UNIVERSITATEA
DE MEDICINĂ ȘI FARMACIE
VICTOR BABEȘ | TIMIȘOARA

Mărioara Boia
Daniela Iacob
Anikó Manea
Camelia Budișan
Ileana Enătescu
Mirabela Dima
Oana Costescu

PRACTICAL NOTIONS OF GROWTH AND DEVELOPMENT

COURSE

Editura „Victor Babeş”
Timişoara, 2020

Editura „Victor Babeş”
Piaţa Eftimie Murgu nr. 2, cam. 316, 300041 Timişoara
Tel./ Fax 0256 495 210
e-mail: evb@umft.ro
www.umft.ro/editura

Director general: Prof. univ. emerit dr. Dan V. Poenaru

Colecţia: MANUALE
Coordonator colecţie: Prof. univ. dr. Sorin Eugen Boia

Indicativ CNCSIS: 324

Traducere: Dr. Maciu Ana Maria Cristina - medic rezident Neonatologie

ISBN 978-606-786-182-2

Table of contents

CHAPTER I

INTRODUCTION

Infant care represents a prophylactic side of pediatrics and consists of an assembly of means which ensure both somatic and mental growth and development of a child, from birth until adolescence, in a way that it maintains the child's good health. Infant care interests the child and its family, the socioeconomic environment, for maintaining both a good health and development of physical and intellectual performances of an individual.

CHAPTER II

CLASSIFICATION OF INFANT CARE

1. **Preconceptional care**

Represents all the preventive measures which can be taken by a couple, in order to conceive a healthy foetus and it targets the avoidance of teratogenic factors that determine prenatal insults:

a) *Infectious factors*: Rubella virus, Cytomegalovirus and Toxoplasma Gondi infection lead to different major anomalies and determine almost 2% of the total complex malformations. Other infectious diseases related to malformations are as follows: Herpes virus, Coxsackie virus, Varicella Zoster virus, Treponema palidum, urinary tract infections.

The following are examples of plurimalformative syndromes which appear due to certain infectious diseases:

- **Congenital Rubella**- causes the following anomalies: congenital cataract (fig. 1), congenital heart defects, IUGR, hearing loss, prolonged and severe jaundice, intellectual disability, liver and spleen diseases, pneumonias.

Fig. 1. Newborn with congenital rubella - congenital cataract.

- **CMV infection - the most severe anomalies:** sensorineural hearing loss, visual acuity insult, neuropsychic and neuromotor disorder such as seizures, tetraparesis, diplegia, dyslexia, dysgraphia, adjustment disorders, intellectual disability, demise (20-30%), liver failure (fig. 2), DIC.

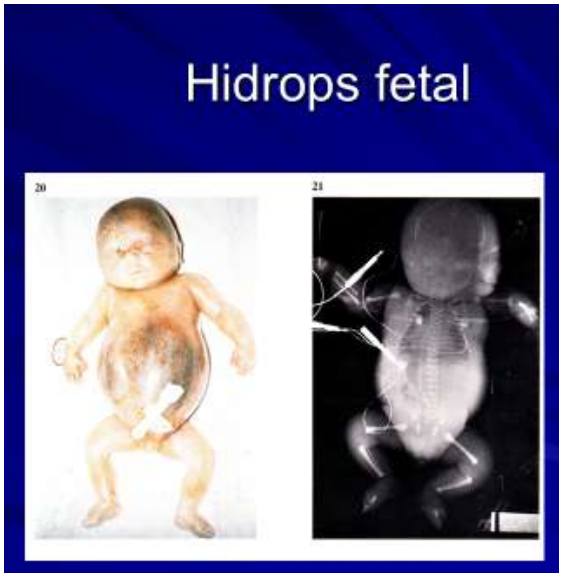


Fig. 2. Newborn with severe congenital CMV infection, hydrops fetalis

- **Congenital toxoplasmosis - frequent anomalies:** prematurity, IUGR, sight loss, brain calcifications, hydrocephalus, congenital heart defects, jaundice, hearing loss.

b) *Non-infectious maternal diseases*: *manifest diabetus mellitus* may lead to various malformations; *phenylketonuria*may lead to heart defects and intellectual dissability; *spotting* during the first trimester of pregnancy.

c) *Actinic factors* (ionizing radiation): these have a mutagen effect when they act upon the zygote (chromosomal aberrations).

d) *Chemical factors*: *thalidomide* which leads to various malformations; *organomercury* leads to neurological lesions, *nicotine*causes small gestational age newborns; *alcohol*causes small gestational age newborns, dismorphism/ malformations, intellectual dissability; *drugs*- anticonvulsants given during the first trimester; anticoagulants given during the first trimester; heparin may cause intrauterine fetal death, cytostatics always lead to malformations.

e) Other teratogenic factors:
   - Nutrition: amino acid deficiency; vitamins E, A, folic acid; oligoelements: Zn, Iodine;
   - The ideal maternal age for conceiving is 25 to 35 years.

Fig. 3. Newborn with Down Syndrome

Fig. 4. Occipital myelomeningocele

2. Prenatal infant care

Prenatal infant care targets the protection of the expectant mother and the intrauterine development of the foetus.

Goals: early pregnancy detection; follow-up of the expectant mother's health state (monitoring, early detection and treatment of the mother's possible diseases, admission of the high risk patients), following a regular life and work schedule; vitamin prophylaxis, proper alimentation.

The normal pregnancy timeline consists of 280 ±10 days.

3. Postnatal infant care

Postnatal infant care consists of an ensemble of measures taken for the supervision, correct alimentation, environmental hygiene, psychoaffective state within family and community.

The main purpose is decreasing infant mortality which acts upon the average life expectancy and rate of natural increase.

Infant mortality (I.M.) can be measured using the following formula:

I.M. = (Number of deaths to live born infants under one year of age) / 1000

Infant mortality, is still high in Europe, even if it has been significantly decreasing (26,9‰ in 1990 - 11‰ in 2008). The average **infant mortality** in the EU is 4,59 to one thousand live born infants. In our country, the mortality rate dropped to 6‰.

Among the states with a low mortality rate are Sweden, Slovenia, Norway, Japan, Italy, Finland, Czech Republic, Switzerland, Spain.

CHAPTER III

GROWTH AND DEVELOPMENT

Postnatal growth and development

Growth represents a normal process of cell multiplication and volume growth, which leads to body size upsurge and the apparition of new tissue, respectively.

Development represents a normal process which includes functional complexities like the formation of new structures and enzymatic maturation.

Growth and development follow a neat pattern, almost the same for all children, but with certain variations between normal ones, depending on age and reflecting the growing body's response to multiple factors.

In humans, maturity is slowly obtained, 1/3 of life is a preparation for the other 2/3 of it.

A. Growth general laws

Growth general laws were assessed according to the general aspects of growth, but also through careful observation and investigation of each segment of the body:

Alternation laws - refers to the elongation of the bones, followed by callosity.

Proportion laws - from birth until maturity, each body segment has its own growth behaviour compared to height.

Puberty laws - before puberty, height rises especially in the inferior members area, and then in the trunk area. At puberty, elongation is seen first, and after that the thickening of the body.

B. Growth factors

During the process of growth and development, several categories of factors arise:

1. ***Genetic factors*** (hereditary, intrinsic)

   These factors hold an important role in determining the growth rhythm due to genetic controlling of the structural proteins and their enzymes.

   Genetic pathology is quite complex and multifarious, but generally the following genetic disorders are seen (see "Growth disorders due to genetic causes").

   - *aneuploidies* (abnormal number of chromosomes), which can be classified as follows: monosomy - the absence of one chromosome of a pair; trisomy and polysomy - more than one chromosome added to a normal pair.

- *structural anomalies* (morphological), from this category there are: deletions - a portion of the chromosome is missing; translocation - a portion of the chromosome is reattached to a different chromosome; inversions; isochromosomes.

2. Hormonal growth factors

Hormonal factors have an important role in the modulation of both growth and development processes; these act in several phases of life due to genetic information. The main growth hormones are:

- *Growth hormone* (G.H.) - has a role in cell multiplication and chondrogenesis, acts upon the cartilage with the help of somatomedin. Hyperfunction leads to gigantism. Hypofunction leads to harmonic dwarfism (short stature, normal intellect).
- *Thyroxine and triiodothyronine*, with the help of the hypothalamic-pituitary system act upon the growth cartilage, realizing bone mineralisation, but also upon the central nervous system and dental maturation.

  Hypersecretionmay lead to hyperthyroidism. Hypofunction leads to disharmonic dwarfism and intellectual disabillity (imbecility).
- *Parathyroid hormone* controls the calcium homeostasis and is involved in the skeletal calcification.
- *Insulin* is involved in the protein, fatty acids and glycogen synthesis.
- *Androgynous hormones* - initially they activate the growth mechanism, but during puberty they limit it, by accelerating the bone maturation.
- *Estrogens and progesterone* contribute to the growth cartilage calcification.
- *Cortizone* has a negative effect (diminishes the number of cells) and a positive one (favours the enzyme maturation).

3. ***Environmental factors***

Environmental factors act upon the growth process both in the intrauterine life, as well as after birth. During the intrauterine period, these factors act by chemical, actinic and infectious agents. After birth, the growth process may be influenced by acute and chronic diseases, alimentation and geographic environment (pollution, sunshine, UV, humidity). These factors mainly influence the first 5 years of life.

Other factors:

a. Socioeconomic factors: financial status, home quality, hygiene, medical facilities and civilization;
b. Cultural and educational factors;
c. Emotional factors (maternal deprivation);
d. Physical exercises: circulation activation, increase the O_2 flow to the tissues.

4. ***Pathologic factors***

Pathologic factors, which act both in the intrauterine period, as well as after birth, have a restrictive effect on growth and development. For example:

- intrauterine: maternal-fetal infections;
- postnatal: acute and chronic digestive disorders, chronic organ injuries, metabolic and endocrine disorders, infantile chronic encephalopathy, congenital heart defects, of the central nervous system, etc.

C. Types (growth charts)

During the growth period, 4 types of growth can be seen:

1. **Neural type -** defining for the central nervous system, which grows very fact during intrauterine life. After birth, there is an intense increase until the age of 5, and after that a slower rate until adolescence.
2. **Skeletal type -** rapid growth during intrauterine life and until the age of 2, slow growth until puberty, rapid growth during puberty and then a slow rate during adolescence.
3. **Lymphatic type -** progressive development until 5-6 years of age (lymph nodes, tonsils and thymus), then it reduces and the thymus regresses.
4. **Adipose tissue-** rapid growth until 1 year of age, after that with a slower rate between 1 and 2 years, and then with a steady rate.

D. Growth and development assessment

Growth and development assessment is based upon the comparison between the somatometric parameters of a certain child and the ones of other healthy children, of the same age, gender, geographic region, country.

Growth assessment uses different parameters.

For comparing the parameters, certain charts were made, based on measurements obtained after evaluating lots of healthy children, of all ages, both genders, from different countries.

Based on the given data, certain „gaussian" charts and dynamic charts were made, or certain „continous" channels, mathematically derived, so called „percentiles„ or standard deviations (after the used formula).

1. On the „gaussian" charts the weight, height, head circumference values, at a given age, are as follows:
    - The mean value is on top, the negative values on the ascending branch, the positive values on the descending branch.
    - Normal values = $\pm$ 2 S.D. (standard deviations)
        1. S.D. includes 66,6%;
        2. S.D. includes 95%;
        3. S.D. includes 99,7%.
2. The percentiles indicate the presence of a typical seriated measurement of 100.
    - 10^{th} percentile = the child is bigger than 9% of the same age and gender children.
    - 50^{th} percentile = an equal number of children are smaller than the measured one.
    - 1^{st} percentile = -3 S.D. P. „84" = + 1 S.D.
    - 3^{rd} percentile = -2 S.D. P. „97" = + 2 S.D.
    - 16^{th} percentile = -1 S.D. P. „99" = + 3 S.D.

By comparing the measured child's data with the charts, these can evaluate the growth pattern, which can be:

- ✓ Regular - if it is constantly situated on the same channel;
- ✓ Irregular- with periods of slow down and acceleration.

3. Growth charts

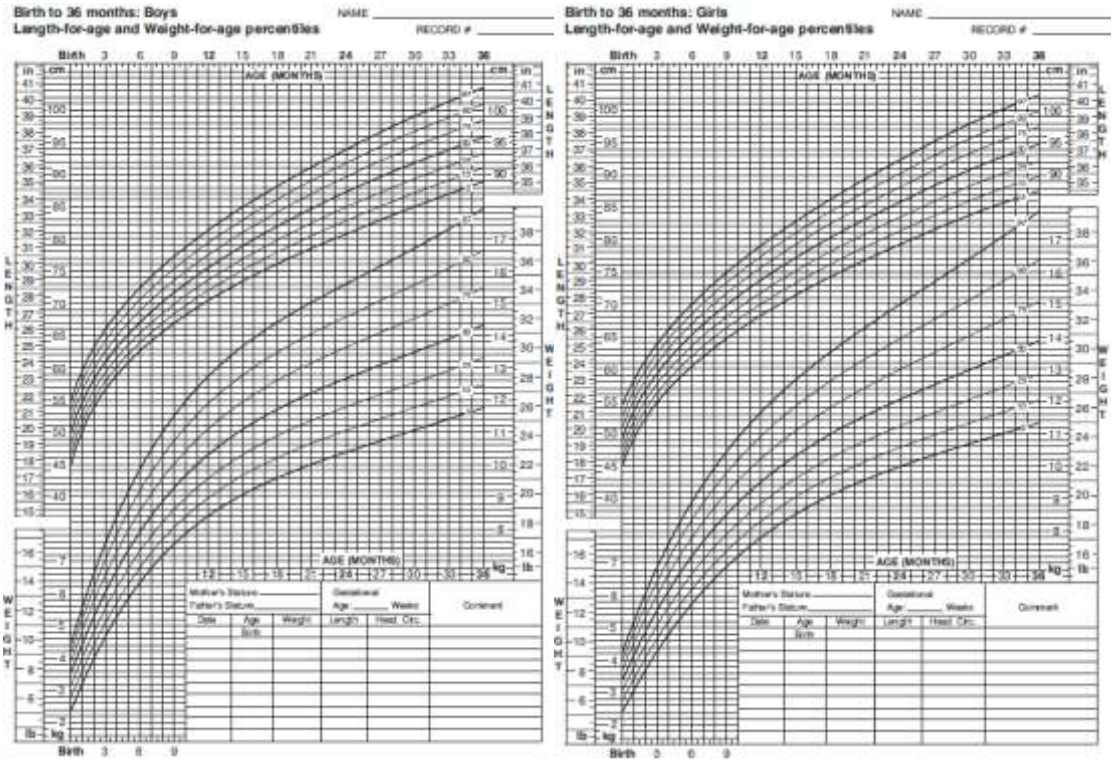


Fig. 5. Postnatal growth charts, by gender

For the evaluation of growth and development, *the most used parameters* are:

1. Weight

Is the most useful index in appreciating a child's growth and nutritional status.

Parameters that influence growth are: genetic factors, gestational age, maternal malnutrition, alcoholism, tabacism, drug addiction, intrauterine infectious diseases, placental insufficiency, multiple pregnancies, diabetus mellitus.

The mean annual spore of ponderal growth in the first year of life is:

Between 0-4 months = 750 g/month;

Between 5-9 months = 500 g/month;

Between 9-12 months = 250 g/month.

Weight is doubled by 4 months, tripled by 1 year of age, quadrupled at 2 years of age, it increases 6 times by the age of 5, 7 times by the age of 7, 10 times by the age of 10.

In the first 2 years of life, boys have a plus of 0,5 kg compared to girls.

In the second year of life, children have a growth rate of 200 - 250 g/month (2-3 kg/year), between 3-5 years with 2 kg/year, between 6-10 years boys have a growth rate of 3-3,5 kg/year. Between 6-12 years of age, girls have a growth rate of 3-3,5 kg/year.

The evaluation of a child's weight can be done using Herman's formula:

W = 9 x 2A

W = weight;

9 = weight by the age of 1;

A = age in years.

2. ***Length or height***

The measurement is made in the dorsal decubitus position by the age of 5-6.

At birth the normal length is 50 $\pm$ 2 cm.

The minimal increment if height increase in the first year of life is:

I^{st} months = 4 cm

II^{nd} - III^{rd} months = 3 cm

IV^{th} month = 2 cm

V^{th} - XII^{th} month = 1 cm

At 1-year-old, length is 50% higher than the one at birth. The statural increment in the first year is 20-30 cm.

Between 1 - 2 years of life it is of 1 cm/month (12 cm/year).

In the first two years of life, boys are higher by 0,5 cm.

Between 2 - 5 years it increases by 6 - 8 cm/year.

Height is doubled by the age of 4 and tripled by the age of 13.

Height growth stops between 17-19 years in girls and by 20 years in boys.

The evaluation of height can be done using Geldrich's formula:

H = 80 + 5 A

80 = lengthat the age of 1 in cm;

A = age in years.

It represents an advisory tool.

3. ***Head circumference (H.C.)***

Head circumference measurement is important until the age of 2-3.

At birth, the head circumference is between 34- 36 cm.

The head circumference grows by 10 cm during the first year of life, of which 50 % during the first 4 months. From 1 to 17 years it grows about 10 cm. The central nervous system represents by 6 months 50 % of the adult's dimension, at by 12 years 75 %.

During adolescence, head circumference grows on behalf of the bone tissue and soft tissues.Head circumference growth is possible due to cranial sutures and fontanels.

Head circumference can rapidly grow because of certain severe diseases: hydrocephaly, intracerebral hemorrhage, intracranial tumors, cerebral malformations; it can be smaller in cases ofcraniostenosis, intrauterine chronic hypoxia, genetic disorders. Both micro and macrocephaly can be inherited.

4. Dental maturation

The major determinants of the dental morphology and dimensions are genetic factors, but *other factors* can be involved as well: *nutritional disorders, rickets, endocrinopathies, and some antibiotics*.

a. The first dentition (milk teeth) is formed by 20 teeth.

The moment of eruption has wide limits, between 1 and 15 months. Exceptionally, at birth there can be present an erupt tooth, between 1/1500 - 1/3000 of births(fig. 6), with no pathological meaning or semnification of future dental eruption.

The order of apparition in most cases is as follows:

- 6^{th}-8^{th} month - inferior central incisors
- 8^{th}-10^{th} month - superior central incisors
- 10^{th}-12^{th} month - lateral incisors
- 1^{st} year -1^{st} and a half year - first molars
- 1^{st} and a half year-2^{nd} year - 4 canine teeth
- 2^{nd} year - 2^{nd} and a half year (3^{rd} year) - second molars.

Rarely, there can be a precocious eruption (4^{th} month), usually with genetic cause, and the eruption can be seen in rickets, 21 trisomy, myxedema, chronic metabolic diseases.

The associated symptoms with dental eruption are: agitation, slight digestive disorder, subfebrility.

Calcification starts in the 5^{th} month of pregnancy and ends by 2 1/2 - 3 years of life.

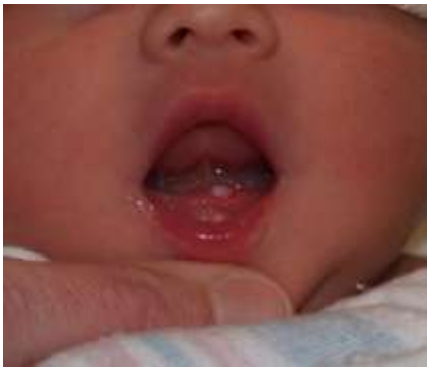


Fig. 6. Newborn with dental eruption present at birth.

b. Permanent dentition

Permanent dentition starts by the age of 6 with the first molar (the 6th year molar).Calcification starts in the first postnatal month and goes on until 25 years of life.

Between 7-12 years of life, the milk teeth shed in the same sequence they appeared.

The replacement of first dentition with the permanent one is generally as follows:

Between *6-8* years - central incisors;

Between *7-9* years - lateral incisors;

Between *9-13* years - canine teeth;

Between *9-12* years - first premolars;

Between *10-12* years - second premolars;

Between *10-14* years - second molars;

Between *18-20-25* years - third molars.

Dental maturation needs input of:Ca, P, vitamins A, C, D. The first molar, the one from 6 years, consists the foundation for the development of permanent dentition, which consequently determines the final form of the maxilla and the neat arrangement of teeth.

5. Bone maturation

It is the most loyal indicator of growth, bone age must be concordant to the chronological age.

The ossification process starts in the 5th month of pregnancy, ends with adolescence and starts at the ossification nuclei. The term newborn has 3 to 4 ossification nuclei:

- *Beclard nucleus* - situated on the distal femoral epiphysis;
- *Tappon nucleus* - situated on the proximal epiphysis of the tibia;
- *Cuboid bone nucleus*;
- *Humeral head nucleus* (inconsistent).

The evaluation of the ossification is done by radiographic examination: under the age of 1 at the lower limb level, after the age of 1 at the upper limb level, or at the radiocarpal joint level. In the first year, 10 ossification nuclei appear, for one hemiskeleton.

Establishment of bone age is based on the number and dimension of the nuclei, their form and density and by the delimitation of the bone extremities edges, the distance which splits the epiphyseal centers.

Bone age is finalized around 12 years for girls and around 13 years for boys. Bone maturation is estimated also by studying the number of bone sutures, which appear between 13 and 18 years.

6. Other growth appreciation criterias

In the current medical practice, other criterias can be used for growth appreciation:

- *measurement of the biacromial and biiliac diameter*;
- *arm and thigh circumference*;
- *skinfold thickness* (tricipital andsubscapular). This type of measurement is a valuable criteria for appreciating the nutritional status;
- *antimicrobial resistance appreciation*;
- *neurologic development assessment.*

Essential characteristics of these measurements

For their applicability in the current medical practice, the measurements must fulfill certain criterias:

- to be obtained through standardised methods

- compare the results to normal values obtained from the significant statistical cross-section, from one infant population of the same age, gender, geographic zone, comparable socioeconomic status.

Any deviation will be appreciated based upon the somatic traits of the genitors (growth genetic potential) and the child's own growth chart.

GENETIC GROWTH DISORDERS

Approximately 2-3% of the newborns are seen with a congenital defect which is diagnosed at birth; a higher percentage can be seen in countries where the diagnose is given later. The modern methods of early diagnosis and intensive care make survival options possible for a large number of these patients. The first step is the development of the classification methods used to identify certain anomalies, as well as understanding of the terminology used to describe them.

Classification and definition of congenital anomalies

Malformation- morphogenetic anomaly determined by *intrinsic factors* which intervene in the development of a certain structure.

Mechanism: formation, development ortissue differentiation realized by genetic, mesologic or both causes.

Examples: spina bifida, cleft lip or cleft palate, congenital heart defects, syndactyly.

Deformation - morphogenetic anomaly determined by *extrinsic factors* which intervene in the formation and development of a certain structure.

Mechanism: intrauterine fetal constraint.

Examples: craniofacial asymmetry, ear anomalies, feet deformities, clubfoot.

Disruption- morphogenetic anomaly, given by *distructive forces* which act upon the development of a structure.

Mechanism: cell death or tissue distruction determined by vascular, microbial or mechanical factors.

Examples: absence of fingers or members, facial cleft.

Dysplasia - morphogenetic anomaly determined by *the abnormal arrangement and function of cells* from a certain tissue.

Mechanism: major mutant genes.

Examples: skeletal disorders, ectodermal dysplasia, connective tissue disorders.

Diagnosis of congenital anomalies

Specifying the correct diagnosis of different congenital anomalies supposes the main following steps:

1. Family medical history (as well as personal history);
2. Clinical examination;
3. Paraclinical investigation;
4. Formulating the complete diagnosis;
5. Establishing a treatment schedule, follow-up, making sure the family benefits from adequate examination and genetic advice.

Family medical history (and personal history)

The target of this is following the next aspects:

- the diagnosis of patients with obvious problems;
- identifying other potential problems that patients might have;
- identifying other individuals with high risk from the same family;
- identifying the conditions which raise the suspicion of a genetic disorder (genic or chromosomial) within the family:
    - ✓ consanguinity: increases the risk of autosomal recessive disorders;
    - ✓ the abnormal traits of one or both parents, which are also present in our patient, can be transmitted autosomal dominant;
    - ✓ the similar impairment transmitted through the maternal line and its presence in boys suggests the X-linked transmission;
    - ✓ history of reproductive failure (miscarriage, sterility, stillbirth) or death in the neonatal period suggests the possibility of balanced chromosomal rearrangement from the genitors.

*Pre- and perinatal history*refers to: genitors age, ethnicity, socioeconomic and psychosocial status of the family (alcoholism, tabacism, substance abuse, depression, suicide); parity (number of pregnancies); uterine malformations or reduced pelvic dimensions; data from the actual pregnancy:

- fetal position,
- beginning and intensity of the fetal movement,
- gestational age,

- quantity of amniotic fluid,
- placental morphology and length of umbilical cord,
- spotting or infectious episodes.

– hazardous environment for the fetus through maternal exposure and injury:
  - infectious agents: viruses (rubella, CMV, herpes, herpes-zoster), bacterias (treponema pallidum), parasites (toxoplasma Gondii);
  - physical agents: radiation, high body temperature (internal - through fever or external - solarium, sauna);
  - drugs and chemical substances, prescribed (anticoagulants, antineoplastics, anticonvulsants, isotretionin), or unprescribed (alcohol, cocaine);
  - maternal diseases: diabetus mellitus, phenylketonuria, myotonic dystrophy, systemic lupus erythematosus, epilepsy.

- birth data:
  - ✓ type of birth (normal, c-section, forceps extraction),
  - ✓ labor complications,
  - ✓ the newborn's presentation,
  - ✓ placenta: size, aspect.

- newborn's state:
  - ✓ APGAR score,
  - ✓ birth weight (small/large for gestational age),
  - ✓ somatometric indexes.

Clinical examination

A. ***Morphologic alteration inventory***

Any deviation from normal will be carefully observed and noted, even if it seems unique and has only a cosmetic connotation. The spectrum of craniofacial dysmorphism can be very comprehensive: facial or general asymmetry, small, dysmorphic and low-set ears, shortened palpebral fissures, with mongoloid or anti mongoloid slits, hypertelorism, or hypotelorism, ptosis or palpebral edema, coloboma, nystagmus, strabismus, microphtalmia, macroglossia or pseudomacroglossia, lip cleft or palate cleft, facial cleft, micrognathism, retrognathism, micro or macrocephaly etc.

Trunk and members alterations will also be observed: limb agenesis, ectrodactyly, brachydactyly, syndactyly, polydactyly, arachnodactyly, segmental hypoplasia, column, sternum, limb deformations, the presence of certain hyperpigmented or hypopigmented areas.

Following the nervous system's functionality, certain anomalies can be seen, like: muscle tone anomalies, archaic reflexes, motility, the presence of facial paresis or limb paresis.

The examination of the cardiovascular system and morphology of the external genital organs must not be neglected; a certain degree of sexual ambiguity could be revealed.

B. Congenital anomalies classification

1. Major and minor anomalies or normal versions
   a. *Major anomalies* – appear at approximately 3-5% of newborns and they usually need medical or surgical intervention.
   b. *Minor anomalies* – are versions that have or not a certain medical or cosmetical signification; these can be seen at approximately 4% of the newborns.
   c. *Normal versions*– traits that do not exceed the spectrum of normality.

Minor anomalies and normal versions can serve as an indicator of altered morphogenesis and may lead to the anomaly pattern.

2. Performing the somatometrical measurements, which allow the quantitative appreciation of the physical anomaly, whenever possible.
3. Comparing the patient with other family members.
4. Brief appreciation, but correct, of children with life potential, which will need specific treatment.

Laboratory testing

- cytogenetic investigations (karyotype, sex chromatin);
- biochemical testing;
- radiographies, tomographies;
- echographies, EKG;
- any other paraclinical explorations which can complete the diagnosis of the disorders found at birth, with specifying the complexity and severity of the anomalies, establishing the prognosis and formulating the differential diagnosis;
- postmortem examinations and explorations.

Formulating a complete diagnosis

The necessary studies and investigations needed for formulating a diagnosis are usually done by a team of specialists and conclusions are debated with a multidisciplinary team (obstetrician, neonatologist, pediatrician, geneticist).

When the diagnosis is completely formulated, a conference type discussion is held with both parents, which has to allow the explaining of the diagnosis, immediate and long term implications and the possibilities of recurrence on other descendants, or manifesting disease in other family members. Giving appropriate genetic advice can remain in the geneticist's care, but we must ensure this has been taken care of, if the geneticist is not participating when the discussion with the family takes place.

Examples of common dysmorphic syndromes

1. Dysmorphic syndromes of chromosomial cause

Down Syndrome ***(trisomy 21)***

Characteristic dysmorphisms: round face, brachycephaly, mongoloid palpebral fissures, hypertelorism, epicantus, flat nasal bridge, pseudomacroglossia, short, thick neck, hypotonia, brachydactyly.

Pätau Syndrome*(trisomy 13)*

Facial dysmorphisms: beveled forehead, microphthalmia, coloboma, hypertelorism, lip or cleft palate, severe central nervous system anomalies, renal and skeletal anomalies, genital organs anomalies.

Edwards Syndrome*(trisomy 18)*

Diverse and nonspecific facial dysmorphisms, marked muscular hypertonicity, occipital anomalies, calcaneal anomalies, pectus excavatum, finger anomalies, cardiac malformations.

2. Dysmorphic syndromes of genetic cause

Treacher Collins Franceschetti Syndrome(mandibulofacial dysostosis)

Facial dysmorphisms: hypoplastic facial bones, especially the superior maxilla, mandible and zygomatic arch, macrostomia, micrognatism, aquiline nose, coloboma, antimongoloid palpebral fissures, ear malformation, hypoplastic ear lobe or absent, big "fish like" mouth, high-arched palate, dental anomalies.

Pierre Robin Syndrome*(mandible hypoplasia)*

Craniofacial dysmorphysms: micrognathism, glossoptosis, various types of cleft palate, low inserted ears, microphthalmia, multiple skeletal anomalies.

Mucopolysaccharidosis type I ***(Hurler disease)***

Characteristic face traits, with gargoylic dysmorphism: grotesque, rough, with bulgy forehead, faded nasal bridge, large nostrils, thick lips, bulky tongue, small teeth. The trunk presents with a large anteroposterior diameter, dorsolumbar kyphosis. Big abdomen, deformed limbs, limitation of the joint movement, big "claw-like" fingers, dwarfism.

3. Dysmorphic syndromes of multifactorial polygenic cause

Anencephaly*(acrania)*– monstruosity incompatible with life.

Congenital lip-palate cleft

Studies have shown families with high incidence of this defect, and so, with a higher risk, which sustained the multifactorial polygenic determinism. The anomaly can be determined by chromosomes (trisomy 13, 18) or by teratogen factors action during intrauterine development.

Spina bifida

This represents a congenital anomaly which consists of a lack of closing of the vertebral arches in different parts of the spinal column. The anomaly can be open (aperta), when in the place of defect the soft tissue is missing and closed (oculta), when the skeletal defect is covered by muscle and skin; the defect is usually covered by a strange pilosity in the area.

4. Dysmorphic syndromes of multifactorial polygenic cause

a. Rubeolic embryopathy

Is characterised by 4 types of anomalies: ocular (microphthalmia, cataract, strabismus, nystagmus), auricular (malformations of the external ear), heart defects (septal defect, persistent arterial duct, tetralogy of Fallot) and dental (dental hypoplasia - so severe that it leads to edentation; enamel alteration). Sometimes, facial and skeletal anomalies can be present.

b. Diabetic embryopathy

Large for gestational age, with "swollen" aspect, moon shaped facies, skin edema, syndactyly, ophtalmic anomalies, heart defects, congenital foot anomalies.

c. Syphilitic embryopathy (congenital syphilis)

Specific facial dysmorphism (high forehead, small nose, "saddle nose", altered teeth - Hutchinson teeth, mulberry molars, palatoschisis), nail deformities, maculopapular or erythematous rash.

CHAPTER IV

CHILDHOOD STAGES

Childhood represents a stage of human life. One third of it represents the grooming of the other two thirds of it. Out of morphofunctional and pathological reasons, childhood is divided into 3 periods, each having its own subperiods.

Infancy- 0-3 years

Infancy has the following periods:

1. *The neonatal period* which represents the first 28 days, of which the first 7 days represent the early neonatal period. It is a period of adaption of all aparatus and systems to the extrauterine life, along with various pathology and high mortality.
2. *Infant period* = 1 month - 1 year and is characterized by:
    - accelerated statural growth - from 50 ± 2 cm at birth to 80 cm at 1 year of age
    - accelerated ponderal growth - from 3250 g (medium weight) at birth to 9000g at 1 year of age
    - head circumference growth from 34-36 cm at birth to 44 cm by the age of 1
    - high metabolic demands
    - digestive functions development (for complementary feeding)
    - appearance of the first teeth
    - neuropsychic development
    - self immunity development
    - high morbidity, high mortality
    - maternal attachment.
3. *Small child period*: from 1 to 3 years and has the following traits: head - trunk - limbs ration is modified, completing the first teeth eruption, diverse alimentation; perfection of the motorfunctions, vocabulary enrichment, intensification of the affective relationships, development of certain habits (sleep, eating schedule, sphincters control); reduced morbidity (respiratory, contagious, intoxications, insults); reduced mortality.

Early childhood (preschooler) - 3-6 years

The main characteristics of this period are:

- *the first permanent molar tooth* appears (6 year molar);
- *slow-down of the statural and ponderal growth*;
- *less nutritive needs*, alimentation close to the adult one;
- *complex development of the central nervous system*: higher knowledge, understanding, memory, discernment capabilities; the brain has similar dimensions to the adult one; grammar-like language; by 5 years of age, there is reasoning; high sensibility, needs affection (without excess); playing has an educative purpose, it develops thinking and discipline;
- high independency need;
- *anti infectious capacity* - self and using vaccines;
- *specific pathologies*: communicable diseases, immune diseases and allergies, accidents, intoxications, mortality is lower.

Middle childhood (schooler)

Middle childhood has more subperiods (see chapterXI):

1. ***Small scholar***: from 7 to 11 years, and has the following particularities:
    - slow statural and ponderal growth at first, and then accelerated during puberty;
    - first dentition is replaced by the permanent one;
    - slower metabolism;
    - alimentation is closer to the adult one;
    - intense intellectual development, depending on the instructional and educational processes;
    - reduced morbidity (mostly caused by acute articular rheumatism, tuberculosis, malignant hemopathies, accidents)
    - reduced mortality.

2. *Puberty (big scholar)* is a difficult period to differentiate, this being a genetic phenomenon, sensible to the geographical (country, epoch), nutritional, socioeconomic and psychological factors. Puberty advance is higher in some countries, due to the aforesaid factors.

During puberty, there can be:

Adrenal puberty determined by the androgynous stimulation.

- Clinically, no changes can be seen, or the possible apparition of pubic hair;
- Biologically, the secretion of androgynous hormones begins.

Gonadal puberty - appears 2 years after the adrenal one. The gonadotropic secretion begins gradually, as well as the steroid hormone secretion.

Normal puberty's course

The beginning of puberty and the age of debut depend on a variety of factors and range as follows: girls 9 - 13 years (mean age 11 years) and boys 10 - 15 years (mean age 12 years).

There is a *correlation between the beginning of puberty and the degree of bone maturation* (for example, the concordance between the beginning of puberty and the start of the ossification of the sesamoid bone).

During this period, *statural growth is intense*: for boys, in the first year it is of 8,7 cm and the second year 6,5 cm and ends after approximately 5 years after its beginning. For girls, the growth increment is 7,5 cm in the first year and 5,5 cm in the second one.

Characteristic psychological changes are:

- affective maturity
- presence of libido (adolescence crisis);
- accepting the body changes;
-intellectual maturity;
- development of abstract thinking.

The evolution of puberty, for both the physical and psycho-affective traits for both genders are summarized in the Tanner stages.

a. Clinical stages of pubertal development (Tanner)

For girls*:*

Stage I: infantile - S1 (breasts), P1 (pilosity);

Stage II: breast budding, elevation of the papillae; increased diameter of the areolae (S2), apparition of pubic pilosity, and then axilar pilosity (P2);

Stage III: development of the mammary glands, enlargement of the areolae (S3), pilosity becomes coarser (P3), development of the labia (minora and majora);

Stage IV: complete breast development, the areola becomes bulgy (S4), complete pilosity (P4);

Stage V: the first menstrual cycle appears(2 years after the beginning of puberty); regularization of the menstrual cycles (ovulation appears approximatelly 2 years later).

For boys:

Stage I: infantile;

Stage II: the beginning of testes enlargement, pubic pilosity appears, then the axilar one;

Stage III: coarse pubic hair, upper lip pilosity appears, voice changes start to show;

Stage IV: adult type pilosity, muscle mass development, widening of the back;

Stage V: beard growth, ejaculations appear.

b. Biologic stages of puberty

They can be delimitated using hormonal dosing. These are applied only in puberty anomalies, they are difficult to interpret and are expensive.

1. Pituitary gonadotropins

These hormones are without gender specificity, they realize gonadic growth, gamete maturation, adrenal C androgen sexual hormones secretion, for both genders. The level of the gonadotropins increases progressively in blood and urine, all along puberty.

For girls, the plasmatic level of FSH rises, which begins by 11 years, and the maximum level is reached within 2 years from the beginning of secretion. L.H. level increase appears later, has a higher duration, with fluctuations until the menstrual cycle becomes regular.

For boys, the increase of the *FSH* level begins by the age of 12 and is paralel to the enlargement of the testicles.

2. ***Sex steroids***

- *Estrogen* levels increase with the development of the mammary glands. From stage III there are hormonal fluctuation present, in correlation to the cyclical activity of the ovaries.
- *Androgens* begin to increase in level from 6-7 years of age (beginning of adrenal maturation). These hormones rise along with testosterone levels during puberty (gonadic maturation).
- *Plasmatic progesterone* begins to rise with the prepubertary stage; its level remains low until the apparition of menstrual cycles.

c. ***Physiological variations of puberty***

Recognizing these variations is possible along with the apparition of the secondary traits which match the skeletal age, so the chronological one.

Differential diagnosis is done with:

*1) Real sexual precocity*in which the sexual traits appear before the skeletal age of normal puberty, along with bone maturation. In this situation, there is a risk of definitive short stature.

2) Real delayed puberty is characterized by: absence of the secondary sexual traits, bone pubertar age is overcome. The etiology can be within the family history or a pathologic growth reason. In this situation, psychological problems appear.

3) Dissociation of puberty arises prematurely and isolated, as a secondary trait. The child's development is normal. Examples: premature development of the pubic pilosity, of breasts, with no other signs of pubertal evolution.

Pubertal gynecomastia in adolescent males

It can appear during a normal pubertal process. The testes volume is normal for the pubertal stage. The prognosis is good if the phenomenon regresses in a few months (at most a few years). It induces important psychologic consequences.

CHAPTER V

TERM NEWBORN

The neonatal period includes the first 28 days of life and represents the transition from the intrauterine life to the extrauterine one. It's an extremely vulnerable period for the newborn, who finalizes a lot of the physiologic traits needed for the extrauterine survival.

The transition from the intrauterine to the extrauterine life requires multiple biochemical and physiological readjustments.

The disparition of the maternal circulation through the placenta presumes a series of readjustments. Otherwise, the newborn lung takes the gas exchange function, the intestinal tract takes the absorption of the nutritional factors, the kidney takes the excretion function and the sustaining of the hydroelectrolytic and acid-base balance, the liver takes the neutralization function and excretion of the toxic substances and the immune system the protection against infections. The cardiovascular system and the endocrine system adapt, as well, for functioning independently.

The first 7 days of life are called the perinatal period or early neonatal period.

Evaluation of the gestational age

Fetal evaluation using various means, more or less invasive, is justified with fetal and neonatal risk assessment. For this purpose, gestational age is being evaluated, along with the functional maturity, intrauterine growth and development and prenatal specific diagnosable diseases. Gestational age is evaluated using several methods:

- ✓ last menstrual period: Mc Donald formula – 7 days are added to the last menstrual period, starting with the first day and then 3 months are substracted;
- ✓ clinical examination of the newborn.

After birth, the best way to evaluate gestational age is using the *Ballard score, modified by Dubowitz* (**table 1 and 2**). The error extent of this estimation is +/- 2 weeks. This method is not accurate enough for the premature newborn or the sick one.

Dubowitz/Ballard score– evaluates the general aspect, skin texture, motor function, reflexes.

- Physical maturity - general examination- can be appreciated well in the first 2 hours of life (table 1).
- Examination of the neuromuscular maturity (table 2)- is realized in the first 24 hours.

Classification of newborns

Based on gestational age, newborns as classified as follow:

- Preterm: gestational age < 37 weeks;
- Term: gestational age between 38-42 weeks;
- Postterm: gestational age > 42 weeks.

Based of *birthweight*:

Newborn with appropriate birthweight ≈ 2500 g;

Newborn with very small birthweight< 1500 g;

Newborn with small birthweight< 2500 g.

Newborns with small birthweight will be evaluated also by maturity and *gestational* age, as follows:

Appropriate for gestational age preterm newborn;

Small for gestational age preterm newborn;

Very small for gestational age preterm newborn;

Table 1. Ballard score. Physical maturity

	0	**1**	**2**	**3**	**4**	**5**	**6**
Skin	Sticky, friable, transparent	Gelatinous, red, translucent	Smooth, pink; visible veins	Superficial peeling and/or rash; few veins	Cracking pale areas; rare veins	Parchment, deep cacking; no vessels	Leathery, creacked, wrinkled
Lanugo	None	Sparse	Abundant	Thinning	Bald areas	Mostly bald	
Plantar surface	None	Almost visible	Faint red marks	Anterior transverse crease only	Creases anterior 2/3	Creases over entire sole	
Breast	Imperceptible	Barely perceptible	Flat areola, no bud	Stippled areola, 1-2 mm bud	Raised areola, 3-4 mm bud	Full areola, 5-10 mm bud	
Eye/ Ear	Lids fused loosely or tightly	Lids open; flat pinna; stays folded	Slightly curved pinna; soft slow recoil	Well curved pinna; soft but steady recoil	Formed and firm, instant recoil	Thick cartilage, stiff ear	
Genitals (male)	Flat, smooth scrotum	Empty scrotum, faint rugae	Testes in the upper canal, rare rugae	Descending testes, few rugae	Testes are down, good rugae	Pendulous testes, deep rugae	
Genitals (female)	Prominent clitoris, flat labia	Prominent clitoris, small labia minora	Prominent clitoris, enlarged labia minora	Majora and minora usually prominent	Majora larga, minora small	Labia majora covers clitoris and labia minora	

Table2. Ballard score. Neuromuscular maturation

a)

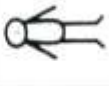
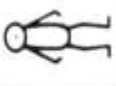
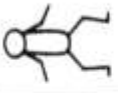
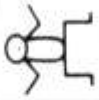
	-1	0	1	2	3	4	5
Postura							
Articulaţia mâinii (flexia mâinii pe antebraţ)	 >90°	 90°	 60°	 45°	 30°	 0°	
Reculul braţului (retracţia braţului)		 180°	 140°-180°	 110°-140°	 90-110°	 <90°	
Unghiul popliteu	 180°	 160°	 140°	 120°	 100°	 90°	 <90°
Semnul fularului							
Manevra călcîi-ureche							

Table 3. Ballard score and gestational age ratio

SCORE	WEEK
-10	**20**
-5	**22**
0	**24**
5	**26**
10	**28**
15	**30**
20	**32**
25	**34**
30	**36**
35	**38**
40	**40**
45	**42**
50	**44**

Morphofunctional particularities

Based on *gestational age*, the term newborn is born between 38-42 weeks, and based on *birthweight* between 2500 – 4000 g.

Other important parameters, which characterize the term newborn are:

- *length*, with values between 48-52 cm;
- *head circumference*, with values between 34-36 cm;
- *chest circumference*, with values between 33-34 cm;
- *abdominal circumference*, with values between 31-32 cm.

The initial examination of a newborn must be done as soon as possible, after birth, for the identification of a certain anomaly and to establish a base for the next examinations to come. For high risk births, this examination must happen in the labor room, and must concentrate upon congenital anomalies and physiopathological alterations which can interfere with a normal cardiovascular and metabolic adaptation to the extrauterine life. Congenital anomalies can be present at 3-5% of births.

The second, more detailed examination must be done within 24 hours of birth, in the Neonatal Care Unit.

The examination of a newborn takes patience, softness and procedural flexibility.

The clinical exam of a newborn must follow the antropometric parameters, on one hand (weight, height/length, head, chest and abdominal circumference) and the complete examination on apparatus and systems on the other hand. All followed aspects are carefully watched and noted: pulse (normal: 120-160 bpm), respiratory rate (normal: 30-60 rpm), temperature, weight, length, head circumference and the dimensions of any visible or palpable structural anomaly.

Blood pressure is determined only in the ill newborn's case.

Skin

Skin is completely developed, both anatomically and functionally and is pinkish-red (fig. 7).

At birth, we can observe that the skin is covered in a waxy, yellow substance called *vernix caseosa*, which is high in cholesterol, glycogen, fatty acids and proteins. It is produced by the amniotic epithelium and the fetus sebaceous glands. It has a lubrication role, protects against bacteria and the cold and is usually covering the pits, or in the dorsal region or shoulders.

On the skin, soft hair, named *lanugo* can be observed, usually on the forehead, shoulders and back. On the face and nose *«facial milia» (miliaria sebaceous)*is remarked, represented by numerous sebaceous glands of gray-white color. Upon skin examination, certain nevi can be seen as well:

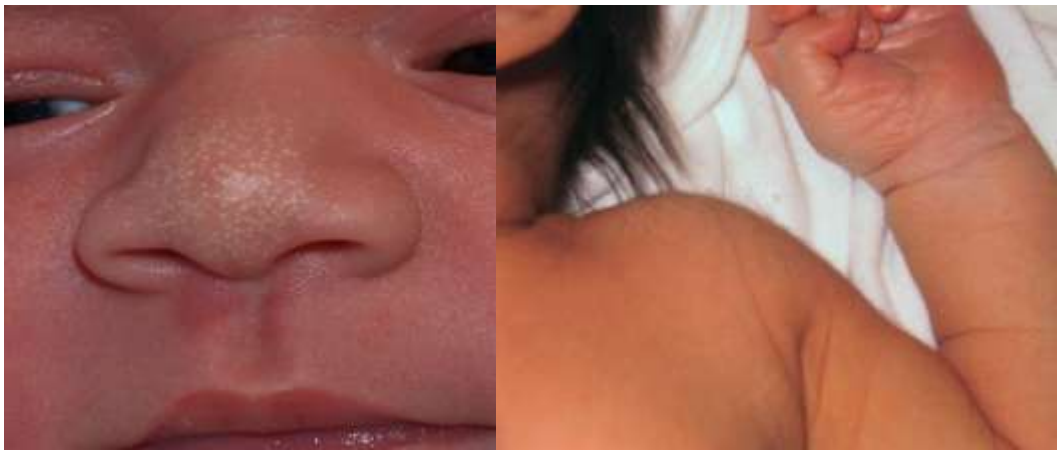


Fig. 7. Newborn skin aspect. Color, miliaria sebaceous, lanugo.

