

## Individualizing insulin therapy for optimum glycemic control

Don't let the increased risk of hypoglycemia keep you from prescribing intensive insulin therapy. By choosing carefully among the different types of insulin and adjusting dosages to lifestyle, you can help the patient achieve optimal metabolic control.

**S**ince the Diabetes Control and Complications Trial demonstrated that intensive therapy can prevent or delay the development and exacerbation of microvascular complications in type 1 diabetes mellitus, treatment standards have tightened.<sup>1</sup> The goal now is to maintain glucose levels as close to the normal range as possible (see Table 1, page 36). As a result, patients are being asked to accept major responsibility for self-monitoring and making frequent adjustments to their insulin regimens.

### INSULIN REGIMENS

Intensive therapy is recommended for compliant patients older than 13 years who do not have advanced complications of diabetes and are familiar with and sensitive to the signs and symptoms of hypoglycemia. Because many elderly diabetic patients are insensitive to the signs of hyperglycemia, especially tachycardia, they are often excluded from intensive therapy. This program is also not advisable for those in whom sympathetic manifestations of moderate hypoglycemia, such as tachycardia and hypertension, would be hazardous. Other reasons to avoid intensive insulin therapy include a tendency toward seizures, compromised mental status, and low hypoglycemic awareness.

### Types of insulin

The average time of onset, peak action, and duration of action for various types of insulin need to be considered (see Table 2, page 37). Many patients do not fit these "average" profiles and, therefore, monitoring should be done to discover individual variations.

In healthy persons without diabetes, continuous basal insulin secretion occurs, with boluses related to food intake. The basal component restrains hepatic glucose production, keeping it in equilibrium with tissues that are obligate glucose consumers. For insulin therapy to be effective, the basal and mealtime component must be identified. Basal insulin may be provided in one of the following ways:

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**This article at a glance**

**Individualizing insulin regimens**

- Intensive insulin therapy is possible if the patient is motivated and educated about insulin adjustment.
- Intensive therapy is not recommended for patients for whom moderate hypoglycemia would exacerbate underlying cardiovascular or neurologic disease.
- Multiple injections allow better glucose control and flexibility with regard to meals and exercise but require self-monitoring of glucose levels before meals and at bedtime.

**Monitoring and delivery options**

- Regular monitoring is essential to prevent hypoglycemia in well-controlled patients.
- Insulin should be decreased appropriately for exercise planned for 1 to 3 hours after a meal.
- An external pump can be useful to patients who need 3 or 4 daily injections of insulin and require flexibility in terms of meal schedules and daily activities, including travel.

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- Bedtime intermediate-acting insulin, with or without morning intermediate-acting insulin
- Ultralente insulin or insulin glargine
- Insulin pump therapy.

**Short- and rapid-acting insulins** Regular insulin is used primarily to provide postmeal coverage and thus should be taken about 30 minutes before the meal to achieve maximum effectiveness without inducing postmeal hypoglycemia. The effect of regular insulin is sustained in most people

because of molecular aggregation, so this type of insulin provides some coverage for 6 to 8 hours.

Insulin lispro is ideal for the control of post-meal glucose levels when the meal is high in carbohydrate. Studies of patients with type 1 diabetes show that insulin lispro significantly improves postprandial glucose peaks during the day compared to regular insulin, and insulin lispro also results in lower nighttime blood glucose levels, which is important for reducing hypoglycemia.<sup>2,3</sup> In patients with type 2 diabetes who take oral agents such as sulfonylureas, the addition of insulin lispro has been shown to significantly improve postprandial glucose peaks, which in turn leads to improved fasting glucose levels.<sup>4</sup> The duration of action is too short for premeal boluses to provide sustained coverage throughout the day or for a very high-fat meal. Insulin lispro must be combined twice a day with bid and intermediate-acting insulin to achieve adequate control of diabetes. For meals high in fat and low in carbohydrate, regular insulin coverage is preferred.

Recently, insulin aspart received FDA approval (see "The role of insulin aspart," page 38). Unfortunately, this new analog's role in insulin regimens is not yet clear as studies have compared it to regular insulin but not to insulin lispro.

