**CHRONIC NUTRITIONAL DISORDERS IN CHILDREN:OBESITY, DIABETES, PATOLOGY OF THYROID GLAND**.

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**DIABETES MELLITUS**

Type 1 diabetes mellitus (T1DM), one of the most common chronic diseases in childhood, is caused by insulin deficiency following destruction of the insulin-producing pancreatic beta cells.

It most commonly presents in childhood, but one-fourth of cases are diagnosed in adults.

T1DM remains the most common form of diabetes in childhood, despite the increasing rate of type 2 diabetes mellitus (T2DM).

*Epidemiology.*  In 2019, there were 227 580 incident cases of childhood diabetes worldwide. Cases of childhood diabetes increased by 39.37% (95% uncertainty interval [UI], 30.99%-45.45%) from 1990 to 2019.

The global incidence rate increased from 9.31 (95% UI, 6.56-12.57) to 11.61 (95% UI, 7.98-15.98) per 100 000 population.

Age and sex – The age of presentation of childhood-onset T1DM has a bimodal distribution, with one peak at four to six years of age and a second in early puberty (10 to 14 years of age).

*Risk factors.* Risk of diabetes is also increased when a parent has diabetes and this risk differs between the 2 parents: The risk is 3-4% if the mother has diabetes but 5-6% when the father has diabetes.

* In monozygotic twins, the concordance rate ranges from 30-65%, whereas dizygotic twins have a concordance rate of 6-10%. Islet cell autoantibodies (ICAs) have been identified in 85 percent of patients with newly diagnosed type 1 diabetes and in prediabetic subjects
* Target autoantbodies: Studies on the NOD (nonobese diabetic) mouse model indicate that proinsulin/insulin itself is the likely primary target for the autoantibodies.
* Perinatal factors — maternal age >25 years, preeclampsia, neonatal respiratory disease, and jaundice, especially that due to ABO blood group incompatibility;
* A variety of viruses and mechanisms may contribute to the development of diabetes in genetically susceptible hosts. Coxsackie B virus-specific immunoglobulin M (IgM) responses have been found in 39 percent of children with newly diagnosed type 1 diabetes, compared with only 6 percent of normal children.

Exposure to enteroviruses, both in utero and in childhood, can induce beta cell damage and lead to clinical diabetes.

* Role of diet — Several dietary factors may influence the development of type 1 diabetes, with most attention having been paid to cow's milk

Other dietary factors that have been suggested at various times as playing a role in diabetes risk include omega-3 fatty acids, vitamin D, ascorbic acid, zinc, and vitamin E.

* Psychologic stress.

*Pathogenesis.*

In T1DM, a genetically susceptible host develops autoimmunity against the host’s own β cells.

An injury to the pancreas causes the release of β-cell antigens (such as GAD65), which are captured by antigen-presenting cells (APCs) and presented to CD4 T cells.

The type and activation stage of the APCs, as well as the cytokine environment during CD4 T-cell activation, determine the differentiation of autoreactive T cells into diabetogenic T-helper type 1 (Th1) cells, T-helper type 2 (Th2) cells, or antigen-specific regulatory T cells.

A dominant Th1 autoimmune response leads to the recruitment and activation of cytotoxic CD8 T cells, which attack the pancreatic β cells. This results in a significant release of β-cell antigens, epitope spreading, and the destruction of the pancreatic islets.

*Clinical manifestations.*

Signs and symptoms of type 1 diabetes in children include the following:

* Hyperglycemia
* Glycosuria
* Polydipsia
* Unexplained weight loss
* Nonspecific malaise
* Symptoms of ketoacidosis

The decreasing β-cell mass with worsening insulinopenia, progressive hyperglycemia, and eventual ketoacidosis all imply that symptoms steadily increase, from early intermittent polyuria to DKA and coma, over weeks usually, rather than months.

• Initially, when only insulin reserve is limited, occasional postprandial hyperglycemia occurs.

• When the serum glucose increases above the renal threshold, intermittent polyuria or nocturia begins.

• With further β-cell loss, chronic hyperglycemia causes a more persistent diuresis, often with nocturnal enuresis, and polydipsia becomes more apparent.

