ENDOCRINE SYSTEM IN CHILDREN

Endocrine system of regulation means endocrine glands' cells production of the special matters – hormones which go into a blood, are carried by it and carry out functions' regulation of organs and tissues-targets (strengthening or weakening depending on the necessities of organism).

Hormones **are peculiar envoys, commands, coded by a chemical way. Depending on composition of their nature they can be peptides or steroids (derived from cholesterol).** ***Peptide hormones*** **react with specific receptors on the surface of cellular membranes.** ***Steroid hormones*** **react directly with DNA inside the cells, freeing the effects of genes with achievement of the proper effects.**

There is general conformity to the law of the endocrine system action– as more hormones are excreted, as much intensity of execution of organs' and tissues' function. Lack of hormone conduces to the function's stop or its very low level.

Organization of hormonal management in an organism is based on doubling (a few hormones can approximately execute similar aims), and counter- regulation: there are antagonistic counter-hormones.

The *feedback principle* – in condition of disappearance of necessity in strengthening of function automatically the intensity of hormones making goes down or counter-hormones switch on.

Endocrine glands possessing an intra-secretory function include a *hypophysis (pituitary gland, pituitary cerebri), epiphysis (pineal gland), adrenal (or suprarenal gland), thyroid gland (glandula thyroidea), parathyroid glands, thymus (thymic gland), pancreas, sexual glands (or gonades).*

Each of the endocrinal glands possesses a specific function, but all of them are in close intercommunication with each other and with CNS, providing unity of organism's functions regulation, that is reflected in the often used term *"neuroendocrine (neurohumoral) regulation".*

The main organizing center **which provides regulation in the conditions of intensive stream of neuroendocrine impulses and participates in feedbacks forming is *hypothalamus*.**

Efficiency of *hypothalamus*` work is explained that it is a part of brain and is regulated by direct communications with the numerous neurons of CNS. In its turn the hypothalamus possesses by hormonal activity, synthesizes relysing-hormones which stimulate formation of hypophyseal hormones tropic to the endocrine glands. The functional state of endocrine glands, especially of hypothalamo-hypophysial «axis», has the enormous value for children, because determines their growth and development.

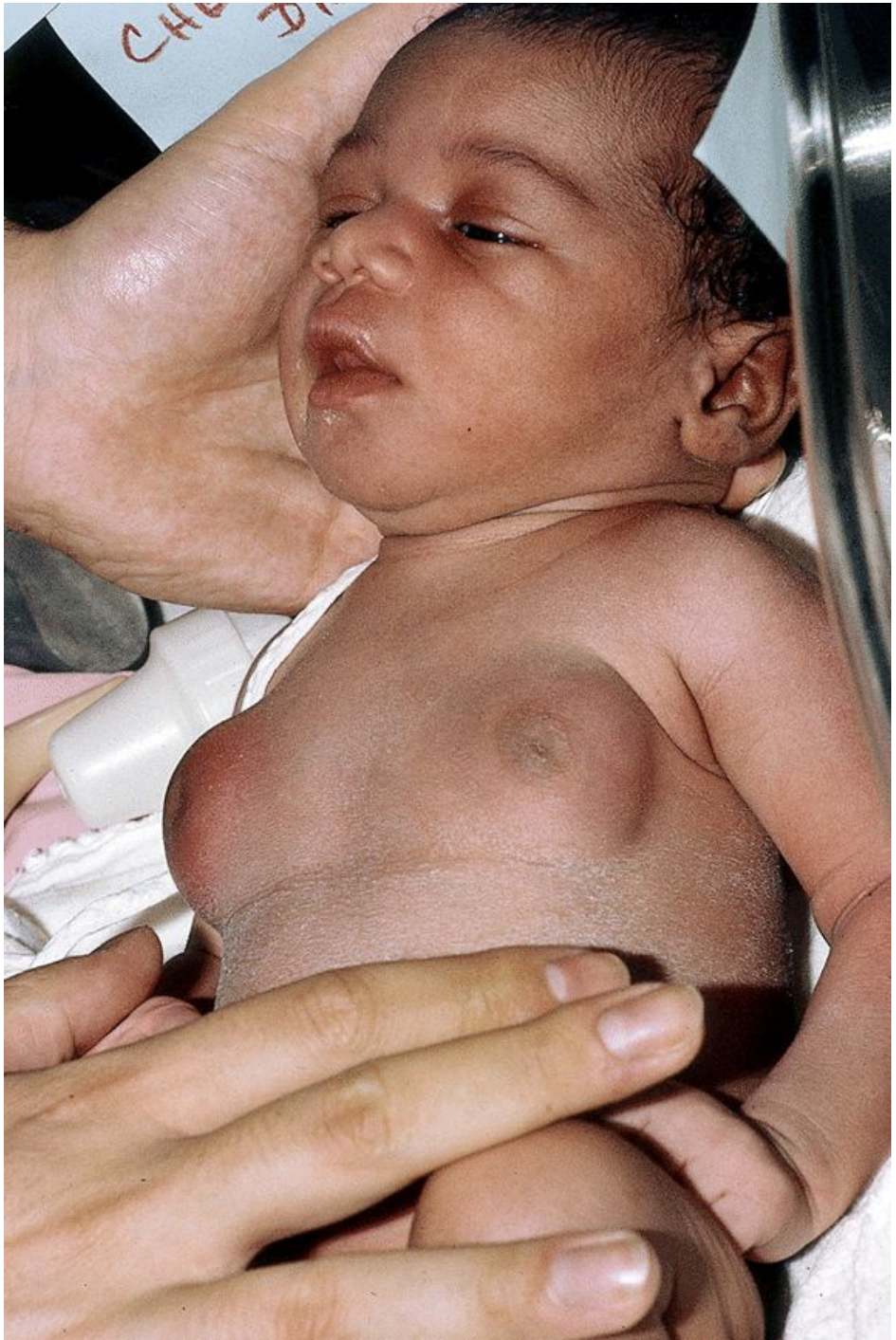
The system of the endocrine regulation depends very much on ability of cells and tissues` receptors to react specifically in answer of the hormonal impulses.

The features of endocrine system in different periods of childhood.

Most endocrine glands' organogenesis and the hypothalamus` formation begin on 5 — 6th week of embryonic phase. The hormonal synthesis begins after organogenesis' completion in the first trimester of pregnancy.

From positions of embryology it is necessary to define the hypothalamus, hypophysis and epiphysis as derivative structures of cerebrum. Thymus (thymic gland), thyroid and parathyroid glands are derivated from embrionic branchial pockets. Pancreas is formed from middle bowel's diverticulum of embryo. Adrenal glands` forming takes place together with the renal cortex. In the II trimester the participation of the systemic axis called hypothalamus - hypophysis - adrenal cortex is already expressed in regulator activity. At the moment of birth the hypophysis possesses distinct secretory activity, which is confirmed by a presence in the umbilical cord blood of fetus and newborn a high contents of ACTH. Functional activity of adrenal cortex in a prenatal period is also proved.

The fetal development especially on an early stage, undoubtedly, is happening under close control of mother's hormones which a child gets with a placental blood and continues to get with motherly milk in postnatal period.



Benign gynecomastia in a newborn due to hyperestrogenemia in a mother.

The endocrine diseases of mother with high concentrations of hormones in blood can cause similar diseases in a fetus and newborn (for example, thyrotoxicosis in newborns).

Two male infants (twins) with neonatal congenital hyperthyroidis

Clinical features include lack of subcutaneous tissue and wide-eyed, anxious stare.

Summary:

In prenatal period **the hypophysis and thymus achieve the most anatomic and functional development.**

After birth **the adrenal, pancreas, thyroid and parathyroid glans are advancing quickly while the hormonal activity of thymus is exposed to reverse fase.**

Teens **- the turbulent development of sexual glands begins at onset of pubertal period. The definitive forming of them signifies ending of childhood and their age involution means old age coming.**

The essence of endocrine regulation in human organism.

The hormonal system of regulation is organized by the feedbacks.

For example, thyreotropin-dismissive hormone of hypothalamus promotes making of anterior hypophysial lobe's the thyroid-stimulating hormone (TSH, thyrotrophin, thyrotropic hormone) which in its turn stimulates making of thyroid hormones–triiodothyronine and thyroxin. The sufficient contents of thyroxin brakes hypothalamus and its stimulating function fades.

Principles on which the clinical research of endocrinal system is based on.

1/ Detection of signs and syndromes which are characteristic of hyper- or hypoproduction of hormones in a patient.

2/ Determination of hormones' concentrations in blood serum, taking into consideration the principle of feedback. It means if the countent of eventual effectoring (tissue) hormone is low the simultaneouse increasing of hypophysial and hypothalamic fuction happens with proper tropic and releasing hormones production. (And vice versa).

3/ Detection of abnormal organs' and cells-targets' reaction for hormones (for instance, the feminizations` phenomenon in boys having testicles with their development on a womanish type also called as a testicular feminization due to ignorans of body cells to react to testosterone).

4/ Determination of endocrine glands' sizes and their other specifications.

The increase of endocrine gland's sizes is not necessarily accompanied by hormonal production increase. For example, in case of euthyroid goiter when there is the compensating increase of thyroid gland in size due to lack of iodine in food.

Description of ductless glands in children, effects of their hormones on organs and cells-targets, semiotics of insufficiency or surplus of activity of endocrine glands.

Hypothalamus.

Hypothalamus is the part of cerebral trunk and simultaneously supreme organ in the system of feedbacks and direct communications in the system of endocrine regulation. As a part of nervous system the hypothalamus participates in forming of major vegetative functions such as senses of *hunger* and *thirst*, maintenance of *body temperature*, *arterial pressure*, *sweating (perspiration)* and many others. At the same time as an organ of endocrine system the hypothalamus produces *releasing hormones (factors)* able to excite the hypophysial humeral production. *It means that the hypothalamic hormones are mainly directed on target-cells of hypophysis.*

The *innate* structural abnormalities of hypothalamus, as a rule, are not compatible with life. More frequently in medical practice it is necessary to deal with the *acquired diseases of hypothalamic area* like a consequence (sequelle) of acute viral encephalitises.

Semiotics of hypothalamic lesions.

The hypothalamic syndrome (hypothalamic disfunction) proves by various vegetative disorders (like *bulimia* or *excessive appetite*, *unmotivational thirst, body temperature fluctuations* which so-called as the *fever related with CNS damege*, *asymmetry of perspiration, arterial hypertancion).* In this cases appropriately there are disorders of many other endocrine glands. Their activity can be both increased and weakened as a result of hypothalamic disorders development. The patients' appearance often corresponds to *severe obesity* with surplus mass reaching up 200% and more over normal. It is so-called hypothalamic obesity. It develops very quickly after the inflammatory disease of CNS with the hypothalamic area lesion.

