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# PARACETAMOL ANALGESIA VERSUS MEPERIDINE ANALGESIA IN PEDIATRIC SURGERY

Mihaela Coşofreţ<sup>1</sup>, Nida Boşnac<sup>1</sup>, Asan Rucni<sup>1</sup>, Enache Florin<sup>1</sup>, Constantin Tica<sup>1</sup>

## Abstract

The study tracked the impact of pediatric surgery, age and time of day on postoperative analgesia of a group of children hospitalized in the pediatric surgery department SCJU Constanta. The analgesics we used were those with central action (meperidine) and those with peripheral use (paracetamol). The study was prospective and was performed on age groups and surgery type (visceral, orthopedic, plastic, urology).

**Key words:** Postoperative pain, meperidine, paracetamol, analgesia

## Introduction

Acute postoperative pain (APP) is a particular form of acute pain that occurs in response to tissue injury, visceral distension or disease. APP is that expression of autonomic responses, psychological and behavioral which causes unpleasant and undesirable sensory-emotional experience. [6] This topic was chosen for many reasons, such as:

- difficulties in postoperative pain assessment and reassessment on children;
- the wrong idea of the medical staff that children, especially infants and babies, do not feel pain like adults do, and it has harmful consequences (lack of medical staff training); [5]
- adverse reactions from drugs analgesics, including respiratory depression and addiction; [4]

## Purpose

The aim is to evaluate effective means implemented to control postoperative pain of children in pediatric surgery service in Constanta County Emergency Hospital, as well as to compare the requirements imposed by the reality of pain management, in order to identify specific targets for improving clinical practice with positive effects on patient satisfaction and the cost of hospitalization (reduce the medication doses, use of available medication, hospitalization period).

## Materials and methods

Research sample consisted of 200 children aged between 0 -192 months with an average of 71 months. The

children's weight was from 2 kg to 97 kg, with an average weight of 23.200 kg.

The period in which the study was made, was from December 2008 to May 2009, which corresponded to the following criteria:

- The surgical operation must be done with general anesthesia or locoregional anesthesia;
- After surgery patients are monitored in the intensive care unit (ICU);

Children were divided into four categories according to their age, as follows: Category A: newborns between 0-6 months, B: infants: 6 to 24 months; Category C: early childhood: 2 to 6 years; category D: children over 6 years.

The included population distribution by age and type of surgery is shown in the figure below (fig.1).

Data collection was performed within 48 postoperative hours for each patient using a three parts questionnaire:

- Preoperative data - related to the patient's observation chart;
- Intraoperative data - related to the anesthesia record;
- Postoperative data - postoperative analgesia.

The results were processed statistically and expressed as a percentage, as this expression is more faithful to the expression of absolute values. Comparison between age groups was performed using the following types of statistical analysis: Student t test, chi square test Cohen.

## *Postoperative analgesia*

All the children included in this study have received at ICU intravenously painkiller, and not intramuscular.

1. Peripheral painkillers - Paracetamol alone - in 90% of cases, and in combination with ketoprofen in 6% of cases.
2. Central pain relievers - in 25% of postoperative prescriptions, 86.5% meperidine and 13.5% morphine (for 7 children over 6 months) - prescribed on request.

The average dosage of paracetamol reported to the average weight of the included children, was 15 mg / kg body weight and grip. Paracetamol was prescribed up to 4 injections in 24 hours. The average dosage of meperidine reported to the average weight of children was 1 mg / kg [1]. It wasn't prescribed systematically but according to patient's needs. The number of allowed administrations was up 4-6 injections in 24 hours.

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Adding a peripheral with a central painkiller represented 22% of postoperative analgesia. Paracetamol alone was used in 90% of cases and in association with ketoprofen in 6% of cases. Meperidine is 86.5% of central painkillers and it was prescribed according to patient's needs.

The comparative study of paracetamol and meperidine was based on the following criteria: age, day-night report, the number of doses depending on the type of surgery.

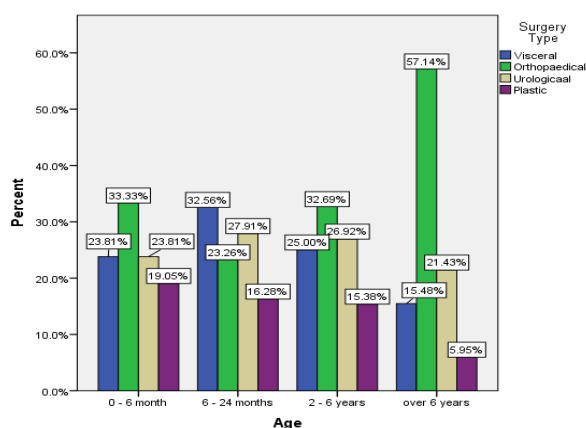


Figure 1 – Included population distribution by age and type of surgery.

## Results

### 1. Influence of age on paracetamol and meperidine administration.

Results are expressed as mean number of injections in 12 hours.

The average number of injections of paracetamol in 12 hours was statistically significantly higher during the day, the first day after surgery (D 0/day) at children older than 6 years ( $p = 0.03$ ) (fig. 2). The average number of injections

of meperidine in 12 hours was statistically significantly lower at children less than 6 months old (fig. 3). The percentage of children in category A (0-6 months), administration of meperidine was 62% lower (administrations/ in 12 hours) compared to the average for other categories. The children from A category (0-6 months) have not required treatment with meperidine from the second day after surgery.

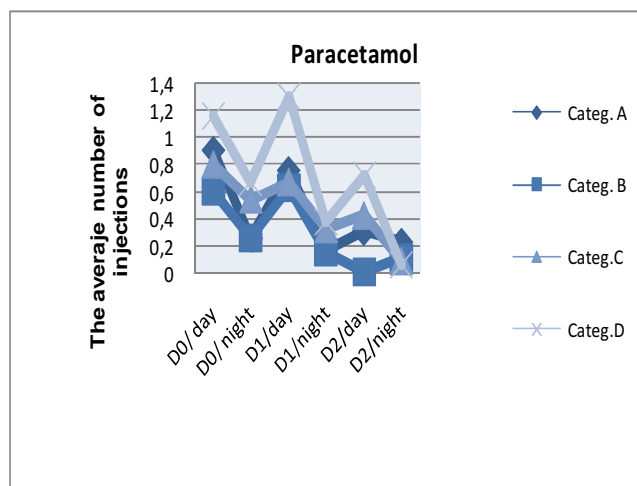


Figure 2 – Influence of age on paracetamol administration.

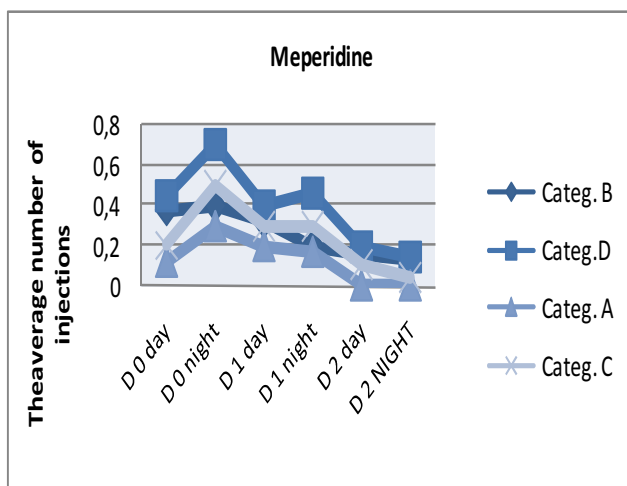


Figure 3 – Influence of age on meperidine administration.

### 2. Influence of day and night over the painkillers management (figure 4).

The average number of paracetamol injections was higher during diurnal phases. The average number of meperidine injections was higher in nocturnal phases. These

results are likely to be real ( $t(6) = 3.12$ ,  $p < 0.05$ ) because of the different effects each used products have. Top of meperidine injection within the first night. Meperidine – it keeps nycthemeral rhythm in order to facilitate sleep, with strong analgesic and sedative effect.

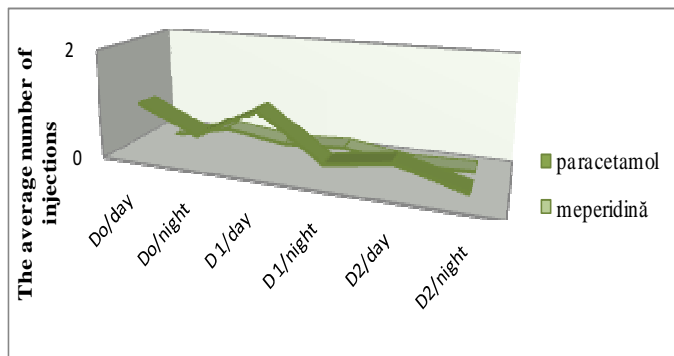


Figure 4 – Influence of day and night over the painkillers management.

### 3. Number of doses of painkillers according to the type of surgery.

The average number of injections of paracetamol and meperidine was more important in major surgery than in minor surgery (figure 5 and 6). For meperidine, statistical analysis results show a probability with 50% higher for

children undergoing major surgery to receive more treatment with this drug compared to children undergoing minor surgery. Paracetamol - 66% probability to obtain a larger quantity for a major surgery than a minor surgery. Meperidine - 50% probability to receive a larger quantity for a major surgery than a minor surgery.

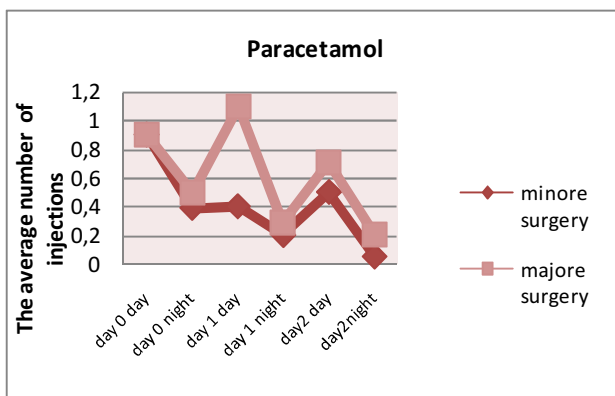


Figure 5 – The average number of injections of paracetamol according to the type of surgery.

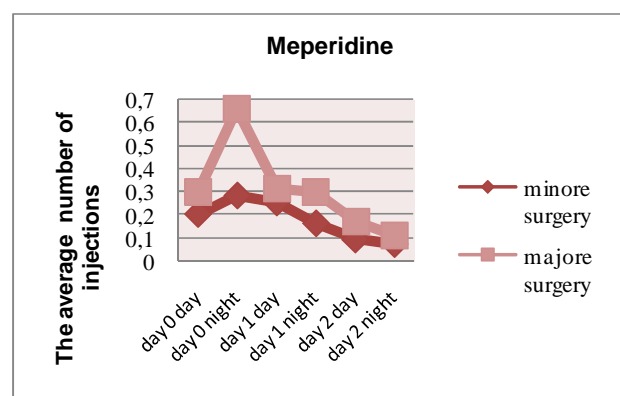


Figure 6 – The average number of injections of meperidina according to the type of surgery.

### 4. Number of doses of pain relievers according to the hospital sections

Variations in the average number of meperidine and paracetamol injections in 12 hours were similar in visceral and orthopedic hospital sectors. So, there are no statistically significant differences in terms of taking paracetamol between visceral and orthopedic sectors (chi square is below the limit, = 1.55 and  $p = 0.2$ ).

### Conclusions

All children included in the study have received postoperative painkillers; the dosage related to children weight is not influenced by age. Two classes of analgesics are routinely used: paracetamol and meperidine.

Peripheral analgetics are found in 90% of prescriptions, systematically prescribed, and correspond to level one of pain; in our study paracetamol was used in 90% of cases.

Meperidine, essential in central painkillers prescriptions (86.5%) was prescribed mostly on request,

influenced by age (for 85% of children in category D) but not of surgery type.

Paracetamol is widely prescribed in the service and without distinction between age groups. The average dosage is 15 mg / kg, which is consistent with normal dosage.

Prescriptions for central painkillers in 86.5% of cases are for meperidine. Often prescribed on request, as required. Unfortunately, these prescriptions are based on a classical dose adapted to a limited number of patients, and prescriptions according to the need are often less possible.

Paracetamol associated with meperidine is prescribed in 22% of cases. The combination corresponds to the concept of balanced analgesia, interesting is that allows for actions to take place in the periphery (paracetamol) and central level (meperidine). Nociceptive transmission can be effectively altered and modified at various levels ranging from the periphery to the centers of the trunk [3].

In our study, the number of injections of painkillers, peripheral or central, is influenced by age. Of total average number of injections of meperidine, the lowest is at infants

less than 6 months old. That might explain the reluctance to opioid administration, reluctance about the risk of respiratory depression and sedation [2]. The increased number of meperidine injections to children of category D in relation to other age groups, we attribute it to the nurse - patient communication, according to their satisfaction level.

In the analgesia efficacy study, we didn't take into account the presence of parents in our study, one of the key parameters in the management of analgesia [4]. No study of our knowledge was made in the attempt of taking in count these multiple parameters.

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# ELASTIC STABLE INTRAMEDULLARY NAILING (ESIN) FOR THE TREATMENT OF SIMPLE BONE CYSTS

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## Abstract

A unicameral bone cyst, otherwise known as a simple bone cyst, is a fluid-filled cavity in the bone, lined by compressed fibrous tissue. It usually occurs in the long bones of a growing child between the ages of 5 to 15, especially in the upper part of the humerus (50 - 60% of the time) or the upper part of the femur (25-30% of the time). Other bones, however, can be affected.

Since Virchow first described the unicameral bone cyst (UBC) in 1876, several methods for management were proposed. Currently performed surgical procedures include curettage combined with bone grafting, allografting with freeze-dried crushed cortical bone, use of homologous cancellous bone chips, the application of high-porosity hydroxyapatite, and cryosurgery. Decompression with multiple drill holes and intralesional injections of either steroids or bone marrow have also been used to treat UBC, with variable success rates. Elastic stable intramedullary nailing for the treatment of UBC in long bones has been rapidly gaining popularity.

The objective of the present study was to evaluate the results of intramedullary nailing for the treatment of unicameral bone cysts with or without a pathological fracture.

Intramedullary nailing is a minimally invasive method, which permits early stability and decompresses the cyst allowing healing. Significant differences were not observed among results from different locations.

Six children with symptomatic simple bone cysts were surgically treated with percutaneous cyst decompression, curettage, and intramedullary nailing. Patients were observed in-clinic with serial examinations and radiographs. Fracture healing and cyst recurrence were determined at follow-up.

All patients returned to activities of daily living with full range of motion and were completely asymptomatic. All fractures healed. There were no surgical complications or refractures.

**Key words:** Unicameral bone cyst, intramedullary nailing, decompression

## Introduction

Simple bone cysts, also known as unicameral or solitary bone cysts, are benign fluid-filled cavities occurring predominantly at the proximal ends of long bones in children. Approximately half of these occur in the proximal humerus (Figure 1) [1]. The etiology of simple bone cysts is not yet well understood. Early treatment of these lesions included open curettage and bone grafting with either autogenous or allogeneic bone. In addition to significant surgical morbidity [2], this method resulted in recurrence rates of 35% to 45% [2-6].

In the late 1970s, Scaglietti et al [7, 8] popularized the use of percutaneous aspiration and corticosteroid injection, but recurrence rates remained high and multiple injections were often required [8-11]. More recent methods have included trephination with or without bone grafting, [12-14] injection of autogenous bone marrow, [15-19] and intramedullary nailing [20, 21]. These methods have reduced recurrence rates. However, with many of these percutaneous techniques, radiographic evidence of cyst persistence is evident. Despite an absence of described clinical sequelae, activity restriction is frequently recommended by practitioners to avoid refracture.

The purpose of this study was to evaluate the effectiveness of a percutaneous approach to the treatment of simple bone cysts that includes percutaneous decompression, curettage, and injection of bone replacement material, in comparison with elastic stable intramedullary nailing. We hypothesize that these maneuvers will facilitate bone healing and reduce cyst recurrence, with improved radiographic restoration of normal bone such that activity restriction would not be necessary.

## Patients and Methods

Five children were admitted in our institution for a unicameral bone cyst between 2008 and 2011. There were 3 boys and 2 girls with a mean age of 11.4 years (range, 2 to 15 years) at the time of surgery. These patients have been followed until currently for the purpose of this study. The diagnosis was based on typical imaging, cystographic features and histology.

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Previous studies have used the cyst index [22] and the cyst diameter [23] to measure the state and progress of cystic activity. We employed a radiographic ratio to ascertain the severity of the lesion. The extent of the lesion on the longitudinal axis was divided with the normal expected diameter of the long bone at the site of the lesion



Figure 1 – 3D Computer Tomography of a humeral cyst.

All patients had large and active metaphyseal lesions adjacent to the physis of a long bone. Four cysts were located at the proximal humerus and one cyst was located at the neck of the femur.

One of the 5 patients had been referred with a pathological fracture of the proximal humerus. In this patient, diagnosis was obtained using imaging techniques including standard radiographs and computed tomography scans. The fracture had been initially treated non-operatively with closed reduction and cast immobilization. Treatment of the cysts initiated 6 weeks after the occurrence of the fracture, to prevent recurrence, and to provide stability to the bone and early mobilization of the patients.

#### Operative technique

For the cyst located at the neck of the femur the procedure was as follows: with the child under general anesthesia, fluoroscopy is used to locate the cyst and the physis. After full skin preparation and draping, a thin trocar is used to perforate the bone cortex and evacuate the cyst by aspiration of fluid. A cystogram was performed; a venous drainage was not observed. The cyst would not have been injected with artificial bone replacement if a large venous drainage was observed. Using a thin curette under fluoroscopic guidance tissue was obtained for histology. Histology sections showed a unicameral bone cyst. After

(Figure 2). The presented herein method of treatment has been performed in large simple bone cysts that occupied more than 2 times the physiologic diameter of the long bone at the site of the lesion.



Figure 2 – The longitudinal diameter of the cyst is more than 2 times of the diameter of the long bone at the site of the lesion diameter of the long bone at the site of the lesion.

that we have prepared the bone replacement and injected in the cavity under fluoroscopic guidance.

In the other four cases, with humeral cysts, under fluoroscopic guidance, retrograde intramedullary nailing (Figure 3, a & b) was done using flexible intramedullary nails in 2 cases and in the other two was used a antegrade nailing. These nails are 2 to 4 millimeters in diameter and can be trimmed to the appropriate length.

The diameter and length of the nails were selected on the basis of measurements made with a tape on the preoperative anteroposterior radiograph; the enlargement on radiographs was taken into account. The chosen length of the nails was then rechecked with the image intensifier after placement of the nail on the anterior surface of the corresponding bone. The longest nails that did not encroach on the proximal growth plate were used. The diameter of the nails was selected such that two nails would occupy approximately 80% of the medullary canal. One straight incision were made in the distal region of the involved part of the extremity, laterally, approximately one to two centimeters proximal to the joint line. The cortical bone was exposed by blunt dissection; under image-intensifier control, two holes were drilled in appropriate positions on top of the other at about 1 cm distance, longitudinally. Then one by one the two nails were inserted, one of it in “C” shape and the other in “S” shape. Both nails were directed to pass through the bone cyst, one at a time. The proximal and distal



physes were avoided. The distal ends of the nails were appropriately trimmed and left protruding from the bone without acute bending to avoid irritation of the soft tissues while ranging the adjacent joint.

### Evaluation

All patients were reviewed clinically and radiographically at 2 and 6 weeks and then every 3 months.

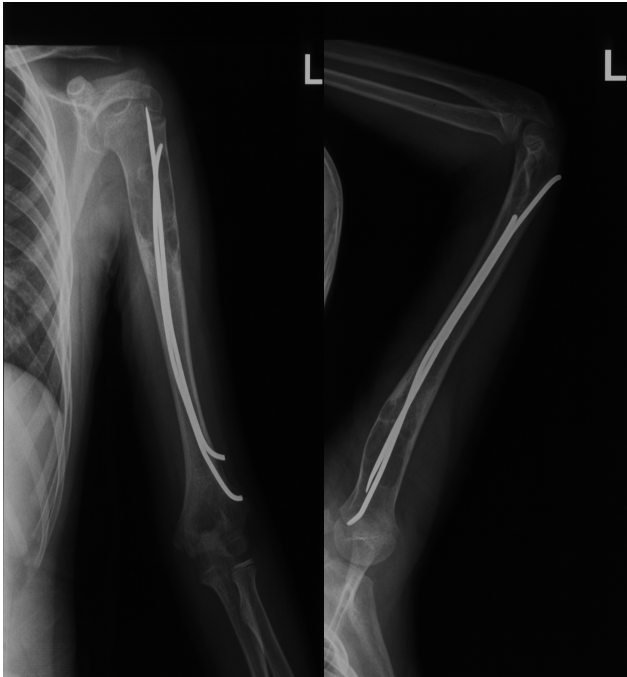


Figure 3 a& b – Xray control, retrograde intramedullary nailing.

Clinical evaluation included the presence of pain, the participation in daily living activities, the range of motion of the adjacent joints and the occurrence of a fracture or re-fracture.

Healing of the cysts was assessed on plain radiographs according to the criteria of Neer [24]. No nail has been retrieved at the time of this study (Figure 4 a & b).



Figure 4 a & b – The cyst started to heal – 3 months Xray control.

### Results

The longest follow-up was 32 months. Mean ratio of the cysts at diagnosis was 4.6 (range 3.2 to 6.3). The volume of artificial bone replacement in one case was 25 ml. The mean hospital stay of the patients was 36 hours.

At 6 weeks postoperatively, all patients were pain free and had full range of motion of the adjacent joints. Full activity including weight-bearing was resumed within this time in all children. Until the latest examination, there was no clinical or radiological evidence of fracture or re-fracture and recurrence of the cysts.

The only complications reported were irritation at the entry sites of the nails. Radiographic signs of cyst healing were present at 6 months in all patients.

According to the classification system of Neer, there are 4 stages of cyst healing:

- Stage I include complete cyst filling;
- Stage II include partial cyst filling with thickening of the cyst wall and small lucencies of less than 3 cm;
- Stage III include recurrence of the cyst and lucencies of more than 3 cm;
- Stage IV include no response of the cyst [24].

In the present series, review radiographs showed that all 5 cysts had consolidated completely or partially (Neer

stages I and II); 1 cyst were graded as Neer I, and 4 cysts were graded as Neer II.

