## CONTENTS

1. **CHILDHOOD OBESITY: BETWEEN NATURE AND NURTURE**  
   Corina Pienar, Maria Puiu, Adela Chiriță-Emandi, Simona Dumitriu, Cristina Popa, Iulia Jurca-Simina, Ioana Micle, Smanarad Arghirescu .......................................................... 3

2. **FUNCTIONAL AND PSYCHOLOGICAL OUTCOMES 50 YEARS AFTER A JUVENILE AMPUTATION**  
   GA Aiordachioae, A Pop, H Haragus, D Vermesan, I Stoia .................................................................................. 9

3. **LEFT-SIDED PNEUMONECTOMY IN ONE-YEAR OLD CHILD A RESULT OF COMPLICATED PLEUROPNEUMONIA**  
   A Uchikov, P Stefanova, B Ivanov ............................................................................................................................ 15

4. **USE OF A EQUIMOLAR MIXTURE OF NITROUS OXIDE AND OXYGEN IN THE PAIN MANAGEMENT OF PEDIATRIC PATIENTS – OWN EXPERIENCE AND REVIEW OF LITERATURE**  
   NF Tepeneu, Daniela Alina Chiru .......................................................................................................................... 19

5. **PROPRANOLOL TREATMENT OF INFANTILE HEMANGIOMA: OUR PRELIMINARY RESULTS**  
   Corina Stănculescu, CM Popoiu, Anca Popoiu, Şt. Lazea, A. Lăcătușu, Patricia Cristodor, VL David, Emanuela Verenca, ES Boia ........................................................................................................ 24

6. **TREATMENT OPTIONS FOR JUVENILE OSTEOCHONDRAL KNEE DEFECTS**  
   D Crisan, D Vermesan, R Prejbeanu, S Nîtescu, C Bogdan .......................................................................................... 32

7. **PLASMA CONCENTRATION OF ZINC IN CHILDREN AGED 0-3 YEARS**  
   Nicoleta M Negruț, Eugenia M Domuța, Mircea V Nanulescu .................................................................................. 45

8. **SEVERE PROXIMAL HYPOSPADIAS REPAIR – ONE STAGE VERSUS TWO STAGE REPAIR**  
   RI Spataru, Niculina Bratu, Monica Ivanov .................................................................................................................. 53

9. **TUMOR-LIKE RECTUS FEMORIS PELVIC OSSIFICATION IN A TEENAGE ATHLETE – CASE PRESENTATION**  
   ML Mioc, D Vermesan, R Prejbeanu, V Iman, H Haragus ........................................................................................ 58

10. **PREVALENCE OF INFECTION IN LOW BIRTH WEIGHT INFANTS**  
    Mirabela Dima, C Ilie, Marioara Boia, Daniela Iacob, Aniko Manea, Nicoleta Ionita, Simona Sipos, Daniela Chiru, RE Iacob .................................................................................. 99

11. **TREATMENT BY INJECTION WITH BLEOMYCIN OF RISK HEMANGIOMAS CASE PRESENTATION**  
    D Teacă, C Tica, FD Enache ....................................................................................................................................... 84

12. **DUODENAL ATRESIA REPAIR - CASE REPORT**  
    A Surd, H Gocan, Rodica Muresan .......................................................................................................................... 88

13. **OVERVIEW OF CLINICAL FEATURES, DIAGNOSIS AND AETIOLOGY OF PARAPNEUMONIC EFFUSION AND EMPYEMA IN CHILDREN**  
    Anca Budusan, I Paraian, H Gocan, I Dobrescu, Bela Farkas .................................................................................. 90

14. **POSSIBILITIES OF COMPLEX REHABILITATION THERAPY IN GENETIC NEUROMUSCULAR AND OSTEOARTICULAR DISORDERS**  
    Cristian Milicin, Dan Nemeș, Elena Amâriță, Liliana Cățan, George Puenea, Daniel Popa .......................................................................................................................... 79

15. **THE SEVERITY OF MITRAL VALVE PROLAPSE IN CHILDREN CORRELATES WITH DIFFERENT TYPE OF SYMPTOMATOLOGY**  
    I Gyalai, H Branea, Oana Ancușa .......................................................................................................................... 102

16. **PREVALENCE OF INFECTION IN LOW BIRTH WEIGHT INFANTS**  
    Mirabela Dima, C Ilie, Marioara Boia, Daniela Iacob, Aniko Manea, Nicoleta Ionita, Simona Sipos, Daniela Chiru, RE Iacob .................................................................................. 107

17. **21. PREVALENCE OF INFECTION IN LOW BIRTH WEIGHT INFANTS**  
    Mirabela Dima, C Ilie, Marioara Boia, Daniela Iacob, Aniko Manea, Nicoleta Ionita, Simona Sipos, Daniela Chiru, RE Iacob .................................................................................. 111
CHILDHOOD OBESITY: BETWEEN NATURE AND NURTURE

Corina Pienar$^{1,2,*}$, Maria Puiu$^1$, Adela Chirita-Emandi$^2$, Simona Dumitriu$^2$, Cristina Popa$^1$, Iulia Jurca-Simina$^2$, Ioana Micle$^{1,2}$, Smaranda Arghirescu$^{1,2}$

Abstract
Introduction: In the last decades, the incidence of overweight and obesity has reached epidemic proportions. Both genetic and environmental factors are involved. When a disease clusters in a family our first instinct is to search for a genetic cause, but where obesity is concerned, careful evaluation is required. Purpose: to discuss the possible factors related the early and severe weight gain of three morbidly obese siblings. Methods: Mădălina, Denisa and Cătălin were referred to our Medical Genetic department for evaluation. We performed a complete assessment. Results: The siblings were born to obese parents. The family had chaotic eating habits and lived a profoundly sedentary life and did not attend kindergarten or school. Mădălina, the oldest, had multiple admissions to the hospital for obstructive sleep apnea (OSA). Anthropometric measurements confirmed the severe obesity. Their facial features resembled each other’s and their mother’s. Only Mădălina presented with acanthosis nigricans, while all 3 children had skeletal complications of obesity. Metabolic markers were in normal range, Mădălina’s leptin and Denisa’s adiponectin levels were low. In all 3 children the abdominal ultrasound was suggestive for nonalcoholic fatty liver disease. All children proved to be under stimulated and below average intellects were found. Lifestyle modifications recommendations were made and after 2 months all children lost weight. They also underwent psychological counseling. Mădălina’s OSA improved. Conclusions: Nurture is the major determinant of the siblings’ severe obesity. While on the short term prognosis is fair, on the long run, the multiple comorbidities associated with obesity make it reserved.

Key words: childhood obesity, genetics, environmental factors

Introduction
In the last decades, the incidence of overweight and obesity has reached epidemic proportions, affecting all ages, races, and sexes, and becoming a major health problem worldwide (1,2). Most worrisome is that increasing numbers in childhood obesity will have huge implications on adult morbidity and mortality (3).

In Romania, childhood overweight and obesity is estimated at 18.2% and 7.2%, respectively (4).

Both genetic and environmental factors are involved in the etiology of obesity. Although, there has not been such a dramatic change in mankind’s genetic profile to explain the ascending trend of obesity we are facing, it is clear that not all individuals exposed to obesogenic environments become obese. A genotype predisposition for weight gain must exist for the environment factors to result in an overweight/obese phenotype. Twin, family, and adoption studies estimate a heritability for obesity/overweight ranging from 50% to over 90% (1,2).

An easy access to cheap, high caloric foods and beverages combined with a sedentary lifestyle defines an obesogenic environment and represents the main culprit of the obesity epidemic (2,5). Parents play a crucial role in shaping a healthy lifestyle in their children (5,6).

Usually, when a disease clusters in a family our first instinct as physicians is to search for a genetic cause. Where obesity is concerned, due to the multiple and intricate factors involved, matters tend to be more complicated and careful evaluation is required.

Purpose
Our aim was to discuss the possible factors related the early and severe weight gain of three morbidly obese siblings.

Materials and Methods
Mădălina Nicoleta- 7 years and 6 months old, Denisa- 6 years and 1 month old and Cătălin Andrei- 3 years and 7 months old were referred to our Medical Genetic department for evaluation regarding the morbid obesity of all siblings. We performed a complete assessment that ranged from obtaining a detailed medical history to karyotyping and multidisciplinary consults.

Results
Mădălina Nicoleta was born to non-sanguineous, obese parents that came from an urban setting. She was the first born, from a physiological pregnancy, at full term, weighing 3.2 kg- appropriate for gestational age (AGA). She was exclusively breastfed for 2 months, than was started on cow’s milk; solid food was introduced at 1 year old. Currently, her eating habits were chaotic, she was not involved in any form of physical activity and does not attend kindergarten or school. Her medical history was positive for multiple admissions to the hospital for obstructive sleep apnea (OSA).

Physical assessment: the anthropometric measurements are represented in Figure 1.

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The facial phenotype was similar to the mother’s: epicantus, hypertelorism, convergent strabismus of the right eye. No stretch marks were present, but she had acanthosis nigricans in the cervical area. The distribution of adipose tissue was generalized (Figure 2). The girl had thoracal kyphosis, thoracolumbar scoliosis and inwards rotation of both thighs.

Figure 1 From left to right: Mădălina Nicoleta, Denisa, Cătălin Andrei

The blood work-up revealed polycythemia, secondary to chronic and severe sleep apnea. Basal glycaemia, oral glucose tolerance test (OGTT), glycated hemoglobin (A1c), lipids’ profile and transaminase were in normal range. Basal insulinemia and the calculated Homeostasis Model Assessment (HOMA= insulin x glucose/22.5), C peptide and adiponectin were in normal range. Leptin was very low.

The karyotype was 46 XX. We performed a fluorescence in situ hybridization (FISH) test to detect a possible deletion on the 15th chromosome (Prader-Willi syndrome). It was negative.

Imaging studies: X-rays revealed a cardiothoracic index of 0.66 (normal range for age 0.5-0.4), thoracal kyphosis, thoracolumbar scoliosis, bilateral coxa valga, genu valgum and patellar subluxation.

The ECG showed an extreme deviation to the right of the heart axis (QRS +150°), while the heart ultrasound was normal.

The abdominal ultrasound revealed an enlarged liver (right hepatic lobe 15 cm, left hepatic lobe 12-13 cm, caudate lobe 3 cm) with high echogenicity, an uneven structure and posterior attenuation.

Consults: The pneumologist reconfirmed the diagnosis of OSA and recommended Continuous Positive Airway Pressure (CPAP) therapy during sleep. The otolaryngology consult found a sub-acute adenoiditis. The pediatric orthoped confirmed the skeletal complications associated with morbid obesity. The pediatric endocrinology consult reviewed the anthropometric measurements, recommended additional hormonal investigations and made lifestyle modifications recommendations: nutritional and physical activity plan.

Figure 2 Mădălina Nicoleta: Left: BMI > 97th WHO percentile; weight loss after 2 months. Right: height > 97th WHO percentile
A psychology consult found an IQ (Raven) of 80 (below average) due to inappropriate cognitive stimulation, polymorphic dyslalia, low prosexia capacity, irritability, limited social skills and low self-esteem.

Auxologic measurements confirmed the diagnosis of severe obesity; comorbidities are shown in Table 1.

Denisa was the second born, from a physiological pregnancy, at full term, weighing 3.1 kg, AGA. She was exclusively breastfed for 2 months, than was started on formula; solid food was introduced at 6-7 months. Identical to her sister, the eating habits were chaotic; she was not involved in any form of physical activity and does not attend kindergarten.

Figure 3 Denisa: Left: BMI > 97th WHO percentile; weight loss after 2 months. Right: height > 50th WHO percentile

Figure 4 Cătălin Andrei: Left: BMI > 97th WHO percentile; weight loss after 2 months. Right: height > 97th WHO percentile
Physical assessment: the anthropometric measurements are represented in Figure 3. The facial phenotype was similar to her mother and sister. No stretch marks or acanthosis nigricans were present. The distribution of adipose tissue was generalized.

He had mild thoracolumbar scoliosis, inwards rotation of both thighs. The blood work-up revealed normal basal glycaemia, OGTT, A1c, lipids’ profile and transaminase. Basal insulinemia and HOMA, C peptide and leptin were in normal range. Adiponectin was low.

Table I Obesity associated comorbidities, complete diagnosis: *NAFLD= nonalcoholic fatty liver disease; ** only ultrasound criteria

<table>
<thead>
<tr>
<th>Morbidity/Child</th>
<th>Mădălina Nicoleta</th>
<th>Denisa</th>
<th>Cătălin Andrei</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skeletal (lumbar spine deformities, femur/tibia/foot deformities)</td>
<td>Thoracic kyphosis</td>
<td>Mild thoracic kyphosis</td>
<td>Thoracolumbar scoliosis</td>
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<td>Thoracolumbar scoliosis</td>
<td>Thoracolumbar scoliosis</td>
<td>Bilateral genu valgum</td>
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<td>Bilateral coxa valga</td>
<td>Bilateral genu valgum</td>
<td>Bilateral pottelar subluxation</td>
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<tr>
<td>Pulmonary (bronchiolitis, asthma, sleep apnea)</td>
<td>Obstructive sleep apnea</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cardiologic (high blood pressure, ischemic heart disease, heart failure)</td>
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<td>-</td>
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</tr>
<tr>
<td>Metabolic (diabetes, hyperlipidemia, NAFLD*)</td>
<td>NAFLD**</td>
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<tr>
<td>Hormonal (insulin resistance, hypoadiponectinemia, high leptin levels)</td>
<td>Acanthosis nigricans</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Psychological (limited social skills, introversion, isolation, depression)</td>
<td>Limited social skills</td>
<td>Introversion</td>
<td>Psycho-motor delay (mainly due to inappropriate stimulation)</td>
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<td>Low self-esteem</td>
<td>Isolation</td>
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The karyotype was 46 XX. We performed FISH test to rule out Prader-Willi syndrome, which came out negative. Imaging studies: X-rays revealed a mild thoracic kyphosis, thoracolumbar scoliosis, bilateral genu valgum. A spina bifida occulta was found. The ECG and heart ultrasound were unremarkable. The abdominal ultrasound revealed an enlarged liver (right hepatic lobe 12 cm, left hepatic lobe 8 cm) with high echogenicity, an uneven structure and posterior attenuation. Consults: The pediatric orthopedic and endocrinology consults were similar to the older sister. The psychology consult showed an IQ (Raven) of 80 (below average) due to inappropriate cognitive stimulation, limited social skills; introversion and isolation. Aside severe obesity, the complete diagnosis is shown in Table 1. Cătălin Andrei was the youngest of the 3 sibling, from a physiological pregnancy, at full term, weighing 3.2 kg, AGA. He was started on formula from birth; solid food was introduced at 6-7 months. Identical to his sisters, the eating habits were chaotic and he was not involved in any form of physical activity and does not attend kindergarten. Physical assessment: the anthropometric measurements are represented in Figure 4.

The girl had mild thoracal kyphosis, thoracolumbar scoliosis and inwards rotation of both thighs. The blood work-up revealed normal basal glycaemia, OGTT, A1c, lipids’ profile and transaminase. Basal insulinemia and HOMA, C peptide and leptin were in normal range. Adiponectin was low.

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The facial phenotype was similar to his mother and sisters. No stretch marks or acanthosis nigricans were present. The distribution of adipose tissue was generalized.

Discussions

Anthropometric considerations

The growth of a child is of high importance for us pediatricians. Genetic, hormonal and nutritional factors are responsible for normal growth. When evaluating a child
with obesity, height is the anthropometric measurement that differentiates between primary (due to unhealthy lifestyle) and secondary (syndromic) obesity. Overweight and obese children and adolescent are generally taller than their peers during childhood and early puberty (7). Genetic and endocrine diseases that have obesity as a symptom (Cushing’s syndrome/disease, hypothyroidism, Laron syndrome etc) are all associated with height deficit.

It is obvious that the siblings do not present with impaired height, on the contrary their respective heights tend to be above average. This makes a diagnosis of secondary obesity unlikely.

**Metabolic considerations**

While all of the metabolic markers were in normal range, it is clear to us that the metabolic risk of these children is significant. Furthermore, in spite of a normal insulin level, as well as HOMA index, Mădălina’s siblings do not present with impaired height, on the contrary their respective heights tend to be above average. This makes a diagnosis of secondary obesity unlikely.

**Leptin and adiponectin profile**

We strongly believe that the leptin and adiponectin disturbances are a consequence of primary obesity, rather than its cause.

Leptin is almost exclusively excreted by the adipocyte, dependent of the fat cell volume, invoking satiety and ceasing nutritional intake. Increased levels have been found in obese. The release of leptin is partly dependent on sleep timing, duration and quality. The human leptin profile is mainly dependent on meal intake, with a morning minimum and increasing levels throughout the daytime, followed by a nocturnal maximum (maybe to inhibit hunger during the overnight fast). Leptin levels were lowest in a state of sleep debt, signaling the brain an unnecessary need for extra caloric intake (11).

The low levels of leptin found in Mădălina may reflect her prolonged OSA, but this is debatable because several studies found high levels of leptin in adult patients with OSA (12,13).

Adiponectin is a hormone secreted exclusively by the adipose tissue. It correlates inversely with obesity and insulin resistance and has been linked with features of the metabolic syndrome in obese children and adolescents (14).

It has been suggested that adiponectin may be a useful biomarker to identify children at risk of cardiometabolic adverse effects of adiposity (15), but its role as an early marker of the metabolic syndrome in overweight and obese children is unknown. Furthermore, there are only a few studies of adiponectin in preschool children (16).

Denisa’s low adiponectin may reflect a more precarious metabolic homeostasis in comparison with her siblings.

**Nature versus nurture**

While genetic factors may be suspected, it is clear to us that nurture played a significant role in the development of the siblings’ severe obesity. Their meals are unorganized, uncontrolled, lacking nutrients and including high amounts of bread, refined sugars and unsaturated fats. In addition, the family lives a profoundly sedentary life. All children proved to be under stimulated with psychological age appropriate deficits. The socioeconomic status significantly affects families like this one all over the world: unhealthy lifestyles are more common among those with lower education and poor financial conditions (17,18).

**Outcome**

On the short term prognosis is fair: the family was given dietary and activity recommendations and after 2 months all children lost weight (Figures 2-4). They also underwent psychological counseling and will be closely follow-up. Mădălina’s OSA improved and she does not require CPAP therapy.

On the other hand, the long term prognosis may be reserved due to the frequent drawbacks and inability to maintain the weight loss. An emphasis must be made: in an obese child, most excess weight before puberty is gained before 5 years of age (19). Furthermore, early weight gain is associated with inflammation, endothelial activation and major metabolic risks (20, 21).

It is encouraging that early prevention and intervention on risk aimed at managing obesity in preschoolers seems to be the most effective (22, 23). Needles to say a supportive parent is mandatory.

**Conclusions**

Nurture is the major determinant of the siblings’ severe obesity. Signs of metabolic disturbance are already present and hormonal disturbances are a consequence of primary obesity, rather than its cause. While on the short term prognosis is fair, all children having already lost weight, on the long run, the multiple comorbidities associated with obesity make it reserved..
References

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FUNCTIONAL AND PSYCHOLOGICAL OUTCOMES 50 YEARS AFTER A JUVENILE AMPUTATION

G. Aioirdachioae¹, A Pop¹, H Haragus², D Vermesan², I Stoia³

Abstract
The results after amputation compared to a salvaged lower limb are currently debated. For below the knee the outcomes vary and there is no consensus. We therefore consider important to present long-term outcomes of pediatric amputations. Our case has had half a decade of active living after a juvenile amputation. The now elderly patient was evaluated using gait analysis and functional outcome scores and compared to similar level amputees adjusted for age and gender from a group of 18 lower limb amputees that performed gait analysis as part of a larger study to determine gait modifications in below the knee amputees. The measurements were taken using a Zebris spatial detection instrument. The reason for amputation was severe trauma (crush injury) at the age of 5. The female patient had a transtibial amputation of the left leg that subsequently underwent repeated prosthetic fittings. The Gillette gait index revealed abnormal gait for the entire group of 18 participants, including the juvenile amputee. For this case the score was 42.1 compared to a mean of the group of 39.7. This can be interpreted as a poorer function compared to the mean of the study group. The Prosthesis Evaluation Questionnaire: for Appearance, Frustration, Perceived Response, Social Burden, Well Being, Satisfaction, Self efficacy and Importance the juvenile amputee produced higher values compared to the group average. These were considered significant since they were more than 15% better. For Ambulation, Residual Limb Health, Sounds, Utility, Pain, Transfer and Prosthetic care the values were below this cut-off value and thus were deemed comparable. Qualitative increased asymmetry can be found for adduction-abduction and inward-outward rotation of the hip and inward-outward rotation of the ankle. We conclude that juvenile below the knee amputations can be successful procedures for severe trauma. They produce favorable outcomes up to 50 years. The psychological results are dependent on time from index surgery and personality and are not necessarily correlated to function and gait symmetry, but more to acceptance of the disease.

Key words: juvenile amputation, gait analysis, psychological outcome, prosthesis evaluation questionnaire, Gillette gait index

Introduction
Lower limb amputations are one of the oldest major surgical procedures still in use. They predate even anesthesia and are highly debilitating. With limited use these procedures are used in children mainly in treating malignancy or severe trauma. With all advancement in limb salvage and reconstruction there are still situations where below the knee amputations will be applied to children.

The results after amputation compared to a salvaged lower limb are currently debated. For above the knee amputation, studies provide superior function and physiological results favoring limb salvage. However, for below the knee the outcomes vary and there is no consensus. Some find limb-salvage surgery offers better gait efficiency and return to normal living but does not improve the patient's perception of quality of life [1]. A study on combat injuries found that lower limb amputees had increased risk for infectious complications but not post traumatic stress disorder and proved better use of rehabilitation clinics [2].

A meta-analysis of observational studies found that overall hospital stay and costs are higher for limb salvage patients with comparable long-term functional outcomes, self-reported disability, pain and return to work. The most interesting finding is that at the time of injury patients prefer limb salvage, but the majority of failed salvage patients would opt for early amputation if they could decide again [3].

Factors that are considered to have the largest impact on decision-making for an elective amputation are pain and function, whereas body image and peer perception had less influence. Satisfaction with the surgical outcome is mostly related to how closely the result matched the patient's expectations [4].

For pediatric patients in particular, there are certain complications associated with amputations. One less frequent is secondary tibia vara after synostosis formation. This later has been found to contribute to the development of a progressive varus deformity and should be monitored during a child's growth [5]. A more common incident is osseous overgrowth. Metaphyseal and diaphyseal amputations are likely to develop some degree of overgrowth requiring revision whereas joint disarticulations never develop overgrowth. Traumatic amputations more frequently require stump revisions compared to elective procedures [6]. This is important since apex stump growth may lead to skin perforation, pressure ulcers, and difficulties in accommodating the prosthesis. Different stump capping procedures have been proposed to reduce this event [7].

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Fig. 1 Ground reaction forces recorded in stance phase of the gait.

Fig. 2 Flexion-extension movement in hip joint.

Fig. 3 Adduction-abduction of the hip joint in a gait cycle.
Fig. 4 Inward-outward rotation of the hip joint in a gait cycle.

Fig. 5 Flexion-extension movement in knee joint.

Fig. 6 Adduction-abduction of the knee joint in a gait cycle.
We therefore consider important to present long-term outcomes of pediatric amputations. Our case has had half a decade of active living after a juvenile amputation. The now elderly patient is evaluated using gait analysis and functional outcome scores and compared to similar level amputees adjusted for age, gender, level and prosthetic type.

**Material and Method**

From a group of 18 lower limb amputees that performed gait analysis one had the amputation as a child. The cause was severe trauma (crush injury) at the age of 5. The female patient had a transtibial amputation of the left leg that subsequently underwent repeated prosthetic fittings (8). The patient is now 64 years old and has had a normal life throughout. She had two natural births, has worked full time for 40 years at a manufacturing plant and is now caring for two grandsons. She is independent and walks without any assistive device.

The gait analysis was performed as part of a larger study to determine gait modifications in below the knee amputees. The measurements were taken using a Zebris spatial detection instrument. The functional outcome was determined by computing the Gillette gait index (formerly known as normalcy index) as described by Schutte et al [8]. This instrument was developed to assess the abnormal gait in children with cerebral palsy. It uses 16 gait parameters that have been shown to have less variability in adults compared to children, which makes it more sensitive. In addition, in the mature population this score is more dependent on one parameter among the ones initially proposed – time of peak flexion. Nonetheless it has been proved useful also in adults [9].

The patient perception of handicap, function and prosthesis was determined using the Prosthesis Evaluation Questionnaire, developed by the Prosthetics Research Study [10]. This complex evaluation tool consists of eighty-two questions with a linear analog scale response format. Nine scales are computed from forty-two items (ambulation, appearance, frustration, perceived response, residual limb health, social burden, sounds, utility, well being).

**Results**

The Gillette gait index revealed abnormal gait for the entire group of 18 participants, including the juvenile amputee. For this case the score was 42.1 compared to a
mean of the group of 39.7. This can be interpreted as a poorer function compared to the mean of the study group.

The Prosthesis Evaluation Questionnaire: for Appearance, Frustration, Perceived Response, Social Burden, Well Being, Satisfaction, Self efficacy and Importance the juvenile amputee produced higher values compared to the group average. These were considered significant since they were more that 15% better. For Ambulation, Residual Limb Health, Sounds, Utility, Pain, Transfer and Prosthetic care the values were below this cutoff value and thus were deemed comparable.

The charts below (Fig.1-8) represent the measured left to right gait symmetry of the juvenile amputee compared to a matched age, gender, prosthetic type and level control from the study group of 18. Qualitative increased asymmetry can be found for abduction-abduction and inward-outward rotation of the hip and inward-outward rotation of the ankle (Fig. 3, 4 and 8).

Discussions and Conclusions

There are limitations to this study. There is only one patient with such long term follow-up and pediatric amputation. Therefore, we only compared to a matched age, gender, prosthetic type and level since statistical processing would have yielded biased results. Nonetheless, we still find important to present the functional and psychological outcome of an old adult with juvenile amputation. This can be an example of long term outcome for present candidates that might help decide on therapeutic management regarding amputation or limb salvage.

Patients after a lower limb amputation reflect differently on body image and function. The handicap is reflected differently depending on the patient's awareness of the impairment [11]. A meta-analysis of amputation versus limb salvage in mangled lower limb injuries found that reconstruction is more acceptable psychologically to limb salvage in mangled lower limb injuries found that outcomes were comparable [12].

The psychosocial adjustment to lower-limb amputation is time dependant. Depression and anxiety can be high up to two years post-amputation. Positive adjustment to limb loss can be predicted by increased time since amputation, plentiful social support, higher satisfaction with the prosthetic device, active coping, an optimistic personality type, lower level of amputation and stump pain [13]. The same authors call for longitudinal rather than cross-sectional studies that can include immediate reactions, adjustment during postoperative rehabilitation period and development of changed identity [13].

Elderly people with lower limb amputations are high consumers of health care resources. Mobility is essential to regain independence and such skills are achievable. However, a literature review of the studies that included all subjects undergoing a lower limb amputation reported that less than half of the elderly reached this goal, mainly due to co morbidities [14]. Impairment variables predicting activity limitation are linked to strength, balance, demographics, time, cause and level of amputation. In one particular study, strength of the hip extensors was found to be the strongest predictor, judged by the six minute walk scores [15].

Vascular amputees are an important subgroup of elderly patients. Many are able to remain independent despite infrequent prosthesis use and outdoor ambulation. Ability to predict ambulation after below the knee amputations in the vascular population is unreliable but preservation of the knee is essential in regaining mobility [16].

Optimal treatment of pediatric lower limb malignancy has not reached a consensus. Studies have showed that physical and emotional outcomes in patients treated with an expandable endoprostheses are good but complication rates remain high. Amputation and rotationplasty are successful alternative treatments if patients agree [17].

Juvenile amputation overgrowth has remained a minor setback for this subgroup. Alternative surgical procedures have been proposed either with the use of a synthetic cap [18] or by using different stump apex techniques such as the Ertl amputation [19].

We conclude that juvenile below the knee amputations can be successful procedures for severe trauma. They produce favorable outcomes up to 50 years. The psychological results are dependent on time from index surgery and personality and are not necessarily correlated to function and gait symmetry, but more to acceptance of the disease.

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LEFT-SIDED PNEUMONECTOMY IN ONE-YEAR OLD CHILD A RESULT OF COMPLICATED PLEUROPNEUMONIA

A Uchikov¹, P Stefanova², B Ivanov²

Abstract

Pleuropneumonia in children with heavy complications often requires surgical treatment. In the accessible literature a couple of cases with pneumonectomy in children of different ages are described. Procedure is not often done because of intervention difficulty and the high risk of intra and postoperative complications. A clinical case of one-year old child with left-sided pneumonectomy because of chronic pleuropneumonia is presented. Taking the decision for removal of a pair organ is difficult and responsible, but in the presented case it solves a number of complications and improves the quality of patient’s life.

Key words: pleuropneumonia, pneumonectomy, child

Introduction

The inflammatory lung process in children has a tendency to quickly progressing destructive pleural and parenchymal complications.(1) Pleuropneumonia in children with life threatening condition is usually supported with parenchymal damage of lung as: necrotizing pneumonia, pulmonary abscess, fungal infection or gangrene of lung (1,2) Surgical treatment includes thoracocentesis, thoracotomy with decortication, atypical resections, segmentectomies or when the whole lobe is affected - lobectomy and in non-working lung pulmonectomy is required.(2)

Pneumonectomy in early pediatric age in case of inflammatory lung diseases is considered a procedure of high risk because of the complex operative technique and postoperative complications.(5) In a couple of publications the authors consider that the procedure should be avoided when is possible. (6) Despite that, there are situations when pneumonectomy and pleuropneumonectomy continue to be the only way of treatment in inflammatory destructive lungs diseases. (1,6)

Children, who underwent pneumonectomy have less functional disturbances compared with adults. (7)

Clinical case:

A one year old boy was admitted in the Department of Pediatric surgery of UMHAT St. George with diagnosis: complicated left-sided pleuropneumonia with difficult respiratory insufficiency. On the chest X-rays is total left-sided pneumothorax – fig. 1

Thoracocentesis was done in the 6th intercostal space and 100 ml. purulent exudate was evacuated, and the Bulau chest drainage was put fig.2 The condition of the boy remained serious and second thoracocentesis is done - fig.3

Condition of child remained still serious. A CT/computer tomography/ of lung is done - Fig.4

The child stayed in serious condition. Clinical process of disease and data from computer-tomography check-up imposed taking a decision for thoracotomy. With lateral thoracotomy in 6th intercostal space the chest cavity is opened. The thick coalesced visceral to parietal pleura was separated as well as from the diaphragm and pericardium. The pulmonary tissue is atelectatic in the phase of hepatization. The attempt for unfolding the lung is without result. The decision of left pneumonectomy is taken. A thoracic drainage was put in the 7th intercostal space.

Histopathology – atelectatic pulmonary parenchyma with hyperemia and subpleural haemorrhages and interstitial fibrosis. After intensive care and antibiotic therapy the condition of child significantly improves and he gradually recovered and was discharged from the hospital.

After 4 mounts, a radiology control and physical examination is done –fig.5 and fig.6

Argument

The destructive diseases of lung supported by necrosis of pulmonary parenchyma are the final stage of deteriorated passing pneumonia leading to serious complications and inconvertible changes in parenchyma which are seldom met in children.(1) The inflammatory lung diseases such as bronchiectasis, tuberculosis, necrotizing pneumonia, pulmonary abscesses, fungus infections, pulmonary gangrene, bronchial structure and congenital malformations , the affected lung doesn’t have proper function, with visible lack of perfusion and ventilation (1, 2) In the literature data bronchiectasis remain the most frequent reason for chronic supplicative destructive diseases in children’s lungs, followed by tuberculosis. (1,3,4,5,13) In our case the presented child hasn’t prior congenital or gained lung pathology and the destructive processe develop on the base of complicated pleuropneumonia, uninfluenced by applied standard conservative and operative therapy.
Fig. 1 Total left-sided pneumothorax

Fig. 2 Left lung half is almost completely dimmed. Presence of inflammatory changes in the pulmonary parenchyma with taking on the pleural cavity

Fig. 3 Extra-alveolar air collections were not estimated in the left side. The same chest half is homogeneously shaded. Combination of pleural effusion and atelectasis
Fig. 4 The whole left lung is with disturbed aeration and is presented with homogeneous structure with density about 45 HE and missing air bronchogram – finding corresponds to atelectasis. Small effusion basally.

Fig. 5 4 mounts, a radiology control

Fig. 6 After 4 mounts physical examination

Nissen in year 1931 in Europe and Haight in year 1932 in North America did the first successful pneumonectomies with children (3). In 1956 F. J. Sambrook Gower, reports for pneumonectomy with newborn on the occasion of congenital cystic malformation of right lung (10). In the accessible literature publications about pneumonectomy are very rare, especially in children under one year (1, 9, 12). According to authors, pneumonectomy as a choice of treatment is one of the quickest and effective means preventing organism from coming serious
complications as: massive spitting blood, secondary fungus infections, secondary amyloidosis, pussy infections, septicemia, pulmonary hypertonia and chronic respiratory insufficiency. (1, 8)

Pneumonectomy in children because of inflammatory lung diseases is a high risk procedure connected with intra and postoperative complications.(1, 2, 3, 8, 9, 11, 12) This operative intervention in children is much more complicated, compared with adults.(1, 3, 4, 8, 9, 11, 12) The difficulty in the presented case is mainly due to the patient’s age, the small chest, the tightly covered lung and the applied endotracheal anesthesia.

After total pneumonectomy, the often met complications are post-pneumonectomy empyema, bronchial, bronchial-pleural fistula and post-pneumonectomy syndrome.(1, 3, 11, 12) In some of the cases after removal of one lung the remaining one is predisposed to edema and 100% mortality is registered (1,11,13)

In our case such complications are not observed. Preoperative application of the antibiotic therapy, antituberculosis patent medicines with proven case of tuberculosis and multiple lavage of the chest cavity after pneumonectomy contribute to decrease the percentage of sick and death rate in children (1,8,9), algorithm to which we keep also.

