# MODERN MANAGEMENT OF ACUTE COMPLICATIONS OF DIABETES MELLITUS

***Learning guide for***
***the 5th and 6th year students, trainee physicians,***
***paediatricians, endocrinologists, general practitioners***

**МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ**
**Харківський національний медичний університет**

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# СУЧАСНИЙ МЕНЕДЖМЕНТ ГОСТРИХ УСКЛАДНЕНЬ ЦУКРОВОГО ДІАБЕТУ

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## INTRODUCTION

Type 1 diabetes mellitus (T1DM), one of the most common chronic diseases in childhood, is caused by insulin deficiency resulting from the destruction of insulin-producing pancreatic beta cells. In children and adolescents with T1DM, the most common complications include hypoglycemia, hyperglycemia, diabetic ketoacidosis (DKA), and psychiatric disorders.

The incidence and prevalence of type 1 diabetes among young people are increasing globally, while prevention is progressing more slowly than expected. The prevalence of type 1 diabetes among children and adolescents under the age of 15 is estimated to be increasing by around 3 %, with strong geographical variations. Therefore, the treatment and monitoring of paediatric diabetes is central to clinical practice. The rising incidence of diabetic ketoacidosis (DKA) in newly diagnosed children with type 1 diabetes is unabated in most countries, including those with free healthcare. In children with established diabetes, DKA occurs at a rate of 6–8 % per year [1]. DKA can also occur in children with type 2 diabetes (and especially in obese African American adolescents), although at a lower rate than in type 1 diabetes. Continuous monitoring of the incidence of DKA is essential to prevent this terrible complication in children. After the diagnosis of type 1 diabetes is made, regular self-monitoring of blood glucose and ketones, if indicated, is an integral component of type 1 diabetes management. Severe hypoglycaemia (SH) in children with type 1 diabetes has decreased over the past decades, but is still a common problem and is a major obstacle to achieving good metabolic control. Although new advances have improved glycaemic control and reduced the number of hypoglycaemias, long-term complications are still a constant burden for diabetes patients, and 1 in 3 young people with type 1 diabetes has at least one diabetes complication. Risk factors for diabetes complications begin to emerge in childhood and adolescence, and some young people may be diagnosed with chronic complications before they reach adulthood.

Diabetes complications can be divided into acute and chronic. Acute complications include diabetic ketoacidosis, hypoglycaemia and hyperosmolar hyperglycaemic syndrome.

## *ACUTE GLYCEMIC COMPLICATIONS*

**Hypoglycemia** – Hypoglycemia is the most common acute complication of T1DM in childhood. Hypoglycemia is a common complication of type 1 diabetes mellitus (T1DM) in childhood [2]. It can occur in any child in whom the dose of administered insulin exceeds the insulin requirement.

An international consensus group has identified the following important thresholds for the classification of hypoglycaemic episodes in children with type 1 diabetes [3]

## BLOOD GLUCOSE THRESHOLDS FOR CATEGORIZING HYPOGLYCEMIA

• Clinical hypoglycemia alert – Blood glucose < 70 mg/dL (3.9 mmol/L); this is commonly used as a threshold for recognizing and initiating treatment for hypoglycemia.

• Clinically important or serious hypoglycemia – Blood glucose < 54 mg/dL (3.0 mmol/L); values in this range tend to be associated with defective glucose counter-regulation, impaired hypoglycemia awareness, and, sometimes, cognitive dysfunction.

• Severe hypoglycemia – An event associated with severe cognitive impairment (including coma and seizures), requiring assistance of another person to correct, including administration of carbohydrates or glucagon or intravenous (IV) dextrose.

## RISK FACTORS

• Insulin regimen – is an important predictor of hypoglycaemia risk, this regimen improving glycaemic control and is likely to also reduce the risk of hypoglycaemia.

• Episodes of hypoglycaemia are more common and severe in younger children because food intake, activity and adherence to treatment schedules are less predictable in younger children compared to older children.

• Exercise is a well-recognised cause of hypoglycaemia, because exercise increases insulin sensitivity, increases glucose utilisation and increases insulin absorption. Recommendations for avoiding hypoglycaemia during and after physical activity include:

- monitoring glucose levels before, during, and after intense exercise. If this is a new activity, monitoring should be done up to 12 hours after exercise due to possible delayed effects.
- eating a snack before and/or during vigorous activity.
- increase the dose of the last insulin dose before the start of activity.
- reducing the basal rate of the insulin pump during and for a period after exercise.

• Alcohol consumption is a common cause of hypoglycaemic episodes in adolescents and young adults.

• Acute illnesses – during acute illnesses accompanied by nausea, vomiting and anorexia, hypoglycaemia can occur due to insufficient oral intake if insulin doses with meal-related peaks are not properly adjusted.

