DIABETES MELLITUS IN CHILDREN AND TEENAGERS

I. DEFINITION

Diabetes mellitus is one of the most frequent chronic conditions in children characterized by an absolute or relative INSULIN deficit with the loss of the body's ability to use carbohydrates as a source of energy. Consequently, the blood glucose level increases (hyperglycemia), the glucose passes into the urine (glycosuria) and the proteins and lipids are used to provide body energy.

II. CLASSIFICATION

Here is the etiological classification recommended by the American Diabetes Association and the WHO Expert Committee:

a) The type 1 diabetes mellitus is the most frequent form of diabetes in children and teenagers, with an occurrence of > 90%. It occurs due to an absolute INSULIN deficit caused by the destruction of the β pancreatic cells, with 2 sub-types:

☐ autoimmune
☐ idiopathic

b) The type 2 diabetes mellitus occurs due to a relative INSULIN deficit (by the decrease of the insulin secretion ability and/or by insulin resistance)

c) Specific types caused by:

- Genetic defects of the β cells function (various types of MODY)
- Genetic defects of the INSULIN action
- Exocrine pancreatic diseases: pancreatitis, tumors of pancreas, hemochromatosis, cystic fibrosis, etc.
- Endocrine diseases: Cushing syndrome, acromegaly, pheochromocytoma, hyperthyroidism, etc.
- Types caused by medicines or other chemicals: corticoids, thyroid hormones, thiazide, nicotinic acid, alpha interferon, vacor, etc.
- Infections: inborn rubella, cytomegalovirus infection
- Rare autoimmune forms (antireceptor insulin antibodies)
- Rare genetic syndromes sometimes associated with diabetes (Wolfram syndrome, Turner syndrome, Klinefelter syndrome, Prader-Willi syndrome, myotonic dystrophy, etc.)

d) **Pregnancy diabetes** that occurs through the mechanisms of the type 1 or 2.

**TYPE 1 DIABETES MELLITUS**

**III. ETIOPATHOGENESIS**

The production mechanism is autoimmune, the destruction of the β pancreatic cells being initiated in persons with genetic predisposition (HLA DR3 and DR4 antigens) by certain environmental factors (viruses, chemical and harmful agents, nutrition factors).

**IV. EVOLUTION STAGES**

1. Pre diabetes that precedes the clinical onset of the actual diabetes by several months or years.

   The initial normal blood sugar level stage is followed by the decrease of glucose tolerance or changes in the basal blood sugar level suggesting the transition from a normal blood sugar level to hyperglycemia.

2. State period or manifestation of the actual diabetes.

3. Partial remission period (« honey moon »).

4. Permanent insulin addiction stage.

**V. POSITIVE DIAGNOSIS**

The positive diagnosis is based on clinical and laboratory signs. The onset of the disease may be acute, intermediate or slow:

- **the acute onset** characterizes about 4% of the patients, being more frequent in suckling and infants, the diabetes coma symptoms being visible within 1-2 days;
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- **the intermediate onset** characterizes most patients (89.7%), the specific symptoms (polyuria, polydipsia, polyphagia and inexplicable weight loss) occurring within the 2-4 to 6-8 weeks before diagnosis setting. Therefore, the **anamnesis** is of the utmost importance in order to detect the disease before ketoacidosis onset;

- **the slow onset** characterizes children and teenagers (6.3%) and the symptoms occur several months before diagnosis setting. Gradual weight loss may result into the onset of the height-weight retardation, and the dermatological manifestations (staphylococcus infections, candidosis not responding to treatment) may draw attention to this diagnosis.

