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TRISOMY 18 AND AGENESIS OF CORPUS CALLOSUM: A CASE REPORT

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Abstract
Trisomy 18 syndrome is caused by the presence of an extra number 18 chromosome, which leads to multiple abnormalities. Many of these malformations make it hard for infants to live longer than a few months. We present a case of trisomy 18 with agenesis of corpus callosum in a newborn male with intrauterine growth retardation that was investigated for growth retardation and facial dismorphia. The cytogenetic analysis revealed a complete trisomy 18 karyotype.

Key words: trisomy 18, multiple abnormalities

Introduction
Edwards et al. and Smith et al. first described trisomy 18 separately in 1960. Edwards syndrome or complete trisomy 18, is the second most common autosomal trisomy in newborns, after Down syndrome, with a prevalence at birth of about 1 in 6000 [Root and Carey, 1994]. It is a chromosomal disorder that was widely described resulting from three copies of the chromosome 18 in every cell. The additional chromosome 18 usually results from maternal non-disjunction in 90% of the cases and of paternal non-disjunction in 10% of the cases. The affected patients manifest multiple congenital malformations, mental retardation, feeding difficulties, developmental delays. Surviving rate is very low about 55-65% of newborns with trisomy 18 die in the first week of life, and 90% have died by 6 months of age and only about 5-10% of infants are alive at 1 year of age [Root and Carey, 1994]. Children born at term and females have a better surviving rate than premature births and males [Niedrist et. al., 2006].

Case report
The proband (Fig.1, Fig 2) a newborn male is the second child of a healthy couple. Mother’s age at birth was 30 years and father’s was 38 years. The newborn had intrauterine growth retardation, he weight at birth 2330 g, head circumference was 31 cm, length: 48 cm and thoracic circumference: 31 cm. Ultrasonographic examination was performed during pregnancy but no worrying signs were found therefore antenatal screening was not completed.

Fig.1, Fig 2. The male newborn – the second child of a healthy couple.
The proband was investigated at birth for growth retardation and facial dismory. On examination the following anomalies were observed: microcephaly, ocular hypertelorism, short palpebral fissures, microstomia, micrognathia, low set, malformed ears, arthrogryposis, clenched hands with the index finger overriding the middle finger and the fifth finger overriding the fourth finger, rocker-bottom feet. The newborn showed signs of neonatal hypotonia.

Brain ultrasonography was performed and the pathological findings were: minor enlargement of posterior horns of the lateral ventricles and agenesis of corpus callosum.

Cardiac system was investigated, and the physical examination with a stethoscope revealed a heart murmur and at the transthoracic echocardiogram a ventricular septal defect was discovered.

Renal ultrasonography was also a part of the investigations, as the anomalies of this system are known to be frequent, but no signs of renal malformations were revealed.

**Cytogenetics**

Chromosome analysis from peripheral blood lymphocytes was performed. A total of 50 metaphases were counted and in all cells a supernumerary chromosome 18 was present. Thus the chromosomal investigation revealed a complete trisomy 18; the karyotype was 47,XY,+18 (Fig. 3, Fig. 4).

**Discussions**

The phenotypical appearance of our patient was suggestive for trisomy 18 as the informative findings for this syndrome were present. The patient anomalies that are found in more than 50% of the trisomy 18 cases are: intrauterine growth retardation, short palpebral fissures, microstomia, micrognathia, prominent occiput, low-set, malformed ears, short neck with excessive skin folds, clenched hand, crossed fingers, hypoplasia of toe nails, short dorsiflexed hallux, rocker-bottom feet, mild hirsutism of the forehead and back, neonatal hypotonia. Anomalies present in 10-50% of the cases are microcephaly, foot valgus. Agenesis of corpus callosum is one of the less common findings in trisomy 18 cases. It is known to be present as associated malformation in less than 10% of the cases and among the CNS malformations is very infrequent also [Case et al. 1977].

The cytogenetic analysis made certain the phenotypical suspicion for trisomy 18. The karyotype was of a complete trisomy (47,XY,+18). There have been described in the literature cases of mosaic trisomy 18, partial trisomy 18 (18p, 18q) and even double aneuploidies, three copies of chromosome 18 and an extra 21, X or Y chromosome in the same cell. Complete trisomy 18 results from meiotic non-disjunction, which is in 90% cases maternal. More recent studies have provided the information that in contrast to Down syndrome and Patau syndrome, in Edwards syndrome meiosis II non-disjunction prevails. Baty et al. have concluded in a study that the risk for trisomy 18 after the occurrence of one case with free trisomy is about 0.5%.

Survival of the patient with trisomy 18 is very short as most of the affected children die within the first year of life. There has been little documentation of the precise reason for death in infants with trisomy 18 [Carey, 2001]. The most frequent cause of death in newborn period cited in the literature was sudden cardiac or cardiopulmonary arrest, but all of the patients had congenital heart malformations. Later on the main causes of death are aspiration pneumonia, seizures, cardiac and renal failure.

In conclusion because trisomy 18 is not absolutely fatal, our patient must be followed in evolution to establish the possible complication and the prognosis advitam.
References


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THE ROLE OF FLUORESCENCE IN SITU HYBRIDIZATION IN ASSESSING THE CYTOGENETICALLY DIAGNOSIS IN CRYPTICAL MOSAICISM ANEUPLOYDIES

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Abstract
Clinical cytogenetics has evolved into an indispensable diagnostic tool for the identification of chromosome abnormalities. Cytogenetics has become increasingly important for the identification of aneuploidy and unbalanced structural rearrangements in patients that have suggestive phenotype. Although aneuploidy and many chromosomal abnormalities are revealed through cytogenetic studies, conventional cytogenetic analysis peripheral blood lymphocytes cannot reliably detect rearrangements of genomic segments smaller than 5–10 million base pairs (Mb) and might not detect a cryptic mosaicism aneuploidy. The aim of this paper is assessing the role of molecular cytogenetics techniques and in particular fluorescence in situ hybridization (FISH) in detecting cryptic mosaic aneuploidies in three cases, one case with suspicion of homogeneous 4p deletion and two cases with suspicion of mosaic trisomy 21. Aneuploidy detection using FISH in the interphase nuclei is a proven diagnostic application.

Key words: aneuploidy, karyotype, fluorescence in situ hybridization (FISH).

Introduction
Cytogenetics is an indispensable technique for the identification of aneuploidy and unbalanced structural rearrangements in patients that have suggestive phenotype for a chromosomal syndrome. Although aneuploidy and many chromosomal abnormalities are revealed through cytogenetic studies, conventional cytogenetic analysis from peripheral blood lymphocytes cannot reliably detect rearrangements of genomic segments smaller than 5–10 million base pairs (Mb) and might not detect a cryptic mosaicism aneuploidy. Also, microscopic examination of the chromosomes may not reveal the chromosomal origin of small supernumerary marker chromosomes and may not identify subtle rearrangements of the subtelomeric regions.

The resolution of detecting chromosomal anomalies has been improved by molecular cytogenetic and molecular techniques such as fluorescence in situ hybridization (FISH), multiplex ligation-dependent probe amplification (MLPA) and comparative genomic hybridization (CGH). FISH was the first molecular cytogenetic technique to overcome the resolution limitations of conventional cytogenetic analysis and also offered a solution for rapid chromosomal detection for common aneuploidies in interphase nuclei. A variety of probe types can be used to detect chromosome rearrangements and aneuploidy. For example, repetitive sequence probes that are unique to each centromere are most commonly used to identify trisomies of the common aneuploidies for chromosomes 18, X and Y. These probes are also often used to identify the chromosomal origin of marker chromosomes. Whole chromosome painting probes may be used to characterize translocations on metaphase and locus specific probes may be helpful for the identification of particular deletion syndromes, based on phenotypical findings (e.g., cardiac defect for Velo-cardio-facial/DiGeorge syndrome) or used for those chromosomes for which unique centromere probes are not available (e.g., chromosomes 13 and 21). However, most FISH assays will reveal only abnormalities from the genomic segments for which the probes have been designed. One exception to this is comparative genomic hybridization (CGH). CGH has the distinct advantage of being able to reveal imbalances across the genome. In CGH, DNA is extracted from a control individual with a known normal karyotype and from an individual with an unknown karyotype or a known abnormal karyotype that requires further investigation. These two DNA specimens are differentially labeled with two different fluorochromes and applied to metaphase chromosomes prepared from a karyotypically normal individual. Discrepancies between the fluorescent intensities along the extent of each chromosome will reveal gains or losses of genomic segments [Levy et al., 1998]. Multiplex ligation-dependent probe amplification (MLPA) was first described in 2002 [Schouten et al., 2002]. The method was designed to detect gene dosage abnormalities in a wide range of diseases by the relative quantification of up to 45 different DNA sequences in one reaction. The results are usually available after 2–3 days.

Material and methods
This work is presenting cytogenetics diagnose of cryptic mosaic aneuploidies in three situations, one case with suspicion of 4p deletion in homogeneous karyotype and two cases with suspicion of mosaic trisomy 21.

First case, a boy, was initially investigated at the age of one (Fig.1) for development milestones delay. He came from a foster home so no data regarding the parents were available.
The birth weight was 1500 g and length was 44 cm, the newborn presenting severe growth retardation. Upon clinical examination facial features were suggestive for Wolf-Hirschhorn syndrome: high forehead with a prominent metopic suture, high frontal hairline, prominent glabellum, hypertelorism, epicanthic folds, sclera with a blue tint, broad nasal root, prominent philtrum, thin upper lip, down turned mouth low-set ears. Cytogenetic analysis from peripheral blood lymphocytes was performed. Metaphase slides were prepared from peripheral blood cultures chromosome analysis was performed according to routine methods and GTG-banding technique. All 30 metaphases examined revealed a deletion of short arm of chromosome 4 (4p16.3del). The boy was reevaluated at the age of 4 for severe mental retardation and a change in phenotypical appearance that was suggesting a Williams syndrome: small upturned nose, long philtrum (upper lip length), wide mouth, small chin, and puffiness around the eyes (Fig.2).

The cytogenetic analysis was performed again and surprisingly from the total number of 30 cells counted 28 showed a deletion 4p and 2 euploid cells were found. FISH analysis was available and it was performed for interphase cells as well as in metaphase cells from cultured lymphocytes from peripheral blood using Vysis Wolf-Hirschhorn Region Probe LSI WHS Spectrum Orange (4p16.3) and CEP 4 Spectrum Green on one slide and Vysis
Williams Region Probe (7q11.23 LSI ELN Spectrum Orange and 7q31 D7S486, D7S522 Spectrum Green) on another slide because of the Williams syndrome phenotype. 200 cells were counted in interphase nuclei on the first slide and mosaicism for del 4p16.3 was found (35% normal cells)(Fig. 3, Fig. 4).

The second slide turned out to be negative for Williams syndrome as both orange and green signals were present on both chromosomes 7 in all metaphases and interphase cells examined (Fig. 5).

Fig. 3. Metaphase spread containing normal chromosomes 4 with the presence of the LSI WHS (4p16.3) Spectrum Orange and the CEP 4 Spectrum Green signals.

Fig. 4. Metaphase spread containing one chromosome 4 with the CEP 4 Spectrum Green but without the LSI WHS Spectrum Orange signal.

Fig. 5. LSI ELN Metaphase spread without deletion for Williams syndrome.
The other two cases evaluated were both trisomy 21 patients, newborns, that had a typical phenotype for Down syndrome and the clinical examination did not raise any diagnostic difficulty. The cytogenetics analysis was performed to confirm the clinical diagnosis and the conventional method from peripheral blood lymphocytes revealed in each case metaphases with normal karyotype. Taking into account that in literature the proportion of cryptic mosaicism was reported and the fact that mosaic trisomy 21 patients have a better later development we considered as necessary to reevaluate these cases by performing a molecular cytogenetics technique. FISH was carried out using Vysis LSI 21 Spectrum Orange probe on interphase nuclei and metaphase cells from cultured lymphocytes from peripheral blood from the two newborns (Fig. 6, Fig. 7). The possibility of mosaicism was unfortunately ruled out, because in all nuclei and metaphases examined in both patients three signals for chromosome 21 were present.

Discussions and conclusions

Previous studies have demonstrated the potential of FISH analysis to detect cryptic mosaicism aneuploidies in patients who have phenotypical dysmorphism for a chromosomal syndrome. To assess the rate of mosaicism, both conventional cytogenetic analysis and FISH analysis should be performed in such cases. Our results demonstrate the importance of using FISH for diagnosing numerical and structural chromosomal anomalies. This study confirmed cryptic mosaicism for one case and declined it for the other two situations.