**TABLE 1**  
**Suggested therapeutic goals for blood glucose and HbA<sub>1c</sub> levels**

Desired glucose control level	Fasting blood glucose (mg/dL)	2-h postmeal glucose (mg/dL)	2-4 AM blood glucose (mg/dL)	Hemoglobin A <sub>1c</sub> (%)
Normal	65-109	140	60-70	<6.8
Intensive	65-126	180	60-80	<7.0
Acceptable*	80-150	<200	<150	<8.0

**Note:** Goals are based on improvements in complications noted in United Kingdom Prospective Diabetes Study.

\*These values are used for patients for whom intensive glucose control would be dangerous.

**Intermediate-acting insulins** Neutral protamine Hagedorn (NPH) insulin is one of the most frequently used insulins. The risk of nocturnal hypoglycemia and fasting hyperglycemia is increased with insulin regimens using nighttime NPH insulin in combination with regular insulin and/or insulin lispro before meals. Fasting hyperglycemia can be improved when NPH insulin is administered at bedtime instead of with the evening meal. Usually, effective glucose control requires at least a twice-a-day regimen with one of the intermediate-acting insulins, either NPH or lente insulin.

**Long-acting insulins** The long-acting insulins (ultralente insulin and, to a greater extent, insulin glargine) allow 24-hour peakless coverage with 1 injection per day (see "A new long-acting insulin available," page 41). For adequate overall control, they must be used in combination with a short-acting insulin. Mixing the short-acting preparations with the long-acting insulin is not recommended. These insulins are particularly helpful in patients for whom intermediate-acting insulin does not provide adequate coverage between the evening meal and the morning. Injected before the evening meal or at bedtime, ultralente insulin or insulin glargine may adequately prevent morning hyperglycemia.

**Mixtures** In those with predictable schedules and habits, stable NPH/regular mixtures (70/30 or 50/50) may be used once or twice per day. In elderly patients or patients taking corticosteroids who have mainly postmeal hyperglycemia, a single morning injection may be sufficient. Caution elderly patients taking insulin before the evening meal or before bedtime that the short-acting component in these mixtures produces a rapid reduction in glucose levels after the evening meal and may lead to hypoglycemia early in the night.

**Patient-mixed insulins** More patients are mixing their own insulin preparations to improve blood glucose control. The American Diabetes Association (ADA) has established guidelines for optimal mixing of insulins:

- When rapid-acting insulin is mixed with either an intermediate- or long-acting insulin, the mixture should be injected within 15 minutes before a meal.
- Mixing of short-acting and lente insulins is not recommended.
- Phosphate-buffered insulin—such as NPH insulin—should not be mixed with lente insulin.<sup>5</sup>

Because the action profiles of NPH and regular insulins are maintained when mixed in the same syringe, a majority of patients use this mixture. Precautions must be taken since the introduction of intermediate-acting insulins—such as NPH—into a bottle of regular insulin can change the duration of action of the regular type. To avoid contamination, instruct patients to draw regular insulin into the syringe first and then

**TABLE 2**  
**Comparison of human insulins**

Insulin preparations	Onset of action	Peak	Duration of action
SHORT- AND RAPID-ACTING			
Lispro	5-15 min	1-2 h	4-5 h
Regular	30-60 min	2-4 h	6-8 h
INTERMEDIATE-ACTING			
NPH	1-3 h	5-7 h	13-18 h
Lente	1-3 h	4-8 h	13-20 h
LONG-ACTING			
Ultralente	2-4 h	8-14 h	18-30 h
Glargine	2-4 h	Peakless	>24 h
<p><b>Key:</b> NPH, neutral protamine Hagedorn.</p> <p><b>Note:</b> There are marked individual variations with these averages.</p> <p>Adapted with permission from IB Hirsch. Intensive treatment of type 1 diabetes. <i>Med Clin North Am.</i> 1998;82:689-719; and updated by the article consultant.</p>			

### The role of insulin aspart

The newest rapid-acting human insulin analog to receive FDA approval is insulin aspart. In this analog, aspartic acid takes the place of proline at position B28.<sup>1</sup> Like insulin lispro, insulin aspart is injected immediately before a meal for fast control of blood glucose levels and needs to be combined with an intermediate-acting insulin for optimal glycemic control. Insulin aspart has not yet been compared directly to insulin lispro for effectiveness.