Hypophysis (pituitary cerebri).

The pituitary gland is also derived part of brain and its meninges. However the hypophysis has all attributes of the independent endocrine gland. Its secrets penetrate into the blood reaching other endocrine glands and regulate their activity. Anatomically the pituitary gland is located in the bones` hollow on the skull basis' internal surface called "*turkish saddle*" (lat. *sella turcica*).

The anterior hypophysial lobe (anterior pituitary) produces several tropic peptide hormones. They are the somatotropic hormone (STH, somatotropin) or growth stimulating hormone, adrenocorticotropic hormone (ACTH), which stimulates adrenal cortecal hormones` production, thyrotropic (TSH) and gonadotropics (GTH) hormones.

What is the physiological role of STH in childhood period?

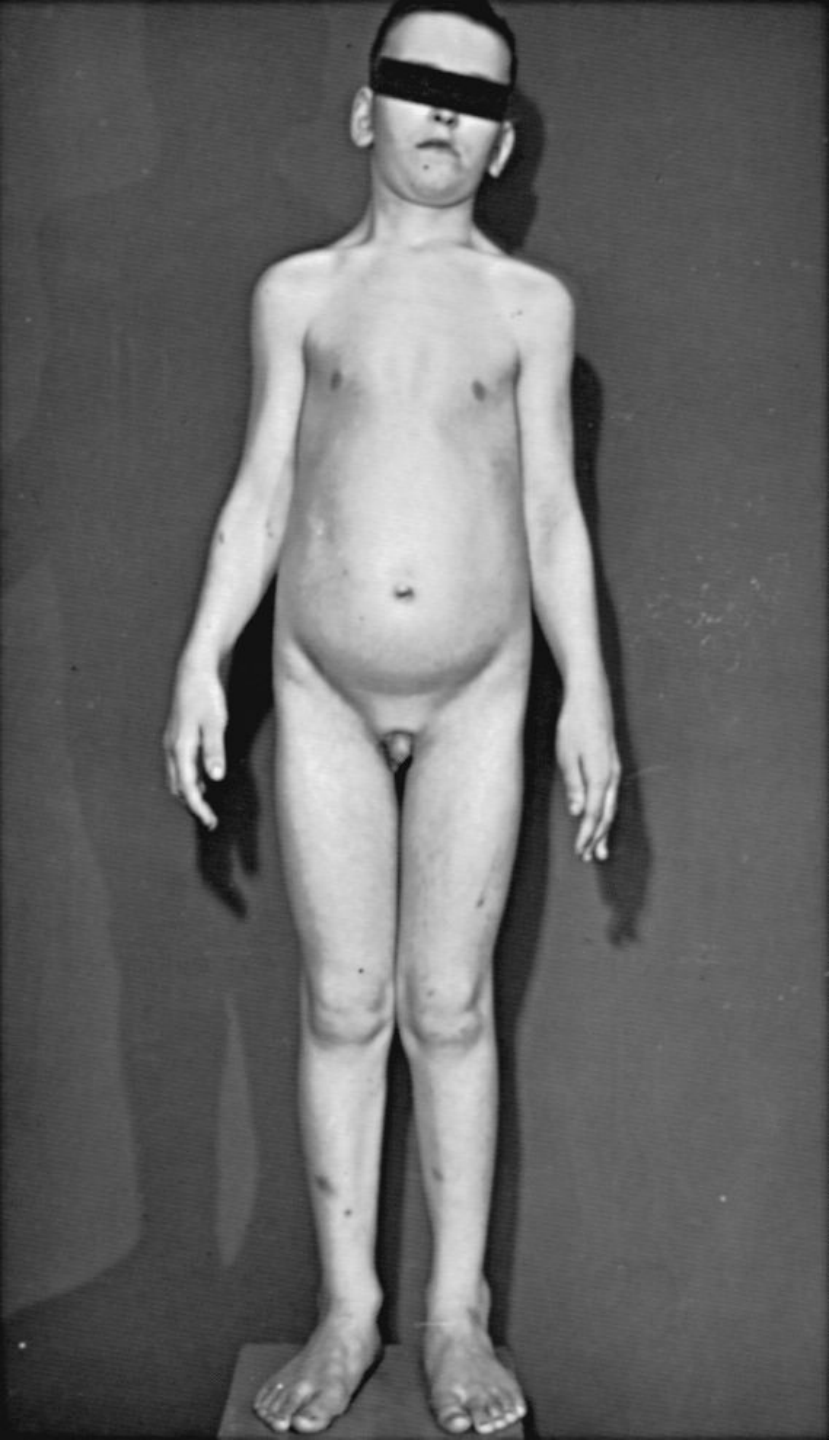
In postnatal period the STH is the main metabolic factor influencing on all types of metabolism. Under its action directly in body tissues the factor of growing similar to insulin is forming up which biological role consists in ensuring of body growing up and maturation as biological phenomena pro se.

The posterior hypophysial lobe (posterior pituitary) is anatomically closely connected with hypothalamus (hypothalamo - hypophysial axis-system). The posterior hypophysial lobe is the main producer of ***oxytocin*** which intensifies contraction of womb and mammary ducts in breast in nurses women and ***vasopressin (antidiuretic hormone - ADH)*** which takes part in regulation of the water balance in any ages. The regulation of ADH syntheses and its coming in blood are controlled by hypothalamus.

Semiotics of pituitary gland's lesions:

hyper – and hypofunction

The *anterior hypophysial lobe's hyperfunction* (commonly due to *adenoma*) occures like a rare disease. The adenoma shows itself by high values of STH and pathological influences upon the growth. It leads to hypophysial ***giantism*** (do not mix up with family tall stature!). The anterior lobe hormonal active adenoma of pituitary gland's with high level of STH content in blood develops mostly in teenagers and adult persons. In these patients the definitive body length alredy has achived and people can not grouth up more. Equal to abnormal grouth in patients with pituitary hyperactive adenoma in clinical practice this condition leads to ***acromegalia***. The acromegalia is nominated as an unusual increasing of the limbs in their distal parts and face (nose, lips etc.).



Cerebral gigantism in an 8-yr-old boy. The height age was 12 yr; the bone age was 12 yr; IQ was 60.

Notice the prominence of the forehead and the jaw and the large hands and feet.

The adult height is 208 cm. He wears size 48 shoes.

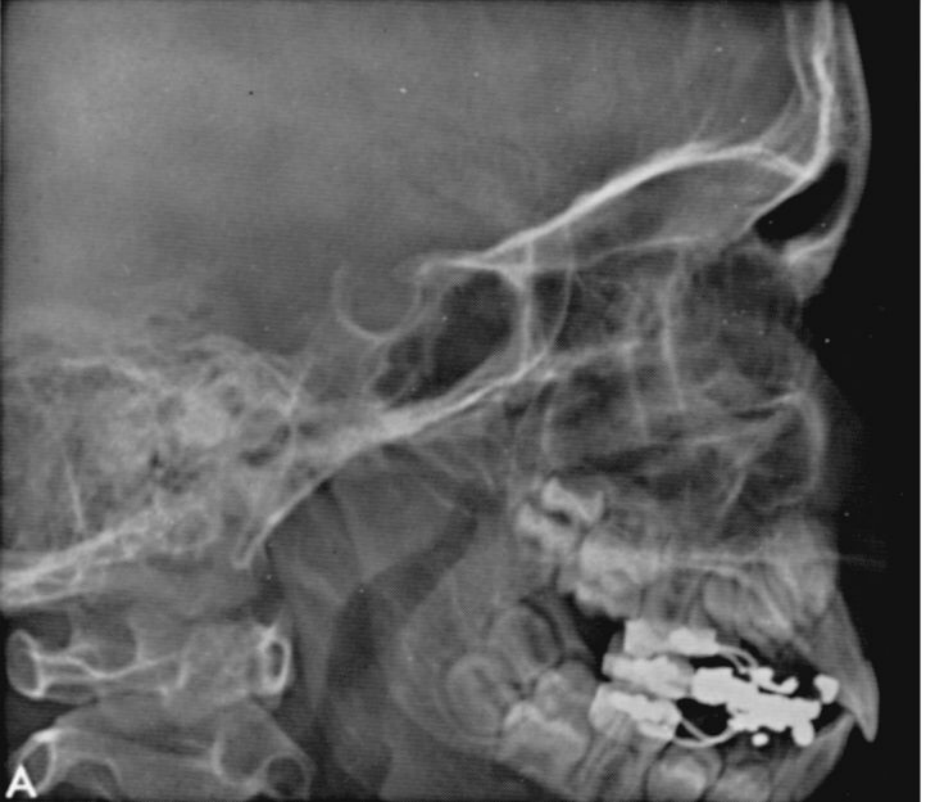
If the hormonal active adenoma of anterior lobe of pituitary gland is accompanied by *hyperproduction of ACTH* it leads to *hypophysial form of Cushing's disease*. The Cushing's disease or syndrome is characterised by high levels of serum *gluco-* and *mineralocorticoids* in plasma. There are also symptoms of *hyperglycemia*, *"similar to buffalo" type of obesity, hypernatremia, hypokalemia, arterial hypertension* and *edematouse skin*.

