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APWR

ASOCIAȚIA PRADER WILLI ROMÂNIA



*Universitatea de
Medicina și
Farmacie
“Victor Babeș”
Timișoara*



Prima conferință est-europeană:

MULTIDISCIPLINARY APPROACH IN THE MANAGEMENT OF PWS

Comitet organizatoric

Dorica Dan, presedinte
Christel Nourissier
Maria Puiu
Ioana Rotaru

Comitet științific

Maria Puiu, președinte

Christel Nourissier
Victor Pop
Natalia Cucu
Margit Șerban
Aurelia Szekeley
Ruxandra Rășcanu
Calin Popoiu
Norbert Hoedebeck-Stuntebeck

Dorica Dan

Sussane Blichfeldt
Hubert Soyer
Corin Badiu
Valerica Belengeanu
Mihai Gafencu
Emilia Severin
Cristina Rusu
Gabriela Anton

Deadline for registration :10th April 2009

Registration and information are open on the following website:

<http://www.simbotours.ro/go/conference;>

<http://anbraro.wordpress.com/2009/03/27/conferinta-est-europeana-privind-sindromul-prader-willi/>

**ASOCIATIA PRADER WILLI DIN ROMANIA
UNIVERSITATEA DE MEDICINA SI FARMACIE TIMISOARA
SOCIETATEA ROMANA DE GENETICA MEDICALA**

are organizing

the 1st Eastern European Conference on PWS

"Multidisciplinary approach in the management of PWS" and the main themes will be: clinic, genetic and epigenetic aspects in PWS; weight management and behavior therapy."



TIMISOARA

24-25 APRIL 2009

TIMISOARA

The first record of the city of Timisoara, built on the site of an ancient Roman fortress called Castrum Regium Themes, dates back to 1212. Over the years, Timisoara, the largest city in western Romania, has been influenced by many cultures. The Romans used it as an important crossroads fortress until the Tatars destroyed it in the 13th century. Conquered by Turkish armies in 1552, Timisoara remained under their protection until 1718 when the region of Banat came under Austrian rule for two centuries. Timisoara later became a vital medieval commercial and manufacturing town. Turks, Austrians, Germans and Serbs all left their mark and their influence can be seen in neighborhoods throughout the city even today.

The charm of this city, settled on the northern bank of the Bega River, lies in its distinct architectural character and vibrant cultural life. Frequently referred to as "Little Vienna," Timisoara is home to year-round musical and theatrical performances, art galleries, museums and a buzzing nightlife. A progressive, cosmopolitan place, Timisoara was the first city in Europe and second in the world after New York, to use electricity to illuminate its public streets.

Thanks to a Mediterranean climate, life is best observed outdoors, in the many public squares and lush green retreats. Timisoara is easy to explore on foot. If you get tired, a tram will be along in a moment; the system is fast,

frequent and efficient.

Timisoara abounds with churches of several denominations, a Jewish quarter, an elegant baroque square and a pedestrian-only downtown area. Some of the monuments in the heart of the city afford panoramic views, while the many parks in this "city of flowers" provide an idyllic spot to take a break from sightseeing.

Interesting facts:

Timisoara was the first European city to introduce horse-drawn trams (in 1869) and electrical street lighting (in 1889).

Timisoara was built on a swamp; the Metropolitan Cathedral has 5000 oaks supports underneath it; Johnny Weissmuller, Hollywood's **original Tarzan, was born here.**

Some of the city's most interesting sites are its elegant baroque buildings, spread around town and particularly along the main square, Piata Victoriei, which stretches from Opera Square (*Piata Operei*) to Loga Boulevard.

The focal point is the towering **Romanian Orthodox Metropolitan Cathedral** (*Catedrala Ortodoxa Mitropolitana*) at the south side of the square. Built between 1936 and 1946, its green and red roof tiles are arranged in a mosaic design. In front of the Cathedral is a memorial to those who lost their lives during the 1989 Revolution that overthrew Communist rule.

The **Memorial Museum of the 1989 Revolution** (*Muzeul Revolutiei*) offers a full insight into the revolution in Timisoara.

We are waiting you to learn together about PWS and to enjoy the beauties of this Transylvanian town.

We are looking forward to welcome you again in Romania!

Dorica Dan – president RPWA/ RONARD.

Maria Puiu, UMF Timisoara, vicepresident RONARD.

