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# I. GENETICS

## STERNUM MALFORMATIONS AS A RESULT OF BMP4 DEFICIENCY

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### Abstract

Recent data shows that the Bmp4 plays significant roles in a large number of developmental processes, including branching morphogenesis of the lung, tooth development, lens development, neuroepithelial cell differentiation, primordial germ cell formation, and not least most importantly bone formation and development.

The purpose of this study was to identify the Bmp4 expression and its role in the development of ribs and sternum and analysis of the skeletal phenotypes caused by the genetic inactivation of Bmp4, along with the study of its expression patterns.

This conclusion of this study is based in part on the finding that some heterozygous mutants, which presumably produce half the amount of active BMP protein as wild type appear to have some skeletal defects with regards to the sternum and ribs.

**Key words** : bone morphogenetic protein, bone, development, transgenic mice, sternum, ribs

### Introduction

BMPs are multifunctional cytokines that are members of the TGF-beta superfamily proteins, which consist of 43 members.<sup>10</sup>

The role of the TGF- beta superfamily involves cell growth, differentiation, and embryonic pattern formation. Currently, approximately 20 BMPs are known, including the addition of various growth/differentiation factors (GDFs) based on sequence homology, that are responsible for inducing ectopic bone formation, chondroblast formation, and visceral development. So BMPs are involved in cell proliferation, differentiation, apoptosis, and morphogenesis.<sup>10</sup>

They are broadly divided into three subclasses based on derived amino acid sequences.

The first subclass is the BMP-2 and BMP-4. They differ mainly in the amino terminal group.

The second subgroup is BMP-5, 6, 7 and 8.

These molecules are larger than the first group. The third subgroup is BMP-3 (osteogenin), which is more distantly related.<sup>10</sup>

Bone morphogenic proteins (BMPs) are known to promote osteogenesis, and clinical trials are currently underway to evaluate the ability of certain BMPs to

promote fracture-healing. The optimal BMPs to be used in different clinical applications have not been elucidated, and a comprehensive evaluation of the relative osteogenic activity of different BMPs is lacking.<sup>10</sup>

The function of BMPs is multifaceted. Besides involvement in bone and cartilage formation, BMPs create an environment for red bone marrow formation and contribute to systemic hematopoietic production.<sup>10</sup>

Recent data shows that the Bmp4 gene plays significant roles in a large number of developmental processes, including branching morphogenesis of the lung, tooth development, lens development, neuroepithelial cell differentiation, primordial germ cell formation, and not least most importantly bone formation and development.<sup>12</sup>

Bmp4 is actively expressed during early sternum and rib morphogenesis and plays an important role in the development of the bony thorax..<sup>12</sup>

Despite increasing experimental insight into the Bmp4 gene regulation in vitro, the in vivo mechanisms controlling Bmp4 expression during development are unknown.<sup>12</sup>

The sternum originates from two distinct mesenchymal condensations (sternal bands) that arise dorsally, extend caudally while migrating toward the ventral midline, and eventually fuse. Rib anlagen emerge independently from the sternal bands. Upon cell proliferation they grow toward the ventral midline and fuse to the sternal bands [Chen, 1952 a; Storm and Kingsley, 1996]. It is generally considered that the ribs and the sternum arise from distinct mesenchymal condensations.<sup>24</sup>

Anterior body wall defects in the thoracic region may be severe, leading to ectopia cordis, or mild, as in skin-covered sternal clefts. The embryologic basis for other sternal abnormalities, such as pectus excavatum and pectus carinatum, is not clear; however, abnormalities of rib morphogenesis and growth are the most likely causes.

Ethiopathogenesis of pectus excavatum and carinatum remains unsettled.

Disturbances in endochondral ossification and growth of costal cartilage seem to be more probable cause of the deformities than diaphragm underdevelopment.

The etiology of sternal cleft deformity is unknown. A familial predisposition has not been described.

Sternal clefts vary from minor “V”- shaped defects associated with an orthotopic heart to complete separation of sternal halves to the xiphisternum associated with thoracic or thoracoabdominal ectopia cordis, the “pentalogy of Cantrell”. The latter conditions are associated with intrinsic cardiac anomalies and a far higher mortality.<sup>9</sup>

Isolated sternal clefts are rarely associated with significant intrinsic cardiac defects.

Several anomalies of somatic fusion have been reported, including fibrous bands extending from the defect to the umbilicus and diastasis recti.<sup>9</sup>

### Material and Methods

The purpose of this study was to identify the Bmp4 expression and its role in the development of ribs and sternum and analysis of the skeletal phenotypes caused by the genetic inactivation of Bmp4, along with the study of its expression patterns.<sup>24</sup>

Bmp4 lacZ mice, where expression of the inserted lacZ is controlled by the entire endogenous Bmp4 gene, were used for mapping all Bmp4 expression domains in the bones that form the thorax.

Although Bmp4 is widely expressed in different tissues during development, we chose to examine its expression in the ribs and sternum.

### Mouse Bmp4 promoter lacZ constructs:

Three fragments of the Bmp4 1A promoter and part of 5'-exon 1 (2372/+258, ) 1140/+212, and )260/+212) were linked to pUC19/AUG b-gal containing the lacZ gene.<sup>12</sup>

Expression of lacZ in mice harboring this construct is a sensitive reflection of expression of the entire endogenous Bmp4 gene.<sup>12</sup>

### B-Galactosidase expression assay and immunostaining:

To examine the onset of endogenous Bmp4 expression in ribs, heterozygous Bmp4 lacZ newborn mice (PN1) were utilized for analysis of B-gal activity.

B-Galactosidase staining was assessed in newborn mice using the method described by Lawson et al. Briefly newborn mice were fixed with ice-cold 4% paraformaldehyde for 30 min to 1 h, and then washed three times with PBS for 5 min each. The specimens were then stained overnight in freshly made X-Gal solution (1 mg/ml) at 32°C.<sup>12</sup>

### Bone and cartilage staining:

The ribs and sternum from newborn mice were dissected and the stained with alcian blue and alizarin red for bone and cartilage.

The chemicals used in the fetal skeletal processing— ethanol, potassium hydroxide (KOH) and glycerin.<sup>2</sup>

The specific stains used in the study were Alizarin Red S and Alcian Blue (Sigma Chemical Co. ).<sup>2</sup>

Before preparation of the staining solution, stock solutions of Alcian Blue and Alizarin Red S were prepared

as follows: Alcian Blue 0.15% (w/v) in 70% ethanol and Alizarin Red S 0.1% (w/v) in 95% ethanol.<sup>2</sup>

The clearing solution was 70% ethanol: glycerin: 100% benzyl alcohol solution (2:2:1) and the holding solution was glycerin 50% (v/v) in 70% alcohol.<sup>2</sup>

The double-staining procedure described in the methods section was effective at staining both ossified and cartilaginous skeletal structures in the newborns. The ossified structures are stained red and the cartilage is stained blue.

### Results

External analysis of the newborn pups did not reveal any significant abnormality for the Bmp4, heterozygotes. In particular, no differences in size were observed, indicating the absence of major patterning and growth defects.

At this stage Bmp4 lacZ signals are present in the perichondrium along the entire course of the ribs from the vertebrae to the sternum sometimes being dispersed but often being more intense towards the outerlayers.

As shown in figure 1, initial Bmp4 signals are evident in the ribs and sternum at post natal day 1.

Asynchronous ossification of inferior sternal segment 5 was recorded. This ossification segment differed from all the other four centers and had a modified shape. We have noticed that in some cases this center was reduced in size and in others fused with segment 4 giving it an unusual shape as seen in the figure 2.

Ectopic calcification of the site of rib attachment to the sternum was not detected in any of the single heterozygote analyzed.

Even when patterning defects were observed, each rib attached to a cartilaginous region of the sternum and these cartilaginous regions were clearly separated by ossified areas.

It has been proposed that the process of rib attachment to the sternum inhibits ossification and/or promotes chondrocyte proliferation at the site of fusion, and that this process is controlled at least partly by Bmps [Storm and Kingsley, 1996; Solloway et al., 1998].

This is consistent with the hypothesis that rib extensions inhibit ossification at the site of fusion [Chen, 1953]. The number of ribs attached to the sternum was always normal in the Bmp4 heterozygous mice.<sup>24</sup>

The sternum is formed by the progressive anterior to posterior fusion of two parallel sternal bands, a process that is normally completed by 15.5 dpc [Chen, 1952b].

The presence of an unfused distal part of the sternum neonatally indicates a severe delay in the completion of this process.<sup>24</sup>

Analysis of the xiphoid process revealed some defects in Bmp4 heterozygotes.

Both the cartilaginous and ossified part of this element was split medially, while wild-type animals have a completely fused process.

As seen in figure 2 the sternum malformation was associated in all cases with the defect of ossification at the level of the inferior sternal segment 5.

Very mild modifications of the ossification center | 4 were noted in correlation with the malformed 5<sup>th</sup> center.

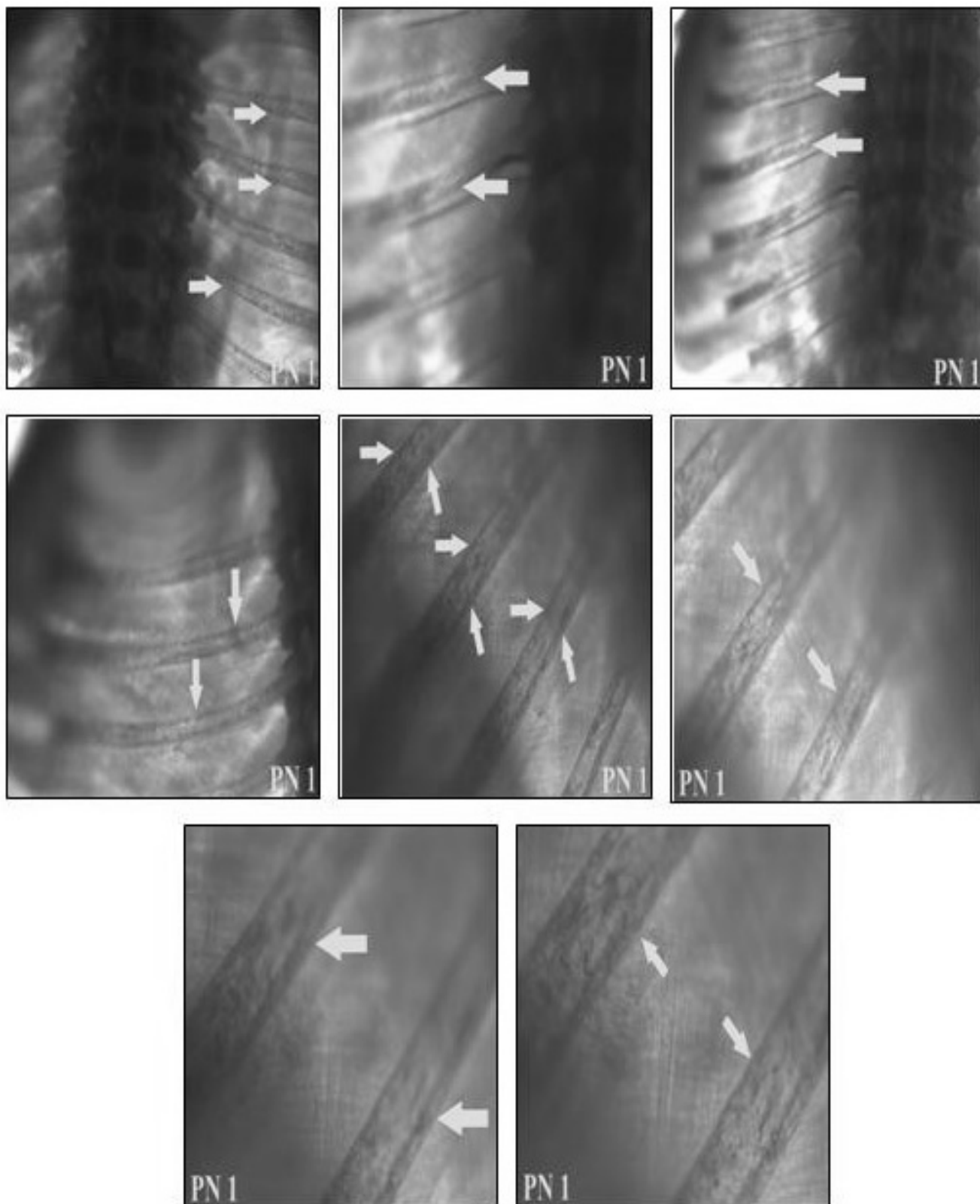


Fig. 1. Bmp4 lacZ signals are present in the perichondrium along the entire course of the ribs from the vertebrae to the sternum sometimes being dispersed but often being more intense towards the outerlayers. The arrows show the blue lacZ staining.

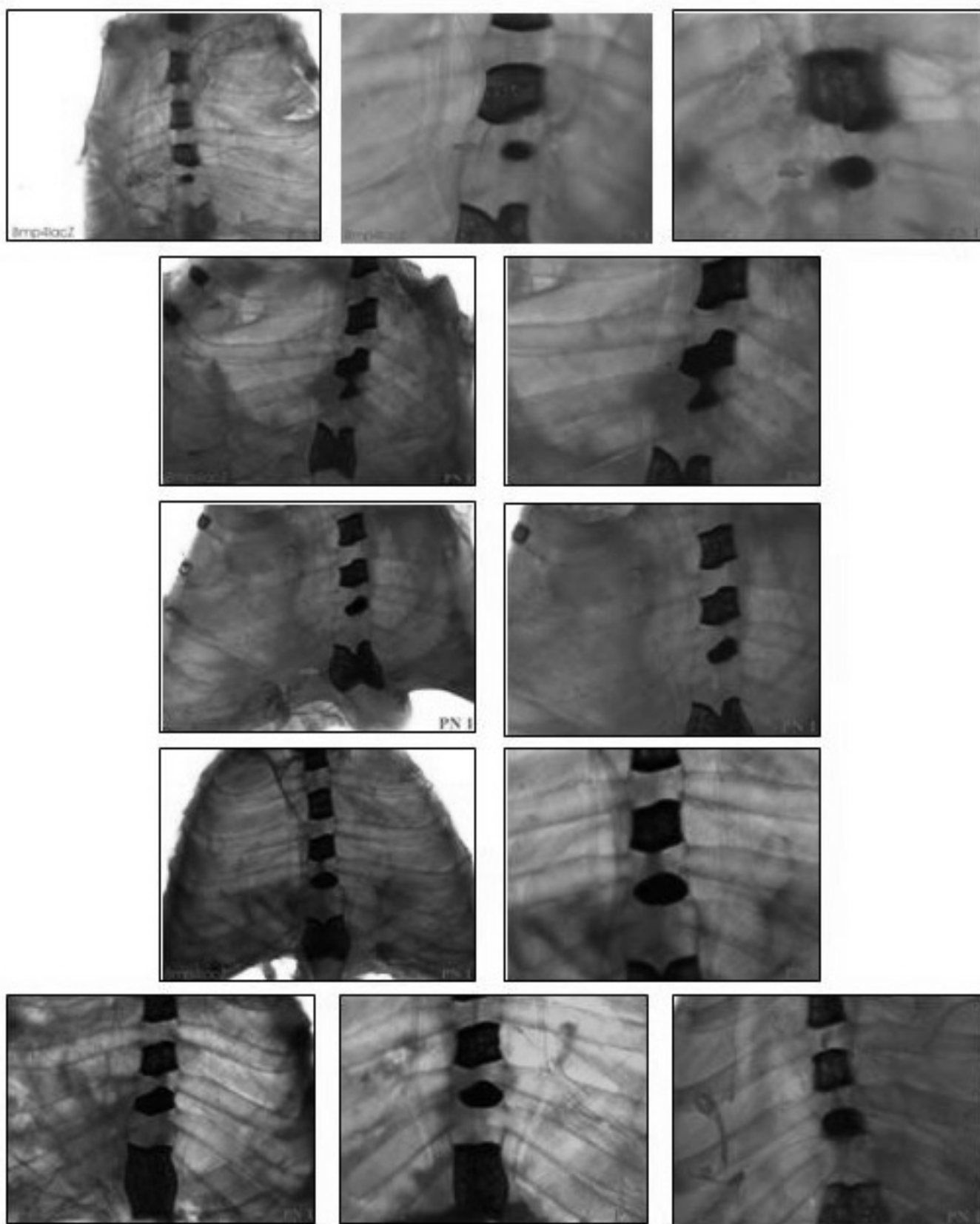


Fig. 2 Asynchronous ossification of inferior sternal segment 5 was recorded at the BMP4 +/- mice as shown by the pointing arrows. (Alcian blue/ alizarin red staining).

## Conclusions

These results indicate that Bmp4 gene dosage is essential for the normal development of the sternal bone and ribs.<sup>17</sup>

Whatever the precise mechanism, the amount of BMP4 secreted by a signaling source appears to be important for achieving the appropriate response in a target tissue.<sup>17</sup>

This conclusion is based in part on the finding that some heterozygous mutants, which presumably produce half the amount of active BMP protein as wild type appear to have some skeletal defects with regards to the sternum and ribs.

## Discussions:

These noted malformations in the mouse model might not have a major effects on the future development of the chest cavity largely because of the fact that the mouse does not have a vertical position of the body so that even if

Findings suggest that a nonossified sternal segment is abnormal and is an indication for further imaging in humans. Few investigators in recent articles have addressed the issue of timing of ossification of the sternal segments.<sup>25</sup>

In many anatomic regions in young children, bone structures ossify in a predictable fashion. A lack of knowledge of the order of ossification can lead to misinterpretation of these findings.<sup>25</sup>

These sternal ossification abnormalities have been reported in human subjects to occur in infants with

there are any tendencies of the sternum to sink in the excavatum shape the chest internal organs will act as a force that will keep the sternum in the right position.

With regards to the human body which has a vertical position thus any changes in the consistency of the anterior chest wall will not be contrabanced by an internal force to prevent the sternum from sinking.

If the ossification of the sternum occurs with delay the possibility that the anterior chest wall will modify its shape increases.

A more detailed analyses of these modifications will determine the efficacy of osteogenesis that we know may depend not only on the type of BMP or the combination of BMPs that is present but also on the cell types that are present.

The timing of ossification of the xiphoid, or sternal segment 5, varies and the xiphoid may remain nonossified for years in humans. Some researchers think that asynchronous ossification of one of the five ossification sites may be suggestive of a number of disease processes that involve the anterior chest wall.<sup>25</sup> congenital heart disease and in patients with several of the bone dysplasias.<sup>25</sup>

Dysplasias associated with delayed sternal ossification include camptomelic dysplasia, Noonan syndrome, and trisomy 17–18 in humans.<sup>25</sup>

It can be suggested that there is a possibility of a normal variation in sternal ossification centers with regards to their presence or absence, shape and size, not investigated.

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## II. NEONATOLOGY

### COMPLICATIONS OF PERI/ INTRAVENTRICULAR HEMORRHAGE

**Marioara Boia<sup>1</sup>, Aniko Manea<sup>2</sup>, Daniela Iacob<sup>1</sup>, Dana Mihut<sup>2</sup>, ES Boia<sup>1</sup>, RE Iacob<sup>1</sup>**

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#### Abstract

Peri/Intraventricular hemorrhage is one of the most frequent diseases of the premature newborn with low birth weight. The most severe complications are: evolving hydrocephalus and multicystic encefalomalacia. The authors intend to present the posthemorrhagic encephaly as a severe and invalidating complication. Cranial ultrasound is used for optimal diagnosis of the disease, dimensions follow-up of the ventricular system, to establish the moment of placing the derivation valve and shunt dynamic follow-up.

**Key words:** intraventricular hemorrhage, hydrocephalie

#### Introduction

The most frequent and serious complication is posthemorrhagic hydrocephalus which appears at 75% from the survivors of severe forms (degree III and IV).

Generally patients with intracranial hemorrhage evolve to regression in 75% of cases and to ventricular dilatation in 25% of cases.

Only in 10% of cases with ventricular dilatation is needed a ventriculoperitoneal shunt.

From the echographic point of view the dilatation of trigon and occipital horns, before frontal horns, could be the only sign of hydrocephalus development. Initially these areas are the only one dilated in small hemorrhage, while in large hemorrhages the entire ventricular system is dilated.

Posthemorrhagic ventricular dilatation can be asymmetric and can affect more the lateral ventricles than the III<sup>rd</sup> ventricle. The volume increase of the IV<sup>th</sup> ventricle is very rare and usually, represents a ventriculitis override to a hemorrhage or an obstruction of Sylvius aqueduct and also of Luschka and Magendie orifice, leading to an isolated ventricle IV.

#### Posthemorrhagic hydrocephalus

Posthemorrhagic hydrocephalus occurs by modifying the normal flow of CSF during the organization process and reaction to the blood in ventricles leaking secondarily through the fourth ventricle into pericerebellar leptomeninges.

At the distance of two weeks after hemorrhage, ultrasound will show small protein- containing particles floating about in the CSF and most probably contributing to

the obliteration of its distal flow. Obstruction may be found in the lateral ventricle, near the foramen of Monro, in the cerebral aqueduct, near the foramina of the fourth ventricle, in the pericerebellar cisterns, near the tentorial groove, in the pericerebellar arachnoid spaces and in the arachnoid granulations of sinuses.

Depending on the obstruction location can occur unilateral, bilateral, internal, external or mix hydrocephalus (of communicating type).

In four out of five cases can appear communicating variant due to obliterative arachnoiditis in the pericerebellar and pericerebral spaces. In some situations both aqueduct and foramina of the fourth ventricle may be obstructed, giving rise to an “isolated fourth ventricle”: continued CSF production in the plexus of the lateral and fourth ventricle gives rise to hydrocephalus above and below the tentorium despite occlusion of the aqueduct. Isolation of the fourth ventricle is a rare complication especially after resealed (or revision) repeated shunt. It may be accompanied by transtentorial upward herniation of that ventricle.

Ventricular widening increases progressive in the weeks after hemorrhage from 5% in the case of hemorrhage grade II up to 40-80% for grades III and IV. The immediate and distance prognosis is modifying at infants with posthemorrhagic hydrocephalus in comparison with those who present only hemorrhage. Factors contributing to this may be subependymal damages from within the ventricular cavity and cerebellar cortical injury from within the leptomeninge. Injury to the inferior olive may follow cerebellar cortical damage. Some authors observed a slow first stage of ventriculomegaly which in 50% of cases subsequently regresses but in other 50% persists, evolving towards symptomatic hydrocephalus. Clinical signs may nearly always be anticipated by serial sonography of the cranium.

Cranial ultrasound plays an important role in the detection and follow-up of posthemorrhagic complications.

1. Evaluation of the severity of ventriculomegaly via repeated measurements: it is possible to determine the laterolateral diameter of both lateral ventricles together on a coronal section through the foramen the foramen of Monro, the roof to floor diagonal height on the same section, and

then proceed to precise measurement of the third ventricular width in an axial section through the sphenoidal fontanelle. The latter measurement is facilitated by the existence of dense ependymal lining. As for lateral ventricular diameters, normal values have been established for gestational age. Treatment will be almost certainly necessary when this value is above the 97<sup>th</sup> centile.

