PART 2

Self management of insulin-dependent diabetes mellitus

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Insulin dosages and the monitoring thereof

Insulin

The beta cells in the islets of Langerhans in the pancreas secrete insulin in response to the blood glucose level. Human insulin is manufactured in the form of proinsulin, which consists of two peptide chains linked by a connecting peptide - a total of 81 amino acids. Prior to release in the pancreatic vein, the proinsulin is separated into the insulin molecule and the connecting peptide. The half-life time of insulin in the blood circulation is approximately 7 - 10 minutes, since insulin is inactivated in the liver and kidney. After oral glucose ingestion, the insulin level begins to rise within 3 - 5 minutes, with peak levels of approximately 6 - 8 times the basal levels reached in 30 - 60 minutes and a return to basal levels after 3 - 4 hours.

Although insulin is not the only mechanism responsible for glucose homeostasis, it is the prime factor which accomplishes this important function. Insulin is measured in units with a non-diabetic secreting approximately 25 - 50 units per day.

Porcine insulin differs from human insulin in only one amino acid and is therefore least antigenic in man. Two types of insulin are generally available on the market: A proinsulin-freed mixture of porcine and bovine insulin, and a monocomponent insulin of even higher purity, usually containing only porcine insulin. Monocomponent insulin is preferred since it has fewer side effects. The concentration of insulin refers to the number of units per millilitre. Various insulins generally available in the RSA are shown in the table *.

A typical daily requirement for an insulin-dependent diabetic is 0,7 - 1 units/kg bodyweight. Since the pancreas releases insulin in response to the blood glucose level, and since the insulin-dependent diabetic is totally dependent on outside insulin, the objective of any insulin therapy is to mimic nature exploiting the insulin action profiles shown in the table. Note that these action profiles are guidelines only, and may change from patient to patient.

* Other manufacturers supply a similar range of insulin.

There are four basic insulin dose regimens
● Single daily dose of lente insulin. Although this is the easiest to administer, it is often difficult to control a patient throughout the day.
● Mixed insulin dosage. This consists of a single injection of a combination of regular and lente insulin *. A typical combination is 2 parts lente to 1 part regular.
* Monocomponent insulins from NOVO can be freely mixed with each other, but not with other insulins, e.g. NPH.
● Split insulin dosage. This consists of two daily injections of semi-lente or lente insulin.
● Split-and-mixed insulin dosage. This provides two injections of insulin, each consisting of both regular and semi-lente (or lente) insulin, thus yielding four components of insulin action. Each component can by altered individually, thus providing con-

siderable flexibility. A typical approach is to inject ²/₃ of the total units in the morning, with the balance in the evening.

(See Table Overleaf)

Diet

The dietary principles for a non-obese insulin-dependent patient are as follows: (All kilojoule values are rounded off)

For children, the total number of daily kilojoules required is given by 4 200 for the first year of age, plus 420 kJ for each additional year. (The formula is valid up to age 12 to 14 years).

For adults, the following formula can be used: Let the desirable bodyweight by N (kg), then basic kilojoules 92 N (kJ). Add activity requirements:
● Sedentary occupation : 27,6 N (kJ)
● Moderate activity : 46 N (kJ)
● Strenuous activity : 92 N (kJ)

These kilojoules are provided by protein (17 kJ/gm), carbohydrates (16 kJ/gm) and fat (37 kJ/gm). For growing children the daily requirement is 3 to 4 gm protein/kg bodyweight. A carbohydrate-to-fat mass ratio of approximately 2 : 1 is commonly used, although the fat content may be reduced for low-fat diets.
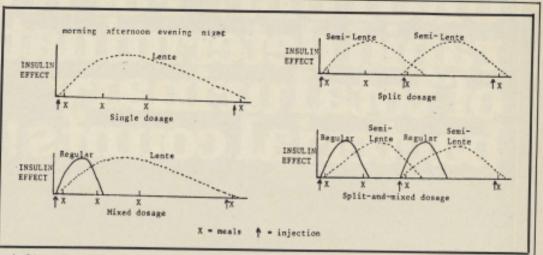
In order to prevent glucose loads onto the body, the total number of kilojoules is spread equally between breakfast, lunch, dinner and the three snacks (mid-morning, mid-

Description	Trade Name	Type	Onset/end of effect (hours after injection)	Maximum effect (hours after injection)
Regular (short-acting)	Actrapid	Porcine insulin	½ - 7	2½ - 5
Semilente	Rapitard	Mixture of 25% porcine and 75% bovine insulins	1 - 22	4 - 12
	Semitard	Porcine insulin	1½ - 15½	4½ - 9½
Lente (intermediate-acting)	Lentard	Mixture of 30% porcine and 70% bovine insulins	2½ - 24½	6½ - 14½
	Monotard	Porcine insulin	2½ - 22	6½ - 14½
Ultralente	Ultratard	Bovine insulin	4 - 36	10 - 30

Monocomponent insulins from NOVO Industries (M.I.M.S., Vol. 20, No. 9, Sept. 1980)

* Other manufacturers supply a similar range of insulin.

afternoon and late-night), i.e. 25% each. The time delay between food intake and peak blood glucose value for various types of foods is as follows: Simple carbohydrate (sugars): 15 - 30 minutes; complex carbohydrates: 30 - 60 minutes; fats and starches: 90 minutes; proteins: 3 hours. By manipulating the types of food taken during each meal or snack, the absorption delays can be used to further equalise the blood glucose level. For example, the late-night snack should contain a lot of protein to prevent nocturnal hypoglycemia.

morning afternoon evening night

INSULIN EFFECT — Lente
X = meals   ↑ = injection
Single dosage

INSULIN EFFECT — Regular — Lente
Mixed dosage

INSULIN EFFECT — Semi-Lente   Semi-Lente
Split dosage

INSULIN EFFECT — Regular   Semi-Lente   Regular   Semi-Lente
Split-and-mixed dosage

X = meals   ↑ = injection

The number of kilojoules in each meal or snack is made up of a few so-called food exchanges. The food exchange method is based on six basic exchange lists: Milk, vegetables, fruits, bread, meat and fat. Some basic lists are further subdivided, e.g. low-fat, medium-fat and high-fat meat exchange lists. Each list contains various types of foods and a portion size for each, so that a portion of each type of food contains a fixed amount of carbohydrates, protein and fat.