The **laboratory diagnosis** is based on the presence of one of the following criteria:

a) 2 basal blood sugar levels ≥126 mg/dl or

b) one blood sugar level at any time during the day ≥ 200 mg/dl or

c) after TTGO (1.75g glucose/kg max 75 g is administered) with the setting of the diabetes dg, when the blood sugar levels are:

- ≥ 126 mg/dl – basal blood sugar level
- ≥ 200 mg/dl – 2 hours after glucose intake

Other investigations required:

- glycosuria
- ketones blood level
- ketones urine level
- for ketoacidosis, Astrup parameters determination
- Hb A1c
- Insulin plasma level
- **plasma C peptide**
- immunity markers determination (ICA, Ac anti GAD, Ac anti INS) for the confirmation of the autoimmune mechanism.

To **conclude** with, **positive diagnosis** is based on the presence of specific symptoms and on a plasma sugar level ≥ 200 mg/dl or at least 2 values ≥ 126 mg/dl of the basal blood sugar level or after TTGO.
VI. DIFFERENTIAL DIAGNOSIS

a) differential diagnosis of onset acidoketosis coma with:
   - accidental poisoning (for instance acetylsalicylic acid poisoning)
   - encephalitis, meningitis
   - other neurological causes

b) symptoms due to ketosis (nausea, vomiting, abdominal pain) with acute abdominal pains in children and teenagers and acute dehydration syndrome in suckling

c) there should be made a distinction between polydipsia and polyuria in diabetes mellitus and diabetes insipidus

d) with temporary hyperglycemia due to:
   - insufficient development of the endocrine pancreas
   - pancreas overstress (higher iv glucose intake, medication causing hyperglycemia)
   - stress (hyperadrenergic factors)
   - by the decrease of peripheral glucose consumption

e) metabolic acidosis of hereditary metabolism diseases.

VII. TREATMENT

The treatment objectives are as follows: ensuring a normal growth rate and development of the child, preventing acute metabolic complications (hypoglycemia and ketoacidosis), chronic complications and ensuring a life to the patient as close to normal as possible, with a good psychosocial and professional integration.

These desiderata are achieved by the long-lasting maintenance of a normal blood sugar level.

The therapeutic means are:

a) insulin treatment
b) nutrition
c) exercise
d) specialized medical education of the patient and his/her family
e) blood and urine sugar self-check
The therapeutic approach depends on individual needs and is adjusted to the
disease, to the child and his/her family.

A. Insulin treatment

!!! For patients suffering from type 1 diabetes, insulin treatment has no other
alternative

- purpose: achievement of blood sugar levels as close to normal as possible
- daily insulin intake ≈ 1iu/kg/day of which
  - basal intake = 0.35 iu/kg
  - prandial intake = 0.65 iu/kg
  - decreases during remission < 0.5 iu/kg/day
  - increases at puberty and adolescence up to 1.5- 1.8 iu/kg/day
- insulin preparation choice: there have been used in children especially
  « human » rapid acting (Actrapid HM, Humulin R, Insuman R) and
  intermediate acting insulins (Insulatard, Humulin N) insulins, as well as
  rapid (Humalog, Novo Rapid, Apidra ) and basal (Lantus, Levemir) insulin
  analogs.

- Treatments diagrames:
  - the multiple daily injection therapy (MDI) consists of the administration of
    4 injections/day, of which 60-70% is rapid insulin (IR) and 30-40% long-acting
    insulin (II)
  - this treatment corresponds to the physiological secretion of the pancreas:
    the long-acting insulin administered in the evening tries to cover the basal
    needs and the 3 rapid insulin injections before the main meals try to imitate
    the postprandial secretion of a normal pancreas.
  - allows a relative freedom in the meals timetable, but
  - it requires insulin doses adjustment, which means a rigorous self-check of
    blood sugar levels
  - recommendations: at the beginning, at puberty, adolescence, in case of
    morning hyperglycemia
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☐ **conventional insulin therapy:**

- 2-3 injections/day
- 30-40% rapid-acting insulin and 60-70% intermediate-acting insulin
- it needs nutrition adjustment after insulin action
- it requires the strict observance of meal times and carbohydrates intake
- recommendations: in remission, in infants for whom doses distribution is difficult, in case of lack of compliance of the patient and/or the family as concerns the treatment