The lateral ventricles can be symmetrically dilated, isolated ventriculomegaly or ventricular asymmetry can occur. Thus, it could be only a widening of the posterior horns of the lateral ventricles, situation called colpocephaly (discrepant overdistention of the occipital horns). Also, on a

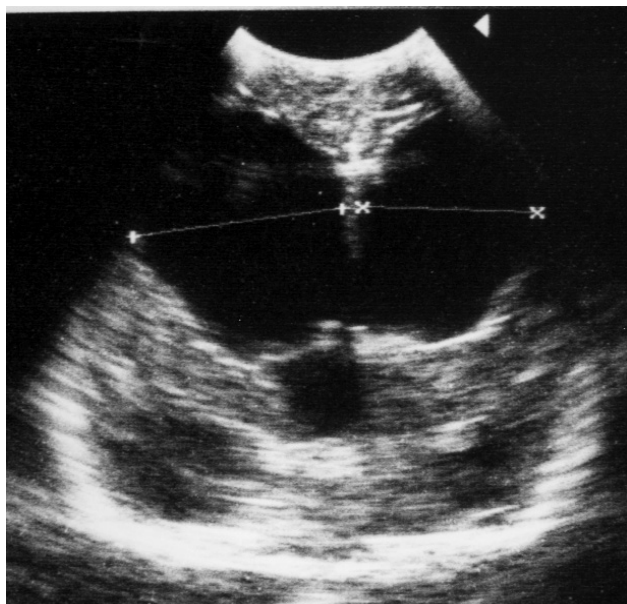


Fig. 1. Coronal section. Severe dilatation of frontal horns.

The position of the neonate does not have a significant influence on the ventricles' shape. Some of the authors underlined that if the baby lies on its side the underlying lateral ventricle may widen more than the proximal ventricle.

Any follow-up of ventriculomegaly in the case of an infant with a fontanelle opening should be done with ultrasound. Depending on the devices' performances and on the scanhead dimension both ventricular system and cerebral parenchyma can be followed-up until the complete ossification of the cranium. It can be also determined the moment of placing the ventriculoperitoneal derivation valve and shunt follow-up. Due to ultrasound performances repeated CT scanning is unjustifiable.

2. Sagittal and axial sections reveal a discrepancy between dilatation of the supratentorial ventricles and the fourth ventricle. In these cases can be well seen the aqueduct of Sylvius, even in the case of stenosis (shape of a cleft); it can be underlined a discrepant dilatation of the fourth ventricle and, in the absence of a large cisterna magna, can be predicted the absence of communication between the fourth ventricle and the pericerebellar spaces.

Normally, the fourth ventricle shows like a triangular structure following the third ventricle, near the

coronal section can be observed the boomerang – shape of the frontal horns above the caudate nuclei. Balloon – shaped frontal horns are usually an indicator for treatment (fig.1).

Besides the lateral ventricles in posthemorrhagic hydrocephalus is very reliable the monitoring of the third ventricle, best estimated in sagittal and parasagittal sections. We also mention that the third ventricle does not necessarily widen uniformly and quite late after the lateral ventricles (fig.2). Normally the width of neonatal third ventricle does not exceed 2 mm (or 2,8 mm by some other authors).

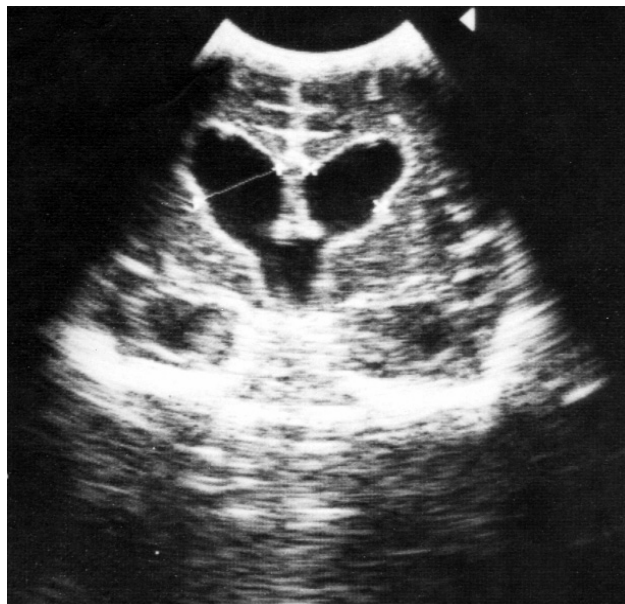


Fig. 2. Coronal section. Dilatation of lateral ventricles.

brainstem. When dilating, will attempt to find the way of least resistance and form a round or more tubular structure in the cerebellar vermis. In the severe forms, when dilatation happens suddenly, a life-threatening pressure can be generated on the vital centres in the brainstem.

3. Sonographic measurements before and after lumbar puncture are used in medical practice to show the communication between the ventricular system and the lumbar subdural space. The shape of the lateral ventricle can be also significantly changed.

4. In case of posthemorrhagic hydrocephalus, the severity of intracranial hypertension can be evaluated by several methods: recording the head circumference; measuring the pressure by means of applanation tonometry over the anterior fontanelle; serial measurements of ventricular diameters. Ultrasounds also give the possibility to study the transependymal CSF resorption.

The measurement of arterial flow rates by means of calculation of the resistance index is useful for evaluating the functionality and the vascularization of the cerebral parenchyma. Either due to the mechanical pressure on the arteries caused by the ventricle contours, or more likely due to intracranial hypertension, can be observed that hydrocephalus requiring treatment induces a decrease or

even inversion of diastolic flow rates in the anterior, middle or cerebral arteries. Resistance indices above 0.8 ( $RI = S - D/S$ , where S=systolic peak rate and D=end diastolic rate) suggest that the vessel bed has been affected. Necrosis of the medial part of the occipital lobe occurs with

hydrocephalus and is probably the result of compression of the posterior cerebral artery.

5. The installation of the derivation shunt can be guided by ultrasound: in order to avoid early plexus in – growth it is ideally to position the shunt tip in the frontal and not in the temporal horn (fig. 3).

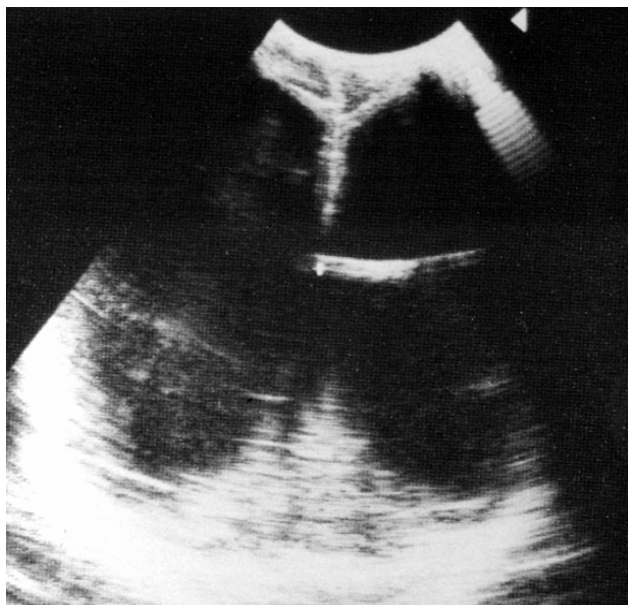


Fig. 3. Two months premature newborn with severe evolutive hydrocephaly - derivation shunt.

### Conclusions

1. Posthemorrhagic hydrocephalus is the most severe complication of the periventricular hemoraege. It occurs in 75 % of the surviving severe cases.
2. Cranial ultrasound plays an important role in the detection and follow-up of the disease: the enlargement

of the lateral ventricle; increase of the diameter of the III- rd ventricle; the measuring of the remaning cerebral parenchim.

3. Finding the proper moment for ventriculo- peritoneal shunt and fallow-up of the derivation.

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### III. PEDIATRICS

## IN FRONT OF THE GATES OF THE EU: A DIFFERENT PERSPECTIVE FOR CYSTIC FIBROSIS

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#### Summary

Cystic fibrosis (CF) is one of the most common recessive genetic disease in caucasian population. The improved knowledge about the pathophysiology of the disease and the spectacular advances in the delineation of the genetics of the defect have brought hope that a cure for CF may not be so far away. The paper present a background about perspectives of CF in the begining of a new milenium.

**Key words:** cistic fibrosis, genetic disease, caucasian population

First recognized as a clinical entity in the late 1930s, Cystic Fibrosis (CF) is one of the most common life limiting recessive genetic disease in caucasian population. It is characterized by chronic and obstructive lung disease, pancreatic insufficiency and high sweat electrolyte levels.

There are at least some explanations for the great interest in CF currently in the western world. Life expectancy has changed dramatically, more so, today life span for an infant diagnosed soon after birth is certainly very much longer than only a few decades ago when many children did not reach school age.

For those patients who attend specialized CF centers, life expectancy could reach 40 years, this being the result of improved traditionally treatment based on controlled airway infection, physiotherapy, reduction of inflammation and better nutrition.

The improved knowledge about the pathophysiology of the disease seems to provide new ways to attack pharmacological approaches.

In the same way, the spectacular advances in the delineation of the genetics of the defect have brought hope that a cure for CF may not be so far away.

Over time, the survival and quality of life for CF patients have improved markedly, due in large to regular periodic evaluation, monitoring of complications, aggressive intervention by physicians and other healthcare workers specifically trained in the management of CF.

Recorded median survival has risen from under 5 years of age in the 1950s to more than 30 years of age in 1995 (1,2).

Despite being a monogenic disease, CF appears to be very heterogeneous. First, since the cystic fibrosis transmembrane conductance regulator (CFTR) gene was cloned in 1989, more than 1,300 mutations have been described (3-5). And second – the distribution of these

CFTR mutations vary widely between countries and/or ethnic groups.

The cloning of the CFTR gene and the ongoing identification of many mutations have promoted intensive research into the association between genotype and phenotype in attempt to find prognostic factors for the outcome.

Several studies have shown that some mutations (e.g. the  $\Delta F508$  as the most common mutation worldwide) are associated with severe disease presentation (6), while other mutations are associated with a milder phenotype (e.g. R553X and others).

There is, however, considerable heterogeneity in disease severity between different individuals, who share even an identical CFTR genotype.

It is widely recognized that the age at diagnosis and the type of severity of symptoms at the initial presentation reflect the clinical heterogeneity of CF.

In this respect it has been hypothesized that early diagnosis with an intensive therapeutic program may result in a better prognosis. It has also been shown that infants presenting with gastrointestinal symptoms are diagnosed earlier than those with pulmonary symptoms.

It seems that patients with pulmonary involvement at diagnosis exhibit the highest mortality. (7).

The hallmark of CF and the cause of death in more than 90% of patients is chronic progressive pulmonary disease. The bacterial endobronchial infection resulting in host inflammatory response appears to be the most important process occurring right after birth in CF patients. There are several other factors such as environmental, genetic, which seem to influence the colonization of the airways and further outcome of lung disease.

Meantime, further studies should determine whether early severe lung disease, associated with early death is related to CF genotype or if severe malnutrition at the time of diagnosis is related to poorer outcomes.

It will be a question if early detection in terms of early intervention and maybe environmental changes would improve outcomes.

It is important to underline the fact that early intensive treatment in CF will be beneficial for patients only in organized, staffed CF centers.

It has been shown that there are striking differences in the condition of people attending different CF centers, far more marked that can be accounted for by

climate, socio-economic circumstances, age of diagnosis or variation in prevalent gene mutations.

There has been recently published a European Consensus upon standards on care for patients with CF (8) defined as optimal service provision necessary to deliver the best outcomes possible.

The guidelines of the consensus are based on the belief that intensive treatment – both prophylactic and as a response to acute events decrease morbidity and increase survival and quality of life.

When speaking of early diagnosis and intervention as a necessary tool for improving outcome – it has to be done through developing programs for organizing care in Regional CF Centers, with trained physicians and nurses, with availability of diagnostic and treatment facilities.

What can we improve for our patients who are often severely malnourished when diagnosed with CF or who attend our clinics after years from diagnosis with severe lung disease?

We have to attempt the ultimate effort which is needed standing in front of the gates of the EU: to try to be organized and provide care at European standards, following protocols and guidelines in order to correct evaluate our patients. The way we treat, the way we'll see the results.

The emphasis on improving care is an important initiative in any disease; this should have a major favorable influence on the quality and duration of life of many people with CF.

The latest ECFS document that sets out the standards of care should be an aim for all people engaged in the management of CF.

We also dare to hope that along the transformation that has to happen when becoming an EU member, the approach to a life-limiting disease as CF will be different and will provide another perspective for the patients.

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## VENTRICULAR ARRHYTHMIAS IN CHILDHOOD

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### Abstract

Isolated premature ventricular beats may be seen in 15% of normal newborns, 30% of normal adolescents and 66% of adolescents with repaired heart disease. Sustained ventricular arrhythmias are relatively rare in young normal hearts. Sudden cardiac death is also rare in young with normal hearts, although there is an increased incidence in dilated and hypertrophic cardiomyopathies and following repair of particular congenital heart lesions.

Patients with cardiomyopathy (CM) often have ventricular arrhythmias, although the risk of mortality is more closely linked to ventricular function. There are many infants and pediatric patients with apparently normal hearts who have asymptomatic nonsustained ventricular tachycardia.

The main concern is to identify diagnoses such as long QT syndrome associated with recurrent cardiac syncope so that appropriate choices can be made regarding drug and/or device therapy.

**Key words:** Ventricular tachycardia, sudden death, cardiomyopathy, congenital heart disease.

**Ventricular arrhythmias** may occur in the setting of congenital heart disease, cardiomyopathies and inflammatory myocardial disease, electrical myopathies, or even in a structurally and functionally normal heart.

Arrhythmias can be identified on incidental examination or because of symptoms such as palpitations, chest pain, or syncope. The primary concerns are identifying patients at risk of sudden cardiac arrest and attempting to modify that risk. The relative frequency of ventricular arrhythmia and the relative rarity of sudden death in pediatric patients complicate management choices and introduce controversy and uncertainty when interpreting historical data.

The frequency and natural history of ventricular arrhythmias is highly dependent on the underlying substrate. More than 50% of pediatric patients with sustained or symptomatic ventricular arrhythmias have evidence of organic heart disease. Of those without overt heart disease, up to 50% may have at least subtle evidence of myopathy. With organic heart disease, ventricular arrhythmias are common, with frequent ventricular ectopy detected in up to 60%, particularly following late repair of tetralogy of Fallot, aortic valve replacement, or with pulmonary vascular disease. Without apparent heart disease, isolated premature ventricular contractions (PVCs) are seen in 10% to 15% of infants and 20% to 35% of adolescents, whereas higher grade ectopy and ventricular tachycardia are uncommon.

Ventricular arrhythmias are a clear mechanism of sudden cardiac arrest, although other cardiac concerns can contribute to both mortality and symptoms.

Hemodynamic impairment also contributes to outcome, complicating our understanding of mortality risk.

### 1. Congenital Heart Disease

Several congenital heart defects have been associated with late sudden death, in particular tetralogy of Fallot. There are no data on the incidence of ventricular ectopy when these patients reach adolescence. Because of its high prevalence, low-grade ventricular ectopy cannot serve as an adequate marker of patients at high risk, but the absence of ectopy may be one marker of lower risk.

Tetralogy of Fallot is the most frequent form of cyanotic congenital heart disease and has the longest follow-up, providing a model for assessing risk associated with ventricular arrhythmias.

The incidence of isolated premature ventricular contractions and nonsustained ventricular tachycardia in postoperative patients with tetralogy of Fallot is relatively high. When electrocardiogram (ECG), Holter, and exercise reports are combined, up to two thirds of older tetralogy of Fallot patients will have frequent PVCs and 8% will have nonsustained ventricular tachycardia (VT). The frequency of PVCs is notably lower in early school age children repaired in infancy and with transatrial repairs. These patients were repaired at a younger age and with modern techniques of cardiac protection, which may contribute to these encouraging results.

Sustained ventricular arrhythmias are much less common. Certainly some congenital heart disease patients present with spontaneous sustained monomorphic ventricular tachycardia (VT), although large population-based data are lacking. Sudden death may occur in 2.7% to 6% of surgical case series and is presumed to be due to ventricular arrhythmia.

Hemodynamic, historical, and ECG markers continue to be used for initial identification of patients at risk. These include residual right ventricular outflow tract obstruction, residual ventricular septal defect, prior shunts, older age at initial surgery, pulmonary insufficiency, and longer duration of follow-up. ECG markers are proposed to further or more easily stratify risk: The results are dependent on the apparent prior risk of the group. Several studies have correlated risk of mortality and/or induced sustained monomorphic VT with QRS durations  $\geq 70$  to 180 msec and/or increased QT/QTc dispersion. Individually these approaches have potentially spectacular test characteristics, although examination of the

data suggests they are dependent on the preexisting risk of the underlying population.

Together these studies suggest that noninvasive markers offer hope for rapid, although imprecise stratification of individual patients. There are no current techniques to exclude the risk of sudden cardiac death. Marginal hemodynamics, well recognized for each type of congenital heart disease, clearly contribute to mortality and cannot be fully corrected. Although more data are clearly required, a combination of multiple noninvasive risk factors, including symptoms in young adults with repaired congenital heart disease, and inducible VT on programmed ventricular stimulation is likely to identify a group with exceptionally high risk of sudden cardiac death. Unfortunately, therapy choices also remain imperfect. For this group of patients, approaches such as pulmonary valve replacement and implantable cardioverter–defibrillator therapy alone or in combination with antiarrhythmic therapy may be justified.

## 2. Structurally Normal Hearts

Risk assessment and management of ventricular arrhythmias in structurally normal hearts involves identifying reversible causes (intracardiac catheters, isolated cardiac trauma, marked metabolic disturbances, and some drug toxicities). Once these isolated triggers are identified and treated, the risk associated with that ventricular arrhythmia is removed. For most other patients with structurally and functionally normal hearts, the key issue is appropriately classifying them as having benign VT or uncommon but identifiable electrical myopathies with associated risk of sudden cardiac death. For patients with depressed ventricular function, an additional goal is identifying those with reversible causes of cardiomyopathy (as tachycardia mediated CM) and those who have irreversible cardiomyopathy for which supportive care and transplant may be required. There are specific patterns that help distinguish these groups. Selective use of echocardiography, ambulatory ECG and Holter monitoring, and exercise testing each offer complementary information. Further investigations, including the use of intracardiac studies, biopsies, angiography, and magnetic resonance imaging, may provide potential information but are recommended selectively.

## 3. Cardiomyopathy

### a. Dilated Cardiomyopathy and Inflammatory

#### *Myocarditis*

The prognosis of pediatric patients with dilated cardiomyopathy is poor, with 25% to 30% 1-year mortality in infants and younger children and possibly worse in older symptomatic patients. Mortality is frequently associated with complex ventricular and supraventricular arrhythmias. Risk stratification beyond following congestive symptoms and ventricular function is controversial. The presence of inducible VT during programmed stimulation does not increase this precision, suggesting that the substrate of sudden death may be different from either spontaneous nonsustained VT or induced VT. Initial implantable cardioverter–defibrillator

experience in adults suggest some benefit from implantable cardioverter–defibrillator therapy in patients with recurrent sustained VT awaiting transplant. Studies comparing implantable cardioverter–defibrillators, amiodarone, or beta-blockade are in progress in adults. There are not adequate data to make these choices in either adults or children.

In myocarditis aggressive supportive and antiarrhythmic therapy, possibly including mechanical support, allows time for evaluation and management of the underlying process. Even when myocardial performance improves following apparent myocarditis, there remains a background incidence of ventricular arrhythmias of uncertain significance

### b. Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy is generally an autosomal dominant condition secondary to defects in sarcomeric protein genes. Male athletes may have sufficient left ventricular hypertrophy to consider the diagnosis of hypertrophic cardiomyopathy, although intraventricular cavity diameters are preserved, wall thickness is generally less than hypertrophic cardiomyopathy, and deconditioning will resolve the hypertrophy. With an overall incidence as high as 1/500, there is heterogeneity in presentation, penetrance, and prognosis with referral populations having incidence of sudden cardiac death of 3% or higher, whereas less select populations have mortality incidences of 1% or lower.

Nonsustained VT on ambulatory monitoring or surface ECG is common and seen in 10% to 16% of children with hypertrophic cardiomyopathy. Sustained VT can be a cause of syncope, sudden cardiac arrest, and mortality. Younger age at diagnosis, nonsustained VT on Holter, syncope, left ventricular outflow tract obstruction on echo and examination, exercise-induced hypotension, inducible VT with programmed stimulation, QRS prolongation, QT prolongation and increased dispersion, have all been proposed as identifiable risk factors for sudden death in hypertrophic cardiomyopathy.

Although the utility of any of these findings in young adults to predict outcome is controversial, their utility in pediatric patients is even less clear. Until genotype/phenotype identification is improved, careful monitoring for symptoms, exercise restriction, and antiarrhythmic drug and device therapy in selected patients represents a reasonable stepwise approach.

Beta-blockade, verapamil, myectomy, and possibly dual-chamber pacing or septal ablation appear to have a role in decreasing symptoms although they do not appear to modify survival. Managing associated Wolff Parkinson–White syndrome and other supraventricular tachycardia is clearly part of the overall arrhythmia management of this difficult population.

## 4. Electrical Myopathy

In contrast to patients with clinically apparent ventricular arrhythmias, or known congenital heart disease, long QT syndrome (LQTS) and many other rare causes of sudden cardiac death may only present with recurrent

cardiac syncope or unexpected sudden cardiac death. It is not clear that these conditions are substrates for recurrent nonsustained VT. Hypertrophic cardiomyopathy is the most common cause of sudden cardiac death in apparently healthy athletes. Primary electrical myopathies, such as LQTS, Brugada syndrome, arrhythmogenic right ventricular dysplasia and catecholaminergic VT, are much less common.

Untreated, the annual mortality in LQTS may be as high as 3%, with particular risk in LQTS infants presenting with functional 2:1 block and marked QT prolongation. The challenge with these disorders is in recognizing the patients (and families) and then planning effective therapy. Abrupt onset of unconsciousness, injury, or onset of symptoms with exercise all potentially indicate cardiac syncope, although each can be seen with neurally mediated syncope. Benign causes of related symptoms, such as neurally mediated syncope, are very common, with up to 0.1% of the adolescent population seeking medical care for syncope and more than 25% reporting episodes of near syncope in response to head-up tilt. Even in apparently high-risk settings, such as syncope with exercise, there may be benign explanations.

Because the diagnosis of neurally mediated syncope is essentially both a diagnosis of exclusion and a diagnosis based on a typical history, the lack of diagnostic precision identifying LQTS and related rare disorders is a major challenge.

For most of these patients, sufficient investigation includes detailed review of the event history, family history, ECG, and probably a Holter and exercise testing specifically searching for repolarization abnormalities. Echocardiography is useful to evaluate structural causes of cardiac syncope not apparent on physical examination: Hypertrophic and dilated cardiomyopathy and anomalous coronary patterns are the most frequent diagnoses in unexpected sudden death in young people.

In patients with documented VT/ventricular fibrillation who do not yet have a diagnosis after echo, ECG monitoring, and detailed history, there is potentially a high

yield with intracardiac programmed atrial and ventricular stimulation: Recurrence risk is difficult to accurately assess, although it is certainly related to the specific diagnosis. Implantable cardioverter-defibrillator therapy, often in combination with beta-blockade or other antiarrhythmic therapy, offers the potential for secondary prevention, even without a clear diagnosis.

Survival advantage of any of these therapy choices is not yet demonstrated in pediatric patients. The potential for drugs, including tricyclic antidepressants and cisapride to induce repolarization changes and arrhythmias suggests the possibility of a pool of individuals genetically susceptible to QT prolongation who can be identified with systematic screening. Certainly, in patients with apparent cardiac syncope and even intermediate probability of LQTS by clinical criteria, avoidance of these drugs appears prudent.

