Dr. Reem Lecture note + illustrated (no slide)

- Regarding lecture the doctor mentioned illustrated as reference book as well as the important (example) for calculation.

……

What is the definition of polyuria? it is increases in amount (volume). It is not Increased in the number of time in urination (frequency).

- 2L/m2/day. (Stander) based on BSA not age.

First part: Diabetes Mellitus (DM1)

- **Case**: 2 y/o child have frequent urination and drinking water
  - What further Questions in history you want to obtain? Please focus on **age**
    - HPI: onset (2 week), water drinking habits, increases appetite, urinary symptoms, breathing smells, how many times you change the diaper (full or not, change the bed)....
  - what is your DDx?
    - DM1, DM2، Central and nephrogenic Diabetes Insipidus (DI). Psychogenicpolydipsia
    - Chronic renal failure and Acuterenal failure (early phase presentationis oliguria, later phase is polyuria), called polyuric phase of acute renal failure
    - UTI, RTA and Fanconi Syndrome
    - Medications (Diuretics)
    - Electrolytes abnormalities (hypercalcemia and hypokalemia)

Box 26.1 Classification of diabetes according to aetiology

- **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, more common in some ethnic groups (e.g. Black and Asian children)
- **Other types**
  - Maturity onset diabetes of the young – various types caused by genetic defects in β-cell function. Strong family history.
  - Drugs, e.g. corticosteroids
  - Pancreatic insufficiency, e.g. cystic fibrosis, iron overload in thalassaemia
  - Endocrine disorders, e.g. Cushing syndrome
  - Genetic/chromosomal syndromes, e.g. Down and Turner
  - Neonatal diabetes: transient and permanent secondary to defective B cell function.
  - Gestational diabetes

- **Type of Diabetes**:
  - DM1, DM2
  - Maturity onset diabetes of young(MODY)
  - Gestational diabetes, mitochondrial diabetes
  - diabetes secondary to medication (steroids)
  - Diabetes secondary to endocrine disorders (Cushing's, acromegaly)
- **Pathophysiology** of DM1 (in basic to explain it to parent):
  - واحد أكل بيروح الأكل من الفم للمعدة بينهضم ويتكسر لجزيئات بسيطة في المعدة ثم يروح للأمعاء الدقيقة عشان يمتص، طيب ايش هي هذي الجزيئات البسيطة ؟ الجزيئات الصغيرة من البروتين ، السكريات و الدهون تمتص هذه الجزيئات وتروح للدم عشان يغذون الخلايا، طيب ايش هو غذاء الخلايا الوحيد؟ السكر وحتى لو حرمت نفسك من السكر الجسم بيكسر البروتين و الدهون ويحولها لسكر لأنه غذائها الوحيد عشان كذا علاج مرض السكر مو بايقاف تناول السكر!، طيب بيطلع السكر عشان يغذي الخلية في كل خلية فيه بوابات تدخل السكر للداخل هذي البوابات ما تفتح إلا بوجود الانسولين نسميه مفتاح الخلايا يجي الانسولين من البنكرياس لكن في حال قل الانسولين او ما صار البنكرياس يطلعه بكمية كافية (مرض السكر) هنا نواجه ارتفاع في السكر بسبب تراكم السكر في الدم وعدم القدرة للدخول للخلايا لان البوابات مقفلة و المفاتيح غير موجودة او قليلة، في هذه الحالة الخلية مو جالسة تتغذى بتصير عندها مجاعة، فيقوم الجسم يكسر البروتين و الدهون (ينحف الطفل) عشان يجيب جلكوز و كيتون ويدخل الجسم في اعراض الكيتونية (الحمضية)بسبب ارتفاع الكيتون في الجسم وكمان بسبب ارتفاع السكر اللي مو قادر يدخل لاخلايا وهي جوعانة و الشخص هذا باقي ياكل لان الخلايا جوعانة (بوليفيجيا) فيزيد السكر كمان طيب فين يروح؟ يطلع مع البول (بولييوريا) لان الكلى سليمة فتحاول تطلع السكر من الدم لانها ما تقدر تمتصه عندها حد (ثريشولد) كم هذا الحد؟ ١٨٠-١٧٥ طبعا بعد كثرة التبول اللي حاصلة الجسم بيفقد سوائل ويبدأ يجيه جفاف عشان كذا تلاقي عندهم (بوليديبسيا) يشربون مويه كثير تعويض للي يطلع وتستمر هذه الدائرة (يعطش يجوع ويتبول كثير) لما يدخل في مرحلة الكيتونية تستغرق قرابة الاسبوعين بالأخير يجي الطفل للطوارئ بسكر مرتفع وحموضة في الدم.
  - Renal threshold for glucoses? 175-180 mg/dl. For all ages.
  - The typical story of DM1 2 week of symptoms(polyuria, polydipsia and polyphagia) present with DKA. If someone came with same symptoms but duration is month or year this is not any more DM1, think for other ddx such as DI (without polyphagia)or DM2.
- **Etiology** for DM1:
  - Autoimmune (not infection, not high sugar intake and not emotional stress):
    - Genetic predisposition in HLA and trigger (unfortunately trigger are hypothetic not proven).
    - T cell start to attach the pancreatic beta cell (months and years before) then it dies once it is die there is no more insulin then develop diabetes type 1 (insulin dependent). When symptoms appear then 90-95% of the beta cell are destroyed.
    - please don't ask the parents about recent infection, they will feel that is the cause and they will blame themself. Ok infection can trigger but not cause. كمان السؤال عن التريقر غير منطقي لأن المناعة انضربت من شهور او سنين ما راح يصير الهجوم قبل اسبوع من المرض لازم نفرق تماما بين وقت ظهور الاعراض الى الدخول في الحمضية اللي تستغرق اسبوعين تقريبا وبين بداية الهجوم المناعي و ظهور الاعراض اللي تستغرق شهور وسنين.