GENERAL PROGRAM

24th of April 2009

08.30-09.00	REGISTRATION
09.30-10.00	OPPENING OF THE CONFERENCE EXPECTED SPEAKERS FROM MINISTRY OF HEALTH, UNIVERSITY OF MEDICINE AND PHARMACY TIMISOARA, APWR, APL.
10.00-10.30	COFEE BREAK, POSTER VIEWING
10.30-13.00	PLENARY SESSION SPW diagnostic and management–European models/ Co- chairs: FRAMBU + PW No (Norwegian experience)
10.30-10.50	APPROACH OF PWS IN NORWAY - Ragnhild Arnesen, parent delegate IPWSO
10.50-11.10	FRAMBU EXAMPLE AT EUROPEAN LEVEL - Dr. Kaja Giltvedt
11.10-11.30	NORO PROJECT “NORWEGIAN – ROMANIAN PARTNERSHIP FOR THE PROGRESS IN RARE DISEASES” - Psychologist Dorica Dan, President of APWR/ ANBRaRo / Launching OF the project
11.30-11.50	PWS PATIENTS’ EXPECTATIONS AT EUROPEAN LEVEL REGARDING THE DIAGNOSIS AND HEALTHCARE SERVICES - Christel Nourissier, Secretary of General EURORDIS
11.50-12.10	PROJECT: CORRELATION OF CLINICAL, GENETICS AND EPIGENETICS ASPECTS FOR UNDERSTANDING THE ETIOLOGY PRADER WILLI/ANGELMAN SYNDROMES – A MODEL OF INTERDISCIPLINARY APPROACH OF RARE DISEASES IN ROMANIA - coordinator Prof. Dr. Maria Puiu
12.10-13.00	HEALTH STATE IN PWS (CHILDREN)- Prof. Dr. Susanne Blichfeldt
13.00-14.00	LUNCH
14.00-15.45	PLENARY SESSION
14:00-15.00	EXCHANGES OF GOOD PRACTICES – GUIDELINES AND STANDARDS OF CARE IN PWS. PRESENTATION OF THE RESULTS OF THE FIRST CARETAKERS CONFERENCE FROM HERNE, GERMANY - Psychologist Norbert Hoedebeck-Stuntebeck and Psychologist Hubert Soyer
15.00-15.20	THE FLUORESCENCE IN SITU HYBRIDIZATION (FISH) ANALYSIS IN PWS - Assist. Prof. Dr. Monica Stoian, UMF Timisoara
15.20-15.40	EPIGENETICS, CONCEPT AND PRACTICAL - Prof. Dr. Natalia Cucu, University of Bucharest
15.40-16.00	SLEEP APNEA IN PWS – CAUSES, DIAGNOSIS AND TREATMENT - Assoc. Prof. Dr. Stefan Mihaicuta, UMF Timisoara
16:00-18.30	WORKSHOPS - MULTIDISCIPLINARY MANAGEMENT + RESULTS PRESENTATION

	<p>Communication, cognitive development and behavior of children with PWS- Assist. Prof. Dr. Violeta Stan, UMF Timisoara</p> <p>The structure of the living environment and of the work place for patients with PWS- Hubert Soyer, Germany</p> <p>Management of the crises and psychological aspect of the person with PWS- Norbert Hoedebeck-Stuntebeck and, Germany</p> <p>European research networks. Means of working together. Christel Nourisier, General Secretary EURORDIS (France), Prof. Dr. Maria Puiu, UMF Timisoara, Psychologist Dorica Dan, APWR</p>
18.30	DINNER

