.) Serum creatinine concentration—if adjusted for age, sex, weight, cyesis, and renal failure—will, he implies, give a better measure of renal function. Should we accept this? Has the time come to abandon creatinine clearance?

Plasma clearance was first introduced by Van Slyke and is derived from the formula UV/P (where U=urinary concentration of clearance substance, P=plasma or serum concentration, and V=the volume of urine in ml/minute).[4] Measurement of clearance is necessary because it is a more precise measure of renal function than either plasma urea or phosphate concentrations: random plasma urea concentrations are influenced by many factors and should not be used as measures of renal function. Glomerular filtration rate is often thought of as equivalent to creatinine clearance, but the two become increasingly disparate with declining renal function.[2]

Endogenous creatinine is the only practical substance to use in routine measurements of clearance. Assaying creatinine in a biological fluid costs about £4, and thus a clearance test costs £8. Using chromium-51 edetic acid to measure clearance is very accurate but costs £40 or more and demands the use of γ radiation; it cannot be recommended for routine use.

Clearance measurements are needed in patients with known or suspected renal disease, after kidney transplantation, or when a systemic condition may be affecting renal function. They are also essential when prescribing potentially toxic drugs that are excreted through the kidneys.

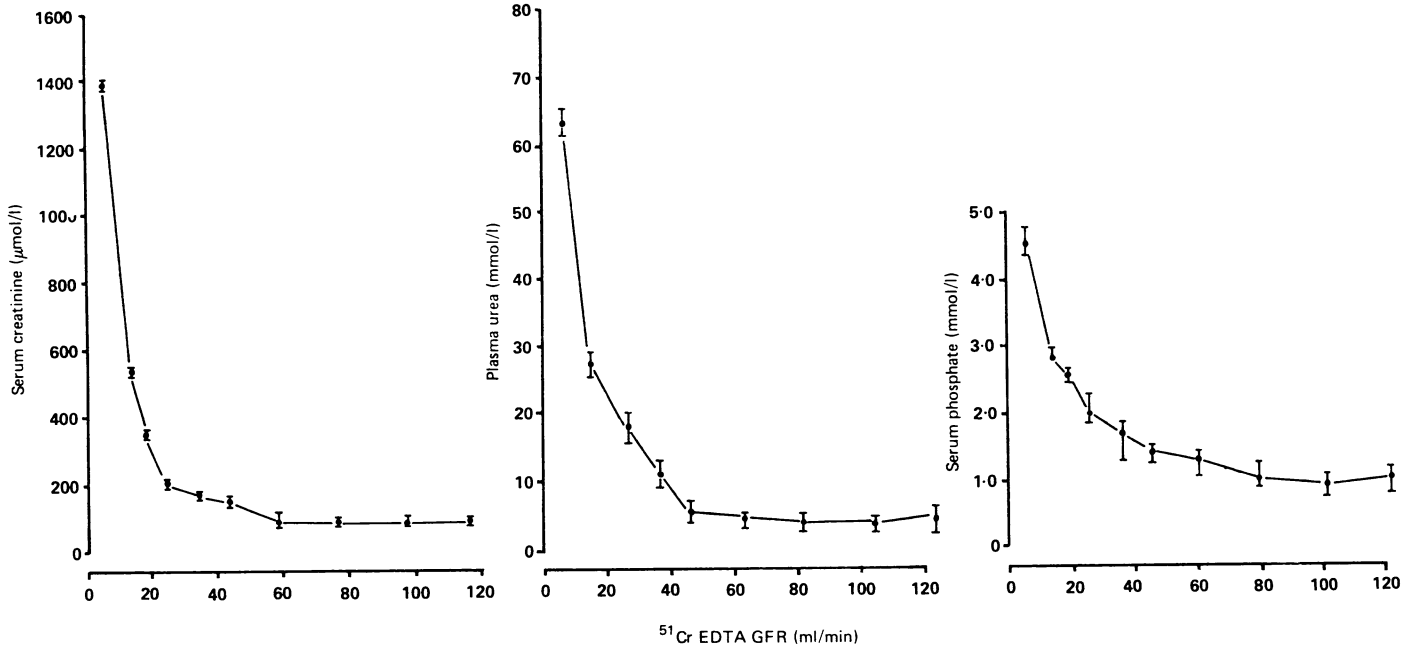
Serum creatinine does not have a linear relation to clearance (see figure) so clearance measurements are held to be the more useful. Various workers have proposed formulas[5-7] or nomograms[8] from which an equivalent of glomerular filtration rate can be calculated from serum creatinine concentration, but these have not gained widespread acceptance.