The development of molecular cytogenetic technologies has increased the ways to detect chromosomal aberrations. The target would be towards the development, selection, and assessment of molecular techniques that will be suitable for use in routine diagnostic settings. For sure, these techniques will have a major contribution in establishing the chromosomal basis of fetal anomalies in an efficient manner that will permit the detection of chromosome abnormalities associated with phenotypical manifestations, allowing for early intervention in the newborn child. However, until these newer techniques become standard of care in some form, these should be considered additional to the standard karyotype.

References


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ETIOLOGIC AND POSITIV DIAGNOSIS OF CRANIOSYNOSTOSIS

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Abstract
In this material authors aim to make a short presentation of most frequent shape and structure modifications of cephalic extremities.

The start point of this study was, on one hand, the growing addressability, in pediatric rooms, of patients with modifications of head shape and dimensions, and on the other hand, diagnosis errors that could appear; particular aspect could be seen as pathologic. We would like to present these anomalies from the clinical and paraclinical point of view and to get them into a diagnosis entity.

Key words: cranyostenosis, newborn, sutures

Introduction
The head perimeter of a healthy, term newborn is about 34 – 36 cm. In the first year of life perimeter grows with approximately 10 cm, so that at the age of 1 year it reaches about 46 cm and in the following 20 years the perimeter grows with another 10 cm, so that at one adult it has about 56 – 57 cm. The modifications in plus (macrocephaly) and in minus (microcephaly) from these dimensions could be pathologic. The most frequent cause of microcephaly is craniosynostosis.

Craniosynostosis represents the premature fusion of one or more cranial sutures leading to modifications of head shape and/or dimensions. Craniosynostosis can be classified as: primary and secondary. Primary craniosynostosis may result from a primary defect of ossification; secondary craniosynostosis is characterized by a failure of brain growth and secondary ossification.

Craniosynostosis can also be classified by the number of sutures involved: simple craniosynostosis (one suture involved) and complex craniosynostosis (multiple sutures involved).

Incidence
By some authors the incidence is 0,4 / 1000 birth, sagital suture being involved mostly.

Causes
The most frequent causes, from literature, are: idiopathic, endocrine (hyperthyroidism, hypophosphatemia, vitamin D deficiency, renal osteodystrophy, hypercalcemia), hematologic (thalassemia), genetic (Apert syndrome, Crouzon syndrome, Pfeiffer syndrome).

There are also mentioned some risk factors as: caucasian mother, maternal age, male infant, maternal tobacco abuse, fertility treatments, treatments with nitrofurantoin, chlorpheniramine.

Clinical forms
Ossification of the cranial vault is circulary, starting from central region of each cranial bone and extending outward toward the cranial sutures and fontanelles (fig.1).
- The metopic suture separates the frontal bones;
- The coronal suture separates the frontal bones from the parietal bones;
- The sagittal suture separates the parietal bones;
- The lambdoid suture separates the occipital bones from the parietal bones.

Clinical diagnosis
Consists of several steps: anamnesis – to emphasize the presence since birth, physical exam which reveals: asymmetry, particular aspect, ossification of sutures and fontanelles, measurements of the cranial perimeter to evaluate Hydrocephalus and Microcephaly, evaluation for any other musculoskeletal abnormalities (ex.: torticolis, fingers and toe abnormalities)

Ossification of Metopic Suture (Metopic Synostosis)
The ossification of metopic suture determines the appearance of trigonocephaly (fig. nr. 2)

The shape of the shead is pointed, as a triangle; anteroposterior diameter is small, eyes appear closer together, forehead more pointed. It is, usually, a mild affection and does not need surgery.
Normal Skull of the Newborn

- Frontal Bones
- Metopic Suture
- Anterior Fontanelle
- Coronal Suture
- Sagittal Suture
- Parietal Bones
- Posterior Fontanelle
- Lambdoid Suture
- Occipital Bone

Trigonocephaly

Fused metopic suture

Fig. nr.2 Trigonocephaly.
Bicoronal Ossification (Bicoronal Synostosis)

The determined affection is brachycephaly (fig. nr.3), through premature ossification of both coronal sutures. Biparietal diameter is widened and the anteroposterior one is smaller. It is a severe disease associated with premature ossification of metopic suture with modifications of skull bones, face hypoplasia, flattened nose. Frequently associated with Crouzon syndrome and Apert syndrome. It is a serious affection and needs surgery, usually in the first year, to increase anteroposterior diameter.

Unilateral coronal synostosis = Frontal Plagiocephaly (fig. Nr.4).

Occurs by premature ossification of coronal suture; it is characterized by decreased anteroposterior diameter, flattened forehead.

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Fig. nr.3 Brachycephaly.

Fig. nr.4 Plagiocephaly.
Unilambdoid synostosis = Occipital Plagiocephaly (fig. Nr. 5).

   Occurs due to premature ossification of lambdoid suture.
   It is characterized by decreased anteroposterior diameter.

   At this form may be taken into consideration positional modifications
   Sagittal synostosis = Scaphocephaly
   Early ossification of sagittal suture is the most frequent craniosynostosis (1/4000 newborns) especially at male infants. It occurs more at premature; anteroposterior diameter is longer and the biparietal narrower.

   Primary craniosynostosis occurs when one or more sutures fuse prematurely, while the brain is still increasing. In this situation intracranial pressure can increase, with all its consequences.

   Secondary craniosynostosis is more frequent than the primary type and results from primary failure of brain growth (microcephaly). Usually is not accompanied by increased intracranial pressure; does not compromise normal brain growth and does not need surgery.

Differential diagnosis

Several affections can be taken into consideration, with modifications of cefalic extremity: cerebral tumors, hydrocephaly, hidranencephaly, endocrine diseases, craniovertebral dysraphism.

In the etiologic diagnosis must be considered: Apert syndrome, Crouzon syndrome, Pfeiffer syndrome, and all other affections mentioned at causes.

Paraclinic investigations

For a precise diagnosis and in order to localize the premature ossificated suture there are needed:
   - Skull radiography with anterior-posterior and lateral views
   - CT and RMN especially when surgery is being considered
   - Transfontanellar ultrasound (if anterior fontanella is open), shows ventricular dilatation (when craniosynostosis is associated with a malformation syndrome), hydrocephalus, corpus callosum agenesis
   - Endocrine evaluation

Complications

Severe, untreated craniosynostosis can lead to complications: increased intracranial pressure, face asymmetries, abnormal dental occlusion, orbit asymmetry associated with secondary strabismus

Treatment

Medical care

Practically there is no medical treatment, only hospitalization and prevention: monitor signs and symptoms of elevated intracranial pressure, measure head
circumference, ophthalmologic consult at patients with high intracranial pressure

**Surgical care**

It is the election treatment for infants with microcephaly (secondary craniosynostosis). Surgery is complicated and it is not performed currently.

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**References**

14. Fig.1 Fig.2 Fig.3 Fig.4 Fig.5 www.gfmer.ch/genetic_diseases_v2/gendis_detail_list.php?cat3=86

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STUDY ON ACUTE LYMPHADENITIS IN CHILDREN

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Abstract

In this study, we followed the clinical and paraclinical manifestations of the acute adenitis in children, taking into consideration that they represent the most frequent cause of acute lymphadenitis during childhood. The infectious adenitis represented the most frequent cause of increasing lymphatic ganglions in children, being present in 694 cases (62.4%). Pyogenic adenitis mostly affected small children (37.1%), the frequency gradually decreasing towards the older child. The pyogenic adenitis appears most frequently after a recent regional infection (89%) in the drainage area of the affected lymphatic ganglions. The most frequent localization of the pyogenic adenitis was at the level of cervical (63.3%) and submandibular regions (21.1%). The pharynx infections were the most frequent (37%), followed by the cutaneous ones (29%).

Key words: Pyogenic adenitis, etiology, frequency, children.

Introduction

Pyogenic adenitis is a localized adenitis, determined by microbial agents which may primitively affect the ganglion or may accompany a regional infection, being a satellite to the infectious processes which are found in the corresponding drainage area.

Microbial adenopathies with common germs often accompany a rhynopharinx infection. The adenopathy may be unilateral or bilateral, painful, surrounded by a moderate periadenitis, without the modification of adjacent teguments. After the pathogen agent penetrates the lymphatic ganglion, the polimorphonuclear cells increase in number and the suppuration occurs. Without treatment, it can evolve to adenophlegmon.

Material and method

We carried out a retrospective study in 313 patients with acute lymphadenitis, aged between 2 weeks and 16 years, who were admitted in the Pediatric Clinics of the Emergency County Hospital in Craiova, from 1996 to 2005.

For this group, we followed: pyogenic adenitis frequency; case distribution according to age groups, sex and environment; anamnesis particularities related to onset; local and general clinical examination; careful clinical examination of the drainage areas in the affected ganglionary area; correlation between the type of infection and the localization of the adenopathy; specific (cultures from the ganglionary product and from other pathologic products) and unspecific paraclinical examinations (neutrophilic leukocytosis, acute phase reactants).

Results and discussions

Within an ampler study, carried out over a period of 10 years, on a group of 1112 children with lymphadenitis, the infectious adenopathies represented the most frequent cause of increasing lymphatic ganglions in children, being present in 694 cases (62.4%). Bacterial etiology was found in 324 cases (46.6%), viral in 255 cases (36.7%), mycobacterial in 99 cases (14.2%), parasitary (toxoplasmosis) in 16 cases (2.3%). We did not register cases of adenopathy caused by fungi (Table 1).

<table>
<thead>
<tr>
<th>Infectious Causes of adenopathy</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial (N=324)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pyogenic adenitis</td>
<td>313</td>
<td>45.1</td>
</tr>
<tr>
<td>Cat’s scratch disease</td>
<td>11</td>
<td>1.5</td>
</tr>
<tr>
<td>Viral (N=255)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV Infection</td>
<td>184</td>
<td>26.5</td>
</tr>
<tr>
<td>Infectious Mononucleosis</td>
<td>36</td>
<td>5.2</td>
</tr>
<tr>
<td>Rubella</td>
<td>28</td>
<td>4</td>
</tr>
<tr>
<td>Measles</td>
<td>4</td>
<td>0.6</td>
</tr>
<tr>
<td>CMV Infection</td>
<td>3</td>
<td>0.4</td>
</tr>
<tr>
<td>Mycobacteria (N=99)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tuberculous adenitis</td>
<td>87</td>
<td>12.5</td>
</tr>
<tr>
<td>Adenitis with atypical mycobacteria</td>
<td>12</td>
<td>1.7</td>
</tr>
<tr>
<td>Parasitary (N=16)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Toxoplasmosis</td>
<td>16</td>
<td>2.3</td>
</tr>
<tr>
<td>Fungi (N=0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hystoplasmosis, Aspergillosis</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>694</td>
<td>100</td>
</tr>
</tbody>
</table>
In our study, the pyogenic adenitis represented the most frequent cause of acute adenitis (45.1%) within infectious adenitis.

The group characteristics related to age, sex, and environment are given in Table 2.

<table>
<thead>
<tr>
<th>Age group</th>
<th>Sex</th>
<th>Environment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>male</td>
<td>female</td>
</tr>
<tr>
<td>0 – 1 year</td>
<td>51</td>
<td>16.3</td>
</tr>
<tr>
<td>1 - 3 years</td>
<td>116</td>
<td>37.1</td>
</tr>
<tr>
<td>3 - 6 years</td>
<td>71</td>
<td>22.6</td>
</tr>
<tr>
<td>6 - 10 years</td>
<td>49</td>
<td>15.6</td>
</tr>
<tr>
<td>10 - 16 years</td>
<td>26</td>
<td>8.3</td>
</tr>
<tr>
<td>Total</td>
<td>313</td>
<td>100</td>
</tr>
</tbody>
</table>

Taking into account the case distribution according to age groups, we can notice that pyogenic adenitis mostly affects infants (37.1%), the frequency gradually decreasing with toddlers. For the 0-3 year age group, immunity is low, and the frequency of the respiratory and cutaneous infections is high. We found pyogenic adenitis in 6 cases for the newborn (2%), while for the infant, in 45 cases (14.3%).