- The capillary hemangioma is frequently seen on the eyelids, base of nose and the occipital area. This vascular mark fades and completely disappears after several months.
- Prominent vascular hemangiona - can be present at birth, it continuously grows for a few months and later regresses spontaneously by the age of 1 or 2.
- Cavernous hemangiomas – do not have a spontaneously regressing evolution and can easily complicate with thrombosis, ulceration or consumption coagulopathy (fig. 8).
- Pigmented nevi – often covered in hair, are placed on the back or the gluteal region. A variation is represented by a blue area situated on the skin, named "mongoloid spot", specific for the hyperpigmented race (fig. 9).
- Petechiae - can show up on the scalp or face, after a difficult delivery.

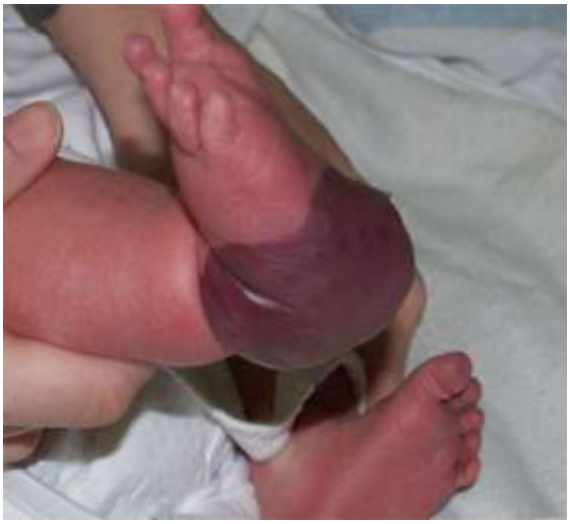


Fig. 8. Gigantic cavernous hemangioma.

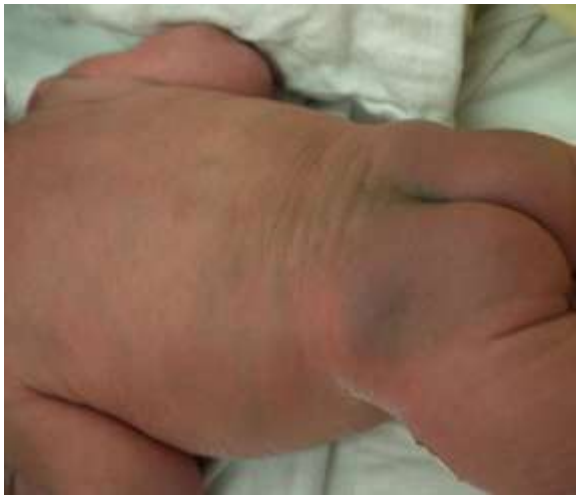


Fig. 9. Mongoloid spot

The vasomotor instability and scarce peripheral circulation are brought out by deep redness or cyanosis when the newborn is crying, the intensity of the violaceous color can intensify the glottic closure during crying.

The mottled aspect of skin can follow a general circulating instability and can be associated with serious diseases or can be connected to a transitory cutaneos temperature fluctuation.

Cyanosis can be masked by the palour from circulatory insufficiency or by anemia.

Emphasised palor of the skin can indicate a severe asphyxia, shock or edema. Severe anemia with an early debut can be seen in: fetal erythroblastosis, subcapsular liver or spleen hematoma, subdural hemorrhage, fetomaternal transfusion or twin-twin transfusion syndrome. Postterm newborns can have paler and thicker skin than the preterm or term newborns, with no signs of anemia.

The intense red color of the skin is seen in polycythemia.

In the area the vernix is situated, and around the umbilical cord the skin can have areas of yellowish-brown color; if this happens, that means the passing of the meconium took place before or during labor, the most frequent cause being intrauterine hypoxia.

Preterm babies have an intense red color of the skin, thin skin and very sensible to physical, chemical and infectious agents. The ones that are extremely preterm have an almost gelatinous skin, with high risk of bleeding and diverse traumatic lesions.

The preterm can have an intensification of lanugo, especially on the head, forehead and face area. The areas covered with pilosity from the lumbosacral region can raise suspicion, like spina bifida, sinus tracts or tumors.

Nails are rudimental for the preterm newborns, but can be over the curve of the fingers in postterm newborn; these can also have pergamentos skin with descuamation.

After approximately 3 days of life, there can be seen an erythematous area, followed by a papular rash, the pustular and vesicular rash being of white color. This benign skin rash, named *toxic erythema,* lasts for about a week, is high in eosinophils and is distributed to the face, upper body and limbs.

Transient neonatal pustular melanosis is a benign lesion which is frequently seen in the dark-skinned newborns, is filled with neutrophils and is seen at birth as a vesicular and pustular rash, located on the chin, neck, back, limbs, hand, sole and usually passes after 2 or 3 days.

Both lesions must be differentiated by other infectious, more severe, vesicular eruptions, like the ones caused by herpes simplex and staphylococcus aureus.

The presence of amniotic bands in the intrauterine life can lead to major skin and limb anomalies. As such, the amniotic bands can separate skin, limbs (amputation, constriction, syndactyly), face (fissures) or trunk (abdominal or thoracic wall defect). Their etiology is uncertain, but can be associated with a rupture of amniotic membranes or their vascular compromise, along with the formation of fibrous bands.

The excessive fragility and elasticity of the skin, associated with joint hypermobility is seen in severe diseases: Ehlers-Danlos syndrome, Marfan syndrome, congenital arachnodactyly or other colagen synthesis disorders.

The epidermis is thin, the stratum corneum is thin, the elastic connective structure of the dermis is underdeveloped, the basal and germinal layers are less developed.

The sweat glands have no activity during the neonatal period.

The head

The head is voluminous and represents 1/4 of the newborn's length; the neurocranium is bigger. The skull has 8 membraneous sutures and 6 fontanelles. The palpable fontanelles are: anterior fontanelle of rhomboidal shape, has a diameter of 2,5/3,5 cm, closes at 14-16 months; posterior fontanelle, which has a triangular shape, is present at 25% of the newborns and has diameters of 1,5/1 cm; it closes in the first 4-8 weeks of life.

The head circumference is between 34-36 cm.

The head can be big (macrocephaly), in case of: hydrocephaly, or familial large head, or macrocephaly associated with intellectual disability (rarely), achondroplasia, cerebral gigantism, neurocutaneous syndromes, inborn metabolic error or hereditary (fig. 10).

The head of a preterm baby can suggest hydrocephaly due to the accelerated brain growth rate compared to the other organs and a larger head to body proportion (the head represents 1/3 of the body, while in a term newborn the head is 1/4 of the body).

A skull depression (indentation, fracture, "ping pong ball sign").

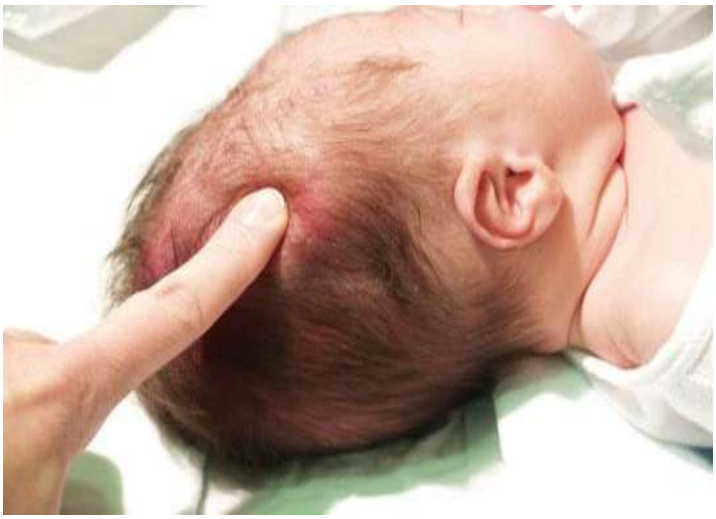


Fig. 10. Term newborn, caput succedaneum, depresible, with edema.

Microcephaly (small head) can be «apparently small» in the newborn from diabetic mother, but the head circumference is within normal limits.

Microcephaly can be hereditary and is not accompanied by intellectual disability or can be secondary to the following anomalies: intrauterine growth restriction, cytomegalic inclusion disease, congenital toxoplasmosis, chromosome anomalies (fig. 12).

The presence of large fontanelles, associated with large sutures can lead to congenital hypothyroidism suspicion, congenital rubella or chromosomal anomaly.

The head can have certain *mechanical alterations*, due to edema, intrauterine positioning or laborious births (caput succedaneum) (fig. 10).

The head can be deformed in the following situations as well: *caput succedaneum* is produced by a hemorrhagic edema of the scalp tissue and is usually situated in the occipital area, does not respect the suture limit and is rapidly reabsorbed; *cephalhematoma* (fig 13) is produced by the subperiostal hemorrhage, is well defined within the skull sutures and can persist for months; sometimes it has a calcification tendency.

The fontanelles and suture dimensions, sunken of bulged fontanelles can be evaluated best after the first few days of life.

Bulged fontanelles can be seen in meningitis, cerebral hemorrhage, cerebral edema, hydrocephaly, cerebral tumors, cerebral malformations. The bulging of the anterior fontanelle suggests the rise of intracranial pressure. High intracranial pressure can be also seen during crying.

Examination of the *cranial sutures (sagital, metopic and coronalsutue)* shows their dimensions, if the parietal bones are overlapped, having a tendency to overlap the occipital and frontal bones, especially in the preterm newborn, which can lead to severe, particular situation, even the apparition of craniostenosis. Craniostenosis represents the premature closure of the fontanelles, followed by the ossification of the sutures, which leads to microcephaly and neuropsychomotor disability.

Head asymmetry can be cause by multiple factors.

The skull can be elongated due to the intrauterine position, if it is the first one born or if it was engaged for a long period of time.

Craniotabes is sometimes identified in the parietal bones area, near the sagital suture. It is frequently seen in preterm babies and the ones exposed to uterine compressions. Usually, the evolution is good, but if it is persistent, tests must be done and the treatment and cause must be established.

Generalized craniotabes can appear in calcification disorders, like the ones from osteogenesis imperfecta, cleidocranial dysostosis, lacunar skull, imbecility, and, occasionally Down Syndrome.

A positive diagnosis is established using paraclinical investigations, the most useful being cranial transillumination and transfontanelar ultrasound.

Fig. 11. Secondary macrocephaly to evolutive hydrocephaly.

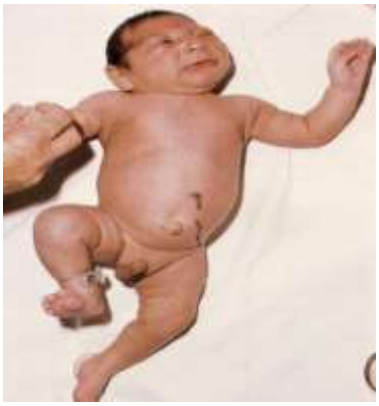


Fig. 12. Microcephaly

Fig. 13. Bilateral arieto - occipital cephalhematoma

Facies

General examination looks for the general aspect of facies, with careful observation of the dysmorphic anomalies, like hyperpilosity, protruding forehead, epicantus, hypertelorism, microphtalmia, low-set ears, which are associated with congenital malformations, most of the time.

Facial asymmetries are seen in: paralysis of the VIIthnerve, hypoplasia of the depressor anguli oris muscle, abnormal fetal posture; if the maxilla was fixed on the opposite shoulder side during intrauterine life, the mandible can easily deviate from the median line.(fig. 14). The symmetrical facial paralysis suggests the absence or the hypoplasia of the VIIth nerve nucleus (Mobius syndrome).

Fig. 14. Facial paralysis

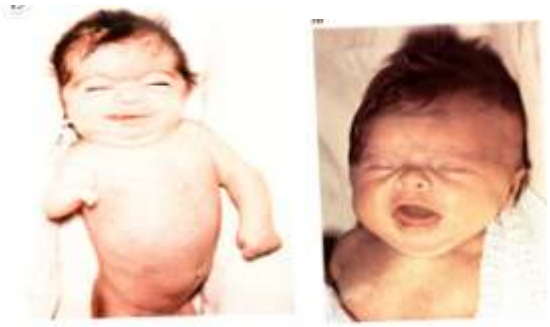


Fig. 15. Facial deformity

Eyes

Eye examination of a newborn is difficult because newborns have a tendency of keeping them closed.

Based on inspection, several modifications can be seen: eye agenesis (fig. 16), palpebral ptosis, congenital cataract, eyelid coloboma.

Fig. 16. Unilateral eye agenesis.

Eyes are opening, spontaneously most of the tine, if the newborn is held upward and lightly moved back and forth. This maneuver, the result of the tonic labyrinthine reflex and tonic neck reflex is the most useful tool for eye examination, rather than forced opening of the eyes. A good examination can be done by face illumination using a flashlight when the newborn opens its eyes.

Conjunctival hemorrhages and retinal ones do not havea pathologic semnification. The retinal hemorrhage can be seen in: severe hypoxia, subdural hematoma or subarachnoidal hemorrhages.

The conjugated eye movement are present immediately after birth, but they become permanent only after a few weeks.

Nystagmus is a common manifestation immediately after birth. In the first 10 days, the eye have a fix position, following the movement direction of the head - the test of "doll eyes". The presence of nystagmus after a few days of life is a pathological sign present in a neurologic or ocular disorder and usually indicates vision disorders.

Pupillary reflex is present after 28-30 gestational age. The pupils must be equal in size, symmetrical and reactive to light.

Blinking and corneal reflexes are present at birth.

A cornea with more than 1 cm diameter, in a term newborn, suggests congenital glaucoma and needs emergency ophthalmologic consult.

The iris must be examined for finding eventual coloboma and heterochromia.

The apparition of a white outline around the iris isn't always a pathological sign. It is usually seen in newborns with Down Syndrome, but can also appear at a healthy newborn..

Leukocoria (white pupillary reflex) appears in a series of severe disorders, like: cataract, tumors, chorioretinitis, retinopathy of prematurity or persistent hyperplastic primary vitreous and requires emergency ophthalmologic consult.

During the ophtalmoscopic examination, there can be identified: retinal anomalies, chorioretinitis and retinoblastoma.

During the first 6 months of life, intermittent convergent strabismus can be present, which has no pathologic semnification. Its persistence after 6 months of life, its unilateral persistence or the presence of a divergent strabismus can indicate a diminished visual acuity or diminished ocular muscles motility.

Conjunctivitis can be present in the first few days of life. The chemical conjunctivitis usually appears after the instilation of silver nitrate 1% drops in the conjunctival sac for the prevention of gonococcal conjunctivitis. Is manifests as eyelid edema and conjunctival inflamation along with purulent drainage (fig. 17).

Fig. 17. Purulent conjunctivitis

Visual acuity is appreciated using the photomotor reflex, the corneal reflex and the pupillary reflex. Central vision progresses from birth, when the newborn perceives only light, until the age of 6, when he reaches the adult's level of acuity.

Visual tracking and fixation are progressively developing: at 2-4 weeks he can fixate certain objects placed in his visual field for a few seconds; by 6 weeks he can track an object placed in his visual field; by 3 months, the infant has convergent eye movements and starts to distinguish the shapes and colors of different objects.

The nose

The nose can be slightly obstructed by the mucus collected in the tight nostrils. The nostrils must be identical. Nostril permeability can be tested using a catheter which easily passes through the nasal duct. Complete obstruction can be seen in bilateral choanal atresia, which can be a cause of respiratory insufficiency (fig. 18).

Fig. 18. Choanal atresia

Ears

The ear examination can bring both pathological data, but also elements of maturation level. The ear examination must establish the presence of the auditory canal, the dimensions of the pinnas, the parched or normal aspect.

The presence of preauricular small tumors can lead the examiner to a certain renal malformation.

Hearing

In the first days of life, hearing is tested with extreme difficulty. From 2 weeks, the cochleopalpebral reflex can be tested, which consists of a flinch and a wink of the eyelids as a response to unexpected sounds.

Ear loss screening using special tools is more accurate.

Mouth

During mouth and oral cavity inspection, we are interested first of all in color, which can be a great indicator of cyanosis.

Normally, early dentition appears rarely (inferior incisor or aberrant location). In pathologic conditions, neonatal dentition appears in Ellis-van Creveld syndrome, Hallermann-Streiff syndrome, and others. Extraction is not recommended.

Hard and soft palate must be inspected for identifying an eventual cleft (complete or partial), ogival arch or bifid uvula (fig. 19).On the hard palate there can be seen epithelial cells accumulation, named Ebstein pearls. Cystic retention, of similar aspect, can also be observed on the gums. Both disappear spontaneously, a few weeks after birth.

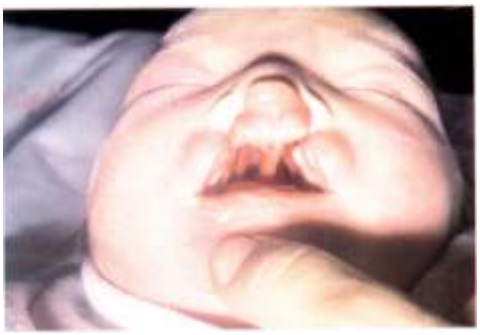


Fig. 19.Bilateral cheilopalatoschisis

On the anterior tonsil pillars, in the first 2-3 days of life, there can frequently be seen small follicles, of white or yellow color, or ulcerous areas on erythematous base. They are of unknown cause and disappear in 2-4 days without any treatment.

There is no active salivation in the first 3 weeks of life. The presence of a small quantity of saliva can suggest the presence of a tracheoesophageal fistula.

The tongue seems relatively large, the frenulum can be short, but must rarely be incised. Ocasionally, the sublingual mucous membrane forms a prominent fold.

The cheeks are abundant on both sides, internal and external, as a result of fat acummulation, which contributes to the development of the sucking apparatus. These, along with the labial tubercle from the upper lip disappear when breastfeeding stops, especially after 1 year of life.

The newborn's pharynx is hard to differentiate due to its arched palate shape, but even so, it must be carefully inspected for indentifying certain anomalies of the posterior palate or uvula. The tonsils are small.

The neck

The neck appears relatively short. The anomalies at this level are not frequent. They include goiter, cystic hygroma, residual brachial cleft, sternocleidomastoid muscle lesions, traumatic or due to intrauterine position, which can lead to hematomas and fibrosis.

Congenital torticollis (fig. 20) establishes the head orientation toward the affected part, and the face toward the opposite direction. If it is not treated, plagiocephaly, facial asymmetry and hemihypoplasia can appear.

For fracture identification, both clavicles should be palpated.

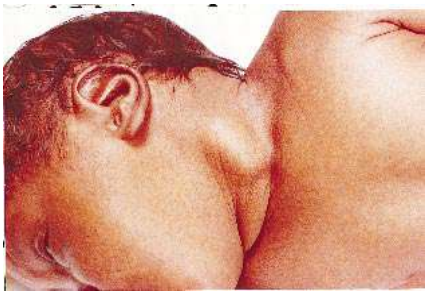


Fig. 20. Congenital torticollis. Sternocleidomastoid tumor.

Mammary glands

Breast hypertrophy is frequently seen and sometimes, in the presence of a genital crisis (under the influence of maternal estrogens), lactation can be present as well. Asymmetry, erythema, induration and sensitivity suggests a mammary abcess. Supranumerary nipples or large internipple distance, along with shield shaped chest can be present in the Turner syndrome.

Pelvic genital region

The external genital organs have a characteristic aspect for each gender. For boys, fimosis is physiological; the testes are frequently palpated in the inguinal canal; uni or bilateral hydrocele can be observed.

For girls, the labia minora appears slightly more developed. There is often observed a mucous, white or sanguinolent secretion, secondary to the transplacentary hyperestrogenism.

Meconium is usually eliminated in the first 12 hours after birth; 99% of the term newborns and 95% of the preterm ones pass the meconium 48 hours after birth.

Anal imperforation is not always visible; it can easily be detected by rectal examination (usually with the help of a tube).

The presence of an irregular skin fold on the sacrococcygeal median line, can be easily mistaken for neurocutaneous sinuses.

Limbs

The limb examination observes the existence of certain posture alterations, especially in the case of pelvic fetal presentation. The suspicion of a fracture or nerve lesion, birth associated, is brought out by observing the limb movement during spontaneous movement or stimulated ones. Hands and feet must be checked for anomalies: polydactyly, syndactyly, abnormal dermatoglyphics, such as simian crease.

Functional adaptation

Respiratory system

- The respiratory system has 4 anatomic components:
  - superior respiratory tract: nasal cavities, pharyngeal sinuses, larynx, trachea – which warms, mixes and filters the inspired air
  - inferior respiratory tract: bronchi and bronchioles – which distribute the air toward the lung
  - respiratory parenchima: respiratory bronchioles, alveolar ducts, alveoles– where gas exchanges happen
  - muscular and elastic structures: intercostal muscles, diaphragm, elastic lung tissue - which realize the respiratory excursions.

Knowing the normal lung development is important for understanding the way in which this can be alterated by different factors and for picking the best treatment methods which can prevent pulmonary injury. The degree of lung development is the main factor in determining the survival of the newborns, especially the preterm, and response to intensive treatment.

Fetal lung development has 5 stages until final maturation:

- embrionar phase which lasts until 5-6 weeks
  - the respiratory primordium appears on day 22 (postconception) by widening of the caudal end of the lanryngo-tracheal canal
  - during this period, developmental anomalies are determined by the formation of the lung bud, the separation of the trachea and esophagus, formation of the superior aerial ducts and initiation of the pulmonary lobes formation. These anomalies can manifest by: laryngeal, pharyngeal, tracheal, esophageal atresia, tracheal and bronchi stenosis, esotracheal fistula, pulmonary agenesis, ectopic lobes, bronchogenic cysts, arteriovenous malformation.
- pseudoglandulary phase which lasts until week 17.
  - major events: tracheobronchial treecomplete development until 16 weeks of gestation, development of the pulmonary arterial bed parallel

to the bronchial ramification, differentiation of the basal, ciliated, Goblet and neuroepithelial cells.

- only the pulmonary limph system, the cartilage, the mucous glands and the smooth muscle is developed. Pleuroperitoneal cavities are closing.
- the anomalies met during this stage are: renal agenesis with pulmonary hypoplasia, pulmonary intralobar sequestration, cystic adenoid malformation, congenital diaphragmatic hernia.

– canalicular phase (acinar) – between weeks 16-26.

- pulmonary acini, formation of the alveolocapillary membrane and the capillary network. Differentiation of the type I and II alveolar cells and the apparition of the lamellar cells within the type II cells is produced during this stage.
- anomalies: renal dysplasia and renal hypoplasia, alveolocapillar dysplasia, respiratory insufficiency, surfactant deficiency.

– saccular phase – weeks 24 – 38.

- air space distension continues along with their growth, formation of the sacs, thinning of the mesenchyme, septal walls contain a double network of capillaries, surfactant synthesis begins in the type II alveolar cells and fetal breathing occurs.
- type II cell maturation is associated with an increase of phospholipid synthesis from the surfactant and associated proteins (A, B, C, D).
- glycogen content is reduced, mitochondrial enzymatic activity increases, indicating a movement toward the aerobic cycle of the oxidation.
- surfactant concentration is still low and the composition of its phospholipids is significantly different from the newborn one.
- for the newborn and adult, the width of the alveolocapillary membrane is 0,6 mycrons, which allows the passive diffusion of O_2 and CO_2 between the alveolar and the capillary bed.
- the immature lung contains relatively small amounts of elastin fibers and collagen and can easily rupture, having a low elasticity coefficient.

        - anomalies associated to this stage: alveolocapillar dysplasia, respiratory insufficiency, surfactant deficit, hyaline membrane disease, transient tachypnea, prematurity apnea.
    - alveolar phase– can start by 30 weeks but usually around 36 weeks of gestation and lasts until the age of 3.
        - a term newborn has approximately 50 million alveoli.
        - this phase is characterized by: secondary sept formation along with subdivization of the alveolar sacs, loss of connective tissue and narrowing of the alveolar septs, and as a result an increase in the pulmonary alveolar bed. The capillary network fuses to a single network and the actual maturation is produced by: collagen, elastin and fibronectin deposit and an increase in the surfactant production within type 2 alveolar cells.
        - in the first 3 months after birth there takes place a slow down in the alveolar development, and then a rapid increase in its numbers in the first year of life, so that by the age of 3 they reach 300 millions comparable to the adult alveolar number.
        - associated anomalies: persistent fetal circulation and pulmonary hypertension, lobar emphisema, meconium aspiration syndrome, pneumonia, respiratory distress syndrome associated with protein B surfactant defficiency.
- the anatomic traits of the respiratory tract of a newborn contributing to respiratory adaptation are:
    - big head – short neck
    - narrow nostrils– big mouth
    - soft palate – big epiglottis
    - high glottis position (C3- C4)
    - oblique vocal chords – narrow cricoidian ring
    - posterior angulation of the subglottic cavity
    - small lung –orizontal movement of the thoracic cage

- the newborn has a nasal respiration. Flux resistance through the nasal passage represents almost 45% of the total resistance.
- big and soft epiglottis, relatively high situated in the pharynx, big tongue, in contact with the soft palate, it occupies a great part of the oropharynx, so it makes the mouth breathing more difficult.
- the subglottic cricoidian region is narrow, there is a risk of stridor from the mucous edema after detubation.
- the tracheal bifurcation angle is different to the left and to the right, so there is always a difficulty of intubation, there is a risk of intubating the right bronchus.
- main breathing muscles: diaphragm and intercostal muscles are normally innervated, but in the preterm newborns there appears muscular fatigue after stimulation. This is mainly because there is little muscular mass and a relatively small percentage of type I muscular fibers with oxidative capacity (10% compared to 25 % in the term newborn and 50-55% in the adult).
- during inspiration, the inferior ribs are moving inward at an angle that in more orizontal then the insertion of the diaphragm, resulting alterations of the pulmonary volumes and costal retraction.
- abdominal distension can lead to respiratory insufficiency due to the fact that the diaphragm is being pushed up.

Before birth, the lung is filled with a liquid which is secreted at this level, and which composition is different from the one the amniotic fluid has. During the passing through the birth canal, a small part of the pulmonary fetal liquid is eliminated with the help of thoracic compression, but the most of it is absorbed through the sanguine and limphatic vessels in the first minutes after birth. Absorption of the intrapulmonary liquid is made due to the rapid increase of the sanguine flow and the decrease of the pulmonary vascular resistance. The increase of PaO_2, decrease of PCO_2 and increase of pH favours the decrease of the pressure in the pulmonary circulation, so the sanguine flow rises.

The first breath is induced by a series of factors: acidosis and moderate hypoxia, rise of PCO_2, hypothermia and the increase of blood pressure in the general circulation by clamping of the umbilical cord. The difference between intrauterine pressure and the atmospheric one, the pleural void, produces air aspiration, which reaches the alveoli and excites the vagus nerve pulmonary endings, leading to expiratory reflex. Tactile stimuli

induce gasping type breathing, without initiating a sustained respiration. Pulmonary compliance and vital capacity increase abruptly and after 12 hours reach values that are proportional to the ones of adults.

During the first 60 minutes after birth, the newborn has an irregular breathing, with tachypnea (60-90 breaths/min), intermittent grunting, nasal flaring, subcostal and intercostal retractions, bronchus rales and bubbly secretion in the oral area. After this period of high reactivity, there comes a sleeping period, with rapid and superficial breathing. Next, the respiratory rhythm is stabilized at a frequency of 30-50 breaths/min.

Using inspection, and observing the breaths of the newborn, several aspects can be identified. Amplitude and rhythm fluctuations depend on the physical activity, wakefulness state or crying. Because these fluctuations are rapid, the respiratory frequency must be recorded during a whole minute, in rest state, preferably sleep state of the newborn. Under these circumstances, the normal respiratory frequency of a term newborn is 30-50 breaths/minute.

For preterm babies the rate is bigger and with larger fluctuations. A constant frequency is defined at 60 breaths/minute. During the regular periods of breathing, this usually indicates cardiac or lung disorders. A preterm baby can breathe in a Cheyne-Stokes rhythm, known under the name of periodic breathing, or with a complete irregular rhythm. The periodic breathing is rare during the first 24 hours of life.

Irregular gasping, followed by spasmodic movement of the mouth and chin, indicates respiratory center disturbances.

Newborn's breathing is almost entirely diaphragmatic, so that during the inspiration time, the soft tissue of the thorax is drawn inward, and the abdomen is protruding. If the child is calm, relaxed, has a normal skin tone, this "paradoxal movement" does not necessarily indicate respiratory insufficiency. On the other hand, a difficult respiration is an important sign of respiratory distress syndrome, pneumonia, anomalies or mechanic lung perturbation.

Nasal flare, subcostal and intercostal retractions, along with polypnea, peripheral or generalized cyanosis are signs of lung injury.

Pulmonary injury suspicion is based on the vesicular murmur, rales and anomalies found at percution, which must always be confirmed by cardiopulmonary radiology or other paraclinical investigations.

Lung ventilation includes at first the anterior and superior parts, then followed by basal and paravertebral ones.

Usually, immediately after birth, massive quantities of surfactant are released in the respiratory tract (from type II alveoli). Once released, the surfactant is continously mobilized through the bronchial tree, with the help of vibrating cilia.

Fetal lung maturation can be accelerated by the administration of glucocorticoids (betamethasone) to the pregnant women, which has a threatened preterm labor. The administration of this therapy, at least 2 days before birth, is followed by the reduction of idiopatic respiratory distress syndrome incidence. Crepitant rales can be heard during auscultation.

The oxygen saturation rises from 65% to 95% after 3 hours of life. The current respiratory volume is 20-25 ml, total respiratory volume is 160 ml, vital capacity during crying is 120 ml, total inspiratory volume is 80 ml. Functional residual capacity is 80 ml.

Cardiovascular system

Prenatal development of the cardiovascular system

This is the first functional apparatus of the embryo, it starts to function at the end of the 3rd week of intrauterine life:

- between the 13th and the 15th day, from the embryonic mesoderm starts angiogenesis.
- after the 17th day the intraembryonary angiogenesis starts as well.
- by the end of the 3rd week, in the cardiogenic mesenchymal plate 2 endocardial tubes start to show. These fusionate in a single endocardial tube which receives connections with the intra and extraembryonary vessels, around the 21st day.
- by the 24th day, the cranial-caudal embryonic curve is seen.

The primitive heart tube, almost rectilinear, has a cranial (arterial) pole and a caudal (venous) one. In cranial-caudal way, the segments can be seen: the bulb of the heart, which continues with the arterial trunk, the primitive ventricle, the primitive atrium, the venous sinus, the 2 horns of the venous sinus. During this phase, the embryo is sustained with the help of nutrients received at the ombilical vesicle level, through the vitelline or omphalomessenteric circulation.

The primitive cardiac tube has an accelerated growth rhythm, by 23 days it takes the position of a "laid down S letter" and forms a bulboventricular loop with 2 components: a venous extremity, from which the venous and atrial sinuses derive and arterial extremity with 2 other components - the ventricle and the bulb.

From the primitive atrium 2 big lateral evaginations will develop, the following definitive atriums. The right ventricle will develop from the primitive ventricle wall.

The arterial trunk is a fibrous segment, situated in the upper part of the valves, continued by the ventral aorta (aortic sac), from which the next great arterial vessels will develop.

At birth, along with the umbilical cord clamping and exclusion of the placental circulation, the blood pressure and the peripheral vascular resistance increase abruptly. Along with the disruption of this circulation, the Arantius venous duct is closed.

Once the oxygen reaches the pulmonary tissue, this determines a decrease of pulmonary spasm, and increase of blood flow.

Immediately after birth, the resistance from the pulmonary circulation becomes almost equal to the one from the systemic circulation. This way, through the arterial duct, there is produced a small left-to-right shunt. along with its complete closure, the shunt diminishes and disappears. During the first day of life, pulmonary resistance drops by half, reaching the adult level at the end of the first week.

The apexian shock can be observed in the 3^{rd}-4^{th} left intercostal space, outside the inter-nipple line; the cardiac sounds are equal, the blood pressure is 75/40 mmHg.

The peripheral circulation is slow, the extremities are cold and cyanotic most of the time, even though the oxygen concentration is normal. The capillary fragility and vascular permeability are increased.

The presence of a murmur in the first day of life is benign, but its persistance may need further investigation.

Congenital heart diseases may not determine a murmur initially, this can appear later in evolution; there is a risk of 1:12 that a murmur identified at birth can mean a heart disease.

Radiographic, echographic and electrocardiographic cardiac evaluation are essential when a heart disease is suspicioned.

Heart rate can normally vary, from 90 beats/min to 180 beats/min, stabilising after a few hours around 120-140 beats/min. A higher heart rate must be evaluated using an EKG.

Preterm babies, whose normal heart rate is usually 140-150 beats/min, can have an abrupt debut of sinus bradycardia.

The pulse should be palpated at both the upper extremities and the lower ones, for the eventual detection of a coarctation of the aorta. Measuring of the blood pressure can be very helpful for a sick newborn. The auscultatory method is acceptable, most of the times, if the stethscope is adapted to the newborn.

The Doppler method has a higher accuracy in the examination of the diastolic and systolic pressure. The oscillometric method is the easiest one at the moment and is the most precise non-invasive method, disponible in the NICU.

Hematologic adaptation

Blood volume is approximately 85 ml/kg (limits 50-100 ml/kg). The red cell particularities during the neonatal period are:

- erythrocytes have a diameter of 8-8,5 microns,
- anisocytosis is frequent,
- red blood cells have a decreased quantity of reduced glutathione,
- there is a transitory deficit of glucose-6-phosphate-dehydrogenase, favoring a severe hemolysis,
- the number of red blood cells is 5,6-6 millions/ mm^3, of which the number of nucleated red cells is 500/mm^3. Red blood cells have a high fragility, a shorter life span and a high metabolic activity
- reticulocytes values during the first 3 days are of 3-5% and stabilize at values of 1% after 7 days of life.

Hemoglobin is of 17-18g/dl in the blood drawn from the umbilical chord. Hemoglobin is of fetal type, which represents 80% of the total Hb, is more oxydable, and by 3 month is transformed in the adult type. Erythrocytes and hemoglobin drop in the first 2-3 months, but then normalize until 2 years of life. The values are influenced by the volume of placental transfusion; if the clamping of the umbilical cord is done belatedly, the level of Hb and hematocrit level are higher; these values also differ based on birthweight and gestational age.

Hematocrit at birth is 55% and 45% after 10 days of life. The serum iron level decreases gradually.

White blood cell count and differential count is rapidly modifying during the first days of life (table 4):

Table 4. White blood cell count and differential count

	FIRST DAY	**1 WEEK**
Leukocytes (mm^3)	18000-20000	12000
Polymorphonuclears (%)	55-60	45-50
Lymphocytes (%)	30	40
Monocytes (%)	10	5-10
Eosinophils (%)	2	2

Platelets have after birth values between 150 000 – 300 000/mm^3. Coagulation mechanisms are imperfect, so the hemorrhagic disease prophylaxis must be done by administering vitamine K. RBC velocity is of 6 mm/hour in the first 3 days of life and the below 11 mm/hour after the first week.

The newborn bone marrow is initially hypercellular, then it decreases by the end of the first week.

Gastrointestinal function

Even though the gastrointestinal tract is sufficiently developed from 28-30 gestational weeks, for allowing absorption and nutritive substances use, this function is not sufficiently mature in the moment of birth. So, the coordination of deglutition and esophageal peristaltis is weak and predisposes toward regurgitation.

Most of the enzymes are present at birth, with one exception, the ones that break down starch.

Digestion and absorption are very good for carbohydrates, good for proteins and low for lipids. Biliary secretion is present from the 3rd month of pregnancy, but the bile is deficitary in salts, and its elimination is inappropriate.

The intestinal lactase and pancreatic lipase are present from the 8th month of pregnancy. The first stool is named meconium, has a dark green color and contains residues from the digestive tract secretions, desquamation cells and bile. Its elimination appears after 24 hours and is final after 1-3 days. The following days "transitional diarrhea" is present, which consists of gelatinous, greenish or faded stools, 6-7 times per day. This false diarrhea is the consequence of microbial invasion at the intestinal level, of the laxative effect of colostrum and immaturity of the digestive function.

Digestive tract invasion with microbial flora is produced after 12-20 hours, while the intestinal tube is sterile. This invasion is produced upward and downward as well. There follows a period of characteristic constitution of flora, with bifidus bacillus, which represents 85-90% of the flora, and is specific to the breastfed newborn.

Intestinal absorption of immunoglobulins, iron and vitamin B12 is good for newborns. The liver can be palpated at 1-2 cm under the right costal margin.

Renal function

I. Renal embryogenesis and functional development

A. Embryogenesis

The mature human kidney is the final stage of three phases of embryonary development: pronephros, mesonephros, metanephros.

The transitory pronephros, the first structure that holds the rudimentary tubes, disappears by the end of the 4th gestational week.

After that, the mesonephros is developing, which holds well developed nephrons, that have vascularized glomeruli connected to the distal and proximal renal tubes and which drain the mesonephric duct.Eventually, the mesonephros fusionates with the cloaca, contributing to the formation of the urinary bladder, and for males, contributing to the formation of the reproductive organs.

The metanephros can be identified around the 5th or 7th week of gestation, this being the last element from the developmental period. It has 2 components: ureteric bud and the metanephric mesenchyme. With each division of the metanephric bud, the stem cells produce a new layer of nephrons. The metanephros reached the lumbar position after 8 weeks of gestation.

The development of the nephronal system and the collecting system differs: the nephronal system comes from the mesenchymal cells, and the tubes are formed starting with the ramification of the ureteric bud. The proximal portion of the proximal ureteral bud appears in the 28th day of gestation, and it branches with a nephron at each tip. These branches form the the final collecting system (tubes, renal pelvis, ureter, urinary bladder trigone).

Most nephrons are formed from the 36th week of gestation. Their number varies from 300.000 to 1.800.000 (mean of 900.000) nephrons per kidney; nephrons cannot regenerate.
There are 4 stages of nephron development:

- Stage I – the renal vesicle appears;
- Stage II – transformation of the renal vesicle in a "S" shaped body
- Stage III – capillary loop
- Stage IV – maturation stage, including the proximal tubes, Henle's loop, distal tubes, juxtaglomerular complex development and a part of the afferent arteriole.

During this stage, the renal interstitium is differentiated into several components: cortical, medular, etc. A perturbance of any part of this sequence can lead to a reduction in the nephrone number.
Once a number of nephrones is formed, the postnatal factors (injuries from acute or chronic renal failure) can only decrease their number.

B. **Functional development**

At birth, the kidneys replace the placental function as the main homeostasis organ, maintaining the fluid, electrolyte balance and elimination of harmful substances.

This transition appears along with the increase of renal blood flow, glomerular filtration rate and tubular functions.

Due to this postnatal transition, the level of renal function is correlated more with postnatal age rather than gestational age.

1. **Renal blood flow**

During fetal development, the blood flow remains low, representing only 2-3% of the cardiac output, then it rapidly rises, to 15-18% of the cardiac output.

This is due to the: decrease in renal vascular resistance, rise in the systemic blood pressure, and increase from the inner part to the outer part of the cortical blood flow.

2. **Glomerular filtration**

Starts immediately after the formation of the first nephrons, the eGFR increasing along with body growth and renal growth (1ml/minute/kg body count).

At birth, it is smaller at most of the preterm babies, and increases dependent on the prematurity grade. At term babies, the GFR rises rapidly, doubling by 2 weeks of age and reaches the adult level at 1 year of age.

3. **Tubular function**

a. Sodium control (Na^+). Renal capacity of natrium reabsorption is developing after 24 weeks of gestation, even though the tubular reabsorption is low until 34 weeks of gestation. After 34 weeks gestational age, sodium reabsorption becomes more efficient, so that 99% of the filtered Na+ can be reabsorbed, resulting a FENa of < 1%, compared to the renal hypoperfusion (prerenal state).

b. Water control. The newborn has a limited capacity of urine concentration, due to the limited concentration of urea in the renal interstitium (reduced input of protein and anabolic growth). The result is a decrease in the interstitial osmolarity which leads to a decrease of concentration capacity, and so a reduced capacity of water absorption. The maximum urine concentration (osmolarity) is only 500 mOsm/l for preterm babies and 800 mOsm/l for term babies.

c. Potasium control (K^+). The limited capacity of preterm babies to excrete large quantities of potasium is strictly tied to the distal tubular secretion of potasium, as a result of low

sensitivity to aldosterone, reduced activity of Na+- K+ -ATP – ase and reduced GFR. Preterm babies have higher concentrations of serum K+ compared to infants or bigger children.

d. Bicarbonate and acidity control. It is limited by a low serum level of bicarbonate in the proximal tube (14-16 mEq/l for preterm and 18-21 mEq/l for term newborns), which advances along with the Na+- K+ -ATP – ase maturation and Na+- H antiporter. In essence, preterm babies are born with a light renal proximal tubular acidosis which advances along with maturation.

e. Phosphorus and calcium control. The input and ultrafiltration of the phosphate, parathyroid hormone and growth factors adjust the renal phosphate transportation. Also, phosphorus renal reabsorption is modified based on gestational age, rising from 85% by 28 weeks to 98% at 40 gestational weeks.

Calcium urinary excretion is lower in preterm babies and is correlated with gestational age. For term newborns, calcium urinary excretion rises and persists until 96 months, approximately.

Neonatal stress and therapies that involveintense use of fluids and furosemide administration increase Ca^{2+} excretion, worsening the tendency toward hypocalcemia or nephrocalcinosis.

4. **The contribution of fetal urine to amniotic fluid volume**is minimal in the first half of the pregnancy (10ml/h), but increases significantly at an average of 50 ml/h. Oligohydramnios or polyhydramnios can relate to renal developmental disfunctions.

Oligohydramnios can be associated to: renal agenesis, renal dysplasia. Polycystic kidney disease leads to severe obstruction of the urinary tract.

Polyhydramnios can be observed in complicated pregnancies due to gestational diabetes or fetal anomalies (esophageal atresia, anencephaly).

Overall, in the first days, the renal function is deficitary: the GFR is reduced, the permeability of the filtration membrane is high, the tubular reabsorption is high, the secretion is deficitary, the dilution and concentration insufficient, excretion of the acids and electrolytes decreased, bases conservation reduced.

The newborn's metabolism is more intense, reported to the renal excretion capacity. There is a relatively renal inefficiency, predisposing the newborn to water and salt retention and edemas occurance (precaution to the dose and nature of renal elimination of drugs).

The urine macroscopic aspect is cloudy, there is a transient albuminuria in the first few days. The diuresis is approximately 100 ml/kg/24h.

Immunologic adaptation

The apparition and maturation of the immunologic mechanisms of anti-infectious defense is realized during the intrauterine life.

Nonspecific defense is realized through:

- cutaneous defense – deficitary, permeable to germs;
- mucous defense – deficitary, secretory IgA appear after 2 weeks;
- phagocytosis is reduced, and the chemotactic response of the leukocytes is weak in newborns;
- nonspecific serum factors – opsonization is relatively good (deficitary for E.coli), propertine (bactericide, antiviral and opsonizing activity) is ½ compared to the adult; the serum complement is 70 mg for 100 ml (50% less than the adult), lizozyme (unties the mucous polipeptidic complexes of certain bacterial membranes)is present.

Specific immunitary defense:

- T dependent cellular immunity is not elaborated in the newborn;
- specific humoral immunity (immunoglobulins):
- most antibodies from the fetal blood are of maternal origin and are represented by IgG; this passes the placenta in the last trimester;
- during intrauterine life, the antitetanic, anti-diphteria, anti-poliomyelitis antibodies and stuck Rh antibodies pass the placenta;
- anti-salmonella, anti E.coli antibodies, reagines and complete anti-Rh antobodies do not pass the placenta;
- IgG of maternal origins decrease in the first 3 months after birth, determining the aparition of a "physiologic hypogammaglobulinemia", which is low at 3 months;
- IgM of maternal origin do not pass the placenta. From the 4^{th} day of life a rapid increase of IgM is produced. IgA is absent at birth. Secretory IgA, appear after 2 weeks in tears, bronchus, digestive tract, etc.

Immunologic differences of a newborn determine infection generalization, giving them a septicemic aspect.

Thermal adaptation

The healthy, newborn with normal weight can maintain a constant temperature of 36,5 Celsius degrees at the abdomen skin level, or 36,5-37 Celsius degrees if the newborn is being placed in a warm room (25 degree Celsius) and is wrapped in tight clothing. Generally, the newborn must be held in a neutral thermal environment. This is defined by the interval of external temperature and the oxygen consumption at a minimum, while the newborn maintains its body temperature within range. A normal body temperature imposes a balance between heat production and heat loss.

Heat production

The newborn's capacity of heat production, using muscular contraction (shiver) is null. The necessary amount of heat is provided by the metabolism. Thermogenesis is realized at the brown adipose tissue level. This represents 2-6% of the total body weight and is distributed along the neck, subscapular region, mediastinum and perirenaly. The cells of this type of fat differ from the normal adipose tissue by the fact that they are richer in mitochondrias and contain a high number of vacuoles. This areas are very well vascularized and when the newborn is placed in a cold area, with the help of cutaneous receptors, norepinephrine secretion is boosted and the eliberation of fatty acids, as well. These are oxidized or re-esterificated, their reactions being accompanied by heat loss.

Heat loss

Heat loss within inside the body to its surface (internal gradient) are vasomotor adjusted. For stabilisation of a thermal comfort zone, the rectal temperature control is insufficient. This is an indicator that modifies when the thermic adaptability of the organism has been exceeded. Capturing the thermal adaption efort early can be realized by simultaneously measuring the central and cutaneous temperature.

Heat loss from the body surface (external gradient) is realized only by physical mechanism: radioation, convection, conduction and evaporation.

In the first hours after birth, the temperature drops by 1-3 Celsius degrees and comes to normal in the next 8 hours. A tendency toward hypothermia or overheating is observed.

Hypothermia complications appear when the body capacity of compensating heat loss is surpassed:

- coagulation disturbances such as intravascular disseminated coagulation and pulmonary hemorrhage
- shock with drop of systemic arterial blood pressure, plasmatic volume and cardiac output
- intraventricular hemorrhage
- severe sinus bradycardia
- high neonatal mortality
- low oxygen reserve and hypoxia due to the high oxygen consumption
- secondary hypoglycemia due to the glycogen reserve depletion
- metabolic acidosis caused by hypoxia and peripheral vasoconstriction
- slow growth
- apnea crisis
- pulmonary hypertension due to hypoxia and metabolic acidosis.

