Diabetes type 1: Clinical management (2)

– Glycemic targets & Insulin treatment-

AHLAM HAMDI DAHADHA

DM I – Glycemic targets/Assessment

Assessment of Glycemic Control:

Two primary techniques available to assess effectiveness of management:

1. **Patient self-monitoring of blood glucose (SMBG)**
2. **A1C**

Continuous Glucose Monitoring (CGM) or interstitial glucose may have an important role assessing the effectiveness and safety of treatment in selected patients.

American Diabetes Association Standards of Medical Care in Diabetes.
Glycemic targets. Diabetes Care 2017; 40 (Suppl. 1): S48-S56

DM I – Glycemic targets / SMBG

Most patients on multiple-dose insulin (MDI) or insulin pump therapy should do SMBG

- Prior to meals and snacks
- At bedtime
- Prior to exercise
- When they suspect low blood glucose
- After treating low blood glucose until they are normoglycemic
- Prior to critical tasks such as driving
- Occasionally postprandially

DM I – Glycemic targets / SMBG- Adults

- SMBG results may be helpful to **guide treatment decisions and/or patient self-management** for patients using less frequent insulin injections or noninsulin therapies.

- Ensure Pt receives ongoing instruction and regular evaluation of SMBG technique and results, and ability to use SMBG data to adjust therapy.

American Diabetes Association Standards of Medical Care in Diabetes.
Glycemic targets. Diabetes Care 2017; 40 (Suppl. 1): S48-S56

DM I – Glycemic targets /CGM - Adults

- Assess individual readiness for continuing use of CGM prior to prescribing.

- Robust diabetes education, training, and support are required for optimal CGM implementation and ongoing use.

DM I – Glycemic targets/CGM - Adults

- When used properly, CGM in conjunction with intensive insulin regimens is a useful tool to lower A1C in selected adults (aged ≥ 25 years) with type 1 diabetes.
- Although the evidence for A1C lowering is less strong in children, teens, and younger adults, CGM may be helpful in these groups.

→Success correlates with adherence to ongoing use of the device.

- CGM may be a supplemental tool to SMBG in those with hypoglycemia unawareness and/or frequent hypoglycemic episodes.

American Diabetes Association Standards of Medical Care in Diabetes.
Glycemic targets. Diabetes Care 2017; 40 (Suppl. 1): S48-S56

DM I – Glycemic targets / SMBG- Children & adolescents

- Ongoing monitoring allows the child and family to become familiar with the patient's glycemic response to different types and amount of foods, exercise, and stress

- Decrease the frequency of severe hypoglycemic episodes.

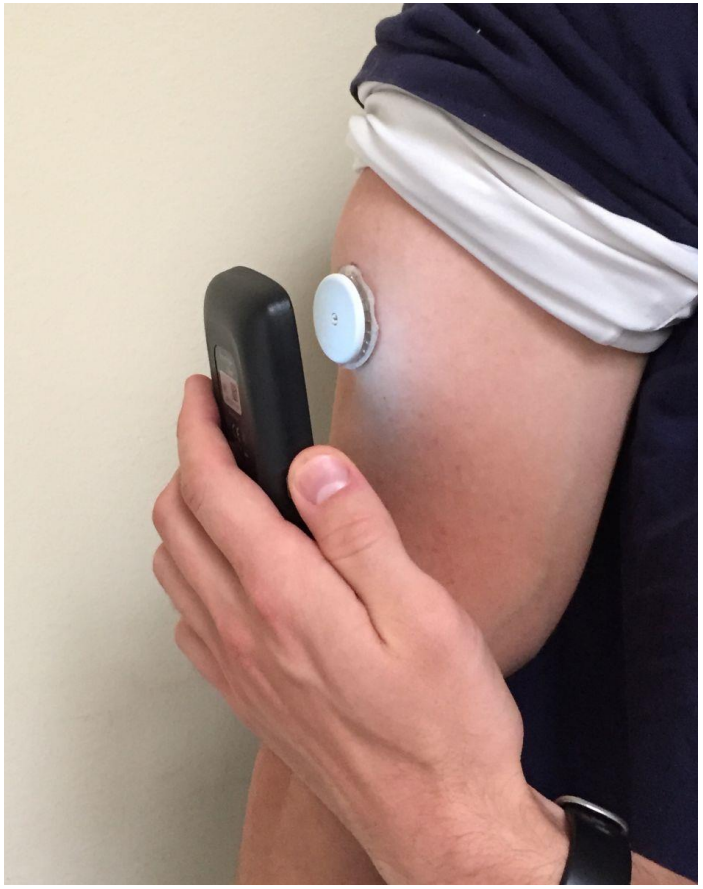
- Generally , the frequency of SGMB is highest in children under the age of six years and decreases with increasing age

DM I – Glycemic targets / SMBG & CGM- Children & adolescents

- **Fingersticks** — ADA recommends at least four times a day, more frequent monitoring may be required/ in intensive management ?

- **Continuous glucose monitoring** — **Subcutaneous glucose sensors** that continuously measure interstitial fluid glucose levels are now available and approved for use in children.

