Lesson of the Week

A change to 100-unit insulin dosage will reduce errors

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Patients with diabetes were first treated with insulin in 1922. Insulin was then prepared at a concentration of 20 units/ml, but later insulin strengths of 40 and 80 units/ml were introduced to reduce the injected volume. For patients needing very large doses, strengths of 320 and 500 units/ml have also been manufactured. The original insulin syringe was designed with 20 divisions (marks) per ml for use with 20 units/ml insulin. Though many new syringes were made in gradations to match U40 and U80 insulins in the United Kingdom, the syringe with 20 marks/ml bearing the British Standard Number BS1619 became the standard. This syringe is recommended for all diabetic patients in the UK, and it is specified in the Drug Tariff as an approved appliance that can be prescribed by general practitioners under the Family Practitioner Services of the National Health Service. This has led to the need to calculate and prescribe unit doses in terms of syringe divisions with 2 units/"mark" for U40 and 4 units/"mark" for U80. Not surprisingly, many errors are made in insulin dosage—not only by patients but also by doctors and nurses unfamiliar with the system. Many have even now failed to grasp the system of marks and units. Errors in dosage ranging between four times and one-quarter the intended unit dose are being given. Hypoglycaemia or ketoacidosis may result, sometimes with serious sequelae.

Investigation

The British Diabetic Association asked the doctors in its Medical and Scientific Section to record on a questionnaire their recent experiences of clinical problems—hazards and misadventures—arising directly out of the confusion over the various strengths of insulin that are available. The inquiry was not intended to estimate the frequency of such misadventures, which would be much more complex and time consuming, but was made simply to illustrate (with details of cases given confidentially) the existence of problems and the form that they might take. Eighty-five replies were received in 10 weeks. The names of consultants, hospitals, and patients are confidential. Fifty-five replies specified instances of dosage errors arising from the confusion between the strengths of 40 and 80 units/ml of insulin. Twenty-six replies confirmed that the consequences

Introducing a single strength of insulin will eliminate severe dosage errors

varied from trivial to very serious clinical events. Four doctors wrote that they had no knowledge of errors or confusion arising from the use of the existing strengths. The 55 cases of dosage errors reported are summarised in the table.

Analysis of errors in insulin dosage in 55 patients with diabetes

Age of patients (years)	No
< 20	10
20-29	5
30-39	9
40-49	4
60 +	11
Effect of error	No
Metabolic instability	14
Hypoglycaemic attack(s) (no admission)	23
Admission with hypoglycaemia	6
Admission with ketoacidosis	6
Survived with permanent sequelae	3
(1) Aged 20, pregnant, half correct dose given, rapid deterioration of control, stillbirth	
(2) Aged 60, man was taking 320 instead of 80 units, hypoglycaemia, psychiatric and domestic sequelae	
(3) Aged 73, given 32 instead of 16 units, severe hypoglycaemia, reduced mental capacity	
Death	3
(1) Aged 23, woman in ketoacidosis given 80 instead of 20 units intravenously, hypokalaemia, cardiac arrest, renal failure	
(2) Age unknown, given tenfold dose in excess (U mistaken for 0), hypoglycaemic death	
(3) Age unknown, hypophysectomy, took double the correct dose, severe hypoglycaemia, brain damage, death	
Responsible for error	No
Patient or relative	19
Nursing staff	15
Medical staff	11
General practitioner	5
Pharmacy	5

Discussion

This analysis, though semi-anecdotal, highlights the confusion caused by insulin being available in several different strengths. This is but a fraction of the total cost, disability, and danger that occurs and is within the experience of the great majority of doctors treating patients with diabetes. There is therefore an overwhelming case for providing one strength of insulin linked to a standard syringe that is graduated directly in units of insulin. This has long been the view of the British Diabetic Association and is now its policy.