The case distribution according to sex emphasizes a clear dominance of males with 197 cases (62.9%), as compared to 116 cases of females (36.9%); from the environment point of view, we notice an increased frequency of children coming from rural areas - 184 cases (58.8%), as compared to urban areas with 129 cases (41.2%).

The adenopathy onset was acute, 1-3 weeks before the hospitalization.

The clinical characteristics of the affected ganglions were: the ganglions diameter was between 2 and 6 cm; they were spontaneously painful or when touching them; they had a hard, fluctuant consistency which was present in 1/3 of the cases; they were adherent to deep planes; modified adjacent teguments (local fever, erythema, edema). The adenitis evolution to suppuration was recorded in 58 cases (18.5%) which required incision and surgical drainage.

The pyogenic adenitis appears most frequently after a recent regional infection, in the drainage area of the affected lymphatic ganglions.

In most cases - 279 cases (89%), we have found out various locoregional infections, after a thorough examination.

The pharynx infections were the most frequent, in 116 cases (37%), followed by the cutaneous ones - 91 cases (29%), infections of the oral cavity - 39 cases (12.5%), otic infections - 17 cases (5.4%), conjunctival infections - 16 cases (5.1%); the infection center was not obvious the moment when the adenitis was diagnosed in 34 cases (11%). (Table 3).

<table>
<thead>
<tr>
<th>Infection localization</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amygdalian</td>
<td>116</td>
<td>37</td>
</tr>
<tr>
<td>Cutaneous</td>
<td>91</td>
<td>29</td>
</tr>
<tr>
<td>Oral cavity</td>
<td>39</td>
<td>12.5</td>
</tr>
<tr>
<td>Otic</td>
<td>17</td>
<td>5.4</td>
</tr>
<tr>
<td>Conjunctival</td>
<td>16</td>
<td>5.1</td>
</tr>
<tr>
<td>Without specified infections</td>
<td>34</td>
<td>11</td>
</tr>
<tr>
<td>Total</td>
<td>313</td>
<td>100</td>
</tr>
</tbody>
</table>

A correlation between adenitis localization and regional infections in the afferent drainage area is shown in Table 4.

The pharynx infections were present in 116 cases (41.5%), being accompanied by laterocervical adenitis in 96 cases (34.4%) and submaxillary and submentonier adenitis in 20 cases (7.1%).

Cutaneous infections in the drainage area of the affected ganglions were registered in 91 children (32.6%). Infections of the hairy skin of the head (seborrheic dermatitis, impetigo, and pediculosis) were present in 61 children (21.8%). These infections determined the appearance of satellite adenitis, with a laterocervical, occipital, retroauricular localization. Acute piodermitis was found in 20 children (7.1%), especially in sucklings, being accompanied by laterocervical, axillary and inguinal adenopathy. We registered infected wounds at the upper limb level accompanied by axillary adenitis in 6 children (2.1%), while at the lower limb level accompanied by inguinal adenitis in 4 children (1.4%).
Infections of the oral cavity were registered in 39 children (13.9%) - 21 children (7.5%) showed signs of gingivostomatitis, and 18 children (6.4%) dental abscess. These infections led to the appearance of submandibular, submentonier and laterocervical adenopathies.

Otitis externa was found in 17 children (6.1%), being accompanied by laterocervical and retroauricular adenopathy, while conjunctivitis, accompanied by preauricular adenopathy was registered in 16 children (5.7%).

Among the paraclinical investigations, in order to set the diagnostic, the cultures from the ganglionary product, the infected cutaneous lesions and the pharynx exudate were most edifying. The presence of the leukocytosis with neutrophily and of the acute phase reactants held an unspecific, but helpful role.

The cultures from the ganglionary product were performed in 58 cases (18.5%) and they were positive for:
- staphylococcus aureus in 28 cases (9%);
- streptococcus β-hemolytic in 14 cases (4.5%);
- streptococcus group B in 4 cases (1.2%);
- anaerobic germs in 12 cases (3.8%).

The cultures from the pharynx exudate revealed the presence of the streptococcus β-hemolytic in 24 cases (7.6%) and of the staphylococcus aureus in 16 cases (5.1%); the cultures from the overinfected cutaneous lesions were positive for the staphylococcus aureus in 18 cases (5.7%).

Leukocytosis was present in 286 cases (91.3%), with values between 10,000-25,000/mm³, while neutrophily with values over 60% was present in all children.

Among the acute phase reactants, the ESR with values between >30mm/hour was present in 243 children (77.6%), the reactive C protein was present in 86 children (27.5%), the fibrinogen with values over 400 mg% was present in 226 children (72.2%), while α₂ globulins with values >8% were present in 48 children (15.3%).

The moderate anemia with Hb values between 9 and 11 gr % was found in 87 children (27.7%).

The laboratory findings are shown in table 5.

Ganglionary biopsy was performed in 36 children (11.5%) where the bacterial etiology was not obvious after the clinical exam and the usual paraclinical investigations. In these children, the hystopathological exam emphasized a lymphocytary, reticular, plasmocitary cell hyperplasia, with big, basophile cells. Both these cells and the polymorphonuclear ones showed major dystrophic phenomena.

Cenghiz (2004), in a study carried out on a group of 132 children aged between 2 and 15 years, noticed that pyogenic adenitis cases were most frequently localized at the level of the cervical region (43.2%) and submandibular (27.3%), while the cultures were positive in 23.5% of the studied cases.

Kelly (1998) specified that infections with staphylococcus and streptococcus are most frequently found in children aged between 1 and 4 years.

Maureen (2002) noticed that 85% of the pyogenic adenitis cases have as etiology the infection with staphylococcus aureus or streptococcus β-hemolytic group A. Kelly (1998) pointed out the presence of the anaerobic bacteria in 38% of the cultures performed in cervical adenitis, in children aged between 2-16 years.

Kelly (1998) presented the following distribution of bacterial adenitis, according to localization: submandibular 50 - 60%; upper cervical 25 - 30%; submentonier 5 - 8%; occipital 3 - 5%; lower cervical 2 - 5%.

Other causes of pyogenic adenitis may also be represented by: H influenzae, Pseudomonas aeruginosa, Yersinia pestis, Chlamydia, Mycoplasma pneumoniae, Treponema pallidum.

When etiology is not obvious, one may occasionally require ganglionary biopsy. From the gathered product, one can make cultures for pyogenic germs, mycobacteria, and sometimes PCR.

In patients with fluctuant lymphatic ganglions, with a suspicion of abscess formation, the ganglionary x ray can bring additional data.

In adenophlegmon, the fine needle aspiration can be performed in order to point out the germs, although in these situations, we usually need an incision and the surgical drainage.
Table 5. Paraclinical explorations in pyogenic adenitis (N=313).

<table>
<thead>
<tr>
<th>Paraclinical explorations</th>
<th>Results</th>
<th>No</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukocytosis</td>
<td>10,000 – 25,000/mm³</td>
<td>286</td>
<td>91.3</td>
</tr>
<tr>
<td>Neutrophil</td>
<td>&gt; 60 %</td>
<td>313</td>
<td>100</td>
</tr>
<tr>
<td>ESR</td>
<td>&gt; 30 mm at 1h</td>
<td>243</td>
<td>77.6</td>
</tr>
<tr>
<td>Protein C reactive</td>
<td>present</td>
<td>86</td>
<td>27.5</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>&gt; 400 mg%</td>
<td>226</td>
<td>72.2</td>
</tr>
<tr>
<td>α_2 globulin</td>
<td>&gt; 8%</td>
<td>48</td>
<td>15.3</td>
</tr>
<tr>
<td>Positive cultures from the ganglionary aspirate</td>
<td>- staphylococcus aureus</td>
<td>28</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>- streptococcus β-hem.</td>
<td>14</td>
<td>4.5</td>
</tr>
<tr>
<td></td>
<td>- anaerobic germs</td>
<td>12</td>
<td>3.8</td>
</tr>
<tr>
<td></td>
<td>- streptococcus group B</td>
<td>4</td>
<td>1.2</td>
</tr>
<tr>
<td>Positive cultures from the pharynx exudate</td>
<td>- streptococcus β-hem.</td>
<td>24</td>
<td>7.6</td>
</tr>
<tr>
<td></td>
<td>- staphylococcus aureus</td>
<td>16</td>
<td>5.1</td>
</tr>
<tr>
<td>Positive cultures in cutaneous lesions</td>
<td>- staphylococcus aureus</td>
<td>18</td>
<td>5.7</td>
</tr>
<tr>
<td>Ganglionary biopsy</td>
<td>Characteristic modifications</td>
<td>36</td>
<td>11.5</td>
</tr>
</tbody>
</table>

Conclusions

1. Pyogenic adenitis represented the most frequent cause of acute adenitis (45.1%) within the infectious adenitis.
2. Pyogenic adenitis mostly affected small children (37.1%), the frequency gradually decreasing towards the older child.
3. In most cases - 279 (89%) – after a thorough examination, we discovered various locoregional infections; we mainly found pharynx infections in 116 cases (37%).
4. The most frequent localization of the pyogenic adenitis was at the level of cervical (63.3%) and submandibular regions (21.1%).
5. Bacterial etiology was confirmed through cultures from ganglionary product in 18.5% cases, staphylococcus aureus (9%) and streptococcus β hemolytic group A (4.5%) being most frequently isolated.

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THE TEENAGERS WITH SUICIDE AND PARASUICIDE ATTEMPTS AND THEIR FAMILY

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Summary
The adolescence, considered as "the age of the second birth" is characterized by the spectacular aspect of the transformations that the individual is going through, in all respects, including that of personality development. The purpose of the study is represented by the evaluation of the familial impact on the motivation in the teenage suicidal attempt. The study group was made up of 60 teenagers, hospitalized in the Pediatric Clinic II Timisoara, diagnosed with suicidal attempt and eventually taken in charge by the Neuropsychiatry department of the Center for Children Diagnose and Treatment. Conclusions: the teenage suicidal attempt represents a phenomenon with an increasing incidence. The dynamic factors of the family life are involved in the psychogenesis of the maladjusted suicidal behaviour.

Key words: suicidal attempt, teenage, personality development.

Introduction
The adolescence, considered as "the age of the second birth" is characterized by the spectacular aspect of the transformations that the individual is going through, in all respects, including that of personality development. The teenage model of personality is influenced by the family environment. In the context of the above-mentioned aspects, the suicidal act can be the expression of maladjustment to the family environment.

Purpose of the paper
The purpose of the study is represented by the evaluation of the familial impact on the motivation in the teenage suicidal attempt, by taking into consideration two aspects: the familial environment and the teenager personality.

Material and method
The study group was made up of 60 teenagers, hospitalized in the Pediatric Clinic II Timisoara, diagnosed with suicidal attempt and eventually taken in charge by the Neuropsychiatry department of the Center for Children Diagnose and Treatment.

The patients have been analyzed from the following points of view:
- identity data
- characteristics of the family environment
- triggering factors of the suicidal act.

THE IDENTITY DATA of the study group reveal:
- average age: 15.5 years
- sex: the females represent 80%, the males represent 20%
- family environment: 70% of the cases come from numerous families (with more than 4 children)
THE CHARACTERISTICS OF THE FAMILY ENVIRONMENT
- dysfunctional families: 19 cases
- family environment deprived of affection, unsupportive: 23 cases
- physical and emotional abuse: 2 cases
- inadequate education: 9 cases
- low social and economical status: 4 cases
- psychiatric disorders in the family: 3 cases

TRIGGERING FACTORS OF THE SUICIDAL ACT
- family or school conflicts: 34 cases
- failure in school: 3 cases
- c (separation from a girlfriend/boyfriend): 2 cases
- psychiatric disorders of the subject, depression: 3 cases
- anxiety: 6 cases
- behavioral disorders: 12 cases

For the psychological evaluation, we have used: Zung self-rating depression scale, the ASI anxiety index, associated with projective tests (the family test, the Draw-a-person test, the Draw-a-tree test) and the Raven test, in order to establish the subject intelligence level (IQ).

Results and discussions
The teenage suicidal attempt represents a phenomenon with an increasing incidence.

In full development, the teenager starts to separate from the state of family dependency and tends to the adult independence and autonomy. It is the period when the personality is defining; the teenager adapts himself and develops the biological, psychological and social potentialities, makes progresses, combining several hierarchical levels: the satisfaction of the biological needs, the social interaction and adaptation, the accepted rules of moral behaviour.