*Non-emergency presentations*

* Non-emergency presentations of diabetes include:
* Recent onset of enuresis in a previously toilet-trained child, which may be misdiagnosed as a
* urinary tract infection or the result of excessive fluid ingestion.
* Vaginal candidiasis, especially in prepubertal girls.
* Chronic weight loss or failure to gain weight in a growing child.
* Irritability and decreasing school performance.
* Recurrent skin infections.

*Emergency presentations*

The usual emergency presentation of diabetic ketoacidosis in a child or adolescent includes:

* Severe dehydration.
* Frequent vomiting.
* Continuing polyuria despite the presence of dehydration.
* Weight loss due to fluid loss and loss of muscle and fat.
* Vomiting and abdominal pain, which may be misdiagnosed as gastroenteritis.
* Flushed cheeks due to the ketoacidosis.
* Acetone detected on the breath.
* Hyperventilation of diabetic ketoacidosis (Kussmaul respiration) is characterised by a high
* respiratory rate and large tidal volume of each breath, which gives it a sighing quality.
* Disordered sensorium (disoriented, semicomatose or rarely comatose).
* Decreased peripheral circulation with rapid pulse rate. Hypotension and shock with peripheral
* cyanosis (a late sign and rare in children with diabetic ketoacidosis).
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DKA occurs in 20-40% of children with new-onset diabetes and in children with known diabetes who omit insulin doses or who do not successfully manage an intercurrent illness.

***Hypoglycemia***

• Low blood glucose: treated when less than 60 mg/dL

• Develops because the body doesn’t have enough glucose to burn energy

• Can happen suddenly

• Can be treated quickly and easily by eating or drinking a small amount of glucose rich food

*The signs and symptoms include:*

Low blood glucose

Hunger

Headache

Confusion, shakiness, dizziness

Sweating

*Diagnosis.*

1. *Blood glucose.* Blood glucose tests using capillary blood samples, reagent sticks, and blood glucose meters are the usual methods for monitoring day-to-day diabetes control. Diagnostic criteria by the American Diabetes Association (ADA) include the following[1] :

- a fasting plasma glucose (FPG) level ≥126 mg/dL (7.0 mmol/L), or

- a 2-hour plasma glucose level ≥200 mg/dL (11.1 mmol/L) during a 75-g oral glucose tolerance test (OGTT), or

-a random plasma glucose ≥200 mg/dL (11.1 mmol/L) in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis.

The criteria for diagnosis of diabetes mellitus in children and adolescents are symptoms of diabetes mellitus such as polydipsia, polyuria, and unexplained weight loss plus casual glucose concentration ≥ 200 mg/dL (11.1 mmol/L) in venous plasma, fasting glucose ≥ 126 mg/dL (7.0 mmol/L) in venous or capillary plasma, or two-hours glucose during oGTT ≥ 200 mg/dL (11.1 mmol/L) in venous plasma or capillary whole blood sample.

1. Recently revised American Diabetes mellitus Association (ADA) criteria allow utilization of *hemoglobin A1c (HbA1c) ≥ 6.5*% for diagnosis of diabetes mellitus.
2. Emergency presentation

|  |  |
| --- | --- |
| Initial Labs  • Blood glucose  • Urine ketones  • Venous blood gas  • Basic blood chemistry  • Electrolytes  • BUN, creatinine  Magnesium, calcium, phosphorus | Additional labs  • CBC  • Osmolality  • Serum beta-hydroxybutyrate (β-OH)  • Hemoglobin A1c (HgbA1c)  • Pancreatic antibodies  • Additional testing as indicated  • CXR, non-contrast Head CT, Cultures (blood, urine, throat) |