Central nervous system

Embryonary development of the central nervous system has 3 important stages: neurulation, formation of the cerebral vesicles (prosencephalisation) and neurogenesis (maturation).

1. Neurulation represents a complex process which consists of the formation and closure of the neural tube, which was previously floating through the amniotic fluid in the form of neural tube.

Neurulation takes place at the end of the pre embryonary period, starting with day 14 and ending by the 4^{th} week. Neurulation defects from the neonatal pathology consist of: anencephaly, encephalocele, spina bifida.

2. Prosencephalisation starts from the first 25-30 days and continues until day 80-90, when the cerebral hemispheres are formed. Initially 3 evaginations are produced: prosencephalon (anterior brain), mesencephalon (midbrain) and rhombencephalon (hindbrain) Over time, the lateral parts of the prosencephalon appear as 2 evaginations - out of which the optical nerves and a part of the eyes will develop.

The following processes take place:

- By day 36, the prosencephalon is posteriorly divided in diencephalon and anteriorly in 2 telencephalic vesicles. The vesicles form the 2 cerebral hemispheres.
- The telencephalic cavities appear out of which the cerebral ventricles are formed.
- Rhombencephalon is divided into 2 layers: anterior one, which constitutes the next pons and cerebellum and posterior one - the next bulb and medulla oblongata.
- The cavities become the 4th ventricle.
- From the mesencephalus the cerebral peduncles and the quadrigeminal plate are being formed.

The perturbances that appeared during this stage can determine major morphologic malformations: holoprosencephaly, arhinencephaly, agenesis of corpus calossum.

3. Neurogenesis starts at 8-10 weeks, continues after birth and consists of prolipheration and migration of neurons. At 20 weeks gestational age the total number of neurons is formed by multiplication of the neuroblasts from the periventricular germinative areas. The last migrating neurons are settled on the external side, so that the superficial structures of the cortex can later develop, rather than the profound ones.

Anomalies during this period lead to:

- microcephaly, agyria and lissencephaly - caused by migration reduction
- cerebral dysplasia - disorders in the placeoccupied by neurons in the cerebral cortex
- heterotopias - through agglomerations of neurons in the white substance, which do not arrive at their place, in the cerebral cortex.

Maturation of the nervous system is finished several years after birth, even though it starts in the fetal period. During the 3rd intrauterine month, the central nervous system appears drafted, as a general structure. Even in rudimental form, all the brain, medulla and sense organs (eye and ear), tight to the nervous system development, exist. During the next step, connections between the lateral ventricles start to show and the 3rd ventricle reduces in size. Next, there comes the differentiation of the other structures: interhemispheric commissures, corpus callosum and the anterior white comissure.

During the last 20 weeks, which represent the second period of maturation, the cerebral growth is realized, tied on one hand by the multiplication of the glial cells, and on the other hand by the start of myelination and growth of the cellular extensions (axonal). In parallel, the cerebral enzymologic system develops.

Myelination is considered the main indicator of the nervous system maturation. It is underdeveloped at birth, continues after birth, until the age of 3 and is genetically determined. So, there is an order of myelination of different fascicles, the ascendant ones are myelinated before the descendant ones. The pathological aspects that appear during this period are distructive processes, ischemic or infectious and not necessarily malformative.

During the postnatal period, starting from birth, the cerebral hemispheres are considered well developed (macroscopically), but the maturation process continues, in a more alert manner.

Structural and functional maturation are complex process, and of duration, and it unwinds as follows:

- for the neurologic functions, the maturation is finished around 10 years of age,
- for age functions, around 13-14 years.
- the weight a newborn's brain has is around 320-340 g,
- it reaches the adult's weight by the age of 12-15;
- the exterior aspect can be compared to the adult one at 2 years of age.
- cerebellum is maturating later, and by 7-10 years is similar to the adult one
- neurons - at birth they are totally present (14-22 billions) - are progressively maturating (cellular body, neuronal extensions, synapses) realizing more complex circuits.
- the glyal cells are developing during the first 6 months of life and reach maturity by 2-3 years of age.

At birth, the central nervous system is not completely functionally mature, excepting the brain stem, which assures the vital functions. That is why, the newborn is said to be a subcortical being, but with a rapid developmental rhythm.

Gradually, there appear new functions, a progressive corticalization appears which implies a functional hierarchization with a subordonation of the inferior structures.

The neurologic exam of a newborn means appreciating the posture, passive muscle tone, active muscle tone and primary reflexes (see "Infant Care Practical Course").

The newborn's posture is that of hypertonia, with flexor muscles predominance, along with the appearance of short-tem clonical movement of the mandible and extremities (which will be differentiated from seizures).

The deep tendon reflexes can be normally absent. The presence of Babinski sign is not pathological.

In the process of morphofunctional development of the central nervous system, a series of reactions characteristic to a certain stage take place; these specific transitory reflexes appear only at a certain age, so the lack of their appearance, as well as their persistence for a longer than usual period of time defines a pathological state.

- ✓ *The rooting reflex*

  Is examined by gently touching the infant's cheek with a soft object; the response consists of the mouth opening and turning of the chin toward the stimulus. In the first month of life, the response consists of repeated turns of the infant's head, with lateral oscillations which decrease as amplitude and which end by touching the stimulus with the lips. After a month, the head turns with one movement toward the stimulus source. This reflex disappears by the end of the first year of life.

- ✓ *The sucking reflex*

  Is shown by gently touching the newborn's lips or cheek; the response consists of opening of the mouth and rhythmical sucking movements. It is present at birth and disappears at the end of the first year of life. In can appear during sleep until 5-10 years, with no pathological meaning.

- ✓ *The swallow reflex*

  Usually follows the sucking reflex. Through sucking, saliva accumulates in the reflexogenous zone of the pharynx. This induces the swallowing reflex, which is shown by the ascension of the hyoid bone. The disorders of the sucking and/or swallow reflexes are frequent manifestations of severe cerebral injury, consequences of hypoxia or obstetrical trauma. The persistence of the swallow reflex after the age of 1 usually indicates a cortical dysfunction.

- ✓ *Cardinal points reflex*

  If a finger is moved across a labial comissure, gently touching it, the lower lip will descend and the tongue will be oriented toward the finger. A sucking movement is also present and even a slight head rotation. If the finger movement stops, the finger will be placed upon the lips and sucked. If the finger is progrssively withdrawn, a head flexion is observed.

- ✓ *The support reflex (static attitude test)*

  Holding an infant below the armpits, with the dorsal foot in direct contact with the table's edge, he will respond by characteristically rising the foot and placing it on the examination table. It is present until the end of the first year of life.

- ✓ *The stepping reflex (automatic walking reflex)*

  It is similar to the support reflex and consists of a series of stepping moves, if the infant is held below the armpits and if the feet are in direct contact with a flat surface. It appears at birth and disappears generally after the 6^{th} - 7^{th} month.

- ✓ *Ventral suspension reflex*

  It is observed by the infant's suspension in a vertical position, with the head facing upward. Until he reaches 4 months of age, the infant flexes the lower extremities. Crossing the two lower extremities suggests Little disease.

- ✓ *The parachute reflex*

  The infant is held in the air, vertically, by the trunk; if we make him descend abruptly, his arms will extend and his fingers will spread.

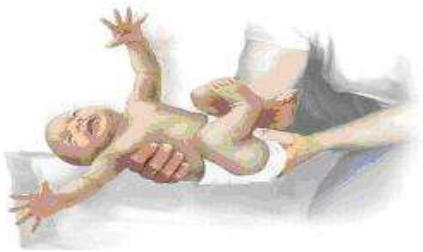


Fig. 21. Moro reflex

- ✓ *Moro-Freudemberg reflex*

  A sudden stimulus (abdominal percussion, an intense noise, a sudden blow on the infant's face, suddenly pulling the diaper from beneath him) determines an abduction and extension movement of all four extremities, usually followed by a slower reverse movement. The reflex is present at birth, fades by 4 months, but can also persist until 6 months of age. If so, it can be proof of a chronic cerebral injury. The asymmetrical movements of the upper extremities can suggest a brachial plexus palsy or a clavicle fracture.

- ✓ *Landau reflex*

  The newborn is held horizontally, with the face down. If the head extends, the trunk and the lower extremities will extend, realizing a quadrant with inferior convexity. If

the head is flexed, the trunk and the lower extremities are also going to flex, realizing a quadrant with superior convexity. This reflex is useful for detecting hypo- or hypertonia. In case of no response, or of an exaggerated one, cerebral disorders of the vertebral column or myopathic ones can be suspected. It is not present at birth, appears after 3 months of life, it is very well noticed between 6 and 10 months and fades after the second year of life.

- ✓ *Tonic labyrinthine neck reflexes*

  Changes in the head positioning in relation to the trunk lead to movements or tonic variation of the infant's extremities. A sudden head spin in one way will determine the extremities which face the front of the body to extend, and those which face the back of the body to flex. They are present at birth, more clear at the upper extremities level than the lower ones; sometimes they are only adumbrated and they fade after the 6^{th} or 7^{th} month of lige. Asymmetrical responses, with stronger reactivity on the left or the right part, can be the consequence of neurological disorders, with cerebral origin. The persistence of these reflexes can suggest a brain injury, while their absence can indicate a spine disorder.

- ✓ *Peiper's tonic reflex*

  If a strong light is projected against the eyes of a newborn, its head will be thrown backwars, in the opistotonus posture.

- ✓ *The grasping reflex*

  From birth, until 3 to 4 months, the infant strongly clenches his fists around an object which is placed on the skin of the palm. Any attempt to take the object will intensify the grasp. The grasping reflex starts to fade from the 3^{rd} - 4^{th} month, being replaced by the same movement but while the infant sees the object or exteroceptive stimuli are present. If the object is taken from the infants hand, the magnet reaction can be observed, which consists of chasing the object with the upper extremity. The absence of this reflex at birth can be the consequence of a peripheral motor neuron damage (brachial palsy, if the absence is unilateral) or severe central motor neuron damage. Its presence after 4 months reflects the release of cerebral tonigenic mechanism, as observed in hydrocephaly, or striate nuclei damage.

Newborn assessement in the delivery room

In the delivery room, assessing the newborn's status is realized after the score done by V. Apgar (1953), which must be done at 1 and 5 minutes after birth. It is appreciated based on 5 clinical signs (**table 5**).

Table 5. Apgar score

	0	**1**	**2**
A = aspect or color of the skin	cyanotic/pale all ove	peripheral cyanosis only	pink
P = pulse	0	<100 b/min	>100 b/min
G = grimace	no response to stimulation	grimace (facial movement)/weak cry when stimulated	cry when stimulated
A = activity	floppy	some flexion	well flexed and resisting extension
R = respiration	apneic	slow, irregular breathing	strong cry

The score is a practical method of evaluation immediately after birth. A score at 1 minute indicates the need of immediate reanimation and at 5, 10, 15 and 20 minutes the score indicates the success of a probable reanimation of the newborn.

An Apgar score between 0-3 at 20 minutes predicts high mortality and morbidity.

The care of a newborn with an **Apgar score of 7-10** - situation seen at 90% of births, imposes a rapid oropharyngeal aspiration, tactile stimulation and skin drying.

The care of a newborn with an **Apgar score of 5-7** - additionally, oxygen is administered. If the clinical state does not improve, positive pressure ventilation is administered, with a rhythm of 30 respirations/min; the acidosis, hypoglicemia and hypocalcemia must be corrected.

The care of a newborn with an **Apgar score of 3-4** - these newborns present with hypoxia and severe acidosis or have received depressant medication. They need immediate positive pressure ventilation. The pressure will not exceed 25-30 cm H_2O. An umbilical venous catheter will be placed for the correction of: acidosis with sodium bicarbonate 4,2%; hypoglicemia by establishing a perfusion line and administering 5% or 10% glucose solution, with a dose of 6mg/kg/h; hypocalcemia by administering calcium gluconate 10% with a dose of 1-2 mg/kg.

Gastric dilatation must be avoided by introducing in the stomach a catheter which will stay in place during ventilation.

The basic assistance of a newborn:

Newborns with a low risk must be placed with the head facing downward immediately after birth for carefully clearing (using gravity) the mouth, pharynx and nose of the mucus, blood and amniotic fluid; also, careful suction with a catheter must be done.

Clearing of the mouth and pharynx must be done carefully, so that no scratches, ulcerations or infections will appear (exceptionally, the infection of the dental bud can appear, or maxillary osteomyelitis and formation of retrobulbar abscess).

If the newborn has a satisfactory state, he can be passed to the mother immediately.

If there is any respiratory problem, newborns must be placed on a radiant warmer and reanimation should be started.

The newborn's gastric content for the ones born from c-section holds more amniotic fluid than the ones born vaginally. Their stomach should be emptied using a suction catheter, for prevention of gastric content aspiration.

Compared to weight, the newborn's body surface is approximately 3 times bigger than the adult one, and the low birth weight babies have a thinner subcutaneous fat tissue.

Heat loss rate is approximately 4 times higher than the adult. Below the usual medium temperature of 20-25ºC from the delivery room, the skin temperature drops by 0.3º C/min, and the central one by 0.1º C/min, immediately after birth, resulting a loss of 2-3 ºC from the central body temperature(correspondent to a loss of heat of approximately 200 kcal/kg).

Term newborns, that are exposed to cold after birth, can develop metabolic acidosis, hypoxemia, hypoglicemia and an increase in the water renal excretion due to their effort to prevent heat loss. They increase the heat production by boosting the metabolism and oxygen consumption and norepinephrine discharge which results from fat oxydation, especially brown fat. What's more, the muscle activity can grow. The hypoglicemic or hypoxic child cannot increase oxygen consumption when placed in a cold environment, so their central body temperature decreases.

After labor and natural birth, many newborns present with moderate metabolic acidosis, which will be compensated through hyperventilation, which is a difficult thing to realize if the newborn is depressed or exposed to thermal stress in the delivery room. This way, we have to make sure the skin is dry and during the skin-to-skin contact with the mother, he will be covered in cloth, or placed under a heat source.

For reducing the incidence of skin and periumbilical area infection (omphalitis), the skin and the umbilical cord should be cleaned in the delivery room of after placing the

newborn in an incubator, using sterile fields with warm water or soap. The child can be rinsed with warm water, dried, clothed and placed in an incubator.

For decreasing the risk of transmission of pathogens in the incubator, the external cloth can be left near the incubator's door.

For decreasing the risk of contacting Staphylococcus aureus or other pathogenic bacteria, the umbilical stump will be treated daily with antiseptic solutions. As an alternative, in cases of S. aureus epidemy, a single bath with hexachlorophene can be done. Repeated baths can be neurotoxic, especially to the newborn with low birth weight.

The medical staff must use disinfectant or antiseptic soap for routinely hand washing before touching a newborn. Hands must be washed to the elbows 2 minutes initially, then 15-30 seconds for the next washings; this is recommended to the visitors as well. Short washes, but meticulous are necessary between child manipulations.

Prevention of the gonococcal infection is done by instillation drops of silver nitrate 1%,. Eyedrops of erythromicine (0,5%) or tetracycline (1%), sterile ophtalmic solution in the conjunctival sac are alternative measures in case of clamydial conjunctivitis.

For preventing the newborn hemorrhagic disease, all newborns have to receive after birth 1 mg of vitamin K (Phytomenadione). Higher intravenous doses predispose to hyperbilirubinemia and nuclear jaundice and should be avoided. Administration of vitamin K to the mother during labor is not recommended due to the unpredictable placentary transfer.

Neonatal screening is available for different genetic, metabolic, hematologic and endocrine diseases. Common screening tests, taken from several blood droplets from the child's heel are the ones for: hypothiroidism, sickle cell disease, phenylketonuria, homocystinuria, galactosemia, androgenital syndrome, HIV infection, maple syrup urine disease.

The newborn without risk, after examination in the delivery room, can be places in an incubator, or in the mother's room, if the environment allows it.

The incubator should be of transparent plastic (the walls) for a good visibility and care and must be frequently washed. All caring should be done inside the incubator, including the physical examination, clothes changing, temperature measuring and other procedures; if there procedures are done in other place, the infectious risk rises. Clothing and bedding should be minimal, only necessary to the newborn's comfort; the incubator temperature must be held at 24 ºC.

Temperature monitorization must be done several times per day, by rectal and axillary measurement; it should be measured at maximum 4 hours in the first 2-3 days and then at 8 hours.

The axillary temperature of 36,4-37 ºC is within limits.

Weighing must be done at birth, and after that, once per day.

Vernix disappears spontaneously in 2-3 days, most of it remain attached to clothing, which must be changed daily. The diaper must be checked before and after feeds or when he cries. It must be changed whether it is wet or dirty.

Meconium or fecal matter must be cleared with sterile fields and sterile water.

Child-parent connection

The normal newborn development partially depends on the affective relationship between him and his mother; this kind of relationship binds them psychologically, as well as physiologically. This bond is facilitated and maintained by a loving husband and family. Attachment can be important for some mothers, for offering care during the neonatal period and later, during childhood.

This is initiated before birth, along with planning and pregnancy confirmation and by accepting the growth of a fetus as an individual.

Immediately after birth and in the weeks to follow, visual and physical contact between the mother and her child develops a variety of enjoyable interactions, such as touching the newborn's hands and face or lightly massaging the back.

Touching the newborn's cheek produces the turn of the baby's head toward the mother, looking for the mother's nipple, and breastfeeding is a strong stimulus for the mother's prolactine secretion.

The first contact between the mother and her child should take place in the delivery room, with the opportunity of continuation after one hour, if possible. Any delay in the contact can appear due to prematurity, pathologies of the newborn or mother, malformations, family problems, and all these can affect a child's development and a mother's capacity of care.

Specific aspects of the neonatal period

The transition from the intrauterine to the extrauterine life determined several aspects or specific manifestations otherwise known as "physiologic incidents". The most frequent ones are:

Physiological jaundice, common or idiopathic newborn jaundice, has an incidence of 60-80% (mean 70%). It has 3 phases of evolution:

- erythrodermia phase with a duration of 24 hours;
- jaundice phase - is manifested within the 2nd - 3rd day, appears on the face, thorax, conjunctives, linings and has a yellow-orange shade;
- decline phase - appears after 5 - 7 days, jaundice totally disappearing after 7 - 14 days.

During the more severe formes, the newborn is sleepy, sucks with difficulty, loses weight. The stools are of normal color, and urine does not contain bile pigments. There is no hepatosplenomegaly. The bilirubin values reach 10-15 mg%, of which indirect bilirubin represents 90-95% of the total. The yellow color of a newborn appears at values of 4-8 mg%.

Jaundice pathogeny is complex and the following factors are involved:

- a transitory deficit of hepatic glucuronidation determined by the decreased activity of glucuronyltranspherase and transitory deficit of uridine diphosphate glucuronic acid;
- slow down in bilirubin excretion by the maternal organism;
- excess of prehepatic pigment secondary to neonatal hyperhemolysis;
- plasmatic albumine insufficient binding due to hypoproteinemia;
- diminuation of bilirubin capture in the hepatocyte due to protein y and z deficiency.

Hypoxia, acidosis and hypoglicemia have an aggravating role.

Currently, newborn jaundice does not require treatment.

In the intense and prolonged formes, glucuronyltranspherase induced synthesis is imposed within the hepatic microsomes with fenobarbital or bilirubin elimination using phototherapy.

Physiologic weight loss takes place in the first few days after birth, being the consequence of a limited alimentary and fluid intake and urine, stool and perspiration elimination.

Ponderal loss is between 5-8%, losses above 10% being pathological. These losses are limited using early intake (glucose 5%, human milk); until the 10th day of life these losses are recovered.

Physiologic descuamation starts in the intrauterine life and continues the following weeks. It has a lamellar, furfuraceous aspect. Sometimes, microvesicles with clear content appear. Descuamation is emphasised in preterm babies, dysmatures, toxemia of pregnancy. The treatment consists of application of vegetal oils.

Umbilical cord involution is produced in consecutive steps: from the white initial color, the umbilical stump suffers a mumification process gaining a dark brown color; a delimitation area is formed, by leukocyte infiltration (aseptic necrosis); the fall out of the stump takes place after 5-10 days and the healing takes 3 to 4 weeks. Both the stump and the scar need daily application of sterile fields and cleaning, for preventing infection.

Genital crisis (hormonal) appears between the 3rd and 6th day of life and consists of swelling and growing of the mammary glands (if expressed, a white secretion will appear). The mammary tumefaction can appear in both genders.

At females, a descuamative vaginitis can appear, and at males a growth in the testicular volume can appear, with or without associated hydrocele and penile edema.

The duration can be of several weeks, being the consequence of the maternal hormones' presence in the newborn's blood. No other treatment but local hygiene is necessary.

Sometimes, other phenomena can appear, noted as **paraphysiologic:**

1. ***allergic erythema***- rare, after 48-72 hours of life, has a polimorph aspect: erythema, papules, vesicles, localized on the face, eyelids (sometimes palpebral edema and conjunctivitis). It is associated with micropoliadenomegalies, catarrh, splenomegaly, hyperexcitability. Blood testing reveals eosinophilia (this is the main hypothesis - the allergic pathogeny on the phenomena; other consider it a enterotoxin eliminated by the bacterial flora which invaded the intestines);
2. ***dehydration fever (thirst)*** **-** a febrile state appears after 3 - 4 days of life with values of 39-40º C, with a duration of 12-14 hours. It is frequently associated with hyperexcitability, influenced general state, ponderal loss. Most frequently, this is secondary to overheating and an insufficient fluid intake;
3. ***difficult adjustment syndrome*** appears at underweight children and manifests as: slow reactivity, difficult breastfeeding, deficitary ponderal curve, intense and prolonged jaundice. This syndrome will differentiate dormant infections of cerebral hemorrhage.

CHAPTER VI

HIGH RISK NEWBORN

The high risk newborn is a term or preterm newborn which is born under pathologic circumstances, of maternal or fetal cause, these causes being isolated or associated. The etiological factors most frequently seen, associated to the high-risk newborns and the type of associated pathology are as follows:

Maternal factors and fetal or neonatal associated risk

1. Mother's age: age over 40 leads to associated neonatal pathology, such as: chromosomal anomalies, macrosomy, intrauterine growth restriction (IUGR), blood loss (interruption or previa)

   - age below 16 years - IUGR, prematurity, neglected/abused child (the mother herself could be abused).

2. Social factors are represented by**:**

   - socioeconomic factors -determine prematurity, IUGR, infection
   - smoking - high perinatal mortality, IUGR
   - substance abuse or alcohol - IUGR, fetal alcohol syndrome, withdrawal syndrome, sudden death syndrome, neglected/abused child.
   - poor diet - slight IUGR to fetal death.
   - trauma (acute or chronic). Placental rupture, fetal death, prematurity.

3. Medical afflictions:

- diabetus mellitus leads to: fetal death, followed by suffering at birth, macrosomy, respiratory distress syndrome, hypoglicemia, congenital anomalies.
- thyroid disorders - goiter, hypothyroidism, hyperthyroidism.
- renal disorders - fetal death, IUGR, prematurity.
- urinary tract infections- prematurity, sepsis.
- cardiac of pulmonary disorders- fetal death, IUGR, prematurity.
- high blood pressure- both chronic or pregnancy related- can determine**:** fetal death, IUGR, prematurity, asphyxia.
- anemia - fetal death, IUGR, hydrops, prematurity, asphyxia.
- isoimmunization - fetal death, hydrops, anemia, jaundice.
- alloimmunization (platelet antigen**)** - fetal death, bleeding.
- thrombocytopenia - fetal death, bleeding.

2. Obstetrical history

- history of newborn with: prematurity, jaundice, IUGR, anomalies.
- medication during pregnancy.
- bleeding during the first trimester, fetal death, prematurity.
- hyperthermia, fetal death, fetal anomalies.
- bleeding in the 3rd trimester, fetal death, anemia.
- premature membrane rupture, infection, sepsis.
- TORCH syndrome.
- trauma at birth, fetal death, prematurity.

Fetal factors and associated fetal or neonatal risk

- Multiple pregnancy is associated with: IUGR, twin-to-twin transfusion syndrome, prematurity, birth trauma, asphyxia.
- IUGR - fetal death, congenital anomalies, asphyxia, hypoglicemia, polycythemia.
- Macrosomy - congenital anomalies, birth trauma, hypoglicemia.
- Abnormal fetal presentation or positioning - congenital anomalies, birth trauma, hemorrhage.
- Heart rate or rythm anomalies - fetal cardiac insufficiency, cardiac blockage, hydrops, asphyxia.
- Activity decrease-fetal death, asphyxia.
- Polyhydroamnios - anencephaly, other central nervous system disorders, neuromuscular disorders, swallow disorder, chylothorax, diaphragmatic hernia, omphalocele, gastroschisis, trisomy, tumors, hydrops, isoimmunization, anemia, cardiac insufficiency, urine concentration inability, large for gestational age, maternal diabetes.
- Oligohydroamnios - fetal death, placentary insufficency, IUGR, renal agenesis, pulmonary hypoplasia, deformations, intrapartum distress, postterm birth.

Labor and birth associated factors and risk assessment of the fetus and newborn

In this category, the following factors are included: preterm birth, postterm birth, maternal fever, maternal hypotension.

Other frequent factors:

- precipitate delivery - birth trauma, intracranial hemorrhage, lung fluid retention/transient tachypnea.
- prolonged delivery - fetal death, asphyxia, birth trauma.
- abnormal presentation - birth trauma, asphyxia.
- uterine tetany- acute asphyxia
- meconium - stained amniotic fluid- fetal death, asphyxia, meconium aspiration syndrome, persistent pulmonary hypertension.
- cardiac failure - fetal death, asphyxia.
- cesarian - RDS, pulmonary fluid retention/transient tachypnea, sanguine loss.
- obstetrical anesthesia and analgesiasi - RDS, neurogenic distress, hypotension, hypothermia.
- placental anomalies:
    - small placenta - IUGR.
    - big placenta - hydrops, diabetus mellitus, large infant.
    - placental or umbilical vessels rupture - blood loss.

Neonatal high risk associated factors:

- Prematurity - IUGR, other prematurity traits.
- APGAR score under 5 at 5 minutes
- APGAR score under 5 at 15 minutes - neurologic disorders.
- Palor or shock
- Bad amniotic fluid smell - infection
- Small for gestational age.
- Postmaturity syndrome.

CLASSIFICATION BASED ON GESTATIONAL AGE AND BIRTH WEIGHT

Newborns should be classified based on gestational age, if possible, because, as a psychological matter, this is far more important aspect than birth weight.

A. Gestational age classification.

1. The assessment based on **obstetrical information** is included in CHAPTER I. Gestational age based on the first trimester ultrasonography evaluation is exact only for 4 days.
2. For confirming or completing obstetrical data, the Dubowitz examination (**Ballard**) can be useful in estimation gestational age. There are certain limitations with this method, especially in evaluating the neuromuscular component of the sick newborns.
3. **Newborn classification based on postmenstrual gestational age**
   a. Preterm. Less than 37 complete weeks of gestation (259 days).
   b. Late preterm. Represents a subgroup of infants born between 34 and 36 weeks of gestation (238-258 days).
   c. Term. Between 37 and 41 6/7 weeks (260-290 days).
   d. Postterm. 42 weeks (295 days) or more.

B. Classification based on birth weight. Even though there isn't a universal agreement, the most common definitions are:

1. **Normal birth weight** (**NBW**). From 2.500 to 4.500 g.
2. **Low birth weight**(**LBW**). Less than 2.500 g. While most LBW preterm infants are born preterm, others are term newborns with small gestational age. LBW infants can be classified as follows:
   a. **Very low birth weight (VLBW)**. Less than 1.500 g.
   b. **Extremely low birth weight (ELBW)**. Less than 1000 g.

Newborn from twin pregnancy

The incidence of twin pregnancies is estimated around 1:80, and of monozigote or identical twins of 1:200. Prematurity and/or IUGR are the main risk coordinates of twin pregnancies. Unlike small fetuses, prematurity and dysmaturity of the twins is due to mechanical factors, and in small amount due to other factors.

The risk of neonatal mortality and morbidity is, also different for the two twins. During natural birth, the second twin is more affected due to the intranatal stress factors.

The optimal time of delivery of the second child is within 15 minutes after the expulsion of the first one. After an interval of 30 minutes, if the expulsion of the second twin does not begin, this will be considered retained, with a high risk of demise or injury.

All twin pregnancy risks develop proportionally, even exponentially with the number of fetuses.

Congenital malformations or malformative syndromes are more frequent for twins, especially monozygotes.

There are *at least 3 types of structural defects*(especially monozygotes twins):

- malformations or complex malformative syndromes, with early signs, which apparently have the same basis that determines twin pregnancies: renal agenesis, anal atresia, tracheoesophageal fistula, anencephaly, holoprosencephaly, situs inversus;
- vascular anomalies, secondary to abnormal vascular communications within a single placenta; these are secondary to thrombosis and IDC that produce at a deceased fetus and can apply the healthy twin: cutaneous aplasia, intestinal atresia;
- plastic deformations, due to mechanical action from the uterus; are normally found at both categories of twins.
- *twin-to-twin transfusion syndrome* - occurs only at *monochorionic twins*and is due to vascular connections which establish between the two fetal circulations. *The donor* will suffer a degree of IUGR, with a slowdown of the organs global mass, anemia and hypotensions, and the *receiver* will have the following: polyglobulia, cardiomegaly, arterial blood pressure and polyhydramnios.

Newborn from diabetic mother

The clinical aspect of these infants is particular, with the following aspects: birth weight>90^{th} percentile for gestational age (macrosomic); cushing-like aspect, swollen, short neck, abundant hair; visceromegaly (excepting the thymus and the brain, sometimes smaller in size) compared to birth weight; head circumference is small (characteristic aspect).

In literature, it is described as a "*giant with clay feet*", because he is exposed to many risks, like:

- cardio - respiratory adaptation disorders, due to associated polyglobulia;

- respiratory distress syndrome (an important percent of macrosomes are preterm);
- morphologic disorders; frequent and of variable intensity;
- renal veins thrombosis, rare, but frequent in the general population;
- cytosteatonecrosis;
- metabolic disorders: hypoglycemia, hydroelectrolitic imbalance (extracelullar dehydration, hypocalcemia), hyperbillirubinemia, hypoproteinemia.

The malformative risk is augmented by the lack of therapeutic control and gravity of the maternal injuries. Congenital malformations are various and can affect any organ or system.

Other categories of risk newborns:

- newborn from epileptic mother (major malformation risk, hemorrhagic risk, withdrawal syndrome);
- newborn from alcoholic mother(major malformation risk, neuropsychomotor injury risk);
- newborn from HBP mother (preterm birth risk, IUGR and cerebral hemorrhage);
- postterm newborn (cerebral injury risk and late neuropsychomotor disorder risk).

CHAPTER VII

SMALL BIRTH WEIGHT NEWBORN

PRETERM NEWBORN

The definition of a preterm newborn takes into account two major criterias: gestational age and birth weight. After the WHO, preterm newborns are those born before 37 weeks gestational age.

Other classification, by weight and gestational age:

- ✓ ELBW - Extremely low birth weight is the weight below 1000 g. Most of these babies are preterm, born before 27 weeks gestational age.
- ✓ VLBW - Very low birth weight is the weight below 1500 g.
- ✓ LBW - Low birth weight, are the ones with weight below 2500 g.
- ✓ AGA - Appropriate for gestational age newborns
- ✓ LGA - Large for gestational age newborns
- ✓ SGA - Small for gestational age newborns; also names newborns with intrauterine growth restriction (IUGR).

ELBW (extremely low birth weight) newborns survive if modern therapeutic means are used: surfactant therapy, maternal corticosteroids and advanced neonatal technology.

Prematurity and IUGR are associated with high neonatal mortality and morbidity. Ideally, the definitions of low birth weight newborns should be based on homogenous genetically and epidemiologically data.

Prematurity holds a major role in determining the perinatal mortality and morbidity.

Generally, a preterm is considered a baby born before 37 weeks gestational age, weighing under 1500 grams, having a length below 47 cm. The inconvenient of gestational age appreciation is not knowing exactly, by some women, the last menstrual cycle's date.

Another classification system, elaborated by WHO in 1948 and largely used in the medical practice, base on the birth weight was:

- prematurity grade I birth weight between 2000-2500 g;
- prematurity grade II birth weight between 1500-2000 g;
- prematurity grade III birth weight between 1000-1500 g;
- prematurity grade IV birth weight below 1000 g.

A weight of 2500 g as a limit for prematurity is also unsatisfactory, because 1/3 of these newborns are dysmature (small birth weight, but normal gestation) and 10% of the newborns with birth weight over 2500 g and gestational age lower than 37 weeks are wrongly called sick newborns.

Maternal diabetus mellitus can be associated with preterm birth; these newborns, even if they are large for gestational age, raise the issues of prematurity.

Along with the mentioned aspects, there are several other criteria to define prematurity, such as: neurologic criteria by Saint-Anne Danassier, EEG criteria (appreciates the electrical activity of the brain), anatomopathologic criteria which appreciates the brain conformation (cerebral scissures, circumvolutions), hystologic criteria (appreciates the nucleo-cytoplasmic index).

The incidence of prematurityvaries based on regions and populational groups between 4 and 14%.

Etiology of prematurity

Has multiple and varied causes, which are frequently associated or intricate, making their contributional distinction very difficult.

Out of the most common ones, we are mentioning:

- preterm births in the mother's history,
- infantile uterus,
- nuchal cord,
- vicious insertions of the placenta,
- hydramnios,
- placenta praevia,
- premature rupture of membranes (PROM),
- uterus and adnexial tumors,
- uterine malformations,
- incompetent cervix
- maternal diseases (TBC, lues, nephropathies, heart disease, hepatitis, toxic pregnancy, acute infections, diabetus mellitus),
- short interpregnancy interval,
- twins,
- primiparity at a young age,

- high multiparity,
- abnormal presentations,
- Rh or group incompatibilities,
- proteins or vitamins deficiency,
- social factors - illegitimate couples, intense professional activity of the mother,
- unknown factors (between 30-50%).

Morphologic pathologies of a preterm baby

The head represents 1/3 of the height, the head circumference is below 33 cm, the cranial sutures are dehiscent, the fontanelles open, the facies is small, of triangular aspect, with sharp chin and underdeveloped ears, with a poor maturation of the cartilage.

Pectus excavatum is frequently seen (the ribs are cartilaginous), thoracic circumference is around 31 cm, underdeveloped intercostal muscles, which favors the tirage.

The abdomen is bulky due to abdominal muscle hypotonia and high liver volume; diastasis recti, inguinal hernia and umbilical hernia are frequently seen. The umbilical cord is inserted closer to the pubic symphysis.

The skin is thin, with visible vascular drawing, with a large surface compared to the body volume, reduced or absent vernix, abundant lanugo on the face, limbs and posterior part of the thorax. Lamellar descuamation is prolonged.

The skin appendages are smooth and do not exceed the curve of the finger.

The subcutaneous tissue is reduced or absent. Bichat's fat pad is underdeveloped in grade III, IV preterm newborns; their face has an old man's look.

The muscle system is reduced and with hypotonia, the skeletal system is insufficiently mineralized; the ossification nuclei, Beclard and Tappon are missing.

The genitals are insufficiently developed. In boys, the testicles are not always descended and in girls, the labia majora does not cover the labia minora and the clitoris. The genital crisis is of low intensity.

Functional particularities

Respiratory system

The respiratory system has the following traits: narrow thoracic cage, horizontal and incompletely mineralizedribs, hypotonia, high position of the diaphragm which limits pulmonary extension and favors tirage.

The respiratory tract is narrow, the pulmonary tissue elasticity is low.

Pulmonary alveoli are immature, with thick ealls and distanced from the sanguine capillares by an abundant mesenchimal tissue, which makes the pulmonary exchange difficult.

There is a quantity and quality surfactant deficit. Synthesis and eliberation of surfactant from the pneumocytes is unsatisfactory before 34 weeks gestational age. The surfactant deficit (maintains the superficial tension of the alveoli) from the alveolar fluid favors alveolar colabation.

Ventilation disorders determine a high resistance in the pulmonary circulation.

What's more, the immaturity of the respiratory nervous centers contributes as well to the respiratory function deficiency. During hypoxia, the apneustic center (upper bulb) stops its activity, and the inferior bulbar center (older) invervenes, which determines a periodic respiration, realized by a profound, jerky inspiration, along with spasmodic movement of the mouth and mandible, interrupted by respiratory breaks (gasping). This type of breathing can be a prelude to respiration shutdown.

Even though hypoxia is partially compensated in the preterm baby, the oxygen is highly utilized by the fetal hemoglobin (HbF=90%), which has a high affinity for oxygen and attached difficultly CO_2, favoring its elimination; on the other hand, the use of anaerobic glycolysis as a main source of energy for the central nervous system, while the hypoxia is severe, drives the depletion of carbohydrates reserves and lactic acids accumulates.

A metabolic acidosis is created, which adds to the respiratory one through hypercapnia.

Preterm acidosis is prolonged because the liver function is not capable of conjugating intermediar catabolism products, and the renal function is limited by phosphate elimination H^+ and base conservation. Severe acidosis depresses the miocardic, renal and brain activities. A vicious circle is realized, and acidosis hinders hematosis by pulmonary arterioles vasoconstriction. The resultant of these respiratory deficiencies is the "respiratory distress" which means dyspnea, apneic crysis with cyanosis and paradoxal inefficient respiratory movements.

The number of breaths is of 50-60 /min.

Cardiovascular system

Is maintained after birth by the permeability of Botalo's orifice and ductus arteriosus, along with correspondent murmur. The right ventricle is enlarged and at the EKG examination a deviation of the electrical axis to the right is observed and ST depression. All mentioned aspects last several weeks after birth. Heart beats are weak and irregular, heart rate is 140-160/minute.

Oxygen reserves are low and the low oxygenation of the myocardium favors the installation of the ergodynamic heart insufficiency.

Blood pressure is between 45-70 mmHg (max) and 30-45 mmHg (min), leading to slow and weak peripheral irrigation.

The arteries, especially the cerebral ones, have an underdeveloped elastic and connective tunic; the consequence is vascular fragility which favors the apparition of hemorrhages, tissue hypoxia and acidosis. The retinal vessels are very friable. The high permeability of capilaries and hypoproteinemia favors the apparition of edemas.

Blood

The blood volume is high (108 ml/kg) until week 7 due to a rise in plasmatic volume.

The bone marrow has small extent, but hematopoiesis is also present in the liver, spleen, kidney.

The number of erythrocytes is of 5000000/mm^3, with anisocytosis, poikilocytosis and the presence of young, macrocitar elements.

The average time of life for red blood cells is reduced, approximately 78 days, haematocrit is 46% at birth and drops at 16% by week 7. Fetal hemoglobin is 90% and persists. Postnatal hemolysis is intense. Both hemolysis and medullar hypofunction generate an early normochromic anemia which lasts until 7 weeks of life. After depletion of the iron reserves, the anemia becomes hypochromial and microcytic.

The leukocyte number is of 8-10000/mm^3 with polymorphonuclear cell predominance, at birth, and after that appears lymphocytosis.

Platelets are around 100000-150000/mm^3.

The coagulation factors are lower than the term newborn's values. The high tendency toward hemorrhages is due to the vascular fragility and coagulation disorders.

Digestive system

The mucous membrane of the oral cavity is dry and permeable, the salivary secretion is low, aspects that favor the appearance of stomatitis.

The sucking reflex is absent at most preterm babies, and others lack the swallow reflex; salivary amylase is present at birth.

The gastric capacity is reduced (30-90 ml), the mucous layes has a few folds, the glands and muscular fibers are underdeveloped and gastric evacuation is delayed.

Chlorhidric acid secretion is good. The labferment, pepsin and gastric lipase are present at birth.

The intestinal musculature is hypotonic, the peristalsis is slow, favoring meteorism and constipation.

The intestinal mucose has a high permeability. Lactase is deficitary during the first week after birth, and is stimulated by offering substrate.

The pancreas has a satisfactory activity at birth by the presence of tripsine, lipase activity is reduced by 20% compared to the term newborn and amilase secretion is absent.

The liver has many deficiencies in seric protein and coagulation factor synthesis. Glucuronyltransferase activity is reduced (10% compared to normal), and is responsible of the duration and intensity of preterm physiologic jaundice, which can evolve up to hyperbilirubinemic encephalopathy.

Bile secretion is deficitary, bile acid values are low, due to the fact that the gallbladder concentrates the acids insufficiently, and the bile acid loss through stools are big.

Digestion and absorption of the human milk proteins are good.

Digestion and absorption of lipids from milk is deficitary due to the reduced activity of pancreatic lipase, small quantity of bile acids, phosphorylation disorders and low activity of serum lipoprotein lipase. Human milk lipids have a superior absorption quality (90%) due to the presence of two milk lipases (lipoprotein lipase and bile salt-dependent lipase). Cow milk lipids are absorbed around 60 - 70%.

Digestion and absorption of milk lactose is normal after one week of life.

The establishment of intestinal microbiome is slow and vulnerable for prematures. The digestive tolerance is generally reduced.

Urinary tract and excretion function

More recent data have confined the notion of excretion function deficiency for healthy preterm newborns, showing that these are capable of assuring the water homeostasis at an intake of 200 ml/kg/day from the third day of life.

It was shown that the constant maintenance of GFR can be done at 0,92 ml/kg/min using tubulary reabsorption, appropriate elimination with negative balance and dilution - concentration capacity in the first 7 days of life, at a normal serum urea concentration.

The oscillations of the urine osmotic pressure between 80-400 mOsm/l, at a constant filtration rate, confirm the renal homeostatic capacity during the first week of life. In the light of these events, it appears that the preterm baby's edemas are due to hypoproteinemia rather than sodium retention.

Studies done in 1987 show that the preterm baby can adequately absorb the HCO_3^- ion in moderate acidosis, during the first week of life.

The proximal tubular reabsorption of bicarbonate is dependent on the carbonic anhydrase activity, which is present in the intrauterine life, before birth.

Hydroelectrolytic metabolism

Maintaining the hydroelectrolytic balance is essential for the organ well functioning. The hydroelectrolytic imbalances can aggravate certain diseases such as: patent ductus arteriosus, intraventricular hemorrhage and chronic lung disease (bronchopulmonay dysplasia).

Compared to term newborns, extremely low birth infants have a larger quantity of fluid in the extracellular compartment and a higher percent of their weight is attributed to the fluid component.

During the first days after birth, there can be observed a weight loss of 10-20% due to diuresis, loss that can be aggravated through phototherapy and radiant heat use inside incubators.

These newborns also have a deficitary renal function, because of the low GFR and low bicarbonate absorption capacity. Because of the immaturity of the tubular of the renal function, the capacity to secrete potassium and other ions is decreased, along with a relative incapacity of urine concentration. Immediately after birth, at the renal tubular level, creatinine reabsorption takes place; its serum values birth do not represent an abnormal renal function. Water balance is monitored using daily weighing (sometimes twice per day), water balance (ingestion/excretion) and ionogram.

These newborn are prone to nonolyguric hyperkaliemia.

Hyperkaliemia is defined by potassium levels higher than 6,5 mmol/l. Such values can cause cardiac arrythmias and demise.

Hypernatremia and hyponatremia are due to free water alteration (dehydration with the rise of serum sodium or hyperhydration with dillutional hyponatremia). At very low birth weight infants, dehydration can be produced by exposure to heat or phototherapy. For these children, hypernatremia can be combatted by administration of hypotone fuids for fluid loss replacement.

For maintaining an adequate hydration state, one can administer up to 200-250 ml/kg/day. Such quantities of fluids can decompensate cardiac disorders (eg: patent ductus asrteriosus). Fluid loss by insensible perspiration can be reduced by use of "double wall" incubators.

In case of hyponatremia, the fluid intake will be restricted and sodium supplements will be given.

The calcium and phosphate metabolism: prenatal calcium reserves are low due to short gestation. The intestinal calcium absorption is good, but the alimentar intake does not provide the adequate necessities of a preterm newborn, so he always has a tendency of clinic manifested hypocalcemia.

Iron metabolism: is defficitary, even though the intestinal absorption and elimination are normal, but the iron supplies are low (168 mg), dietary intake from milk is decreased, and the high intensity hematopoesis generates iron deficiency anemia around 3 months of age.

Nervous system

Circumvolutions and brain scisures are hardly seen and there do not exist clear lines between the white and grey matter.

The cortical and subcortical areas are low vascularised, in contrast with the rich vascular network if the periventricular area. This areas are the place of numerous hemorrhages, causing death by ventricular flood.

The vital function control activity (respiratory, cardiac, thermoregulation) is defficitary.

The preterm baby presents a high muscular excitability, seen as muscular contractions, present during sleeping as well.

The preterm movements have an athetosic nature. Nystagmus, anisochoria and strabismus are frequently seen, but they are transient.

The osteotendinous and abdominal cutaneous reflexes are present, but the swallowing reflex is absent at small preterm newborns. The presence of archair reflexes is conditioned by the duration of the gestation period; it represents a criteria of the nervous system development assessment.

The EEG shows hypovolted route during the first 5 - 6 months.

The CSF is xantochromial, with albuminorachia of 1,5 g% and a number of 5-6 elements/field.

Thermoregulation

After birth, the preterm's temperature drops by 2-3 degrees and normalizes in 2-7 days. Preterm newborns have a high thermolability with a tendency toward hypothermia. This thermolability is the consequence of high thermolysis, deficitary thermogenesis and imaturity of the thermoregulator centers.

High thermolysis is a consequence of high surface of irradiation through the thin, well vascularized skin, with a high water content and lack of adipose tissue; this determines an unsatisfactory thermal insulation.

Thermogenesis is limited by the low lipid reserves, low dietary intake and intestinal absorption, low basal metabolism and low muscle activity. Maturation of thermoregulation take place at 3-5 months of age. That's why the preterm newborn is dependent on the environmental temperature. The thermal comfort zone is of 32 degrees Celsius, which allows a minimal oxygen consumption.

Protection against cold is done through chemical thermogenesis, more exactly by general increase of cellular oxydations, especially brown fat. The brow fat triglycerides from the base of the neck, mediastinum and interscapular area are hydrolized by cathecolamine action into fatty acids, which, by oxidation, release heat. This type of chemical thermogenesis is noneconomic, is done with high energy consumption, taking the oxygen from other vital functions. Overheating determines hyperthermia.

Immunity

Immunity and infection resistance are low. Immunologic deficiency manifests both as nonspecific and specific defense.

Mucous immunologic deficiency is due to high permeability and secretory IgA shortage. The fagocytic activity represents 53-60% of the adult values, due to the decreased chemotactic leukocytic response.

The complement, opsonins and properdin reach about 17-50% of the adult values.