### Discussion

Simple or unicameral bone cysts are characterized by their tenacity and their prevalence of recurrence after treatment. To some extent, this explains the diverse methods used to achieve consolidation of the cyst [11].

Initial treatment of unicameral bone cysts consisted of curettage and bone grafting [11, 24, 25]. However, the success rate following open procedures has ranged from 55% to 65%. The remaining 35% to 45% of patients have had recurrence of the cyst, requiring additional open surgical procedures [4, 9-11, 26-28].

In addition, aggressive surgical options have been related to more complications including infection, coxa vara, physeal damage, epiphyseal arrest and shortening of the limb, increased intraoperative blood loss, intraoperative fractures, and a prolonged period of postoperative immobilization [1, 4, 9, 10, 26, 27]. Campanacci et al [1] reported 14% of retardation of longitudinal growth and limb-length discrepancy, possibly ensuing from a surgical lesion of the growth plate rather than the action of a cyst located adjacent to the physis.

The treatment of simple bone cysts has significantly evolved since the percutaneous injection of methylprednisolone acetate was introduced by Scaglietti et al in 1974 [16, 17]. The mechanism of action of methylprednisolone is unclear. It is postulated that the membranous wall of the cyst degenerates after the injection of corticosteroids, thus eliminating the production of fluid in the cyst and inducing the onset of osteoblastic activity [16-18].

However, long-term studies of percutaneous injection of methylprednisolone acetate have not proven the initial satisfactory results. Multiple percutaneous corticosteroid injections may be required with unpredictable results for recurrent cysts and cysts showing no response, and patients have to avoid strenuous activities for as long as the cyst heals [1, 29].

Several authors have advocated percutaneous multiple drilling with Kirschner wires [30], or prolonged decompression of the cyst using cannulated screws left in place without corticosteroid injection [25]. The mechanism of action of percutaneous drilling and decompression of the cysts is based on the concept that the lesions are caused by the interstitial fluid that is unable to escape from the bone because of a bony plug and venous obstruction (Figure 5). Drilling leads to a continuous decompression and decrease of the internal pressure within the cyst because of drainage of fluid through the cyst wall [25, 31].

Biological methods of treatment of simple bone cysts such as autogenous or allogenic bone grafting and injection of bone marrow or bone substitutes have also been reported [19-24]; these methods have been based on clinical studies that have suggested that aspirated bone marrow has value as a bone-graft material [32].

Although almost all the previously described methods including injection of steroids, bone marrow or bone substitutes, and decompression may produce consolidation of the cyst, they do not provide an early mechanical stability to the weakened bone.

In 1981, Catier et al reported successful results of flexible intramedullary nailing for the treatment of a unicameral bone cyst in the proximal femur in 2 patients [27]. The essential feature of this method is the same as that described in earlier series that is the decompression of the cyst and the decrease in the intracystic pressure [30].

Although a small series that lacks a control group, results were excellent without any major complications or need for re-operations. Radiographic evaluation showed complete or partial healing of the cysts in all patients. The time to healing was not very long and patients return to full daily activities without restrictions or protective splints once there was no functional pain.

### Conclusion

Mechanical treatment of large and active simple bone cysts in long bones using elastic intramedullary nailing for cyst cannulation, decompression and stabilization is effective.

The proposed herein radiographic cyst ratio can be employed as an alternative to the already known cyst indexes for the selection of patients that can be treated with this treatment method.

Elastic intramedullary nailing has the twofold benefits of continuous cyst decompression, and early immediate stability to the involved bone segment, which permits early mobilization and return to the normal activities of the pre-teen patients.

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# OSTEOARTHRITIS IN NEW-BORN BABIES AND INFANTS

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## Abstract

In the case of newborns and infants two general types of infections can occur. Early-onset infections occur in the first week of life, with an average onset age of 20 hours. Approximately "half of these children have signs of infection at birth with a group B streptococcal infection." (1,2) This infection is acquired during or shortly before birth, from the microorganisms colonizing the maternal genital tract. Surveillance studies have shown that 40% of women are carriers of group B genital or rectal streptococci (1). Approximately "50% of children born via genital way by infected mothers become colonized" (3), although only 1-2% of those colonized develop a clinically obvious infection. Prematurity and maternal risk factors are frequently encountered. (prolonged labor, obstetric complications and maternal fever). The aspect of early-onset infection is the same as other forms of neonatal sepsis. Typical signs include: respiratory distress, lethargy, hypotension. All neonates presenting an early-onset of the disease had: bacteremia, 1/3 up to 1/2 had pneumonia and / or respiratory distress syndrome and 1/3 had meningitis. "Delayed-onset infections occur in infants aged between one week and three months, with an average age of 3-4 weeks" (1). Microorganisms can be acquired during birth- as in early-onset cases-or later, through contact with colonized mother, medical staff or other contaminated sources. "The most common manifestation of delayed-onset infection is meningitis," (2) which in many cases is associated with type III encapsulated strain infections. Infants have: fever, lethargy, refusal to eat, seizures. Signs of poor prognosis are: hypotension, coma, status epilepticus, neutropenia. Over 50% of survivors have some degree of "long-term neurological damage from a slight delay in the appearance of language or hear loss, to the profound mental retardation, blindness and seizures that cannot be controlled" (5). A variety of late-onset infections can occur including "bacteremia without an identified source, osteomyelitis, septic arthritis and facial cellulitis associated with preauricular or submandibular adena." (4) "Nowadays, streptococcus B represents, together with Escherichia coli B, represents the main cause of neonatal infection." (6) B streptococcus is responsible for 40% of neonatal infections; infections caused by this germ affects 5% of newborns, 3% are early infections and 1.5% delayed infections. The prevalence of B streptococcus neonatal infections could be the consequence of: improvement of bacteriological screening techniques; use of preventive antiseption against

Staphylococcus that favored the Streptococcus development; antibiotic treatment of pneumococcal infections, that inhibits the formation of pneumococcal antibodies for the mother and, in particular during childhood. Approximately 60% of cases are caused by type III, which contrasts with the distribution of types I, Ib, Ic, II and III in "colonized" women and asymptomatic infants.

**Key words:** Group B streptococcus infection, epidemiology, pathogenesis, pathology, diagnosis: positive differential development, treatment, prevention, new-born.

## Introduction

### 1. EPIDEMIOLOGY, PATHOGENESIS

"After contamination time, there are two ways:

- ante or perinatal contamination (maternal-fetal infection)
- postnatal contamination (secondary infection).

a) Ante or perinatal contamination or maternal fetal infection. It's the most frequently encountered way involving:

- B streptococcus maternal infection;
- pathogen transmission to the fetus;
- "colonization" and / or fetal infection.

#### • *Maternal colonization.*

It is asymptomatic and is also known as maternal 'porting'. The origin of "colonization" is essentially sexual; 55% of the "carrying" women's sexual partners are "colonized" in the urethra. Factors that favor the maternal "colonization":

- B blood group;
- under 20 years of age;
- first pregnancy, twins;
- the use of an intrauterine device.

No correlations were observed between "colonization" and the use of contraception, sexually transmitted diseases, prior use of antibiotics and gynecologic symptoms. The frequency of premature rupture of membranes and premature birth is 8% and, respectively, 2% of all pregnancies, while they are 15% and 5% if the cervix sample is positive for streptococcus B.

#### • *Pathogen transmission from mother to fetus.*

It is done in various ways:

- marrow ("germs cross the placenta" (3) during a maternal bacteremia);

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-upward (germs from the vagina and/or cervical contaminate the amniotic fluid in relation with the premature rupture of membranes or after the transmembranal infection of the lower pole of egg);

-genital chain crossing (with inhalation of vaginal secretions).

- *Infection or "colonization" of the fetus.*

The current incidence of group B streptococcus infections does not exceed an average of 3 in 1000 births, there is about a new-born baby infected from 50-100 "colonized" babies. There are two common ways of infections. Sometimes the fetus is affected by "transplacental marrow"(3), directly or through a placenta outbreak, the germs pass into the umbilical veins, then in general circulation, "causing fetal bacteremia"(4). After the occurrence, one can observe abortions, fetal death, and birth of a premature baby presenting an "early sepsis" (4) or sometimes an early localized infection.

Most frequently, the fetus is affected via *amniotic way (ascending path)* or during *passage through the genital chain*. It produces a digestive and/or air "colonization", which is the starting point of an infection. "The infection can be localized with secondary generalization (may occur before or after birth) or generalized *d'emblée*, infection is usually early."(1,2)

Infection could be due to a germ, particularly virulent, streptococcus B III, while streptococci that are only "colonized" should be less virulent.

An essential role is played by a number of factors such as:

- "prematurity;
- fetal hypotrophy;
- shortage of maternal IgG antibodies against the germ in question"(3);
- lack of natural food.

b) *Postnatal contamination: secondary infection.*

The contamination is attested by the increased concentration levels of neonatal porting between birth and dismissal from maternity. The cause of this contamination could be:

- the mother (throat porting or the presence of germs in mother's milk);
- Maternity-staff ("colonization" in 25-44% of cases);
- other newly-born babies (transmission from one child to another is done through medical staff). Contamination results in porting or, quite rarely, in the baby's infection.

This possible infection is rather delayed (after 2 days of life), while the maternal-fetal infection is usually early (within 48 hours of life).

## 2. PATHOLOGY

Anatomo-pathological lesions are variable, depending on the age at which death occurred and the treatment that the child received.

*Lungs.* Macroscopically, the lungs are dark, dense and poorly aerated. The recesses are atelectatical; there are found hyaline membranes, identical to those encountered in

premature babies suffering from hyaline membrane disease. Within the inter-recessive septa is found interstitial edema, leukocyte infiltration and gram positive cocci. Sometimes, interstitial and/or intra-recessive hemorrhages are observed or pulmonary outbreak. The existence of pleural effusions is also quite frequent.

*Damage of the meninx.* It is common in cases \ of early death, pathological examination showing only minimal inflammatory changes. In the cases in which death occurred after several weeks of life, damage to the meninges is obvious and, characterized by significant local changes associated with the presence of thick pus.

## 3. CLINICAL PICTURE

B streptococcal infections developed in uterus can cause fetal death and premature termination of pregnancy.

There are described:

- early forms of disease, with the onset in the first 48-72 hours of life and even before birth;
- forms of delayed-onset between 2 and 4 weeks of life up to 16 weeks.

### *Early form.*

It's the most frequent B streptococcus type of infection. The following symptoms are observed:

- maternal fever, before, during or after birth (in 50% of the cases)
- amniotitis (in 30% of cases)
- prematurity (in 40% of cases)
- premature rupture of the water bag (in 60% of the cases)
- a low Apgar score (less than 5-7)
- stained amniotic fluid without any obstretical explanation.

All these events are reminiscent of maternal- fetal infection. The clinical picture is characterized by a bacterial pneumonia or septicemia. The pneumonia often begins at birth or within the first 6 hours of life. The following symptoms are observed:

- Severe respiratory distress;
- Marked expiratory groan;
- Frequent bouts of apnea.

An aspect resembling the hyaline membrane disease is achieved, associated, often in premature babies, with a pleural effusion.

B streptococcus septicemia is characterized through:

- early onset, within the first 4-6 hours of life;
- in 1/3 of the cases there is a free interval of 6-24 hours, and in 1/3 of the cases this interval exceeds 24 hours;
- severe respiratory failure is associated with a marked expiratory groan;
- bouts of apnea;
- septic shock, sometimes;
- disseminated intravascular coagulation and,
- in 1/3 of the cases, purulent meningitis"(4).

The evolution is severe. In 50% of cases, death occurs within few days or hours, sometimes before the beginning of the treatment; "neutropenia and the presence of a high antigen streptococcus concentrations in blood form a severe prognosis."(8) In the case of respiratory forms, modern methods of treatment have improved the prognosis. In the

case of surviving children, the reoccurrence of the group B streptococcus infection can be observed after one or more weeks after the treatment ended. It is difficult to determine whether the recurrence is of exogenous origin or caused by initial streptococcus strain, knowing that the B streptococcus may persist at the level of the mucous membrane, despite treatment.

#### *Delayed form.*

Onset disorders occur, generally between the 2nd and 4th week of life, but they may occur up to 16 weeks of life. The delayed form is, in the vast majority of cases, due to the IIIrd B group streptococcus. "The infection is postnatal and occurs in term delivered infants"(9); more rarely, the infection may have as a starting point the maternal-fetal infection, attenuated but not cured by the maternal antibiotic or a "preventive" antibiotic treatment in the newborn. Most frequently it develops into a meningitis, rarely, with an acute onset and a brutal evolution, usually, with an subacute, insidious appearance, which may complicate a subdural empyema or brain abscess that evolves to death or to a perfect recovery without sequelae.

Other clinical pictures are also possible:

- *Focal infection*: arthritis and /or osteitis with multiple locations (they are late clinical manifestations, which are most common after meningitis), media suppurative otitis ethmoid, conjunctivitis, facial cellulitis, necrotizing fasciitis, pulmonary infection;

- "*Rare delayed sepsis*, which complicates a localized form, and are also the starting point. Evolution of the delayed form is made according to clinical type. Delayed meningitis has a mortality of 45% and common sequelae (30% of cases)"(4,10). A successful treatment is found especially in case of short treatment (10 days) with a single antibiotic. Ventricle disease is common. Arthritis and osteitis complicate, through, the sequelae their functional outcome.

Other clinical forms occur between the 2nd and the 14<sup>th</sup> day of life. They would be due to an antenatal infection *in utero*. It's characterized by many clinical pictures:

- septicemia or
- localized infections (pulmonary, meningeal, osteoarticular).

Clinical expression is more severe as the onset is earlier and is more insidious and discreet as the onset is delayed. The prognosis is variable, generally favorable, thanks to the establishment of early treatment. Sometimes we can see recurrent infections.

#### 4. DIAGNOSIS

*Positive diagnosis.* It is based on the following data:

- the occurrence of infection
- clinical and
- laboratory data

Among laboratory data, some demonstrate the presence of infection, without focus on the nature of the pathogen in question, respectively:

- leukocytosis with polinucleosis and myelomiasis;
- high report between non segmented neutrophils / segmented neutrophils

- increased levels of thrombocytopenia, fibrinogen, C-reactive protein;

Bacteriological investigations allow identification of infection and highlight the next causative pathogen; it is recommended that these investigations take place before the introduction of antibiotic. During these investigations it is noticed:

- identification of "specific soluble antigens that can be highlighted in the blood and especially in urine, CSF, by contraimmune- electrophoresis or latex agglutination test."(6)

- positive blood cultures

- identification the pathogen at the site of the infection;

"The presence of group B streptococcus in the samples taken from nasal pharynx, ear, gastric fluid, anus or meconium, allow assertion of the "colonization" if, that is present in the first 12 hours in 3 different places and not infection."(1,2) Placental smears are important in specifying the nature of the pathogen in a newborn with an early infection.

*Differential diagnosis.* The differential diagnosis is made in two stages: emphasize of infection and identification of the pathogen that caused it.

- *Emphasize of infection* is the most important stage. Pulmonary disease makes us think of the membranes disease, amniotic fluid inhalation, and delay of the alveolar fluid resorption. Sepsis and localized forms bring multiple problems, according to the clinical picture.

*-Identification of the causative pathogen.*

After identifying the causative pathogen, the differential diagnosis is made with other bacterial or viral infections.

#### 5. EVOLUTION

Evolution takes place according to the date of occurrence of disturbances, the type of infection developed and also the earliness and quality of treatment. Overall, mortality reaches 25-30% and neurological sequelae are present in 40% of babies who survived meningitis.

#### 6. TREATMENT

*Curative treatment.* It is based on clinical presentation. General antibiotic therapy is essential. Before identifying the pathogen, the following association is used: ampicillin (200 mg/kg/day in 2-3 iv injections, in premature and newborn babies within the first 7 days of life and 3-4 injections after the 7<sup>th</sup> day of the term delivered baby) with gentamicin (5mg/kg/day i.m. or i.v., before the 7<sup>th</sup> day of life kg/day, after the 7<sup>th</sup> day of the term delivered baby, each dose being divided into 2-3 injections of 2.5mg/kg).

Once the pathogen is identified, the combination ampicillin-gentamicin replaces the isolated administration of ampicillin (200-300 mg/kg/day) or penicillin 200,000u/kg /day, in 2 i.v or i.m injections within the first 7 days of life, and, in prematures, 3 iv or i.m injections, after the 7<sup>th</sup> day after the baby is delivered. The combination of ampicillin – gentamicin was continued for 10 days; after this, the procedure continues only with ampicillin for a total of 15 days in the case of sepsis, pulmonary infection,

osteoarthritis, and for, at least, 21 days for meningitis. In general antibiotics the following association is used:

- the intra-rahidian administration of antibiotics in meningitis, is a very questionable measure, since the general path is enough;
- symptomatic treatment;
- if necessary, in severe cases: exchange transfusion, transfusion of fresh blood, transfusion of leukocytes, fresh frozen plasmainfusion.

*Preventive treatment.* Involves the mother and the new-born baby.

For the mother:

- eradication of pathogens likely to infect the fetus (maternal infection screening and treatment);
- antistreptococcal vaccination to achieve high levels of maternal antistreptococcal B III antibodies.

For the new-born babies: systematic detection of maternal porting, followed by:

- clinical supervision;
- peripheral samples from the babies whose mothers are carriers.

Under these conditions, neonatal infection can be detected early and treated very quickly, resulting in lower mortality caused by early streptococcal infection.

Septic arthritis, known as infectious, is the direct invasion of the joint space by various microorganisms (bacteria, viruses, mycobacteria and fungi), a sterile inflammatory process may be a consequence of infection in the body, located at a distance.

Although any infectious agent may cause arthritis, bacterial pathogens are the most significant due to the rapid destructive nature.

The two main classes of suppurative septic arthritis / or gonorrhea are bacterial non-gonococcal. Although Neisseria gonorrhoeae remains the most common pathogen - 75% of cases among sexually active young people, Staphylococcus aureus is a major cause of acute bacterial arthritis in adults and children over 2 years. This pathogen is the cause of 80% of the arthritis affected by the rheumatoid arthritis.

Species such as Streptococcus viridans, Streptococcus pneumonia and group B streptococci represent over 20% of cases. Aerobic gram-negative cocci are involved in 20-25% of cases. Most infections occur in the elderly or very young people, treated by immunosuppression, intravenous drug abuse. Sternoclavicular or sacroiliac joint infection with Pseudomonas aeruginosa or Serratia species occur exclusively in the case of drug addicts.

Polymicrobial infections - 10% of cases and infections with anaerobic organisms are a consequence of trauma or abdominal infection.

In the pre- antibiotic era, death was a common complication in septic arthritis. Those who survived the acute infection had severe joint destruction with fibrous or bone ankylosis. Tuberculosis infection causes fibrous ankylosis. Antibiotic therapy has reduced morbidity and mortality of the disease. The mortality rate is below 10%. Approximately 60% of patients completely recovered. An immediate treatment limits the long-term destruction.

Patients who are asymptomatic more than 7 days before the diagnosis, tended to report severe joint damage. Staphylococcus aureus and gram-negative bacilli tend to be more destructive. "Children with septic arthritis of the hip have long-term disability"(11). The prognosis is better for older children. Long term complications can occur together with growth disorders, bone or fibrous ankylosis of the femoral head.

Pathogens invade the joint by direct inoculation, by contiguity from the infected periarticular tissue or blood. The normal joint has several protective components. Synovial cells have a phagocytic activity and the synovial fluid has a bactericidal activity. Rheumatoid arthritis and systemic lupus erythematosus alter the defensive functions lowering the chemotaxia and phagocytosis. Previously altered joints, especially those with rheumatoid arthritis are the most susceptible to infection. "Synovial membranes of these joints have an increased neurovascularisation and adhesion, conditions that increase the chance of bacteremia. Some microorganisms link to sialoprotein joint, fibronectin, elastin, hyaluronic acid and prosthetic material."(11,12) The major consequence of bacterial invasion is joint destruction. As the destructive process of erosion continues, "it begins shaping cartilage erosions on the sides of joint."(11) Large effusion infections occur in the hip, which affect the blood supply and cause the septic necrosis of the bone.

In children and infants is difficult to diagnose. Infants and children present insidious inflammatory signs. Symptoms including fever, poor appetite and irritability without apparent damage to joints can lead to an incorrect diagnosis. Besides the obvious open fractures, foreign objects, and trauma, finding a remote infection is important. The clinical presentation of a child is similar to that of the adult. Yet the child cannot bear that the affected joint is touched. Additional symptoms may be present and leading to confusion, such as: nausea, vomiting, headache, pharyngitis and abdominal pain. Ear infections are the most common source of bacteria for septic arthritis.

"Tuberculous arthritis is usually, monoarticular, affecting the knee or hip"(12) Most patients are middle-aged or elderly. Unlike the pyogenic arthritis, tuberculosis causes chronic joint pain and minimal signs of inflammation. This condition leads to a delayed diagnosis. Synovial cultures and histological evaluation establish the diagnosis.

### **The aim of the paper**

The paper highlights the idea that osteoarthritis, in the case of newborns and infants, should be known by many doctors and, in particular by the neonatologist and the family doctor because they are the ones who first see the sick child and the prognosis of this condition depends on their early diagnosis. A very good training and knowledge of the disease correlated with a close collaboration improves surgical prognosis of the disease.

Knowing the signs of the disease by the great part of physicians who care for these children makes the disease to be recognized in time, and the child sent to the surgeon, who

set a clear diagnosis as result of investigations, and applies the proper treatment.

Treatment of osteoarthritis in new-born and infants is not a problem now days, if children are guided, after the onset of illness, in a service where they are treated surgically with good results.

### Material and method

The authors have conducted a retrospective study on a group of 15 patients hospitalized between January 2005 and December 2010, diagnosed with osteoarthritis and have analyzed the clinical symptoms, their duration, the existence of underlying diseases, diagnostic methods used, and

conservative and surgical treatment. The diagnostic methods were the clinical history, objective clinical examination and paraclinical examination – supported by radiography.

### Results

The study group consists of 8 girls (53.38%) and 7 boys (46.62%); (Fig. 1) an equal prevalence of disease is observed in women and men.

Their origin environment was urban in 7 patients (39.96%) and 9 patients (59.54%) came from rural areas (Fig. 2). The age of patients in the study group was variable, between 7days and 4months, the highest rate of infant age, in particular up to 4 months of life.