The dynamic factors of the family life are involved in the psychogenesis of the maladjusted suicidal behaviour. Here we can include the quality of interpersonal relationships with the family members and the quality of the
emotional communication in the family. Most of the times, the dysfunctional family creates severe psychosocial stress in teenagers vulnerable to stress, determining a modification of the conflict perception, a negative cognitive distortion, pushing them towards a suicidal behaviour.

The temperament, in a close connection with the IQ, has an important role in the suicidal inclination. Thus, the teenagers with a high IQ respond positively and adapt to the stress conditions, while those with a lower IQ are more vulnerable in similar conditions.

The suicidal attempt must not be considered as a pathologic element, but it must be understood as an aspect of an evolution associating both progress and regress.

Conclusions
1. It is important that the family should have knowledge about the psychological problems faced by the teenager during the period in which his personality structure is defining.
2. The difficulties of expression of the suicidal teenager are generally connected to the adolescence itself. We can mention some constant features of the suicidal teenager, i.e. the capacity to isolate and the difficulty to identify himself which were noticed in all the cases studied.
3. The need to elaborate programs in order to prevent the mental illness in children and the need for children to adopt precocious adaptable measures in order to prevent the suicidal act.
4. The establishment of a program of psychological assistance in special institutions, for teenagers passing through difficult existential moments, the availability of “hotline” centers during the night.

References

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CONGENITAL INFECTION WITH CMV IN THE PEDIATRIC PATHOLOGY

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Summary
Discovered in early XXth century, the cytomegalovirus is the most frequent cause for mother to fetus infection. The multiple forms of manifestation of this congenital infection are characterized by a large palette starting with asymptomatic forms up to varied clinical manifestations. A number of 65 cases have been analyzed (new born and sucklings) suspected from the anamnestical / clinical point of view of congenital infection with CMV, hospitalized in the Clinic II of Pediatrics Timisoara. For 27 cases, the infection has been confirmed from the serological point of view by dosing the specific antibodies of the type IgG and IgM. The authors analyze the casuistry from the epidemiologic, clinical, paraclinical and evolutive (neurosensorial consequences) point of view. From the epidemiologic point of view the incidence of the infection with CMV has obviously prevailed in suckling, with a slight predominance in male subjects, with no significant difference as to their origin (rural/urban).

The conclusions of the research as to the clinical manifestation, paraclinical investigation and in particular as to the evolution from the neurosensorial point of view of the casuistry have determined the authors to conclude that the infection with CMV represents nowadays a significant issue of public health in mother-child couple.

Key words: Cytomegalovirus, neurosensorial consequences, children.

Introduction
Discovered at the beginning of the XX century, the citomegalic virus represents the most frequent fetomaternal infection cause. According to the data in the specialized literature, the prevalence of the congenital infection is of 0,2 – 2, 4 % and the fetopathy consequent situates on the first place within the frame of the fetomaternal infections.

Although the possibility of evolution may be variable in both forms of disease, the evolution towards decease in the symptomatic forms (25-30% of the children) as well as of the installation of some serious consequences (70-80% in the symptomatic forms, respectively 15% in the asymptomatic ones) draws the attention on this infection.

Scope of the study
The scope of this study is that in emphasizing some aspects regarding the frequency of the infection, the diagnostic ages, complications and consequences produced by the citomegalic virus, virus known as having aggressive potential on the young tissues, in formation.

Material and Method
There was performed a study with a number of 65 cases (new-born and nursling) anamnestically / clinically suspected of congenital infection with CMV hospitalized in the Clinic II Pediatrics Timisoara for a period of 2 years (January 2005 – January 2007).

The new-born and the nursling were analyzed with regard to the data regarding:
- sex
- provenience medium
- the form of disease from the clinically point of view (symptomatic and asymptomatic)
- laboratory examinations: evidencing atc.Anti CMV of type IgG, IgM by means of the method ELISSA.
- complementary clinical investigations: audiometry in biannual prospective way in the first year and then annually applied to all of the 27 children that formed part of the study, the average mean of the last examination being 39 months.

The loss of neurosensorial hearing has been defined as the air conduction threshold, >25dB, with auditory brain stem response (ABR) >20dB, on and audiogram correlated with the normal values for a child normally developed for the respective age. Progressive loss of hearing has been defined as neurosensorial decrease of hearing with 10dB or more, for any ABR frequency or threshold, documented by two different evaluations.

Results and conclusions
Among the 65 studied cases, the infection with the citomegalic virus was confirmed at a number of 27 children (40%) by dosing atc anti CMV of type IgG and IgM.

Children diagnosed with congenital infection in different phases of evolution had a greater incidence over the masculine sex (65%) compared to the feminine sex (35%).

With regard to the medium of provenience of the patients I have noticed an incidence equal in the rural and the urban one.
From the point of view of the age to which was established the infection diagnostic with CMV, a greater balance has distinguished at the age group of 0-6 months (19 cases) followed by the age group 6-12 (8 cases).
The clinical manifestations found at the studied patients were polymorphic, dependent of the patient’s age, symptomatic form (19%) or asymptomatic of disease (81%). Symptomatic form of disease was suspected by the presence of some suggestive clinical signs including: spots and hepatosplenomegaly – 3 cases, retard of intrauterine growth – 1 child, microcephaly –2 cases.

Following the audiometric evaluations, the loss of the hearing appeared at 14% (3 of 22) of the children with asymptomatic form of disease and 80% (4 of 5) at those with symptomatic form of disease. Among the symptomatic form of disease of the infection with CMV, the loss of hearing during the analysis appeared to all of the children with spots and hepatosplenomegaly (3 cases) and 1 child with microcephaly.
Conclusions
1. The results of this study show that the congenital infection with CMV represents a problem of public health that due to the polymorphic clinical expression can determine diagnostic confusions.
2. It is necessary an early diagnosis of the infection with CMV before the installation of the after-effects phase.
3. The disease disseminated at birth, proved by the presence of the hepatosplenomegaly spots, intrauterine retard growth, microcephaly, represents an important factor in losing the hearing at the children.
4. The infection with CMV is underdiagnosed at the current moment, which is why it is necessary an active localization of the cases and the performance of some centralized statistic information.

References

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POSITIVE AND NEGATIVE PREDICTIVE VALUE OF SEROLOGICAL TESTS IN CELIAC DISEASE CHILDREN BASED ON HISTOLOGICAL FINDINGS

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Abstract
The authors tried to establish the positive predictive value and negative predictive value of serological tests used in celiac disease screening on target population. Positive diagnosis of gluten intolerance was established assessing the histological villous alteration using Marsh classification (1992) modified by Oberhuber (1997). In order to optimize the serologic diagnosis during celiac disease screening among risk population, maximum specificity and sensitivity are obtained by using combination of antiendomisium and antitransglutaminase antibody assessment.

Key words: celiac disease, children, antiendomisium antibody, antitransglutaminase antibody

Introduction
Nowadays, the gold standard of celiac disease diagnosis is represented by intestinal biopsy showing characteristic villous lesions. The biopsy sample can be taken by using Watson capsule or during upper digestive endoscopy. Recent, a non-invasive diagnosis algorithm of serological tests for celiac disease developed.

Objectives
We intended to establish sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of serologic tests used for celiac screening. The diagnosis was based on histological intestinal injury, using Marsh classification.

Material and methods
70 consecutive patients (medium age 6.5 years, sex ratio G/B 48/22) presenting high suspicion of celiac disease (chronic diarrhea, small stature, weight loss, recurrent abdominal pain, or anemia resistant to oral martial therapy) were enrolled in this study during April 2004 until March 2007 – group A. All patients enrolled in group A underwent intestinal biopsy using upper digestive endoscopy (patients aged more than 4 years), or Watson capsule (patients aged less than 4 years).

During the same period, a lot of 62 consecutive, randomized patients – lot B of study, (medium age 9 years, sex ratio G/B 38/24) underwent upper digestive endoscopy for different causes, non-related to gluten intolerance: recurrent vomiting, dyspepsia, gastritis, gastric or duodenal ulcer, hematemesis, cirrhosis with esophageal varices, alternating bowel habits). For each patient from group B a sample of intestinal biopsy was taken during upper digestive endoscopy.

All biopsy sample were blindly classified, using Marsh criteria (1992) modified by Oberhuber (1997): type I infiltrative, type II hyperplastic (infiltrative lymphoplasmonic lesions in villous corion, associated by glandular crypt enlargement) and type III destructive (including partial, subtotal villous atrophy – type IIIa, IIIb and total villous atrophy – IIIc). (1)

At the time of admission in this study, a serum sample was taken for total serum immunoglobulin A level and also for IgA and IgG antigliadin antibody (AGA), IgA anti-endomisium antibody (EMA) and IgA anti – human tissue transglutaminase antibody (anti hu-tTG). 2 patients from lot B with selective IgA deficiency were excluded from this study.

For IgA EMA detection we used immunofluorescence technique using smooth muscle of monkey esophagus (ImmunoGlo™Anti-Endomysial Antibody (EMA) Test Kit – provided by „IMMCO DIAGNOSTICS”). Detection of anti tTG antibodies was performed using ImmuLisa™ anti-hu tTG ELISA. Test kits were provided also by „IMMCO DIAGNOSTICS”.

Results and discussions
14 patients from 70 enrolled in group A of study (20%) and 1 patient from 60 remained in group B after IgA deficiency subjects exclusion (1.67%) presented villous lesions corresponding to Marh type II, IIIa, IIIb and IIIc. The 115 remained patients with normal intestinal morphology were considered the control group. All 15 subjects with histologically confirmed celiac disease tested positive for IgA EMA and tTG, while both IgA and IgG AGA were positive only in 10 of 15 patients (66,7%). None of the patients from control group had positive IgA EMA, but 6 patients from 115 (5%) tested positive for IgA anti hu-tTG antibody. 15 control subjects (13%) tested positive for IgA AGA and 30 control subjects (26 %) tested positive for IgG AGA.

Assessing these data, we calculated EMA and tTG sensitivity as 100% and IgA, IgG AGA 66%. The specificity was 100% for EMA, 95% for tTG, 87% for IgA AGA and 87% for IgG AGA. The negative predictive value was 100% for EMA and tTG, 94% for IgG AGA and 95% for IgA AGA. The positive predictive value was 100 % for EMA, 71% for tTG (p = 0, 03% vs. EMA), 25 % for IgG AGA and 66% for IgA AGA. Most of the control subjects who false
positive for were anti - hu tTG antibody had Crohn’s disease or chronic liver disease.

Recent studies described a high number of asymptomatic (latent, silent) or atypical form of celiac disease. In many cases, this condition is indicated by intestinal morphology alteration observed after upper digestive endoscopy performed for dyspeptic syndrome, or to evaluate an irritable bowel syndrome non-responsive to classic therapy. It is estimated that 5% of patients with irritable bowel syndrome corresponding to Rome II criteria have celiac disease. (2), (3)

Typical form of disease presents classic clinic manifestation, positive serology and characteristic intestinal alteration.

Atypical form of disease presents different and/or minimal clinic manifestation (dermatitis herpetiformis, dental enamel hypoplasia of permanent teeth, osteopenia/osteoporosis, short stature, delayed puberty s.a.), positive serology and characteristic intestinal alteration.

Silent form of disease associates positive serology and intestinal villous injury in non-symptomatic patients.

Latent form of disease is characterized by positive serology without bowel morphology alteration in non-symptomatic patients.

Studies regarding atypical, silent or latent form of celiac disease have generated a great interest for methods of serologic screening in gluten enteropathy diagnosis. Using different serologic tests since 1997 permitted a better selection of cases for intestinal biopsy in celiac patients. (4)

Anti-reticulin antibodies used previously for gluten intolerance diagnosis proved to have low sensitivity and specificity, so these antibodies are excluded from diagnosis protocols.

IgA and IgG antibodies (AGA) are quantitative assessed using ELISA technique. There is a great number of false positive patients for AGA, mostly of them presenting milk protein intolerance, parasitic enteritis – Giardia Lamblia, s.a. Lately, specialized researchers developed a new serologic test for IgA and IgG AGA, based on deaminate gliadine peptides, with high accuracy. This new assay has a higher sensitivity and specificity compared to conventional IgA and IgG AGA assay. (5)

EMA are detected on the smooth muscle of monkey esophagus or human umbilical tissue using indirect immunofluorescence. EMA decrease slowly after gluten exclusion and have a rapid increase tendency after gluten challenge. It is known that indirect immunofluorescence technique is operator dependent and there are different sources of error: number of function hours of fluorescence source, lens quality, microscope diaphragm opening s.a. (6)

Since 1998, IgA and IgG tTG have been detected using ELISA technique. Recent, researchers developed a rapid diagnosis test for tTG, dot blot assay with similar sensibility and specificity as ELISA. (7)

As many studies concluded, enzyme linked immunosorbent assay based on human tissue transglutaminase outperforms the guinea pig based tissue transglutaminase assay (8), so we used in this study human antigen for tTG antibody.