**Use** Insulin aspart is an attractive option for use at mealtimes to ameliorate postmeal hyperglycemia. The rapid taper of its metabolic effect may be beneficial in reducing the occurrence of late postmeal hypoglycemia.

**Compared to regular insulin** In a recent study of 884 patients with type 1 diabetes, those who used insulin aspart immediately before meals had significantly better glycemic control than did those who used human insulin 30 minutes before meals.<sup>2</sup> The glycosylated hemoglobin level was significantly lower for the insulin aspart group than for the human insulin group (7.8% vs. 7.9%), and postprandial glucose levels were significantly lower after each meal. The overall risk of severe or mild hypoglycemic episodes was similar for both insulins, but fewer nocturnal hypoglycemic episodes occurred in patients receiving insulin aspart (16%) than in those receiving human insulin (34%).

1. Mudaliar SR, Lindberg FA, Joyce M, et al. Insulin aspart (B28 aspartulin): a fast-acting analog of human insulin. Absorption kinetics and action profile compared with regular human insulin in healthy subjects with diabetes. *Diabetes Care*. 1999;22:1501-1506.
2. Raskin P, Jovanovic L, Guthrie RA, et al. Insulin aspart (Iasp) improves glycemic control compared to human insulin (HI) for patients with type 1 diabetes [abstract]. *Diabetes*. 1999;48(suppl 1):A115. Abstract 0496.

add the intermediate- or long-acting preparation.

Prefilled syringes may be especially beneficial to those dependent on other persons to draw their insulin and to those traveling or eating in restaurants. These predrawn insulins are stable for up to 30 days when stored in the refrigerator in a vertical position, with the needle pointing upward so that suspended insulin particles do not clog the needle.

### Intensive therapy for type 1 diabetes

The simplest effective regimen for type 1 diabetes uses NPH insulin with breakfast and at bedtime as the basal insulin, and short-acting insulin—either lispro, regular, or a combination

of the two as needed—for the evening meal (see Table 3, page 42). Short-acting insulin coverage for other meals may be added as necessary. A reasonable starting dosage for a patient with type 1 diabetes is 0.5 U/kg/d. The distribution is dependent on the patient's food plan and exercise habits. In many patients, better metabolic control may be achieved using ultralente or glargine insulin as the bolus insulin, with short-acting insulin added to cover food intake. This regimen avoids nocturnal hypoglycemia.

### Regimens for type 2 diabetes

When insulin therapy is used in type 2 diabetes, normalization of glucose values is recommended to decrease microvascular complications and improve associated lipid abnormalities. Experts had been concerned that the large doses of insulin necessary to control glucose levels in this disease would increase cardiovascular risk, but the United Kingdom Prospective Diabetes Study demonstrated no increase in cardiovascular events in patients whose diabetes was controlled with insulin.<sup>6</sup>

Insulin is used in type 2 diabetes to control acute episodes of hyperglycemia and as chronic therapy when oral agents are no longer sufficient. In either case, intermediate- or long-acting insulin may be added at bedtime to the patient's existing oral-agent regimen to suppress hepatic gluconeogenesis and normalize fasting glucose levels. With this strategy, weight gain is less than if insulin is substituted for oral agents. Because of the insulin resistance characteristic of type 2 diabetes, insulin requirements will be greater than in type 1 diabetes—usually about 1.5 U/kg/d of ideal body weight. A mixed insulin starting at 10 U/kg/d given before the evening meal is an alternative therapy that can improve control with little weight gain.

If a single dose of insulin is insufficient to achieve control, other regimens should be select-

ed and the oral agents gradually decreased. Combination therapy with at least one oral agent is frequently useful to avoid unacceptable weight gain and to decrease insulin requirements.