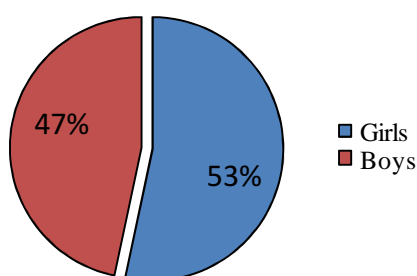


Fig. 1. Sex distribution.

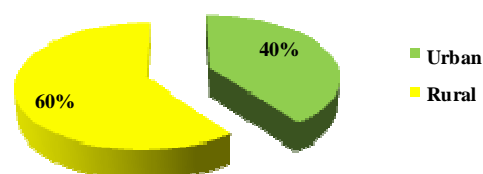


Fig. 2. Origin environment.

Patients have come directly to our surgery service (10cases - 66.60%), in an emergency, sent from other medical services, where they were initially hospitalized and treated for other diseases (2patients - 13.32%) and sent to our clinic on suspicion of osteoarthritis or other surgical

conditions (Fig. 3). The methods used for diagnosis were: clinical history, clinical examination, and radiography and laboratory examination. Surgery was performed on 12 patients.

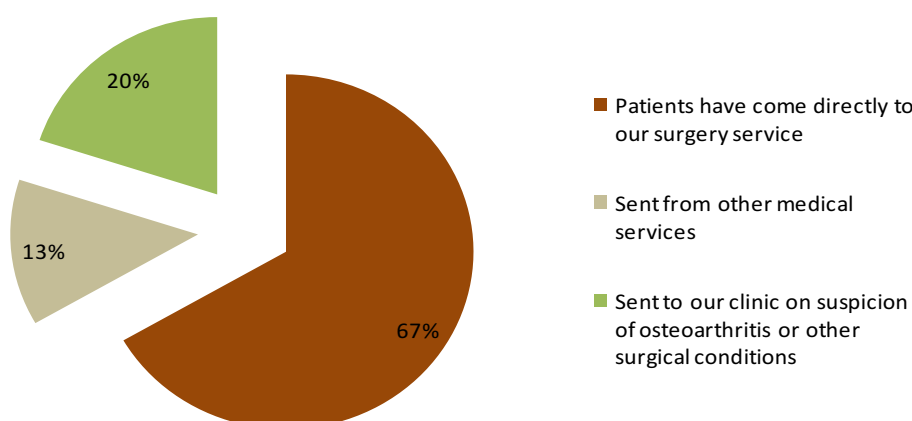


Fig . 3. Patients treated in our unit.



## Discussions

Osteoarthritis is a cause of disability in infants and toddlers. The diagnosis is, mainly, based on the clinical history, followed by imaging investigations.

The most common clinical picture consists of:

### Local symptoms:

- pain, especially in the shoulder, hips, knees or legs and sometimes in the spine;
- major functional impotence of the affected limb;
- serious, increased pain and swelling on palpation;
- deformed joints (especially in late stages of osteoarthritis).

### General symptoms:

- fever or even the lack of fever in advanced stages;
- alteration of general condition: loss of appetite, tachycardia, anxiety, lethargy;
- the association with other diseases that can mask the onset of osteoarthritis (pneumonia, meningitis, otitis).

Increased pain and the patient's altered state should alarm parents to report immediately to the doctor's. Patients

are detained and treated in the pediatric surgery service and orthopedics. Surgery should be performed early in cases that do not show indication for conservative treatment.

## Conclusions

- Group B streptococcus, represents, together, with *Escherichia coli*, the first cause of neonatal infection.
- *Ante or perinatal contamination*: maternal-fetal infection is the most frequent way, involving B streptococcal maternal "colonization", transmission of the pathogen in the fetus, "colonization" and/or fetal infection.
- B streptococcal infections developed *in utero* can cause fetal death and premature interruption of pregnancy.
- Osteoarthritis is a serious and disabling disease of the newborn and infant.
- Diagnosis is difficult and often delayed, with poor outcome of the affected joints;
- Before identifying the pathogen, the administration of general antibiotics is essential.

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## ROLE OF UROTHERAPY IN VOIDING DYSFUNCTIONS TREATMENT IN CHILDREN

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### Abstract

The study's *objective* was to implement a bladder therapy schedule to children with voiding dysfunctions and evaluate its efficiency. *Material and methods.* The study has been conducted between January 2005 and December 2009 at 3<sup>rd</sup> Pediatric Department, Cluj-Napoca. The study included 46 patients with voiding dysfunction symptoms, 40 females (86.9%) and 6 male (13.1%) with an average age of  $9.7 \pm 2.48$  years. They were investigated clinically and by renourinary ultrasound. The bladder capacity and post-void residual volume was determined by ultrasound. Each patient had kept a bladder and intestinal journal. The urotherapy consisted of multiple stages, the key element being the timed voiding. Has been determined the daytime incontinence evolution, bladder capacity and post-void residual volume. *Results.* The rate of therapeutic response at 6 months from therapy initiation was 86.9%, 26.1% were full response, 6.5% response, while 54.3% partial response. Only 13.1% did not respond to the therapy. The bladder capacity has increased significantly and post-void residue has diminished as a therapy result. *Conclusion.* Urotherapy can be considered standard therapy for children suffering lower urinary tract symptoms. The therapeutic success rate at 6 months was 86.9% with a full response of 26.1%.

**Key words:** voiding dysfunction, urotherapy, children

### Introduction

Toilet training develops during the first 4 to 6 years of life and it is a complex phenomenon. Besides the normal anatomy of the lower urinary tract, a complex neuronal system exists and is connected and controlled by the central nervous system (1).

In a meta-analysis published in 2008, regarding the bladder and intestinal control gaining, Mota et al analysed 473 articles published between 1960 and 2007. They concluded that bladder control gaining appears more late in most countries and an incorrect training can produce in time a bladder and intestinal dysfunction, causing social problems to the child and his family (2).

About 10% of children aged 5 to 6 years have daytime urinary incontinence. The prevalence decreases with age, it is about 4% between 12 and 18 years. (3-5). Daytime urinary incontinence, a common complain of voiding dysfunctions causes a major stress at school age and it affects the quality of life. It is mandatory to make an early diagnose and treatment to reduce the social and psychological impact of urinary incontinence and also to prevent the renal impairment and the development of renal scars.

Urotherapy was described for the first time in the late 1980s in Scandinavia. Today it is widely used in children with voiding problems. It is defined as a nonsurgical and non-pharmacological therapy of the lower urinary tract. It consists in the re-education of the bladder and its aim is to correct the filling and the evacuation phase (6).

The studies published in literature show a therapeutic success of 75-90% (3,7-9,10).

Bladder therapy includes the implementation of a normal "working schedule" of the bladder. It involves voluntary initiation of micturition at specific times, at 1-3 hours, without having voiding urgency before, for exercising the voluntary control on the bladder. It is necessary to establish a journal of micturitions, intestinal transit and liquid intake. After evaluation of liquid intake and the alimentary habits, rules for a regular and fixed liquid intake are made (3,10-13).

A central place in urotherapy is occupied today by timer voiding. It was demonstrated that despite the using of biofeedback therapy and pelvic floor training, the therapeutic results had improved after the introduction of timed voiding. Allen et al showed, in a study published in 2007, that timed voiding has a therapeutic success rate of 45% in patients with urinary incontinence. That's why they recommend this therapy to be used from the beginning in treatment of voiding dysfunctions, before using anticholinergic agents. They also sustain the idea that anticholinergic therapy appears to be overused as a first-line treatment for children with daytime urinary incontinence (11).

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The **aim** of the study was to implement a bladder therapy schedule for the children with symptomatic voiding dysfunctions and to evaluate the efficiency of this therapy.

### Material and methods

The study was performed during January 2005 and December 2009 in the III<sup>rd</sup> Pediatric Clinic, Cluj-Napoca. It was a prospective and observational study, performed with the informed consent of the parents, according to the Ethics Committee rules. The study included 46 patients with symptomatic voiding dysfunction, 40 were female (86.9%) and 6 were male (13.1%) with an average age of  $9.7 \pm 2.48$  years (%CI de 8.96-10.44 years).

The symptoms were represented by: urgency, daytime urinary incontinence and frequent voiding, more than 8 in 24 hours. Patients with neurogenus bladder and organic obstruction were excluded from the study.

A complete clinical examination and a history were performed for all patients. The bladder capacity was measured and compared with the values expected for the age, calculated by the formula:  $CV = 30 + [30 \times \text{age (years)}]$ . The values of bladder capacity were written as % from the age values. Examination for detecting urinary infection and a renourinary ultrasonography were performed for all patients.

Renourinary ultrasonography was performed with a SA 6000 C device, using a multifrequency transducer adapted for the patient age. Bladder capacity and post-voiding residue were determined. Bladder capacity was determined by measuring the transversal, longitudinal and anteroposterior diameters. After voiding, the post-voiding residue was also measured using these three diameters. A post-void residual volume over than 20 ml was considerate pathological.

Before starting the treatment, all patients wrote a journal about the hour and urine volume, the hour and the intensity of incontinence, the liquid intake and the intestinal transit as consistence and frequency of encopresis.

Urotherapy was performed several times. The first time a dialogue about the voiding dysfunction took place between therapist and the child and his family. After that a schedule was done about how and when the micturition to take place. The importance of a relax position was underlined so that a complete evacuation of the bladder to be done. The best position for pelvic relaxation is sitting with the thorax gently sloping in front with the thighs supported and slightly apart. When the micturitions are to take place: for that the journal of micturitions was evaluated for minimum three days. According to this, the initiation of micturitions at specific times, 1-3 hours without voiding urgency before, was recommended for practicing the voluntary control of the bladder. For those with significant residue a double micturition was recommended, meaning voiding again after few minutes so that a complete evacuation of the bladder to be done.

Patients with night-time urinary incontinence followed a wakening programme: day one waking hourly in the first 3 hours after bedtime (each time the child was asked if he wants to urinate and the last time he was made to urinate). In

the second day at three hours after bedtime, day three at 2 hours and a half after bedtime, day 4 at 2 hours after bedtime, day 5 at one hour and a half after bedtime, day 6 at one hour after bedtime and day 7 the child was left to wake alone. If he had involuntary voiding during this time the programme was repeated.

After evaluating the journal of intestinal transit, a therapy for constipation was given, where necessary, 1 ml/kg/day, maximum 40ml/day of paraffin oil.

The program lasted 6 month, after that a re-evaluation took place.

The therapeutic response was evaluated according to the number of urinary incontinence episodes, according with the International Children's Continence Society (ICCS) recommendations: no response (decrease between 0-49%), partial response (decrease between 50-89%), response (decrease with 90%) and full response (absence of symptoms or less than one symptom in one month)(14). The urinary incontinence episodes were evaluated by a severity scoring system: loss by drop-1 point, little dashes-2 points and wetting of upper clothes- 3 points. The amount of these symptoms was calculated during one week and the value was compared with the one obtained at the end of the therapy. The percentage obtained represents the decrease in number and severity of daytime episodes of urinary incontinence in one week (3,14). An ultrasonographic measurement of bladder capacity and residue was also performed.

All data were statistically processed using MedCalc programme for Windows version 9.3.2.0. The results were reported as arithmetic average, confidence interval 95% CI or percentage. The analysis of the parameters was obtained using Student Test for pairs and a correlation coefficient was applied. A p value under 0.05 was considerate statistically significant.

### Results

The demographic, clinical and ultrasonographic data are shown in table I.

The therapeutic success rate, evaluated after 6 month of therapy, was 86.9%. A 26.1% had a full response, 6.5 % were responding and 54.3% had a partially response. Just 13.1% did not respond to the therapy and needed anticholinergic therapy (Table II).

In table III are shown the clinical aspects, associated conditions and the ultrasound modifications, at the end of urotherapy, according to the response category.

The ultrasonographic evaluation performed showed a significant growth of bladder capacity after the end of treatment ( $p < 0.0001$ ;  $r = 0.84$ ) (Figure 1). Although, at the end of the study 21 patient still had a low bladder capacity for age, the values improved. At the beginning of the study, ultrasound showed an average value for post-voiding residue, of  $40.7 \pm 9.7$  and at the end of the study it was  $12.9 \pm 13.4$ , meaning a statistically significant decrease ( $p = 0.0008$ ;  $r = 0.70$ ) (Figure 2). At the end of the study 10 patients still had post-voiding residue, but with an improved value, under 40 ml.

Table I. The demographic, clinical and ultrasonographic data.

Parameters	Patients n (%)
Age	9.7±2.48
Sex    female	40 (86.9)
male	6 (13.1)
Urgency	25 (54.3)
Daytime incontinence	46 (100)
Nighttime incontinence	19 (41.3)
Frequency	22 (47.8)
Constipation	17 (36.9)
Recurrent urinary tract infection	24 (52.2)
Reduced bladder capacity	32 (69.5)
Post-void residual urine	21 (45.6)

n- number of patients

Table II. Results for study group patients with daytime incontinence at the end of urotherapy.

Urotherapy results	Patients (%)
Full response	12 (26.1)
Response	3 (6.5)
Partial response	25 (54.3)
No response	6 (13.1)

Table III. The clinical aspects, associated conditions and the ultrasound modifications at the end of urotherapy, according to the response category.

	Full response n (%)	Response n (%)	Partial response n (%)	No response n (%)
Urgency	0	0	3 (6.6)	4 (8.8)
Frequency	0	0	4 (8.8)	5 (10.8)
Daytime incontinence	0	3 (6.6)	25 (54.3)	6 (13)
Nighttime incontinence	0	0	3 (6.6)	3 (6.6)
Recurrent urinary tract infection	0	0	2 (4.4)	3 (6.6)
Constipation	1 (2.2)	1 (2.2)	2 (4.4)	2 (4.4)
Reduced bladder capacity	0	1 (2.2)	14 (30.4)	6 (13)
Post-void residual urine	0	0	4 (8.8)	6 (13)

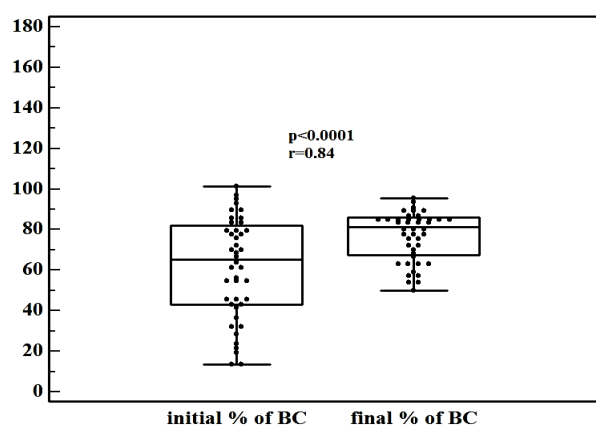


Figure 1. The graphs illustrated that the bladder capacity increased significantly after the end of urotherapy.  
BC-bladder capacity

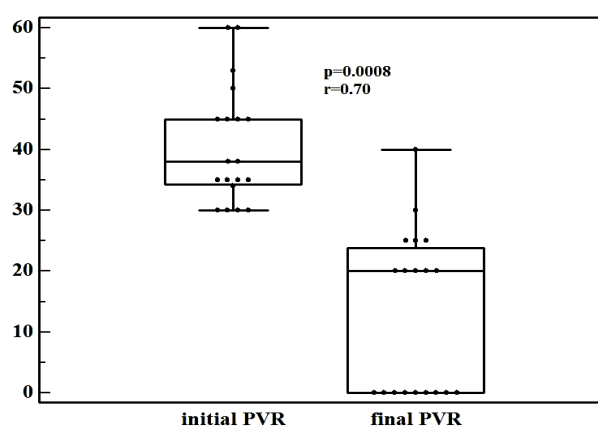


Figure 2. The graphs illustrated that the post-void residue decreased significantly after the end of urotherapy.  
PVR-post-void residue

Among all 24 patients with recurrent urinary infections just 5 of them (10.8%) still had urinary infection episodes but they associated important post-voiding residue.

After urotherapy and laxative agents the intestinal transit improved significantly the evolution of these patients, just 6 of them (13%) still had constipation at the end.

### Discussions

Urotherapy is now considerate to be the standard therapy for children with lower urinary tract dysfunction. Anna Helena Hellstrom published for the first time, positive results using this therapy (15). After that the Utrecht group reported a therapeutic success of 80 %. (6,16).

Despite the absence of randomized trials, different studies had shown favorable results of urotherapy. The voiding program is considered the best, with best results at lower costs. Bower and al said that “The learning of skills require practice and correction and repeated performance of the optimal maneuvers”, objective can be obtained by different therapeutic ways as long as the aim of the practice is the same (6).

In 2010, Mattsson et al reported a therapy success rate of 76%, sustaining the therapy in small groups of 2-5 persons as an alternative to the individual therapy. The positive results could be due to an increase confidence and a better perception of bladder and intestine function but also due to the modifications of voiding habits (17). Hoebeke notes that more important than the educative skills of the therapist, is the initiation of an individual program for each patient (6).

In the present study the therapeutic success rate after 6 month of urotherapy was 86.9%, according with the literature (3,5,8). Disappearance of the symptoms, increase of the bladder capacity and absence of post-voiding residue were present only in 26.1% of patients. Hellstrom et al reported a complete resolution rate of the urinary incontinence in 51% after 1 year and Hagstroem et al reported a rate of 55% (5,18).

A direct compare of the therapeutic results is difficult. First of all there is a big variability between the inclusion criteria and different treatment programs (1,6,19). Second, the seeking intervals were different. In long term studies the evaluation of daytime urinary incontinence showed a constant reduction of episodes, this means that the results of this therapy are not limited to couple of months (19).

Although the response rate is lower than in the literature, this probably is due to many factors such as the absence of 2 therapeutic elements: biofeedback and pelvic floor training (3,5). Programmed voiding before urgency appears, was the main therapeutic element use in this study. Hagstroem et al showed in a study published in 2008 that up to 70% of children previously refractory to urotherapy respond to treatment when timer-watch is added to therapy (15). Timed voiding seems to be a key factor in standard urotherapy (5,11,20).

In the responsive group patients (6.5%) and partial responsive group (54.3%) the main symptom of voiding dysfunction, urinary incontinence evaluated by a severity score, was present in 61.8% patients. These patients

achieved a decrease of urinary incontinence episodes during one week and an evident improvement of bladder capacity and post-voiding residue.

An important element in evaluation of patients with low urinary tract dysfunctions is bladder capacity, which improved considerably during urotherapy ( $p<0.0001$ ;  $r=0.84$ ).

Although at the end of the study, 45.6% of patients still had a reduced bladder capacity for age, this had increased compare with values found at the beginning of treatment. Low values were found in patients with partial response and no-response to treatment.

Mattson et al performed a study with 206 healthy, school age, children in order to evaluate the bladder capacity in children with normal lifestyle. The conclusion was that healthy children urinate when they want not necessary when they feel the need to urinate and only occasionally when the bladder is full. The voiding pattern is dependent of social activities (21).

Post-void residue determination represents o screening method for recognition of patients with low urinary tract dysfunction, but also a method for evaluating therapeutic response. Studies made on infants and healthy children showed that they do not empty their bladder with each voiding. (22-24). Delayed post-voiding ultrasound, with few minutes shows the presence in the bladder of 5 ml urine, which makes difficult to interpret the result. That's why ICCS considers as pathological a value of post-voiding residue over 20 ml (14). In present study at first, 21 (45.6%) of patients had post-voiding residue. After treatment and especially after double micturition, a statistically significant decrease of the post-voiding residue was obtained ( $p=0.0008$ ;  $r=0.70$ ). The average value of post-voiding residue at the beginning of the study was  $40.7\pm9.7$  and at the end it was  $12.9\pm13.4$ .

Constant presence of post-voiding residue increases the risk of urinary infection (25). Before starting the therapy, urinary infection was present in 24 (52.1%) of patients. Under therapy a significant reduction of post-voiding residue was obtain and also the numbers of urinary infection episodes. At the end of the study only 5 (10.8%) of patients still had recurrent urinary infections and persistent post-voiding residue.

The limits of this study are a small number of patients and a reduced possibility to compare the results with those in the literature because of the absence of randomized trials and the absence of a standardized method of urotherapy.

### Conclusions

Urotherapy can be considered standard therapy for children suffering lower urinary tract symptoms. The therapeutic success rate after 6 months was 86.9%, with a complete response on 26.1% of patients. Along with the disappearance/improvement of daytime urinary incontinence, an increase in bladder capacity, disappearance of post-voiding residue and reduce episodes of urinary infection, were obtained.

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# THE IMPORTANCE OF EARLY DIAGNOSIS IN THE SPLEEN RUPTURES. CASE PRESENTATION.

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## Abstract

**Introduction.** Duodenal stenosis is a narrowing or partial blockage of a portion of the duodenum. This condition is clinically manifested at birth or later in childhood. Clinical manifestations can range from loss of appetite, a downward weight curve and vomiting, to the sensation of filling up quickly or excessive hunger. **Case report.** We illustrate the clinical observation of a child admitted in our hospital for surgical solution of a subvateriene duodenal stenosis. Symptoms that led to the diagnosis was the episodes of bilious vomiting, bulk, both during and outside feeding. These symptoms implicitly achieve weight loss with a weight below the appropriate age. After surgical correction, the evolution was favorable, with subsequent absence of vomiting and achieving adequate weight curves. **In conclusion,** duodenal stenosis remains a disease with surgical solution and good postoperative prognosis.

**Key words:** duodenal stenosis, Ladd's band, child

## Introduction

Duodenal stenosis is a condition caused by incomplete recanalization of the duodenal lumen in the womb. The obstruction occurs most often near the ampulla of Vater. The clinical onset is variable and generally consists of recurrent vomiting, weight loss, abdominal distension, or halitosis due to undigested food in the stomach. Emergency therapy is represented by appropriate hydration, and gastric decompression by nasogastric probe. After stabilization, the patient follows surgical therapy which, if done properly, shows an excellent prognosis.

## Case presentation

We present the clinical observation of a patient admitted to our clinic with the suspicion of a duodenal stenosis.

D.B., a two month old baby boy, is hospitalized in the Second Pediatric Clinic from Cluj-Napoca, to investigate a vomiting syndrome. From the age of 3 weeks the baby has had frequent vomiting and bilious regurgitation, unsystematized, both during and outside the alimentation period. This syndrome became worse in the last few days and associated periods of extreme agitation. About a week after the onset of the vomiting syndrome, the baby had a maculo-papulous rash initially located in the scalp and was

spreading. During an episode of skin rash, he associated eyelid edema, which is why the eruption was interpreted as being an allergic one.

