MANAGEMENT OF TYPE - 1 DIABETES MELLITUS

INVESTIGATIONS AND TREATMENT

MANSI NAIK
VII SEMESTER

INVESTIGATIONS

FASTING BLOOD SUGAR

PLASMA GLUCOSE

HEMOGLOBIN A_{1c}

SYMPTOMS OF TYPE 1 DIABETES MELLITUS

- **Polyuria**
- **Nocturia**
- **Polydypsia**
- **Recent weight loss**
- **Polyphagia and**
- **Fatigue**

CRITERIA FOR DIAGNOSIS OF DIABETES

Random glucose in random sample	> 200mg/dL (>11.1mmol/L)
Fasting Plasma Glucose	> 126mg/dL (7.0mmol/L)
2h plasma glucose during an OGTT	>200mg/dL(11.1 mmol/L)
HbAic	>6.5%

ESTABLISHING THE DIAGNOSIS OF DIABETES

With symptoms

- Fasting glucose **>126mg/dl** or random glucose **>200mg/dl**

Without symptoms

- They should have a second confirmatory test

Diabetes should not be diagnosed by capillary blood glucose levels

TREATMENT

Goals of treatment:

- To eliminate symptoms related to hyperglycemia
- To reduce and delay the complications
- To achieve a normal lifestyle and normal emotional and social development
- To achieve normal physical growth and development
- To detect associated diseases early

TREATMENT

INSULIN THERAPY

NUTRITIONAL THERAPY

PHYSICAL ACTIVITY

INSULIN THERAPY

- Patients with type 1 diabetes mellitus (DM) require lifelong insulin therapy. Most require 2 or more injections of insulin daily, with doses adjusted on the basis of self-monitoring of blood glucose levels.
- The aim of treatment in type 1 DM is to provide insulin in as physiologic a manner as possible.

BASAL INSULIN	PREPRANDIAL INSULIN
EITHER LONG OR INTERMEDIATE ACTING INSULIN	EITHER RAPID OR SHORT ACTING INSULIN

FEATURES OF DIFFERENT INSULIN PREPARATIONS

PREPARATION	PROPERTIES	ONSET	PEAK	EFFECTIVE DURATION
Rapid-acting				
Lispro	Faster onset, shorter duration	15 minutes	0.5-1.5 hr	3-4 hr
Insulin Aspart	Faster onset	15 minutes	0.5-1.5 hr	3-6 hr
Glulisine				
Short-acting				
Regular insulin		30 minutes	2 hr	3-6 hr
Intermediate-acting				
NPH insulin	Slower onset, longer duration	2-4 hr	6-10 hr	10-16 hr
Lente	Slower onset , longer duration	3-4 hr	6-12 hr	12-18 hr
Long-acting				
Ultra Lente	Slower onset, longer duration	6-10 hr	10-16 hr	18-20 hr
Glargine	Slower onset, longer duration	4 hr	-	24 hr
(Lantus)	No peak			

RAPID ACTING INSULIN

Rapid-acting insulins include:

LISPRO, ASPART AND GLULISINE

These insulins are:

- absorbed more quickly
- have a rapid onset of action (5-10 minutes),
- a short interval to peak action (45-75 minutes) and
- a short duration of action (2-4 hours).

Therefore, they can be administered shortly before eating.

SHORT ACTING INSULIN

Short-acting insulin includes:

REGULAR INSULIN

- Regular insulin is a preparation of zinc insulin crystals in solution.
- When administered subcutaneously :
  - its onset of action occurs in 0.5 hours,
  - its peak activity comes at 2.5-5 hours, and
  - its duration of action is 4-12 hours.
- The standard strength of regular insulin is 100 U/mL .

INTERMEDIATE ACTING INSULIN

Intermediate-acting insulin include:

NPH INSULIN, a crystalline suspension of human insulin with protamine and zinc.

- The onset of action usually occurs at 1-2 hours,
- the peak effect is noted at 4-12 hours and
- the duration of action is normally 14–24 hours.

NPH provides a slower onset of action and longer duration of action than regular insulin .