• Inconsistent carbohydrate intake – fluctuations in the timing and content of carbohydrates in food lead to unstable glycaemic effects and an increased risk of hypoglycaemia.

• Psychological and social factors – an increased risk of hypoglycaemia is associated with low socioeconomic status and mental disorders.

• Concomitant autoimmune disorders – celiac disease, Addison's disease and autoimmune thyroiditis are associated with T1D and may increase the risk of hypoglycaemia. These disorders should be excluded in children with recurrent unexplained hypoglycaemia.

## SYMPTOMS AND SIGNS

• *Adrenergic symptoms* – Tremor, pallor, rapid heart rate, palpitations, and diaphoresis. These are caused by sympathetic neиral activation and epinephrine release. However, episodes of hypoglycemia aan lower the threshold at which these symptoms occur, leading to "hypoglycemia unawareness" and increasing the risk for subsequent severe hypoglycemia.

• *Neuroglycopenic symptoms* – Fatigue, lethargy, headaches, behavior changes, drowsiness, unconsciousness, seizures, or coma. These symptoms result from direct effects of hypoglycemia on the central nervous system. The severity of neuroglycopenic symptoms increases with the severity of hypoglycemia and resultant central nervous system glиcose deprivation.

• *Behavioral symptoms* – Behavioral symptoms include irritability, agitation, erratic behavior, unusual quietness, or tantrums and are most common in younger children. These behavioral symptoms are probably a consequence of adrenergic and neuroglycopenic responses

## MANAGEMENT

Hypoglycaemia can be asymptomatic or manifested by low blood glucose concentrations in the absence of symptoms. If the patient is asymptomatic, the blood glucose level should be measured to confirm the suspicion of hypoglycaemia.

Clinical classification of severity – The severity of hypoglycaemia is classified according to the symptoms and response required for successful treatment.

*Mild Symptoms* – include adrenergic and mild neuroglycaemic manifestations:

− Older children can usually recognise the symptoms (palpitations, headache, sweating, tremors) and treat themselves adequately with oral administration of rapidly absorbed carbohydrates.

− In infants and young children, symptoms of hypoglycaemia include lethargy, poor feeding, nervousness and hypotension; these symptoms can occur across a range of blood glucose concentrations. Young children are unable to communicate their symptoms to caregivers and may not show the same adrenergic signs as older children. Therefore, caregivers should be trained to recognise and treat nonspecific symptoms associated with hypoglycaemia in this age group.

Moderate symptoms – include sufficient neurological impairment to require a second person to administer oral therapy.

*Severe symptoms* – include neurological impairment that precludes oral therapy, requiring intervention with intranasal, subcutaneous or intramuscular glucagon or intravenous (IV) dextrose. Symptoms may progress to loss of consciousness, seizures or coma.

Mild to moderate hypoglycaemia – blood glucose < 70 mg/dL [3.9 mmol/L] and/or adrenergic and neuroglycaemic symptoms should be treated with oral treatment with a concentrated and rapidly absorbed source of simple carbohydrates (10 to 15 g of glucose). Options include:

- Glucose tablets – 5 g per tablet
- Glucose gel – 15 g per tube
- Fruit juice – 12 g carbohydrate per 4 oz (120 mL)
- Regular soda (not diet) – 12 g carbohydrate per 4 oz (120 mL)
- Honey – 17 g carbohydrate per 1 tablespoon (15 mL)
- Table sugar (granulated sugar) – 12.5 g sucrose per 1 tablespoon
- Skittles – 10 g carbohydrate (sucrose) per 10 candies

In patients with poor oral absorption during gastroenteritis or other diseases, glucagon in minimal doses is effectively used to prevent impending hypoglycaemia or to treat mild hypoglycaemia at home.

Dosing is as follows, using a standard U100 insulin syringe:

– Children under 2 years of age – 2 "units" (20 micrograms) of glucagon subcutaneously

– Children aged 2 years and older – 1 unit of glucagon (10 micrograms)/year up to 15 units (150 micrograms).

A repeat dose (twice the initial dose) is administered if the blood glucose level does not rise within 30 minutes.

Severe hypoglycemia – Patients with severe neurological impairment and/or who cannot take oral glucose require urgent treatment with glucagon. Every person with T1DM should have a glucagon kit on hand and easily accessible at all times.

Standard (lyophilized) glucagon – Glucagon may be administered subcutaneously or intramuscularly at the following doses:

- ≤ 20 kg body weight – 0.5 mg (or 0.02 to 0.03 mg/kg)
- > 20 kg body weight – 1 mg

Intranasal glucagon – Dosing for intranasal glucagon is:

- 3 mg intranasally initially (for ages ≥ 4 years)
- Administer an additional 3 mg dose (using a new device) if there has been no glycemic response after 15 minutes

Intravenous dextrose – in patients with severe hypoglycaemia, dextrose should be administered intravenously if intravenous administration is available and appropriately trained healthcare personnel are available.