**Treatment Overview**

*Treatment goals*

 Prevent death and alleviate symptoms

 Achieve biochemical control

 Maintain growth & development

 Prevent acute complications

 Prevent or delay late-onset complications

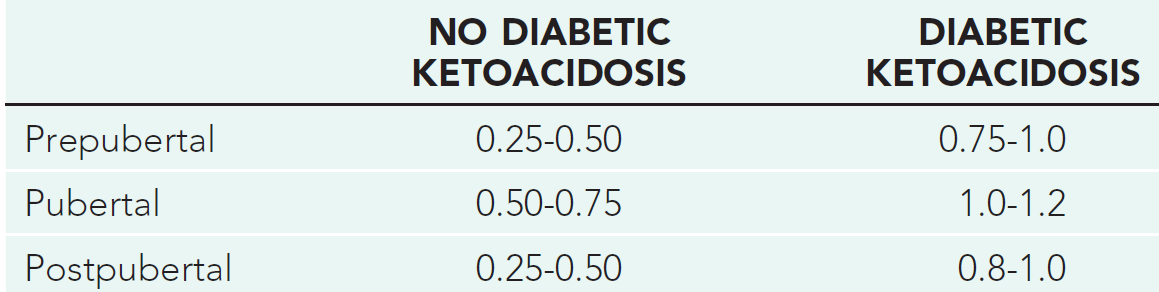
Insulin Therapy

• The dose is usually higher in pubertal children.

• It is also higher in those who are in DKA at the time of presentation.

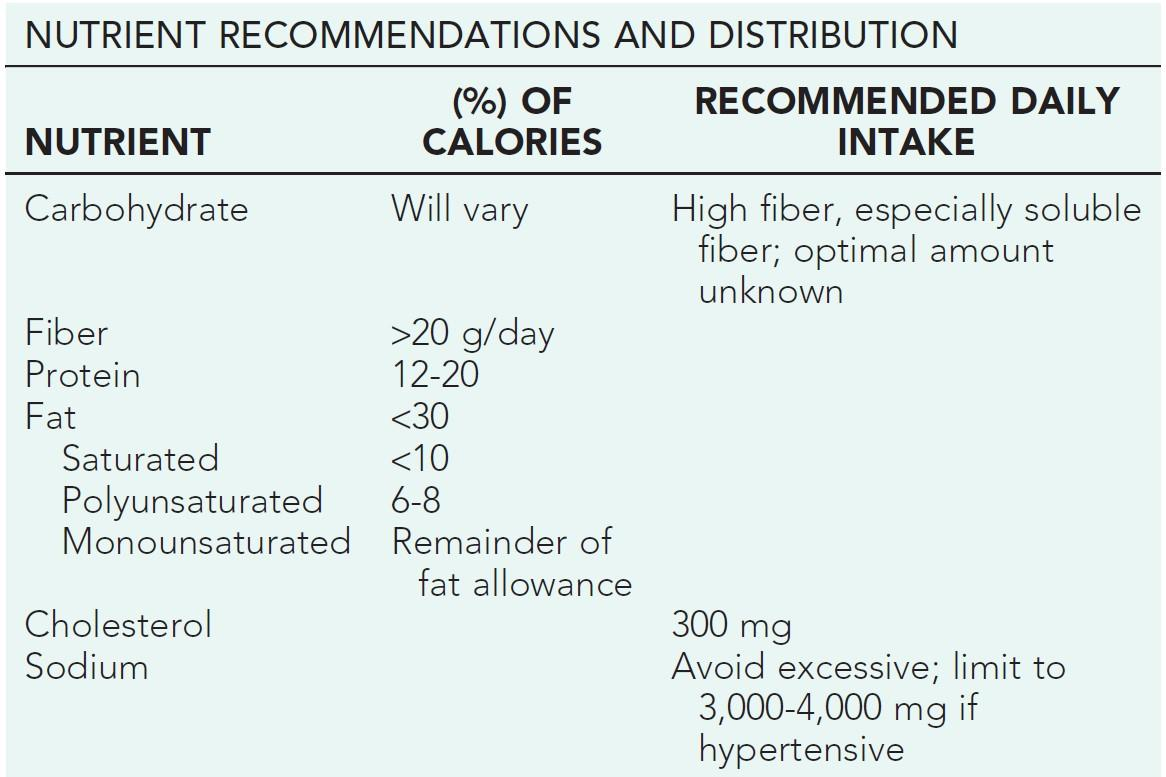
• The optimal insulin dose can only be determined empirically, with frequent self-monitored blood glucose levels and insulin adjustment by the diabetes

team.