DM I – Glycemic targets / SMBG & CGM



DM I – Glycemic targets/ A1C- Adults

- Perform A1C test at least 2x annually in patients that meet treatment goals.
- Perform the A1C test *quarterly* in patients whose therapy has changed or who are not meeting glycemic goals.
- Use of point-of-care (POC) testing for A1C provides the opportunity for more timely treatment changes.

American Diabetes Association Standards of Medical Care in Diabetes.
Glycemic targets. Diabetes Care 2017; 40 (Suppl. 1): S48-S56

Mean Glucose Levels for Specified A1C Levels

	Mean Glucose					
	Mean Plasma Glucose*		Fasting	Premeal	Postmeal	Bedtime
A1C%	mg/dL	mmol/L	mg/dL	mg/dL	mg/dL	mg/dL
6	126	7.0				
<6.5			122	118	144	136
6.5-6.99			142	139	164	153
7	154	8.6				
7.0-7.49			152	152	176	177
7.5-7.99			167	155	189	175
8	183	10.2				
8-8.5			178	179	206	222
9	212	11.8				
10	240	13.4				
11	269	14.9				
12	298	16.5				

professional.diabetes.org/eAG

American Diabetes Association Standards of Medical Care in Diabetes.
Glycemic targets. Diabetes Care 2017; 40 (Suppl. 1): S48-S56

DM I – Glycemic targets/ goals in adults

Glycemic Recommendations for Nonpregnant Adults with Diabetes

A1C	<7.0%* (<53 mmol/mol)
Preprandial capillary plasma glucose	**80–130 mg/dL* (4.4–7.2 mmol/L)**
Peak postprandial capillary plasma glucose†	**<180 mg/dL* (<10.0 mmol/L)**

* Goals should be individualized.

† Postprandial glucose measurements should be made 1–2 hours after the beginning of the meal.

American Diabetes Association Standards of Medical Care in Diabetes. Glycemic targets. Diabetes Care 2017; 40 (Suppl. 1): S48-S56

DM I management in children & adolescents/ Glycemic goals

Values by age	Plasma blood glucose goal range (mg/dl)		A1C	Rationale
	Before meals	Bedtime/overnight		
Toddlers and preschoolers (<6 years)	100-180	110-200	<8.5 percent	Vulnerability to hypoglycemia
				Insulin sensitivity
				Unpredictable dietary intake and physical activity
				A lower goal (<8 percent) is reasonable if it can be achieved without excessive hypoglycemia
School age (6-12 years)	90-180	100-180	<8 percent	Vulnerability to hypoglycemia
				A lower goal (<7.5 percent) is reasonable if it can be achieved without excessive hypoglycemia
Adolescents and young adults (13-19 years)	90-130	90-150	<7.5 percent	A lower goal (<7 percent) is reasonable if it can be achieved without excessive hypoglycemia