Despite the high risk which pneumonectomy hides with the vast destructions of lung is not expected to be avoided as a method of treatment when all the other means are spent. (1, 8, 9, 12) A couple of authors share that children who went through pneumonectomy as an operative intervention have good physical growth. ( 7, 8, 10, 11, 12 )

Children who underwent similar operations grow and develop normally and according to the Stiles and co. have bigger potential of growth, they tolerate better duly pulmonectomy as a result of which have lesser functional disturbances compared with adults (7), as we estimated during control check-ups in our case does not show diversion from the norm.

References

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USE OF A EQUIMOLAR MIXTURE OF NITROUS OXIDE AND OXYGEN IN THE PAIN MANAGEMENT OF PEDIATRIC PATIENTS – OWN EXPERIENCE AND REVIEW OF LITERATURE

NF Tepeneu¹, Daniela Alina Chiru²

Abstract
Pain is one of the most common causes for consultation of a paediatrician and represents a major problem in paediatrics. Simple self-reporting and behavioural pain scales are suitable for assessment of intensity of acute pain. Acute pain of whatever origin should be treated immediately. The high analgetic, anxiolytic and sedative effects of nitrous oxide have been known worldwide for a very long time, but the inhalative administration has been approved in our country only in the early beginning of 2011 (authorization number 3143/2011) [1]. The principle of an anxiety and pain-free treatment necessitates, particularly in childhood, a standardized age-related pain management. The oral, rectal or i.v. administration of a sedative/analgesic in pediatric surgery is mostly accompanied by a great deal of stress for all involved and the alternative of general anesthesia is often not readily available or even not available at all. Nitrous oxide is a good alternative to the other mentioned methods for pain management in the pediatric patient. It is absorbed and eliminated through the lungs and because metabolism does not take place in the body fasting is unnecessary. Side effects may occur, but are completely reversible at the end of the application.

Keywords: Children. Pain. Anxiety. Nitrous oxide. Trauma. Pediatric surgery.

Introduction
The principle of an anxiety and pain-free treatment is particularly in childhood a very big challenge for all persons involved: patient, parents and medical staff. A standardized age-related pain management is needed. The presence in the unknown environment of the hospital triggers the fear in the mind of a small child. Also a painful diagnostic or therapeutic maneuver will remain for a long time as a horrifying experience [2,3,4,5].

The oral, rectal or i.v. administration of a sedative/analgesic in pediatric surgery is mostly accompanied by a great deal of stress for all involved and the alternative of general anesthesia is often not readily available or even not available at all. Also the problem in emergency situations would be that the child has not been fasting before and a sufficient analgesia/anaesthesia is not possible to be administered [2,5].

The high analgetic, anxiolytic and sedative effects of nitrous oxide have been known worldwide for a very long time [5,6,7,8,9,10,11,12]. It is a good alternative to the other mentioned methods for pain management in the pediatric patient. It is absorbed and eliminated through the lungs and because metabolism does not take place in the body fasting is unnecessary. Side effects may occur, but are completely reversible at the end of the application [1,6,9,10,11,12].

The analgetic properties of nitrous oxide have been discovered by the dentist Horace Wells in 1844. Further uses were discovered in England in 1961 when a 50% mixture of nitrous oxide and oxygen under the name ENTONOX® was used in the control of birth related pain with very good results. The 50% mixture of nitrous oxide and oxygen

(EMONO:"equimolar mixture of oxygen and nitrous oxide"; MEOPA: "melange equimoleculaire oxygène/protoyde d’azote") is being used for several years now under different commercial names in Europe: ENTONOX® in England, Poland, Cyprus, Spain, Czech Republic, Greece, Hungary, Slovak Republic, Romania, MEDIMIX® 50 in France and Switzerland, RELIVOPAN® in Belgium, Holland, Luxembourg, LIVOPAN® in Germany, Denmark, Finland, Island, Italy, Norway, Portugal, Sweden.

American dentists are using it very successfully for sedation [2].

The application of nitrous oxide in everyday practice is done by the pediatric surgeon or by a trained nurse. The presence of an anesthetist is not required [2]. While using nitrous oxide the the requirements of occupational safety have to be taken into consideration, the gas should be applied only in a room with windows or a good ventilation system [6,1].

Since August 2008, the solid mixture of 50% nitrous oxide and 50% oxygen under the name of LIVOPAN® is approved in Germany for children and adults [6,7].

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The nitrous oxide-oxygen mixture is supplied in 2, 2.5, 5 or 10-liter pressure tanks with integrated pressure regulator and flow controller (demand-driven gas flow or constant). The inflow tube runs via a filter, the demand valve and a face mask to the patient [7]. When using a demand valve the awake and addressable patient controls through breathing the needs and even the effect of the gas. The application with a continuous flow is an alternative for younger patients. The compliance of the child can be enhanced by special masks and additional fragrances applied on the inside of the mask. The absorption and elimination of nitrous oxide takes place over the lungs, via the lungs, metabolism of the gas will not take place. The combination with other analgesics is possible. Side effects may occur, but they are completely reversible with the completion of the application. Minor side effects with an incidence of 5 % include nausea, vomiting, dizziness and paresthesia. Major effects appear with a frequency of 0.33 % and are: decrease in oxygen saturation, bradycardia and loss of contact with the patient due to oversedation [7,12,13,14].

Material and method

Since August 2010 a solid mixture of 50% nitrous oxide and 50% oxygen under the name of LIVOPAN® is used in the Pediatric Surgery Clinic of the the University Mannheim for pain management. It is used for elective and emergency small or medium procedures for inpatient or on an outpatient basis.

The procedure was discussed with the patients and their parents regarding the application of the gas and the expected effects, possible complications and alternatives for analgesia. Oral informed consent from the parents was obtained. The nitrous oxide was applied over a suitable face mask. Patients under 2 years of age were excluded from the study because of lack of compliance. Additional fragrances (strawberry, orange) were applied on the inside of the mask to enhance compliance of the patients. The mask was held by the patients themselves or the parent. The application of the gas occurred in a fully equipped ambulant operating room. A pulseoxymeter was applied on the finger of the patient before beginning of the procedure and a full survey of the patient by a trained nurse was undertaken. Before the actual procedure the mixture of 50% nitrous oxide and 50% oxygen was applied for at least 3 minutes. The application of nitrous oxide was stopped with the ending of the procedure, there was no need for further application of oxygen. The patients could be discharged shortly after the procedure. For the evaluation of treatment outcomes a documentation form for parents, caregivers and the doctors was created. Because of the nitrous oxide-induced retrograde amnesia an objective evaluation of outcome from the perspective of patients was not possible.

<table>
<thead>
<tr>
<th>Emergency procedures</th>
<th>Elective procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>32 wound closures</td>
<td>22 removal of Kirschner wires (fractures)</td>
</tr>
<tr>
<td>6 burns</td>
<td>2 removal of external fixateur</td>
</tr>
<tr>
<td>1 suprapubic catheter</td>
<td>13 cast wedge</td>
</tr>
<tr>
<td>2 reduction of paraphimosis</td>
<td>35 burns</td>
</tr>
<tr>
<td>2 incision of abscesses</td>
<td>17 placements of Foley urinary catheter for cistography</td>
</tr>
<tr>
<td>9 removals of foreign bodies</td>
<td>2 removal of preputial adhesions</td>
</tr>
<tr>
<td>24 closed repositions of minor displaced forearm fractures</td>
<td>1 removal of a sole wart</td>
</tr>
<tr>
<td>3 repositions of patella dislocation</td>
<td></td>
</tr>
<tr>
<td>2 repositions of elbow dislocations</td>
<td></td>
</tr>
<tr>
<td>3 repositions of finger dislocations</td>
<td></td>
</tr>
<tr>
<td>13 reposition of finger fractures</td>
<td></td>
</tr>
<tr>
<td>2 repositions of metacarpal fractures</td>
<td></td>
</tr>
<tr>
<td>1 reposition of metatarsal fracture</td>
<td></td>
</tr>
<tr>
<td>1 knee joint aspiration</td>
<td></td>
</tr>
<tr>
<td><strong>Total= 101 procedures</strong></td>
<td><strong>Total= 92 procedures</strong></td>
</tr>
</tbody>
</table>

Table 1. Procedures performed
Results
In the period between the 01.10.2011 and 30.09.2012 a number of 162 children with the age between 2 and 16 years (mean age 7.5 years) in need of a acute or elective surgical intervention were treated with a solid mixture of 50% nitrous oxide and 50% oxygen and 193 procedures were performed (some children required multiple procedures) (Table 1). In- and outpatients over the age of two years with no significant other comorbidities whoicked elective or emergency small or medium procedures were included. The exclusion criteria included the age under 2 years, relevant comorbidities and the rejection of nitrous oxide by parents or the patient. The patient lot was composed of 91 male patients(56,18 %) and 71 female patients (43,82 %). Fasting before the procedure was not necessary.

The range of indications consisted in procedures for:
- Pediatric trauma (95/49.22 %)
- Burns(41/21,24 %)
- Wounds (32/16,58 %)
- Urologic procedures (22/11,39%)
- Septic surgery(2/1,03%)
- Dermatologic surgery (1/0,51%)

There were 101 (52,34%) emergency procedures and 92 (47,66%) elective procedures performed in the 162 children. The surplus of procedures is mainly attributed to the pediatric patients with burns, but also patients with multiple wounds, multiple Kirschner wire removal or multiple foreign bodies.

Monitoring of side effects under application of the solid mixture of 50% nitrous oxide and 50% oxygen was done by pulseoxymeter, as well as observation by trained nurse and physician. The presence of the parents as well as their support had also positive effects on the success of the procedure.There were no problems observed during monitoring of the patients. There were no side effects in 154 patients (95,06%), 6 patients accused mild nausea and 2 accused dizziness. These symptoms disappeared quickly after the application of nitrous oxide was stopped. Also there were light positive psychotropic effects (laughing, singing) in 32 patients (19,75%).

Very good analgetic and anxyolitic effects as well as retrograde amnesia were observed in 158 patients(97,53 %). In 4 patients the effects were not satisfactory, 2 of them presenting with forearm fractures, 1 with a elbow dislocation and 1 with a wound to the head. In 2 cases the procedure had to be interrupted, the patients were excluded from the study.

The satisfaction and acceptance of the solid mixture of 50% nitrous oxide and 50% oxygen in the ranks of patients, parents and physicians were very high. All parents would choose a application of solid mixture of 50% nitrous oxide and 50% oxygen under similar conditions again if there was the case, although only 6 parents or couples of parents have heard before that of this procedure.

Discussion
There is a great need for proper analgesia even for small procedures in children. The high analgetic, anxiolytic and sedative effects of nitrous oxide are well suited for this purpose. It is a good alternative for oral, inhalative or intravenous analgesics. There is also a very low rate of side effects reported.

In emergency room conditions there are very often problems because of pain and fear of traumatized patients and the fact that they are not fastened or there is no capacity for a general anesthesia for the moment.

Proper and age related analgesia and anesthesia are very important in the pediatric population. Burnweit et. al [12] observed the patients must not fasten before the procedure. They advised for the regular use of nitrous oxide in an emergency room in the USA and also Babl et al.[9] in Australia and Annequin et al. in France [8]. Nitrous oxide is applied in practice by special trained nurses or the pediatric surgeon himself [11,12,13,14,18,19,20,21].

Several authors reported that the use of a demand-valve in the administration of nitrous-oxide can reduce the complications rate [11,12,13,14,15,16,17,18,19,20,21]. The presence of a parent during the procedure can increase the compliance of the child[13].

Patients under 2 years of age were excluded from the study because of lack of compliance. By law there is a age related barrier of 4 years for pediatric patients in France[15]. Annequin et al. [8], Burnweit et al. [12] und Reinoso-Barbero et al. [19] reported better results in patients over 3 years of age. Burton et al. [13] reported about good results in a pediatric population with the age between 2 and 7 years. Gal et al.[15] described the emergency and elective application of nitrous oxide and also possible complications.

The therapeutic range of nitrous oxide is large but should not be overextended[9,13,22]. Gregory and Sullivan[16] reported of the quicker reposition of a forearm fracture when comparing nitrous oxide with regional anesthesia but Henrikus et al.[17] published a significantly high rate of therapy failures using nitrous oxide in the treatment of displaced forearm fractures.

Before the actual procedure the mixture of 50% nitrous oxide and 50% oxygen must be applied for at least 3 minutes[7,8,10,19]. The effects of nitrous oxide have a quick onset and also a quick ending. Intensive observation and application of 100 % oxygen like Bar-Meir et al. [10] and Ekbom et al.[14] and suggested is not needed.

Gall et al.[15] reported minor and major side effects after 7511 applications of nitrous oxide in a pediatric population. They reported a incidence of 5 % minor side effects and 0,33% major side effects. We did not encounter any major side effects, minor side effects were seen in 4,93 % of patients (minor nausea, dizziness). These minor side effects disappeared with the termination of the application of nitrous oxide, concording with the observations of Annequin et al. [8]. Annequin et al.[8] reported a rate of 12% dissatisfaction from the medical staff. The satisfaction and acceptance of the solid mixture of 50% nitrous oxide and 50% oxygen in the ranks of patients, parents and physicians in our lot was 100%. This is correlated maybe with a good preparation of the patient and parents before the procedure. Babl et al.[9] reported about the problem of self assessment in children with the age under 5 years, mainly because of the known issue of retrograde amnesia.
Burnweit et al.[12], Babl et al.[9,23] Reinoso-Barbero et al.[19] and other authors[13,14] have stated that nitrous oxide is a safe method for anesthesia and analgesia in pediatric patients. Babl et al.[23] recommended the application of nitrous oxide in patients with ages between 1 and 3 years as safe. However, it must be assumed that these were small interventions in otherwise healthy children. Other authors like Fröhleke et al.[24] and others[25,26,27,28,29] report about various side effects, some of them very serious[24], but especially in patients with associated diseases. The administration of nitrous oxide in critically ill children, children with a polypharmacy and systematically treated with folic acid antagonists may not be assessed as safe automatically [24,26,27]. Further studies are needed to clear this aspect.

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Conclusion
If technique, indications, as well as side effects are well taken in consideration we can agree that nitrous oxide is a safe method for anesthesia and analgesia in pediatric patients. The major disadvantage is the fact that it is not a widespread and popular method, and as this fact only 6 couples of parents from our lot had heard about this method. The high percentage of acceptance of the method encourages us to recommend the usage of nitrous oxide in pediatric patients in Romania for elective as well as emergency small or medium surgical or orthopaedic procedures.


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PROPRANOLOL TREATMENT OF INFANTILE HEMANGIOMA: OUR PRELIMINARY RESULTS

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Abstract

Infantile hemangiomas (IH) are the most common benign vascular tumors in childhood, affecting 4-5% of Caucasian infants in their first year of life.

We performed a prospective study of 34 cases of IH treated with propranolol from May 2010 to December 2012. Beta blocker treatment was administered in 21 girls and 13 boys aged 2 to 14 months (mean age 5.4 months). All patients were evaluated with electrocardiography and echocardiography prior to start of treatment. Propranolol was administrated at a dose of 1mg/kg/day divided in 3 equal parts (day 1) and 2mg/kg/day divided in 3 equal parts (day 2), continuing with this dose throughout the rest of the treatment. The treatment was initiated during a 24-48 hours hospitalization, time during which blood pressure and heart rate were measured every 6 hours. After 24 hours of hospitalization we performed an EKG and measured the blood glucose level. None of our patients developed hypotension, hypoglycemia or bronchospasms.

The results are: very good-70.96%, good-16.12%, partial-6.45%, no response- 6.45%. Three patients were uncooperative and after 1 month to treatment they have not presented to control and stop the treatment.

Keywords: infantile hemangioma, propranolol, treatment, beta blocker

Introduction

What is hemangioma? What is infantile hemangioma? What is congenital hemangioma? The terminology used for vascular lesions has been very confusing until 1982, when Mulliken and Glowacki classified the common cutaneous vascular lesions of childhood into two categories, based on endothelial cell characteristics: hemangiomas and vascular malformations [1,2,3,4].

In 1996, the International Society for the Study of Vascular Anomalies (ISSVA) accepted the classification of vascular anomalies into vascular tumors and vascular malformations, based on clinical, radiological and pathological characteristics [5,6]. Hemangiomas represented the most vascular tumor of infancy and can be divided into two categories: infantile hemangiomas and congenital hemangiomas. IH is the most common benign vascular tumor of infancy, occurring in an estimated 4-5% of Caucasian infants [7,8].

The typical IH is not present at birth, appearing a few days postnatally, it rapidly grows during the first year and regresses slowly by the age of 7 years. One third of IH may be apparent as a stain at birth. They are more common in females (3:1) and premature babies with birth weight of less than 1500 grams. The lesions may be classified by clinical type into superficial, deep and mixed [9]. Medical history should focus on determining whether or not the lesion is present at birth, its growth rate (proportional versus disproportional), and if episodic enlargement occurred at any point [10].

The diagnosis of IH is based on medical history and physical examination. Imaging techniques are sometimes used to evaluate the extent of the lesion, differential diagnosis and follow-up of response to treatment [4].

Two approaches can be adopted in the management of infantile hemangiomas: the expectant “wait and see” attitude or the therapeutic (either medical or surgical) attitude. The methods of treatment include: systemic corticosteroid therapy, intralesional corticosteroids, interferon α, Vincristine, laser therapy, cryotherapy, surgical excision [10].

By a chance, Leaute-Labreze C et al. [11] discovered the propranolol’s effects for infantile hemangioma. They treated for hypertrophic myocardiopathy an infant with a nasal infantile hemangioma with enlarging lesion despite corticoid treatment and observed propranolol’s inhibitory effect on hemangioma proliferation.

Synthesized by James W. Black [12] in the early 1960s, propranolol has been used extensively in children and neonates in pediatric cardiology. The indications for propranolol use have now exceeded the spectrum of cardiology, as the drug has been proven useful in pathologies like migraines, infantile hemangiomas, portal hypertension, post-traumatic stress and cancer [11,13,14,15].

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24
### Table 2. Characteristics of the patients

<table>
<thead>
<tr>
<th>No</th>
<th>Gender</th>
<th>Localization</th>
<th>Type of IH</th>
<th>Age at onset</th>
<th>Age at end</th>
<th>Duration</th>
<th>Response</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>Periorbital</td>
<td>Deep</td>
<td>9 mo</td>
<td>15 mo</td>
<td>6 mo</td>
<td>Very good</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Capillary malformation of major labia</td>
<td>-</td>
<td></td>
<td></td>
<td>No response</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>Periorbital</td>
<td>Deep</td>
<td>5 mo</td>
<td>13 mo</td>
<td>8 mo</td>
<td>Very good</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>Face (cheek)</td>
<td>Deep</td>
<td>14 mo</td>
<td>20 mo</td>
<td>6 mo</td>
<td>Very good</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>Scalp (occipital) and lower lip</td>
<td>Mixed</td>
<td>5 mo</td>
<td>13 mo</td>
<td>8 mo</td>
<td>Very good</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>Forearm and scalp</td>
<td>Superficial</td>
<td>6 mo</td>
<td>16 mo</td>
<td>10 mo</td>
<td>Very good</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>Periorbital</td>
<td>Deep</td>
<td>6 mo</td>
<td>14 mo</td>
<td>8 mo</td>
<td>Very good</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>Cervical area and forearm</td>
<td>Superficial</td>
<td>6 mo</td>
<td>-</td>
<td>Ongoing</td>
<td>Good</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>Right calf</td>
<td>Superficial</td>
<td>7 mo</td>
<td>15 mo</td>
<td>8 mo</td>
<td>Very good</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>Face (chin)</td>
<td>Superficial</td>
<td>5 mo</td>
<td>6 mo</td>
<td>1 mo Retract</td>
<td>Uncooperative patient</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>Forehead</td>
<td>Superficial</td>
<td>5 mo</td>
<td>8 mo</td>
<td>3 mo Retract</td>
<td>No response Surgical excision</td>
</tr>
<tr>
<td>11</td>
<td>F</td>
<td>Forearm and abdominal wall</td>
<td>Superficial</td>
<td>3 mo</td>
<td>12 mo</td>
<td>9 mo</td>
<td>Very good</td>
</tr>
<tr>
<td>12</td>
<td>M</td>
<td>Fingers</td>
<td>Superficial</td>
<td>5 mo</td>
<td>11 mo</td>
<td>6 mo</td>
<td>Very good</td>
</tr>
<tr>
<td>13</td>
<td>F</td>
<td>Left hand</td>
<td>Superficial</td>
<td>5 mo</td>
<td>-</td>
<td>Ongoing</td>
<td>Very good</td>
</tr>
<tr>
<td>14</td>
<td>F</td>
<td>Right breast</td>
<td>Mixed</td>
<td>2 mo</td>
<td>-</td>
<td>Ongoing</td>
<td>Good</td>
</tr>
<tr>
<td>15</td>
<td>F</td>
<td>Left breast and scalp</td>
<td>Superficial</td>
<td>6 mo</td>
<td>-</td>
<td>Ongoing</td>
<td>Good</td>
</tr>
<tr>
<td>16</td>
<td>M</td>
<td>Ear lobe</td>
<td>Superficial</td>
<td>2 mo</td>
<td>8 mo</td>
<td>6 mo</td>
<td>Very good</td>
</tr>
<tr>
<td>17</td>
<td>F</td>
<td>Labia major</td>
<td>Superficial</td>
<td>7 mo</td>
<td>8 mo</td>
<td>1 mo Retract</td>
<td>No response Uncooperative patient</td>
</tr>
<tr>
<td>18</td>
<td>F</td>
<td>Face</td>
<td>Superficial</td>
<td>5 mo</td>
<td>6 mo</td>
<td>1 mo Retract</td>
<td>No response Uncooperative patient</td>
</tr>
<tr>
<td>19</td>
<td>F</td>
<td>Upper eyelid, thorax, fingers</td>
<td>Superficial</td>
<td>2 mo</td>
<td>-</td>
<td>Ongoing</td>
<td>Good</td>
</tr>
<tr>
<td>20</td>
<td>F</td>
<td>Abdominal wall</td>
<td>Superficial</td>
<td>4 mo</td>
<td>12 mo</td>
<td>8 mo</td>
<td>Very good</td>
</tr>
<tr>
<td>21</td>
<td>F</td>
<td>Abdominal wall</td>
<td>Superficial</td>
<td>8 mo</td>
<td>16 mo</td>
<td>8 mo</td>
<td>Very good</td>
</tr>
<tr>
<td>22</td>
<td>M</td>
<td>Shoulder</td>
<td>Superficial</td>
<td>8 mo</td>
<td>9 mo</td>
<td>1 mo Retract</td>
<td>No response Surgical excision</td>
</tr>
<tr>
<td>23</td>
<td>M</td>
<td>Abdominal wall</td>
<td>Superficial</td>
<td>2 mo</td>
<td>8 mo</td>
<td>6 mo</td>
<td>Very good</td>
</tr>
<tr>
<td>24</td>
<td>F</td>
<td>Face</td>
<td>Mixed</td>
<td>5 mo</td>
<td>-</td>
<td>Ongoing</td>
<td>Very good</td>
</tr>
<tr>
<td>25</td>
<td>F</td>
<td>Scalp and right calf</td>
<td>Superficial</td>
<td>4 mo</td>
<td>-</td>
<td>Ongoing</td>
<td>Very good</td>
</tr>
<tr>
<td>26</td>
<td>M</td>
<td>Scalp and thorax</td>
<td>Superficial</td>
<td>8 mo</td>
<td>-</td>
<td>Ongoing</td>
<td>Very good</td>
</tr>
<tr>
<td>27</td>
<td>M</td>
<td>Lower lip</td>
<td>Mixed</td>
<td>14 mo</td>
<td>-</td>
<td>Ongoing</td>
<td>Very good</td>
</tr>
<tr>
<td>28</td>
<td>F</td>
<td>Lower eyelid</td>
<td>Superficial</td>
<td>3 mo</td>
<td>9 mo</td>
<td>6 mo</td>
<td>Very good</td>
</tr>
<tr>
<td>29</td>
<td>F</td>
<td>Left calf</td>
<td>Superficial</td>
<td>6 mo</td>
<td>12 mo</td>
<td>6 mo</td>
<td>Very good</td>
</tr>
<tr>
<td>30</td>
<td>F</td>
<td>Thorax</td>
<td>Mixed</td>
<td>2 mo</td>
<td>14 mo</td>
<td>12 mo</td>
<td>Partial</td>
</tr>
<tr>
<td>31</td>
<td>M</td>
<td>Forehead</td>
<td>Superficial</td>
<td>5 mo</td>
<td>-</td>
<td>Ongoing</td>
<td>Partial</td>
</tr>
<tr>
<td>32</td>
<td>F</td>
<td>Right ankle</td>
<td>Superficial</td>
<td>2 mo</td>
<td>-</td>
<td>Ongoing</td>
<td>Very good</td>
</tr>
<tr>
<td>33</td>
<td>M</td>
<td>Scalp</td>
<td>Superficial</td>
<td>2 mo</td>
<td>-</td>
<td>Ongoing</td>
<td>Very good</td>
</tr>
<tr>
<td>34</td>
<td>F</td>
<td>Face and cervical</td>
<td>Mixed</td>
<td>6 mo</td>
<td>-</td>
<td>Ongoing</td>
<td>Good</td>
</tr>
</tbody>
</table>

### Materials and methods

We present our preliminary data from 34 children with 44 infantile hemangioma treated with oral propranolol, during the May 2010 to December 2012 timeframe. (Table 1.)

Informed consent from the parents/guardians of each patient was obtained in all cases. Clinical pictures have been taken before the start of treatment and at each subsequent visit. Inclusion criteria were infants newly diagnosed with IH who had not been previously treated with local or systemic corticosteroids.

Beta blocker treatment was administered to 21 girls and 13 boys aged between 2 months and 14 months (mean age 5.4 months). Treatment was discontinued if the lesion completely disappeared, if parents decided to cease the
medication or if after 1 or 3 month of treatment there was no improvement, and the family was offered surgical treatment.

Prior to administration of the drug, all patients were clinically evaluated by a pediatric cardiologist, then underwent electrocardiography (EKG) and echocardiography.

We have used the Prof. Dr. Cremer therapeutic scheme: propranolol was administrated at a dose of 1mg/kg/day divided in 3 equal parts (day1) and 2mg/kg/day divided in 3 equal parts (day 2), continuing with this dose throughout the rest of the treatment[16,17]. We have initiated the treatment during a hospitalization of 24-48 hours. The blood pressure, blood glucose and the heart rate were carefully monitored every 6 hours. After 24 hours we have remeasured child blood glucose and registered the EKG profile. In all cases, the drug was well tolerated and the treatment was continued at home. Monthly, we have evaluated the clinical and photographic evolution of the hemangioma, and we monitored the heart rate, blood pressure, blood glucose and performed an EKG. A repeat echocardiogram was performed after 2 months of treatment.

During the period of observation, the family was instructed to report any evidence of evolution, and none reported or received other therapies for other medical problems.

Fig. 1. Case 1: A. Before treatment; B. After 5 months; C. After 8 months; D. After 9 months from treatment cessation.

Fig. 2. Case 2: A. Before treatment with Propranolol; B. After 9 months; C. After 12 months.
Fig. 3. Case 3: A. Before treatment; B. After 3 months; C. After 6 months.

Fig. 4. Case 4: A. Before; B. After 8 months; C. After 1 years and 6 month.
The outcome of each lesion was defined by its status at the last recorded patient visit. Outcomes are classified as: 1-very good if the final observation indicates that the lesion has more than 90% disappeared, 2-good if the lesion has more than 70% disappeared, 3-partial if the lesion has less than 50% disappeared, 4-early removing from study by parents.

**Results**

The distribution of the 44 hemangiomas was as follows: 24 cases on the head and neck (2 forehead, 3 periorbital, 2 upper eyelid, 1 lower eyelid, 2 lower lip, 5 facial, 2 cervical, 1 at ear lobe, and 6 scalp); 8 cases on the trunk (3 thorax, 2 breast and 3 abdominal wall); 11 cases on the extremities, and 1 case in the anogenital region. Lesion type was multifocal in 9 cases.

Three patients left the study after only 1 month of treatment, based on parent’s decision.

The treatment did not affect blood pressure and heart rate. None of the parents reported wheezing, and food intake was regular.

Outcomes are: 22 cases (16 completed treatment)-very good (70.96%), 5 cases (still in treatment)- good (16.12%), and 2 cases –partial response (6.45%).

In two cases (6.45%) after 1 month and 3 months of treatment, the lesions did not respond to propranolol and the surgical excision was performed.

One case present one deep infantile hemangioma of the periorbital area and a capillary malformation of the major labia. After 6 months the treatment with propranolol, the periorbital infantile hemangioma present total regression, but the capillary malformation is unchanged.

Only one patient, with a large facial and cervical infantile hemangioma, received another form of treatment (cryotherapy) before propranolol. No relapses were observed in the 16 cases who completed the treatment.

**Case presentation**

Case 1: 8 month old boy with a calf IH having a rapid growth over a month. Hemangioma was present in the first week of life as a small red stain. Noteworthy to mention, patient also has dextrocardia. After 8 months of treatment solely a teleangiectasia remained on the spot of the hemangioma. 9 months after treatment cessation, the color of skin became normal (Fig. 1).

Case 2: 3 month old girl with an forearm IH present at 3 week of life in the form of little red stains, and having a rapid growth during the last 2 months prior to treatment initiation. After 12 months of treatment the result was very good (Fig. 2).
Case 3: two month old boy with IH of left ear lobe which began growing during the first week of life and entered an accelerated growth phase 2 weeks prior to initiating therapy, time during which the parents noted bleeding of the hemangioma. After 6 months of treatment the result was very good (Fig. 3).

Case 4: 6 months old girl with a large facial and cervical mixed infantile hemangioma. The lesion was present at birth as a two small red stains and began growing after the first month of life. The patient was treated with cryotherapy, without good result. At 6 months of life start the treatment with Propranolol 2mg/kg body/day. The results is very good, the treatment is still ongoing (Fig. 4).

Case 5: Six months old boy with deep infantile haemangioma, who started in the second month of life. A. The photo is at 4 months of age, with 2 days before started treatment with propranolol. B. After 8 month of propranolol treatment at 2 mg/kg body/day the eye is open and we stoped the therapy. C. After 1 year and 6 months at the cessation the treatment. The right eye is open (Fig. 5).

Discussion

IH are composed of multiple cell types: a majority of endothelial cells associated with pericytes, dendritic cells, and mast cells. Histological analyses of IH have generated many developmental theories suggesting an embryonic or primitive cell origin and these debates will finally determine the best treatment for children [18].

North reported on the GLUT-1 positive staining of IH, suggesting a relation of hemangioma to placental tissue [19]. Bree speculated that invasive angioblasts, differentiated by a type of placental cells, or embolized placental cells may initiate the vascular tumors. However, the study does not demonstrate that placental trophoblast is the cell of origin for IH [20].

The new theories focus on progenitor cells, derangement of angiogenesis, mutation in the cytokine regulatory pathway, and developmental field defects [21,22].

The etiology and pathogenesis of hemangiomas remains unknown. Most IH regress without therapy, so for small and uncomplicated hemangiomas the “wait and see” approach may suffice [23].

The methods of treatment, when required, includes: systemic corticotherapy, intraleosional corticosteroids, cytotoxic drugs (bleomycin, vincristine, cyclophosphamide), systemic pharmacologic treatments (interferon α, vincristine and cyclophosphamide), laser therapy, cryotherapy, surgical excision, radiotherapy [10]. Until recently, the first line therapy for complicated IH was systemic corticosteroids [24-26]. The second and third line treatments are vincristine and interferon α, both of which were however linked to severe neurotoxic side effects [26]. In spite of the belief that systemic corticosteroid treatment of IH is very safe [27,28] numerous complications (aseptic necrosis of the femoral head, diabetes, osteoporosis, adrenal insufficiency, cataracts, glaucoma, infection, gastric irritation, elevated blood pressure, cushingoid like aspect, and hypothalamic-pituitary-adrenal axis suppression) have been described [29-33].

After Léauté-Labrèze observation [11] of propranolol’s effects on hemangiomas, numerous reports describing the same effects have appeared [18,34,35,36,37].

The new treatment for severe IH is a noncardioselective beta adrenergic receptor blocker: propranolol [38,39]. The mechanism of action of propranolol on IH remains unknown. Regulators of hemangioma growth and involution are poorly understood. During the growth phase, two major proangiogenic factors are involved: basic fibroblast growth factor (bFGF) and vascular endothelial growth factor (VEGF). During the involution phase, apoptosis has been shown [40,41]. Potential explanations for the therapeutic effect of propranolol on IH include vasoconstriction, which is immediately visible as a change in color, associated with a palpable softening of the hemangioma; decreased expression of VEGF and bFGF genes through the down-regulation of the RAF–mitogen-activated protein kinase pathway [42,43] (which explains the progressive improvement of the hemangioma); and the triggering of apoptosis of capillary endothelial cells [43].

The mechanism of action of propranolol on IH is open for research but the results obtained seem encouraging.

Conclusion

For the past 40 years, the use of propranolol has been shown to be safe in children with cardiac disease. In 70.96% of cases, we observed the fading in color and softening of the hemangioma following the administration of propranolol, with no adverse reactions. We consider that systemic therapy with the nonselective beta-adrenergic receptor antagonist propranolol is an effective treatment for IH, due to its rapid therapeutic effect and good drug tolerability.

We believe that the propranolol will become the first line of treatment for IH, although randomized controlled trials should be developed to compare propranolol and corticosteroid therapy.

Ongoing research is bringing us closer to an understanding of the cause of hemangiomas, which will provide opportunities for personalized therapies.

References


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TREATMENT OPTIONS FOR JUVENILE OSTEOCHONDRAL KNEE DEFECTS

D Crisan¹², D Vermesan¹², R Prejbeanu¹², S Nitescu², C Bogdan²

Abstract
Articular cartilage is a avascular, aneural and alymphatic tissue that covers the articular ends of bones. It serves as al low friction high wear resistance surface to ideal provide mobility and strength. However due to its poor vascularization it has rather limited regenerative capabilities.

