• Type 1. Most childhood diabetes:
  – Destruction of pancreatic β-cells by an autoimmune process

• Type 2. Insulin resistance followed later by β-cell failure:
  – Usually older children, obesity-related, positive family history, not as prone to ketosis, commoner in some ethnic groups (e.g. Indian subcontinent)
Type 1 Diabetes Mellitus

- **Background**
  
  - **Genetic factors**
    
    - Human leukocyte antigen (HLA)
      
        - DR3 and DR4 carries the greatest risk of type 1 diabetes mellitus
    
    - Child or sibling of T1DM: 4-6% risk
  
  - **Environmental factors e.g.**
    
    - Enteroviral infection, congenital rubella
    
    - Viral infection is the most important environmental factor
    
    - Breastfed infants have a lower risk for type 1 diabetes

Autoimmune destruction of the beta cells in the pancreas
Figure 25.1 Stages in the development of diabetes.
Type 1 Diabetes Mellitus

• Diagnosis
  – Fasting plasma glucose (FPG) level ≥ 126 mg/dL or
  – 2-h plasma glucose level ≥ 200 mg/dL or
  – Random plasma glucose ≥ 200 mg/dL with symptoms of hyperglycemia
  – HgbA1C ≥ 6.5 % • Glycated hemoglobin
Type 1 Diabetes Mellitus

Diagnosis

- Positive autoimmune markers
  - Glutamic acid decarboxylase [GAD] antibodies
  - Insulin islet cell antibodies
  - Zn transporter antibodies
Type 1 Diabetes Mellitus

- Management
  - Insulin therapy
  - Injections of insulin daily
  - Basal insulin
    - long-acting (glargine or detemir)
  - Preprandial (premeal) insulin
    - Rapid-acting (lispro, aspart, or glulisine)
Treatment

- Insulin
- Nutrition

The eatwell plate is based on 5 food groups:

- Fruit and vegetables
- Meat, fish, eggs, beans, and other non-dairy sources of protein
- Milk and dairy foods
- Bread, rice, potatoes, pasta, and other starchy foods
- Food and drinks high in fat and/or sugar
# Types of Insulin

<table>
<thead>
<tr>
<th>Type of Insulin</th>
<th>Onset</th>
<th>Peak</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid acting</td>
<td>15 minutes</td>
<td>60-90 minutes</td>
<td>3-4 hours</td>
</tr>
<tr>
<td>Short acting</td>
<td>30 minutes - 1 hour</td>
<td>2-3 hours</td>
<td>3-6 hours</td>
</tr>
<tr>
<td>Intermediate</td>
<td>2-4 hours</td>
<td>4-10 hours</td>
<td>10-16 hours</td>
</tr>
<tr>
<td>Long acting</td>
<td>1-2 hours</td>
<td>No peak</td>
<td>24+ hours</td>
</tr>
</tbody>
</table>

**Type of action** | **Chemical name** | **Brand name**
---|-------------------|-----------------
Rapid | Insulin lispro | Humalog
    | Insulin aspart | NovoRapid
    | Insulin Glulisine | Apidra
Short | Soluble insulin | Actrapid
    | Humulin S | Insuman Rapid
Intermediate | Isophane insulin suspension/NPH | Humulin I and Insulatard
    | Insulin zinc suspension | Hypurine Bovine
Long | Insulin glargine | Lantus
    | Insulin detemir | Leveimir
    | Insulin degludec | Tresiba
### 2. New-Onset Diabetes without Ketoacidosis

#### Insulin requirements:

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Start with 0.5 IU/kg/day</td>
</tr>
<tr>
<td>Pre-pubertal</td>
<td>0.7-1.0 IU/kg/day</td>
</tr>
<tr>
<td>During puberty</td>
<td>1 and even up to 2 U/kg/day</td>
</tr>
</tbody>
</table>

The correct dose of insulin is that which achieves the best glycaemic control.