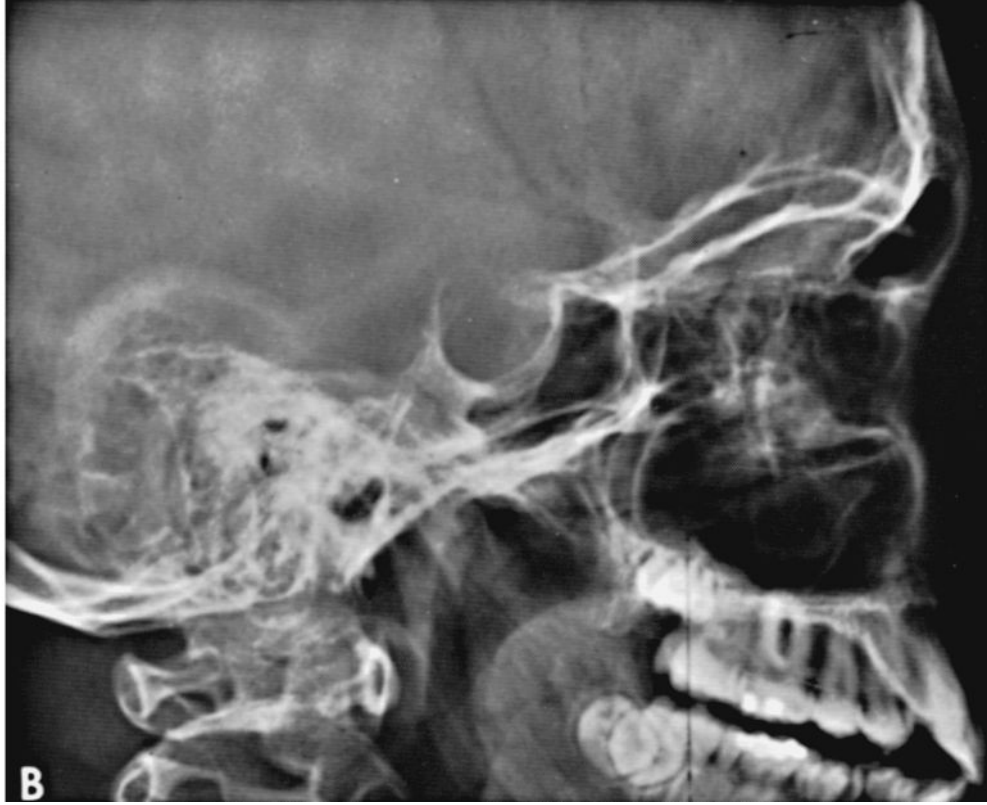
*The **hypofunction of anterior lobe of pituitary gland*** usually proves itself by concentrational *decrease of STH*, *insulin like growth factor* and *gonadotropic hormone (GTH).* The condition causes the ***hypophysial proportional dwarfism (nanism) with delay of sexual developement.***

The common functional disturbances of anterior hypophysis can provoke disturbance touch all sides of gland's activity. This syndrome is called as *dispituitarism* and quite often it appears only in teens.

Hypophysail posterior lobe's dysfunction.
Due to *insufficient production of ADH* the symptoms of pathological ***polyuria*** and ***polydipsia (diabetes insipidus)*** develop in condition of absence of hyperglycemia and glucosuria.

Objective visiul stady of the pituitary gland is possible observing size of the sella turcica on *lateral roentgenogram of the skull*. This is one of visualising methods in endocrinology and is broadly used in clinical endocrinologic practice.





Roentgenograph of the skull of a 9-yr-old boy with polydipsia, polyuria, nocturia, and enuresis. Urine specific gravity was 1.010 after water deprivation. Growth was normal, and the sella turcica was considered roentgenographically to be at the upper limit of normal but was probably enlarged. Over the ensuing 6 mo, the symptoms of diabetes insipidus abated.

The patient returned at 14 yr of age because of growth failure and delay in sexual maturation. Studies revealed a deficiency of growth hormone, gonadotropins, corticotropin, and thyrotropin. Note the enlargement of the sella turcica. There was exacerbation of diabetes insipidus with the administration of hydrocortisone and thyroxine. At surgery, a large *craniopharyngioma* was found.

Adrenal glands

Adrenal cortex produces more than 60 biologically active materials and tissues` hormones of *steroid* nature, which because of their influence on metabolism are divided on *glucocorticoids (cortisone), mineralocorticoids (aldosteron, 11-desoxycorticosterone)* and *sexual hormones - androgens (17-ketosteroids and testosterone)* and very small concentrations of female sexual hormones – *estrogens* (for example, *estradiol*).

The production of cortico - and mineralocorticosteroids are found under control of hypophysial ACTH and interconnected with it. These hormones provide the catabolic effects releasing energy, possess an antistressal and immunoregulating properties. The mineralocorticoids participate in regulation of fluids and sults balance. They predispose to delay of sodium and remove the potassium.

The *role of adrenal glands' sexual hormones* is especially important in prenatal period. This role consists in forming of primary sexual signs which differentiate phenotypically children on boys and girls.

In period of human life since the birth till adolescens the small amouts of adrenal sexual hormones regulate only anabolic reaction and support the growing. The bodies of children in their 8-9 years practically do not differ too much in boys and girls. The genitalias formed according to genotypical sign are an exception.

At the beginning of pubertal stage (approximately in 11 years old girls and 13 years boys) obeying to hypothalamic and hypophysial humoral signals the adrenal glands react by transitory increasing of adrenal male gonadial hormone production (testosterone) both in boys and in girls. The body transformation cascade of sexual puberty starts. First of all the *pubarche* (growing of lean light hair on pubis) appears.

Subsequently only the sexual glands' activity for all time of sexual puberty will provide forming of secondary sexual signs.

After the age dependant involution of gonades the adrenals again will become a source of testosterone like in early childhood and this hormone will maintaine the anabolic reactions in olderness.

Semiotics of adrenal cortex' lesion

About adrenal cortex' activity the clinicians consider basing on *ACTH, corticosteroids', mineralocorticoids' contents in blood, on serum potassium, sodium and chloride* which disturbans should be indirect signs of *hypo- or hyperaldosteronism*, on concentrations of *17-ketosteroids in urine*, on *Cushing's, Addison's symptoms performance*, on *correctness of external genitalia' forming in girls* (subjects with genotype 46, XX), on possible signs of *premature puberty* in boys and girls.

The acute adrenal insufficiency syndrome

The signs are *weak and rapid pulse*, *arterial hypotention, hypoglycemia, bluish spotted skin (livedo).*

The chronic suprarenal insufficiency (Addison's disease)

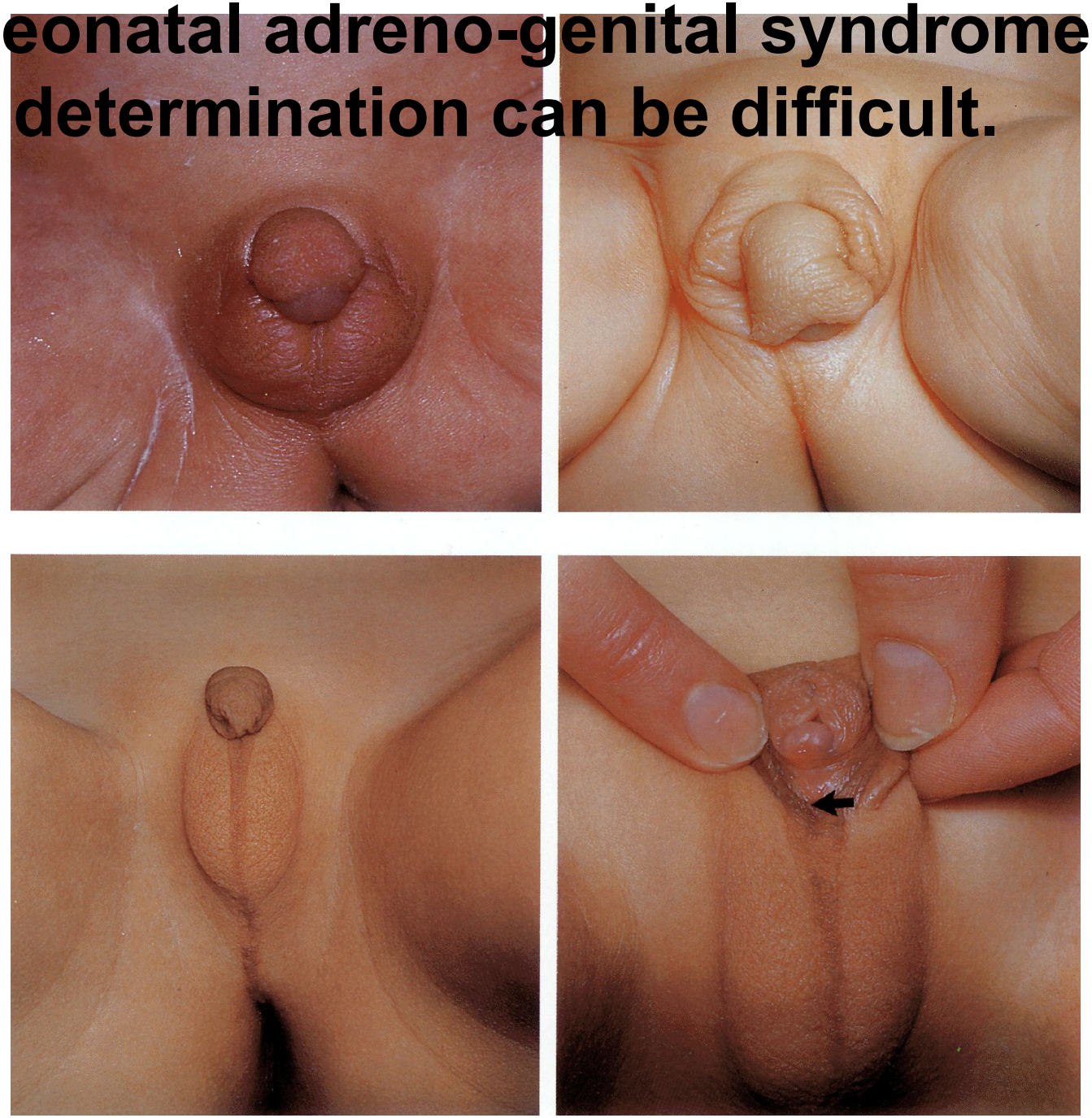
The signs are the *weight losing*, edvanced *muscular weakness*, peculiar *brownish skin* colouration on abdomen, on area of genitalia and joints (*"bronze disease").* The serum *hyponatremia* and *hyperkalemia* are characteristic.**Both for acute and for chronic forms of adrenal insufficiency it is characteristic of serum low levels of glucocorticoids and mineralocorticoids. Besides, for chronic form of insufficiency it is typical of high concentration of serum ACTH as result of futile pituitary`s signals to intensify the suprarenals` function.**

The abnormally ***increased function of adrenal cortex*** with *hypersecretion of glucocorticoids, androgens* and *partly mineralocorticoids* cause the suprarenal form of the *Cushing's syndrome*. In children this condition develops basically as a result of adrenal cortexs' hormonal active tumor. In these cases the level of *ACTH* in plasma is low.