IgG from the mother represents 10% of the term newborn's level; the transfer is made during the last 3 gestational months.

The preterm newborn's infections have a quiescent evolution, without fever, but with alteration of the general state, with a septicemic trait.

Complications of prematurity

Preterm babies have a series of specific disorders, associated with difficulty of adaption to the extrauterine life, secondary to different organs and systems immaturity. The most severe and frequent disorders, that lead an increase in neonatal mortality are:

1. Respiratory distress syndrome

A serious and early prematurity of high risk complication is the respiratory distress syndrome (RDS), and its main cause is the surfactant deficiency.

The RDS incidence is inversely proportional to gestational age, with an incidence of 60% by 29 weeks of gestation. In the US, RDS affects 40.000 newborns yearly (most of which have very low birth weight).

Specific clinical signs are: tachypnea (>60 breaths/min.), cyanosis, intercostal retractions, nasal flaring, expiratory grunting.

Untreated, RDS increases the oxygen need during the first 24-72 hours of life. The cardio-pulmonary x-ray shows a uniform reticular and granular image, with air bronchogram. Due to the surfactant shortage, alveoli collapse, edema appears along with a decrease of total pulmonary capacity.

The surfactant decreases the tension in the small respiratory duct walls, so that the alveoli remain open, without oxygen supplementation or ventillatory support.

Common complications are: chronic lung disease (bronchopulmonary dysplasia) and retinopathy of prematurity.

Prophylactic surfactant administration for preterm babies born below 28 weeks of gestation decreases the ventillation necessity, but does not decrease the risk of bronchopulmonary dysplasia occurrence. Synthetic surfactants do not have in their structure certain proteins that are found in the natural surfactant structure, which makes them less effective.

The RDS incidence can be significantly reduced by the use of prenatal corticosteroids and early surfactant therapy.

Prenatal use of steroids also decreases the indicence of patent ductus arteriosus and intraventricular hemorrhages, but there still exists the possibility of neuropsychic disorders during the administration of repeated doses of steroids.

In the last decade, surfactant was often used in the treatment of RDS, so it was concluded that it should be prophylactically used for all born before 30 weeks of gestation, which would lead to unnecessary surfactant administration for some preterm babies. While a small number of newborns are intubated at birth, prophylactic surfactant administration via intubation cannot be realized. Newborns that are not intubated at birth, can be given oxygen via nasal canula, with continuous positive pressure (it improves the endogenous production of surfactant). If this measure does not pay off (rise of PaCO2, clinical signs of respiratory distress, increase of oxygen need), the next therapeutic option remains intubation and surfactant administration. Studies (Geary et al.) have shown that such a therapeutic protocol decreases the incidence of chronic lung disease.

If the surfactant prophylactic administration is wanted, it should be done immediately after birth. If it is used as a curative treatment, it should be administered as soon as the clinical signs of respiratory distress start to show or if the respiratory syndrome does not improve after initial reanimation.

One of the most severe prematurity complications is the **chronic lung disease (bronchopulmonary dysplasia - BPD)**, which is defined by: oxygen necessity supplementation or ventillatory support until a gestational age of 36 weeks. An older definition was: oxygenotherapy dependency after 28 days of life. The incidence is between 19% (1990) to 23% (1996) at newborns with less than 36 weeks gestational age, with a weight< 1500 g.

2. ***Intraventricular hemorrhage (IVH)***

It's the most common prematurity complication, with the subependimal germinal matrix as a starting point and it can progress in the presence of aggravating factors, to the whole ventricular system and/or periventricular parenchyma, leading to peri or intraventricular hemorrhage.

The incidence and severity of the hemorrhage are inversely correlated with gestational age. Extremely low birth weight infants have a high risk, due to the high germinal matrix vulnerability and because the cerebral protective self-regulation is not yet developed.

3. Periventricular leukomalacia

Commonly seen pathology in bigger preterm infants, the second pathology after intraventricular hemorrhages; it represents an area of ischemic necrosis of the white periventricular substance, localized closely to the external angle of the lateral ventricles. Its incidence was appreciated around 7-26% within autoptic studies. The frequency is higher for preterm newborns with a birth weight under 1500 g, with a history of severe hypoxia or ischemia (80-90% of the cases are seen in preterm babies), newborns from laborious births, along with cranial trauma or babies with cardiorespiratory disorders during the neonatal period (heart failure, patent ductus arteriosus, repeated crisis of apnea, septicemia).

4. Apnea of prematurity

Apnea is defined as an interruption of breathing for a period longer than 20 seconds or any respiratory break with a shorter period but associated with cyanosis, bradycardia or both.

Apnea is frequently seen in a preterm baby. It is caused, most of the time, by a transient disorder of respiratory control (apnea of prematurity) or rarely by a more severe state, such as: septicemia, hypoglicemia, intracranial hemorrhage, seizures or mother ingestion of certain drugs.

5. Patent ductus arteriosus

For a fetus, the blood oxygenation is realized through the placenta, so the blood passage through the lungs is not necessary. The ductus realizes the connection between the pulmonary artery and the aorta, so that on the whole pregnancy period, the blood bypasses the lungs. At term, the ductus closes, generally after the first 48 hours of birth due to the constriction done by oxygen. This constriction has a decreased effect on the ductus arteriosus on preterm newborns, so that 80% of the ELBW or VLBW ones still have a ductus at birth, with important clinical severity, depending on the shunt intensity between the systemic and pulmonary circulation, left to right shunt.

The clinical symptomatology is diverse: systolic murmur of different degrees, dyspnea. If the PDA is of a high caliber, a negative effect is produced onto the cerebral oxygenation, a decrease of the systemic blood flow due to the left to right shunting, decrease of the urinary flow, food intolerance or hypotension.

6. Necrotising enterocolitis (NEC)

NEC represents a digestive disorder, specific for the preterm newborn, which determines mucous injuries and intestinal vascularisation disorders and it represents the most frequent intestinal emergency of prematurity. The incidence is directly correlated to gestational age: 1-8% of the newborns admitted to the NICU, with a mortality rate of 10-50%.

7. Hyperbilirubinemia

Most of the VLBW newborns develop hyperbilirubinemia (jaundice) which needs treatment. Hyperbilirubinemia is produced under the following circumstances: exaggerated hemolysis, liver immaturity that is incapable of conjugating and eliminating the resulted bilirubin. What's more, most premature babies have a low intestinal motility due to the insufficient oral intake, so the results are: late meconium passing (which contains bilirubin) and an increase in the enterohepatic circulation of the conjugated bilirubin. Due to these prematurity complications and other contributory factors (group or Rh incompatibility, sepsis), these newborns have a high risk of nuclear jaundice at lower bilirubin values than the term newborns.

8. Retinopathy of prematurity

It represents a disease of the preterm retina, which has not been yet vascularized. Slight changes in oxygen exposure have been incriminated in the distruction of the vascular trajectory and can lead to abnormal growth of the vessels, which can lead to retinal detachment and blindness.

The retinopathy risk factors are represented by prematurity and oxygen exposure. All VLBW babies should have an ophtalmologic examination by 4 weeks of age (or postconceptional age of 31 weeks) and, based on the results, every other 2 weeks until the retina is completely vascularized.

If the disease is present, treatment assessment will be done based on stage and location, from frequent check-ups to laser intervention or even vitrectomy.

The presence of another disorder or the sinuosity of the retinal vessels represent a poor prognosis and require immediate treatment.

Preterm newborns with retinopathy have a high risk of developing sequelaes, such as myopia, strabismus or amblyopia.

9. Metabolic disorders

Hypoglycemia (less than 20 mg%) and hypocalcemia (less than 8 mg%) are common. Fetal euglycemia (normal blood glucose level) is maintained during the whole pregnancy by the maternal placenta. VLBW newborns can have difficulties in maintaining their glucose levels immediately after birth when the glucose maternal source has been cut-off. Besides, these newborns have a higher risk compared to term newborns and do not have sufficient glycogen reserves.

Hypoglycemia is considered when the plasmatic level of glucose is below 45 mg/dl.

10. Hypothermia

As a result of a high ratio of the body and small weight, the decrease of brown fat reserves, immaturity of the skin and decrease of glycogen reserves make the ELBW susceptible to heat loss immediately after birth. Hypothermia can appear as a result of hypoglycemia, apnea or metabolic acidosis, as well.

Temperature monitorization is important for all categories of preterm newborns and is realized using radiation heating devices or double wall incubators.

Hypothermia (<35ºC) has been associated with a bad prognosis, including chronic dependence on oxygen; that's why, special protection measures are imposed. Thereby, after expulsion, the newborn must be dried and put on a radiant heating sourse, and his head must be covered with a hat or something else. Studies show that using a plastic bag immediately after the baby has been dried, seems to minimalize the temperature loss thorugh evaporation and convection.

For the newborn transportation from the delivery room to the NICU it is necessary that the baby is covered in warm blankets or cellophane. For long distances transportation, the newborn must be places in a double-wall heated incubator.

The delivery room and the NICU must be maintained heated for the prevention of hypothermia of such preterm newborns.

11. Infections

Predisposition to infection is based both on immunologic immaturity, but on other immaturities as well, that indirectly influence the rise of the infectious risk: nutrition difficulties, with a risk of pulmonary aspiration, multiple maneuvering or explorations, catheterisations or extended iv fluid therapy. Infection still remains an important factor of VLBW neonatal mortality and morbidity.

Preterm newborn nutrition

Preterm baby's nutrition must be appropriate for his digestive particularities and high nutritional needs. Maintaining an ascending growth curve for these newborns remains a challenge. Weight is monitored continuously (daily weighing) and so are the anthropometric indexes: length and head circumference (weekly).

The growth curve can be influenced by specific complications, such as pulmonary disorders or sepsis. Another contributing factor is the inadequate calories and proteins intake.

Initiation of enteral nutrition is frequently delayed, due to the risk of NEC apparition. For VLBW babies, parenteral nutrition provides the necessary energy and protein requirements during the first weeks of life.

The optimal parenteral nutrition was realized by the use of special amino acid solution, glucose, minerals, electrolytes and it names total parenteral nutrition. A 20% lipidic emulsion is added to the nutritional scheme.

It is considered that the total protein requirement for stimulating the protein anabolism is of 4 g/kg/day. The nutrition for these preterms must be supplemented with essential amino acids such as cysteine, glutamine and minerals (iron, iodine, zinc, copper, selenium, floride). Chrome, molybdenum, manganese and cobalt can be added especially to the newborns with long term parenteral therapy. In some centers, L-carnitine is added. Lont term parenteral nutrition use has secondary effects, such as: cholestasis and high trygliceride levels.

Caloric requirements are high compared to the reduced nutritional absorption and metabolism. During the first week of life, caloric intake requirements are 60-90 cal/kg/day, during the second week 100-120 cal/kg/day, and after that 130-140 cal/kg/day.

Fluid requirements are influenced by temperature and humidity of the environment. During the first week, there is a tendency of sodium and water retention, which is why the fluid intake starts by 60 ml/kg/day and increases up to 150 ml/kg/day; during the second week of life: 150-180 ml/kg/day, and at the end of the first month of life: 200 ml/kg/day.

Protein requirements are high, between 2,5 – 4 g/kg/day. Cysteine and histidine are considered essential amino acids. Because the VLBW infants are losing 1,2 g/kg/day of endogenic proteins, they require the same amino acid quantity per day and 30 kcal/kg/day for maintaining the protein balance. It is recommended that the nutritional supplementation should be done using protein substances during the first 12-24 hours, for avoiding protein catabolism.

Lipid needs are of 2-3 g/kg/day, and it is known that preterm babies have a malabsorption for lipids. Linoleic acid requirement is 5% of the total caloric intake need. The lipid intake varies depending on tolerance and must be initiated during the first 24 hours of life for an optimal nutrition. Lipid supplementation can be delayed due to possible infection or hyperbilirubinemia occurence.

Carbohydrate needs are of 4-6 g/kg/day during the first week of life (when the preterm has a lactase deficiency) and rise up to 12-18 g/kg/day due to the high glucose requirements, which is done by the organ functioning and brain glucose need.

Mineral needs are bases on insufficient prenatal reserves and high needs during the growth process.

The calcium requirement is of 40-50 mg/kg/day, phosphorus of 30-40 mg/kg/day, iron 1-2 mg/kg/day.

Nutrition should be early initiated because the preterm newborn has low reserves, high energy consumption and the environmental aggressions along with associated disorders increase the nutritional needs.

Oral nutrition starts with 5% glucose solution for reducing the incidence of hypoglycemia. After 12 hours, human milk is progressively added, related to his weight and general state.

The dosing of small milk quantities every 2-4 hours can be initiated from the first day of life. If the nutrition is well tolerated (low gastric residual), the food ration can be increased by 10-20 ml/kg/day. Bolus nutrition is physiologic, but some preterm newobrns do not tolerate it and require continuous enteral feeds.

Clinical research shows that the enteral fed preterms, which tolerate higher quantities of milk have an ascending growth curve and a lower infection risk.

Contrary to the fact that early enteral feeds could favor the apparition of NEC, studies have not shown a correlation between the nutritional techniques (the age for enteral feeding initiation, rhythm of ration increase) and NEC.

The number of feeds should be 7 for preterms over 32 - 34 weeks gestational age and 8-10 for VLBW and ELBW, depending on tolerance and associated pathology (see "Infant care-practical course", chapter IV). When the weight of 2000g is reached, the number of feeds should drop to 7, no matter the degree of prematurity.

Human milk is considered to be the best choice for enteral feeding and it has been shown that is has a protective effect on NEC.

Human milk is the best food for a preterm baby, due to its protein specificity, low mineral values, amino acid intake, essential fatty acids, biologic value and optimal absorption. It can provide, along with the fluid requirements, the caloric needs of proteins, lipids, carbohydrates and minerals.

LBW newborns have a high requirement of micro and macronutrients, similar to the one from the intrauterine life. The gastrointestinal immaturity does not allow an adequate nutritional intake, if we are talking about growth needs.

In spite of multiple immunologic and nutritional advantages, a diet based solely of human milk, with no supplementation, is energy inefficient and needs calcium, phosphorus and protein supplementation, so that bone mineralisation and growth rate maintain similar rates to the intrauterine ones.

Mother's own milk should be supplemented with a caloric, protein and mineral addition, especially calcium and phosphorus. Without these essential elements, protein - calorie malnutrition can appear, along with hyponatremia, osteopenia of prematurity or rickets. To this end, human milk fortifiers are used, with special formulas for preterms, mineral supplements, vitamin supplements, with different brand names: liquid PreNan, stage I and II, Prematil, HumanaO, Enfamil, Similac Human Milk Fortifier - powder and Similac Natural Care Liquid Fortifier - liquid.

Complications of human milk fortifiers use are: nutritional imbalance, high osmolality, bacterial contamination.

There are a numerous number of formulas, specially designed for preterm babies that cannot be breastfed.

The nutritional balance is very important during the neonatal period. Studies show that a high intake of carbohydrates during this period is associated with a growth above limit and insulin resistance, increasing the risk of metabolic syndrome during the adult life.

The nutrition technique is individualized based on the presence or absence of the swallowing and sucking reflexes. The vigorous preterm baby will be breastfed, while the ones that cannot suck, but have the swallowing reflex can be fed using a spoon or using a bottle, and those with no swallowing reflex using gavage feeding (fig. 22). The ones with RDS are fed via parenteral nutrition until pulmonary ventilation is normalized and after that oral nutrition is started.

Fig. 22. Preterm newborn, placed in an incubator, fed via gavage.

Vitamins intake: vitamin C, 50 mg/day, necessary for the phenylalanine and tyrosine metabolism; vitamin D for rickets prophylaxis, 1000 UI per day, starting from day 10; vitamin E, 10-15 mg/day, prevents hyperhemolisis; vitamin A, 2000 UI/day, necessary because of the low liver reserves and lipid absorption insufficiency; folic acid, 2,5 mg/day, for establishing the intestinal microbiome.

Preterm babies catergories

- 24- 29 weeks old preterm baby (650-1250 g) will be placed in a NICU. Hypoxia will be prevented by strict monitoring and, at need, assisted ventilation will be applied for preventing severe complications such as interventricular hemorrhage. Mortality is between 30-100%.
- 30-34 weeks old preterm baby (1250-2000 g): hypoxia will be prevented, along with RDS. Mortality is between 10-40%.
- 34-37 weeks old preterm baby (2000-2500 g), in most cases has a favorable outcome; techniques of nutritional care will be applied in the hopes the growth curves are appropriate. Mortality is around 5-10%.

The ELBW preterm newborn, has a growth chart that maintains below 10%, sometimes even until school age.

Fig. 23. Preterm newborn with physiologic jaundice.

Evolution

Physiologic weight loss is reduced, and the return to the initial weight is slow, by 2-3 weeks.

The rhythm of growth is emphasized: by 2-3 months the weight is doubled, by 6 months - tripled, by 1 year the weight can be 6-7 times bigger; this is the case if the nutrition and care are adequate.

The stature and growth deficite will be recovered after 2 years. There aren't specific normal values for the preterm's normal growth rhythm.

Physiologic jaundice is more intense and prolonged, along with a risk of bilirubin induced encephalopathy. The hormonal crisis is missing or appears later in evolution.

The neuropsychic development can register several neurologic disorders, sensory, intellectual deficits, behavioral disorders in 10-50% of cases.

It appears that the preterm baby's evolution is more difficult that the term newborn's. The smaller the weight, the higher the neurodevelopmental disorder risk.

The most common neurologic disorders are: spastic diplegia, hemiparesis, hydrocephalus. The sensory deficits are: hypoacusis, strabismus, vision disorders, retinopathy. Some deficiencies can be prevented or, if present, can be corrected. Behavioral disorders (anxiety, aggresion) and speech disorders have a major importance in school adaptation.

Prognosis depends upon: grade of prematurity, the cause that determined preterm birth, hypoxia, care, late morbidity.

Early prognosis is uncertain due to the high neonatal mortality, generated by RDS, traumatic encephalopathies, hemorrhagic disease.

Late prognosis reveals the frequency of bronchopulmonary dysplasia, NEC, iron deficiency anemia, neuropsychic deficiencies, statural and growth restriction. The recovery possibility depends on how early the deficiencies are diagnosed and how well they are treated.

INTRAUTERINE GROWTH RESTRICTION

Intrauterine growth restriction, or IUGR, represents a newborn with a weight below the 10^{th} percentile, related to gestational age; the clinical examination shows signs of intrauterine malnutrition. It is also known as delayed intrauterine growth (DIUG) or limited intrauterine growth (LIUG) and the basic feature is represented by the significantly reduction of the fetal growth and of birth weight.

Other names were used as well: small for gestational age, dysmaturity, fetal malnutrition, placentary dysfunction syndrome. After WHO, IUGR means a newborn with a birth weight less than 2500 g and a gestational age higher than 37 weeks.

Etiology of IUGR

In IUGR multiple factors are involved:

- maternal causes: toxemia, chronic hypertension, kidney diseases, cyanotic heart disease, juvenile diabetes, hemoglobinopathies, malnutrition, alcoholism, tabacism, abnormal uterine structure.
- placental causes: structural and inflammatory lesions, twin pregnancy, placental infarction, twin-to-twin transfusion syndrome, abnormal umbilical cord insertion.
- fetal causes: intrauterine infection (toxoplasmosis, rubella, cytomegalovirus, herpes virus); major fetal anomalies, especially the one interesting the gastrointestinal tract and the cardiovascular system.
- other factors:

Nicotine, acts upon the placental function by: increasing the benzpyrene hydroxylase activity has degenerative placental influences; a decrease in the amino acid plasmatic level, carotene, reduction in the pyruvate kinase activity inside the leukocytes and decreasing of ARN synthesis. It's also noticed a reduction in the respiratory movement of the fetus.

Alcohol is unanimously recognised, as it produces: small birth weight, microcephaly with facial dysmorphism, plurimalformative syndrome (renal, pulmonary, cardiovascular, digestive, neurologic, ocular malformations).

Anemia of pregnancy can be a risk factor for small birth weight.

Anti-epileptic drugs can produce a restriction in skull development.

In IUGR secondary to maternal and/or placental causes, it is observed a larger weight decrease compared to length and head circumference (brain sparing phenomenon). In IUGR caused by fetal factors, the reducing of weight is proportional to the head circumference.

Genetic factors hold an important role; the existence of a single umbilical artery *as an associated anomaly* involves a nutritional component of genopathies or cromosomopathies, by a decrease in placentary flow.

The placentary insufficiency (small, ischemic placenta, placental infarction) represents a known cause of IUGR.

It is not know how the incriminated factors determine IUGR. 30% of the cases do not have an exact etiology.

Prenatal conduct during the IUGR pregnancy

Supervising the IUGR pregnancy means a close monitoring of both the mother and the fetus. A close mother supervision means: detection and treatment of maternal causes (hypertension, toxemia, infection).

Monitoring the fetal state has three main objectives:

- congenital anomalies finding; there is a high risk for the women over 36 years of age.
- evaluation of lung maturity, by determining the lecithin/sphingomyelin ratio in the amniotic fluid (amniocentesis). If the ratio is 2/1 or above, it represents a mature lung, with a low probability of RDS.
- determining the fetus well being by: serum or urinary estriol determination (in case of IUGR the estriol is low); serum prolactin for appreciation the feto placental integrity; following the fetus movement using ultrasonography; following the fetal breaths (normally, a rythmic respiration); monitoring the fetal heart by recording or amniocentesis.

When the mother's or fetal state are damaged, but the fetal lung is mature, immediate birth is recommended. In case of IUGR, prolonging the pregnancy after 38 weeks has a high mortality risk for the fetus (decline of nutrient intake to the brain).

Diagnosis of IUGR in the prenatal period

Confirmation of the diagnosis is done by several methods:

- ultrasonography, which allows the measurement of the head to toe length; biparietal diameter measurement.
- bone densitometry can determine the total intrauterine volume, using tridimensional measurements integrated in mathematic formulas.

By evaluating the ratio between the fetal head and body, 2 types of IUGR occured:

flat, late type, in which the head growth process is reduced only by the end of pregnancy; newborns are small and asymmetrical, they have a dysproportion between the head and body. The head is larger and is "protected" by the fact that the circulation is directed to the brain. In this case, maternal or placental factors are involved.

slow growth type, in which the biparietal diameter growth is slow from the start, resulting in a small, symmetrical newborn, with a probable fetal cause.

Diagnosis of IUGR at birth

During the clinical examination, the thin aspect draws attention, along with low fat tissue, skin descuamation, and meconium stained body. Prader (1983) distinguishes 2 forms of IUGR:

1. *Asymmetrical or dysarmonic form,* in which:
    - weight is smaller compared to length, and the length is smaller compared to the head. The newborn has different degrees of growth deficit, a decrease of adipose tissue, muscular mass and dry skin;
    - the onset is produced at the end of gestation;
    - postnatal recovery is good;
    - this form corresponds to an intrauterine malformation and can be confirmed by a restrictive nutritive intake, by a placental insufficiency or a twin pregnancy. It is seen in 2/3 fetuses with IUGR.
2. *The symmetrical form, harmonic*, in which:
    - weight, length and head circumference are proportional and the newborn has an aspect of "perfect miniature";
    - the onset is during the early gestation period;
    - postnatal recovery is difficult;
    - this form corresponds to some primary fetal anomalies which interest the brain development. It is due to genetic causes, embripathies, fetopathies, dysmorphic syndromes. It is seen in 1/3 cases with IUGR.

Immediate postnatal conduct

Based on the newborn's clinical state, the attitude in the delivery room is different:

- reanimation initiation in the case of neonatal asphyxia;
- respiratory tract suction of meconium was found in the amniotic fluid before birth;
- umbilical cord clamping during the first 15 seconds after birth, for avoiding postnatal placental transfusion; it is dangerous due to high erythropoiesis in neonatal hypoxia;
- thermal comfort assurance.

Specific neonatal complications of SGA newborn

The main issues of IUGR newborn are the causes that determine this disorder, the restriction degree and clinical form; the most common complications are:

- hypoglycemia;
- perinatal asphyxia;
- meconium aspiration syndrome;
- patent ductus arteriosus;
- acute renal injury;
- thermoregulation disorders;
- polycythemia with hyperviscosity;
- postasphyxic encephalopathy;
- hypocalcemia;
- intrauterine infection sequelae;
- symptoms related to chromosomal aberrations.

Asphyxia at birth is seen at 2/3 of dysmature newborns, with a low APGAR score and associated with meconium aspiration.

During the first 48 hours, cerebral edema can be seen, along with seizures. In this cases, anticonvulsants, mannitol sol 10% and diuretics should be given.

Pulmonary hemorrhage appears during the first 2-4 days, and is fatal in most cases. Left heart failure is pathogenic in this case and meconium aspiration syndrome.

Hypothermia is due to a decrease of subcutaneous tissue and increase of body surface. Due to the high amount of brown fat (which appears at 20-30 weeks of gestation) and a high tone on the flexor muscles, the dysmature baby has a higher resistance toward hypothermia than the preterm newborn.

Hyperhydration is caused by an excess of extracellular water, proportionally to the malnutrition degree. Simultaneously, a decrease in the cellular volume occurs, due to intracellular water and solid substances. These are in high contrast to the clinical aspect of dehydration.

The mixed acidosis is not accented but it is compensated during the first 24 hours. Its persistence over 24 hours is a bad prognosis sign.

Neonatal hypoglycemia is favored by a tardiness in oral nutrition during the first 24 hours of life. The substrate of this metabolic complication is a reduction of the glycogen reserves from the liver and myocardium. Glycemia at birth is around 30 mg/dl. The clinical manifestations are variable, leating to hypoglycemic seizures. Therapy consists of glucose administration via iv perfusion, in doses of 6mg/kg, until the glycemia is normal.

Early nutrition, if started during the first 6 hours of life, initiates gluconeogenesis.

During perinatal asphyxia, hyperviscosity can occur, due to: high level of erythropoietin secondary to hypoxia, with erythropoiesis stimulation and increase of eryhtrocyte number (polycythemia); also, intrauterine transfusion can appear because of late umbilical clamping after birth.

All these lead to polycythemia, hemoconcentration and increase of hematocrit up to 65%.

Clinical expression of polycythemia is unspecific, as it can lead to heart failure, respiratory, digestive and neurologic disorders.

Treatment consists of exchange transfusion and replacement of 10% of the blood volume with albumin, saline solutions, which decrease the risk of hyperbilirubinemia by reducing the hemoglobin mass.

Respiratory distress syndrome is a rare complication of the IUGR newborn and is more frequently seen in the preterm below 32 weeks of gestation.

Evolution

In case of no pathologic incidents, the evolution is good, with a growth recovery time of 3 months. The required energetic substrate for growth will be assured by a higher milk quantity, with a dose of 190 ml/kg or by hypercaloric feeds, of 170 kcal/kg during the first 6 weeks of life. Growth recovery is related to higher protein consumption. Gastric capacity is high in these newborns.

Sometimes, the evolution is unsatisfactory due to erythrocyte immaturity and by a reduction of the intestinal mucosal absorption surface.

The neurodevelopment, for these newborns with IUGR started before 26 weeks of gestation, is associated with significantly reduced intelligence tests and learning disabilities.

The following neurologic issues that appear can have many forms, which depend on the intensity and the duration of the phenomena:

- important neurologic anomalies, up to cerebral palsy;
- minor neurologic anomalies, represented by minor cerebral dysfunction, for about 25% of cases, manifested as: hyperactivity, attention disorders, hyperreflexia, learning difficulties, school adaption deficits. An important role is held by their manifestation in social environment.

Large for gestational age newborns (LGA)

Represents a category of newborns with a weight above average by two standard deviations above the 90^{th} percentile.

The etiology is various, and the most common factors are:

- constitutionally large newborns (large parents)
- newborns from diabetic mothers
- transposition of the great vessels
- fetal erythroblastosis
- Beckwith-Wiedemann syndrome
- parabiotic twin syndrome.

These newborns usually associate with birth trauma, including brachial plexus injury, perinatal depression and polycythemia. Early starting of feeds is necessary because the can have hyperinsulinism and therefore are predisposed to hypoglycemia (newborns from diabetic mothers of Beckwith syndrome or erythroblastosis).

Dysmaturity is defined by exceeding of the normal gestation period over 42 weeks. The cause remains unknown in most cases. Sometimes, it is associated with anencephaly, trisomy 13, 18, Seckel syndrome.

Dysmature syndrome

In the literature it is described in newborns with normal length and head circumference. Sometimes it is associated with small birth weight, but compared to SGA children they have a good evolution, due to the fact that they have a normal development until the pregnancy reaches 42 weeks.

Dysmature newborns are classified as follows:

1. Stage I

- dry and cracked skin, in bulks or wrinkled;
- painless aspect
- decrease of subcutaneous tissue
- skin too large for the newborn
- eyes wide open, alert newborn

2. Stage II

- all characteristics from stage 1
- meconium stained
- perinatal depression (in some cases)

3. Stage III

- stage I+II
- meconium stained umbilical cord and nails
- higher risk of fetal, intrapartum or neonatal demise.

There is a certain correlation between low placental weight and higher mortality in dysmature infants. One study has shown that an average placental weight of 452g was seen in deceased newborns, for surviving ones a weight of 580g and when the placental weight was above 700g, no demises were seen.

From the therapeutic attitude perspective, the following aspects are pursued:

- prepartum: careful estimation of the real gestational age, close fetal monitoring;
- intrapartum: fetal monitoring use and preparation for the possible neonatal depression and meconium aspiration;
- postpartum management.

The assessment of the possible dysmaturity complications; the most frequent ones are:

- congenital anomalies
- perinatal depression

- meconium aspiration
- persistent pulmonary hypertension
- hypoglycemia
- hypocalcemia
- polycythemia.

Early initiation of feeds can contribute to both complication prevention but also to early recovery and achieving the optimal nutritional status.

CHAPTER VIII

VITAL SIGNS MONITORING IN NEONATOLOGY AND PEDIATRICS

SPECIFIC PATHOLOGY ANTICIPATION

Vital signs monitoring is an important part of maintaining a normal health status for the newborns and infants. For early detection of the worsening of clinical state, each patient needs vital monitoring.

The pulse oximetry can record the vital parameter of respiratory frequency, heart rate, blood pressure, temperature, and when certain changes appear, the medical staff will be notified.

Vital signs include:

- breath
- pulse
- blood pressure
- temperature

This monitorisation is necessary as an indicator of the health status or disease, especially under the following circumstances:

- when a change in he general status occurs
- before and after invasive diagnosis procedures
- before and after surgical interventions
- before and after medication administration, with impact on the respiratory and cardiovascular system
- patient admitted in the ICU
- during transportation

Normal values of the vital signs

A. Respiratory rate - normal values

Table 6 . Normal values of the respiratory rate

Newborn	45-55 per minute
During the first 3 months	40-45 per minute
At the end of the 1st year	35 per minute
At 2 years	32 per minute
At 3 years	30 per minute
At 5 years	27 per minute
At 11 years	24 per minute
Adult	15-16 per minute

- **Type of breathing**
  - *Newborn:*
    - abdominal breathing
    - nasal breathing in case the respiratory tract is not permeable
    - sometimes irregular rhythm
  - *Infant:*
    - the breathing becomes thoracoabdominal progressively
    - after 6 months of age, he can breath orally
  - *After 2 years of life:*
    - breathing identical to the adult

B. Heart rate normal values

Table 7. Normal values of heart rate

Age	**Minimal rate**	**Maximal rate**
Newborn	80	160
3 months	120	200
1 year	100	180
8 years	65	120
12 years	60	110

Newborn	140 - 150 beats per min
6 months	130 beats per min
1 year	125 beats per min
2 years	120 beats per min
4 years	100 beats per min
8 years	90 beats per min
12 years	85 beats per min

C. Blood pressure normal values

Table 8. Normal values of the blood pressure

AGE	**mm/Hg - MAX--MIN**
Infant	90-60
2-3 years	95-60
4-6 years	100-65
7-9 years	105-65
10-12 years	110-70
13-15 years	120-80

Average blood pressure values of newborns depending on birth weight

Table 9. Average blood pressure values for newborns

	< 1000 g	**1000-1500 g**	**> 2500 g**
At birth (mmHg)	33 ± 15	39 ± 18	49 ± 19
1 week (mmHg)	41 ± 15	47 ± 18	60 ± 19
2 weeks (mmHg)	45 ± 15	50 ± 18	64 ± 19
4 weeks (mmHg)	48 ± 15	53 ± 18	68 ± 19

The optimal measuring method should be simple, noninvasive, painless and should offer continunous measurements; till now, such a method isn't available.

The most used method for the measurement of blood pressure is the oscillometric one. The average blood pressure is measured by the oscillations within the arterial wall and then the systolic and dyastolic pressures are measured based on an algorithm. The method is accurate enough for everyday use, if the cuff is right for age. The oscillometric method has the advantage of being easy to use and measures the heart rate as well.

D. Temperature - normal values

- ✓ **Rectal temperature**
  - normal values: *35,5 – 37,5°C*
  - is measured using the mercury thermometer, which is introduced intrarectally at an agle of 30°, 3 cm at a term newborn and 2 cm at a preterm.
  - duration: 1 minute
  - is not used in NEC

- ✓ **Axillary temperature**
  - is measured at the armpit level, for 3 minutes
  - normal values: *35,6 – 37,3°C*

- ✓ **Abdominal cutaneous temperature** (skin temperature)
  - normal values:
    - term newborn: *35,5 – 36,5°C*
    - preterm newborn: *36,2 – 37,2°C*
  - is measured using a cutaneous sensor placed on the abdomen (avoiding the liver area or the bone of the costal arch). The electrode will be fixed using an adhesive.

✓ **Plantar temperature**

- normal values: *34,5 - 35°C*

➢ **Temperature monitoring:**

✓ *Continuous*

- preterm newborn with weight below 1.500 grams
- term newborn with central temperature below 34°C, until its normalization
- severe birth asphyxia
- septic shock
- meningocerebral hemorrhage

✓ Discontinuous (intermittent)

- every hour until the stabilisation of the central temperature during the first 24 hours
- every 4 hours, from day 2-3
- every 8 hours, from day 4-7
- every 12 hours, after the 8^{th} day

➢ **Types of thermometers:**

✓ *standard Benchmark mercury glass thermometer*

- measurement over 3 minutes
- breaking risk, poisoning by mercury evaporation
- is not used anymore in neonatal units

✓ *electronic thermometer* –the most often used

- thermal sensor can be thermoresistent or thermocoupler
- the signal t^0 is processed and displayed digitally
- measurement time below 45 seconds
- the thermometer has small dimensions, easy to handle

✓ *infrared electronic thermometer*

- infrared sensitive sensor which detects the infrared radiant energy from the tympanic membrane
- the sensor converts the infrared signal in an electrical one which will be processed and digitally displayed as t^0
- measurement time below 2 seconds.

ANTICIPATING SPECIFIC PATHOLOGIES

- **Important clinical signs of the respiratory system**

✓ **Thoracic deformities**

- emphysematous thorax: asthma, bronchial chronic obstructive pulmonary diseases
- paralytic chest (phthisic): malnourished children or children with severe bronchopulmonary disorders
- infundibuliform thorax: Marfan syndrome, Ehles Danlos syndrome
- chest affected by rickets: severe rickets
- kyphotic chest: vertebral column deformation
- unilateral chest bulging: foreign body aspiration with ball-valve mechanism, pleurodesis, pneumothorax
- unilateral chest retraction: pulmonary atelectasis, unilateral pulmonary fibrosis.

✓ **Coughing** - reflex act of protection, started by the stimulation of the irritative receptors within the respiratory tract. Extremely common, the mechanism is always the same, no matter its cause.

Clinically, several aspects are distinguishable, which are extremely useful in the etiological diagnosis:

- ***dry irritating cough:*** dry nocturnal throat, adenoid vegetations, respiratory infection debut.
- ***dry, irritative, progressive cough:*** inflammatory process of the pharynx, larynx, trachea, bronchi.
- ***productive cough, with expectoration (older children):*** respiratory tract infection, bronchitis, pneumonia.
- ***nocturnal cough, barking-like cough****:* acute laryngitis, laryngotracheitis.
- ***periodical, suffocating, dry cough****: foreign body.*
- ***paroxysmal, tormenting cough, with white mucous expectoration****:* whooping cough, adenoviral infections (sometimes).

- ***cough with serious aphonia****:* diphteria.
- ***metallic, loud cough:*** psychiatric causes, tracheitis.
- ***jerky, painful, contained cough:*** dry pleurodesis.
- ***weak, dry, pertussis-like cough:*** interstitial pneumonia, mucoviscidosis.
- ***weak, dry cough with aerated expectoration:*** pulmonary edema, circulatory stasis.
- ***paroxysmal, dry cough with mucous expectoration:*** obstructive bronchitis, asthma
- ***tormenting, dry cough with purulent expectoration****:* bronchiectasis.
- ***bitonal cough:*** foreign body, trachea compression, bronchus compression.
- ***hemoptoic cough****:* the ORL area, tongue trauma, foreign bodies, pulmonary, abscess, cavern, hemangiomas, arteriovenosus disorders.

✓ **Stridor** – obstruction of the upper respiratory tract, characterized by a rough sound made by the passing of the turbulent air flow through a partially obstructed segment.

- Causes
  - acute laryngitis, laryngotracheitis
  - allergic laryngitis (pseudocrup)
  - laryngeal edema (angioedema)
  - epiglotittis
  - foreign body aspiration in the upper respiratory tract
  - laryngeal malformations
  - supraglottic mass
  - adenoid vegetation hypertrophy, abscesses, periglottic tumors.

✓ **Hemoptysis** –the elimination of blood coming from the inferior respiratory tract (laryngo-tracheo-bronchic or alveolar spaces) by coughing.

- Causes
  - infections in the bronchopulmonary respiratory system
  - staphyloccocal, pneumococcal pneumonia (lobar pneumonia)
  - pulmonary destructions, pulmonary abscess, necrotising enterocolitis
  - pulmonary tuberculosis
  - foreign bodies in the respiratory tract
  - trauma of the thoracic organs

- ✓ **Tachypnea** – acceleration of breath
    - Causes
        - respiratory insufficiency sign
        - pneumonia informative sign
        - chronic bronchopulmonary process exacerbation

- ✓ **Bradypnea** - slow breathing which can influence the inspiratory and expiratory times

- ✓ **Orthopnea:** dyspnea that doesn't allow the supine position and forces the child to sit on a chair of stand up.

- ✓ **Apnea -** the breathing stops for a longer or shorter period of time. If it is <10 seconds and with no bradycardia or cyanosis, it is considered physiological in a newborn.

- ✓ **Prematurity apnea** - the interruption of breathing for more than 20 seconds or any respiratory break of a shorter period of time but associated with cyanosis, bradycardia or both. It is usually caused by a transitory disorder of the respiratory control (prematurity apnea) or, rarely, by a severe state like: sepsis, hypoglycemia, intracranial hemorrhage, seizures or drug ingestion by the mother.

- ✓ **Groan -** expiratory sound heard due to the partial occlusion of the glottis, which maintains an intrathoracic pressure which opposes to the alveolar collapse. It represents a sign of struggle in case of a diminished compliance when acute newborn dyspnea happens.

- ✓ **Thoracic cage retractions**- the retraction of the thoracic cage, in its lower part.
    - Causes
        - severe respiratory insufficiency signs
        - severe pneumonia signs
        - asthma attack
        - chronic pulmonary diseases.

- ✓ **Dyspnea** – sensation of difficult breathing reported by the patient. Its etiology is polymorphic.
    - Clinical types:
        - inspiratory
        - expiratory
        - mixed
    - Causes
        - phyisiological - effort dispnea of healthy children
        - restrictive dyspnea from pulmonary fibrosis, throracic cage deformities
        - obstructive dyspnea – asthma, laryngitis, foreign body aspiration
        - epiglottitis
        - pulmonary parenchyma impairment - pneumonia
        - ventilatory disorders in case of pneumothorax, pleural effusion
        - upper respiratory tract congenital malformations
        - pulmonary hypoplasia
        - congenital cysts
        - progressive congenital pulmonary emphysema
        - hernia, relaxation, diaphragmatic paresis

- ✓ ***Nasal flaring*** - the nostrils widen with every breath. Due to the fact that nasal and pharyngeal resistance represent 50% of the newborn's respiratory tract resistance, the effort of breathing is probably decreased by the widening of the nostrils.

- ✓ **Wheezing** - high-pitched, whistling breathing conditioned by the bronchial obstruction (partial, localized, diffuse).
    - Causes
        - recurrent wheezing, bronchial hyperresponsiveness, atopia, cutaneous allergic reactions
        - effort induced asthma
        - cough, suffocation during physical practice
        - asthma
        - broncho obstructive syndrome with anti-inflammatory treatment
        - asthma bronchitis

- bronchial hyperresponsiveness, irritating cough when exposed to inhalatory allergens (tabacism, smoke, exhaust gase, fog)
- viral infections (respiratory syncytial virus)
- atypical infections - chlamydiasis, mycoplasma infection
- bacterial infections

✓ **Cyanosis –** bluish colour of the skin and mucous membrane. Physiopathologically, cyanosis is an oxygen desaturation of the blood flowing through the cutaneous capillaries, appearing when the reduced hemoglobin concentration is above 5 grams/dl in the peripheral circulation.

- Causes
  - respiratory insufficiency
  - oxygen transfer disorder through alveocapillary membrane
  - low pulmonary perfusion or the pulmonary territories low ventilated/not at all
  - amniotic fluid aspiration syndrome
  - hyaline membrane disease
  - pneumonias
  - Mikity-Wilson syndrome
  - bronchopulmonary dysplasia
  - pulmonary arteriovenous shunt
  - mechanical causes which interfere with the pulmonary ventilation: lobar emphysema, diaphragmatic hernia, pneumothorax, pneumomediastinum, thorax malformations, thracheoesophageal fistula, bronchogenic cyst, choanal atresia, mediastinum tumors.

➢ **Clinical signs in heart rate changes**

✓ **Sinus bradycardia -** heart rate of 100 b/min and less

- tachy brady syndrome (sick sinus syndrome)
- atrioventricular block:
  - Ist degree
  - IInd degree - Mobitz I
  - IInd degree - Mobitz II
  - IIIrd degree - congenital
  - IIIrd degree– acquired

✓ **Sinus tachycardia** - heart rate of 180 beats per minute and more

- *supraventricular tachycardia:*
- atrial flutter,
- atrial fibrillation
- ectopic atrial tachycardia
- multifocal atrial tachycardia
- AV nodal reentrant tachycardia
- WPW syndrome
- accessory pathway entrant tachycardia
- *ventricular tachycardia (VT)*
- monomorphic ventricular tachycardia
- polymorphic ventricular tachycardia
- focal ventricular tachycardia
- torsade de pointes

✓ **Cardiac dyspnea**

- heart insufficiency
- can appear in case of paroxistic tachycardia
- in different pathological situations of cardiac decompensation

➢ **Blood pressure alterations**

✓ For a newborn, hypotension is determined by a combination of abnormal peripheral vascular adjustment, myocardic dysfunction and hypovolemia, usually having a multifactorial etiology.

- Causes
  - severe respiratory distress syndrome
  - hypovolemia**:** placental abruption, placental hemorrhages, fetal-maternal hemorrhage, fetomaternal transfusion syndrome, birth trauma
  - cardiogenic shock: asphyxia, arrhythmia, congenital heart defects (ductal-dependent heart defect and total anomalous pulmonary venous return), cardiomyopathy, myocarditis.
  - sepsis and septic shock
  - drugs: prostaglandin E1

✓ High blood pressure is represented by the following signs:

- headache
- vertigo
- epistaxis
- dyspnea
- apnea
- drowsiness

➢ **Temperature important clinical signs**

✓ **Hypothermia -** body temperature below 36°C (rectal temperature)

- Causes
  - room temperature below 22°C
  - cold scale or diaper
  - unheated reanimation source
  - cold oxygen into the newborn's face
  - handling of a naked newborn in the incubator, in an unheated ward
  - open/closed defect incubator
  - alteration of the adjusting temperature mechanisms (nervous system malformations, meningocerebral hemorrhage, severe infections, etc).

✓ **Clinical signs of hypothermia in a newborn:**

➢ **Skin and mucous membranes**

- usually reddish and cold to touch
- can associate with central cyanosis or pallor, edemas or scleroderma on the face or extremities

➢ **Breathing**

- bradypneic, irregular, superficial, associated with expiratory grunt
- relapsing apnea, especially in the small gestational age preterm newborn

➢ **Heart**

- bradycardia

- **Abdomen**
  - abdominal distension
  - vomiting

- **Kidneys**
  - oliguria

- **Behavioral changes**
  - alimentation refusal
  - weak cry
  - lethargic, with weak response to pain
  - tremors, rarely seen in newborns
  - nervous system depression

- **Metabolic disorders**
  - hypoglycemia
  - metabolic acidosis
  - hyperkalemia
  - modified coagulation tests, which determine a general hemorrhagic disease, or frequently pulmonary hemorrhage, which is the main cause of death

✓ **Hyperthermia -** body temperature above 37,8°C (rectal temperature)

- Causes
  - excessive clothing
  - when room temperature exceeds 36°C
  - incubator dysfunction, or of the radiant heater
  - local or systemic infection
  - dehydration
  - alteration of the central thermoregulation mechanisms, such as severe neonatal asphyxia or malformations (hydranencephaly, holoprosencephaly, encephalocele)
  - hypermetabolism.

✓ **Body's response to overheat**

- vasodilatation
- tachycardia
- hyperpnea
- sweating

✓ **Clinical signs of overheat hyperthermia**

- erythematous, warm skin (especially in the thoracic area and extremities)
- fever, agitation, grunt, irritability and apnea (Perlstein, Belgaumkar)
- diarrhea, disseminated intravascular coagulation, liver and renal insufficiency (Bacon)
- seizures → lethargy → coma
- thermic shock death, with severe metabolic modifications

✓ **Clinical signs in septic fever**

- pallor
- pallor-cyanotic, cold extremities
- central temperature higher than cutaneous temperature

CHAPTER IX

PAIN MANAGEMENT OF A NEWBORN

Introduction

The progress made in the latest years has established that the newborn can experience acute or chronic pain, and that the correct management has benefits on both short term and long term.

Term newborn and preterm newborn can experience pain and have the right to efficient analgesic therapy, in safety. That's why, pain prevention is a goal for both doctors and parents.

Newborn cannot verbalize pain and therefore others must recognize it, evaluate and manage it; the newborn has a higher sensitivity to stimuli and is predisposed to pain and its consequences.

As a result of different studies, there are significant changes in biochemical and physiological markers as a result of pain stimuli, even for preterm newborns, higher than the adult response.

About 10-15% of the total number of term newborns and a vast majority of the preterm ones are hospitalized in the NICU, so they represent the highest risk category of developing neurologic anomalies. Among consequences, a modified sensitivity is seen, with prologed pain until adolescence, neuroanatomic permanent anomalies and comportamental, emotional and learning anomalies.