LONG ACTING INSULIN

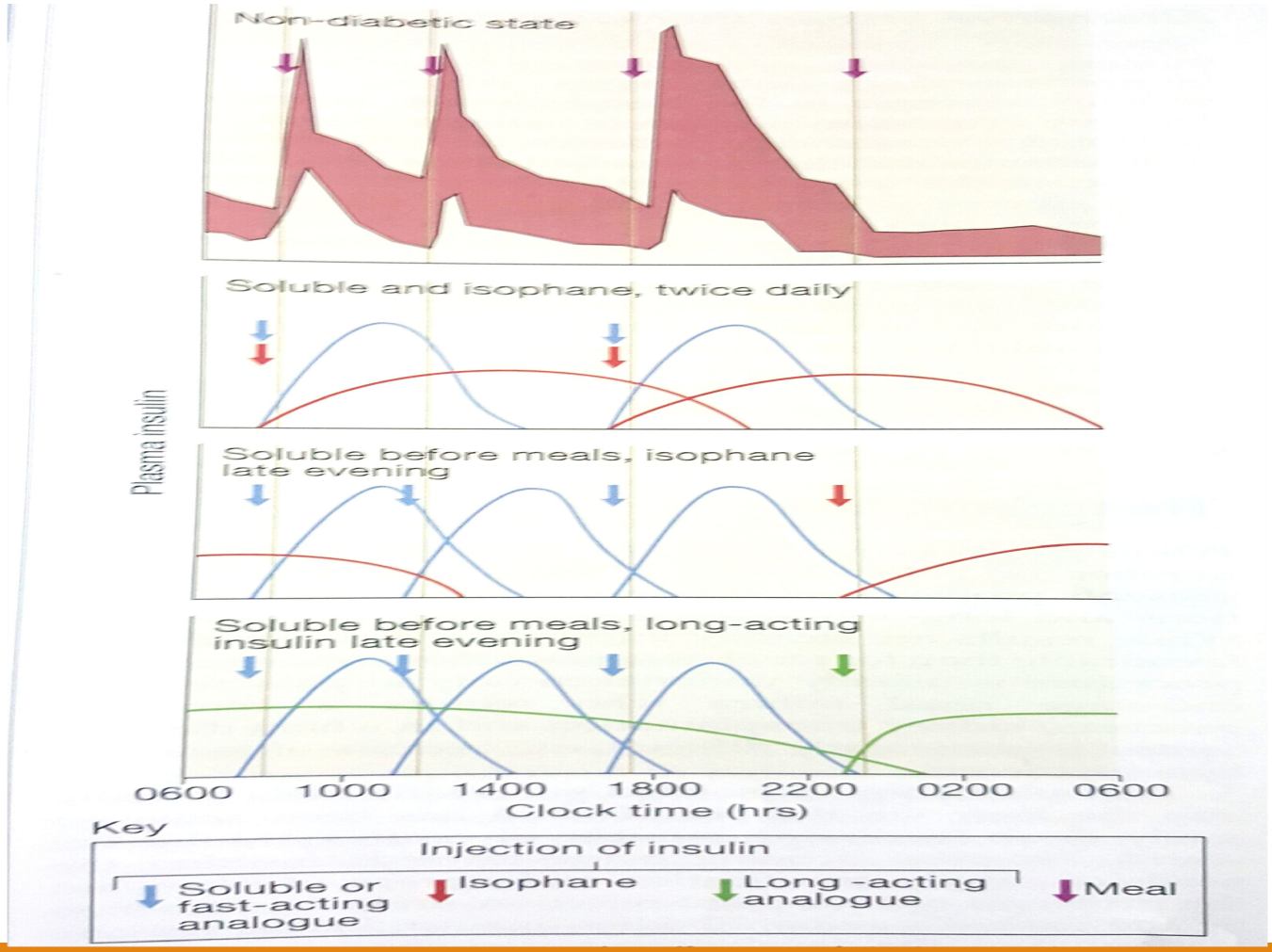
Long-acting insulins include:

INSULIN GLARGINE AND INSULIN DETEMIR

- Insulin glargine has no peak and produces a relatively stable level lasting more than 24 hours.
- Insulin detemir has a duration of action that may be substantially shorter than that of insulin glargine but longer than those of intermediate-acting insulins.

- Mixtures of insulin preparations with different onsets and durations of action frequently are administered in a single injection by drawing measured doses of 2 preparations into the same syringe immediately before use.
- The exceptions are insulin glargine and insulin detemir, which should not be mixed with any other form of insulin.
- Preparations that contain a mixture of 70% NPH and 30% regular human insulin (eg, Novolin 70/30 and Humulin 70/30) are available, but the fixed ratios of intermediate-acting to rapid-acting insulin may restrict their use.