25th of April 2009

09.00-11.30	PLENARY SESSION
09.00-09.45	HEALTH STATE IN PWS (ADULTS)- Prof. Dr. Susanne Blichfeldt
09.45-10.00	MULTIDISCIPLINARY APPROACH FOR THE MANAGEMENT OF INDIVIDUALS WITH PRADER-WILLI-SYNDROME - Prof. Dr. Greco D, Italy
10.00-10.30	EXPECTATIONS OF PEOPLE LIVING WITH PRADER-WILLI SYNDROME ON DIAGNOSIS AND CARE IN EUROPE - Christel Nourissier, Secretary General EURORDIS
10.30-10.45	SELF INJURY AND PRADER-WILLI SINDROME - Prof. Dr. Buono S, Italy
10.45-11.00	EFFECTS OF GH THERAPY IN TEN SUBJECTS WITH PRADER-WILLI SYNDROME - Prof. Dr. Ragusa L, Italy
11.00-11.30	COFFEE BREAK, POSTER VIEWING
11.30-13.00	PLENARY SESSION
11.30-11.45	ENDOCRINE APPROACH IN PWS PATIENT - Prof. Dr. Corin Badiu, "C.I.Parhon" National Institute of Endocrinology, Bucharest, Romania
11.45-12.00	GENOTYPE-PHENOTYPE CORRELATION IN PRADER WILLI SYNDROME - AN OVERVIEW OF THE LITERATURE - Assist. Prof. Dr. Cristina Skrypnik, University of Oradea, Faculty of Medicine and Pharmacy, Genetics Department
12.00-12.15	ORTHOPEDIC AND SURGICAL APPROACH IN PWS PATIENTS - Assist. Prof. Dr. Calin Popoiu, UMF Timisoara
12.15-12.30	ELEMENTS OF DIAGNOSIS AND CLINICAL FOLLOW-UP IN PWS – Assoc. Prof. Dr. Otilia Marginean, UMF Timisoara
12.30-12.45	WS' QUALITY OF LIFE: SOCIAL ADJUSTMENT AND COGNITIVE SKILLS - Prof. Dr. Achutegui, I, Italy
12.45-13.00	SLEEP APNEA SYNDROME: PATHOGENY, DIAGNOSTIC, TREATMENT - Conf. Dr. Stefan Mihaicuta, UMF Timisoara
13.00-13.15	COGNITIVE DEVELOPMENT AND BEHAVIOR OF CHILDREN WITH PWS - Assist. Prof. Dr. Violeta Stan, UMF Timisoara
13.15-13.30	NEW TECHNIQUES OF DIAGNOSIS IN PWS - Assoc. Prof. Dr. Cristina Rusu, Medical Genetics, UMF Iasi

13.30-14.30	LUNCH
14.30-15.30	PLENARY SESSION
15.30-15.50	IMPLICATION OF NGO IN EDUCATION OF PATIENTS WITH RARE DISEASES AND GENERAL POPULATION - Assist. Prof. Dr. Mihai Gafencu, President of Save the Children Foundation
15.50-15.10	VOLUNTARY ACTIVITY, STUDENTS AT FACULTY OF MEDICINE FOR RARE DISEASES PROMOTION - Prof. Dr. Maria Puiu, Stud. Andrada Borlovan, UMF Timisoara
15.10-15.30	COFFEE BREAK, POSTER VIEWING
15.30-17.30	WORKSHOPS- MULTIDISCIPLINARY MANAGEMENT
	<p>Trainig for teachers inclusive methods, Psiholog Mihaiela Fazacas – APWR, Psiholog Mirona Marcu, UMF Timisoara</p> <p>Fitness, sport si nutritive – programe de reabilitare in SPW, Susanne Blichfeldt, Dr. Ioana Rotaru (FUNDATIA ACASA)</p> <p>The management of sleep apnea syndrome in PWS- Assoc. Prof. Dr. Stefan Mihaicuta, UMF Timisoara</p> <p>The Development of health services for PWS patients– Prof. Dr. Maria Puiu, UMF Timisoara, Dorica Dan – APWR</p>
17.30-18.30	CONCLUSIONS. BEST POSTERS AWARDS HANDLEING OF THE DIPLOMA. CLOSING OF THE CONFERENCE
18.30	DINNER

We are organizing The First Eastern European Conference on *PWS* in Timisoara as we are grateful to the Medical University Timisoara, "Salvati Copiii" Organization and the *Children Hospital* "L. Turcanu" which are very active and supportive in our common projects in the field of *rare diseases*. Also, we recognize as very important the contribution of the Local Authorities Timis in this area.

The primary aim of the conference is to raise awareness and promote Prader Willi Syndrome and rare diseases as a public health priority in Eastern Europe, but also to share the best practice at European level and learn from each other as we intend to create also a platform of cooperation among parents and professionals.

The secondary aim is to help define strategies useful to these countries to evaluate the needs and to establish priorities to approach *PWS* using European models. The strategies should support diagnoses, treatment and care for rare disease patients throughout Balkan and Eastern European countries. The conference targets are all the stakeholders contributed on methodologies that could best drive forward the needs of patients, their families and professionals.