### Conclusions

The primary concern of families with ventricular arrhythmias and of the pediatricians and cardiologists caring for these families is to prevent the sudden cardiac death. Fortunately, with rare exceptions, the prognosis of congenital heart patients with ventricular arrhythmias is very good. Unfortunately, the ability to identify patients at particularly high risk of sudden death is limited in most clinical situations. Alternative causes of symptoms, including supraventricular tachycardia and neurally mediated syncope, are relatively common. Therapy remains imperfect and may also contribute to mortality.

The basic approach with documented or possible ventricular arrhythmias is to always worrisome, observe and manage selective patients carefully. Recognizing benign patterns of ventricular arrhythmias allows a more permissive management approach: these are almost always characterized by normal sinus rhythm repolarization patterns, lack of serious symptoms, normal ventricular function, and no significant past medical history or family history of early mortality.

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## CONSIDERATIONS ON A CASE WITH ACUTE RENAL FAILURE OF UROLOGIC NATURE IN INFANCY

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### Abstract

The paper presents the case of a 6-month old infant hospitalized in Clinic II Pediatrics for congenital bilateral ureteral stenosis with subclinical evolution before this age. Clinical course revealed the occurrence of the urinary tract infection associated with the malformation, with unfavorable and rapid evolution to acute pyelonephritis, and acute renal failure with demise in the 5<sup>th</sup> day of hospitalization. The case was referred to our clinic from a Pediatric Ward where he was admitted for a respiratory infection and the diagnosis of polycystic kidney was suspected based on an ultrasound examination.

**Keywords:** congenital bilateral ureteral stenosis, acute pyelonephritis, acute renal failure.

### Introduction

Congenital bilateral ureteral stenosis is a rare abnormality of the urinary tract, more frequent in boys, ureteral stenosis being situated wherever between the ureteropelvic and the ureterobladder junctions<sup>1</sup>.

Clinical signs represent an outcome of the complications occurred because of the urinary obstruction, and are recurrent urinary infections, ureterohidronephrosis (pseudo tumor kidney), chronic renal failure and more rare acute renal failure.<sup>1</sup>

Excretory urogram examination represents the most important method of examination for a certain diagnosis. It shows the uretero-pyelo-calyceal supragenital dilatation with a delay or even absence of elimination of the contrast substance.

### Case presentation

The 6-month old infant, G.P., was admitted to our clinic for: fever and vomiting. Family history revealed young and apparently healthy parents. He was the third

child, with normal gestational age, birth weigh 3300g, 2 months breast feeding and then artificial feeding with cow milk. Two days before admittance in our clinic, the child was hospitalized in another pediatric department for Bronchopneumonia being treated with association of antibiotics. Based on an ultrasound examination, a suspicion of polycystic kidney was established. No information regarding diuresis before admittance was available.

Clinical examination showed an infant with 3850g, fever (T=39°C), bad general state, no appetite, sever pallor, warm extremities, enlarged abdomen, liver with inferior margin 2 cm below the right rib. At the examination of the medium right part of the abdomen a 4/6cm pseudo tumor was revealed, with lombar contact, firm, wavy surface, mobile, and another 4/4 cm pseudo tumor was palpable in the hypogastrium and pubian area, firm, immobile, with a smooth surface. Oligo-anuria was present during the entire evolution.

Biologic tests showed: Hb=6,6g%, Er=2,400 000/mmc, L=5,200/mmc, ESR=120/141mm, uree=178mg%, creatinine=1,4mg%, uric acid=9,7mg%, Natrium=146→135→119mEq/l, K=6,5mEq/l, ph=7,07, BE=-19,7mmol/l, pCO<sub>2</sub>=30,3, albuminury, leucocitury, Uroculture with E. Coli>100,000/ml, sterile hemculture.

Renal ultrasonography in different sections revealed sinusal transonic images into the renal parenchyma, wiped pyelocaliceal shadow, and disseminated hyperreflectogen images in the cortico-medullar area. Right kidney appeared with a mixed structure, with hyperefectogen images up to the cortico-sinusal level, with very slight differentiation parenchima-sinusal. Between the liver parenchyma and the renal parenchyma, the renal capsule is highly reflectogene, with wavy contour and invasion of psoas (Fig. 1).

Fig.1 Renal ultrasonography-  
Left lumbar transversal section-  
Transonic images that go into  
the left renal parenchyma.



Bad general state of patient and the presence of acute renal failure did not allow us to perform the excretory urogram. In the absence of the excretory urogram, the diagnosis of that moment was: Congenital anomaly of kidney (probably

bilateral polycystic kidney); Acute pyelonephritis; Acute renal failure. The evolution was unfavorable despite the treatment, with profound alteration of general state and decease within 5 days from admittance.



Fig 2. Macroscopic examination- Both kidney increased in size, wavy surface, bilateral hydroureter. Morphopathologic exam actually allowed us to visualize the patient lesions.

Macroscopy revealed both kidney increased in volume and weight (right kidney 8,5/3,5/5cm, left kidney 6,5/3,5/3 cm) colored in red, highly waved surface, with an aspect of bilateral hydroureter (Fig 2). On the section, the calices appeared dilated, filled with purulent liquid. The left ureter had a narrowing of the lumen through a spin at 3,5cm from the ureteropyelic junction, whereas the right ureter was impermeable, with a severe stenosis 1,5cm from the ureteropyelic junction. Bilateral ureterohydronephrosis and

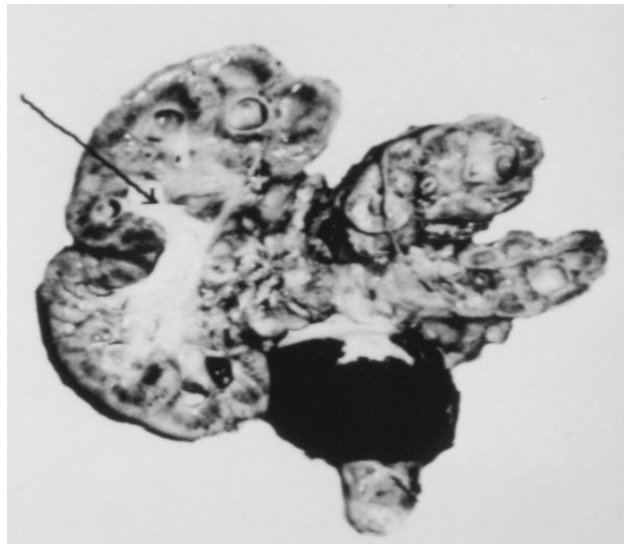


Fig. 3 Macroscopic exam - Dilated calice, filled with purulent liquid.

increased urinary bladder with large walls purulent liquid and necrotic-hemorrhagic mucosa were also noticed (Fig. 3).

Microscopy showed confluent interstitial inflammatory lesions with congestion, interstitial edema, polymorphonuclear infiltration, suppurative necrosis, endotubular necrotic and granulocytic cylindries. (Fig. 4, 5).

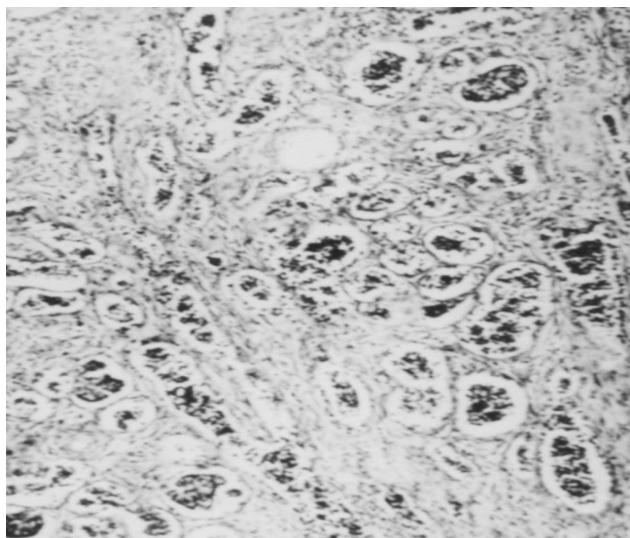


Fig. 4. Microscopic exam - Confluent interstitial inflammatory lesions, polymorphonuclear infiltration, suppurative necrosis.

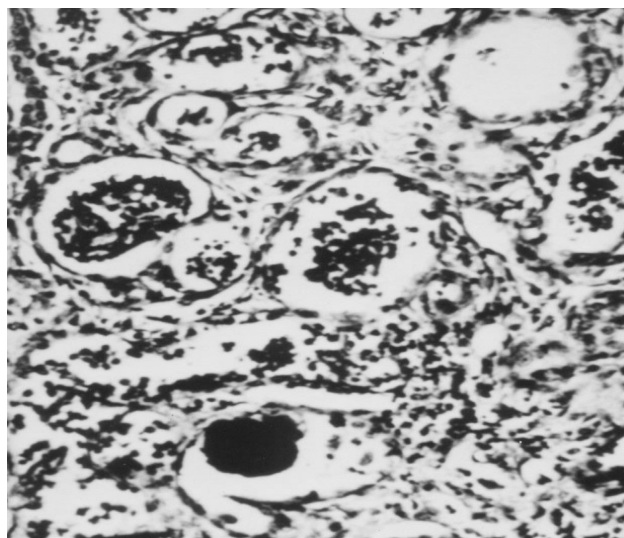


Fig. 5. Microscopic exam - Endotubular necrotic and granulocytic cylindries.

### Discussion

The case was admitted to our clinic with digestive symptoms and fever, which after investigations proved to be the clinical and biological picture of the acute renal failure, following an acute pyelonephritis.

Ultrasound examination did not establish a precise diagnosis, but a suspicion of congenital renal anomaly was clear, most probable a cystic disease of kidney.

Among these, the most frequent disease in children is multicystic dysplastic kidney which goes with increased kidney, palpable at clinical examination, wavy surface, severe and rapid evolution to acute renal failure and decease. In this case, a giant hydronephrosis is developed with the decrease of renal parenchyma to a blade size.<sup>1,4,5</sup>

A second frequent anomaly is represented by polycystic kidney (Potter I polycystic kidney). The kidneys are also palpable at clinical examination, increased in size, wavy surface, but the onset occurs later on in life with signs of portal hypertension (hepatosplenomegaly) through the severe congenital hepatic fibrosis and with chronic renal failure progressively installed.

Polycystic kidney type Potter IV (partial or intermittent obstruction of the urinary flux) presents the most elements similar with our case: palpable kidney, wavy surface, bilateral hidroureter, hypertrophic urinary bladder, severe prognostic with evolution to acute renal failure. This

disease was excluded based on the macroscopic and microscopic examination.<sup>1,4,5</sup>

Another aspect that should be taken into account is the eventuality of a preexistence of chronic renal failure stage II partly compensate on which acute renal failure occurred. Actually, renal malformations determine chronic renal failure at first, acute renal failure occurring as a complication of the chronic stage in the context of hydro-electrolytic perturbation witch was the situation of our case. The patient presented oliguria within 2 weeks ago, at the same moment with the onset of the respiratory disease, and the azotemia increased gradually, simultaneous with hydroelectrolytic and acido-basic perturbations.

### Conclusions:

1. The case represents a regrettable diagnosis error
2. The delayed diagnosis was determined by multiple factors: few clinical signs at the domicile, ambiguous results at ultrasound examinations, and the rapid evolution of pyelonephritis in the absence of therapy to acute renal failure.
3. Excretory urogram with radiopaque medium performed in due time would have been allow a precocious diagnosis and a rapid surgical correction treatment

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# AIR PARTICULATE MATTER (PM) CONCENTRATION IN RESITA A MAJOR DANGER FOR CHILDREN'S RESPIRATORY SYSTEM

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## Abstract

The paper work presents a group of school children with respiratory system diseases caused by air pollution. The causes of the growing number of respiratory diseases are pointed out by the high number of hospital admissions and the increasing number of visits to the family doctors.

**Key words:** air pollution, breath, schoolchildren

## Introduction:

According to the O.M.S. (the World Health Organization), "There is air pollution, when the presence of a foreign substance or a significant variation of the proportion of its components, are likely to cause a harmful effect on the activity and good being of the people." [1] We have decided to assess the causes of the growing number of respiratory diseases also pointed out by the high number of hospital admissions and the increasing number of visits to the family doctors [2], and we drew the conclusion that the main cause is air pollution with PM 10 (particulate matter less than 10 microns). Its concentration is over the maximum limit of 0,150 mg/cubic metre. The information was taken from the Ministry of Environment's site.

## Aims:

a) Establishing the degree of modification of respiratory functions during 1 year (2004- 2005) using spirometry.

b) In this article we want to analyze the respiratory system diseases in children, a group of 300 school children was taken.

## Material and Methods:

We studied a group of 300 school children aged 7-18, 150 were taken from a polluted area where they live and study, this group was considered "exposed" (E+). The other group "not exposed" (E-) lives in a less polluted area. Children from E+ study at two different schools nearby the main pollution source CSR (Combinatul Siderurgic Resita), and the second group (E-) study at two schools situated in a remote area from CSR.

We statistically analyzed the data obtained by means of questionnaires from children, teachers and parents.

The group of children was clinically examined.

We measured twice a year the respiratory functions (RF) using spirometry :

- VC (current volume),
- FVC ( forced vital capacity)
- FEV1( forced expiratory volume at one second)
- PEF ( peak respiratory flow).

## Results:

We first noticed significant differences of RF. Children from E+ had lower RF than children from E-. We measured the parameters mentioned above and the results of VC test are presented in table 1.

Table 1.

VC								
		<50	50-59	60-69	70-79	80-89	>=90	tot
	<b>m</b>	24	17	9	6	3	1	60
<b>E+</b>	<b>f</b>	21	27	18	16	7	1	90
	<b>tot</b>	45	44	27	22	10	2	150
	<b>m</b>	0	4	20	18	11	7	60
<b>E-</b>	<b>f</b>	0	9	26	26	22	7	90
	<b>tot</b>	0	13	46	44	33	14	150
<b>Total</b>		<b>45</b>	<b>57</b>	<b>73</b>	<b>66</b>	<b>43</b>	<b>16</b>	<b>300</b>

We can easily see that:

- in the less polluted area there is not a single child who has VC < 50,
- in the polluted area only two children have VC >90,

- the majority of children from the polluted area have VC values between < 50 and 60.

We measured the second parameter FVC and the results are presented in table 2.

Table 2.

<b>FVC</b>								
		<50	50-59	60-69	70-79	80-89	>=90	tot
	<b>m</b>	37	11	5	4	2	1	60
<b>E+</b>	<b>f</b>	46	23	10	5	3	3	90
	<b>tot</b>	83	34	15	9	5	4	150
	<b>m</b>	0	9	16	19	11	5	60
<b>E-</b>	<b>f</b>	3	12	31	26	11	7	90
	<b>tot</b>	3	21	47	45	22	12	150
<b>Total</b>		<b>86</b>	<b>55</b>	<b>62</b>	<b>54</b>	<b>27</b>	<b>16</b>	<b>300</b>

- in the polluted area the number of children who have FVC < 50 represents 55,33% from the total number of 150,
- in the polluted area the number of children who have FVC >90 represents only 2,66% from the total number of 150 ( 4 children).

polluted area and the low number of children with respiratory diseases from the less polluted area. In the polluted area 70% of children have FEV1 values between < 50 si 60.

We computed the Tiffeneau coefficient [3],[4],[5] using the formula  $FEV1 * VC / 100$  and we found out that 32 children have a low coefficient and they are respiratory monitored : IgE, hemoglobin, pulmonary radiography, the research being in development.

Fev1 values are presented in table 3 and they also underline the significant differences between the high number of children with respiratory diseases from the

Table 3.

<b>Fev</b>								
		<50	50-59	60-69	70-79	80-89	>=90	tot
	<b>m</b>	26	16	9	4	4	1	60
<b>E+</b>	<b>f</b>	30	32	18	3	2	5	90
	<b>tot</b>	56	48	27	7	6	6	150
	<b>m</b>	4	12	16	14	7	7	60
<b>E+</b>	<b>f</b>	9	21	25	15	9	11	90
	<b>tot</b>	13	33	41	29	16	18	150
<b>Total</b>		<b>69</b>	<b>81</b>	<b>68</b>	<b>36</b>	<b>22</b>	<b>24</b>	<b>300</b>

Another studied parameter is PEF.

The results obtained after the statistic analyze are shown in table 4.

Table 4.

<b>PEF</b>								
		<50	50-59	60-69	70-79	80-89	>=90	tot
	<b>m</b>	29	9	11	4	4	3	60
<b>E+</b>	<b>f</b>	49	14	18	5	3	1	90
	<b>tot</b>	78	23	29	9	7	4	150
	<b>m</b>	10	6	10	12	14	8	60
<b>E-</b>	<b>f</b>	11	16	24	22	8	9	90
	<b>tot</b>	21	22	34	34	22	17	150
<b>Total</b>		<b>99</b>	<b>45</b>	<b>63</b>	<b>43</b>	<b>29</b>	<b>21</b>	<b>300</b>

- in the less polluted area 71,33% of children have PEF >60.
- in the polluted area 32% of children have PEF >60.

### Discussions

A very interesting aspect which is easily noticed is the fact that in the polluted area 30% of school children have VC < 50, while in the less polluted area nobody has VC < 50.

In E+ (polluted area) 12% of children have FVC>70, a very low percentage, while in E- (less polluted area) 53% of children have FVC>70, four times higher than the percentage of children from E+.

In E+ 10% of girls have FEV1>70, while in E- 44% of girls have FEV1>70, again four times higher.

Regarding PEF, a very important difference has been observed. The number of school children from the less polluted area with PEF >60 is twice higher than the number of school children from the polluted area.

### Conclusions

What has undoubtedly been proven after the statistical results is that the proportion of school children with modified RF is higher in the polluted area than in the less polluted area and that the number of girls with low RF is higher than the number of boys, and one cause of this matter can be the fact that boys live a more physically active life and spend their holidays in less polluted areas. Another cause can be the fact that girls have more pets than boys. In general, the entire group of 300 children have modified RF.

A very important cause that leads to modified RF in school children is air pollution, high levels of **particulate** matter. Children are among the most sensitive, and this fact is demonstrated by the high number of hospital admissions for respiratory diseases. The number of hospital admissions for some respiratory diseases during four years (2001- 2004) is presented in table 5.

Table 5.

Disease/children 5-14 years	2001	2002	2003	2004
Sinusitis	4	0	5	12
Laryngitis and trachea illness	7	59	31	72
Asthma	54	51	52	117
Bronchitis	67	137	50	128

The growing number of visits to the family doctor and hospital admissions for respiratory diseases in 2004 dovetails with the intensive activity of CSR, and also with the increasing level of air pollution ( over 52 tests exceeding the maximum concentration limit in 2004, while

in the past years there were merely 10, 20 tests exceeding the limit).

Our study aims to point out the negative impact of air pollution on children's health from Resita.

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# SEPSIS WITH STAPHYLOCOCCUS AUREUS IN AN INFANT WITH SEVERE GASTROENTERITIS CASE REPORT

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## Summary

Young age, malnutrition,, leak of breast-feeding, exposure to unsanitary conditions are factors that increase susceptibility to severe bacterial infections. We present the case of a two month old male infant hospitalized in our clinic for severe gastroenteritis with dehydration and sepsis with *Staphylococcus aureus*.

**Key words:** sepsis, infant, *Staphylococcus aureus*, gastroenteritis

## Introduction

Infants smaller than 3 months are at increased risk to serious bacterial infections.(1) Sepsis is a chain of events that begins with a minor infection. There is an increase in sepsis caused by organisms that are resistant to most standard antibiotics. The incidence of sepsis has nearly doubled in the last decade.

Staphylococcal sepsis may be associated with any localized infection. The onset may be acute and marked by vomiting and fever.(1) As the infection worsens staphylococcal bacteria enter the blood stream. The body attempts to defend itself against the infection with a series of inflammatory and antiinflammatory compounds that attack body tissues.

The cell wall peptidoglican elicits endogenous pyrogen production from monocytes, is chemotactic, activates complement, has endotoxin-like properties. (1, 2) Adesion of *S.staphylococcus aureus* to mucosal cells is mediated by teichoic acid in the cell wall (3)

Untreated staphylococcal sepsis is associated with a mortality rate of 80% or grater. Mortality rates have been reduced to 20% by appropriate antibiotic treatment. (4, 5)

Prognosis may be influenced by numerous host facts, including nutrition, immunologic competence and the presence or absence of other debilitating diseases.(1, 6, 7)

## Case report

We present a two months old male infant, admitted in the 1<sup>st</sup> Pediatric Clinic in „Louis Țurcanu” Children’s Hospital Timișoara on 04.10.2002. He is the second child of an young healthy couple from the country. The pregnancy was not followed up and the child was born in term, with o weight of 3100g and Apgar score 9. He was fed with breast milk for 21 days and then with powder milk. The socio-economic status of the family was low. The weight growth was inadequate.

## The history of illness

For 72 hours the infant presented severe watery diarrhoea, vomiting and high fever 39°C. The treatment at home with Smecta, antipiretics and diet didn’t stopped the symptoms, so the patient was admitted in our hospital.

## Clinical findings

The infant was lethargic,with generalized hypotonia, hypothermia (core temperature=36°C and cutaneous temperature=35,6°C). He’s weight was 3300 g. The skin was very pale, mottled , with prolonged capillary refill time over 3 sec, cold extremities and persistent abdominal cutaneous fold. (Fig.1) The anterior fontanel was depressed and mucous membranes were dry. Eyes were sunken. There were present tachypnea 60 breaths/min and tachycardia 150/min. The peripheric pulse was weak .The blood presure was 46/25 mmHg. There was abdominal distention and the stools were watery. Oliguria was present. There was no stiffness of the neck.



Fig.1 Clinical aspect.

Laboratory findings

Table 1. Blood cell count

Data/variabila	04.10.2002	11.10.2002
Hemoglobin g%	6,5,	8,3
Erythrocyte/mm <sup>3</sup>	2410000	3200000
Hematocrit %	24	28
Leucocyte/mm <sup>3</sup>	29100	9300
Immature forms %	13	0
Granulocytes %	77	68
Lymphocytes %	10	32

Table 2. Tests for coagulation

Data/variabila	04.10.02	11.10.02
Platelet count/mm <sup>3</sup>	31000	107000
Bleeding time	6'30"	3'15"
Coagulation time	8'30"	5'
Prothrombin time	55"	15"
Fibrinogen level g/l	1,2	2,2

Table 3. Arterial blood gases

Date/hour/variable	04.10.02 18.45	04.10.02 22.51	07.10.02
PH	6,95	7,17	7,38
BE mmol/l	- 29,4	- 23	- 2,3
PCO <sub>2</sub> mmHg	28	31	39

Table 4. Serum glucose level

Date/hour/variable	04.10.02 18.45	04.10.02 20.30	05.10.02
Glucose mg%	203	118	104

Table 5. Serum electrolytes level

Date/variable	04.10.02	07.10.02
Na mmol/l	125	139
K mmol/l	2,9	4
Ca mmol/l	2,4	2,55
Cl mmol/l	90	103

- Acute – phase reactants: CRP positive; ESR: 20 mm/1h
- Serum iron: 5,4 micromoli/l

Table 6. Renal function

Date/variable	04.10.02	08.10.02
Serum urea level mmol/l	13,30	5,3
Serum creatinine $\mu$ mol/l	139	35

Table 7. Cultures

Specimen	Result
Blood	Staphylococcus aureus
Throat swab	Staphylococcus aureus
Nasal swab	Staphylococcus aureus
Stool	Negative
Urine	Sterile

Treatment

Antimicrobial agents: Ceftriaxone 0,3 g/day and Pierami 0.045 g/day iv ; Colimicină 100000ui/kg/day po 3 days.