INSULIN REGIMENS


Non-diabetic state
Soluble and isophane, twice daily
Soluble before meals, isophane late evening
Soluble before meals, long-acting insulin late evening
Plasma insulin
0600
1000
1400
1800
2200
0200
0600
Clock time (hrs)
Key
Injection of insulin
Soluble or fast-acting analogue
Isophane
Long -acting analogue
Meal

MULTIPLE DAILY INJECTIONS

Multiple subcutaneous insulin injections are administered to control hyperglycemia after meals and to maintain normal plasma glucose levels throughout the day. This may increase the risks of hypoglycemia. Therefore, patients should be well educated about their disease and about self-monitoring of plasma glucose levels.

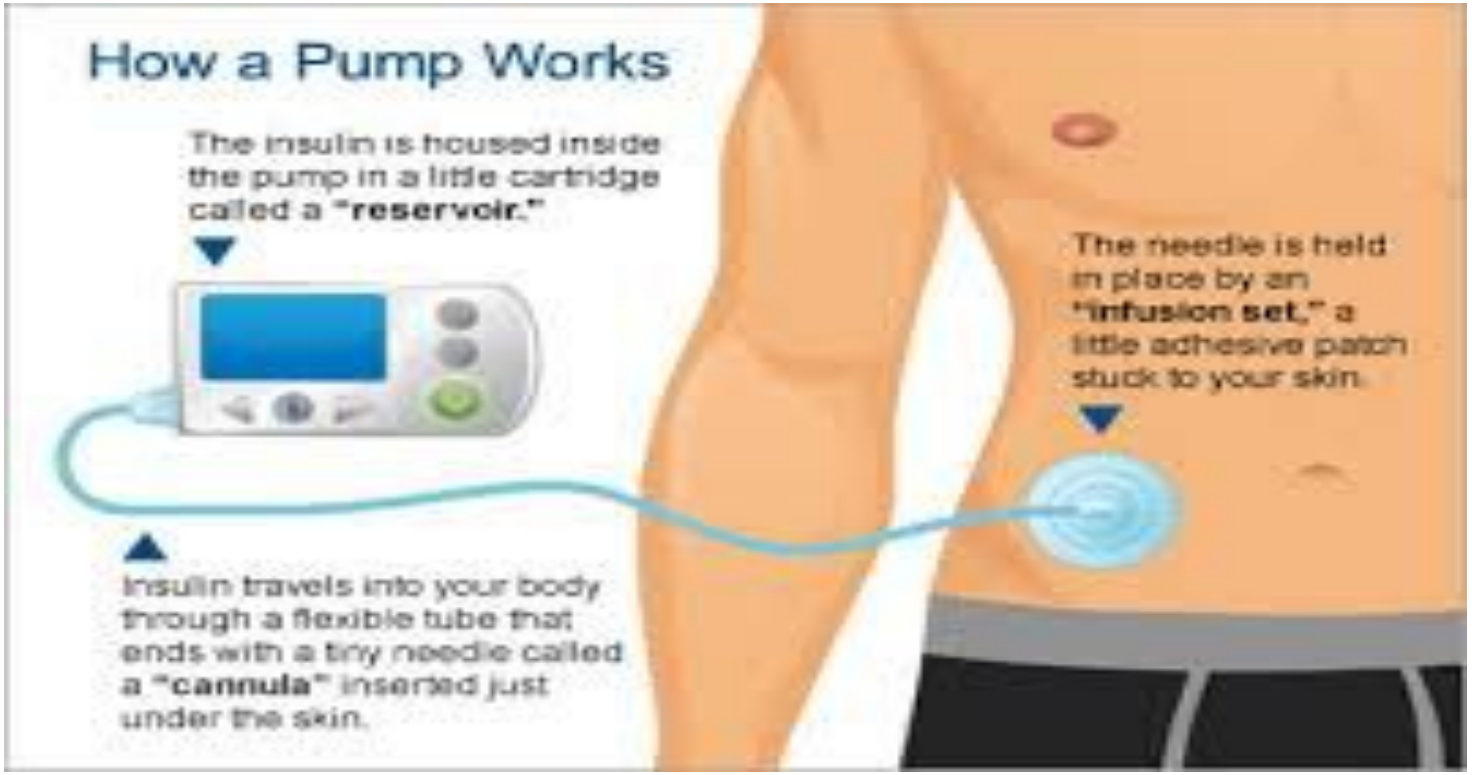
4 DOSE REGIMEN

- 25% of the total daily dose is administered as intermediate-acting insulin at bedtime,
- with additional doses of rapid-acting insulin before each meal (3 meals).