☐ **pump therapy ( continuous subcutaneous insulin infusion - CSII )**

- imitates the natural action of the pancreas

- providing a constant supply of insulin to the body and extra doses as needed

- the pump continuously supplies the body with the insulin

- unlike MDI therapy, the pump only supplies fast-acting insulin

- supplemental doses are steel needed

- CSII improves metabolic control while giving the patient greater freedom and enhanced quality of life

- factors influencing insulin treatment
  - ☐ the « dawn » phenomenon is the morning hyperglycemia determined by the growth hormone secretion increase, which determines temporary insulin resistance in the first morning hours (if the 3 a.m. blood sugar level is normal, then we can speak of the dawn phenomenon)
  - ☐ the Somogy phenomenon is the occurrence of morning hyperglycemia caused by a night hypoglycemia (the 3 a.m. blood sugar level is low).
- adverse reactions and complications
  - hypoglycemia represents the main fear of diabetic children and their parents
  - insulin allergy
  - abscess at the injection place
  - post-insulin edema
  - insulin resistance
  - lipodistrophy

B. Nutrition
- objectives
  - achievement of a well balanced blood sugar level and a normal metabolic rhythm
  - normal growth and development rhythm
  - maintenance of an ideal body weight
- general principles
  - nutrition similar to non diabetic children
  - constant daily carbohydrates intake
  - best proportion of nutritive principles
  - adjustment depending on age, sex, exercise
  - gastrotechnical variation
- diet composition
  - energy needs
    - Kcal/day = 1000 + 100 x age (years)
    - Kcal/kgb/day = 90 – 3 x age (years)
  - nutritive principles proportion
    - G (carbohydrates) = 50-55%
    - L (lipids) = 30-33%
    - P (proteins) = 13-15%
  - sweeteners: artificial and natural, calorigenic and non-calorigenic (for instance Saccharine, Cyclamate, Aspartame, etc.)
We recommend their use by turns, in order to avoid the use of the same sweetener for a long time, which may lead to adverse effects.

- fibers are recommended as they decrease the sugar level of foods
- meal times → synchronize meal times and insulin treatment
  3 main meals + 3 snacks
  carbohydrates distribution: 30% - lunch, 20% - breakfast and dinner, 10% - snacks
- diet education should begin on the first hospitalization and continued throughout the disease

C. Exercise
- decreases blood sugar levels by:
  - increasing the sensitivity of the peripheral tissues to INSULIN (functional changes at the level of insulin receptors )
  - increasing INSULIN absorption in the subcutaneous tissue
- practical recommendations
  - blood sugar level self-monitoring
  - additional carbohydrates intake
  - preventive INSULIN dose adjustment
  - avoidance of INSULIN injection in a body area subjected to exercise

D. Medical education
- purpose
  - achievement or improvement of metabolic balance
  - gradual taking over of treatment responsibility by the child
  - acute and chronic complications reduction
  - best psychosocial integration
  - regaining the will to live
- it is performed by a multidisciplinary team
- it is addressed both to the child and his/her family
- it is performed on an individual or group basis
- it starts on the first hospitalization (at the onset of the diabetes mellitus)
- it continues on an individual basis on periodic checks (out-patient clinics) or in groups (scheduled hospitalization or hospitalization caused by metabolic disorders)
- it is completed in medical camps
- it is adjusted to the cognitive abilities of the child, it is structured on topics
- methods: verbal, visual-suggestive, audio-visual
- it is periodically assessed and completed

E. Self-monitoring and insulin doses adjustment

Self-monitoring
- it means the performance of blood sugar level determination and urine tests (glycosuria-ketonuria) by the patient, at home

Purpose
- maintenance of a glycemic homeostasis enabling a harmonious growth and development and preventing acute and chronic complications