Interpretation of serologic test in celiac disease must consider IgA selective deficiency source of false negative results for IgA EMA and tTG. Also ESPGHAN criteria for celiac disease do not recommend serologic tests in patients aged less than 2 years, due to high frequency of false negative results. (9)

In 2007 at Barcelona, during ESPGHAN (European Society of Pediatric Gastroenterology, Hepatology and Nutrition) Symposium, a researchers group leaded by S. Niveloni from Mucosal Biology Research Center and Center for Celiac Research, Maryland University, Baltimore, USA, have comunicated their results regarding a new serologic diagnosis algorithm for celiac disease with positive and negative predictive value of 100%. This protocol with high accuracy is able to diagnose celiac disease without performing intestinal biopsy and associates EMA, anti-actine antibodies, tTG and serie level of protein zonulin. (10)

Conclusions

Although anti - tTG antibody evaluated in our study showed an optimum sensitivity, their low specificity determined positive predictive values wich were significantly lower than those of EMA assay.

In accordance with others studies, the positive predictive values of Ig A and IgG AGA were to low to warrant submitting a patient to intestinal biopsy for suspected celiac disease only performing AGA serology.

In order to optimize the serologic diagnosis of celiac disease, screening tests among risk population must associate a combination with maximum specificity and sensitivity - EMA and tTG antibodies assessment.

Low values of IgA and IgG AGA sensitivity and specificity compared to EMA and tTG, can reduce or even exclude these tests from celiac disease serologic screening.

In order to develop a non-invasive diagnosis algorithm for gluten enteropathy, further studies on different age groups are needed regarding deaminate gliadine peptides antibody, anti-actine antibody, or zonulin. Until these tests will be available and accessible in any laboratory, intestinal biopsy remains the gold standard for celiac disease diagnosis.

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HISTIOCYTOSIS WITH LANGERHANS CELLS
- CASE PRESENTATION -

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Abstract
The authors present the case of a 9 month old male nursling, hospitalized in the clinic for unilateral installed othorragia. The clinical exam corroborated with the radiological exam (skull, thorax, limbs) established the histiocytosis diagnosis with Langerhans cells. The final diagnosis is the histopathological and imunohistochemical one of the biopsied material from the tumoural bleeding system of the external auditory conduct.

Key words: histiocytosis, diagnosis, nursling.

Presentation of the case
We present the case of a 9 month old male nursling, from the rural environment, hospitalized in the Second Pediatric Clinic of the Districtual Craiova Hospital (OS 29954/2007) for abrupt installed othorragia (24 h before coming to the hospital)

The heredocollateral antecedents are insignificant.
From the personal physiological antecedents: first child, born at term, W=3000 g, unknown Apgar score, naturally alimented at the hospitalization time, incorrectly diversified at 6 months of age, properly vaccineted and vitaminised.
Pathological personal antecedents: a respiratory intercurrence, ambulatory treated.

The hospitalization objective exam shows a 9 month old male nursling, in good nutrition state, afeverish, with intensely pale teguments and mucous, facies suffering, excited, with subangulomandibular adenopathy with mobile 0.5 – 1 cm ganglions, right othorragia, normal appearance mouth cavity, pulmonary without pathological alteration, AV = 132/min, systolic breath of second degree on the whole cardiac area, liver with the inferior edge 1 cm under the rim, impalpable splen, diminished whimsical appetite, normal intestinal transit, spontaneous, physiological mictions, irritability, agitation.

The laboratory exams and the paraclinical exploration have shown: Hb=9.03 g/dl, T=500000/mmc, L=14200/mmc, NN=4%, NS=37%, Lf=40%, M=8%, anisocytosis, hipocromia,
During the hospitalization, the anemia has accentuated Hb=8,30 g/dl, T=460000/mmc, L=6000/mmc (NS=38%, E=8%, Lf=51%, M=3%), anisocytosis ++++, poikilocytosis+++ , hipocromia+++ (ovalocyte, skizocyte, anulocyte) sideremia = 13µg/dl, =52/98mm →61/80mm →70/115, after 1 and 2 hours. The rest of the biological investigations had normal limits.

The ORL exam: bleeding tumoral formation of the external right conduct.

The skull x-ray: at the level of the cranial calotte several round ovalar zones of osteolysis can be observed with dimensions between 4 – 14 mm diameter, with a thin line [fig. 1].

Fig. 1. The skull x-ray.
The pulmonary x-ray: without modifications of pulmonary transparency, heart with the accentuation of the inferior left arc. Bone structure modification of the left scapula, left C II and C V, C V arc given by the resorption through the osteolysis of the exostosis at the level of the ribs, the density grows of the collateral soft parts left C II.

Global T10 sag [fig. 2]. Osteolysis zones have been radiological traced also at the level of the left humerus and at the level of bilateral femur.

Abdominal ultrasound offers normal data.

The performed paraclinical exploration, toghether with the clinical exam and the laborotary exams, establish the histiocytosis diagnosis with multiple bone determinations. The diagnosis is sustained by the histopathological and immunohistochemical exam from the biopsied material from the level of the tumoral system of the right external auditive conduct (which continued to bleed during the entire period of hospitalization).Histopathological study - the morphological picture is dominated by the Langerhans cells proliferation, which are a particular type of histiocytes. The cells have an abondant acidophilic cytoplasm, are generally multinucleated and present multiple vesicular nucleus with small nucleolus. Togther with the multinucleated histiocytes, granulocytes can also be observed. The multinucleated histiocytes are found on the squamous epithelium ulceration and subjacent to the ulceration. The cells have an acidophilic cytoplasm, irregular multiple nuleuses, with small nucleus. At the immunohistochemistry there is a positive marking for CD15, S100 and CD68 protein:

- the CD15 is positive granulocytes and negative in histocytes [fig. 3 si 4].
- the S100 protein is a marker for histiocytes (the positivation for S100 have been obtained) [fig.5].

- the positivation for CD68 has been obtained in numerous multinucleated histiocytes [fig. 6] and CD68 is negative in the intravascular granulocytes [fig.7].

The nursing has been transferred in the Marie S. Curie Hospital where the medicamentous treatment according to the LCH III protocol: Vinblastime and Prednisone induction.

**General Data**

Langerhans cells histiocytosis (HCL) is a disease which is a part of the histiocitary syndrom which include: reactive histiocytosis (secondary to some immunodeficiencies and infections) and malignant histiocytosis.

In HCL takes place the uncontrolled proliferation of some cells belonging to the fagitomononucleous and which lead to the infiltration and distruction of the normal surrounding tissues. HCL reunites in only one entity the following syndromes:

- the Letterer Siwe disease (for children under 2 years old)
- the Hand Schuller Christian syndrome (characteristic to the preschool child)
- the eosinophilic granuloma (for the big child and adult)
- spontaneous resolutive congenital histiocytosis (Hashimoto Pritzker syndrome)
- pure cutaneous histiocytosis.

Until 1985, HCL, reunited under the name of histiocytosis X the first three entities (different according to the premises and extension of the lesions) the distinction between them being difficult.

The actual data show that the incidence of the disease is reduced (4-5.4 cases/million/year), the medium debut age being 2-3 year of age and mainly affecting the male sex. It is considered that under the age of 5 half of the cases with bone lesions appear.

The clinic picture of the disease: the skeleton and the skin are the most often interested. The bone lesions can be localized at the level of the skull, the long bones, the vertebrae, the renal pelvis and the ribs and can be unique or multiple.

The symptomatology consists in pain, fracture, soft parts tumefaction (in the mastoeidian localisation). The bone affectation can be latent, asymptomatic, the x-ray identifies different size osteolysis hotbeds clearly delimited. The mandibular localisations produces pain, tumefaction and reactive adenopathy, even teeth fall. The superior jaw is rarely affected. When affected the vertebral corpus, appear the effect of plane vertebra. Signs of mandibular compression appear with the extension of the granulome in the muscular space. The invasion of the bone marrow is more frequent, the evolution is imposed by the extension of the granulome in the skull x-ray (with the accentuation on the osteolysis zones HCL characteristic). The general state of the nursing was modified before the diminished appetite othorragia debut, irritability, the tegument and progressively accentuated mucous pallor (the hipocrome anemia being explained by the diminishing of the appetite, the sanguine loses, the alimentary deficiency). The positive diagnosis has been made by joining the clinical and radiologic data, but also the anatomopathological exam from the bleeding tumoral system from the auditive conduct has been imposed.

The HCL prognosis is different in function of the disease type, of its localization, the lesions extension and the dysfunction of the interested organs.

**Discussions**

In the presented case, the affection is of only one system (the bone system), but with numerous localizations (skull, thorax, backbone, limbs), the speciality litterature showing a large frequency of the acute disseminated forms under the age of 3. The skeleton is the most frequently affected (in our case being the sole localization). The debut of the disease was particular othorragia which led to the taking of the skull x-ray (with the accentuation on the osteolysis zones HCL characteristic). The general state of the nursing was modified before the diminished appetite othorragia debut, irritability, the tegument and progressively accentuated mucous pallor (the hipocrome anemia being explained by the diminishing of the appetite, the sanguine loses, the alimentary deficiency). The positive diagnosis has been made by joining the clinical and radiologic data, but also the anatomopathological exam from the bleeding tumoral system from the auditive conduct has been imposed. In HCL exists a positive marking for the S100 protein, vimentin, CD1, CD14, CD15, CD68. In the presented case the positivation for the S100 protein and CD68 has been obtained; CD15 has been positive for granulocytes.

The specific treatment for the disease has been started, the prognosis is reserved in HCL with multifocal debut – chronic evolution with an unique or multiple relapse (especially under the age of 2 at the debut) like in the presented case.

**Conclusions**

The debut of the disease in the 9 month old nursing was particular: othorragia and irritability. The diagnosis was specified following the corroboration of the clinical data with the radiologic exam.

The histopathological exam and the immunohistochemical study established the final diagnosis.

**References**


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CURRENT ISSUES IN INTESTINAL FAILURE IN CHILDREN – CAUSES AND MANAGEMENT

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Abstract
The concept of intestinal failure (IF) is currently defined as a critical reduction of functional gut mass below the minimum amount necessary for adequate digestion and absorption to satisfy body nutrient and fluid requirements for growth in children or maintenance in adults. Causes of IF include intestinal hypomotility disorders, intestinal mucosal disorders, and the short bowel syndrome. We present the actual possibilities in the management of the IF – enteral and parenteral nutrition, non-transplant surgery and intestinal transplantation, analysing their indications, contraindications, and complications.

Key words: intestinal failure, parenteral nutrition, intestinal transplantation, child

DEFINITION OF INTESTINAL FAILURE:
The concept of intestinal failure (IF) is currently defined as a critical reduction of functional gut mass below the minimum amount necessary for adequate digestion and absorption to satisfy body nutrient and fluid requirements for growth in children or maintenance in adults. According to the recent consensus of the IF Working Group, IF is characterized by the inability of the body to maintain the balance of proteins, energy, electrolytes or micronutrients\(^2,3\). The real incidence and prevalence of IF are not known\(^4\). If children on home parenteral nutrition (PN) are taken into account, the incidence of IF in the general population is 2-5/1 million\(^6\). The incidence of short bowel syndrome (SBS) in the general population is 2-6.8/1 million\(^7\). The incidence of short bowel syndrome (SBS) in children is 2-5/1 million\(^8\).

