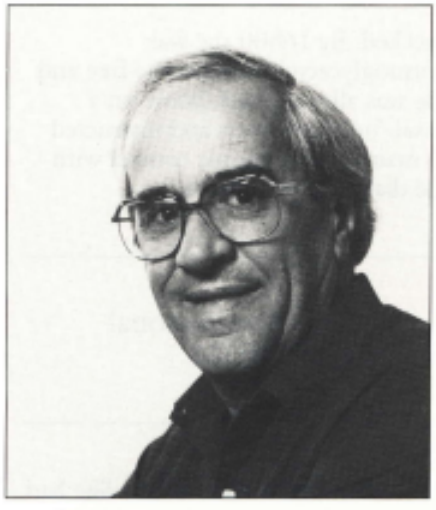
Diabetes Mellitus: Part II
Insulin-dependent diabetes mellitus

— LI Robertson



Dr LI Robertson
MBChB, MFGP (SA).

Curriculum vitae

Dr LI Robertson studied at Cape Town University where he received the MB ChB in 1954. He did some post-graduate training at Mc Cord Zulu Hospital (Durban) and St Monica's Home (Cape Town), received the MFGP (SA) in 1975 and has been in Private Family Practice in Durban since 1957. He has a wide interest in different fields of medicine, and at the moment still holds the following posts: Senior Medical Officer – Diabetes Dept (Addington Hospital), Medical Director – Child Guidance & Research Centre (Durban/Westville), Medical Director – Institute of Human Sexuality. He also makes time to serve on several committees. He is Vice-chairman of the council of SA Academy of Family Practice/Primary Care; he is an elected member of the SA Medical and Dental Council and gives time to many other committees serving the community. Dr Robertson has presented many papers at Medical Conferences, has published several scientific papers and contributed to two medical textbooks. He is married to Barbara and they have 4 children.

Summary

IDDM or Type I diabetes is no longer called "juvenile-onset diabetes". After the discovery of insulin, patients can today enjoy excellent control, but it still remains a serious, life-threatening disorder. Unfortunately no epidemiological survey has been done in the RSA on IDDM to illustrate the extent of the disease, but the clinical features like polyuria, polydipsia, tiredness, weight-loss etc, are classsical. More and more patients are being diagnosed early on, before symptoms are profound, and patients are much better controlled today than their earlier counterparts.

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Insulin-dependent diabetes and Type 1 diabetes are terms which are synonymous and have replaced 'juvenile-onset diabetes'. For the purpose of these articles I shall be using the term insulin-dependent diabetes (IDDM). Note that the important word is 'dependent' which denotes that without insulin these patients cannot live, and this distinguishes them from the large number of Type II diabetics who require insulin for good control but can survive without injections of the hormone. And as we shall see in a later article, an increasing number of black diabetics fall into this latter category.

IDDM is the classical, life-threatening form of the disorder, the treatment of which was revolutionised by the discovery of insulin by Banting and Best.[1] It is the form which continues to attract most clinical researchers, not unexpectedly, as the bulk of the research funding comes from companies making insulin. It is salutary to reflect, however, that IDDM only constitutes a minor percentage, probably no more than 15%, of the total diabetic population.

We have no idea of the magnitude of the problem in the Republic as there has never been an epidemiological survey, though this ought not to pose insurmountable difficulties, given the fact that all of these patients require insulin for life, as this must be dispensed or prescribed. Dare one suggest that such a survey might be usefully undertaken by the various Academy members scattered throughout our urban and rural areas? Three recent large British surveys[2] quoted overall prevalence rates of about 1% of which only about one quarter are truly insulin-dependent.[3] The average hospital diabetic clinic population does not reflect the prevalence in the community because it usually contains a considerably higher proportion of IDDM patients. There is also increasing evidence that the incidence of IDDM is rising in childhood, perhaps of the order of a two-fold increase per decade.[4] As this does seem to be largely a disease of the higher socio-economic classes, the increase may be a reflection of relative affluence.[5] Add the fact that an increasing number of Type II diabetics are now on insulin and one begins to get an idea of the major health-care problem posed by insulin-treated diabetes to a cash-strapped economy like ours.