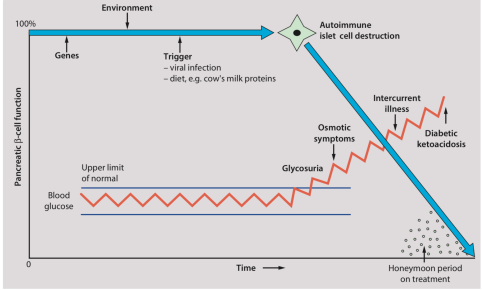


Figure 26.1 Stages in the development of diabetes.

- **Stages**: for all the stage you can detect antibodies (AB) in blood عشان كذا الحين هم يشتغلون انهم يعالجون الشخص قبل يوصل المرحلة الثالثة انهم يسوون سكريينينق يلقطون منها وجود الانتيبوديز بس لسى تحت الدراسات.
  - Stage 1: **normal** blood sugar but you can detect the AB in blood.
  - Stage 2: **Abnormal** blood sugar and AB without symptoms.
  - Stage 3: symptoms start clinical diagnosis and AB
  - Post dx: chronic long term phase.
- **Symptoms**:
  - Classical: polyuria, polydipsia, polyphagia and weight loss
- **Diagnosis**:
  - Hx and PE,
  - Lab test To confirm diabetes:
    - OGTT (=>200 mg/dl)
    - Random (=>200) + symptoms.
    - Hb A1c (=>6.5)
    - Fasting plasma glucose (=>126 mg/dl)

Box 26.2 Symptoms and signs of diabetes

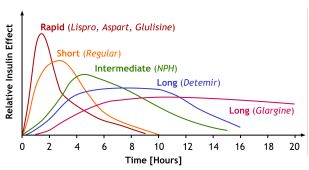
Early

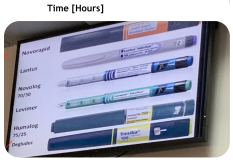
Most common – the 'classical triad':
- excessive drinking (polydipsia)
- polyuria
- weight loss

Less common:
- enuresis (secondary)
- skin sepsis
- *candida* and other infections