### Dosage adjustments

To achieve glucose control, adjustment of both the basal long-acting or intermediate-acting insulin and the bolus insulin—insulin lispro or regular insulin—is required (see Table 4, page 44). Self-monitoring of blood glucose levels is necessary to determine insulin dosages.

To help the patient learn to determine the amount of short-acting insulin to be used to cover food intake in intensive insulin therapy, carbohydrate counting should be taught. The carbohydrate content in a meal is quantitatively more important than the protein or fat content. With this method, patients are taught to count the number of grams of carbohydrate they antic-

Drugs mentioned in this article	
<b>INSULINS</b>	
<b>Insulin analog [insulin lispro] (Humalog)</b>	<b>Isophane insulin suspension [NPH]</b>
<b>Insulin aspart (NovoRapid)</b>	<b>Isophane insulin suspension [NPH]/insulin (Humulin 50/50)</b>
<b>Insulin glargine (Lantus)</b>	<b>Isophane insulin suspension [NPH]/insulin (Humulin 70/30, Novolin 70/30)</b>
<b>Insulin lispro protamine suspension [NPL]/insulin lispro (Humalog 75/25)</b>	<b>Regular insulin</b>
<b>Insulin zinc suspension, extended [ultralente] (Humulin U Ultralente)</b>	<b>OTHER AGENTS</b>
<b>Insulin zinc suspension [lente]</b>	<b>Glucagon (Glucagon Emergency Kit)</b>
	<b>Glucose</b>

ipate eating in a meal and the dose of regular insulin or insulin lispro to be taken before the meal. The dosage is then calculated based on the ratio of insulin to carbohydrate content. For example, 1 unit of insulin lispro may be appropriate for every 15 g of carbohydrate in a meal. When carbohydrate counting is not possible, insulin coverage for meals can be estimated (for

### A new long-acting insulin available

Insulin glargine is an extended-action biosynthetic human insulin. This insulin is produced by recombinant DNA technology with 2 modifications of the native human insulin structure: substitution of the amino acid glycine for the native asparagine at position A21 of the A-chain of human insulin and the addition of 2 arginine molecules to the NH<sub>2</sub>-terminal end of the B-chain of human insulin.

**Use** Insulin glargine works well as a basal insulin in combination with short-acting insulin used to cover caloric ingestion. It should not be used in pregnant women and in situations where the patient is not taking either oral agents or short-acting insulin to cover meals. Insulin glargine can be administered as a once-daily SC injection at bedtime. It should not be diluted or mixed with any other forms of insulin.

**Compared to NPH insulin** In patients with type 1 diabetes, the onset of action of insulin glargine was shown to be later, the duration of action longer, and the time-action profile flatter than that of NPH insulin. Four large clinical trials have shown that a single bed-

time dose of insulin glargine, in combination with preprandial short-acting insulin, is as effective or more effective than once or twice daily NPH insulin plus short-acting insulin in improving glycemic control in patients with type 1 diabetes.<sup>1</sup> Two other large studies that included patients with type 1 and type 2 diabetes found insulin glargine to be as effective as NPH insulin in achieving glycemic control. However, the prevalence of nocturnal hypoglycemia was significantly lower in those treated with insulin glargine than in those who were treated with NPH insulin. Also, the insulin glargine group had less weight gain than the NPH group, 0.9 lb versus 3.1 lb.<sup>2,3</sup>

- Gillies PS, Figgitt DP, Lamb HM. Insulin glargine. *Drugs*. 2000;59:253-260.
- Rosenstock J, Schwartz S, Clark C, et al. Efficacy and safety of HOE 901 (insulin glargine) in subjects with type 2 DM: a 28-week randomized, NPH insulin-controlled trial [abstract]. *Diabetes*. 1999;48(suppl 1):A100. Abstract 0432.
- Ratner RE, Hirsch IB, Mecca TE, et al. Efficacy and safety of insulin glargine in subjects with type 1 diabetes: a 28-week randomized, NPH insulin-controlled trial [abstract]. *Diabetes*. 1999;48(suppl 1):A120. Abstract 0516.