The conception of pain perception

“The concept of pain and suffering comes from the simple sensorial limit determination. It contains emotional, cognitive, comportamental components, as well as developmental, environmental and sociocultural components.” (AAP and American Pain Society policy statement, September, 2001)

Ethics

“Determination and treatment of the algic syndrome - main components in the pediatric practice, refusal of assuring the adequate analgesis represents an unethical and unprofessional comportament."

Definition

Pain was defined by the International Association for the Definition of Pain as an "unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage."

Also, the incapacity of verbally or non-verbally communicating pain does not deny its existence.

Stress: a disturbance of the dynamic balance between a newborn and his environment, resulting a physiologic response.

Stress or response to pain: physiologic response of an individual to pain or stress, characterized mainly by changes in four areas - endocrine and metabolic, autonomous, immunologic and or comportamental.

Types of pain in newborns

A. Birth trauma

Neonatal pain associated to birth trauma is a result of vacuum extraction.

→ Vacuum - face or head bruising as a result of passing through the pelvic canal

→ Forceps extraction - temporary marks of face/head bruising

→ Cephalohematoma - frequent in forceps extraction births or vacuum extraction

→ Clavicle fracture - the most common fractures seen at birth

B. Acute procedural pain

In the NICU, newborns can be exposed to painful procedures, as arterial or venous punction, lumbar punction, intramuscular injections, peripheric or central cathererisation, endotracheal intubation. ELBW or VLBW preterm newborns are handled 150 times per day and have less than 10 minutes of uninterrupted rest.

A newborn can feel pain in the hyperalgesia areas and inflammation around tissue lesions, abrasions caused by the sensors for oxygen saturation, monitoring electrodes and local disinfectant agents.

C. Acute pain after surgery

After surgery pain still remains an important issue in the NICU.

Routine pain management should be done using a specific scale, for prolonged post-surgery pain.

D. **Chronic pain**

Chronic pain is still insufficiently researched in Neonatology.

- chronic pain is an extension of acute, uncontrolled pain.
- means of pain evaluation - validated measurements of chronic pain

Response to pain

Immediate response to pain is different from one newborn to the other, preterms being more aware of the pain stimulation than the term baby. A healthy newborn can react energetically to a painful stimulation, while a sick newborn can have no reaction whatsoever. Preterms respond to pain by a physiologic and comportamental obvious reaction and by hormonal, metabolic manifestations, which can lead to destabilising effects on the short and long term.

Comportamental modifications to pain

- Facial expression: grimace, nasal flare, chin trembling, nasolabial fold deepening, atypical tongue movement, frown.
- Body movement: body arching, back of the head hypotonia, finger gripping, hypotonia/trembling of the extremities, squirming; active movement as a way to withdraw from the painful stimulus.

Physiological modifications to pain

The painful stimulus activates the compensatory mechanisms from the autonomous nervous system, which as a response, has heart rate changes, respiratory rate changes, blood pressure, oxygen saturation, cellular metabolism acceleration changes, high oxygen need, reduction of the tidal volume, pupil dilation.

Neuroendocrine modifications to pain:

- Pallor, skin erythema, midriasis, repeated swallowing.
- Reduction of cerebrovascular autoregulation, with rise in the intracranial pressure, with a high risk of intraventricular hemorrhage.
- High liberation of: cortisol, norepinephrine, glucagon, GH, renin, angiotensin, aldosterone, ADH.

Pain evaluation in a newborn - the fifth vital sign

Pain evaluation in a newborn is complicated by its incapacity to verbalize pain. There are numerous scales and scores of pain evaluation, based on different context indicators (gestational age, sleep/waking status), comportamental response, physiologic response or combinations of oxygen saturation, BP and facial expression.

Due to communication difficulties, it is necessary to differentiate between pain and agitation, because each of them must pe treated and assessed differently.

Facial expressions are the most sensitive and specific indicators of pain and are included in most of the scales and scores of pain evaluation of the neonatal pain. The following have been subject to comportamental evaluation and have proven valid, reliable and feasible to neonatal pain assessment.

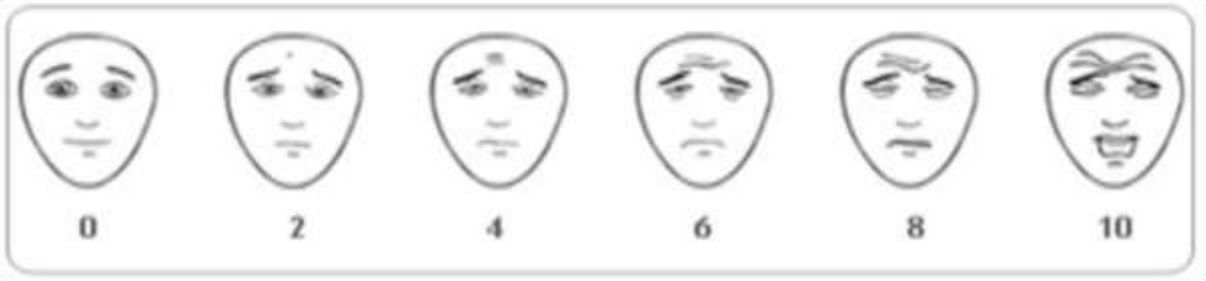
1. Neonatal Index Pain Scale (NIPS) is used for assessing pain before and after interventions at normal weight newborns and preterm babies. It uses comportamental and physiologic variables: facial expression, superior and inferior extremity state; during crying or the intensity of crying during awakening; breathing pattern.

The baby is appreciated with 1-10 points according to clinical status. A score of 0-3 means an adequate analgesis management.

2. Facial pain score - is assessed by the changing of the face expression and it can be used by parents, clinicians and researchers.

The baby is appreciated with 1-10 points. 0- the pain is missing; 2-minimal pain.

Fig. 24. Facial pain aspect.



3. Premature infant pain profile (PIPP). It is a method that includes the evaluation of face expression and physiologic responses in association to gestational age and newborn's clinical status and is the sole validated method of acute pain assessment for preterm babies.

The intensity of pain is determined by measurement of 7 indicators: comportamental indicator (face expression) and physiologic ones (heart rate and oxygen saturation) and their correlation to gestational age and sleep/wakening index.

A score less or equal to 6 points indicates the lack of pain or minimal pain. A score of more than 12 points indicates moderate to severe pain.

4. The score of severe pain appreciation is based on observation of the baby's behaviour (Douleaur Aigue du Nouveau Né - DAN). The score is used for assessing the newborn's behaviour and includes grimace, limb movement, crying (non-intubated infants), crying equivalence (intubated infants); it is the sole method of pain assessment for intubates babies.

The score interpretation: minimum - 0 (no pain), maximum - 10 (the most powerful pain).

Table 10. *Scales and scores used in pain assessment*

Nr. crt.	Scala	Indicatori	Vârsta gestațională	Cauza durerii
1	PIPP (Premature Infant Pain Profile) (27 de săptămâni – termen)	FC, SpO_2, Expresie facială, status somn/veghe, VG	28-40 de săptămâni	Procedurală, Postoperator (minor)
2	NIPS (Neonatal Infant Pain Scale) (28-38 de săptămâni)	Expresie facială, caracter plâns, caracter respirații, mișcări membru, status somn/veghe	28-38 de săptămâni	Procedurală
3	NFCS (Neonatal Facial Coding System)	Expresie facială	Nou-născut prematur și la termen - sugari de 4 luni	Procedurală
4	N-PASS (Neonatal pain, Agitation, and Sedation Scale)	Caracter plâns, iritabilitate, status, expresie facială, tonus extremități, semne vitale	Ziua 0-100 și se ajustează în funcție de VG	Postoperator, Procedurală, Nou-născuți ventilați
5	DAN (Douleur Aigue Nouveau-nè)	Expresie facială, mișcările membrelor, plânsul (nou-născuți neintubați), echivalente ale plânsului (nou-născuți intubați)	Nou-născut prematur sau la termen - sugar de 3 luni	Procedural, Nou-născuți ventilați
6	CRIES (Cry, Requires O_2, Increased vital signs, Expression, Sleeplessness)	Caracter plâns, necesar O_2 pentru SpO_2>95%, AV, semne vitale, expresie facială, stare de veghe prelungită	32-36 de săptămâni	Postoperator
7	COMFORT Scale	Mișcări, agitație, expresie facială, starea de alertă, FR, FC, TA, AV	0-3 ani	Postoperator, stare gravă, sedat, ventilați
8	PAT Tool (Pain assessment Tool)	FR, FC, SpO_2, TA, postura, tonus, expresie facială, caracter plâns	Nou-născuți prematuri și la termen	Acută
9	EDIN (Echelle de la Douleur Inconfort Nouveau-Ne')	Expresie facială, mișcări membre	25-36 de săptămâni (prematuri)	Durere cronică

For acute pain (procedural, after surgery):

- Premature Infant Pain Profile (PIPP)
- For infants - Neonatal Pain Scale (NIPS)
- Douleur Aigue du Nouveau-Né (DAN)
- Crying, Requires increased oxygen administration, Increased vital signs, Expression, Sleeplessness (CRIES)
- Neonatal pain, agitation and sedation scale (N-pass)
- Pain Assessment tool (PAT)

For chronic pain:

- Neonatal pain, agitation and sedation scale (N-pass)
- Echelle Douleur Inconfort Nouveau-Né (EDIN)

The medical staff should steer after the institution's guidelines. Each institution should select an instrument, educate the staff for establishing the an optimal and documented pain management.

Pain management

Objectives:

- stress minimisation.
- reducing the number of painful procedures or stimuli that are unnecessary.
- prevention of CNS injury.
- minimisation of pain mediators eliberation at tissular level.
- stress response recovery.
- prevention/reducing of acute pain by supplying analgetics as a prevention method for every painful procedure, which includes a combination of non-pharmacological and pharmacological methods.
- monitoring patient response to analgetics using scales and scores of assessment validated and provided if needed.

Non-pharmacological actions

The following approach can efficiently reduce pain and discomfort by routine care and minor procedures.

In some situations, these combinations can remove the pharmacologic use or can help dosage reduction and frequency and, as a consequence, diminishing of the secondary effects.

a. Breastfeeding/mother's own milk administration/non-nutritive sucking.

b. Music therapy.

c. Wrapping, maintaining a satisfactory body position, Kangaroo-care.

d. Invasive procedures are done only with trained staff.

e. Increasing the break period between painful procedures.

Each Neonatology Unit should have and follow a minimal stimulation protocole, that shoud take into account:

- decrease of the number of light and sound stimulus.
- permanent monitoring, instead of heart auscultation
- a correct positioning of the newborn must be maintained, that allows him to breath well; if a desaturation occurs, he should be moved.
- the number of invasive handling should be brought to a minimum; grouping the investigation sampling.
- an umbilical artery catheter is preferred for newborns that need often arterial gas assessment.

Pharmacological actions

Pharmacocynetic and pharmacodinamics are different for newborns, especially the preterm ones, compared to other groups of age. It should be taken into considerration the fact that the sedative-hypnotic medication is not analgesic as well.

Pharmacological actions vary based on pain severity, from local analgesis to systemic analgesis.

CHAPTER X

CLINICAL AND BIOLOGICAL PARTICULARITIES OF INFANTS AND SMALL CHILDREN

The infant period lasts from the age of 1 month until 1 year of life. The small child period is from the first year of life until 3 years.

Clinical and biological traits of an infant:

1. Skin

Represents a complex protective shell, both structurally and functionally, being in a continuous exposure to environmental aggressions.

Color:

- white-pink, soft in breastfed newborns
- pale in newborns fed with formula

During the infant period, the thickening of the epidermal corneum layer and the pigmentation of the basal cells; the chromatophore cells start to develop, leading to the occurence of infection and physicochemical factors increased resistance.

The dermis is maturing, the dermal papillae are multiplying and the capillaries stretch and take the form of a hairpin, resembling the ones from the adult life.

The sebaceous glands are well developed even from birth and determine a crust on the scalp.

The sweat glands are developing at 2-3 months and by 2 years of life they reach the whole functional activity.

The hair changes its color in time, and once puberty starts, facial, axillary, anterior thoracic level, pubic and limb hair appears.

The infant's skin is elastic, the skin fold comes to its initial form, and in dehydration states, the skin fold becomes slow or persistent.

The surface area of the human skin is big raported to weight and reduces by age; it's calculated by Lassabliere's formula:

Surface area of human skin $=L^2 \times 0,92$

It represents the ratio between skin surface and weight: **surface area of human skin (cm^2)/W(kg)**.

Based on age, the following values occur:

- newborn=660 cm²/kgc
- 1 year=420 cm²/kgc
- adult=220 cm²/kgc

2. *The subcutaneous tissue*

The adipose tissue is well represented in a newborn; it initially develops on the face, limbs, thorax and after 6 weeks, on the abdomen; in case of malnutrition, it disappears.

Clinical: nutrition state is appreciated by measuring the skin fold of the thorax (normal value=1,5-2 cm), of the abdomen (normal values=1,5-2 cm) and the presence of adductors creases on the internal surface of the thigh and by the presence of turgor.

Turgor is assessed by pressure resistance which the examiner induces between the index and the thumb on the external surface of the thigh.

In malnutrition, the subcutaneous tissue decreaes, the turgor is diminished and doughy in infants that receive a lot of farinaceous dishes.

3. Sebaceous and sudoriferous glands

They develop progressively, and by 3 months of age have a normal secretion.

4. Lymphatic node system

It is present from birth, and during the first months of life the lymph vessels are larger, nodes are less developed, which leads to an easier way for bacteria and toxins to cross into the blood flow and cause septicemias.

5. Muscular system

Represents 25% of the total body weight, unlike the adult's musculature which represents 40%.

Its development is unequal, the lower limbs have a well represented musculature.

Muscular tone is increased, with physiologic hypertonia in newborns, that after 1 month decreases, becoming normotonia.

Neuromuscular excitability, researched with galvanic power, shows that at a normal infant it can be acquired a muscular contraction of an at least 5 mA intensity, with negative pole toward the opening; the apparition of muscular contraction at a lower intensity, indicates a neuromuscular hyperexcitability, tetany or hypocalcemia.

6. Skeletal system

Represents at birth around 15-20% of the newborn's weight.

In infants, there is a gap between the increase of the skeletal organic substrate and the body's possibility of calcification using an usual nutritional intake, so that physiologic osteoporosis occurs; this phenomenon can appear again during puberty; that's why the direct resistance to trauma is very low.

The skeletal tissue has a high vascularization during the childhood period; this explains the high recovery capability in children and the intensity of the inflammatory reactions at that age.

The ossification of the skull begins during intrauterine life; at birth, the fontanelles are present. The anterior fontanelle has rhomboidal shape, diameters of 2,5/3,5 cm and closes at 14-16 months; the posterior fontanelle has a triangular shape, has diameters of 1,5/1 cm and closes during the first 4-8 weeks of life.

The vertebral column is rectililear at birth and its curvature appears by mechanical forces, that develop parallel to motor functions:

- 3 months: cervical lordosis (the infant holds his head)
- 6 months: dorsal kyphosis (the infant sits)
- 9-12 months: lumbar lordosis (the infant begins to walk)

The thorax has a cylindrical shape, the ribs are horizontal, forming a straight angle with the column after 6 months of age, and the ribs are becoming oblique. The transverse diameter becomes equal and then exceeds the antero-posterior one, the thorax takes a conical shape; these modifications change the type of breathing from abdominal-diaphragmatic in infants to thoracic in children.

The pelvis has a funnel shape, maintaining its form for boys, but for girls it changes, becoming cylindrical during puberty.

The lower limbs grow faster and have a brackety shape because the internal condyles of the tibia are less developed than the external ones.

7. Respiratory system

The upper respiratory tract is narrower in infants and their inflammation leads to mucous tumefaction and breathing difficulties.

The maxillary sinus and the ethmoidal cells are well represented, the frontal sinus has a slow development until the age of 6 years.

The pharynx represents the Waldeyer's tonsillar ring and its hypertrophie happens easily. The tonsills gradually grow until 4-6 years of age (physiological hypertrophy) and then regress by 11-12 years along with the regression of the whole lymphatic system.

The larynx is higher than the adult one. Its higher position allows the infant to suck and breathe at the same time. It develops slowly, from 5 years of age; at puberty, the rythm of growth accelerates along with voice change during puberty. Glottic spasm is often seen in children.

Trachea lacks elastic tissue, the pressure resistance is low, weakly attached and easy to move.

The bronchi are richer in muscular fibres in children compared to adults and larger. The right bronchus has a smaller angle of bifurcation than the left one. The mucous membrane is poor in mucous glands.

The respiration is abdominal and diaphragmatic in infants. The diaphragm is raised, it's dome reaches the 4^{th} rib.

Lung weight: in newborns it is about 60 g, by 1 year 130 g and at puberty around 1000 g.

Lung aeration and increase of the pulmonary blood flow determines the alveoli development. The alveoli rise in volume and size which ultimately lead to lung blood flow increase. The interalveolar septum is thicker in infants and it becomes thinner with age.

The elastic fibers are less developed at infant age so this favors athelectasis.

The lungs have a rich vascularization, which predisposes to infection occurence.

Respiratory rate (RR) – normal values based on age:

infant: 40-45 b/min

1 year: 35 b/min

3 years: 30 b/min

5 years: 25 b/min

15 years: 16 b/min

The breathing amplitude is unequal, with irregular rhythm sometimes. During sleep certain respiratory breaks can occur, sometimes even Cheyne-Stokes breathing.

Upon physical examination, during pulmonary auscultation, a vesicular murmur is perceivable, transmitted to both pulmonary areas and tightened murmur due to reduced width of the thoracic wall.

Hiccups represent a reflex act of diaphragm contraction and occur frequently in healthy infants during the first month of life, without any pathological significance.

8. Cardiovascular system

The heart is placed horizontally in infants, due to the short thorax and high diaphragmatic dome; after the age of 2, the heart is placed vertically.

Heart apex: V^{th} intercostal left space; apex shock: IV^{th} intercostal left space outside the medial clavicle line by 1-2 cm.

The heart weighs in infants around 70 g, and during puberty around 400 g.

The atrias are big, the heart has a round shape, with increased transversal diameter.

At birth, the left ventricle wall is thicker than the right one, so that at puberty the left ventricle is 3 times bigger than the right one. This kind of growth is a result of elastic and connective tissue development and continues until adult life.

In children, the thin thoracic wall allows during auscultation a stronger perception of heart sounds. Frequently, mesodyastolic murmurs can be heard, inconsistent and with rhythmic intensity, with no pathologic semnification.

Newborn pulse= 160 b/min

infant= 120 b/min

2 years= 110 b/min

5 years= 100 b/min

8 years= 90 b/min

14 years= 80 b/min

Blood pressure is low although the cardiac output and the circulation speed are increased (big vessels, high wall elasticity).

BP during the first year of life = 80/50 mmHg

Systolic BP= $2X + 80 (\pm 10)$, X represents age in years

9. Digestive system

The oral cavity is small, with large tongue that exceeds the dental line and is in contact with the cheek mucous. It is adapted to sucking, having a role of aspiration pump, and the tongue represents the piston.

The saliva quantity is around 50-100 ml/day, it contains amylase, lipase and secretory IgA. IgA synthesis provides the infant with antiinfectious defense properties.

The salivary amylase is found in a comparable quantity to the adult at the age of 6-12 months. In case of physiologic deficit of pancreatic amylase in a small infant, the salivary amylase ensures starch hydrolysis from the decoction or rice mucilage.

The lingual lipase intervenes in the digestion of milk lipids, in the stimulation of milk lipases and pancreatic lipases during the infant period.

The stomach is transversely placed with the great curvature placed caudally, with the pilor at 2 cm to the right of the medial line. After 2-3 years it will be placed vertically. The stomach glands and crypts grow in size and number under the influence of gastrin. After the start of nutrition, the parietal gastric cells response to secretory stimulus increase significantly.

Gastric capacity – 1 month – 100 cm^3;
– 3 months – 150 cm^3;
– 1 year – 300 cm^3

The free hydrochloric acid secreted by the parietal cells and pepsinogen are low in infants. After 3 months of age, as a result of an increased gastrin receptor activity the gastric pH drops at 2,5-3,5 in breastfed infants, while the infant fed by formula has a higher pH.

The gastric secretion contains:

- proteolytic pherments: pepsin, cathepsin, rennet;
- lypolytic pherments: lipase, lypo kinase.

Gastric evacuation is done after 2 hours in the breastfed infant, after 3 hours in the formula fed infant, and after 4 hours in complementary fed infants. In bigger children, the evacuation of gastric content is done by peristaltic movement followed by the opening of the pilor.

The infant's intestine is about 3,4 m, longer than the adult one related to height, being in fact an adaption to the growing body. This relation decreases progressively with advanced age. The lymphatic vessels form a rich network, the lymphatic tissue from the Peyer's patches and lymph nodes present a hypertrophy by the age of 6 years.

The rectum is long, fixed by the sorrounding organs, that's why the tendency toward prolaps occurs.

After 3-4 months of life, the facultative anaerobic flora diminishes in the infant's colon (Enterobacteriacae, Lactobacillus, Streptococcus, Staphilococcus) in favor of the strict anaerobic one (Bifidobacterium, Eubacterium, Clostridium Bacteriodes); the fecal flora is close to the adult one.

The bowel movement is done during 6-8 hours through the small intestine, and by the large intestine in 6 to 12 hours.

The infant stools are from 1 to 4 per day. In the breastfed infant, stools have a yellow-orange color, are semi consistent, adherent to the diaper, with acid pH. The stools of the

artificially fed infant are of yellow-gray color, consistent, do not adhere to the diaper and have an alcaline pH.

Liver – at birth, the right lobe is twice as big as the left one, and in bigger children, three times bigger.

The gallbladder reaches the liver's edge by 3 months.

The hystological structure of the liver is definitive around 1 year and a half.

The inferior liver margin is found 2 cm below the right inferior costal margin, on the right medial clavicle line.

The superior margin is found in the V^{th} or VI^{th} intercostal space, on the intermamelonar line, in the axilla at the VII^{th} intercostal space, and the IX^{th} intercostal posterior space.

The liver makes iron supplies and can intervene in case of anemia. After 5 months of age, the iron deposits are low, so the infant can develop hypochromic anemia if the nutrition is not iron-sufficient.

Bile secretion is decreased in infants, and the necessary bile salts for lipid emulsion and absorption are low.

The newborn pancreas weighs 3 g, by 1 year 9 g and by 10 years 30 g. Its histological structure is characteristic in infants due to the fact that it has a rich interlobullar, interacinar fibrous tissue and abundant vascularization.

10. Urinary system

The kidneys are lobulated; this lobulation disappears in the second year of life.

The kidney weight is of 35 g.

The ureters have a L=10 cm by 1 year of age. The renal pelvis and ureters have muscular end elastic fibers that are underdeveloped during the infant period; the walls are hypotone, which favors the stasis and infection.

The urinary bladder has an anterior wall in relation to the abdominal wall at birth; the small infant has the apex of the urinary bladder at half the distance between the navel and pubis. After 1 year, the urinary bladder descends in the pelvis and its anterior wall is found behind the pelvis.

The partially distanced urinary bladder reaches half into the pelvis, half into the abdomen, and when it is full, it is entirely in the abdomen.

The female urethra has a L=1,5 cm and diameter of 4 mm, and the male urethra has a L=5 cm and a diameter of 4 mm. The urinary density is of 1010-1012 in infants.

The urinary pH in the breastfed infant is of 6,8-7,8 and in the formula fed it is of 5.

The infant diuresis 75-100 ml/kgc.

Micturition - 10-15-30/day.

When urinary bladder control appears, the micturitions become rare - 6-8/day. In infants, micturition is done by automatic reflex.

By 1-2 years of age the child has a need to evacuate his bladder and voluntarily contracts his sphincter.

By the age of 4, the voluntary urinary control is complete. From here starts the necessity of initiation of certain educational reflex habits and potty training during the infant period, as well as getting used to ask for the potty after the age of 1.

The hematopoietic system

In infants and small children, hematopoiesis is produced in the bone marrow for the erythrocitary, granulocytary line and platelets, and for the limphocytary in the lymph nodes and bone marrow.

From 6 months, in the long bones, the bone marrow starts to be replaced with embrionar cells, capable of multiplication and to fulfill the hematopoietic potential. This process of transformation is finished by 12 years of age, so the hematopoiesis in the bigger child takes place within the short and wide bones: ribs, vertebrae, skull, clavicle as well as the long bones epiphysis.

The blood volume reduces after birth, so that by 2 months it reaches the adult values (75-80 ml/kg/day).

The lymph organs are the thymus, lymph nodes, Peyer's patches, tonsils, subepithelial lymph nodes and spleen, with lymphopoietic and immunity roles.

The bone marrow and lymph organs in children have a capacity of rapid transformation and reaction to different factors, so that in medullary metaplasia, when the hematoformator capacity is low, the hematopoiesis is done in the parenchimal organs: liver, spleen, lymph nodes.

CHAPTER XI

CLINICAL AND BIOLOGICAL PARTICULARITIES OF A PRESCHOOLER AND SCHOOL-AGE CHILD

I. **Preschool child**- the period between 3 and 7 years.

Growth and development during the second childhood period (preschool age)

Physically speaking, the development is obvious during the preschool age period. Between the age of 3 and 6, growth occurs from a height of +/- 92 cm to +/-116 cm and weight from +/-14 kg to +/-22 kg. At the same time, the muscle structure develops, the adipose tissue diminishes, the skin becomes more elastic and thicker, the ossification process is intense in the long bones epiphysis, thoracic bones and clavicles, the provisory dentition starts to deteriorate and the permanent dentition to develop. The organism as a whole becomes more elastic, the movement supple and firm.

Even from this period, a series of differences between girls and boys start to show. In boys, it can be seen a certain agitation that is less frequent in girls, and a stronger cooperation in girls, followed by a richer verbal activity; a tendency of isolation in activities of building is seen in boys.

During this phase, the growth is slower. Growing in length can be calculated using:

$L = 5A + 80$

where L = length; A = age.

Length growth is about 6-8 cm/year during this phase.

Weight is calculated using the formula:

$W = 2A + 9$

where W = weight; A = age

Weight growth is done by 2 kg/year. By 2 years of age, the child will weigh 12 kg and will have 85 cm in length, and by 3 years – 15 kg and 95 cm.

The body configuration changes. The lordosis and prominent abdomen from the first childhood will disappear. The face grows more than the head. The limbs grow alternatively, at 3 years the upper limbs and at 4 years the lower limbs.

By 3 years of age, he can go up the stairs by alternating the feet, and at 4 years he can go down the stairs by alternating the feet.

Intelligence development enters a new phase. From the symbolic phase, after 3 years of age, intelligence goes through an inventivity period that prepares the complex operative thinking. The thinking makes obvious progress, even so. By 3 years of age, the child knows to use the words "ME", "YOU", "HIM", starts to use verbs at different tenses, understands the notion of male and female. This is the age of "Why?", "How?", "What for?".

By 4 years he establishes a certain independence and adjusts his program to the schedule made by adults.

At 4-5 years the child reaches a degree of motor development that allows him to execute isolated movements with different segments of the body (tricycle riding). He executes movement with higher degrees of difficulties (jumping, climbing). The language is improved and the child has a certain level of independence, adapts easily to the daily routine.

Between the age of 4 and 5, the child goes through a period of appetite loss, frequently determined by the lack of variety in the diet or affective tensions. Affection discomfort influences the appetite and the child's involvement during meals.

Progressive changes are done in the area of progressive culturalization in the terms of clothing and hygiene. These conducts involve a lot of skills but the ability to chose the clothing based on several factors as well, keeping things tidy, washing and using the toilet. Until the end of this period, the child can adapt efficiently by acquiring a set of adequate skills.

Around 6 years, almost all motor functions are mastered without difficulties; the logical thinking occurs, along with anxiety and frustration. Here act aspects related to temper.

Nutritional hygiene, hand washing, hair and teeth brushing reflect de degree of development and self-image forming. Aspects related to sleep are essential. The child doesn't want to go to sleep, because of the interest of interacting with others; he becomes more and more receptive to the thing the adults do, as well as feeling the pleasure of playing. The protest against going to sleep can be done verbally, elusively, by procrastinating and is filled with all sorts of transactions, like the necessity of having certain preferences such as: the mother being present, or a source of lighting, music or silence.

The preschooler crosses the knowledge stage by enlargement of his behavior related to the social and cultural environment, from which he assimilates life models that determine a more active integration of the human condition.

PSYCHOLOGIC DEVELOPMENT AND PERSONALITY TRAITS SHAPING

The preschool period is one of the most intense stages of psychic development. This takes place under social, cultural pressure by the influence of mass-media and institution attendance (kindergarten), where the child is in contact with the multiple demands regarding the autonomy and adaption to living environment.

The small preschooler (3-4 years) is unstable, cries laughing and passes from one mood to the other by living explosively and totally the events that impress him. However, the child is more insensitive toward the meaning of events and adopts conducts that are adequate to social convergence on a basis of affective fragility with tantrums. The middle aged preschooler (4-5 years) becomes more sensitive to the events that surround him and is capable of making relatively correct appreciations about the behavior of others. By structuring volitional traits, the child can enter longer activities and seeks to help the adults.

The big preschooler (5-6/7 years) manifests a higher adaptability and intelligence, reluctance to slight awkward situations as a result of a correct understanding of certain situations and causality reports in the producing of events. The child maintains a certain opposition toward the adult, that manifests rather spontaneously and is followed by a desire of reconciliation. The desire to be helpful is seen clearly. Becomes more and more careful, mimics the adult behavior and takes part in the adult occupational activities. The learning capacity becomes active and is doubled by knowledge interests.

II. School aged child

The third childhood: - small school child phase: 6-11 years

This period, from the start of school to the end of elementary school is appreciated by some as the ending of childhood. It's specific that for all this phase there are descriptions centered on school and learning adaption issues without neglecting the fact that some cerebral structures develop as a result of the fact that during the early childhood and preschool phase the most important adaptive and attitude experience takes place.

Therefore, during the small school age period, important traits develop and progress is made in the psychic activity due to the awareness of the learning process - the learning becomes the fundamental activity. This means that the educational activity will intensely use the intellect; a knowledge aquisitional process is realized and the child will be given different learning strategies, the role of attention and repetition will be emphasised, writing, reading and calculus skills will be developed.

The first 4 years of school will modify the diet, tension and event planning, that dominate the child's life.

The adaption process amplifies and centers its attention on a new adult, that is not limited by parents anymore. This adult (teacher) starts to play an important role in the child's life. For the child he is the representative of high order and ensures that the rules of society and school are exercised, trains the psychic energy, imposes patterns of behaviour and thinking.

The child becomes highly sensitive to the new dimension of the group and the affective equality of the school environment, which requires the need to win an independent statute within the group.

Growth and development during the third childhood and the school period

The growth is slow, but will be emphasised during the puberty phase, when a new growth spurt will be registered. The mean growth is done by 3,5 kg/year, height by 6 cm/year, head circumference, very slow, from 51 to 53-54 cm. By the end of this period, the brain size reaches the adult dimensions.

School years form a period of intense activity. The vertebral column becomes stronger, but at the same time exposed to dephormations, by incorrect positioning.

Around the age of 7, the first permanent tooth erupts, along with the first molar. Teeth replacing is done by 4 teeth/year for a period of 5 years. The second permanent molar appears by 14 years of age. The third molar can appear around 20 years of age, as well.

Once with family detachment, the child starts to spend time outside of it, at school or on playgrounds. Conflictual situations between parents and children occur.

The daily routine must be maintained and respected.

Unlike the previous program, in the daily program of the small child, several changes appear:

- the activity program is more stable, meaning that the waking hour and the bed time must be followed strictly, so that the school activity can be carried on optimally.
- the time spent at school is much more organized and full of activities that are more and more different from the ones done in kindergarten.
- after the return at home, the child must have a period of studying by himself, that can be assisted by the parents but not substituted.
- the playing must remain in the daily schedule, but the moment and time are dependent on the school necessities.

The small child needs 10 to 11 hours of sleep at night and especially the stability and following of the bed time. Sleep insufficiency leads to attention span, memory deficiency and a decrease in thinking performances.

The most important aspects of the physical development are as follows:

growth in length is slightly slower between 6 and 7 years, then the rhythm is increased and by the end of this phase the mean height in boys is around 132 cm and in girls around 131 cm. There is a tendency that girls have a slight advance compared to boys; weight growth is relatively constant and it is up to 29 kg in boys and 28 kg in girls.

The ossification is the most important during this phase and is done in the following areas: vertebral column, but the lumbar curvature is still unstable and in danger of deformation if the school child has a bad positioning for writing or carries heavy loads; in the pelvic area, hands (carpal and phalanges); continous dentition change. The joints are strengthening and the general resistance of the skeletal system increases.

The most important improvements of the muscle system are at the hand level, more precisely of the groups implicated in writing.

At the nervous system level, the following changes are important:

a) the brain mass increases up to 1200-1300 g;

b) the neuronal structure becomes almost as the adult one

c) the frontal lobes develop functionally

d) the speed of neuron connection formation increases.

The general motor activity develops and improves, especially autocontrol. The motor abilities are developing as a result of physical activity. The child aged between 6-7/10-11 years can practice any sport: cycling, swimming, skating, handball, on the terms that he is sustained and stimulated accordingly.

Attention considerations of small school aged child

Attention is shaped based on school solicitations.

During the first 6-7 years of life, attention is defined as an expression of orientation and psychic activity concentration. Generally, the child of 6-7 years cannot pay attention for more than 25-30 minutes during activity time. After entering school, the attention is well developed (the voluntary attention is less outlined). The stability and the duration is included in the instructive - educational process by stimulating the child's interest to fulfill an activity and generally by realizing a positive motivation about learning.

The psychic development profile of a small school child

Remarkable event: entering school.

This period is appreciated by some authors as the ending of childhood and the first year of primary puberty. The problems seen in this stage are linked to the school and learning adaptation.

Around the age of 6-7 years, the child encounters an important event: entering school. His whole physical and psychical development will be influenced by this factor. Learning becomes the fundamental type of activity, determining the developments of learning capacities and strategies. Parallel to this process, the child realizes important acquisitions: writing and reading skills, that become the condition and instrument of the other acquisitions to come.

School learning is radically distinguished from all the learning acts until this moment, both by content and by type of deployment. The volume, quality and diversity of the content after 7 years of age shape each child's future.

The development of perception and observational capacities appear between 6 and 10 years.

The visual perceptions are shaped by the reading and writing activity.

The evolution of perceptions and observational capacities are marked by the nature of the learning contents.

The increase of the general visual sensitivity is done by 60% compared to the preschooler and the differential one by 45%. Under these circumstances, the perceptions become clearer and more precise: starting with the age of 6, children can rapidly establish symmetry and asymmetry in the images they start to see, and when they learn how to read and write, they observe the graphical signs of small dimensions, letter differences, small space orientation and form perceptive diagrams for small and large letters, hand-written or print, that ensure the correspondant speed of reading and writing.

The ocular movements during reading: fixation, anticipation, regression, transition from one row to the other. They increase in speed by 1-3 hundredth of second and, during the act of reading, the eyes realize the following types of movements:

a) fixation of the letters and sylables that are pronounced at that moment;

b) anticipation of the one to follow by better functioning of the perypheral vision field;

c) regression, meaning coming back to the ones read already for the control and understanding of the meaning;

d) transition from one line to the other (this transition is done by following the row with the finger);

The other categories of perception increase, the ones referring to objects, mathematics symbols, geometrical shapes.

The auditory phonetics is highly trained.

Auditory perceptions progress especially around auditory phonetics. This is sistematically trained in tasks such as:

a) identification of the sounds from one word;

b) identifications of the words from one sentence;

c) analysis of the position of a sound in a word;

d) division into syllables;

e) the correct passing to graphic signs from hearing the correspondent signs. The musical hearing progresses and the children sing well songs that fit them.

The tactile perceptions become smooth, richer and start to be trained in writing.

Main aspects about language development between 6 and 10 years of age

The appropriation of reading and writing has an effect upon other dimensions of language, such as:

- an increase of passive vocabulary up to 4000-5000 words, doubling by the ones from the preschool age, and the active vocabulary over 1000 words. Other progresses refer to the semnification of words and understanding of the figurative meaning, rigour in the right use of words.

Perfectioning: speaking, reading, writing.

The language development is very good and ensures a basic condition in the development of all cognitive processes.

Memory and immagination - characteristic aspects of the small school age.

The voluntary memory and logic dominates. Memorization methods are insured. Memory refers to fixation of the school information, in such a way that the pupil recognizes and orally or in writing reproduces what he memorized. Fixation, recognizing and reproduction are strictly linked to the level of intelligence development in children. All that's fixated in the memory without the understanding of the child is rapidly forgotten - short term memory.

The specific of affective life in a small school child

The control of emotional and expressive conduct increases - self-control on emotional and expressive capacities increases.

Motivation and will - specific manifestations.

Motivation for learning is active and in progress.

The small school aged child's motivation is on one hand a premise of well adaptability in school, and on the other hand, a progress area realized by the support he gets in school.

CHAPTER XII

PUBERTY AND ITS INFLUENCE ON GROWTH. PUBERTY LAWS

Puberty is defined by:

- rapid initial growth, followed by a slow growth rate;
  - modifications of the dimensions and proportion of different body segments;
  - apparition of period in girls and sperm in boys;
  - intense intellectual development, high psychic lability;
  - dental and bone maturation;
  - decreased sensitivity and resistance to infection, lower mortality.

Dental maturation

The permanent dentition appears at 6 years of age, along with the first molar. Between the age of 7 and 12 years, the milk teeth are replaced by permanent ones, as follows:

- 6-8 years - central incisors
- 7-9 years - lateral incisors
- 9-13 years - canines
- 9-12 years - first premolars
- 10-12 years - second premolars
- 10-14 years- first molars
- 18-20 years- second and third molars

The permanent dentition has 32 teeth. The 6 year molar serves as foundation for the development of the whole permanent dentition and for the neat teeth arrangement. Permanent dentition calcification starts during the first month of life and ends at 25 years of life. For this process to unfold naturally, an adequate intake of calcium, phosphorus and vitamins must be realized (vitamins A, C, D).

Bone maturation

The bone maturation assessment is considered the most truthful indicator of general growth, the bone age has to be consistent with the chronological age.

Bones are formed based on a cartilaginous matrix, the ossification process starts by the Vth month of intrauterine life and ends in adolescence. The ossification appears at the femural

bone nucleus and can be seen by radiographic examination after 36-37 weeks of gestation; as for the superior tibial nucleus - after the 38 week gestational age. At birth, the child has another nucleus, at the cuboid bone level and sometimes the humeral head.

The assessment of the bone maturity is done by radiologic examination of the lower limbs by the age of 1, and after this age, other areas can be investigated as well.

Establishing of the bone age is based upon: the dimensions and numbers of the epiphyseal centers at a given age; the dimensions, form, density and delimitation of the bone extremities contours; the distance that separates the epiphyseal centers from the calcification area or the fusion degree of these two elements.

The apparition and fusion of the diverse centers of ossification follows a relatively well-based "schedule" from birth until maturity. From birth until the age of 5-6, the number of ossification nuclei increases; after this age, the rhythm of apparition diminishes.

The ossified diaphysis and epiphysis remain for a long time separated by an area called "conjugation cartilaje"; growth in length is realized at this level. The welding of these elements takes place in a certain order, at precise ages (more or less) and after this, the natural stopping of growth takes place.

An essential reference of puberty consists of bone age. Puberty is triggered at an average of 12 years in boys bone age and 10-11 years in girls.

Bone age is definitive by the apparition of all the nuclei of ossification. There is a coincidence between the onset of puberty and the appearance of the sesamoid nucleus of the thumb.

The apparition of secondary sexual traits in puberty

The apparition of secondary sexual traits in puberty represents the last step in the physiologic process of sexual differentiation. Puberty is defined by the maturation of the genital function, having as biologic support the hypothalamic-pituitary-gonadal axis; its consequence is the acquiring of the capacity of procreation.

The onset age is variable depending on gender, and from case to case it is influenced by the factors mentioned above. Compared to the previous century, a tendency toward pubertary advance is seen.

The onset of puberty depends on the maturation of the hypothalamic-pituitary-gonadal axis, the hypothalamus secretes "releasing factors" specific for hypophysis gonadotropic hormones (FSH, LH). The increase of gonadotropic concentration is practically constant in boys, but for girls it is a cyclic curve, fact that induces ovulation.

Basal values and the one after stimulation of these hormones during different phases of puberty are seen in the table below (Sizonenko, 1982).

Puberty changes in boys

1. 8-9 years: the infantile body aspect persists
2. 10-11 years: the internal and external genital organs grow
3. 12 years: pubic pilosity appears (pubarche)
4. 13 years: prostatic secretion takes place and breast areola develops (thelarche); gynecomastia phenomena can occur
5. 14-15 years: axillar pilosity, voice changing
6. 15-16 years: facial pilosity, gonadal cells mature
7. 16-17 years: pubic pilosity gains a male aspect, gynecomastia phenomena disappear; juvenile acne can occur
8. 17-19 years: the cartilages of conjugation are ossifying.

Puberty changes in girls

1. 8-9 years: the uterus is slowly developing
2. 10-11 years: the uterus is developing rapidly, the myometrium appears, the vaginal secretion with acid pH, pubic pilosity (pubarche), breast areola develops (thelarche)
3. 11-12 years: axillar pilosity occurs, mammary glands enlarge along with the pelvis
4. 12-14 years: monthly cycle occurs (menarche) - irregular and anovulatory
5. 14-15 years: menstrual cycle becomes ovulatory
6. 15-16 years: juvenile acne can occur
7. 16-17 years: the cartilages of conjugation are ossifying.

Tabble 11. Tanner stages of sexual maturation assessment

Stage	Boys		Girls
	External genital organs	Pilosity	Breasts
I (infantile)	0	0 (smooth hairs)	0
II	progressive englargement of the testicular volume	small hair and pigmented skin in the pubic region	breast bud, the breast grows in diameter, the areola grows
III	the penis begins to lengthen	hair becomes more coarse and curly and begins to extend lateraly	breast begins to become more elevated, extends beyond the borders of the areola, which continues to widen but remains in contour with the surrounding breast
IV	penis continues to increase in length; the scrotum englarges further	adult-like hair quality, extending across pubis but sparing medial thighs	increased breast sizing and elevation; areola and papilla form a secondary mound projecting from the contour of the surrounding breast
V	adult scrotum and penis	hair extends to medial surface of the thighs	breast reaches final adult size; areola returns to contour of the surrounding breast, with a projecting central papilla

The gonadotrope hormones stimulate the growth of the gonads, their synthesis function and eliberation of specific sexual hormones. These hormones are responsible of the apparition of specific body changes during puberty, also known as secondary sexual traits. Meanwhile, there is a pubertary maturation of the adrenal glands; the androgens are responsible of the growth spurt during puberty in both genders and the apparition of pubic and axillar pilosity in girls.

PHYSIOLOGIC PUBERTY IN GIRLS

The secondary sexual traits that appear during puberty are represented by the ovarian secretion of estrogens (gonadotropin stimulation) and the high androgen secretion due to adrenal glands secretion.

The first modification is represented by the onset of thelarche. The mammary gland development leads to the estrogenic ovarian activity. The onset can be unilateral, asymmetrical, painful. The complete development is done after 2-3 years.

The pubarche, pubic pilosity appears a few months after the telarche onset and the axillar pilosity soon after the pubic one, by the adrenal gland's action. A spurt of statural growth is always present, of 6-12 cm/year after the onset of menarche.

At the external genital organ level a slight hypertrophy of the major labia is observed, along with physiological leucorrhoea. The vaginal mucosa becomes pinkish, matte, with acid pH. The cytological and vaginal smear show a presence of the acidophilic superficial cells, which means estrogenic impregnation. The uterus grows as well.

After 2 to 5 years after the onset of thelarche, the menarche appears, which represents the action of gonadotrope hormones: the FSH determines the growth in volume of the ovaries, maturation of the Graaf folicles and stimulation of the ovarian secretion of estrogen, while LH stimulates the secretion of progesterone from the yellow body in the second part of the cycle. The first cycles are usually anovulatory.

Table 12. Pubertary stages in girls

Stage	Thelarche	Pubarche and axillar pilosity	External genital organs		
			Major labia	Minor labia	Vaginal mucosa
P1	absent	absent	infantile	undeveloped	glossy
P2	incipient	incipient	incipient development	incipient development	slightly matte
P3	average	average	average development	average development	matte
P4	well developed	abundent	well developed	well developed	matte
P5	menarche onset				

Ovulation

The ovary fulfills two functions: ovulation and ovarian steroidal hormones synthesis (estrogen and progesterone). Ovulation starts at pubery and is a process that assures reproduction. During the pubertary period, the ovary has only primary folicles formed by a layer of glanular cells, which cover an ovogonia found in prophase. The interruption in prophase of the germinative cells is maintained from puberty until menopause. The cellular meiosis is a maturation process that occurs during each menstrual cycle.

The number of germinative cells is approximately 2 million from birth, and at puberty around 100.000. The monthly production of a sole ovule needs around 400 ovogonies. All other ovogonies are destroyed by an atresia process, during the folicle phase. As a result, 99,6% of the existant germinative cells at puberty will be destroyed and the ovule which will eventually be fertilized, is the process of an intense selection. The ratio selection/atresia is of 1/20.000.

During the last day of the luteal phase of a cycle and during the first part of the follicle phase of the next cycle, under the influence of the initial increase of FSH and locally secreted estrogens, a group of 6-12 follicles start to grow and are transformed in secondary follicles. These are characterized by the presence of several granular cells layer and by increasing the dimensions of the oocyte. Of these follicles, only 1 maturates, the rest of them regress. The "selected" follicle is progressively developing, the oocyte grows and the granular cells proliferate.

In time, certain modifications in the adjacent ovarian stroma appear, the ajacent stomal cells arrange in concentric layers around the follicle: the inner sheath (adjacent to the follicle) and the outer sheath (periphery). At the same time, in the defined area, surrounded by the granular cells, a fluid starts to accumulate, that contains mucoid substances and steroids.

The sheath and granullary cells secrete higher quantities of estradiol, the most active estrogenic hormone. This phenomena has two major consequences: the increase of the intraovarian concentration of estrogenic hormones, which will favor the development of the adjacent follicles, and the increase of the blood concentration of estrogenic hormones, which will lead to a feed-back control on the secretion of LH and FSH. The blood concentration of estradiol increases slowly at first, and then rapidly, being at a maximum right before the sudden increase of LH and FSH - during ovulation.

In blood, the progesterone concentration decreases during the first days of the menstrual cycle, is reduced during the middle phase of the follicular stage and then increases in parallel with the increase of LH.