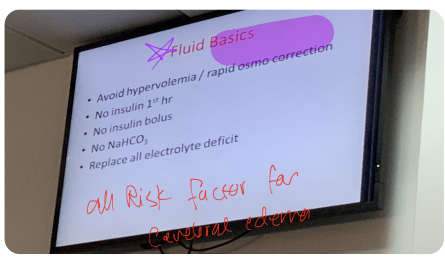
Late – diabetic ketoacidosis
- Smell of acetone on breath
- Vomiting
- Dehydration
- Abdominal pain
- Hyperventilation due to acidosis (Kussmaul breathing)
- Hypovolaemic shock
- Drowsiness
- Coma and death

- **Management**:
  - Education and counseling: check blood glucose at least 3 times daily before meal, Exercise and food.
  - Blood glucose measurements. How?
    - **Glucometer** (most accurate)
    - Continuous glucose monitoring device دقته اقل لانه يقيس الجلكوز في الانترستيشيوم يتاخر تقريبا خمس دقايق لكنها مره تساعد كل خمس دقايق تعطي قراءة وتنبيه لو ارتفع او انخفض
  - Replace the insulin. How?
    - Subcutaneous injection, Insulin pen, Insulin pump (ultra short only) and Inhaled insulin.
    - Where to inject? Any area with subcutaneous fat.
    - Type: Rapid, Short, Intermediateالعكر, Mix (short and intermediate) and Long (3 types):
      - Detemir insulin (Levimer) for 18h.
      - Lantus insulin (Glargin) for 24h.
      - New one tresiba insulin (Degludec) for 72h.

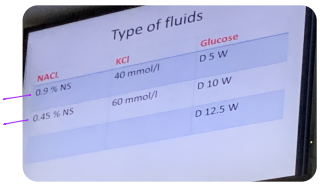




- **Complication**:
  - **hypoglycemia**: know the s/s.
    - **Diabetic**: less than 70 mg/dl or <4 mmol/l
    - **Non diabetic**: less than 55 or 2,2 mmol/l
    - **How to treat**: simply give glucose لما يكون صاحي معك اعطيه ملعقة عسل او ثلاث حبات تمر او كوب عصير لا تعطون تشوكلت ولا حليب ولا مشروبات غازية ، لكن لما يفقد الوعي اعطيه قلوكاجون او لو عندي اي في اكسس اعطيه محلول سكري على طول
    - **Complication**: affected brain function, seizures, hypoglycemia unawareness.
  - **DKA**:
    - **Risk factor**: new onset DM, acute illness, skip insulin or meal and pump malfunction.
    - **Clinical manifestation**: classical DM symptoms + abdominal pain , lethargic, acetone breath, confusion, drowsiness, LOC, and N/V. If present late the presentation will be worse even may die!
    - **Diagnosis**:
      - Hyperglycemia >200 or >11
      - Ketonemia and ketonuria
      - Low blood pH < 7.3 (every change in pH by 0.1 will change the severity) or HCO3 < 15 (change by 5 in severity)
    - **Management**: ABC Then know the severity of DKA to measure fluid
      - Fluid replacement: deficit + maintenance
        - **Fluid deficit = 10 x weight x degree of dehydration%**
          - **Degree of dehydration (severity of DKA):** لما يصير فيه اختلاف بين الحمضية والبايكارب ناخذ الاسوأ نحدد منها السيفرتي
            - Mild = 5% (24h) , pH = 7.2, HCO3 <15
            - Moderate = 7% (48h), pH = 7.1, HCO3<10
            - Sever = 10% (48h-72h) , pH<7.1 ,HCO3<5
        - **Maintenance = (100,50,20 per day or 4,2,1 per hour)**
      - Starting fluid: (first hour)
        - Mild and Moderate: no bolus
        - Sever: bolus if in shock