Dosing is 0.25 g/kg (maximum single dose 25 g). This is supplied by:

- 2.5 mL/kg of 10% dextrose solution or
- 1 mL/kg of 25% dextrose solution

## HYPERGLYCEMIA AND DIABETIC KETOACIDOSIS

Diabetic ketoacidosis (DKA) is a common and potentially life-threatening complication of T1D. It can be present at the onset of T1D or can occur in a patient with known diabetes. It is caused by insufficient insulin levels, which leads to hyperglycaemia and lipid breakdown with the formation and accumulation of keto acids. Avoid the complication of (DKA) needs frequent blood glucose testing or continuous glucose monitoring.

### DEFINITIONS

**Diabetic ketoacidosis (DKA)** – according to the consensus statement of the International Society for Childhood and Adolescent Diabetes in 2022 [4].

Hyperglycemia – Blood glucose > 200 mg/dL (11 mmol/L)

- Metabolic acidosis – Venous pH < 7.3 or serum/plasma bicarbonate < 18 mEq/L (18 mmol/L)
- Ketosis – Presence of ketones in the blood (> 3 mmol/L beta-hydroxy-butyrate) or urine

*Assessment of severity of diabetic ketoacidosis in children*

| Defining features | Severe | Moderate | Mild |
|---|---|---|---|
| Venous pH | < 7.1 | 7.1 to < 7.2 | 7.2 to < 7.3 |
| Serum bicarbonate (mEq/L) | < 5 | 5 to 9 | 10 to < 18 |

Factors that increase the risk of developing DKA in a child with primary manifestation of type 1 diabetes include [5]:

− age less than 5 years old

− advanced diagnosis of diabetes mellitus, including seeking medical care

− low social status, lack of health insurance

− children living in countries with low incidence of type 1 diabetes mellitus.

In children with established diabetes, Groups with increased risk for DKA include:

• Children with poor metabolic control (higher hemoglobin A1c [HbA1c] values and higher reported insulin requirements)

• Gastroenteritis with vomiting and dehydration

• Peripubertal and pubertal adolescent girls

• Children with a history of psychiatric disorders (including eating disorders) or unstable family circumstances

• Children with limited access to medical care (underinsured)

• Inadvertent or intentional omission of insulin, including disloodgement and occlusion of insulin pump infusion tubing

Common risk factors for DKA include wing:

• Metabolic imbalance or missed insulin doses

• Diseases – intercurrent diseases

• Medications – medications, such as corticosteroids, L-asparaginase and diazoxide atypical antipsychotics, tacrolimus, , accelerate the development of DKA in people who have not previously been diagnosed with type 1 diabetes, alcohol.

## CLINICAL FEATURES

Onset of diabetes are manifested with hyperglycaemia and polyuria (due to glucose-induced osmotic diuresis), polydipsia (due to increased urinary water loss), fatigue, weight loss, nocturia and enuresis, vaginal or cutaneous moniliasis may occasionally occur.

Decreased energy and activity, irritability, and physical signs of dehydration more typical for infants, may be severe candidal diaper rash on the skin.

Acute complications of diabetes usually have anorexia, nausea, vomiting and abdominal pain. Abdominal pain needs to performs differential diagnosis

with appendicitis or other intra-abdominal pathology. Polyphagia may be observed at the beginning of the disease. When insulin deficiency increases and keto-acidosis develops, appetite is suppressed. Diabetes decompensation for infants may be with hyperpnoea and tachycardia. Children with decompensation have fruity breath secondary to exhaled acetone. Neurological symptoms, which range from drowsiness, lethargy and confusion to coma, are mainly related to the severity of acidosis.

## EVALUATION

All patients with suspected DKA should be rapidly evaluated as follows.

Clinical assessment

• Decreased blood pressure, decreased peripheral pulse, tachycardia, and significant postural changes in blood pressure more typical abnormality of vital functional.

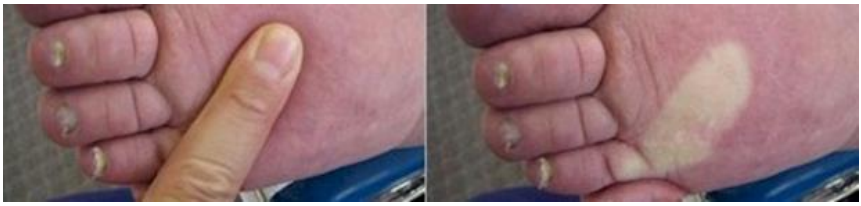
• Measure weight to calculate fluid replacement volume and insulin infusion rate.

• Assess the degree of dehydration.