Insulin Pump Therapy- can be programmed with a patient’s personal insulin dose algorithms.

Continuous Glucose Monitoring Systems- provide glucose readings to permit finer control of insulin administration by patients and families. To avoid hypoglycemia the glucose sensor sounds an alarm.



Long-term complications

• Complications of DM can be divided into 3 major categories:

(1) microvascular complications, specifically, retinopathy and nephropathy;

(2) macrovascular complications, particularly accelerated coronary artery disease, cerebrovascular disease, and peripheral vascular disease;

(3) neuropathies, both peripheral and autonomic, affecting a variety of organs and systems.

**OBESITY IN CHILDREN**

In 2019, an estimated 38 million children under the age of five were classified as overweight, with over 340 million aged 5-19 falling into the overweight or obese category.

In pre-school children aged 0-5 years, overweight and obesity are defined as the proportion of children with a sex- and age-specific body mass index-for-age value above +2 Z-score and above +3 Z-scores of the 2006 WHO recommended Growth Standards, respectively.

In school age children and adolescents aged 5-19 years, overweight and obesity are defined as the proportion of children with a sex- and age-specific body mass index-for-age value above +1 Z-score and above +2 Z-scores of the 2007 WHO recommended Growth Reference, respectively.

BMI should be calculated and documented in the medical record on all children ages 2-18 at least annually, ideally at a well child visit

***Etiopathogenic factors associated with obesity in children***

Genetic factors

Environmental and behavioral factors:

-dietary factor

-physical activity

-screen time

-sleep duration and quality

Iatrogenic factor (medications)

Endocrine factor (hypothyroidism, Cushing's disease, hypothalamic obesity, GH deficiency)

***Clinical picture***

• Fine facial features on a heavy-looking taller child

• Larger upper arms & thighs

• Genu valgum common

• Relatively small hands & fingers tapering

• Adiposity in mammary regions

• Pendulous abdomen w/ striae

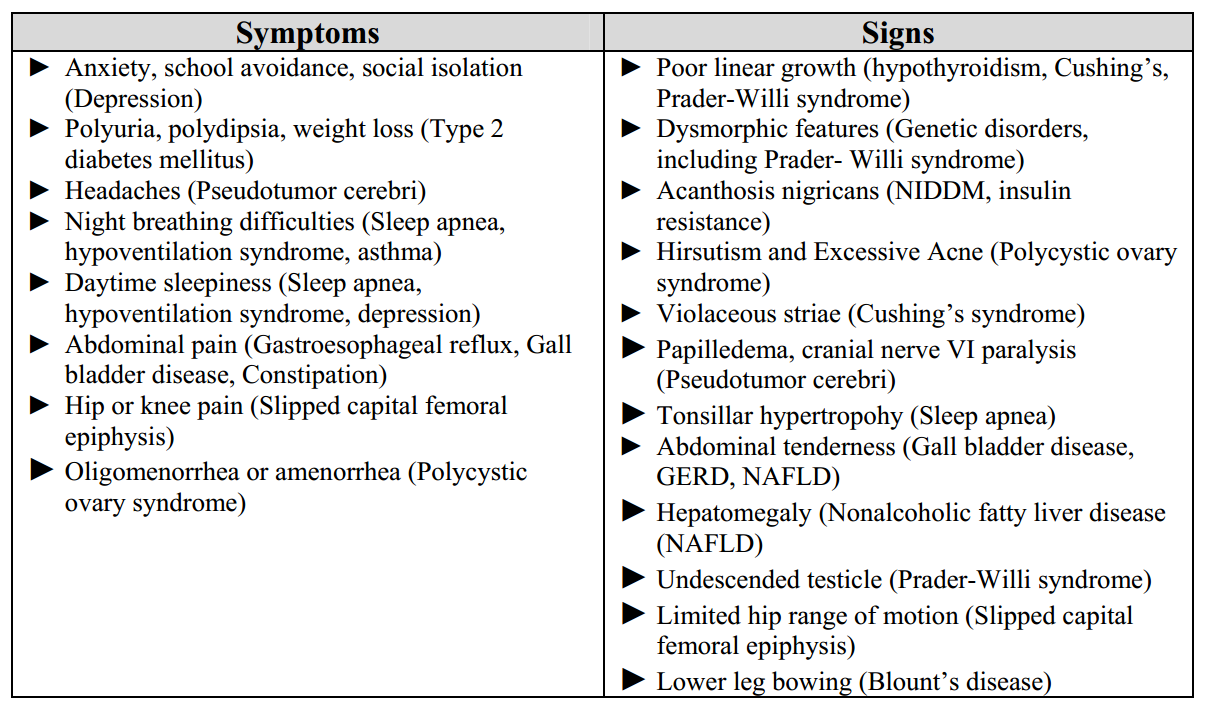
• In boys, external genitalia appear small though actually average in size