Physical examination at admission in the pediatric clinic reveals a baby weighing 4700 grams, a weight index of 0,94 and a nutritional index of 1,09. The general condition is good, the skin and mucous are normally colored and hydrated; the limbs are slightly cold but the time of recoloring is normal; cardio-pulmonary balanced, with no abdominal organomegalia at palpation. From the child's personal pathological history we retain a physiological pregnancy evolution, natural birth and a birth weight of 3,600 grams.

Laboratory investigations detected a tendency to metabolic alkalosis, slightly hyposodemia, leukocytosis and lymphocytosis, an increased level of immunoglobulins type A, M and G.

Upper digestive endoscopy of the stomach reveals a large amount of bile and an open pylorus. A gastrografen esogastroduodenal examination showed subvaterian duodenal stenosis with expansion above it (dilation of the first portion of the duodenum and stomach which looks volvulated) and the evacuation was delayed (Fig. 1). The abdominal ultrasound describes the same issue of obstruction of the duodenum which is dilated (predominantly proximal, but apparently also in the distal portion), large pylorus and duodeno-gastric reflux.

The case was interpreted as subvaterian duodenal stenosis in an infant with cow's milk protein intolerance and was translated in the Department of Pediatric Surgery from Cluj-Napoca to perform the surgical therapy of the duodenal stenosis.

In our clinic, it was decided to perform an exploratory laparotomy. After practicing a supraumbilical incision on the midline and then a subumbilical dissection of the musculo-cutaneous plans, we entered the peritoneal cavity. While inspecting the contents, we saw the appendix and the cecum to the left and a short mesentery. Subsequently we proceed to assess the extrinsic obstruction at the terminal portion of D3. At its entrance by the mesocolon flaw, we proceeded to its enlargement, with a thorough haemostasis. We ligated and cut the vascular arch of the mesocolon to allow an optimal dissection. After cutting off the obstruction we passed to the decolation of Treitz's angle which was in excess acolyte.

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We continued to free and fully mobilize the D3 and D4 duodenal portions. Subsequently, we noted the presence of a Ladd band which we cut and then we moved on to reconstruct the mesocolic bursa. In the last stage of surgery we placed drain tubes into the laterocolic and subhepatic spaces.

After surgery we adopted a particular lifestyle and therapeutic plan. Postural therapy was used and we used antiinfective and antiacid medication. The evolution was favorable, although in early days the weight curve was stationary. At discharge, the weight reached an appropriate age value.

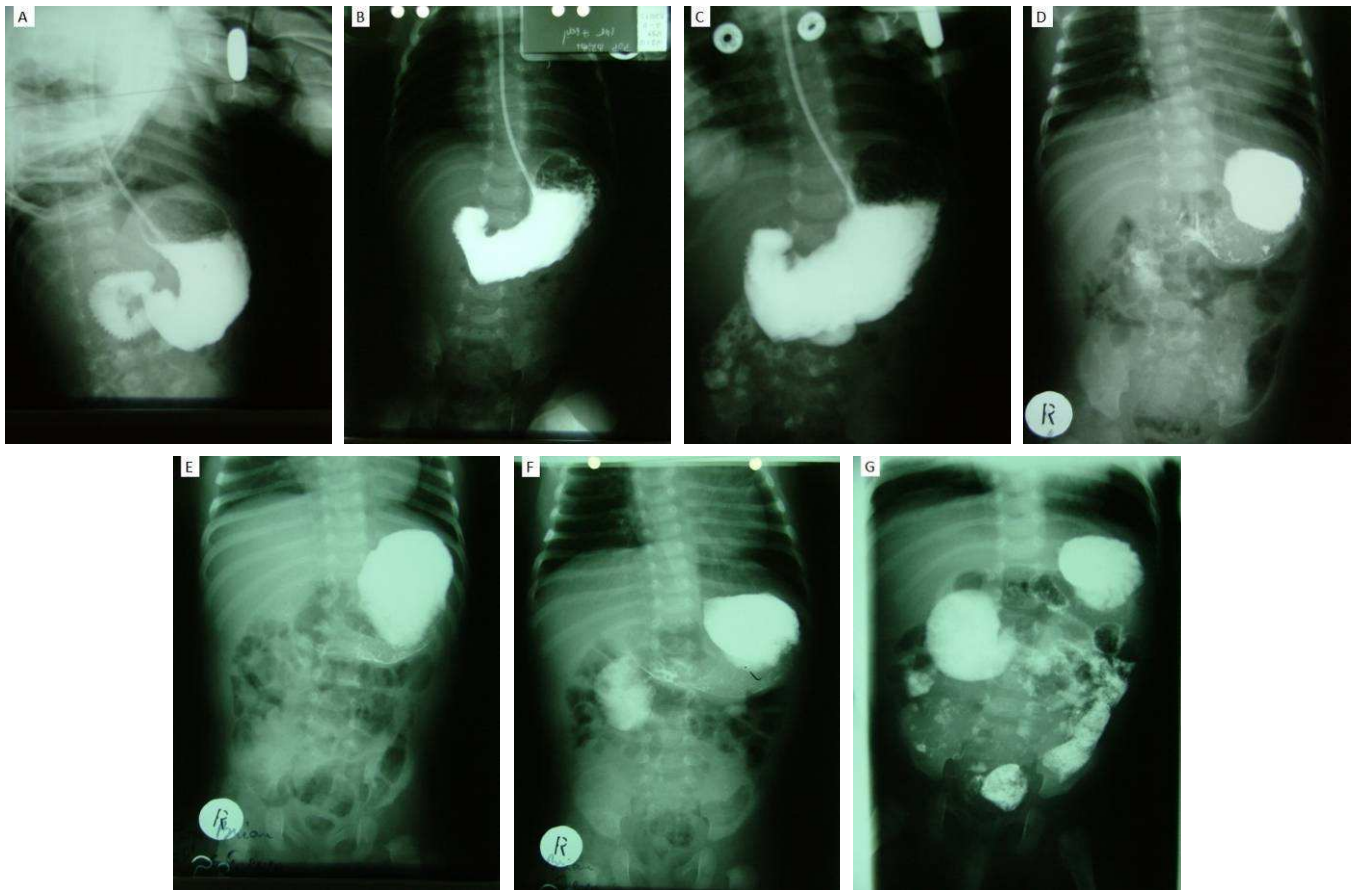


Fig. 1. Multiple radiographs with contrast (Gastrografin) showing contactions of the proximal duodenum (A,B), dilatation of the stomach and proximal duodenum (C,D,E,F), and little passage of contrast material distal to the site of stenosis (G).

## Discussion

Congenital obstruction of the duodenum was first reported by Calder in 1733. Cases resulting in duodenal obstruction may be represented by duodenal atresia and stenosis, annular pancreas or peritoneal bands secondary due to the incomplete rotation of the intestine.

Duodenal obstruction was often reported to be associated with Down syndrome, esophageal atresia or esophageal fistula. Other associated malformations include vertebral anomalies, congenital heart disease, mental retardation and Meckel diverticulum (1).

The incomplete nature of the obstruction in duodenal stenosis leads to variable clinical picture that can sometimes start at an advanced age. Detection of duodenal obstruction can be made by prenatal ultrasound, usually after polyhydramnios is detected. This issue causes intestinal failure to absorb the amniotic fluid.

Most obstructions are located distal to Vater's ampulla so, the clinical onset is typical of bilious vomiting without abdominal distension. Obstruction at a higher level will cause the appearance of symptoms from the early days of life, while less severe obstructions may allow the clinical setting after a few months or even years after birth. If onset occurs in the first stage of life it is usually manifested through weight loss, dehydration and metabolic hypochloremic alkalosis. The onset in adulthood can manifest as gastro-esophageal reflux or peptic ulcer.

Laboratory investigations indicated in cases of duodenal obstruction include dosage of pH meters and ionogram, this disease being characterized by loss of fluid and electrolytes.

Imaging investigations are mainly represented by the empty abdominal radiography, gastro-intestinal study using dye, abdominal ultrasound.



The empty abdominal radiograph usually reveals a distended stomach accompanied by significant expansion in the first part of the duodenum (the characteristic appearance of "double bubble") and the absence of air after the second air bubble.

The investigation of the digestive tract using a dye is important in establishing the exact diagnosis. If a small amount of air is observed below the obstruction, we are faced with a case of duodenal stenosis or other causes of partial intestinal obstruction.

An abdominal ultrasound is useful in detecting the renal abnormalities or the annular pancreas.

Initial therapy consists in stabilizing the patient. This process involves relieving flatulence through a nasogastric tube and acido-basic hydration by administering intravenously fluids.

After stabilizing the patient, the surgical treatment of the disease is performed. This involves excision of partially obstructed duodenum, followed by reconnecting the remaining healthy parts of the duodenum.

Surgery in duodenal stenosis includes duodenoduodenostomia (believed to lead to a faster recovery after surgery in terms of anastomotic function) or duodenojejunosomia (2).

The localisation of the obstruction is made by detecting the difference in terms of size bowel above and below the

obstruction and by placing the nasogastric tube below the obstruction.

In patients with malrotations, the Ladd procedure is performed, in which the Ladd band or bands detected are excised, the mesentery corresponding to the small intestine is widened, the appendix is removed and both cecum and colon are placed on the left side.

After surgery, the nasogastric tube remains and the patient will receive oral diet gradually, only after the appearance of the intestinal noises and stools.

There are a number of immediate and late complications that may occur after surgery. These are reported to occur in 14-18% of cases. Among the immediate complications we remember the ones related to prematurity, the presence of associated congenital malformations and those caused by parenteral (parental or prenatal) nutrition. Also, during the initial period after surgery, intestinal obstruction secondary to adhesions secondary can occur (3).

Late complications may occur months or years after surgery, and may include abnormal function of the duodenum, duodeno-gastric reflux and gastritis, peptic ulcer, gastro-esophageal reflux, colestasis (4, 5, 6).

Survival rate in duodenal stenosis is about 90-95 %. Mortality increases when the patient associates prematurity or congenital anomalies.

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# EPIDEMIOLOGIC, CLINICAL, PARACLINICAL AND THERAPEUTIC STUDY IN NEONATAL SEPSIS

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## Abstract

One of the major causes of morbidity and mortality in neonatal period is represented by sepsis. Sepsis study takes such great importance, is constantly developing modern means of diagnosis and treatment. In relation to the time distinguish *maternal-foetal infection* (early sepsis) is clinically evident from birth or the first seven days of life and has its debut in the intrauterine life, and *postnatal infection* (late sepsis) starts after birth, the source of infection being either maternal germs (ill or carrier mother) or environmental, often intra-hospital germs. This paper aims to review current means of diagnosis and therapeutic methods used in neonatal septicemia.

**Key words:** neonatal sepsis, diagnosis, treatment.

## Introduction

Sepsis is one of the major causes of neonatal morbidity and mortality. Considering the high incidence and gravity of the disease, the study of sepsis is extremely important and thus modern tools of diagnosis and treatment were developed.<sup>1-4</sup>

*Maternal-foetal infection* (early sepsis) is clinically evident from birth or the first seven days of life. This kind of infections has its debut in the intrauterine life.

*Postnatal infection* (late sepsis) starts after birth, the source of infection being either maternal germs (ill or carrier mother) or environmental, often intra-hospital germs.<sup>5-10</sup>

Prevalence of neonatal sepsis is of 1 case per 1,000 full-term neonates born alive and 4 per 1,000 preterm neonates born alive. Sepsis incidence in the case of low birthweight newborns hospitalised over a long period of time increases dramatically to 300 cases per 1,000 low birthweight newborns.<sup>11-13</sup>

Predisposing factors in neonatal sepsis may be grouped into: mother-related factors and newborn-related factors, in newborns within the first seven days of life.

## Purpose of the paper

This study has both retrospective and prospective character and aims at analysing the current diagnostic tools and therapeutic methods used in case of neonatal sepsis.

## Material and method

This study covers the period between 2005 and 2010 years in the newborns department within the "Louis

Turcanu" Paediatric Clinical Emergency Hospital in Timisoara.

During this above mentioned period, 10,683 babies were borned, out of which 1,092 were preterm newborns, and 177 cases of sepsis occurred.

**Newborns with sepsis were divided into two groups:**

- **Group I:** 137 newborns with early sepsis – disease onset in the first 7 days

- **Group II:** 40 newborns with late sepsis – disease onset after 7 days

Positive diagnosis of sepsis was established after anamnestic, clinical and paraclinical criteria.

### Study protocol for each patient included:

- detailed anamnesis intending to obtain as many as possible data related to the risk factors for infection

- full clinical examination performed daily, aiming at identify the clinical signs characteristic to the infected newborns and follow-up of each case's evolution

- suggestive paraclinical investigations and appraisal of diagnostic value on the studied groups

- application of therapeutic conduct and assessment of treatment on the studied newborns' groups

- anatomo-pathologic examination of all the deceased newborns, in which anatomical samples harvesting and bacteriological inseminations from organs (lung, brain, liver, spleen, kidney) were performed.

### The present study comprised:

- an analysis of the main risk factors for infection, both for early and for late sepsis. We have grouped these factors in major and minor risk factors.

- we have followed the clinical manifestations that occur more frequently in the neonatal sepsis and we have assessed the weight of clinical signs in the evolution of sepsis. As the clinical manifestation did not differ between the two groups, they were studied generally.

- we have conducted a study of the main investigations performed in order to establish the positive diagnosis. In the same time, we have calculated the diagnostic value of each investigation and we have developed a positive diagnostic score in sepsis.

- we have analysed the main therapeutic means used to fight against neonatal sepsis as effectively as possible.

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## Results and discussions

### Risk factors

#### Risk factors for early sepsis

The study was performed on 137 babies with maternal-foetal infection in the newborns department of "Louis Turcanu" Paediatric Clinical Emergency Hospital in Timisoara between 2005 and 2010 years.

#### **Gestational age**

Prematurity was the risk factor most frequently associated with maternal-foetal infection.

In the period between 2005 and 2010 years 10,683 neonates were born, out of which 1,092 preterms.

The correlation between prematurity and maternal-foetal infection has two explanations:

- premature membrane rupture might be a direct consequence of maternal chorioamnionitis
- premature membrane rupture of obstetrical cause favours ascension of germs forming microbial flora in the cervix and vagina and newborns' infection.

Infection (not only colonisation) is possible, as anti-infectious defence means are not fully developed in newborns.

#### **Maternal infection**

Among the studied cases, 36% of pregnant women had proved infections (chorioamnionitis).

Maternal infections more frequently encountered during the study that generated chorioamnionitis were urinary and genital infections (cervico-vaginitides and endometrioses).

**Urinary infection** was of great importance and frequency in the anamnesis of newborns with sepsis.

Correlation between urinary tract infection and maternal-foetal infection was as higher as the urinary infection was more severe or was treated more superficially (not treated or not fully treated).

Secondary bacteremia is a possible explanation, which can infect the newborn by the transplacental route.

**Genital infections** (cervico-vaginitides and endometrioses)

The pathogene germs infected the newborn by either ascendant route, after membrane rupture, or contiguity, during the passing through the pelvi-genital tract.

**Fever over 39°C during the labour** or within the first hours after birth is a major risk factor for maternal-foetal infection.

### **Cervico-vaginal transmission of pathogene germs (E.coli)**

Pathogene germs present in the vagina of pregnant women may infect the newborn during birth either by contiguity or by pathologic inhalation of vaginal secretions.

### **Prolonged time between membrane rupture and labour onset**

The longer the period of time between membrane rupture and onset of labour, the higher the infection risk. Two thirds of the newborns infected via this route had broken membranes for over 24 hours.

#### **Neonatal infection is more frequent in males (61%)**

Higher incidence of sepsis in males is mentioned in several studies in the literature. It is probably related to the existence of only one X chromosome, but there is still no explanation for this phenomenon.

### Risk factors for late sepsis

#### **Prematurity**

This was the main risk factor involved in late sepsis (97.5%). The causes for prematurity being so often involved in late sepsis are as follows:

- immaturity of anti-infectious defence in preterms
- frequent contacts with the maternity hospital personnel
- use of oftenly invasive care methods (perfusions, catheterisms, gavages).

#### **Prolonged hospitalisation**

Microbial flora in the hospital is a permanent threat for all the newborns because of their unusual susceptibility to infection.

**Severe diseases of the newborn** (hyaline membrane disease, pulmonary atelectasis) represent a risk factor for neonatal infection as these babies present pulmonary areas with ventilation and vascularisation disturbances and need invasive intensive care (mechanical ventilation, perfusions, catheterisms). Prolonged contact with intra-hospital microbial flora favours the onset of lung infection.

We have divided these risk factors into major and minor.

Major risk factors have a high correlation with neonatal infection and their presence suggest a high risk of infections. They are listed in table 1.

Minor risk factors have a reduced correlation with infection and their presence suggest a lower risk of infections. They are listed in table 2.

Table 1. Major risk factors.

<b>Major risk factors</b>	Prematurity Chorioamnionitis Fever during labor Maternal urinal infection Cervicitis, endometritis Membrane rupture over 24 hours
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Table 2. Minor risk factors.

<b>Minor risk factors</b>	Cervicovaginal portage of pathogen germs Membrane rupture 8-24 hours Male gender Care techniques (perfusions, gavage)
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**Clinical manifestations**

We have traced the clinical manifestations more often encountered in neonatal sepsis.

Clinical signs and proportion in which they were seen among the studied cases are shown in table 3.

Table 3. Clinical signs.

Clinical signs	Manifestations	Percentage
Thermoregulations disorders	Hypothermia, hyperthermia	25%
Behavioral disorders	Lethargy, irritability, spontaneous moan	88%
Cutaneous disorders	Acrocyanosis, pallor, marmoratis, purpura, edema, scleredema	55-65%
Respiratory disorders	DRNN, apnea with cyanosis, tachypnea	55-60%
Circulatory disorders	Early septic shock Refractory septic shock	75% 12%
Digestive disorders	Intestinal ansa distension, digestive intolerance, hepatomegaly	46%
Neurological disorders	Lethargy, irritability, seizures, abnormal movements of the eye balls, hypotonia, hypertonia, disappearance of the archaic reflexes	35%

Within this large and unspecific symptomatology, more suggestive clinical signs which correlated for the most part with the maternal-foetal infections were:

- grunting in the absence of respiratory distress syndrome
- tachycardia in the absence of fever or arterial hypotension
- skin marmoration
- purpuric petechia
- crises of apnea with cyanosis
- lethargia
- edemas, scleredemas

**Investigations**

We have studied the main investigations performed to establish the positive diagnosis of neonatal sepsis. For this, we have selected a group of tests useful for the diagnosis of neonatal sepsis depending on the experience and possibilities of the hospital.

None of the lab tests in this group has the specificity and sensitivity needed to get the sepsis diagnosis. For this reason, we have determined the positive predictive value and correlation coefficient between that investigation and sepsis for each investigation.

Based on the correlation coefficients, a diagnostic score was established which to be useful in the positive diagnosis of sepsis when associated with the risk factors and the mentioned clinical signs.

**Bacterial cultures****Blood culture**

Blood culture is a bacteriological diagnosis method by which identification of bacteria in the blood is made.

In order to perform the blood culture one can use both classical and automatic devices of detection. Blood cultures

were done for each baby with risk factors present in the anamnesis and with suggestive clinical signs of infections.

***Based on the results from blood cultures, the systemic infection has been divided into four groups:***

1. Sepses with germ identified in blood culture with clinical and biological context present, 33 cases (18.6%).
2. Asymptomatic bacteremias without clinical and biological context, but with risk factors for infection present in anamnesis, 22 cases (12.4 %).
3. Sepses with germ not identified in blood culture or in septic foci in which the clinical context is evident and biological context is present ("suspected sepsis"), 34 cases (19.2%).
4. Sepses with germ identified in septic foci in which clinical and biological aspects are present, blood culture is negative, but there are at least two positive cultures from septic foci that can communicate only by hematogenous route, 88 cases (49%).

In conclusion, depending on the presence or absence of pathogenic germ in the blood culture, the studied cases are distributed into four groups:

Regarding the etiological spectrum of the positive blood cultures, the results were the following:

Most common microbial flora was formed of gram negative bacilli, 47 cases (85.4%). The most frequently encountered germs were:

These results are consistent with the microbial flora encountered both in maternal and nosocomial infections.

- **Candida albicans** was the etiological factor in 3 cases (5.4%). Candida sepsis was seen in all the 3 cases in newborns weighing under 1,500 gr., cu infecție maternofetală.

- **Sepsis with pathogen staphylococcus-** 5 cases (10%). Out of these, 2 children had abscesses at the site of venous puncture, 1 child had lately inserted umbilical catheter, the umbilical stump being colonised by pathogen

staphylococcus and in two children the access route was not identified.

#### **LCR examination**

Examination of cephalorachidian liquid of each newborn included cytological, biochemical and bacteriological examinations.

Cytological and biochemical examination is less relevant immediately after birth considering the values normally increased of the leukocyte count and proteinorachia both in full-term and preterm newborns.

Meningitis incidence was 4.5%.

#### **Endotracheal culture**

In this study endotracheal cultures were performed in each babies intubated and mechanically ventilated (108 cases).

By corroborating the results of endotracheal cultures with clinical symptoms, risk factors and other investigations, the study results were:

- 68 cases – congenital pneumonia (63%)
- 23 cases – ventilator-associated pneumonia (21.5%)
- 17 cases– sepsis without respiratory infections (15.5%)

These results suggest the high weight of respiratory infections (congenital pneumonia, ventilator-associated pneumonia) within neonatal sepsis.

#### **Gastric liquid culture**

Positive cultures of gastric liquid in absence of clinical symptoms and characteristic smear are not proofs of infection, but of the colonisation of the newborn.

In the current study we have analysed digestive infection in newborns with both early and late sepsis.

In early sepsis, digestive infection occurred in the context of maternal chorioamnionitis, possibly by ingestion of infected amniotic fluid and it was part of the maternal-foetal infection (2.1%).

In late sepsis, digestive infection was present in 21 children (52%) out of which the most were II and III degree preterms fed by gavage and kept more than 7 days in the intensive care unit.

The significantly increased percentage of digestive infection within late sepsis proves the importance of the risk factors for the transmission of nosocomial infection (gavage feeding, prolonged hospitalisation, prematurity).