#### Insulin regimens

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>50% of the total daily dose</td>
<td>Rapid -acting insulin (NovoRapid Pen) divided up between 3 pre-</td>
</tr>
<tr>
<td></td>
<td>meal boluses</td>
</tr>
<tr>
<td>50% of the total daily dose</td>
<td>long-acting insulin (Lantus® (insulin glargine Pen)) single</td>
</tr>
<tr>
<td></td>
<td>evening injection</td>
</tr>
</tbody>
</table>
Figure 25.3 Basal-bolus insulin regimen and continuous pump insulin regimen, showing the basal levels of insulin programmed into the pump (blue bars) and the bolus insulin (red pulses) given before each meal/snack according to carbohydrate intake.
Insulin Injection Sites

Insulin injection sites:
- Outer arm
- Abdomen
- Hip area
- Thigh
Type 1 Diabetes Mellitus

- Insulin pump
  - Same method of calculations for injection
  - No long acting insulin only rapid insulin
  - Can use smaller dose than the injection
  - Less injection per day but requires measurements before each bolus same as injection
  - Site changed every 3 days
  - Change the site if develop ketosis and use injection until resolved.
Some Children Wear Insulin Pumps

An insulin pump administers insulin through a catheter in the abdominal fat to help control a person's blood sugar levels.
Type 1 Diabetes Mellitus

- Monitoring
  - Hemoglobin A1c
    - Target HbA1C <7.5% in all pediatrics
    - Hb A1C = 7% average 150 over 3 months
    - Measurement reflects 3 months control
  - Screening Type 1 DM 5 years, Type 2 at the time of diagnosis
    - Microalbuminuria: >30 Alb/Cr ratio is positive
    - Dilated eye examination
  - Careful neurologic examination screen every 5 years after diagnosis
  - TSH every 1-2 years
Blood glucose monitoring should ideally be carried out **4-6 times a day**, however, this is dependent on the availability of testing strips.

**Recommended target blood glucose levels:**

<table>
<thead>
<tr>
<th>Blood Glucose Targets for Most People with Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>During the day</strong></td>
</tr>
<tr>
<td><strong>Overnight &amp; pre breakfast</strong></td>
</tr>
</tbody>
</table>
• Regular exercise; improves glucoregulation by increasing insulin receptor number.

• No form of exercise, including competitive sports, should be forbidden to the diabetic child.

• In patients who are in poor metabolic control, vigorous exercise may precipitate ketoacidosis because of the exercise-induced increase in the counter-regulatory hormones.

• A major complication of exercise in diabetic patients is the presence of a hypoglycemic reaction during or within hours after exercise.
Regular assessment of the child with diabetes

Assessment of diabetic control:
- Any episodes of hypoglycaemia, diabetic ketoacidosis, hospital admission?
- Is there still awareness of hypoglycaemia?
- Absence from school? School supportive of diabetes care?
- Interference with normal life?
- HbA\textsubscript{1c} results – 58 mmol/mol (7.5%) or less?
- Diary of blood glucose results – if monitoring, is he reacting to results?
- Insulin regimen – appropriate? Correction bolus doses given?
- Lipohypertrophy or lipoatrophy (Fig. 25.6a and b) at injection sites?
- Diet – healthy diet, manipulating food intake and insulin to maintain good control?

General overview (periodic):
- Normal growth and pubertal development, avoiding obesity – measure each visit
- Blood pressure check for hypertension yearly (age-specific centiles)
- Renal disease – screening for microalbuminuria yearly from 12 years
- Eyes – photography for retinopathy or cataracts, yearly from 12 years
- Feet – maintaining good care – yearly
- Screening for coeliac and thyroid disease at diagnosis, thyroid screening yearly, coeliac again after 3 years or if weight gain poor.
- Annual reminder to have flu vaccination

Knowledge and psychosocial aspects:
- Good understanding of diabetes, would participation/holidays with other diabetic children be beneficial? Member of Diabetes UK?
- Becoming self-reliant, but appropriate supervision at home, school, diabetic team?
- Taking exercise, sport? Diabetes not interfering with it?
- Leading as normal life as possible?
- Smoking, alcohol?
- Is ‘hypo’ treatment readily available? Is stepped approach known?
- What are the main issues for the patient? Are there short-term goals to allow engagement with improving control?

