Insulin Administration

Insulin is necessary for normal carbohydrate, protein, and fat metabolism. People with insulin-dependent (type I) diabetes mellitus do not produce enough of this hormone to sustain life and therefore depend on exogenous insulin for survival. In contrast, individuals with non-insulin-dependent (type II) diabetes are not dependent on exogenous insulin for survival. However, over time, many of these individuals will show decreased insulin production, therefore requiring supplemental insulin for adequate blood glucose control, especially during times of stress or illness.

An insulin regimen is often required in the treatment of secondary diabetes, i.e., diabetes occurring in relation to other disease states such as pancreatic disease. Insulin is also used in some cases of gestational diabetes to obtain optimum blood glucose control. In all instances of insulin use, the insulin dosage must be individualized and balanced with food intake and exercise.

This position statement addresses issues regarding the use of conventional insulin administration (i.e., via a needle and syringe) in the self-care of the individual with diabetes. It does not address the use of insulin pumps.

INSULIN—Insulin is obtained from beef or pork pancreas or is made chemically identical to human insulin by recombinant DNA technology or chemical modification of pork insulin.

Insulin is available in short-, intermediate-, and long-acting forms that may be injected separately or mixed in the same syringe. Short-acting insulins include regular and semilente. Intermediate-acting insulins include lente and NPH. Insulin preparations with a predetermined proportion of NPH mixed with regular, such as 70% NPH to 30% regular, are considered intermediate acting. The only long-acting insulin is ultralente.

Different companies have adopted different names for the same short-, intermediate-, or long-acting forms of insulin or their mixture. Human insulins have a more rapid onset and shorter duration of activity than pork insulins, whereas beef insulins have the slowest onset and longest duration of activity.

Insulin is commercially available in concentrations of 100 or 500 U/ml (designated U-100 and U-500; 1 U equals ~36 μg of insulin). U-500 is only used in rare cases of insulin resistance when the patient requires extremely large doses. U-500 is the only insulin that requires a prescription. It is critical that the person with diabetes purchase the correct syringe to match the concentration of insulin to be used. Insulin preparations are sometimes formulated individually for use in infants (e.g., U-10) with diluents provided by the manufacturer. In these instances, special care must be taken to ensure that the correct dose of the diluted insulin is administered with an ordinary insulin syringe.

Different types and species of insulin have different pharmacological properties. Human insulin is preferred for use in pregnant women, women considering pregnancy, individuals with allergies or immune resistance to animal-derived insulins, those initiating insulin therapy, and those expected to use insulin only intermittently. Insulin type and species, injection technique, insulin antibodies, site of injection, and individual patient response differences can all affect the onset, degree, and duration of insulin activity. Changing insulin species may affect blood glucose control and should only be done under the supervision of a health professional with expertise in diabetes. Human insulin manufactured using recombinant DNA technology is replacing insulin isolated from pigs and cows in many parts of the world. However, certain animal insulin preparations are useful in some circumstances. The choice of species of insulin to be used should be discussed with the patient and should take into account its current and future availability, its cost, and other factors such as immunogenicity and absorption characteristics.

Pharmacists should not interchange insulin species or types without the approval of the prescribing physician and without informing the patient of the type of insulin change being made. If an individual is admitted to a hospital, the type of insulin he/she has been using should not be changed inadvertently. If there is doubt about the principal species, human insulin should be administered until adequate information is available. When purchasing insulin, the patient should make sure that the type and species are correct, that if a specific brand has been prescribed it is dispensed, and that the insulin will be used before the expiration date.

Storage

Vials of insulin not in use should be refrigerated. Extreme temperatures (<36 or >86°F, <2 or >30°C) and excess agitation should be avoided to prevent loss of potency, clumping, frosting, or precipitation, particularly with human and pork insulins. Insulin in use may be kept at room temperature to limit local irritation at the injection site, which may occur when cold insulin is used.

The patient should always have available a spare bottle of each type of insulin used. Although an expiration

ORIGINALLY APPROVED OCTOBER 1989. APPROVED OCTOBER 1990 AND REVISED IN 1993.

date is stamped on each vial of insulin, a slight loss in potency may occur after the bottle has been in use for >30 days, especially if it was stored at room temperature.