... Insulin-dependent Diabetes

There is a well-described seasonal variation in the presentation of IDDM, with clustering in autumn and winter.[6] In the younger age groups slightly more males are affected but this tends to even out at older ages of presentation.[3] Although

IDDM or Type I diabetes –no longer called "juvenile – onset diabetes"

still mainly 'juvenile-onset' it can present at any age and about 10% of new elderly (over 65) diabetics may require insulin.[7]

Clinical features

The classical symptoms are polyuria, polydipsia, severe tiredness and weight-loss in the presence of a normal appetite, but other minor symptoms are common, such as leg-cramps, skin-infections, penile or vulvar pruritus from candidiasis and blurred vision from osmotic changes in the lens. Nausea, vomiting and drowsiness are indications of keto-acidosis and impending coma. One finds that more and more patients are being diagnosed early on before symptoms are profound and a fairly typical presentation of IDDM is illustrated in the patient story, which also emphasises our reluctance to admit these patients unless grossly metabolically deranged, and also our efforts to keep them from school or work for as short a time as possible.

Patient Story: insulin-dependent diabetes

Julie A. University Speech and Drama student.

4th February. Having noticed that she was rather more thirsty than even the humid Durban climate warranted, she visited her cousin, one of our IDDM clinic patients. He cajoled her into presenting a tentative finger for his lancet and did a capillary blood-glucose using his reflectance meter. It was 14,8mmol/L. He dragged her off to our clinic on the next day.

5th February. Her fasting level was 19,8mml/L and her urine showed 1+ ketones. She was kept in our Out-patient Metabolic Unit after extracting a promise from me that she would be allowed out in order to sing the female lead in her University production of "Fiddler on the Roof" that night. She was given an insulin-in-saline infusion and her blood glucose rapidly dropped to under 5mmol/L. She was taught to inject herself using a pen-injector for bolus insulin and a syringe for her bed-time 'Humulin L', as well as the correct method of performing capillary blood-glucose estimations on a loan reflectance meter. She had the first of many sessions with the dietitian and the diabetes specialist nurse. At

Many black diabetics fall in the category NIDDM

16h00 she was allowed home, gave her first bolus injection before supper, sang that night and gave herself her bedtime basal insulin.

6th February. Back at the Unit and on insulin-infusion as her pre-breakfast blood sugar was back to 15mmol/L, and her urine again had ketones. Self-monitoring technique checked. By 16h00 she was normoglycaemic and ketone-free and she was allowed back home on a basal/bolus regimen and instructed to maintain telephonic contact with the diabetes specialist nurse.

A well-described seasonal variation in IDDM

13th February. Back at clinic. She had maintained an average home blood glucose of 6mmol/L and had had no further symptoms or ketonuria. She continued to get rave reviews.

Aetiology and natural history of IDDM

The major aetiological factors are a genetic predisposition (identified by specific HLA class II antigens such as DR3, DR4) together with viral infections or other environmental agents. Beta-cells are destroyed by autoimmune damage. Interestingly, although the clinical onset is abrupt and dramatic, the actual autoimmune process destroying the Beta-cells may have been present for many years previously. Circulating antibodies to the pancreatic islet-cells have been found up to seven years prior to the clinical presentation of some cases of IDDM. During this pre-clinical phase the intravenous glucose tolerance test may reveal abnormalities but symptoms are absent and the oral glucose tolerance normal.[8]

After the commencement of insulin therapy many patients enjoy excellent control with minute doses of insulin. This 'honeymoon period',[9] which is

not a feature of IDDM in the very young, may last from a few months to a year or more and patients often wonder if they are 'cured'. The physician should resist the temptation to stop the insulin, but should rather continue using a small dose, possibly a once-daily long-acting insulin, our preference being 'Humulin L'. The likelihood is that the honeymoon reflects temporary improvement in Beta-cell function resulting from lowering glucose levels below those which result in Beta-cell toxicity.[10]

A small proportion of patients with IDDM appear to retain some endogenous insulin production, and, in effect, seem to maintain their 'honeymoon'. There is evidence that these patients have better glycaemic control and might, therefore, be less prone to diabetic complications. We can identify these more fortunate IDDM patients by checking their residual 'C-peptide' activity, as will be described in a later article. Recent years have witnessed a number of

No epidemiological survey done in RSA to establish the magnitude of the problem of IDDM

attempts to try and prolong the honeymoon period, or to try and secure a true remission of IDDM. Hyperglycaemia itself is Beta-cell toxic, and, as witnessed in our patient story, one useful approach is to impose tight blood-glucose control immediately upon the diagnosis. Attempts to suppress the auto-immune process have been made using, chiefly, the immunosuppressive agent cyclosporin, but as this is itself Beta-cell and nephro-toxic, and has been associated with lymphomata, its ill-effects far outweigh any possible advantages. For some years we have been using nicotinamide on our newly diagnosed IDDM patients, as there were reports that this might prolong the life of the remaining Beta-cells. There are now ongoing research studies investigating the value of the drug in this situation.