Figure 25.6 Lipohypertrophy from insulin injections. (a) Injection sites. (b) Lipohypertrophy (arrow) from insulin injections.
**Diet**

**Fats:** Fat typically doesn't break down into sugar, and in small amounts, it doesn't affect blood glucose levels.

**Proteins:** Protein doesn't affect blood glucose unless the patient eat more than the body needs.

**Carbohydrates:** Carbohydrates affect blood glucose more than any other nutrient.
The same total caloric intake as usual in non DM child is given with the same ratio

50% CHO

35% Fat

15% Proteins

Number of meals is preferred to be three fixed major with two snakes in between.
What is Carbohydrate (CHO) Counting?

• is a method of matching your insulin requirements with the amount of carbohydrate you eat and drink.
• It is an effective way of managing the condition that, once mastered, will lead to better blood glucose control, greater flexibility and freedom of lifestyle.
To be successful using carbohydrate counting, you need to:

• be motivated and able to take the time required to improve diabetes management
• do simple arithmetic (add, subtract, multiply and divide)
• understand insulin action
• read food labels
• count carbohydrates
• understand the relationship between carbohydrate and insulin
Count your Carbs & Calories with over 1,700 Food & Drink Photos!

Carbs & Cals

UK No1 Bestselling Book for Diabetes, Weight Loss & Healthy Eating!

by Chris Cheyette & Yello Baloua

In association with Diabetes UK Care, Connect, Campaign.

500 new food & drink photos added! Now includes protein, fat, saturated fat & fibre!

Pasta Twists

Tiramisu

Please select your portion size
Carbohydrate Counting and Insulin Correction

- adjusting insulin
- Calculate amount of carbohydrate that patient eat.
- Think about activity/exercise
- Check blood glucose level.
- Ideally, the measurement after the meal should be within 30-50 points or (2 mmol/l) of the pre-meal levels. If it's not, need Carb Counting, Meal Plans, and Insulin Adjustment?
• Roughly according to Age the Insulin to CHO ratio:
  • Less than 5 years: 1 unites / 25 gm
  • 5 to 8 years: 1 unites / 20 gm.
  • 8 to 11 years: 1 unites / 15 gm.
  • 11 to 18 years: 1 unites / 10 gm
• **Note:** In general these 3 factors will aid in estimating correct mealtime doses of insulin (rapid acting insulin)

1. Check blood glucose
2. Estimate amount of carbohydrate about to be eaten.
3. Consider any exercise done before this meal or any exercise after meal.
Psychological support & Education

Team Clinic

- Ice-breakers
- Patient-driven, facilitator-mediated
- Set visit goal

Patient

- Patient one-on-one with provider

Provider

- Review Goals
- Discuss Plans
- Answer Q's

Family

- Normal development + diabetes
- Set visit goal
Screening for complications and associated conditions

- height and weight & state of injection sites at each clinic visit.
- **Thyroid disease & coeliac disease** at diagnosis and annually.
- annual **foot** care reviews.
- Regular **dental and eye** examinations every 2 years.
- from the age of 12 years: **blood pressure, retinopathy, microalbuminuria & S.Creatinine.**
Special consideration

- Partial Remission or Honeymoon Phase in Type 1 Diabetes
- Somogi Phenomena
- Dawn Phenomena.
- Management of DM during Infection.
Partial Remission or Honeymoon Phase in Type 1 Diabetes

- Insulin requirements can decrease transiently following initiation of insulin treatment.
- This has been defined as insulin requirements of less than **0.5 units per kg** of body weight per day with an **HbA1c < 7%**.
- **Ketoacidosis** at presentation and at a young age reduce the likelihood of a remission phase.
- It is important to **advise the family** of the transient nature of the honeymoon phase to avoid the false hope that the diabetes is spontaneously disappearing.
- **Treatment** by reduce the dose of Insulin Accordingly.
In children with high dose of insulin at Night (Long acting), Hypoglycemia will increase late night (3-4 a.m.) counter regulatory hormone.