There is a collective wish to share experience as well as an agreed necessity to have tailor made approaches whilst optimizing resources. In other words, there will be promoted an atmosphere of solidarity, with a European vision. To date FRAMBU model and Nordic European countries seems to have the best expertise in the field. We will be all together in the conference, trying to share knowledge, expertise and all the love we have for our children.

This is how most of the projects are born all over the world. The project that we will be launching during this Conference "Norwegian – Romanian Partnership for Progress in Rare Diseases NoRo" has been born based on these principles and we are sure that it will create a difference and a better future for our children!!!!

Dorica Dan - *President RPWA, RONARD, BoD Eurordis, IPWSO*

I. ABSTRACT REPORTS / ABSTRACT WORKSHOPS

1. APPROACH OF PWS IN NORWAY

Ragnhild Overland Arnesen

Parent delegate International Prader-Willi Syndrome Organization

In the last decade, Norwegian paediatricians have acquired more knowledge about PWS and most children born with the syndrome are now diagnosed in the neonatal period using a DNA blood test. Most children with PWS get growth hormone treatment from 1-2 years of age. Restricted energy intake and increasing energy consumption are the most important tasks for caretakers of children, youth and adults with PWS. The parents need a lot of support to handle living with the stress of having a person with PWS in the family. In Norway children with PWS start in daycare when they are around 12 months of age. The children receive follow up from physiotherapists and educational staff. Most of the children start in regular elementary schools, but later on they often attend classes for children with special needs. In order to support the family and plan transitions well, the service providers and the parents have regular meetings. The families also get some financial support. Both the parents and the person with PWS need respite services that are provided by the government. This is a good arrangement for siblings, parents and the person with PWS.

As adults, most people with PWS in Norway move from their family home to a group home. These are

most often owned by the municipality. There they are provided service as needed: food and diet, personal hygiene, exercise, medicine, household etc. Most adults with PWS also have adapted work.

The older grownups with PWS in Norway often have an obesity problem. It seems like this is a problem which will be reduced in the future, with early diagnosis, better treatment, and most important, use of growth hormones. The Norwegian PWS Association is working to establish group homes for only PWS persons as experiences show that this gives a better quality of life for PWS than mixed homes.

The Norwegian PWS Association has a close cooperation with Frambu. One of our projects of common interest is the Scandinavian Growth Hormone Project, testing the effect of using growth hormones on adults with PWS.

Ragnhild Overland Arnesen is mother of a 30 years old PWS woman, and has for several years been member of the board of The Norwegian PWS Association. She has for many years been responsible for The PWS members' magazine, and she is also the Norwegian delegate for IPWSO. In civil life she is information senior adviser in The City of Bergen.

2. FRAMBU EXAMPLE AT EUROPEAN LEVEL

Kaja Giltvedt

Frambu - Centre for Rare Disorders, Norway

Frambu Resource Centre for Rare Disorders in Norway is responsible for approximately 100 different diagnoses, and among these is PWS. The Centre is a government funded supplement to the regular health care system in Norway. Frambu arranges one week courses for families with members with PWS. Costs for travel, room and board are covered. The participants at these courses are provided with lectures,

workshops sessions, and leisure activity follow-up during evenings. Children are provided with educational follow up. Every summer Frambu arranges Health Camps for children and adolescents with rare disabilities. The camps accommodate young people, unaccompanied by their parents, in two weeks.

Kaja Giltvedt has her physiotherapy education from Oslo, Norway 1981 and a Bachelor of Physical

Therapy Degree from the University of Manitoba, Canada 1984. She has a Masters in Health Sciences from the University in Oslo 2001 and is certified Paediatric Physiotherapist. Since 1990, she has worked with children from 0-18 years both in community care,

at the Ullevål University Hospital in Oslo and at Frambu Resource Centre for Rare Disorders where she has met many of the children and adolescent with PWS in Norway.

3. NORWEGIAN ROMANIAN PARTNERSHIP FOR PROGRESS IN RARE DISEASES – NORO

Dorica Dan

President RPWA, RONARD, BoD Eurordis, IPWSO

Project Aim:

To contribute to the improvement of the quality of life for people affected by rare diseases in Romania by providing equal access to early diagnosis, quality treatment and rehabilitation services through a comprehensive and accessible network of facilities and resources as set forth by the National Plan for Rare Diseases.