Intravenous fluid resuscitation:

Isotonic sodium chloride solution intravenously in numerous boluses of 20 ml/kg; glucose 10% and electrolytes (Na Cl 5,8%; KCl 7,4%)

- Correction of metabolic acidosis with sodium bicarbonate

Oxygen 8l/min via face mask and monitor saturation with a pulse oximeter.

Sympathomimetic agent: Dopamine 0,5% 3  $\mu$ g/kg/min for 10 hours.

- Transfusion with packed red cells  
Smecta by mouth  
Antipiretic medication (algalmin iv)  
Parenteral administration of vitamins B<sub>1</sub>, B<sub>6</sub>  
Parenteral nutrition with Aminovenos and

Intralipid

Vital signs and patient's perfusion were carefully monitored.

Diet:

- Oral glucose electrolyte solution (Gesol)
- Low-lactose formula

Evolution

With treatment the vomiting and diarrhoea stopped, the severe dehydration reversed, the digestive tolerance restored. The weight increase was of 1500 g.

The infant was discharged after 8 days with following recommendations:

- following up by family doctor for iron deficiency anemia and mild protein-caloric malnutrition
- feeding with powder milk
- treatment with iron in oral solution Ferrum Hausmann 3x10 drops/day and Pikovit syrup 2,5 ml/day 1-3 months
- active immunizations according to schedule
- administration of Vigantol and calcium by mouth

Discussions

Infants are more susceptible to dehydration because of the greater basal fluid and electrolyte requirements per kilogram (1) Early aggressive volume resuscitation has been shown to improve survival.

Disseminated disease with Staphylococcus aureus may occur after a viral infection that suppresses neutrophil or respiratory epithelial cell function. (1, 2, 7) Sepsis is revealed by clinical findings (hyperthermia, tachycardia, cold extremities with prolonged capillary refill, oliguria) and laboratory manifestations (positive blood culture; metabolic acidosis; anemia; leukocytosis and increase in juvenile forms). (6, 7, 8) Antibiotics remain one of the few therapies that improve the outcome in sepsis (8, 9)

Conclusions

1. Small infants are particularly vulnerable at severe infections.
2. Malnutrition, anemia, leak of breast-feeding, are factors that increase susceptibility to severe diarrhoea.



3. Management of dehydration remains the corner-stone of therapy of severe gastroenteritis
4. Optimal management of severe sepsis depends of rapid recognition, aggressive restoration of circulating

volume with fluid boluses, initiation of appropriate antibiotic therapy, and implementation of adequate monitoring.

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## OUR EXPERIENCE IN PEDIATRIC SEPSIS

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### Abstract

Despite the existence of an international consensus regarding both pediatric sepsis-related definitions, and the management of this serious condition, there is no detailed analysis of the epidemiology, diagnosis and prognosis of pediatric sepsis in Romania. We sought to determine the influence of age, gender, microbiologic etiology, and underlying condition on the incidence, outcome, and associated hospital resources use of sepsis and its complications in pediatric patients. We analyzed our Clinic's patients' files for the years 2003 and 2004. Of 2876 hospitalizations for an infectious process in children, 248 met the International Pediatric Sepsis Consensus Conference definitions for sepsis, or 124 cases of pediatric sepsis per year. The incidence was highest in infants (12 per 100 infected children) and fell constantly with age. The incidence of sepsis in children did not vary significantly by sex in any of the age groups. One third of the cases had underlying disease (33%). The majority of infections causing sepsis were respiratory (64%). Microbiologic etiology was determined in 25% of all cases, with Gram-negative bacteria being the most important pathogens. Hospital mortality was 5% overall, with a mortality of 53% for the patients presenting with septic shock. The mean length of stay was 12 days. Several factors were significantly associated ( $p < 0.005$ ) with a poor outcome: shock, metabolic acidosis, increased serum bilirubin and creatinine levels, the presence of 4 or more organ dysfunctions. The therapy with corticosteroids was found to improve the outcome of pediatric patients with severe sepsis or septic shock. Sepsis is a significant healthcare problem in children and is associated with the use of extensive healthcare resources. We therefore need to make efforts to increase awareness and adopt the existing evidence-based recommendations for the management of sepsis and its complications.

**Keywords:** sepsis, severe sepsis, septic shock, children, epidemiology, clinical features, treatment, mortality, prognostic factors.

### Introduction

The worldwide burden of sepsis in children is tremendous. Latest reports suggest that in the United States alone, there were estimated 4,400 pediatric deaths from sepsis every year, with hospital costs of \$ 1,7 billion, and sepsis being the fourth leading cause of hospital admissions. However, most research has focused on adults, and information about sepsis in children is limited.

A description of pediatric-specific definitions for systemic inflammatory response syndrome (SIRS), sepsis, severe sepsis, septic shock, and multiple organ dysfunction

syndrome was recently published (1). Still, there is no detailed analysis of the epidemiology, diagnosis, treatment, and prognosis of pediatric sepsis in Romania. We therefore sought to explore our Clinic's sample of pediatric sepsis in more depth. Specifically, we analyzed the impact of age, gender, underlying pediatric disease, and microbiologic etiology on the incidence, mortality, and length of hospitalization of children who develop sepsis; as well as several clinical features occurring in children with sepsis; and the existence of a series of parameters, which could be used as outcome-predicting factors.

### Purpose

The main goal of our study was to determine the importance of sepsis and its complications in the general morbidity and mortality in the pediatric population. Secondly, we tried to identify those parameters, which could be used as prognostic factors. And last - we analyzed the results of the various management strategies currently applied in the treatment of sepsis and its complications in our Clinic.

### Materials and methods

#### Data sources

We constructed a patient database for the calendar years 2003 and 2004 based on the analysis of the patients' files. We extracted demographic characteristics (age, gender, social background), principal and all secondary admission and discharge diagnoses, clinical parameters (community/hospital-acquired infection, SIRS criteria, organ dysfunction parameters: respiratory, cardiovascular, digestive, hepatic, neurologic, renal, hematologic, shock), laboratory parameters (erythrocytes sedimentation rate, white blood cells count, hemoglobin, hematocrit, platelets count, fibrinogen, procalcitonin, C-reactive protein, pH and blood gases, serum electrolytes, coagulation parameters, BUN, creatinine, bilirubin, AST and ALT, chest radiograph, other imaging examinations, electrocardiogram, blood cultures and other cultures and antibiogram results), therapeutical measures and duration (antibiotics, fluids resuscitation, inotropics, vasopressors, transfusions, corticosteroids, intravenous immunoglobulin, GM-CSF, oxygen), length of sepsis, length of stay, and hospital discharge status.

#### Case selection and definitions

We identified cases with sepsis, severe sepsis or septic shock by analyzing all hospitalizations for a bacterial or fungal infectious process from our Clinic within the 2-years period.

We defined children as patients who are 18 years old or less, and divided them into 6 clinically and

physiologically meaningful age groups for age-specific vital signs and laboratory variables to meet the diagnosis criteria, as recommended by the Consensus Panel (1). (Tables 1 and 3).

The diagnosis was based on the current specific definitions of systemic inflammatory response syndrome, sepsis, severe sepsis, septic shock, and organ dysfunction for neonates and children (1). (Tables 2 and 4).

**Table 1:** Pediatric age groups for sepsis definitions

Age-group	Age
Newborn	0 days to 1 month
Infant	1 month to 1 year
Toddler	1 to 3 years
Preschool	3 to 6 years
School age child	6 to 12 years
Adolescent	12 to 18 years

**Table 2:** Definitions of SIRS, infection, sepsis, severe sepsis and septic shock

#### *SIRS\**

The presence of at least two of the following four criteria, one of which must be abnormal temperature or leukocyte count:

- Core\*\* temperature of  $>38.5^{\circ}\text{C}$  or  $<36^{\circ}\text{C}$ .
- Tachycardia, defined as a mean heart rate  $>2$  SD above normal for age in the absence of external stimulus, chronic drugs, or painful stimuli; or otherwise unexplained persistent elevation over a 0.5-to 4-hr time period OR for children  $<1$  yr old: Bradycardia, defined as a mean heart rate  $<10^{\text{th}}$  percentile for age in the absence of external vagal stimulus,  $\beta$ -blocker drugs, or congenital heart disease; or otherwise unexplained persistent depression over a 0.5-hr time period.
- Mean respiratory rate  $>2$  SD above normal for age or mechanical ventilation for an acute process not related to underlying neuromuscular disease or receipt of general anesthesia.
- Leukocyte count elevated or depressed for age (not secondary to chemotherapy-induced leucopenia) or  $>10\%$  immature neutrophils.

#### *Infection*

A suspected or proven (by positive culture, tissue stain, or polymerase chain reaction test) infection caused by any pathogen OR a clinical syndrome associated with a high probability of infection. Evidence of infection includes positive findings on clinical exam, imaging, or laboratory tests (e.g., white blood cells in a normally sterile body fluid, perforated viscus, chest radiograph consistent with pneumonia, petechial or purpuric rash, or purpura fulminans).

#### *Sepsis*

SIRS in the presence of or as a result of suspected or proven infection.

#### *Severe sepsis*

Sepsis plus one of the following: cardiovascular organ dysfunction OR acute respiratory distress syndrome OR two or more other dysfunctions (defined in Table 4).

#### *Septic shock*

Sepsis and cardiovascular organ dysfunction as defined in Table 4.

\*See Table 3 for age-specific ranges for physiologic and laboratory variables; \*\* core temperature must be measured by rectal, bladder, oral or central catheter probe.

**Table 3:** Age-specific vital signs and laboratory variables (lower values for heart rate, leukocyte count, and systolic blood pressure are for the 5<sup>th</sup> and upper values heart rate, respiration rate, or leukocyte count for the 95<sup>th</sup> percentile).

Age group	HR beats/min		R	Leukocyte Count $\times 10^3/\text{mm}^3$	SBP
	$\uparrow$	$\downarrow$			
Newborn	$>180$	$<100$	$>50$	$>19.5$ or $<5$	$<65$
Infant	$>180$	$<90$	$>34$	$>17.5$ or $<5$	$<100$
Toddler	$>160$	NA	$>29$	$>16.5$ or $<5$	$<100$
Preschool	$>140$	NA	$>22$	$>15.5$ or $<6$	$<94$
School age child	$>130$	NA	$>18$	$>13.5$ or $<4.5$	$<105$
Adolescent	$>110$	NA	$>14$	$>11$ or $<4.5$	$<117$

HR- heart rate;  $\uparrow$ -tachycardia;  $\downarrow$ - bradycardia; RR- respiratory rate; SBP- systolic blood pressure; NA- not applicable.

**Table 4:** Organ dysfunction criteria

#### *Cardiovascular dysfunction*

Despite administration of isotonic intravenous fluid bolus  $\geq 40$  ml/kg in 1 hr:

- Decrease in blood pressure (hypotension)  $<5^{\text{th}}$  percentile for age or systolic BP  $< 2$  SD below normal for age.

OR

- Need for vasoactive drug to maintain BP in normal range (dopamine  $>5$   $\mu\text{g/kg/min}$  or dobutamine, epinephrine, or norepinephrine at any dose) OR

- Two of the following:

Unexplained metabolic acidosis: base deficit  $>5\text{mEq/l}$ ;

Increased arterial lactate  $>2$  times upper limit of normal;

Oliguria: urine output  $<0.5$  ml/kg/hr;

Prolonged capillary refill:  $>5$  seconds;

Core to peripheral temperature gap  $>3^{\circ}\text{C}$ .

#### *Respiratory*

- $\text{PaO}_2/\text{FiO}_2 <300$  in absence of cyanotic heart disease or preexisting lung disease;

OR

- PaCO<sub>2</sub> >65 torr or 20 mmHg over baseline PaCO<sub>2</sub>; OR
- Proven need of >50% FiO<sub>2</sub> to maintain saturation ≥92%; OR
- Need for nonelective invasive or noninvasive mechanical ventilation.

#### Neurologic

- Glasgow Coma Score ≤11; OR
- Acute change in mental status with a decrease in Glasgow Coma Score ≥3 points from abnormal baseline.

#### Hematologic

- Platelet count < 80,000/mm<sup>3</sup> or a decline of 50% in platelet count from highest value recorded over the past 3 days (for chronic hematology/oncology patients); OR

- International normalized ratio >2.

#### Renal

- Serum creatinine ≥2 times upper limit of normal for age or 2-fold increase in baseline level.

#### Hepatic

- Total bilirubin ≥4 mg/dl (not applicable for newborn); OR
- ALT 2 times upper limit of normal for age.

Surgical cases were not taken into account. We defined cases as surgical if they had a major surgical procedure other than tracheotomy.

#### Statistical analysis

We constructed the databases and conducted analyses in Microsoft Excel (Microsoft Corp., Redmond, WA). We compared categorical data by chi-square test and continuous data by Student and Anova test as appropriate.

#### Results

##### Epidemiology

We identified 248 cases of sepsis within the 2 years. The age- and sex-adjusted annual incidence of sepsis was 8.5 cases per 100 children hospitalized for a bacterial or fungal infection or 124 cases of sepsis per year. The incidence was highest in infants (12 per 100 infected children, 38% of the cases,  $p=0.001$ ) and fell constantly with age. The mean age was 46 months (median, 24 months). The incidence of sepsis in children did not vary significantly by sex for any of the considered age groups.

One third of all children with sepsis (33%) had underlying comorbidity. Drug-induced conditions (drug-induced Cushing-syndrome or chemotherapy-induced neutropenia) were the most common categories of underlying disease overall (23%), followed by malnutrition (20% of the cases).

##### Site of infection and microbiologic etiology

The majority of infections causing sepsis were respiratory (64%), followed by digestive and urinary tract infections (18% and 12% respectively). (Table 5).

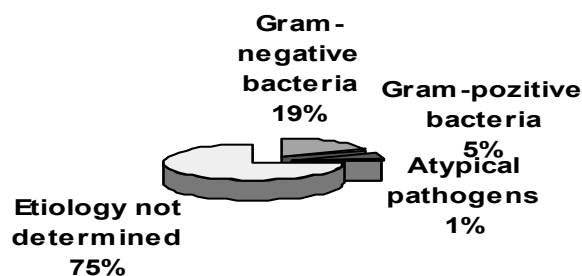
**Table 5:** The source of infections causing sepsis

Source	Number of cases	%
Respiratory	156	63%
Digestive tract	42	18%
Urinary tract	30	12%
Central nervous system	6	2.4%
Ear/nose	3	1.2%
Central venous or ventricular catheter	3	1.2%
Cutaneous/soft tissues	1	0.4%
Peritonitis	1	0.4%
Undetermined	6	2.4%

Respiratory infections predominated in toddlers (45% of the cases), whereas digestive sepsis was particularly common in infants (36%).

The microbiologic etiology was only determined for 25% of the patients. As shown in Figure 1, Gram-negative bacteria caused the majority of infections that evolved with sepsis.

**Figure 1:** Microbiologic etiology of infections in patients with sepsis



*Enterobacteriaceae* caused most of Gram-negative infections (59%), with *Escherichia coli* (56%) and *Klebsiella pneumoniae* (12%) being the most frequent pathogens. *Pseudomonas aeruginosa* (10%) was the third most frequent agent of Gram-negative sepsis. The most common Gram-positive infecting organism was *Staphylococcus aureus* (75%). Atypical pathogens were identified in a minority of patients (4%).

##### Diagnosis and Clinical Features

Our study showed that only 19 (7.66%) out of the 248 cases of sepsis, which we found, had been correctly diagnosed during the hospitalization period. Other 27 cases (10.8%) were diagnosed as sepsis, septic shock or septicemia without fulfilling the diagnosis criteria or were diagnosed as 'septic- or toxico-septic state'.

Most frequently patients presented with 3 out of the 4 diagnosis criteria (56% of the cases,  $p=0.00002$ ). The most common were changes in core temperature (either fever or hypothermia) (98% overall); significant changes in the heart rate occurred in 90% of the patients; tachypnea occurred in 38% of the cases; leukocyte count abnormalities were encountered in 95% of our patients.

Children with sepsis were found to present with a large variety of symptoms and signs, or alteration of the laboratory variables. (Table 6)

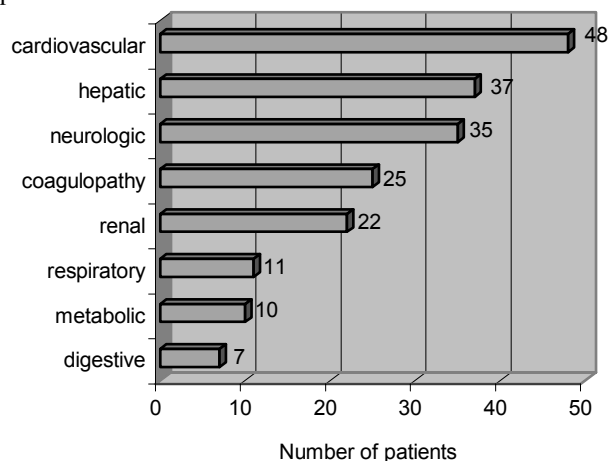
**Table 6: Symptoms and signs in pediatric septic patients**

Symptoms and signs	No of patients	%
Neurological	35	14%
Cardiovascular	22	9%
Respiratory	11	4%
Digestive	7	3%
Hepatic	25	10%
Renal	20	8%
Cutaneous	20	8%
Coagulopathy	20	8%

Up to 24% of the patients included in our study had a severe evolution: severe sepsis occurred in 17% of all cases, and septic shock affected 7%. The majority of infections causing severe sepsis were either respiratory (48%) or digestive (31%), as well as for the septic shock, which actually occurred only as a consequence of respiratory (65%) and digestive (35%) infections. The incidence of both severe sepsis and septic shock was the highest in infants (31% and 35% respectively).

Most patients with MODS presented with an association of 4 or more organ dysfunctions (35%,  $p<0.005$ ). As shown in Figure 2, the most common organ dysfunction was the cardiovascular organ dysfunction (occurring in 17% of the children with sepsis).

**Figure 2: The organ dysfunctions in children with sepsis**



## Treatment

The recommendations of the Consensus Conference were followed in less than 5% of all patients.

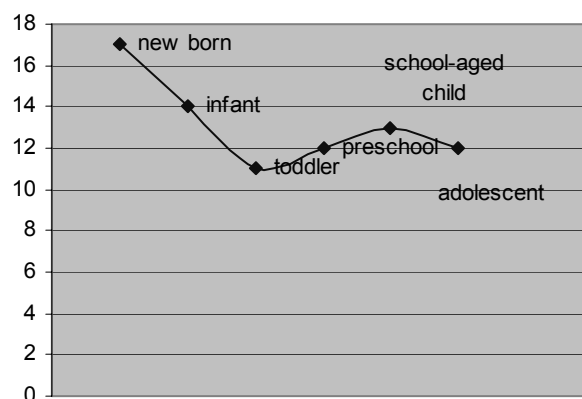
Initial empirical anti-infective therapy included a mean of 2 antibiotics per patient, with a minimum of 1 and a maximum of 7 antibiotics per patient. An antibiogram was performed in only 4% of all patients. The mean duration of anti-infective therapy was 10 days, with a minimum of 1 day and a maximum of 91 days. The most commonly used were 3rd generation Cephalosporins (71%). The most frequently used was Ceftriaxone (30%). The most frequent association of 2 antibiotics was Ceftazidime + Amikacin (39%).

Fluid resuscitation was used for the therapy of 93% of the patients with severe sepsis and septic shock. Inotropic therapy and vasoactive drugs were used in 10% of all patients with severe sepsis and septic shock. A number of 20 patients with severe sepsis and septic shock received intravenous corticosteroids (hydrocortisone), mostly those with sepsis of respiratory origin.

## Hospital Resource Use

The mean length of stay (LOS) was 12 days, with a minimum of 1 day and a maximum of 91 days. Forty percent of the total hospital days were incurred by newborns, who had a higher mean LOS than other children (18 vs. 7 days,  $p<0.00001$ ). (Figure 3). Mean LOS was similar between boys and girls. The mean LOS was also high in patients with underlying disease (21 days). Nonsurvivors had a much lower LOS, but higher hospital costs, than survivors (1 vs. 13 days,  $p<0.0001$ ).

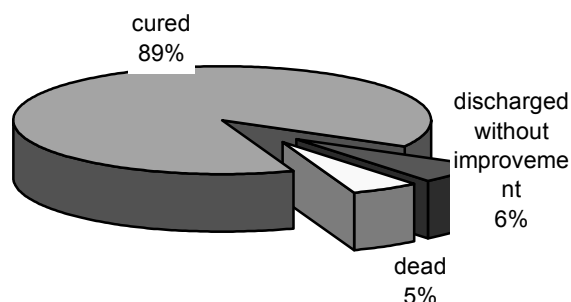
**Figure 3: The age – mean length of stay curve**



## Mortality

Sepsis and its complications were incurred for more than 25% of the general hospital mortality in our clinic.

Of 248 patients with sepsis, 13 died before discharge, and 15 were discharged with no signs of improvement. (Figure 4). The annual age- and sex-adjusted mortality rate was 5 per 100 children.

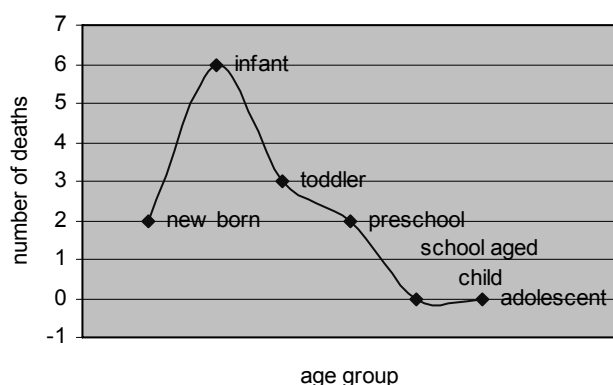
**Figure 4:** The outcome of the patients with sepsis

Hospital mortality generally varied little with age, except for the significantly higher rate among infants, who were incurred for 47% of all deaths. Because hospital mortality varied little with age, the number of deaths per population paralleled the incidence rate, with a high rate in infants that fell dramatically in older children. (Figure 6). There was no gender-related difference in hospital mortality.

The mortality rate was significantly increased by the severity of the septic process: among the severe sepsis cases the mortality rate was 5%, whereas among the patents with septic shock it was much higher: 53%.

Hospital mortality was higher in children with underlying disease (11% vs. 1.8%,  $p < 0.002$ ).

More than three quarters of deaths occurred within the first 2 days from admission.

**Figure 5:** The age- number of deaths curve

### Prognostic factors

Several factors were found to significantly influence the outcome of the pediatric patients with sepsis. First of all there was the presence of changes in core temperature ( $p=0.0019$ ), tachypnea ( $p=0.00004$ ) or tachycardia ( $p=0.009$ ) on admission. Secondly we found the respiratory ( $p=0.0003$ ) or digestive ( $p=0.0002$ ) origin to be associated with a poor outcome. There was also the occurrence of increased serum bilirubin ( $p=0.001$ ) or creatinine ( $p=0.0002$ ) level, or metabolic acidosis ( $p=0.003$ ). The risk of death also increased with increasing number of failing organs, from 3.8% for those with single organ dysfunction

to 53.2% for those with four organ systems or more failing ( $p=0.0001$ ).

On our sample of patients, therapy with corticosteroids was found to significantly increase survival in the severe sepsis and septic shock cases ( $p=0.0049$ ).

### Discussions

We found sepsis and its complications to be a major health problem in children, with more than 120 cases and 6 associated deaths per year in our clinic only.

Infants were at highest risk. More than any other single factor, age influences the epidemiology of sepsis. Infants and older children are two epidemiologically distinct pediatric populations, with different incidences, underlying diseases, sites of infection, infecting organisms, and organ dysfunctions.