Timed urine collections for measuring creatinine clearance are often inaccurate, and two or three attempts may have to be made before a 24 hour collection of urine can be obtained from an inpatient. The completeness of outpatient collections is always suspect. The laboratory must receive urine and blood from the patient together, and often this fails. Thus measuring creatinine clearance is beset with difficulties.

The next problem comes with assaying creatinine. The measurement also identifies other non-creatinine chromatogens—in particular, acetone and glucose falsely raise creatinine concentration. The concentration may also be spuriously raised by hyperbilirubinaemia or rifampicin. Tubular secretion of creatinine is reduced by salicylate, cimetidine, and trimethoprim, falsely raising the blood concentration.[1] At low concentrations of serum creatinine (normal renal function) the accuracy of the assay diminishes. Furthermore, a muscular man with a normal glomerular filtration rate has a higher blood concentration of creatinine than a small woman.[9] Clinical chemists remain unhappy with the assay[10] despite the coefficient of variation for creatinine being only about 2% in a modern laboratory (J Glenn—personal communication).

With regard to dietary meat, in one study serum creatinine concentration rose by 70-80% after an unphysiological meal containing 300 g protein.[11] The source of protein is probably important since 90 g of milk protein did not change the creatinine clearance, while in the same group of eight healthy volunteers 90 g of meat protein increased the clearance by 18%.[12] To avoid possible alterations in serum creatinine concentration blood should be sampled either with the patient fasting or after a light breakfast. This also controls for any possible circadian variation. In women clearance increases up to 20% premenstrually, slightly reducing the serum creatinine concentration.[13] Adequate reference values for premenstrual serum creatinine concentrations are not available but may not be important since the change is only about 5 μmol/l.

If serum creatinine is to replace creatinine clearance doctors will require age related ranges of serum creatinine concentration (and 95% confidence intervals) for men and



Relation between glomerular filtration rate measured using chromium-51 edetic acid (^{51}Cr EDTA GFR) and serum creatinine, phosphate, and urea concentrations in patients being investigated for renal disease. Values are means and ranges (unpublished data from Roberts B, Gabriel R, 1975).

Conversion: SI to traditional units—Creatinine: 1 μmol/l≈0·0113 mg/100 ml. Urea: 1 mmol/l≈6 mg/100 ml. Phosphate: 1 mmol/l≈3·1 mg/100 ml.

women, in pregnancy, in childhood, and in renal impairment. The figures from one large study of 50 000 subjects will provide the data for serum creatinine concentrations in healthy men and women,[14] and preliminary figures for pregnancy are available,[13 15] but data for infancy and childhood are sparse.[15 16] No reference ranges are available for people with renal impairment.

If implemented Payne's suggestion could be used to define normal renal function in both sexes over all age ranges. If serum creatinine concentration were raised then one would have to resort to clearance, the use of a formula, or a guess. It is not widely appreciated that when the serum creatinine concentration is only just above the normal range then the patient has functionally lost one kidney. Serum creatinine concentrations are not easy to interpret when the clearance is 30-45 ml/minute, and an increase in the serum creatinine concentration of only 30-40 μmol/l is associated with a 15-20% further decrease in clearance (see figure). Yet it is precisely at this stage that further treatment may prove effective since once glomerular filtration rate is persistently less than 30 ml/minute progressive loss of function is usually irreversible.