**TABLE 3**  
**Common daily insulin regimens**  
**in type 1 or type 2 diabetes**

Morning	Noon	Evening	Bedtime
REGIMENS FOR TYPE 1 OR TYPE 2 DIABETES*			
NPH	—	SS-regular/ lispro	NPH
Lente	—	Regular/lispro	Lente
SS-regular/ lispro	SS-regular/ lispro	SS-regular/ lispro	Lente
SS-regular/ lispro	SS-regular/ lispro	SS-regular/ lispro	Ultralente, glargine†
MORNING-EVENING BID REGIMENS FOR TYPE 2 DIABETES			
NPH*	—	NPH	—
70/30‡	—	70/30	—
50/50§	—	50/50	—
75/25	—	75/25	—
<p><b>Key:</b> NPL, neutral protamine lispro; NPH, neutral protamine Hagedorn; SS, sliding scale.  <b>Note:</b> Total insulin dosage usually is approximately 0.5 U/kg of actual body weight/d. Total dosage depends on insulin resistance. Starting dosage of 1.0 U/kg of ideal weight/d is reasonable.</p> <p>* A sliding scale is used to add regular insulin or insulin lispro as needed. Two thirds of the total daily dosage can be given 30 min before breakfast and one third 30 min before the evening meal.          † Given once a day at bedtime.          ‡ Commercially available, premixed preparation of 70% NPH and 30% regular insulin.          § Commercially available, premixed preparation of 50% NPH and 50% regular insulin.             Commercially available, premixed preparation of 75% NPL and 25% insulin lispro.</p>			

example, 3 units for breakfast, 2 units for lunch, 4 units for supper) and modified by postmeal glucose determination and added to the sliding scale. The amount of premeal insulin would then be the sum of the insulin by scale and the estimated carbohydrate coverage.

For snacks, a bolus insulin may be injected as necessary but should be used only with caution at bedtime. If patients plan to exercise after a meal, the premeal food coverage dose of insulin should be decreased.

**Nocturnal hypoglycemia** When long-acting or evening intermediate-acting insulin is adjusted, the patient should monitor glucose levels once at

2 or 3 AM. Nocturnal hypoglycemia is common in the elderly and in patients with renal insufficiency and inadequate gluconeogenesis. Stable insulin mixtures (such as 70/30 insulin) can also produce nocturnal hypoglycemia when given before the evening meal. The substitute of 75/25 insulin, a mixture of NPL and lispro insulins with an earlier action peak than other mixed insulins, may decrease the incidence of nocturnal hypoglycemia.

**Flexible meal scheduling** For patients who need to vary their meal patterns, a single dose of long-acting insulin at bedtime with regular insulin or insulin lispro used for meal coverage is an excellent regimen. If regular insulin is used, then NPH once at bedtime may offer sufficient coverage.

#### ENSURING ADEQUATE MONITORING

A cornerstone of diabetes care is self-monitoring of glycemic status. For most patients with type 1 diabetes,

self-monitoring is recommended 3 or 4 times daily. Studies have shown that testing at least 3 times a day can help patients with diabetes reduce complications by up to 60%.<sup>7</sup>

The optimal frequency of self-monitoring for patients with type 2 diabetes is variable. Monitoring should be used to assist with treatment decisions. Insurers usually allow insulin-treated patients 2 or 3 test strips per day, but providers may indicate the need for more frequent monitoring for conditions such as brittle diabetes, fluctuating glucose levels, or hypoglycemia. Illness, traveling, and any changes in routine (such as increased exercise and a different diet during

vacation) may require more frequent monitoring.

According to the ADA, the glycosylated hemoglobin (HbA<sub>1c</sub>) level should be measured every 3 to 6 months to determine the glycemic control profile. A pager-sized device measuring HbA<sub>1c</sub>, known as Digital Response, displays results digitally in 8 minutes and has recently received FDA approval. This new monitoring device is suitable for use in the physician's office or lab, as well as for home testing by prescription.

### Self-monitoring of blood glucose

Numerous self-monitoring devices are available, allowing even visually and physically handicapped patients to obtain accurate glucose values. Meters with memory and printout capacity are helpful to avoid both mistakes in transcription and misinterpretation.