The diet then consists of a number of exchanges for each meal, e.g. lunch having one exchange of each of the following: Milk, fruit, bread, medium-fat meat and fat (1 300 kJ). The patient may select a portion of whichever type of food, within the specified exchange list, he fancies to make up a certain exchange. For example, a medium-fat meat exchange contains 322 kJ and consists of 0 gm carbohydrates, 7 gm protein and 5,5 gm fat. This could be made up of amongst many others, 30 gm beef, pork or veal (all fat removed), or ¼ cup creamy cottage cheese, or one egg. The use of the food exchange method allows a patient to adapt his diet to his own tastes and preferences whilst satisfying dietary requirements. Some foods can be used at will, e.g. diet cold drinks (2 - 4 kJ per 100 ml) and some types of raw. vegetables (e.g. lettuce). These do not have to be counted in the diet.

Since many foods have nutritional information on their packaging, it is possible to expand the exchange list. For example, a 50 gm PVM diet bar contains 678 kJ and is roughly equivalent to 1 bread exchange

and 2 medium-fat meat exchanges, with 1 fat exchange to be omitted elsewhere. One 8 gm slice of Ry-king turns out to be equivalent to 1 vegetable exchange. Reference 15 is an excellent cookbook based upon the food exchange method.

To further smooth out glucose peaks, check the 24-hour absorption profile. This consists of the superposition of triangular curves (the peaks of which are the kilojoules provided and correspond to the absorption delay) for each carbohydrate, protein or fat component for each food exchange at each meal or snack.

Other dietary objectives, e.g. for low-sodium or low-fat diets can be easily incorporated into the above principles.

Tables of ideal weight and height as a function of age and sex are important in monitoring the growth of children.

In the case of vomiting during sick days, calories can be provided using liquids, e.g. regular cold drinks or fruit juices.

Fortunately these dietary principles are not critical, e.g. the exact kilojoule distribution and relative proportions of fat, protein and carbohydrate can be deviated from significantly without a catastrophic collapse in diabetic control.

Monitoring

Proper control of diabetes requires that the blood glucose level be kept within strict limits and this invariably means that the patient must be regularly monitored. There are four basic monitoring tests, depending on whether urine or blood is used and whether spot or averaged values are measured.

1. Urine testing. This test is done on a second-voided urine

specimen obtained by passing urine from a full bladder, waiting 10 - 15 minutes for the bladder to partially refill and using the second urine specimen for testing. A Keto-Diastix (Ames Company) * reagent strip is dipped into the specimen. After fixed time intervals, colour changes are used to semi-quantitatively estimate glucose and ketone concentrations. Heavy glycosuria implies hyperglycemia, whereas a combination of heavy glycosuria and ketonuria implies impending ketoacidosis. These urine tests are considered spot checks of glycosuria, even though they represent values averaged over ½ to 1 hour.

2. Twenty-four-hour urine test. This very useful and easy test based on urinalysis ascertains average control over 24 hours. A 24-hour urine specimen is collected by discarding the first-voided specimen and saving all further specimens for 24 hours, including first voiding the next morning. The glycosuric concentration is measured. Using the measured volume of the 24-hour specimen, the amount of glucose (in grams) lost in a 24-hour period can be calculated. Expressed as a percentage of the total carbohydrate intake, this is used to assess diabetic control.

3. Blood glucose measurement. Blood glucose monitoring in the home environment consists of drawing a drop of capillary blood, normally from a fingertip, placing this on a plastic strip (e.g. Ames' Dextrostix) * and using colour changes to obtain a semi-quantitative estimate of the blood glucose value, or using a reflectance meter to obtain a quantitative estimate.

Blood glucose monitoring has become very popular in recent years. Its accuracy and validity is beyond doubt. Blood glucose measurements are spot estimates.

4. Glycosylated hemoglobin. Glycosylated hemoglobins consist of derivatives of glucose covalently bound to hemoglobin A. Their rate of synthesis depends on the blood glucose concentration. As a result, glycosylated hemoglobin levels correspond to the time-averaged blood glucose concentration over the hemoglobin's 120 day life span. It is unaffected by short-term fluctuations in blood glucose concentration caused by food ingestion, exercise or insulin therapy. It is thus a quantitative and reliable index of long-term diabetic control.

The popularity of monitoring glycosuria for spot estimates is mainly based on the ease of urinalysis methods. It is well known that the use of glycosuria as an estimate of the blood glucose level (which after all is the relevant parameter) has serious weaknesses. These are that the renal threshold for glucose is not known, differs from person to person, varies with age and that the glycosuria level lags the blood glucose level by several hours. Studies have shown that there is not much correlation between glycosuria and blood glucose values. It appears that glycosuria values can be seriously misleading, should be treated with due caution and whenever possible be verified with blood glucose measurements.

It is very important to keep detailed records of all measurements taken to monitor the patient.