Approach to the Management of Hyperglycemia

Patient/Disease Features

Risk of hypoglycemia/drug adverse effects

Disease Duration

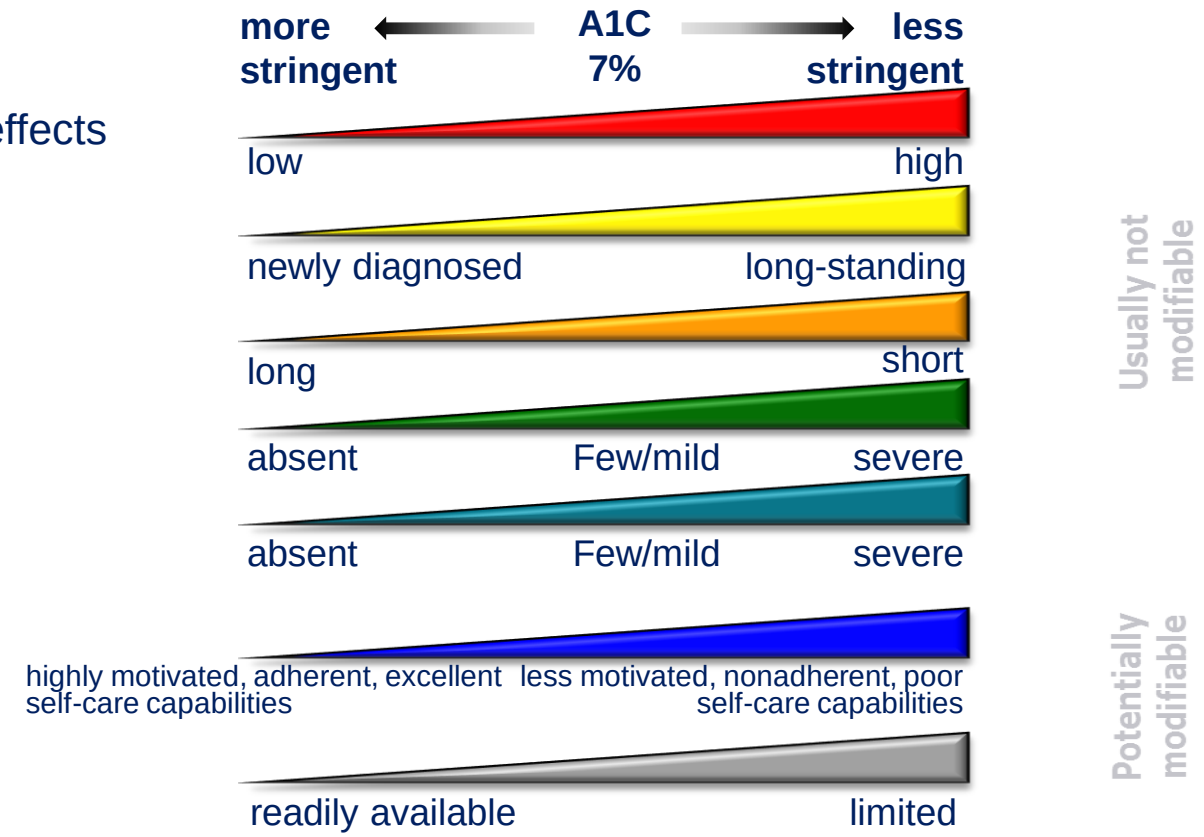
Life expectancy

Relevant comorbidities

Established vascular complications

Patient attitude & expected treatment efforts

Resources & support system



American Diabetes Association Standards of Medical Care in Diabetes. Glycemic targets. Diabetes Care 2017; 40 (Suppl. 1): S48-S56

American Diabetes Association Standards of Medical Care in Diabetes. Glycemic targets. Diabetes Care 2017; 40 (Suppl. 1): S48-S56

DM I management in children & adolescents

- **Why is it different from adult care:**

- Differences in the size of the patients.
- **Developmental issues** → unpredictability of a toddler's dietary intake and activity level
- **Medical issues** → increased risk of hypoglycemia and diabetic ketoacidosis.

** **Because of this , the management of a child with type 1 diabetes must take into account the age and developmental maturity of the child** **

DM I management in children & adolescents / Successful management:

- **Balancing strict glycemic control**, which reduces the risk of long-term complications, **and avoidance of severe hypoglycemia.**
- **Setting realistic goals for each child and family.**
- Maintaining normal growth, development, and emotional maturation.
- **Training the patient and family** to provide appropriate daily diabetes care.

DM I management in children & adolescents

Training and care of the patient and family is divided into two management phases:

- ✓**Initial management** — Initiate therapy with insulin , age-appropriate essential skills for optimal diabetes care

- ✓**Ongoing management** — Continued care, education, and support for the child and family

DM I management in children & adolescents / Initial management

At the time of diagnosis, in the first few days:

- **Basic understanding-** Cases and treatment
- **Insulin administration-** insulin types, dosage and injection sites.
- **Blood glucose testing-** Frequency & timing, glucometers.
- **Ketonuria-** Check urine for ketones.
- **Hypoglycemia-** recognize signs and symptoms, treatment.

DM I management in children & adolescents/ Ongoing management

After the initial phase, the diabetes team continues to provide care, teaching, and support to the child and family.

- The interaction of insulin, diet, and exercise on blood glucose concentrations.
- Management regimen specific for each patient
- Strict glycemic control to prevent long-term sequelae
- Age-appropriate psychosocial support for the patient and the family.
- Age-appropriate care- in previous lecture.

DM I – Insulin treatment

DM I – Insulin replacement

- The objective of insulin replacement is to **mimic the insulin** secretion pattern in the person without diabetes with multiple subcutaneous injections.
- In the person without diabetes, there is normally a rapid increase in plasma insulin after meals, triggered by glucose absorption into the bloodstream.
- This surge in insulin limits postprandial glycaemia by stimulating hepatic and peripheral glucose uptake.

DM I – Insulin replacement

- During fasting and between meals, insulin measurements drop to much lower levels (**often called basal or steady state**) which are sufficient to maintain blood glucose in the range 65-100gm/dl.

•Even after a prolonged fast, it is possible to detect circulating insulin.

•Basal insulin levels tend to be highest in the **early morning**, probably in response to the well-described surge in growth hormone and cortisol at that time of day.

–These counter-regulatory hormones tend to increase blood glucose and this has been termed the '**dawn phenomenon**'.

DM I – Insulin replacement

- Insulin is usually injected subcutaneously .
- Other routes such as intravenous infusion or intramuscular injection have **not proven practical in the long term** and despite intensive research, oral insulin preparations are not yet available.
- Until the 1980s, insulin was extracted and purified from animal sources.

→ Porcine and bovine insulins are still available but have been largely replaced by human sequence insulin produced **from genetically engineered bacteria**. Recently modified human insulin molecules (so-called analogues) have now been developed.

DM I – Insulin replacement

Insulin regimens comprise:

–short-acting / rapid acting (soluble, regular or analogue) insulin to simulate the normal mealtime surge

–A longer acting insulin which is used to provide the background or basal concentration.