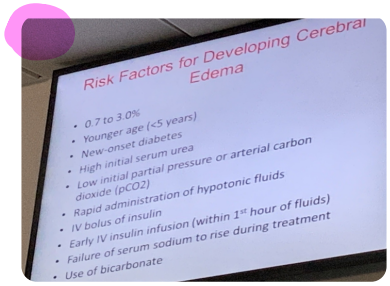


- **Example** for fluid replacement: 10 year old girl with 2 week history of polyuria, polydipsia and vomiting for 1 day. Glucose (30mmol/l), urine ketones +4, gas (pH =7.1, HCO3 = 4 , Co2 = 12) and weight = 30 kg. calculate the require fluid in 24h.
    - Sever dehydration.
    - Fluid deficit = 10 x weight x degree of dehydration% = 10x30x10 =**3000** 48h = 1500 24h.
        - In this example the patient have sever DKA (HCO3=4) so the result of deficit will be in 48h so we divided by 2 for 24h. If the case is mild you don't have to divide the result it is in 24h.
    - Maintenance fluid = (100,50,20 per day or 4,2,1 per hour) = (4x10)+(2x10)+(1x10) = 40+20+10= **70ml**/kg/h. = 1680 ml/kg/day
    - Fluid replacement = 1500+ 1680 = 3180 ml/kg/day.
    - Required fluid in the first 24 h = 132.5 ml/kg/h.



- Type of fluid: depends on glucose and electrolytes (Na and K). Aim to correct the acidosis
- **No insulins in first hour**. (شوفو الصورة بالصفحة السابقة)
- Monitor ketone , glucose , RFT , electrolytes and gas every 2 h.

- **Risk of developing cerebral edema**
    - **Risk factor:** >>> pic.
    - **S/S + criteria** >>>pic
    - **Diagnosis**: by criteria you have to memorize them>>> pic
        - If dx clinically you don't have to confirm it radiologically start Tx! Immediately.
    - **Treatment >>>pic**
- **Chronic complication rare in pediatric** start screening 5 years after dx
    - Neuropathy, Retinopathy , Nephropathy and Macrovascular.



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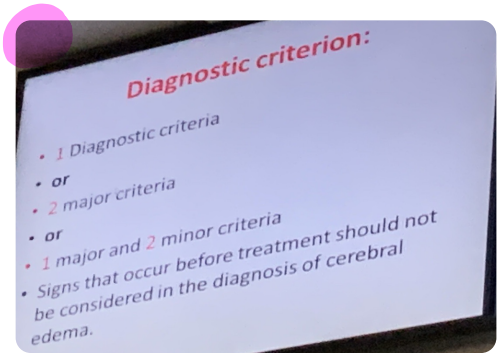
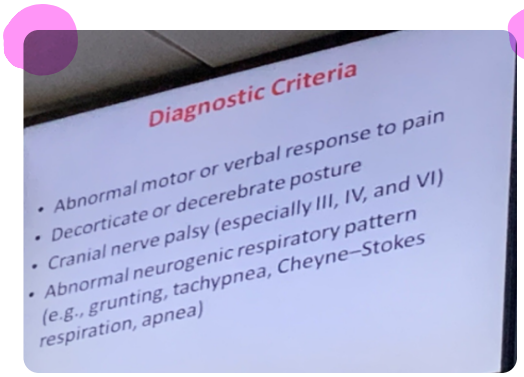
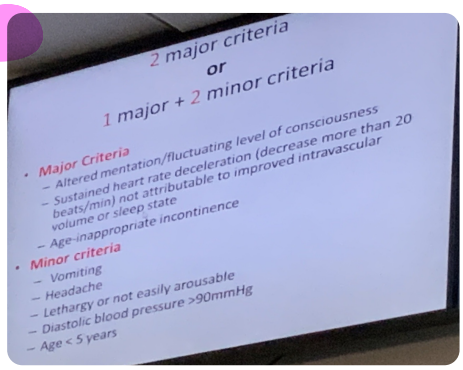
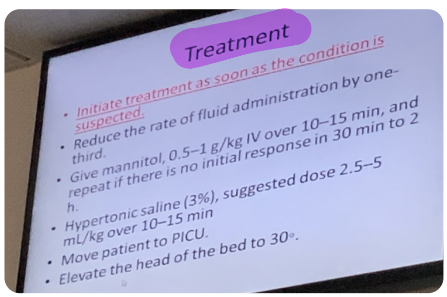








Insulin may be injected into the subcutaneous tissue of the anterior and lateral aspects of the thigh, the buttocks, and the abdomen. Rotation of the injection sites is essential to prevent lipohypertrophy or, more rarely, lipoatrophy.