By complete maturation of the preovulatory follicle, a sudden increase of LH-FSH induces the ovulation and the transformation of the respective follicle happens, at the corpus luteum. The ovulation process consists of a slow expulsion of the egg, as a response to the increased LH secretion and local cellulary changes.

Postovulatory, the granular and inner sheath cells suffer numerous mitosis, a rapid numerical increase and an intense metabolic activity. Along with this process, the follicle turns into corpus luteum, which grows progressively, reaching the maximum dimension at 2-8 days after ovulation. If the fertilisation and implantation process don't happen, at 8-9 days postovulation, the corpus luteum, suffering a hyaline degeneration process turns after 3 months into corpus albicans.

Usually, 10-16 days after ovulation, the corpus luteum actively secretes sterdoids.

The ovulation process is under the control of gonadotropic hormones, dependent on a specific "releasing-factor" (RF), gonadotropin releasing hormone (GRH), a decapeptide secreted by the neurons from the hypothalamus.

The ovarian hormones biosynthesis starts from cholesterole and the final products are: estrogens (estradiol, estrone), progesterone and a small amount of androgens (testosterone and androstenedione).

The menstrual cycle

Under the influence of ovarian hormones, the endometrium suffers modifications important to the physiology of reproduction. In the first half of each menstrual cycle, the progesterone concentration is low, while the estradiol one grows gradually, being maximum at 24 hours before ovulation. This phenomenon stimulates the endometrium, which grows in width, from 1mm during the first 4-6 cycle days to 3-5mm around ovulation.

At 36 hours after ovulation, under the influence of progesterone, the endometrium, prepared by estrogen, suffers specific hystologic changes. If the egg is fertilized, its implantation takes place, usually in the 8th day after ovulation. If the ovulation does not occur, the glandular secretion decreases, and in the 11th day after ovulation, the endometrium is invaded by lymphocytes and in the 14th day after ovulation, the egg starts to detach and remove along with the rapid decrease in the progesterone and estradiol concentrations. These hormonal changes initiate the gonadotrope secretion, involved in the induction of a new menstrual cycle.

PHYSIOLOGICAL PUBERTY IN BOYS

The growth of the testicular volume represents the first specific change of boys puberty, followed by the penis development and the pigmentation of the scrotum. After a few months, the pubic pilosity shows, then the axyllar one and, variably, the one from face and trunk. Among the ones mentioned above, several other aspect occur: growth spurge, voice changing, muscle mass apparition. One third of the cases can present with an intumescence at the mammary gland level, unilateral or bilateral, which can reach a diameter up to 2 cm and it can also be painful. This usually regresses after a few months.

All these changes are secondary to the increased testosterone synthesis from the Leydig cells as a response to the LH hypophysary secretion. At the same time, the FSH stimulates the maturation of the seminifeous tubules and spermatogenesis, this way completing the sexual maturation.

Table 13. Pubertary stages in boys (after Tanner and Tarib)

Pubertary stages	Testicles	Penis	Penis length (cm)	Pubic and axillary pilosity	Facies (pilosity acne)
	Testicular volume index (cm)	Length			
PI	2.8±0.6	-	3-8	absent	absent
P2	4.8±1.7	2.5-3.2	4.5-9	onset	absent
P3	9±2.1	3.3-4	4.5-15	average	absent
P4	-	4.1-4.5	-	developed	present
P5	13.2±2.1	4.5	9,18	male pubic type	present

Spermatogenesis and the testicular hormonal biosynthesis

The parenchyma of testis is formed by two seminiferous tubules, surrounded by connective tissue which contains Leydig cells, blood and lymph vessels. The cytoplasm of the Leidig cells contains an abundance of endoplasmic reticulum which is organically involved in the synthesis of steroids.

The testis has a double function, being responsible for both the spermatogenesis and the steroid hormonal synthesis, when the androgenic hormone synthesis is predominant.

Spermatogenesis is the process of sperm formation from the immature germ cells. It takes place in the epithelium of the seminiferous tubules, under the control of FSH. The new formed sperm is transported into the epididymis, where they are stored until complete physiologic maturation.

The spermatogenetic cycle starts from the germ cell named spermatogonium. This is the least differentiated cell. It is divided to form the spermatocyte, which forms, by meiosis or reductional division, the spermatid. The spermatid is a haploid cell. It will suffer a complex process of metamorphosis process, which forms a mobile, flagellated cell, named sperm cell.

At the Leydig cell level, the testicle synthetizes a series of steroids, mostly androgens and in a small amount, estrogens.

Androgens are the steroid hormones that realize the differentiation and development of the male reproductive organs, development of the secondary sexual traits and male behaviour.

The testicles secrete the following androgenic hormones: testosterone, androstenedione and dehydroepiandrosterone. What's more, the 5-alpha-dihydrotestosterome is considered the 4th testicular hormone; it comes from the metabolization of testosterone under the action of 5-alpha-reductase.

The estrogens secreted by the testes are represented by estradiol and estrone. They come from the transformation of testosterone and androstenedione, respectively. These hormones can be directly secreted by the testes or can result from the metabolic transformation of early mentioned androgens. This way are provided 30-95% of the total circulating estrogen hormones in males. The testes secretes daily 10-15 micrograms of estradiole and more importantly, estrogen. The estrogens stimulate the growth of the mammary glands in boys during puberty and have a role in the FSH secretion (males).

The testicular hormonal synthesis is regulated by the hypophyse, by the LH hormone. This stimulates the androgenous steroidogenesis, having a role in the development and differentiation of the Leydig cells during puberty, on which they act upon with the help of a specific receptor (messenger) and cyclic AMP (secondary messenger).

The testosterone determines the differentiation of internal genital organs, the suppresion of the mammary ridge, the penis growth in length, muscle mass, spermatogenesis, voice change, male psychosexual orientation.

Dihydrotestosterone determines the differentiation of the external genital organs, the growth of the prostate gland, pubic and body pilosity development, acne and temporal alopecia.

The intimate mechanism of action involves the protein-specific cellular receptor, coded by a gene localized on the X chromosome.

PRECOCIOUS AND LATE PUBERTY

The real precocious puberty manifests by the apparition of menstrual cycles before the age of 8 years. The cycles are followed by ovulation and preceded by successive and complete stages, previous to menarche: statural growth, thelarche, adrenarche and pubarche.

Precociuous pseudopuberty is manifested by an early hormonal sexualization, due to gonadic causes or extragonadic ones, by tumors or adrenal hypertroplasy. It can appear as a iatrogenic cause, by intempestive estrogenotherapy.

Idiopatic precocious puberty: is characterized by the premature maturation of the CNS with a pulsatile secretion of LRH (gonadotropin releasing hormone).

Neurogenic precocious puberty (nervous lesions)

Precocious pseudopuberty: is determined by a premature secretion; the sexual hormones usually lead to the apparition of secondary sexual traits, without a pulsatile secretion of gonadotropes and with no ovulations, by complete lack of gametogenesis.

Incomplete precocious puberty

a. Premature thelarche can be seen from time to time in girls with ages between 6-18 months, when a transient breast enlargement appears, with no other signs of precociuos puberty.

b. Premature pubarche is charaterized by the apparition of a pubic pilosity, not very intense, with a slow evolution until the normal apparition of puberty.

Late puberty

It is considered when the apparition of the secondary sexual traits show up after the age of 13 years, and menarche is not present until 16 or 18 years.

The most common form is the one genetically constitutional and can be taken into consideration if the family reveals similar delays in other family members.

NUTRITION DURING ADOLESCENCE

Adolescence is a period of dramatic growth and development. During this interval, a complex of physiologic and psychologic changes take place. All these require special nutritional needs.

Although the weight gained during adolescence is considerable, the tissue composition differs from one gender to the other. The male grows more and faster based on muscle mass, while the female gains weight by increasing the muscle mass and the adipose tissue. The energetic needs will keep in mind, among other things, the energetic balance. The inactive subjects can become obese even if their energetic intake is below the recommended one; on the other hand, the more active ones will require an increased intake.

The protein intake will be between 12-14% of the total energetic needs during childhood and adolescence. The peak of the protein intake matches the energetic one by the age of 12 for girls and 16 for boys. This peak is represented by 100 g/day for boys and 80g/day for girls.

If the protein intake decreases, the synthesis of new tissue will be negatively influenced and a decrease of growth occurs.

Studies realized in the USA, on a lot of 5000 subjects show that for ages between 12 and 13 years, the girls consume around 2550 kcal/day, and at the age of 18 years of age the energetic intake drops by 300 kcal/day. In boys, the average energetic intake until 16 years of age is about 3470 kcal/day and during the following years 3000 kcal/day. The fact that both genders have and intake higher than the recommended intake is significant. It is important that the meals should be consumed based on appetite and not necessarily keep track of absolutely all the recommendations (table 1).

The minerals requirements (especially calcium, iron and zinc) increase substantially during the period of growth; the calcium - for the enhancement of the muscle mass; iron - for the expansion of the muscle mass and blood volume; zinc - for the skeleton and the muscle tissue.

Calcium retention varies based on the growth rate. The boys acquire an average of 290-400 mg of calcium/day during the growth period, and the girls around 210-240 mg/day.

The recommended diet ration is of 1200mg/day for both genders, being intended for the coverage of the rapid growth rate during puberty.

It should be mentioned the difficulty of an intake of 1200 mg of calcium because a daily diet that consists of bread, butter, potatoes, vegetables can provide only 300 mg/day; for ensuring the difference up to 1200 mg/day, according to recommendations, 6 cups of milk should be consumed, which is hard to accept by adolescents.

It was noted, as well, that around 5% of girls consume less than 2/3 of the recommended calcium intake. It is uncertain if the process is compromised by this decreased intake. We remind of the fact that the ratio between calcium and phosphorus should ideally be of 1:1. The inadequate intake of iron is reflected upon the high anemia prevalence among adolescents.

Iron is necessary due to blood volume and muscle mass expansions which realise during growth. Because this expansion has a more rapid rate in boys, they need around 42mg/day. Girls lose iron via menstruation, which represents around 0,5mg/day; as a result, the requirement is approximately the same for both genders.

The recommended iron intake for both genders is 180 mg/day. Observation shows that very few adolescents consume the recommended iron intake. This aspect probably explains the low level of hemoglobin, of hematocrit and iron in this age category.

For the improvement of these events, it is recommended to add to the diet products rich in iron: meat, beans, green vegetables, peanuts, nuts and other fruit or cereals that are high in iron. The ingestion of food high in ascorbic acid, along with the ones that contain iron favors iron absorption.

Zinc has a recognized role in the process of growth and in the sexual maturation of adolescents. The severe zinc deficit in boys leads to dwarfism syndrome, anemia and hepatosplenomegaly. High zinc deficiencies seem to determine growth restriction and a delay of sexual maturity in teenagers.

Zinc retention is estimated at 400 micrograms/day, during adolescence. The recommended diet intake is 15 mg/day.

Richer sources of zinc are the animal products such as: meat, fish, eggs, milk. In fact, a correlation has been observed between zinc and protein content of the animal products. The plant products have a lower zinc content.

The vitamin requirements during adolescence are high compared to small children, due to a high energy consumption, which requests more thiamine, riboflavin and niacin.

The high rate of tissue synthesis during adolescence requires high quantities of folic acid and vitamin B12, for the metabolism of the DNA and the RNA. The high rate of skeletal growth requires high intakes of vitamins D, A, C and iron. The recommended intake is shown in table 1.

The dietary habits of adolescents

During the last years, in our country, especially in the urban environment a certain behaviour can be observed: the habit of eating outside of home (bars, stands). The way in which these adolescents "skip meals" is an accepted aspect by a lot of families.

Breakfast and lunch are the most commonly skipped meals. Scholar and social activities can as well be a reason of skipping dinner. Due to the tight schedules, adolescents consume "economically", buying meals that are of inferior quality. These snacks decrease the appetite and are low in nutrients, vitamins, minerals and proteins, but high in carbohydrates and lipids.

Low calories aliments are not recommended because during the growth period there is a high requirement of calories and food principles.

The rapidly served meals, also known as snacks, have little fruit and vegetables, leading to a decrease in vitamin C, A and folic acid. In exchange, they can be rich in lipids and sodium, poor in fibers, favoring the apparition of degenerative diseases. In case there are

certain motivations regarding the rapid eating of meals and snacks, the nutritional balance must be improved by supplementation of fresh fruit, vegetables and limitation of the high lipid food content.

Vegetarian diet

Adolescents turn more and more toward the vegetarian diet. A lot of people adopted this way of alimentation due to moral, health, religious or ecologic reasons.

During adolescence, the problem with the vegetarian diet lies in the fact that the growth and development requirements are high. The diet guide from table 2 has more details. If a lacto-vegetarian diet is adopted, this can provide the recommended intake for all nutrients, including vitamins and minerals.

The vegetarian diet, which eliminates all animal products is poor in vitamins B6, B12 and riboflavin, minerals, especially calcium, iron and zinc. Vitamin B12 is found only in animal products.

Calcium can be supplemented by the consumption of fresh greens, beans, nuts, seeds. Iron can be supplemented by the consumption of vegetables, fruit, beans, nuts, seeds. Zinc sources are the products of wheat and beans.

Spinnach and parsley contain oxalates which bind the minerals, making them hard to absorb. The phytates from cereals can decrease the absorption of iron and zinc.

Alimentation and obesity during adolescence

There is a period when the individual forms and develops an image of himself, so obesity can have a great adverse effect on the psychological development. The obese teenager is discriminated by his antourage most of the time. This attitude can determine a sentiment of social isolation and subestimation. Unfortunately, this sentiment frequently leads to an increase in alimentary consumption and, as a consequence, an aggravation or maintaining of the obesity condition.

Some of them, teenagers, or adults, look for ways to rapidly lose weight.

One of the most widespread methods includes the exclusive consumption of protein products, due to the fact that proteins save the muscle tissue, and the fatts are burnt for assuring the energetic requirements. It must be emphasised that the animal protein does not contain all the necessary vitamins and minerals. As a result, they should be supplemented by drug prescriptions.

Severe restriction is not recommended during growth period, because it limits the protein use necessary for tissue synthesis that will be attracted by the catabolic processes. An obese must eliminate from the diet the excess brought by fats, snacks and desserts.

As an example, the aliments from table 2 will be recommended, except for the fatts. This diet permits a normal growth, with no adipose tissue buildup.

The programme of obesity control will include physical activity as well. Different authors report cases of obese adolescents that practically do not eat anything more than non-obese patients, but are less active. Physical activity will be encouraged and established as a permanent component of the teenager's life, not only for energy consumption, but for the loss of adipose tissue accumulation.

Nutrition and sport

In many schools and sport clubs different wrong informations and concepts are heard regarding the nutrition recommended for athletes.

By some, the solution would be the protein supplementation as a way to cover the needs during practice, but it is known that the proteins do not constitute the main source of energy for the muscle tissue. Some additions can be necessary for the synthesis of muscle mass during workouts, but these demands can be done by a diet that can offer 1 g/kg/day of proteins for the mature athlete and 2 g/kg/day for the one in growth. Supplementation above these values is not beneficial for the physical performances.

Another misconception refers to vitamin and mineral supplementation during practice. If the athletes have an adequate diet, the vitamin supplementation is not necessary. If the doses of vitamin A and D are above limits, these will have toxic effects, that will reflect upon athletic performance.

Sodium and potasium are minerals that are frequently lost during hard physical practices. The ensuring of these minerals is done by non-alcoholic drinks, high in electrolytes, by the adding of NaCl in diet, as well as the addition of fruits rich in potasium, such as oranges and bananas. The ingestion of electrolyte tablets is not recommended, except from rare cases of physical practice.

Iron deficiency occurs in female athletes as a result of an inadequate intake, menstrual loss and increase of tissue needs. As a result, a supplementation of 30-60mg/day can be recommended.

During physical exercise, the whole body water can decrease, as a result of sweating, but from urinary losses and evaporation from the respiratory tract, as well.

By increasing the environmental temperature, along with the intensity of the exercises, the water requirements increase. These losses are recommended to be replaced by an intake of small and frequent quantities of fluids during practice. Before the event, the teenager should be well hydrated, because dehydration can lead to fatigue, limitation of the effort capacity, temperature rise and thermic shock, eventually. The conception that water ingestion is in the detriment of athletic performances is proven to be dangerous.

Maintaining the body weight by water and food restriction is as well indesirable because this method can lead to tissue degradation, electrolytic inequity and dehydration.

Alimentation during pregnancy in adolescence

The increase of pregnant teenagers has become a serious health issue. Pregnancy at a very young age is considered of high risk due to the frequency of preeclampsia, preterm delivery and small birth weight. 10% of the children born from mothers with age between 15 and 19 years have a small birth weight.

It is known that adolescent girls have variations that interest growth and sexual maturation. For many girls, the sexual maturation is definitive only 4 years after the onset of menarche (around 17 years of age).

During the growth period, the needs of a female teenager are high. If at the same time a pregnancy occurs, the nutritive requirements increase more, for the coverage of the fetal growth. The pregnant teenager is considered with nutritional risk. The nutritive needs of the pregnant adolescent can be estimated by adding the necessary supplements, as in adult pregnancies, related to gestational age (see table 1). Iron supplementation will be added, 30-60mg/kg/day, necessary for both the maternal and fetal bodies.

The use of oral contraceptives during adolescence and their effect on metabolism

Oral contraceptives can induce a series of metabolic disorders: decrease of plasmatic albumins, increase of triglycerides. For people with familial hypercholesterolemia the risk of cholesterol increase after contraceptive use is high. For the ones with diabetes mellitus, an abnormal glucose tolerance can occur.

For vitamins, a certain increase of the plasmatic level of vitamin A, ascorbic acid, riboflavin, pyridoxine, folic acid and vitamin B12 is observed. Retention of fluids is also seen, which influences the weight and body composition.

All these disorders are reversible after the interruption of contraceptive administration.

Alcohol abuse and its impact on nutrition

In many countries, the number of teenagers that consume alcohol is rising. Although teenagers consume less alcohol than adults, the use of narcotics along with alcohol is more frequent at this age.

Drug use can enhance the dangerous effects of alcohol. The chronic alcoholism can seriously alter the nutritional status of the adolescent, each gram of alcohol produces 7 kcal and this energy supplements the one from the diet. This way, a decrease of the protein, vitamin and minerals is produced. In parallel, an irritation of the gastric mucose occurs, that by the loss of appetite, reduces aliment consumption.

The urinary zinc excretion is high in alcohol abuse. On the long tern, it can lead to a reduction of vitamin A, as well as affecting the erythrocite function from the small intestinal wall, so that the nutrient absorption is altered. The teenager has high nutritional needs for growth and development and can be severely susceptible to nutritional deficiencies done as a result of alcohol abuse.

Table 14. Recommended diet for teenagers

	Quantity	Boys		Girls		Pregnancy	
		11-14 years	15-18 years	11-14 years	15-18 years	11-14 years	15-18 years
Weight	kg	45	66	46	55	46	55
Energy	kcal	2700	2800	2200	2100	2500	2500
Proteins	g	45	56	46	46	76	76
Vit.A	UI	5000	5000	4000	4000	5000	5000
Vit.D	UI	400	400	400	400	600	600
Vit.E	mg	8	10	8	8	10	10
Vit.C	mg	50	60	50	60	70	80
Folacine	µg	400	400	400	400	800	800
Niacine	mg	18	15	15	14	17	16
Riboflavin	mg	1.6	1.7	1.3	1.3	1.6	1.6
Vit. B6	mg	1.8	2.0	1.8	2.0	2.4	2.6
Vit. B12	µg	3.0	3.0	3.0	3.0	4.0	4.0
Calcium	mg	1200	1200	1200	1200	1600	1600
Phosphorus	mg	1200	1200	1200	1200	1600	1600
Iodine	ug	150	150	150	150	175	175
Iron	mg	ÎS	18	18	18	18+	18+
Magneziun	mg	350	400	300	300	450	450
Zinc	mg	15	15	15	15	20	20

PART II

CHAPTER I

GENERAL PRINCIPLES OF NUTRITION AND ALIMENTATION

The optimal use of nutritive principles -*proteins, lipids and carbohydrates* from diet, is done with the purpose of ensuring a cerebral and somatic growth, so that growth can be maintained on the specific age graphic.

The major nutrition principles: *proteins, lipids and carbohydrates* are the main energy providers, but the ration has a non energetic part as well, represented by *water, mineral substances, oligoelements, fibers and vitamins,* with a role of cofactor in the synthesis and degrading processes, assuring the nutritional yield.

The nutritional needs vary with age, gender, genetic constitution, growth rate of different tissues, stage of maturation, body structure, physical activity, environment. They form a curve that is parallel to the weight and body length, leading to an adequate growth.

The recommended dietary ration (RDR) represents the amount of energy and nutrient principles, considered sufficient for maintaining a health status from a given population (97% of the individuals). Generally, the RDR exceeds with 20% the minimum need for a specific aliment. Nutritional imbalances, generated by an insufficient or excessive diet intake can lead to disorders such as: malnutrition, obesity, degenerative disease (anemia, rickets), early atherosclerosis, diarrhea, high blood pressure.

Energetic requirements

In infants and children, the caloric requirements is calculated based on: caloric consumption on age groups, taking into account the ideal weight, body composition, environment, growth process and physical activity. The caloric needs represent the correspondent of daily energetic expenditures, such as:

a) ***Maintenance metabolism***, which contains:

- basal metabolism, which varies based on age: 35 Kcal/Kg/24h in newborns; 50 Kcal/Kg/24 h in infants; 25-30 Kcal/Kg/24h in big child and teenager; 20 Kcal/Kg/24 h in adult;
- the dynamic specific action of aliments represents 10% of the basal metabolism

b) ***Thermoregulation***, requires 20 Kcal/Kg/24 h.

c) ***Growth***, requires a different caloric consumption based on age, parallel to the growth pattern:

1. 50 Kcal/Kg/24 h between 0-2 months;
2. 25-27 Kcal/Kg/24 h between 2-6 months;
3. 10-11 Kcal/Kg/24 h between 6-12 months.

The growth requirements, as a whole, represent 3-4,5 Kcal for each gram of growth spurt.

d) ***Physical activity***, the energy consumption is reduced during the first months of life and suffers individual variations from one day to the other:

- 10-20 Kcal/Kg/day during the first 6 months of life (nervous crying infant);
- 25 Kcal/Kg/day after 6 months.

The caloric requirements during the first year of life are between 90-120 kcal/kg/day, and then, for each following stage of 3 years, drop by 10 Kcal/Kg/day (**table 6**). The maximum admitted limit for a newborn is of 165-180 kcal/kg/day.

Table 15. Caloric requirement based on age

Age	**N.C./Kg/day**
0 - 3 months	120-110
4 - 6 months	110-100
6 - 12 months	100-90
1 - 3 years	90
4 - 6 years	80
7 - 16 years	60-50

For assuring an optimal growth, with a moderate amount of fat (20%) and a maximum use of nutrient principles, it is imperative an ideal ratio of calories/nutrient principles. For this, 40-50 % of the calories must come from carbohydrates metabolisation (1 g carbohydrates = 4,2 Kcal), 35 - 40 % from lipid metabolisation (1 g lipids = 9 Kcal) and 10 % from protein metabolism (1 g proteins = 4 Kcal).

Water requirements

Water, the main body component has an essential role on the whole organs and systems, with an active role in growth and development and in health status maintenance.

The role of water is vital, it takes part of all the nutrient substances because:

- it takes part in organ and tissue structure;
- it transports the excreted metabolits from the kidney;
- component of sweat;
- thermoregulatory role;
- umidifier for the respiratory tract.

The water quantity from the human body is different based on age:

- 75 % of the weight of a newborn;
- 70% of a child's weight;
- 60-65% of the adult weight.

The water distribution, between different compartments is variable with age:

- ✓ **0-6 months -** extracellular water represents 40% of weight (35% interstitium, 5% in plasma), while the intracellular water represents 35% of weight.

- **after 6 months**
  - ✓ extracellular water represents 25% of weight(20% interstitium, 5% in plasma), while the intracellular water represents 50% of weight.

The water from the intersitial sector is variable and maintains the homeostatic balance between the intracellular and vascular sector. The water exchange from the two compartments depends on the protein content and the electrolyte concentration.

Fluid requirements is inversely proportional to the postnatal age, being higher during the infant period: it begins with quantities of 100-140 ml/kg during the newborn period, reaches 180 ml/kg at the age of 1 months; during the infant period the requirement decreases until 120 ml/kg by 1 year of age, during the small child period (100 ml/kg at 3 years) reaching 40/ 50 ml/kg by the age of 18 years.(**table 7**).

The calculation of hydric ration depends on *age* and *caloric content* (approximately 12 ml of water for each 100 Kcal),

The water requirements are calculated based on *daily loss, caloric intake, nutritional diet* (especially the content of protein and minerals).

Daily losses are: insensible perspiration 63 - 66%, urine 17 – 23%, feces 3 - 15 %.

Table 16. Water requirement based on age

Age	Water requirement ml/kg/day
0 - 3 months	180 - 160
4 - 6 months	150 - 130
7 - 9 months	130 - 125
10 - 12 months	125 - 120
2 years	115
4 years	100
6 years	100 - 90
10 years	50 - 80
14 years	50 - 60
18 years	40 - 50

The water requirements are assured by the dietary fluids (exogenous water) and by oxidation of the nutritional principles (endogenous water).

For a *breastfed healthy infant*, the fluid requirement is assured by human milk. This intake becomes insufficient in case of temperature increase of the environment, when the intake can be supplemented up to 200 ml/Kg/day.

In case of pathologic events: vomiting, diarrhea, increased diuresis, fever, respiratory distress, phototherapy, etc., the fluid requirement must be increased, sometimes by parenteral supplementation.

In infants, a dehydration of over 10% can lead to colapse, hypoxemia, acidosis and coma. A dehydration over 22% of the weight is incompatible with life.

Protein requirements

Proteins represent the essential elements for growth, they have a major role in the organism, are the structure of all organs and systems. A dietary ratio with an optimal amount of proteins is the basis of any nutritional balance and a growing body and represents around 10% of the caloric value.

The biological value of proteins is given by the amino acid structure. Out of all 24 amino acids, 9 are essential (cannot be synthesised and must be given to the infant): *threonine, valine, leucine, isoleucine, triptophan, lisine, tryptophan, phenylalanine, metionine and histidine*. For the *preterm newborn* arginine, cysteine and taurine are added, which cannot be synthetised due to enzymatic deficiencies.

Carnitine is an amino acid synthetised in the liver and kidney from lisine and methionine. In foods, they are especially found the animal products, but in some plants as well, such as soy, but in smaller quantities. The cell natural component has a fundamental role in the energy production, transport and entering of the fatty acids in the mythochondries. The highest quantity is found in the bone muscles, and in case of hypoxia, stress, the quantity of carnitine increases in the myocardium.

Protein intake is different with age.

RDR is of:

- 3-3,5 g/kg/day between 0-6 months and formula feedings;
- 1,8-2 g/kg/day between 0-6 months and breastfeeding;
- 2 – 2,2 g/kg/day during the infant period;
- 23 g/day between 1-3 years;
- 30 g/day between 4-6 years;
- 34 g/day between 7-10 years;
- 50 g/day in adolescence.

Digestion coefficient(DC) - represents the ratio between the absorbed nitrogen and the ingested one and is:

- 1 for human milk proteins;
- 0,95 for cow milk proteins;
- 0,50 - 0,80 for vegetable proteins.

Net protein utilization (NPU) related to DC and the biologic value has different values according to the protein provenance:

- NPU = 100 for human milk proteins;
- NPU = 90 for egg proteins;
- NPU = 84 for beef meat;
- NPU = 83 for fish proteins;
- NPU = 50 for plant proteins.

The exclusive source of protein from the diet of the first months of life is the human milk or formula, which ensures an appropriate intake by quality and quantity. During complementary feeding, the animal proteins represent 50% of the dietary ration (milk, meat, egg, fish, cheese). Caseine, serum and egg are considered the ideal source of protein because they contain essential amino acids.

The hypoproteic diet from the infant and small child period *leads to* the stopping of growth, Kwarshiokor malnutrition, hypoproteic edemas, stopping of cellular multiplication (CNS included).

The hyperproteic diet from small ages *leads to:* acidosis, high urea values, favoring the rotting process and multiplication of the pathogens, increasing of the adipose tissue and obesity.

Lipid requirements

Optimisation of the lipid requirements from the infant and small child's diet, due to the energetic role they have in the human body, are at the basis of the nutritional balance on the whole period of growing, especially during puberty.

In the establishment of the dietary ration during childhood, it must be taken into account on one hand the energetic requirements according to age (lipids are 35-40% of the total caloric ration) and on the other hand, of the *structural role and the transportation role* for liposoluble vitamins, so that the ration has an optimal content of polyunsaturated essential fatty acids chain tryglycerides.

Lipid digestion capacity is different based on *age*.

In newborns, the lipid absorption is variable and the digestion is limited. The pancreatic lipase and the bile acids are decreased during the neonatal period, that's why the lingual lipase and the process of gastric lipolysis are important. Term newborns with normal birth weight absorb human milk lipids around 95-98% and the cow milk lipids 85-90%.

In preterms the absorption is around 75% from the human milk and 60% from cow milk. A good absorption and digestion from the human milk is due to the high content of poly-unsaturated fatty acids with long chain (C_{20}-C_{22}). These are integral components of the cell membranes, which permeability they ensure along with enzyme activity. At the same time, they have a role in the cerebral development, especially the brain of the fetus and small child.

The special formulas used in artificial feeding or mixed of newborns and preterms have a high content of long chain polyunsaturated acids, because the capacity of lipid digestion and absorption is reduced during the neonatal period.

The high cholesterole concentration from human milk is important for establishing a diet from the first life period. Cholesterole is the precursor of sterolic structure hormones and has a role in the formation of the cellular membranes.

Cholesterole can be synthetised in a low percentage in the preterm newborn's liver, that is why the specific formular must contain 5 mg/dl of cholesterole for an optimum growth rate.

Adequate nutritional diet in nutrient principles must contain *tryglygerides* (98%) as well *as natural dietary sources* of lipids. Medial chain triglycerides are absorbed intactly, with no previous hydrolisis, directly into the portal circulation. These are the indispensable components of the dietary infant products, indicated in the intestinal absorption disorders.

The essential fatty acids are added to the milk formulas for infants (because they cannot be synthetised) due to the fact that they have a primordial role in the development of the brain and retina, influencing directly the postnatal growth curves. These are represented by: *linoleic acid (C_{18}), linolenic acid (C_{18})* and *arachidonic acid (C_{20}),* considered facultative because it can be synthetised from the linoleic acid.

The linoleic acid from formulas must represent 3% of the total caloric value. The decrease of the ration below 1% determines growth stopping and the decrease below 0,1% cutaneous changes, biochemical changes of the phospholipids from the erythrocyte membrane. The linoleic acid is found in corn oil (55%), soy oil (51%), sunflower oil (52%) and olive oil (16%).

The lipid requirements from diet is based on age:

- 3-6 g/kg/day in infants;
- 4-4,5 g/kg/day between 1-3 years;
- 2 g/kg/day after this age.
- the minimum quantity of lipids is of 1,5 g/kg/day
- 35-40% of the total caloric ratio

The minimum intake of lipids is of *1,5 g/kg/day.*

The hypolipidic diet during infancy leads to:

- reduction of the liposoluble vitamin absorption;
- perturbation of the growth process;
- cutaneous changes (seborrheic dermatitis, parakeratosis) - linoleic acid< 0,1%;
- decrease of the arachidonic acid synthesis, prostacyclin and thromboxane (linoleic acid< 0,1%);
- lipid fraction imbalances with hyperlipidemia and hypercholesterolemia (linoleic acid<0,1%);
- biochemical changes from the erythrocyte membrane.

The hyperlipidemic diet determines: obesity; hormone disorders; higher incidence of HPB; hypercholesterolemia; excess of polysaturated acids induces a relative deficit of vitamin E, which in preterm newborns and small infants leads to: hemolytic anemia, seborrheic dermatitis and sebum.

Carbohydrate requirements

Carbohydrates represent the *most important energy source* for the body; they are present in the alimentary ration under the form of: *monosaccharides* (glucose, fructose, galactose), *disaccharides* (lactose, sucrose, maltose) and *polysaccharides* (starch and glycogen). The only *source of carbohydrates storage* is the *glycogen,* from liver and muscles.

The dietary intake of carbohydrates during the first trimester of life is represented by the milk *lactose*, which during the digestion processes is split by the *intestinal lactase* in a molecule of glucose and one of galactose. Galactose is used for the synthesis of cerebrosides, for the mielination of the CNS and has a major role in the hepatic glucuronoconjugation and its epuration. The quantity of lactose that is not the subject of intestinal enzymatic process is fermented by the intestinal flora present in the large intestine, ensures an acid pH in stools and favors the development of the lactobacillus bifidus; it also facilitates the calcium, magnesium and mangane absorption.

The glucose molecule from the milk lactose has an energetic role and is absorbed by an active mechanism in the small intestine, by equimolar conjunction with sodium; it does not require specific enzymatic action.

Starting from these statements, the milk formulas for preterm infants are enriched with glucose, which also covers the high caloric requirements of this category of newborns. on the other hand, the preterms with GA of 30-40 weeks have a low lactase activity, with 50% compared to term newborns, that is why they cannot tolerate formulas with a standard lactose content.

Disaccharides are a part of the infant's diet as *sugars, dextrin-maltose* and are introduced in some milk formulas in variable concentrations based on tolerance and indications.

Starch a glucose polymer, is found as a liniar form or with branched structure (amylopectin). The starch digestion is assured by the amylase of pancreatic or salivary origin.

The newborn digests starch with the help of the intestinal glucoamylase. The plant starch can be introduced in the infant's diet from the first day of life as rice powder, exceptionally, in pathologic situations. It is found in the composition of special milk formulas. The farinaceous is usually introduced after 4-6 months, during complementary feeding.

Alimentary fibers (pectine, cellulose, lignin, hemicellulose) are not caloric sources and are present in the infant's diet until the complementary feeding is introduced.They intervene in the regulation of the bowel movement, stools texture, water, organic acids, minerals absorption, they modify and reduce the intestinal flora, tie the bile acids, induce hypocholesterolemia and hypolipemia.

Carbohydrates requirements are of 12 g/kg/day in infants and of 10 g/kg/day in small children and represent 40-50% of the caloric value.

A decrease of the carbohydrate intake leads to *hypoglycemia,* which influences the normal functionality of the Krebs cycle, growth disorders (malnutrition), hunger ketosis and stopping of growth.

An increase in the carbohydrate intake leads to wight gain and obesity.

Electrolyte and olygoelements requirements

Sodium (Na^+)

It represents the main electrolyte, the main extracellular cation, which intervenes in the *regulation of the osmotic pressure, acid-base balance, hydroelectrolytic and the regulation of neuro-muscular excitability.*

Serum level is around 135-145 mEg/l.

The sodium requirement is of 2-5 mmol/Kg for newborn and 0,7 mmol/Kg in adults. Human milk contains 8 mEg/l, and the cow milk 28 mEg/l.

The sodium excess from the cow milk can determine in the newborn and small child osmotic diarrhea, hypernatremic dehydration with severe consequences on the central nervous system.

The high intake of Na^+in the daily diet can *lead to:* hydric retention, hypervolemia, hypernatremia, edemas. It is also believed that a high intake of sodium during the infant and small child period and predisposes to high blood pressure during maturity.

Chlorine (Cl^-)

Is the main anion of the organism, it accompanies the intake and elimination of sodium and intevenes in:

1. osmotic pressure regulation;
2. hydroelectrolytic and acid-base balance;
3. takes part in the composition of the HCl from the gatric secretion.

Normal serum values are of 99-100 mEg/l.

Cl deficit appears in: prolonged vomiting, excessive sweating; glucose perfusion without electrolytic intake; long term treatments with ACTH.

The hypochloremic dietary ration leads to hypochloremic alcalosis.

Potasium (K^+)

Is a predominantly intracellular electrolyte (98%), the highest part being in the bone muscle level.

Intervenes in the body in: muscle contraction, conduction of the nervous impulse, heart rhythm and regulation of the osmotic pressure and the hydroelectrolytic balance.

Normal serum values are of 4-5 mEg/l.

The daily recommended intake is of 1-2 g or 1,5 mEg/Kg/day, the important sources being meat, fish, vegetables, dry fruit, milk, which insure an intake of 2,5 mmol/ 100 /Kcal/day.

Hypopotasemia determines: digestive disorders (nausea, vomiting), abdominal meteorism, tachycardia and nervous irritability.

*Hyperpotasemia*leads to modifications in the heart rhythm, and at values of 10 mEg/l atrioventricular block is produced.

Calcium (Ca^{++})

Is a major component of the bones and teeth (99 %), a small proportion (1 %) is found intravascullary, interstitially, cytoplasmatically and mithocondrially.

Role of calcium in the body*:*

1. regulates the homeostasis by immediate ionic exchanges;
2. in the mineralization process, in relation to phosphorus, vitamin D and parathyroid hormone;
3. participates in the muscle contraction and neuromuscular excitability;
4. intervenes in coagulation, being a blood coagulating factor;
5. activates some enzymes.

The normal values are: *9-11 mg %* or *5 mEg/l*. In the body, calcium is under ionized, difusable and unionized form (bound by plasmatic proteins or as salt).

Calcium requirements vary with age, being around 180-*200 mg/day,* respectively 180 mg /day during the first 4 months.

Sources of calcium are represented by: cow milk, green vegetables, egg yolk, meat, fish, raw fruits, wheat flour. Although cow milk contains a higher quantity of calcium, 117 mg/100 ml, this is only absorbed around 23-30 %. In human milk, the content is smaller 34 mg/100 ml, but the absorption is realized in proportion of 70 %, due to theratio of Ca/P = 2, ideal to absoption.

The calcium deficit can lead to many manifestations:

- newborns fed with cow milk can develop hypocalcemic seizures, of nutritional cause (the ratio Ca/P is inadequate - excess of P);
- the former preterm newborns can develop osteopenia if they were fed preterm start formulas with a content less than 70-80 mg/100 ml calcium;
- rickets, tetany, spasmophylia.

Phosphorus (P)

Is the main component of bones (80%) and muscles (9%). Vitamin D intervenes in the absorption and excretion of the phosphorus.

Role - intervenes in:

- bone metabolism;
- forms the structure of the nucleus and cellular cytoplasm;
- in the structure of the CNS;
- has a role in the cellular membrane permeability;
- is an important source of energy;
- takes part from the composition of certain substances involved in the metabolic phosphorylation and dephosphorylation of the nutrition principles.

The serum level of phosphorus is of 4 - 7 mg %.

The phosphorus requirement is different, according to age:

- 160 mg/day during the first 4 months of life;
- 250 mg/day during the first 6 months of life;
- 300 mg/day until the age of 1 year;
- 800 mg/day after 1 year.

The dietary sources are: meat, liver, fish, egg yolk, cheese, milk, green vegetables, fruit.

The ratio of Ca/P is 1,7 at birth and 2 in adults.

The phosphorus deficit is manifested by hypotonia and fatigue. The decrease of phosphorus from severe malnutrition is an indicator of the severity and of bad prognosis.

Hyperphosphatemia associated to hypocalcemia takes place during the period of rickets recovery.

Magnesium (Mg)

It represents an important intracellular cation; half of it is found in bones and the rest in the soft tissues. The body quantity varies with age from 760 mg at birth to 28 g in young adults. It is an enzyme cofactor in the mythocondria, as well as an important ion in maintaining the neuromuscular excitability.

The serum level is of 1,9-2,5 mEq/l.

An *intake* of 60 mg/day in infants is recommended, which will increase up to 300-400 mg/day in adolescence.

Human milk contains approximately 4 mg/100 ml, and cow milk around 12 mg/100 ml, and during complementary feeding the green vegetables represent the main magnesium source. It is an important component of the chlorophyll.

Hypomagnesemia is seen in some *refractary neonatal tetanies to the calcium therapies and in protein-calorie severe malnutrition,* in which neuromuscular manifestations are observed.

Iron (Fe)

Is the *main component* of *hemoglobin and myoglobin.* It is found in cytochromes as iron deposits in liver and spleen and in the whole body will circulate as combined, tied to a betaglobulin.

The iron quantity from birth is of 250-300 mg (75 mg/kg), and in adults 4 g (60 mg/kg), deposits that are sufficient until 4 months of age.

Dietary iron absorption is around 10%, but this percentage is influenced by many factors: the iron from spinach is absorbed around 1-2%, while the one from meat around 10-20%.

Iron requirement during the first 5 months is of *de* 6 mg/day and 10 mg/day until 1 year of age. In preterms, a daily intake of 2mg/day is recommended, starting from 2 months of life.

Human milk has *a low iron content,* but with *an absorption of 40%* due to the presence of lactase, lactoferrin, ascorbic acid and relatively decreased quantity of casein.

Start formulas used in the enriched formulas have a content of 0,7-0,14 mg/100 ml, and the continuation ones 0,7 -0,9 mg/100 ml. Therefore, the anemia during the first weeks of life (6-8 weeks) is caused by the morphofunctional particularities of the hematopoietic system of the newborn: erythrocyte life span is shorter, of the ones that contain fetal hemoglobin; the decrease of the hemoglobin quantity and erythroid progenitors, postnatal erytropoiesis decrease.

Zinc (Zn)

Is the *component* of *metalloenzymes.* It is deposited in different organs. The mature human milk has a low content of zinc, its quantity is bigger in colostrum. Some formulas, especially start formulas, are enriched with zinc up 200 - 300 μg/100ml.

Zn intake from human milk is of *2 mg/day*, sufficient quantity for the protective effect against enteropatic acrodermatitis. The presence of phytates in the organism decreases zinc absorption.

Zn deficiency is manifested as *anorexia and failure of growth.*

Iodine (I)

Is *absolutely necessary for thyroid hormone synthesis.*

Iodine requirements for preterms are of *30-40 mg/kg/day*, for a term newborn of 7-10 mg/kg/day, and adults 50-100 mg/day. The most important sources of iodine are aliments, especially seafood. The water is not iodine sufficient, that's why in endemic areas, alimentation must be supplemented.

Sulphur (S)

Has an important role in growth, being a component of cellular proteins. *Sulphur requirement* is between 0,5-1 g/day, being covered by aliments high in protein.

Vitamin requirements

Vitamins are *essential body elements*, being essential cofactors for metabolism and growth. They are classified as *liposoluble* (A, D, E, K) and *hydrosoluble* (group B and vitamin C).

Vitamin requirement is ensured by a balanced diet, but it varies with age and aliment composition.

Vitamin A (retinol)

The main function is the *synthesis of rhodopsin* in the retinal cone cells. It has a role in cellular membrane stability, stimulation of the messenger RNA, protein and glycoprotein synthesis, cellular growth, epithelial integrity, growth of bones and teeth, lyzozime secretion and immunitary defense.

The daily requirement is of 10 mg/kg/day (30 UI/kg/day) or 400 mg/day.

Hypovitaminosis A can determine *a decrease of the night vision,* and in severe formes *xerophtalmia (dry cornea).* It can appear after *prolonged parenteral alimentation with no vitamin supplementation, in the generalized malabsoption syndrome, chronic diarrheic diseases, bile duct obstruction, pancreatic, livel diseases of hypothyroidism.*

Hypercarotenemia is seen in the *congenital enzyme absence*, the enzyme that converts caroten into vitamin A and secondary in *conditions that interfere with this process* (liver diseases, hypothyroidism, diabetus mellitus) or by *prolonged use of carrot in the diet.* It manifests by the yellow color of the skin, the sclera is the exception.

Milk formulas for infants ensure an intake of 250 UI of vitamin A/100kcal. During the complementary feeding, the natural sources are represented by milk, egg, fish, liver.

Vitamin D

Is represents a *hormone vitamin, that is essential* for growth and the regulation of the phosphorus and calcium metabolism. It acts upon a lot of organs and systems:

- at the intestinal level *it favours the absorption of Ca and P;*
- at *bone level it mobilizes Ca,* as oposed to the action of parathormone; the increase of extracellular action is an essential condition for the deposit inside the bone matrix in the presence of phosphates;
- at *the urinary system level it favors the reabsorption of Ca;*
- *in the muscle it favors the synthesis of proteins,* contractions and formation of the ATP system by organic phosphate incorporation in the muscle cell;
- in the parathyroid it controls the synthesis of the parathormone.

The main source of vitamin D has its origin in the skin, where the 7-dehydrocholesterol is transformed in colecalcipherol under the direct action of UV light.

Human milk has a small amount of liposoluble vitamin D, but rickets appears rarely, due to the existence of a hydrosoluble (vitamin D sulphate) and *an optimum ratio of Ca/P.*

Cow milk, that contains small amounts of vitamin D and an inadequate ration of Ca/P is considered a rickets-inducing aliment.

The recommended vitamin D dose is of 800-1000 UI/day. No milk formulas enriched with vitamin D (40 mg/100 Kcal) cover the requirements, so that for the necessary climate conditions from our country, *a daily mandatory supplementation* is necessary until 1 year of age.

The adverse effects of vitamin D appear in different situation of hypervitaminosis D: weakness, digestive symptoms (inappetence, nausea, vomiting, constipation), polyuria, polydispsia, dehydration.

Biological signs are: *hypercalcemia* (16-17 mg%), *hyper-phosphatemia and hypercholesterolemia*. Secondary to hypercalcemia, the calcium depositing in the soft tissues is realized along with skeleton demineralisation.

The treatment of hypervitaminosis consists of suppression of the calcium intake from alimentation and administration of corticotherapy.

Vitamin E

It is considered essential for growth and development, its most important function is *cell protetion against oxidation substances.* It assures the integrity of polyunsaturated acids from the cell membrane structure; protection of vitamin A and ascorbic acid in the intestinal lumen and intracellular; stabilisation of biologic membranes.

Vitamin E is found in 2 groups of natural substances: tocopherols (a,b,g,d) and tocotrienols. The most active one is a-tocopherol.

The recommnended dose is 3 mg/dayduring the first 6 months of life, then 4 mg/day. In preterm newborns, during the first days of life, the vitamin E dose can be up to 15mg/day. Drug administration in a *preterm newborn* has a favorable effect in determining the diagnosis of *retinopathy of prematurity.*

Vitamin E deficit in preterms can lead to a form of *hemolytic anemia. The most important biologic effect is attributed to the antioxidant action.*

The deficit of vitamin E is frequently seen in:

- perturbation of the transplacentary transfer(seen in IUGR newborn);
- prematurity, due to the decreased supplies, the existence of malabsorption for lipids and by the rapid growth process which imposes high requirements;
- in the potassium and calcium malnutrition and in the malabsorption syndromes from cystic fibrosis, celiac disease, chronic cholestasis, bile cirrhosis;
- the use of milk formulas than hold large quantities of polyunsaturated fatty acids;
- oral treatment with Fe, along with vitamin E administration, determines the oxidative distruction of this one.