Most laboratory reports are now produced by computers, and reference ranges might be added together with reciprocal values of serum creatinine concentration for those who want this transformation. Yet in practice it would be difficult to implement Payne's logical suggestion, although pilot studies in renal units could be tried. Rather, doctors must improve techniques for collecting urine: a 24 hour collection is merely a habit, and two consecutive 24 hour periods may compensate for variations in creatinine excretion and errors in collection. This, however, expects too much of even well motivated patients, and a sound argument can be made for overnight collection of urine. Everyone empties the bladder before going to bed, and the patient could note the precise time, discarding the urine just passed. Urine passed during the night would be saved, and in the morning the bladder would again be emptied, the urine saved, and the exact time noted. A sample of blood should be obtained as soon as practicable thereafter, labelled, and taped to the urine container and both should then be sent to the laboratory. In this way complete and accurately timed urine collections and serum would be available for assay. This system is virtually foolproof, is clinically feasible, and would also control for circadian changes in creatinine excretion.[3]

Creatinine clearance with urine collected under controlled conditions remains the simplest, cheapest, and most useful measure of renal function. Yet this may be replaced by the concentrations of serum creatinine once adequate tables correcting for age, sex, weight, pregnancy, and renal failure become available.

ROGER GABRIEL

Renal Physician,
Renal Unit,
St Mary's Hospital,
London W2 1NY

1 Payne RB. Creatinine clearance; a redundant clinical investigation. *Ann Clin Biochem* 1986;**23**: 243-50.
2 Bauer JH, Brooks CS, Burch RN. Clinical appraisal of creatinine clearance as a measure of glomerular filtration rate. *Am J Kidney Dis* 1982;**2**:337-46.
3 Pasternack A, Kuhlbäck B. Diurnal variations of serum and urine creatinine and creatine. *Scand J Clin Lab Invest* 1971;**27**:1-7.
4 Möller E, McIntosh JF, Van Slyke DD. Studies of urea excretion. II. Relationship between urine volume and the rate of urea excretion by normal adults. *J Clin Invest* 1929;**6**:427-86.
5 Mawer GE, Knowles BR, Lucas SB, Stirland BM, Tooth JA. Computer-assisted prescribing of kanomycin for patients with renal insufficiency. *Lancet* 1972;i:12-5.
6 Cockcroft DW, Gault MH. Prediction of creatinine clearance for serum creatinine. *Nephron* 1976;**16**:31-41.
7 Beranek P, Gabriel R. Creatinine clearance without urine. *Abstracts of the European Dialysis and Transplant Association* 1985:62.
8 Kampmann J, Siersbaek-Nielsen K, Hansen JM. Rapid evaluation of creatinine clearance. *Acta Med Scand* 1974;**196**:517-20.
9 Dunea G, Freedman P. Serum creatinine. *JAMA* 1968;**204**:163.
10 Rosano TG, Brown HH. Analytical and biological variability of serum creatinine and creatinine clearance: implications for clinical interpretation. *Clin Chem* 1982;**28**:2330-31.
11 Jacoben FK, Christensen CK, Mogensen CE, Heilskov NSC. Evaluation of kidney function after meals. *Lancet* 1980;i:319.
12 Jones G, Lee K, Swaminathan R. Glomerular filtration response to acute protein load. *Lancet* 1985;ii:838.
13 Davison JM, Noble MCB. Serial changes in 24 hour creatinine clearance during normal menstrual cycles and the first trimester of pregnancy. *Br J Obstet Gynaecol* 1981;**81**:10-17.
14 De Lauture H, Cacès E, Dubost P, *et al*. Concentrations of cholesterol, uric acid, urea, glucose and creatinine in a population of 50 000 active individuals. In: Siest G, ed. *Reference values in human chemistry*. Basle: Karger, 1973:141-52.
15 Moniz CF, Nicolaides KH, Bamforth FJ, *et al*. Normal reference ranges for biochemical substances relating to renal, hepatic and bone function in fetal and maternal plasma throughout pregnancy. *J Clin Pathol* 1985;**38**:468-72.
16 Rudd PT, Hughes EA, Placzek MM, Hodes DT. Reference ranges for plasma creatinine during the first month of life. *Arch Dis Child* 1983;**58**:212-5.