• Using the Glasgow Coma Scale (GCS) or a similar assessment for assess the neurologic state

### Degree of Dehydration

| Symptom | Degree of Dehydration | | |
|---|---|---|---|
| | Mild (< 3 % body weight lost) | Moderate (3–9 % body weight lost) | Severe (> 9 % body weight lost) |
| Mental status | Normal, alert | Restless or fatigued, irritable | Apathetic, lethargic, unconscious |
| Heart rate | Normal | Normal to increased | Tachycardia or bradycardia |
| Quality of pulse | Normal | Normal to decreased | Weak, thready, impalpable |
| Breathing | Normal | Normal to increased | Tachypnea and hyperpnea |
| Eyes | Normal | Slightly sunken | Deeply sunken |
| Fontanelles | Normal | Slightly sunken | Deeply sunken |
| Tears | Normal | Normal to decreased | Absent |
| Mucous membranes | Moist | Dry | Parched |
| Skin turgor | Instant recoil | Recoil < 2 seconds | Recoil > 2 seconds |
| Capillary refill | < 2 seconds | Prolonged | Minimal |
| Extremities | Warm | Cool | Mottled, cyanotic |
| Adapted from King CK, Glass R, Bresee JS, et al. Managing acute gastroenteritis among children: oral rehydration, maintenance, and nutritional therapy. *MMWR Recomm Rep*. Nov 21 2003; 52 (RR-16): 1–16 | | | |



Skin with decreased turgor remains elevated after being pulled up and released


**The capillary refill time (CRT) is the time taken for return of skin color after gentle pressure for 5 seconds and release**

## Glasgow Coma Scale and Pediatric Glasgow Coma Scale

| Sign | Glasgow Coma Scale[1] | Pediatric Glasgow Coma Scale[2] | Score |
|---|---|---|---|
| Eye opening | Spontaneous | Spontaneous | 4 |
| | To command | To sound | 3 |
| | To pain | To pain | 2 |
| | None | None | 1 |
| Verbal response | Oriented | Age-appropriate vocalization, smile, or orientation to sound; interacts (coos, babbles); follows objects | 5 |
| | Confused, disoriented | Cries, irritable | 4 |
| | Inappropriate words | Cries to pain | 3 |
| | Incomprehensible sounds | Moans to pain | 2 |
| | None | None | 1 |
| Motor response | Obeys commands | Spontaneous movements (obeys verbal command) | 6 |
| | Localizes pain | Withdraws to touch (localizes pain) | 5 |
| | Withdraws | Withdraws to pain | 4 |
| | Abnormal flexion to pain | Abnormal flexion to pain (decorticate posture) | 3 |
| | Abnormal extension to pain | Abnormal extension to pain (decerebrate posture) | 2 |
| | None | None | 1 |
| **Best total score** | | | **15** |

The Glasgow Coma Scale (GCS) is scored between 3 and 15, with 3 being the worst and 15 the best. It is composed of 3 parameters: best eye response (E), best verbal response (V), and best motor response (M). The components of the GCS should be recorded individually; for example, E2V3M4 results in a GCS of 9. Traditionally, the GCS defines the severity of traumatic brain injury (TBI) as follows: ≤ 8: severe brain injury, 9 to 12: moderate injury, and a score ≥ 13 or higher: mild injury. However, a significant minority of patients with TBI and a GCS score of 13 have potentially life-threatening intracranial lesions. While a revised classification has not been widely adopted, a GCS score of 9 through 13 likely best represents the TBI population at moderate risk for death or long-term disability (ie, "potentially severe").

The Pediatric Glasgow Coma Scale (PGCS) was validated in children 2 years of age or younger.

*Data from:*

*1/. Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet 1974; 2:81.*

*2. Holmes JF, Palchak MJ, MacFarlane T, Kuppermann N. Performance of the pediatric Glasgow coma scale in children with blunt head trauma. Acad Emerg Med 2005; 12:814.*

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**Laboratory testing should include the following:**

Immediate (point-of-care) testing

- Blood glucose
- Blood beta-hydroxybutyrate (BOHB) or urine ketones (acetoacteate)
- BOHB is the most direct and reliable measure of the degree of ketoacidemiia.

Additional testing

- Blood glucose
- Electrolytes, including serum bicarbonate concentration
- Blood urya nitrogen (BUN) and creatinine
- Venous pH and partial pressure of carbon dioxide (pCO2)
- Calcium, phosphorus, and magnesium

**TREATMENT OF MODERATE AND SEVERE DIABETIC KETOACIDOSIS**

Treatment of DKA includes the administration of insulin to eliminate ketosis and reduce hyperglycaemia, correction of dehydration with intravenous fluids, and correction of electrolyte disturbances with electrolyte replacement.