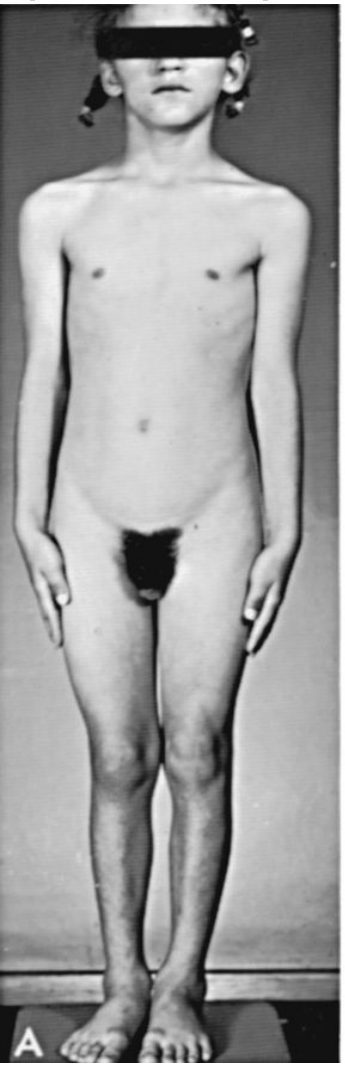
The genetically determined disturbances with ***hyperproduction of 17- ketosteroides*** (testosterones` line) by suprarenal glands, possible, *with simultaneous deficit of mineralo-* and *gluco-corticoids* in plasma.

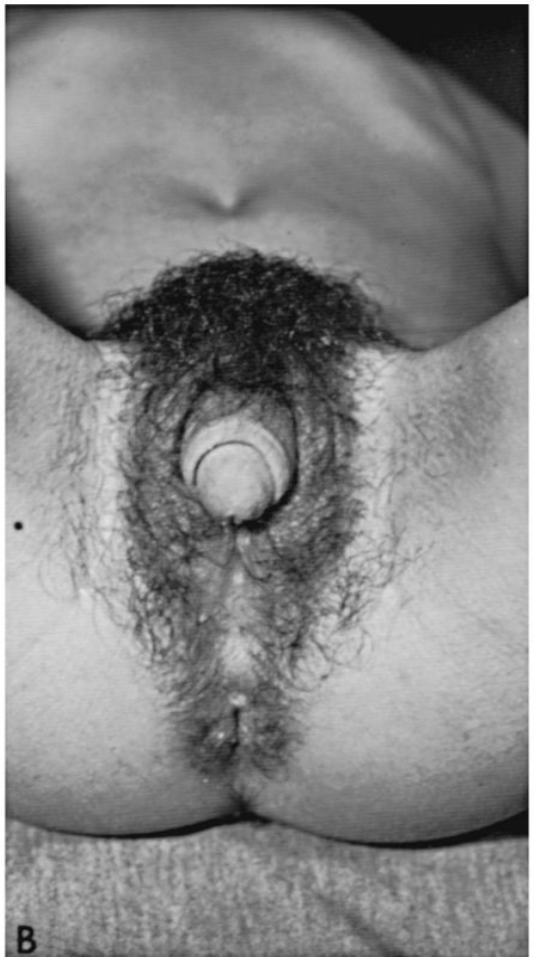
The affected children develops so-called *adreno-genital syndrome*. The clinical pattern of syndrome is the most tipical in girls. In them the external genitails' *virilization* can occur in children even in utero. The external genitalias are getting masculine: the clitoris hypertrophies and labia becomes to look like a scrotum. The sex determination in newborn becomes difficult. Some forms of adreno-genital syndrome are accompanied with lack of mineralocorticoids and *phenomenon of sodium loss* with urine and severe *vomiting.* The affected children are getting dehydrated.

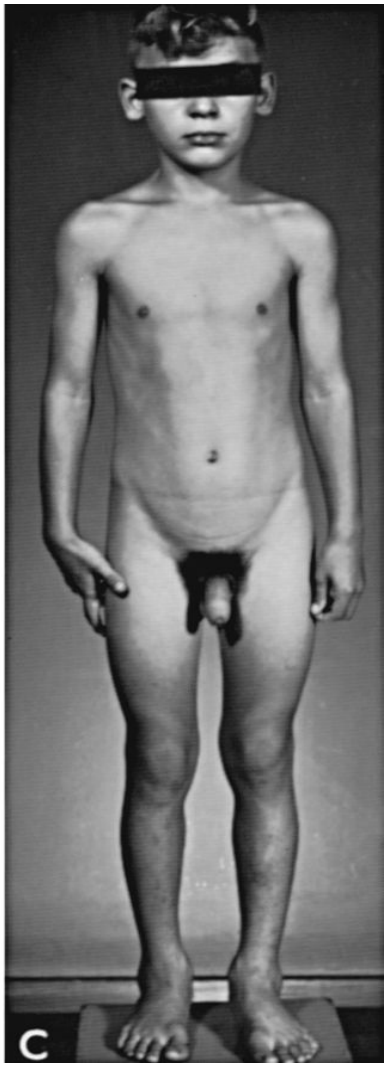
In neonatal adreno-genital syndrome the sex determination can be difficult.



In elder age (between 3 and 8 years in girls and 3 - 11 years in boys) the symptoms of late adreno-genital syndrome are the *virilization* in girls and *premature (precox) puberty* both in girls and in boys.







A. A 6-yr-old girl with congenital adrenal hyperplasia. The urinary 17-ketosteroids were high (50 mg/24 hr).

B. B. Notice the clitoral enlargement and labial fusion.

C. Five-yr-old brother was not considered to be abnormal by the parents. The urinary 17-ketosteroids were also high (36 mg/24 hr).

Semiotics of selective lesion of suprarenal medulla.

The main hormones of adrenal medulla are ***adrenaline*** and ***noradrenaline***. They influence on the level of arterial blood pressure and regulate adaptive reactions in stress. The *pheochromocytoma* (hormone-active tumor of suprarenal medulla) is a rare in children disease and is characterized by severe attacks of *arterial hypertension* due to *hypercatecholaminemia*. The laboratory studies reveal the high levels of *adrenaline, noradrenaline* and/or their metabolities in blood and urine.

Thyroid gland

The thyroid gland synthesizes two main hormones: *triiodothyronine (T3)* and *thyroxin (T4).* These hormones are regulators of basic metabolism, consequently, determine child's growing and influence on excitability of nervious system. The function of thyroid gland is closely connected with pituitary gland function which adjusts its activity on feedbacks' principle using *TSH.*

Thyroid gland functional insufficiency

Thyroid gland functional insufficiency or *hypothyroidism* is one of the most frequent endocrine diseases in children. The hypothyroidism can develop as an innate or acquired disease. It can be caused by congenital aplasia of thyroid gland or acquired lesion. The size of the gland can be normal or enlarged (the *goiter or struma*).

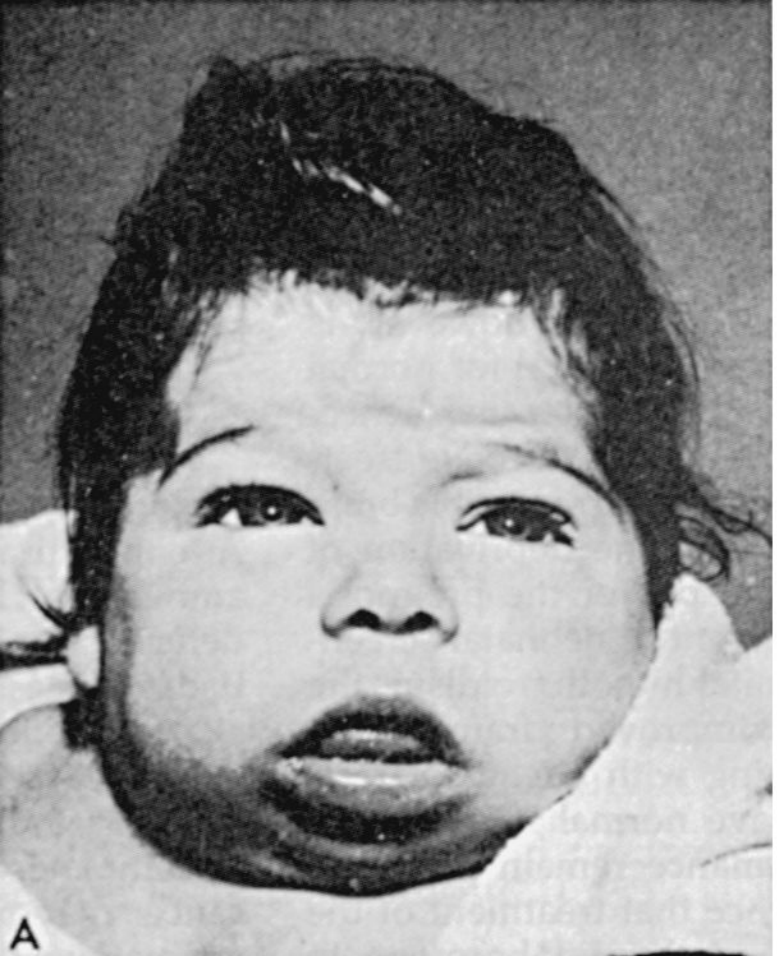
The clinical manifestations of *congenital hypothyroidism* appear in neonatal period or early infancy in form of the ***cretinism***.

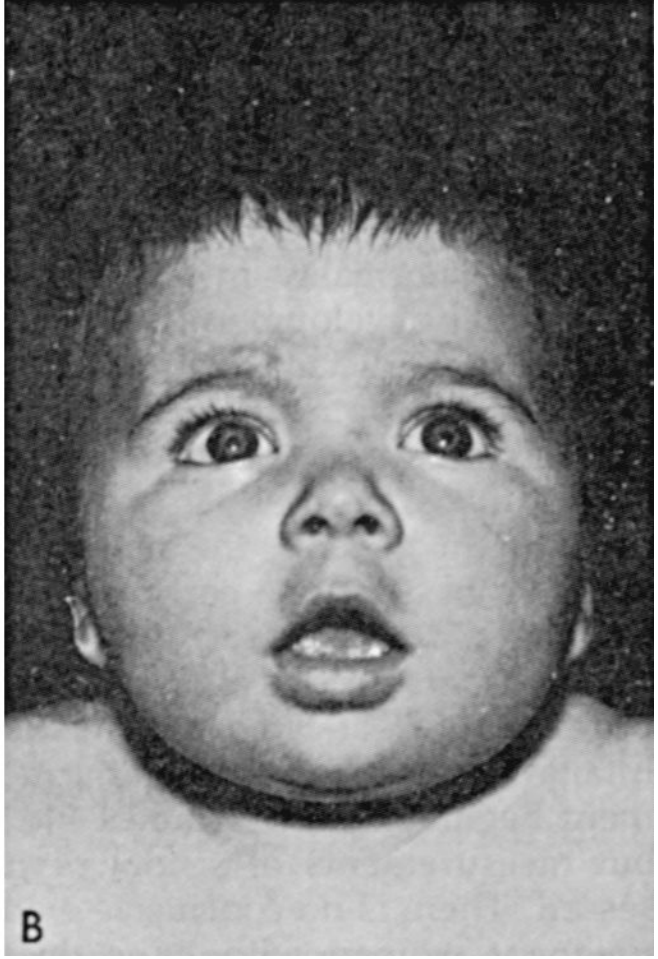
The cretinism means the *dwarfism* with *mental retardation*.