- Where available, a basal insulin such as glargine or detemir is preferred to NPH. These patients may need additional intermediate- or long-acting insulin in the morning for all-day coverage.
- Patients should adjust their daily dosage(s) on the basis of their self-monitoring of glucose levels before each meal and at bedtime.
- Patients should also assess their plasma glucose levels at 2:00-4:00 AM at least once per week during the first few weeks of treatment and thereafter as indicated.

CONTINUOUS SUBCUTANEOUS INSULIN INFUSION (INSULIN PUMP)

- A small battery-operated infusion pump that administers a continuous subcutaneous infusion of rapid-acting insulin can provide selected, programmed basal rate(s) of insulin and a manually administered bolus dose before each meal.
- The patient self-monitors preprandial glucose levels to adjust the bolus dose(s).


How a Pump Works
The insulin is housed inside the pump in a little cartridge called a "reservoir."
Insulin travels into your body through a flexible tube that ends with a tiny needle called a "cannula" inserted just under the skin.
The needle is held in place by an "infusion set," a little adhesive patch stuck to your skin.

USES OF INSULIN PUMP

1. The ability to vary basal insulin during day and night by using multiple basal rates and allowing adjustment of insulin dose for nocturnal and daytime requirement

2. To prevent early morning hyperglycemia secondary to Dawn phenomena due to early morning hormonal surges

3. Allowing alteration of basal rates during exercise and preventing post activity hypoglycemia

INITIATION OF INSULIN THERAPY

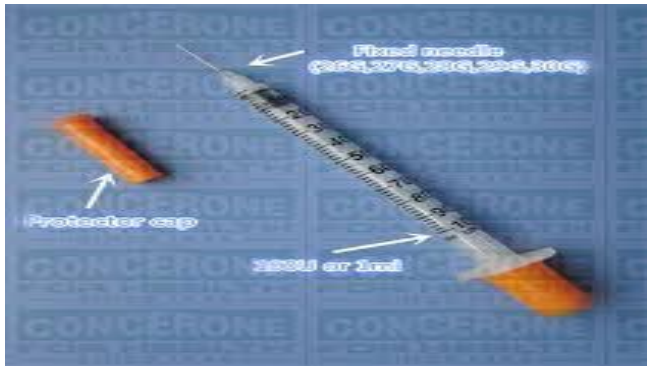
- The initial daily insulin dose is calculated on the basis of the patient's weight.
- After selecting the initial dose, adjust the amounts, types, and timing according to the plasma glucose levels. Adjust the dose to maintain pre-prandial plasma glucose at 80-150 mg/dL (i.e, 4.44-8.33 mmol/L).
- The insulin dose is often adjusted in increments of 10% at a time, and the effects are assessed over about 3 days before any further changes are made. More frequent adjustments of regular insulin can be made if a risk of hypoglycemia is present.

How to inject insulin subcutaneously?

- Needle sited at right angle to the skin
- Subcutaneous (not intramuscular) injection
- Delivery devices: Glass syringe (requires re-sterilization)
  Plastic syringe (disposable)
  Pen device (reusable, some disposable)
  Infusion pump