CAUSES OF INTESTINAL FAILURE:
- Intestinal motility disorders\(^9\): chronic intestinal pseudo-obstruction\(^1,4\), Hirschsprung disease – especially the rare form of total aganglionosis with jejuno-ileal involvement\(^1\);
- Intestinal mucosal disorders\(^5\): primary epithelial abnormalities\(^7\) (epithelial dysplasia, microvillus inclusion disease, congenital disorders of glycosylation) and immune mediated disorders (severe combined immunodeficiency, severe hypogammaglobulinaemia, autoimmune enteropathy with nephropathy, unclassified autoimmune enteropathy);
- Short bowel syndrome – following extensive intestinal resections with reduction of functional gut mass\(^1\):
  - in neonates: gastrochisis, necrotising enterocolitis, small bowel atresia, malrotation with volvulus\(^4\), mesenteric arterial and venous thrombosis\(^1\);
  - after the neonatal period: Crohn’s disease, radiation enteritis, tumors, trauma, mesenteric infarction\(^4\), extensive angioma\(^1\), arterial thrombosis\(^1\), complicated intussusception\(^1\).

In children, SBS is the most common indication for long-term PN\(^2\). Intestinal resections can be either short (leaving 100-150 cm of small intestine), large (leaving 40-100 cm) or massive (leaving less than 40 cm)\(^9\). The age at the time of resection, degree of cholestasis (IF associated liver disease), type of the small bowel remaining (ileum adapts better than jejunum), residual length of the small bowel, preservation of the ileo-caecal valve, preservation of at least the right colon, functional integrity of the remaining small intestine, and early establishment of intestinal continuity are all factors that are considered very important for adaptation\(^9\). The time of resection is also essential because at birth, the small bowel is 250 ± 40 cm long and its increase in length is maximal during infancy\(^9\). It doubles its length during the last trimester of pregnancy, which accordingly confers a benefit of full-term birth compared to a premature birth\(^9\).

In summary, the favourable factors for intestinal adaptation are therefore residual small bowel longer than 15 cm, presence of the ileo-caecal valve, preservation of the colon and the functional integrity of the remnant intestine\(^10\).

But the residual intestine may become dilated and dysmotile, leading to stasis of intestinal nutrients and small bowel bacterial overgrowth (SBBO). SBBO may lead to malabsorption and bacterial translocation, with potential sepsis\(^1\). SBBO is more likely to occur in the case of ileo-caecal resection\(^1\). In addition, SBBO exacerbates hepatotoxicity related to PN\(^9\).

CLASSIFICATION OF INTESTINAL FAILURE:
With so many causes, IF may have various degrees of severity and duration\(^1\):
- a) According to the duration, IF may be acute (reversible within 6 months) or chronic (longer than 6 months, and even permanent)\(^5\);
- b) According to the type (this classification has been established in adults)\(^10\):
  - type 1: self-limiting IF – usually following abdominal surgery
  - type 2: IF in severely affected patients with extensive intestinal resections, with septic, metabolic and nutritional complications, and necessitating a multidisciplinary approach
  - type 3: chronic IF – patients need long-term PN.
MANAGEMENT OF INTESTINAL FAILURE:
A multidisciplinary approach\textsuperscript{11,12} is mandatory, including a pediatric gastroenterologist, pediatric surgeon, surgeon specialized in liver and intestinal transplantation, dietician, PN pharmacist, social nurse, and nutritional nurse.

A. MANAGEMENT OF SHORT BOWEL SYNDROME
I. Medical management
Parenteral nutrition is the cornerstone of management, promoting normal growth in children with SBS\textsuperscript{1}. The duration of PN varies according to the residual intestine length and the presence of the ileo-caecal valve\textsuperscript{1}.

Following resection, enteral nutrition (EN) is the most important factor in promoting intestinal adaptation and intestinal hyperplasia\textsuperscript{4}. Therefore, early oral feeding/enteral nutrition is recommended, leading to enhancement of gastrointestinal secretion, salivary epidermal growth factor and gallbladder motility\textsuperscript{4}. Breast milk with its trophic factors, such as epidermal growth factor, is the best choice in the first few months of life\textsuperscript{13}. Conceptually, a protein hydrolysate or amino acid based formula seems to be more appropriate in patients with SBS due to the decreased luminal contact time, but there is no convincing evidence to support their use in preference to a polymeric feed\textsuperscript{4} (amino acids would be only less antigenic\textsuperscript{14}). Some children have disaccharide intolerance and a glucose polymer based formula may be used\textsuperscript{4}. A high fat diet (60\% of the calories) may be beneficial (providing energy) and does not have a significant impact on stool volume or losses in children with an end-jejunostomy\textsuperscript{13,15}.

Continuous nasogastric feeding initially, followed by overnight nasogastric feeding and bolus feeding during the day, is recommended in order to use the residual small bowel function and to encourage oral feeding\textsuperscript{4}. It is important to maintain a urinary sodium/potassium ratio of at least 2:1 with an absolute urinary sodium concentration of over 10-20 mmol/l in children with significant fluid and electrolyte losses\textsuperscript{4,16}.

Currently, there is no convincing evidence to support the routine use of pectin, glutamine, growth hormone, or IGF-1 as trophic factors in the process of intestinal adaptation\textsuperscript{15}. A promising agent in the promotion of intestinal adaptation is glucagon-like peptide-2 (GLP-2), a pro-glucagon derived peptide secreted from the ileal and colonic mucosa after feeding\textsuperscript{16}. GLP-2 induces marked proliferation of the small intestine epithelium in patients with SBS, increasing body weight and nutrient absorption\textsuperscript{16}.

Various antibiotic regimens can be used for 7 to 14 days, with 14 to 28 days of interruption\textsuperscript{17}, but very cautiously to preserve the intestinal bacterial flora for production of short chain fatty acids and/or avoid the emergence of multiresistant strains of bacteria\textsuperscript{1}. Metronidazole (10-20 mg/kg/day) can be used, either alone or in association with trimethoprim-sulfamethoxazole.

Probiotics might be helpful, although there is no significant evidence for this in children\textsuperscript{18}.

II. Surgery
Besides intestinal transplantation (IT), non-transplant surgery can be used to provide maximum mucosal contact without disturbing motility or reducing total absorptive mass\textsuperscript{4}. The Bianchi procedure (bowel lengthening), intestinal placation or tapering and the serial transverse enteroplasty procedure (STEP) are examples of such methods\textsuperscript{11}.

Patients with dilated bowel segments need to meet some anatomical criteria in order to be selected for longitudinal intestinal lengthening and tailoring, including intestinal diameter > 3 cm, length of residual small bowel > 40 cm and length of dilated bowel > 20 cm\textsuperscript{1}. The STEP procedure has some advantages over the Bianchi procedure, since the intestinal blood supply remains undisturbed, and it can be performed on smaller dilated segments as well as on dilated bowel segments after a previous Bianchi procedure\textsuperscript{2}. They are effective especially in children with mild liver disease and without significant portal hypertension, and can be performed also after liver transplantation\textsuperscript{1}.

B. PARENTERAL NUTRITION
PN can be partial or total, temporary (helpful for SBS) or permanent (for intestinal motility disorders and intestinal mucosal disorders)\textsuperscript{4}. After 4 years, the survival rate in patients with home PN is 80\% for SBS and 70\% for motility disorders. Some complications can be encountered associated with long term use of PN: central venous catheter related infections; thrombosis leading to impaired venous access\textsuperscript{4}; intestinal failure associated liver disease (IFALD) – expression that replaces the old name of parenteral nutrition associated liver disease\textsuperscript{1}; and bone disease (dual-energy X-ray absorptiometry, as well as phosphorus and calcium serum levels should be assessed)\textsuperscript{4}. In a recent study, the following complications of total PN were reported: complications associated with the central venous catheter (mechanical – 52\%, infectious – 26\%), metabolic (3\%) and hepatic (19\%) complications\textsuperscript{29}.

- Central venous catheter related infections (potentially leading to sepsis) – can cause a rise in bilirubin level of higher than one third and cholestasis may develop in 90\% of infants after the first infection. Frequent infections may contribute to progressive liver disease\textsuperscript{30}.
- Vascular thrombosis – the repeated episodes of line infections with multiple surgical procedures to remove and insert catheters may predispose to thrombosis\textsuperscript{24}. Percutaneous vascular insertion techniques using Doppler ultrasound, with minimal trauma, may be more helpful\textsuperscript{23}. It seems that the use of anticoagulants for prevention of vascular thrombosis is not beneficial\textsuperscript{26}. Pulmonary thromboembolism occurs in 39\% of the children, and have a fatal potential\textsuperscript{27}. In asymptomatic children yearly echocardiography and ventilation-perfusion scanning are recommended\textsuperscript{4}.
- IFALD – occurs in 40-60\% of the infants on long term PN (versus 15-40\% in adults on home PN)\textsuperscript{28}. In a recent study, IFALD occurs in 25\% of the children on home PN\textsuperscript{29}. IFALD includes steatosis, cholestasis, hepatic fibrosis and cholelithiasis\textsuperscript{28}. Progression of liver disease towards biliary cirrhosis, portal hypertension and hepatic failure occurs in a minority of patients, but it is more common in newborns and infants than in adults\textsuperscript{28}. Abnormalities in hepatic enzymes are often seen within the
first four weeks of onset of PN in children. Due to the risk for development of gallstones, abdominal ultrasound is recommended twice a year.

Multiple factors are involved in the pathogenesis of IFALD:

- in infants: prematurity, low birth weight, duration of PN, repeated laparotomies for SBS, recurrent sepsis, and direct hepatotoxicity due to the hepatic immaturity; in addition, premature babies also present deficiencies of taurine or cysteine;

- other important mechanisms include:
  - deficiency of choline (at any age), associated with steatosis and cholestasis;
  - absence of enteral nutrition (leading to a reduction of intestinal hormones and, following intestinal resections, to a decrease of the enterohepatic circulation and of biliary flow, thus promoting cholestasis and the accumulation of toxic bile acids causing cholestasis);
  - SBBO, catheter infections release endotoxin and pro-inflammatory mediators;
  - lipids (notably polyunsaturated fatty acids); generally, high level of serum lipids is associated with IFALD;
  - aluminium, chromium or iron overload;
  - magnesium toxicity (at any age), associated with steatosis and cholestasis;

- in adults, IFALD is less common and varies with age, duration of PN, energy intake, excessive intake of lipids or glucose.

Prevention of IFALD requires:

- a multidisciplinary approach to management of PN
- stimulation of early enteral nutrition
- use of aseptic catheters to reduce the incidence of sepsis
- supplementation of PN with choline, taurine and cysteine
- reduction of iron and aluminium intake in the solutions for PN
- oral ursodesoxycholic acid (30 mg/kg/day) to improve bile flow and reduce biliary stasis
- use of appropriate intravenous fat emulsions (not more than 2–2.5 g/kg/day), containing various combinations of medium and long chain triglycerides
- control of the lipid supply and rate of delivery, including stopping intravenous lipids as soon as thrombocytopenia, hyperbilirubinemia and/or jaundice appear
- ingestion of long-chain triglycerides, breast milk, or injection of cholecystokinin analogs, for stimulation of the enterobiliary axis
- limiting glucose intake to prevent insulin resistance and hepatic steatosis
- performing cyclic PN (instead of continuous PN) thereby reducing hyperinsulinism and liver steatosis.

Prognosis of IFALD is correlated to the rapid progression of the disease, requiring early intestinal transplantation. Children referred with a plasma bilirubin concentration of higher than 200 µmol/l have a life expectancy without intestinal transplantation of 6 months. In children with cirrhosis, survival at 12 months is 30%. The development of coagulopathy and portal hypertension with varices reduces survival to less than 8 weeks. In patients with SBS, isolated liver transplantation may be performed.

C. INTESTINAL TRANSPLANTATION (ITx)

Small bowel transplantation is a salvage procedure for those patients with IF where total PN is not efficient and/or has severe side effects. In July 2005 more than 1300 ITx have been performed worldwide in 65 centres in 19 countries.

The indications for ITx are irreversible IF (requiring parenteral intake of more than 50% of calories) despite all medical and/or surgical attempts at digestive autonomy (discontinuation of PN), and associated with one of the following conditions:

- vascular thrombosis with impaired venous access (more than 2 thrombosis in the subclavian, jugular or femoral veins);
- progressive liver disease (with coagulopathy, bilirubin levels over 3 mg%, splenomegaly, gastroesophageal varices, thrombocytopenia, ascites and encephalopathy);
- severe, recurrent catheter-related sepsis (2 episodes of sepsis per year, 1 episode of line-related fungemia, septic shock or acute respiratory distress syndrome);
- metabolic disorders that are ineffectively treated with PN and that affect the growth of the child;
- underlying disease leading to uncontrollable water-electrolyte losses, recurrent severe acute dehydration (life-threatening condition if PN is not used after 24 hours) – e.g. intractable diarrhea;

Factors influencing the survival of children with IF referred for ITx include age below 1 year, surgical disease, bridging fibrosis and cirrhosis, bilirubin levels over 3 mg% and thrombocytopenia.