–This combination is called the **‘basal-bolus’** regimen or multiple daily injection (MDI) therapy

DM I – Insulin replacement

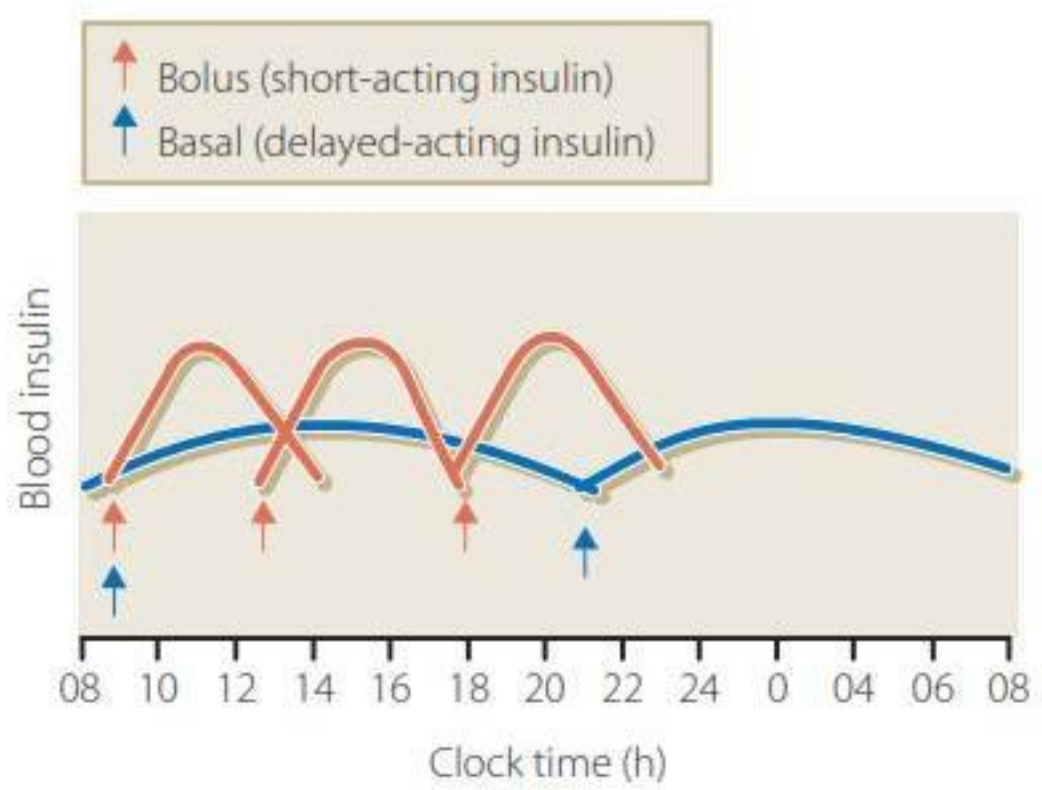


Figure 10.2 Basal-bolus insulin regimen.

Type	Onset (Hrs)	Peak (Hrs)	Duration (Hrs)	Comments
Rapid-acting				
Lispro Insulin	0.25	1	2-3	Shouldn’t be used intravenously
Insulin Aspart	0.25	1	2-3	
Short-Acting				
Regular Human Insulin	0.5-1	2-4	4-6	Longer action if larger dose (mass action effect)
Intermediate-Acting				
NPH Human	0.5-1	4-6	8-16	
Long-Acting				
Insulin Glargine	0.5-1	none	23-26	Basal insulin-minimal or no peak- cannot be mixed with other

DM I – Rapid-acting and short-acting insulin

Rapid-acting and short-acting insulin:

- **T**ypically administered as a premeal bolus (5 to 15 mins pre-meal) for the rapid-acting, and 20 to 30 mins for the short-acting type)

- **Dosage is based on : (1) carbohydrate content of food and (2) the blood glucose level.**

- If necessary, rapid-acting insulin can be administered after meal in younger children when intake is unpredictable.

- **Rapid- and short-acting insulins delivered by continuous subcutaneous infusion via an insulin pump provide basal insulin levels.**

DM I – Rapid-acting Vs. short- acting insulin

- Faster onset and shorter duration than regular insulin (short-acting)

→ modifications have been made in the insulin molecule to prevent it from forming polymers and other complexes that slow absorption and delay action.

It has the following advantages when compared to regular insulin:

- It decreases the postprandial rise in blood glucose concentration.

- More convenient → it can be injected 10 to 15 minutes prior to or immediately after meals,

BUT regular insulin should be given 30 to 45 minutes or more before meals to optimally match the high blood suger after a meal.

DM I – Rapid-acting Vs. short- acting insulin

Despite these advantages, the results from clinical trials have been somewhat disappointing.

→ **Meta-analyses of randomized trials (involving 5925 patients with type 1 diabetes) that compared rapid-acting insulin analogues with regular insulin showed only a minor benefit of insulin analogs in terms of A1C values**

** One disadvantage of rapid-acting insulins is their higher cost

DM I – Intermediate and long acting insulin

- **Intermediate-acting NPH insulin**

- NPO (neutral protamine Hagedorn, named after its inventor); an insoluble suspension of insulin made by combining it with the highly basic protein protamine, together with zinc, at a neutral pH.

- Usually given two or three times a day, but may be given in a targeted manner in combination with long-acting insulins.

- Provides some coverage for meals (eg, NPH insulin given before breakfast will cover lunch).

- Because of the duration of action , there was a tendency for patients to develop **nocturnal hypoglycaemia.**

DM I – Intermediate and long acting insulin

As a result of this, two longer-acting insulin analogues have been developed which have **a flatter absorption profile**

–Glargine (no significant effect on glycemic control, better for hypoglycemia)

- **Long-acting insulin preparations**

- Given once or twice a day.