**Initial volume expansion**

The main task of initial volume expansion is to restore effective circulating blood volume by acutely replacing some of the sodium and water losses and improving glomerular filtration rate to increase the excretion of potassium and glucose. An initial volume increase of 10 to 20 ml/kg should be administered as an intravenous bolus using isotonic saline (0.9 % sodium chloride [NaCl]) or Ringer's lactate infused over 20 to 30 minutes [7].

**Subsequent fluid administration** – Once the child is hemodynamically stable, additional IV fluids should be administered, calculated to replace the remaining fluid deficit over 24 to 48 hours, using IV fluids with 0.45 to 0.9 % NaCl.

**Hyperglycemia** – intravenous insulin infusion should be started approximately one hour after the patient has been given intravenous fluids. Insulin administration suppresses hepatic glucose excretion and ketogenesis, and stimulates peripheral glucose uptake and metabolism to serum glucose concentrations and restore keto acid levels. In addition, evaporation reduces serum glucose concentrations by diluting it and by impairing renal perfusion. Insulin should be administered as an intravenous infusion at a rate of 0.1 U/kg/h. Insulin can be dissolved in saline (0.45 or 0.9 % NaCl) and administered using a syringe infusion pump to control the rate of administration [8].

**Adding dextrose to intravenous fluids** – adding dextrose to intravenous fluids – when the serum glucose concentration falls to 250–300 mg/dl (13.9–16.7 mmol/l), dextrose should be added to the intravenous fluid infusion. If the blood glucose level drops below 150 mg/dl (8.0 mmol/l) before ketoacidosis is completely resolved, the concentration of dextrose in the IV solution should be increased

(e.g. to 10 or 12.5 %) to allow the insulin infusion to continue. In order to avoid hypoglycaemia or hyperglycaemia, it is recommended to maintain a blood glucose concentration of 100–150 mg/dL in older children (5.5–8.3 mmol/L) or 150–180 mg/dL (8.3–11.1 mmol/L) in younger children throughout the insulin infusion.

Very impotent is correctional of electrolytes balance. Potassium replacement should generally be initiated after the initial volume increase, at the same time as insulin therapy. If the patient is normokalemic and does not have a bowel movement, potassium replacement should be started with the start of insulin therapy. The usual starting concentration is 40 mEq/L (40 mmol/L) of potassium added to the intravenous solution (but not to the initial bolus). If the patient is hypokalemic, potassium replacement should be started immediately and insulin infusion should be delayed until the serum potassium concentration returns to near normal. The serum potassium concentration should be monitored hourly and replacement therapy should be adjusted if necessary. If the patient is hyperkalemic, delay potassium replacement therapy until the serum potassium level is returned to normal and urine output and adequate renal function are documented. Potassium replacement should be administered as a mixture of potassium phosphate and potassium chloride or acetate (see Phosphates section below). Administration of potassium chloride alone should be avoided to reduce the risk of hyperchloremic metabolic acidosis. Serum potassium levels should normally be monitored every two to four hours and the potassium concentration of intravenous fluids should be adjusted as necessary to maintain normal serum potassium levels. Electrocardiographic monitoring is recommended for most patients with DKA, but especially for patients with hyperkalaemia or hypokalaemia.

The insulin infusion should continue at 0.05 to 0.1 units/kg/hour until all of the following conditions are met:

- Serum anion gap reduced to normal (12±2 mEq/L) or serum BOHB ≤ 1 mmol/L (10.4 mg/dL)
- Venous pH > 7.3 or serum bicarbonate > 18 mEq/L
- Blood glucose < 200 mg/dL (11.1 mmol/L)
- Patient is tolerating oral intake

**Bicarbonate** should not be administered to treat acidosis, except in specific rare circumstances.

## TREATMENT OF MILD DIABETIC KETOACIDOSIS

The condition of these patients often improves significantly after intravenous (IV) fluids and subcutaneous insulin administration. Rapid-acting insulin can be administered at an initial dose of 0.1 U/kg every one to two hours with close monitoring of blood glucose levels and adjustments to the

insulin dose based on clinical response. Further treatment can be carried out at home. Ongoing home treatment includes rapid-acting insulin subcutaneously every three hours (with dose adjustments based on response), rehydration with oral fluids, and frequent monitoring of blood glucose and ketones.

**Hyperglycemic hyperosmolar state** – DKA must be distinguished from hyperglycemic hyperosmolar state (HHS), which is characterized by:

- Marked hyperglycemia (plasma glucose > 600 mg/dL [> 33.3 mmol/L])
- Minimal acidosis (venous pH > 7.25 or arterial pH > 7.3 and serum bicarbonate > 15 mmol/L)
- Absent to mild ketosis
- Marked elevation in serum osmolality (effective osmolality >320 mOsm/kg)
- Altered consciousness (e.g., obtundation, combativeness,seizures)

HHS can occur in young patients with type 2 diabetes, type 1 diabetes and in infants, especially those with transient neonatal diabetes mellitus associated with 6q24. It can occur as a complication in people without diabetes after severe burns, peritoneal dialysis or haemodialysis. Patients taking certain medications, such as methadone, diuretics, corticosteroids, beta-blockers, phenytoin and diazoxide, are also at increased risk of developing HCV. The incidence of HCV is increased in adolescents with type 2 diabetes and obesity.