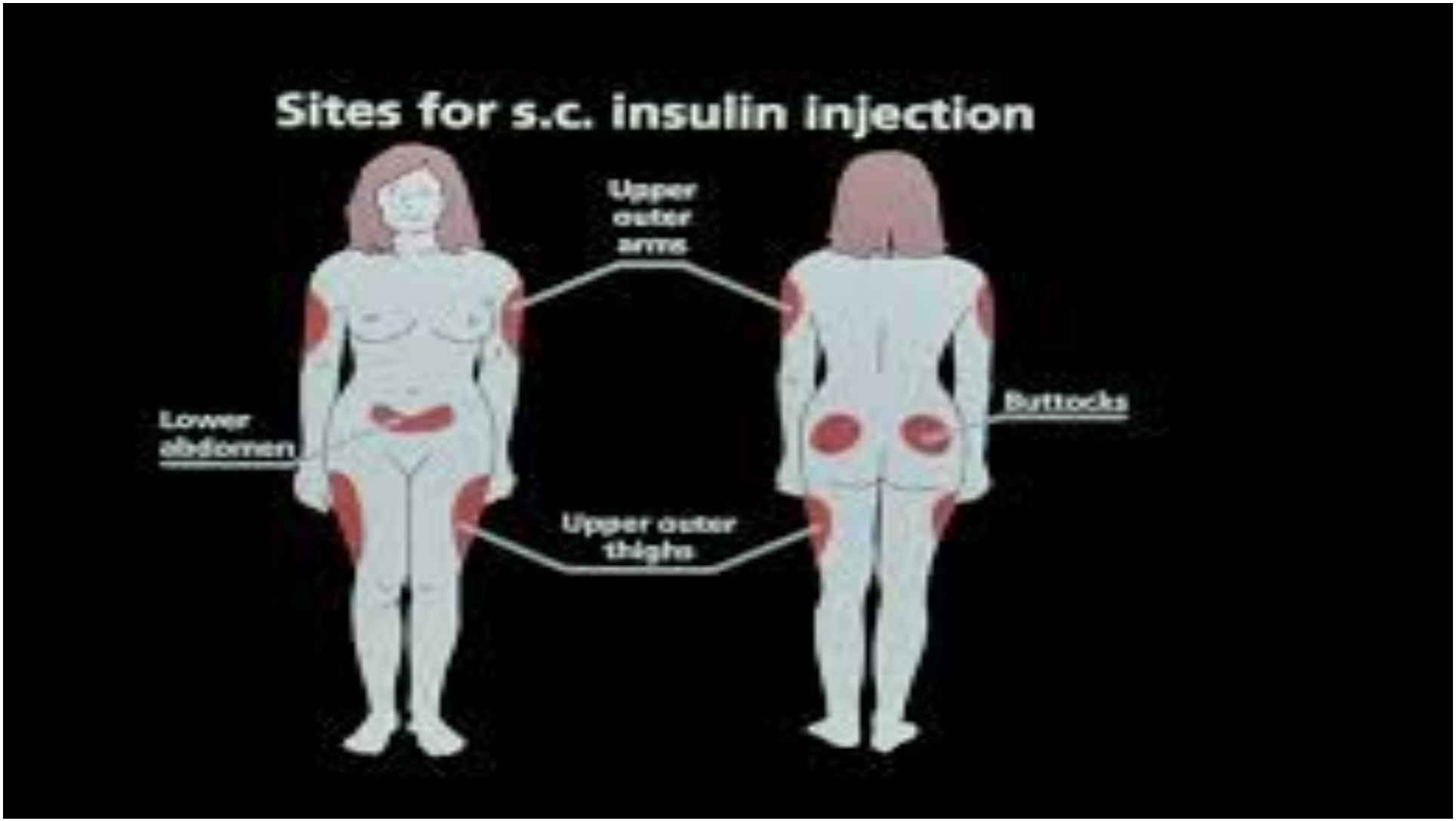
GLASS SYRINGE

PLASTIC SYRINGE



INSULIN PEN DEVICE

INSULIN PUMP


Sites for s.c. insulin injection
Upper outer arms
Lower abdomen
Buttocks
Upper outer thighs

PRECAUTIONS

- Insulin is sensitive to heat and exposure to oxygen. Once a bottle of insulin is opened, it should be used for no more than 28 days and then discarded; even if there is still some insulin in the bottle, it may have lost its clinical effectiveness.
- Insulin kept in a pump reservoir for longer than 3 days may lose its clinical effectiveness.

