inaccuracies in the amount of insulin injected—which is particularly important when a mixture of short and intermediate acting insulins is used; and, secondly, when the glass syringe and needle are kept in spirit the fluid in the dead space is likely to be a mixture of insulin and spirit. This has to be ejected by forcible use of the plunger before the next injection and results in a wastage of about 5 units of insulin at each injection. This represents an estimated annual cost to the NHS of £2 million.[9]

These disadvantages must, however, be kept in perspective, and anybody who has seen children drawing up their insulin at diabetic camps can be under no illusion about the accuracy with which prescribed insulin is drawn up—and older patients may be even less accurate.[10] Furthermore, the amount of insulin lost in the dead space of glass syringes is probably negligible compared with the insulin left in discarded insulin bottles. For in the NHS there is no reward for thrift and few penalties for profligacy, and little heed is paid to either the amount of insulin dispensed or the insulin used.

The Secretary of State would do well to have another look at the choice of syringes. It is specious to argue that the sterility of the disposable syringe cannot be guaranteed after single use. What guarantee is there that glass syringes remain sterile after use, or indeed are sterile before use? Disposable syringes have been shown to be more convenient and are safe to reuse. They should be freely available to all diabetics needing insulin.

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Measuring serum calcium

Not long ago a fair argument was raised in these columns that in most cases the corrected plasma calcium concentration was an adequate measure of ionised calcium.[1] With increasing interest in disorders of calcium metabolism, the widespread measurement of serum calcium, and the development of new methods of measuring the different serum fractions this view may now be challenged.

Interpretation of total serum calcium concentrations is difficult because of the presence in serum of a diffusible and a non-diffusible fraction of calcium.[2,3] The non-diffusible fraction (about 40% of the total) is bound to protein, mainly albumin, and is not physiologically important. The diffusible fraction is distributed throughout the extracellular fluid and is present in interstitial fluid and filtered by the kidney. It comprises ionised or free serum calcium (about half of the total) and calcium complexed to anions such as bicarbonate, phosphate, and citrate (about a tenth of the total). The ionised calcium is the fraction of most importance clinically. Common examples of difficulties which may arise from measuring the total serum calcium concentration include the effects of prolonged haemostasis during venepuncture and of changes in posture. These increase serum protein concentrations and thus increase the total serum calcium concentration without changing its ionised fraction.[4,5] Conversely in hypoalbuminaemic states a low total serum calcium concentration may not be associated with low concentration of ionised calcium. Calcium binding to proteins is also affected by pH so that acute acidosis or alkalosis may raise or lower the amount of ionised calcium without affecting the total serum calcium value.[6] (Nephrologists still occasionally induce tetany by giving intravenous infusions of bicarbonate to patients who are acidotic.)

The correlation between the total serum calcium and albumin concentrations has been used to construct appropriate algorithms for "correcting" the serum calcium concentration when serum albumin concentrations differ from a selected normal value.[3,7-9] A commonly used adjustment is to add or subtract 0·02 mmol/l for each g/l that serum albumin is less than or exceeds 40 g/l.[1] The aim of the adjustment is to derive a value which reflects the concentration of ionised calcium more accurately.

These algorithms have several limitations. Firstly, large changes in pH are not accounted for by these adjustments. Secondly, calcium is not bound exclusively to albumin and indeed may be bound more avidly to some globulins, though they circulate in lower concentrations.[10] Thus any disorder resulting in abnormal plasma proteins may influence the amount of protein bound calcium, and changes of clinical importance have been seen in patients with cirrhosis and myeloma.[11,12] The third problem is the wide individual variation in the amount of calcium bound to albumin (0·007-0·053 mmol/g, a sevenfold range). This undermines the validity of using a single coefficient for all patients[5] and may account for reports indicating that none of the published algorithms gives a reliable correlation between total and ionised calcium values when many patients are studied prospectively.[9,13] Indeed, adjusting the total serum calcium concentration in this way may be counterproductive because it induces a false sense of security in the physiological importance of the derived value.

So what alternative ways are there to assess calcium concentrations accurately? Methods are available to measure ultrafilterable, dialysable, and ionised serum calcium.[10] Measurements of ionised calcium require special apparatus, samples need to be collected anaerobically, and the assays are time consuming to perform. Ion selective electrodes are, however, becoming more reliable and more widely available, and a reasonable case may be made for measuring ionised calcium concentrations in patients in whom there is a high index of suspicion that the total serum calcium concentration might be misleading. Ion selective electrodes, however, measure the activity of the calcium in solution rather than its concentration, and this must be multiplied by its activity coefficient, which is dependent on the ionic strength of the solution.[14] In plasma this is largely determined by the sodium and potassium concentrations and is thus fairly constant in most patients. Of perhaps greater importance, but less widely appreciated, is that the ionised calcium value correlates with the concentration of serum albumin in both

patients and control subjects.[15] This relation is probably due to a Donnan effect, whereby calcium ions are attracted electrostatically to albumin in the serum within the vascular compartment. This suggests that measuring ionised calcium in the presence of albumin will overestimate the concentration of ionised calcium in the interstitial fluid. The way in which this may be clinically misleading was discussed in a recent *BMJ* article, which indicated that even ionised calcium values do not provide a true gold standard for assessing calcium state.[16]

A technique hitherto neglected is the measurement of the dialysable (ionised plus complexed) fraction of total serum calcium, and methods have been devised for automated use with a high degree of precision and accuracy.[17 18] Prince *et al* in this issue (p 735) report their experience of measuring dialysable calcium in both patients and control subjects and compare this with measurements of other fractions of serum calcium. Although the clinical validation of the method requires more work, it overcomes many of the problems associated with the presence of albumin but does not take account of large changes in anion concentrations—such as the increased bicarbonate of compensated respiratory acidosis, which will increase the complexed, but not the ionised, fraction of serum calcium.

The debate will continue about the fraction of serum calcium that offers the most advantages in terms of cost, ease of analysis, and ability to reflect the biological state of patients. Whether we move towards measuring ionised or dialysable serum calcium (or the ionised fraction of dialysable calcium), probably the measurement of total serum calcium with or without adjustment will be regarded increasingly as a second best option.

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Regular Review

Blood pressure measurement: current practice and future trends

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Most doctors and nurses appreciate the importance of recording blood pressure, but many are unaware of the limitations of the commonly used methods of indirect sphygmomanometry. Recent research has suggested that the time honoured methods of measurement may not be sufficient for accurate diagnosis and prognosis in hypertension. Automated devices for measuring blood pressure are now being marketed with more emphasis on commercial considerations than in the interest of improving the accuracy of measurement. Often the sales literature of these devices makes extravagant claims of accuracy unsupported by independent assessment. This review will consider current techniques and instruments for the routine measurement of blood pressure. The evidence that reliance on conventional clinic or office measurement may be misleading will also be examined, together with recently developed techniques that may improve the management of hypertension.

Standard method

The standard method of the indirect measurement of blood pressure is based on the principle of arterial occlusion and blood pressure detection by various techniques, the first of which was palpation, described by Scipione Riva-Rocci in 1896.[1] Theodore Janeway in 1901 was the first to recognise the occurrence of sounds during deflation of the cuff,[2] but it was Nicolai Sergeyovitch Korotkoff in 1905 who related these sounds to systolic and diastolic pressure, thus introducing the auscultatory method of blood pressure detection.[3] Korotkoff identified three phases of sound, and in 1907 Ettinger elaborated on these by describing five phases.[4] The technique has changed little over the years but recommendations for its standardisation have been published and revised regularly by the American Heart Association since 1939,[5] and reviews of the subject have attempted to