**Pathophysiology of HHS**

Stress/precipitating event i.e. infection, trauma, substance abuse, undiagnosed diabetes

↓

Insulin deficiency/ resistance + rise in counter-regulatory hormones (cortisol, glucagon, epinephrine, growth hormone)

↓

Extreme hyperglycaemia with minimal/absent ketogenesis

↓

Hyperosmolality

↓

Prolonged osmotic diuresis

↓

Volume depletion leading to severe dehydration + electrolyte depletion

**Signs and symptoms of hyperosmolar hyperglycemic state**

Vital signs related to HHS include the following:

− Tachycardia
− Orthostatic decrease in blood pressure
− Hypotension
− Tachypnea
− Hyperthermia, if infection is present
− Management

Acute respiratory failure is an emergency condition. Urgent treatment of ARF is aimed at general resuscitation, rapid restoration of intravascular volume, replenishment of fluid and electrolyte deficiency, correction of hyperglycaemia and hyperosmolality.

**Monitoring of children during treatment for diabetic ketoacidosis**

| Parameter | Frequency | Comments |
|---|---|---|
| Vital signs | Hourly | Decrease in heart rate (not related to sleep or rehydration) or severe hypertension suggest possible cerebral injury |
| Fluid intake and output | Hourly | Ensure ongoing positive fluid balance |
| Neurologic status | At least hourly | Use GCS or similar assessment (refer to UpToDate content on cerebral injury in children with DKA) |
| Blood glucose | Hourly | Use a point-of-care meter, but cross-check with laboratory tests to ensure correlation |
| Blood BOHB | Every 2 to 4 hours, if available | Perform if test is available.<br>Resolution of DKA is indicated by BOHB ≤ 1 mmol/L (10.4 mg/dL) |
| Electrolytes, BUN, creatinine, venous blood gas | Every 2 to 4 hours | Timing of initiating potassium replacement depends on initial serum potassium level (refer to UpToDate topic text).<br>**Calculate the anion gap:**<br>•Anion gap = sodium − (chloride + bicarbonate)<br>•Normal anion gap = 12±2 (in mEq/L or mmol/L); indicates resolution of DKA*<br>**Calculate the corrected sodium concentration:**<br>▪ Corrected sodium = measured sodium + 1.6 (glucose − 100 mg/dL)/100<br>**NOTE** – For glucose measured in mmol, use: (glucose − 5.56)/5.56 |
| Calcium, magnesium, phosphorus | Every 4 to 6 hours | More frequent measurements may be required for patients with significant derangements in these laboratory values |
| ECG monitoring | Continuous, if available | Required for patients with severe DKA or significant electrolyte abnormalities (particularly potassium), but recommended for all patients |

GCS: Glasgow Coma Scale; DKA: diabetic ketoacidosis; BOHB: beta-hydroxybutyrate; BUN: blood urea nitrogen; ECG: electrocardiogram.
* Ketoacidosis can be considered resolved when the anion gap is normal (12±2 mEq/L or mmol/L), serum BOHB is ≤ 1 mmol/L (10.4 mg/dL), and venous pH is ≥ 7.3

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## THE LIST OF THEORETICAL QUESTIONS TO BE STUDIED IN PRACTICAL CLASSES:

1. Etiology of the diabetic ketoacidosis (DKA), hypoglycemia, hyperglycemic non-ketotic state; microangiopathies, macroangiopaties?
2. Pathogenesis and stages of DKA, hypoglycemia, hyperglycemic non-ketotic state; microangiopathies, macroangiopaties?
3. Pathomorphology of DKA, hypoglycemia, hyperglycemic non-ketotic state; microangiopathies, macroangiopaties?
4. Clinical presentation of the DKA, hypoglycemia, hyperglycemic non-ketotic state; microangiopathies, macroangiopaties?
5. Additional methods of examination (laboratory, instrumental)?
6. Principles of treatment (protocols) of the DM, DKA, hypoglycemia, hyperglycemic non-ketotic state; microangiopathies, macroangiopaties?

## TASKS

**1.** A 15-month-old girl is brought to the emergency room because she is lethargic and may have had a seizure. Her appetite has been decreased for 24 hours because of an intercurrent viral illness. Urinalysis reveals 3+ ketones and blood chemistry evaluation reveals:

Na = 140 mEq/L
K = 5.0 mEq/L
Cl = 100 mEq/L
CO2 = 19 mEq/L
Glucose 31 mg/dl

Based on the history and initial laboratory evaluation of this child, which is the most appropriate mode of action?