• In girls, external genitalia normal & menarche not delayed

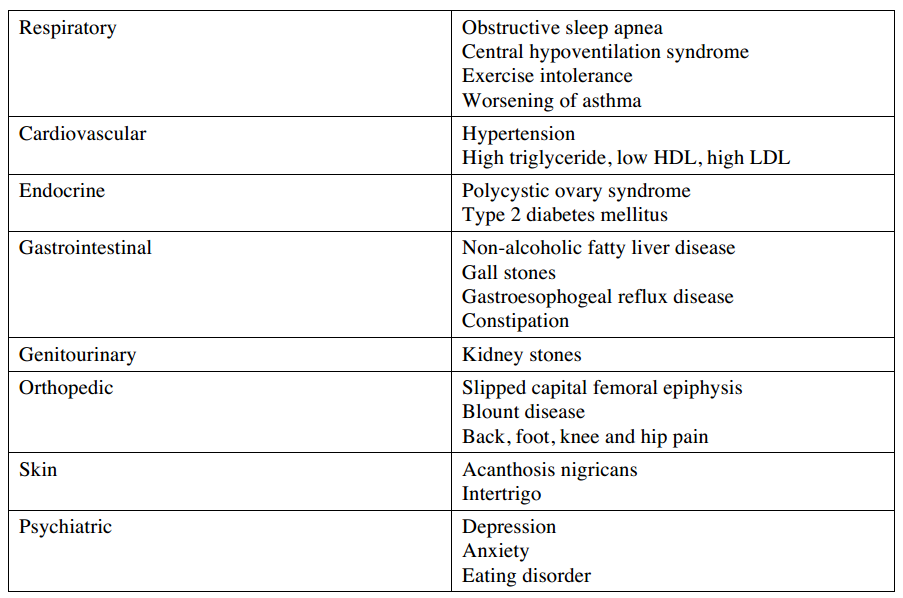
• Psychologic disturbances common

• Bone age advanced

*Symptoms and Signs of Conditions Associated with Obesity*



***Major and Minor Comorbid Conditions Associated with Obesity***



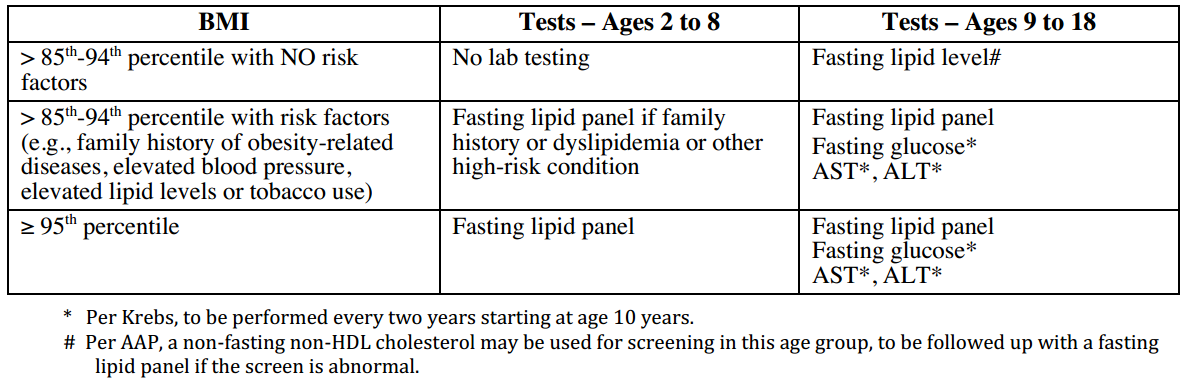