Early manifestation in neonatal period include:
feeding difficulties (lack of interest and choking spells;
respiratory difficulties (nasal obstruction or labored and noisy respiration;
prolonged physiological jaundice as an important sign for suspicion.

The *late symptoms* of innate hypothyroidism, as a rule, are the result of late diagnosis. The affected children start to loss an intellect and coarse features of appearance are getting evident.

The *coarse features* are: *large head, coarse hair, low anterior hair line, wrinkled forehead, swollen eye lids and thick protruded tongue*. Sometimes the *hoarse voice* attracts attention on. The *umbilical hernia* is present. Simultaneously the *motor* (the child does not head support, delayed sitting, standing) and *mental* (does not smile, laughing, recognize of mother etc.) *delay* is progressing.

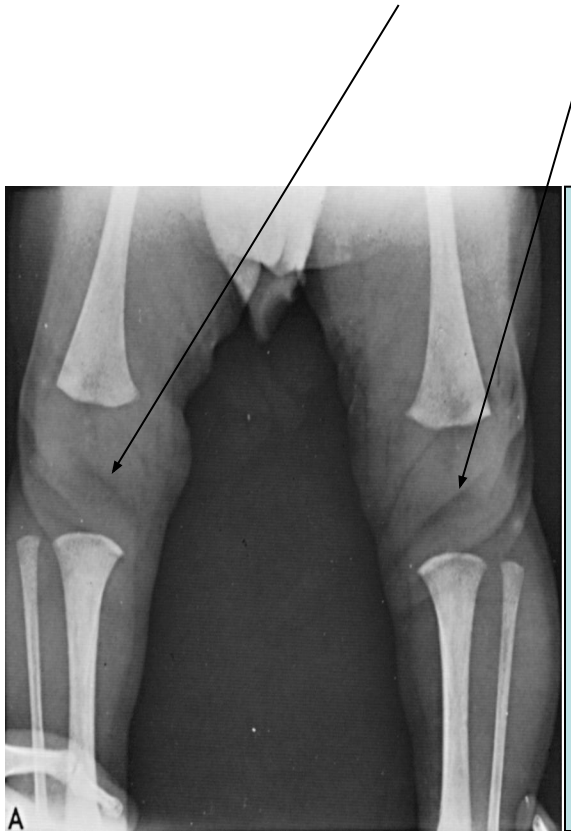




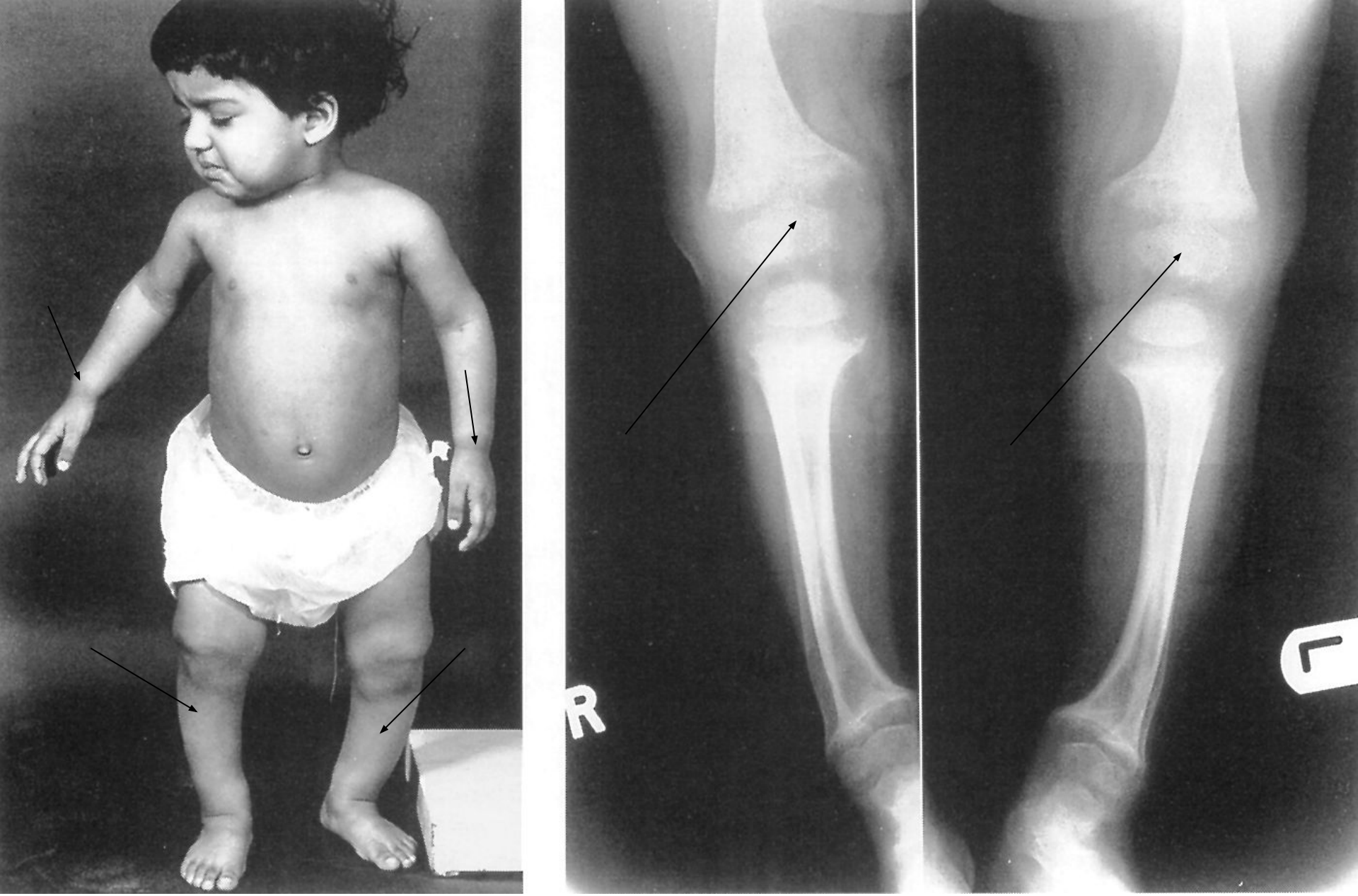
Congenital hypothyroidism in an infant 6 mo of age. The infant fed poorly in the neonatal period and was constipated. She had a persistent nasal discharge and a large tongue; she was very lethargic; and she had no social smile and no head control.

A.Notice the puffy face, dull expression, and hirsute forehead. Osseous development was that of a newborn.
B. Four mo after treatment, notice the decreased puffiness of the face, the decreased hirsutism of the forehead, and the alert appearance.

Among additional confirmatory investigations the X-Ray symptome of bone ossification delay is important. In infants suspected as hypothyroid it is enough to make the rontgenologic study of knee joint. The lag of hip epiphysises ossification means that hypotireoidism started before childs` delivery.



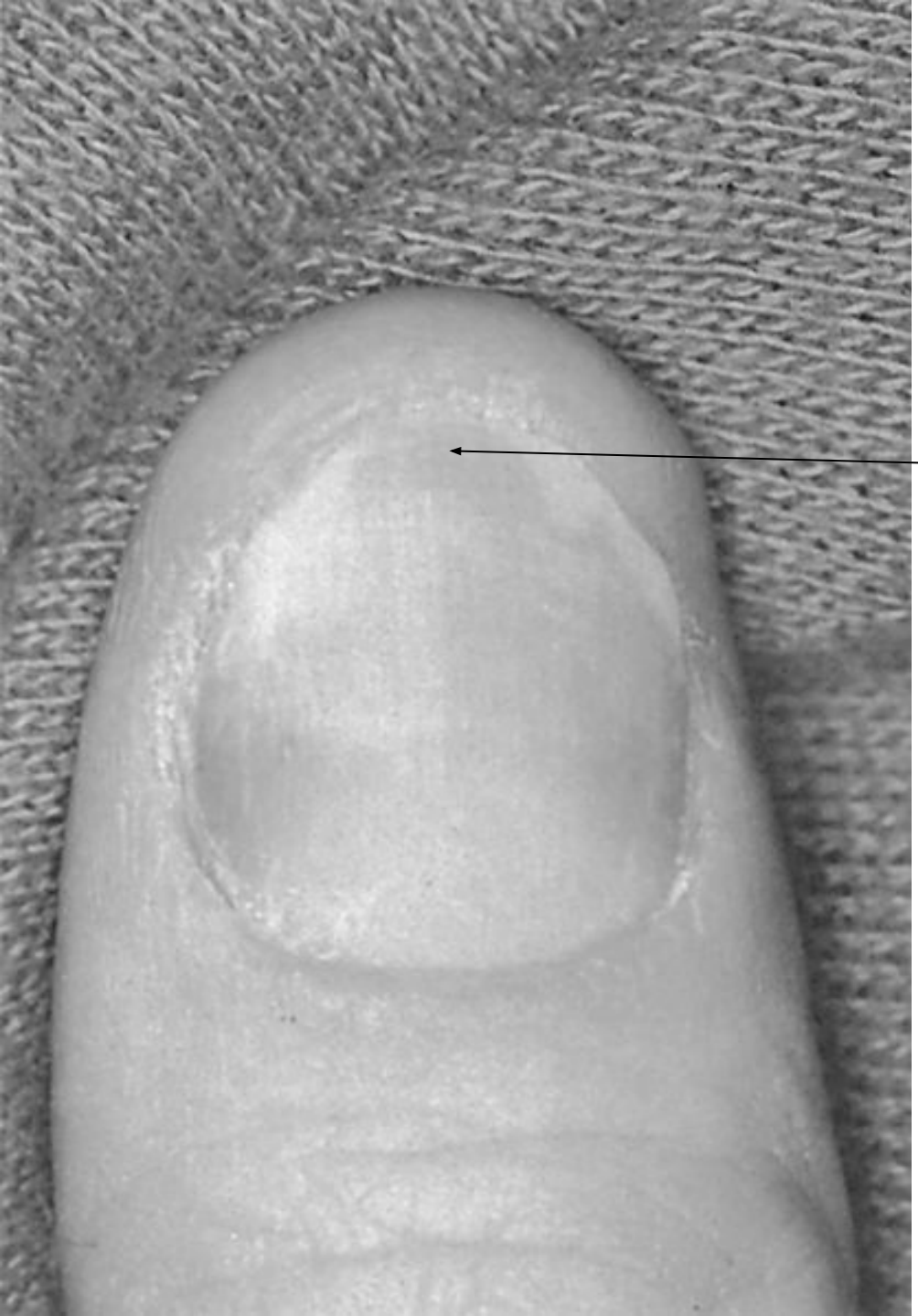
Congenital hypothyroidism:
Absence of distal femoral epiphysis in a 3-mo-old infant who was born at term. This is evidence for the onset of the hypothyroid state during fetal life.