Natural sources of vitamin E are represented by plant oils (soy, sunflower).

Vitamin K

The essential function of vitamin K consists of *prothrombine activation*, inactive biologic protein, situated in the liver cell.

There are three important situation of avitaminosis K:

- newborns before intestinal colonisation with flora;
- malabsorption syndromes(including bile athresia);
- oral antibiotherapy with broad spectrum.

In newborns, the vitamin K deficit can produce *early hemorrhagic syndrome* due to the synthesis disorders of the liver coagulating factors. *Late hemorrhagic syndrome* appears after 10 days and up to 3 months and is caused by the prolonged antibiotic treatment or the malabsorption syndrome. The disorder is characterized by hemorrhage, predominantly intracranial.

Human milk has a small quantity of vitamin K and does not offer protection against the hemorrhagic syndrome. The infant soy milk formula is not supplemented with vitamin K and can lead to the same effects.

Hemorrhagic syndrome prophylaxis is done by parenteral administration of vitamin K to the newborn, in doses of 0,5-1 mg. In case of prolonged antibiotherapy, it is recommended that the dose should be repeated once a week.

Supradosage of phytomenadione favors hyperbilirubinemia, especially in preterm newborns that associate a G6PD deficit.

Vitamin B_1(thiamin)

It is the coenzyme of the decarboxilation processes. It acts in many forms:

- phosphorilated form - cocarboxylase;
- thiamine pyrophosphate - cofactor role in the enzymatic processes of the glucidic metabolism;
- thiamine triphosphate - in the physiologic processes of the CNS.

The requirements of vitamin B_1 are 0,3-0,7 mg/day (40mg/100 Kcal). It is found in the liver, meat and cereal germs.

Vitamin B_1 deficit appears in the poor dietary regime (decorticated rice), in case of low absorption (chronic diarrhea, severe liver diseases) and exaggerated consumption of vitamin B_1 (fever, hypercatabolism).

In severe deficiencies beriberi disease can occur, on a background of malnutrition.

Vitamin B_2 (riboflavin)

It is contained in the flavin-nucleotides, having a role of oxydoreductor. It is largely distributed in the alimentary sources (milk, vegetables, meat).*The recommended dose is 100 mg/100 Kcal.*

Vitamin B_6 (pyridoxine)

Vitamin ***B_6*** named as pyridoxine is implied in numerous metabolic processes, especially *protein metabolism*. It also intervenes in: conversion of tryptophan in nicotinic acid; transformation of linoleic acid in arachidonic acid; incorporation of Fe in the molecule of hemoglobin; it is necessary the glycogen metabolisation; the cellular and humoral mediated processes.

The vitamin B_6 is of 0,4 mg/day at 1 year of age and 2 mg/day at 18 years.

Nutritional deficiency is exceptional, pyridoxine is found in a lot of aliments. The deficit can be seen in:

- competitive inhibition (treatment with HIN, penicillin, hydralasine);
- malabsorption syndromes of chronic digestive disorders;
- pregnancy, infectious states, growth period.

Intrauterine deficiency of vitamin $B_6$is incriminated in the production of renal and nervous malformations incompatible with life.

Vitamin B_6 deficiency manifests by: *fatigue, apathy, irritability, hyposideremic hypochrome anemia, cutaneous lesions, glossitis.*

A prolonged deficit determines nevritis and *pyridoxine-dependent seizures, especially in newborns.*

Vitamin B_9 (folic acid)

Participate as a form of *coenzyme* in numerous metabolic processes. At cellular level, folates - in the presence of vitamin B_1 and ascorbic acid - are transformed in tetrahydrofolates, which participate in the DNA synthesis. It also participates in the synthesis of purinic and pyrimidinic bases, hemoglobin synthesis, maturation and regeneration of erythrocytes and protein synthesis.

RDR is *in infants of 30-65 mg/day, and in bigger children 40 mg/1000 Kcal*.

In human milk, the folates are about 35-45 mg/l, but their biodisponibility is supperior.

The adapted formulas or partially adapted ones have an appropriate content, while cow milk has the same content as human milk, but *the absorption is deficitary*. Goat milk has a

low content (below 10 mg/l). Excessive diet with goat milk determines a particular form of megalobrastic anemia.

Folic acid deficit is seen in: prematurity (insufficient reserves), protein-caloric malnutrition, parenteral alimentation, malabsorption syndrome, vitamin B_6 intermediary metabolism blockage, congenital enzymatic defects.

Vitamin B_{12} (cyancobalamin)

Has a similar structure to the porphyrinc ring. *It is an enzymatic cofactor* and has a role in *the mielination of the CNS.* For the absorption, it needs a glycoprotein that is secreted by the parietal gastric cells (intrinsic factor).

The vitam B_{12} deficiency is rarely seen in infants due to:

- congenital absence of the intrinsic factor;
- intestinal malabsorption;
- chronic diarrhea;
- prolonged treatment with neomycin, aspirin, tuberculostatics.

The deficiency of B_{12} leads to *pernicious anemia*.

Vitamin B_{12} requirement varies between 0,3 mg/day in infants and 3 mg/day in adolescents.

Vitamin C (ascorbic acid)

It has an *essential role* in the human body due to its multiple imprications in the metabolic processes:

- collagen and cholesterol synthesis;
- hydroxylation of the tryptophan, some steroid and norepinephrine;
- tyrozin catabolism;
- hematopoiesis process.

It protects certain vitamins such as: thiamine, riboflavin, folic acid and pantothenic acid.

The daily requirements of vitamin C are of 20-30 mg/day. *The main sources are of dietary origin* exclusively, generally represented by fruit (citrus fruits) and green vegetables.

The aliments that are *believed to induce scurvy* are: pasteurized cow milk, formula milk with no added vitamins, non-enriched essential flours.

Clinical manifestations of deficiency are: inappetence, fatigue, irritability, muscle hypotonia, low scholar efficiency.

CHAPTER II

PARENTERAL NUTRITION

It consists of the administration of nutritional principles necessary for an appropriate somatic and cerebral growth, endovenously, due to the incapacity of digestive tube use caused by immaturity and severe medical and surgical disorders.

Parenteral nutrition can be partial or total, complementary to enteral feeding and is frequently used in pediatrics, but especially in term and preterm newborns with severe disorders at birth.

Based on the present pathology and the anticipated duration of administration, parenteral nutrition can be done by peripheral or central line. The peripheral line is the easiest to use, especially if it is for 4-6 days and are needed glucose solutions of <12,5% concentrations, lipid emulsions that must cover the caloric and nutritional requirements. The peripheral line avoids complications, especially septic ones, but has a series of disadvantages when used for a long period of tine: limits the number of peripheral vessels, requires a high quantity of fluids, high risk of phlebitis and necrosis, ensures a lower caloric intake.

The central venous catheter can be also placed percutaneously or by venectomy, on the following vessels: umbilical vein, introduced in the inferior vena cava, jugular vein, subclavian vein and femural vein. The use of this way of perfusion is necessary when parenteral nutrition is for a long time, or when the peripheral veins are depleted, when the newborn needs several iv accesses or when a hyperosmolar solution, with higher than 12,5% glucose concentration are required for administration. The use of central venous catheter has the advantage of administering a large quantity of fluids, with high amounts of glucose, on a prolonged period of tine (over 3 weeks), but special measures must be taken for preventing complications: embolism, septis, thrombosis.

Indications

The major indications for total parenteral nutrition are:

1. respiratory distress syndrome;
2. bronchopulmonary dysplasia, with the incapacity to tolerate enteral feeds;
3. birth weight<1500 g; these newborns cannot be integrally supported by enteral nutrition, due to the gastrointestinal tract hypomotility and low gastric capacity;

4. severe gastrointestinal disorders, such as NEC;
5. liver failure;
6. digestion and absorption disorders – short bowel syndrome or refractary diarrhea; unspecific chronic diarrhea;
7. surgically corectable diseases (omphalocele, gastroschisis, esotracheal fistula, malrotation with volvulus).

Components of parenteral nutrition

As any other type of nutrition, parenteral nutrition must ensure the optimum intake of nutrients by which the organism must cover its losses and assure an optimal nutrient intake for growth using specific components: fluids, carbohydrates, electrolytes, proteins, lipids, vitamins, minerals.

Caloric intake

In parenteral nutrition, the caloric intake must be gradually increased so that it provides at least 100-110 cal/kg/day, which will progressively be replaced by enteral nutrition, by small quantities at first, as tolerated.

The caloric requirements are lower that the ones for enteral nutrition.

They must assure:

- the base metabolism,
- losses,
- thermoregulation,
- physical activity,
- dynamic specific action (synthesis processes),
- realize an adequate ponderal growth.

For preterms, the caloric requirements are higher than the ones of term newborns which must ensure, aside from the losses caused by the basal metabolism, minimum muscle activity, fecal losses and the caloric requirement for the stress caused by cold and thermoregulation. At the same time, the postnatal growth is accelerated, as a way to recover the statural and ponderal growth requires a higher caloric intake than the term newborns, up to **150-175 cal/kgc/day** (BPD or heart defects).

Fluids requirements

Establishing the fluid need in total parenteral nutrition, it must be held into accound that the indications of this type of nutrition are in most cases ELBW preterms, with associated pathology, or term newborns with severe disorders:

- ordinarily, it is started with 80-100 ml/kg/day;
- it can be gradually increased by 10 ml/kg/day (if there are no losses or abnormal growth increases or fluid restriction necessity) and up to 150-175 ml/kg/day;
- weight must be monitored at least once a day, at the same time, each day;
- newborns with birth weight<1000 g, during the first weeks of life, or newborns <1500 g in the first week of life, must be weighed twice per day;
- diuresis monitorization;
- the quantity of fluid administration must consider, firstly the caloric requirement and then the next factors: gestational age, postnatal age, associated pathology, the used heating system (incubator – 65 ml/kg/day, radiant heater– 180 ml/kg/day, the use of humidifier);
- the requirement care be increased by 10-20 ml/kg if the newborn benefits from phototherapy, if he is with fever (10-20 ml/kg/day for each Celsius degree over 38 temperature), hyperventilation (5-20 ml/kg/100 kcal/day) in a high humidity environment (humidity over 50%);
- preterms, based on their birth weight, have a different fluid requirement. Small preterms (ELBW and VLBW) will start with 40 -60 ml/kg/day and will gradually increase the intake to 140-150 ml/kg/day by the end of the first week, reaching 180-200 ml/kg by the end of the first month of life;
- in parenteral nutrition, the maximum amount of fluids tolerated by the newborn body is of 300 ml/kg;

Fluid restriction will be used for newborns with:

- ✓ bronchopulmonary dysplasia;
- ✓ patent ductus arteriosus;
- ✓ heart failure;
- ✓ kidney failure;
- ✓ respiratory distress syndrome;
- ✓ mechanical ventilation with humid atmosphere;

- ✓ a weight increase higher than 25 g/kg/day for these newborns, during the first days of life is more of an unwanted fluid restriction rather than an increase of the body mass.

Carbohydrate requirements

Starting from the fact that the main nutrients are the carbohydrates, these are early introduced, in gradually increased quantities, in different concentrations, depending on age and the used venous access:

- the carbohydrates used are dextrose and glucose - solution of 5%, 8% or 10%;
- the intake represents 50% of the total caloric needs and offers 3,4 kcal/g;
- the quantity is adapted at the end, based on the total calorie deduction of all other fluid and caloric intakes and from the total recommended fluids for the specific case;
- it can be started with quantities of 5-9 mg/kg/min via peripheral vein;
- the term newborn can receive variable quantities, based on his pathology, from 7-8 mg/kg/min to 10-14 mg/kg/min;
- the preterm tolerates small quantities of glucose 6-7 mg/kg/min, concentrations up to 10%, the risk of hyperglycemia is high.
- glucose administration, in doses of 7 mg/kg/min can ensure the high caloric requirement of this category of newborns;
- a higher than 7 mg/kg/min rate is associated with fat synthesis, and the higher dose of 20 mg/kg/min can lead to hepatic steatosis;
- the used glucose solution can be variable, depending on tolerance, access, gestational age, birth weight;
- on a peripheral vein, the maximum concentration is of 12,5% glucose.
- small preterm (< 1000 g) will start with 5% solutions and the bigger ones with 10%.
- Concentration increases will be done gradually, by 0,5-1%/day, under the strict glycemia control (<120 mg% - the glucose concentration can be increased, between 120 and 180 mg%, the same glucose concentration will be maintained and >180 mg% the glucose concentration will be decreased).

Protein requirements

- the protein intake represents 12-15% of calories; it is known that 1 g of proteins provides 4 cal;
- the used proteins from parenteral nutrition favor normal amino acid concentrations, such as: glycine, thyrozin, histidine, glutamic and aspartic acid and small quantities of phenylalanine, methionine.
- the cysteine quantity is sufficient for the small gestational age newborn - the enzyme cystathionine, that converts methionine into cysteine is absent or present in small amounts in this category of newborns;
- protein hydrolysates have the disadvantage that 50% of amino acids are found as peptides with hard metabolisation and risk of acidosis, azotemia and hyperaminoacidemia;
- all sources of proteins can determine a rise of serum transaminases of direct bilirubin, without the need of stopping the parenteral nutrition;
- the initially administered quantity is of 0,5 g/kg/day;
- it is increased by 0,5 g/kg/day, each day until the maximum admitted dose that covers growth requirements;
- protein requirement: 2-2,5 g/kg/day - term newborn, with progressive addition, from the first or second day;
- for preterms, the protein requirements are 3-3,5 g/kg/day.

Lipid requirement

- the lipids used in parenteral nutrition have the most caloric density of all components;
- the calories intake is of 35-40% of the total intake, 1g of lipids delivers 9 cal, based on the used solution: 10% -1,1 kcal/ml, 20% - 2 kcal/ml
- the main essential fatty acids found in this emulsion are: linoleic (54%), oleic (26%), palmitic (9%) and linoleic (8%);
- the essential fatty acids ensure 4-10% of the daily caloric needs;
- the deficit of essential fatty acids is manifested as: stationary ponderal curve, thrombocytopenia, thin and translucent skin, slow wound healing;

- lipid adding to the parenteral nutrition is done gradually: the recommended initiation dose is of 0,5 g/kg/day Intralipid 20%; the dose is increased by 0,5 g/kg/day, every day until a maximum dose of 3 g/kg/day.
- Factors that influence the lipid requirements are represented by the value of serum bilirubin (between 8-10 mg %) and serum albumin value (between 2, 5-3 g%), when a reduction of the dosage is recommended, down to 0,5-1 g /kg/day.

Complications of hypertriglyceridemia are:

- iv lipid deposits in the reticuloendothelial system (RES) and the possible blockage of the RES function;
- the adverse effects upon the oxygen diffusion capacity from the lungs;
- erythrocyte increasing and thrombocyte aggregation;
- competition between free fatty acids and bilirubin for the albumin binding sites;
- the dose is reduced or interrupted during acute sepsis, respiratory distress syndrome, thrombocytopenia and severe hyperbilirubinemia (close to the limit level). A small dose of Intralipid can be administered in these situations, toprovide essential fatty acids, as long as the serum triglyceride level is <100 mg/dl.

Electrolytes

Essential electrolytes, provided by the parenteral nutrition solutions must cover the growth intake as well as the eventual losses but, the provided quantity must not exceed (along with proteins) the maximum osmolarity of 800 mOsm/l.

The essential electrolytes that we supply and individualy monitor are:

Sodium

- the main extracellular ion, 80% of it is metabolically disponible, the rest is found in bones;
- the normal requirements are 3 mEq/kg/day;
- very small infants have a higher requirement due to deficient tubular function: up to 8-10 mEq/kg/day;
- congestive heart failure, kidney failure or chronic therapy with diuretics, because they need careful monitoring and particularity of Na intake.

Potassium

- it is located inside the cell where it is the main cation (75%);
- the serum concentration is highly influenced by changes in the acid-base balance;
- it is important in the assimilation of glucose and synthesis of glycogen by other cells; hypoK can determine glycosuria despite of the fact that insulin is normally secreted;
- the normal intake of K is of 2 mEq/kg/day.

Chlorine

- is an extracellular anion;
- the main effect of its excess or shortage is manifested upon the acid-base balance;
- the normal intake of Cl is 2-6 mEq/kg/day.

Calcium

- almost all body Ca is located inside the bones;
- Ca is administered as Ca gluconate 10%;
- usual dose - 2 ml/kg/day for term newborns and 4 ml/kg/day in preterms;
- the dose can be increased if diuretics are administered, in case of osteopenia, newborns with severe asphyxia or newborn from diabetic mothers.

Phosphorus

- it has an important role in human metabolism;
- it is a vital substrate for bones, is involved in energy transfer, transport and eliberation of oxygen, it influences the leukocyte fagocitosis and pathogenic resistance;
- usual dose - 1mEq/kg/day, delivered as K posphate;
- large quantities of phosphorus can be necessary for children with prolonged parenteral nutrition that develop osteopenia and/or fractures.

Ratio Ca/P

- the targetted ratio, based on weight, during parenteral nutrition is 1,7;
- a normal ratio leads to the optimal bone mineralization;
- a decreased Ca/P ratio can lead to hypocalcemia, increased secretion of PTH (which leads to urinary phosphate loss), osteopenia.

Magnesium

- 60% is firmly fixated in bones and the rest in mostly intracellular;
- usual dose - 0,5 mEq/kg/day.

Microelements

Their introduction is recommended in the nutrition solution for the maturization of the cellular enzymatic system.

- **Chrome** is necessary for glucose use; the recommended dose is 0,2 mcg/kg in term newborns and up to 5 mcg/kg in children;
- **Copper** deficiency is seen in: hyporchomic anemia, leukopenia, osteopenia. The recommended dose is 20 mcg/kg in newborns and up to maximum 300 mcg/kg in children; excessive administration leads to hepatic cirrhosis;
- **Selenium** is essential with an antioxidant role; its deificit leads to hair color change, of the skin, macrocitosis, miositis, cardiomiopathy. The recommended dose is of 0,8 -2 mcg/kg in newborns and to a maximum of 30 mcg/kg in children;
- **Magnesiun** is important for gluconeogenesis enzymes and production of mucopolysaccharides; tonic potential onto the nervous cell. The recommended dose is of 10 mg/kg.

Vitamins

The intake of vitamins in preterm newborns or term newborns is done by adding vitamins to the solution for parenteral nutrition. These solutions must contain all vitamins: Biotin, Dexapanthenol, Folic acid, Niacin, Riboflavin, Thiamine, Vitamin A, B6, B12, C, D, E, K.

These are administered according to the requirements for kg/day.

The complications of total parenteral nutrition

- liver diseases, usually after 2 weeks of parenteral nutrition;
- hepatomegaly;
- colestasis (high direct bilirubin);
- abnormal hepatic enzymes; the exact etiology of this hepatic disease is not known;
- hyper- or hypoglycemia;
- electrolytic;

- azotemia;
- acidosis;
- hyperammonemia;
- hyperTG;
- excesses and deficits of vitamins;
- osteopenia;
- pathologic fractures;
- sepsis;
- air embolism;
- catheter embolism;
- catheter thrombosis;
- thrombocytopenia;
- abnormal position of the catheter;
- SVC or right atrium calcifications;
- prolonged parenteral nutrition can cause a decrease of the pancreatic exocrine secretion, decrease of the parietal cell mass and intestinal mucose atrophy.

Next, we will present a parenteral nutrition scheme:

1. first day of life: 60-90 ml glucose 10% solution, which can be increased until day 3 with up to 100-125 ml/kg/day.
2. from the 2nd and 3rd day of life, electrolytes are added;
3. from day 3, if enteral feeds are not possible, the glucose solution will be completed by proteins;
4. after the first week, Intralipid will be added (if IB<8mg% or IB<5mg% for preterms <1000g).

It is started with 15 ml/kg/day, they are increased by 5ml/kg/day up to a maximum of 40 ml/kg/day.

Parenteral nutrition, the one that ensures the parenteral and growth requirements, needs to cover an intake of 12,5 g/kg/day of carbohydrates 2,25 g/kg/day of proteins and 4 g/kg/day of lipids for a fluid intake of 165 ml/kg/day.

Parenteral nutrition requires careful monitoring of the following parameters:

- weight;
- length and head circumference;
- glycemia, azotemia, ammoniemia;
- electrolytes and daily pH during the first 4 days, then 2 times per week;
- calcemia, phosphatemia, Mh, Ht - 2 days per week;
- transaminases, IB and proteins - weekly;
- urine exam (density, glucose, ketonic bodies and volume) daily;
- if Intralipid is administered, the following will be determined daily: lipemia and weekly: thrombocytes, leukocytes, erythrocites, tryglycerides and cholesterol.

CHAPTER III

BREASTFEEDING

Breastfeeding represents the alimentation of a newborn and infant using breast milk for the first 6 months of life. It is the ideal aliment of all categories of newborns and infants because human milk is perfectly adapted to the nutritional needs of infants, it is an aliment with high biological value, including enzymes, antibodies, vitamins and minerals.

Breastfeeding advantages:

1. assuring a balanced nutritional diet;
2. automatic adaption of the infant's needs;
3. offers protection against infection and allergies;
4. protective role against necrotising enterocolitis;
5. important economical implications (free and easy to reach);
6. contraceptive effect (lactation amenorrhea), which allows the spacing of pregnancies up to an optimal interval of 2 years;
7. anti-carcinomatous action (prevents the apparition of breast cancer in the women that breastfeed);
8. protective role against NEC;
9. passive immunity transfer;
10. best protection against: marasmus, obesity, tetany, infections, diabetes;
11. has growth modulators (epidermal growth factor, nerve growth factor);
12. the breastfed infant's intestinal flora has bacillus bifidus, which produces lactic and acetic acid, which diminishes the pH of stools and increases infection resistance.

Composition of human milk

The composition of human milk depends upon *the lactation stages, preterm birth, mother's age, beginning or ending of a feeding, milk requirement,* as well as individual maternal factors. Of all these, the most important one is *the lactation stage.*

Based on these, **HM can be of 3 types**(lactation stages):

- **Colostrum**

  Is secreted during the first 5 days after birth - 10-100 ml/day. Compared to the mature milk, the colostrum is thicker, has a high density and is rich in proteins and mineral salts, poor in lactose, lipids and some hydrosoluble vitamins. It is richer in fat-soluble vitamins and immunoglobulins. Due to the high content of mineral salts has slight laxative properties, favoring meconium elimination. Although it contains large quantities of oligoelements and minerals (mostly zinc), it is well tolerated during neonatal period of immature kidney. Its caloric value is of 520-570 cal/l.

- **Transitional milk**

  Is secreted between day 6 and 10; it has a composition of constant biochemical and immunologic change: the quantity of protein and minerals decreases, while lactose concentration and vitamins from group B increase.

- **Mature human milk**

  It has a constant concentration on the whole lactation period, with medium variations (**table 17**).

Table 17. Composition of human milk compared to cow milk (g/l)

Composition	Human milk	Cow milk
Proteins (g/l)	9	35
Carbohydrates (g/l)	70	50
Lipids (g/l)	40	35
Minerals (g/l)	2,5	7,5
Caloric value (cal/l)	690	660

Proteins

Are represented by casein (40%) and lactoserum proteins (60%). The balance *casein/lactoserum proteins* is subunitary *40/*60; human milk is an "albumine" type of milk. The supramatured milk has a balance of 50/50, compared to cow milk, where the balance is 90/10.

Casein

- precipitates at acid pH;
- is formed of myceliums that contain calcium and phosphorus; is easy to digest;
- holds a large branched amino acid proportion (leucin, valine);
- holds a small aromatic amino acid proportion (phenylalanine, tyrosine);

- together with BSSL – bile-salt stimulated lipase – has an important hormonal biologic, enzymatic action and hormone-like substances;
- the balance *metionine/cysteine=1*; this is of great importance for term and preterm newborns, which lack the cystathionine enzyme for the transformation of methionine into cysteine.

Lactoserum proteins

- *alfa-lactalbumin* is predominant and intervenes in the lactose enzymatic synthesis;
- *beta-lactoglobulin*, the allergy protein of cow milk is absent in human milk.

Free amino acids

- *total nitrogen* of HM is less than in cow milk, represented by proteic nitrogen (casein and lactoserum proteins);
- *non-proteic nitrogen*, 20-30% of the whole nitrogen quantity varies with the mother's nutritional state. It is represented by free amino acids: glutamic acid and taurine. The glutamic acid is an energy source for the tricarboxylic acids, for erythrocites. Taurine improves lipid absorption, is a neurotransmitter and neuromodulator, favors the intestinal colonisation with bacilus bifidus.

Carbohydrates

Lactose

- *is the main carbohydrate* from milk; is found in proportion of 6 - 7 g/100 ml;
- is composed of *a molecule of glucose and one of galacose*, being the only source of galactose.
- has *an energetic value* due to the glucose composition;
- it has a role in *the stimulation of intestinal lactase;*
- represents *the only source of galactose* (major role in the mielinisation of the CNS and the glucuronoconjugation processes);
- *favors* the metabolisation processes of *calcium and phosphorus;*
- by fermentation, it allows *an acid intestinal pH*, an optimal environment for the development of the microflora.

Nitrogen oligosaccharides

- are represented by 9 structures;
- in quantity of 10 g/l – energy source;
- compositional sources intervene in the formation of sphyngomyelin and gangliosides.

Lipids

- in quantity of 3-6 g/l, ensure *55%* of the caloric intake;
- the ratio *saturated fatty acids/unsaturated fatty acids=48/52* compared to 65/35 for cow milk;
- *linoleic acid* represents 8-10 % of total lipids;
- are found in a quantity of ≈ 40 g/l, are represented by *tryglycerides* (98-99%), while cholesterol, cholesterol esters and phospholipids represent 1-2%;
- the tryglycerides are composed of poliunsaturated fatty acids and saturated fatty acids, in almost equal proportions (in cow milk - saturated fatty acids are more abundant);
- *essential fatty acids* (linoleic and linolenic) represent 10-12% of the total fatty acids of HM. The *linoleic* acid is in a quantity of approximately 5 times bigger in human milk and intervenes in the formation of arachidonic acid and maturation of the CNS. Long chain polyunsaturated fatty acids are found in a concentration of 25-42 g/100 ml, which represents 0,76-1,62% of the total milk quantity. These are the precursors of structural lipids, prostaglandins, leukotrienes and thromboxans;
- *the cholesterol* from mature human milk (10-20 mg/100 ml) is an important component of cellular membranes, sexual hormones, vitamin D, having an essential role in the mielinisation of the CNS;
- human milk lipids are better absorbed the the ones from cow milk;
- *the composition and the level of lipids from HM variates during a day, during the same breastfeed and during the lactation period.* It is higher by the end of breastfeeds, contributing to the realization of the "repletion sensation".

Minerals

The electrolyte composition of HM variates with the lactation moment (is higher in colostrum); the small quantity of minerals 2-2,5 g/l, 3-4 times smaller than from cow milk realizes a small osmotic charge - of 80 mOsm/l, compared to 300 mOsm/l,the value from cow milk.

- ✓ ***Na*** *and* ***Cl*** are present as 10-12 mg%; therefore, the overcharge of the kidney function is avoided - immature in newborns.

- ✓ ***Calcium and phosphorus,*** present in small quantities in human milk (Ca approximately 3-4 times and P 6-7 times), but the ratio Ca/P = 2 in human milk, optimal for a good absorption (in cow milk = 1,2).
- ✓ ***Fe*** - in small quantity in human milk, its biodisponibility is bigger in cow milk, regarding both intestinal absorption as well as its incorporation in the hemoglobin molecules.
- ✓ ***Cu***- is present in colostrum in large amounts and less in mature HM and decreases as breastfeeding is prolonges; the double quantity compared to cow milk would explain the reduced frequency of anemia due to dietary origin.
- ✓ ***Zn*** - is found in high quantity in colostrum and in smaller, similar quantities in cow milk and mature HM, but the presence of a ligand favors its absorption and explains the exclusive role of human milk in prevention and treatment of enteropathic acrodermatitis.

Ohter minerals present in human milk, but in smaller quantities are: *I, Mg, Se, Mn, Mo.*

The reduced minerals and proteins from HM, determine *a reduced osmotic charge of breastfed* infants. In opposition, integral cow milk nutrition can lead to hyperosmolarity and hypernatremia.

Vitamins

Human milk contains both *liposoluble and hydrosoluble vitamins,* in variable amounts, in relation to maternal intake.

- ✓ ***Vitamin A***, 1000 UI/l, *sufficient* for protecting cutaneous infections;
- ✓ ***Vitamin D***, 22 UI/l, quantity considered *insufficient*, inferior to the requirements of the newborn (800-1000 UI/zi);
- ✓ ***Vitamin K*** is present in smaller quantity in colostrum, and is *insufficient to the needs of newborns,* that is why the *supplementation is needed,* with 0,5-1 mg at birth, for prevention the neonatal hemorrhagic disease;
- ✓ ***Vitamin E*** is present in large quantities in human milk than in cow milk; *it is sufficient* for term newborns, but requires supplementation in case of infants with small birth weight;
- ✓ ***Vitamins of group B,*** are generally *insufficient* in HM;
- ✓ ***Vitamin C*** is present in quantities of 50 mg/l *and covers the infant requirements* if the mother is a non-smoker and has a correct diet.

The small amount of minerals and proteins from HM determine a reduced osmotic charge in the breastfed infants. As opposed, the alimentation with integral cow milk will lead to hyperosmolarity and hypernatremia.

Table 18. Essential and conditioned essential amino acids form human milk

For 100 kJ1		**For 100 kcal**
Cystidine	9	38
Hystidine	10	40
Isoleucin	22	90
Leucin	40	166
Lysine	27	113
Methionin	5	23
Phenylalanin	20	83
Treonin	18	77
Tryptophan	8	32
Tyrosine	18	76
Valine	21	88

Table 19. Composition of mature human milk

Energetic value	65-67 kcal/100 ml
Proteins	0,85 g – 0,90 /100 ml; 1,27 g/100 kcal
Lipids	3,8 -4,2 g/100 ml
Carbohydrates	6,9-7,2 g/100 ml
Lactose	55-70 g/l;8,2-10,4 g/100 kcal
Sodium	15 mg/100 ml;0,87=0,45 mEq/100 kcal
Potassium	55 mg/100 ml;1,65=0,27 mEq/100kcal
Chlorine	33 mg/100 ml;1.68=0.69 mEq/100kcal
Vitamin A	150-1100 ug/l;22-160 ug/100 kcal
Vitamin D	4-110 UI/l; 0.015-0.4 ug/100 kcal
Vitamin E	2-5 mg/l(0.5-1.6 mg a-TE/g PUFA)
Vitamin K	0.6-10 ug/l
Vitamin C	30-100 mg/L; 4.5-15 mg /100 kcal
Vitamin B1 (thiamine)	30-35 ug/100 kcal
Vitamin B2 (riboflavin)	60-90 ug/100kcal
Vitamin B3 (niacin)	1100-2300ug/L; 164-343 ug/100kcal
Vitamin B5 (pantothenic acid)	2-2.5 mg/l; 269-552ug/100kcal
Vitamin B6 (pyridoxine)	70-310 ug/l; 10.4-46.3 ug/100kcal
Vitamin B12 (cyanocobalamin)	0.16-0.64 ug/l; 0.02-0.09ug/100kcal
Folic acid	24-141ug/l;3.8-20.9 ug/100 kcal
Biotin	5-9ug/l; 0.75-1.3 ug/100kcal
Calcium	194-268 mg/l; 29-40 mg/100kcal
Phosphorus	107-164 mg/l; 16-24 mg /100 kcal
Ratio calcium:phosphorus	2:1
Iron	0.02-0.04 mg /100 ml
Magnesium	31.4-35.7mg/l; 4.8-5.5 mg/100kcal
Copper	220 ug/l; 33 ug/100kcal
Zinc	0.5-4.7 mg/l
Manganese	3.5 ug/l
Fluorine	0.007-0.011 mg/l
Iodine	10-20ug/l – peste 300 ug/13
Selenium	15-17ug/l

Human milk enzymes

In human milk are found 20 enzymes with role in digestion and antiinfectious defense. *The most important ones are:*

1. ***lysozyme*** or muramidase, bactericide substance produced by the macrophages;
2. ***lipases***, stimulated by the bile salts, with part in milk tryglyceride digestion;
3. ***antitrypsin;***
4. ***alpha-amilase***, catalyzes starch hydrolysis into maltose;
5. ***galactosyltransferase***, intervenes lactose synthesis, binds Mn, Zn, Ca and Co;
6. ***lactoperoxidase*** produced by macrophages has a bactericidal action against E.coli and salmonella;
7. ***ribonucleases*** catalyse the action of RNA;
8. ***xanthine oxidase*** takes part in the purine, pyrimidine and aldehyde oxidation;
9. ***produces protease inhibitors*** that have a high activity in the colostrum, they catalyse the protein hydrolisis.

Antiinfectious protection factors

Cellular factors

The Donne corpuscles are large macrophages that protect against NEC; they transport and eliberate secretory IgA, the C_3 and C_4 fractions of the complement, lactoferrin and lysozyme; the polimorphonuclear neutrophils, *large and small from T and B line lymphocytes*.

Immunoglobulins

In human milk, the secretory type *IgA prevails* (IgAs), which compensates the transient autonomous secretion of Ig by the intestinal submucouse cells in newborns and infants. *IgAs* is found *in a large proportion in colostrum* (20-50 mg/ml) and *decreases at* 1 mg/ml *after day 6 of life.*

The deficit of secretory IgA from human milk favors the apparition of respiratory infections and chronic diarrhea. IgM is found in high amounts in colostrum (150-170 mg/ml) compared to mature milk (30-60 mg/l). IgG is present in very small amounts.

Lactoferrin

Is a whey *glycoprotein*with bacteriostatic and even bactericide role, which is found in high amounts in human milk; it is considered an important growth factor. It has also been identified in intestinal and pancreatic juice, even in tears and sweat.

Its concentration in the colostrum is of 3,5-4 mg/ml, and in the mature HM 1,7 mg/ml. Lactoferrin *reversibly ties two molecules of trivalent iron* from HM, which are then secreted in the gastric acid; in the jejunum, it ties again iron which is later released to the receptors from the brush border level and so it is taken before it can reach pathogenic microorganisms. In the presence of anti-E. coli antibodies and bicarbonate, lactoferrin has *a strong bacteriostatic role by the deformation of transport RNA.*

Lysozyme *(muramidase)*

It is found in *HM* in a *3000 times higher concentration than cow milk.* It *splits proteoglycans* from the bacterial wall (*direct bactericide effect)* and acts as an antimicrobial *associated with complement and secretory IgA (direct bactericide effect).* It appears lysozyme has a bifidogenic effect.

Lactoperoxidase

Has a *bactericidal action against streptococcus, E. coli and Salmonella.*

Fractions C3 and C4 of the complement

It favors *phagocyte chemotaxis and* intracellular including of different particles.

Antistaphylococcal factor

It is represented by an unsaturated fatty acid that inhibits the growth of S. aureus.

Bifidus factors

- are represented by *oligosaccharides, polisaccharides that contain N-acetylglucosamines, glycopeptides and glycoproteins.*
- *they favour the growth of bifidus lactobacillus* inside the colon of breastfed infants, as a role in vitamin B and K synthesis.
- also, they *acidify the intestinal medium* by the production of lactic and acetic acid, having a role in growth inhibit of pathogenic bacretia (inhibits the growth of E. coli, shigella and yeast).
- it favors the absoption of *iron, calcium, lipids and vitamin D.*
- *influence the nitrogen retention.*

Lipase represents a lethal factor for lamblia.

Antiviral nonspecific role substances

Are represented by non-immunoglobulinic macromolecules, $\square_2$-macroglobulin-like, ribonuclease, hemagglutinin inhibitors, milk-cells (with a role in the production of inter-pherone and lymphokins, IgA); a lipidic factor against herpes simplex has been described.

Growth modulators from human milk

Are represented by the following substances:

1. ***Epidermal growth factor***

   Stimulates the growth and differentiation of pulmonary and gastrointestinal epitheliums; has a role in pH regulation.

2. ***Neuronal growth factor***

   It is essential for the development of intestinal sympathetic nervous system and maturation of the sensitive neurons.

3. ***Insulin-like growth factors (IGF-1*)**

   Are the cellular "effectors" of STH by somatomedine's help.

4. ***Human milk growth factors (HMGF I, II and III)***

5. ***Lymphocyte B stimulating factor***

   Has a role in the prolipheration of B lymphocytes and Ig production.

6. ***Lipase***

   Is stimulated by the bile salts with a role in the destruction of Giardia lamblia.

7. ***Sulfate hydroxylase***

   Is a substance that participates in the IgAs synthesis.

8. ***Taurine***

   Has a role in the prolipheration of the retinal cells and the olphactory bulb. It is found in high concentrations in tissues that are developing, especially during the *rapid cellular prolipheration periods.*

9. ***Z growth factor (bifidum factor).***

Other human milk substances

STH, insulin, somatostatin, relaxin, calcitonin, neurotensin, GRS, prolactin, TRH, TSH, T_3, T_4, ovary steroids, adrenals, erythropoietin.

In human milk there are all circulatory maternal hormones present; their concentration is variable with lactation stage. Prolactin decreases in time, and T_3 and T_4 level increase. Their role in infants and newborns is not known.

Prostaglandins E_2 and F_2.

Exogenous substances excreted in milk (especially drugs).

Physiology of lactation

The mammary glands milk secretion begins during pregnancy and is due to estrogens and progesterone. After placental elimination, which has an inhibitory role upon lactation, the two main reflexes intervene: secretion reflex and milk ejection reflex.

a. *Secretion reflex or prolactinic reflex*

Is triggered by nipple stimulation, by suction, which induces, by a neurohormonal reflex, the production of prolactin in the anterior pituitary gland; this hormone stimulates and maintains milk secretion.

As long as the sucking is more complete and vigurous, the more milk is secreted.

b. *Milk ejection reflex (let-down reflex)*

It is a psycho-somatic reflex on which depends the act of breastfeeding. The reflex arc runs from the nipple, to the posterior pituitary gland, where it stimulates the production of oxytocin. This passes into the circulation and determines cell concentration from the glandular alveoli.

By this mechanism, the milk reached the galactophoric ducts, then into larger ducts and cysterns. This process continues during breastfeeds, the empty mammary gland can continue its secretion under the influence of prolactin.

The mother's anxiety or confidence can influence the ejection reflex, which can be inhibited or stimulated. After two weeks of lactation (crucial for the success of breastfeeding), the mammary gland gains autonomy (mammary automatism phase). Emotional tension, stress, inhibits the reflex, decreases the local blood flow leading to lactation insufficiency.

The factors that influence lactic secretion

a) Before birth

1. *mother's information on the importance of breastfeeding and techniques;*
2. *stimulation* on nipple formation during the last months of pregnancy (by rubbing with a rough towel);
3. *periodic nipple expression* - colostrum secretion.

b) At birth

1. avoiding anesthetics during labor;
2. should be avoided: pain, fatigue, mother's anxiety, routine episiotomy.

c) After birth

1. the integrity of the esophagus will be checked with an aspiration tube, for discovering an eventual atresia;
2. early initiation of breastfeeds;
3. complete breast emptying during each alimentation;
4. avoiding stress, anxiety during lactation period;
5. the mother should have a balanced diet with a caloric supplementation of 700-800 Kcal/day, fluid intake (tea, water, milk - maximum of 500 ml/day);
6. alcoholic drinks, coffee, tobacco, narcotics use is strictly forbidden.

Contraindications of breastfeeding

a) temporary - mother related temporary contraindications:

- ✓ acute infections, with fever, treated with antibiotics;
- ✓ bloody nipple fissures;
- ✓ mastitis;
- ✓ umbilicated nipples.

- infant related temporary contraindications:
  - ✓ hyperbilirubinemie due to inhibited conjugators: pregnane, 3-alpha,20-beta-diol.

b) permanent

- mother related permanent contraindications:
  - ✓ septicemia, nephritis, eclampsia;
  - ✓ active tuberculosis;
  - ✓ HIV infection;
  - ✓ malaria;
  - ✓ renal or heart failure;
  - ✓ neoplastic disease, cachexia, psychiatric disorders;
  - ✓ multiple sclerosis;
  - ✓ pregnancy >20 weeks of gestation;
  - ✓ imbalanced maternal diabetes;
  - ✓ thyrotoxicosis;
  - ✓ oral birth control;
  - ✓ antineoplastics, diazepam, litium.
- infant related permanend contraindications:
  - ✓ galactosemia, phenilketonuria;
  - ✓ congenital lactose intolerance.

Drugs excreted in breast milk

A lot of chemical substances are passed on through milk to the newborn; the transfer rate is usually 1% of the daily dose received by the mother. The risk of accumulation in the newborn system is high, due to the fact that their weight is 15-20 times smaller that their mother's, the metabolism is slower, with reduced desintoxication possibilities (renal immaturity, bilirubin competition, cholestasis).

This depends on many factors:

1. *drug binding to plasmatic proteins:* only free fractions, not binded, can be easily excreted in lactic secretion;
2. *drug's blood concentration; the higher the concentration, the higher the excretion (immediately after breastfeeds);*
3. *transmammary transfer mechanisms;*
4. *cumulative effect by fetal and transnatal transfer.*

A drug's action, that passes the placenta during pregnancy (long-term medication) is continued after birth as well due to slow desintoxication and tissular drug fixation.

If the drug is continued after birth, *summation phenomenon can appear:* hypertonia, sleepiness, respiratory or alimentary difficulties. This type of manifestations have been described in *antiepileptic drug administration* (phenobarbital, benzodiazepines, phenytoin); their administration requires strict supervision and sometimes weaning.

Some *administered drugs* to the mother can induce certain *deficiencies in the newborn* by creating digestive absorption disturbance mechanismsin mothers:

- digestive chelators such as paraffin oil or cholestyramine can block liposoluble vitamin absorption, leading to hemorrhagic manifestations (vitamin K deficiency) or rickets (vitamin D) in the breastfed infant.
- antiepileptics administered to the mother induce vitamin D deficiency or K by enzymatic induction.

Neonatal jaundice can be aggravated by some drugs with different mechanisms:

1. competition for free bilirubin in the fixation locus on albumin (sulfonamides);
2. aggravation of normal hemolysis (vit K, antioxidant agents).

Some of the medication administered to the mother and tranfered in milk act upon *normal echology of the digestive tube,* leading to normal saprophit microbe balance alteration and selection of resistant germs, eventually pathogens (prolonged administration, high dosage).

- Cloramphenicol - for the apparition of "gray baby syndrome" the concentration is too low; these is a possibility of medullary depression.
- Tetracyclins - dentition discoloration; perturbance of calcium absorption.
- Nalidixic acid - hemolytic anemia, acidosis, hemolysis.
- Aspirin and salicylates -hemorrhagic risk, especially in newborns.

CHAPTER IV

ARTIFICIAL FEEDING

Artificial feeding represents the infant's nutrition for the *first 4-6 months* of life, using artificial milk formulas or cow milk.

The differences between mother's own milk and cow milk are numerous and extremely important; the unmodified cow milk is not recommended for an infant's normal growth and development.

Because artificial milk is obtained from cow milk by quality and quantity modifications of the composition, all references to milk formulas report to the cow milk composition.

Cow milk composition (CM) compared to human milk (HM)

CM has a hydric content of 87,5% and dry substance 12,5%.

CM proteins

- ✓ high quantity - 3,4 g/100 ml, 3 times higher than in HM (1-1,5):
- ✓ *proteic excess* is transformed in the liver into urea, glucose, lipids and acids (sulphuric acid), with possible liver hypertrophy by exhaustion;
- ✓ *the excretion* of high osmotic charge and urine acidity can affect the immature kidney of the artificially fed infant;
- ✓ *the balance between casein* (90) and *lactoserum proteins* (10) is over the unit, CM has 6 times more casein than HM;
- ✓ *the casein from CM* precipitates in high vials, is hard to digest, *along with slow gastric evacuation and delayed intestinal transit;*
- ✓ the cazein from CM is high in proline and lacks cysteine, *has a high content or aromatic and branched; these are incompletely metabolized by the infant;*
- ✓ out of the lactoserum proteins, highly prevalent is *β-lactoglobulin*, an allergenic protein (strong antigenic fraction) that is involved in the respiratory allergy in infants, rashes, digestive hemorrhages, abdominal cramps or even sudden death syndrome;
- ✓ *lactoferrin* is present in small quantities, *favoring the apparition of iron deficiency anemia;*
- ✓ *imunoglobulins* from the CM are *ruined* by proteolytic enzymes;

- ✓ *unabsorbed proteins* from CM favor *the development* of a highly putrefaction flora, rich in E.coli, at the colon level;
- ✓ *the effects* of protein excess are: *hypertone dehidration, hyperammonemia, metabolic acidosis and nitrogen retention.*

Carbohydrates from cow milk

- ✓ are in smaller quantity than in human milk, assuring a less caloric intake (29%);
- ✓ the lactose from cow milk is around 4,5-5%, and in HM 6,5-7%;
- ✓ cow milk has 2 times less galactose, which takes part in the mielination processes and in the galactocerebrosides synthesis.

Lipids from cow milk

- ✓ are, in general, *in similar quantity with those from human milk*, ensuring 40-50% of the total caloric value;
- ✓ *the main lipids from* cow milk and human milk are *tryglycerides, oleic acid, palmitic and stearic acid;* but human milk has twice as more absorbable oleic acid than cow milk;
- ✓ *are inferior by quality* by the high amount of saturated fatty acids content (70-75% of the total of fatty acids);
- ✓ the low percentage of polyunsaturated fatty acids (20%) explains the reduction of the absorption coefficient of fats from cow milk - up to 80-85%;
- ✓ *cow milk lipids* can lead to *steatorrhea and neonatal hypocalcemia* (more frequent in preterm neonates), the apparition of *rickets and hypercholesterolemia.*

Minerals from cow milk

- ✓ are *3 times more present* (7,5 g/l) than in HM, out of which sodium is of 23 mmol/l.
- ✓ along with proteins, it competes in the realisation of *a high osmolarity*, and it can overcome the renal excretion capacity of the newborn and small infant;
- ✓ *iron* is present as 0,5 g/l, *below the infant's requirements.* Its absorption is diminished by the protein excess from cow milk;
- ✓ *the balance Ca/P is inadequate* for calcium absorption;
- ✓ *minerals excess* can lead to: *hyperosmolarity, sudden death syndrome, neonatal hypocalcemia.*

Vitamins from cow milk

- ✓ are *well represented, excepting vitamins D and C*, which are present in *insufficient quantities.* Vitamin C is partially distructed by boiling;
- ✓ cow milk has more vitamin K than HM;
- ✓ the *vitamin A content is adequate for the small infant.*

Bacterial contamination

Cow milk is usually contamined, but in most cases, with unpathogenic bacteria. It is a good growth medium for pathogens and it can be a way of transmission for: *streptococcal infection, diphteria, typhus, brucellosis.* That is why, cow milk *will be sterilised* before alimentation.