Early morning Hyperglycemia.

Treatment: Reduce the dose of Long acting Insulin at Night.
In children with Normal dose of Insulin at Night & Normal midnight glucose (Normoglycemia), Counter regulatory hormone may normally increase Early morning Hyperglycemia.

Treatment: Increase the dose of Long acting Insulin at Night.
Management during Infection

• Infection may precipitate hyperglycemia or DKA.

• **Mild infection** should be treated + increase the dose of Insulin by **10 – 15%**.

• **Sever infection** necessitate hospitalization.
Important information

• Do not shake the insulin as this damages the insulin?
• After first usage, an insulin vial should be discarded after 3 months if kept at 2-8°C or 4 weeks if kept at room temperature.
• Intermediate-acting **and** short-acting/rapid-acting insulin, can be combined in one Syringe.
• Use 4mm needle for injection of Insulin SC.
Two Emergencies of Diabetes

<table>
<thead>
<tr>
<th>HYPOGLYCEMIA</th>
<th>HYPERGLYCEMIA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Due to:</strong></td>
<td>Presence of ketones</td>
</tr>
<tr>
<td>Low blood glucose</td>
<td>Fast - within seconds</td>
</tr>
<tr>
<td>Fast – within seconds</td>
<td>Too much insulin</td>
</tr>
<tr>
<td>Too much insulin</td>
<td>Too little food</td>
</tr>
<tr>
<td>Too little food</td>
<td>Too much exercise without food</td>
</tr>
<tr>
<td>Insufficient insulin</td>
<td>Missing or delayed meals/snacks</td>
</tr>
<tr>
<td>Missed insulin dose(s)</td>
<td>Stress/overexcitement in young children</td>
</tr>
<tr>
<td>Infections/illness</td>
<td>Blood glucose:</td>
</tr>
<tr>
<td>High (greater than 200 mg/dL)</td>
<td>Low (less than 60 mg/dL)</td>
</tr>
<tr>
<td>Moderate/large in urine or blood</td>
<td>None in urine or blood</td>
</tr>
</tbody>
</table>

KETOACIDOSIS/DKA

<table>
<thead>
<tr>
<th><strong>Blood glucose:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (less than 60 mg/dL)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Ketones:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>None in urine or blood</td>
</tr>
</tbody>
</table>

**Time of onset:**

Fast – within seconds | Slow - within hours or days

**Causes:**

Too much insulin | Insufficient insulin
Too little food | Missed insulin dose(s)
Too much exercise without food | Infections/illness
Missing or delayed meals/snacks | Stress response
Stress/overexcitement in young children |
Classic Triad of DKA

The biochemical criteria for the diagnosis of DKA\textsuperscript{3,4}

- **Hyperglycemia** - blood glucose greater than 200 mg/dL

- **Ketosis** - ketones present in blood and/or urine

- **Acidosis** - pH less than 7.3 and/or bicarbonate less than 15 mmol/L
Clinical Presentation

Nausea, vomiting
Polyuria
Polydipsia
Weight loss
Fruity breath odor
Abdominal pain
Lethargy/drowsiness
Confusion
Coma
Diabetic ketoacidosis

Box 25.4 Essential early investigations

- Blood glucose (>11.1 mmol/L)
- Blood ketones (>3.0 mmol/L)
- Urea and electrolytes, creatinine (dehydration)
- Blood gas analysis (severe metabolic acidosis)
- Urinary glucose and ketones (both are present)
- Evidence of a precipitating cause, e.g. infection (blood and urine cultures performed)
- Cardiac monitor for T-wave changes of hypokalaemia
- Weight
**Pathophysiology of DKA**