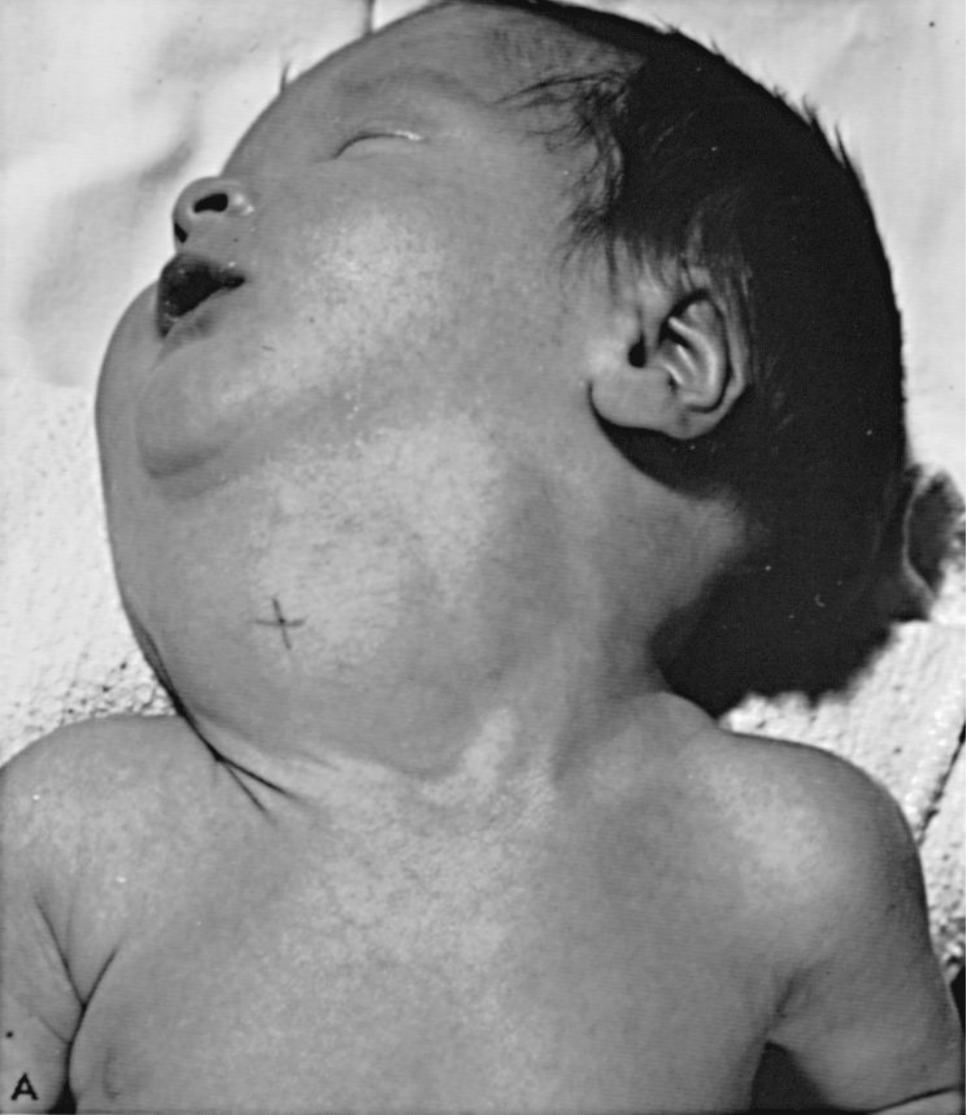
Rickets in a 2-year-old child presenting with bowing of legs, abnormal gait, and associated hypotonia. The condition has to be differentiated with infantile cretinismus. Note prominence of wrists and lower femoral epiphyses.

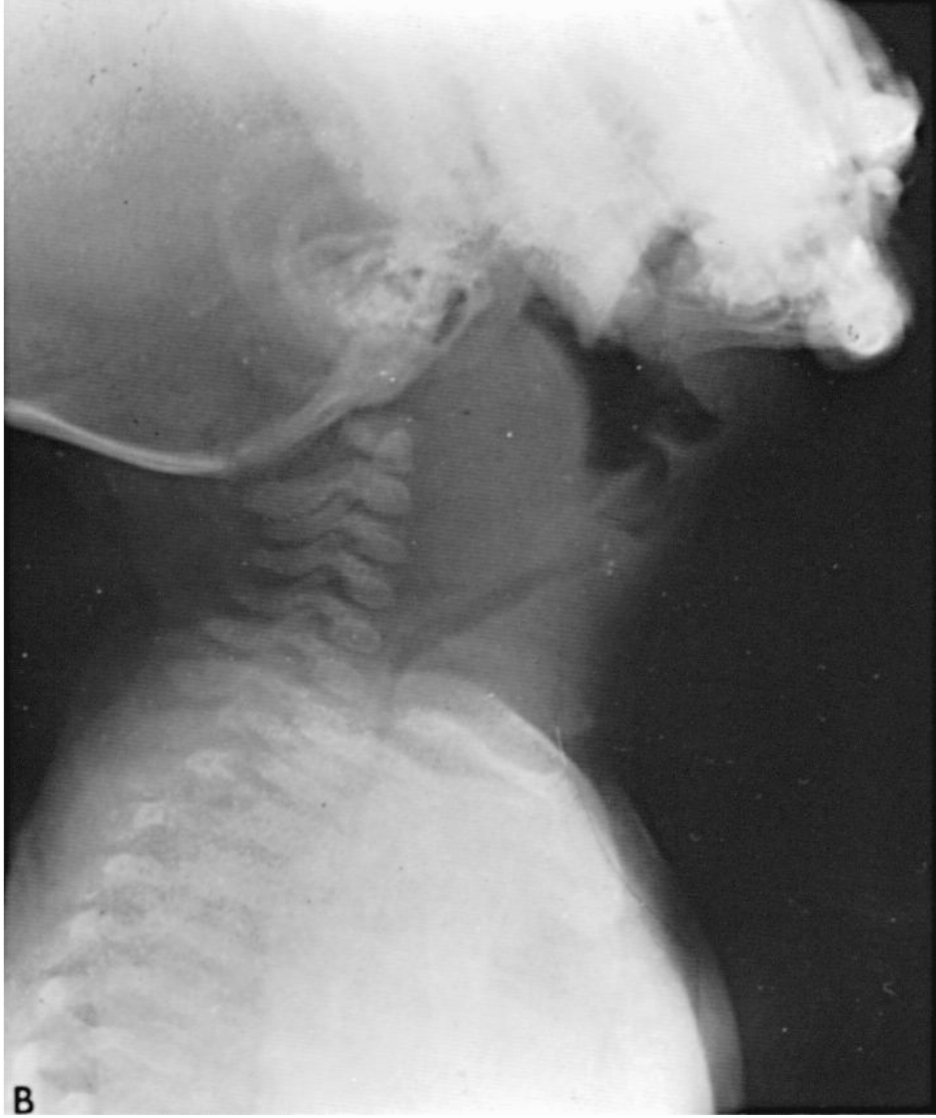
The laboratory study confirms the diagnosis. The serum concentration of TSH is increased and T3, T4 are decreased.

Hyperthiroidisms ***(exophthalmic goitre, Graves' disease, thireotoxicosis*** **and other names). The symptoms are emotional lability, hyperperspiration, fever, arterial hypertension, typical nails and ocular symptoms. The laboratory studies reveal low level of TSH and simultaneously high serum concentrations of T3 and/or T4.**



Onycholysis associated with hyperthyroidism





The sizes and other characteristics of thyroid gland should be estimated by visual examination and palpation. The enlargement of thyroid gland is called goiter or struma. The goiter can develop in utero and cause the severe disturbances of breathing (respiratory distress) in newborn.