Table 1. Percentage of patients affected by different diabetic complications with increasing duration of diabetes (after Pirart, 1978.)[11]

Duration of DM (years)	Neuropathy (%)	Retinopathy (%)	Nephropathy (%)
0	8	5	0
5	15	16	2
10	26	26	5
15	31	40	8
20	40	48	10
25	49	50	14

Long-term natural history

Both IDDM and NIDDM have a long-term history marked by the appearance of serious complications in many patients. These include retinopathy and nephropathy (usually termed 'microangiopathic' or 'microvascular' complications), and atherosclerosis, or 'macrovascular' disease. In addition, most patients develop varying degrees of nerve complications, sometimes symptomatic. The IDDM patient of early onset is particularly liable to microvasculopathy, although the 'clock' for complications only seems to start 'ticking' after puberty, a fact which has allowed us to reduce the stricter control in our tiny tot patients, to the relief of their parents. The now-famous study of the Belgian diabetologist, Jean Pirart[11] is illustrated in Table 1, which demonstrates the cumulative prevalence of complications with increasing duration of diabetes.

This study, and others, strongly suggest that the complication-risk in

The IDDM patient of early onset is particularly liable to microvasculopathy

IDDM is also related to the degree of glycaemic control. Final proof that good control may retard or prevent the development of complications will have to await the outcome of the massive '*Diabetes control and complications*' study due out in a couple of years time, but, in the meantime, the assumption is almost an article of faith in our current approach to achieve the best possible diabetic control.

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For diabetic patients overall, the risk of premature death is twice that of the age-matched, non-diabetic population.[12] IDDM patients are even more at risk. The mortality is 4 to 5 times normal,[13] and up to 7 times normal for those whose disease presents in childhood.[14] Overall life expectancy is reduced by about 25%. The major causes of premature death are shown in Table 2, which also highlights the different causes of death in IDDM and NIDDM.[15] Renal and cardiac disease account for 70% of deaths in IDDM whereas in NIDDM, 70% of deaths are due to cardiac and cerebral arteriosclerosis. Mortality rates seem to peak at about 15-25 years after the onset of IDDM and thereafter decrease.[16]

Whilst these figures are singularly depressing, it should be remembered that only a minority of patients develop complications and in most cases these are asymptomatic or cause few problems. Blindness and renal failure affect only a small proportion. Also, almost all the above data are derived from patients diagnosed and treated during the 'dark ages' of the years prior to the mid-1970s when glycaemic control was not considered important. Our patients today are far more likely to be better controlled than their earlier counterparts, and one hopes that this will be reflected in reduced complication and mortality rates in the future.[2] Despite the potential problems of IDDM some patients do remarkably well in the long-term. A case in point is that of a dear friend and colleague who was diagnosed a year after the famous discovery of Banting and Best. When he first came under my care he was in his eighties and related, with a chuckle, the fact that when he was one of the founder members of his group practice he was unable to get partnership insurance due to his IDDM. At the time of relating the story he was the only survivor of the practice, the others having long departed. He had had bilateral cataract-extractions but had otherwise excellent vision and still drove his own car. He had no nephropathy and only asymptomatic neuropathy. Significantly, his mean glycosylated haemoglobin was at the lower end of the reference range. He eventually passed on from non-diabetic causes.

Table 2. Causes of mortality in insulin-dependent (IDDM) and non-insulin dependent (NIDDM) diabetes[15]

	IDDM (%)	NIDDM (%)
Cardiovascular disease	15	58
Cerebrovascular disease	3	12
Nephropathy	55	3
Diabetic 'coma'	4	1
Malignancy	0	11
Infections	10	4
Others	13	11

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