Several new devices are being developed to make glucose self-monitoring easier for patients. Recently, meters have become available that use 0.1 to 0.3  $\mu$ L of blood and have been approved for sampling from the forearm, upper arm, or thigh. One of these, the AtLast System (about \$63) creates a small break in the skin of the arm or thigh using a custom-made lancet. Another similar lancet device, the FreeStyle (about \$69), has the added benefit of minimal interference from substances in the blood such as vitamin C or acetaminophen, which can result in inaccurate readings on many other systems. Many practitioners also find the FreeStyle device to cause less bruising than other lancet devices. The correlation with fingerstick meters is comparable under most circumstances.

Close to FDA approval, the GlucoWatch Biographer (about \$300, with pads at \$4 each) detects blood glucose levels through the skin. The device, which uses small electric currents to open the skin and draw fluid to a special sensor pad attached to the back, takes readings every 20 minutes.

The FDA advisory committee cautioned that

25% of the time, GlucoWatch readings can differ from traditional blood tests by about 30%. As a result, the FDA recommended that patients should perform a fingerstick test first to double-check the watch's results. The only other safety concern the FDA expressed was that most patients experienced mild to moderate skin irritation, which cleared up when the watch was removed.

### Dealing with hypoglycemia

The incidence of hypoglycemic reactions increases with intensive insulin therapy, with the thin and the elderly most affected by such episodes. All persons requiring insulin should carry at least 15 g carbohydrate to be eaten or taken in liquid form in the event of a hypoglycemic reaction. Patients should also be given a prescription for a glucagon kit, and family members, roommates, and coworkers should be instructed in its use for situations when these patients are not able to take a carbohydrate orally.

**Mild** With mild hypoglycemia, symptoms such as diaphoresis, tachycardia, palpitations, and hunger may occur. Values of less than 70 mg/dL are treated with food—for example, 4 oz of milk or 2 oz of a drink with concentrated sugar, such as a soda.

**Moderate** This form of hyperglycemia may include not only symptoms of sympathetic nervous system overactivity, but also neuroglycopenic symptoms. One or two starches followed by a protein, such as a sandwich and an 8-oz glass of low-fat milk, should be consumed. Glucose tablets or instant oral glucose may be used. The blood glucose level should be higher than 100 mg/dL within 30 minutes of eating.

Be alert for patients who overreact to minor symptoms of hypoglycemia and consume excess food. This may lead to weight gain and increased insulin requirements. Consumption of several

**TABLE 4**  
**Insulin adjustment guidelines**

Cause	Action/solution
FASTING HYPERGLYCEMIA (when 2-3 AM glucose level is checked OR 2-3 AM glucose level $\geq$ 100 mg/dL)	
Inadequate bedtime insulin	Increase bedtime insulin by 2 U q2-4d* and monitor 2-3 AM glucose level
FASTING HYPERGLYCEMIA (2-3 AM glucose level $\leq$ 65 mg/dL)	
Nocturnal hypoglycemia with rebound hyperglycemia	Decrease bedtime insulin by 2 U q2-4d and monitor 2-3 AM glucose level OR change evening intermediate-acting insulin to bedtime, and use insulin lispro to cover evening meal OR use insulin glargine at bedtime
ELEVATED BLOOD GLUCOSE BEFORE EVENING MEAL	
Inadequate morning insulin OR early NPH peak	Increase morning intermediate-acting insulin by 2 U q2-4d until target glucose level is reached If this causes hypoglycemia before lunch, switch starch from lunch to breakfast or in early PM, add starch to lunch OR decrease AM NPH and give small amount of NPH at lunch
ELEVATED BLOOD GLUCOSE AT BEDTIME	
Excessive food intake at evening meal or inadequate insulin for evening meal coverage	Review meal plan, decrease food intake OR increase short-acting insulin supper coverage
FASTING HYPOGLYCEMIA	
Omission of bedtime snack or insufficient snack OR excessive evening or bedtime insulin	Review and adjust snack contents OR use insulin lispro to cover evening meal or decrease bedtime insulin by 2-4 U q2d until target glucose level is reached
HYPOGLYCEMIA BEFORE EVENING MEAL	
Excessive morning insulin OR insufficient food intake at lunch	Decrease morning intermediate-acting insulin by 2-4 U q2-4d until target glucose level is reached OR add either starch at lunch or a mid-afternoon snack
BEDTIME HYPOGLYCEMIA	
Excessive regular insulin before evening meal OR late bedtime with exercise after evening meal	Decrease dose before evening meal or use insulin lispro
<p><b>Key:</b> NPH, neutral protamine Hagedorn.</p> <p>*Interval with insulin glargine should be longer.</p>	