There was no significant gender-related difference in the occurrence and evolution of sepsis.

As with adults, underlying illness was very common in children who develop not only sepsis, but also severe sepsis and septic shock.

These findings are consistent with those of prior studies (2).

In a great majority of cases the microbiologic etiology was not determined, leading to a prolonged duration of the treatment. There are several reasons why it is important to try and make a microbiological diagnosis in septic patients. First, and most important, is to ensure that effective antimicrobial therapy is given. There is strong evidence to support the intuitive belief that patients given appropriate therapy are more likely to survive than those given inadequate or inappropriate treatment (3). Secondly, obtaining microbiological information will contribute to the local epidemiological database, without which logical prescribing is difficult, if not impossible. There are substantial differences between ICUs in the microbial ecology, including the prevalence of methicillin-resistant *Staphylococcus aureus*, and vancomycin-resistant *Enterococcus faecalis*. Antimicrobial resistance patterns also vary widely, for example, penicillin-resistance in *Streptococcus pneumoniae*, and gentamicin-resistance in *Enterobacteriaceae*. Furthermore, these patterns are constantly changing, and an up-to-date awareness of these patterns is obviously essential when considering empirical therapy. Finally, knowledge of the microbial cause may be important in the choice of adjunctive future therapies (for instance- antiendotoxin agents) (3).

In the cases in which a pathogen was identified, the etiology was found to be quite diverse, implying that any preventive strategies must be multifaceted. The predominance of Gram-negative bacteria in the etiology of sepsis is reported in literature for the 70's and the 80's, with an increase of the proportion of infections caused by Gram-positive bacteria (4).

Unfortunately, there still remain a very large number of cases in which sepsis is either not diagnosed, or is recognized very late in the evolution, far beyond the optimal therapeutic moment. Even more, there is still an extensive use of old, outdated language.

Patients' symptoms and signs, as well as the laboratory parameters values, vary a lot, mainly because of the different sites of infection, but also because of the various occurring organ dysfunctions.

Regarding the treatment of sepsis, we found a constant lack of a protocol – not only in the treatment of severe sepsis and septic shock, but also in the use of anti-infective therapy (5).

Children who develop sepsis consumed substantial healthcare resources, with average length of stay in excess of most conditions.

One fourth of the patients with sepsis have a severe evolution, with a significantly higher rate of hospital mortality (53% in our study vs. 9-12% reported in the literature), sepsis being the most important cause of death

in our clinic, together with poisonings. We could blame this on the delayed diagnosis, the deficiencies in the laboratory diagnosis, as well as on the lack of therapeutical protocols and of a team specially trained for the treatment of severe sepsis and septic shock.

There were several major limitations of our study, mainly due to the variations in filling patients' files, as well as the absence of a protocol of investigation and surveillance of the pediatric patients with sepsis, which made us therefore unable to select all the required data for our patients. There was also the lack of precise administrative data, making us unable to determine the exact cost of hospitalization for the pediatric patients with sepsis.

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## CONSIDERATIONS ON A STURGE-WEBER-KRABBE CASE

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### Abstract

The Sturge-Weber-Krabbe syndrome is a complex form of neuroangiomas, having as diagnostic elements cutaneous, cerebral and ocular angioma. The authors present a 9 years old male patient diagnosed with extensive cutaneous angiomas. The child requires follow-up, as the evolution and prognosis of the disease can be unfavourable, by neurologic disorders and mental retardation aggravation.

**Key words:** Sturge Weber, diagnosis, child.

### Introduction

Sturge-Weber-Krabbe angiomas (SWK) is a complex form of neuroangiomas, characterised by ocular, cutaneous and cerebral angiomas. The disease is sporadic; there is no direct evidence of a hereditary transmission. Like other neurocutaneous syndromes, SWK syndrome has an incomplete penetrance, with a great variability of clinic manifestations. The disease is rare, the frequency is 1/10.000 live births, without sex predilection.

### Case presentation

The authors present an 8 years old male patient diagnosed with extensive cutaneous angiomas, accompanied by ocular and neuropsychiatric disorders.

The parents are young and healthy, and have other three healthy children. Both maternal and paternal relatives have no pathology associated to the case.

Personal history: first born child, from a normal pregnancy, delivered normally at full term, weight at birth 3000g, with no neonatal suffering, was natural alimentation up to 6 months, current vaccinations done adequately.

Psychomotor development milestones were delayed; the child presents a moderate mental retardation accompanied by behavioral disorders.

### Clinical examination:

- adequate staturo-ponderal development: weight 24kg, height 130cm;
- extended deep red, flat, non-prominent angioma on head, neck, right hemithorax, upper limbs and right lower limb;
- recurrent right anterior epistaxis;
- congenital hyperpigmentation of the iris – iris heterochromia;
- moderate mental retardation, normal neurological findings, and intermittent episodes of seizures;
- the rest of clinical examination found no other abnormalities



Fig. 1. Non-prominent angioma on head, neck, right hemithorax.



Fig. 2 extended deep red, flat, non-prominent angioma on head, neck, , right hemithorax, upper limbs and right lower limb



### Paraclinic investigations

*Biological tests:* hemogram and complete blood count, acute phase reactants, seric proteins electrophoresis, common urine tests, seric levels of calcium, phosphate and magnesium, alkaline phosphatase, urea, creatinine, aminotransferases – all found in normal limits.

*Ophthalmologic examination:* anterior segment of the right eye – flat well-circumscribed angioma surrounding

the sclerocorneal limbus, violaceous sclera on a 4-5mm perilimbic-ring. Bilateral – congenital iris hyperpigmentation, heterochromia of iris. Visual acuity: right eye- light perception, left eye -1.

Fundus examination: normal discs, congenitally pigmented retina, and normal retinal blood vessels.

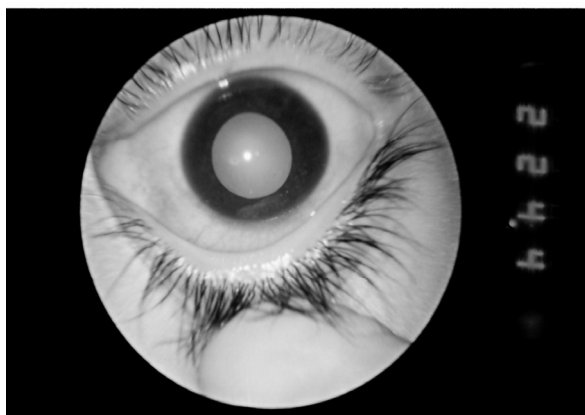


Fig. 3: Right eye, violaceous sclera on a 4-5mm perilimbic-ring.

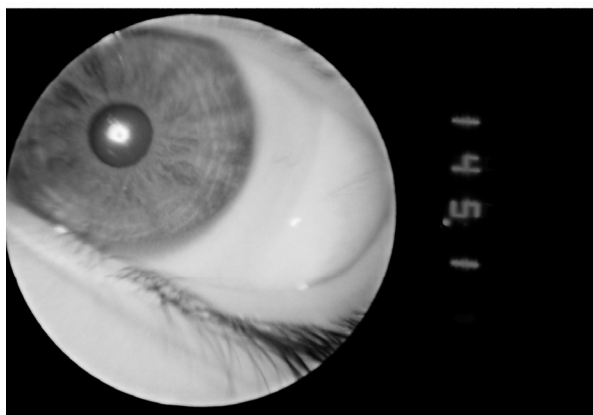


Fig. 4: Left eye.

*Electroencephalogram:* dominant alpha slight high voltage activity with irregular aspect, slow polymorph delta

and gamma waves; isolated, sharp high voltage synchronic waves – all in central derivations.

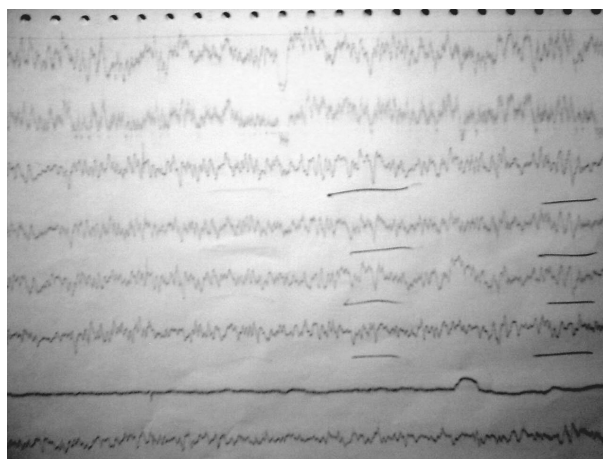
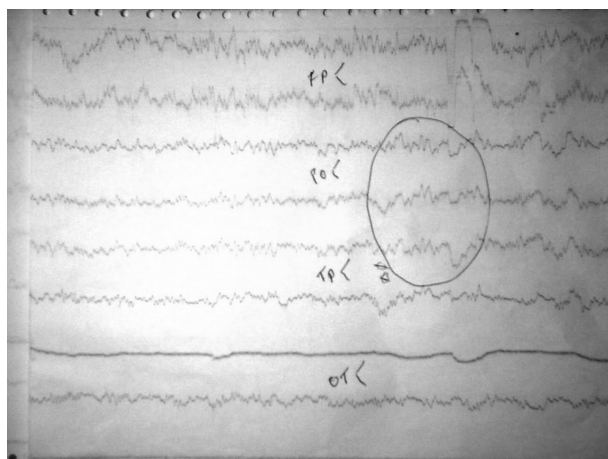


Fig. 5: E.E.G.

*Cranial, thoracic and abdominal CT-scan* – showed no evidence of angioma.

*Otorhinolaryngologic exam* found angioma placed on the nasal mucosa.

### Discussions

The diagnosis was made on the presence of cutaneous lesions: multiple, extensive flat angiomas, predominant on right hemibody, repeated convulsions,

accompanied by moderate delayed cognitive skills and on anamnestic dates – absence of related pathology in family members.

We consider that the expression of cerebral angiomas are EEG alterations, seizures and the mental retardation and behavioral disorders, although cranial CT-scan found no signs of cerebral angioma.

Ocular manifestations include: flat angiomas – right eye, violaceous sclera, congenital hyperpigmented iris,

iris heterochromia, and congenital pigmented retina – bilateral. Right eye decreased visual acuity is probably explained by a tumoral compressive mass of the optic pathway which couldn't be found at CT-scan.

No manifestations of congenital glaucoma were found.

The SWK Syndrome was first described in 1879, and then Weber in 1922 and Krabe in 1934 made a complete description. Association of cutaneous and cerebral angiomas together with ocular manifestations characterizes the complete encephalotrigeminal angiomatosis.

Cutaneous lesions can lead to making the diagnosis from the first presentation. Classical angiomas are found on lower face, in the trigeminal nerve territory. Often angiomas extend also to the neck, trunk and abdomen as in our case. Cutaneous angiomas are presented in 90% of cases.

Cerebral angiomatosis is the second characteristic of the disease. Clinical manifestations are: seizures, migraine episodes in later childhood, hemiparesis, hemiplegia, constant and progressive mental retardation.

The most frequent ocular manifestations are: choroidal haemangioma and glaucoma. Classic forms of the disease include glaucoma- if this misses, in the presence of cutaneous and cerebral angiomas, the association is called Jahnke syndrome.

Other crude paucisymptomatic forms were included into distinct syndromes:

- Schirmer syndrome – with precocious glaucoma and buphthalmos;

- Lawford syndrome – late glaucoma with chronic evolution, without buphthalmos;

- Moles syndrome – choroidal angioma, without enlargement of the eye;

- Brushfield-Wyatt – association of face angioma and calcified angioma in the contralateral cerebral hemisphere.

These entities are no longer considered as apart syndromes, but as forms of SWK syndrome.

The Roach Scale is used for classification:

- type I - includes facial and leptomeningeal angiomas; may have glaucoma;

- type II – facial angioma alone, no cerebral involvement; may have glaucoma;

- type III –isolated leptomeningeal angioma, or another cutaneous localization; usually no glaucoma.

### Conclusions

The particularity of the case is the extension of cutaneous lesions accompanied by neuropsychic manifestations (seizures, mental retardation) in a child whose cerebral lesions and glaucoma were not found during investigations.

The child requires follow-up, as the evolution and prognosis may become dramatic, by aggravation of the neurological and mental disorders.

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## IV. PEDIATRIC SURGERY

### LOCAL EFFECTS OF GROWTH HORMONE ON INTACT CONDRÓ-COSTAL CARTILAGE

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#### Abstract

Pectus excavatum is the most common chest wall deformity seen in children.

We are trying to develop a new nonsurgical method of correcting the deformity.

The local and systemic effects of human growth hormone ( Norditropin ) injected at the surface of intact condro-costal cartilage in 9 two weeks old Sprague Dawley rats were investigated.

The cartilages were injected every two days for 21 days.

Every second day one of the subjects was sacrificed and the injected condro-costal cartilage site, tibial bone and mandibula were histologically analyzed.

At the level of the tibial bone and mandibula no systemic effects of the growth hormone was found.

Histological analysis confirmed the presence of ossification and calus formation at the site of injection and modified shape of the cartilage.

A local increase in periosteal bone deposition and new bone formed was found after transversal sections of the condro-costal cartilage were performed.

Further studies will conclude if the local injection of growth hormone in the cartilage will open a new gate in the treatment of this malfomation.

**Keywords:** condro-costal cartilage, periosteal bone, pectus excavatum

#### Introduction

There have been a great variety of methods tried for the correction of funnel chest, but all of them can be divided in two main categories: the lifting or the overturn of the sternal bone. In both procedures recurrency is the most common complication by far, and it is determined by insufficient fixation of the sternum or by deterioration of the local blood flow.

However, there have been many procedures –50 – until nowadays, often very ingenious, it has not been found the best solution yet. Actually, the problem is not the elimination of pectus excavatum, but the maintenance of

the newly created form after the surgical procedure. The sternum must be adapted for sustaining all the forces that appear – those resulted by respiratory movements, as well as those determined by growth – thus the stability of mechanism not to be put in danger at any time.

The self- repair capacity of the cartilage is poor. If there is a lesion on the cartilage and repair is begun, then this is done only by the perichondrium and usually only during the growing process, in young patients. In an adult, tipically, cells of the perichondrium proliferate to initiate repair, but proliferation is poor, resulting a few, insufficient cells. In this case, the process ends up with the production of merely dense connective tissue. However, not rarely, in adults, the development of new blood vessels at the site of healing enhances the growth of bones rather than that of cartilage. The limited capacity of the cartilage to self- repair may cause great difficulties for the surgeon, when the rib cartilages have to be cut in order to get into the thorax cage for a by-pass procedure or a sternochondroplasty, for instance.

At the site of repair, bone is produced instead of cartilage because chondrocytes spread in this area are not properly oxygenated.

The local and systemic effects of human growth hormone ( Norditropin ) injected at the surface of intact condro-costal cartilage in 9 two weeks old and 9 mature Sprague Dawley rats were investigated.

The aim of the study is to investigate the possibility to replace the surgical correction of pectus excavatum is a new non surgical method by local injection of human growth hormone at the surface of intact condro-costal cartilage.

#### Material and method

The present study was conducted at the “Pius Branzu “ Center for Laparoscopic Surgery and Microsurgery in Timisoara.

The histological analysis of the condro-costal cartilage was conducted at the Department of Pathology at

the Children Hospital “Loius Turcanu “, Timisoara, Romania.

The animal experiments were conducted on two weeks old Sprague Dawley rats in total a number of 18 subjects.

There are several reasons why we choose to use the Sprague Dawley rats a few of them beeing the fact that, it is an accepted animal model, the reproductive rate of these animals is high and last but not least the similarity with the humans.

Two groups were used each with 9 subjects as following; the first group received a human growth hormone (Norditropin) injection at the surface of intact condro-costal cartilage and the control group.

The rats were caged with 12 hours light and 12 hours darkness, and had free access to tap water and pellet food.

The drugs used in this study were Norditropin<sup>TM</sup> PenSet<sup>R</sup> 12 manufactured by NovoNordisk.

The rate of the injection of these substances was every two days for 21 days.

The first step was the anesthesia of the animals this beeing done with a mixture of Ketamin (for human use)

and Xylazin (veterinary use) administered for each individual with regards to body weight.

The animal was then placed on the operative desk and the fur was shaved from the anterior thorax. After a previous cleaning of the chest skin surface with a Betadine<sup>R</sup> solution a 1.5-2 cm incision was performed and the muscular and bony structures of the chest were revealed.

The surface of condro-costal cartilage was reached after a careful dissection of the pectus major muscle on the right side using microsurgery fine tools and the microscope.

We delivered the hormone product at the desired site using an insuline syringe of 1 ml and the aid of the microscope. At this stage I would like to mention the fact that a great amount of patience and skill is required to inject the dilution right at the condro-costal cartilage site since in two weeks old rats this structure is quite hard to reveal.

At the end of the procedure the skin of the chest was closed using a 4.0 coated Vicryl<sup>R</sup> suture.

Every second day one of the subjects was sacrificed and the injected condro-costal cartilage site, tibial and femur bones and mandibula was harvested for histological analysis.



Fig.1 The thorax, femur and mandible harvested from the rats at the end of the study for histological analysis.

Subsequently, 3.5-um-thick sections were cut perpendicular to the longitudinal direction of the bone using a microtome.

The tissue formed during the injection period was identified using a trichrome stained sections (light microscopy) and unstained sections (polarization microscopy).

## Results

It is well known that systemic administration of growth hormone (GH) increases diaphysial bone mass by periosteal bone formation in both young and old rats.

The aim of the study is to investigate the possibility to replace the surgical correction of pectus excavatum is a new non surgical method by local injection of human growth hormone at the surface of intact condro-costal cartilage.

At the injected site on the right side of the thorax, the doses of GH induced new bone formation at the periosteal surface, and the responses were located at the medial and lateral surfaces corresponding to the areas where GH was injected.

Local GH treatment of the right hemithorax did not influence the left hemithorax bony structures dimensions, volume, length.

At the GH-injected location, increased external bone dimensions were seen, and the responses to rGH was noted to be dose dependent. The new bone formed at the periosteal surface was woven bone.

External callus dimensions at the site of the administration of hormones was increased in the GH group compared with the control group, whereas body weight changes during the healing period were also present.

The light microscopy aspects of the cartilage correspond to those found in electronic microscopy and are suggestive for the adaptive nature of both chondrocytes and matrix to mechanic injuries, inflammations, hypoxia.

The obtained modification were similar to those reported in the case of the study of the cartilage in pectus excavatum.

Particular similar patterns were seen since in both cases we deal with a form of hypertrophy.

Electron microscopy study of rib cartilage in pectus excavatum reveals particular aspects of cartilaginous matrix components as well as of cellular ones (chondroblast–chondrocyte).

Thus, the cellular lacuna is covered with an osmiophil material (MOs). Around the lacunae there are collagen fibers (Fs) and extracellular material with calcium (Ca) deposits. In contrast to the matrix from the connective tissue of the perichondrium, the cartilage matrix (Mx), with

the exception of calcium deposits, looks homogenous in a lower power view, containing fine fibers (5-20 $\mu$ ). These fibers are collagen type 2 with smaller diameter and less obvious periodicity compared to collagen type 1. The free spaces of the matrix network are irregular and large. Lipids (L) and secretion granules accumulate at the periphery of the cartilaginous cell.

Chondrocytes have an irregular cellular surface, presenting microvilli (Mv), and are covered with matrix with a fibrillar aspect. These surfaces covered with microvilli account for the resorptive activity of the chondrocyte.

Being a poorly nourished tissue, cartilaginous cells contain lipid and rich glycogen inclusions within their cytoplasm. This aspect is common in chondrocytes in young tissues as well as in degenerated cartilage, a fact we could also confirm in the control group.

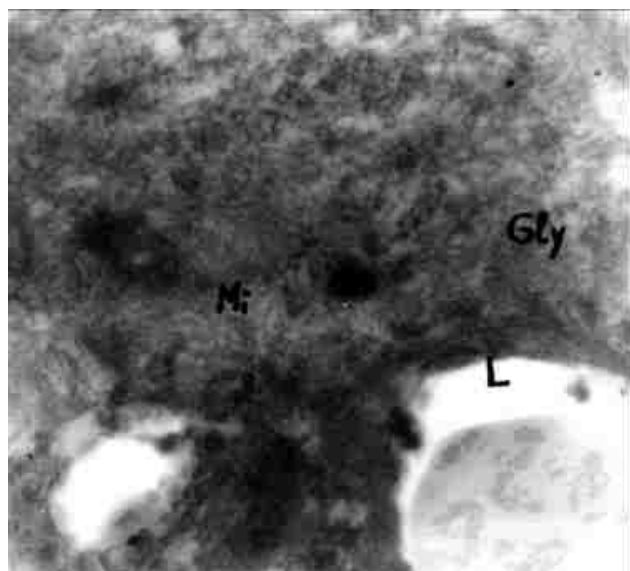


Fig. 2 Lipids and glycogen deposits in the cytoplasm of a chondrocyte; density of mitochondrias within the cytoplasm differs from one territory to another; x 4000.

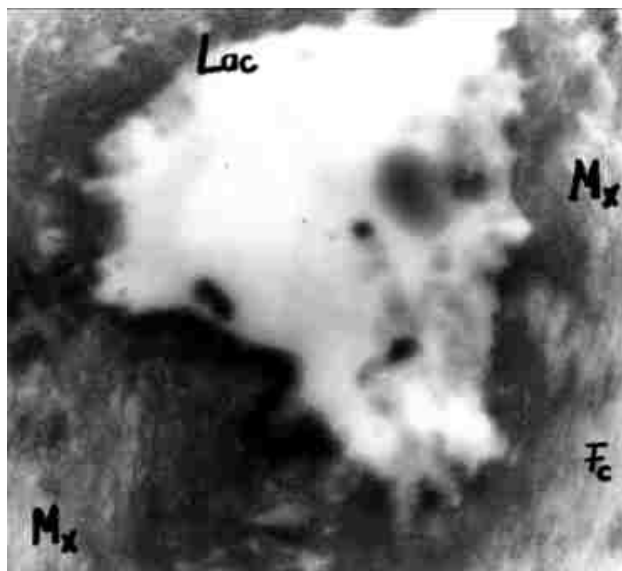


Fig. 3 Ultrastructural aspect of a lacuna (lac), surrounded by territorial matrix (Mx) and condensed collagen fibers in perilacunar capsule; this lacuna contains an electron-dense waste material after chondrocyte degradation; x 12930.

A more detailed histological analysis of the ribs and sternum together with the tibial bone and the mandibula is still in progress and further results will be available in a short amount of time.

### Discutions

Endochondral bone formation during vertebrate genesis is a highly regulated process resulting, in the case of long bones, in increased length.<sup>1</sup>

During this process, young chondrocytes initially undergo rapid proliferation; then cease proliferation to become mature chondrocytes, producing a large amount of extracellular matrix, and subsequently become hypertrophic.

At the stage of hypertrophy, the cells exhibit a number of changes (Nurminskaya and Linsenmayer, 1996), including de novo synthesis of collagen type X.<sup>1</sup>

These events change the composition and, conceivably, the properties of the cartilage matrix in the hypertrophic zone (Chen et al., 1992), allowing the invasion of blood vessels and the ultimate replacement of the cartilage matrix by bone. Thus, the proper control of chondrocyte development, i.e., appropriate regulation of cell proliferation and the subsequent differentiation to hypertrophy, is of critical importance to the formation of a normal bone.<sup>1</sup>

Studies of transgenic mice with local GH expression in either the osteoblasts or the erythroid tissue of

the bone marrow have revealed increased tibial and femoral cortical thickness in the transgenic animals.<sup>1</sup>

This strongly indicates a local effect of GH on intact cortical bone, although the transgenic mice lines developed in these experiments also showed increased weight gain and linear growth.