PRECAUTIONS

- **<u>If drawing a mixed dose,</u>**

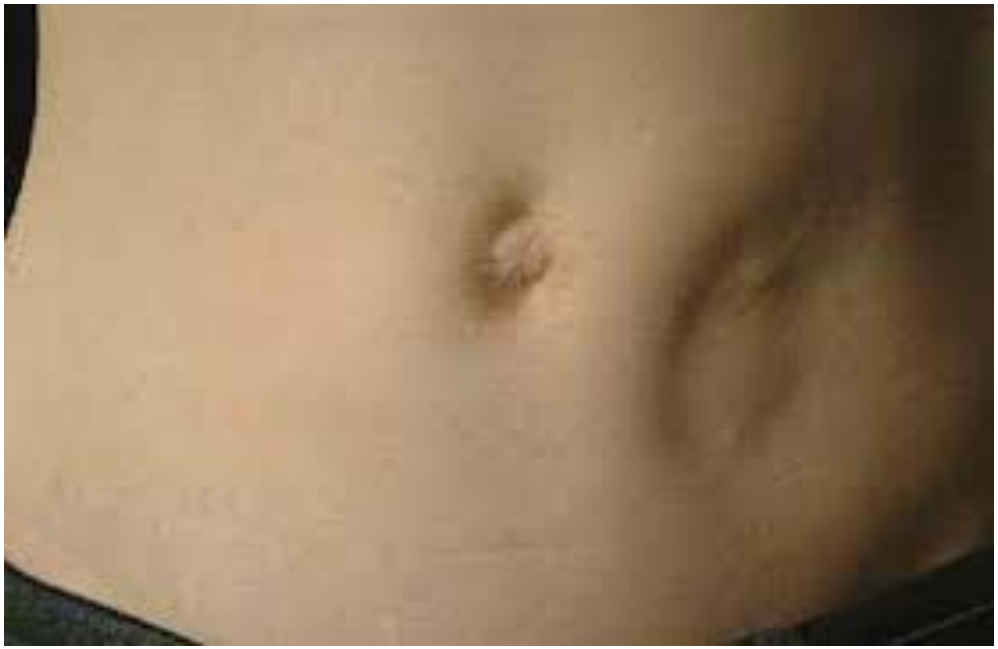
✓Short acting insulin is drawn before intermediate acting(cloudy) insulin as accidental introduction of long acting insulin in short acting insulin can increase the duration of action of short acting insulin.

✓Meals are planned as 3meals per day incorporating 2or 3 snacks

SIDE-EFFECTS OF INSULIN THERAPY

- Hypoglycemia
- Weight gain
- Peripheral edema (insulin treatment causes salt and water retention in short term)
- Insulin antibodies(with animal insulin)
- Local allergy (rare)
- Lipohypertrophy and lipoatrophy at injection sites

LIPODYSTROPHY



TRANSPLANTATION

- Whole pancreas transplant is carried out in a small number of patients every year.
- At present, it is undertaken only in patients with end stage renal failure who require both kidney and pancreas transplant and in whom diabetes control is particularly difficult.
- However, following whole pancreas transplantation problems relating to exocrine pancreatic secretions and long term immunosuppression are yet to be overcome.
- Transplantation of isolated pancreatic islets has been achieved safely in increasing number of patients worldwide.

NUTRITIONAL THERAPY

Diet management includes:

- A daily caloric intake prescription
- Recommendations for amounts of dietary carbohydrate, fat, and protein
- Instructions on how to divide calories between meals and snacks

….contd.

- The minimum protein requirement for good nutrition is 0.9 g/kg/day (usual range, 1-1.5 g/kg/day), but a reduced protein intake is indicated in cases of nephropathy.
- Fat intake should be limited to no more than 30% of the total calories, and a low-cholesterol diet is recommended.
- Patients should minimize consumption of sugars. Carbohydrates intake should be limited to 45-60% of diet.
- Fruits and vegetables : 5 portions daily
- Adequate fiber intake.

….contd.

A recommended distribution consists of:

- 20% of daily calories for breakfast,
- 35% for lunch,
- 30% for dinner and
- 15% for a late-evening snack.

PHYSICAL ACTIVITY

- Patients should be encouraged to exercise regularly.
- Educate the patients about the effects of exercise on the blood glucose level. If patients participate in rigorous exercise for more than 30 minutes, they may develop hypoglycemia unless they either decrease the preceding insulin injection by 10-20% or have an extra snack.
- Patients must also make sure to maintain their hydration status during exercise.

GOALS 0F BLOOD SUGAR AND GLYCATED HEMOGLOBIN

	TODDLERS AND PRE-SCHOOLERS (0-6 YEARS)	SCHOOL AGE (6-12 YEARS)	ADOLESCENTS AND YOUNG ADULTS
PRE-MEAL GLUCOSE	100-180 mg/dL	90-180mg/dL	90-130 mg/dL
BEDTIME AND OVERNIGHT GLUCOSE	110-200 mg/dL	100-180 mg/dL	90-150 mg/dL
Hb A_{1c}	<8.5%	<8.0%	<7.5%

SICK DAY CARE

- Children with diabetes require careful monitoring at home when they are ill or ketotic.
- Children who have high blood sugars >240 mg/dL and or are ill should be tested for ketosis.
- Beta-hydroxybutyrate and acetoacetic acid can be measured in blood or urine.
- Based on level of ketosis additional insulin is provided every 2hr. This ranges from 5-20% of total daily dose as short acting insulin.
- Blood sugar is monitored and patients are advised to administer additional oral fluids.
- Children are to be brought to emergency if there are any signs of persistent ketosis.