- Provide a basal insulin level that suppresses hepatic glucose production and maintains near-normal glucose levels in the fasting state.

DM I – insulin administration/types

Insulin is administered by needle and syringe, pen, or pump.

Needle and syringe:

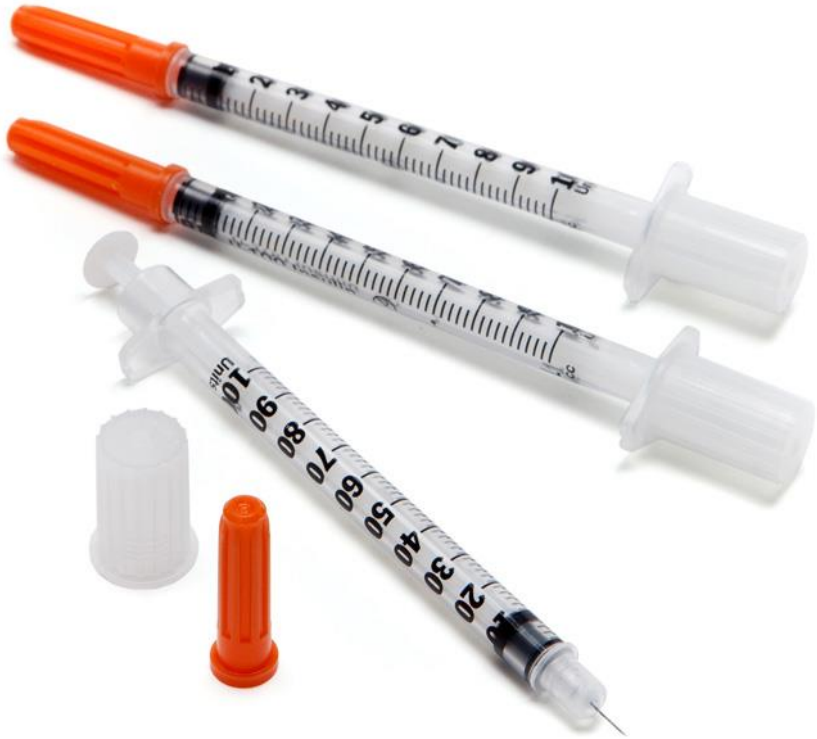
- An advantage of needle and syringe is that NPH and short- or rapid-acting insulins can be mixed in a single injection, thereby reducing the number of injections.
- However, insulin glargine cannot be mixed with any other form of insulin and must be administered separately.
- Syringes are available in 30 (0.3 mL), 50 (0.5 mL), and 100 (1 mL) unit sizes.

DM I – insulin administration/types

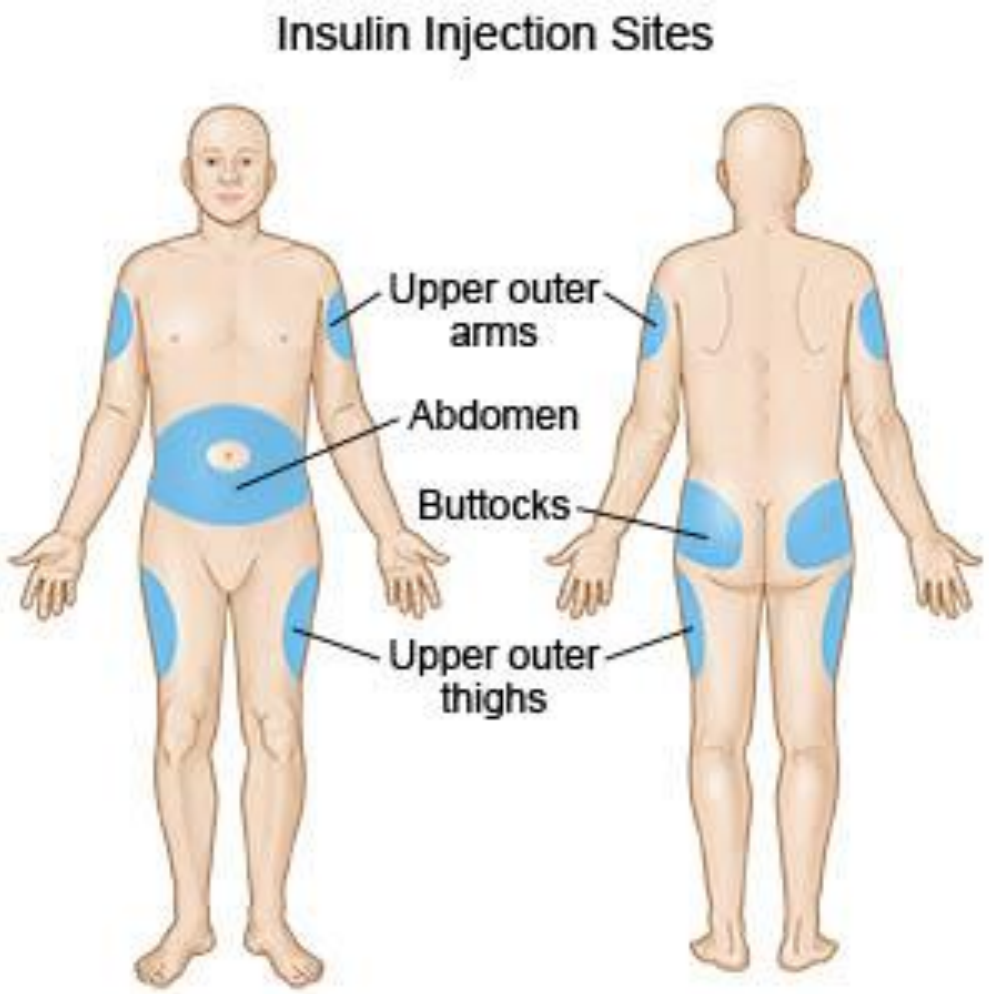
Pens :