Cartilage lesions of the knee are rather common in children and adolescents representing a more difficult pathological entity due to the young age of the patients and the risk of secondary degenerative disease in case of a poor management. Osteochondral fractures (OCF) are most prevalent in this age group due to a higher risk of direct knee trauma, skeletal immaturity in girls predisposing them to lateral patellar dislocation with secondary OCF and a more elastic ligamentary apparatus. Juvenile osteochondritis dissecans (JOCD) has been a recognized entity for more than 100 years and despite extensive research there is no clear explanation of the cause of this disease, although repetitive trauma seems to play an important role in its pathogenesis.

Treatment options vary from conservative treatment in minor lesions to arthroscopic or open knee surgery. Arthroscopic surgery has the advantage of a minimally invasive technique, but there are cases where a conversion to open or a combined approach are necessary. Different techniques are available, depending on the size and stability of the defect and the stage of the disease such as internal fixation, bone marrow stimulation, allograft and autograft transplants (OATS) and ACI.

We propose a clinical presentation of the techniques used for arthroscopic management of osteochondral defects in skeletally immature patients.

Introduction
Lesions to the articular cartilage are a more frequent pathological entity with a potentially disabling outcome on the affected joint and overall life and activity level modifying results on the skeletally immature patient which can in turn result in a sedentary lifestyle. The most important lesions that affect the articular cartilage of the knee are osteochondral fractures, acute, traumatic lesions that regularly involve the condylar or patellar cartilage or juvenile osteochondritis dissecans, a chronic pathology that is believed to be caused by repetitive trauma (1-3)

JOCD has been recognised as a pathological entity for more than 100 years] but its pathogenesis is still widely debated, with no certain cause having been pinned down.

Youth is involved in a wide array of sports that require intensive family support, thus early recognition of osteochondral lesions of the knee is easier to make.(3, 4) Osteochondritis dissecans OCD of the knee can be classified in an adult form and a juvenile form. However, these two forms of OCD have a different natural evolution in terms of the disease and the outcomes that they produce. JOCD has a better outcome under conservative treatment than the adult form with high degree of family involvement and commitment, the "compliance triad" of physician, parent, and child being the key element when a conservative treatment plan for JOCD is initiated. JOCD can be further subdivided in an adolescent form a juvenile form, depending on the status of the growth physis:(1, 5, 6)

- Juvenile Osteochondritis Dissecans: wide open physis
- Adolescent Osteochondritis Dissecans: closing physis
- Adult Osteochondritis Dissecans: closed physis.

The incidence of JOCD in global population is of about 15 – 29 per 100 000 according to Kocher et. al. and it is more frequent in children than in adults, with a reported prevalence of approximately 6 cases per 10,000 men and 3 cases per 10,000 women.(7)

Even though the name of the disease wrongly suggests an inflamatory etiology it probably should have been better named “ostechondrosis” it stuck since in 1888, Konig used this term to describe the pathologic process that led to traumatic loose bodies of the knee and hip joints.

The etiology of JOCD was the center of a decades of debate with many hypotheses postulated, the cause of OCD was believed to be inflammatory, genetical, ischemical, repeated microtraumatisms on the articular cartilage or heterotopic ossification. Much discussion and arguments have been advocated for all of these but more recently most authors seem to agree to a multifactorial etiology centered around microtrauma. Trauma has been described as a potential etiology of OCD but the result of direct trauma is often a OCF but the predilection of OCD for the posterolateral portion of the medial femoral condyle suggests indirect trauma as a more likely cause, this is also supported by the repetitive impingement of the tibial spine on the lateral portion of the medial femoral condyle that takes place during the internal rotation movements of the tibia during gait.(7-10)

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The typical presentation of a young patient with knee OCD includes dull, nonspecific, poorly localized pain in the early stages of the disease, without knee trauma as opposed to a osteochondral fracture that produces sharp pain over the knee, caused by a traumatic event. Classic OCD pain will be antero-medial to the patella, accompanied by joint effusion and joint stiffness. Later stages of the disease can be accompanied by more severe symptoms such as locking, catching and giving away, usually indicative of a loose body if symptoms are constant and severe. The progressive nature of the lesion is indicated by symptoms that are increasing in frequency and intensity.

Method
Imaging of osteochondral lesions of the knee is regularly started with a X-ray in standard incidences (anteroposterior and lateral) and a special views, the tunnel view for the notch and the sunrise view for investigating the patellar articular surface. This can provide some information on the level of the injury, OCFs can be detected by standard radiographs take in the emergency department(fig.1), but in the early stages of OCD radiographic modifications can be absent. Knee MRI would be the next imaging modality that is often used in evaluating the osteochondral injured knee. It is useful both in acute lesions and in OCD detecting lesions invisible on standard radiographs and it also visualized chondral loose bodies, bone edema, joint fluid accumulation and associated pathology. Ultrasound has the advantage of dynamic scanning and decreased cost over MRI, in the hands of an experienced musculoskeletal operator it can prove to be a reliable investigation. Bone scintigraphy with technetium (99mTc scintigraphy) it can detect subclinical bilateral lesions as well as the degree of healing, which is proportionally higher with 99mTc uptake in the bone. This makes scintigraphy a useful tool in evaluating the joint status in a conservatively treated juvenile patient.(11-15)

Two classification systems are widely used for staging JOCD, the Hefti classification, based on MRI aspects and the arthroscopic Guhl classification.

The Hefti classification:
- Stage 1: Small change without clear margins of fragment
- Stage 2: Osteochondral fragment with clear margins but without fluid between fragment and underlying bone
- Stage 3: Fluid is visible partially between fragment and underlying bone
- Stage 4: Fluid is completely surrounding the fragment, but the fragment is in situ.
- Stage 5: Fragment is completely detached and displaced (loose body).

The Guhl classification
- Stage I: Intact Lesions
- Stage II: Lesions showing signs of early separation
- Stage III: Partially detached lesions
- Stage IV: Craters with loose bodies (fig 2,3 and 4)

Treatment of osteochondral lesions of the juvenile knee should be coordinated with the degree of articular cartilage impairment and the size of the lesion and most importantly the type of lesion. While conservative treatment for JOCD has a demonstrated success rate, with a secondary surgical indication, for acute OCF the primary indication is arthroscopic, open or combined refixation of the fragment while chronic lesions benefit from arthroscopic treatment as well.

For juvenile patients with OCD the first line of treatment is conservative therapy for which relatively good outcomes have been reported, Cahill reported a 56% success rate on a series of 92 knees followed scintigraphically for an average of 4.2 years with no knee immobilization and a complete restriction of athletic activities.

Other authors report similar success rates, with or without immobilization the higher number of stable lesions and healing under conservative treatment demonstrates that juvenile OCD has a much better prognosis than adult OCD. There is still debate over the role and length of immobilization but a general phased conservative treatment protocol has been produced (13, 16-19)

Phase 1 (Weeks 0 – 6):
- Knee immobilisation (cast or brace)
- Partial weight bearing with crutches
- Pain free knee is a criteria for phase 2

Phase 2 (Weeks 6 – 12)
- No knee immobilization
- Weight bearing as tolerated
- Physical therapy: ROM and low impact strengthening (quads, hams).
- No sports
- X-ray - healing with clinical improvment - phase 3.

Phase 3 (from 3 – 4 months)
- A complete absence of symptoms allows for gradually loading the knee (running, jumping and eventually sports) with progressively increased intensity
- Follow-up MRI/scintigraphy shows the degree of lesion healing.

Treatment and results
While conservative treatment is indicated for most patients with JOCD as the first line of treatment and surgical therapy is usually reserved for cases that failed to show signs of healing at follow-up, there are situations that imply surgery as the first line of treatment such as unstable lesions on MRI evaluation and articular loose bodies from a lesion with a detached osteochondral fragment. Also the surgical indication is definitive in cases of acute OCF.

Surgical therapy for osteochondral lesions includes several options such as bone marrow stimulation techniques, subchondral drilling, loose fragment fixation, cartilage abrasion, loose body removal, allograft transplant, OATS and ACI. Treatment algorithms have been conceived to address these lesions, one of the most useful is the one described by Garrido et. al., presented below (fig.5)(17, 20)
Fig. 1 Osteochondral fracture in a skeletally immature patient

Fig. 2, fig.3 and fig.4 This MRI shows a OCD Stage IV lesion on coronal T1 GFE, coronal STIR and sagital T1.
Fig. 6 Stable JOCD treated antegrade drilling.

Fig. 5 Treatment algorithm for OCD (Garrido et al).
Bone marrow stimulation include drilling the lesion for grade I and II stable JOCD and microfractures for chronic JOCD and OCF. Microfractures represent the piercing of small holes in the area of the defect to allow for nutrient and growth factor rich blood to penetrate trough to the joint space. This will allow the cartilaginous defect to be filled with fibrous cartilage. Subchondral drilling creates vascular channels in low grade stable OCD lesions or as a suplement to fragment fixation. Antegrade drilling (Fig. 6 Antegrade drilling) is done orthogonally under direct arthrosopic visualization using the standard portals or separate accessory portals. Retrograde driling necescitates C-arm radiosopic control to avoid joint penetration or the secondary mobilisation of the osteochondral fragment or ACL tibial aiming device with or without sonography. Iliac crest bone graft supplementation has also been added to help in healing. Good and excellent results have been reported in literature. The healing rate was of 80% in adolescent JOCD patients, with 70% or more being able to return to sports. (2, 17, 21-26)

Higher grade lesions (3&4) with unstable osteochondral fragments with a totally or partially detached fragment (trap door) and acute OCF’s have an indication for fixation of the fragment. This can be achieved via metal screws (Herbert), metal or bioabsorbable pins or bio-screws (fig. 7). Each have their advantages, some authors prefer the use of metal implants that need hardware removal surgeries to benefit from this second look arthroscopy to check the status of the cartilage.(15, 20, 24, 26-29)

Grafting the lesion is the most complex treatment method, reserved for the chronic, large size JOCD lesions. Autograft transplantation is a surgical option but availability is reduced to a small number of patients. It represents the harvesting of a osteochondral plugs from nonweightbearing areas of the joint and implanting them in the bed of the defect. One plug is sufficient for 2cm2 of lesion surface. Allografting is permitted in some countries by legislation, with isstrumentation sysytems available to size and match the defect. NWB rehabilitations is started postoperatively. Good rates of survival have been reported for osteochondral grafts.

Autologus condhrocite implantation allows the repair of defects up to 10cm2 and up to 8mm in depth. Chondrocytes are harvested, grown in a cell culture in a lab and inserted in the defect in a pouch made by autologus periosteum or a synthetic colagen patch (fig. 8)(2, 5, 20, 30).

Conclusions
In conclusion, while JOCD if detected in a timely fashion with a compliant patient and adult supervision has a generally good outcome by conservative treatment, surgical options are available even for cases with advanced destruction of the articular cartilage with simillarly good results.

References


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PREVALENCE OF REFRACTIVE ERRORS IN SCHOOLCHILDREN IN ROMANIA

Luminita Turcin¹, Afilon Jompan²

Abstract
The main aim of this study is to establish the refractive errors prevalence in rural and urban schoolchildren from Arad county.

Materials and Methods: We have examined 1121 pupils aged 6 to 11 years enrolled in elementary classes of 5 schools from Arad rural and urban environments during January - March 2012. We have investigated the following parameters: age, sex, objective refraction, visual acuity, family income. Refraction was measured with Potec 5000 autorefractokeratometer under cycloplegia which was obtained with cyclopentolate 4 times in one hour. Myopia was defined as refractive errors of at least -1.0 SD, hyperopia +1.5 SD and astigmatism 1.0 CD.

Results and discussions: Out of the total of 1121 children, 612 were in rural and 509 in urban environment. In rural environment we found 427 were emmetropic and 185 were found with refractive errors. There were 31 cases of myopia, 65 of hypermetropia and 89 cases of astigmatism. We found 12 new myopia cases, 23 new hyperopia cases and 48 new astigmatism cases.

In urban environment, 379 were emmetropic and 130 were found with refractive errors. There were 17 cases of myopia, 43 of hypermetropia and 70 cases of astigmatism. Fifty children were newly discovered with ophthalmic refractive pathology and 33 didn't wear optical correction although they knew about their condition.

Conclusion: The most prevalent ophthalmic pathology in Arad rural and urban schoolchildren is astigmatism, followed by hyperopia and myopia. In rural environment astigmatism is more prevalent in girls and hyperopia is more prevalent in boys. Family income is another important risk factor in which correlates especially with the neglected ophthalmic refractive conditions. Elementary schoolchildren are a high risk group for developing refractive errors.

Key words: refractive errors, children, amblyopia, myopia, hyperopia, astigmatism

Introduction
Visual impairment of schoolchildren is one of the most common and addressable health problems. It is also the second leading cause of treatable blindness (1). Visual impairment is mainly cause by refractive errors like myopia, hypermetropia and astigmatism. Most of the children with uncorrected refractive errors are asymptomatic (or present mild symptoms like: frequent eye scratching, conjunctival congestion, epiphora, etc) and hence screening for myopia, hypermetropia and astigmatism helps in early detection and timely interventions. In countries with high attendance schools (like Romania), integration of vision screening within screening for other health issues is recommended. (2) Differences in the availability of eye care services (preferably conducted by eye specialist) and even the magnitude of refractive errors between rural and urban schoolchildren are not considered. (3) These study will discuss rural and urban ophthalmic pathology in preschool- and schoolchildren, the differences between the two environments, risk factors and possible consequences.

In a different study, Bucsa D. and collaborators concluded than the most common disorders in preschool- and schoolchildren are refractive errors. (4) Therefore, for early detection and consequence prevention are imperative.

Reliable data on prevalence and distribution of refractive errors from population-based surveys are needed to plan cost-effective programs devoted to the reduction of visual impairment and blindness.

Undiscovered and untreated refractive errors are an important cause of low visual acuity or amblyopia. Defining how visual impairment affects health and social outcomes is complex. Is the person more affected by deficits in distance visual acuity, in near visual acuity, or in the simultaneous use of both eyes? We found little recent data in the romanian literature regarding the prevalence of myopia, hypermetropia and astigmatism at schoolchildren in Romania. We found no comparative study between urban and rural environment regarding prevalence of those refractive errors. Therefore, our objective is to determine the prevalence of this pathology in children from both rural and urban environment and to identify ways we can improve ophthalmic childcare. We must underline the importance of the screening of refractive errors because of the negative consequences that result from the early misdiagnose of these health problems. When visual impairment is present, there may be further effects on overall health, self-perception, educational attainment, job choices, and a number of other social factors. (14)

Amblyopia (also known as lazy eye) and its risk factors, is a decrease in visual acuity resulting from abnormal visual development in children. Due to its baneful consequences amblyopia is a major public health problem. Amblyopia is the most common cause of monocular or in some cases binocular vision loss in infants and young adults (7).

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Amblyopia affects approximately 2-4% of the population (8). Most cases are associated with eye misalignment, usually esotropia in infancy or early childhood (9-10). Anisometropia is the difference in refractive error between the two eyes. It is associated with amblyopia. Anisometropia or a combination of strabismus and anisometropia are causally associated with amblyopia. In children under 7 years, amblyopia was associated with strabismus in 38% of cases, with anisometropia in 37% of cases and with both strabismus and anisometropia in 24% of cases (11). Correction of refractive errors is the first step in treating amblyopia. Correction alone has been shown to significantly reduce amblyopia. Occlusion is another important part of amblyopia treatment. Less frequent occlusion can be just as effective as more extensive occlusion. (11)

In the present work, prevalence and pattern of refractive errors (myopia, hyperopia, astigmatism) among school children in Arad has been studied for planning appropriate eye care programs to reduce the burden of visual impairment among younger population in this area. An important component of general medical care for people with visual impairment is the burden that they have in terms of quality of life.

Materials and methods

The study was conducted between September 2011 and March 2012. Verbal consents of school director, teachers and parents were obtained for screening the children. The research protocol adhered to the provisions of the Declaration of Helsinki for research involving human beings.

Target group size was calculated by the means of Kish and Leslie's formula for an expected prevalence of 30% with confidence limit of 5% and confidence level 99.99%.

We have examined 1121 pupils aged 6 to 11 years enrolled in elementary classes of 5 schools in Arad county rural environment and 5 schools from Arad city. There was no acute pathology that would have influenced refraction. The distant vision of a child was tested utilizing Snellen’s ‘E’ chart. The visual acuity was tested with the chart at 6 meters. If uncorrected vision was <0.6 in either eye, the child was declared to have defective vision. A cover-uncover test was then performed to confirm the diagnosis of strabismus. If eyes moved after removal of the cover, the child was considered to have a “phoria”; and if the degree of deviation did not change on cover and uncover, the child was considered to have a “tropia” (> 5 degree / 10 diopter (D)]. The eye movements were tested in 6 cardinal directions to rule out paralytic or restrictive strabismus. Anterior segment was examined with flashlight to detect cataract; congenital anomalies like anophthalmos, microphthalmos, large corneas; and evidence of previous eye surgery. Objective refraction was measured with Potec 5000 autorefractokeratometer under cycloplegia which was obtained with cyclopentolate 1% 4 times in 1 hour. This procedure was applied to all children, regardless of visual acuity. Family member income was voluntary stated by one parent.

Statistical analysis was conducted with Epi Info 7. Emmetropia was defined as a spherical equivalent between -1.00 and +1.00. Myopia was considered when the measured objective refraction was more than or equal to –1.0 spherical equivalent diopters in one or both eyes. Hyperopia was considered when the measured objective refraction was greater than +1.50 spherical equivalent diopters in one or both eyes provided no eye was myopic. Astigmatism was considered to be visually significant if ≥1.00 D. Results are presented in tables and charts below.

All children with uncorrected refractive error were given low cost spectacles . Children with eye diseases were further examined and managed at the base clinic free of charge. The study results were shared with the scientific fraternity and policies for improving eye care of children were proposed.

Table 1. Number of children and distribution of refractive errors over classes.

<table>
<thead>
<tr>
<th>Class</th>
<th>No. pupils</th>
<th>Total refractive errors</th>
<th>Myopia</th>
<th>Hyperopia</th>
<th>Astigmatism</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>147</td>
<td>38</td>
<td>9</td>
<td>12</td>
<td>17</td>
</tr>
<tr>
<td>II</td>
<td>124</td>
<td>44</td>
<td>5</td>
<td>15</td>
<td>24</td>
</tr>
<tr>
<td>III</td>
<td>168</td>
<td>47</td>
<td>10</td>
<td>18</td>
<td>19</td>
</tr>
<tr>
<td>IV</td>
<td>173</td>
<td>55</td>
<td>7</td>
<td>20</td>
<td>29</td>
</tr>
<tr>
<td>Total</td>
<td>612</td>
<td>185</td>
<td>31</td>
<td>65</td>
<td>80</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Class</th>
<th>No. pupils</th>
<th>Total refractive errors</th>
<th>Myopia</th>
<th>Hyperopia</th>
<th>Astigmatism</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>139</td>
<td>37</td>
<td>5</td>
<td>9</td>
<td>18</td>
</tr>
<tr>
<td>II</td>
<td>149</td>
<td>40</td>
<td>5</td>
<td>12</td>
<td>23</td>
</tr>
<tr>
<td>III</td>
<td>112</td>
<td>29</td>
<td>3</td>
<td>10</td>
<td>16</td>
</tr>
<tr>
<td>IV</td>
<td>105</td>
<td>29</td>
<td>4</td>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td>Total</td>
<td>509</td>
<td>130</td>
<td>17</td>
<td>43</td>
<td>70</td>
</tr>
</tbody>
</table>
Results

We found the following results: out of the total of 1121 children, 612 (54.59%) were in rural and 509 (45.41%) in urban environment.

In the rural environment we found 427 (69.77%) were emmetropic and 185 (30.23%) were found with refractive errors (ammetropic). There were 31 (5.06%) cases of myopia, 65 (10.62%) of hypermetropia and 89 (14.54%) cases of astigmatism. This means that 30.23% of children from rural environment included in the study have ophthalmic refractive pathology. Results are shown in Table 1.

Out of the total of 509 children examined from urban environment, 379 (74.46%) were emmetropic and 130 (25.54%) were found with refractive errors (ammetropic).

There were 17 (3.34%) cases of myopia, 43 (8.45%) of hypermetropia and 70 (13.75%) cases of astigmatism. We didn't find any statistical significant difference in the prevalence of total number of refractive errors or in any specific error.

In rural environment we examined 289 (47.22%) boys and 323 (52.78%) girls. We discovered 17 (54.83%) cases of boys and 14 (45.17%) cases of girls with myopia. There is no statistically significant difference between sexes in myopia. We discovered 41 (63.07%) cases of boys and 24 (36.93%) cases of girls with hyperopia. We discovered 29 (32.25%) cases of boys and 60 (67.75%) cases of girls with astigmatism. Prevalence of astigmatism was higher in girls (67.75%) than boys (32.25%) [p<0.00001], while hypermetropia was more prevalent in boys (63.07%) than in girls (36.93%) [p<0.005].

<table>
<thead>
<tr>
<th></th>
<th>Pupils</th>
<th>Myopia</th>
<th>Hyperopia</th>
<th>Astigmatism</th>
<th>Refractive errors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Male</strong></td>
<td>289</td>
<td>17</td>
<td>41</td>
<td>29</td>
<td>87</td>
</tr>
<tr>
<td><strong>Female</strong></td>
<td>323</td>
<td>14</td>
<td>24</td>
<td>60</td>
<td>98</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>612</td>
<td>31</td>
<td>65</td>
<td>89</td>
<td>165</td>
</tr>
</tbody>
</table>

Table 2. Distribution of refractive errors over sexes.

<table>
<thead>
<tr>
<th></th>
<th>Pupils</th>
<th>Myopia</th>
<th>Hyperopia</th>
<th>Astigmatism</th>
<th>Refractive errors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Males</strong></td>
<td>230</td>
<td>7</td>
<td>25</td>
<td>23</td>
<td>60</td>
</tr>
<tr>
<td><strong>Females</strong></td>
<td>279</td>
<td>10</td>
<td>45</td>
<td>70</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>509</td>
<td>17</td>
<td>43</td>
<td>70</td>
<td>130</td>
</tr>
</tbody>
</table>

Table 3. Newly and neglected refractive errors distribution.
In urban environment in this study we examined 230 (45.18%) boys and 279 (54.82%) girls. We discovered 7 (41.17%) cases of boys and 10 (58.83%) cases of girls with myopia. There is no statistically significant difference between sexes in myopia. We discovered 28 (65.11%) cases of boys and 15 (34.89%) cases of girls with hyperopia. We found 25 (35.71%) cases of boys and 45 (64.29%) cases of girls with astigmatism. Prevalence of astigmatism was higher in girls (64.29%) than in boys (35.71%) \(p<0.001\), while hypermetropia was more prevalent in boys (65.11%) than in girls (34.89%) \(p<0.005\).

Comparing the pupils from the two target groups (rural/urban) we didn't found any statistical significant variation in the prevalence of myopia, hyperopia or astigmatism based on sexes. Data are displayed in Table 2.

Out of the 612 children from rural environment examined, 185 (30.23%) were found with refractive errors. Eighty-three (44.86%) children were newly discovered with ophthalmic refractive pathology and 71 (38.37%) didn’t wear optical correction although they knew about their condition. Hence, 154 pupils overall didn’t wear optical correction for their ophthalmic pathology, because either they didn’t know about it or they were not compliant with the treatment.

In the urban environment out of the total number of 509 children examined, 130 (25.54%) were found with refractive errors. Fifty (38.46%) children were newly discovered with ophthalmic refractive pathology and 33 (25.38%) didn’t wear optical correction although they knew about their condition. Hence 83 pupils overall didn’t wear optical correction for their ophthalmic pathology, because either they didn’t know about it or they were not compliant with the treatment.

Table 4. Age groups distribution of refractive errors.

<table>
<thead>
<tr>
<th>Age</th>
<th>No. pupils</th>
<th>Myopia cases</th>
<th>%</th>
<th>Hyperopia cases</th>
<th>%</th>
<th>Astigmatism cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>45</td>
<td>7.35</td>
<td></td>
<td>7.69</td>
<td></td>
<td>8.99</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>115</td>
<td>18.79</td>
<td></td>
<td>10.77</td>
<td></td>
<td>16.85</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>97</td>
<td>15.85</td>
<td></td>
<td>11.92</td>
<td></td>
<td>21.35</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>120</td>
<td>19.61</td>
<td></td>
<td>12.46</td>
<td></td>
<td>12.36</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>112</td>
<td>10.3</td>
<td></td>
<td>14.21</td>
<td></td>
<td>19.1</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>123</td>
<td>20.1</td>
<td></td>
<td>16.52</td>
<td></td>
<td>21.35</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>612</td>
<td>100</td>
<td></td>
<td>100</td>
<td></td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

Table 5. Income / family member relations with refractive errors.

<table>
<thead>
<tr>
<th>Income/Year</th>
<th>No. of pupils</th>
<th>Refractive Errors</th>
<th>Refractive Errors</th>
<th>Refractive Errors</th>
<th>Refractive Errors</th>
</tr>
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<tbody>
<tr>
<td>&lt;700</td>
<td>179</td>
<td>29.25</td>
<td>45</td>
<td>24.32</td>
<td>40</td>
</tr>
<tr>
<td>700-1500</td>
<td>285</td>
<td>46.57</td>
<td>93</td>
<td>50.27</td>
<td>26</td>
</tr>
<tr>
<td>1500-3500</td>
<td>103</td>
<td>16.83</td>
<td>34</td>
<td>18.39</td>
<td>5</td>
</tr>
<tr>
<td>&gt;3500</td>
<td>45</td>
<td>7.35</td>
<td>13</td>
<td>7.03</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Income/Year</th>
<th>No. of pupils</th>
<th>Refractive Errors</th>
<th>Refractive Errors</th>
<th>Refractive Errors</th>
<th>Refractive Errors</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;700</td>
<td>62</td>
<td>12.18</td>
<td>38</td>
<td>25.23</td>
<td>18</td>
</tr>
<tr>
<td>700-1500</td>
<td>155</td>
<td>30.45</td>
<td>50</td>
<td>38.45</td>
<td>11</td>
</tr>
<tr>
<td>1500-3500</td>
<td>190</td>
<td>37.33</td>
<td>30</td>
<td>23.09</td>
<td>3</td>
</tr>
<tr>
<td>&gt;3500</td>
<td>102</td>
<td>20.04</td>
<td>12</td>
<td>9.23</td>
<td>1</td>
</tr>
</tbody>
</table>
In rural environment 31 (5.06%) children examined wore optical correction at the time the study was conducted. Forty-seven (9.23%) of the 509 children examined form urban environment wore optical correction at the time the study was conducted. There is a statistical significant difference in the prevalence of optical correction. [p<0.006].

In rural children we found 12 (6.48%) new myopia cases, 23 (12.43%) new hyperopia cases and 48 (25.94%) new astigmatism cases. The number of new cases, expressed as percentage of total number of children examined, was as follows.: 1.96% myopia cases, 3.75% hyperopia cases and 7.48% astigmatism cases.

In rural children we found 11 (5.94%) known and neglected myopia cases, 19 (10.27%) known and neglected hyperopia cases and 41 (22.16%) known and neglected astigmatism cases. The number of known and neglected cases, expressed as percentage of total number of children examined, was as follows: 0.98% myopia cases, 3.53% hyperopia cases and 6.70% astigmatism cases.

In urban children we found 5 (3.84%) new myopia cases, 18 (13.86%) new hyperopia cases and 27 (20.76%) new astigmatism cases. The number of new cases, expressed as percentage of total number of children examined, was as follows: 0.78% myopia cases, 2.75% hyperopia cases and 2.94% astigmatism cases. Forty-seven (9.23%) from the 509 children examined wore optical correction at the time the study was conducted. Results are shown in Table 3.

Considering each type of refractive errors in rural environment we have 38.70% new myopia cases, 35.48% known and neglected myopia cases, 35.38% new hyperopia cases, 29.23% known and neglected hyperopia cases 53.93% new astigmatism cases and 46.07% known and neglected astigmatism cases. In urban environment we have 21.41% new myopia cases, 23.52% known and neglected myopia cases, 41.86% new hyperopia cases, 32.55% known and neglected hyperopia cases 38.54% new astigmatism cases and 21.42% known and neglected astigmatism cases.

In rural environment 74.19% of the children with myopia, 64.61% of the children with hyperopia and 100% of the children with astigmatism didn't wear optical correction at the time of examination because either they didn't know about their pathology or they have shown low compliance with the treatment. Related to the total number of children from rural environment examined, we found 3.76% untreated myopia cases, 6.86% untreated hypermetropia cases and 14.54% untreated astigmatism cases. Statistically significant differences can be seen between myopic and astigmatic cases (3.76% and 14.54% p<0.00001) and between hyperopic and astigmatism cases (6.86% and 14.54% p<0.00001). There was no statistically significant difference between hypermetropic and myopic cases.

In urban environment 52.94% of the children with myopia, 74.41% of the children with hyperopia and 60% of the children with astigmatism didn't wear optical correction at the time of examination because either they didn't know about their pathology or they have shown low compliance with the treatment. Related to the total number of children from urban environment examined, we found 1.77% untreated myopia cases, 6.17% untreated hypermetropia cases and 8.25% untreated astigmatism cases. Statistically significant differences can be seen between myopic and hypermetropic cases (1.77% and 6.17% p<0.001) and between myopic and astigmatism cases (1.77% and 8.25% p<0.0001). There was no statistically significant difference between hypermetropic and astigmatism cases.

Comparing the two environments we found higher prevalence of known and uncorrected refractive errors in rural environment (71 cases) than urban environment (33 cases). [p<0.005]. Similar, we found a higher prevalence of known and uncorrected astigmatism in rural environment (41 cases) than urban environment (15 cases). [p<0.01].

The prevalence of myopia, hyperopia and astigmatism over age groups in the two environments studied are shown in Table 4. There was no statistically significant difference in the prevalence evolution over these age groups in neither of the studied refractive pathologies. There is no difference between the 2 environments either.

Another interesting aspect was the influence of family income over the prevalence and treatment of those refractive errors. Findings are presented in table 5.

In rural environment we found 179 pupils who lived in families with less the 700 ron/family member from which 45 had refractive errors and 40 neglected them. We found 285 pupils who lived in families with income between 700 and 1500 ron/family member from which 30 had refractive errors and 11 neglected them. We found 103 pupils who lived in families with income between 1500 and 3500 ron/family member from which 34 had refractive errors and 5 neglected them. We found 45 pupils who lived in families with income over 3500 ron/family member from which 13 had refractive errors and none neglected.

In urban environment we found 62 pupils who lived in families with less the 700 ron/family member from which 38 had refractive errors and 18 neglected them. We found 155 pupils who lived in families with income between 700 and 1500 ron/family member from which 50 had refractive errors and 11 neglected them. We found 190 pupils who lived in families with income between 1500 and 3500 ron/family member from which 30 had refractive errors and 3 neglected them. We found 102 pupils who lived in families with income over 3500 ron/family member from which 12 had refractive errors and one neglected.

In both environments, referring to the neglected refractive errors there is a statistical significant difference in the <700 and 700-1500 groups over the 1500-3500 and >3500 groups. In the rural environment there is a statistical significant difference in the neglected refractive errors between the <700 and 1500-3500 groups [p<0.00003] and 700-1500 and >3500 groups [p<0.01]. In the urban environment there is a statistical significant difference in the
were increased with worsening distance acuity. Visually unskilled manual labor job and were more likely to be impaired. If impairment was unilateral, were more likely to have an greater number of injuries at work or at home or in juries impaired people were not found to be more likely to have a unable to work because of permanent illnesses. These odds of elementary schoolchildren have refractive errors. The 28.09% ammetropic. This could mean that about one quarter 71.91% of children from the study were emmetropic and schoolchildren are refractive errors. (4) We found that the most common disorders in preschool- and related to sports than were people with normal sight. (15)

In a study on rural India schoolchildren, Dandona R. (13) reported the prevalence of myopia (-0.50SD) of 4.1% (similar to our study 4.28%), of hyperopia (+2.0SD) 0.78% and of astigmatism (0.75CD) of 2.8%. There are many papers on childhood refractive error in the international literature, reporting a broad, worldwide variation in the prevalence of myopia and hyperopia. Substantial differences in methods, definitions, and demographics are an important source of results variation. (2)

In 2003, Budau M. and collaborators conducted a screening of refractive errors of children investigated at “Luis Turcanu” Hospital's Ambulatory. They concluded that: out of the 646 children, 407--63% (CI95 = 59.1-66.7) had refraction errors, out of which 1.5% (CI95 = 0.8-2.9) were myopic, whereas 49.8% (CI95 = 45.9-53.8) were hyperopic. Astigmatism was found in 11.8% (CI95 = 9.4-14.6), and the mean age was 10.7 years (6). Compared to their study we found higher prevalence of myopia (4.28% in our study and 1.5% in the cited study [p<0.0001]). Differences in prevalence are found in astigmatism cases, which we found to be most frequent, while in the above mentioned study hyperopia had the highest prevalence. We believe the differences arise from the different definitions of the studied pathology. Our target group is from rural environment only. In the cited study there was no differentiation between the two environments in which regards the target group. Patients who went to “Luis Turcanu” Hospital's Ambulatory already had some symptoms and possibly a current disease. This could be a good explanation for the high percentage of refractive errors found (63%), Their target group doesn't have a classification of the child’s developing environment. Our study group is form exclusively of schoolchildren aged 6 to 11 from rural areas of Arad County.

In a study, Bucsa D. and collaborators concluded that the most common disorders in preschool- and schoolchildren are refractive errors. (4) We found that 71.91% of children from the study were emmetropic and 28.09% ammetropic. This could mean that about one quarter of elementary schoolchildren have refractive errors. The quality of life can be altered in those untreated children. Rahi et al found that those with impaired vision, even if the impairment was unilateral, were more likely to have an unskilled manual labor job and were more likely to be unable to work because of permanent illnesses. These odds were increased with worsening distance acuity. Visually impaired people were not found to be more likely to have a greater number of injuries at work or at home or injuries related to sports than were people with normal sight. (15)

In 2001, Hendrickson K., Bleything W. conducted a screening of Romanian children and adults. They found the following data: 45% of the children were emmetropic, 27% were myopic, and 28% were hyperopic. When compared with other nations, the prevalence of myopia was higher in the Romanian children. With-the-rule astigmatism had the highest occurrence when compared to other axis orientations, yet the overall occurrence of astigmatism was less than that found in other nations for both children and adults. Incidence of astigmatism was lower compared to other nations in both children and adults. The prevalence of strabismus and other ocular diseases was lower in the Romanian children as compared to other nations. (5) Refractive errors were more likely to have a manual (versus non-manual) occupation and to be separated, divorced or widowed, and less likely to be in social or professional organizations. There is also some evidence that they are more likely to express concern, embarrassment and frustration about their eyesight and worry about coping with life.