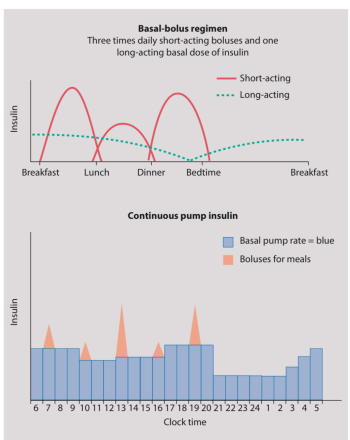
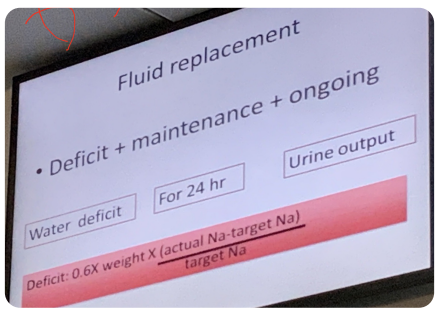


Figure 26.3 Basal-bolus insulin regimen and continuous pump insulin regimen, showing the basal levels of insulin programmed into the pump (blue bars) and the bolus insulin (red pulses) given before each meal/snack according to carbohydrate intake.

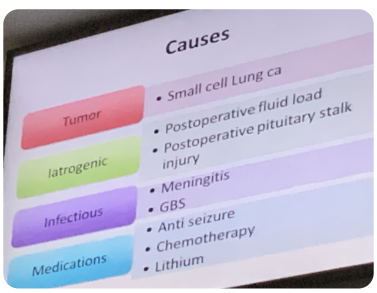
Second part: Diabetes Insipidus (DI)

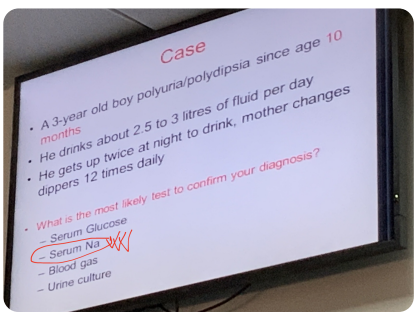
- **Type** of DI:
  - Central: we will talk mainly about it.
  - Nephrogenic
  - Psychogenic
- **Central DI**
  - **Pathophysiology**: ADH manufacture in hypothalamus and stored in posterior pituitary, ADH controlled how much water reabsorbed from renal tubules, so if you don't have ADH you will loss water كانها حنفية مفتوحة (uncontrolled) = **polyuria** then develop **polydipsia** because of this loss، then the Na concentration will become high due to this loss (**hypernatremia**)
  - **Symptoms**: polyuria, polydipsia, dehydration, weight loss, hyperthermia, irritability and FTT (if child).
  - **Etiology**:
    - Congenital pituitary malformation <1 year mostly
    - Brain Tumor >1 year
    - Iatrogenic
    - Meningitis
    - Idiopathic
  - **Diagnosis**:
    - **Water deprivation test**: stop drinking water then **every hour** check Na, osmolarity and urine specific gravity. (Patient fail to concentrate the urine even with fasting = ADH deficiency) then give ADH to differentiate between central and nephrogenic
      - If central > responds (no continues urination)
      - If nephrogenic> no response
    - **Na in blood and urine hypernatremia**
    - **Osmolarity** in blood and urine (high in blood low in urine)
    - **urine specific gravity**
  - **Management**:
    - desmopressin (ADH) replaces the missing hormone.
    - Free water access to prevent dehydration.
  - How to **replace fluid** in DI:
    - Fluid deficit + maintenance + ongoing (urine output)
      - Deficit= 0.6 x weight x [(actual Na-target Na)/ target Na]
    - For 24 hours
    - Target Na كم انا ابغى الصوديوم يوصل