- Supplied pre-filled with insulin and may be either disposable or reusable.
- The ease of use and portability are appealing to many patients.
- Although mixed insulin preparations are available ; these are not tailored to the needs of children.
- Mixed insulin pens are usually reserved for individuals who are limited in their ability to make dosing decisions and, as a result, glycemia is not usually as strictly controlled.
- Pens that deliver aspart and lispro are available ; offer the flexibility of ½ unit delivery.

DM I – insulin administration/types



DM I – insulin administration/injection sites



DM I – insulin administration/issues to consider

- Insulin absorption is fastest in the abdomen and slowest in the thigh and buttocks

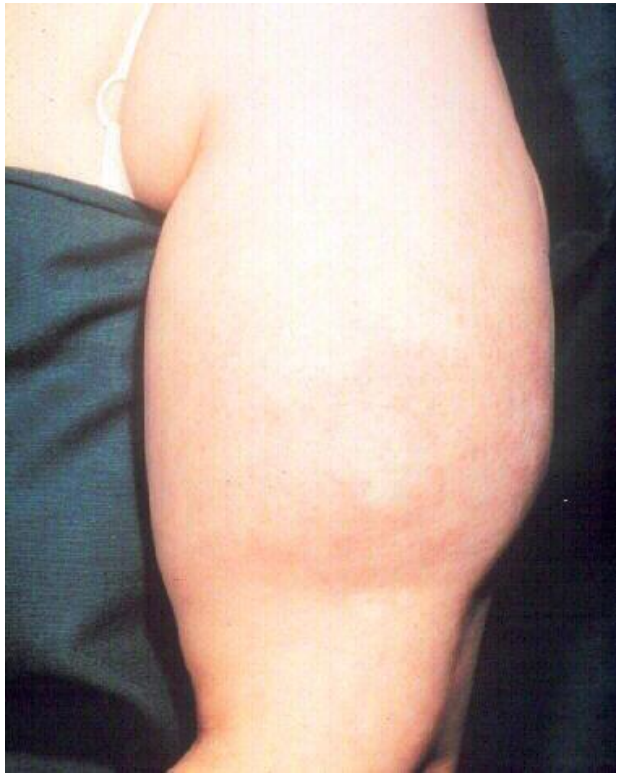
–It can be accelerated from these sites by exercise or taking a sauna or warm bath.

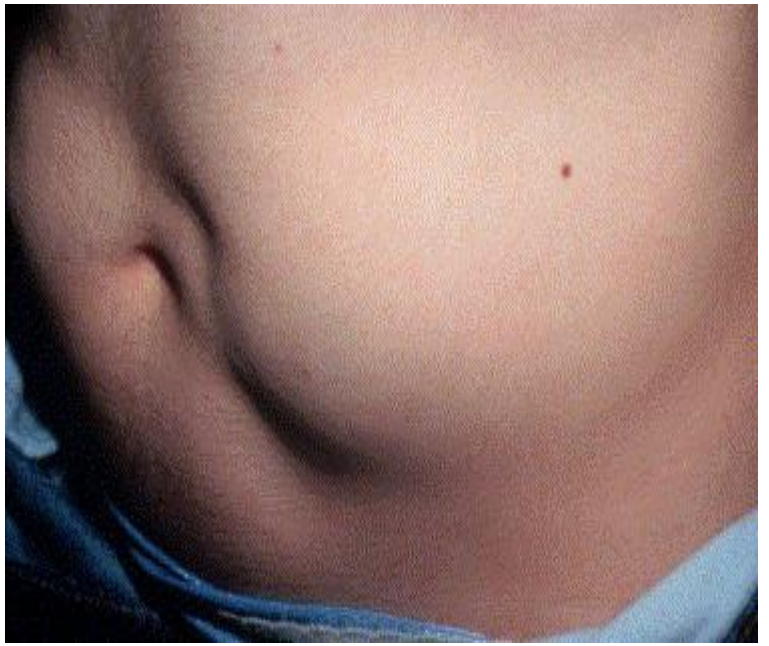
–Short-acting insulin is usually given into the abdomen, which is less affected by exercise

–longer acting insulins into the thigh

- **Repeated injection into the same subcutaneous site may, in the long term, give rise to an accumulation of fat (lipohypertrophy) because of the local trophic action of insulin**

DM I – insulin administration/issues to consider





DM I – types of regimens /Conventional regimen

- Administration of NPH at least twice a day (at breakfast and a second dose either at dinner or bedtime), with a rapid-acting or short-acting insulin 2 or 3 times a day.
- The rapid- or short-acting insulin would be given at any main meal or with the afternoon snack depending on blood glucose concentrations.
- **This regimen is fixed and the patient must adjust lifestyles so that meals and vigorous physical activity occur on a relatively fixed daily schedule**.
- 2/3 of the total daily dose is administered before breakfast and 1/3 before dinner and at bedtime as rapid.