*A. Treat with intravenous glucose and admit to hospital for (diagnostic) 24-hour fast.*
*B. Treat with intravenous glucagon.*
*C. Perform oral glucose tolerance test.*
*D. Let the child eat and discharge from emergency room.*
*E. Obtain an electroencephalogram and begin treatment with phenobarbital.*

**The answer is A.** This child is hypoglycemic and ketonuric. The differential diagnosis includes idiopathic ketonic hypoglycemia, growth hormone (GH) deficiency and cortisol deficiency a well as some rare inborn errors of metabolism. After the acute episode is treated with intravenous glucose, the child should be fed and observed as she recovers from her intercurrent illness. She should then be admitted to the hospital for a 24-hours fast with frequent monitoring of blood glucose and urinary ketones. If she becomes hypoglycemic (blood glucose level

less then 40 mg/dl), blood should be obtained for measurement of electrolytes, cortisol, GH and organic acids (blood and urine). If the patients GH and cortisol levels are elevated (as they should be during the hypoglycemic stress) and she is not acidotic, the most likely diagnosis is idiopathic ketonic hypoglycemia. An oral glucose tolerance test is not an appropriate test for a child with hypoglycemia and ketonuria. In the presence of ketonuria, intravenous glucagon is unlikely to raise the blood sugar, therefore it is not an appropriate treatment.

**2.** A 10 year old boy admitted to the hospital because of sweating, lethargy, slurred speech. One month ago the boy had acute respiratory infection. The boy is sick by diabetes mellitus. The child was hospitalized in ICU. Glucose of blood – 1,9 mmol\l. All of the fallowing may be manifestations of an insulin reaction (hypoglycemia) in an diabetic patient EXEPT:

*A. Loss of appetite.* *C. Lethargy.* *E. Slurred speech.*
*B. Sweating.* *D. Bizarre behavior.*

**The answer is A.** Type 1 diabetes mellitus is characterized by a loss of insulin secretion by pancreatic beta cells. With the loss of insulin – the major anabolic hormone – a catabolic state develops. When treating DM with insulin there is a risk of relative insulin excess, with resultant hypoglycemia. Symptoms of hypoglycemia may be related to a sympathetic discharge and include sweating, tremulousness and hunger (not loss of appetite). More severe symptoms (e.g.,lethargy, bizarre behavior, slurred speech, seizures) are caused by glucose deprivation to the central nervous system.

**3.** Autoimmunity is thought to play a pathogenetic role in which of the following conditions?

*A. Hypophosphatemic rickets.* *D. Diabetes mellitus (type 1).*
*B. Familial hypercholesterolemia.* *E. 21-Hydroxylate deficiency.*
*C. Congenital hypothyroidism.*

**The answer is D.** Diabetes mellitus (type 1) is thought to have an autoimmune basis. Evidence for this is the presence of circulation islet cell antibodies in most newly diagnosed patients and the association of DM with other autoimmune disorders, such as Hashimoto thyroiditis, Graves disease and Addison disease. The other disorders listed in the question are not thought to be autoimmune in nature. Hypophosphatemic rickets is caused by defect in renal phosphate handing, familial hypercholesterolemia is caused by an inherited deficiency of low-density lipoprotein receptors and congenital hypothyroidism is caused by thyroid dysgenesis or defective thyroid hormone synthesis. 21-Hydroxylate deficiency – inherited defect of adrenal glands with variable degree of masculinization of external genitalia.

## TEST TASKS

**1.** A 12-year-old girl presents with irritability and tearfulness for about a year. A year ago she was also found to have diffuse enlargement of the thyroid gland (II grade). This condition was regarded as a pubertal manifestation, the girl did not undergo any treatment. The girl's irritability gradually gave place to a complete apathy. The girl' face is puffy, soft tissues pastosity, bradycardia, constipations. Skin pallor and gland density progressed, the skin has a waxen hue. Which of the followingt can be assumed?

*A. Subacute thyroiditis.* *C. Thyroid carcinoma.* *E. Diffuse toxic goiter.*
*B. Juvenile basophilism.* *D. Autoimmune thyroiditis.*

**2.** A 9-year-old boy, diagnosed with diabetes mellitus three years ago, was admitted to the hospital in a hyperglycemic coma. Primary dose of insulin should be prescribed basing on which of the following calculation:

*A. 0,05 units/kg of body mass per hour.*
*B. 0,1–0,2 units/kg of body mass per hour.*
*C. 0,3–0,4 units/kg of body mass per hour.*
*D. 0,2–0,3 units/kg of body mass per hour .*
*E. 0,4–0,5 units/kg of body mass per hour.*