***Approaching the obese child***

1. Measure body mass index (BMI), plot results on a growth chart to classify weight status, and track changes over time.

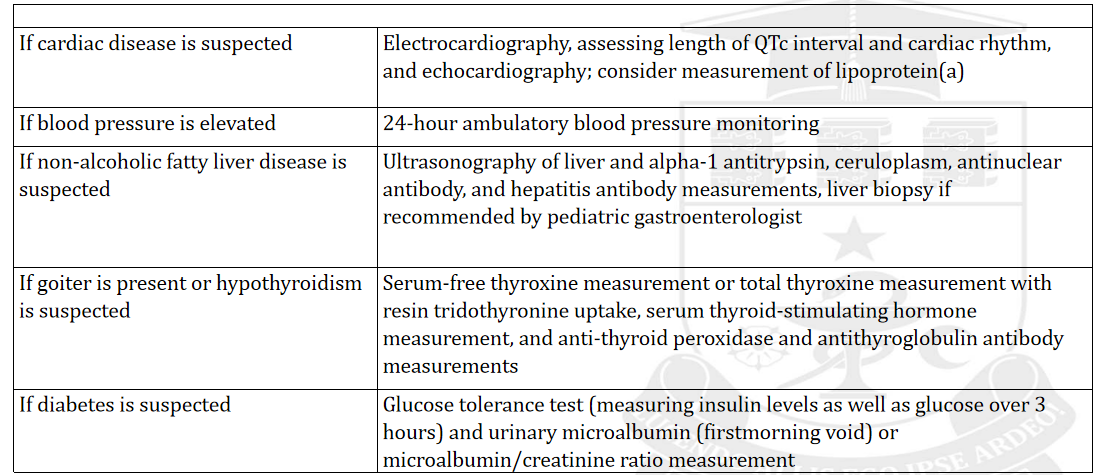
2. Screen for comorbidities in overweight/obesity in children: Focused review of systems,Blood pressure, Periodic laboratory monitoring

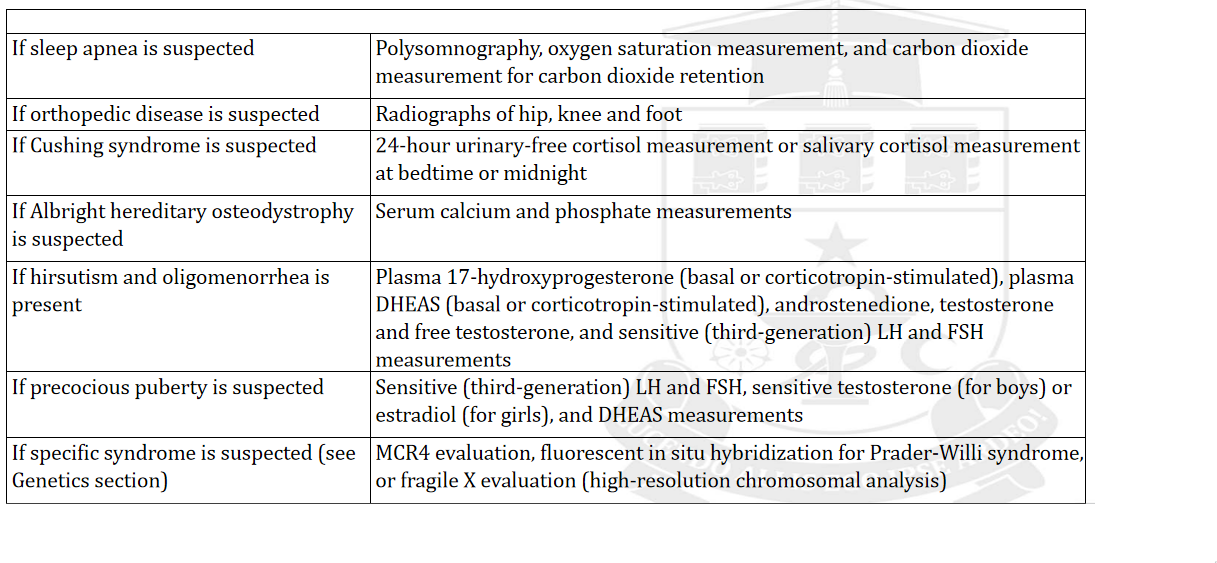
3. Effective lifestyle and behavior interventions.