Rahi et al reported the use of the Vision-Related Quality of Life Core Measure 1 and these investigators found that impairment of vision-related quality of life was strongly correlated with impairments in visual acuity at both distance and near and with impaired stereopsis. Impaired vision-related quality of life was strongly associated with inability to work and with not currently being married. (15)

Conclusions

The most prevalent ophthalmic pathology in Arad rural and urban schoolchildren is astigmatism, followed by hyperopia and myopia. In rural environment astigmatism is more prevalent in girls and hyperopia is more prevalent in boys. There is no statistically significant difference in the prevalence of myopia cases in the two sexes.

Comparing the two environments we didn't found any statistical significant difference in the prevalence of total number of refractive errors or in any specific error.

In urban environment the prevalence of optical correction was statistically significant higher than in rural environment. We didn't find any variation of prevalence between age groups from 6 to 11 in any of the studied refractive pathology.

The most prevalent newly discovered ophthalmic pathology in rural schoolchildren is astigmatism, followed by hypermetropia and myopia.

Elementary schoolchildren are a high risk group for developing refractive errors. From those astigmatism is the main risk factor of developing amblyopia, followed by hyperopia and myopia.

The most prevalent known and uncorrected (neglected, poor treatment compliance) ophthalmic pathology in rural schoolchildren is astigmatism, followed by hypermetropia and myopia. Basically, no child with astigmatism had any optical correction.

We believe that the newly discovered refractive errors can be addressed by screenings like this one. It is a good way to discover and treat children ophthalmic pathology and prevent amblyopia. Visual acuity screenings are needed to discover refractive pathology in children. The screening of school and preschool children should be carried out
periodically. Most children are unaware of their refractive errors.

Family income is another important risk factor in which correlates especially with the neglected ophthalmic refractive conditions. Interesting is that at the same level of income there is no difference between the two environments.

References

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PLASMA CONCENTRATION OF ZINC IN CHILDREN AGED 0-3 YEARS

Nicoleta M Negruț1,2, Eugenia M Domuța3, Mircea V Nanulescu4

Abstract
Purpose: Our research aimed at establishing the values of plasma zinc level and the presence of zinc deficiency, in healthy children aged 0-3 years in Bihor County, Romania.
Methods: A total of 96 healthy children aged 0-3 years were included in the study during 2009-2011. Plasma concentration of zinc was determined using the 5-Br-PAPS endpoint colorimetric method.
Results: Mean plasma concentration of zinc in the study group was 15.33±1.49 µmol/l, higher for children who had less than 3 episodes/year of acute respiratory infections compared to those who experienced more than 3 episodes/year (15.89±1.46 µmol/l versus 14.2±0.76 µmol/l, p<0.001). Conclusions: In healthy children, aged 0-3 years, from Bihor County we recorded a mean plasma concentration of zinc of 15.33 ± 1.49 µmol/l, a value falling within normal limits. Children with more than 3 episodes of acute respiratory infections/year had lower values of mean plasma concentration of zinc than those with maximum 3 episodes/year. The children in our study showed no zinc deficiency.
Key words: zinc, diarrhea, acute respiratory infection, children.

Introduction
Zinc modulates the specific and nonspecific immune response in the human body and plays a role in the metabolism of the nucleic acids, in the enzyme activity (a catalytic, regulatory and structural role), entering the composition of over 300 enzymes (1), being necessary for growth and development processes (2).

Its presence in the human body in a very small amount (about 1.5 to 2.5 g) (3, 4) associated with storage failure causes a continuous need for dietary intake.

Zinc requirement is 2 mg/day for children aged 0-6 months and 3 mg/day for children aged 7 months-3 years (3). A part of ingested zinc becomes absorbed and then can be used by the human body. Its absorption is inhibited by the presence of phytates, oxalates, polyphenols, fibers, divalent cations and antibiotics such as florquinolones and tetracyclines (4).

Sources of zinc are the foods rich in protein such as meat, seafood, eggs, dairy, wheat germs and brewer's yeast. These foods are usually expensive, leading to the prevalence of zinc deficiency of 30% in children worldwide (especially in developing countries), at ages when there is a maximum vulnerability for this deficiency.

The first reference to human zinc deficiency was made in 1958 by Bert L. Vallee et al (5), in a study on zinc metabolism in patients with Laennec cirrhosis. Later, in 1961 Prasad et al described the clinical characteristics of zinc deficiency in Iranian children (6).

Zinc deficiency determines the decrease of the immune system's defense capacity (7).

Zinc deficiency is associated with the stunting rate, if there is deficiency, the rate of stunting is higher (8). The rate of stunting is calculated according to the formula (Cstunt/Ctotal)*100, where Cstunt is the number of children under 5 years showing height growth retardation and Ctotal is the total number of investigated children aged under 5 years. It is considered to be a stunting growth when the height of the child is below the average height specific for that age and gender with 2 standard deviations (SD). In 2002 Romania recorded on the national scale a 12.8% stunting rate, according to the latest data reported in 2013 by the World Health Organization (WHO) (9). According to this data, Romania belongs to the list of countries with a low prevalence of zinc deficiency (less than 20%) (10).

The exact level of zinc deficiency in children from developed and medium developed countries is not precisely known (11). Therefore it is important to know the situation in Romania, in the group most vulnerable to zinc deficiency, respectively toddlers (0-3 years).

Our research aimed at establishing the plasma zinc level and the presence of zinc deficiency, in healthy children aged 0-3 years in Bihor County, Romania.

Patients and methods
The source population included 98 healthy children, aged 0-3 years, who addressed in 2009-2011 the office of the ‘Gavril Curteanu’ Municipal Hospital of Infectious Diseases Oradea, for laboratory investigations on demand.

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3 Faculty of Medicine and Pharmacy, University of Oradea
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The study was conducted by 'Iuliu Hatieganu’ University of Medicine and Pharmacy
E-mail: Negrut.Mihaela@umfcluj.ro, maria.domuta@yahoo.com, nanulescumircea@yahoo.com
Patients included in the study were clinically healthy children aged 0-3 years who addressed during the study period the hospital’s laboratory in order to perform routine medical tests for inclusion in the community (nursery, kindergarten), for analysis on demand or who came for the mandatory inspection at 2 years after acute viral hepatitis A.

Patients with a history of illness during the last three months, those who have followed previous therapy with zinc, calcium, copper, iron, laxatives, antacids containing magnesium, and those who did not have the written consent of parents were excluded from the study.

To determine the sample cases of healthy children (n) under the age of 3 years, we used the valid formula for studies in which the tracked feature is an alternative (present case: healthy-sick), with 95% probability, error limit of 0.1 and community volume of 32,420 (data provided by Bihor County Statistics Department) (12,13). The sample will include at least 96 at a population of over 10,000.

During the study period, 98 children were included in the study, 2 children were excluded at the parents’ request, leaving 96 children in the study. For each patient a written consent of parents or legal guardian was requested. All procedures involving human subjects were approved by the Ethics committee of the hospital.

Children included in the study were clinically examined by a MD Infectious Disease Specialist, the day of sample collection. There were declared clinically healthy only children who after the history and physical examination showed no symptoms or clinical signs of disease.

For each child included in the study a questionnaire form was filled in, Table no. 1.

Minimum family monthly income required to ensure satisfactory conditions for the growth and development of the child was considered to be 330 EURO, (2 minimum wages at the time of the study). For the distribution of cases by determination period, the 4 seasons of the year were taken into account, namely: Winter: December to February; Spring: March to May; Summer: June to August; Autumn: September to November. Children’s diet was considered excessive for the 5 types of food, if they have exceeded the recommendations of the nutrition guidelines by age group (14, 15).

Plasma concentration of zinc (PCZ) was determined to the subjects included in the study. Venous blood sampling was done in basal conditions, during the time segment 7-9.30, after fasting, from the median cubital vein with Becton-Dickinson (BD) holder-vacutainers closed system, in BD vacutainers for heavy metals containing heparin lithium as anticoagulant. PCZ determination was obtained from the plasma after centrifugation. A colorimetric method was used to determine the PCZ. This method is based on the reaction between zinc and 2 - (5-Bromo-piridilazo) -5 - (N-propyl-N-sulfo-propylamino)-phenol (5-Br-PAPS). The inter-assay coefficient of variability of the method was 2.95% and the corresponding intra-assay coefficient of variability was 1.46%. The detection limit of the method was 0.61 µmol/l. Reading was performed using the CX5 Beckman Synchron automatic analyzer (Beckman Coulter Inc, USA).

<table>
<thead>
<tr>
<th>No.</th>
<th>Determination date dd / mm / yy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Demographic data</td>
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<tr>
<td></td>
<td>place of residence</td>
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<tr>
<td></td>
<td>age</td>
</tr>
<tr>
<td></td>
<td>sex</td>
</tr>
<tr>
<td></td>
<td>area of origin</td>
</tr>
<tr>
<td>2.</td>
<td>Pathological medical history no. of episodes/year</td>
</tr>
<tr>
<td></td>
<td>acute respiratory tract infections</td>
</tr>
<tr>
<td></td>
<td>acute diarrheal disease</td>
</tr>
<tr>
<td>3.</td>
<td>Socio-economic parameters</td>
</tr>
<tr>
<td></td>
<td>number of family members</td>
</tr>
<tr>
<td></td>
<td>family monthly income</td>
</tr>
<tr>
<td>4.</td>
<td>Child nutrition considered excessive, amount/day (It will be considered as excessive food the one that was consumed by the child in quantities that exceeds the value in the grey area of the table, according to the child's age)</td>
</tr>
<tr>
<td></td>
<td>Age</td>
</tr>
<tr>
<td></td>
<td>Dairy</td>
</tr>
<tr>
<td></td>
<td>Cereals</td>
</tr>
<tr>
<td></td>
<td>Meat</td>
</tr>
<tr>
<td></td>
<td>Fruits and Vegetables</td>
</tr>
<tr>
<td></td>
<td>Chocolate</td>
</tr>
<tr>
<td>0-4 months</td>
<td>&gt;1 liter</td>
</tr>
<tr>
<td>4-6 months</td>
<td>&gt;1 liter</td>
</tr>
<tr>
<td>6-8 months</td>
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<tr>
<td>8-12 months</td>
<td>&gt;500g</td>
</tr>
<tr>
<td>1-2 years</td>
<td>&gt;500g</td>
</tr>
<tr>
<td>2-3 years</td>
<td>&gt;100g</td>
</tr>
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</table>

Table no.1. Questionnaire form

*dd-day, mm-month, yy-year*
<table>
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<th>NO.</th>
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<th>ABSOLUTE NUMBER</th>
<th>%</th>
</tr>
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<td>1.</td>
<td>Gender</td>
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<tr>
<td></td>
<td>Female</td>
<td>43</td>
<td>44.7</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>53</td>
<td>55.3</td>
</tr>
<tr>
<td>2.</td>
<td>Area of origin</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Urban</td>
<td>45</td>
<td>46.8</td>
</tr>
<tr>
<td></td>
<td>Rural</td>
<td>51</td>
<td>49.2</td>
</tr>
<tr>
<td>3.</td>
<td>Age</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>0-6 months</td>
<td>14</td>
<td>14.6</td>
</tr>
<tr>
<td></td>
<td>7-12 months</td>
<td>25</td>
<td>26.0</td>
</tr>
<tr>
<td></td>
<td>13-24 months</td>
<td>28</td>
<td>29.2</td>
</tr>
<tr>
<td></td>
<td>25-36 months</td>
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<td>30.2</td>
</tr>
<tr>
<td></td>
<td>mean age</td>
<td>19.5±10.48 months</td>
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</tr>
<tr>
<td>4.</td>
<td>Pathologic personal history</td>
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<td>Acute respiratory infection</td>
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<tr>
<td></td>
<td>≤ 3 episodes/year</td>
<td>41</td>
<td>42.7</td>
</tr>
<tr>
<td></td>
<td>&gt;3 episodes/year</td>
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<td>32.3</td>
</tr>
<tr>
<td></td>
<td>Acute diarrheal disease</td>
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<tr>
<td></td>
<td>≤ 1 episode/year</td>
<td>32</td>
<td>33.3</td>
</tr>
<tr>
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<td>&gt;1 episodes/year</td>
<td>10</td>
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<td>5.</td>
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<td></td>
<td>number of family members</td>
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<tr>
<td></td>
<td>≤ 4 members</td>
<td>73</td>
<td>76.1</td>
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<tr>
<td></td>
<td>&gt;4 members</td>
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<td>23.9</td>
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<tr>
<td></td>
<td>family monthly income</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>≤1500RON</td>
<td>33</td>
<td>34.3</td>
</tr>
<tr>
<td></td>
<td>&gt;1500RON</td>
<td>63</td>
<td>65.6</td>
</tr>
<tr>
<td>6.</td>
<td>Predominant food or in excess</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>1. Predominant food</td>
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<tr>
<td></td>
<td>dairy</td>
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</tr>
<tr>
<td></td>
<td>grain</td>
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<td>11.5</td>
</tr>
<tr>
<td></td>
<td>vegetables and fruits</td>
<td>23</td>
<td>23.9</td>
</tr>
<tr>
<td></td>
<td>meat</td>
<td>11</td>
<td>11.4</td>
</tr>
<tr>
<td></td>
<td>2. Excess food</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>chocolate</td>
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<td>4.1</td>
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<tr>
<td>7.</td>
<td>Period for determining the</td>
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<td></td>
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<tr>
<td></td>
<td>plasma concentration of zinc</td>
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<tr>
<td></td>
<td>winter</td>
<td>26</td>
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</tr>
<tr>
<td></td>
<td>spring</td>
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<tr>
<td></td>
<td>summer</td>
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<td>19.8</td>
</tr>
<tr>
<td></td>
<td>autumn</td>
<td>29</td>
<td>30.2</td>
</tr>
</tbody>
</table>

Table no.2. Characteristics of subjects included in the study
Parameter Mean PCZ (µmol/l) p
Gender
  female 15.19±1.31 0.31
  male 15.51±1.69
Area of origin
  rural 15.10±1.51 0.14
  urban 15.54±1.45
Diet
  1. Predominant food
     meat 16.19±1.89*
     dairy 15.67±1.55
     cereals 15.57±1.84
     vegetables and fruits 15.24±1.16
  2. Excess food
     chocolate 15.23±1.47
Socio-economic parameters
  1. Number of family members
     ≤4 members 15.52±1.62 0.19
     >4 members 15.08±1.30
  2. Monthly family income
     ≤330 EURO 15.26±1.36 0.65
     >330 EURO 15.40±1.64
Season
  winter 15.66±1.12**
  spring 15.40±1.26
  summer 15.22±1.22**
  autumn 15.28±1.05

Table no.3. Mean plasma concentration of zinc according to gender, area of origin, diet, socio-economic parameters and season

* p - the value of p for children who eat mostly meat versus other foods (dairy p=0.487, grains p=0.326, vegetables and fruits p=0.393, chocolate p=0.304), ** p – the value of p for children from group winter versus other seasons (spring p=0.45, autumn p=0.2, summer p=0.22), PCZ - plasma concentration of zinc

Figure no. 1. Plasma concentration of zinc in the group of healthy children
PCZ-plasma concentration of zinc, M-mean, SD-standard deviation, n-total number of children

M±SD=15.53±1.49
n=96
Figure no. 2. Box plot diagram of plasma concentration of zinc by age.
The boxes represent the interquartile range. PCZ-plasma concentration of zinc, M-mean, SD-standard deviation. Means PCZ are indicated by red solid square. The whiskers connect the most distant values of PCZ in each study group. Mean PCZ±SD was 15.77±1.01µmol/l (age group 0-6 months), 14.69±1.18µmol/l (age group 7-12 months), 15.15±1.58µmol/l (age group 13-24 months), 15.97±1.58µmol/l (age group >24 months). Statistical differences: ▶ p>0.05, ◀ p=0.005, ◇ p<0.001.

Figure no. 3. PCZ according to the pathological medical history.
PCZ-plasma concentration of zinc, M-mean, SD-standard deviation, ADD-acute diarrheal disease, ARI-acute respiratory infection. The black solid circles represent the PCZ values. Mean PCZ±SD was 15.89±1.46µmol/l (group ≤3ARI/year), 14.23±0.76µmol/l (group >3ARI/year), 15.49±1.44µmol/l (group ≤1ADD/year), 15.09±1.56µmol/l (group >1ADD/year). Statistical differences: ▶ p>0.05, ◀ p<0.001.
Reference values for population aged 0-3 year were 49.5 to 99.7 µg/dl (7.6 to 15.3 µmol/l) for neonates and 3.8 to 110 µg/dl (9.8 to 16.8 µmol/l) for older children (16).

Statistical analysis was performed using EPHINFO application, version 6.0, software program of the Center for Disease Control and Prevention (CDC) in Atlanta and WHO, adapted to the processing of medical statistics. There were determined means, standard deviations and tests of statistical significance (Student’s t test) (12, 13). Harvard Graphics software program, version 3.0 was used for drawing the graphs.

Results

Mean value of PCZ (M) in the group of children was 15.33±1.49 µmol/l. In 80.20% of the children we recorded normal values for their age, ranging from 9.8 to 16.8 µmol/l, while the PCZ values were above the upper limit of normal in 19.8% of children. There were no low levels of PCZ, Figure no.1. Over 80% of children had values in the range M±2SD (80.44%) and 90.22% between M±2SD. PCZ coefficient of variation is 9.71%.

There is no statistically significant difference between the mean PCZ of groups depending of gender, area of origin, children diet, socio-economic parameters and season, Table no.3.

The highest mean PCZ value was recorded in the age group>24 months, significantly higher than in the age group 7-12 months and compared to the age group 13-24 months, but slightly higher than in the age group 0-6 months. Mean PCZ value in the age group 0-6 months was significantly higher than in the age group 7-12 months, but insignificantly higher than in the age group 13-24 months. There were no statistically significant differences between the mean PCZ value in the age group 7-12 months than in the age group 13-24 months, Figure. no. 2.

Subjects with more than 3 episodes of acute respiratory infections (ARI)/year had a statistically significant lower value of PCZ as compared to those who had less than 3 episodes/year. There are no significant differences between those who had an episode of acute diarrheal disease (ADD)/year and those who had more than 1 episode/year, Figure. no. 3.

Discussion

Zinc is an essential micronutrient in children’s growth and development. Our survey revealed that the mean PCZ, in Bihor County, in young children was 15.33±1.49 µmol/l (100.19±9.7 µg/dl), value falling within the range of normal reference values of the laboratory, age-appropriate for the subjects. A percentage of 80.20% of PCZ values was within this range. Minimum normal value of PCZ with the method studied was 9.8 µmol / l. In a 2012 study conducted on a sample group of 2115 healthy children aged 0.5 -18 years in Utah, United States, Chia-Ni Lin et al. found a mean PCZ of 89 ± 17 µg/dl (18). There is no data so far concerning the value of PCZ in the healthy children aged 0-3 years in Europe (19, 20). There was no records of a child aged 0-3 years, in our study, with PCZ values lower than 9.98 µmol/l. According by WHO, zinc deficiency is defined by decreased of the value of PCZ below the 9.98 µmol/l (4). A percentage of 19.8% of children had PCZ over the normal maximum value of 16.8 µmol/l. The specialized literature indicates that increased levels of PCZ can be found in cases of increased intake of zinc or accidental exposure to zinc. Intake of quantities of 10 to 15 times the recommended daily dosage according to age and gender may cause side effects, but the medical literature doesn’t mention the minimum PCZ value that can cause them to occur (21). There is no zinc deficiency in the general population of Bihor County, in this age group and for the period studied. There is no data so far concerning the value of PCZ in the pediatric population in Romania. Globally, Romania is considered as having a low prevalence (12.8%) of zinc deficiency for children under 5. The estimation was made in 2007 by WHO, using the nutritional stunting rate, last calculated for Romania in 2002 (10).

Children older than 24 months had a significantly higher PCZ mean compared to children aged 7-12 months, 13-24 months, but not significantly different from the children aged 0-6 months. Mean PCZ value in the age group 0-6 months was significantly higher than in the age group 7-12 months. These differences are explained by the fact that until the age of 6 months the infant diet is almost exclusively made up of breast milk, which represents an important source of zinc, the intestinal absorption of zinc is not influenced by the presence of phytates, fibers or oxalates from vegetables and fruits (22). After the age of 6 months the child’s nutrition includes vegetables, fruits and grains that decrease the intestinal absorption of zinc and after the age of 24 months the child’s nutrition coincides with that of the adult, meat being an important source of protein and zinc, respectively. Chia-Ni Lin et al. reported in 2012 that there were not found any statistically significant PCZ values different according to age in a study conducted on a group of 2115 healthy children in the United States. The results were explained by the authors by the fact that in this region fortification of foods with zinc has been used since 1987 (18).

Children with more than 3 episodes of ARI/year had a mean value of PCZ significantly lower than those who had less than 3 episodes/year. Decrease in zinc concentration distorts the functioning of the immune system, leading to the body's propensity to infections. Studies in the literature confirm that the normal level of zinc in the body protects the child from ARI (23, 24, 25). We have not found statistically significant differences between the mean PCZ in children with 1 episode of ADD/year and those with more than 1 episode/year. Literature data refer only to the effect of zinc administration to prevent ADD, the results being discordant, Walker CL, et al supports the idea of decreased incidence of acute diarrhea after zinc intake (26), while Boran P. et al denies the favorable effects of zinc on the development and severity of the illness (27). Our results can be explained by the fact that the comparison was made at a low incidence of diarrheal episodes/year (less than 1/year versus over 1/year), the small number of children with more than 1 episode of acute diarrhea/year didn’t allow stratification in this segment.
We obtained slightly elevated values of the PCZ mean in males versus females, however the difference was not statistically significant. The data are consistent with the literature (15, 28).

The group of children from urban areas had a higher PCZ mean compared to those in rural areas, the difference could be explained by a lower socio-economic level in rural areas correlated with lower access of children from these areas to food rich in zinc, which are generally more expensive. Differences between PCZ values in urban versus rural areas are not statistically significant. The data are consistent with the literature in different parts of the world (26, 29).

Meat is an important source of zinc. PCZ values in children who eat particularly these kinds of food were slightly higher than in those who have a diet based mostly on vegetables and fruits, cereals, milk or chocolate consumed in excess (30). Grains contain large amounts of zinc that are lost through processing, fruits and vegetables contain small amounts of zinc which is why the body can not properly absorb the zinc in vegetable proteins compared to the zinc in animal proteins (4). Zinc ion absorption is inhibited by the presence of oxalates, polyphenols, phytates and fibers.

Mean values of PCZ were higher in children from families with a higher socio-economic level (children from families with up to four members, and those from families with monthly income over 330 EURO). The difference can be explained by the fact that foods rich in zinc are generally more expensive, access to them is restricted by the socio-economic level of families in which the person concerned. The results are consistent with the literature (26), but the differences are not statistically significant.

We recorded higher mean values of PCZ in winter compared to spring, summer and autumn, which can be explained by the more frequent consumption during this period of food of animal origin (rich in zinc), to the detriment of the food of vegetable origin (available mainly in the warm season of the year). Zinc absorption is influenced by its concentration in the food as well as by the animal or vegetable origin of the food. Its absorption from plant proteins is very low compared to that from animal protein (4). Differences were not found statistically significant.

This study is the first of its kind in Romania, conducted on human subjects aged 0-3 years (11).

Conclusions
1. In healthy children, aged 0-3 years of Bihor County we recorded a mean PCZ of 15.33±1.49 μmol/l, a value falling within normal limits.
2. We didn’t find zinc deficiency in children tested.
3. We recorded elevated values of PCZ in children over 24 months, compared with children in the age groups 7-12 months and 13-24 months. The age group 0-6 months had an increased mean PCZ versus the age group 7-12 months.
4. Children with more than 3 episodes of ARI/year had lower PCZ values than those with maximum 3 episodes/year.

Acknowledgement: This paper is part of a doctoral study.

Conflict of interest declaration: No conflict of interest exists.

Abbreviations:
WHO – World Health Organisation
PCZ – Plasma concentration of zinc
BD – Beston-Dickinson
CDC – Center for Disease Control
M – Mean
SD – Standard deviation
ARI – Acute respiratory infections
ADD – Acute diarrheal disease

We recorded elevated values of PCZ in children over 24 months, compared with children in the age groups 7-12 months and 13-24 months. The age group 0-6 months had an increased mean PCZ versus the age group 7-12 months.

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SEVERE PROXIMAL HYPOSPADIAS REPAIR – ONE STAGE VERSUS TWO STAGE REPAIR

RI Spataru 1, Niculina Bratu1, Monica Ivanov1

Abstract
Background: Proximal hypospadias repair represents a major challenge for the pediatric and urologist surgeons. Many patients suffer a high number of interventions with poor results. We describe our personal experience in surgical treatment of severe forms of hypospadias in the last 5 years and the progress being made from previous surgical techniques. Material and methods: We retrospectively reviewed the records of patients who underwent hypospadias repair between 2007 and 2011 and we selected only 15 patients with severe proximal hypospadias. Proximal hypospadias was considered as urethral opening defect which extends from the proximal third of the penile shaft to the perineum. The severity of proximal hypospadias was reassessed during surgery. The techniques of repair were transverse island preputial flaps and buccal mucosa grafts in one step and two steps respectively. All patients were followed for complications at 1, 3, 6 months and 1 year. Results: Mean age at first procedure was 5.6 years. 4 cases we previously operated on. Transversal preputial island flap was used in 11 patients. Mean operative time was 3 hours. No flap necrosis was encountered. 8 patients (72.5%) developed postoperative fistula which was closed after 6 months. Staged buccal mucosa urethroplasty was performed in 4 patients. Complications after Bracka repair: 1 case (25%) developed postoperative fistula, 2 cases (50%) had relatively narrow buccal mucosa graft requiring additional tissue for urethroplasty. Conclusion: In severe forms of hypospadias, both transverse preputial flap and buccal flap are good choices regarding long term results. Final outcome of hypospadias surgery can only be evaluated once the patient reaches adulthood.

Background
Proximal hypospadias repair still represents a major challenge for the pediatric and urologist surgeons proven by the high number of surgical techniques available, none without complications. Many patients suffer a high number of interventions with poor function and esthetics results. One stage repair has the advantage of using skin that is unscarred from previous surgical procedures, with undisrupted blood supply (1) and decreased number of hospitalization days but it is also dependent on surgeons' expertise and family request. On the other hand, it is often associated with re-interventions to correct complications in severe cases and poor cosmetic results. Two-stage repair is usually chosen in severe primary proximal hypospadias or revisional hypospadias.

The assessment of hypospadias severity is based on meatal position, quality of the urethra and urethral plate, and presence or absence of penile chordae (2). In general, hypospadias surgery involves three main steps: straightening of the penis (i.e., correction of chordae); reconstruction of the missing urethra (i.e., urethroplasty); and reconstruction of the tissues forming the ventral radius of the penis (i.e., glans, corpus spongiosum, and skin) (3). Hadidi (4) in his hypospadias classification recommends that “surgeons conduct both a preoperative assessment based on the clinical site of the meatus and an intraoperative assessment based on the position of the meatus after straightening of the penis”.

Material and methods
We retrospectively reviewed the records of patients who underwent hypospadias repair between 2007 and 2011 to determine the location of the native meatus, type of repair and postoperative complications and we selected for our study only 15 patients with severe proximal hypospadias.

Proximal hypospadias was considered as urethral opening defect which extends from the proximal third of the penile shaft to the perineum during presurgical evaluation. The severity of proximal hypospadias was reassessed during surgery based on the presence of chordae and the need for a straightening procedure, the quality, location and width of the distal urethra after dissection, presence of hypoplasia of the ventral wall of the urethra, shallow or no urethral plate groove, small glans. We also included proximal hypospadias re-interventions because of the technical challenges they represent due to scarred local tissue and poor quality of local flaps.

The techniques of repair in our patients were: one stage transverse island preputial flaps used as a tube or onlay and two stage Braka technique using buccal mucosa grafts (BMG) with ventral skin coverage as onlay and tube. For the transverse island preputial flap technique we used a tubularized/onlay pedicle flap of mucosal foreskin that was interposed between the ectopic meatus and the glans (figure 1).

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Figure 1 a-d. Urethroplasty with transverse island preputial flap. a: preop aspect; b: degloving the penis; c: neourethra from transverse preputial flap; d: postoperatory aspect.

Figure 2. a-e. Scrotal hypospadias - surgical steps. a: preop. aspect; b: buccal mucosa graft harvesting; c: accurate hemostasis at the donor site; d: attaching the buccal graft at the recipient site; e: tubularization of the neo urethral plate, final aspect.
Buccal mucosa grafts were easy to harvest (figure 2-b) with clearly identification and preservation of the Stenon duct opening, performing accurate hemostasis at the donor site (figure 2-c), as wide as possible and attaching the center of the buccal graft at the recipient site for preparation of the urethral plate (figure 2-d). In the second stage - after 6 months - we performed the tubularization of the neo urethral plate (figure 2-e).

All patients were followed for complications at 1, 3, 6 months and 1 year respectively. We analyzed postoperative complications with respect to early complications (viability of the flap, hematoma, infections and wound dehiscence) and late complications (urethrocystostomy fistula, proximal strictures, meatal stenosis, recurrent UTIs, cosmetic dissatisfaction).

Results

From the total 15 patients with severe proximal hypospadias after the preoperative evaluation 5 had meatus opening at the proximal gland, 9 penoscrotal and 1 case was scrotal (table 1). At the time of surgery 13 patients required release of the moderate or severe chordae, 9 had shallow or no urethral plate groove and a full substitution of the missing urethra had to be performed, 7 had very thin urethral orifice at dissection, 5 patients had a small glans associated with small penis (we don’t administer testosterone injections preoperatively) and in 6 patients ventral urethral wall was hypoplastic at catheterization (table 2).

Mean age at first procedure was 5.6 years. 4 cases were previously operated on: 1 patient had one failed intervention, 2 patients had 2 interventions and 1 patient 5 reinterventions after an initial Thiersch-Duplay technique.

Mean operative time was 3 hours. No infections, hematoma or flap necrosis was encountered in our cases. 8 patients (72.5%) developed postoperative fistula which was closed after 6 months. Most of the fistula occurred in cases with transverse island preputial flaps used as a tube due to poor margin vascularization of the flap.

A 14 years old patient with scrotal hypospadias initially operated using a Thiersch-Duplay technique was admitted to our department after 5 interventions followed by repeated hair clew extraction from the neourethra. We gave up on this neourethra (Figure 3-a) and perform a 2 stage Bracka repair up to the proximal penile region (Figure 3-b,c,d,e,f) and finishing the neourethra using ventral skin (Figure 3-h,i,j,k).

Complications encountered after Bracka repair were: 1 case (25%) with postoperative fistula and 2 cases (50%) with relatively narrow buccal mucosa graft, requiring additional tissue for urethroplasty (table 4).

Discussion

Until 7 years ago, in our hospital the main surgical technique used in the repair of the severe proximal hypospadias was Thiersch-Duplay repair. Hair-bearing penoscrotal skin is now avoided in hypospadias reconstruction but was used in the past. When incorporated into the urethra, it may be problematic and can result in urinary tract infection or obstruction at the time of puberty. This generally requires cystoscopic depilation using a laser or cautery device or, if severe, excision of hair-bearing skin and repeat hypospadias repair. This was the case of one of our patients with 5 reinterventions.

Successful hypospadias surgery ensures a cosmetic penile appearance, voiding in the standing position and unhampered sexual function in adulthood. Despite great surgical interest in short-term functional and cosmetic results, and the incidence of problems such as fistula and stricture, there are only a few studies regarding the long-term outcome of hypospadias surgery compared with control subjects (5).

<table>
<thead>
<tr>
<th>No patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal penile</td>
</tr>
<tr>
<td>Penoscrotal</td>
</tr>
<tr>
<td>Perineal</td>
</tr>
</tbody>
</table>

Table 1: Anatomical location of the meatus before release of chordee

<table>
<thead>
<tr>
<th>No patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate/severe chordae</td>
</tr>
<tr>
<td>Shallow/no urethral plate groove</td>
</tr>
<tr>
<td>Very thin urethral orifice</td>
</tr>
<tr>
<td>Small/poor glans</td>
</tr>
<tr>
<td>Hypoplasia of the ventral urethral wall</td>
</tr>
</tbody>
</table>

Table 2. Factors involved in determining the severity of the proximal hypospadias
<table>
<thead>
<tr>
<th>Types of surgical procedures</th>
<th>No of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transversal preputial island flap onlay</td>
<td>4</td>
</tr>
<tr>
<td>Transversal preputial island flap tube</td>
<td>7</td>
</tr>
<tr>
<td>Buccal mucosa graft (BMG)</td>
<td>1</td>
</tr>
<tr>
<td>BMG with penile skin flap</td>
<td>3</td>
</tr>
</tbody>
</table>

Table 3. Types of surgical procedures

<table>
<thead>
<tr>
<th>One stage repair</th>
<th>Two stage repair</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. Tubular</td>
</tr>
<tr>
<td>Infection</td>
<td>0</td>
</tr>
<tr>
<td>Necrosis</td>
<td>0</td>
</tr>
<tr>
<td>Wound dehiscence</td>
<td>5</td>
</tr>
<tr>
<td>Fistula</td>
<td>6</td>
</tr>
<tr>
<td>Meatal stenosis</td>
<td>2</td>
</tr>
<tr>
<td>Urethral stenosis</td>
<td>2</td>
</tr>
<tr>
<td>Recurrent UTIs</td>
<td>1</td>
</tr>
<tr>
<td>Cosmetic dissatisfaction</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 4. Complications related to the surgical technique

Figure 3. a-k. Complex re-do staged urethroplasty for scrotal hypospadias.
Powell et al. compared the outcomes of flaps with
grafts for the single-stage treatment of proximal
hypospadias, confirmed that complication rates of
vascularized flaps compared similarly to those of free grafts,
and concluded that the use of vascularised flaps offered no
advantages. They also showed that the incidence of
postoperative fistulae was 10–32%, stricture 4–12%, and
stenosis 0.4–3% (6).