The person administering insulin should inspect the bottle before each use for changes (i.e., clumping, frosting, precipitation, or change in clarity or color) that may signify a loss in potency. Visual examination should reveal short-acting insulin to be clear and all other insulin types to be uniformly cloudy. The person with diabetes should always try to relate any unexplained increase in blood glucose to possible reductions in insulin potency. If uncertain about the potency of a vial of insulin, the individual should replace the vial in question with another of the same type.

Mixing insulin

Administration of mixtures of short- and intermediate- or long-acting insulins will produce a more normal glycemia in some patients than use of a single insulin. The formulations and particle size distributions of insulin products vary. On mixing, physicochemical changes in the mixture may occur (either immediately or over time). As a result, the physiological response to the insulin mixture may differ from that of the injection of the insulins separately. Therefore, mixing of insulins should follow these guidelines:

- Patients who are well controlled on a particular mixed-insulin regimen should maintain their standard procedure for preparing their insulin doses.
- No other medication or diluent should be mixed with any insulin product unless approved by the prescribing physician.
- Use of commercially available premixed insulins is preferred to extemporaneous mixing by the patient if the insulin ratio is appropriate to the patient's insulin requirements. Mixing insulins from more than one manufacturer should be avoided.
- Currently available NPH and regular insulin formulations may be used immediately or stored for future use.
- Lente insulins do not interact with each other; they may be mixed together in any ratio and are stable when mixed.
- Mixing of regular and lente insulins is not recommended except for patients already adequately controlled on such a mixture. On mixing, Zn^{2+} present in lente insulins will bind with the regular insulin and delay its onset of action. The degree and rate of binding varies with the ratio and species of the two insulins; binding equilibrium may not be reached for 24 h. If regular-lente mixtures are to be used, the patient should standardize the interval between mixing and injection.
- Phosphate-buffered insulins (including protamine zinc insulin and NPH insulin) should not be mixed with lente insulins. Zinc phosphate may precipitate, and the longer-acting insulin will convert to a short-acting insulin to an unpredictable extent.
- Insulin formulations may change; therefore, the manufacturer should be consulted in cases where its recommendations appear to conflict with the American Diabetes Association guidelines.

SYRINGES—Conventional insulin administration involves subcutaneous injection with syringes marked in insulin units. There may be differences in the way units are indicated, depending on the size of the syringe and the manufacturer. Insulin syringes are manufactured with 0.3-, 0.5-, and 1-ml capacity. Regulations governing the purchase of syringes vary greatly from one state to another.

Syringes must never be shared with another person because of the risk of acquiring a blood-borne viral infection, e.g., acquired immune deficiency syndrome or hepatitis.

Disposal

Regulations in some states require the destruction of used insulin syringes and needles. Recapping, bending or breaking a needle increases the risk of needle-stick injury. Unless the syringe will be reused, it should be placed in a puncture-resistant disposal container or needle-clipping device, which retains the clipped needle in an inaccessible compartment. In areas with container-recycling programs, placement of containers of used syringes, needles, and lancets with materials to be recycled is prohibited. Local trash-disposal authorities should be consulted to determine the appropriate disposition of such containers. The likelihood of reuse of a syringe by another person is decreased if the plunger is separated from the barrel at the time of disposal.

Syringe reuse

Manufacturers of disposable syringes recommend that they be used only once, because the sterility of a reused syringe cannot be guaranteed. However, some individuals prefer to reuse a syringe until its needle becomes dull. Most insulin preparations have bacteriostatic additives that inhibit growth of bacteria commonly found on the skin. For many patients, it appears both safe and practical for the syringe to be reused if the patient so desires. The syringe should be discarded when the needle becomes dull, has been bent, or has come into contact with any surface other than the skin; if reuse is planned, the needle must be recapped after each use.

Syringe reuse may carry an increased risk of infection for some individuals. Patients with poor personal hygiene, an acute concurrent illness, open wounds on the hands, or decreased resistance to infection for any reason should not reuse a syringe. Patients reusing a syringe should periodically inspect the skin around an injection site for unusual redness or signs of infection. Individuals should consult their physicians before initiating the practice of syringe reuse and whenever injection-site infection is suspected.