- Insulin deficiency
- Excess counter-regulator hormones:
  - glucagon, cortisol, catecholamines, and growth hormone

- Ketogenesis
- Hyperglycemia
- Glucosuria
- Acidosis
- Osmotic diuresis
- Dehydration
<table>
<thead>
<tr>
<th>Age</th>
<th>Respiratory Rate (breaths/minute)</th>
<th>Heart Rate (beats/minute)</th>
<th>Systolic Blood Pressure (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborn</td>
<td>30 - 60</td>
<td>100 - 180</td>
<td>&gt; 60</td>
</tr>
<tr>
<td>3 months</td>
<td>30 - 60</td>
<td>110 - 160</td>
<td>&gt; 70</td>
</tr>
<tr>
<td>6 months</td>
<td>30 - 60</td>
<td>110 - 160</td>
<td>&gt; 70</td>
</tr>
<tr>
<td>9 months</td>
<td>30 - 60</td>
<td>110 - 160</td>
<td>&gt; 70</td>
</tr>
<tr>
<td>12 months</td>
<td>30 - 60</td>
<td>110 - 160</td>
<td>&gt; 70</td>
</tr>
<tr>
<td>2 years</td>
<td>24 - 40</td>
<td>90 - 150</td>
<td>&gt; 70</td>
</tr>
<tr>
<td>4 years</td>
<td>22 - 34</td>
<td>90 - 150</td>
<td>&gt; 75</td>
</tr>
<tr>
<td>6 years</td>
<td>18 - 30</td>
<td>70 - 120</td>
<td>&gt; 80</td>
</tr>
<tr>
<td>8 years</td>
<td>18 - 30</td>
<td>70 - 120</td>
<td>&gt; 80</td>
</tr>
<tr>
<td>10 years</td>
<td>18 - 30</td>
<td>70 - 120</td>
<td>&gt; 80</td>
</tr>
<tr>
<td>12 years</td>
<td>12 - 16</td>
<td>60 - 110</td>
<td>&gt; 90</td>
</tr>
</tbody>
</table>

Follow established guidelines
Consider need for consultation and transfer to higher level of care
Recognize and prevent serious complications such as cerebral edema
Maintain strict NPO
IV fluids
Phase I
Initial volume expansion
Phase II
Replacement of fluid deficit
Maintenance fluids
Insulin administration (begins after the initial fluid resuscitation)
Continuous IV insulin infusion
Subcutaneous/Intramuscular
Electrolyte replacement
Reassessment and ongoing monitoring
Start IV fluids: 10-20 mL/kg of 0.9%NS over the first hour
In a severely dehydrated patient, this may need to be repeated
Fluids should not exceed 50 mL/kg over first 4 hours of therapy

Clinical assessment of dehydration to determine fluid volume
Children with DKA have a fluid deficit in the range of 5-10%
Mild DKA 3-4% dehydration
Moderate DKA 5-7% dehydration
Severe DKA 10% dehydration
Shock is rare in pediatric DKA

Replace fluid deficit evenly over 48 hours

REMINDER: Serum sodium decreases by 1.6mEq/L for every 100-mg/dl increase in serum glucose concentration above 100mg/dl, therefore no electrolyte correction is needed

ALL PATIENTS WITH DKA REQUIRE SUPPLEMENTAL FLUIDS
Start replacing potassium after initial fluid resuscitation and concurrent with starting insulin therapy.

**MONITOR CLOSELY!!!**

In general, in patients with DKA, there is a significant potassium deficit that must be replaced.