***Laboratory Workup***



***Further Clinical Comorbidity Assessment***





***Νսtritiοո education and support***

* Physical activity education and support
* Behavior change strategies to establish these new behaviors in a nonstigmatizing way
* Family involvement in the program and targeting the household, in healthy changes
* Intensive interventions, so called because at least 26 hours of face-to-face contact over 3 to 12 months

The 5210 Toolkit is a nationally recognized weight management strategy aimed specifically at childhood obesity:

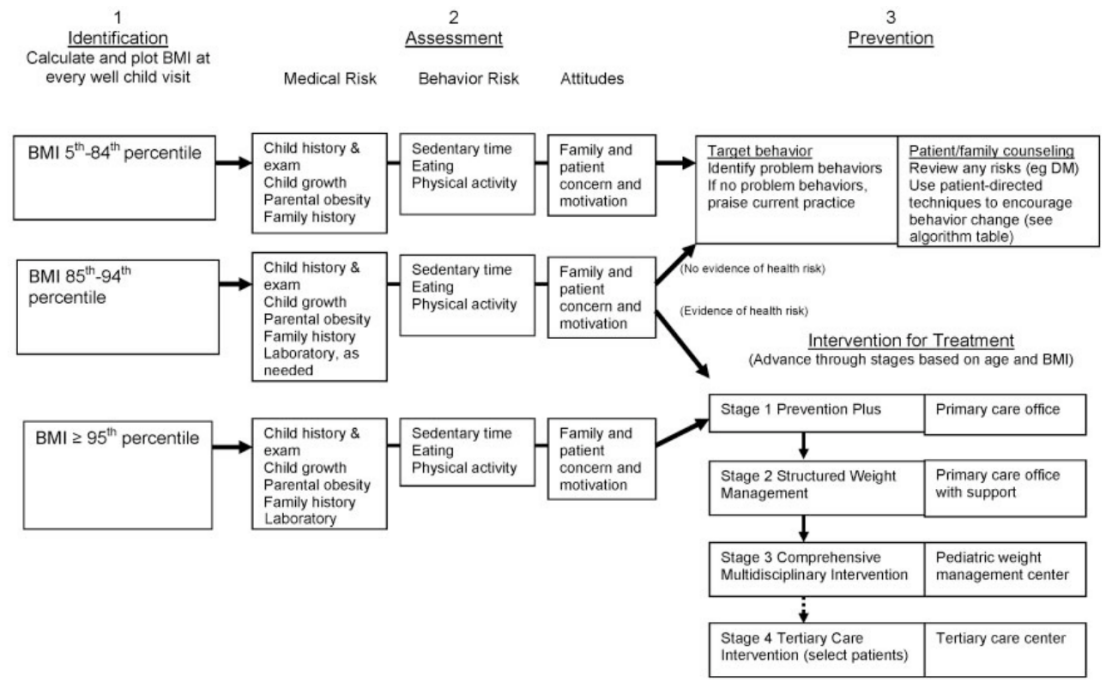
-5 or more fruits and vegetables

-2 hours or fiever recreational screen time

-1 hour or more of physical activity

-0 sugar drinks more water and only low-kalorie milks

***Universal assessment of obesity risk steps to prevention and treatment***



**CONGENITAL HYPOTHYROIDISM**

Congenital hypothyroidism is a partial or complete loss of function of the thyroid gland (hypothyroidism) that affects infants from birth (congenital).

*Epidemiology.* Congenital primary hypothyroidism, occurring in approximately 1:2000 to 1:4000 newborns, is one of the most common preventable causes of intellectual disability worldwide.