Parathyroid glands

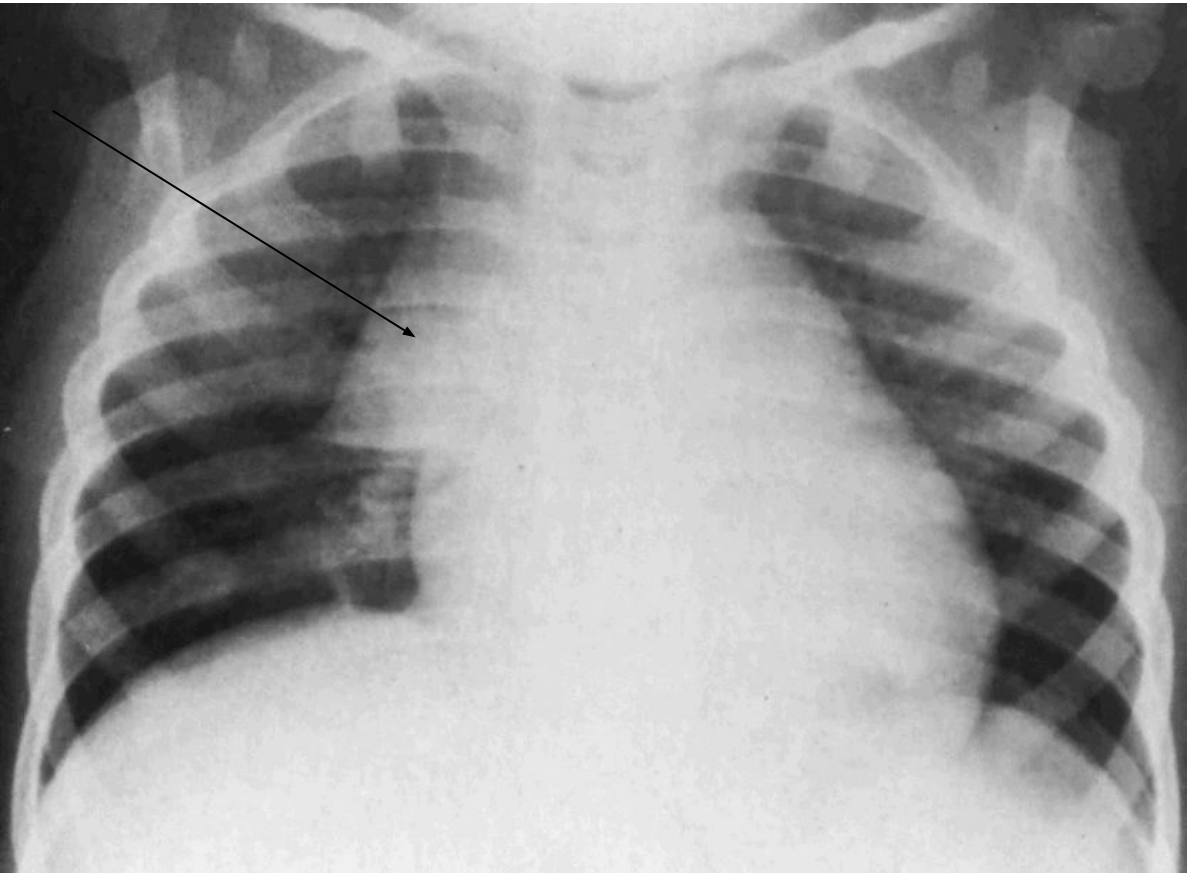
Parathyroid glands are derived from branchial pockets, shaping in embryo simultaneously with thymic gland and arc of aorta. So the embryopathies of these organs are often combined.

The parathormone which synthesis occurs in parathyroid glands participates together with vitamin D in regulation of phosphoric-calcium metabolism. The function of parathyroid glands is autonomous and does not controlled by pituitary gland.

Functional insufficiency of parathyroid glands (due to their aplasia, damages in labour or as a result of excessive surgery operation on thyroid gland) results in *hypocalcemia* and *hyperphosphatemia*. This condition is characterized by high neuro-muscular excitability and even *spasmophilia*. The last one manifests itself spontaneously and/or after mechanical irritation of periftral nervous showing involuntary muscular spasms possible as well as to generalize on maneure of tonic cramps (spasms). Hypocalcemic cramps as a rule does not accompany by loss of consciousness like a typic brein-releted.

Innate hyperparathyroidism is accompanied by *hypercalcemia* with nephrocalcinosis development and *nephrolitiasis* in urine tract (renal pelvis and urinary bladder).

The hypertrophy (hyperplasia) of thymus if it is revealed in young children on routine chest X-Ray is frequent benign sign and reflects individual feature of childs` physiology. As a rule it is not connected with pathological conditions. In many cases the rengenological enlargement of thymus does not mean thimic hyperfunctional condition. Now the pediatricions do not take this sign in account.



Thymic "sail sign".

Epiphysis (pineal gland).

In children the epiphysis (breins` derived gland) has biger size than in adult persons. It works out the hormones influencing upon common *gonadial cycle, lactation, carbohydrates` metabolism and water-salts regulation. The epiphyseal activity correlates with account of leukocytes in blood.* The clinical importance of epiphyseal disfunction is not studied enough yet.

Pancreas

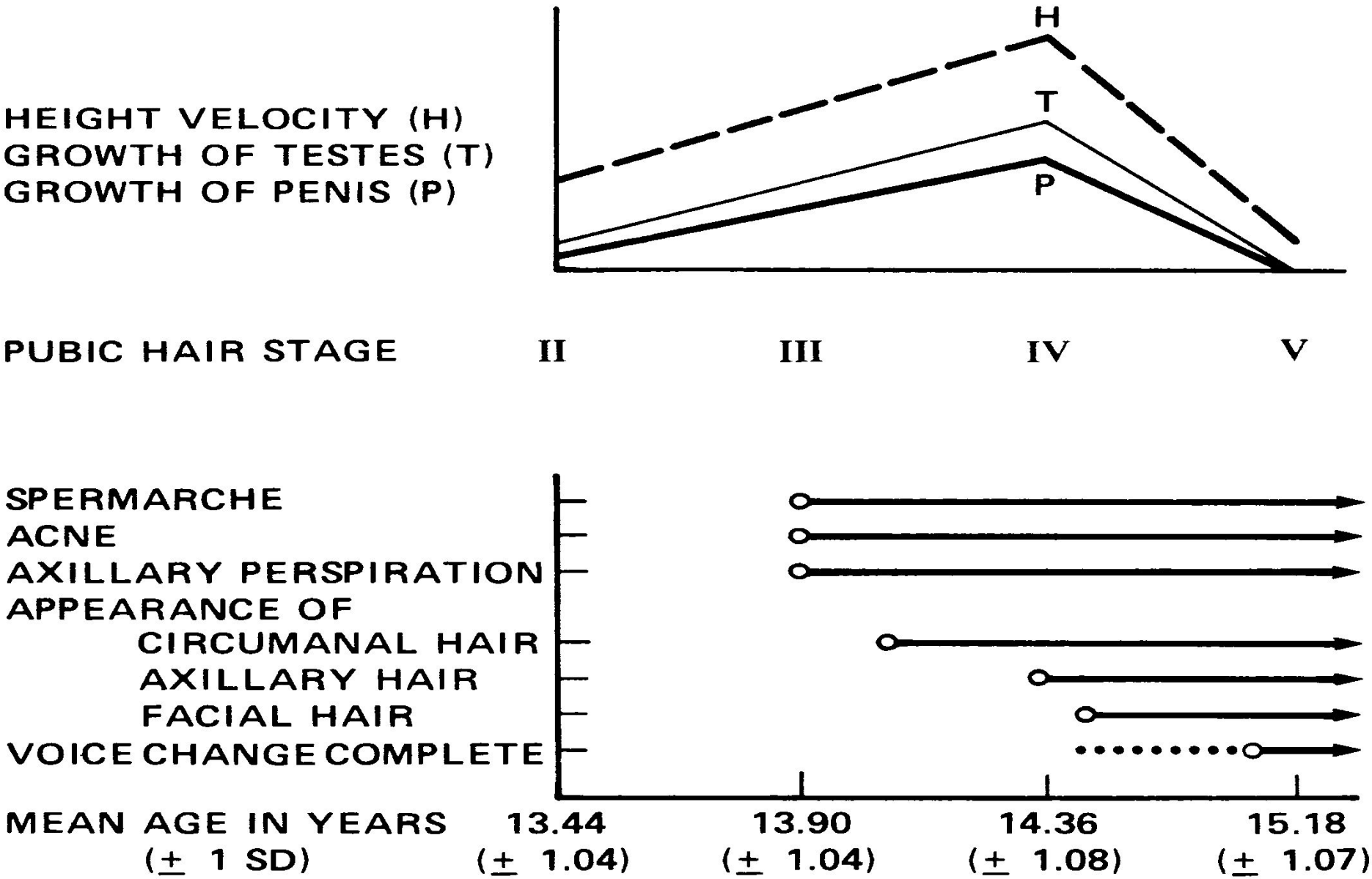
Pancreas as an organ of endocrinal system works out insulin and glucagon. They act like antipods and adjust the level of glucose in blood and its utilization by body` cells. The insufficient production of insulin as a result of pancreas' insulin-producting cells' destruction in children is known as a *diabetes mellitus* of the first (juvenile) type. The symptoms of recently appeared and progressing juvenile diabetes mellitus are connected with hyperglycaemia (abnormally high level of glucose in blood) and cells` impossibility to assimilate glucose from the blood. This is only list of these symptoms: hyperglycaemia, glucosuria, polyuria due to osmotic diuretic effect of glucosuria, relentless thirst and hunger, polydipsia and polyphagia, dehydration, severe metabolic disturbances leading to cerebral coma.

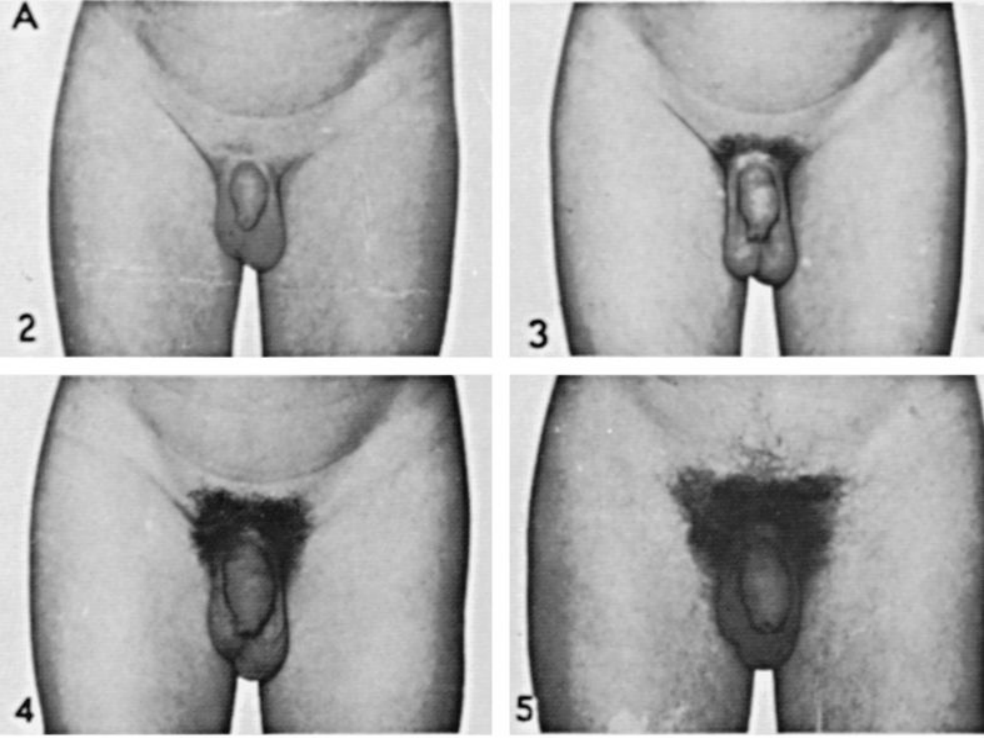
Gonadial glands development and puberty.

Boys' puberty.