Third part: Syndrome of Inappropriate Antidiuretic Hormones (SIADH)

- **Pathophysiology**: no water loss (opposites of DI) all of the fluids will reabsorbed again فيضان داخلي بالجسم as the excess water in body there will be low Na (diluted **hyponatremia**)
- **Symptoms**: anorexia, coma, muscle cramps, nausea, weakness, confusion, seizure
- **Etiology:** >>> pic
- **Fluid maintenance:** Fluid deficit + maintenance + ongoing (urine output)
  - For fluid **excess**
    - Deficit= 0.6 x weight x [(actual Na-target Na)/ target Na]
    - Same as DI عشان بس النتيجة بتطلع بالناقص و هي الكمية اللي المفروض المريض يطلعها يرجع لتوازن السوائل الطبيعي.
- **Diagnosis**:
  - Na in blood and urine: low in blood
  - Osmolarity in blood and urine: low to normal in blood, high in urine
  - High urine specific gravity
- **Management**: fluid restriction سهل بالكلام واصعب شيء بالتطبيق المريض بالعناية وكلهم يبغون بعطونه سوائل ونقولهم لا تعطونه لما تطلع الزايدة
- **Case**:>>>pic





Diabetic ketoacidosis

Box 26.4 Essential early investigations in diabetic ketoacidosis

- Blood glucose (>11.1 mmol/L)
- Blood ketones (>3.0 mmol/L)
- Urea and electrolytes, creatinine (dehydration)
- Blood gas analysis (severe metabolic acidosis)
- Evidence of a precipitating cause, e.g. infection (blood and urine cultures performed)
- Cardiac monitor for T-wave changes of hypokalaemia
- Weight (compare with recent clinic weight to ascertain level of dehydration)

(b)

(c)

(a) Diabetic ketoacidosis management

Follow this regimen if: hyperglycaemia (blood glucose >11 mmol/L, acidosis (pH <7.3 and/or bicarbonate <15 mmol/L), blood ketone usually >3 mmol/L and clinical dehydration and/or vomiting, drowsy or clinically acidotic.
(Follow guidelines from the British Society of Paediatric Endocrinology and Diabetes to reduce the risk from hypokalaemia, aspiration and cerebral oedema).

1. Fluids →
If in shock, initial resuscitation is with 0.9% saline (10 ml/kg). Dehydration should then be corrected gradually over 48 hours (see Fig. 26.7b and c). Rapid rehydration should be avoided as it may lead to cerebral oedema. Initial rehydration fluids need to be taken into account in calculating fluid requirements. 0.9% saline with 40 mmol/L KCl is recommended for first 12 hours, adding 5% glucose when blood glucose <14 mmol/L. After 12 hours, if plasma sodium level is stable, 0.45% saline/5% glucose with 40 mmol/L KCl is recommended. Monitor:
- fluid input and output
- blood glucose (hourly), blood ketones (1-2 hourly), electrolytes, creatinine and acid–base status 2–4 hourly
- neurological state.

Consider transfer to PICU and central venous line (CVP) and urinary catheter if shocked or in coma.
A nasogastric tube is passed for acute gastric dilatation if there is vomiting or depressed consciousness.

2. Insulin →
Insulin infusion (0.1 units/kg per h) is started after intravenous fluids running for 1 hour. Do not give a bolus. Monitor the blood glucose hourly. Aim for gradual reduction of blood glucose . Change to a solution containing 5% glucose when the blood glucose has fallen to 14 mmol/L to avoid hypoglycaemia.