The GH receptor has been found on osteoblast-like cells, and in vitro experiments have shown that GH directly induces proliferation in a number of osteoblastic cell lines. However, this proliferative activity induced by GH can be abolished if antiserum to IGF-I is added to the cell system. GH also stimulates the production of type I collagen, osteocalcin and alkaline phosphatase in osteoblastic cells.<sup>1</sup>

In two previous experiments, the local effect of GH on healing bone defects have been investigated by different authors.

In rat mandibular defects covered with osteopromotive membranes, GH was applied locally by mini-osmotic pumps.<sup>1</sup>

The defects were analyzed after 4 weeks by semiquantitative histomorphometry, and the results revealed an enhanced bone formation (bone union, bone maturity) when GH was given in doses of 2 and 20 ug/day, respectively.<sup>1</sup>

Macroporous biphasic calcium phosphate implants loaded with GH were inserted into rabbit bone defects located at the distal end of the femurs.

After 3 weeks, a dose-dependent increase in bone ingrowth and ceramic resorption was found in the GH-loaded implants.<sup>1</sup>

A number of studies with regards to the effect of the human growth hormone on the costal cartilage are ongoing at the moment and there is a clear indication that this form of therapy will someday be able to substitute extensive surgical procedures specially in the field of orthopedics.

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## ORTHOSES , SPLINTS , BRACES AND OTHER ORTHOTIC DEVICES

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### Abstract

Orthotics is concerned with the design and fitting of supportive devices to patients who because of muscle weakness or deformity have disabeling conditions of the limb or spine.

**Key words:** orthoses, splints, braces, serial casting

"L'Orthopedie ou L'art de Prevenir et de Corriger dans les Enfants, le Derformitees du Corps" was the title given by Nicolas Andry to his book written in 1741, and so the notion of orthopaedy was born, based on the greek "orthos" (= straith) and " paideuein / pais"(bring up/child).

Orthopaedic pathology was common since dawn of mankind (tuberculosis of the bones, postraumatic fractures).

But the conservative treatment was initiated by Hippokrates, the correctiv grips he described are used till ower days. He was using bandages with corrective role as well as shoes that could maintain the position of the foot.

Plaster casts were used for the first time by arab doctors in the X-th century, but europeans started to use them at the end of the XVIII-th century. During the middle ages the ancestor of the brace was born :an iron-built armour, but with no corrective rol. Documents about the use of splints to reduce contracture of the knee or elbow appear in Strassburg in 1517. Ambroise Pare used iron plates to correct deformities in scoliosis in the XVI-th century.

Braces , as well as other orthotic devices ,suffered a constant improvement (metal, wood,fabric ) during ages. Today they are made of synthetic materials and have an important corrective-functional part.

The concept of bracing was considered to be the shoring up of falling or paralyzed body segments. With the use of thermoplastics this concept has shifted to a more dynamic idea of promoting improved functional efficiency. This new view has led to developments in orthoses that provide minimum stabilization while restoring proper structural and biomechanical alignment. The orthotic devices cover a wide range of products including collars to support the neck, spinal supports, splints, belts, corsets, leg callipers and splint and special footwear.

Goals of intervention with lower extremity orthoses and splints in pediatric population :

- prevention of contractures and deformity for children with cronic neuromotor impairment (protects cartilaginous and soft tissues from deforming effects of weight-bearing strains)

- correction of deformity ( casts, splints orthoses are used to stabilize bony structures during growth and to apply corrective forces to the weight-bearing joints over a prolonged period of time.

- provision of optimal joint alignment in order to respond appropriately to direction and degree of force applied by muscle and weight-bearing.

- selective,minimal restriction of motion

- protection of weak antigravity muscles (weakness occurs following surgery or following prolonged disuse of a muscle group, and can lead to overstretch of the muscle tendon and places very high compensatory demands upon other muscle groups.)

- control of tone and tone- related deviations (structural alignment in the foot promotes an improved balance of muscle power and reduces compensatory excessive muscle tone )

- enhancement of experience (supportive devices provide the nonambulatory child with the experience and physiologic benefits of the standing position without deforming the feet.

- attention to cosmesis and weight.

The role of orthoses and splints is primarily limited to maintenance of achievable alignment and reduction of functional deformity in children.

Lower extremity splints are an alternative to expensive orthoses for small children who grow rapidly while exhibiting changes in foot size and alignment; as a short-term distal support system during rehabilitation (after hamstrings lengthening, tendo-Achilles lengthening); as an evaluation tool in clinical decision making; as interim support to the delivery of an orthoses; as a means of providing a variety of function-specific support systems.

The stabilizing foot splint is used in managing mild to moderat pronation deformity in children with neuromotor impairment( pes planovalgus due to ligament laxity or hypotonia, calcaneus varus deviation).

In cases of equinovalgus deformity( which combines pronation of the foot with limitation of mobility into ankle dorsiflexion) or equinovarus deformity( the combination of equinus with supination of the foot) an ankle- foot splint is indicated when the foot structures can be passively realigned or an ankle-foot orthosis-whether solid or hinged-when the deformity is fixed.

The genu recurvatum related to equinus in children with cerebral palsy is managed with a knee hyperextension splint.

The primary factor to crouch deformity is



weakness in the triceps surae group, so a crouch-control ankle-foot splint could be of help.

Using corrective progressive casts in series is a conservative intervention measure by which casts are applied and removed in succession in order to help regain or increase extensibility in muscle and connective tissue surrounding the casted joint. Casting is undertaken gradually enough to allow the cellular growth changes to occur. The two types of contracture in cerebral palsy are: hypoextensibility related to imbalance of hyperactivity between the agonist and the antagonist muscles and a more passive type of hypoextensibility revealing a dysfunction in trophic or growth regulation ( muscle growth does not keep pace with bone growth, so contracture worsens steadily with growth ). Tardieu et al. advised using three casts in a three week period to gain extensibility in the triceps surae group. The casts extended from the foot to either below or above the knee (with involvement of the gastrocnemius muscle ) and gain of up to 15 degrees of dorsiflexion range were possible with progressive casting.

Disadvantages of serial casting are muscle atrophy; the inconvenience of plaster -heavy; pressure sores; risk of peroneal nerve damage; possible diminish of range of motion gained by casting in six to twelve months depending of follow-up management, growth rate, changes in activity level, illness, family stress. Repetition of the progressive casting might be required every year or two to maintain or regain extensibility. If the casting process fails, surgical correction have to be considered.

The advantage of a serial cast course followed by consistent night splinting may serve to prevent the need for surgical lengthening of muscle tendon.

An other orthotic device applied to the body to limit motion, correct deformity, reduce axial loading or improve function is the brace.

The cervical spine is the most mobile spinal segment with flexion greater than extension, good rotation and bending. The thoracic spine is the least mobile and has a greater flexion than extension. Lateral bending increases in caudal

direction, axial rotation decreases in caudal direction.

The lumbar spine has minimal axial rotation. The greatest movement in the lumbar spine is flexion and extension.

Immobilization of the spine increases erector spinae muscle activity since normal rotation that occurs with ambulation is limited by the orthosis.

The biomechanical principles in orthotic design include horizontal forces, fluid compression, distraction, construction of a cage around the patient, placement of an irritant to serve as a kinesthetic reminder and skeletal fixation.

Orthotic devices are named by the body regions that they span :

- cervical orthotics - soft or hard collar ( kinesthetic reminder to limit neck movement)
- head cervical orthotics -include chin and occiput and decrease range of motion - the Philadelphia collar
- cervical thoracic orthotics - halo device- treatment of unstable cervico-thoracic fractures
- thoracolumbar orthotics -anterior spinal hyperextension brace, Jewett hyperextension brace (thoracic and lumbar spine fractures)
- thoracolumbosacral orthosis or custom -molded body jacket offers best control in all planes of motion indicated in compression fractures, bracing for idiopathic scoliosis
- lumbosacral orthotics-chairback brace-indications for unloading intervertebral discs, relief low back pain, limits flexion and extension.

The main goal of a brace in scoliosis is to prevent further deformity and prevent or delay surgery (Milwaukee brace -CTLSO, Boston brace- TLSO, Charleston bending brace -maximum side bending correction).

Most adolescents diagnosed with idiopathic scoliosis are prescribed bracing treatment if their curve is between 25-40 degrees, from a point (usually 45 degrees) surgery might be considered. Therefore patients who are braced should have lower rates of surgery than those who are not braced.

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# COMPREHENSIVE TREATMENT OF COMPLEX TIBIAL DEFORMITIES BY SINGLE-CUT CORRECTIVE OSTEOTOMY

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## Abstract

Complex tibial deformities imply simultaneous correction of varus deformity and internal rotation of the tibia, axis realignment, restoration of joint surface congruity and treatment and prevention of limb length discrepancy. Four patients were treated in our department using the single-cut osteotomy described by Paley. Osteosynthesis was achieved by an external fixator in two cases, K-wires in one case and plate in one case. At follow-up, all patients were satisfied, with normal lower limb alignment and no limb length discrepancy.

**Key words:** tibia vara, single-cut osteotomy, CORA, Blount disease, hypophosphataemic rickets

## Introduction

Limb deformities can be classified according to cause (congenital, developmental, posttraumatic), location (bone or joint contracture, extra- or intraarticular), geometry (angulation, translation, rotation, length discrepancy), severity (magnitude), and progression (static or progressive). Orthopedic surgical correction must consider all of these factors (1).

Limb deformities may lead to dysfunction, pain, and joint degeneration. To patients, appearance may be of primary concern. For bone deformities, the mainstay of treatment has been osteotomy, whereas for joint-contracture deformities, extra- and intraarticular soft-tissue releases have been the standard of treatment (1).

Many innovative osteotomies have been developed to treat limb deformities. The results are frequently subjectively acceptable but objectively inaccurate. Secondary deformities often result from primary correction. The significance of this has only recently been recognized (2;3). Inaccuracy of correction in children has often been excused by the time-honored pediatric orthopedic motto, "It will remodel with time." In some cases, this has been true. In many cases, however, residual and secondary translation and angulation deformities have gone untreated into adult life. Although most of these residual and secondary deformities are asymptomatic in children, many lead to degenerative changes and disability in adults. During the 20th century, high postoperative complication rates were often reported: neurovascular complications owing to acute correction with stretch injury and compartment syndromes (4) and bone complications owing to extensive exposure and methods of fixation. During the last 10 years of the

20th century, a revolution occurred in the management of children's deformities because of improved biologic and mechanical techniques.

Gradual correction reduces the operative exposure needed to cut the bone (5). Acute surgical morbidity is greatly reduced by these percutaneous techniques. Furthermore, progressive correction avoids stretch damage to the neurovascular structures that are at risk. The magnitude of correction, which was previously the limiting factor in how much deformity correction could be achieved, is no longer an obstacle with gradual correction of bone or joint deformities. The accuracy of correction, which was usually only  $\pm 5^\circ$ , improved greatly (6) with gradual correction because of postoperative adjustability of external fixation.

With the advent of radiographs just over 100 years ago, our understanding of the geometry of deformities increased greatly. A wide variety of configurations of osteotomy were developed to correct these deformities. The most commonly used have been the opening and closing wedge osteotomies and the dome osteotomy (1).

Despite improvements in imaging techniques and methods of internal and external fixation, the study of the geometry of deformities remained greatly unexplored until the past 10 years. The level of the apex of deformity was always considered intuitively, and the level of osteotomy relative to the apex depended on the location of the physis and the space needed for the hardware. This approach more often than not created secondary translation deformities. Paley et al. (2;3) described the concept of the center of rotation of angulation (CORA). They demonstrated that when the axis of correction and the osteotomy are at a level different from that of the CORA, secondary translation deformities occur. They developed a simple method to identify rapidly and accurately the level of the CORA. Because the concepts of the CORA and the axis of correction are basic principles of deformity correction, they are independent of the method of fixation used. Although in the past, the tendency has been to make the osteotomy accommodate the fixation, the current concept is to consider the principles of deformity correction as preeminent and to make the fixation and osteotomy adhere to the principles. In other words, instead of osteotomy being slave to fixation, fixation becomes slave to osteotomy. With this approach, we can eliminate secondary deformities after osteotomy (1).

A more recent development has been to harness the capriciousness of the physis by temporary hemiepiphyseal stapling (7). Epiphyseal stapling was a popular method for treating angular deformities in adolescence during the 1960s and 1970s. It became less popular as osteotomy techniques improved during the 1980s and 1990s. Stevens et al. (8) recently showed that it is a safe technique to use in young children, with little risk of growth plate closure.

### Purpose

Tibia vara can be difficult to treat because of frequent associated deformities, including distal femoral varus, proximal tibial procurvatum and distal tibial valgus that contribute to lower limb malalignment. We present a comprehensive approach that addresses all components of

the deformity and allows restoration of the anatomic and mechanical axes.

### Materials and methods

Five limbs in four patients presenting with tibia vara were operated on between 2004 and 2005. There were three girls and one boy. Average age at surgery was 8 years 6 months. The diagnosis at initial presentation was: vitamin D-resistant hypophosphataemic rickets (VDRR) in two cases, Blount's disease in one case and genu varum post septic osteoarthritis of the knee in one case (Table 1). Two patients had previously undergone two valgus osteotomies each.

Patients were analyzed clinically and radiologically according to leg axis and length, knee mobility and stability and pain.

Table 1. Synopsis of patients

<i>Pt. No.</i>	<i>Age at surgery</i>	<i>Sex</i>	<i>Diagnosis</i>	<i>No. of previous osteotomies</i>	<i>Varus</i>	<i>Internal rotation</i>	<i>Procurvatum</i>	<i>LLD</i>
1.	14 yrs	F	VDRR	2	16°	0	32°	0
2.	3 yrs	M	Blount's disease	0	30° (R) 30° (L)	40° (R) 35° (L)	0	0
3.	7 yrs	F	Genu varum post septic osteoarthritis of the knee	0	20°	43°	0	6 cm
4.	10 yrs	F	VDRR	2	20°	30°	0	0

VDRR —vitamin D-resistant hypophosphataemic rickets; LLD —limb length discrepancy

### Preoperative planning

Angular deformity of the tibia involves angulation not only of the bone but also of its axes.

We calculated the amount of deformation using the Paley et al. method. The point at which the proximal and distal axis lines intersect is called the center of rotation of angulation (CORA). The axis line of the proximal bone segment is called the proximal mechanical axis (PMA) or proximal anatomic axis (PAA) and the axis line of the distal bone segment is called the distal mechanical axis (DMA) or distal anatomic axis (DAA) (9).

We draw the PMA or PAA and the DMA or DAA lines and identified the CORA at their points of intersection. We measured the magnitude of angulation in the frontal plane.

When rotation and angulation deformities are both present, the axis of rotation and the axis of angulation can be defined as two separate axes or can be resolved into one axis that defines both deformities. The axis of angulation is

in the transverse plane. The axis of rotation is the longitudinal axis that is perpendicular to the transverse plane. That axis that defines both angulation and rotation is inclined between the longitudinal and the transverse axes of rotation and angulation, respectively (9).

We calculated the orientation of this longitudinally inclined axis using a modification of the graphic method.

### Operative technique

The first step is a 2-cm segmentary resection of the fibular diaphysis at the junction between the middle and lower third.

We then expose the anteromedial aspect of the tibial metaphysis or diaphysis at level of the determined CORA.

Combined torsional and angular deformities of the tibia are corrected creating a single osteotomy which is oriented so that rotating the two fragments on the created osteotomy plane allows to correct all deformities in one step (Fig. 1).



Fig. 1. The orientation of the osteotomy plane.

#### Patient 1

A 14 years old girl presented with vitamin D-resistant hypophosphataemic rickets (VDRR), for which she underwent two valgisation/derotation osteotomies on the left side. On the left side she had  $16^{\circ}$  varus deformity and  $32^{\circ}$  procurvatum of the tibia. She had no limb length discrepancy. Radiographs showed  $16^{\circ}$  varus deformity in the frontal plane and  $32^{\circ}$  procurvatum deformity in the

sagittal plane.  $30^{\circ}$  oblique radiograph showed no deformity of the tibia (Fig. 2). We performed the correction osteotomy in the transverse plane, inclined  $30^{\circ}$  from the sagittal plane. The stabilization of the osteotomy was obtained by an external fixator. The fixator was removed 3 months postoperatively. No pin-site infection was observed. At 1 year follow-up, the patient had normal leg alignment, no limb length discrepancy and no pain (Fig. 3).

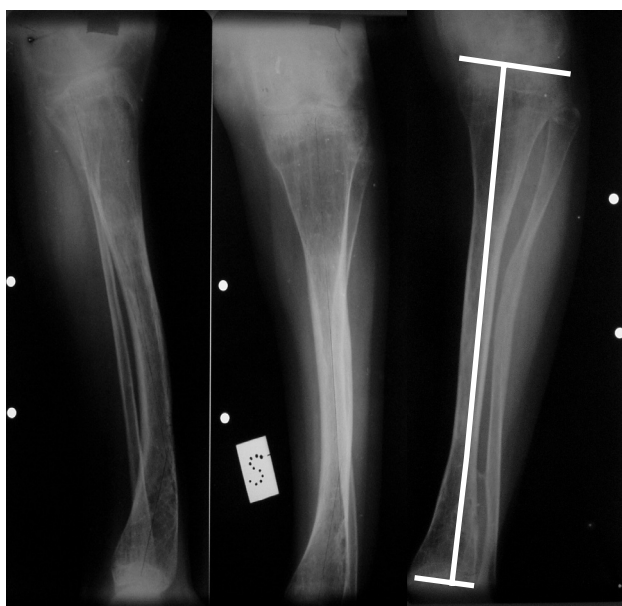


Fig. 2. Patient 1:  $32^{\circ}$  procurvatum deformity in the sagittal plane,  $16^{\circ}$  varus deformity in the frontal plane and no deformity in the  $30^{\circ}$  oblique plane.

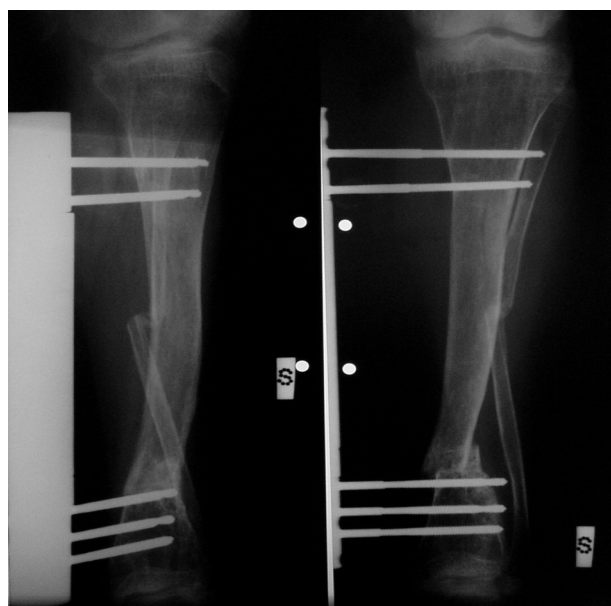


Fig. 3. Patient 1: Postoperative appearance.

#### Patient 2

A 3 years old boy presented with bilateral Blount's disease (Fig. 4). He had  $40^{\circ}$  internal rotation and varus deformities on the right side and  $35^{\circ}$  internal rotation and varus deformities on the left side. Radiographs showed  $30^{\circ}$  metaphysodiaphyseal angle (MDA) on both

sides. We performed a single-cut osteotomy on the left side and then on the right side, followed by percutaneous K-wires fixation and long leg plaster cast immobilization for 6 weeks. At plaster cast removal we removed the K-wires also. At follow-up the boy had normal leg alignment (Fig. 5).



Fig. 4. Patient 2: Bilateral Blount's disease, operated on the left side.

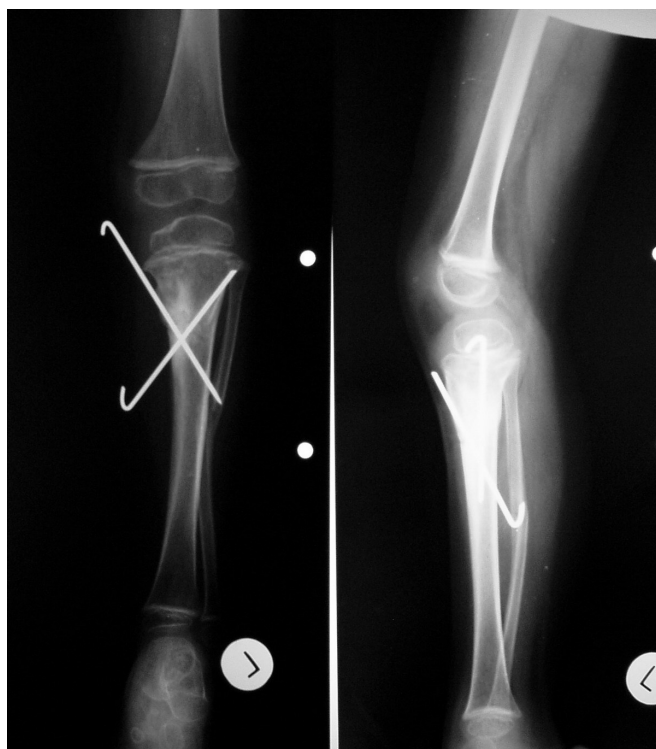


Fig. 5. Patient 2: normal tibial alignment on the left side postoperatively.

#### Patient 3

A 7 years old girl was examined in 2004 for left side  $20^{\circ}$  varus,  $43^{\circ}$  internal rotation and 6 cm limb length discrepancy following septic growth arrest of the proximal tibia (Fig. 6). We performed single-cut osteotomy, fixed by external fixator which allowed us to make the lengthening

of the tibia. Oral antibiotics were used to treat a pin-site infection. The fixator was removed after 8 months postoperatively. At 1 year follow-up the patient had normal leg alignment, no limb length discrepancy and fixed extension contracture of the left knee (because of initial septic osteoarthritis of the knee) (Fig. 7).

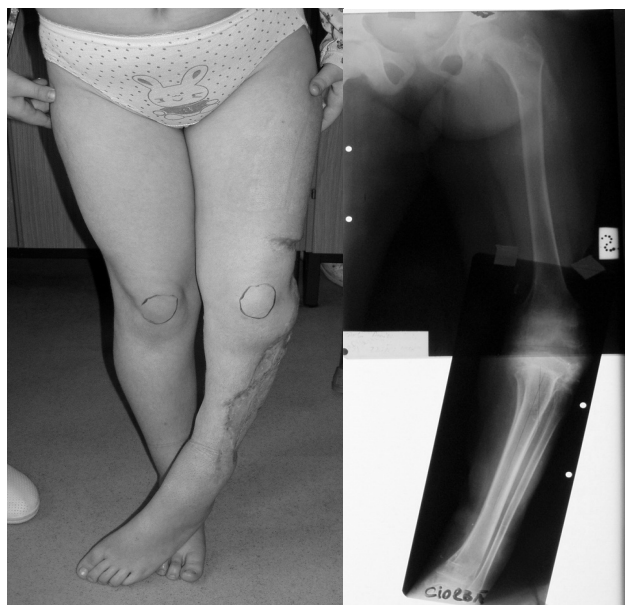


Fig. 6. Patient 3:  $20^{\circ}$  varus,  $43^{\circ}$  internal rotation and 6 cm limb length discrepancy following septic growth arrest of the proximal tibia.