Contraindications to ITx are:

- absolute: severe neurological disorders, non-resectable malignancies, and life-threatening or other irreversible diseases unrelated to the digestive system;
- relative: severe congenital or acquired immunological deficiencies, multisystem autoimmune diseases, insufficient vascular patency to guarantee vascular access for up to 6 months after transplant, and chronic lung disease of prematurity.

There are several types of operation:

- isolated ITx (in patients with mild liver disease – no evidence of portal hypertension, mild hepatic fibrosis on biopsy);
- small bowel and liver transplant (in patients with moderate to severe liver disease);
- multivisceral transplantation (more than the liver and small bowel are transplanted, usually stomach and whole pancreas) – in patients with extensive disease, e.g. motility disorders or desmoid tumours.

The preferred technique is the composite graft where the liver and intestine with bile ducts, duodenum and the head of pancreas can be implanted en bloc with minimal disruption to the vascular and other structures connecting the organs, or the organs can be retrieved from the donor,
survival at 5 years after isolated ITx or liver and intestinal transplantation. Statistical reports show that small bowel transplant (± colonic) represents 44% of grafts, liver and intestinal transplantation 48%, while multivisceral transplantation (small bowel, stomach, pancreas, and liver) make up 11%66. Due to the lack of availability of size-matched organs, 50-60% of the children die on the ITx waiting list, the majority of these being infants and less than 10 kg weight. In order to overcome this problem, the technique of en bloc reduction can be performed, using the liver and small bowel from much larger adult donors, by excision usually the right lobe of the liver and mid-section of the small bowel graft. Graft survival at 1 year increased to 65% for isolated ITx and to 59% for liver and intestinal transplantation34. Overall survival at 5 years after isolated ITx or liver and intestinal transplantation is 50%-25.

ITx related complications were common in the past and included significant surgical morbidity, moderate to severe acute rejection and opportunistic infections4,36. The incidence and severity of rejection has improved considerably after the advent of IL-2 blockers and other immunosuppression strategies4,36. Generally, following transplant forms of induction (thymoglobulin, IL-2 receptor antagonists) and maintenance (tacrolimus) therapies need to be used34. Tacrolimus is the most widely used drug to prevent rejection (in 75% of the patients)34. Studies have shown that rejection rate is lower in liver and intestinal transplantation. Currently, rejection, bacterial, fungal and viral (Cytomegalovirus, Epstein-Barr-virus) infections, post-transplant lymphoproliferative disease and graft versus host disease are the most common complications after intestinal transplantation. However, with the use of an appropriate cytomegalovirus prophylaxis regimen and Epstein-Barr virus polymerase chain reaction monitoring techniques for prevention of neoplastic post-transplant lymphoproliferative disease, the incidence of these complications decreased significantly36.

In the experience of Birmingham Children’s Hospital, 212 children with IF were assessed for ITx between 1989 and 2005. They were categorised into three prognostic groups: stable on PN (n=82); unsuitable for transplantation (n=43) due to end stage liver disease and/or other co-morbid conditions; or recommended for transplantation (n=87). Of the 87 children recommended for transplantation, 9 families declined ITx, 22 children died on the waiting list, 2 children improved, while 38 ITx (median age 2.3 years, median weight 11 kg) and 16 intestinal and liver transplantation (median age 0.8 years, median weight 7.8 kg) were performed8. In 2006, 18 of 38 children with ITx and 9 out of 14 isolated liver transplant children were still alive (overall 5 year survival rate of 52%)9. There is evidence that quality of life in 10-16 year old ITx recipients is similar to healthy children, although their parents remained more anxious than the parents of healthy children38.

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CONGENITAL DYAPHRAGMATIC HERNIA - CASE REPORT

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Abstract
Congenital diaphragmatic hernia (CDH) constitutes a major surgical emergency in the newborn, and the key to survival lies in prompt diagnosis and treatment. CDH is characterized by a variable degree of pulmonary hyperplasia associated with a decrease in cross-sectional area of the pulmonary vasculature and dysfunction of the surfactant system. The lungs have a small alveolar capillary membrane for gas exchange, which may be further decreased by surfactant dysfunction. In addition to parenchyma disease, increased muscularization of the intraacinar pulmonary arteries appears to occur. In very severe cases, left ventricular hypoplasia is observed. We report a case of a 3 year old girl presented with congenital diaphragmatic hernia to which we applied surgical treatment.

Key words: congenital diaphragmatic hernia, pulmonary hypoplasia, posterolateral Bochdalek hernia

Abbreviations
CDH- congenital diaphragmatic hernia
PPHN- persistent pulmonary hypoplasia in the newborn

Introduction
The diaphragm is the major muscle of respiration and the second most important muscle within the body after the heart. Then a decrease in diaphragmatic function occurs, a concomitant respiratory dysfunction occurs. However, no compensatory mechanisms are in place to prevent respiratory compromise in the setting of decreased diaphragmatic excursion. Congenital diaphragmatic hernias (CDH) occur through embryologic defects in the diaphragm, and most patients present early in life rather than later[1]. However, a subset of adults may present with a smaller congenital hernia that was undetected during childhood[3]. The diaphragm initially develops as a septum between the heart and liver, progresses posterolaterally, and closes at the left Bochdalek foramen at approximately 8-10 weeks' gestation. The herniation of viscera in CDH usually occurs during the pseudoglandular stage of lung development. Lung compression results in pulmonary hypoplasia that is most severe on the ipsilateral side, although both lungs may be abnormal. Pulmonary hypoplasia is associated with fewer bronchial, alveolar and arterial generations. Pulmonary capillary blood flow is decreased because of the small cross-sectional area of the pulmonary vascular bed, and flow may be further decreased by abnormal pulmonary vasoconstriction. Pulmonary hypertension and pulmonary hypoplasia have been recognized as the 2 cornerstones of the pathophysiology of CDH. In recent years, evidence suggests that cardiac maldevelopment may further complicate the pathophysiology of CDH[3,4,5].

Etiology
Genetic factors: The initiating factor responsible for the development of CDH is unknown. Wide variations (7-31%) have been noted in the reported prevalence of chromosomal abnormalities (trisomy 13, trisomy 18, and tetrasomy 12P mosaicism) in patients with CDH. The prevalence is higher in cases of CDH associated with other defects. Familial occurrence has been noted in fewer than 2% of CDH cases[6,7,8]. The role of drugs and environmental chemicals in the development of CDH is uncertain, but quinine, thalidomide, phenmetrazine, and polybrominated diphenyls have been used to induce CDH in various species.

Frequency
In the US, CDH occurs in 1 of every 2000-4000 live births and accounts for 8% of all major congenital anomalies. Worldwide, the frequency is the same as that in the United States.

Classification of CDH
The 3 basic types of CDH are the posterolateral Bochdalek hernia (occurring in utero at approximately 8-10 weeks of gestation), the anterior Morgagni hernia, and the less-common hiatus hernia. The left-sided Bochdalek hernia is seen in approximately 90% of cases. The major problem in a Bochdalek hernia is the posterolateral defect of the diaphragm, which results in either the failure of the pleuroperitoneal folds to develop or the improper or absent
Because of associated PPHN (persistent pulmonary hypertension in the newborn) and pulmonary hypoplasia, medical therapy is directed toward optimizing oxygenation while avoiding barotrauma. In the delivery room, if the infant is known or suspected to have pulmonary hypoplasia, immediately place a nasogastric tube and connect it to continuous suction to prevent bowel distension and further lung compression. For the same reason, avoid mask ventilation and immediately intubate the trachea. Avoid high peak inspiratory pressures and be alert to the possibility of early pneumothorax if the infant does not stabilize.

Surgical Care:

Fetal surgery: Harrison et al reported the first human fetal surgery for CDH in 1990[14]. However, a randomized trial published in 1998 showed that in utero repair did not improve survival compared with standard therapy. Currently, fetal intervention is not indicated in CDH.

Postnatal surgical care: until recently, specialists believed that reduction of the herniated viscera and closure of the diaphragmatic defect should be emergently performed following birth. However, a delayed surgical approach that enables preoperative stabilization decreases morbidity and mortality. This change in protocol is due to the recent understanding that the medical problems of pulmonary hypoplasia and PPHN(persistent pulmonary hypertension in the newborn) are largely responsible for the outcome of CDH and that the severity of these pathophysiologies is largely predetermined in utero. Herniated viscera in the chest does not appear to exacerbate the pathophysiology as long as bowel decompression with a nasogastric tube is continuous. Several reports indicate that circulatory stability, respiratory mechanics, and gas exchange deteriorate after surgical repair. The ideal time to repair a CDH is unknown. Some suggest that repair 24 hours after stabilization is ideal, but delays of up to 7-10 days are typically well tolerated, and many surgeons now adopt this approach. Some surgeons prefer to operate on these neonates when normal pulmonary artery pressure is maintained for at least 24-48 hours based on echocardiography[15,16].

Complications of CDH

Pulmonary hypoplasia

The main problem lies in the presence of pulmonary hypoplasia, which may be unilateral or bilateral. Pulmonary hypoplasia is thought to result from long-standing intrauterine (embryonic) compression of the lungs by the hernia. Mortality in babies with CDH is largely confined to those with bilateral pulmonary hypoplasia, but hypoplasia is always more severe in the lung ipsilateral to the hernia. The pulmonary vasculature is also affected to a greater degree than the bronchial tree[17]. Infants with the largest and longest-standing hernias have the most-hypoplastic lungs and are less likely to survive after birth. If a diaphragmatic hernia develops toward the end of pregnancy or after birth, pulmonary hypoplasia does not occur.

Gastric volvulus

Gastric volvulus can occur in early infancy as a complication of CDH, and it usually produces acute gastric
obstruction. Radiographic findings usually consist of an
inverted distended stomach [11, 18].

**Rotational abnormalities and midgut volvulus**

Intestinal malrotation is commonly observed in
children with CDH (30-62%), and it also occurs in 37-40% of the cases of right-sided CDH. Volvulus is a complication in a small minority of these cases [19].

**Gastric or other intestinal perforations**

Gastric or other intestinal perforations occur rarely.

**Hypoplasia of the left ventricle with a left-sided
hernia or pleural effusions due to the right-sided
involvement**

The pleural effusion is believed to be the result of lymphatic obstruction secondary to the compressive effects of the hernia.

**Bilateral renal hypertrophy**

The kidneys are often enlarged and hyperplastic [20].

Some have suggested that an embryonic liaison exists
between the kidneys and the lungs wherein the kidney
produces a pulmonary growth factor (Proline) that
influences normal lung development. Conversely when the
lung is hypoplastic, it produces a renotropic substance and
causes the kidneys to hypertrophy.

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**Case report**

We present a 3-year old girl, 10 kilograms weight
who was admitted to our Department of Pediatric Surgery
with bilious emesis, signs of respiratory distress (retractions,
cyanosis, grunting respirations), colicky abdominal pain and
lack of stools for 5 days. Physical examinations revealed
asymmetric chest and also asymmetric abdominal distension
(more on the left side). The auscultation of the lungs
revealed no air entry on the left side with bowel movements
on the left pulmonary aria, with a shift of cardiac sounds
over the right chest. Chest-abdominal plain films with
contrast substance showed dilated stomach and also some
dilated loops of small bowel in left-side of the thoraces, and
a few air-fluids levels in the left chest and abdomen.

Blood analyses revealed nutritional anemia,
dehidratation with hypovolemia, mixed acidosis and
intestinal parasitosis. We diagnosed congenital
diaphragmatic hernia with acute bowel obstruction. First
time we applied non-operative treatment for acute bowel
obstruction (gastric aspiration, hydro-electrolitic and
metabolic equilibrated and also total parentheral nutrition).
After this period we continued the investigations. A CT-scan
of chest and abdomen confirmed our diagnosis and excluded
a possible diaphragmatic relaxation. (Figure no 1 and 2).

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After these completed investigations and the
treatment of upper respiratory tract infection and intestinal
parasitosis we decided that this patient fullfield conditions
for surgical treatment. The surgical procedure was made
under general endotracheal anesthesia. (figure 3). We
approached with laparotomy so that abdominal contents
could be inspected adequately. The hole in the diaphragm is
found (figure no 4) and a tube is placed in the chest to
equilibrate the pressures. We gently reduced the herniated
viscera: stomach, spleen, complete small bowel, ascending
and transverse colon (hepatic flexure) (figures no 5 and 6).