DM I – types of regimens /Intensive regimen

- **Provides insulin in a manner that more closely approaches physiologic insulin secretion than does conventional therapy.**
- Includes an insulin preparation that will maintain:

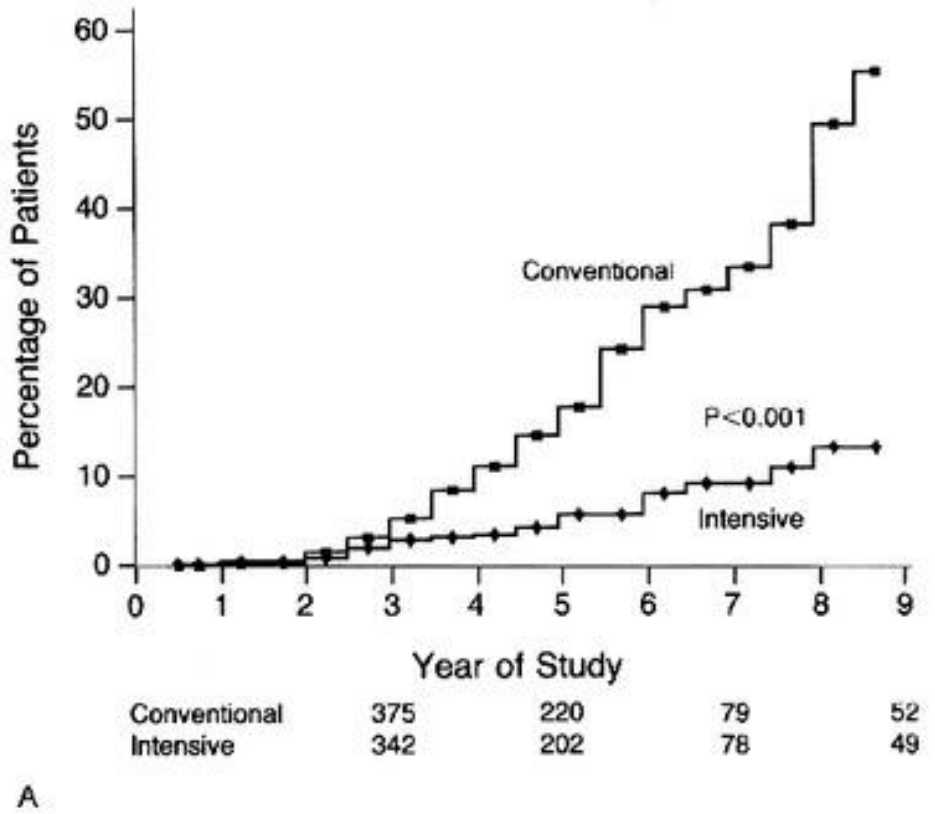
  - **A basal insulin level** and suppress lipolysis and hepatic glucose production
  - **Pre-meal boluses** of rapid- or short-acting insulin to minimize postprandial elevation of blood glucose.

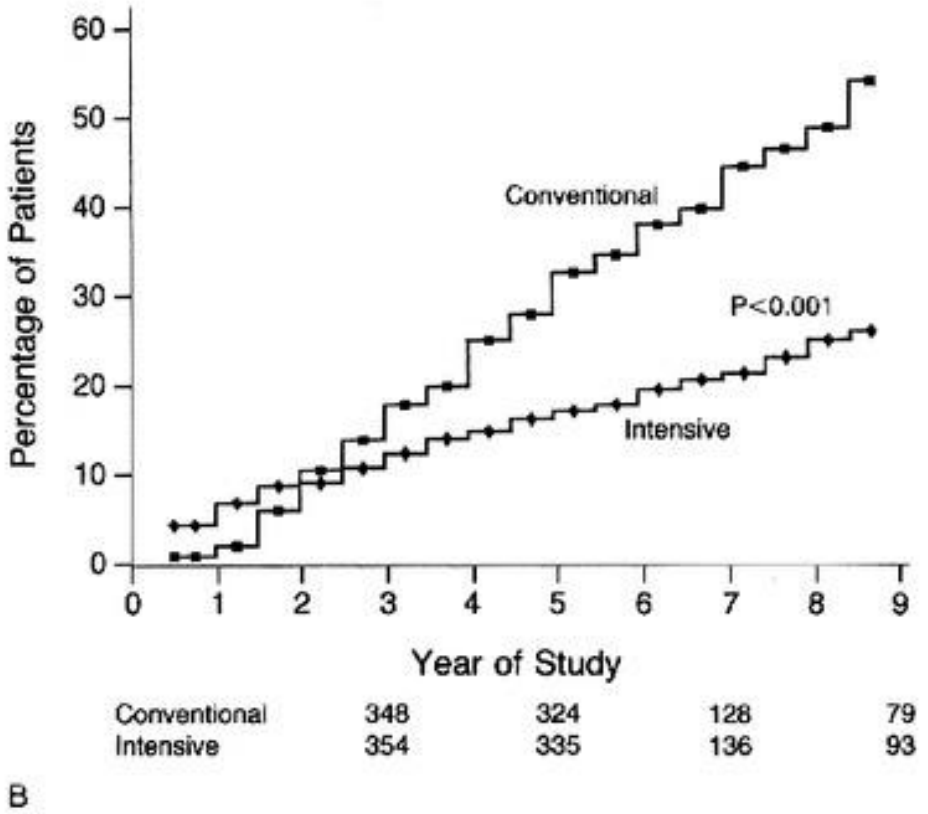
- These boluses are adjusted according to the carbohydrate content of meals as well as the current blood glucose level.

