fiered by 1.0 nmol/L or more. These samples came from 13 patients: 10 men, three women, ages 70 ± 12 years. The only drugs being taken in common, apart from digoxin, were furosemide (10 patients) and amiloride (four patients). The patients could be categorized into three groups according to clinical and/or biochemical evidence of impairment: 1—renal, 2—renal and hepatic, 3—hepatic, and group 4—no evidence of either. The samples were also measured with the Wellcome Dac-Cel radioimmunoassay kit (RIA); results agreed well with those by the FPIA.

Possible explanations for the large discrepancies between the FPIA and the FETI are: (a) the presence of digoxin-like immunoreactive substance(s) (DLIS) and (b) interassay differences in the percentage cross reactivity of digoxin metabolites.


It is now well established that measurement of maternal serum alpha-fetoprotein (MSAFP) is valuable in the screening of pregnant women for fetal neural tube defects (NTD) and Down syndrome. Most commercial kits were developed to yield good precision and accuracy in the mid to high range, which is adequate for NTD screening. MSAFP in a Down syndrome fetus tends to be low, depending upon gestational age, in the range of 0 to 30 int. units/mL. MSAFP results are reported in terms of the multiple of the median (MoM). By integrating maternal age and MSAFP, it can be seen that a pregnant woman at age 20 years with an MSAFP of 9 int. units/mL (0.35 MoM) at 16 weeks or a 34-year-old with an MSAFP of 19 int. units/mL (0.72 MoM) at 16 weeks has a risk for a fetus with Down syndrome equivalent to that for a 35-year-old woman based on age alone. Most commercial kits are not adequately sensitive in the low range, and inaccurate assay results not only can have serious psychological effects but also incur additional costly diagnostic tests to the patient.

We have modified the Clinical Assays (Travenol-Genentech Diagnostics, Cambridge, MA) Alpha-Fetoprotein RIA kit procedure to enhance low-end sensitivity without compromising high-end sensitivity. The Clinical Assays AFP kit is a conventional double-antibody RIA procedure. We tried several experimental approaches. The modification that satisfied our requirements consisted of changing the original protocol to a sequential scheme with a 1-h incubation of samples, standards, and controls with the anti-AFP antibody, followed by addition of the 125I tracer and further incubation for 2 h. All incubations were at room temperature and the volumes used were those specified in the original standard protocol. We evaluated a total of 63 patients and three controls by both the standard and sequential scheme for correlation. The coefficient of correlation (r) was 0.99, r² = 0.98. The equation for the regression line was y = 0.92x + 6.62, where y is the sequential and x is the standard protocol. The calculated sensitivity, based on 20 replicates of the zero standard, was 1.1 int. units/mL for the sequential compared with 8.0 int. units/mL for the standard protocol. The standard curve was also modified to include a 5.0 int. units/mL standard and the 400 int. units/mL standard was deleted. The range of the standard curve was 0 to 200 int. units/mL. We believe this sequential procedure offers significant advantages of precision and accuracy over the standard protocol.


Determination of small increases above normal of albumin in diabetic urine has been reported as indicating early, still reversible, diabetic nephropathy. A simple, rapid method for assaying large numbers of urines at low cost has been developed for use with the Encore centrifugal analyzer (Baker Instruments Ltd., Egham, Surrey, U.K.).

To evaluate the method, we used calibration material of human origin for specific protein assay (SPS-01) from the Protein Reference Unit, Royal Hallamshire Hospital, Sheffield, U.K., for preparing the standard curve. Goat antibodies to albumin from the same source (specific antibody concentration 10.5 mg/L) was diluted 40-fold with polyethylene glycol 6000 (PEG) in isotonic saline (NaCl 150 mmol/L). The diluted wash was PEG 35 g/L, in distilled water. Turbid urines were filtered before analysis. The reagent blank contained all reagents, but isotonic saline was substituted for urine. Volumes were: sample 18 μL; antibody 250 μL; diluent 30 μL. The temperature was 30 °C, wavelength 340 nm. Curve fit was by cubic spline. Absorbance was read at 100 s, then at 2-s intervals until it no longer increased. Absorbance readings >1.0 A were rejected. The within-batch CV was 3.0% (SD 0.066%) for albumin concentrations between 4 and 75 mg/L. The between-batch CV was 4.9% (SD 0.84%) at an albumin concentration of 17.25 mg/L and 3.7% (SD 2.2%) at 58.4 mg/L. Analytical recoveries were 102% (for 4.3 mg/L added albumin), 95% (18.1 mg/L), 99% (38.2 mg/L), and 102% (72.4 mg/L). The detection limit for albumin was 4.0 mg/L. Correlation with a radioimmunoassay procedure (Metachem Diagnostics Ltd., Northampton, U.K.) gave a correlation coefficient of 0.99, slope 1.04, and intercept −0.9. For 43 assays in duplicate the cost was £3.95 ($5.73) with a 1-h assay time, compared with the radioimmunoassay cost of £197.81 ($286.82) and an assay time of 2.5 h.

**Two Spectrophotometric Methods Compared for Measuring Low Concentrations of Ascorbate in Plasma and Urine, A. H. Chalmers and B. C. McWhinney (Department of Pathology, Mater Misericordiae Public Hospitals, South Brisbane, Queensland, Australia 4101)**

We have simplified considerably Roe's method (1) for measuring ascorbate with 2,4-dinitrophenylhydrazine (DNPH) and compared it with a phosphotungstic acid (PTA) method (2) for measuring plasma and urinary ascorbate concentrations less than 200 μmol/L. The PTA method was