Then we approximated the edges of the diaphragm
with nonabsorbable suture (figure no 7).
FIG. 3 Pre-surgical aspect.

FIG. 4 Intraoperator aspect (the hole in the diaphragm).

FIG. 5 Intraoperator aspect (herniated viscera).
The defect was large (approximately 8 cm in diameter) but prosthetic mesh was not necessary. A tube is placed in the left chest to allow air, blood, and fluid to drain so the lung can re-expand. In our case, the left lung was not functionally, but the mediastin took the normally placed. Pain management required intravenous narcotics and non-steroidal anti-inflammatory drugs (NSAIDs) seven days. Protective anthybioterapy and parentheral nutrition was necessary for 3 days. The patient left the hospital 10 days after surgery.

**Follow-up care**

Once an anatomic defect has been corrected, periodically assessing pulmonary function and obtaining chest radiographs is important. Although spontaneous recurrence of a repaired diaphragmatic hernia is low, small defects in the repair site have been reported, so surveillance is essential.

**Conclusions**

The prognosis in CDH is different. For the baby who is born with respiratory impairment and is immediately symptomatic, the chance of survival is poor unless an almost perfect resuscitative effort is accomplish without delay. Other baby who presents with symptoms after 24 hours of life and becomes compromised more slowly has an excellent prognosis. Our case confirms the hypothesis that CDH is a major medical emergency but a delayed surgical emergency.
References

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THE HYPOSPADIAS AND THE PSYCHO-AFFECTIVITY CASE REPORT

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Abstract
In this study we take a close look to the surgical treatment of hypospadias which leads to the appearance of some psychological implications. The psychological implications became more obvious as the reconstructive surgical therapy is considered at the age of puberty or adolescence.

We tried to show these aspects in four case studies in which we use the following methods of psychological investigations: interview with the child and his owners, observation of the children’s behavior before and after the surgical treatment, the projective test Machover and the projective test of the Family.

Regarding the conclusions, we are able to prove now the importance of cultural level, the importance of the interaction between the mother and her child, child’s feeling of culpability and anxiety, the high need of affection especially from the father which the patients tries to identify with.

This study tries to show the importance of the association between the very needed surgery and psychical influences.

Key words: hypospadias, psychological influences

Introduction
The main idea of our case studies were implemented at the end of the 50’s when the real cognitive movement started. These cases are approving that the surgical treatment of hypospadias could leads to the appearance of some psychological implications. The hypospadias is a congenital malformation of the masculine urethra characterized by an abnormal opening of the urethra on the ventral face of the penis, near the top of the gland where the meat normally opens. It is a frequent malformation which effects 8.2% of the new-born male.

The etiology of hypospadias is doubtful. It is quite known there is a genetic factor implicated. There are studies¹ which prove the hereditary factor is taken into consideration on a secondary plan, but we also know this factor is not fœble.

The malformation is located at the genital area and it causes a lots of psychological issues. Those problems are more pregnant when surgical intervention is delayed until the age of puberty or adolescence, a period dominated by sexuality, a period with unasked questions about the children’s normality as future adults.

The basic ideology which leads us to an adequate treatment of hypospadias changes many times trying to coordinate itself with the last perfected microsurgery techniques. Also, an important point is understanding the psychological aspects of pediatric surgery so we can try to minimize physical and psychological trauma.

It is absolutely necessary to know these aspects and put them head to head with the imminent surgical intervention in order to solve future cases of hypospadias.

Material and methods
Regarding our four case studies we use the following methods of psychological investigations:
1. The method of interview (were interviewed both child and his parents).
2. The method of observation (of the child before and after the surgery).
3. The projective test of the Family.

The tests were applied in standard conditions and we tried to show the psychological changes related to the hypospadias. It has been taken into consideration the age of the child, the capacity to admit his disease and all the related future problems which could emerge from actual disease. This study could not be generalized because the group we tasted is not representative.

Case report
Having as a started point the applications of Gestalt Psychology (where are also the roots of cognitive movement on which the concepts of our study are based on) we will expose some aspects regarding a boy who suffered 11 surgical interventions until the age of 9 (case: S.V. -9 years old, diagnosis: balanic hypospadias).

The anamnesis reveals the fact that this child came from a monoparental family, the boy’s father leaving the family because of the disease his son suffers (from the mother’s declarations).

During the tests, the patient requires additional information, demands approval and he uses his entire set of colors. (Fig. 1).

Opened colors – yellow, blue, red - used to picture himself shown us a brave child who likes being active.

Dark colors- black- reveals the anxiety and the sentiment of culpability.
The combination of colors—red and black, yellow and red—proves the sociability, but also the aggressiveness associated with the feeling of anxiety. He verbally denies his father is a part of his family, but in this picture he puts himself between the two parents of his. (Fig. 1).

The child is fighting with a feeling of culpability regarding his father’s leaving, he shows low confidence in himself, fear and shyness, all those being covered by an aggressive verbal behavior especially for his father. S.V. is one of the patients who needs psychological help.

Conclusions

Regarding the conclusions, we could notice the importance of cultural level, the importance of mother-child interaction in the first years of life, the relationship between his parents. The culpability feelings associated with high anxiety were present throughout the study. It was also obvious the need for affection especially from the father who the patients try to identify with. The denying tendencies of their disease were remarked, also the ineffable wish of the boys to be integrated in the society.

As far as the recommendations for the evaluated cases, we advise psychological counseling for the child and his family, which has the purpose of helping finding ways and means of communication between the parents and their child. Without a sure attachment mother-child in the first months of life, the entire future life of the baby could be affected and he could also reveal such behavior to his own future family.

It is very important that the child to be familiarized with the hospital environment and the surgeon. Therapeutics methods vs. psychological implications are going to continuously contribute to the improvement of the surgical techniques and last but not least to the establishment of the psychological counseling.

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FEED-BACK LOOP EVALUATION OF THE ORAL HEALTH EDUCATION MESSAGE

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Abstract
Considering the general situation of oral hygiene in children, a special attention must be payed to institutionalized children. For this reason, Rotary Club Timișoara, District 2241, under the coordination of President Mihai Avram, started, at the beginning of 2006, a project on oro-dental health education of institutionalized children. This project was run in cooperation with the „Centre for Promotion of Health Education and Motivation of Prevention in Dentistry” accredited by the National Board of Higher Education Scientific Research (CNCSIS) Bucharest (collaboration contract no. 226/2006). The Centre activates in the Department of Preventive, Community Dental Medicine and Oral Health of the Faculty of Dental Medicine – „Victor Babes” UMP Timișoara.

The aim of the project was to make aware and motivate these children with a special situation, in order to achieve and maintain an appropriate oro-dental hygiene.

Key words: institutionalized children, prevention, oro-dental hygiene, motivation, bacterial plaque

Introduction
“Preventive dental medicine” is a constitutive part of dental medicine, connected to the study and implementation of protective measures and early treatments – both at individual and community level – with the aim of accomplishing and maintaining the integrity of oro-dental structures throughout human life. In the World Health Organization classification, oro-dental diseases are situated on the third place as a worldwide plague. This shows that dentists must make all efforts for this “leading” role to disappear. For this, prevention of oro-dental diseases must become a priority on every specialist’s agenda. Patients must be educated towards a certain number of behaviours, because the best results are obtained by individualized education. Behaviours with which patients must become familiar are: hygiene measures, periodic control visits, an appropriate diet.

Considering the general situation of oral hygiene in children, a special attention must be payed to institutionalized children. For this reason, Rotary Club Timișoara, District 2241, under the coordination of President Mihai Avram, started, at the beginning of 2006, a project on oro-dental health education of institutionalized children. This project was run in cooperation with the „Centre for Promotion of Health Education and Motivation of Prevention in Dentistry” accredited by the National Board of Higher Education Scientific Research (CNCSIS) Bucharest (collaboration contract no. 226/2006). The Centre activates in the Department of Preventive, Community Dental Medicine and Oral Health of the Faculty of Dental Medicine – „Victor Babes” UMP Timișoara.

The aim of the project was to make aware and motivate these children with a special situation, in order to achieve and maintain an appropriate oro-dental hygiene. From previous studies we observed that in most cases dental brushing is restricted to an apparent cleanness, an action performed under constraint. But, as most of the oro-dental diseases may be prevented by addressing the causes, performing oro-dental hygiene is primordial.

The need to change habits and behaviours is obvious; but this change occurs neither spontaneously nor easily. In order to make the patient active and especially in order to keep the quality and constance of cleaning, we must create an imperious need, a deep motivation. This ambitious goal may be achieved only by an intelectual endeavour of a “communication professional”, by use of educational materials matching the age and understanding level and with a lot of patience. To educate means to transmit a messaage; and in order to succeede you must have an appropriate experience, to know effective techniques and to respect certain psychological principles.

The objective of this project was to offer oro-dental health education and prevention services for over 200 institutionalized children in orphanages, actions financed by the project: „Feed-back Loop Evaluation of the Oral Health Education Message”. Children who benefited were from the Rudolf Walther Home (194) and from the Childrens’ Home in Bulgaruș village (17). These children were aged between 5 and 17 years.
This project went through the following stages:
- clinical examination, monitoring, assessment of the initial state of dental hygiene, age group specific oro-dental health education lectures, leaflets, games and interactive sessions;
- performing of actual prevention actions; and
- assessment of the perception of the oro-dental health education message.

Each patient was examined, a dental and a prevention file were filled in with the initial examination data: the bacterial plaque index was calculated after marking with revealing substances and the degree of oral hygiene was established. In this study we used the Quigley-Hein Index which is based upon assessment of the bacterial plaque covering the dental crown, without taking into account its thickness, and it is scored from 0 to 5 (0 for total absence of plaque and 5 for plaque covering more than 2/3 of the tooth). Then, each patient was individually educated and given elementary notions on teeth composition, proper brushing and the way dental caries occur. Following dental plaque revealing, they were made aware on the existence of unbrushed food debris on dental surfaces and could improve their brushing by insisting on retention areas. After that, professional brushing was performed and, in some cases, ultrasound and abrasive powder scaling were used.

During the following visits, revealing of bacterial plaque was repeated in order to check the way they improved dental brushing and preventive procedures were performed. All caries-free molars and premolars were sealed for further protection and a topical fluoride gel application was done in order to strengthen the enamel superficial layer. WHO included sealing of groves and fossets among the 4 dental caries prevention methods, together with oro-dental hygiene, general and local fluoride application and food hygiene. It may be stated that sealing contributes by mechanical blocking to the increase of hard dental structures facing cariogenic attacks, being the most effective prophylactic measure against occlusal caries.

In parallel, age-group specific oro-dental health education lessons were given: slide presentations and puppet theatre with Dr. Knabel bunny for preschool children, as well as Power Point and poster presentations for pupils. During community dental medicine stages, our department staff together with Dental Medicine students went to these homes for children where students gave health education lectures.
Interactive discussions were permanently organized stimulating children to describe things they understood and to exemplify proper dental brushing by use of demonstration models. Flyers with notions on proper dental brushing, dental plaque and its role in dental caries and periodontal disease were spread; notions on the use of dental floss and mouth rinse and a game which gave each child the opportunity to check during one month if he or she does or does not forget morning and evening brushing.

Throughout the period this study was performed, we observed that the position of children towards the visit to the dentist changed a lot. As soon as the second session, most children came without fear, even showing pleasure and impatiently waiting for the treatment. The aspects which pleased us most were that the message we sent was receptioned, fact proven by the decrease of bacterial plaque index (on a 0 to 5 scale) from a mean value of 3.17 in the first session to an average of 2.30 in the last check-up and the increased interest and preoccupation of these children for a better oro-dental hygiene.
References


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MANUSCRIPT
REQUIREMENTS

The manuscript must be in English, typed single space, one column on A4 paper, with margins: top – 3 cm, bottom – 2.26 cm, left – 1.5 cm, right – 1.7 cm. A 10-point font Times New Roman is required. The article should be organized in the following format: Title, Names of all authors (first name initial, surname), Names of institutions in which work was done (use the Arabic numerals, superscript), Abstract, Keywords, Text (Introduction, Purpose, Materials and Methods, Results, Discussions and/or Conclusions), References, and first author’s correspondence address.