In a previously reported North American survey, Cook
et al. found that the preferred surgical procedure to correct
proximal hypospadias without penile curvature was one-
stage repair (TIP repair and onlay island flap repair were
each preferred by 43% of participants). When considering
the preferred surgical urethroplasty to correct proximal
hypospadias with severe penile curvature, 40% of urologists
in that study preferred the Duckett repair, 11% preferred the
onlay island flap, and 3% preferred the TIP repair (7). What
emerges from the interesting study of Springer and
coauthors is consistently different [8]. The authors tried to
identify actual international trends in the management of
hypospadias by inviting pediatric urologists, pediatric
surgeons, urologists, and plastic surgeons worldwide to
participate in an anonymous multiple-choice online
questionnaire. Completed questionnaires were obtained
from 377 participants from 68 countries. From the results, it
appeared that two-stage repair was the preferred method to
correct proximal hypospadias for 43.3–76.6% of
participants, which is in contrast to the results of the North
American survey in which one-stage procedure was the
method of choice (7). This technique seems to represent a
reliable solution when a full circumference urethroplasty is
required or when the urethral plate is of dubious quality. It is
particularly appropriate for severe hypospadias associated
with a poor plate and chordee (8).

Conclusion

There is no single technique which is completely free
from complications regardless of the apparent less severe
preoperative assessment. Most types can be solved using
one stage repair but on severe forms of hypospadias, both
transverse preputial island flap and buccal mucosal graft are
good choices regarding long term results. Final outcome of
hypospadias surgery can only be evaluated once the patient
reaches adulthood.

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Abstract
In the current practice, clinicians are often placed in the difficult situation of diagnosing and treating rare lesions. Bony over-use injuries are a known fact among young performance athletes. These types of lesions pose challenges in differential diagnosis and therapeutic decisions.

We present a patient treated in our clinic a few months ago. He was referred to our clinic with pain during sport practice and during high range of motion hip mobilization. The lesion was detected on pelvic X-rays and CT scan as a bony structured lump situated on the anterior edge of the pelvis, proximal to the acetabular rim. Our treatment of choice was block-resection of the tumor and histopathologic tests performed on the extracted fragments. At 3 months after surgery, the patient has no residual pain, no range of motion restraint, is back to practicing sport and presents with a good overall outcome.

Even though it may be considered a complicated process to manage, these types of lesions must always be differentially diagnosed with tumors. Concluding, overuse manifestations should be suspected but tumors should be first excluded.

Key words: heterotopic ossification, rectus femoris origin, overuse injury, young athletes, enchondroma, snapping hip.

Introduction
Overuse lesions in young athletes are a known issue which poses a great deal of difficulties for orthopedic surgeons. They are known to affect young boys who practice performance sport and have a very active lifestyle. For this reason, the feeling of not being able to practice sport is what pushes the patient towards the doctor, not the paint itself.

Overuse injuries are sports-related microtraumas that result from repetitively using the same parts of the body, usually by overtraining. The peak incidence for sport related injuries is situated between 5 to 14 years of age with more than 750,000 visits to the doctor being estimated in the U.S.A.[1]

This group of affections includes golfer’s elbow, jumper’s knee (patellar tendonitis), osteochondritis dissecans, Osgood-Schlatter disease, Sever’s disease (calcaneal apophysitis), shin splints, spondylolysis, swimmer’s shoulder, tennis elbow. The treatment methods range between rest, physical therapy, corticosteroids and infiltrations and surgery. The reason for this higher incidence in young athletes is because sports-oriented children tend to push themselves, ignore the pain, or are not able to connect it to certain repeatable actions they make.

The rectus femoris muscle arises from two tendons. One – the anterior or straight originates from the anterior inferior iliac spine, while the other – the posterior or reflected tendon originates from a groove above the rim of the acetabulum. These two tendons unite at a sharp angle and form the aponeurosis from which the muscle arises. This type of anatomy makes it possible for many problems to appear during effort and overusage.

A very common injury of the rectus femoris is a tear in one of its tendons. Garcia et al studied a series of ten professional soccer players that presented with rectus femoris proximal ruptures. All of them were treated surgically, either by direct suture with non-absorbable sutures (6 cases) or by the use of bone anchoring sutures. A consensus regarding the optimal treatment was not found, but it is clear that surgical treatment has a low recurrence rate and it is a steady indication for these cases.

Spindel et al. described a case of pelvic chondroma in a 15yo male, which was operated multiple times prior to diagnosing, for multiple chondro-osseous exostoses. The patient underwent two more major surgical interventions until the pelvic mass was removed. The follow-up was good, the urinary retention was gone, locomotion improved and the gastrointestinal disturbances ceased. One must always keep in mind that from dealing with ossifications, the situation can change drastically in a short period of time.[2]

Great caution must be taken when differentially diagnosing a tumor in this age group, as the disease has a greater life impact than it would on elders. This is where the experience of the doctor and the advances in modern medicine comes into place. The surgical procedure is very demanding and requires for a very well thought pre-operative planning.

Case presentation
Medical history
A 14yo male was referred to our clinic for persisting hip pain, which aggravated during sport activities. Medical history revealed that the pain had started 3 months ago, insidiously, without the existence of a significant starting trauma. The patient had no other medical history, presented with no loss of weight over the past months.
Clinical examination

He presented with stable vital signs and a normal clinical examination overall. The range of motion of his right coxo-femoral joint was slightly affected due to pain and impingement. The complaints usually involved specific moments of the sport activity, climbing steps and running on faulty terrain.

Imaging studies

The antero-posterior and lateral view X-rays that we performed on his pelvis revealed a bony prominence located on the anterior edge of the right pelvic bone, directly above the acetabular rim. It had approximately 4cm in diameter and it stood on the insertion point of the rectus femoris muscle. The MRI findings showed shape and signal modifications at the level of the antero-inferior iliac spine, presented under the shape of a septated formation of 42/26mm which had no other influences on the surrounding tissue. We performed a CT scan with 3D reconstructions that pointed at a benign tumor, most probably and exostosis (fig.1 and 4).

Laboratory workup

Our patient’s blood tests revealed no signs of inflammatory process or infection, but instead showed an increased level of AP (alkaline phosphatase) of 245U/L.

Surgical treatment

Excision surgery was performed through an 8cm incision with an anterior, modified Smith-Petersen approach. The superficial and deep layers were dissected through, until the ossification was reached. High attention was aimed at not harming the lateral femoral cutaneous nerve, the femoral nerve and the ascending branch of the latter. The ossification was easily excluded with the aid of X-ray. A biopsy was sent to the lab in order to get the exact histopathologic provenance of the tissue.

Histopathological exam

The histopathologic findings were as follows: osseous remodeling aspect, most probably reactive, and callus-like aspect or heterotopic ossification. After putting it into a clinical setting the latter was our final diagnosis.

Follow-up visits

After surgery we performed CT and X-ray scans for visual and documented confirmation of the excision (fig 3, 2, 5). The antero-posterior and lateral view X-rays showed no more evidence of the existing ossification, while the CT scans and the 3D reconstructions ensured us that the lesion was gone. Confirmation MRI was not needed, as it was only an investigation used for differential diagnosis. Range of motion was fully regained by the patient, especially hip flexion and abduction (which was the hardest point of motion to achieve before surgery). The patient now presents with no pain considering what existed before the surgery. The patient’s recovery period of 10 weeks has fully reintegrated him in his daily activities and he has now returned to his sport activity routine, carrying out demanding physical exercises.

Differential diagnosis

Enchondromas – are usually located at the level of the proximal humerus, distal femur and the short tubular bones of hands and feet. Patients usually are in their third decade when affected by enchondroma. The disease is equally spread at men and women. It’s long and oval shape resembles our lesion but all the rest of the criteria do not match.[4]

Osteoma – Widely met at the bones of the skull and face, this type of benign tumor is known to appear at the level of the pelvis as well. It is thought to be some sort of inflammatory reaction since it is often found in the ear canal of cold water swimmers or divers, but the etiology still remains unclear. Enneking described the X-ray aspect of osteomas as "one-half of a billiard ball" attached to the underlying bone. [5]

Femoroacetabular impingement - arises from an unfit incongruence between the femoral head and the acetabulum. Though it may present with the same symptoms as our patient, this affection is easily excluded with the aid of X-ray and MRI visualization.

Epiphyseolysis capitis femoris juvenilis lenta – usually occurs between 10 and 15 years old and consists of the separation between the head and neck of the femur at the level of the growth cartilage, after repeated micro-trauma due to intense physical activity. This results in a deformity that can be measured on X-ray.

Proximal rectus femoris rupture – is a common traumatic injury sustained by soccer players during sporting activities. 90% of the cases were acute ruptures, while the rest were chronic.[3] The injury often occurs while hitting the ball, when a large amount of pain can be felt at the level of the groin. MRI is used to confirm the diagnose the lesion, and usually after the surgical procedure, every patients can restart running after a mean time of 2 months and can play soccer again after a mean time of 3.8 months.

Anterior snapping hip – is usually met in athletes, with a good muscle development and high sporting activities. Usually the snapping sensation is not painful, but in time it can create a bursitis of the joint, thus creating inflammation and pain. As the hip is bent, the rectus femoris tendon shifts across the head of the thighbone, and when it comes back to a straight position, the tendon shifts again. Clinical diagnosis can be easily performed and the treatment ranges from physical therapy (stretching exercises) to open or arthroscopic surgery.

Discussion

Overuse injuries in young athletes are a common and controversial discussion amongst orthopaedic practitioners. This is partially due to the high number of affections that can be seen surrounding this joint and affecting this type of patients.

Ekstrand et al concluded, after a big cohort study carried out on almost 3000 soccer injuries, that more than 92% of all of the injuries recorded affected the 4 main muscular groups of the lower limb (hamstrings – 37%, adductors – 23%, quadriceps – 19% and calf muscles – 13%). These muscle injuries represented one third of all time-loss injuries in soccer.[6]
Fig. 1. Axial and sagittal CT scans revealing the ossification located on the anterior side of the iliac crest.

Fig. 2. Axial and sagittal CT scans showing the excision spot and the local bony anatomy after the surgery.

Fig. 3. Antero-posterior and lateral X-ray views of the right hip, that show no more evidence of the ossification.
In 2003, Straw et al presented a case report on the surgical of a chronic rupture of the rectus femoris muscle in a soccer player. Surgical reattachment was obtained by a 20cm incision, No 2 Ethibond sutures were used for tendon suture. After 6 months, the patient presented with no pain, with a clinically normal thigh and good functional results.[7]

In a recent article, Hjort et al, brought up slipped capital femoral epiphysis as a concerning problem amongst children with immature skeleton. Groin, hip or knee pain are a few of the symptoms which can be found and they are always aggravated by sports. Early diagnosis is crucial regarding this affection, as a late doctor presentation can lead to disabling complications.[8]

Kaplan stated in one of his articles that femoroacetabular impingement is often a cause of groin pain. Physical examination and careful x-ray analysis is very important in diagnosing and treating these patients before the impingement begins to create further chondral lesions that will lead to arthritis.[9]

In 2012, Herget et al presented a study case of a 21yo boy, professional bodybuilder which presented with progressive hip pain and increasing disability in carrying out daily routine. His initial response do NSAIDs was satisfying, and after the arthroscopic intervention and the biopsy, sinovitis was revealed to be the cause of the inflammation. After a re-evaluation and a CT scan, it was clear that the signs were pointing out to an osteoid osteoma, causing cam impingement and monoarthritis. Arthroscopic excision and femoral neck trimming were performed with good postoperative results.[10]

In another study, Donthineni et al performed a retrospective review of 115 cases of patients diagnosed with enchondroma. The concluded that most of these patients were diagnosed accidentally, the main source of problem being the effect this tumour has on the adjacent joint. More resources should be spend on teaching radiologists and general orthopaedists how to diagnose such maladies, as most of them were mistaken with sarcomas.[11]

Heterotopic ossifications are a common known complication of repeated sport trauma. In a study conducted in 2009, Jackson et al. tried to evaluate the osteogenic potential of the mesenchymal progenitor cells (MPCs) that appear in traumatically injured muscle. Upon osteogenic induction, MPCs showed increased alkaline phosphatase activity, but their final conclusion was that these traumatized muscle-derived MPCs have the potential to function as osteoprogenitor cells when exposed to the appropriate biochemical environment.[12]

Even though it may be considered a complicated process to manage, these types of lesions must always be differentially diagnosed with tumors. Concluding, overuse manifestations should be suspected but tumors should be first excluded.

References

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RECTOSIGMOIDIAN RESECTION IN CHILDREN.
A COMPARATIVE STUDY BETWEEN LAPAROSCOPIC AND OPEN TECHNIQUE

M Oancea¹,², Lorena Vatra², Anna Kadar²

Abstract

Background Minimal invasive surgery, particularly laparoscopy has dramatically changed the treatment options in congenital megacolon, facilitating the diagnostic and considerably reducing the operative trauma. The paper presents a comparative analysis between two groups of patients with rectosigmoidian resection and abdominoperineal pull through, performed by the same surgical team using laparoscopic or open transabdominal approach. Methods A number of 43 patients diagnosed with Hirschsprung’s disease or chronic constipation were operated on between 2002 and 2013. 7 patients (medium age 2y 9m) were operated on using Duhamel technique. One of these patients needed a surgical correction after an insufficient resection performed by the same technique. 36 patients (medium age 4y 2m) were operated on performing laparoscopic rectosigmoidian resection. In 15 cases the diagnostic was confirmed by the full thickness laparoscopic colic biopsy. We performed this as an initial surgical stage during the laparoscopic resection in 7 patients. The diagnostic approach, the operative trauma, immediate and long term postoperative outcome became the criteria in our comparison between these two clinical series. The main criteria regarding the therapeutic success were a regular and spontaneous bowel movement without anal incontinence phenomenon. Results: We noticed a prolonged operative time during our initial laparoscopic procedures, but an important decrease in the quantity of the analgesic and antibiotic drugs. There was also a reduced period of intensive care unit and general hospitalization stay in the laparoscopic series. Oral intake was possible in 36 hours for the laparoscopic series and in 72 hours for the open surgery series. First bowel movement was noticed in 1 to 3 days in case of the laparoscopic series, versus 3 to 5 days in case of the Duhamel technique. Medium hospitalization period was 23 days in case of the open technique series compared to 9 days for the minimal invasive surgery series. We registered one death in case of the open technique series after 6 months from surgery. There was a redo surgery performed in laparoscopic series in order to correct an insufficient resection at the time of the first surgery. We also used the minimal invasive surgery for this procedure. In this series were noted two cases of anastomotic leak and one case of anastomotic stenosis. Long term follow-up did not revealed patients with constipation or the need for supplementary therapeutic measures. In the laparoscopic series 4 patients presented soiling with favorable response to medical treatment. Comments: Evaluation of the surgical technique, immediate postoperative outcome and long term results reveal that laparoscopic rectosigmoidian resection represents a superior method of treatment compared to the open technique, especially to the retrorectal transanal pull through with perineal excess bowel segment as in our series. In laparoscopic series enterocolitis and soiling are clinical manifestation of limited results, compared to rectal stump impaction in open technique.

Key words: rectosigmoidian resection, pullthrough laparoscopy, Hirschprung’s disease

Background

Resection of the aganglionic bowel and restoration of the intestinal continuity with sphincteric structures preservation was first applied as the treatment of choice for Hirschsprung’s disease in 1948 by Orvar Swenson.(1) Swenson technique represents a low rectal resection performed by combined abdominal and perineal approach presenting potential risks for genito-urinary and sphincteric complications. B. Duhamel (1956) and F. Soave (1964) introduced a surgical technique in clinical practice which maintains total or partial aganglionic rectum in transit.(2,3) Surgical technique analysis shows similar general results, with variable success rate and postoperative complications specific to each surgical technique. Facilitating the specimen collection for the histologic examination and diminishing the intraoperative trauma, the laparoscopy has dramatically changed the surgical approach for congenital megacolon. (4) In 1994 K. Bax reproduced the Duhamel technique using laparoscopic approach. The approach proposed in 1995 by K. Georgeson, which is now currently used in practice, reproduces the Swenson technique borrowing surgical stage from Soave technique. (5,6) Rectosigmoidian resection and rectocolic biopsy using laparoscopic approach have been used in our surgical team since 2002. This paper reveals the applicability of this surgical method and evaluates clinical results.

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**Fig.1.** Congenital megacolon. 
Acute intestinal obstruction.

**Fig.2.** Enema of a neonatal congenital megacolon.

<table>
<thead>
<tr>
<th></th>
<th>Every 1-2 days</th>
<th>Every 3-4 days</th>
<th>Every 5-7 days</th>
<th>Over 8 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous</td>
<td>30 pt</td>
<td>20 pt</td>
<td>10 pt</td>
<td>5 pt</td>
</tr>
<tr>
<td>Need for medical therapy</td>
<td>5 pt</td>
<td>10 pt</td>
<td>15 pt</td>
<td>20 pt</td>
</tr>
<tr>
<td>Soiling</td>
<td>5 pt</td>
<td>10 pt</td>
<td>15 pt</td>
<td>20 pt</td>
</tr>
<tr>
<td>Not continent</td>
<td>0 pt</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 1.** Analytic score of rectal evacuation.

<table>
<thead>
<tr>
<th></th>
<th>Laparoscopy</th>
<th>Open surgery</th>
<th>Re do lap</th>
<th>Re do open</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cases</td>
<td>36</td>
<td>7</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Excellent</td>
<td>23</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>6</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fair</td>
<td>5</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>2</td>
<td>none</td>
<td></td>
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</tbody>
</table>

**Table 2.** Comparative stooling score
Materials and methods

There were 43 patients operated on between 2002 and 2013 diagnosed with congenital megacolon and chronic constipation. In 7 cases (6 boys and 1 girl) aged between 7 months and 10 years, (medium age 2y 9m) we practiced abdominoperineal pull through according to Duhamel technique, preserving an excess colic segment at the perineum. One case was a redo surgery for an initial insufficient resection practiced according to the same procedure. A number of 6 from 7 patients were diagnosed with chronic intractable constipation. There was only one patient presenting acute bowel obstruction syndrome, admitted as an emergency case. Diagnostic methods were plain abdominal X ray combined with contrast enema confirmed by the intraoperative histologic examination.

Mean intraoperative time was 160 minutes (between 130 and 200 minutes), excluding the waiting time for the histologic exam. Bowel resection was done proximal from the dilated colon in order to avoid transitional zone. According to the standard procedure used in our Clinique at that moment, each case was finalized abandoning an excess colic segment in the perineum after the retrorectal and transanal abdominoperineal pull through. After 14 days, we practiced the excision of the exteriorized bowel and applied a forceps on the common rectocolic septum, which was detached after 19-26 days (medium 22 days). We allowed clear liquid intake after 3 days, depending on the return to normal bowel function. The patients from this surgical series were released from the hospital in approximately 23 days (medium period). There were follow-up visits monthly in the first 3 months, every 3 months in the first year and every 6-8 months in the next 3 years. The following were evaluated: frequency of the spontaneous bowel movements, continence, sense of fullness, tendency to constipation, episodes of enterocolitis, perianal erosions. We performed laparoscopic rectosigmoidian resection in case of 36 patients aged between 13 days and 17 years (medium 4y 2m). Six of these patients (2 neonates) were admitted with acute intestinal obstruction syndrome and the others presented chronic constipation syndrome. The diagnostic was made using plain abdominal X-ray and contrast enema. Multiple colic biopsies were taken using laparoscopic approach before the definitive surgery in 15 cases for which the diagnostic was confirmed. We usually take samples for histologic exam at the time of colostomy/ileostomy (10 cases) or intraoperative when we performed the definitive pull through. When the patient presents a colostomy prior to definitive surgery we usually keep it during laparoscopic dissection for the benefit of colonic “suspension” at the abdominal wall with a good mesocolon exposure.

Mean time of surgery in laparoscopic cases is of 240 minutes (175minutes and 300minutes), excluding the waiting time for histologic examination. Oral intake of liquids is allowed from the day of surgery and solid food after 36 hours. We usually keep the patients in the intensive care unit until the return of the digestive functions (medium 3 days) and we release the patients from the hospital in 9 days (medium) with a prolonged period for the neonates and infants (14 days). We settled the follow-up visits once a month in the first 3 months after surgery, every 3 months for the first year and in every 6-8 months for the next 3 years. The follow-up criteria were the same: frequency of the spontaneous bowel movements, continence, sense of fullness, tendency to constipation, episodes of enterocolitis and the appearance of the perianal erosions.

Results

We noticed a prolonged operative time during our initial laparoscopic procedures, but an important decrease in the quantity of the analgesic and antibiotic drugs. There were also a reduced period of intensive care unit and general hospitalization stay in the laparoscopic series. Recovery of the intestinal bowel movement was noticed 3-5 days after surgery in the laparoscopic series, versus to 3-5 days in the open Duhamel technique. Mean hospitalization period was 23 days in open series versus to 9 days in laparoscopic series. Due to repeated episodes of bowel adhesions which necessitated 3 redo operations we registered 1 death at 6 months after surgery in open series. There was the need for a redo laparoscopy to correct an insufficient bowel resection. We registered 2 cases of anastomotic fistula, one of which requiring colostomy and one rectal anastomatic stenosis due to a partial anastomotic leakage. Anastomatic stenosis was treated with rectal dilatations. None of patients presented constipation or the need for special therapeutic measures long time after surgery. There was a higher frequency (2-6 stool/day) of bowel movement 4 to 6 months after surgery in laparoscopic series. This was a limited condition with special diet, but in 5 cases we had to administer Loperamid for 2-4 months. We registered 3 cases of repeated postoperative enterocolitis. One patient has been requiring nutritional therapy during 3 years after surgery. Intermittent soiling was noticed in 4 cases from laparoscopic series and 2 of these patients showed favorable response to medical treatment. The postoperative results regarding spontaneous rectal evacuation and anal continence were evaluated according to a personal clinical score (table 1 and 2).

Discussions

Evaluation of the surgical technique, immediate postoperative outcome and long term results reveal that laparoscopic rectosigmoidian resection represents a superior method of treatment compared to the open technique, especially to the retrorectal transanal pull through with perineal excess bowel segment as in our series. Preoperative multiple full-thickness intestinal biopsy is an excellent definitive diagnostic method. Suction rectal biopsy, which is the most used method, offers only a confirmation of the disease, not an extension of the lesion, so it must be accompanied by intraoperative biopsy. The mean operative time for laparoscopic procedures is increased compared to the open technique: 240 min vs. 160 min. Increased operative time may be attributed to rectal dissection and Anastomosis but we must consider that in open technique this operative time represents another scheduled surgery, after 14 days. Patients are admitted in the intensive care unit until the recovery of the general status and digestive functions. This period consists of 3 to 5 days.
postoperative days in case of the laparoscopic surgery group compared to 18 days in case of the open technique group. They also need close supervision of the exteriorized bowel segment and necessitate a large amount of antalgics and antibiotic drugs. If we talk about laparoscopic surgery, the shorter period of hospitalization after an important surgical intervention comes from the diminished intraoperative trauma. The absence of parietal incision, atraumatic manipulation of the bowel segments, fine dissection of the structures due to magnification are technical details which favor this decreased intraoperative trauma. Laparoscopic rectosigmoid resection with coloanal anastomosis is, in fact, a Swenson technique although the rectal mucosal dissection plane for a variable (2-4cm) length represents a technical element of the Soave technique. Promoting a better control of the rectal dissection, avoiding the main genitourinary trauma, laparoscopy avoids the main complication of the Swenson technique. Better postoperative results after laparoscopic approach has been reported also for the initial series, during the learning curve.(10) Evaluation of the patients after surgery did not reveal any case of constipation. Limited results consist of soiling and episodic enterocolitis in laparoscopic series vs. rectal stump impaction in open series. It is assumed that soiling after surgery is due to excessive exposure of the anal canal during the endoanal dissection, but we have to notice that Duhamel technique consists also of a perineal stage with exposure of the anal canal, and soiling is not reported as a complication after surgery. If we talk about the results in Hirschsprung’s disease, we have to notice a permanent search for better results which goes parallel with more detailed pathologic knowledge and more diagnostic methods: histochemistry and immunohistochemistry. Continuous studies and progresses regarding neuroenteric pathology discovered new entities such as neurointestinal dysplasia and chronic intestinal pseudoobstruction, entities which are difficult to document in current clinical practice. Their symptoms are superposed on the Hirschspring’s disease so this may be the explanation for limited postoperative results. .... “I would like to conclude that definitive surgery in the sense of a cure for Hirschprung does not exist. So let us stop talking about perfect results”… N.Bax (9).

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**BEHAVIORAL PHENOTYPES**

Simona Dumitriu¹, Adela Chirita-Emandi¹, Tiberiu Mircea¹, Maria Puiu¹

**Abstract**

Complex phenotype in neurogenetic disorders raised scientific interest and implication of novel technologies having the purpose of defining them at different levels: genetic, structural and functional, cognitive and behavioral. This article suggest that that their behavioral phenotype is not a juxtaposition of impaired learning abilities, attention deficit/ hyperactivity disorders or pervasive symptoms and increasing acknowledgement we can design appropriate/ individualized intervention programs for patients, family and community.

Key words: behavioral phenotype, neurogenetic disorders, rare diseases

**Background**

Behavioral genetics focuses on human traits and behavior study, analyzing the differences that arise in connection with a trait in the individuals of a population. The advancement in neuroscience knowledge, the interdisciplinary between biology, epigenetics, ethology statistics, psychology and genetics, have created the path to a better understanding of biological bases of behavior, going towards identifying the neurobiological mechanisms underlying behavioral patterns.

Molecular genetic studies are trying to establish new directions for the mechanisms trough which the human genome fundaments behavioral phenotypes. An argument in this direction is that careful observation of behavior is compulsory when approaching therapeutic interventions in neurogenetic disorders. However, due to reduced incidence of some of these disorders and their complex genetic mechanism, it is difficult to establish the validity of the syndrome-behavioral phenotype association.

A definition considers behavioral phenotype to be a pattern of motor, cognitive, language and social dysfunction characteristics that are associated with a biological disorder. The presence of the behavior is not required in any situation, but the likelihood of its recurrence is increased. [1]

Typical examples are self-mutilation of fingers and lips in Lesh Nyan syndrome (LNS), hyperphagia and compulsive eating behavior in Prader Willi syndrome (PWS); reduced emotional contact in fragile X syndrome (FRX), and superficial sociability, tachylalia, and language disorders in Williams syndrome (WS). When present, the symptoms suggest the syndrome. [2] Using this method, Rett syndrome behavioral phenotype, with stereotypes characteristic of wave motion of the hands, hand-mouth game, made this type of autism identifiable many years before its genetic origin was recognized.

Behavioral phenotypes identification in these disorders was just a step towards a complex work of which can correlate a gene with one or tens of proteins, different genes with the same behavior, more genes and mutations involved more complex the mechanism. [2] However, despite the presentation of behaviors that define the syndrome, not all patients, will present the classic symptoms, but the probability to occur is higher. Behavioral phenotypes also influences acquired disorders, such as, for example in fetal alcohol syndrome. The impact of alcohol on cells is now well known, its consequences are related to cell death, brain median line developmental abnormalities, behavioral problems and learning difficulties.

**Why should we be interested in the concept of behavioral genetics? How can it help us?**

Firstly, it has clinical value. Identification of these phenotypes may provide clues regarding underlying genetic cause which can explain developmental and behavioral alterations. Increasing awareness of professionals in this field may facilitate access to early diagnosis and development of specific interdisciplinary intervention programs.

The knowledge derived from studies on genetic abnormalities and their behavioral phenotypes in these syndromes are also relevant for studies concerning the biological determinants of human behavior.

For many parents it may be difficult to deal with the illness of their child with unexplained behavior, different from everyone in the family. Parents can be informed that certain behavior patterns are characteristic for their illness (learning disorders or facial dimorphisms) and together they shape their child's specific disease manifestations. Families find empowering the access to full knowledge about their family members' genetic conditional not only by facilitation of the grief process but, more important, helping the coping mechanism, by the access to resources and peer support from other groups with the same condition. Additionally genetic counseling brings further understanding.

This article will detail the patterns of behavior in genetic disorders.

**Specific behavioral phenotypes in several rare genetic diseases**

A. Lesh-Nyan syndrome (LNS)

Is a X-linked transmitted, recessive disorder with an incidence of 1: 380,000. It involves an inborn error of purine metabolism, due to the absence (or very low levels) of hypoxanthine-guanin phosphoribosyltransferase (HPRT) enzyme. The enzyme deficiency prevents normal hypoxanthin metabolism and produces excess serum accumulation of uric acid, with symptoms of gout in absence of specific treatment.

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Fig. 1. 4.5 year old boy with spastic tetraparesis, and severe motor regression because of LNS.

Fig. 2. Male patient at age of 4. Note the fair skin, clearly nonspecific brown eyes, the hypotonic face with prominent lower jaw, wide mouth, tongue thrusting, and relative microcephaly.

Fig. 3. Our 5 year old patient. Note the lack of contact and interest for the human face.

Fig. 4. A 5 year old boy with FRX, showing some of the facial features: long face, large and protruding ears, low muscular tone.
Page and Nyan suggested a correlation between the severity of motor symptoms, the presence of self-aggressive behavior, the cognitive assessments and the HPRT level. [3]

Behavioral phenotype

Self-aggressive behavior of LNS was conceptualized as a compulsive behavior that the child tries to control, but which is usually hard to resist. The topography of these can be predicted: the most common, biting of fingers, lips, and oral mucosa, in early years and other maladaptive behaviors (hitting the head, trunk and eyes, nail pulling) or psychogenic vomiting later. Usually these involve mutilating of only one part of the body. Compulsive behavior is preceded by anxiety. These children become anxious when they start to see a part of their body as being threatening. The boys and young men seem to welcome protective restraining devices and appear to become threatening. The boys and young men seem to welcome protective restraining devices and appear to become extremely agitated when these are removed. [4] A verbal pattern can be represented by chronic stutter and coprolalia. Moreover, the child may have aggressive impulses and pinch, scratch, or direct verbal insults against other children.

Case report

We report a 4.5 years male patient. Parents reported “orange sand” in their son’s nappies in the first week. He started to manifest severe restless episodes, insomnia and difficult acceptance of the bottle around 3 month. Around 6-7 month he started to show developmental delay and motor incoordination. He was diagnosed with LNS around the age of one, already at this age presenting self-injurious behavior like hitting the head and frequent vomiting. They started Allopurinol immediately after the diagnosis. The present developmental status is: cognitive concordant with the age of 36 months. The language is severely impaired; he can use very short sentences of 2-3 words. Motor skills: spastic tetraparesis with uncontrolled extrapyramidal movements. Usually a happy child, he learned to anticipate the self-aggressive outburst and to ask his mother to protect him. Even wearing special gloves, pacifier and helmet he mutilated his lips, teeth and gingival mucosa. The parents report that the medical management included a whole range of medical treatment including SSRIs, antipsychotics, dopamine antagonists, anxiolytics and opiate antagonist, gum shields and some teeth removing.

B. Prader-Willi Syndrome (PWS)

PWS is caused by the loss of paternal copies located in the region 15q11-13 usually by deletion. The maternally inherited copies of these genes are virtually silent due to imprinting in this region, only the paternal copies of the genes being expressed. Other genetic mechanisms include: uniparental disomy (UDP), sporadic mutations, chromosome translocations, and gene deletions. Deletion of the same region on the maternal chromosome causes Angelman syndrome (AS).

Despite its prevalence of 1/10,000 up to 1/15,000 the behavioral phenotype came to be remarked in relation with Angelman syndrome, which has a different behavioral phenotype although both genomic imprinting disorders are involving the same region on chromosome 15. PWS and AS represent the first reported instances of imprinting disorders in humans.

Behavioral phenotype

Specifically, the syndrome includes a particular eating behavior (a compulsive search for food, non-selective non-discriminatory ingestion of large quantities of food and also, stealing food), irritability, reduced tolerance to frustration, stubbornness, anger, pinching skin, associated, in the vast majority of patients with mild mental retardation. Behavioral control problems appear as the child grows, initially in transition from one activity to another, and then, associated with binge eating behavior.

Typically, the behavioral difficulties reach a peak in adolescence or in early adult life. Binge eating is the most severe and debilitating behavior disorder, leading to obesity, diabetes and severe respiratory difficulties. Usually, patients are happy and open to interpersonal networking, participating with interest in behavioral training. They can learn to structure their daily routine activities, rewards, breaks, boundaries and firm rules.

An extensive study focused on assessing self-aggressive, stereotyped and obsessive compulsive behavior in individuals with PWS and showed that skin picking is the most common self-aggressive behavior, observed in 19.6% of individuals, with low frequencies of nose pinching, kicking and pulling nails and lips hair. From the compulsive behavior category, the compulsive eating is the most common. Less common are the rigidity and inflexibility to environmental changes, strict arranging of objects, repeated checks, compulsive washing of hands. [6 7]

Standardized assessments have identified high levels of depressive, anxiety and compulsive symptoms, with functioning impairment, which are not explained by developmental delays, difficulties in nutrition or by obesity in patients with PWS. [8]

Case report

We report a 12 years old male patient diagnosed at age of 2 as having PWS after a history of neonatal hypotonia and difficulties in achieving the important developmental milestones. The parents manage to control his compulsive alimentary behavior by controlling the environment and cognitive behavioral therapy. He is able to follow a complete behavioral program every day, however, when frustrated he has difficulties in avoiding a binge episode. During this episode he still needs one of his parents to help him relax and not transform the frustration of not finding anything in the fridge in a temper tantrum. BMI at the moment is 28.77kg/m2. He controls the pinching skin habit relatively well. The psychological evaluation revealed: mild mental retardation, severe deficit of executive functions, dyslalia, severe attention deficit and anxiety. He finds difficulties in interacting with children of his age and
Case report

We report a 4 years old boy with a history of delayed motor milestones and delay in general development later, absence of speech and poor understanding of language until 1.5 years when he had the first seizure. Soon after the seizure he was seen laughing out loud, hand flapping as the most happy child while having 41 degrees Celsius of fever. The EEG ruled the gelastic phenomenon during this episode, which was confirmed by the child's apparent happiness. The parents learned to deal with his episodic severe insomnia, sensitivity to heat, feeding problems and to use his fascination for water as a reward for appropriate behaviour.