glucose tablets usually relieves hypoglycemic symptoms promptly without the need to over-correct with carbohydrate foods.

**Severe** Instant glucose gel may be placed into the mouth in cooperative patients and is prefer-

able to food in this situation. No fluids should be given when consciousness is impaired since aspiration may occur. Instead, glucagon should be used to mobilize glycogen stores and rapidly raise blood glucose levels.

*Continued on page 47*



## INSULIN DELIVERY OPTIONS

Insulin absorption varies in relation to the injection site and according to the degree of exercise experienced in the area into which the drug is injected. Studies have shown that absorption is more rapid in the abdomen than the arms, buttocks, or thighs. The current recommendation is to vary the position over the surface of the abdomen because this area is least affected by exercise and has a considerable portion of SC tissue over which injections can be distributed.

**Injectors** Several penlike devices and insulin-containing cartridges are available that deliver insulin SC through a needle. These devices may improve accuracy and be more convenient for patients who are visually or neurologically impaired and for those using multiple-daily-injection regimens. Although more expensive, these devices are excellent for beginning insulin therapy. Insurers may reimburse only for insulin and not for delivery devices; in those situations, a nondisposable pen with insulin cartridges may be prescribed.

**Pumps** Smaller than a deck of cards, insulin pumps can be hooked to a belt. Continuous SC insulin infusion (CSII) delivers insulin continuously in microliter amounts through a tube inserted under the skin. Medicare recently approved the reimbursement of these pumps (about \$5000) for people with type 1 diabetes who require at least 3 injections per day and have demonstrated for at least 6 months the ability to accurately self-monitor their blood glucose levels at least 4 times per day. Most important, patients must be highly motivated to improve glucose control and demonstrate accurate use of an insulin pump. An external pump can be useful to patients whose lives require flexibility with meal schedules and daily activities, including travel. Even more so than other diabetes treatments, CSII requires extensive patient education.

Improved catheters, an increase in the ability

to change the number of basal rates, and smaller pump size have made CSII an important option to many people who use insulin to control diabetes. Bolus insulin may be administered by activating the pump before meals to provide sufficient insulin for anticipated carbohydrate consumption. Therefore, if basal insulin dosage is correct, it should be possible to delay or omit the meal without a significant compromise in glycemia. Until the introduction of insulin lispro, it was frequently difficult to determine if 3- to 5-hour postprandial blood glucose levels were more dependent on the previous bolus insulin or due to the basal insulinemia. Because of the pharmacokinetics of regular insulin, it is difficult to know precisely which insulin component is responsible for any particular blood glucose level. □

## REFERENCES

1. The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group: Retinopathy and nephropathy in patients with type 1 diabetes four years after a trial of intensive therapy. *N Engl J Med.* 2000;324:381-389.
2. Holleman F, Schmitt H, Rottiers R, et al. Reduced frequency of severe hypoglycemia and coma in well-controlled IDDM patients treated with insulin lispro. The Benelux-UK Insulin Lispro Study Group. *Diabetes Care.* 1997;20:1827-1832.
3. Gaie EA. A randomized, controlled trial comparing insulin lispro with human soluble insulin in patients with Type 1 diabetes on intensified insulin therapy. The UK Trial Group. *Diabet Med.* 2000;17:209-214.
4. Feinglos MN, Thacker CH, English J, et al. Modification of postprandial hyperglycemia with insulin lispro improves glucose control in patients with type 2 diabetes. *Diabetes Care.* 1997;20:1539-1542.
5. American Diabetes Association. Position statement: Insulin administration. *Diabetes Care.* 2000;23(suppl 1). No. S86. Available at: <http://journal.diabetes.org/FullText/Supplements/DiabetesCare/Supplement100/s86.htm>. Accessed July 5, 2000.
6. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet.* 1998;352:837-857.
7. American Diabetes Association. Position Statement: Implications of the Diabetes Control and Complications Trial. *Diabetes Care.* 2000;23(suppl 1). No. S24. Available at: <http://journal.diabetes.org/FullText/Supplements/DiabetesCare/Supplement100/s24.htm>. Accessed July 5, 2000.