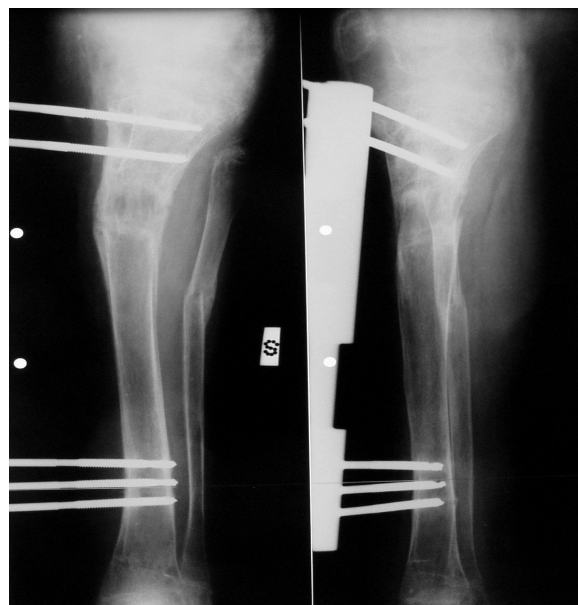


Fig. 7. Patient 3: At follow-up normal leg alignment, no limb length discrepancy.

*Patient 4*

A 10 years old girl presented with VDRR for which she underwent two valgisation osteotomies on the left side. On the left side she had 20° varus and 30° internal rotation deformities of the distal tibia (Fig. 8). We



Fig. 8. Patient 4: 20° varus and 30° internal rotation deformities of the tibia.

performed single-cut osteotomy in the lower third of the tibia, fixed with a 4-holes plate. The union was obtained after 2 months, with normal leg alignment and no pain (Fig. 9). The hardware implant was not removed yet.

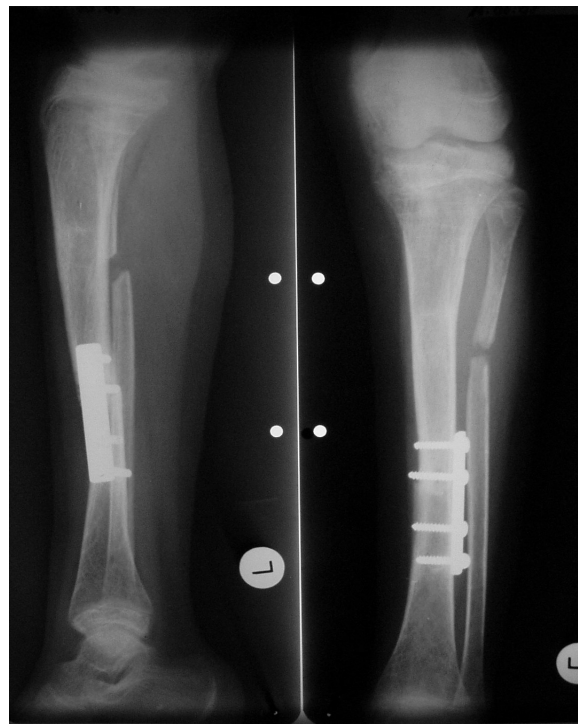


Fig. 9. Patient 4: the union was obtained after 2 months, with normal leg alignment and no pain.

## Results

Average follow-up was 8 months. Average preoperative varus deformity was 23,2° versus 3,5° after correction. Average preoperative internal rotation was 29,6° compared to 1,8° postoperatively.

The fixation hardware was left in place for an average of 6 weeks, allowing a longer period (8 months) for the patient who required limb lengthening.

The patients were satisfied and had no residual deformities. Radiographically, all patients had correct alignment and articular congruency.

We had only one complication: pin-site infection requiring oral antibiotics.

## Discussions

Blount's disease is characterized by progressive varus deformity of the proximal tibia associated with internal rotation of the tibia. It is caused by a growth disorder of the medial portion of the medial tibial physis. The turning point in the evolution of the disease is the development of a metaphyseal epiphyseal bony bridge of the medial proximal tibia (10). It is widely accepted that early treatment diminishes the recurrence rate of Blount's disease (11;12).

If performed before age 4 to 5 years, the rate of recurrence following valgisation is low, hence improving the long-term prognosis (11;12). However, we are sometimes confronted with advanced recurrent disease with several deformities to deal with. The prerequisite for treatment is evaluating the magnitude of all tibial deformities. Using the Paley's method of preoperative planning, we are able to evaluate and correct all deformities in one step avoiding secondary deformations due to osteotomy. Lower limb frontal and sagittal plane alignment and joint orientation have significant consequences for function and wear on the hip, knee and ankle. There is a normal range for the orientation of these joints relative to the mechanical and anatomic axis of the femur and/or tibia. We can use the normal joint orientation to accurately plan realignment of a deformed femur or tibia. In the frontal plane we use both anatomic and mechanical axis lines for planning. In the sagittal plane, the mechanical axis has less relevance and, therefore, only the anatomic axis is used for planning (9).

Monticelli and Spinelli (13) described four cases of one-step surgical procedure using an Ilizarov device to treat several deformities.

It is widely accepted that genu varum encourages femorotibial medial arthrosis. Depression of the medial

tibial plateau increases joint incongruity. Zayer (14) found 7 cases of knee arthritis in a population of 17 patients aged 30 to 60 with juvenile Blount's disease. Doyle et al (11) found 6 cases of arthritis in a series of 17 patients aged 16 to 35 years. Ingvarsson et al (15) found, in 49 patients followed to adult life (average 38 years old), 11 cases of knee arthritis in 8 patients and 15 cases of knee surgery in adulthood (10 meniscectomies, 4 valgisation osteotomies, 1 total knee prosthesis).

The majority of authors recommend correction of all deformations in one-step surgical procedure.

Single-cut osteotomy is an innovative technique developed by Paley et al. We use single-cut osteotomy for correction of complex tibial deformity in each case.

### Conclusions

One-step surgical management of the complex tibial deformities is an original technique that results in a decrease in both hospital stay and the number of operations. For these reasons, it could be classified as a minimal invasive procedure. This, however, does not eliminate the need for regular follow-up; this type of treatment requires full patient and family collaboration.

This comprehensive approach allow restoration of the mechanical and anatomic axes of the lower limb in patients with tibia vara, resulting in a resolution of symptoms as a result of normalization of the weight-bearing forces across the knee and ankle. We believe that this approach will decrease the risk of early degenerative arthritis of the knee.

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# CONSIDERATIONS UPON A 29 CASES WITH ESOPHAGEAL ATRESIA

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## Abstract

Esophageal atresia with or without tracheoesophageal fistula is a surgical emergency, presenting during first moments of extrauterine life. It is frequent associated with other congenital anomalies and it is usually complicated due to aspiration of gastric contents leading to pneumonia and respiratory distress. Ligation of fistula and reconstructive anastomosis of the ends of esophagus is mainstay of treatment.

Anesthesia and skill of anesthesiologist during pre, intra and post operative periods play an important role in successful treatment and survival of neonate.

**Key words:** esophageal atresia, tracheoesophageal fistula, reconstructive anastomosis

## Introduction

*Esophageal atresia* (EA) is a congenital disorder when proximal and distal portion of esophagus do not communicate. The proximal blind pouch has thick musculature and bigger diameter, while the distal portion has thin musculature.

*Tracheoesophageal fistula* (TEF) is a congenital disorder, with abnormal connection between anterior esophagus and posterior membranous trachea.

These two congenital malformations can occur as separate entities but commonly they occur together and the five different combinations are:

1. EA with distal TEF
2. EA with proximal TEF
3. EA with proximal and distal TEF
4. Isolated EA ( without TEF)
5. Isolated TEF ( without EA)

## Aims of study:

To evaluate:

- the incidence of EA/TEF, in a specific period, in the Department of Pediatrics Surgery and Orthopedics, Timisoara, Romania
- the distribution of EA/TEF in Western Romania
- the frequency of different types of EA/TEF
- the common used investigation for diagnosis of EA/TEF in our hospital
- the common used treatment for EA/TEF in our hospital
- the frequency of associated malformations and complications

## Material and method

The study being done on 29 cases of esophageal atresia and tracheoesophageal fistula during 1995- 2004, surgically resolved at Clinical Emergency Hospital for Children “Louis Turcanu” Timisoara, Department of Pediatrics Surgery and Orthopedics.

This study is an example of retrospective study, conducted with the help of:

- observation files
- operation protocols

The following parameters for every esophageal atresia - tracheoesophageal fistula case where studied:

1. Clinical findings for each case of EA-TEF
2. Time distribution of EA-TEF - during years 1995-2004
3. Place distribution of EA-TEF - according to localities – either rural or urban
4. Person distribution of EA-TEF- according to sex
5. Age at presentation of EA-TEF
6. Frequency of EA-TEF - according to type of EA-TEF
7. Associated anomalies
8. Diagnosis
9. Management
10. Prognosis and complications

## Results

### 1. Clinical findings.

#### a. Pregnancy history

##### Course

Most of pregnancies followed normal course and very few presented with complications. E.g. toxemia

##### Maternal age

In our study maternal age is <30 yrs in 70% of cases, while text says that frequency of EA-TEF increases with increase in maternal age (>30 yrs).

##### Polihydroamnios

Our study shows only 7% of pregnancies had having history of polihydroamnios. These were from cities, where follow up facilities are generally good. We know from experience that TEF presence decrease the amount of amniotic fluid.

##### Mode of Delivery

Most pregnancies had spontaneous or natural mode of delivery, very few needed cesarean section.

#### b. Prematurity

As we know EA/TEF is commonly associated with premature birth because of polihydroamnios.

##### Grade



Every case has demonstrated some degree of prematurity, according to APGAR SCORE, most common being prematurity grade 2.

#### Birth Weight

About 25% of cases weighed less than 2500 gm at birth.

#### *c. General physical examination*

##### Cutaneous Tissue

Most cases presented with generalized cyanosis, especially when crying and with attempted feeding, also physiological icterus was common, depending upon stage of prematurity.

##### Sub-cutaneous Tissue

Almost every case had some deficiency in subcutaneous adipose tissue.

##### Muscular Tissue

Every case presented with hypotonia, but about 4% cases presented opisthotonia because of associated nervous tissue disorder.

##### Lymphatic Tissue

No lymphadenopathy detected.

#### *d. Respiratory system*

##### Inspection

Most of cases presented with use of accessory muscles of respiration, cyanosis, and intercostals retractions with inspiration and choking especially with attempted feeding.

##### Palpation

There were no palpable deformities except those with vertebral column defect. E.g. scoliosis.

##### Percussion

Most of cases had dullness on percussion because of high association of aspiration bronchitis and pneumonia.

##### Auscultation

Most of cases presented with abnormal respiratory sounds bilaterally, rales or crepitations depending upon the underlying pathology.

#### *e. Cardiovascular system*

##### Inspection

Generally normal except when there was associated congenital cardiac malformation, leads to cyanosis.

##### Palpation

Apex beat normally palpable and peripheral pulses was normal.

##### Percussion

Almost every case had normal cardiac limits.

##### Auscultation

Most cases presented with normal cardiac sounds except in congenital cardiac malformation, there was holosystolic murmur.

#### *f. Digestive system*

##### Inspection

- Every case had been presented with excessive salivation and drooling.
- With attempted feeding there were episodes of gagging, choking and cyanosis.
- Most of cases had distended abdomen.
- 14% cases had anorectal atresia with no visible anal aperture.
- Most of cases had intestinal transit with history of passed meconium.
- 4% cases presented with anal ectopia

##### Palpation

Most of cases had soft abdomen on palpation with no hepatosplenomegaly.

##### Percussion

Most of cases had increased tympani on percussion because of distension, with normal hepatic limits.

##### Auscultation

Most of cases had normal borborygmy because history of present intestinal transit.

Those with absent intestinal transit had no audible borborygmy sounds.

#### *g. Genito-urinary system*

Most cases presented with normal micturation and normal aspect of urine, except in 4% cases with congenital renal malformations and also with normal genital system on inspection and palpation except 4% cases with bilateral ectopic testes.

#### *h. Nervous system*

Almost every case had normal nervous system examination with 4% cases of abnormal examination. E.g. absent spinal reflexes.

**2. Time distribution of EA-TEF - during years 1995-2004** (fig. 1) was: 3 cases in 1995, 4 cases in 1996 and same number in 1997, 2 cases in 1998 and also 2 in 1999, 3 cases in 2000 and 3 in 2001, 5 cases in 2002, only 1 case in 2003 and 2 cases in 2004.

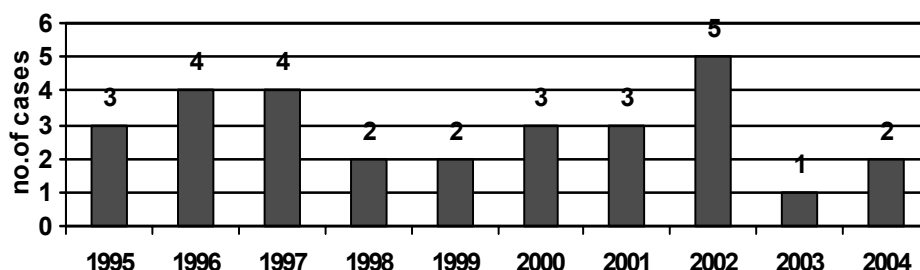


Fig. 1. - Time distribution of cases between 1995 – 2004.

3. Place distribution of EA-TEF cases according to localities indicated both the rural and urban areas had almost equal number of cases (fig. 2) , although urban areas had slightly more cases:

- rural area - 48% of cases
- urban area - 52% of cases

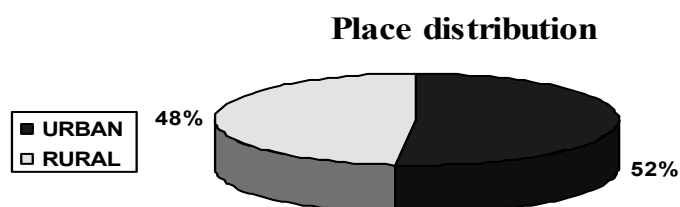


Fig. 2. – Place distribution of EA-TEF cases.

4. Distribution of EA-TEF cases according to sex in our study shows male (18) to female (11) ratio of 1.63.

5. Age at presentation of EA-TEF: according to time between delivery and presentation in our department, most

of the cases (21) was hospitalized in the first 36 hours of life (fig. 3).

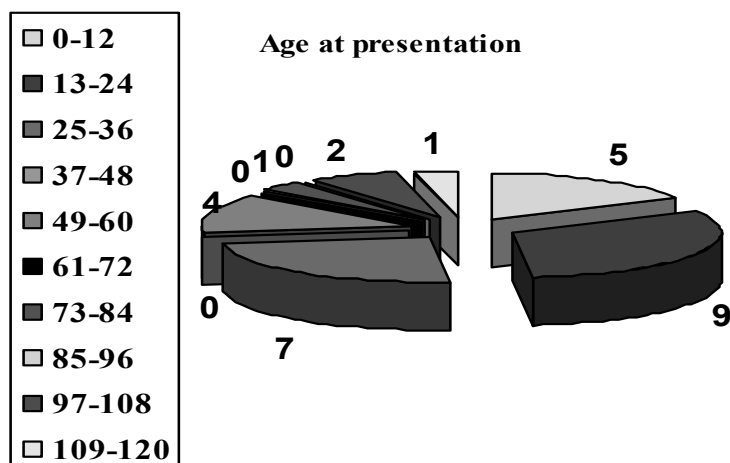


Fig. 3. – Distribution of cases according to age of presentation.

6. Frequency of type of EA-TEF in our study shows type 3 being most common:

- Type 3 (86%) 3A (20%) 3B (80%)
- Type 4 (7%)
- Type 1 (3%)
- Type 2 (3%)
- Type 5 (1%)

7. Associated anomalies – the presence of associated anomalies shows:

- 28% of cases had VACTERL association (fig. 4), most common being anal and cardiac. In contrast, studies conducted outside shows 50% VACTERL association.
- increased risk of VACTERL association with birth weight less than 2500 gms, which is consistent with outside studies.

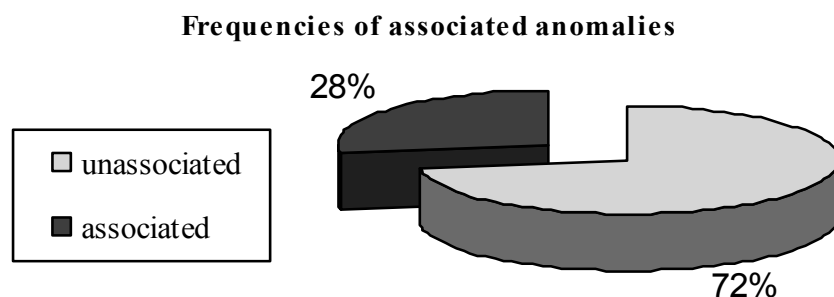


Fig. 4. – Frequencies of associated anomalies.

### 8. Diagnosis

As we know in new born prematurity, polihydroamnios and any demonstrable element of VACTERL, warrants a more thorough search for EA-TEF. Also, prenatal diagnosis of EA-TEF by maternal sonography is possible but requires highly experienced hand.

Postnatal nasogastric intubations followed by simple whole abdomen and chest radiography and if needed contrast studies are mainstay of diagnostic investigation for EA-TEF. Contrast studies helps to locate exactly the

position of TEF, type of EA-TEF and to measure the distance between two ends of esophagus.

In our hospital, mainstay of postnatal diagnosis of EA-TEF is radiography with nasogastric tube (NGT), with 41% of cases being diagnosed with this technique (table 1). This is consistent with diagnostic approach outside Romania.

Radiography with contrast medium being done on 38% of cases is not a preferred approach because it increases the chances of chemical tracheobronchitis and pneumonia, adding to further considerable morbidity.

Table 1. Radiological diagnosis in EA-TEF

Method of radiography	No. of cases
Radiography with NGT	12
Radiography with Contrast Medium	11
Radiography with NGT and Contrast Medium	06
TOTAL	29

### 9. Management

Immediate surgery is the only treatment of EA-TEF.

Approach adopted in our hospital to treat EA-TEF, is consistent with the approach adopted outside Romania and depends on the length of gap between proximal and distal ends of esophagus. Our study shows long gap situation 28% and small gap situation 72%, small gap situations being treated with single surgery approach and long gap situation being treated with stepped surgical approach.

#### a) *Small Gap Situation:*

- single surgery is required.
- 4<sup>th</sup> intercostals right space thoracotomy and extrapleural approach.
- azygos vein is divided.
- ligation of TEF.
- esophagus is mobilized and primary anastomosis is usually achieved.

#### b) *Long Gap Situation*

- stepped surgery is required.
- 1<sup>st</sup> ligation of TEF, cervical esophagostomy and gastrostomy.

- 2<sup>nd</sup> surgery is performed 2-3 weeks onwards includes esophagoplasty either with stomach or colon.

### 10. Prognosis and complications

Our study shows high Case Fatality Rate and low Survival Rate of 69% and 31% respectively.

A) *Case Fatality Rate* (CFR) = Total number of deaths due to particular disease / Total number of cases due to same disease x 100 = 69%.

B) *Survival Rate* = Total number of patients alive after five years / Total number of patients diagnosed or treated x 100 = 31%.

This high CFR is due to immediate postoperative life threatening complications. Most common being:

- cardiopulmonary failure
- acute septic shock- enterobacter species
- acute bronchopneumonia- staphylococcus aureus
- out of 31% who survived, very few have presented with postoperative stricture at site of primary repair of esophagus and recurrence of TEF.

### Conclusions

After the study, we have reached some conclusions, which are as follow:

- there is approximate equal, rural and urban distribution of this condition.
- male to female ratio being 1.63, with male sex at increased risk of having this condition.
- 73% cases presented to us within first 36 hours of life.
- type 3 of EA is the most common form of the condition with 86% of total cases, rest is as follows type 4(7%), type 2(3%), type 1(3%), and type 5(1%).
- 28% of cases had been associated with VACTERL anomalies, out of which most common were anal and cardiac anomalies.
- 59% of cases were diagnosed with the help of contrast radiography, while rest 41% with simple whole thoracoabdominal radiography with NGT.

- choice of therapeutic approach depends upon length between two ends of oesophagus:
  - small gap situation- single surgery
  - long gap situation- stepped surgery
- now, in days of highly sophisticated aseptic surgical techniques, we still have severe complications with fatal evolution in approximative 70% of cases in our hospital, most common postoperative complications are:
  - cardiopulmonary failure
  - acute septic shock- due to enterobacter species
  - acute bronchopneumonia- due to staphylococcus aureus
  - hepatorenal failure
  - disseminated intravascular coagulation
- postoperative complications are main cause of mortality rather than EA-TEF itself

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## BRIEF CASE REPORT: EXTENDED SMALL BOWEL VOLVULUS ASSOCIATED WITH SIGMA VOLVULUS

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### Abstract

Volvulus is a common surgical emergency and in most of the cases requires prompt diagnosis and treatment in order to evolve favorably. We present you a case of a 6-year-old male with a massive volvulus involving a large portion of small bowel and sigma that did not evolve favorably. There are no prospective, randomized studies comparing treatment options and the most frequently raised questions are: when to perform the resection if such an intervention is needed and how long should the resected portion of the bowel.

**Key words:** small bowel volvulus, sigma volvulus, laparotomy.

### Introduction

Small bowel obstruction (SBO) is a common cause of emergency surgical admission. The most frequent causes are well known and may often be safely treated conservatively in the first instance. However, some of the most rare causes of small bowel obstruction require prompt diagnosis and treatment so that they will not to progress rapidly to gangrene.[1]

Small bowel volvulus (SBV) presents with classical features of intestinal obstruction.

The outstanding symptom is central abdominal pain, the severity of which may be out of proportion to the apparent degree of obstruction. The diagnosis should be particularly considered if the pain does not respond to narcotic analgesia, although in such cases frank gangrene is often already present.[1]

Laboratory tests are often not conclusive for these patients such as the case of the studied patient.

Although the haematocrit, serum liver enzymes, amylase and lactate dehydrogenase are frequently raised, they do not show a consistent correlation with SBV.[1]

A white cell count, greater than  $18.000/\text{mm}^3$ , has been shown to be correlated with the presence of gangrenous bowel.[1,3]

In a review of 229 patients with small bowel obstruction no single hematological test was found to reliably differentiate gangrenous from viable small bowel.

Muchas et al [6], in their series, showed a 55% hyperamylaemia and abnormal serum lactate levels in 86% of patients with gangrenous small bowel, in contrast to 5% and 4%, respectively, in those with other causes of small bowel obstruction.

In contrast to the specific radiological features of colonic volvulus, the plain abdominal radiography in SBV

shows non-specific features of small bowel obstruction with either distended loops or a featureless/gasless abdomen.[7,8,9]

Upper gastrointestinal barium series, angiography, computerized tomography (CT) and magnetic resonance imaging (MRI), however, may be beneficial in establishing the diagnosis of SBV.[1]

### Case report

A 6-year-old male was admitted to the emergency department with acute abdominal pain of several hours' duration accompanied by nausea, vomit and diarrhea.

At the initial examination, the patient had no abdominal distension, no fever and the blood pressure and the pulse were in normal limits.

Results of blood work and urinalysis were, except high blood sugar, between normal limits.

Abdominal radiography showed 2 air-filled structures in the left upper abdomen cavity (fig. 1).

The following hours the patient's abdominal pain increased and the abdomen became distended. We decided that an immediately surgical intervention is necessary. After a median laparotomy we discovered a massive volvulus that involved large portions of small bowel and sigma.

The volvulus was formed by two separate axes: one of the ileum and a small part of the jejunum and the other one of the sigma with both axes forming a common axis. Both the small bowel and the sigma suffered from lack of blood supply and presented changes in color and consistency.