#### **Urine culture**

It is the bacteriological diagnosis method by which isolation and identification of bacteria in the urine is done. Non-invasive harvesting of urine was performed in each newborn.

In early sepsis were recorded 6 cases of de pyelonephritis (4.3%), kidney infection was considered the methastatic localisation of a maternal-foetal infection transmitted on transplacental route from mother to foetus.

In late sepsis were recorded 16 cases of urinary infections (40%), which spread in this situation by ascending route starting from cystitis, or, more rarely, the secondary localisation of a systemic infection with other access route.

Predominance of urinary infection in newborns with late sepsis suggests the importance of environmental microbial flora.

#### **Umbilical culture**

In all the newborns with periumbilical erythema or umbilical secretions umbilical cultures were performed.

In neither case the omphalitis as nosocomial infection became systemic infection.

#### **Complete blood count**

##### *Leukocyte count*

Leukocyte count is a useful, although not specific test for infections. When interpreted, the physiological variations in the leukocyte count in newborns were taken into account. The detailed study of different types of leukocytes revealed however that neutrophil count represent a more precise test and more valuable for the bacterial infection diagnosis.

Neutropenia is characteristic for neonatal bacterial infection, which is the reduction of the total neutrophil count under 1,500 cells/mm<sup>3</sup>.

To determine the positive predictive value of neutropenia in neonatal sepsis we have performed complete blood counts within 12 – 24 hours in all the newborns with risk factors for infections.

High incidence of neutropenia recorded in the infected newborns gives importance to the positive predictive value of neutropenia, 68%, while de correlation index with sepsis was 0.7.

More precise results are acquired by seprate determination of mature and immature neutrophil counts (promyelocytes, myelocytes and metamyelocytes).

Normal value of the immature neutrophils/ total neutrophils (I/T) ratio is lower than 0.2. Increase of this ratio over 0.2 is characteristic for infections.

##### **I / T < 0. 2 normal**

##### **I / T 0.2 infections**

I/T ratio is also a suggestive test for bacterial infection prognosis.

##### *Platelet count*

Normal values of platelets in full-term and preterm newborns are similar to those of the adults: 150,000 – 250,000 elements/mm<sup>3</sup>. Thrombocytopenia is the reduction of platelet count under 100,000 elements/mm<sup>3</sup>.

Thrombocytopenia occurs lately in severe bacterial infection and inspite of this often is recorded as the first sign suggesting infection.

High incidence of thrombocytopenia in sepsis (48%) determines its remarkable positive predictive value and the correlation index 0.5.

#### **C-reactive protein**

C-reactive protein is a globulin present in blood in the acute stage of inflammatory disease.

It doesn't pass the placental barrier; therefore its presence in the blood is due to its direct synthesis by the foetus or newborn.

All the newborns with C-reactive protein were deemed at high risk of sepsis. In each newborn two tests at 48 hours one after another were made. Positive predictive value of C-reactive protein for sepsis was related to the increase of C-

reactive protein in 70% of the infected newborns, which corresponds to a significant correlation coefficient, 0.7.

This test was less useful in the early sepsis diagnosis, but it was useful in establishing the final diagnosis and in the treatment monitoring. Good response to therapy was associated with the decrease of C-reactive protein values.

### **Glycaemia**

Glycaemia dosing is a simple and rapid investigation that has a significant correlation with neonatal sepsis.

### **Acid-base equilibrium**

Disturbance of acid-base equilibrium and metabolic acidosis onset are characteristic for sepsis.

Metabolic acidosis has high positive predictive value for sepsis in both the babies mechanically ventilated and not ventilated. Correlation index of metabolic acidosis with sepsis is 0.4.

### **Bilirubin**

Early jaundice was a clinical sign encountered sometimes at the onset of a systemic infection (12%). Intense jaundice, with bilirubin > 18 mg/dl, was also a clinical sign seen in newborns with sepsis (27.7%).

### **Treatment**

#### **Hygienic-dietetic measures**

Refer to special conditions of placing the newborns, oxygenotherapy, parenteral or enteral nutrition.

#### **Antibiotic therapy**

*Empirical antibiotic therapy in asymptomatic newborn* presenting risk factors for early sepsis was represented by the association of a beta-lactamin (ampicillin) with an aminoglycoside (gentamicin). This combination was utilised in 22 I degree premature newborns (12.4%).

Use of ampicillin as first-line antibiotic therapy is more and more rare; choice of a complex antibiotic formed of beta-lactamin associated with a beta-lactamase inhibitor is preferred. One antibiotic of this kind used in our section is unasyn (ampicillin + sulbactam).

*Empirical antibiotic therapy in symptomatic newborn* was the association of a cephalosporin (cefotaxime, ceftazidime) with an aminoglycoside (gentamicin). This combination was utilised in 110 nou-născuți (80%) newborns.

#### *Targeted antibiotic therapy*

Considering that microbial flora most often found in our department was formed of gram negative bacilli, most used preparations were cephalosporins associated with an aminoglycoside.

#### **Cephalosporins**

Use of II and III generation cephalosporins in the treatment of severe sepsis is due to the more efficient spectrum against all gram negative bacilli, including pseudomonas aeruginosa. In this study 91.5% of the newborns with sepsis were treated with cephalosporins.

#### **Aminoglycosides**

Mostly used aminoglycosides were: gentamicin (90%), amikacin (54%), netilmicin (18%).

Treatment with aminoglycosides lasted on average for 14 days in each newborn.

No nephrotoxic adverse effects were recorded among the studied cases, and data from literature assert that ototoxicity and nephrotoxicity in newborns are not significant.

### **Carbapenems**

Carbapenem class was utilised cautiously, being considered alternates for severe infections, possibly hospital infections; however, one third of the newborns with sepsis underwent this treatment: imipenem (Tienam) (29.3%) and meropenem (Meronem) (6.7%).

More selective use of carbapenems is recommended in order to avoid the development of resistant pathogen strains.

### **Vancomycin**

Vancomycin was used in 46 newborns (33%) out of which 32 had positive cultures with pathogen staphylococcus sensitive to vancomycin on antibiogram.

### **Antimycotics**

Candida sepsis was rare (2%) due to the prophylactic use of fluconazole in all the children with antibiotic therapy exceeding 10 days.

Antibiotic therapy was administered for at least 14 days, extending up to 3 weeks in severe sepsis and 6 weeks in sepsis associated with complications like: osteitis, arthritis, and pyelonephritis.

### **Treatment of septic shock**

#### **Volemic recovery**

Septic shock is a major emergency in the newborn and therefore rapid correction of blood pressure is critical. A fast and handy mean of temporary adjustment of blood pressure is perfusion with physiological serum 10 - 20 ml/kg body weight administered within 30 minutes. Immediate therapeutic effect was good but for a short time.

#### **Corection of tissue perfusion**

To improve the tissue perfusion and maintain the blood pressure, inotropic substances - dopamine, dobutamine - were used even in the first phase of septic shock. On average, the treatment with dopamine/dobutamine lasted for 5 days, the doses being decreased gradually and ventricular allure, blood pressure, and diuresis being monitored.

#### **Plasma**

Persistence of septic shock status and the danger of evolution towards the refractory septic shock imposed the use of plasma. Transfusion of fresh frozen plasma was utilised.

### **Treatment of clotting disturbances**

Clotting disturbances encountered within the studied cases were represented by 71 cases of thrombocytopenia (40.1%) and 8 cases CID (4.5%).

Thrombocytopenia required emergency treatment in order to avoid the severe complications it causes (cerebral, pulmonary, digestive hemorrhage).

Emergency treatment was performed by transfusion of platelet concentrate and fresh frozen plasma, the aim being not to regulate the biological parameters, but to cease the hemorrhagic manifestation.

The treatment of disseminated intravascular coagulation syndrome in newborns means the treatment of

septic shock (administration of fresh plasma, platelet concentrate, antibiotic therapy and control of metabolic acidosis).

#### **Treatment of acute infectious anemia**

When septic shock status was associated with low values of haemoglobine and hematocrite, blood transfusion (erythrocyte concentrate or fresh blood) iso group, iso Rh was performed.

#### **Treatment of metabolic acidosis**

Most times metabolic acidosis was adjusted by volemic recovery.

Adjustment of metabolic acidosis with sodium bicarbonate was done cautiously, especially in preterms, because of the important adverse effects (intraventricular hemorrhage)

#### **Treatment with immunoglobulins**

Treatment with intravenous immunoglobulins in newborns with sepsis is controversial.

We used, however, the drug named Octagam. Results were not significant; evolution, complications, and duration of the treatment were similar in newborns both treated and not treated with immunoglobulins.

#### **Prophylactic treatment**

##### **Early sepsis prophylaxis**

Early sepsis prophylaxis was done by careful monitoring of pregnant women, avoidance of premature deliveries, periodic performance of cultures (urine culture, cervix culture), and correct treatment with antibiotics of any infection during pregnancy.

##### **Late sepsis prophylaxis**

Late sepsis prophylaxis was done by promoting natural diet, avoidance of iatrogenic contamination, avoidance of excessive use of antibiotic.

To prevent the nosocomial infections in the neonatology department, a series of anti-epidemic measures that proved to be useful to this end are in place.

#### **Conclusions**

1) **Sepsis** is one of the major morbidity and mortality causes in the neonatal period. Considering the high incidence and gravity of the disease, the study of sepsis is extremely important and thus modern tools of diagnosis and treatment were developed.

The present study was conducted between 2005 and 2010 on two groups:

Group I consisted of 137 newborns with early sepsis in which the disease started in the first 7 days of life.

Group II consisted of 40 newborns with late sepsis in which the disease started after the first 7 days of life.

2) **The risk factors for neonatal sepsis** were analysed separately on the studied groups. Depending on the degree of correlation with sepsis, the risk factors were divided into two groups: major and minor.

The risk factors that correlated in a high proportion with early sepsis were: chorioamniotitis 80%, urinary infection 60%, fever during labour 80%, premature rupture of membranes 94%.

The minor risk factors that correlated in a lower proportion with early sepsis were: cervico-vaginal transmission of pathogen germs 3.1%, membrane rupture more than 24 hours before birth 2%, cervico-vaginitis 1.9%, and male gender 32%.

3) **Clinical symptomatology** is represented by a large range of clinical manifestations that evolve from the well-known 'the newborn doesn't look good' situation to the septic shock.

Clinical manifestations more frequently encountered in early sepsis were dominated by respiratory manifestations (DRNN, crises of apnea with cyanosis) 55-60%, skin manifestations (pallor, marmoration, early jaundice) 65% and behavioural disturbances (lethargy, irritability, grunting) 80%. In late sepsis clinical symptomatology was dominated by digestive manifestations (abdominal distension, meteorism, vomiting) 46%, thermal regulation disturbances (hypothermia, hyperthermia) 25%, and behavioural disturbances (lethargy, grunting) 88%.

4) **Septic shock** was often seen among the studied cases. Early septic shock, manifested by peripheral circulation disturbances, arterial hypotension, tachycardia, causeless changes in blood pressure, was encountered in 65% of the cases.

Late septic shock manifested through acute renal failure, scleredema, clotting disturbances (thrombocytopenia, CID) was seen in a smaller proportion 18% (CID, 4%)

5) **Paraclinical investigations** performed to establish the positive diagnosis of sepsis were divided upon the positive predictive value as follows: investigations with high positive predictive value, which we considered major, as they were significantly correlated with sepsis, and investigations with lower positive predictive value, which we considered minor, as they had lower correlation with sepsis.

6) **Blood culture** is a bacteriological diagnosis method by which bacteria in the blood are identified.

For blood culture both the automatic (85 cases) and classic (92 cases) methods of detection were used. 3 blood cultures were made on average for each patient: one initial blood culture, one control blood culture after 2 days and one control blood culture after 14 days.

7) **Etiological spectrum of blood cultures** was dominated by the presence of gram negative germs (85.4%). In early sepsis E.coli was involved most often, while in late sepsis there were klebsiella, proteus and pathogen staphylococcus. These results are consistent with those in the literature.

8) **Candida infection** was rare among the studied cases due to the prophylactic use of fluconazole in all the children with broad-spectrum antibiotic therapy exceeding 14 days.

9) **Neutropenia** is the most important and early sign for sepsis diagnosis. From the studied cases 68% of the newborns had neutropenia at the time of infection onset. Occurrence of young myeloid elements was present in 83% of the cases and was a good prognostic factor. I/T > 0.2 ratio is characteristic for infections.

10) **C-reactive protein** had increased values in sepsis, although not on the onset, but after clinical onset and after the change in the leukocyte count. For this reason more relevant for diagnosis was the dynamic increase of C-reactive protein values.

Within the studied cases, 64% of the newborns had C-reactive protein present. The test was also useful for treatment monitoring, decrease of C-reactive protein being associated with good response to therapy.

11) Both neutropenia and positive C-reactive protein were encountered in both study groups, no differentiation being possible from this point of view between early and late sepsis.

12) **Glycaemia** is a simple and rapid investigation that has been correlated with neonatal sepsis as follows:

Hypoglycaemia was seen in 8.7% of cases in early sepsis and in 20% of cases in late sepsis.

Hyperglycaemia was encountered in 29% of cases in early sepsis and in 22% of cases in late sepsis.

13) **Early jaundice** affected 12% of the newborns with sepsis, and intense jaundice with bilirubin > 18 mg/dl affected 27.5% of the newborns. Onset of early and intense jaundice (in absence of isoimmunisation) is a ground for sepsis investigations.

14) **Metabolic acidosis** is characteristic to sepsis. Within the studied cases, 60% of the children had metabolic acidosis.

15) **Empirical antibiotic therapy** in asymptomatic newborn was represented by the association of a beta-lactamin (ampicillin) with an aminoglycoside (gentamicin).

Use of ampicillin as first-line antibiotic therapy is more and more reduced as in the etiology of maternal-foetal infection resistant germs producing beta-lactamases (*E.coli*) emerged. In this context we preferred the choice of a complex antibiotic formed of beta-lactamin associated with a beta-lactamase inhibitor (Unasyn).

16) **Targeted antibiotic therapy** was started either after getting the results of bacterial cultures and antibiogram or by presuming a pathogen germ from the known microbial flora.

II and III generation cephalosporins were used in all the newborns with sepsis.

Carbapenems (Tienam and Merronem) were used with caution to avoid the development of resistant pathogen strains, they being considered the reserve class for severe, possibly hospital infections.

Vancomycin was used in superinfections with pathogen staphylococcus, either proven by positive cultures, or suspected during disease evolution.

17) **Treatment of septic shock** envisaged volemic recovery and correction of tissue perfusion. Rapid, but temporary recovery of blood pressure was accomplished by short perfusions with physiological serum 10-20 ml/kg body weight administered within 30 minutes.

Tissue perfusion improvement and blood pressure maintenance were obtained by using vasoactive substances (dopamine and dobutamine).

Vasoactive substances treatment lasted on average for 5 days, the doses being decreased gradually and ventricular allure, blood pressure, and diuresis being monitored.

18) **Treatment of clotting disturbances** was performed by transfusions of freshly prepared platelet concentrate and plasma.

Platelet concentrate transfusion was performed in all the newborns with hemorrhagic syndrome (spontaneous bleeding, prolonged bleeding after injections) and in newborns without hemorrhagic syndrome, but with platelet count under 30,000/mm. Transfusion of fresh frozen plasma was used quite frequently in the treatment of sepsis in the neonatology department; 43% of the newborns with septic shock underwent plasma treatment.

19) **Treatment with intravenous immunoglobulins** had not the expected effects; the drug named Octagam was however used, administered in a dose of 400 mg/kg body weight/day, repeated after 7 days.

20) **Neonatal sepsis prophylaxis** targets both the early and the late forms.

Early sepsis prophylaxis is done by prophylactic antepartum antibiotic therapy administered to all the pregnant women at infectious risk. Also, early sepsis prophylaxis is made by the correct treatment of any infection during pregnancy, especially the urinary infections and cervico-vaginitides.

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# CONSIDERATIONS ON THREE CASES OF HEMANGIOMA WHICH WERE TREATED WITH INTRALESIONAL BLEOMYCIN INFILTRATION

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## Abstract

Hemangiomas are benign neoplasms of the vasculature frequently encountered in children. Several studies have shown that these tumors are characterized by excessive angiogenesis. Although benign, the lesions can present with complications, and may thus require treatment. There are multiple therapeutic options available for patients with problematic or life threatening hemangiomas, some of which have serious side effects.

The treatment of congenital vascular anomalies is based on an understanding of the clinical behavior and natural history of individual lesions. Most hemangiomas do not require immediate intervention and 90% can be expected to undergo gradual involution before the age of 9 years.

Hemangiomas are classified as capillary, cavernous, and mixed lesions. The incidence in newborns is 1-3%, and this increases to 10% by the age of 1 year. In the biologic classification proposed by Mulliken and Glowacki in 1982, hemangiomas are defined as vascular tumors that enlarge by rapid cellular proliferation.(1,2)

In contrast to hemangiomas, vascular malformations are hamartomatous lesions composed of dysplastic vessels lined by non-proliferating endothelium. They almost never regress and may expand in size.

Complications of hemangiomas are cosmetic and functional, and depend on their location, size, or rapid proliferating phase.

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

Our patients were treated with intralesional injections of 2 mg bleomycin as a 0.4 mg/ml solution in the local area. The injections were repeated after 4-6 weeks for a total of 6-10 times.(3,4,5)

**Key words:** hemangiomas, congenital vascular anomalies, intralesional bleomycin injection

## Introduction

Isolated hemangiomas may be seen in 1-3 % of normal newborns, and 10% of normal children under 5 year old. Hemangiomas and vascular malformations( low flow venous ) represent 84 % from all vascular malformations( Mulliken – 800 cases between 1995- 2007 ).(1,6)

Specialties interested: almost all medical specialties.

Often can be errors of diagnostic and treatments

Basic knowledge of treatment of hemangiomas: INTRALESIONAL BLEOMYCIN INFILTRATION , other sclerotherapy, laser (not longer use ), systemic drugs (propranolol), interventional vascular embolization( for arteryovenous fistulae),surgery as primary and secondary treatment.(7,8)

Hemangiomas represent stem cell tumor from pericyte. Experimental utilization of immunosuppressor drugs and immunomodulators like Rapamicin have good results.(9,10)

## Purpose

The main goal of our study was to determine the importance of intralesional infiltration in decrease of vascular tumor.

The paper present the case of a 2-year old infant hospitalized in our clinic for a vascular tumor.

The child requires follow-up, as the evolution and prognosis of disease can be unfavourable.

This kind of treatment with bleomycin infiltration is representative for our clinic.

Today we can observe a increase number of this type of hemangiomas and vascular malformations.

## Material and method

Study was made using a child who had this vascular tumor since birth.

Ultrasound examination and CT will be used if is necessary

## Case presentation

### First case

The 2-year old infant was admitted to our clinic for fever, unfavorable and rapid vascular tumor grow up.

Family history revealed young and apparently healthy parents. He was the second child, with normal gestation. He's brother have no health problem.

Child has a perianal hemangioma on admission in hospital who look like this (fig 1).

He was treated with intralesional injections of 2 mg bleomycin as a 0.4 mg/ml solution in the local area.

After 4 weeks, when the child was returned in our clinic he look better (fig.2).

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Fig. 1. Perianal uninjected hemangioma.



Fig. 2. After first injection.

Has made a new intralesional injection.

After this second injection tumor was limited both in area and intensity. After 5 weeks tumor look like this (fig3).

Third injection was performed after this 5 weeks and after another 4 weeks, when the child was returned, their tumor size reduced remarkably (fig4).

Last injection was performed after one month.

Now, after a month, vascular tumors is total decreased and remained only slightly pigmented scars (fig.5)



Fig. 3. After second injection.



Fig. 4. After third injection.



Fig. 5. In present, after four injection (slightly pigmented scars).

The second case is present on admission in this way. Note the presence of ulcers in the hemangioma (fig 6).

After the first injection, at intervals of four weeks is seen as ulcers and reduce tumor size was significantly reduced (fig.7).

Proceed to the second injection.

After six weeks of this, notice the disappearance of ulcers and normal skin tissue appearance (fig.8).

It injects the third time remaining hemangioma. After eight weeks we obtain the following tumor appearance (fig.9). It is found almost entirely normalization of skin tissue.



Fig. 6. Laterocervical uninjected hemangioma.



Fig. 7. After first injection.



Fig. 8. After second injection.



Fig. 9. After third injection.

*The third case* shows a hemangioma located in the nasal pyramid which makes it be considered an emergency (fig.10).

It is injected. At an interval of five weeks after first injection is noticed a change in the surface and intensity of hemangioma (fig.11).

Proceed to the second intratumoral injection.

Following this, after two months, the entirely tumor almost disappear, in its place remains an area of hyperpigmentation of the nasal pyramid (fig.12).



Fig. 10. Uninjected hemangioma.



Fig. 11. After first injection.



Fig. 12. After second injection (remains an area of hyperpigmentation).

### Results and discussions

Currently in our pediatric surgery clinic is constant treatment with intralesional bleomycin injection for total of 22 patients, in various stages of treatment.

Also see that evolution was a sure-fire hemangiomas their disappearance and their transformation into scar skin hyperpigmentation.

From aesthetically parents of these children were very happy and did not regret the decision to opt for this method of treatment.

After a period of few months and few Intralesional injections with bleomycin, hemangioma was treated with a very good result both functionally and aesthetically.

For a best treatment is necessary a very good compliance from the patient.

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# NEUROLOGICAL COMPLICATIONS AT EXTREMELY LOW BIRTH WEIGHT PREMATURE NEWBORN

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## Abstract

**Introduction** Premature birth is one of the most difficult, complex and delicate problems of modern medicine. Intraventricular hemorrhage is the most frequent form at newborn, more often seen at premature than at term newborn. Periventricular leucomalacia : an ischemic lesion of periventricular white matter, characteristic to premature.

**Objectives** The study wants to establish: the incidence of extreme prematurity related to other categories of premature, repartition by sex at studied lot, incidence of cranial hemorrhage and hypoxic-ischemic perinatal pathology at studied lot.

**Material and method** The study was carried out in the Premature - Neonatology Department of the Clinical Emergency Hospital for Children „L. Țurcanu”.

**Conclusions** The high incidence of intraventricular hemorrhage (91,83%) can be explained due to its' high incidence in the pathology of extreme prematurity and also due to better possibility to diagnose with transfontanelar ultrasonography, this being performed serially to all premature hospitalized in our clinic. At our studied lot we observed high incidence at IInd degree intraventricular hemorrhage (44,44%).