What should the single strength be? Most of Europe uses only U40, but about two-thirds of patients in Britain on insulin

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use U80. Both doctors and patients would resist doubling the injection volume, which would result if U80 was abandoned and U40 became standard. If we standardised on U80 we would be the only country in the world likely to do so, and old syringes and obsolete instruction leaflets would continue to cause confusion. U100 has already been adopted by the United States, Canada, and Australia, with New Zealand following shortly. After seeing the results from clinical trials at several British centres, considering the experience of other countries, and debating the problems and hazards of change, the British Diabetic Association determined to seek standardisation of insulin strength at U100. Doctors who belong to the BDA voted unanimously for this change. At a meeting in Aberdeen in September 1980 they showed their disquiet that the change was proceeding so slowly. Other professional bodies have also formally welcomed the principle of U100 as the sole insulin strength: the Royal Colleges of Physicians of London, Edinburgh, and Ireland; the Royal College of Physicians and Surgeons of Glasgow; the Royal College of General Practitioners; the British Paediatric Association; and the General Medical Services Committee of the British Medical Association.

With U100 insulin will come a new British Standard U100 insulin syringe, graduated and numbered directly in units of insulin. There will be two sizes—one for injections of up to 50 units, the other up to 100 units and both marked in units. The 50-unit syringe will allow even small doses to be measured and delivered accurately. These syringes have already been shown to be suitable for small children. Plastic syringes for U100 are already available and though in most areas patients still have to

buy them, they are very cheap if used repeatedly, safe,¹ and recommended by most clinics and by the BDA. We hope that the change to U100 will come in 1982. The change-over will probably be largely carried out at diabetic clinics, though general practitioners and all other relevant agencies will be affected. A carefully prepared programme of information and organisation has already been started.

We believe that the great majority of doctors accept that the interest and safety of diabetic patients is best served by this change. Legitimate doubts and hesitations have been expressed—particularly a reluctance to change the practice for a patient already well established for whom there may be no obvious advantage. The whole-hearted support of the medical profession is vital so that the demand for U40 and U80 ends and these strengths are withdrawn. Initiating, organising, and implementing the change to U100 are in the hands of the doctors, for there is no legislative process in Britain by which the withdrawal can be effected. We solicit their support earnestly but confidently.

Reference

- ¹ Greenough A, Cockcroft PM, Bloom A. Disposable syringes for insulin injection. *Br Med J* 1979;ii:1467-8.

Requests for reprints should be made to: the British Diabetic Association, 10 Queen Anne Street, London W1M 0BD.

For Debate . . .

What does "response" in cancer chemotherapy really mean?

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Immense difficulty is experienced in assessing the response to chemotherapy of patients with metastases from the more common tumours. Two response categories, "complete" and "partial," are generally recognised; but in a recent review of interferon as a treatment for cancer an appreciable proportion of patients classified as "responders" were included in a new category of "less-than-partial" response.¹

A clinical response of a human tumour can obviously be defined as some measurable reduction in the patient's total tumour burden. A large proportion of reports, however, have failed to give the exact criteria of response, which should state explicitly what has been measured, the percentage reduction implied by "partial response," and the duration of the response. Even when all these data are available the informed reader often cannot decide whether patients should be treated with a particular chemotherapeutic regimen showing a good partial response rate. The reason is quite simple. Apart from certain

rare tumours—for instance, leukaemias, lymphomas, and chorion carcinoma—there is little hard evidence to show that the duration of life of a good quality is usefully extended. Furthermore, it is difficult to document and present reliably the chemotherapeutic side effects that often seem to be relegated to second place in overall assessment. The sceptically non-committed oncologist instinctively feels that the problems associated with chemotherapeutic combinations far outweigh the dubious benefits and that the partial response criterion is far too crude an indicator on which to base the management of patients.

In this article I attempt to delineate some of the known factors related to our current methods of oncological assessment and some of the fallacies inherent in them. I also attempt to assess critically some of the results of interferon treatment in human cancer in the light of those facts and fallacies.

Current methods of oncological assessment

DEFINITIONS OF TUMOUR RESPONSE

Two categories of objective tumour response are now generally recognised, in line with the recommendations of the International Union Against Cancer (UICC).²

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