**3.** A 17-year-old patient reports excessive body weight, headaches, irritability, and rapid fatigability. Significant weight gain occurred at the age of 14. On examination, the patient weighs 90 kg, with a height of 160 cm, and a proportional body build. Fatty tissue distribution is even, and there are thin pink striae (stretch marks) on the thighs, abdomen, and mammary glands. Blood pressure is 145/90 mm Hg. Which of the following is the provisional diagnosis:

*A. Pubertate dyspituitarism.* *D. Itsenko-Cushing's disease.*
*B. Alimentary constitutive obesity.* *E. Cushing's syndrome.*
*C. Somatoform autonomic dysfunction.*

**4.** The mother of an 8-year-old girl complains that the child is too short and has excessive body weight. On examination, there is obesity with fat deposits on the torso and face (round moon-like face), acne, striae on the thighs and lower abdomen, and hirsutism. Which of the following hormones can cause such symptoms, when in excess?

*A. Cortisol.* *B. Testosterone.* *C. Thyroxin.* *D. Glucagon.* *E. Insulin.*

**5.** In a 11-month-old baby, there are observable signs such as postponed tooth emergence, the closing of fontanels, muscular weakness, and heightened perspiration. The most likely type of hypovitaminosis in this child is which of the following?

*A. Hypovitaminosis A.* *C. Hypovitaminosis B1.* *E. Hypovitaminosis D.*
*B. Hypovitaminosis B6.* *D. Hypovitaminosis C.*

**6.** A 12-year-old girl is experiencing a significant advancement in physical development (+3σ). Her height has increased by 10 cm in a year, double the standard rate for her age group. While the number of permanent teeth aligns with the age norm (20), the development of secondary sex characteristics (Ma, P, Ax, Menarche) is three years ahead of her biological age. Development rate ahead of her biological age can occur due to which of the following:

*A. Acceleration.*
*B. Endocrine disorders.*
*C. Sports training.*
*D. Certain components of her diet.*
*E. Deficient hygienic education.*

**7.** A 13-year-old girl exhibits 30 % excess body mass and has been gaining weight since the age of 3. With a family history of obesity, she has normal height and sexual development, along with an excessive appetite. Periodical headaches are reported, and her blood pressure is 120/80 mm Hg. Subcutaneous fat is evenly distributed, with no stretch marks, and juvenile acne is present. Which of the following is the type of obesity?

*A. Hypothalamic syndrome of puberty.*
*B. Adrenal obesity.*
*C. Alimentary constitutive obesity.*
*D. Hypothalamic obesity.*
*E. Hypothyroid obesity.*

**8.** A 17-year-old girl presents with primary amenorrhea, no pubic hair growth, normally developed mammary glands, and the genotype 46 XY. The uterus and vagina are absent. The most likely diagnosis is: Which of the following is the diagnosis?

*A. Mayer-Rokitansky-Kuster-Hauser syndrome.*
*B. Cushing disease.*
*C. Testicular feminization syndrome.*
*D. Cushing syndrome.*
*E. Sheehan syndrome.*

**9.** A 11-year-old girl is displaying an advanced level of physical development. Over the course of a year, her height has increased by 12 cm, which is double the typical growth rate for her age group. Her permanent teeth count aligns with the age norm, and the development of secondary sex characteristics is three years ahead of her chronological age (Ma, P, Ax, Menarche). Such accelerated development beyond her biological age may be attributed to:

*A. Rapid growth (acceleration).*
*B. Specific components of her diet.*
*C. Inadequate hygienic education.*
*D. Involvement in sports training.*
*E. Endocrine disorders.*

**10.** During a routine examination, a 9-year-old girl diagnosed with type 1 diabetes mellitus presents with a 3 cm diameter, firm, painless swelling on the anterior surface of her hip. The skin over this swelling appears normal in color and temperature, and its location corresponds to where she typically administers her insulin injections. Which of the following is the most likely cause of this clinical presentation?

*A. Formation of post-injection abscess*
*B. Formation of post-injection infiltration*
*C. Development of atrophic lipodystrophy*
*D. Development of hypertrophic lipodystrophy*
*E. Allergic response*

**STANDARDS OF ANSWERS TO TEST TASKS:**

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|
| *D* | *B* | *A* | *A* | *E* | *B* | *C* | *C* | *E* | *D* |

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*Навчальне видання*

# СУЧАСНИЙ МЕНЕДЖМЕНТ ГОСТРИХ УСКЛАДНЕНЬ ЦУКРОВОГО ДІАБЕТУ

***Методичні вказівки***
***для здобувачів вищої освіти 5–6-х курсів***
***за спеціальністю «Медицина», лікарів-інтернів,***
***лікарів-педіатрів, лікарів-ендокринологів,***
***лікарів загальної практики – сімейної медицини***

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