*Etiology.* Congenital hypothyroidism is most commonly caused by an embryologic defect in thyroid gland development (dysgenesis) or a defect in thyroid hormone synthesis (dyshormonogenesis).

Most cases of thyroid dysgenesis are sporadic, while the dyshormonogenesis disorders are inherited in an autosomal recessive pattern. Defects in thyroid hormone transport or action are rare causes of congenital hypothyroidism

*Classification.*

Primary hypothyroidism — Primary hypothyroidism refers to inadequate thyroid hormone production in the gland itself.

Central hypothyroidism — Central hypothyroidism refers to defects in the production of TSH due to either hypothalamic or pituitary dysfunction.

*Clinical picture.*

Asymptomatic newborns. The vast majority (more than 95 percent) of infants with congenital hypothyroidism have few, if any, clinical manifestations of hypothyroidism at birth.

Symptomatic infants. Infants born in regions of the world that lack newborn screening programs typically present with symptoms and signs of hypothyroidism that develop over the first few months of life, which include lethargy, hoarse cry, feeding problems, often needing to be awakened to nurse, constipation, puffy (myxedematous) and/or coarse facies, macroglossia, umbilical hernia, large fontanels, hypotonia, dry skin, hypothermia, and prolonged jaundice (primarily unconjugated hyperbilirubinemia).

If an infant has central hypothyroidism, the clinical manifestations are often related to associated deficiencies of other pituitary hormones and include:

hypoglycemia (growth hormone and adrenocorticotropic hormone),

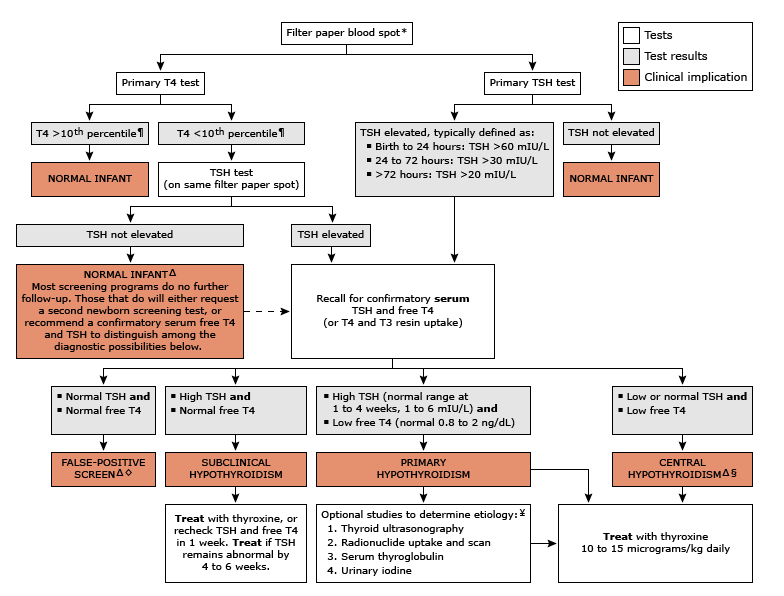
micropenis (growth hormone and/or gonadotropins),

undescended testes (gonadotropins), and,

least commonly, features of arginine vasopressin deficiency (previously known as central diabetes insipidus).

*Diagnostic.*Neonatal Screening. Blood for screening is collected onto filter paper cards after heel prick, and the cards are then sent to a centralized laboratory for testing.

For full-term infants, the sample is optimally collected between 24 and 72 hours after birth.



*Treatment tools.*

Levothyroxine is the recommended treatment for children with primary or central hypothyroidism. The goals of treatment are to restore normal growth and development, including pubertal development.

For patients with subclinical hypothyroidism, treatment decisions often depend on the degree of thyroid-stimulating hormone (TSH) elevation.

Levothyroxine dose — Initial treatment is started with levothyroxine at the following doses, given by mouth, once daily:

●Age 1 to 3 years – 4 to 6 mcg/kg body weight

●Age 3 to 10 years – 3 to 5 mcg/kg

●Age 10 to 16 years – 2 to 4 mcg/kg