Objectives:

1. To define a **team of professionals and patients' representatives (NATIONAL RARE DISEASES TASK FORCE)** to design, implement, monitor and evaluate the National Plan for Rare Diseases in Romania.
2. To contribute to the development of **new high quality services for rare diseases** in Romania on national level through *the creation of a pilot reference center for personalized intervention for those affected by rare diseases.*
3. To **enhance the training capacity** within the country for the prevention, diagnostic, treatment and rehabilitation of rare diseases

- a. to design and implement a **training network for specialists and staff**
- b. to create **accredited online training courses (eUniversity)** about rare diseases for professionals: social workers, psychologists, nurses, teachers, doctors, etc.

4. Permanent development and maintaining of a shared best practice network on RD

Conclusions:

In the absence of a strategic approach for creation of services designated for Rare Diseases and insufficient funding, the collaboration of national and international NGOs, European networks, local authorities, medical, educational and social specialists is essential.

Developing awareness about the needs of children with Rare Diseases and engaging public in a shared strategy for the development of genetic services, will ensure a collaborative international approach in sharing of expertise and experience and will **start a model network** in this field through the development of a strategic partnership: patient organizations from Romania and Norway, Ministry of Health, Local Authorities, State departments, etc;

4. EXPECTATIONS OF PEOPLE LIVING WITH PRADER-WILLI SYNDROME ON DIAGNOSIS AND CARE IN EUROPE

Christel Nourissier, Secretary of General EURORDIS

European organization for rare disease

PWS is a complex disease requiring early diagnosis, pluridisciplinary care and social assistance. Diagnosis should be given with proper information and psychological support. Overall, patients need more

than 11 different kind of medical services, an even larger number of consultations and hospitalizations than other rare diseases. Access to medical services is generally difficult, mostly because of lack of referral,

unavailability or travel hurdles. Patients also need to be accompanied. 8% of patients feel rejected mainly because of the complexity of the disease, their physical aspect or their behavior. 59% of patients do not have access or are unsatisfied with social assistance. One parent in 63% of families, usually the mother, is forced to reduce or stop his activity to take care of his/her child with PWS.

Clinical management has a greater impact on obesity outcomes in PWS than cultural factors. Access to health services and proper organization of care with

centers of expertise for people living with PWS can have a high impact on life expectancy and quality of life.

Ref: The voice of 12 000 patients. Experience and expectations of rare disease patients on diagnosis and care in Europe, 2009

Cross-cultural comparison of obesity and growth in Prader-Willi syndrome. Oenone Dudley, Françoise Muscatelli, Journal of intellectual disability research, 2008

5. CORELATION OF CLINIC, GENETIC AND EPIGENETIC ASPECTS IMPLICATED IN THE ETIOLOGY OF PRADER WILLI/ANGELMAN SYNDROMES: MODEL OF MULTIDISCIPLINARY ABORDATION FOR RARE DISEASES IN ROMANIA

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The aim of the project is the integration of a multidisciplinary approach for Prader Willi and Angelman syndromes, distinct genomic diseases, with a neurodegenerative component. The main lesion is localized on the 15q11.2-13 chromosome caused during genitors' gametogenesis and reproduction process. This deficiency may be represented by deletion, uniparental disomy and altered epigenetic marking through DNA methylation or chromatin modification. Both diseases are caused by changes in parent contributions on the aforementioned region. The modifications in imprinting diseases like Prader Willi and Angelman, require: the study of regional regulation for genetic/epigenetic processes in clusters; the contribution of specific genes regulating the imprinting of cluster formation; enhancer activity, the DNA and chromatin replication timing, as well as correspondence between histones, protein complexes, iRNA and epigenetic processes from DNA. The project envisages the cytogenetic and molecular genetics approaches in the syndromes diagnosis, establishing a European research network partnership. The research will enable: 1. establishment of a strategy in definition for genotypes PWS/AS, 2. correct identification of the genetic defect, 3. deciphering the variation in gene expression/ gene subsequence and their regulation pathway mechanism, 4. the involvement of epigenetic factors that modulate (enhancing/decreasing) the severity of phenotypic

aspects into the diagnosis protocols.

The project envisages the understanding of early development processes and hopefully will contribute to elucidate the basic mechanisms determining the clinical classical modifications. Creation of a database will permit the collection of clinical, genetic and epigenetic data from Romania and further the integration into the European data base. Due to high mortality and morbidity associated with PSW/AS, this project will be the ground for new clinical studies to establish guidelines for diagnosis and treatment in order to improve the quality of medical practice and an improvement of medical and social standard for affected patients with PWS/AS.