**Key words:** neurological complications, extreme prematurity

## Introduction

Premature birth is one of the most difficult, complex and delicate problems of modern medicine.

Intraventricular hemorrhage is the most frequent form at newborn, more often seen at premature than at term newborn. Its' importance is not only in high incidence of this pathology, as the number of small and very small premature survival increases, but also in the major impact on perinatal and post neonatal morbidity and mortality, through secondary neurological sequelarity, through complications and lesional associations.

The figures regarding incidence of intraventricular hemorrhage depends on several factors: years of reference, degree of equipment and performance of perinatal study center, categories of gestational age and birth weight,

gravity of hemorrhage forms, diagnosis methods, use of ultrasound screening, morbid association, prophylaxis methods.(1,2). The frequency of peri and intraventricular hemorrhage is in opposite relationship with the birth weight.

After Perlman and Volpe, at premature with birth weight between 500 700 g the incidence of intraventricular hemorrhage is 62%, out of which 97% are severe forms (degree III and IV), while at those with birth weight between 700 and 1500 g, the incidence is 25% and only 32% are severe forms. These data are related with some offered by other studies. Gleissner shows, in a study, that incidence of intraventricular hemorrhage is 48,5% at 27 weeks of gestation, 32,4% between 28 and 32 weeks of gestation and decreases to 26% after this age.(2,3)

Incidence of peri and intraventricular hemorrhage at premature decreased constantly in the last years, from approximately 40% at children with birth weight <1500g to 20% in recent studies. (4,5,6)

Even the incidence decreased its prevalence amongst the surviving children is still substantial due to high rate of survival of newborn with birth weight under 1000 g.

The frequency of peri and intraventricular hemorrhage at newborn with very low birth weight who survive, depending on its' severity: low 70% (40% with degree I, 30% with degree II), moderate 20%, severe 10%.

From the children with peri and intraventricular hemorrhage degree III-IV, approximately 50% will need treatment for posthemorrhagic hydrocephaly, and 50% will have either static ventriculomegaly or transitory ventricular dilatation.

**Periventricular leucomalacia** (PVL): an ischemic lesion of periventricular white matter, characteristic to premature. At autopsies is revealed at 75% from deceased premature with moderate and severe hemorrhage. Now, the frequency of PVL amongst the children with hemorrhage who survive it is difficult to establish because cranial noninvasive imagistic techniques can very hard make the difference between the two lesions. Ischemic lesions from PVL are, usually, symmetric, at border arterial areas near the lateral ventricle trigon, periventricular.

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By the origin, localization and pathogenetic mechanism they are different from the periventricular hemorrhagic venous infarct. This is of venous origin, frequently unilateral or asymmetrical when it is bilateral, representing a complication of intraventricular hemorrhage and having a triangular shape and periventricular localization anywhere along the lateral ventricles, frontal dominant. More, intraventricular hemorrhage precedes the appearance of PVL, once with the start of intraventricular hemorrhage the risk of PVL is raising 5-9 times. In 25% of the cases PVL complicates with intralesional hemorrhages. One of the risk factors in PVL are coagulating affections.(7)

There are two steps in the diagnosis of HPV/IV: recognizing the child with risk and using a screening procedure. Even multiple imagistic ways are available, ETF is the screening procedure most used.. The prognostic value of examination is higher with the usage of Doppler ultrasonography that allows examination of cerebral hemodynamics, because a big part of neonatal cerebral lesions are of circulatory origin.

Is recommended that ETF screening to be done in the first 7-10 days of life. Because at 20-40% from patients hemorrhage can evolve, it is recommended to repeat ETF at 2 weeks of life in order to establish the maxim evolution of hemorrhage. After major episodes of HPV/HIV, serial ultrasonography must be done weekly to monitor the ventricular size and early track of hydrocephaly. If ETF screening is normal there are not necessary further examinations, in the absence of clinical symptoms.(8,9,10)

## Objectives

The study wants to establish:

-the incidence of extreme prematurity related to other categories of premature.

-repartition by sex at studied lot

- incidence of cranial hemorrhage and hypoxic-ischemic perinatal pathology at studied lot

## Material and method

The study was carried out in the Premature - Neonatology Department of the Clinical Emergency Hospital for Children „L. Țurcanu”.

Here were hospitalized, investigated and treated, between 01.01.2006 and 30.06.2010, a number of 3239 premature and term newborn from that 98 premature with extremely low birth weight.

## Results and discussions

### Annual incidence of newborn with extremely low birth weight

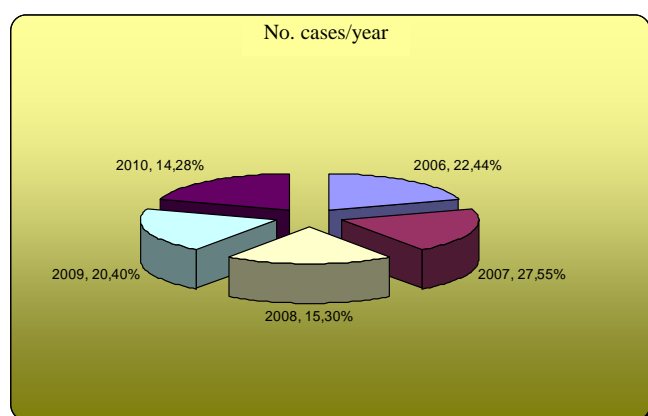
From the 98 cases studied, 22 (22,44%) were registered in 2006, 27( 27,55%) in 2007, 15 (15,30%) in 2008, 20 (20,40%) in 2009, 14 (14,28%) in 2010 until 30.06.(graphic 1)

### Case repartition depending on sex

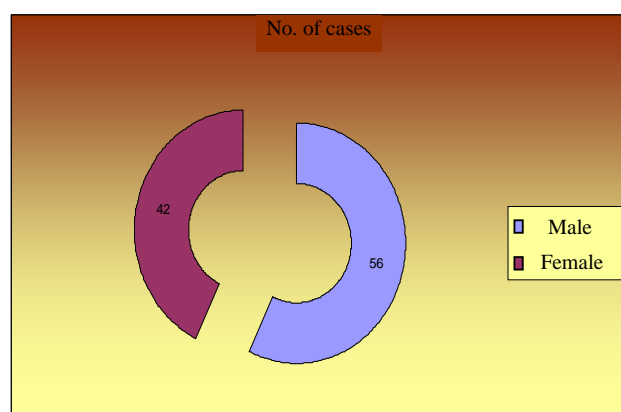
The repartition by sex of the premature newborns from study, by years, revealed the dominance of male gender (graphic nr.2):

- Male gender.....56 cases (57,14%)
- Female gender.....42 cases (42,85%)

Following the repartition by sex and the years of study it is highlighted a slightly dominance of male gender in all the years of study excepting 2008 where the ratio female gender / male gender = 1/2.



Graphic 1. Percentage distribution of cases from the study.



Graphic 2. Repartition by sex of the premature with extremely low birth weight.

Pathology was frequent at the entire lot of premature studied, more rich as the prematurity degree was higher.

Intraventricular hemorrhage is one of the major causes of morbidity and mortality of premature in neonatal period.

Predominance of hemorrhagic lesions is due to cerebral tissue immaturity (especially of the germinal matrix – start

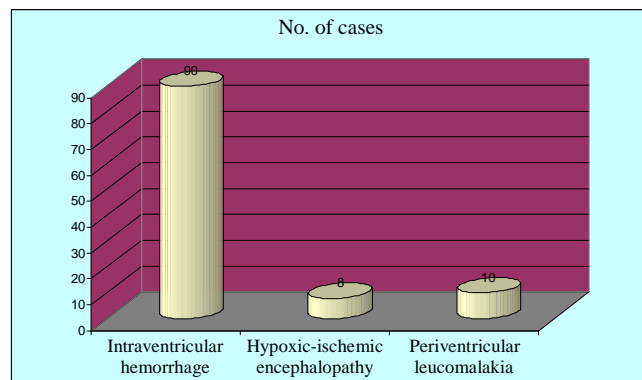
point of this lesion), and to presence of starting factors: acute hypoxia, intrauterine cronical hypoxia).

Incidence of intraventricular hemorrhage is high at the studied lot (91,83%)- 90 cases.

In 8 cases transfontanelar ultrasonography highlighted:

- hypoxic-ischemic encephalopathy in medium form-----5 cases (5,1%)  
 - hypoxic-ischemic encephalopathy in severe form -----3 cases (5,1%) (Graphic nr.3)

În 10 cases there was presented association of intraventricular hemorrhage with periventricular leucomalacia. (10,20).



Graphic 3. Repartition of neurological complications by number of cases.

Due to poor status one case couldn't benefit of this intervention, being deceased later.

Transfontanelar ultrasonography was carried out for all the premature hospitalized in our clinic. Even if in the literature the highest incidence belong to intraventricular hemorrhage of IIIrd and IVth degree, at our studied lot we observed high incidence at IInd degree intraventricular hemorrhage (44,44%).

Our data don't differ from literature. Despite antenatal prophylaxis measures incidence is still high. This is due to major incidence of associated perinatal pathology – SDR, infectious pathology.

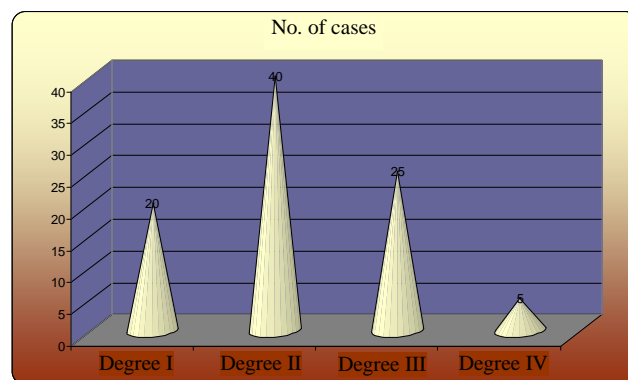
Low Apgar score at 1, 5, 10 and 20 minutes, clinical diagnosis for perinatal hypoxia (depending of severity) and the presence of fetal acute or cronic affection were identified at premature lots of LPV.

Congenital malformations represents, together with respiratory distress syndrome, intraventricular hemorrhage and infections, one of the main causes of death.

It was highlighted a number of 5 cases (4,9%) of cerebral malformations associated with intraventricular hemorrhage.

We can observe the predominance of intraventricular hemorrhage comparative with other pathologies.

Repartition by cases of the intraventricular hemorrhage degree was: degree I = 20 cases (22,22%), degree II = 40 cases (44,44%), degree III = 25 cases (27,77%), degree IV = 5 cases (5,55%) (Graphic 4)



Graphic 4. Graphic representation of intraventricular hemorrhage degree.

## Conclusions

1. The incidence of extreme prematurity at studied lot distributed per years shows us an approximately equal number of cases, with a slightly decrease in 2008 and mention that in 2010 were evidenced only cases hospitalized in 6 month.

2. Repartition by gender of the newborns included in the study, by years showed the domination of male gender 57,14%, towards female gender 42,85%

3. Following the incidence of pathology at the studied lot we can observe that on the first place is intraventricular hemorrhage with a percentage almost equal as the infectious pathology, these two being the main causes of death at this category of prematures.

4. The high incidence of intraventricular hemorrhage (91,83%) can be explained due to its' high incidence in the pathology of extreme prematurity and also due to better possibility to diagnose with transfontanelar ultrasonography, this being performed serially to all premature hospitalized in our clinic. At our studied lot we observed high incidence at IInd degree intraventricular hemorrhage (44,44%).

5. 3 cases were diagnosed with hydrocephaly, 2 of them taking benefit of neuro-surgical intervention in order to set the ventriculo-peritoneal drainage, with favorable evolution in the next period.

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# TREATMENT OF POTENTIALLY DIFFICULT HUMERAL SHAFT FRACTURES USING ESIN (ELASTIC STABLE INTRAMEDULLARY NAILING) – CASE PRESENTATION

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## Abstract

Fractures of the humerus present about 3% of all fractures. The majority are closed fractures (85-90%). In the last two decades an important progress in conservative and surgical treatment of the humeral fractures was achieved. Surgical treatment of humeral fractures was enhanced by the development of new minimally invasive surgical procedures with biologically more appropriate osteosynthesis and better results. Nevertheless, most humeral fractures are still treated conservatively. Malunions with anterior bowing of less than 20° or varus of 30° are functionally and cosmetically well tolerated. Where intervention is indicated there is considerable debate over implant selection with a current vogue for intramedullary fixation.

Detailed knowledge of the region's anatomy, careful study of the fracture type and patient's lifestyle and expectations should be considered in the decision for the type of treatment.

Although to date we have used the implant in only a small series of patients, the results are encouraging. We advocate the use of this elastic intramedullary nail in potentially difficult humeral shaft fractures. This case-presentation and others are clear examples.

**Key words:** humeral shaft fractures, ESIN (Elastic Stable Intramedullary Nailing), minimally invasive surgical procedures

## Introduction

The majority of humeral fractures can be managed non-operatively. Malunions with anterior bowing of less than 20 deg or varus of 30 deg are functionally and cosmetically well tolerated [1,2]. Where intervention is indicated there is considerable debate over implant selection with a current vogue for intramedullary fixation [3,4]. I present a case in which we used elastic stable intramedullary nailing to manage a potential difficult humeral fracture unsuitable for non-operative management. The theoretical advantages which this method offers are discussed. The aim

of this paper was to present the results for a severe fracture in a skeletally immature patient treated using elastic stable intramedullary nails (ESIN).

## Case presentation

Fifteen year old boy has fallen on his left arm and elbow from about one and a half meters. He didn't present any other injuries except a comminutive fracture of the left humeral shaft in the middle third (Fig. 1). The next day he was operated using ESIF.

## Surgical technique

The operative procedure was carried out under general anaesthetic. The affected upper limb was supported by a radiolucent arm table. An image intensifier was positioned so that the long axis of the humerus was in view. Under image intensifier guidance, surface markings were made on the skin for the fracture site, proximal and distal physes. An initial attempt of closed reduction was made. This was performed by gentle longitudinal traction with abduction and external rotation of the arm. An image intensifier was used to monitor reduction. As the closed reduction failed, I proceeded to open reduction utilising an anterior deltopectoral approach.

Two retrograde oblique drill holes were created in this area, one above the other, taking care to drill far enough to get through the solid cortical bone of the humeral shaft [5]. The holes were made slightly larger than the diameter of the chosen nail. The diameter of the nail was selected based on the narrowest diameter of the medullary canal on radiographs using the formula 0.49 diameter of the canal in mm [6,7]. The first pre-bent ESIN was introduced through the inferior hole and passed downwards towards the fracture site. The second ESIN was then introduced and advanced in antegrade fashion to the fracture site. Once reduction was achieved, the ESINs were advanced across the fracture site to the humeral lateral and medial supracondylar ridge. The nails were appropriately rotated to achieve final reduction and a satisfactory position in the distal humerus without violating the cortex or supracondylar area and elbow joint (Figs. 2 and 3).

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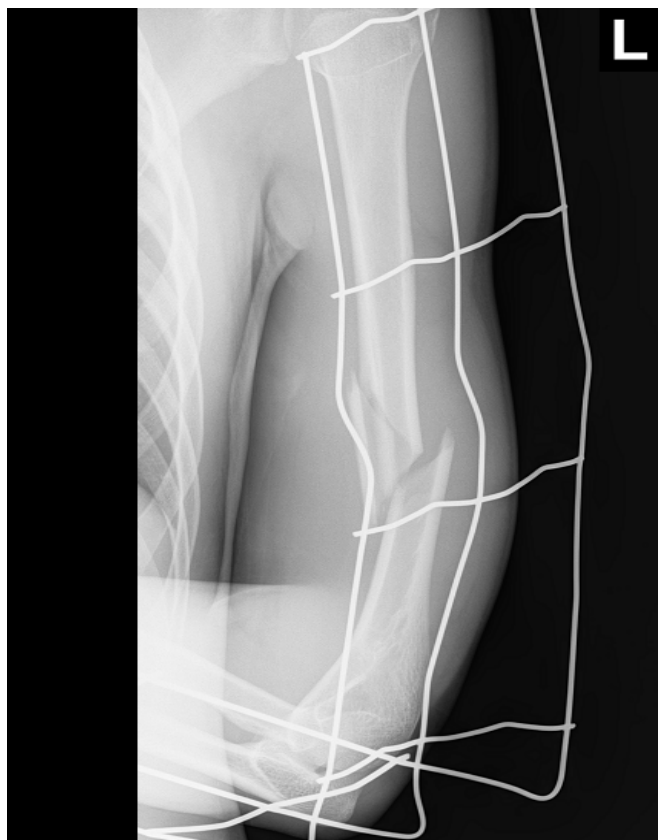


Figure 1 - comminutive fracture of the left humeral shaft in the middle third.



Figure 2 – Anterior X-ray control after nail insertion.

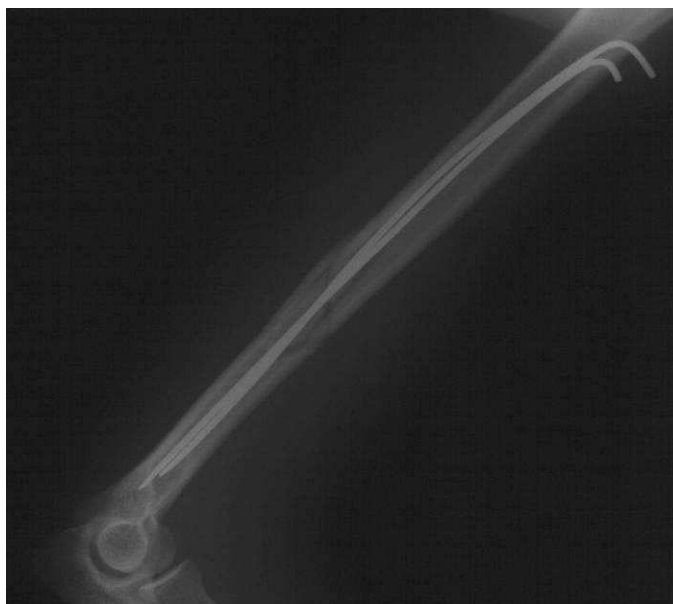


Figure 3 – Lateral X-ray control.

The two ESINs were then bent distally and cut 1 cm from the cortical surface to allow for easy removal at a latter date. Surgical wounds were closed with absorbable Vicryl™ sutures. Skin edges were apposed using absorbable Monocryl™ subcuticular sutures.

The postoperative regime consisted of application of a collar and cuff sling to the operated upper arm for three

weeks. The patient was encouraged to start pendulum exercises of the shoulder as soon as comfortable. Routine removal of the implant was performed as part of considered good practice, and undertaken under general anaesthesia as a daycase procedure at six months (Figs. 4 and 5).



Figures 4 and 5 – Anterior and lateral X-ray control just before removing the rods.

#### Complications

We were fortunate to experience no complication in this case. The humeral shaft healed perfectly, also the skin incision. The movements in the arm, shoulder and elbow joints were not affected. Discussion

Debate continues over the choice of intramedullary implant for use in humeral shaft fractures.

Indications for surgical treatment using ESIF:

- primarily instable fractures,
- secondary movement,
- open fractures,
- comminuted fractures,
- fractures that are associated with vascular and nerve injuries,
- fractures in polytraumatized patients,
- pathological fractures,
- fractures that could not be repositioned (the patient is still under local anesthesia, so we can just proceed with the operation),

- instable fractures in children older than 10 years (ESIF is a method of choice),
- supracondylar fractures.

The nail provides elastic intramedullary fixation by conferring flexible stability at the fracture site whereas the majority of alternative devices available confer rigid fixation but may lack rotational stability and are prone to loosening of the distal fixation [8-10]. If the nail is introduced by a retrograde technique and avoids many of the problems associated with the anterograde approaches including nail migration, rotator cuff pain, shoulder impingement and impaired shoulder function [8-15].

Whereas some techniques have been criticized for their lack of “user friendliness” [8, 9]

the simplicity of the ESIF instrumentation facilitates the introduction of the both nails. Because the technique is quicker radiological exposure is limited when compared with alternative methods.

Reaming is thought to have a deleterious effect on fracture healing and union rates in the

humerus [15, 16, 17]. It has also been implicated in the formation and propagation of iatrogenic fracture [18]. Reaming of the isthmus and fracture site is not required with insertion of the nails. Residual endosteal circulation is therefore preserved. The flexible stability conferred at the fracture site by the nail in combination with preservation of endosteal blood supply may in part be responsible for the relatively rapid union and low complication rates when compared with other techniques.

### Conclusion

- Elastic stable intramedullary fixation (ESIF) is a cheap, safe and easy method of operative treatment of long

bone fractures in children. Even though most long bone fractures in children are still treated conservatively, ESIF already represents the standard method of fixation in some cases, particularly in femoral fractures. Clear indications and the proper surgical technique make ESIF a very successful way of treating our young patients.

- It is well known that higher rates of non-union, infection and other complications accompany the operative treatment of humeral shaft fractures when compared with closed treatment techniques.

- Although to date we have used the implant in only a small series of patients the results are encouraging. We advocate the use of this elastic intramedullary nail in potentially difficult humeral shaft fractures.

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# A MANAGEMENT INFORMATION SYSTEM FOR PATIENTS WITH CHRONIC HEPATIC CONDITIONS

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## Abstract

Nowadays, scientific research in hepatology requires a fast way to record and access all data corresponding to a patient (patient electronic record), for further or real time data processing, and integration with the already existing data. The management of patient data is important for therapeutic procedures in patient's benefit, in enhancing the quality of medical treatments, as well as in scientific research through an active involvement in clinical studies.

The information system will be dedicated to the management of patients with chronic liver disease, with or without cirrhosis, and it will be represented by a complex web platform which will integrate: a multimedia database for the patients' electronic records; a computation component for scores and indices required to evaluate liver fibrosis (like: Fibrotest-Actitest, Metavir, Knodell-Ishack, APRI index, Lok index, Fornes score, FibroIndex, HepaScore, Fibrometer, FIB-4 and others); a component to assure the automatic allocation of corresponding ICD-10 code for the patient's condition; a component to offer rapid statistic processing of data stored in the database; a component to allow the interaction between mobile information collecting devices and the system; a dedicated search engine.

Correlation of all results with those already obtained by other medical studies published in national and international journals will be assured by the dedicated search engine. The system will allow data import/export in .xml format, according to HL7 standard.