Potassium replacement should continue throughout IV fluid therapy.

no faster than 10 mEq/hour thru a peripheral IV or 20 mEq/hour through a central line.
Bicarbonate therapy is generally contraindicated in Pediatric DKA due to increased risk of cerebral edema.\textsuperscript{7,8,9,10}

Bicarbonate therapy should only be considered in cases of:
- Severe acidemia
- Life-threatening hyperkalemia\textsuperscript{11}
Diabetes Ketoacidosis

• Background
  – Diabetic ketoacidosis (DKA) is a severe insulin deficiency state causes metabolic acidosis and dehydration
  – Cerebral edema (most common cause of death in Type 1 DM)
  – Precipitating factors that could lead to the onset of DKA
    • Infection
    • Insulin omission
    • Insulin pump failure
    • Failure to match insulin dosing to metabolic requirements during illness or stress
First hour

Fluid resuscitation
10cc/kg 0.9 NS IV over 1 hour

Second hour

Rehydration fluids:
0.9NS +20meq/L KPhos +20meq/L K Acetate
Rate
Maintenance rate plus the deficit over 48 hours evenly
Rarely fluid rate exceed 1.5-2 maintenance rate

Insulin
0.1/kg/h

When blood glucose level = 250-300
change fluids to:
D5 0.45% NS with 40meq/L (KPho+KCL) the same rate

Resolution of DKA
Ph >7.3
Bicarb >15

D/C IV fluids when PO tolerated
Give SC insulin then D/C IV insulin
Diabetes Ketoacidosis

• Important to know
  - If the blood glucose concentration < 150 mg/dL (8.3 mmol/L), dextrose 10% or even 12.5%, can be used
  - IV insulin therapy should continue as long as the patient still acidotic
  - Decrease IV insulin rate if persistent hypoglycemia despite maximum dextrose administration
Diabetes Ketoacidosis

- Cerebral edema
  - Risk factors
    - Treatment with bicarbonate, young age
    - Overaggressive fluid replacement
    - Too early an introduction of insulin therapy

- Clinical Presentation
  - Vomiting, headache, abnormal drowsiness
  - Altered mental status
  - Sustained and inappropriate bradycardia
  - Age-inappropriate incontinence
  - Diastolic hypertension (>90 mm Hg)
Hypoglycemia in patients with DM

- Conscious patient
  - 15 gram of CHO if >40 mg/dL or 30 gram of CHO if <40 mg/dL
  - Recheck in 15 minutes
  - Repeat if needed if still < 70 mg/dL
  - Once is >70 mg/dL ....Give with fat in order to last longer

- Unconscious or not able to drink
  - Glucagon
    - 1 mg IM (0.5 mg if < 20 kg)
    - Does not work for ketotic hypoglycemia or glycogen storage diseases
  - IV Dextrose if already has an IV
Development of Type 2 Diabetes

- Normal
- Insulin resistance
- Impaired Glucose Tolerance
- Type 2 Diabetes
Type 2 Diabetes Mellitus

Diagnosis

- Family history of type 2 diabetes in first- or second degree relative
- Signs of insulin resistance or conditions associated with insulin resistance
- Random plasma glucose 200 mg/dL or greater in association with polyuria, polydipsia, or unexplained weight loss
Type 2 Diabetes Mellitus

- **Diagnosis**
  - FPG value of 126 mg/dL or greater
  - or a 2-h plasma glucose value of 200 mg/dL or greater during an OGTT
  - HbA1c levels > 6.5 %

- **Indications for OGTT**
  - Fasting glucose is 100-125
  - High suspicious of type2 DM
    - Acanthosis nigricans
    - Family history of DM
    - PCOS
    - High BMI
Acanthosis Nigricans
Type 2 Diabetes Mellitus

- Laboratory results that usually suggest type 2 diabetes are as follows:
  - Elevated fasting C-peptide level
  - Elevated fasting insulin level.
  - Absence of autoimmune markers
Type 2 Diabetes Mellitus

- **Management**
  - Diabetes education and lifestyle changes (diet, exercise, and weight control)
  - Pharmacologic therapy with metformin (drug of choice)
  - Insulin
    - Present with ketosis and DKA
    - HbA1c >9%
    - Random BG 250mg/dL or more
  - Lipid-lowering agents and blood pressure medications to achieve cardioprotection, if necessary