3. Potassium →
Although the initial plasma potassium may be high, due to displacement from cells in exchange for hydrogen ions, it will fall following treatment with insulin and rehydration. Potassium replacement must be instituted as soon as maintenance fluids are started (unlike adults, it can be assumed that the child will have normal renal function and the greatest risk is from total body potassium depletion). Continuous cardiac monitoring and 2–4 hourly plasma potassium measurements are indicated until the plasma potassium is stable.

4. Acidosis →
Although a metabolic acidosis is present, bicarbonate should be avoided unless the child is shocked. The acidosis will correct with fluid and insulin therapy.

5. Re-establish oral fluids, subcutaneous insulin and diet →
Do not stop the intravenous insulin infusion until 1 hour after subcutaneous insulin has been given.

6. Identification and treatment of an underlying cause →
Ketoacidosis may be precipitated by an intercurrent infection. Diabetic ketoacidosis causes neutrophilia but not a fever. Antibiotics may be indicated. If the child was known to have diabetes, consider the reason for the ketoacidosis.

Figure 26.7 **(a)** Diabetic ketoacidosis management; **(b)** boy with severe dehydration and weight loss from diabetic ketoacidosis; and **(c)** 4 months later. (Photos b and c courtesy of Jill Challener.)

Summary

Regular assessment of the child with diabetes

Assessment of diabetes:

- 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_{1c} results – less than 48 mmol/mol (6.5%)?
- Diary of blood glucose results or blood glucose read-out– are appropriate actions to results being taken?
- Insulin regimen – appropriate?
- Lipohypertrophy or lipoatrophy (Fig. 26.8 a 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 height and weight and BMI and plot on growth chart at each visit
- Blood pressure check for hypertension yearly (age-specific centiles)
- Renal disease – screening for microalbuminuria, an early sign of nephropathy, annually from 12 years
- Circulation: - check pulses and sensation
- Eyes – retinopathy or cataracts are rare in children, but should be monitored annually from 12 years, preferably with retinal photography
- Feet – maintain good care, avoid tight shoes and obtain prompt treatment of infections - annually
- Screening for coeliac and thyroid disease at diagnosis, thyroid screening annually, coeliac again if symptomatic.
- Annual reminder to have flu vaccination

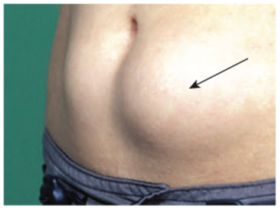
Knowledge and psychosocial aspects:

- 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?

(a)

(b)

Injection sites – check for lipohypertrophy or lipoatrophy



(c)

Figure 26.8 **(a)** The regular assessment of the child or young person with diabetes; **(b)** injection sites; and **(c)** lipohypertrophy (arrow) of abdomen from insulin injections.

Box 26.5 Tests to perform when hypoglycaemia is present

Blood

- Confirm hypoglycaemia with laboratory blood glucose
- Growth hormone, IGF-1, cortisol, insulin, C-peptide, fatty acids, ketones (acetoacetate, 3-hydroxybutyrate), glycerol, branched-chain amino acids, acylcarnitine profile, lactate, pyruvate

First urine after hypoglycaemia

- Organic acids
- Consider saving blood and urine for toxicology, e.g. salicylate, sulphonylurea

Box 26.6 Causes of hypoglycaemia beyond the immediate neonatal period

Fasting

- *Insulin excess*
  - Excess exogenous insulin, e.g. in diabetes mellitus/insulin given surreptitiously
  - β-cell tumours/disorders – persistent hypoglycaemic hyperinsulinism of infancy, insulinoma
  - Drug-induced (sulphonylurea)
  - Autoimmune (insulin receptor antibodies)
  - Beckwith syndrome
- *Without hyperinsulinaemia*
  - Liver disease
  - Ketotic hypoglycaemia of childhood
  - Inborn errors of metabolism, e.g. glycogen storage disorders
  - Hormonal deficiency: GH↓, ACTH↓, Addison disease, congenital adrenal hyperplasia

Reactive/nonfasting

- Galactosaemia
- Leucine sensitivity
- Fructose intolerance
- Maternal diabetes
- Hormonal deficiency
- Aspirin/alcohol poisoning