Before syringe reuse is considered, it should be determined that the

patient is capable of safely recapping a syringe. Proper recapping requires adequate vision, manual dexterity, and no obvious tremor. The patient should be instructed in a recapping technique that supports the syringe in the hand and replaces the cap with a straight motion of the thumb and forefinger. The technique of guiding both the needle and cap to meet in midair should be discouraged, because this frequently results in needlestick injury.

The syringe being reused may be stored at room temperature. The potential benefits or risks, if any, of refrigerating the syringe in use or of using alcohol to cleanse the needle of a syringe are unknown. Cleansing the needle with alcohol may not be desirable, because it may remove the silicon coating that makes for less painful skin puncture.

INJECTION TECHNIQUE

Dose preparation

Before each injection, the hands and the injection site should be clean. The top of the insulin vial should be wiped with 70% isopropyl alcohol. For all insulin preparations except short acting, the vial should be gently rolled in the palms of the hands (not shaken) to resuspend the insulin. An amount of air equal to the dose of insulin required should first be drawn up and injected into the vial to avoid creating a vacuum. For a mixed dose, putting sufficient air into both bottles before drawing up the dose is important. When mixing short-acting insulin with intermediate- or long-acting insulin, the clear short-acting insulin should be drawn into the syringe first.

After the insulin is drawn into the syringe, the fluid should be inspected for air bubbles. One or two quick flicks of the forefinger against the upright syringe should allow the bubbles to escape. Air bubbles themselves are not dangerous but can cause the injected dose to be decreased.

Injection procedures

Injections are made into the subcutaneous tissue. Most individuals are able to lightly grasp a fold of skin and inject at a 90° angle. Thin individuals or children may need to pinch the skin and inject at a 45° angle to avoid intramuscular injection, especially in the thigh area. Routine aspiration (drawing back on the injected syringe to check for blood) is not necessary.

If an injection seems especially painful or if blood or clear fluid is seen after withdrawing the needle, the patient should apply pressure for 5–8 s without rubbing. Blood glucose monitoring should be done more frequently on a day when this occurs. If the patient suspects that a significant portion of the insulin dose was not administered, blood glucose should be checked within a few hours of the injection. If bruising, soreness, welts, redness, or pain occur at the injection site, the patient's injection technique should be reviewed by a physician or diabetes educator. Painful injections may be minimized by

- Injecting insulin at room temperature.
- Making sure no air bubbles remain in the syringe before injection.
- Waiting until topical alcohol (if used) has evaporated completely before injection.
- Keeping muscles in the injection area relaxed, not tense, when injecting.
- Penetrating the skin quickly.
- Not changing direction of the needle during insertion or withdrawal.
- Not reusing needles when they become dull.

Some individuals may benefit from the use of prefilled syringes (e.g., the visually impaired, those dependent on others for drawing their insulin, those traveling or eating in restaurants). Prefilled syringes are stable for up to 3 wk when kept in a refrigerator. If possible, the syringes should be stored in a vertical position, with the needle pointing upward, so that suspended insulin particles do not clog the needle. The predrawn syringe should be rolled between the hands before administration. A quantity of syringes may be premixed and stored. The effect of premixing of insulins on glycemic control should be assessed by a physician, based on blood glucose results obtained by the patient. When premixing is required, consistency of technique and careful blood glucose monitoring are especially important.

Injection site

Insulin may be injected into the subcutaneous tissue of the upper arm, the anterior and lateral aspects of the thigh, the buttocks, and the abdomen (with the exception of a circle with a 2-inch radius around the navel). Intramuscular injection is not recommended for routine injections. Rotation of the injection site is important to prevent lipohypertrophy or lipoatrophy. Rotating within one area is recommended (e.g., rotating injections systematically within the abdomen) rather than rotating to a different area with each injection. This practice may decrease variability in absorption from day to day.

Site selection should take into consideration the variable absorption between sites. The abdomen has the fastest rate of absorption, followed by the arms, thighs, and buttocks. Exercise increases the rate of absorption from injection sites, probably by increasing blood flow to the skin and perhaps also by local actions. Areas of lipohypertrophy usually show slower absorption. The rate of absorption also differs between subcutaneous and intramuscular sites. The latter is usually faster.