**Key words:** databases, patient, electronic record, health, fibrosis scores, fibrosis stage and degree evaluation

## Introduction

Information and communication technology is more and more present in medical fields, offering major enhancements in patients' management. Most hospitals in Romania already use PIMs (Patient Information Management System), benefitting from an integrated format, very flexible and easy to use for a great variety of clinic and research applications.

Research activities in hepatology require an information platform to provide integration of patients' management with the ensemble of laboratory investigations, marker determinations useful to evaluate the health status, functional explorations, all leading to the enhancement of medical treatments quality.

As in the last few years the prevalence of chronic viral hepatitis has increased, and its progression towards cirrhosis which may complicate with the development of hepatocellular carcinoma represents a major health issue, it all leads to the necessity to correctly evaluate the degree and stage of liver fibrosis (using invasive and non-invasive techniques), in order to initiate and evaluate patient's response to antiviral treatment.

Fibrosis is a key component of the healing process occurring in damaged liver tissue, being characterized by deposits of extracellular matrix (ECM) following a dynamic process of ECM synthesis and degradation. Fibrosis progression towards cirrhosis is represented by specific tissue modifications like: hepatic and vascular architecture damage, hepatic function alterations, an increased risk of developing malign transformation, involving also alterations in hepatic functions, morphology and hemodynamic behavior.

An important feature in the progression of hepatic disease is represented by a decreasing number of hepatocytes, due to apoptosis and cellular collapse. Viral aggression initiates the programmed cellular death of hepatocytes - apoptosis, which stimulates inflammation by releasing inflammatory molecules like cytokines identified in hepatocyte's structure (found in cells / at cellular level), or by signaling processes which induce apoptosis. [1] Inflammation implies cellular exudate process and an increase in vascular permeability. Activation and proliferation of hepatic stellate cells (HSC) stimulate production of extracellular matrix, especially type I collagen, but also type IV and III collagen. HSCs produce matrix metalloproteinases (MMPs) synthesized intracellularly and secreted as pro-enzymes, activated by a proteolytic cleavage by membranetype matrix metalloproteinase 1 (MT1-MMP) or plasmin. MMPs are involved, along with their inhibitors, in controlling matrix degradation. HSCs also produce tissue inhibitors of metalloproteinases (TIMPs) which can irreversibly bind the proenzyme or active forms of MMPs and inactivate them. Activation of hepatic stellate cells leads to matrix deposits, but in the same time it prevents its degradation due to TIMPs. Excess production of TIMPs relative to MMPs may be an important factor in liver fibrosis progression.

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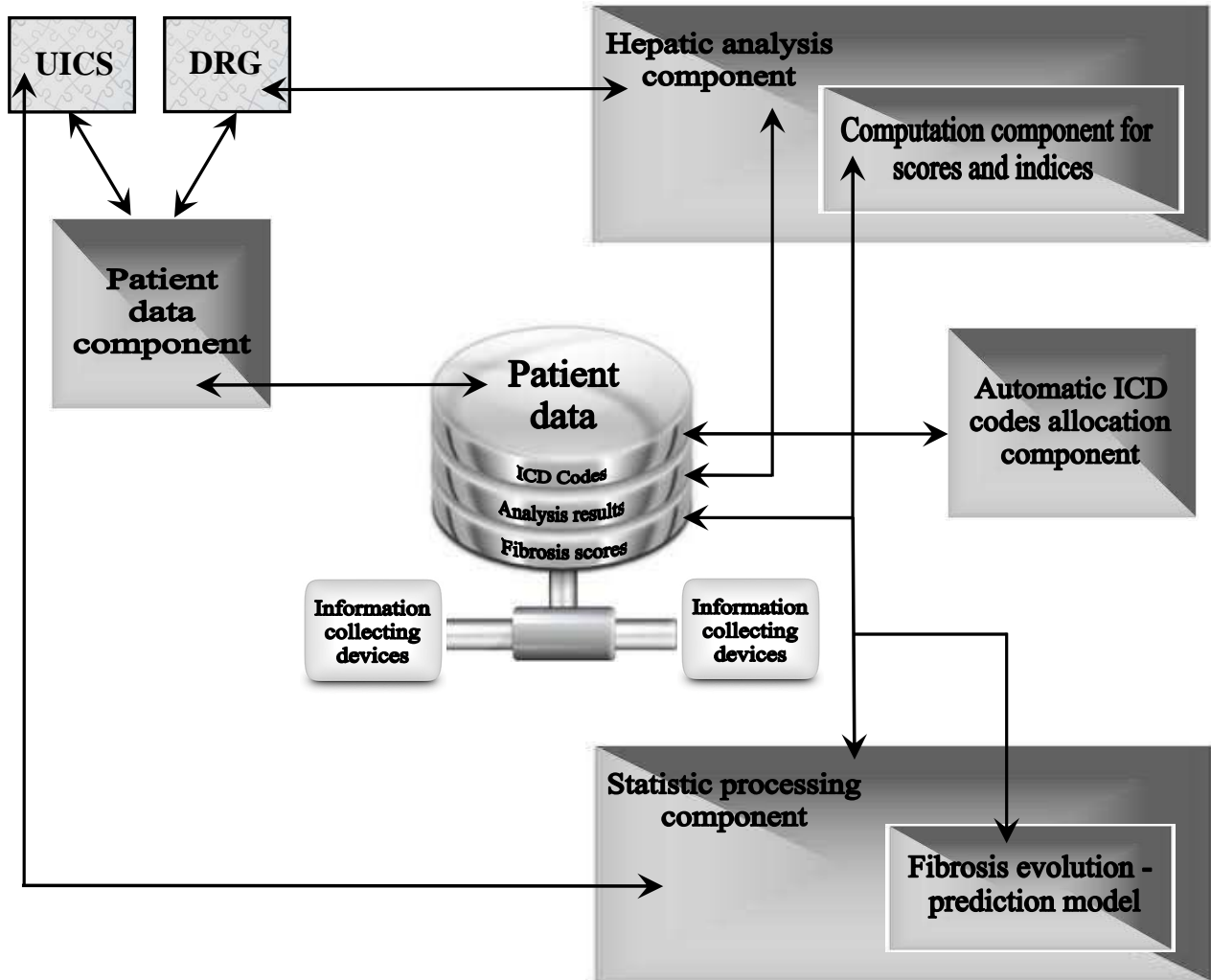


Figure 1. System architecture.

*UICS* - Unique Integrated Computer System

*DRG* - Diagnosis Related Groups

The information system will offer the classic data management, integrated with specific knowledge on hepatic diseases, which will facilitate the determination of patient's hepatic health status. The system will integrate three patient categories:

- patients with chronic viral hepatitis C;
- patients with C viral hepatic cirrhosis;
- patients with hepatocellular carcinoma of C viral etiology.

The patient data management will be accomplished using a database that will include:

- information related to age, sex, life conditions;
- anamnestic, objective and para-clinic pathological alterations, specific for the chronic C viral liver disease;
- results obtained from immunohistochemical, serologic and genetic tests;
- aggravating factors for the chronic hepatic disease, obtained through a questionnaire regarding the diet and behavioral habits of patients (drugs, other medical treatments which may cause hepatotoxicity, alcohol

consumption, smoking, stress levels at work, other diseases that may complicate the hepatic condition).

Each patient will have an associated electronic record, compatible with his electronic record existing in the national Unique Integrated Computer System (all data from the UICS file will be imported in the current record). This electronic record will allow the constant monitoring of patient's health status, in accordance with the prescribed treatment.

The system will be divided in the following components:

- a computation component for scores and indices required to evaluate liver fibrosis status (like: Fibrotest-Actitest, Metavir, Knodell-Ishack, APRI index, Lok index, Fornes score, FibroIndex, HepaScore, Fibrometer, FIB-4 and others), in order to provide patient's hepatic health status; the application will evaluate the degree of hepatic fibrosis, by computation of hepatic scores and indices, based on available tests results; evaluating liver fibrosis severity indicates the progression of viral hepatitis towards cirrhosis;

- a component to assure the automatic allocation of corresponding ICD-10 code for patient's condition;
- a component to offer rapid statistic processing of data acquired and stored in databases; all information available from databases will be used to determine a prognostic method in evaluating progression of liver fibrosis towards cirrhosis, and the potential development of hepatocellular carcinoma, according to factors aggravating the hepatic condition;

- a component to allow interactions between mobile information collecting devices (IPad) and the database;
- a dedicated search engine.

*UICS - Unique Integrated Computer System*

*DRG - Diagnosis Related Groups*

### Patient's hepatic health status

Patient's hepatic health status will be evaluated by the main application, using its corresponding data stored in databases. This process will be accomplished in three phases:

#### 1. Anamnesis

Anamnesis will offer basic information for each patient, regarding:

- identification data: age, sex, residence, occupation;
- personal pathological antecedents: acute viral hepatitis infection, blood transfusions, surgery, family aggregation;
- patient's complaints, structured on syndromes:
  - Dyspeptic syndrome: abdominal discomfort, nausea, vomiting, selective or unselective inapetence;
  - Abdominal pain syndrome: either diffuse or at epigastrium or right hypochondria, intermittent or continuous, in relation with diet and medication;
  - Gaseous syndrome: flatulent dyspepsia;
  - Asthenic syndrome: fatigability or physical asthenia, bradypsychia and impotence;
  - Hemoragipar syndrome: gingivorrhagia, repeated epistaxis, rectorrhage or cutaneous hemorrhage expressed by spontaneous ecchymoses;
  - Neurologic syndrome (central or peripheral): conscience status and degree, sleeping disorders, psychomotor agitation or slowness in motion;
  - Weight loss
  - Extrahepatic manifestations: arthralgia / arthritis, vascular stains;
  - Hormonal (thyroid) manifestations, cardiovascular symptoms (arterial hypertension) and renal (nephritic type) diseases
- Behavior (alcohol consumption, drugs, etc.)

#### 2. Objective examination

Following complete clinical examination, several specific elements will be emphasized:

- hepatosplenomegaly syndrome: size, contour, liver consistency, presence and degree of splenomegaly;
- cutaneous-mucous syndrome: jaundice absent or present with variable intensity, absence of fingernails

alterations, palmar erythema, stellar angioma, purpuric lesions or ecchymoses;

- neurologic syndrome: presence or absence of encephalopathy, with various degrees, alterations of conscience status, sensibility, cutaneous and osteotendinous reflexes;

- ascites syndrome: ascites liquid is present in variable quantity, edema due to hypoproteinemia is present or absent;

- psychic symptoms: insomnia, depression;

- extrahepatic manifestations: articular, cutaneous, vasculites.

### 3. Para-clinic investigation

The database will store results obtained from specific hepatic functional tests used to describe the ensemble of biochemical tests necessary to evaluate liver disease status. Different components are monitored, varying from the severity of hepatocellular necrosis or alterations in liver's capacity of synthesis, up to its excretion function. These tests generally measure hepatic sanguine flux, liver's metabolic capacity and its excretory function.

### Evaluation methods for the degree of hepatic fibrosis

#### I. Invasive methods

Hepatic biopsy is essential not only for diagnosis and prognostic of chronic liver disease, but also in establishing a therapeutic protocol, as well as for assessing patient's response to antiviral therapy. It is a method which provides data regarding liver's regeneration capacity, offering also useful information in deciding the necessity of performing a liver transplant. [2] Advantages, disadvantages and contraindications of hepatic biopsy are summarized in Table 1. In many cases, liver biopsy confirms the etiology of hepatic condition, also remaining the best method to establish the presence or absence of cirrhosis.

For more information regarding the degree and stage of liver fibrosis, the fragments obtained from liver biopsy may also be:

- evaluated using classical histological techniques;
- used to evaluate fibrosis stage and degree using Metavir and Knodell-Ishack scores;
- evaluated using computer-aided quantitative analysis, as well as immunohistochemical techniques.

#### II. Non-invasive methods

Due to the disadvantages of liver biopsy and the heterogeneous distribution of fibrosis in liver, the need of new evaluation techniques for liver fibrosis, especially non-invasive, emerged during the past years. Practically, the purpose of biochemical non-invasive investigations is discriminating between patients without fibrosis or patients with a mild degree of fibrosis (F0 – F1 Metavir score), and those with severe degree of fibrosis (F2 - F4 Metavir score), without requiring liver biopsy.

The serological samples may represent direct and indirect markers, as summarized in Table 2 and Table 3.



Table 1. Advantages, disadvantages and contraindications of liver biopsy.

Advantages of liver biopsy		
1	Diagnostic value	Used to determine the etiology of liver disease and to predict its progression.
2	Identification of hepatic condition etiology	Viral, alcoholic, autoimmune, metabolic / congenital, vascular, etc.
3	Differential diagnosis	Confirms the etiology of liver disease.
4	Evaluation of the degree and stage of fibrosis	<b>Metavir score</b> - ascertains the necroinflammatory activity and the stage of fibrosis. Fibrosis degree is analysed on a scale from 0 to 4.
		<b>Knodell-Ishack score</b> or the Histology Activity Index (HAI score) - is comprised of four distinct components that make one single score. The first component (periportal and/or septal necrosis) is measured on a scale from 0 to 10. The next two components (intralobular degeneration and portal inflammation) are measured on a scale from 0 to 4. The fourth component indicates the amount of scarring in the liver and is scored from 0 (no scarring) to 4 (extensive scarring or cirrhosis).
5	Evaluation of the treatment	Assesses the liver fibrosis after antiviral therapy.
Disadvantages of liver biopsy		
1	Post hepatic biopsy complications	The majority of complications (60%) occur within two hours, and 96% occur within 24 hours following the procedure. The most common complications include mild pain and a slight reduce in blood pressure. More severe complications like inflection, bleeding, and injury to surrounding organs, are very rare (1-5%).
2	Sampling errors	Needle liver biopsy has been shown to have a high rate of sampling error in patients with diffuse parenchymal liver diseases. In these cases, the sample of liver tissue does not reflect the true degree of inflammation, fibrosis, or cirrhosis, despite an adequate sample size. [3]
3	High costs	The cost of liver biopsy is estimated at USD\$1,032 without complications and USD\$2,745 with complications. [4]
4	Sampling subjective analysis	Due to human error in interpretation of liver biopsy.
Contraindications		
5	Multiple contraindications	Coagulopathy, platelet count under $100.000/mm^3$ , ascites, hepatic hydatid cyst, hepatic hemangiomas.

Table 2. Direct serological markers for the evaluation of liver fibrosis degree.

Markers associated with extracellular matrix deposits		
Collagens	pro-collagen I C peptide (PICP)	- it has a low diagnostic importance in chronic hepatitis; - its value increases in alcoholic cirrhosis, indicating the progression disease progression; [5]
	pro-collagen III N peptide (PIIINP)	- there is a correlation between the levels of PIIINP and liver fibrosis in patients with alcoholic hepatic disease, viral hepatitis and primary biliary cirrhosis; [5-8]
	collagen type IV and its fragments (NC1 and PIVNP)	- there is a correlation between the degree of liver fibrosis and the serologic level of type IV collagen in patients with chronic viral hepatitis, hepatic alcoholic disease and cirrhosis, following hemochromatosis; [9, 10]
Glycoproteins and polysaccharides	hyaluronic acid (HA)	- serologic level of hyaluronic acid has an important role in identifying early stages of liver fibrosis in patients with chronic hepatic conditions of different etiology; [11]
	laminin	- its serologic level is increased in patients with chronic liver disease of viral or alcoholic etiology; - it indicates the emphasis of perisinusoidal fibrosis; [12, 13]
	tenascin	- tenascin deposits represent a marker of active fibrogenesis;
	YKL-40 (condrex)	- activated hepatic stellate cells represent the hepatic source of YKL-40; - it has an increased serologic level in severe fibrosis; [14] - in chronic infection with hepatitis C virus, a value greater than 282.8 ng/ml indicates cirrhosis with a sensibility of 80% and a specificity of 78%; [15]
Markers associated with extracellular matrix degradation		
Collagenases and their inhibitors	metalloproteinases (MMPs)	The MMPs and their inhibitors are involved in controlling matrix degradation; [16]
	tissular inhibitors of metalloproteinases (TIMPs)	TIMPs can irreversibly bind the proenzyme or active forms of MMPs and inactivate them. Excess production of TIMPs relative to MMPs may be an important factor for progression of liver fibrosis. [17]
Cytokines and chemokines associated to hepatic fibrosis		
Citokines	tumoral growth factor TGF- $\beta$ 1	- a good correspondence has been demonstrated between serum levels of total TGF – $\beta$ 1, and Knodell scores; [18] - a positive correlation was also observed between TGF- $\beta$ 1 and the rate of fibrosis progression;
	platelet derived growth factor PDGF	- platelet derived growth factor (PDGF) is the main stimulus of HSC proliferation and migration, being upregulated following liver injury. PDGF-BB is the main subunit with the most important role in signalling pathway in HSC activation; [19, 20] - serum level of PDGF–BB has a high value for assessment of liver fibrosis;

Table 3. Indirect serological markers for the evaluation of liver fibrosis degree.

Individual serological markers	
AST/ALT ratio <i>AST – aspartate aminotransferase</i> <i>ALT – alanin aminotransferase</i>	- it has a predictive value, as an AST/ALT ratio of over 1.16 presents a sensibility of 81.3% and a specificity of 55.3% in identifying cirrhosis; [21]
Platelet count	- thrombocytopenia represents a marker for advanced liver disease, but it may also be the result of other conditions like hypersplenism, autoimmune processes, decreased production of thrombopoietin;
Prothrombin index	- prothrombin time is a marker to assess liver synthesis function, being an indicator of hepatic fibrosis presence;
Hepatic fibrosis associated tests	
Fibrotest-Actitest FT-AT	- it is the most known serologic test for evaluating liver fibrosis and hepatic function; - it assesses fibrosis and necroinflammatory activity at hepatic level by combining quantitative results of 6 biochemical seric parameters ( $\alpha$ 2-macroglobulin, haptoglobin, gamma-glutamyl transferase ( $\gamma$ -GT), total bilirubin, apolipoprotein A1 and ALT) with the patients' age and sex; [22]
Forns score	- it includes 4 independent prediction parameters for severe hepatic fibrosis: age, $\gamma$ -GT, cholesterol and platelet count;
APRI index (AST platelet ratio index)	- for values smaller or equal to 0,5 - there is no fibrosis; - the interval 0.5 - 1.5 represents a progressive stage of fibrosis; - values above 1.5 confirm the presence of fibrosis; - it has a 76% sensibility and a 71% specificity in predicting liver cirrhosis;
Hepascore	- it uses the following parameters: bilirubin, $\gamma$ -GT, hyaluronic acid, $\alpha$ 2-macroglobulin, patient's age and sex; - tests values range between 0 and 1;
Lok index	- negative predictive value of Lok index for severe liver fibrosis may reach 99%, for values smaller than 0.2;
MP3 score	- negative predictive value of MP3 score for severe liver fibrosis is 96%, for values smaller than 0.2; - positive predictive value of MP3 score for severe liver fibrosis is 100%, for values above 0.5;
FibroIndex	- it uses the following parameters: AST, platelet number and serum $\gamma$ -globulins;
Fibrometer score	- it uses the following parameters: AST, hyaluronic acid, platelet number, prothrombin time, $\alpha$ 2-macroglobulin, urea and age; - it is a reliable marker for significant liver fibrosis;
FIB-4 score	- it uses the following parameters: AST, ALT, platelet number and age; - it is confirmed for chronic hepatitis C; - it was developed for the co-infection HIV- HCV (hepatitic C virus)

## Conclusions

Patients with chronic liver disease will benefit from enhanced medical treatment through the rapid determination of liver's fibrosis degree and stage, taking advantage in early antiviral treatment, accessible non-invasive monitoring techniques during the treatment, as well as observing their response to the therapy.

The process of collecting and processing patients data involved in scientific research will be optimized and easily accessible, in order to rapidly obtain statistical results. These results will be used in world wide studies, by accessing the most important web directories dedicated to chronic liver disease research.

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# STUDY REGARDING THE EXCESSIVE CONSUMPTION OF ALCOHOLIC BEVERAGES IN STUDENTS FROM TIMISOARA

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## Abstract

**Premises.** The alcohol consumption in large quantities in young adults became frequent in many countries. This type of behavior decreases the self-control and promotes other risk behaviors. It represents the main cause in producing injuries, including road incidents, violence, and especially domestic violence, but also premature deaths.

**Methodology.** The working method was the transversal population survey based on the CORT 2004 questionnaire regarding risk behavior for health in teenagers and young people. The representative sample of students studied totaled 2076 young adults from universities in Timis County, 62.49% (1296) girls and 37.51% (778) boys, with the medium age of 21.1 years. The admission of the young people in the study was conditioned by the freely expressed consent of every participant. Data were analyzed with PASW program, version 18, 2010.

**Results.** 19.6% of the young people declared excessive alcohol consumption, with a boys / girls report of 1.7/1. The most powerful predictor of the status of student consuming large quantities of alcohol in a special occasion was the male gender, boys having 2.5 times more chances to practice this behavior compared to the girls. At the age of young adult a strong influence is represented by the group of friends: the young people whose friends use to consume alcohol, have 2 times more chances to practice binge drinking; those who have friends that get drunk at least once a week have 1.3 times more chances to be alcohol consumers in large quantities in a special occasion.

**Conclusions.** Knowing some characteristics of the adolescents' entourage contribute to the promotion of health programs in the young population.

**Key words:** young people, excessive alcohol consumption, binge-drinking, the influence of the family and of the entourage outside the family

## Introduction

The practice of alcohol consumption in large quantities in young people became frequent in many countries. This type of behavior decreases the self-control and promotes other risk behaviors. It represents the main cause in producing injuries, including road incidents, violence, and especially domestic violence, but also premature deaths [1].

The problems are not necessary the result of the young people beginning to consume alcohol, but the result of the quantities of alcohol they consume. It was proven that the young people have the tendency to consume large quantities of alcohol in the late adolescence until approximately the age of 25 years [2, 3]. The young adults often practice binge drinking [4]. The results of the NESARC study show that 46% of the alcohol consuming young adults have exceeded the minimum alcohol dose recommended daily in the last year [5].

This behavior pattern often leads to tragic consequences, mostly traffic incidents [6]. One third of the young people with ages between 16 and 20 years who deceased in traffic incidents in the USA, had detectable levels of alcohol in their blood, and for those with ages between 21 and 24 years, the percent rose to 51% [7].