D. Rett syndrome (RTT)

RTT is a progressive neurodevelopmental disorder that occurs almost exclusively in females, having an incidence of 1/10,000 to 1/15,000 live births and a penetrance of 100%. [10]. The girls who manifest RTT are usually heterozygous for a de novo mutation in MECP2 gene in 95% of the cases. Other genes have been involved in RS etiology, like CDKL5, FOXG1, NGL1. [11]

Behavioral phenotype

The patients with RTT appear to develop normal until 6-18 month. Some of them achieve appropriate milestones, including the ability to walk and even say a few words. The onset of the developmental regression will be noticed by weight loss, weak muscle posture, progressive microcephaly, scoliosis installation. The neurological deterioration is followed by installation of motor incoordination, ataxia, gait apraxia and seizures. The girls progressively lose the purposeful use of hands and replace it with hand wringing or washing, clapping, flapping and mouthing of the hands movements. Other stereotypical behaviors are the breath abnormalities: hyperventilation, breath-holding, aerophagia, apnea and forced expulsion of air and saliva. These are the most frequently recognized behavior in RTT girls. Other autistic features are unresponsiveness to social cues, loss of eye-to-eye contact, hypersensitivity to sound. After this stage the patients suffer severe physical change: loss of weight and of muscular mass, severe scoliosis which together with breathing abnormalities will cause cardiac abnormalities and generalized dystonia. The behavioral abnormalities include high sensitivity to the external events manifested by anxiety, low mood, teeth grinding, night laughing or crying. [12]
stereotypical behavior seems to be the hyperventilation and breath-holding. Her EEG record did not show abnormal interictal modifications in the last year and her social quotient was very low. She lost the ability to use her hands in the first few months after the symptoms starting and the walking in the following 6-8 month. She is very sensitive to external changes, every change in the daily routine increase her anxiety, and aggravates the stereotypical behaviors. She presents constant respiratory alkalosis. Her MRI brain revealed diffuse cerebral atrophy, which was predominantly cortical, suggestive of RTT. She was diagnosed with RTT syndrome in severe regressive phase.

\textbf{D. Fragile X syndrome (FXS)}

Include a broad of disorders caused by the mutation in the fragile X mental retardation 1 gene (FMR1) at Xq 27.3. Full mutation is caused by >200 cytosine-guanine-guanine repeats (CGG) which led to methylation or silencing of the gene and absence of messenger RNA and subsequently of FMR1 protein. The premutation, between 55-200 CGG repeats, is found in carriers and can act like a gain of function mutation. Some boys carriers of the permutation may manifest attention- deficit or/and hyperactivity disorder and autism spectrum disorder (ASD). The expansion from a premutation to a mutation occurs when FMR1 gene is passed to the next generation. The greater the number of CGG repetition in a female, the greater the risk of expansion to full mutation in the next generation. A carrier mother, having two X chromosomes, has a 50% risk to pass the mutation to the next generation, by having affected/ carrier sons and daughters and also normal children without the FRM1 mutation.[13] When passed by a male, the permutation will only pass to his daughters. The premutation is more frequent and it can occur 1/250 in women and 1/810 in males.[14] The incidence of the full-mutation allele is lower, around approximately 1/2500. Increasing the level of acknowledgment of the cases having the full mutation and high functioning or having the premutation and neurodevelopmental problems may facilitate the access of these individuals to genetic counseling.

\textbf{Behavioral phenotype}

The behavioral phenotype may be more helpful than physical phenotype in diagnosing the children with FXS because of the absence of the typical physical characteristics in prepubertal period. It has been the subject of extensive studies concerning learning difficulties, mental retardation, autistic features, language impairment, perseveration and attention deficit/ hyperactivity disorder. The intellectual deficit manifest more severe in males with FRX, in majority with an IQ lowers than 70, than in females, in which the pattern of inactivation of the second X chromosome may improve the outcome. Females having full mutation and normal IQ and may manifest deficits in executive functioning which will relate with their attention and organizational difficulties and instable social relationships. [15]

The behavior of children with FXS include impulsivity, short attention span/ hyperactivity, hyper arousal and sensitivity to auditory, olfactory, and tactile stimulus and relational difficulties symptoms and perseveration, a broad of symptoms from ADHD, autistic and control impulses spectrum. But what of these is, and how is it specific?

The relational pattern is considered to be juxtaposition between friendly social and pervasive developmental disorder in children with FRX. [16] They tend to be more sociable and interested in interaction than autistic people, but their structural anxiety and hyper arousal in new environments may increase the tendency to social avoidance.

Perseveration, a specific behavioral and communicative feature, may be another common field with ASD. This can be seen in speech, by repeating the same word, the same topic, using repeatedly the same inadequate tone just for the need of repetition, without response to the negative insight of the audience. Behavioral perseveration is often recognized and can direct to an evaluation for autism. They may prefer to repeat some activities like spinning objects, stacking toys, but also the same rituals, like eating the same food, washing hands, watching the same cartoons. Motor perseveration can be self-stimulatory like hand flapping, toe walking, spinning or leaping, but also hands biting, excessively chewing of food or of the clothing items.

It has been suggested that there is interdependence between the arousal regulation, attention, and academic performance. [17] An argument in this direction is a different sympathetic and vagal/ parasympathetic modulation pattern observed in these children with FRX by compare with the controls.[18]

The excessive activation of nervous system witch overcome the regulatory mechanism as response to social or environmental stimulation, called hiper arousal, seems to be implicated in relational and language particularities, anxiety and ADHD symptoms in FRX.

The aspect of one of these hiper aroused state can be similar with every human in this state: the behavior is disorganized, with poor attention focus, low capacity of control behavior or language. Children and adults with FRX can describe in this state the felling of somatic/ internal sick/pain, which is often seen as vomiting or abdominal pain in children. The time for them to calm down, is much longer than in other people and it is also dependent of the existence of a free zone. In this situation the language can become sludge, eye contact cannot be established and maintained, they can manifest tantrum, aggression and perseveration.

Usually not showed in firsts meeting of a child with FRX, language and vocabulary may be their strength. An infant may amaze his parents by the spectacular vocabulary acquisitions with low effort. The difficulty intervenes when the kid has to exercise his language in a social environment. The hiper arousal structural pattern, combined with the anxiety triggered by social conversational participation and less self-monitoring and control then its needed togetherness with lifelong experiencing these difficulties build a language which is inadequately perseverative and tangential in FRX individuals.[16]
The triad, over activity, persistent inattentiveness and impulsivity leads to many children with FXS to be also diagnosed with ADHD. Compared with peers with the same developmental level they showed the same degree of motor activity, but significant more inattentiveness, restlessness, distractibility and impulsivity.\[16\] They show a difficulty to switch visual attention and inhibit repetitive behaviors based on a weakness of executive functions.\[16\]

Particularities concerning hypersensitivity to stimuli, hiper arousal in social environments triggering anxiety, repetitive behaviors, diminishing attention and contact must be approached therapeutically as early as possible by individualized techniques and environment management.

**Case report**

We report a boy age 5 years, born from normal pregnancy, with mildly late developmental milestones. Parents observed hand flapping, perseveration and poor eye contact during the first year. They asked for an evaluation for ASD. Single palmar crest, ear cupping and hyper extensive joints directed diagnosis to test for FRX. After FRX diagnosis the child the family started to work with a therapist trained in ASD intervention. She observed particularities difficult to address: inability to establish eye contact, even though he is a very happy and interested of interaction child, high anxiety to minimal changing of the environment, rocking behavior and sucking his sleeves in these stressful situations. The parents chose “to protect” him as much as they could from highly stimulated environments. They observed that after an hiper arousal event usually triggered by social anxiety, like going to park, he was very difficult to calm down and could remain upset for the entire day. His language progressed satisfactory with little help, but the attention could only be maintained for only a few minutes by the age of three. Based on his self-stimulatory behaviors, poor attention and eye contact it has been decided to follow the program of a preschool center for autistic children. Transition period was a lot longer than in autistic children and was described by the parents and the therapist as regressive. Perseveration in language started to be severe, anxiety episodes on daily basis and aggressive episodes frequent. He started vomiting and after complete pediatric checkup anxiety was considered the only cause. Finally, the solution was to work daily with the same therapist, in one to one session, and that him to serve as a security figure in other settings like sport, going to gym or to supermarket. The cognitive evaluation showed borderline mental retardation with good communication score and lower socialization and motor scores. The evaluation with ADOS, a specific instrument for ASD, did not situate him in the autism range.

**E. Williams syndrome (WS)**

WS is characterized by particular facial appearance, with elfin appearance, cardiac abnormalities/malformations, connective tissue abnormalities, mental retardation or learning disorder, idiopathic infantile hypercalcemia, particular cognitive profile and an unusual personality profile.

The disorder is caused by a deletion of 1.5 megabase the long arm of chromosome 7, including the elastin gene (ELN). The deleted region includes about 25 genes that probably contribute the manifestations of the syndrome, like: LIMK1, GTF21, GTF2IRD1, CYLN2, STX1A, FZD9, implicated in brain development, visual and spatial orientation, synaptic plasticity, motor coordination.\[19 20 21 22 23\]

Perhaps the most interesting perspective offered by animal models is the opportunity to develop and test new therapeutic interventions. It was already shown that some of the most serious cardiovascular abnormalities found in ELN (elastin) mice, can be mitigated by introducing a human ELN gene, suggesting that, although not identical, mechanisms causing the disease are somewhat similar in humans and mice. \[24\] This provides a starting point for pre-clinical testing of pharmaceutical therapies to reduce blood pressure, to decrease smooth muscle cell proliferation and vascular stenosis, which are major causes of mortality in WS. In the future, animal models will probably be just as important for development and testing of new therapies to combat anxiety, disinhibition, visual and spatial deficits, and even mental disability.

**Behavioral phenotype**

All children with WS have delayed development as follows: 75% have the cognitive and adaptive level corresponding \[25 26 27\] to their mental retardation, while the remaining 25% have learning disorders. \[28 29\]

Individuals with WS are described by most experts as being extremely sociable, empathic, unable to go unnoticed in the group becoming too close and friendly, showing a very positive social judgment to unfamiliar people.\[30 31\]. Von Arnim and Engel (1964), were among the first to describe that people with WS show an amazing volubility and a greater ability to establish interpersonal contacts, based on a background of uncertainty and anxiety. \[32\]

Most adolescents and adults with WS present severe anxiety. Children and adolescents with WS have an increased vulnerability to excessive concern, compared with groups with Down or Cornelia de Lange syndrome and manifest clinical anxiety more than those with PWS. This vulnerability to anxiety contributes to “difficult” temper of people with WS.\[33\] Although individuals with WS are extremely close, empathetic and sensitive to other people, they have difficulties to make and maintain friends. These difficulties may be due to absence of certain social knowledge explained by the “theory of mind”. Thus, social knowledge includes an understanding of the mind as a system of representation (e.g. false faith, irony) and the ability to make rapid social judgments about the mental state of others, based on facial expression and body (e.g. emotional and intentional attributions based on immediate perceptual information). In terms of representation, the child must be able to understand another's mental representation of different and be able to predict behavior based on understanding.

The dissociation of language quality and facial and spatial processing was proposed as a mark of the WS.
syndrome. WS phenotype involves a feature of cognitive functions: disturbed spatial processing while processing facial expression is intact. The evaluation of the development level showed small differences between adults and children regarding receptive and expressive language. Tests have documented cognitive profile almost identical to those found in children. Reading, pronunciation, numeracy and social adaptation remains at low levels, along with aging, with functioning appropriate for the age of 6-8 years. In studies on both, children and adults, the peculiarities of intellectual abilities hold up the notion that the syndrome has a particular cognitive, linguistic and functional adaptation patterns. The main difficulties in school adjusting are caused by hyperactivity, lack of concentration and poor attention capacity.[34 35]

Case report

Our patient, an 11 years old girl was diagnosed soon after birth with WS secondary to a severe aortic stenosis and hypercalcemia. At the moment she is a 5th grade student and she is getting extra help at home from a professor to keep her in line with her peers. Global developmental delay was first detected at the age of 6 months. She gained milestones by early education intervention, but she is still has mild mental retardation, scoring better on subtests measuring verbal abilities than on subtests measuring visuospatial construction. The school teacher reported that her vocabulary is within the normal range size, the onset of grammatical acquisition begun later and needed more effort from both of them. She is willing to be thought, to learn and to please the teacher and the parents. Her program has to be scheduled in 20 minutes episodes with breaks, for her attention deficit to be kept under control.

The report from school also describes her as joyful, sociable, overly friendly, perceived by the other children to be empathic, but needing adult’s reassuring when caring for someone her anxiety increases. Emotional and facial decoding is still challenging for her being a hardener for her structural anxiety. She was also diagnosed with unspecific pervasive disorder because of this poor insight for emotions and low ability to create emotional connections and have appropriate response. Even following therapy the cognitive phenotype in WS may be a maintaining factor for anxiety, obsessional thoughts, and bias thoughts about daily routine decisions and in critical points can be reinforced by psychotrope medication.

Conclusion

Studies on behavioral phenotypes in neurodevelopmental disorders demonstrate complex connections that outline the path from genes to cognition and complex behavioral phenotypes. Behavioral phenotypes arise in mendelian transmitted disorders and non-mendelian inheritance (PWS/AS, FRX). Assessments made in these syndromes show that recognition of the genes involved is only the first step. Identifying the proteins involved and their expression in the brain are critical. In order to clarify their mechanism the use of animal models, the study of neuroanatomy trough brain imaging techniques, and detailed descriptions of behavior are mandatory. In addition, comparative studies between partial variants of the Mendelian disorders (WS), those caused by UPD (PWS, AS) as well as the study of atypical subjects, showing all of the characteristics of the disorder (WS) are the key to understanding developmental pathways.

The delineation of behavioral phenotypes can be a difficult task, but should persuade specialists to persist in identifying gene-behavior relationships and behavioral abnormalities. Delimitation of a behavioral phenotype may be the first step toward molecular characterization of behavior.

Acknowledgements:


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Abstract

Purpose. This paper intends to expose and discuss the technical aspects of the transanal endorectal rectosigmoidian resection in children. Colic resection and coloanal anastomosis technique may be performed by totally endoanal or combined endoanal and laparoscopic approach for the mobilization and devascularization of the colon. Both techniques have, as a common surgical stage, the suprasphincteric endorectal dissection and transanal coloanal anastomosis. This paper analyses the indications, contraindications, technical details and surgical complications which strictly depends on the transanal endorectal surgical stage. Materials and methods This study was conducted on a number of 42 patients with rectosigmoidian resection. In 6 cases the resection was performed using exclusively the transanal endorectal approach and in the other 36 cases we used videoassisted technique. The patients were aged between 13 days and 17 years (mean 3y 2m). Five of these patients were admitted as an emergency case and were operated on as a single stage procedure, without performing a colostomy. There were 37 cases admitted as a chronic constipation syndrome with or without aganglionosis. We used exclusively the endoanal technique in children with certified low type of aganglionosis. We practiced laparoscopic devascularization and mobilization of the colon in cases with resection above the rectosigmoid junction. Results and Discussions about operative results take into account only endoanal stage of the surgery, underlining the technical aspects with obvious impact over the postoperative results. There were 9 postoperative difficult outcomes: 2 anastomotic fistulas, 1 anastomotic stenosis, 1 insufficient resection and 4 cases with episodic soiling.

Key words: congenital megacolon, transanal rectosigmoidian resection

Background

Laparoscopic rectosigmoidian resection became very fast a revolutionary point of view in the strategy and technical aspects of congenital megacolon. This technique imposed itself as a single stage procedure, abandoning techniques that preserve aganglionic rectum (Duhamel technique and Soave). This technique was first presented simultaneous by Bax-1994(1) and Smith (2) as a reproduction of the Duhamel technique. After this, K. Georgeson performed the rectosigmoid resection as a reproduction of the Swenson technique using laparoscopic approach. (2) Georgeson’s technique imposed itself very quickly in clinical practice and many authors report improvement of the postoperative results. Starting from the rectosigmoid laparoscopic resection, J. de la Torre and A. Ortega performed an exclusively endorectal approach. (4)

Material and Method

This study take into account 42 patients with rectosigmoidian resection. There were 36 videoassisted surgery and 6 exclusively transanal endorectal procedures. Both techniques consist of a rectal resection after segmental rectal dissection on a variable length through endorectal approach. Mean age of the patients was 3 years and 2 months (aged between 13 days and 17 years). There were 5 patients admitted as an emergency case and operated on without a colostomy as a first stage of the procedure. A number of 37 patients were admitted in the hospital as a chronic constipation, with or without aganglionosis revealed by the preoperative histologic examination. Exclusive endoanal approach was practiced in low type of aganglionosis. We practiced laparoscopic devascularization and mobilization of the colon in cases with resection above the rectosigmoid junction. We practice this technique without infiltration of the submucosal rectal plane. The endoanal stage of this procedure consists of a good exposure of the terminal rectum, starting 1 cm above the dentate line. This is possible by placing a circumferential row of staying suture which realizes a continuous traction over the rectal mucosa (photo 1).

The rectal mucosa is then dissected from the muscular plane on a length of 3 to 4 cm. After crossing the rectal wall, we continue the dissection of the perirectal plane until we reach the peritoneal reflexion (Douglas cull de sac) or until we meet the perirectal dissection plane initiated laparoscopically. Entering the peritoneum, we may exteriorize transanal the dissected colon traction it into the perineum and resect it. (photo 2).

The resection level is settled by the histologic examination performed during the operation or we may use key points settled at the time of laparoscopic preoperative biopsies. Coloanal anastomosis is done in one or two plane, total or half thickness.

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75
Photo 1. Exposure of the anal canal.

Photo 2. Pull-through of the dissected colon.
Results

Perineal stage of the procedure is not significant different in the two procedures. Mean operative time was 75 minutes (between 60 and 110 minutes). We did not take into account the blood loss during the surgery because they are clinical insignificant. Postoperative mean follow-up period was of 3 years. There are two criteria which scores the postoperative outcome: spontaneous rectal evacuation and anal continence. Minimum age that is usually take into account for rectal continence is at 3 years old, but, clinical observation of healthy children demonstrate that we may score continence after 4 years old. There were no postoperative complications in 36 patients. The surgery promotes daily rectal emptying once in 36 hours without laxative and without uncontrolled stool evacuation. There were 6 complicated postoperative outcomes. One patient presented successive anastomotic fistula, anastomotic stenosis and after that recurrent enteroctitis and persistent soiling. Postoperative anastomotic fistula was observed in two patients, one of them requiring colostomy and the other, with minor lesion, was cured after oral nutrition suspension and total parenteral nutrition for 8 days. In patient with colostomy we registered anastomotic stenosis after a period of 4 weeks and we controlled it through regular dilatations for three months. There was one insufficient colic resection and the patient developed an important pseudo-obstructive syndrome which necessitate a redo laparoscopic surgery. There were 4 cases with postoperative soiling, all of them presented in patients with at least 2 enterocolitis episodes in the first 3 postoperative months. One case of soiling appeared in one of the two children with anastomotic fistula. The other 3 cases did not reveal any pathologic findings as an explanation of soiling. In 2 cases we resolved this continence problem through nutritional therapy and Loperamid for 3 to 4 months. One patient presents recurrent postoperative soiling after 2 postoperative years and another after 3 years.

Comments

Laparoscopic surgery and totally transanal approach represent the return of surgery to the basic principles of the Swenson technique which resects the aganglionic rectum and practice coloanal anastomosis, giving up the procedures that maintain in transit the aganglionic rectum. There are, in fact, two clinical criteria which analyse the postoperative results: the frequency of spontaneous rectal evacuation and anal continence. Endorectal resection technique is practiced above the sphincteric structures, far from the anal discriminative reflexing zone, because the dissection starts at lcm above the dentate line. There is an initial submucosal dissection on a bowel length of 4 to 6 cm, after that we enter the perirectal space. This approach preserves the sphincteric structure and genitourinary elements (urethra, seminal vesicles, deferent duct) which remain out of the dissecing plane. This is why the technique may be considered a Soave-Boley technique in cases which extend the dissection until the rectosigmoid junction. (5) Even in that case, the demucosed rectum is resected or cut in a longitudinal manner, anterior and posterior. Without this technical detail the rectum may become a circular stenotic tube which may produce the postoperative incontinence phenomenon. The anal incontinence may appear in postoperative period as a recurrent or permanent complication without a correlation with technical aspects. Although this continence pathology was attributed to excessive dilatation of the internal sphincter with rupture of its elements, we have to notice that there are also other surgical techniques, as Duhame technique which realise this sphincteric dilatation and there are patients presenting perfect postoperative continence even in the absence of the internal sphincter(anorectal malformations treated using posterior sagittal approach) The anal continence and frequency of rectal evacuation may be related also to other technical details: dilatation and thickness of the bowel wall at the level of the coloanal anastomosis, the degree of tension in anastomosis and the level of the colic resection. A coloanal anastomosis with an important colic dilatation is technically difficult and may generate postoperative complications: leakage, fistulas and mucosal prolapse. As a principle, it is recommended to start the resection above the dilated zone so that the anastomosis may be done with a normal colon. In clinical practice, this principle may consists of a too longer colic segment (colic surgery is, in fact, the surgery of the colic vessels -7-) resection with unfavourable postoperative functional outcome (enterocolitis, soiling, perineal erosions). Mucosal prolapse may be avoided by suturing the anastomosis in two planes, with mucous superficial one. It is unanimously agreed that the level of the resection is an essential criteria of a good postoperative result. The usual histologic examinations for Hirschsprung’s disease are limited to direct or indirect (AChE level) determination of the presence of ganglia in the myenteric and submucous plexus. For the rest of the entities, known as neuropathic disorders (chronic intestinal pseudoobstruction and neurointestinal dysplasia), myopathic disorders or connective tissue disorders (colic desmosis) the diagnosis is difficult to document except for the research Cliniques. The presence of these entities may explain the unsatisfactory results even in cases with standardized diagnostic and surgical technique. Another technical aspect is the tension inside the anastomosis. Beside the technical surgical details, a tension –free anastomosis depends on the anaesthesia technique and the relaxation of the sphincteric structures, which can be obtained combining a spinal anaesthesia. One patient was reoperated using endoanal technique after an insufficient resection. This redo surgery had a good postoperative outcome with restoration of intestinal function, without anal incontinence. The decision for the second surgery was made after the histologic finding of the absence of the ganglionic structure in the resected bowel. There are cited cases when endoanal redo surgery was recommended in patients with ganglionic structures present in the full thickness biopsy specimen but with clinical persistent constipation and frequent episodes of enterocolitis.(6)

Conclusions

One can say that endorectal transanal approach represents a technical progress in surgical strategy of
congenital megacolon. This technique is characterized by
significantly diminished intraoperative trauma, avoiding or
minimizing abdominal surgical stage and by rapid recovery
of the general status. This approach can avoid some
postoperative complications specific to surgical
interventions which include pelvic dissection through open

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POSSIBILITIES OF COMPLEX REHABILITATION THERAPY IN GENETIC NEUROMUSCULAR AND OSTEOARTICULAR DISORDERS

Cristian Milicin¹, Dan Nemeș¹,², Elena Amăricăi¹, Liliana Caţan¹, George Puenea¹, Daniel Popa¹,²

Abstract

Introduction: Genetic neuromuscular and osteoarticular disorders causing a motor and sensory deficit raises not only pathological issues related to its presence, but medical issues in general. Purpose of the study: Highlighting the importance of the complex and sustained medical recovery therapy, installed early in patients with Duchenne muscular dystrophy, Becker muscular dystrophy and Pierre Robin syndrome. Material and method: In a period of 5 years, 8 patients with genetic muscular dystrophy were studied, aged between 3 and 13 years, who were evaluated completely and who followed a complex recovery treatment, 3 cures of 15 sessions, with a frequency of 3 sessions per week during one year. Results: By applying the complex, sustained and long-term treatment, we obtained a significant improvement of the clinical and functional parameters, in case of all patients studied. Conclusions: The complex recovery treatment, applied early, leads to stimulation and acceleration of the nervous regeneration process.

Keywords: Duchenne muscular dystrophy, Becker muscular dystrophy, Pierre Robin syndrome, medical recovery, nervous regeneration.

Introduction

Genetic neuromuscular and osteoarticular disorders determines a motor and sensory deficit, with strong implications on economic, professional, social and not least, family level.

It raises not only pathology issues related to its presence, but medical issues in general. This pathology causes particular concern of physicians, patients and their entourage, concern about the physical and mental handicap of patients, about the caregivers, and the technical means available for the physician, about the complex treatment possibilities and the appropriate social integration.

The complex therapy of genetic neuromuscular and osteoarticular disorders and the long-term interdisciplinary collaboration are very important, based on the idea that early, complex and sustained therapy, closely monitored by a multi specialized team consisting of: family doctor, neurologist, dentist, medic rehabilitation physician and psychologist, will have a much higher efficiency than individual therapy. (1- Muresanu, 2002)

Objective of the paper

Revealing the importance of early establishment of the medical recovery treatment in patients with Duchenne muscular dystrophy, Becker muscular dystrophy and Pierre Robin syndrome.

Studying the behavior of clinical, functional and electrophysiological parameters in patients with Duchenne muscular dystrophy, Becker muscular dystrophy and Pierre Robin syndrome, before and after the treatment, comparing the results obtained after three sessions of complex medical rehabilitation therapy.

Analysis of the possibilities for stimulating neuronal regeneration, with probable potential of neuroplasticity, after applying the chosen approach.

Material and method

During the period April 2008 – April 2013, at the BFT Clinical Hospital in Timișoara, we studied 8 patients, 3 with Duchene muscular dystrophy, 3 with Becker muscular dystrophy and 2 with Pierre Robin syndrome, aged between 3 and 13 years.

Each patient underwent complex assessment to determine the severity of the disease:

- General assessment: using the FIM (FUNCTIONAL INDEPENDENCE MEASURE) scale (2 – Nemes, 2001)
- Assessment of the muscle strength:
  - Determining the degree of force by manual method according to the method in 6 steps (0-5) of the National Foundation for Infantile Paralysis (2 – Nemes, 2001)
  - Assessment of muscle strength with the pressure gauge, which registers the grip of the patient's affected hand. The results obtained from the affected limb were compared to the results from the healthy limb.
- Assessment of sensitivity: tactile, thermal, painful, vibratory, proprioceptive, kinesthetic.
- Determination of the adjustment coefficient α:
  - The adjustment coefficient α is defined as the ratio between the intensity of triangular current with a duration of 1000 ms and the intensity of rectangular current with the same duration, for values that produce minimal contractions (2 – Nemes, 2001). Determining the adjustment coefficient is very important because its value reflects the degree of denervation of muscles to be subjected to electro-stimulation.

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- Electrodiagnosis was conducted at the level of affected muscles, thus the adjustment coefficient $\alpha$ was determined.
  (3-Kimura, 2001)
- As a working technique, the bipolar technique for determining curve $I/t$ (normal values for adjustment coefficient $\alpha$: normo-innervated $\alpha=2.5-6$; partially denervated $\alpha=1-2.5$; totally denervated $\alpha<1$). We used the Siemens Universal – Neuroton 826 device (Figure 1A).
- To determine the adjustment coefficient $\alpha$ we used point electrodes that were placed according to the standard methodology.
- Determination of the motor nervous conduction velocity in the affected muscles: We used the principles and the working method standardized by the northern school (4-Milicin, 2008). We used the Keypoint - EMG/EP SySTEM device manufactured by Alpine Biomed Corp. USA. (Figure 1B)

Each patient received an initial comprehensive assessment, as well as complex assessments before and at the end of each cure of complex treatment and rehabilitation. The main objectives of the physiokinetotherapy treatment applied to the 8 patients were as follows:

1. Prevention and correction of deviations with the help of fixed orthoses and passive mobilizations (Figure 2) (5-Stalberg, 1993).
2. Prevention of joint stiffness: passive mobilizations (Figure 3A), auto-passive, passive-active (Figure 3B), active (Figure 3C), and hidrokinetotherapy.
3. Rare vasculotrophic disorders were eliminated using antideclive positions, massage for facilitating the circulation (Figure 4) and elastic gloves.
4. The reeducation of paralyzed muscles was achieved by:
   - Electro-stimulation of partially denervated muscles
   - Initially: elements of facilitation, contra-lateral exercises, PNFs, Kabat diagonals (D1E, D2F), analytical exercises
   - Later we added exercises for increasing muscle strength and resistance (Figure 6).
   - Finally, we applied stability and coordination exercises (Figure 7).

Results and discussion
The overall evolution during the 3 sessions was generally good. Comparing the FIM results, initially, with the intermediary ones (at the end of each cure) and with the final ones (after 1 from the beginning of the treatment) they significantly improved (Figure 8).

Most patients reached 3 points on the muscular strength scale determined manually after the 3 cures (Figure 9A) and presented a growth by 0.4-0.6 of the values of the muscular strength measured with the pressure gauge after the three cures (Figure 9B).

There was an increase by 7-9 of the sensitivity assessment values at the level of the affected limb at the end of the treatment in most cases (Figure 9A).

After the treatment, most patients presented a growth by 0.5-0.8 of the values of the adjustment coefficient $\alpha$ (Figure 9A).
Figure 2. Fixed orthose.

Figure 3A. Passive mobilizations,  Figure 3B. Auto passive-active mobilizations,  Figure 3C. Active mobilizations

Figure 4. Massage for facilitating the circulation.

Figure 5. Electro-stimulation of partially denervated muscles.

Figure 6. Exercises for increasing muscle strength and resistance.
Figure 7. Stability and coordination exercises.

Figure 8. FIM results.

Figure 9. The sensitivity assessment values.
Conclusions
An aggressive approach of the patient with genetic neuromuscular and osteoarticular disorders is essential, but the effort during exercise (regardless of the means of performance) must be progressive, individualized, applied with care, because the increased functional requirements can damage the muscle (as final element in the performance of the movement in the ‘neuro-muscular-artro-kinetic apparatus’) immature or dystrophic, which will not be able to support any over tension (‘overload’).

The clinical and electrodiagnostic assessment of genetic peripheral motor neuron lesions is mandatory to establish the location and the level of nervous damage, as well as a proper therapeutic strategy.

The parameters considered for the study can very well monitor initial deficits and the evolution under treatment.

The stimulation means used were very efficient in the clinical and functional evolution of the genetic peripheral motor neuron syndrome, both for functional and for organic lesions.

The analysis of data from the study allowed us to conclude that the proposed treatment can have two effects for genetic peripheral neuron lesions:
• Stimulation of the nerve by producing supramaximal impulses triggering a motor response
• Stimulation of limb regeneration by accelerating the recovery process of tissues by activating the metabolism and stimulating the cytogenesis.

Taking in consideration the good results obtained in a short time (12 months), we may assume that the used rehabilitation methods also have a neuroplasticity effect.

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TREATMENT BY INJECTION WITH BLEOMYCIN OF RISK HEMANGIOMAS CASE PRESENTATION

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Abstract
Cutaneous hemangiomas are the most common tumors of infant and children. Risk or complicated hemangiomas are considered those hemangiomas located in specific anatomic areas, which can interfere with vital functions and can cause serious deformities, irreversible. Various methods of treatment are described for these complicated hemangiomas. In our clinic we used bleomycin. Article refers to three cases of patients treated with intralesional bleomycin injection which shows hemangiomas located in risk areas: nose, tongue, and ear. After these injections we obtained a significant reduction of vascular tumors and improve organs function. Cases show that intratumoral injection with bleomycin can be considered as an alternative to the surgery.

Key words: hemangiomas, complications, intralesional bleomycin injection

Introduction
Hemangiomas with special location such as neck, face, holes conduct a special approach. Since the last 5 years the number of cases with head and neck damage was predominantly in our clinic. This show the importance of knowing the modality of investigation and treatment of these hemangiomas.

In the table below you can see the distribution of hemangiomas/year (table 1)

This distribution of hemangiomas is very important because, depending on the area and the affected organ, should consider immediate treatment or therapeutic expectation.

As you can see the head and neck damage was predominantly. (Chart 1)

For treating this type of hemangiomas we used bleomycin. This agent produced extensive fibrosis and spontaneous resolution of hemangiomas. (1)

The beneficial effects of intralesional bleomycin injection (IBI) in the treatment of haemangiomas were initially reported by Kullendorf (2) and Saruhan et al. (3) More recently, the effectiveness of IBI was evaluated in 37 patients with haemangiomas in a study conducted by the Pretoria Vascular Malformation Study Group. Complete resolution or significant improvement was seen in 87% of the patients. (4)

Despite the promising results the bleomycin's mechanism of action in haemangiomas remains unknow.

Material and method
I considered for this study cases of hemangiomas whose development may cause significant functional impairment or cosmetic.

This paper consists of three cases of hemangioma.

Working protocol consists in a intratumoral injection of bleomycin solution obtained by diluting 15 mg lyophilized blomycin in 15 ml of normal saline. The injections were made at a variable interval of time, usually three weeks.

Number of injections was between one and six.

Case presentation

First case
The 6-month old infant was admitted to our clinic for fever, unfavorable and rapid vascular tumor growth. CT examination reveals no damage other than the nasal wing. He was treated with intralesional injections of bleomycin as a 0.5 mg/ml solution in the local area. After 4 weeks, when the child was returned in our clinic he look better. Has made a new intralesional injection. After this second injection tumor was limited both in area and intensity. Third injection was performed. After this third injection we see a significant reduction of hemangioma with presence of nasal deobstruated fossa.

The second case
Patient with age of 2.5 years. In the picture below are found a lingual hemangioma, located at the tip of the tongue (fig 6). I decided bleomycin injection of tumor. As shown in the next picture after this single injection, we see a significant reduction angioma (fig. 7. Hemangioma injected after 6. The child resumes normal function of swallowing and speech.