THANK YOU

Tests to Differentiate Type 1 from Type 2 Diabetes

Although the oral glucose tolerance test with insulin levels is usually considered unnecessary for diagnosing type 1 DM, the dramatic increase of type 2 DM in the young suggests that assessment of insulin secretion may become more important. The 2011 American Association of Clinical Endocrinologists (AACE) guidelines note that to help distinguish between the 2 types in children, physicians should measure insulin and C-peptide levels and immune markers (eg, glutamic acid decarboxylase [GAD] autoantibodies), as well as obtain a detailed family history.[61]

C-peptide is formed during conversion of proinsulin to insulin. An insulin or C-peptide level below 5 µU/mL (0.6 ng/mL) suggests type 1 DM; a fasting C-peptide level greater than 1 ng/dL in a patient who has had diabetes for more than 1-2 years is suggestive of type 2 (ie, residual beta-cell function). An exception is the individual with type 2 DM who presents with a very high glucose level (eg, >300 mg/dL) and a temporarily low insulin or C-peptide level but who will recover insulin production once normal glucose is restored.

Most patients who present with undiagnosed type 1 DM have the classic symptoms of uncontrolled hyperglycemia, including polyuria, polydipsia, nocturia, fatigue, and weight loss. In these patients, a confirmatory random plasma glucose level of greater than 200 mg/dL is adequate to establish the diagnosis of DM. On occasion, a patient who is ultimately found to have type 1 DM presents with subtle symptoms because of residual insulin secretion.

Islet-cell (IA2), anti-GAD65, and anti-insulin autoantibodies can be present in early type 1 but not type 2 DM. Measurements of IA2 autoantibodies within 6 months of diagnosis can help differentiate between type 1 and type 2 DM. These titers decrease after 6 months. Anti-GAD65 antibodies can be present at diagnosis of type 1 DM and are persistently positive over time. (See also Type 2 Diabetes Mellitus.)

Testing for islet autoantibodies can substitute for expensive genetic testing in those patients suspected of having maturity-onset diabetes of the young (MODY). The prevalence of these antibodies is the same in patients with MODY as in the healthy population. A positive test for positive islet autoantibodies makes MODY highly unlikely.[66]

Differential Diagnoses

Diabetic Ketoacidosis
Diabetic Nephropathy
Diabetic Ulcers
Insulin Resistance
Lead Nephropathy
Type 2 Diabetes Mellitus

Class Summary

Rapid-acting insulins are used whenever a rapid onset and short duration are appropriate (eg, before meals or when the blood glucose level exceeds target and a correction dose is needed). Rapid-acting insulins are associated with less hypoglycemia than regular insulin.

Currently, short-acting insulins are less commonly used than the rapid-acting insulins in patients with type 1 DM. They are used when a slightly slower onset of action or a greater duration of action is desired.

Intermediate-acting insulins have a relatively slow onset of action and a relatively long duration of action. They are usually combined with faster-acting insulins to maximize the benefits of a single injection.

Long-acting insulins have a very long duration of action and, when combined with faster-acting insulins, provide better glucose control for some patients. In patients with type 1 DM, they must be used in conjunction with a rapid-acting or short-acting insulin given before meals.

Premixed insulins contain a fixed ratio of rapid-acting insulins with longer-acting insulin, which can restrict their use. Premixed insulin is usually not recommended in type 1 DM patients, because of their need for frequent adjustments of premeal insulin doses.

Plasma glucose

Patients with type 1 diabetes mellitus (DM) typically present with symptoms of uncontrolled hyperglycemia (eg, polyuria, polydipsia, polyphagia). In such cases, the diagnosis of DM can be confirmed with a random (nonfasting) plasma glucose concentration of 200 mg/dL or a fasting plasma glucose concentration of 126 mg/dL (6.99 mmol/L) or higher.[2, 61]

A fingerstick glucose test is appropriate in the emergency department (ED) for virtually all patients with diabetes. All fingerstick capillary glucose levels must be confirmed in serum or plasma to make the diagnosis. All other laboratory studies should be selected or omitted on the basis of the individual clinical situation. Intravenous (IV) glucose testing may be considered for possible early detection of subclinical diabetes.