## Material and method

The working method was the transversal population survey based on the CORT 2004 questionnaire regarding the risk behaviors in adolescents and young people, achieved during the research project under the aegis of the National Council of Scientific Research in the University Education (CNCSIS) within the Education and Research Ministry, and the aegis of the University of Medicine and Pharmacy "Victor Babes" Timisoara: Type A CNCSIS grant, cod 1167, 2003-2005, with the title: "The Evaluation of the risk behavior dimension in young people from high-schools, vocational schools and universities in Timis County".

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For the study of the risk behavior for health represented by the excessive alcoholic beverages consumption in young adults, the population of students in the Timis County was chosen. A representative sample was established with the help of the Epiinfo program, version 6.04, 2001. A nest stratified sample was chosen, the primary unit for sampling being represented by the group of students. The admission of the young people in the study was conditioned by the freely expressed consent of every participant [8].

The representative students sample totalized 2076 students from universities in Timis County, 62.49% (1296) girls and 37.51% (778) boys. The participants to the study were part of the young adult age group, 18 – 25 years, with an average age of 21.1 years.

Data were analyzed with the PASW program, version 18, 2010.

### Results and discussions

1. The excessive alcohol consumption in students, for the entire sample and based on the sex criteria (Table 1-3, Figure 1)

Table 1. The students' distribution based on the number of days in the last month when they consumed excessive quantities of alcohol in a short period of time (5 or more portions during a few hours).

Answers	Frequency	Percents
No alcohol consumption in large quantities in the last month	1655	80.4
1 day	180	8.7
2 days	102	5.0
3-5 days	65	3.2
6-9 days	30	1.5
10-19 days	10	0.5
20 or more days	16	0.8
Total respondents	2058	100.0

Non-respondents: 16

19.6% (403) of the *students* had *excessive alcohol consumption*. Of this, most had an excessive consumption in one day in the month, 44.7% (180); 6.5% (26) had an excessive consumption in at least 10 days of the month;

3.9% (16) had *frequent excessive consumption* of alcohol in at least 20 days of the month. There was no case of *daily excessive consumption* reported.

Table 2. The distribution of the male gender students based on the number of days in the last month when they consumed excessive alcohol quantities in a short time period ( 5 or more portions during a few hours).

Answers	Frequency	Percents
No alcohol consumption in large quantities in the last month	510	66.3
1 day	102	13.3
2 days	68	8.8
3-5 days	45	5.9
6-9 days	25	3.3
10-19 days	8	1.0
20 or more days	11	1.4
Total respondents	769	100

Non-respondents: 9

Table 3. The students' distribution based on the number of days in the last month when they consumed excessive quantities of alcohol in a short time period (5 or more portions during a few hours).

Answers	Frequency	Percents
No alcohol consumption in large quantities in the last month	1145	88.8
1 day	78	6.1
2 days	34	2.6
3-5 days	20	1.6
6-9 days	5	0.4
10-19 days	2	0.2
20 or more days	5	0.4
Total respondents	1289	100

Non-respondents: 7

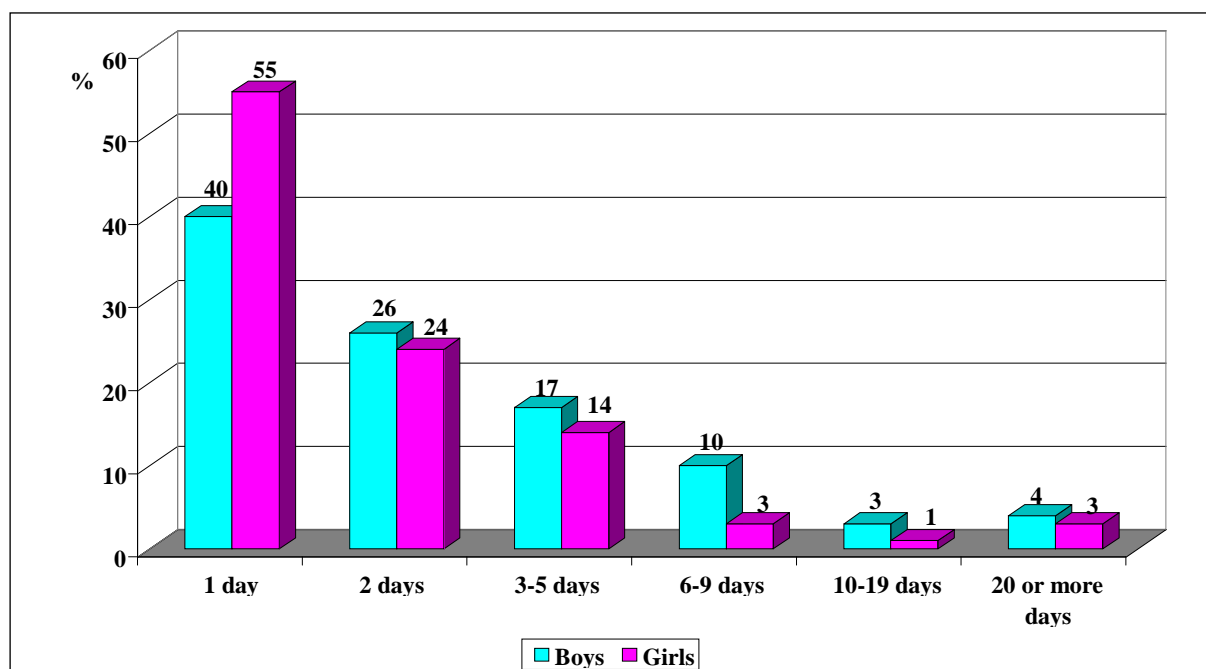


Figure 1. The percentage distribution of the alcohol consuming students based on gender and the number of days with excessive consumption in the last month before the study.

An **excessive consumption** was reported by 51% (259) of the alcohol consuming **male students**, and out of these: in one day of the month, 40% (102); in at least 10 days of the month, 7% (19); a **frequent excessive alcohol consumption** in at least 20 days of the month, 4% (11).

An **excessive consumption** was reported by 12.6% (144) of the total alcohol consuming **female student**, and out of these: in one day of the month, 55% (78); in at least 10 days of the month, 4% (7); a **frequent excessive consumption** in at least 20 days of the month, 3% (5).

## 2. Risk behavior in the family and in the entourage outside of the family

The prevalence of the alcohol consumption registers the highest value for the family members of the young people: 63.6% (1271) for fathers. Next is the consumption among brothers with a prevalence of 34.81% (610), and then the consumption among mothers, 19.4% (403) (Figure 2).

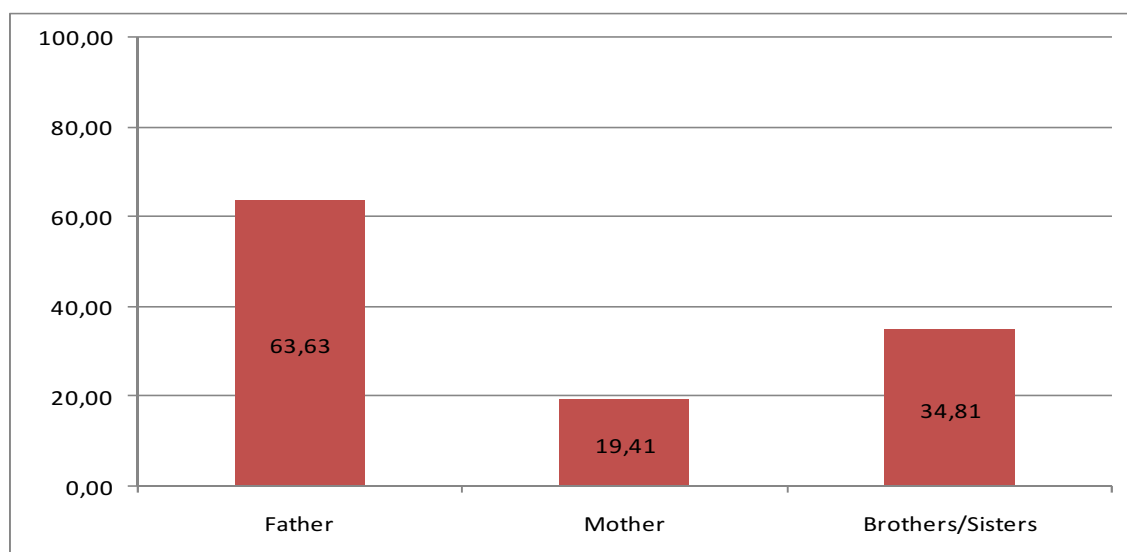


Figure 2. The prevalence of alcohol consumption in family members of the students.

The prevalence of alcohol intoxications, in decreasing order, was 23.1% (455) for fathers, 13.2% (234) for brothers and 1.9% (38) for mothers (Figure 3).

Jessor [9] asserted in 1987 that, the alcohol consumption is a learned behavior, tailored after the norms and expectations of the entourage, and also the particular experiences of the young individual. In a meta-analysis of 30 studies, Foxcroft and Lowe [10], studying the influence of family socialization on the alcohol consumption in teenagers, found a clear negative relation between the family support and the alcohol consumption in teenagers, but also between the control exerted by the parents on their children

and the alcohol consumption in teenagers. Thus, the low parental support and diminished parental control were associated with increased alcohol consumption. They also evinced a negative relation between the family structure and the alcohol consumption; the teenagers with disorganized families have the tendency to consume more alcohol.

Almost one third of the young people, 30.6% (630), have the majority of friends to be alcoholic beverages consumers, and 5.2% (106) indicate alcohol consumption in all friends. A percent of 10.1% (208) of the respondents do not indicate alcohol consumption in friends (Figure 4).

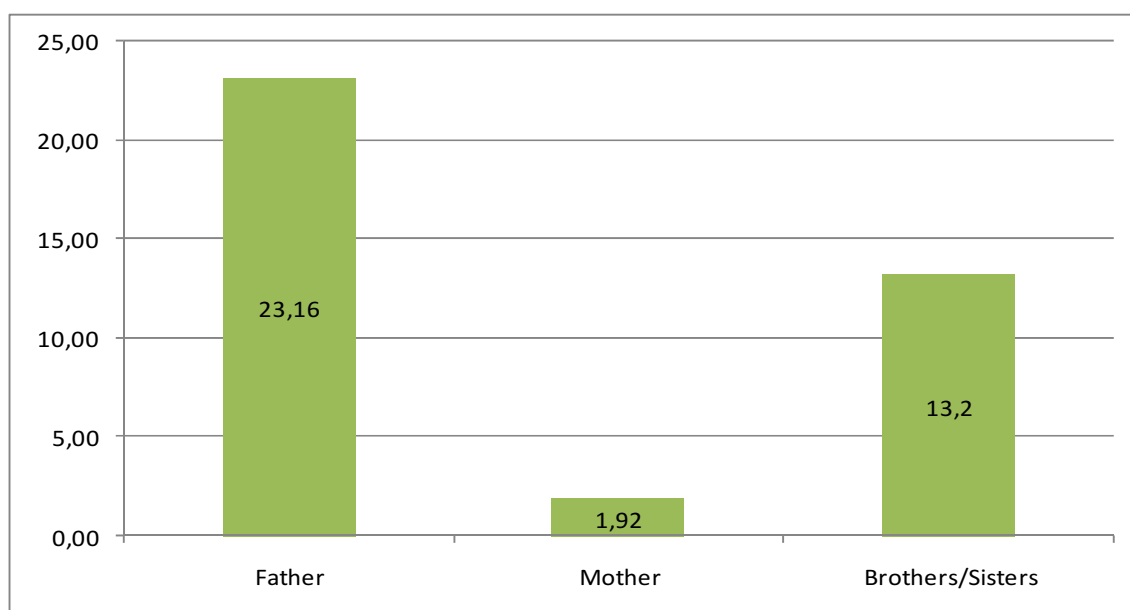


Figure 3. The prevalence of alcohol intoxications for the family members of the students.

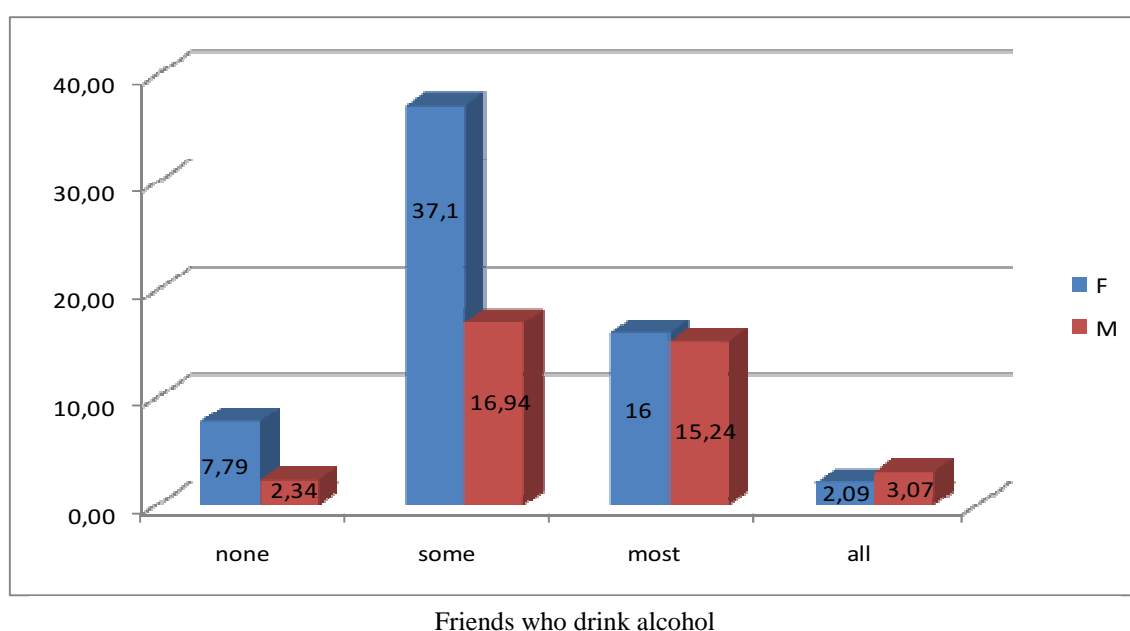


Figure 4. The students' percentage distribution based on the number of alcohol consuming friends.



The results of the present study indicate that the boys have significantly more alcohol consuming friends than the girls,  $U=379988.5$ ,  $z=-9.79$ ,  $p<0.001$ .

Most young people, 48.6% (992) reported they do not have any friend who gets drunk at least once a week. At

least one intoxication every week is reported for most friends by 6.3% (129) of the respondents, and for all the friends by 1.1% (22) of the respondents (Figure 5).

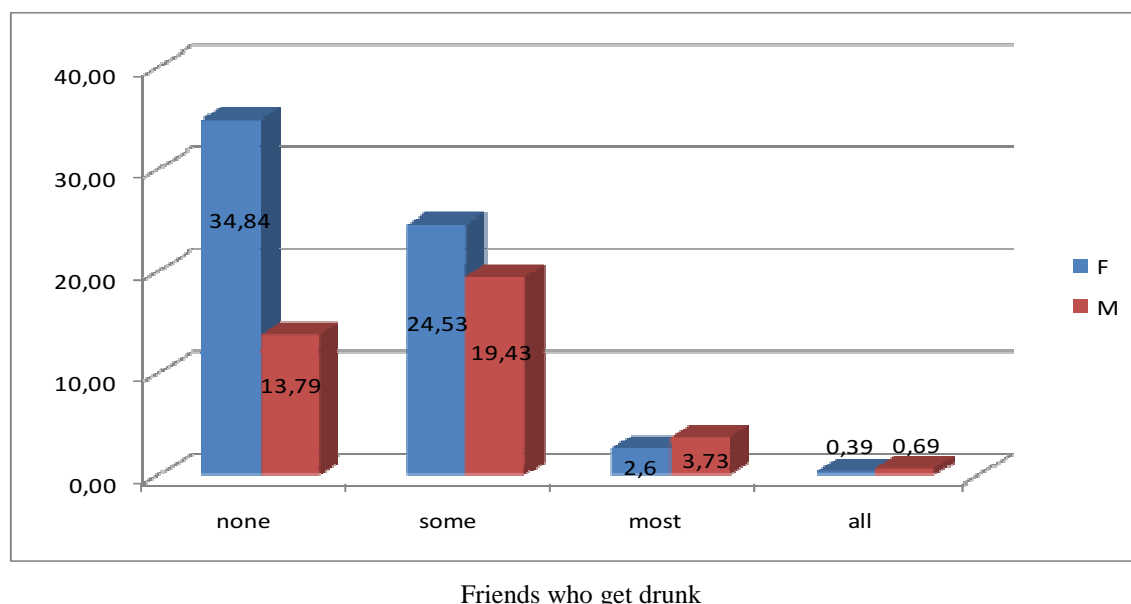


Figure 5. The students' percentage distribution based on the number of friends that get drunk at least once a week.

The present study indicates that boys have significantly more friends that get drunk at least once a week, compared to the girls,  $U=383230$ ,  $z=-9.05$ ,  $p<0.001$ .

In a study intended to highlight the impact of close friends and of the group of friends on cigarette and alcohol consumption in adolescents [11], the results indicated that close friends have increased influence on the onset of alcohol and cigarette consumption. As for the intoxication state, the authors concluded that the adolescents are more influenced by the group of friends, and are less influenced by the close friends.

### 3. The entourage contribution to the excessive alcohol consumption in students

The logistic regression test was performed in order to determine the impact of more factors from the entourage on the alcohol consumption exceeding 5 units in one occasion for the young people. The model contains 18 independent variables (age, sex, last school finished by the father, last school finished by the mother, the frequency of behavior rules being established by the parents, the frequency of respecting these rules, the parents knowledge about the way their children spent the time outside the home, the satisfaction towards the family's financial situation, the number of alcohol consuming friends, the number of friends that get drunk at least once a week, the status of alcohol consuming of the father, mother and brothers, the father, mother, brothers getting drunk and the satisfaction towards the relation with parents and brothers). The model

containing these predictors is statistically significant,  $\chi^2(18)=255.32$ ,  $p<0.001$ , thus meaning that the proposed model can separate the students with this type of behavior from those that do not poses it. The model can explain between 16.3 and 26.1% of the variance of the large quantities of alcohol consuming status in one occasion and may correctly classify 82.7% of the cases.

The strongest predictor of consumer status for large quantities of alcohol in one occasion, for the young people is the male gender, boys having 2.5 times more chances to practice this behavior compared to the girls. At the age of young adulthood a strong influence is created by the group of friends. The young people whose friends have the habit to consume alcohol have 2 times more chances to practice binge drinking, and those having friends that get drunk at least once a week have 1.3 times more chances to consume alcohol in large quantities in one occasion.

The rest of the statistically significant predictors are: not respecting the rules imposed by the parents, the parents not knowing the way their children spent their time, the high educational level of the mother and the satisfaction towards the financial situation.

The predictors without statistically significant contribution to the model are: establishing behavior rules by the parents, the participants' age, the father's level of education, the level of satisfaction towards the relation with parents and brothers, the father's, mother's and brother's status of alcohol consumer and the habit of getting drunk of the father, mother and brothers (Table 4).

Table 4. The logistic regression predicting the binge-drinking behavior in students.

Independent variables	B	S.E.	Wald	df	Sig.	OR	95% C.I. for OR	
							Min	Max
Age	-.066	.051	1.656	1	.198	.936	.847	1.035
Gender (1)	.903	.158	32.664	1	.000	2.467	1.810	3.363
Last school finished by the father	-.048	.078	.389	1	.533	.953	.818	1.109
Last school finished by the mother	-.193	.085	5.139	1	.023	.824	.698	.974
Establishing behavior rules	.117	.096	1.499	1	.221	1.124	.932	1.357
The frequency of respecting these rules	.268	.084	10.131	1	.001	1.307	1.109	1.542
The parents knowledge about the way their children spent their time	.273	.084	10.634	1	.001	1.314	1.115	1.549
The satisfaction towards the family's financial situation	-.169	.083	4.152	1	.042	.845	.718	.994
The satisfaction towards the relation with parents	.142	.163	.759	1	.384	1.152	.838	1.585
The satisfaction towards the relation with brothers	.026	.152	.029	1	.866	1.026	.762	1.381
Father consumes alcohol (1)	.240	.183	1.709	1	.191	1.271	.887	1.821
Father gets drunk (1)	.273	.196	1.943	1	.163	1.314	.895	1.928
Mother consumes alcohol (1)	-.312	.208	2.251	1	.134	.732	.487	1.100
Mother gets drunk (1)	.143	.554	.066	1	.797	1.154	.389	3.417
Brothers consume alcohol (1)	.297	.182	2.660	1	.103	1.345	.942	1.922
Brothers get drunk (1)	.258	.227	1.292	1	.256	1.294	.830	2.019
The number of alcohol consuming friends	.711	.120	34.937	1	.000	2.036	1.609	2.578
Number of friends getting drunk	.273	.120	5.142	1	.023	1.314	1.038	1.663
Constance	-2.757	1.166	5.587	1	.018	.063		

### Conclusions

The excessive alcohol consumption, binge-drinking, of 5 or more alcohol portions in a few hours, is a reality in students, in a percent of 19.6%. The boys are excessive consumers more often than the girls, with a boys / girls report of 1.7 / 1.

The prevalence of alcohol consumption is highest, 63.6% in fathers. Next is the consumption among brothers with a prevalence of 34.81%, than among the mothers, 19.4%. The prevalence of alcohol intoxications, in decreasing order, was 23.1% in fathers, 13.2% in brothers and 1.9% in mothers.

30.6% of the young people reported most friends to be alcoholic beverages consumers, and 5.2% indicated that all their friends consume alcohol. Boys have significantly more alcohol consuming friends than girls. At least one intoxication a week is reported for most friends in a

percentage of 6.3%, and for all the friends in percentage of 1.1%. Boys have significantly more friends that get drunk at least once a week than girls.

The strongest predictor for the status of alcohol consumer in large quantities in one occasion, for the young people is the male gender, boys having 2.5 times more chances to practice this behavior compared to the girls. At the age of young adult a strong influence belongs to the group of friends. The young people whose friends use to consume alcohol, have two times more chances to practice binge-drinking, and those who have friends that get drunk at least once a week have 1.3 times more chances to consume alcohol in large quantities in one occasion.

Knowing some characteristics of the teenagers' entourage contribute to the promotion of health programs in the young population.

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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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