Insulin can be given with jet injectors that inject insulin as a fine stream into the skin. These injectors offer an advantage for patients unable to use syringes or those with needle phobias. A potential advantage may be a more rapid absorption of short acting insulin. However, the initial cost of these injectors is relatively high and they may traumatize the skin if used incorrectly. They should

not be viewed as a routine option for use in patients with diabetes.

Several pen-like devises with insulin-containing cartridges are available that deliver insulin subcutaneously through a needle. In selected patients (e.g., those who are visually and/or neurologically impaired and those using multiple daily injection regimens), these devises may improve accuracy of insulin administration and/or be more convenient.

Pump therapy is as safe as multipe daily injection therapy when recommended procedures are followed.

Other considerations

Whenever possible, insulin should be self-administered by the patient. In the case of children, the proper age for initiating this depends on the individual degree of maturity and receptivity of the child as well as family and social circumstances. It should not be delayed beyond adolescence. In the case of the visually impaired, mechanical aids are available to ensure accuracy. Where this is insufficient, the syringes may be prefilled periodically by a relative, friend, home health aide, or visiting nurse and the dose self-injected. The latter strategy can also be applied to some individuals with borderline dexterity or arithmetical skills. For patients who are completely independent in insulin administration, it is still advisable to have a family member knowledgeable in the technique in case of emergency.

PATIENT MANAGEMENT

Dosing

The appropriate insulin dosage is dependent on the glycemic response of the individual to planned diet and exercise regimens. For virtually all type I and many type II patients, the time course of insulin action requires two or more injections per day to avoid daytime hypoglycemia while allowing adequate blood glucose control overnight. Type I patients may also require both short- and longer-acting insulins. A dosage algorithm suited to the individual's needs and treatment goals should be developed with the cooperation of the patient. The timing of the injection depends on blood glucose levels, food consumption, exercise, and types of insulin used. Variables in insulin action (e.g., onset, peak, and duration) must be considered.

The most commonly recommended interval between injection of short-acting insulin and a meal is 30 min. Eating within a few minutes after (or before) injecting short-acting insulin is discouraged because it substantially reduces the ability of that insulin to prevent a rapid rise in blood glucose and may increase the risk of delayed hypoglycemia. Guidelines should be set by the physician for the suggested interval between insulin injection and mealtime based on factors such as blood glucose levels, site of injection, and anticipated activity during the interval.

Self-monitoring

Whenever possible, insulin-using patients should self-monitor blood glucose (SMBG). Insulin dosage adjustments should be based on blood glucose measurements. SMBG is extremely valuable in patients who take insulin because they experience day-to-day variability in blood glucose levels. This variability is influenced by differences in insulin absorption rates, insulin sensitivity, exercise, stress, rates of food absorption, and hormonal changes (e.g., puberty, the menstrual cycle, and pregnancy). Illness, traveling, and any change in routine (e.g., increased exercise and a different diet during vacation) may require more frequent SMBG under the guidance of a physician. Travel through three or more time zones requires special advice regarding insulin administration. During illness, it is important that insulin be continued even if the patient is unable to eat or is vomiting. When accompanied by hyperglycemia, a positive urine test for ketones during illness indicates a need for extra, not less, insulin. Physicians should obtain information regarding blood glucose values whenever patients need assistance in handling illness or stress.

Hypoglycemia

Excess insulin is a common cause of hypoglycemia. Hypoglycemia may also result from a delayed or missed meal, decreased carbohydrate content of a meal, or increased physical activity. All insulin-requiring individuals should be instructed to carry at least 15 g of fast-acting carbohydrate to be eaten in the event of a hypoglycemic reaction. Family members, roommates, and co-workers should be instructed in the use of glucagon for situations when the individual cannot be given carbohydrate orally. All insulin users should carry medical identification (e.g., a bracelet or wallet card) that alerts others to the fact that the wearer uses insulin.

SUMMARY—The injection of insulin is essential for management of type I diabetic patients and may be needed by type II diabetic patients for intermittent or continuous glycemic control. The species and dosage of insulin used should be consistent, and the patient's injection technique should be reviewed periodically with the diabetes-care team. The effective use of insulin to obtain the best metabolic control requires an understanding of the duration of action of the various types of insulin and the relationship of blood glucose levels to exercise, food intake, and stress; SMBG; and learning to adjust insulin dosage with the support and guidance of the diabetes-care team.