Milk formulas for infants

These represent a milk product that suffered several changes during industrial preparation, with the purpose of *having a similar composition to HM.*

In the artificial nutrition it is recommended the use of adapted and partially adapted milk formulas, due to the advantages compared to cow milk:

1. by thermal treatment, sterilisation and splitting of protein molecules;
2. water addition decreases the protein and electrolyte concentration;
3. lactose addition increases the caloric value;
4. they have a low protein and mineral content;
5. they have vitamin, mineral and olygoelement additions, proportionally appropriate to the infant's requirements.

The milk formulas used in pediatrics have a different composition based on the *infant's age*. Keeping this criterion in mind, they classify as:

Preterm milk formulas

They must be adapted to the morphofunctional particularities of the immature digestive system. They have the following ***traits:***

- *are adapted* to the special growth needs;
- are caloric enriched - *20-24 kcal/30 ml;*
- they contain high amounts of protein 1,8-2,4 g/100 ml - higher than the start formulas.

Proteins

Come from *whey, are supplemented with taurin,* which is well tolerated and realize a profile of plasmatic amino acids, superior to the ones realized from the formulas in which casein is predominant.

Carbohydrates

Are represented *50% of lactose and 50% glucose polymers,* for partial compensation of the lactose intolerance of the preterm newborn.

Lipids

Are represented *50% by the medium chain tryglycerides* for compensating the limited secretion of pancreatic lipase and low quantity of bile acids.

Are prepared with adequate polyunsaturated fatty acid content for which the preterm body has the following benefits: favours the transmembranary transport, assure permeability and affinity to the cellular membrane receptors, have a role in immunity boosting and favours brain and retina development. The polyunsaturated fatty acids excess can produce hemolytic anemia by vitamin E deficiency (antiperoxidal effect onto the polyunsaturated fatty acids from the erythrocyte membrane). That's why, the ratio vitamin E/PFA is twice as increased as the ones from the term newborn formulas.

High concentration of minerals, vitamins and proteins

They have a deffinitive role in the assurance of an accelerated growth rythm, with limited absorption capacity and low limits for large liquid toleration. The phosphorus content is high and proportional to the high requirements of the preterms.

HMF (human milk fortifiers)

Are products that are *added to human milk and are destined for preterm newborns, that are exclusively breastfed and have a birth weight less than 1800 g.* They have a high caloric value. HMFs are used to promote an optimal growth rate and a better bone mineralisation.

Due to their high content of calcium and vitamin D, these products could lead to hypercalcemia. They will be given with precautions to preterm babies which receive over 160 ml milk/kg.

HMFs can be associated with other formulas (not just human milk) if the formulas are not adapted to the preterm newborn. Weekly calcium monitoring is necessary.

Start formulas for infants between 0-4 months

Are milk formulas with *similar composition to the HM,* especially made for assuring *the infant's energetic needs (67-72 cal/100 ml).*The protein source is cow milk; the osmotic charge is low.

Are the most used in the newborn and infant nutrition due to their composition, adapted to the specific digestion and absorption possibilities in this category of age. It is characterized by:

- *caloric value of 64-72 cal/100 ml*;
- *protein content between 14-18 g/l,* with important reduction of the casein quantity and lactoserum protein addition. The balance *casein/lactoserum protein* is similar to HM (40/60)
- ensures an *optimal amino acid composition* by adding *taurin and cystein;*
- *carbohydrates* are mostly represented by *lactose 65-83 g/l*. High intake of galactose intervenes in mielination processes and indirect bilirubin conjugation (synthesis of the uridine - diphosphate - glucuronic acid);
- *lipids* in quatity of 3,2 g/100 ml, are represented mostly by tryglycerides;
- they contain *plant oil,* in variable proportion, *high in PFA,* which leads to an increase of the absorption coefficient up to 85%;
- *the ratio linoleic acid/alpha-linoleic acid* recommended by ESPHGAN (European Society for Pediatric Gastroenterology and Nutrition) is of 5-15; linoleic acid assures 3-5% of the caloric value, which leads to an accelerated growth process (<1% leads to growth rate decrease);
- *cholesterol intake of 1-3 mg/100 ml* is more decreased than HM, unrecommended to preterms, cholesterol intervenes in the growth process, myelin formation, bile salt synthesis and steroid synthesis;
- *minerals* are reduced to intermediate concentrations between HM and recommended superior levels, which ensure a low osmolarity (below 400 mOsm/l);
- *the maximum Na recommended intake is of 12 mEq/100 ml,* and ion sum (Na, K, Cl) must *not exceed 50 mEq/100 ml*for keeping the hydroelectrolytic and acid-base balance;
- *the calcium quantity is of 70-80 mg/dl*

- *the ratio Ca/P is maintained at values of 1,2-2,2,* similar to the ones from HM, assuring an optimal growth rate, bone development, normal cell function and specific enzymatic processes deployment;
- *vitamin and olygoelement supplementation:* the following are added:
  - Fe – 12 mg/l (in some formulas) – prevention of hypochrome anemia;
  - Zn – value below 0,2 mg/100 ml being a limitative growth factor;
  - Cu – in quantity of 20 mg/100 ml.

Continuation formulas

Are milk formulas that have as a protein source cow milk, and are *recommended for infants bigger than 4 months, in parallel with* complementary feeding. Then can be used up to 1 year of age. They are characterized by:

- *caloric value between 60-85 cal/100 ml;*
- *proteins* are around *2-3,3 g/100 ml*, with a ratio *casein/lactoserum proteins of 80/20;*
- *lipids*, in quantity of 2-*4 g/100 ml*, with the enrichment of the PFA content, *represent≈ 35% of the total caloric ratio;*
- *carbohydrates are in quantity of 6,5-8,6 g/100 ml*, lactose is present in proportion of 50%; starch, dextrin maltose and glucose are added;
- *minerals* are present in a relatively high amount, but do not exceed the cow milk concentration;
- have a high osmolarity compared to HM;
- *the ratio Ca/P is of 1,2-1,5;*
- *some products* have an enriched content of *Fe: 0,6-0,9 mg/100 ml.*

Special composition milk formulas

They are also known as "drug aliment" and are milk formulas, specially made for *the dietary treatment of digestive caused disorders such as acute diarrhea.*

They are addressed to a certain group of newborns, infants and children with signs or special pathologic symptoms.

They represent a non homogenous group of formulas, of particular composition and structure, for assuring optimal nutrient digestion and absorption.

Anti-reflux formulas

Are indicated in gastroesophageal reflux and regurgitations because:

- they permit a homogenous milk thickening in contact with the gastric pH;
- lipids rich in medium chain tryglycerides contribute to the gastric evacuation;
- they include starch and carob powder;

Are recommended for:

- children with regurgitation from birth;
- gluten, fructose and sucrose intolerance.

Anti-colic formula (for the digestive comfort)

The characteristics are:

- lactose represents 30% of the carbodydrates;
- galacto-oligosaccharides/fructo - oligosaccharides lead to consistence decline and an increase in the frequency of stools;

Are recommended for artificially fed infants which have frequent colic problems.

Hypoallergenic formula

These formulas have a little under 1% immunoreactive proteins from the total nitrogen source formula, obtained by protein hydrolysis.

The have the following characteristics:

- dietetic products, *structurally modified*, easy to digest and absorb;
- have an optimal quantity of partially hydrolysed protein content;
- *the protein source is enzymatically hydrolyzed casein;*
- the carbohydrate source is represented by *glucose polymers;*
- *lipid source – medium chain tryglycerides (50Î)*, having as source corn oil, soy oil or coconut oil;
- reduces the risk of cow milk protein allergies;
- have in their composition pre- or probiotics;
- contain LC-PUFAs which have an immunomodulation role.

Indications:

- infants that come from families with a history of allergic diseases;
- atopic terrain infants
- allergies to the cow milk proteins.

Delactosed formulas

This category of milk formula has a content enriched with maltodextrin, glucose, fructose and other carbohydrates. They do not have lactose in their composition, but do have an *adequate content of minerals and vitamins* and can be used for a long time without leading to alimentary deficiencies or badly influence the growth rate.

Indication:

- infants with secondary lactose intolerance
- in and after states of acute diarrhea
- after bowel surgery.

Soy formulas

Soy is a protein with a smaller biological value than cow milk proteins, with a decreased digesting degree and biodisponibility.

The composition characteristics are:

- soy protein content instead of cow milk proteins;
- content enriched by methionine, taurine, carnitine, starch and sucrose;
- carbohydrates are represented by *glucose polymers or dextrin maltose;*
- have an enriched content of vitamins and oligoelements.

These formulas are usually *avoided in the treatment of preterm babies, in cystic fibrosis and atopic terrain (*develops cow milk protein allergies and soy milk allergies).

For the preterm newborns, a high content of phytic acid predisposes to hypophosphatemia, slowing the growth rate; determines urea retention, and the quantity of vitamins is insufficient for this category of infants.

Indications:

- milk diarrhea;
- realimentation after a moderate or severe diarrhoea episode;
- cow milk protein intolerance;
- maldigestion, malabsorption, malnutrition;
- celiac disease;
- chronic inflammatory bowel syndrome;
- vegetarian alimentation.

Preparation, storage and manipulation of the infant milk formula

Milk formulas are not a sterile product, it can contain pathogens, some of them extremely invasive, such as Enterobacter, that can lead to serious infection, with septicemic traits, especially during the first 2 months of life.

At home, the milk formula must be prepared before each feeds.

In hospitals and daycares, certain rules are established regarding the preparation and manipulation of milk formulas. If the milk must be previously prepared, it should be daily made and kept at at least 4 C or less, for a period that does not exceed 30 hours.

Contraindications: keeping the formula in heated environments, in the thermostat, thermos or heating in the microwave. The use of different sources of heat can lead to compositional modifications and rises the risk of burns.

The use of liquid sterile formula is recommended for healthy newborns, from maternity.

CHAPTER V

COMPLEMENTARY FEEDING

Complementary feeding refers to slowly replacing breast milk or formula with solid and semi-solid aliments, with the purpose of getting near to the adult alimentation. This is a progressive process, which takes several months and leads to caloric and quantity supplementation, in a moment when milk nutrition does not cover the energetic requirements anymore.

Currently, there is no consensus regarding the optimal age when a non-dairy alimentation should be introduced, they vary with the location, tradition, temperamental and nutritional infant's particularities, family and doctor's preferences. The ESPHGAN established that the optimal interval for solid and semi-solid alimentation inclusion, other than milk, is at 4 - 6 months of age (17 - 26 weeks). WHO underlines the importance of exclusive breastfeeding in the first 6 months of life and continuation until the age of 2, along with complementary feeding.

Starting complementary feeding before 4 months of age can increase the risk of obesity in adult life and favors the apparition of food allergies, even at children who don't have genetic predisposition.

Early complementary feeding can solicit the immature digestive tract early and realizes a big osmotic charge for the functionally underdeveloped kidney. Not ultimately, infants smaller than 4 months do not know how to coordinate the necessary moves for swallowing, so there is a risk of aliment aspiration in the respiratory tract.

On the other hand, adjourning the process of complementary feeding over the age of 6 months can lead to slowing of the growth process (milk is not sufficient to sustain the rapid growth from the first year of life), so the whole process of complementary feeding introduction will be harder; the child will refuse new tastes.

However, for establishing the right moment to start complementary feeding, the following factors must be taken into account:

- biological and neuro-psycho-motor acquisitions, fundamental to the infant's developing process

- taste development and individual preference for certain tastes and textures

- functional maturation of the renal and gastrointestinal system

- success or failure to achieve quantity and quality nutritional requirements, consecutively to the milk diet

- the interaction between socio-economical, cultural factors and local and familial traditions.

General nutritional rules for complementary feeding

- the new aliment will be progressively added, meaning it will be added in small, increasing amounts and slowly reducing the milk quantity, until it is completely replaced
- the new aliment will be administered before milk, using a spoon
- there will not be introduced 2 or more new aliments at the same time; the recommendations are 1 aliment to be introduced at an interval of 3 to 4 days
- if the new aliment is not accepted by the infant, its administration will be interrupted and tried again after a few days
- choosing the first complementary feeding aliment will be done based on the infant's nutrition state: if he is eutrophic, complementary feeding will be initiated with vegetables soup or fruit purée, and if he is dystrophic, instant farinaceous products will be administered (gluten-free preferably) with milk
- domestic (autochthonous) and season products will be chosen to start complementary feeding
- fresh home-cooked or boiled meal is recommended
- choosing and introducing new aliments is done only for the healthy infant, with balanced digestive functions
- if intolerance signs regarding the new aliment appear (diarrhea, vomiting, cutaneous allergies), the specific aliment will be temporarily stopped, and complementary feeding with other new aliments will be reinitiated a few days after recovery
- in the first few months of complementary feeding, the administered meals must be mashed and mushy, purée-like; after this, food granulation will be increased, and through the end of the first year of life, the infant must consume high consistency meals
- after 8 months, the infant will be offered soft bits of food, which he can take and put himself in his mouth, so that self-feeding is encouraged. By one year of life self-feeding using mug and spoon will be encouraged, the infant's clumsiness being precious moments from his development and autonomy
- accidental aspiration of aliments in the respiratory tract can endanger the infant, that's why careful supervision must be done, and parents will be instructed how to apply desobstruction and first aid

- the infant will not be forced to finish the whole quantity of food (there is a risk of oppositional anorexia)
- vitamin supplementation is not necessary in complementary feeding
- after protein or/and electrolyte rich meals, boiled then cooled water must be given
-**high allergic risk aliments** are recommended to be introduced before the age of 1 but not before 4 months of age, in small, progressively increased quantities (ESPGHAN 2016). Among these are egg-whites, fish, nuts (grinded under the age of 3!), peanuts (grinded under the age of 3!), strawberries, wild berries, kiwi, seafood, cow's milk
- aliments that should be avoided until the age of 1 are: honey (risk of infection with Clostridium botulinum), chocolate and cocoa (strong excitant effect on the nervous system), margarine, cold cuts, high-processed cheese, pork and lamb meat, excess of salt and sugar
- replacing the milk meals is done as follows:
    - o vegetables meal with later addition of meat or egg-yolk at lunch
    - o fruit meal at 9 - 10 o'clock in the morning, with biscuit or cow cheese addition
    - o farinaceous dish at 6 o'clock in the evening
    - o keeping a 500 ml quantity in the infant's diet, because the protein and calcium requirement is covered by the administration of breast milk (breastfeeding on demand until the age of 2) or an age adapted formula (integral cow milk is contraindicated to the infant smaller than 1 year- 1 year and a half)
- the best criterion for appreciating the success of complementary feeding is following the individual curves of growth and development.

Depending on the child's history (term birth or preterm, ponderal gain in the first months of life, different acute/chronic conditions), each infant is given by the pediatrician a personalized complementary feeding diet.

Nutritional rules and aliments used in complementary feeding:

1. Proteins:

- meat can be administered mixed with the vegetable soup, and after 8 - 9 months, it can be given as meatballs. Poultry meat can be given from 5 months, and beef and white fish after 6 months
- poultry liver and beef liver is recommended after 6 months and can be replaced with meat during the days it should be administered
- egg-yolk is introduced by 6 months, well cooked, mixed with the vegetables purée, replacing the meat during the days of administration
- fresh cow cheese can be given from 5 months, in a mixture with mashed rice, vegetables or fruit purée; home-made cheese is preferred. Cottage cheese, as well as fresh cheese can be used from 8 - 9 months with pasta, under the form of puddings or cheese dumplings
- yogurt and kefir are recommended after 7 months
- instant cereal powders prepared with breast milk or with formula can be used in artificial alimentation and introduced in complementary feeding starting with the age of 4 months - if they are gluten-free (rice, starch, millet), and after 6 months' products with gluten can be used (wheat, barley, oat, rye)
- pseudocereals (quinoa, chia, amaranth, buckwheat) are gluten-free and require hydration +/- fermentation, so a more laborious preparation. Can be administered together with fruits, being for some days the desert from the child's over 1-year meal
- legumes (beans, green beans, pea, lentil, chickpea) are enjoyed by the children because of their sweetish taste and can be introduced in the alimentation from 9 - 10 months.

2. Lipids:

- vegetable oil is recommended by 4 - 5 months, 2 - 3 g% in the vegetable soup
- poultry, fish, beef meat has in its composition lipids with almost equal proportions between saturated and unsaturated fatty acids
- butter can be given from 5 months in the vegetable purée
- cream, 15 - 25 g/day is recommended starting with 7 - 8 months
- the use of high cholesterol aliments is not recommended, like: egg yolk (2 - 3/week by the end of the first year of life), butter, brain, entrails.

3. Carbohydrates:

- cereals:

- rice mucilage and rice decoction are used in the first months of life, rice cream from 3 months, rice flour from 4 - 5 months for soup thickening of for the farinaceous milk preparation, and rice grains from 8 months
- starch from 4 - 5 months
- wheat, barley, oat, rye flour is recommended for infants older than 6 months due to their gluten composition
- instant industrial flours, simple or complex, are suspended in water or milk; they are flours which dissolve rapidly, and can be administered from 4 - 5 months; the used concentrations are dependent on the product composition and are specified by the producing firm

- fresh vegetables (carrot, potato, tomatoes, green beans, zucchini, salad) are used by 4 - 5 months as vegetable soup and then vegetables purée. Spinach and leek have laxative effects and can be introduced in the alimentation after 6 months. An identical dish, the carrot in the form of carrot soup 30 - 50% can be given after 1 month in diarrhea. Industrial vegetable products or vegetables with flour, meat or fish addition, can be given after 6 months, depending on their composition, due to the high contamination risk (agricultural or industrial); early introduction and extended use will be avoided.

- fruits: fruit juice, rich in minerals, oligoelements and vitamins, is recommended after 6 - 8 weeks, between meals, without being a complementary feeding element; its quantity is progressively increased until 30 ml/day by the age of 3 months and then 50 – 60 ml/day. From 4 - 5 months, fruits represent a complementary feed in the form of apple, peach, banana purée, and can be simply administered or together with cow cheese or biscuits. Raw fruits or compote, as a desert after lunch, can be given after 6 - 7 months. Industrial fruit products simple or with other ingredients added can be given after 6 months.

Complementary feeding has an important influence onto dietary preferences and later taste preferences. Dietary mistakes from the first year of life has serious repercussions upon morbidity, both in childhood and adult life. Particular important situations are in complementary feeding or preterms, which must take account for corrected gestational age and family history of allergies. Taking into consideration the actual tendencies from the adult diet, vegetarian diet, lactovegetarian diet, raw-vegan diet, these diets are not recommended for infants because they do not ensure the protein requirement and iron requirement, both necessary for an optimal development.

CHAPTER VI

SMALL CHILD NUTRITION

General principles of small children nutrition

After the age of one, the child's nutrition must take into account on one hand the morpho-functional particularities age-related, and on the other hand the different and specific physical and intellectual activities. For all age categories, a unique attitude must be adopted: a balanced alimentary ration, rich in nutrients, vitamins and natural fibers.

Starting on this grounds and the fact that between the age of 1 and 2 the nutritional and energetic needs are high because of the increased growth rate and motor activity, *the nutritional ration* is based on the following parameters:

- ✓ caloric requirement: 90 kcal/kg/day
- ✓ fluid requirement: 90 - 100 kcal/kg/day
- ✓ protein requirement: 2 g/kg/day
- ✓ lipid requirement: 4 – 5 g/kg/day
- ✓ carbohydrate requirement: 12 g/kg/day.

The caloric ration will be proportionally distributed as follows:

- ✓ 15% proteins
- ✓ 35% lipids
- ✓ 50% carbohydrates.

Protein sources are: cow milk (500 ml/day), 30 – 50 g poultry meat, beef, fish, liver, brain, egg (2 - 3 per week) and plant protein.

Lipid sources are: vegetable oil, margarine (mostly polyunsaturated fatty acids), butter, cream

Carbohydrate sources: bread, pasta, biscuits, semolina, rice, polenta, fruits, vegetables and sucrose products.

Vegetables that can be used for this age are: potatoes, root vegetables, green beans, peas, cauliflower, zucchinis, spinach, tomatoes. They can be prepared in soups, purées, and after 2 years of age as sautés or salads. The vegetable quantity will be around 200 - 300g/day.

Fruits will be part of the daily alimentation, as: juices, purées, compotes or whole fruit.

Sweets can be offered at the end of the meal.

The child's alimentation has to be varied and esthetically presented, basic radicals should prevail over acid radicals. The menu will be made taking into account the developmental degree and the child's preferences.

After the age of 1, the child can differentiate and develops alimentary preferences. He can have periods when the interest is lost for certain aliments. In these cases, the presentation of the same aliment in other forms must be tried.

5 meals per day will be administered, 3 of which are principal and 2 snacks; the schedule must be respected, because secretory digestive reflexes must be formed. The meals will be prepared tasty, served as attractive as possible and within proper hygienic conditions.

The small child must be encouraged to self-feed and to drink from a mug. Those fed by parents who still use the bottle after the age of 1, can present nervous anorexia, oral and manual motor dysfunctions.

It is optimal that as many meals as possible should be served together with the family, because doing so, the appetite rises, and the parents' supervision will accustom the child with correct habits.

Preschooler's nutrition

At this age, the alimentation is similar to the adult one. The nutritional needs are increased, especially due to the intense motor activity.

The caloric requirement is 80 kcal/kg/day, of which *proteins* will assure *15 - 18%, lipids 25 - 30% and carbohydrates 55 - 60%.* Fluid requirement is of 80 ml/kg/day.

Protein requirement is *2 g/kg/day*, with a ratio of 2/3 animal protein and 1/3 plant protein. Their sources are: milk, 500 - 600 ml/day, which includes yoghurt and kefir, which are well tolerated, cow cheese, low sodium cheese; poultry meat, beef, fish, pork, lamb, mutton, cold cuts which can be administered around 75 g/day, minced; boiled egg, fried egg or omelette, or other way of cooking - puddings, soufflé can be administered as well.

Lipid requirement is of 2 - 3 g/kg/day and can be administered as butter, cream, margarine and vegetable oils.

Carbohydrates requirements is of 10 g/kg/day and can be administered as: bread and pastry, 150 g/day, pasta, cake, fruits, vegetables. Intermediary bread is recommended due to its fiber content and vitamins of group B.

Vegetables are given as purées, puddings or green, as salad. *Fruits* are given raw, preferably, after they are washed.

At this age, the child will receive *3 main meals and 2 snacks*. A tight schedule, when his entourage is out playing, might diminish his appetite. *Water and sweets* are offered *at the end of the meal,* for not affecting the appetite. At least two meals must be served with the family.

The child will be taught to *wash his hands before each meal and to brush his teeth after the main meals.*

The conditioning of accepting a certain meal (for example while listening to stories) represents a mistake, as well as calming hunger with candy, biscuits, juices before meals.

School-child's nutrition

The energetic and nutritional needs of 6 - 12 year olds are destined to the physical, intellectual activity and sexual maturation in particular.

The energetic needs are between *50 - 60 kcal/kg/day,* of which *15% assured by proteins, 30% by lipids and 55% by carbohydrates.*

The fluid requirement is of *80 ml/kg/day.*

The protein requirement is of *2 g/kg/day,* of which 50 - 60% assured by animal origin proteins. *Protein sources* are: cow's milk 400 ml/day, meat 100-150 g/day, cheese 30 – 50 g/day, 1 egg every 2 days and plant origin protein.

The lipid ration is 1,5-2 g/kg/day will be assured by: oil, cream, butter, milk, eggs and some vegetables.

The carbohydrate requirements are of 8 g/kg/day, and will be assured by: bread, pasta, rice, potatoes, fruits, vegetables, pastry products and sweets.

The child will be given *3 main meals and 1 - 2 snacks per day.* It will be insisted upon breakfast.

The school snack will be prepared at home, for a better control over the child's alimentation.

Lunch will have 3 courses, in which raw vegetables and fruits will be present as salads and fruits as desert.

Dinner consists of 2 courses, one of animal protein and a desert.

The school child's alimentation will be supervised because in the absence of parents he tends to skip some of the meals, or grabs a quick bite, which leads to an unbalanced alimentation.

Errors seen in child nutrition

- the parent tendency of forcing the children to eat over their energetic needs, favouring obesity.
- monotonous nutrition, insufficiently tasty and unattractively presented, favours inappetence.
- in pre-adolescents and adolescents psychic instability and vegetative instability are present and lead to behavioral diet changes.

Both *anorexia*, as well as *bulimia* have a high incidence in teenagers.

Nervous anorexia, along with weight-loss means, can have multiple medical consequences such as: cardiovasculary disorders.

CHAPTER VII

NUTRITIONAL DISORDERS

Nutritional disorders are manifested by the alimentary refusal or insufficient ingestion due to behavioral disorders or basic organic pathology. They are frequently seen in newborns and children <6 years of age, but alimentation disorders can appear in bigger children as well.

In reality, just a proportion of 1-5% of newborns and small children have severe nutritional disorders which determine growth failure. In preterm children, severe nutrition disorders appear in 30% of cases, in almost 80% of the patients with neurologic disorders of developmental disorders.

Most of the time, nutritional disorders are transient and can be adjusted in an adequate psychological environment.

General characteristics of avoiding nutritional disorders:

- efficient alimentation duration of approximately 20-30 minutes, without discomfort for parents of children.

- the intervals between meals of 2-3 hours, allow the child to feel hungry.

- regular meals educate children to recognize hunger and satiety, essential for establishing a feed rhythm of its own.

In the medical practice, the most frequent causes of organic disorders are the neurologic ones, followed by structural anomalies of the digestive tube, but generally they can be present as a group of disorders.

Table 20. Organic cause of nutritional disorders

ETIOLOGY	PATHOLOGY
Neurologic disorders	Cerebral palsy
	Myelomeningocele
	Myopathies
	Muscle distrophy
	Miastenia Gravis
	Tumors in the CNS
	Encephalopathy (epileptic, hypoxic-ischemic)
	Craniocerebral trauma
Structural anomalies	Short lingual frenum
	Cleft lip/cleft palate
	Macroglossia
	Esophageal ring
	Esophageal fistula
	Esophageal stenosis
Cardio-respiratory disorders	Congenital heart defects
	Broncho-pulmonary dysplasia
Metabolic disorders	Fructose hereditry intolerance
	Urea cycle disorders
	Organic acidosis
Gastrointestinal disorders	Alimentary allergies
	Gastroesophageal reflux disease
	Esophagitis (drug-induced, infectious, eosinophilic)
	Gastroparesis
	Constipation

Diagnosis methods in nutritional disorders

An interdisciplinary approach is necessary, with a team such as: nutritionist, psychologist, pediatrician, speech therapist. Medical basic evaluation consists of anamnesis, observing the feeding process and diagnosis tests planning.

Medical history must hold data such as:

- pregnancy, birth,
- breastfeeding,
- complementary feeding onset,
- the age at which the child starts to eat by himself,
- tools used during meals (cup, pacifier),
- tolerated textures, accepted aliments, the duration of each meal,
- the child's behavior, along with the parent's during meals,
- the child's capacity of feeding.

If the child suffers from malnutrition, the evaluation of caloric and nutritional intake is important, and it must be done preferentially by dietary journal over a period of 3 days, done by the parents at home.

The psychologic evaluation helps with the identification of parenteral and behavioral factors that can contribute to the apparition of dietary disorders.

If an organic cause is present, complete paraclinical examinations are necessary.

Most children with associated neurologic pathologies will need a thorough evaluation of oral feeding and most of the time, nutritional supplementation is imposed.

Some patients will require behavioral therapy for overcoming the dietary refusal and mechanisms of avoiding nutrition. Each patient is a different situation and requires a complex individual evaluation by a multidisciplinary team, with experience in the nutritional problems.

Long term complications of nutritional disorders

90% of the time, the correct approach has a high efficiency in these kinds of disorders. In preterm born babies, the predisposing factors of dietary disorders are: cerebral palsy, delays in neurologic developmental acquisitions and a discordant relation between child and parent.

Even in severe cases, the therapy success rate can get up to 60%. Surprisingly, gavage alimentation and the presence of deglutition difficulties are the most important factors that will lead to the failure of treatment.

Long term follow-up of children with infantile anorexia, shows that despite partial improvement of the nutritional status, dietary disorders, anxiety and depressive disorders can persist up to the age of 8.

In these cases, a correlation has been observed between alimentation difficulties and emotional overreacting of mothers.

CHAPTER VIII

THE IMPORTANT ROLE OF PARENT-CHILD RELATIONSHIP IN THE CHILD'S SOMATIC AND MENTAL DEVELOPMENT

Even from birth, the child presents numerous abilities and skills. The most important abilities, the ones that condition his whole development is the ability to interact with the adult that takes care of him, that is, most of the time his mother. The period with the most intense changes is the childhood period - more precisely, small child period, until the age of 3 years. Along with the importance of the first 3 years of life, Brazelton used to say that: "This period is capital for the later development of empathy, self-esteem, risk assumption capacity and learning from mistakes - essential quality of maintaining the intellectual development."

The attachment between children and parents is fundamental for the physical, emotional, intellectual and social child development. The desire to ensure a good care is specific to our civilized society, and the child's psychologic needs cannot be satisfied by love and understanding. The securing love is the most important need at an early age, offering the base of future social, family, parental, sibling relationships and friendships. The ability to react and respond to love and later to become a loving parent mostly depends on the amount of love received during childhood. Satisfying this need will later bring security, safety feeling, and trust and later, self-esteem. Loved by the ones around him, the child learns that he is worthy of being loved, that he is valuable, precious. He learns to love himself. The attachment toward his mother or the one that takes care of him, makes a child stronger - if he has good parents, that respect and understand him or can make him weak, vulnerable, if the parents do not know how to respond to the child's needs.

Once with age, the need for new experiences and satisfying those needs is important for the intellectual development and for knowing the world. As food is important for physical growth, experiences are essential fot the cognitive development, playing and language development being the most important ones in this matter. Language is the most important game and through it the child learns how to think and develop social relationships. He must not only be spoken to, but also how he is told different things. When a child asks questions, parents will answer, giving him correct responses, in a manner he can understand. New experiences among schedule and clear routine of family life, lead to predictability and life continuity and generate the identity and feeling of belonging.

Around the age of three, the need of responsibility appears and the child's independence grows. The child learns how to feed himself (eats, bathes, dresses himself). The responsibilities grow with age, and are important by giving the feeling of liberty while realising his own actions. If at the age he requests responsibilities, this need is not valued by parents, later, when they expect certain things from the youngster, he will not know and will not have the initiative or capacity to assume certain responsibilities. By assuming these things, the child learns the rules, when a thing is done a certain way and why. The adult will play the expert, guide or partner role, based on the child's age and maturity. The teenager must have an emotional support but also the capability and liberty of taking decisions and assuming the consequences.

The mistakes made in attending to the child's needs can distort his development. The consequences are dramatic for both the individual and the society. The intolerable tensions between an individual and his environment have an origin in the suffering and dangers the child has passed through.

The most frequently seen form of abuse and violence against children and the less debated and realized is the neglect of physical and psycho-emotional needs by the adult responsible of his development. This kind of neglect can be a non-physical form of violence and represents the incapacity or the adult refusal of assuring the child's development with all the required aspects of his life. After Daro and McCarthy "a child's neglect, represents an unforgiving, silent murder of the human spirit".

The child emotional neglect can be present even from birth, such as alcohol abuse or narcotics by the mother or poor feeding of the newborn. Visible signs are many, but this can be dirty, smelly, appears to be hungry, pale and does not gain weight. Some infants have been left hours without food and no changing; they reacted by crying for food, warmth, due to discomfort or pain, which can be bothering and can arouse the adult's agressivity. The child lives in a world where his needs are rarely perceived, no one gets close to him or shown him he is worthy. The child's development is seriously affected and the lack of response or stimulation can lead to serious psychomotor development delay or speech , along with focus inability. A child of 12 months, can look like one of 6 months. Over time, these children will stop crying and communicate their needs. Their prattling will not turn into normal language. They do not have the chance to explore or learn anything new about the environment other than the place they live in.

Severe neglect is not affecting only the emotional state, but also the physical development. In 1998, The Institute for Mother and Child's Protection from Bucharest presented a report regarding children development in the institutions of abandoned children. The report statues a physical development (length and weight growth) below average and a decrease in immunity, cause of frequent illness. The question was posed if the food was insufficient as a matter of quality and quantity, but an important aspect was missed: emotional abuse. This can generate poor sleep, with frequent interruptions. Also, certain practices, of waking the children and taking them to the toilet for not wetting the bed were done. Growth hormones are secreted during sleep, so if a child does not sleep right, he will not grow right. Another observed aspect was the erase of the sexual characteristics. This has serious consequences on the physical general aspect, knowing the fact that sexual identity is a basic condition for social interaction.

Neglect can be less obvious and not necessarily continuous. The child can be hold only after he cried for long enough. He can receive food but not necessarily sufficient or adequate, he can have clothes, but not adequate or can receive a certain amount of affection, but not enough. The immediate psychological effects are fear, isolation and the incapacity to trust anyone. A lot of children sometimes take the adult role from a young age for compensating what the parents didn't offer. They have to take care of themselves and very often of their parents, as well. This child is frequently praised by adults for his maturity without acknowledging the fact that his behaviour means he is deprived of his childhood.

In youngsters, the effects of emotional neglect manifest by a violent, antisocial behavior and personality disorders. They are impulsive, do not have the patience to wait, are incapable of working, of making an effort for what they desire, do not recognise the rights of others, are irresponsible. They will quit school for jobs that bring immediate profit and will live a sentiment of rejection from society. This leads to the desire to destruct or self-destruct.

If the family or the society do not respond adequately to the child's needs for a healthy development, we risk the very future of society. The way in which we address to the child's needs creates their first experiences, the ones that will represent the base of their future evolution.

BIBLIOGRAPHY

1. Compendiu de specialitati medico – chirurgicale – Util pentru intrarea in rezidentiat,volumul 2, cap.capitolul IX, pg.35-60.
2. Patologia aparatului respirator la copil // Sub red. V. Popescu. Bucureşti, 1999
3. Pediatria. Tratat // Sub red. E.Ciofu, C.Ciofu. Bucureşti, 2001
4. Ştiuca S. Esenţialul în pneumologia copilului. Chişinău, 2005
5. Hlingworth RS – Common symptoms of disease in children, 1 vol, Oxford, 1971
6. Tournier G – Séméiologie respiratoire clinique. In: Pathologie respiratoire de l'enfant, ch. 3, 33 – 37, Ed. Flammarion (Paris), 1975
7. De Jong W. Blood Pressure Variability in Neonates: with a special focus on signal acquisition and signal processing. Eindhoven: Technische Universiteit Eindhoven 2000; 10-20, 43-55.
8. Ong WH, Guignard JP, Sharma A, Aranda JV. Pharmacological approach to the management of neonatal hypertension. Semin Neonatol 1998; 3:149-163.
9. Ribeiro MAS, Fiori HH, Luz JH, Piva JP, Ribeiro NME, Fiori RM.. Comparison of noninvasive techniques to measure blood pressure in newborns. J Pediatr (Rio J) 2011; 87(1):57-62.
10. Spinazzola RM, Harper RG, de Soler M, Lesser M. Blood pressure values in 500 - to 750 - gram birthweight infants in the first week of life. J Perinatol 1991; XI:147-151. 59. Park MK, Menard SM. Accuracy of blood pressure measurement by the Dinamap monitor in infants and children. Pediatrics 1987; 79:907-914.
11. Nafday SM, Brion LP, Benchimol C, Satlin LM, Flynn JT, Edelman CM Jr. Renal Disease. In: MacDonald MG, Mullett MD, Seshia MMK. Avery's Neonatology. Pathophysiology & Management of the Newborn. 6th Ed. Lippincott Williams & Wilkins 2005; 994
12. http://crdm.md/images/ups/protocol/Hipertensiunea arteriala esentiala la copil.pdf
13. https://www.researchgate.net/publication/323540038, Monitorizarea pe durata transportului neonatal_
14. http://www.medtorrents.com/load/pediatrie_si_puericultura/aparatul_respirator_la_copii/21-1-0-1082
15. Anand KJ, Aranda JV, Berde CB, et al. Summary proceedings from the neonatal pain-control group. Pediatrics 2006; 117:S9.
16. Mancuso T, Burns J. Ethical concerns in the management of pain in the neonate. Paediatr Anaesth.2009; 19:953–7. [PubMed]
17. Peters JW, Schouw R, Anand KJ, van Dijk M, Duivenvoorden HJ, Tibboel D. Does neonatal surgery lead to increased pain sensitivity in later childhood? Pain. 2005; 114:444–54.[PubMed]
18. Grunau, RE (2013) Neonatal Pain in Very Preterm Infants: Long-Term Effects on Brain, Neurodevelopment and Pain Reactivity. Rambam Maimonides Medical Journal, 4(4), e0025.
19. Caraceni A, Cherny N, Fainsinger R et al. The Steering Committee of the EAPC Research Network. Pain measurement tools and methods in clinical research in palliative care: recommendations of an expert working group of the European Association of Palliative Care. J Pain Symptom Manage 2002; 23: 239–255.
20. Lawrence J, Alcock D, McGrath P et al. The development of a tool to assess neonatal pain. Neonatal Netw, 1993; 12:59-66.
21. Stevens B, Johnston C, Petryshen P, Taddio A. Premature Infant Pain Profile: development and initial validation. Clin J Pain 1996 Mar; 12(1):13-22.

22. Lawrence J, Alcock D, McGrath P, Kay J, Mac Murray SB, Dulberg C. The development of a tool to assess neonatal pain. Neonatal Netw 1993 Sep; 12(6):59-66.
23. Carbajal R, Paupe A, Hoenn E, Lenclen R, Olivier-Martin M. [APN: evaluation behavioral scale of acute pain in newborn infants]. Arch Pediatr 1997 Jul; 4(7):623-8.
24. Krechel SW, Bildner J. CRIES: a new neonatal postoperative pain measurement score. Initial testing of validity and reliability. Paediatr Anaesth 1995; 5(1):53-61.
25. Hummel P, Puchalski M, Creech SD, Weiss MG. Clinical reliability and validity of the N-PASS: neonatal pain, agitation and sedation scale with prolonged pain. J Perinatol 2008 Jan; 28(1):55-60.
26. Spence K, Gillies D, Harrison D, Johnston L, Nagy S. A reliable pain assessment tool for clinical assessment in the neonatal intensive care unit. J Obstet Gynecol Neonatal Nurs 2005 Jan; 34(1):80-6.
27. Debillon T, Zupan V, Ravault N, Magny JF, Dehan M. Development and initial validation of the EDIN scale, a new tool for assessing prolonged pain in preterm infants. Arch Dis Child Fetal Neonatal Ed 2001 Jul; 85(1):F36-F41.
28. Sharek PJ, Powers R, Koehn A, Anand KJ. Evaluation and development of potentially better practices to improve pain management of neonates. Pediatrics 2006; 118 Suppl 2:S78.
29. Bellieni CV, Cordelli DM, Marchi S, et al. Sensorial saturation for neonatal analgesia. Clin J Pain 2007; 23:219.
30. Golianu B, Krane E, Seybold J, et al. Non-pharmacological techniques for pain management in neonates.
31. Semin . American Academy of Pediatrics Committee on Fetus and Newborn; American Academy of Pediatrics Section on Surgery; Canadian Paeditric Society Fetus and Newborn Committee, Batton DG, Barrington KJ, Wallman C. Prevention and management of pain in the neonate: an update. Pediatrics. 2006 Nov; 118(5):2231
32. Manual de Puericultură şi Neonatologie, Lito UMFT, 2002
33. Manual de Lucrări Practice de Puericultură, Lito UMF, 1992
34. Noţiuni de Puericultură- Cresterea si dezvoltarea postnatala,Colectia „Manuale”2010
35. Esentialul in pediatrie, Ed. Medicala Amaltea, 1997
36. Tratament elementar de pediatrie vol.4, Ed. Casa Cartii de Stiinta Cluj, 2000
37. Pediatrie practica, Ed.Risoprint, Cluj-Napoca, 2006
38. Ciofu E, Ciofu C. Esențialul în pediatrie, Ed. a 2-a, București, Ed. Amaltea, 2002, p.43.
39. Complementary Feeding, link:
40. http://www.espghan.org/fileadmin/user_upload/guidelines_pdf/con_28.pdf
41. Recommendations on complementary feeding for healthy, full-term infants, link: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4464122/
42. https://www.la-pediatru.ro/info/cand-incepi-diversificarea
43. Boțiu V, Ilie C, Boia M. Manual de Puericultură și Neonatologie, Lito UMF, 2002, p.96-98.
44. Ciofu E, Ciofu C. Esențialul în pediatrie, Ed. a 2-a, București, Ed. Amaltea, 2002, p.44-47.
45. American Heart Association, Gidding SS et al. Dietary Recommendations for
46. Children and Adolescents: A Guide for Practitioners. Pediatrics 117(2); 2006.

47. Florescu L, Temneanu OR, Mîndru DE, Nistor N. Alimentaţia diversificată – scurtă trecere în revistă a unor principii corecte pentru o sănătate pe termen lung. Revista Românå de Pediatrie, Vol. LXIV, Nr. 3, 2015, p. 305.
48. Lindberg, L., Bohlin, G. and Hagekull, B. (1991), Early feeding problems in a normal population. Int. J. Eat. Disord. 1991, 10: 395-405.
49. Chatoor, I. Diagnosis and Treatment of Feeding Disorders In Infants, Toddlers, and Young Children. Washington, DC: Zero To Three, 2009
50. Aldridge, V. K., Dovey, T. M., Martin, C. I., & Meyer, C. (2010). Identifying clinically relevant feeding problems and disorders. Journal of Child Health Care, 14(3), 261–270.
51. Schädler, G., Süss-Burghart, H., Toschke, A.M., von Voss H, von Kries R: Feeding disorders in ex-prematures: causes- response to therapy-long term outcome. Eur J Pediatr (2007) 166: 803
52. Burklow KA, Phelps AN, Schultz JR, Mcconnell K, Rudolph C. Classifying Complex Pediatric Feeding Disorders. J Pediatric Gastro-enterol Nutr 1998. 27. 143-147
53. Kerzner B, Milano K, MacLean WC, Berall G, Stuart S, Chatoor I: A practical approach to classifying and managing feeding difficulties. Pediatrics 2015; 135: 344-353.
54. Prasse, J. E., & Kikano, G. E. (2009). An Overview of Pediatric Dysphagia. *Clinical Pediatrics* (*Phila)*, *48*: 247–251.
55. Arvedson JC: Assessment of pediatric dysphagia and feeding disorders: clinical and instrumental approaches. Dev Disabil Res Rev 2008;14:118-127
56. Fischer E, Silverman A: Behavioral conceptualization, assessment, and treatement of pediatric feeding disorders. Semin Speech Lang 2007;28:223-231.Howe T-H, Wang T-N: **55.**Systematic review of interventions used in or relevant to occupational therapy for children with feeding difficulties ages birth-5 years. Am J Occup Ther 2013;67:405-412.
57. Ammaniti M, Lucarelli L, Cimino S, D'Olimpio F, Chatoor I: Feeding disorders of infancy: a longitudinal study to middle childhood. Int J Eat Disord 2012;45:272-280.
58. Foisoreanu V: Nurologia developmentala. A 21-a cosfatuire nationala de Neurologie si Psihiatrie Infato-Juvenila,Vol. lucariilor in extenso.edit. Tragu=Mures 1998 pag 2-31.
59. Menkes J.H: textbook of child neurology editia IV Philadeplhia 1990 pag 209-218.
60. Netter F.H: The Ciba Collection of Medical Illustrations 1986: 1:131-47
61. Danaher, C et al. 2011. Early childhood feeding practices improved after short-term pilot intervention with pediatricians and parents. Childhood Obesity. 7(6): 480-487
62. Engle PL, Black MM, Behrman JR et al (2007) Strategies to avoid the loss of developmental potential in more than 200 million children in the developing world. Lancet, 369: 229-42.
63. Preiser JC, Schneider SM. ESPEN disease-specific guideline framework. Clin Nutr 2011;30:549e52
64. Bell E, Warburton D, Stonestreet BS, Oh W: Effect of Fluid Administration on the Development of Symptomatic Patent Ductus Arteriosus and Congestive Heart Failure in Premature Infants. N Engl J Med 1980; 302:598-604.
65. Alimentaţia enterală a nou-născutului la termen bolnav COLECŢIA GHIDURI CLINICE PENTRU NEONATOLOGIE Ghidul 09/Revizia 025.07.2010

66. Nutrition Committee, Canadian Paediatric Society: Nutrien need and feeding of premature infants. CMAJ 1985;152:1765-1785.
67. Ekhard E Ziegler, Patti J Thureen, Susan J Carlson, Aggressive nutrition of the very low birthweight infant, Clin Perinatol, 2002; 29: 225-244.
68. Weber, A. , Loui, A. , Jochum, F. , Bührer, C. and Obladen, M. (2001), Breast milk from mothers of very low birthweight infants: variability in fat and protein content. Acta Pædiatrica, 90: 772-775.
69. Moro GE, Minoli I: Fortification of human milk; in Ziegler EE (ed): Nutrition of the very low birthweight infant. Nestle nutr Workshop Ser Pediatr Program. Philadelphia, Lippincott Williams & Wilkins, 1999, Vol 43, pp 81-93.
70. Schanler RJ, Shulman RJ, Lau C: Feeding Strategies for Premature Infants: Beneficial Outcomes of Feeding Fortified Human Milk Versus Preterm Formula, Pediatrics Jun 1999, 103 (6) 1150-1157.
71. Goldman HI: Feeding and necroltising electrolitis. Am J Dis Child 1980; 134:553-555
72. Gomella, ediția 25, Newborn Physical Examination, pg 43 – 65
73. Manual of Neonatal Care, seventh edition, Assessment of the Newborn History and Physical Examination of the Newborn, pg 91 -102
74. Manual of Neonatal Care, seventh edition,Care of the Well Newborn, pg 103 -110
75. Tratat de Neonatologie, Iulian Lupea 2005, Examenul clinic al noului nascut la termen, pg 82 -99
76. Tratat de Neonatologie, Iulian Lupea 2005, Clasificarea nou- nascutilor dupa varsta gestationala si greutatea la nastere, pg 205-213
77. Cloherty and Stark's ,Manual of Neonatal Care, ISBN: 9781496343611,2017
78. Puericultură Curs -.Boia Marioara - Puericultură Curs – LITO U.M.F.T, 2005
79. Tricia Lacy Gomella .Neonatology: Management, Procedures, On-Call Problems, Diseases, and Drugs - fifth edition.
80. https://library.med.utah.edu/pedineurologicexam/html/newborn_n.html#28