The main hormone of testicles is *testosterone*. It pertains to anabolic steroids, activates the *growing, muscular tissue developement, dexterity and muscles power* peculiar to male nature. Testosteron causes the cascade of body changes in boys residing in the 1-st stage of sexual development according to JM. Tanner, when boys' and girls' bodies extraordinary remind each other. The *secondary sexual signs* gradually are forming and *spermatogenesis* begins.

Sequence of maturational events in males.

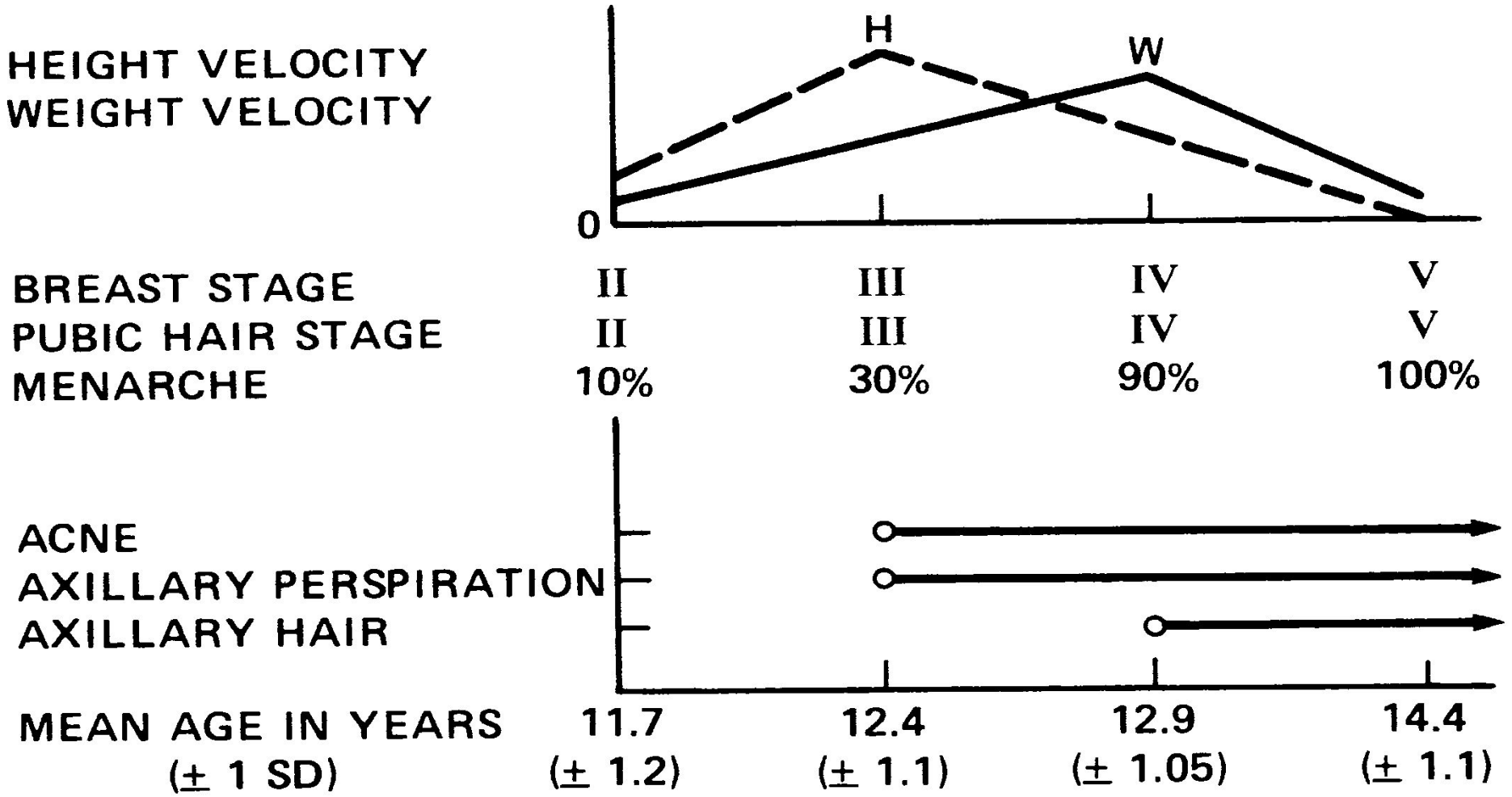


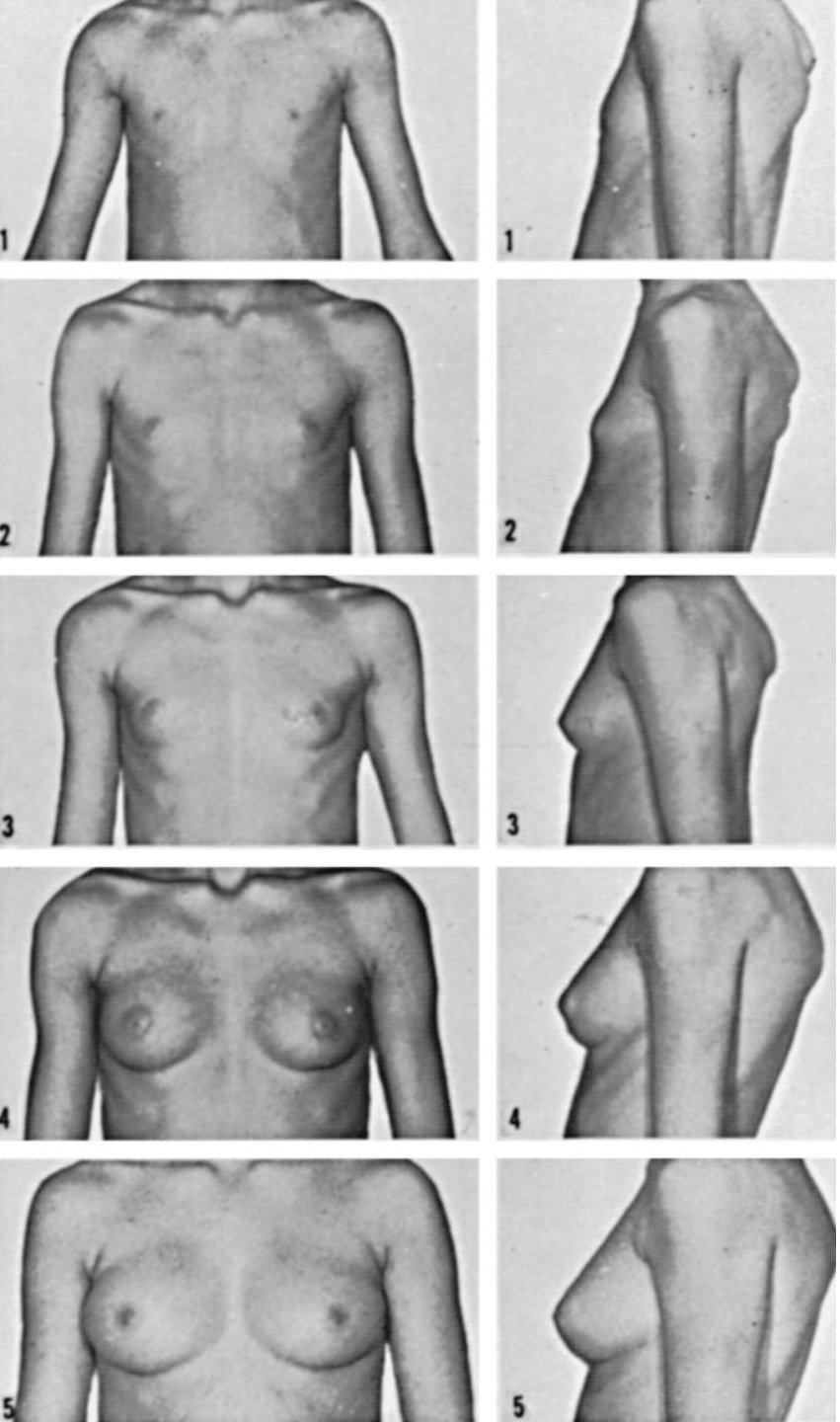


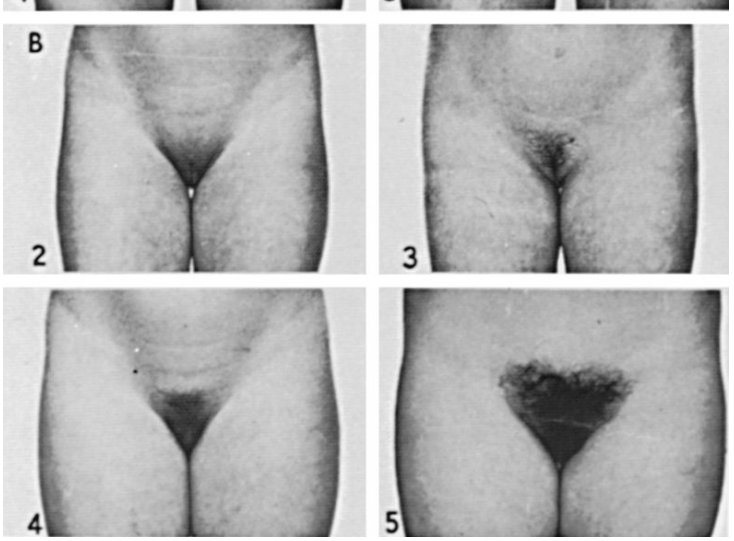
Sex maturity ratings of pubic hair development in adolescent boys. (By JM Tanner, M.D., Institute of Child Health, Department of Growth and Development, University of London, London, England.)

Puberty in girls.

Period of puberty in girls is characterized by gradual body changes occurring due to influence of gonadial hormone - *estradiol.*







The girls aged approximately 14,5 - 15 years reach the definitive rate of sexual maturity (Ah 3, Pu 5, Ma 5). In this age 100% of girls regularly menstruate.

What parts of the hypophysis (pituitary) do you know?

anterior and posterior
medial and lateral
small and large
black and white
right lobe and left lobe

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T4 - thyroxine
TSH – Thyroid stimulating hormone, thyrotropin
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Adrenal medulla produces:

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B. Noradrenalin
C. Dopamine
D. All of the above
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In children with congenital hypothyroidism the serum blood tests reveal:

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Increased TSH
Increased T3
increased T4
decreased TSH, T3, T4

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D. Congenital viral infection
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C. squint
D. frequent blinking
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hyponatremia
hypoglycemia
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Loss of appetite
Sweating
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