Individually measured glucose levels may differ considerably from estimated glucose averages calculated from measured hemoglobin A_{1c} (HbA_{1c}) levels.[63] Therefore, caution is urged when the decision is made to estimate rather than actually measure glucose concentration; the difference between the 2 has a potential impact on decision making.

Hemoglobin A

Hb is the stable product of nonenzymatic irreversible glycation of the beta chain of hemoglobin by plasma glucose and is formed at rates that increase with increasing plasma glucose levels. HbA_{1c} levels provide an estimate of plasma glucose levels during the preceding 1-3 months. The reference range for nondiabetic people is 6% in most laboratories. Glycated hemoglobin levels also predict the progression of diabetic microvascular complications.

American Diabetes Association (ADA) guidelines recommend measuring HbA_{1c} at least every 6 months in patients with diabetes who are meeting treatment goals and who have stable glycemic control. For patients whose therapy has changed or who are not meeting glycemic goals, the guidelines recommend HbA_{1c} testing every 3 months.[5]

Other laboratory studies

Fructosamine levels also test for glucose levels. Fructosamine is formed by a chemical reaction of glucose with plasma protein and reflects glucose control in the previous 1-3 weeks. This assay, therefore, may show a change in control before HbA_{1c} and often is helpful when applying intensive treatment and in short-term clinical trials.

A white blood cell (WBC) count and blood and urine cultures may be performed to rule out infection

The American Association of Clinical Endocrinologists and American College of Endocrinology released a consensus statement on insulin pump management:[96]

Based on currently available data, continuous subcutaneous insulin infusion (CSII) is justified for basal-bolus insulin therapy in patients with type 1 diabetes mellitus.

Only providers whose practice can assume full responsibility for a comprehensive pump management program should offer this technology.

The ideal CSII candidate is a patient with type 1 diabetes mellitus or intensively management insulin-dependent type 2 diabetes mellitus who is currently performing 4 or more insulin injections and 4 or more self-monitored blood glucose measurements daily; is motivated to achieve optima blood glucose control; is willing and able to carry out the tasks that are required to use this complex and time-consuming therapy safely and effectively; and is willing to maintain frequent contact with their health care team.

Adult patients At CSII initiation, the patient should have daily contact with the pump trainer. a return visit with the endocrinologist/diabetologist/advanced practice nurse is advised within 3-7 days after CSII initiation.

Educational consults should be scheduled weekly or biweekly at first, then periodically as needed.

Specialist follow-up visits should be scheduled at least monthly until the pump regimen is stabilized, then at least once every 3 mo.

Pediatric patients CSII is indicated for pediatric patients with elevated hemoglobin A1C (HbA1C) levels on injection therapy; frequent, severe hypoglycemia; widely fluctuating glucose levels; a treatment regimen that compromises lifestyle; and microvascular complications and/or risk factors for macrovascular complications.

Ideal pediatric candidates are those with motivated families who are committed to monitoring blood glucose 4 or more times per day and have a working understanding of basic diabetes management.

Patient age and duration of diabetes should not be factors in determining the transition from injections to CSII.

INSULIN REGIMENS

Common insulin regimens include the following:

- Split or mixed – NPH with rapid-acting (eg, lispro, aspart, or glulisine) or regular insulin before breakfast and supper
- Split or mixed variant – NPH with rapid-acting or regular insulin before breakfast, rapid-acting or regular insulin before supper, and NPH before bedtime (the idea is to reduce fasting hypoglycemia by giving the NPH later in the evening)
- Multiple daily injections (MDI) – A long-acting insulin (eg, glargine or detemir) once a day in the morning or evening (or twice a day in about 20% of patients) and a rapid-acting insulin before meals or snacks (with the dose adjusted according to the carbohydrate intake and the blood glucose level)
- Continuous subcutaneous insulin infusion (CSII) – Rapid-acting insulin infused continuously 24 hours a day through an insulin pump at 1 or more basal rates, with additional boluses given before each meal and correction doses administered if blood glucose levels exceed target levels