Blood sugar level self-monitoring
- essential for diabetes care on the long run
- each diabetic child should dispose of at least 2 blood sugar level check strips per day
- the blood sugar levels are filled out in the treatment book and the insulin doses are adjusted depending on these values

Urine self-monitoring
- if the AG is not possible, glycosuria determination may provide some information
- glycosuria provides a retrospective image of the blood sugar levels between 2 urinations
- the absence of glycosuria DOES NOT necessarily mean a normal blood sugar level
- ketonuria is determined in case of severe blood sugar level disorders and its occurrence requires a prompt therapeutic response

VIII. OUT-PATIENT CHECKOUTS

- periodic meeting with the medical team, on the average once a month
- protocol of a periodic visit:

  **Anamnesis:**
  - general state, hypoglycemic events, exercise, school results
  - check of the treatment book and correlation of the blood sugar levels in the book with the last value of Hb A1c (mean value of the glycemia over the last 3 months)

  **Clinical examination:**
  - weight, height
  - injection places examination
  - puberty development (Tanner stages)
  - check of the possible occurrence of lipid necrobiosis and limitation of joint movements as indicator of early chronic complications
  - the goiter may suggest a diabetes associated with another autoimmune disease (autoimmune thyroiditis)
  - blood pressure determination

  **Biological examination:**
  - quarterly determination of Hb A1c (mean value of the blood sugar levels over the last 3 months) in order to assess the quality of the blood sugar level checks
    - for the diabetic patient, the Hb A1c should ideally be below 7% (7.5% for small children)
  - lipid balance determination two times a year (total cholesterol, TG, HDLc, LDLc)
  - the screening of the chronic complications begins (according to the protocol in effect):
- after 5 years of evolution if the diabetes onset was before puberty
- after 2 years of evolution if the diabetes onset was at puberty
- after that, the checks are performed annually
- in order to detect diabetes retinopathy a simple ophthalmological exam or preceded by a fluorescein angiography is needed
- in order to detect incipient diabetes nephropathy, microalbuminuria is determined, 2 positive values (between 30-300 mg/24 hours) out of 3 successive determinations (performed within 1 to 6 months) being necessary.
- Subclinical diabetes neuropathy by determining the nervous leading speed (VCN)
- screening of other chronic complications (infectious, nutritional)
- other investigations required by the related diseases

From the therapeutic viewpoint, we focus on:
- insulin treatment: treatment diagram, dose/kg, rapid and intermediate insulin ratio
- nutrition: energy needs, carbohydrates intake, number of meals and carbohydrates distribution depending on the treatment diagram
- self-check at home: method, rhythm, accurate INSULIN doses adjustment
- education: theoretical and practical notions check and completion

Discussion with a psychologist is extremely important:
- at the beginning of the disease
- at puberty
- any time the family and the child think it necessary

Vocational guidance – of teenagers
IX. SOCIAL ISSUES

!!! All diabetic children and teenagers SHOULD have the SAME RIGHTS AND SOCIAL OPPORTUNITIES as the non-diabetic children and teenagers.

TYPE 2 DIABETES MELLITUS

This type of diabetes, occurring usually in adults, has been increasingly reported in children, in relation to obesity. There are certain ethnic groups with higher risks (African-Americans, native Australians, native Americans and Canadians, etc.), and is more frequent than type 1 diabetes in Japanese children. Unlike type 1 diabetes, most of the children and teenagers lack symptoms or have minimum symptoms at the time of diagnosis setting.

Another major issue is its relation to obesity, namely in about 80-90% of the patients.
Ketoacidosis may occasionally occur due to infections or other stresses.
Treatment principles:
the treatment is aimed at preventing long-term vascular complications, involving
- a healthy life style
- obesity management
- oral hypoglycemic agents administration (sulphonilureic, metformin, thiazolidindione)
- insulin treatment when the above-mentioned measures are inefficient.
The implementation of obesity prevention programs is very important given the high prevalence in certain population groups of type 2 diabetes related to obesity.