**** Allows greater flexibility than the conventional regimen in terms of timing and carbohydrate content of meals ****

The Diabetes Control and Complications trial (DCCT)

Cumulative Incidence of a Sustained Change in **Retinopathy** in Patients with IDDM Receiving Intensive or Conventional Therapy, (A) primary prevention (76%) , (B) secondary prevention (54%) .





Diabetes Control and Complications Trial Research Group, N Engl J Med 1993; 329:977.

DM I – Intensive regimen /Multiple daily injections

- Combines a baseline level of insulin using a long-acting insulin analog (insulin glargine or detemir) with premeal/snack boluses of rapid- or short-acting insulin.
- Pre-meal and pre-snack bolus doses of a rapid- or short-acting insulin are based upon three factors:

- Premeal blood glucose level
- Estimated amount of carbohydrates to be consumed
- Expected level of exercise after the meal

DM I – Intensive regimen /Multiple daily injections

- Requires increased **blood glucose monitoring and increased frequency of insulin administration**.
- The patients are required to **count dietary carbohydrates**
- Accurately judge the **impact of exercise** on insulin requirements.
- Without patient or family education, the benefits of this regimen are not attained.
- **Before initiation of MDI, the patient and family must understand and accept the increased commitment.**

DM I – Intensive regimen /insulin pump

The insulin pump (continuous subcutaneous insulin infusion) is increasingly used in the pediatrics.

→ In 2006, > 35,000 patients younger < 21 years used a pump.

DM I – Intensive regimen /insulin pump

The ADA, European Society for Pediatric Endocrinology and others recommends insulin pump for patients with one or more of these characteristics:

- ✓Recurrent severe hypoglycemia
- ✓Wide fluctuations in blood glucose levels (regardless of A1C)
- ✓Suboptimal diabetes control (A1C exceeds target range for age)
- ✓Microvascular complications and/or risk factors for macrovascular complications
- ✓Good metabolic control, but insulin regimen that compromises lifestyle

DM I – Intensive regimen /insulin pump

- Deliver a basal rate (small amount every few minutes, evenly spaced over an hour) of either rapid- or short-acting insulin subcutaneously.
- The rate of administration can be transiently increased to give **mealtime or glucose correction boluses.**
- Most insulin pump is now started with a rapid-acting insulin, rather than short-acting insulin.
- Pre-meal/snack boluses are administered to minimize increases in postprandial glucose concentrations.
- **Insulin is delivered through a subcutaneously inserted catheter that is replaced at two- to three-day intervals.**

DM I – Intensive regimen /insulin pump efficacy

The following reports describe some of the beneficial effects of insulin pump therapy:

- An RDT of 32 children demonstrated that insulin pump therapy compared to MDI resulted in lower A1C levels (7.2 versus 8.1 percent).
- A meta-analysis of six randomized controlled trials revealed lower glycated hemoglobin levels and reduction of daily insulin doses in children using the insulin pump as compared MDI .
- A meta-analysis reported a reduction in severe hypoglycemia in patients using the insulin pump compared with MDI.

DM I – Intensive regimen /insulin pump efficacy

- **Insulin pump therapy has also been used in conjunction with a continuous glucose monitoring device**

→To give the patient more information about their blood glucose levels and

→ Allow them to make better-informed decisions about insulin dosing; this approach is known as **sensor-augmented insulin pump therapy.**

DM I – Intensive regimen /insulin pump- negative side

- Similar to MDI therapy, it requires increased blood glucose monitoring, counting dietary carbohydrates, judging the impact of exercise, and making the appropriate adjustments to insulin infusion rates.

→**Without this increased commitment, the benefits of this regimen are not attained.**

- **High** cost of the pump and its supplies.
- Complications of pump therapy, such as infusion pump failure, superficial infection, and minor dermatologic changes such as nodules or scars at the catheter site

DM I – Intensive regimen /insulin pump- negative side

- Because rapid- or short-acting insulin is used alone in insulin pumps and patients have no long-acting subcutaneous depot of insulin;

- → pump failure can result in rapid onset of diabetic ketoacidosis.
- → This is another reason why frequent blood glucose checking is mandated in children on insulin pump therapy.