The Romanian PWS association is involved in PC 6 (The European Prader-Willi Syndrome Clinical and Basic Science Research), project that identifies and pulls together different national teams involved in these topics. The medical research in rare genetic disease supposes to be multicentric and even international due to the limited number of cases. To avoid bias we need large series of patients, to assure statistically correct answers necessary for developing international good practice standards.

The research from Romania should be more active in the rare disease area, that's why we propose an epigenetic new European approach realized by prestigious teams. Through this new type of partnership between universities, research institutes,

hospitals, nongovernmental associations of affected patients we try to redefine connections between fundamental research and the medical

practice, developing a multidisciplinary investigation model for rare disease in Romania.

6. GENERAL AND SPECIFIC OBJECTIVES OF THE PWA-CLIN-EPI-GEN PROJECT

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General objectives

- Implementation of new molecular methods for genetic/epigenetic investigation and establishment of national centers with high expertise in approaching the two syndromes, the rare genetic diseases that will develop educational reference and release centers.
- Evolving efficient partnership with patients associations through specific modalities like dialogue. The power of these associations will propel the research, will inform the patients and will respond to civil society questions.
- Establishing international collaboration and partnerships with researchers having similar scientific preoccupations, establishing partnerships with other National Organizations PWS, IPSWO and affiliated research groups from each country aiming financial support on programs that intend to stimulate collaboration between specialists, researchers and nongovernmental organizations.
- Developing a multidisciplinary partnership to build a common platform of activities for new innovative solutions in respect to rare disease needs. These new bridges of real and effective collaboration will ascertain on the national level the creation of a solid network comprising institutions with high expertise in this domain, well connected to other national or international research networks. Publications of the research work in well-known journals with high impact factors for enlargement of Romanian research

visibility in international space of rare disease.

Specific objectives

- Developing of a clinical interdisciplinary investigation algorithm specified for SPW/SA (comprising the aspects from genetics, paediatrics, endocrinology, neurology, psychiatry, psychology, orthopaedic surgery, neurology, dietetics) and clear evaluation after elaboration of scores that will track down easily the suspicious cases and will permit genetic/epigenetic investigation, aiming a rapid and correct diagnosis and an efficient early treatment.
- Developing of a complex protocol of investigation in SPW/SA through introduction of the genetic /epigenetic tests relevant for subtypes SPW/SA.
- Identification of some possible intrinsic factors (individuals) and extrinsic factors (environmental) responsible for determining alteration of imprinting process, transgenerational based on applying questioners adapted to family belongers, having as much as possible in respect with number of the generation.
- Communication and dissemination of the results of the research through publishing in national and international journals.
- Ascertain of a standardized base for SPW/SA and gathering clinical data, genetic, epigenetic from all the country and European integration, describing a European model resulting a National Registry for Rare Disease.

7. GENERAL HEALTH IN CHILDREN WITH PRADER-WILLI SYNDROME

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Prader-Willi syndrome (PWS) is a well described complex genetic condition. To treat the many clinical symptoms extending from birth into adulthood a multidisciplinary approach is needed.

The presentation focuses on the various medical symptoms of PWS which appear during childhood, as well as their treatment possibilities. In the treatment process, many professionals are involved. However, the important day to day treatment is carried out by the family, teachers and other close contacts. The following symptoms and the possibilities of treatment will be described: Dysfunctions relating to hunger and

satiety, overweight, pain, temperature (including the regulation of), salt balance, sleep, and endocrine disturbances including growth hormone deficiency. Also abnormal symptoms from eyes, teeth, joints, spine and skin, as well as behavioral problems, are considered. The importance of guidelines or checklists for the continuous care of the general health in children is stressed. These guidelines can be of help for the families, medical persons and other professionals, in securing the most optimal treatment and quality of life for children with PWS.

8. A SHORT REVIEW OF THE FIRST CAREGIVERS' CONFERENCE IN HERNE, GERMANY 2008

Hubert Soyer and Norbert Hödebeck-Stuntebeck

In the workgroup "Environmental structures for PWS-living" different forms of residential services for persons with PWS were compared. There is agreement that guidelines for adequate environmental support should comprise the guarantee of food security (e.g. diet plans), but also further areas of life like weight control, a structured daily plan with work, fitness programs, recreation opportunities by trained caregivers. To weigh up the balance between control and self-determination will be the challenge.