We untwisted the bowel and, because a large part of the intestine was affected, we decided not to perform any intestine resection in order to let some portions revitalize.

We infiltrated the mesentery with Xilina<sup>R</sup>, washed the cavity and placed a drain tube in the Douglas recess and closed the abdomen. After the laparotomy under supportive treatment and antibiotic protection the patient's state was stable.

After 24 hours we reopened the abdomen cavity in order to reevaluate the situation and perform the resection of the non viable parts. We found that a large portion of the small bowel had irreversible necrosis lesions and the sigma presented some modest lesions but still having a decent blood supply.

We performed the resection of 1.2 m of the small bowel with an end ileostomy. For the following 6 days the patient had a favorable evolution in the intensive care unit

but in the 7-th day he presented signs of peritonitis. An iterative laparotomy was performed and founded a perforation of sigma with septic fluid in the cavity. We resected most of the sigma with an end sigmoidostomy. After this surgical intervention the patient's state was satisfying but after another 4 days he presented a silent distended abdomen with involuntary guarding. A 4-th

laparotomy was performed and the resection of the distal portion of sigma, where a large perforation was found.

In the following days the patient's evolution was unsatisfying and after another 4 days, the patient died.

The pathologist report revealed that the death was caused by septic shock with C.I.D. and multiple organ failure.



Fig. 1. Abdominal x-ray hours after admission.

## Discussion

The surgical options for SBV consist of derotation, with or without fixation, and resection with anastomosis.

To date, there has been no prospective, randomized study comparing these options, or any study comparing the long term results to the different procedures.

In the presence of gangrenous bowel almost all authors recommend resection, with or without anastomosis.[10] However, the best treatment for non-gangrenous SBV is uncertain.

Simple derotation carries a high risk of recurrence, while fixation of the torsted small bowel is technically difficult, due to the length and anatomy of the small bowel. In view of the excellent blood supply of the small bowel, some authors recommend resection and primary

anastomosis in all cases of SBV, regardless of whether gangrene is present or not.

The obvious risk of resectional surgery is the development of short-gut syndrome, which arises from a substantial loss of small bowel length.

The actual treatment at laparotomy depends on whether the bowel is gangrenous or not. The frequency of gangrenous bowel in industrialized countries is less than 10%, [2,3] compared with rates as high as 25% in developing countries.

Many authors compared the rates of success and mortality in the case of viable bowel and gangrenous bowel. The following table presents a comparative study of different authors:

Author (Year)	Viable bowel		Gangrenous bowel	
	Number	Mortality (%)	Number	Mortality (%)
<b>African Series</b>				
Shepherd (1969)	389	8.0	36	47.0
Schagen van Leeuen (1985)	116	1.7	22	18.0
Ejumu (1985)	21	4.8	3	33.0
Sroujeh et al (1985)	20	10.0	3	33.0
Bagarani (1993)	10	5.8		21.0
Udezue (1990)	3	0.0		18.0
<b>Western Series</b>				
Drapanas (1961)	18	17.0	5	60.0
People et al (1990)	50	0.0	4	75.0
Average mortality		5.9		38.0

Mortality rates of between 4-50% have been reported, depending on the general condition of the patient and presence of concomitant disease.[4,5]

Emergency resection carries a high mortality rate, partly because of the poor general condition of the patient and toxemia from necrosis. If the resected bowel is gangrenous, the mortality ranges between 18-75% compared with 4-12% in the case of viable bowel.[4,5]

There are no prospective, randomized studies comparing treatment options and the most frequent raised questions are: when to perform the resection if such an

intervention is needed and how long should the resected portion of the bowel be. If too much of the bowel is resected, this could lead to a short-gut syndrome and all of its long term consequences. On the other side, nonviable bowel, left inside the abdomen cavity, could be the starting point of peritonitis with fatal end in many cases.

In conclusion, studies regarding results of different treatment methods are necessary to be done in order to establish a sequence of treatment that will lead to lower mortality ranges.

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## V. PSYCHOLOGY

# PSYCHOLOGICAL ASPECTS OF LIFE QUALITY AT CHILDREN AND TEENAGERS WITH CYSTIC FIBROSIS

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### Summary

At the Caucasians the most found inmate disease is cystic fibrosis (CF). It stands as the most feared enemy for patients and their parents. The CF patient's life-style is significantly affected.

After some several researches on CF youngsters, CMVT's team revealed some emotional and behavioural anomalies.

The family factors do have a big time influence as regarding the psychological adaptability to the CF suffering infant.

### Argument

At the Caucasians the most found inmate disease is CF, mainly revealed in childhood.

Therefore it stands as a major concern of paediatricians even if not only-causing interests also for general pathology or several other specialised disciples.

This malady is a constant challenge for the scientist in the field of genetic, physiologic and biochemistry researches. For a practitioner M.D., CF is a painfully but usefully expertise. But it stands as the most feared enemy for patients and their relatives.

For those who suffer and for their families the struggle for surviving remains in a first tempo, even if there have been achieved huge progresses regarding the research and secrets of this type of disease.

### 1. General considerations

#### 1.1. About Life –Quality concept

A wide-accepted definition is given by Flanagan: “generally spoken, Life-Quality is seem as the individual satisfaction generated by life itself or the joy of living given by the fields that a person puts as important”.(I. B. Iamandescu, 2002, p.126 )(3).But as time flew by, the noun developed but still got separated from the now-days concept of HRQL (Health Related Quality of Life).

I. B. Iamandescu and B.L. Plozza stated that HRQL is “the satisfaction given by life aspects that influence or get influenced by health”(2002,p.126)(3).They

are trying to assess and to correlate the variables of health with the one's who's health may be affected by a particular disease. In HRQL concept are included aspects like: disease's influences onto bio-psycho-social aspects of health (in fact, induced influences on physical, social, psychological and emotional or cognitive factors), symptoms, own perceptions on your own health-status and general points of view about Life Quality.

The same authors do mention the most frequent indicators of the HRQL's concept:

Functionality:

-Physical functionality (ability in realising a wide range of physical activities such as walking, staircase climbing and sports );

-Role functionality (limited mainly due to physical disabilities or health status);

-Social functionality (that is shrinking the range of usual social behaviours or habits-meeting friends, group meetings ).

The state of wealth:

-Mentally sane (induces various emotional states, depressions,anxieties);

-Vitality (own energetic tonus);

-Physical Pain (ability to sense pain or aches).

Own assessment of health:

-General own assessment of health condition;

-Significant changes of health during last 12 months.

Non-medical issues:

-Environmental issues (regarding urban environment);

-Social and human factors (social life management at it's various levels, the quality and size of interpersonal relationships).

Also, here is to mention that the patient's personality induces significant variations of all these factors, and mainly on his own, personal assessment ability.

### 1.2. Psychological perspective

#### 1.2.1. Psycho-behavioural changes induced by sickness



I. B. Iamandescu (3) did underlined that the chronic patient's life-style is significantly affected by all hygienically-dietetically privations, drug's secondary effects and, mainly by the "hurt-feelings". These inflicts his personality as accepting this new social status of a "sick-man", with wide implications in his family and socio-professional life. Therefore, modern medicine science has to converge it's goals not only into optimising therapeutically means, but also in assuring a life quality for the affected, as much as possible as similar to the healthy one's.

As B. Luban-Plozza and I.B. Iamandescu (2002)(3) told, even sick-adults tend to regress their affective-behavioural consciousness, even from the very start of the illness, not to mention hereby the affection-seeking dependence or vulnerability of a youngster when sick, as been much more present.

#### *Behavioural main features of a sick person*

- Selfishness and excessive caprice ( that may even lead in terrorising it's own family environment or medical one, due to shrinking the area of interest only to illness);

- Dependency, not only to medical staff but on environment, too;

- Predominancy in some emotional processes of affective (such as crying or anger);

- Aggressiveness, even if in a latent state ( like criticising the care-takers) or in a obvious way;

- Fear/anxiety-as a response to illness, medical care, due to negative feedback about healing perspectives, that may overestimate latent fears;

- Depression-seen as fatigability, lack of interest, lack of eating-appetite, insomnia or hipersomnia;

- Dissimulated depressive state-revealed through some unspecific physical symptoms.

After some several researches on CF youngsters, our team revealed the next emotional/behavioural anomalies ( on a reverse frequency average):

- 57%-attachment disorders;
- 45%-affective immaturity;
- 35%-anxiety;
- 35%-obvious aggressivity;
- 35%-negativeness;
- 35%-irritability;
- 35%-emotional disorders;
- 10%-latent aggressivity
- 10%-emotive lability;
- 10%-hostile attitudes;
- 10%-learning disorders;
- 10%-inhibition.

#### **1.2.2. The urge on a psychological approach to chronic patients**

The main objective of the entire psychological analysis should be focused on the patient, considering in any case factors as his psycho-behavioural problems and

changes and his expectations (B.L.Plozza and I.B.Iamandescu )(3).

In the established bond between the patient and therapist, it's quite important to unleash emotional stress, which will lead to a significant decrease of stress. Two facts could lead in time to decrease or even to disappearance of psycho-behavioural ill-induced changes: depicting psychological problems and establishing a dialogue and a strong bond.

Achievable objectives through a long lasting psychological assessment should in any case include: minimising aggressively, anxiety and depressions, even extinction them, replacing a nocive behaviour with a well-balanced one, and inducing a proper attitude on illness.

#### **2. Case reports**

We used the following methods and tests while investigating our subjects:

Methods:

- Direct observations on subject's behaviour;

- Clinical interview-made for gaining data and understanding the psychological profile of the subject- "focusing the approach on his feelings, as a revealed in the pre-established bond from the interview"(I.Dafinoiu,2002)(2);

- Anamnesis-usefully in collecting data about important events and possible clinical aspects of the patient.

Tests:

- Machover's test;

- The tree test;

- The family test;

- Raven test.

To every patient we did realised a psychological profile, focused mainly on life-quality factors vs. health: physical functionality, social functionality and environment.

#### **Case 1: I.P., male, 5 years old**

##### **Anamnesis:**

##### *1. Physical and psychological development.*

Child born at 9 months of pregnancy, with 3,4 kg weight and 51 cm height. Is the second sibling. Was diagnosed with CF at 3 months, in another paediatric clinic, is listed at CF Centre of Timișoara since 28.02.2002.Isn't suffering of any cerebral diseases.

##### *2. Family scene.*

I.P. has a harmonious family, is beloved and well protected. Has a elder sister.

##### *3. Educational-professional record.*

Due to his age and health conditions, I.P. hadn't follow any institution.

##### *4. Social system network.*

Being pretty spoiled, he's main attraction of his family's interests. His playground mates are his sister and the kid's of family's friends.

##### *5. Psychosomatic illness record.*

Has not.

*6. Present clinical record*

**Diagnose:** CF, complete form, ΔF508, complicated.

Psychological profile

I.P. has an overrated attachment towards his mother-while having to baby sit him 24 hours-a-day. Even while playing I.P. has to assure himself that mom is close, by seeking her all the time. This may be an anxiety sign. The kid is afraid being alone, is scared of being dropped-he doesn't understand his sickness, he's afraid of injections, he dislikes drug's taste and has bad feeding habits.

I.P. is in an specific development stage, he just realised he's different and wishes to show this fact to others. Being shy he needs quite some time to adapt to a new environment. But then he gets talkative. If he feels accepted and beloved, he becomes confident and open to share all he knows: the poems he knows, he plays. When he's not feeling well, he gets irritable and aggressive: throwing toys, rejects food saucer and hits he's mom.

Very sensitive and receptive at all the reactions from people from around, he takes on some of his mom's anxiety. His mom, noticing the digital hypocratism didn't understand the facts and got worried, thinking that her kid will become somewhat freaky. Her worries were transferred to the kid-who got also tensed and worried. The kid got pretty quiet and calm, after the facts were explained to him.

The psychical and senso-mothrical state of development of I.P. is specific to his age. The kid is visiting CMV from time to time, because of his actual well status.

**Case 2: I.I., female, 9 years old**

**Anamnesis:**

*1. Physical and psychological development*

Child born at the age of nine months at 2,5 kg weight, Apgar index 8. Diagnosed at the age of 2, is being held under CMVT supervision since 4<sup>th</sup> march 1996. Has not been suffering of any cerebral diseases.

*2. Family scene*

I.I. is the 5<sup>th</sup> sibling in her family. There's a special team spirit in the family- all brothers and sisters do take care of each other, and all this around mom-the core of the I.I.'s family.

*3. Educational-professional record.*

I.I. is on a regular basis attending school, even if frequently interrupted-due to several nursing periods.

*4. Social system network.*

Beyond normal brotherhood ties, she has usual friendship relations with her cousins.

*5. Psychosomatic illness record.*

Has not.

*6. Present clinical record.*

**Diagnose:** CF-complete clinical form.

Psychological profile.

Even if someone may think about I.I. as being moody and fanciful, in fact she's anxious and mother-dependant (nursed together with her). She may show from time to time signs of sociability and adaptability, but critical episodes do affect strongly her physical functionality-she feels fatigue, tired, with a low energetic tonus-and her emotive status- as being sad and bad-tempered.

Her affective evolution did not follow its optimal course, I.I. has an 6 years old behaviour. The fact is also due to her mother-due to her dual attitude towards punishment-motivation-she even over spoils her, or mistreats her: by neglecting her intentionally or by telling her that she won't be loved if she isn't well-behaved.

The psychological interference was realised through playing therapy. The main objectives where set in minimising tensions and irritability as well as concealing mom in adopting a proper and adequate attitude towards her child-a mother-like, protective attitude, avoiding overrated spoiling and replacing punishments with explanations about the child's mistakes.

The now-days psychological status of I.I. is still oscillatory due to her mother's emotively and anxiety, even if medically speaking the disease is under control and care.

**Case 3: K.B., male, 13 years old**

**Anamnesis**

*1. Physical and psychological development.*

Born at the age of 9 months of pregnancy, at 3 kg weight and 51 cm height, breast feted till 3 months. Was CF diagnosed at the age of 3 months and recorded at Târgu-Mureş Paediatric Clinic; CMVT recorded him in 25/10/02. Hasn't been suffering of any cerebral diseases.

*2. Family scene.*

K.B. is single to his parents, well beloved and protected. This family ties are unite and strong-bonded, all of his relatives are interested by him, and his some age cousins are his best friends.

*3. Educational-professional record.*

He attended regularly kindergarten and school, but now-a-days-because of frequent and extended hospital care-his mother coaches him. K. B. doesn't speak Romanian (even if he knows only a few words) but he comprehends some, he speaks natively Hungarian and learns English.

*4. Social system network.*

Beside his cousins, he doesn't have many friends, but he has some play mates. He is willing to establish relationships with people around him.

*5. Psychosomatic illness record.*

Has not.

*6. Present clinical record.*

**Diagnose:** CF, complete clinical form, homozygote ΔF508, classical phenotype, with complications.

Psychological profile.

We were asked to assess K.B. in order to determine his IQ, because he seemed as not been able to comprehend any of what it was explained to him. His apathy state seemed unchangeable, nor his mother couldn't interfering in Hungarian, not to mention the fact that he don't understands Romanian too. The MD that asked CMVT for assistance did presumed presence of an anxious-phobic disorder, facts that were partially confirmed.

We can state-after examining K.B.-that he has a minimal intelligence, but this can be seen as quite regular, not as being retarded. Even he is hypersensitive, he benefits of his family's support, and regularly he feels as being loved and protected. Pretty helpfully in his struggle comes his stabile and friendly familial environment.

K.B. is a quite skilled drawer, and he proves even to be creative if he can express his own feelings He is able to conceive easily both friendly places and events.

To his health disorders do come some growing-up problems, and, therefore there may appear moments when he acts as easily annoyed or sometimes as trying to act explicit, by using improper attitudes. His anxiety is strongly related to his disease. He gets easily tensed and scared when he doesn't comprehend what happens, or when he doesn't get explanations about the sense of drugs use or when over-examineted. He has also a darkness phobia-as his mother told us.

Direct communication is somewhat difficult, as being used mom's translations and explanations. We used non-verbal gestures, simple words that could reach his own understanding (at least partially) and to dilute some of his fears.

He is attending all medical prescriptions, and well participating in prescript therapy procedures, including physical-therapies ones, and now he looks emotionally well balanced.

**Case 4: B.C., male, 14 years old****Anamnesis:***1. Physical and psychological development.*

Born at 9 months of pregnancy, at 2,9 kg weight, I.A.= 9, was breast fed till 3 months. Is been held under CMVT's supervision since 30<sup>th</sup> June 2000.Hasn't been suffering of any cerebral diseases.

*2. Family scene.*

B.C. is the only sibling, he is in the centre of his family's attention; his parents show some overrated attitude towards his education and in the same time some maximized protection.

*3. Educational-professional record.*

B.C. attends regular school classes with good and even very good marks and results. He has artistic skills: he's a good drawer, he sings and writes poems and tales.

*4. Social system network.*

He hasn't close friends, social relations of him are under strict parental control.

*5. Psychosomatic illness record.*

Has not.

*6. Present clinical record.*

**Diagnose:** CF, respiratory form.

Psychological profile.

B.C. even if he is an teenager, proves to be calm, obedient, hesitant and perfectionist. He tries to be best in all he does. Even his artistically area is a opportunity to reveal perfectionism: he is detail oriented, he re-draws parts of his drawings in order to improve them' he re-builds rhymes from his poems.

Generally, his entire behaviour reveals a pregnant anxiety-he feels a strong urge to control, in the deepest details, in order not to fail.He's quite a good observer and shows prudence when involved in non-familiar duties.

B.C.'s physical activities are minimal, he doesn't attend sports at school or any physic –therapeutically program, on a regular basis. Opposite to this he shows an intellect-oriented behaviour, B.C. needs to express personal values, his idealism, enthusiastic habits, he's ambitious and impressionable, but unable to get frustrated-facts which reveal a childish attitude.

At regular counselling meetings B.C.'s mother isn't a usual participant, and even so it has been observed that auto relaxing is the appropriate technique in dealing with his disease.

**Conclusions about the CF subjects:**

-As concerning Raven's test results-all subjects have a normal mental state.

-Their physical functioning might be temporary affected during severe seizures.

-Even if emotional and behavioural disorders are quite recurrent, they aren't considerable ones, while social functionality is recorded as been under acceptable levels.

-These is to be attested a proper life quality of those CF suffering subjects, due to proper medical care and their families involvement.

**3. The parent-youngster/teenager-disease correlation****3.1. The interconnection parent-youngster-disease.**

The family is a complex system. Here in, any interaction between it's compounds will affect the entire system.But the interference of a strong, sudden vector will daze the entire balance and stability of the interactional area, specific to a family. It is known that through a child birth there do occur significant changes between husbands-they get also a parent role. We can notice that the interaction between mother-child do influence the tie between husbands, but also the relations between the parents do influence the relations with the child. New siblings will also generate changes to family ties.But the discovery of a chronic disease of the child may be seen as a vector that will destroy irreversible the relational balance of a family.

Some chronically disease does alter the child for long periods of time-and even sometimes the entire life, fact that has serious consequences on his relations with mom, family, playmates or school colleagues, and generally speaking with the entire physic and social sphere. The malady does influence all stages of development, generating progress problems in cognitive or psychosocial fields. The effects may vary depending on the child's character, his family's psycho-support (especially from mom ), the medical interferences, age or social assistance (C.Ciofu,1998 p.118) (1).

The basis of the complex human structure is designed in childhood. Starting at early ages the infant learns how to relate to others, observing as models his parents.If inter-human relations in his family are harmonious, the little child will gain a proper psychological basis, which will lead him among his entire life. This basis will also lead to a proper balance from his sub consciousness, also with influence on the emotional balance of his personality.

Unfortunately, both congenital chronic diseases and those from early childhood, do negatively influence inter-familial relations and the emotional balance of the child. Among this diseases with influence is CF.

The family factors do have a big time influence as regarding the psychological adaptability to the CF suffering infant.

Subsequent influential factors do include familial circumstances, such as: size, structure, socio-economic status, parent's health, attitude towards illness, communication among family members ( I. Popa, Z. Popa and L. Pop, 1998 )(5).

When we evaluate familial factors, independently from the illness stage, we mainly seek for:

1. CF's interference on the family.
2. Family's functionality towards illness.

Here can be evaluated the effect on the entire family, towards the parents, on brothers or on the ill-child himself.

M. E. Hodson and D.M. Geddes (4) studies do reveal that trauma's depth and length lead the parents to sacrifices, parents don't have any time or means for specific adult duties. It outcomes a lack of communication among family members, some sort of silence that leads to misunderstandings and family malfunctions. These are still a few studies done on CF ill person's brother's, even if in some cases, there was noticed some CF's acting from younger brothers in order to get a similar treatment ( favourite) from the parents. Elder brothers are generally protective and helpfully. The attitude towards disease tends to change depending on sickness' stage. The care towards the patient is variable depending on the disease's stage.

Familial dysfunctions do affect negatively the behavioural and health's status of the CF's sick infant. There can be established a bond between bad functioning and the amount of behavioural problems of the CF's suffering child.

CMVT's practical experience revealed that:

- A big majority of parents react through a psycho-emotional blockage the very moment they get the diagnose.

For a instance they can't comprehend what kind of disease they are dealing with, and they cannot react affectively in any manner.

- Immediately follows a stage of distinct confusion-they can't be certain if they understood properly what happens or if something bad happens to them.

- Some of them deny the facts that the illness will affect their sibling, and some of them even ask for some new medical analysis.

- As they realise explanations they get, they will react accordingly to their personality-some become excessively anxious, some get depressive, but there could be found parents who will try to keep up emotional balance not to induce additional fears to the ill infant. Also there had been found some cases in which one partner is blamed for the appearance of CF at their infant. We couldn't assess any cases of hostility towards medical personnel or towards medical sciences.

- Generally speaking the parents are open in offering to their sibling the entire support. There could be also found certain dysfunctional family entities wham's relational disorders significantly do influence the youngster.

- The most frequent caring parent are mothers. Many of them will institutionalise themselves only to comprehend in the best form how to care the youngster, therefore the compliance to care is high.

### **3.2. General advices for parents.**

It is seen as mostly important the relatives' support ( mainly the parent's support ) both for the young CF sick child and for other chronic ill ones.

Therefore, here are some advices, such as:

- ♣ Not to highlight the illness state of the youngster, versus creating a proper environment for him to develop properly his own personality.

- ♣ Not to keep the youngster isolated from other same-aged kids, but to encourage him in developing friendship relations.

- ♣ Not to over spoil him, but also not to loose a proper authority towards him.

- ♣ To assign him age-proper duties, and to observe him discreetly.

- ♣ To listen him patiently when he needs to describe feelings or when he needs to confess.

- ♣ Not to give orders, but advices-and only at a proper time.

- ♣ Not to highlight failures, but to praise his achievements.

- ♣ To express an understanding attitude, and to express helping attitudes in overcoming difficult moments.

*Statement and advice.*

As we all agree, CF's suffering children are destiny's victims, and caring specialists shall contribute in helping them face their cruel destiny with a smile under their innocent eyes.

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### **MANUSCRIPT REQUIREMENTS**

The manuscript must be in English, typed single space, two columns (equal width – 8,5 cm, line between and spacing – 0,8 cm) on A4 paper, with margins: top – 3 cm, bottom – 2,26 cm, left – 1,5 cm, right – 1,7cm. A 10-point font Times New Roman is required.

The article should be organized in the following format: Title, Names of all authors (first name initial, surname), Names of institutions in which work was done (use the Arabic numerals, superscript), Abstract, Keywords, Text (Introduction, Purpose, Materials and Methods, Results, Discussions and/or Conclusions), References, first author's correspondence address.