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### Table 1. Cutaneous hemangiomas by anatomic segment affected

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<td>3</td>
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</tr>
<tr>
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<td>1</td>
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<tr>
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<td>0</td>
<td>1</td>
<td>0</td>
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<td>multiple</td>
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<td>1</td>
<td>0</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

**Chart 1.** Distribution of cutaneous hemangiomas in our clinical study per years.

**Fig. 2.** Uninjected hemangioma.

**Fig. 3.** After first injection.

**Fig. 4.** After second injection.

**Fig. 5.** After third injection.
Fig. 6. Uninjected hemangioma.

Fig. 7. After first injection.

Fig. 8. Uninjected hemangioma.

Fig. 9. After first injection.

Fig. 10. After second injection.

Fig. 11. After third injection.

Fig. 12. After the fourth injection.

Fig. 13. After the fourth injection.
The third case

A patient with age of two months, who shows a hemangioma located in the the ophthalmic and ear area which makes it be considered an emergency. As this hemangioma show when the child was presented in our clinic (fig 8). After the first injection, at intervals of four weeks is seen as ulcers and reduce tumor size was significantly reduced (fig.9). Proceed to the second injection. After six weeks of this, notice the disappearance of ulcers and normal skin tissue appearance (fig 10). It injects the third time remaining hemangioma. After 5 weeks tumor look like this (fig 12, 13)

Results and discussions

Six patients with complicated hemangiomas have been treated with this method during a five-years period. The lesions regressed 60-100% during 6-14 months with one to six bleomycin injections. We believe that intraleional BLM injection is simple, and very useful for treatment of complicated cutaneous hemangiomas. And other authors report achieving a response of greater than 75 percent reduction in the size of the hemangioma after bleomycin intraleional injections (6).

Patient age is not a problem. In this context we refer to Asian authors (7) who made injections to a one day newborn and they found a good involution of vascular tumors without major risks to determine the avoidance of injection.

Also, other authors recommend injection of bleomycin, there were no complications or side effects. Bleomycin therapy of painful, massive hemangiomas can be recommended in older children (2).

Intraleonal bleomycin is another method with which to treat hemangiomas in children and may be particularly helpful for large hemangiomas of the head and neck (6).

In the initial phase there is the temptation to straighten the treatment to a surgical one because complications seemed inevitable: ENT complications, impaired swallowing and speech, sphincter damage, impaired respiratory, dermatological and infectious.

A careful monitoring and proper injection of bleomycin in tumors showed that evolution is very good and demonstrated that exist other way than surgery.

Major difficulty lies in convincing patients to follow treatment until complete disappearance of tumor and do not abandon the medical presentation in various stages.

Conclusions

Intraleonal bleomycin injection is an effective treatment in hemangiomas, obviating the need for invasive primary surgery or systemic treatment.

Injection can cause a significant involution of vascular tumors.

In cases of risk hemangiomas have acted immediately, because their growth may influence the organ function, or child aesthetics.

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DUODENAL ATRESIA REPAIR - CASE REPORT

A Surd¹, H Gocan¹, Rodica Muresan¹

Abstract

Background: Duodenal atresia and stenosis is a frequent cause of congenital high intestinal obstruction. Current operative techniques and contemporary neonatal critical care result in a 5% morbidity and mortality rate. Congenital duodenal atresia complicated by wound dehiscence is very rare, yet not uncommon.

Case presentation: A 3-day-old female baby was hospitalized for bilious vomiting since the day before. After the diagnosis was made a diamond shaped duodenoduodenostomy was performed through a midline incision. On the 3rd postoperative day clear yellow peritoneal fluid started draining from the wound. To rule out an anastomotic leakage oral methylene blue was given through the NG tube. Wound repair was performed on the 4th postoperative day.

Conclusion: This complication can be treated by early diagnosis and surgical intervention. A number of factors for abdominal wound dehiscence have been identified but the risk of developing abdominal wound dehiscence can be reduced by using a transverse incision, preventing wound infection, and by applying optimal surgical technique in every patient.

Key words: duodenal atresia, intestinal obstruction, wound dehiscence

Introduction

Congenital duodenal obstruction is one of the most common anomalies in newborns and infants. Several embryological defects in foregut development, canalization or rotation lead to congenital duodenal obstruction such as duodenal atresia, duodenal web and malrotation. In addition, anomalies of the pancreas can cause duodenal obstruction. Although advances in management in neonatal intensive care, respiratory support and nutritional therapy have dramatically increased the survival rate, the relatively high postoperative reoperation rate remains a challenge in the treatment of congenital duodenal obstruction.[1] We report a case who required reoperation after initial repair for a wound dehiscence on the 4th postoperative day.

Case report

A full term, 3-days-old baby girl borned in a private clinic by C-section was referred to our hospital because of recurrent bilious vomiting since the second day of life. Plain and contrast radiographs demonstrated a dilated stomach and a dilated proximal duodenum (Fig 1).

Fig 1. A,B,C: Preoperative radiographs showing a dilated stomach and proximal duodenum.
D,E: Postoperative radiographs showing aerated of the bowel and the presence of the transanastomotic tube.
F,G,H: Contrast radiograph showing passage of gastrografin and no anastomotic leakage.

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Discussions

Congenital obstruction of the duodenum (CDO) including duodenal atresia and stenosis occurs in approximately 1 in 6000 to 1 in 10,000 births.[2,3] Vomiting in the newborn demands early investigation of the alimentary tract, in particular, a plain film or gastrointestinal series, so that these children will be seen and operated on early with the best chance for survival. Although survival in infants, with congenital intestinal obstruction has improved, duodenal obstruction continues to present unique challenges.

The preferred surgical repair of the primary anomaly is a diamond-shaped (proximal transverse to distal longitudinal) anastomosis. For the surgical treatment of congenital intrinsic duodenal obstruction Kimura, in 1977, introduced an anastomotic technique of side-to-side duodeno-duodenostomy in two layers, placing the bowel incisions to form a “diamond-shaped” (DSD) incision and created a larger stoma. In 1990, he refined his technique based on a transverse incision in the distal end of the proximal duodenum and a longitudinal incision in the distal duodenum. The double-layer anastomosis was completed using 5-0 or 6-0 catgut or Vicryl continuous inner and 6-0 silk interrupted outer layer sutures. By this technique the anastomosis recovered its function in a significantly shorter time period and early postoperative feeding could be started.[4,5]

Fascial dehiscence is uncommon in newborns but can have serious consequences when it occurs. There are multiple risk factors for fascial dehiscence, including the type of incision used. Pediatric surgeons often use a supraumbilical transverse incision particularly in infants because of the access this incision provides to the entire abdomen.[6] We used a vertical incision which is more apt to dehisce than transverse incisions in children, particularly babies. Abdominal wound dehiscence is a severe complication of abdominal surgery in children. Its sudden presentation and requirement of surgical repair in the majority of cases underline the stressful character of this complication for both patients and parents. Literature on risk factors for abdominal wound dehiscence in children is limited. Reported incidences range from 0.4–1.2%, with mortality rates reported as high as 45% [6,7-10].

This complication can be treated by early diagnosis and surgical intervention. A number of factors for abdominal wound dehiscence have been identified but the risk of developing abdominal wound dehiscence can be reduced by using a transverse incision, preventing wound infection, and by applying optimal surgical technique in every patient.

References


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OVERVIEW OF CLINICAL FEATURES, DIAGNOSIS AND AETIOLOGY OF PARAPNEUMONIC EFFUSION AND EMPYEMA IN CHILDREN

Anca Budusan1,2, I Paraian1, H Gocan1,2, I Dobrescu2, Bela Farkas1,2

Abstract
The incidence of empyema and Parapneumonic effusion in children in Romania is still high. A retrospective study was undertaken to investigate the clinical features and etiology of cases if empyema and Parapneumonic effusion admitted in department of Pediatric Surgery, Emergency’s Children Hospital, Cluj-Napoca.

Keywords: empyema, children, pneumonia

Introduction
Parapneumonic effusion occurs in approximatively 3 per 100 000 children per year; it occurs more frequently in pre-school children and more commonly in winter and spring and boys. Empyema is defined as the presence of pus in the pleural space. Childhood empyema is an important complication of bacterial pneumonia. It is considered that small pleural effusion may be present in up to 40% of bacterial pneumonias. Parapneumonic effusion (PPE) and empyema (E) lie on continuum: the stage of the effusion is best assessed using chest ultrasound [1]. E and complex PPE effusion represent parts of a spectrum of disease, with three stages of progression being recognized:

- **Stage 1 (“exudative”):** clear, sterile fluid accumulation within the pleural cavity without the presence of loculations (PPE)
- **Stage 2 (“fibrinopurulent”):** fibrin deposition within the pleural space giving rise to loculations; presence of pus (complicated PPE or E); it is usually accompanied by bacterial invasion
- **Stage 3 (“organisational”):** organized multiloculated empyema with lung entrapment and pleural rind formation, functionally impair gas exchange; this is the stage with complications, as chronic empyema, bronchopleural fistula, lung abscess or spontaneous perforation through the chest wall [2].

The etiology of empyema is closely related with that of community-acquired pneumonia[3]. The majority of PPE are due to Streptococcus pneumonia. Staphylococcus aureus is the leading cause of E in developing countries and in children from families with low social economic status; it occurs more frequently in young infants and in summer months when skin infections are more prevalent.

Haemophilus influenzae type b is now an unusual cause of empyema in countries where the Hib vaccine has been introduced into the routine immunization schedule. Anaerobic infections are rare, but may occur in children with neurological disorders at risk of aspiration pneumonia. Mycoplasma pneumoniae is reported to be a common cause of PPE but rarely of E, also Mycobacterium tuberculosis [4].

Children usually present with a severe pneumonia, or a pneumonia that not respond well to initial therapy. Empyema should be suspected in a child with pneumonia who remains persistently febrile despite adequate antibiotic treatment. The clinical features are usually that of pneumonia and accompanying PPE, such as fever, tachipneea, respiratory distress, decrease or absence of breath sounds and dullness on percussion. Severe cases may present with sepsis, dehydration or respiratory failure. Large pleural effusions that cause mediastinal shift will displace the trachea and cardiac apex from the affected side. Pleuritic chest pain or referred abdominal pain may be reported in older children. Tuberculosis pleural effusion may complicate 2-30% of cases of childhood tuberculosis and must be differentiated from PPE or E. A history of persistent cough, weight loss and a household tuberculosis contact is suggestive of childhood tuberculosis. In primary TB, a unilateral PE develops 6 to 12 weeks after infection. It represents a hypersensitivity reaction and is associated with a positive tuberculin skin test (TST) in over 90% of well-nourished immunocompetent children. Tuberculosis alone is a rare cause of empyema and bacterial co-infection is a more likely scenario. Further history and examination should note any evidence of systemic illness that may cause pleural effusion and include congestive heart failure, edema and hypoalbuminemia (as in nephritic syndrome), malignancy, post-streptococcal glomerulonephritis and connective tissue disorders. Questioning and looking for a HIV infection could be important in patients presenting with immunodeficiency.

An anteroposterior chest X-Ray (CXR) should be done in all children with suspected empyema or PPE. Obliteration of the costophrenic angle indicates a fluid collection within the pleural space. Complete “white-out” of the affected hemithorax with mediastinal shift to the contralateral side is seen in large fluid collections.

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Radiological evidence of pneumonia is usually found and the presence of pneumothorax, pneumatoceles or lung cavities suggests Staphylococcus aureus as etiology, or rarely complicated hydatid cysts. Ultrasound is useful to differentiate the pleural fluid, and also is helpful in identifying pleural thickening and loculations, to guide chest drain insertion and perform follow-up. A computed tomography (CT) scan is usually recommended in suspected complicated cases (lung abscess, parenchymal lung abnormalities, mediastinal associated pathology). Further investigations are aimed at identifying an etiological agent. Analysis of pleural fluid using Gram stain and bacterial culture will help diagnosis. Blood culture is very important and may be positive in 10-15% of empyema cases. In cases when TB infection is suspected, microscopy and culture of sputum or gastric lavage and TST are indicated. Acute-phase reactants including white cell count (WCL), CPR and ESR (erythrocyte sedimentation rate) and procalcitonin may have a role in monitoring clinical progress and response treatment.

Most children with PPE and E can be managed by chest tube drainage; still some children may require a thoracotomy and further surgical procedures (debridement, resection of necrotic tissue, closure of fistulas) [5]. Small effusions that are not associated with significant respiratory distress (no need for oxygen therapy, the child does not have high fever and is not in pain) may be managed conservatively. Small effusions may be regarded as being less than 1 cm for children under 2 years of age and under 2 cm for older children. All children with pleural effusion should be initially treated with intravenous antibiotics, and those should be continued after the chest drain has been removed. Oral antibiotics should be given at discharge for 2 weeks (up to 4 weeks in some cases), depend on culture results. Intrapeural fibrinolysis and video-assisted thoracoscopic surgery (VATS) are modern interventions widely used in high-income countries, but most unavailable in our medical society [6], [7]. In the organized stage the goal standard for surgical treatment remains thoracotomy and decortications. Through pleural debridement release of encased lung parenchyma by carefully removing the thick pleural peel from the entire lung surface and making the lung expand meticulous closure of all major leaks and excision of necrotic lung tissue.

Purpose

The aim of this study is to evaluate clinical presentation and etiology of parapneumonic effusion and empyema in children with complicated pneumonia, who required surgical treatment and to identify risk factors for this.

Materials and Methods

Children with empyema were retrospectively recruited over 3 year’s period from January 2009 to December 2011 (included). A case of childhood pleural effusion was defined by the investigators as the presence of fluid inside the pleural cavity in a child with respiratory symptoms, fever and raised serologic inflammatory markers, and the presence of pleural collection was confirmed using chest X-Ray (CXR), ultrasound (US) or computed tomography scan (CT). Presence of pus cells in the pleural fluid was defined as empyema. Clinical data collected included: age, sex, area of residence, risk factors (including chronic illness and other predisposing conditions), clinical presentation, diagnosis tool, stage of inflammation, etiology. We excluded from our study pleural collections due to other causes (accidental chest injuries, postthoracotomy, and perforations of esophagus). A total of 16 patients with empyema were evaluated in this study.

Results

Our study included 16 children, 10 girls and 6 boys, age between 5 months to 17 years. The average age of the 16 patients was 5.15 years (Table 1).

<table>
<thead>
<tr>
<th>Table 1. Number of patients related to age.</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 y</td>
</tr>
<tr>
<td>6</td>
</tr>
</tbody>
</table>

Majority of patients are included in preschool-age (before 7) (68.75%).

Risk factors were identified as in the following chart: poor nutritional status was the most frequent condition, as
25%; two patients had immunosuppressive treatment for leukemia and Hodgkin disease (12.5%), one patient presented with cerebral palsy and conditions for aspirating pneumonia, and one had obesity (6.25% each) (Table 2).

Table 2. Risk factors for developing a complication of pneumonia.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
<td>1</td>
</tr>
<tr>
<td>Malignancies</td>
<td>2</td>
</tr>
<tr>
<td>Malnutrition, poor weight for age</td>
<td>3</td>
</tr>
<tr>
<td>Cerebral palsy, epilepsy</td>
<td>1</td>
</tr>
</tbody>
</table>

Clinical symptoms were related to pneumonia: chills, fever, dyspnea, chest pain, malaise, cough, increased sputum production, in all 16 cases, the median duration of symptoms prior to admission was 7.32 days, (range 3 to 14). Fever, respiratory distress and cough were the main presenting complaints. Aerobic pneumonic infections will tend to present with an acute febrile illness, localized pleuritic chest pain, sputum production and leukocytosis. Infectious with anaerobes tend to lead a more insidious clinical course with less pronounced fever and more generalized systemic symptoms, such as poor appetite and weight loss.

Our patients presented in three different stages of disease (Chart 1):
- Stage 1 (exudative): 2 (14.84%)
- Stage 2 (fibrinopurulent): 8 (50%)
- Stage 3 (organizational): 6 (37.5%)

Diagnosis imaging tools used were: chest-X Ray (CXR), chest ultrasound (US), CT scan. CXR was used as a modality of diagnosis in all 16 patients (100%) ultrasound was used in 8 patients (50%), especially for follow-up and trying to avoid irradiation in children, and CT scan provided further informations for 6 patients, those who had complications in 3rd stage as fistulas, pneumothorax, lung abscess (37.5%).
All these patients had history of intake of broad spectrum antibiotics and for that, etiological diagnosis was difficult.

Needle aspiration of pleural space was performed in every case and pus was sent for culture and sensitivity. Identification of the causative agent in children with empyema is often difficult, necessitating the use of empiric rather than specific therapy.

Etiology was: MRAS 1 case, Staphylococcus aures 1 case, Streptococcus pneumoniae 1 case, tuberculosis 2 cases and remained unknown for other 11 cases, due to previously mentioned antibiotic treatment.

Right side was involved in 6 cases (37.5%), and left side in 10 cases (62.5%).

Acute-phase reactants were at high levels in all cases, as in following table (Table 3):

<table>
<thead>
<tr>
<th>Case no</th>
<th>White blood cell count x10³</th>
<th>Neutrophilia</th>
<th>PCR mg/dl</th>
<th>ESR mg%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>19000</td>
<td>91%</td>
<td>40.8</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>18900</td>
<td>76%</td>
<td>26.4</td>
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</tr>
<tr>
<td>3</td>
<td>24100</td>
<td>75.4%</td>
<td>15.1</td>
<td>20</td>
</tr>
<tr>
<td>4</td>
<td>12200</td>
<td>72%</td>
<td>18.7</td>
<td>73</td>
</tr>
<tr>
<td>5</td>
<td>20500</td>
<td>63%</td>
<td>16.6</td>
<td>110</td>
</tr>
<tr>
<td>6</td>
<td>16700</td>
<td>69.5%</td>
<td>19.8</td>
<td>75</td>
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<tr>
<td>7</td>
<td>20800</td>
<td>71%</td>
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<td>75</td>
</tr>
<tr>
<td>8</td>
<td>18300</td>
<td>36.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>47000</td>
<td>76%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>18500</td>
<td>56%</td>
<td>42</td>
<td>55</td>
</tr>
<tr>
<td>11</td>
<td>12000</td>
<td>64%</td>
<td>12</td>
<td>26</td>
</tr>
<tr>
<td>12</td>
<td>18600</td>
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<td>17.6</td>
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<td>45</td>
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<tr>
<td>15</td>
<td>6700</td>
<td>63%</td>
<td>21</td>
<td>40</td>
</tr>
<tr>
<td>16</td>
<td>18000</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Discussions

Empyema is usually the result of infected pleural effusion that is associated with ongoing, uncontrolled, pulmonary sepsis or pneumonia. Age plays an important role in the development of empyema. Small children and infants are more commonly affected than older children.

The identification of causative agents in children with empyema can be achieved by culturing blood or pleural fluid. Poor socioeconomic groups with pneumonia are more predisposed to progress to empyema.

Pleural infection should be suspected in all patients with pneumonia, in particular those who fail to respond to appropriate antibiotic therapy, as defined by persistent fever, leukocytosis, and raised inflammatory markers such as CPR. Immunosupressed hosts and infants can present with disproportionately mild symptoms – relative to the severity of the pleural infection. The size of pleural effusion varies, and cannot be used to predict infective etiology.

Any patients presenting with pneumonic symptoms or those who are failing to respond to appropriate therapy and/or who have a pleural-based opacity on CXR that obscures the diaphragm, should be considered for further imaging and investigations.

US of the thoracic cavity can reliably demonstrate loculations and septations and increase the success rate and reduces the complications of thoracocentesis. As a result, we suggest that in the pediatric population US should be routinely used, and CT only in special circumstances, when the diagnosis is in doubt and to provide informations on underlying associated abnormalities such as pulmonary abscesses.

Despite the advances in the diagnosis facilities and early referral, empyema is still one of the most serious chest surgical problems in childhood.

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93
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EPIDEMIOLOGY OF BURN WOUNDS IN PEDIATRIC PATIENTS ADMITTED AT THE EMERGENCY CHILDREN’S HOSPITAL OF CLUJ NAPOCA

Doina Elena Zamora¹, I Paraian², H Gocan², Simona Barsan¹

Abstract
The thermal injury and the subsequent burn wound represents one of the great challenges of trauma. The present study addresses the causes and extent of thermal injuries affecting a specific group of the pediatric population: infants and toddlers. This particular group is prone to accidents and abuse being in the direct care of adults, their parents [1].

The 105 patients aged between 0 and 3 years were admitted in our department over a period of 5 years. All the patients have met the internationally recognised criteria for hospitalization and were categorized based on type of thermal injury, depth of the wound, body surface affected, gender and living environment. Within the studied group we found a prevalence of burns caused by scalding mostly localized at the head, neck, chest and lower extremity. There was a slight prevalence of male subjects. Also most of our patients originated from challenging social environments.

The findings of this research are consistent with those published in literature, regarding mechanism, gender, surface and social background [1,2,3,4].

Key words: pediatric patient, harming agent, thermal injury, total body surface, degree of burn wound

Introduction
The thermal injury occurring in the early childhood period encounters a specific biological and immunological terrain, having as a result some particularities regarding treatment and outcome. The immature organism is extremely sensitive to any minor unbalance but it presents also extraordinary healing and recovery capabilities, superior to the adult.

The types of burns and the events preceding the injury are somehow specific in this age category, sometimes raising the doubt if we have to deal either with an accident or an abuse.

The frequent occurrence of this type of injury at an age dependent of the parental and socio-economic factors and also its psycho-social implications over the future adult, confers a wide study base.

Purpose
The purpose of the current study is to identify the most common types of thermal injury, degree of the burn wound and percentage of the total body surface affected in the pediatric population between 0 and 3 years of age. The age range chosen is particularly important due to the role played by the parental supervision, or lack of it. The end goal is to identify the most exposed population and that of establishing some guidelines to prevent thermal injuries of the early childhood.

Materials and methods

The present study includes pediatric patients with ages ranged between 0 and 3 years, admitted in the Department of Pediatric Surgery over a 5 year period from 01.01.2004 until 30.05.2009. Some of these patients were discharged with complete wound epithelization, others were discharged and treated as outpatients until healing.

The total number of pediatric patients studied was 105, the distribution per year is as follows, as seen in table 1:

<table>
<thead>
<tr>
<th>Year</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
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<tbody>
<tr>
<td>Patients</td>
<td>21</td>
<td>20</td>
<td>15</td>
<td>20</td>
<td>13</td>
<td>13</td>
</tr>
</tbody>
</table>

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95
Criteria for hospitalization were those cited in the literature, namely [3,4,5,6]:
1. Second and third degree burns over 10% in patients under 10 or over 50 years
2. Second and third degree burns over 20% in patients of all age groups
3. Burns involving the face, hands, feet, genitalia, perineum, major joints
4. Third degree burns over 5% in patients of all age groups
5. Electrical burns, including those caused by lightning
6. Chemical burns
7. Inhalation injury
8. Pre-existing medical conditions that may complicate treatment
9. Associated injuries, fractures
10. Burns in children admitted to hospitals without qualified personnel or equipment specific to pediatric care
11. Burn patients requiring a special social, emotional support, suspected child abuse, substance abuse

Results
The degree of the burn wounds was I, IIA, IIB, III, IV, in most cases the same patient showing varying degrees of burns, as depicted in table 2. The depth of the burn wound was considered according to the latest classifications [3,4,5,6].

Body surface area affected by thermal aggression ranged between 1 and 80%, (see table 3).
The burned area was calculated using the Lund-Bowder diagram [3,5].

<table>
<thead>
<tr>
<th>Degree</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>0.95</td>
</tr>
<tr>
<td>IIA</td>
<td>6</td>
<td>5</td>
<td>5</td>
<td>9</td>
<td>3</td>
<td>2</td>
<td>30</td>
<td>28.58</td>
</tr>
<tr>
<td>IIB</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>12</td>
<td>11.45</td>
</tr>
<tr>
<td>III</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>0.95</td>
</tr>
<tr>
<td>I, IIA</td>
<td>3</td>
<td>4</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>17</td>
<td>16.19</td>
</tr>
<tr>
<td>IIA, IIB</td>
<td>5</td>
<td>8</td>
<td>6</td>
<td>3</td>
<td>1</td>
<td>6</td>
<td>29</td>
<td>27.63</td>
</tr>
<tr>
<td>I, IIB</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>-</td>
<td>4</td>
<td>3.80</td>
</tr>
<tr>
<td>I, IIA, IIB</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>0.95</td>
</tr>
<tr>
<td>IIA, IIB, IIIA</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>3</td>
<td>-</td>
<td>4</td>
<td>3.80</td>
</tr>
<tr>
<td>III, IV</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>1</td>
<td>0.95</td>
</tr>
<tr>
<td>IIB, III</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>-</td>
<td>2</td>
<td>1.90</td>
</tr>
<tr>
<td>I, II, III</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>-</td>
<td>2</td>
<td>1.90</td>
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<tr>
<td>Granulation</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>0.95</td>
</tr>
<tr>
<td>Total</td>
<td>21</td>
<td>20</td>
<td>15</td>
<td>20</td>
<td>13</td>
<td>13</td>
<td>105</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 3 – Burned area.

<table>
<thead>
<tr>
<th>Area burned%</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1%</td>
<td>3</td>
</tr>
<tr>
<td>2%</td>
<td>11</td>
</tr>
<tr>
<td>3%</td>
<td>9</td>
</tr>
<tr>
<td>4%</td>
<td>13</td>
</tr>
<tr>
<td>5%</td>
<td>12</td>
</tr>
<tr>
<td>6%</td>
<td>3</td>
</tr>
<tr>
<td>7%</td>
<td>6</td>
</tr>
<tr>
<td>8%</td>
<td>4</td>
</tr>
<tr>
<td>9%</td>
<td>3</td>
</tr>
<tr>
<td>10%</td>
<td>9</td>
</tr>
<tr>
<td>14%</td>
<td>1</td>
</tr>
<tr>
<td>15%</td>
<td>7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Area burned%</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>16%</td>
<td>1</td>
</tr>
<tr>
<td>17%</td>
<td>2</td>
</tr>
<tr>
<td>18%</td>
<td>1</td>
</tr>
<tr>
<td>20%</td>
<td>4</td>
</tr>
<tr>
<td>22%</td>
<td>1</td>
</tr>
<tr>
<td>25%</td>
<td>4</td>
</tr>
<tr>
<td>27%</td>
<td>1</td>
</tr>
<tr>
<td>30%</td>
<td>4</td>
</tr>
<tr>
<td>40%</td>
<td>3</td>
</tr>
<tr>
<td>50%</td>
<td>1</td>
</tr>
<tr>
<td>60%</td>
<td>1</td>
</tr>
<tr>
<td>80%</td>
<td>1</td>
</tr>
</tbody>
</table>
The affected anatomical regions were the head, neck, limbs, chest, abdomen, buttocks, genitals, most burns affecting multiple body regions [7]. Overall we treated 268 distinct anatomical regions.

Dividing the anatomical regions arbitrarily we calculated separately the following entities:
1. Cephalic extremity (head and neck) - 36 pieces
2. Chest - 49 pieces
3. Upper limb (shoulder, arm, forearm) - 65 pieces
4. Hand - 25 pieces
5. Leg (buttock, thigh, calf) - 54 pieces
6. Foot - 20 pieces
7. Abdomen - 15 pieces
8. Perineum, groin - 4 pieces

Most of the anatomical regions affected were consistent with the mechanism of „pouring hot liquid”.

Of the 268 regions anatomical treated in 52 cases there was a single area burned per patient, and in 53 cases multiple regions per patient. Regarding the harming agent affecting the studied population, the proportion was as follows: 86 with hot liquids, 3 with fat, 4 contact with hot solid objects, 8 flame, 2 chemical burns, 1 electrocuted, as shown in table 4.

### Table 4 – The mechanism of thermal injury.

<table>
<thead>
<tr>
<th>Year</th>
<th>Hot liquid</th>
<th>Hot fat</th>
<th>Chemical burns</th>
<th>Solid hot</th>
<th>Flame</th>
<th>Electrocuted</th>
<th>Explosion</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004</td>
<td>16</td>
<td>2</td>
<td>-</td>
<td>2</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2005</td>
<td>18</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2006</td>
<td>13</td>
<td>1</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2007</td>
<td>14</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2008</td>
<td>12</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2009</td>
<td>13</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>86</td>
<td>3</td>
<td>2</td>
<td>4</td>
<td>8</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>%</td>
<td>81.90</td>
<td>2.85</td>
<td>1.90</td>
<td>3.80</td>
<td>7.65</td>
<td>0.95</td>
<td>0.95</td>
</tr>
</tbody>
</table>

We found an overwhelming presence of burns caused by hot liquids consisting with scalding.

Regarding the social status and living conditions of the studied subjects, most of the patients originated from rural environment, families with modest income and multiple siblings.

There was also a certain predominance of male patients but not so increased as the one found in older children.

The distribution per gender and area of origin is detailed in tables 5 and 6.

### Table 5 – The distribution of patients by sex.

<table>
<thead>
<tr>
<th>Year</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Girls</td>
<td>9</td>
<td>9</td>
<td>6</td>
<td>8</td>
<td>11</td>
<td>7</td>
<td>50</td>
<td>47.62%</td>
</tr>
<tr>
<td>Boys</td>
<td>12</td>
<td>11</td>
<td>9</td>
<td>12</td>
<td>5</td>
<td>6</td>
<td>55</td>
<td>52.38%</td>
</tr>
</tbody>
</table>

### Table 6 – Distribution of patients by area of origin.

<table>
<thead>
<tr>
<th>Year</th>
<th>2004</th>
<th>2005</th>
<th>In 2006</th>
<th>In 2007</th>
<th>In 2008</th>
<th>In 2009</th>
<th>Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urban</td>
<td>9</td>
<td>11</td>
<td>7</td>
<td>12</td>
<td>5</td>
<td>6</td>
<td>50</td>
<td>47.62%</td>
</tr>
<tr>
<td>Rural</td>
<td>12</td>
<td>9</td>
<td>8</td>
<td>8</td>
<td>11</td>
<td>7</td>
<td>55</td>
<td>52.38%</td>
</tr>
</tbody>
</table>

### Discussions
The results of this study are consistent with those of various other studies and literature [3,8,9,10].

Children are at particular risk from scalding because a given amount of hot liquid from a container will cover a much larger area compared with an adult (between a 6 years old child and an adult, the body surface area increases 6 times) [11,12].

Burns and fire is the fourth most common cause of accidental death in children [4].

Infants and young children suffer the most frequently scald burns or exposure to flame, burns and fire being the
fourth most common cause of accidental death in children [3,4,12].

Most children under 3 years hospitalized for burns, had the cause scalding or contact burns also demonstrated by the affected body areas [4,5,7,12,13,14].

Burns produced by hot tap water and beverages cause more deaths and hospitalizations than other liquids.

The most recognized burn mechanism in infants and toddlers is the contact with hot liquids either by spilling or by immersion [14].

Almost 80% of thermal injuries in children could be prevented although the main causes such as a poor socio-economic status, indifference of the parents and sometimes abuse are problems difficult to manage by the admitting physician [8,11,12].

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MISDIAGNOSED MECKEL'S DIVERTICULUM CAUSING SEVERE HEMORRHAGE - CASE REPORT

H Gocan¹, A Surd¹, Rodica Muresan¹

Abstract
Meckel's diverticulum was first described by Fabricius Hildanus in 1598. The name derives from the German anatomist Johann Friedrich Meckel who described the embryological and pathological features in 1809 [1]. Although it generally remains silent but life threatening complications may arise making it an important structure for having a detailed knowledge of its anatomical and pathophysiological properties to deal with such complications. Meckel’s diverticulum has varied presentations in children and often becomes a diagnostic challenge. We present a 14-year-old boy with a history of recurrent periumbilical pain and one episode of melena. His symptoms were undervalued during a previous hospitalization in a pediatric unit until he was brought to our clinic for abdominal pain and massive rectal bleeding. The intervention performed in emergency identified a perforated bleeding Meckel's diverticulum with massive hemoperitoneum, that was resected. Our observation shows that severe hemorrhage due to a Meckel's diverticulum although exceptional, is possible.

Key words: Meckel diverticulum, abdominal pain, rectal bleeding, hemoperitoneum

Introduction
Meckel’s diverticulum (MD) occurs in about 2% of the population, making it the most prevalent congenital abnormality of the gastrointestinal tract. It can be asymptomatic or mimic common abdominal disorders. We report a case of a child with an intraoperative diagnosis of MD with a long history of recurrent abdominal pain, vomiting and one episode of melena misdiagnosed as a cyclic vomiting syndrome.

Case report
A 14-year-old boy was referred to one of our pediatric unit with a one month history of periumbilical colicky pain with associated alimentary vomiting. The pain usually spontaneously disappeared within a few hours. During the period before our visit, the painful episodes lasted longer and were reported to occur also at night. No diarrhoea was reported, the boy was rather constipated. Previous medical investigations, abdominal ultrasonography and plain abdominal film were negative. Neither abdominal tenderness, nor liver or spleen enlargement, nor abdominal masses were identified at palpation. Complete blood cell count, electrolytes, glycemia, blood ammonia, renal and hepatic function, pancreatic enzymes, C-reactive protein, erythrocyte sedimentation rate, and gamma globulins were within normal ranges.

A plain abdominal film was unremarkable, and a small bowel enema indicated normal transit and normal appearance of the intestinal loops. During the hospitalisation the patient presented one episode of melena. The upper and lower digestive endoscopy were negative. The patient was hydrated and received antibiotics. He was discharged after 5 days of hospitalisation.

On the 4th day he was referred to our clinic with severe abdominal pain, vomiting and fresh blood in stool. Full blood count showed mild leucocytosis with white blood cell count of 11500 and PCR 4.5.

The ultrasound revealed distended bowel loops with slow peristalsis and contining fluid. Also free abdominal fluid was found. The plain abdominal film revealed air-fluid levels and opacification of the pelvic region.

Emergency laparotomy was performed. The intraoperative macroscopic finding was that of an perforated MD with hemoperitoneum and appendiceal reaction. Segmental resection of the small bowel along with appendectomy was performed (Fig.1).