## SUGGESTED READING

- DeFronzo RA. Pharmacologic therapy for type 2 diabetes mellitus. *Ann Intern Med.* 1999;131:281-303.
- Heinemann L, Linkeschova R, Rave K, et al. Time-action profile of the long-acting insulin analog insulin glargine (HOE901) in comparison with those of NPH insulin and placebo. *Diabetes Care.* 2000;23:644-649.
- Hirsch IB. Intensive treatment of type 1 diabetes. *Med Clin North Am.* 1998; 82:689-719.

# BSA

PHYSICIAN'S ORDERS  
Standing Sliding Scale Insulin

AFFIX PATIENT LABEL HERE

## PILOT

### INSULIN PROTOCOL FOR TYPE II DIABETICS

*Not recommended for more than two (2) days as the only method of control.*

**REGIMENS:**

- *Low Dose Regimen:* Suggested as starting point for the thin and elderly.
- *Moderate Dose Regimen:* Suggested as the starting point for average weight.
- *High Dose Regimen:* Suggested as the starting point for overweight patients.
- *Very High Dose Regimen:* Suggested as the starting point for patients with infections or those receiving steroids.

DATE	TIME	ORDER	VERIFICATION
		1. Start sliding scale at _____ dose level.	
		2. All insulin is Humulin-R (regular) insulin given subcutaneously unless otherwise specified.	
		3. If potassium is low (< 3.5 mEq/L), call physician.	
		4. Check capillary blood glucose on prescribed schedule.	
		<input type="checkbox"/> Q 6 H (12 MN-6 AM-12 N-6 PM) <i>Recommended for patients who are NPO.</i> <input type="checkbox"/> AC & HS (30 minutes before meals and at 9 PM) <i>Recommended for patients WHO ARE ABLE TO EAT.</i>	
		5. Changes: <ul style="list-style-type: none"> <li>• Advance to next higher dose regimen if glucose level is &gt; 250 two (2) times in 24 hours and all readings were &gt; 100.</li> <li>• Decrease to the next lower dose regimen if glucose level is between 60 and 100 twice in 24 hours.</li> </ul>	
		6. If any reading is 60 or below, initiate hypoglycemia protocol and notify MD.	
		7. Write a new Sliding Scale Insulin Protocol order sheet with dose regimen changes and send a copy to Pharmacy.	

Glucose Level (mg/dL)	Low Dose Regimen	Medium Dose Regimen	High Dose Regimen	Very High Dose Regimen	Other
Serum FBS < 60	Hypoglycemia Protocol, and call MD	Hypoglycemia Protocol, and call MD	Hypoglycemia Protocol, and call MD	Hypoglycemia Protocol, and call MD	
60-150	0	0	0	0	
151-200	0	4 units	5 units	6 units	
201-250	3 units	8 units	10 units	15 units	
251-300	4 units	10 units	14 units	18 units	
301-350	6 units	12 units	17 units	21 units	
351-400	9 units	16 units	20 units	25 units	
> 400	12 units, and call MD	12 units, and call MD	12 units, and call MD	12 units, and call MD	

Physician's Signature: \_\_\_\_\_ Date: \_\_\_\_\_ Time: \_\_\_\_\_

**Suggested conversion to daily Humulin-N requirement:** Use 3/4 of total daily Humulin-R requirement as the total daily Humulin-N requirement.

**Figure 1.** Sliding scale insulin order form used in pilot project.