Discussions
MD is the most common congenital anomaly of the gastrointestinal tract. The “rule of two” can remind us of some of its main features: occurs in 2% of the population; usually discovered before 2 years of age; occurs within 2 feet of the ileocecal valve; is 2 inches long and 2 cm in diameter [2]. It is the result of an incomplete atrophy of the omphalomesenteric duct. The location of the diverticulum is on the antimesenteric border of the small intestine, most frequently between 30 cm and 90 cm from the ileocecal valve; there can be a fibrous connection to the umbilicus, as the remnant of the partially obliterated vitelline duct.

MD is a true diverticulum, composed of all layers of the intestinal wall, and is lined by normal small intestine epithelium. Gastric heterotopias can be found in roughly 50% of cases, and pancreatic, duodenal, colonic, or biliary mucosa have rarely been reported.

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MD can be silent all through a lifetime: clinical symptoms arise from complications (MD carriers have a 4% lifetime risk of developing a complication) [3]. Hemorrhage is the result of peptic ulceration of the ileal mucosa next to an acid-producing gastric mucosal heterotopia: the presentation of the blood loss varies from recurrent minimal intestinal bleeding, to a massive, shock-producing hemorrhage, and it is usually painless. Diverticulitis can mimic an acute appendicitis: pain is frequently localized in the midline or slightly to the right and, as in appendiceal disease, inflammation can progress until perforation. The diverticulum can invert into the ileal lumen and become the starting point of an ileo-ileo-colic intussusception: symptoms can not be discriminated from those ascribed to idiopathic intussusception, even though the onset of the former is described to occur at an earlier age. A further mechanism by which MD can produce intestinal obstruction is to turn around a fibrous remnant: symptoms may vary from intermittent recurrent subocclusive episodes, as in our patient, to frank occlusion with strangulation features if a complete volvulus occurs [4]. Preoperative diagnosis of a complicated MD can be challenging and often difficult to establish because clinical symptoms and imaging features overlap with those of other disorders causing acute abdominal pain or gastrointestinal bleeding [5].

Initially, our case was misdiagnosed as a cyclic vomiting syndrome and a functional abdominal pain, since neither inflammatory nor bleeding clinical features were present, and laboratory tests were substantially within normal ranges. Considering the episode of melena, although a single one, a 99mTc-pertechnetate scintigraphy would have been indicated: the principle is that a bleeding diverticulum consists of ulcerated ectopic gastric mucosa that can be revealed with 99mTc-pertechnetate. This concentrates in gastric tissue leading to a reported sensitivity of between 60% and 80% [6].

The clinical findings at the second hospitalisation, along with the US and plain radiograph suggested that emergency surgery must be performed. Complicated MD has a spectrum of radiological features which may help in the preoperative investigations, but are not always diagnostic [7-9]. Final diagnosis is almost always done at surgery: exploratory laparoscopy or laparotomy is recommended because it affords the possibility of simultaneous surgical resection, which is the definitive cure of a symptomatic MD.

In conclusion, Although MD is the most prevalent congenital abnormality of the gastrointestinal tract, it is often difficult to diagnose. The diagnosis of MD should be considered in children with intestinal bleeding, unexplained recurrent abdominal pain, and nausea and vomiting suggestive of cyclic vomiting syndrome.
References


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THE SEVERITY OF MITRAL VALVE PROLAPSE IN CHILDREN CORRELATES WITH DIFFERENT TYPE OF SYMPTOMATOLOGY

I Gyalai¹,², H Branea¹,², Oana Ancușa¹,²

Abstract

Introduction: Mitral valve prolapse (MVP), the most common anomaly of the mitral valve apparatus, occurs when one or both mitral valve leaflets excessively billows into the left atrium toward the end of systole. Mitral regurgitation (MR) develops in some patients particularly those with more significant prolapse, when the valve edges fail to close properly. Most patients are asymptomatic and MVP is an incidental auscultatory finding especially in children. Idiopathic MVP may be congenital in some patients, but recognition may be delayed until adolescence or adulthood. Familial cases are known and occur in an autosomal dominant pattern with variable penetrance and expression (familial mitral valve prolapse).

Material and method: A number of 49 patients were included in the study if they meet the following criteria: age between 6-12 years, documented MVP by transthoracic echocardiography and symptomatic patients. The exclusion criteria were: other associated valvular disease, evident structural heart disease, left ventricular hypertrophy, coronary heart disease and severe comorbidities. We divided our patients in two groups regarding the severity of MVP: group 1 – patients with mild or moderate MVP (without MR) and group 2 – patients with severe MVP (with MR). For each group we determine symptoms and percentage of occurrence and we compare between groups. We followed the study protocol for symptoms and each of our patients were asked to fill up a form regarding the symptoms they experienced and they have to mention them in order of appearance and their frequency. We were interested in certain symptoms like: chest pain, palpitations, arrhythmias, panic attacks, dizziness, syncope and skeletal abnormalities (thin children, height-to-weight ratio greater than normal, pectus excavatum, pectus carinatum). We use a VIVID 5 echo machine in order to determine a positive diagnostic of MVP in our patients. This is an essential tool to identify the presence and magnitude of MVP, the thickness of mitral valve leaflets, mitral annulus size, chordae tendineae length, and left ventricular and left atrial size and function; it also reveals any associated heart diseases which can meet the exclusion criteria. We perform a 12 lead ECG and/or 24 hour Holter in each of our patients to catch any rhythm disturbance (ectopic beats, sinus tachycardia), to explain palpitations.

Results: We included in the study, a total of 49 patients (pts.). We divided them in two groups: group 1 – mild or moderate MVP – 25 pts. and group 2 – severe MVP – 24 pts. The groups were homogeneous and they didn’t have any significant differences regarding age, gender, weight and height values. The following symptoms had statistical significance for group 1: palpitations (p=0.008), arrhythmias (p=0.02) and panic attack (p=0.02). Dizziness and skeletal abnormalities had no statistical significance. The following symptoms had statistical significance for group 2: chest pain (p=0.003) and syncope (p=0.022).

We summarized all the symptoms for each group in a chart to understand better the prevalence of them. The association of palpitations and arrhythmias (demonstrated on 12 leads ECG) has a statistical significance (p=0.008) for group 1 and the association of palpitations and panic attacks a statistical significance (p=0.007) also for group 1. The association between chest pain and syncope has a statistical significance of (p=0.027) for group 2.

Conclusions: MVP presents itself in a various type of symptoms. We determined that, in children, some symptoms are more frequent in presentation than the other. Palpitations, panic attacks and arrhythmias caught on ECG are more probably to appear in moderate or mild MVP while chest pain and syncope in severe MVP.

Key words: mitral valve prolapse, children, chest pain, arrhythmias

Introduction

Mitral valve prolapse (MVP), the most common anomaly of the mitral valve apparatus, occurs when one or both mitral valve leaflets excessively billows into the left atrium toward the end of systole. Mitral regurgitation (MR) develops in some patients particularly those with more significant prolapse, when the valve edges fail to close properly. Most patients are asymptomatic [1] and MVP is an incidental auscultatory finding especially in children. Idiopathic MVP may be congenital [2,3] in some patients, but recognition may be delayed until adolescence or adulthood. Familial cases are known and occur in an autosomal dominant pattern with variable penetrance and expression (familial mitral valve prolapse).

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Aim
The aim of the study is to correlate the different type of symptoms and their percentage of occurrence with the severity of MVP.

Method
The patients were included in the study if they meet the following criteria:
- age between 6-12 years
- documented MVP by transthoracic echocardiography
- symptomatic patients

The exclusion criteria were: other associated valvular disease, evident structural heart disease, left ventricular hypertrophy, coronary heart disease and severe comorbidities.

We divided our patients in two groups regarding the severity of MVP:
- group 1 – patients with mild or moderate MVP – without MR
- group 2 – patients with severe MVP – it means the presence of MR

For each group we determine symptoms and percentage of occurrence and we compare between groups.

Study protocol – echocardiographic measurements
We use a VIVID 5 echo machine in order to determine a positive diagnostic of MVP in our patients. This is an essential tool to identify the presence and magnitude of MVP, the thickness of mitral valve leaflets, mitral annulus size, chordae tendineae length, and left ventricular and left atrial size and function; it also reveals any associated heart diseases which can meet the exclusion criteria.

Two-dimensional, real-time echocardiographic pictures from parasternal long-axis window reveal the mitral valve leaflets coming together in systole and billowing into the left atrium beyond the atrioventricular junction.

The echocardiographic description of the MVP include structural changes, such as leaflet thickening, redundancy, annular dilatation, and chordal elongation. A varying degree of noncoaptation of the leaflets is present, and MR can be identified by Doppler-color, pulse wave, and continuous wave. The MR jet can be defined, and its magnitude and direction estimated. The size of the left atrium and left ventricle are increased in the presence of moderate-to-severe MR.

Study protocol – electrocardiography
We perform a 12 lead ECG and/or 24 hour Holter in each of our patients to catch any rhythm disturbance (ectopic beats, sinus tachycardia), to explain palpitations.

Study protocol – symptoms
Each of our patients were asked to fill up a form regarding the symptoms they experienced and they have to mention them in order of appearance and their frequency.

We follow certain symptoms like:
- chest pain
- palpitations
- arrhythmias
- panic attacks
- dizziness
- syncope
- skeletal abnormalities (thin children, height-to-weight ratio greater than normal, pectus excavatum, pectus carinatum)

Statistical analysis
The data was compared using “t-test” for the continual variables, Fisher’s exact test, contingency table and multivariable regression. All the results were expressed in average values ± standard deviation (SD) and the correlation between the measurements was made using the multivariable regression analysis. The statistical analysis was made using the Stat View 6.0 (SAS Institute USA) software.

Results
We included in the study, a total of 49 patients (pts.). We divided them in two groups:
- group 1 – mild or moderate MVP – 25 pts.
- group 2 – severe MVP – 24 pts.

The groups were homogeneous and they didn’t have any significant differences regarding age, gender, weight and height values (Table 1).

We recorded the following number of symptoms in each group (Table 2) and their statistical significance.

Table 1 – group parameters

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Group 1</th>
<th>Group 2</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>Age</td>
<td>8.68</td>
<td>1.749</td>
<td>8.20</td>
</tr>
<tr>
<td>Gender</td>
<td>6 Male</td>
<td>19 Female</td>
<td>5 Male</td>
</tr>
<tr>
<td>Height</td>
<td>125.61</td>
<td>14.022</td>
<td>124.79</td>
</tr>
<tr>
<td>Weight</td>
<td>35.42</td>
<td>9.012</td>
<td>37.21</td>
</tr>
</tbody>
</table>

Mean = average value; SD = standard deviation; p = statistical value
Table 2 – number of symptoms per group and statistical significance

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Group 1</th>
<th>Group 2</th>
<th>p</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palpitations</td>
<td>15</td>
<td>5</td>
<td>0.008</td>
<td>Highly</td>
</tr>
<tr>
<td>Chest pain</td>
<td>10</td>
<td>20</td>
<td>0.003</td>
<td>Highly</td>
</tr>
<tr>
<td>Syncope</td>
<td>8</td>
<td>16</td>
<td>0.022</td>
<td>Very</td>
</tr>
<tr>
<td>Dizziness</td>
<td>10</td>
<td>11</td>
<td>0.776</td>
<td>Not</td>
</tr>
<tr>
<td>Arrhythmias</td>
<td>15</td>
<td>6</td>
<td>0.021</td>
<td>Very</td>
</tr>
<tr>
<td>Skeletal abnormalities</td>
<td>15</td>
<td>16</td>
<td>0.768</td>
<td>Not</td>
</tr>
<tr>
<td>Panic attack</td>
<td>19</td>
<td>10</td>
<td>0.020</td>
<td>Very</td>
</tr>
</tbody>
</table>

The following symptoms had statistical significance for group 1: palpitations (Fig.1), arrhythmias (Fig.2) and panic attack (Fig.3).

Dizziness and skeletal abnormalities had no statistical significance.

The following symptoms had statistical significance for group 2: chest pain (Fig.4) and syncope (Fig.5).

We summarized all the symptoms for each group in a chart (Fig.6).

The association of palpitations and arrhythmias (demonstrated on 12 leads ECG) has a statistical significance (p=0.008) for group 1 and the association of palpitations and panic attacks a statistical significance (p=0.007) also for group 1.

The association between chest pain and syncope has a statistical significance of (p=0.027) for group 2.
Discussions

Regarding the symptoms we determined that palpitations (p=0.008), arrhythmias (p=0.02) and panic attacks (p=0.021) appear most often in group 1 (mild or moderate MVP) and they have statistical significance. Symptoms like dizziness and skeletal changes have no statistical significance for either group.

Chest pain (p=0.003) and syncope (p=0.022) are statistical significance for group 2 (severe MVP).

We go one step further and studied if association of two symptoms has statistical significance for one group or another. We showed that association of palpitations and arrhythmias (demonstrated on 12 leads ECG) has a statistical significance (p=0.008) for group 1 and the association of palpitations and panic attacks a statistical significance (p=0.007) also for group 1.

The association between chest pain and syncope has a statistical significance of (p=0.027) for group 2.

Chest pain may be caused by any of the following factors [4]: excessive stretching of the chordae tendineae, leading to traction on papillary muscles, coronary microembolism from platelet aggregates and fibrin deposits in the angle between the left atrium and the posterior mitral leaflet, inappropriate tachycardia and excessive postural changes and physical and emotional stresses, hyperadrenergic state, which increases myocardial oxygen demand and coronary artery spasm.

Palpitations [5] appearance may be related to cardiac arrhythmia [5], although this has not been conclusively proven.

Skeletal abnormalities are observed in two thirds of patients and do not fit into any of the recognized connective tissue disorders, although an occasional patient may have Marfan syndrome [6] or other related syndromes. Common findings are as follows: hypomastia, thin children, height-to-weight ratio greater than normal [7], arm span greater than height (dolichostenomelia), arachnodactyly, scoliosis [8], narrow anteroposterior chest diameter (straight back), pectus excavatum or pectus carinatum [9] and joint hypermobility. Panic attacks appears in many cases of MVP [10,11].

Limitation

The small number of patients was the main limitation of this study. Also children under the age of six were not included because they were unable to fill up the symptoms form, for themselves.

Conclusions

MVP presents itself in a various type of symptoms. We determined that, in children, some symptoms are more frequent in presentation than the other. Palpitations, panic attacks and arrhythmias caught on ECG are more probably to appear in moderate or mild MVP while chest pain and syncope in severe MVP.

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PREVALENCE OF INFECTION IN LOW BIRTH WEIGHT INFANTS

Mirabela Dima1*, C Ilie2, Marioara Boia2, Daniela Iacob2, Aniko Manea2, Nicoleta Ionita3, Simona Sipos2, Daniela Chiru2, RE Iacob4

Abstract
The newborn has a variable and uneven susceptibility to infection. In term of onset, neonatal sepsis may be early-onset (within the first 4 days of life) and late-onset (after day 14 of life).

Bacteria, viruses and parasites are transmitted to the fetus and newborn in various ways: trans placental, through amniotic fluid or during expulsion. Another category is represented by nosocomial infections. The study was conducted on a total of 596 low birth weight infants who required a hospitalization in NICU with variable duration, representing a group of suspicion for neonatal infectious pathology. We analyzed the distribution of cases by type of birth, time since amniotic membrane rupture until delivery, Apgar score, a positive bacteriological examination.

Keywords: newborn, neonatal infection, low birth weight.

Introduction
Regardless of etiology (bacterial, viral or otherwise), newborn has a variable and uneven susceptibility to infection. Bacterial infection, defined as clinical syndrome resulting from systemic infection proven by a positive blood culture or other origin, occurs in approximately 1-8 newborn in 1000 births and may be accompanied by meningitis ¼ again - infected infants.

In terms of onset, neonatal infection may be:
- Early postnatal onset (within the first 4 days of life) and
- Late onset (after day 14 of life).

Improved techniques methodologies for neonatal intensive care have led to increased survival of preterm infants and / or very low birth weight.

This has contributed greatly to the increased incidence of neonatal infections by increasing nosocomial component become the 3rd largest category of neonatal infections. In terms of time (relative to the time of birth), nosocomial infections can be assimilated as a subgroup of late-onset neonatal sepsis (after day 4 of life). They mostly interested infants with very low birth weight (VLBW = very low birth weight), a 25% of them may have one or more infectious episodes detected before discharge.

Nosocomial infections are responsible for the increased rate of neonatal morbidity and mortality as well, and prolongation of hospitalization known to be long lasting as VLBW category. In general the current studies give a neonatal mortality rate of neonatal infections caused 20-30%, but this may increase to 80-90% in polymorphonuclear neutrophil depletion stored in the bone marrow. In the category of infants with very low birth weight (VLBW), the group most affected by infectious pathology, the mortality rate reported in a study (Jill E. Baley and Johana Goldfarb, 1998) was 21% (versus 9 % in VLBW infants uninfected)

Transmission of infection. Bacteria, viruses and parasites are transmitted to the fetus and newborn in various ways. Trans placental transmission is responsible for the infections occurred immediately postpartum and is well represented in STORCH infections (syphilis, toxoplasmosis, rubella, cytomegalovirus, HIV, HSV). More commonly, infections are transmitted vertically from mother to child through amniotic fluid or during expulsion. Finally newborns can be infected after birth. These infections can be transmitted to other infants, from the medical staff, including the environment contaminated equipment [3].

Early-onset infections. Most early-onset infections occur in the first 12 hours of life, although it can develop in the first 4 days of life. They are usually fulminant and affects multiple systems, mainly the lungs (pneumonia). Most newborns are spared, but infants are often affected, with a mortality rate of 15-20%.

Listeria monocytogenes was also a common cause among VLBW infants (≤ 1500 grams), from 1991 to 1993. Neonatal Research Network reported that early-onset infections were detected in 1.9% of newborns, although antibiotic therapy was continued over 5 days to almost half of newborns, reflecting the uncertainty of diagnosis.

Gram-positive organisms (GBS, Streptococcus viridans, other Streptococcus and coagulase-negative staphylococcus) predominates over Gram-negative organisms (E. coli, H. influenzae and Klebsiella).

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Early onset infections among VLBW infants have higher morbidity, resulting in an increased rate of intraventricular hemorrhage, persistent ductus arteriosus and the need for prolonged assisted ventilation [4,5].

Late-onset infections. Late-onset infections are more subtle onset and more likely to degenerate into a focal infection, especially meningitis. Although pathogens can be acquired during the expulsion, they are most commonly taken from the environment. Late-onset infections are commonly associated with the term newborn in the first week of life and occasionally associated with obstetric complications. The mortality rate is lower than in early-onset infection in 10% -20% [6].

Nosocomial infections. Nosocomial infections follows a different pattern. Are inversely related to low birth weight and gestational age; infected infants were predisposed to prematurity complications (intubation, catheterization, respiratory distress syndrome, prolonged ventilation, bronchopulmonary dysplasia, persistent ductus arteriosus, severe intraventricular hemorrhage, necrotizing enterocolitis).

At least two major events overlap neonatal period, time of onset and / or development of neonatal infectious pathology:

- transient immaturity of a mature newborn, prolonged (weeks or months) for premature infant, the overall capacity of anti-infective defense;
- microbial colonization process whose purpose is the training of saprophytic flora (bowel, mouth, skin), unique process that does not occur in any other period of life, it generally ends after the first 10 to 14 days postnatal life.

The normal microbial colonization is itself an argument (if applicable) of limitation or even ban of the use of antibiotic therapy in this critical period. Therefore, in the first 10-154 days old it is recommended that the use of antibiotics should only be done when the infection is well established and is etiologic labeled.

Objectives

This study aims to address the neonatal microbial infections as a complex that includes:

- particular issues of microbial colonization in perinatal context
- the expansion of procedures in NICU
- dynamics of microbial colonization process in a unit of NICU and its correlation with infectious pathology
- assessment of factors and risk groups for systemic infection;
- diagnosis issues of neonatal infections, evolution, prognostic and therapeutic and prophylactic perspectives.

Materials and methods

The study material is represented by the totality of newborns who were hospitalized in the Neonatal Intensive Care Unit (NICU) Clinic of Neonatology "Bega" Timisoara, and who had infectious pathology in the neonatal period.

There has been case law for a period of 4 years (2009-2012), and in this case law were selected infants who experienced a systemic infection, which allowed the delineation of the study group (with positive blood cultures).

In the batch analysis we started from suspicion and we defined the casuistry only after etiological confirmation.

Results and Discussions

During the period studied there was a total of 9376 infants, of which 833 (8.88%) were classified in the broader group of newborns with low birth weight (≤ 2500g).

A total of 596 newborn (6.35% of total number of births) required hospitalization with variable duration in NICU, which has been a group of suspicion for neonatal infectious pathology. If we compare the total number of infants admitted in NICU (n = 7596), nearly half of them (43.28%) presented the criteria for suspected neonatal infection, the rest (56.72%) were hospitalized in NICU for other specific neonatal medical problems (Fig. 1).

Distribution of cases according to the type of birth (Fig. 2) shows a sensitive predominance, but insignificant, to caesarean birth versus natural delivery.
Material analysis allowed the identification and concrete delineation of perinatal factors of suspicion for the neonatal infectious pathology. We proceeded to isolated analysis and/or multifactorial of their and try to assess their weight in the determinism of a systemic infection.

One of the most important factors of infection remains PRAM (premature rupture of amniotic membranes), cited in our study as an incidence of 39.92% (n = 103). In the following figure (Fig. 3), is illustrated with PRAM distribution of cases in relation to the onset of labor. It is noted that over two thirds of cases, this has occurred with a hospitalization in NICU over 10 days, but mostly over 14 days is typical for systemic infections.

Since all cases of the study group were admitted in NICU, still from birth systematic biological examinations were performed.

Systematic bacteriological examinations performed during the first 24-72 hours of life illustrates a degree of positivity over 50% and the elective areas of microbial colonization are: nose, eyes, skin (vernix axillary).

In relation with the total number of cases of the group study (n = 258), the degree of microbial colonization was 54.26% (n = 140 cases).

Distribution of cases according to the sampling interval - positivity of blood cultures, shows a positivity estimated at 57.89% in the first 4 days of sampling, which is a favorable period to conduct an effective therapy.

At nearly 60% of the study group, length of stay in NICU was > 7 days.

A hospitalization in NICU over 10 days, but mostly over 14 days is typical for systemic infections.

Summarizing the facts in relation to the case law study group (n = 258), we noted the following weight to factors of suspicion for PIN:

- gestational age < 37 weeks (n = 110 = 42.63%), especially < 34 weeks (n = 98 = 37.98%);
- birth weight < 1500g (n = 42 = 16.27%);
- premature rupture and/or early amniotic membranes (n = 103 = 39.92%);
- first pregnancy regardless of biological age (n = 99 = 38.37%);
- 1 minute Apgar ≤ 7 (n = 102 = 39.53%) and especially 5 minutes (n = 8 = 31.39%);
- other pre and perinatal factors: maternal pathology (HTAS pregnancy-induced hypertension, diabetes, epilepsy, etc.); non-traceable pregnancy, couple or single mother illegitimate, birth dystocia (n = 94 = 36.43%).

**Conclusions**

Systemic neonatal infections of microbial etiology, is one of the most common and feared complications of NICU, with increasing incidence.

The diagnosis of sepsis is sometimes difficult, blood cultures are not being always positive, so it is necessary to corroborate the clinical criteria with other useful criteria for a correct diagnosis, in which the goal will be pursued:

- the isolation of the same etiologic agent in at least two outbreaks, one of which will be done by metastatic path;
- the presence of localized infection or suggestive evolutionary complications

In our observations, it appears that the staphylococcal septicemia is dominant, with the entering gate in order of frequency: Nasopharyngeal, umbilical, eyes, nose.

An important risk factor is the prolonged hospitalization that contributes to the appearance of treatment-resistant infections.

By the peculiarities of "land", newborns with low birth weight are the most exposed to this risk, in this category, the systemic neonatal infections are the third cause of death.
after RDS (respiratory distress syndrome) and IVH-intraventricular hemorrhage (normal associate).

The positive blood culture is the categorical criteria for the ethiological diagnosis, and it will be done an antibiotic sensitivity tests to the isolated pathogen agent.

The treatment with antibiotics will be set even in the phase of presumptive diagnosis (after clinical criteria), after which it will be established a 'target' treatment according with the antibiogram.

At least four conditions are necessary to reduce the incidence of:
1. "aseptic" NICU with highly specialized personnel;
2. rapid bacteriological tests and the expansion of "palette" pathogen susceptibility;
3. Minimal enteral nutrition at infants with low and extremely low birth weight..

References

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VARIABLE PROGNOSIS IN TRISOMY 18 (EDWARDS SYNDROME) – 3 CLINICAL CASES PRESENTATION

Simona Farcas¹, Valerica Belengeanu¹, Monica Stoian¹, Nicoleta Andreescu¹, Dragos Belengeanu², Marioara Boia³

Abstract
Trisomy 18 (Edwards syndrome) occurs in 1/3000 to 1/8000 births and it is the second frequent autosomal aneuploidy with a characteristic clinical aspect, easily recognizable in the neonatal period. The severity of the anomalies conditions the life expectancy and the life span varies from 2 weeks to one year of life, only 5-10% surviving beyond the first year of life. Yet, in the literature there are reported cases with variable survival. The purpose of this article is to present 3 cases diagnosed with trisomy 18 with variable survival.

Key words: trisomy 18, cytogenetics, survival

Introduction
Edwards syndrome described in 1960, by Edwards et al and Smith et al, is a plurimaleformative syndrome with an occurrence on 1/3000 to 1/8000 live births, this incidence being influenced by the application of prenatal diagnostic. An important part of the fetuses with trisomy 18 die during the pregnancy, only a small part come to term [1] The ratio between sexes is 0,9 male : female, females being more affected with trisomy 18 than males [2].

In the clinical tableau there are multiple malformations with a specific pattern of signs that allow an early diagnosis in the neonatal period, including growth deficiency, microcephaly, micrognathia, prominent occiput, clenched hands, congenital heart defects, kidney abnormalities.

The median life span as reported in literature varies from 2.5–14.5 days [3, 4, 5].

We present 3 situations of trisomy 18 where: the first patient, a male died at 9 months old, the second case, a female still alive, being 4 years.

Cases presentations
Clinical data as well as the family and pregnancy history of the patients are presented in Table 1. For all our cases the physical evaluation was consistent with trisomy 18. All patients underwent karyotyping by GTG banding in the Genetic Laboratory of the University of Medicine and Pharmacy “Victor Babes” Timisoara. For all the three cases investigated, the cytogenetic analyses were carried out and metaphase spreads were obtained by 72-hr-culture of peripheral blood lymphocytes using standard techniques. For all patients the chromosomal imbalance revealed three chromosomes 18 in all the metaphases visualized (Figure 1-3). In the second case, because the patient survived after 1 year, for exclusion of a possible cryptic mosaic FISH analysis was performed. The FISH analysis using CEP 18 (Spectrum Green) probe showed three signals corresponding to chromosome 18 in all 50 metaphases and 250 nuclei evaluated (Figure 4).

Figure 1. Patient 1 – metaphase showing 3 chromosomes 18.
Figure 2. Patient 2 – metaphase showing 3 chromosomes 18.
Figure 3. Patient 3 – metaphase showing 3 chromosomes 18.

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Table: Patients’ data at birth.

<table>
<thead>
<tr>
<th></th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Parents age</strong></td>
<td>mother 30 years old</td>
<td>mother 34 years old</td>
<td>mother 39 years old</td>
</tr>
<tr>
<td></td>
<td>father 38 years old</td>
<td>father 36 years old</td>
<td>father 39 years old</td>
</tr>
<tr>
<td><strong>Consanguinity</strong></td>
<td>no</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td><strong>Family history</strong></td>
<td>Second child</td>
<td>First child</td>
<td>3 spontaneous abortions</td>
</tr>
<tr>
<td><strong>Pregnancy history</strong></td>
<td>No investigations were done</td>
<td>Nothing relevant</td>
<td>Growth retardation</td>
</tr>
<tr>
<td><strong>Age of gestation</strong></td>
<td>37 weeks</td>
<td>39 weeks</td>
<td>37 weeks</td>
</tr>
<tr>
<td><strong>General data</strong></td>
<td>weight 2330 g head circumference 31 cm length 48 cm</td>
<td>weight 2450 g head circumference 32 cm length 47 cm</td>
<td>weight 1770 g head circumference 31 cm length 42 cm hypotonia</td>
</tr>
<tr>
<td><strong>Craniofacial</strong></td>
<td>prominent occiput, hypertelorism, short palpebral fissures, low set, malformed ears, small oral opening, micrognathia (Figure 5)</td>
<td>slightly prominent occiput, narrow bifrontal diameter, hypertelorism, short palpebral fissures, low set, malformed ears, high arched palate, microstomia, micrognathia, short neck (Figure 6)</td>
<td>prominent occiput, narrow bifrontal diameter, hypertelorism, short palpebral fissures, low set, malformed ears, microstomia, micrognathia, short neck (Figure 7)</td>
</tr>
<tr>
<td><strong>Hands and feet</strong></td>
<td>arthrogryposis, clenched hands with the index finger overriding the middle finger and the fifth finger overriding the fourth finger, rocker-bottom feet, hypoplasia of nails</td>
<td>clenched hands, syndactyly of finger 4 and 5 bilaterally, rocker-bottom feet, hypoplasia of nails</td>
<td>clenched hands with the index finger overriding the middle finger and the fifth finger overriding the fourth finger, simian crease, syndactyly of finger 2 and 3, short hallux, rocker-bottom feet, hypoplasia of nails</td>
</tr>
<tr>
<td><strong>Cardiac</strong></td>
<td>heart murmur and at the transthoracic echocardiogram a ventricular septal defect was discovered</td>
<td>ventricular septal defect, atrial septal defect, pulmonary hypertension, ventriculomegaly</td>
<td>atrial septal defect, anomalous tricuspid valve, enlarged right ventricle, enlargement of right atrium, enlarged pulmonary vein</td>
</tr>
<tr>
<td><strong>Genital</strong></td>
<td></td>
<td></td>
<td>Hypoplasia of labia major with prominent clitoris</td>
</tr>
<tr>
<td><strong>Renal</strong></td>
<td>no signs of renal malformations</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Central nervous system</strong></td>
<td>minor enlargement of posterior horns of the lateral ventricles and agenesis of corpus callosum</td>
<td></td>
<td>intraventricular cerebral bleeding, severe ischemic encephalopathy</td>
</tr>
</tbody>
</table>

Figure 4. Patient 2 - FISH analysis showing 3 signals for chromosome 18.
Patient 1 died at age of 9 months, cause of death being respiratory failure. Patient 2, in evolution (Figure 8) developed severe mental retardation, she can sit and hold her head and she is tube feed. On the psychiatric side, she acquired only a few simple words as mama, papa. An intraoral clinical examination revealed a narrow high-arched palate and anterior open bite. The patient remains under our supervision. Due to the cardiac malformations in the third case the prognostic was very poor and the child survived only 3 days.

Discussions
Aneuploid syndromes are characterized by phenotypic variability and it is also well documented the overlapping of some clinical manifestations between these syndromes. For the numerical chromosomal aberrations there are key features present in all patients, but there is also a wide heterogeneity of clinical manifestations and a large variability as regards of the patient’s outcome and evolution. Due to these characteristics of the aneuploid syndromes it is difficult to establish a correlation between the aberrations of a certain chromosomal region and the clinical features and is practically impossible to make a prediction about the evolution or prognosis.

Our patients present many physical stigmata of trisomy 18 that are the visit card of this syndrome: prominent occiput, short palpebral fissure, microretrognathia, clenched
hands, and rocker-bottom feet. The presented patients have a common set of manifestations found in 50% or more of patients with trisomy 18 as the specific craniofacial aspect, clenched hands, and cardiac anomalies. Additionally, patient 3 presents several hand and feet anomalies as syndactyly of finger 2 and 3, short hallux, simian crease and also genital anomalies that were reported in less than 50% of trisomy 18 patients and were not found in the other two cases reported here.

It is interesting that among the patients with trisomy 18 that survived, some of them had sever cardiac anomalies like Fallot tetralogy and yet reached the age of 20 years [7].

In a study done by Weber in 1967, it was showed that in female patients with trisomy 18 the survival rate is better than in males [4], observation sustain by other reports, [5] but there are other studies that infirm this supposition [8]. There is a diversity regarding the severity of organ malformation as well as of the clinical outcome. The causes of death and of the prolonged survival are not clear yet, there are genetic and epigenetic factors that interfere with the genetic load of the chromosome 18. The common causes of death are most often apneic spells, cardiac failure, or respiratory insufficiency, congenital heart malformations being the major cause of death [7, 9]. The literature presents that the infections are a frequent cause of morbidity and of mortality in older patients.

Cytogenetically it is important to exclude the mosaicism although no precise correlation between the degree of mosaicism and survival was reported [4, 10].

The first report about cases of trisomy 18 with long survival was done in 1978 by Smith who reviewed six patients with survival beyond 10 years and added another case [11].

To the best of our knowledge in the literature we found several individual cases of trisomy 18 patients that had a longer survival, above one year of life: 6 years Raczkowski’s case [12], 8 years Querioz’ patient [13], 13 year Mehta’s case [14], 14 years Hinijoal’s patient [15], 15 years Simon-Bautista’s case [16], 19 years Petek’s case [17], 20 years Kelly’s patient [7], 50 year in Bhanumathi’s case [18]. Other cases with long survival associated Wilms’tumor: 1 year old, Geiser’s case [19], 1.9 years old Miller’s case [20], 4.7 years old, Wang-Wu’s case [21], 5 and 9 years old, Faucett’s patients [22], 5.8, 8.7 and 13.9 years old, Olson’s patients [23], 9.4 years old, Anderson’s case [24], 13 years old, Karayalcin’s patient [25], 21 years old Shanké’s case [26].

As specified by other authors, we sustain the remark that trisomy 18 is not universally lethal. Patient 3, who is still alive will be followed periodically at our department. At prenatal diagnosis, in the cases with abnormal ultrasound findings and/or abnormal biochemical screening for trisomy 18 it is necessary to perform cytogenetic analysis from amniotic fluid. The risk for trisomy 18 implies counseling the parents as regard of giving birth to a trisomic fetus. For the parents, the decision of having the child in these conditions implies a degree of risk that should be taken in consideration.

References

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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 – 1,7cm. 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.

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