The workgroup "Communication with persons with PWS" dealt with the way what you say, when and how you say it considering the unique characteristics of persons with PWS like cognitive rigidity or emotional dysregulation. During disruptive behavior of persons with PWS the caregivers have to avoid several approaches like discussions or reproaches; active listening is a key way of the staff.

The workgroup "Neurological, psychological and cognitive aspects of behavior management" summarized the neuropsychological vulnerabilities of the persons with PWS (e.g. stress sensitivity) and strengths (e.g. good visual processing). Guidelines for an adequate environment should include the aim of prevention in form of stress reduction (food

management, activity plans,...). Adequate forms of behavior management were discussed taking into account reinforcers or contracts with the involved person with PWS.

Workgroup "Sports, fitness and motivation" emphasized the important role of a fitness program with regard to the health of the person with PWS and the weight control. A continuous program is helpful. Different motivation factors were looked for like reinforcers or fitness in groups.

The Workgroup "Nutrition management" demonstrated examples of special diets for persons with PWS due to their low calorie needs. Guidelines involved the suggestions for a lifelong obligatory diet in an individualized form for the persons with PWS, but also further aspects like daily activities. The caregivers need more information about adequate nutrition.

The participants of the workgroup "Crisis management" discussed ways of reducing the frequency and intensity of stress situations for caregivers and persons with PWS due to their typical behavior problems like tantrums. Good prerequisites for coping are for example well-structured teams with continuous reflection, proactive planning,

communication about behavior management and problematic situations.

The participants of the workgroup “Communication between caregivers and families” emphasized the importance of a proactive and routine contact of the caregivers with the families of the persons with PWS, because the persons with PWS often have close relationships with their relations. Active listening is an important way of communication. One goal is the growing independence of the person with PWS and to assist parents accepting this process.

The participants of the workgroup “Environmental supports for work situation in sheltered workshops” compared different work structures of some countries. There is agreement that a clear structure is necessary (e.g. a given food security, clear rules, prepared

changes). A good prerequisite to meet the needs of the persons with PWS is an individual skill assessment for an individual support plan to find the adequate work form with a minimum of stress. The wishes of the persons with PWS should be considered. Challenges for the future will be more inclusion.

The Workgroup “Aspects of psychological work with people with PWS” examined the role of the psychologist with regard to the persons with PWS providing direct supportive counseling or therapy to the person with PWS or indirect counseling of the caregiver team.

For diagnosis, finding out strategies for stress reduction or catalyzing processes the support by a psychologist can be helpful.

9. THE FLUORESCENCE IN SITU HYBRIDIZATION (FISH) ANALYSIS IN PRADER-WILLI SYNDROME

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Fluorescence in situ hybridization (FISH) technique is an important analysis not only in cytogenetic research but also in routine clinical diagnostics for Prader-Willi Syndrome. It is reported in the literature that 70% of PWS patients present the deletion of the 15q11.2-q13 region on the paternal chromosome, deletion that will be diagnosed using FISH analysis with specific probes. About 20-30% of the PWS patients have maternal uniparental disomy, the rest of 2-5% patients displaying an imprinting defect. We have performed, at the Department of Medical Genetics in Timisoara, conventional cytogenetic analysis and FISH technique for the first 5 PWS patients, included in a multidisciplinary study, who were diagnosed according to the clinical criteria of the syndrome. The

cytogenetic analysis, using trypsin and GTG banding revealed normal karyotypes without translocations for all the patients. For four of the patients FISH was performed using Abbott SNRPN (SO)/CEP15 (SG) /PML (SO) probe, and for one patient Abbott LSID15S11 (SO)/CEP15 (SG) probe was used. Surprisingly, all result came out negative for the deletion. This is in contrast to the data from literature. For one of the patients the diagnosis of PWS is confirmed by mutilation analysis, as for the others is still in study. In order to correctly diagnose the molecular class for the PWS patients, besides DNA methylation analysis, DNA polymorphism analysis and mutation analysis for the imprinting center, FISH analysis should also be performed.

10. AN EPIGENETIC GENE REGULATORY SYSTEM PROPOSED TO BE STUDIED FOR ESTABLISHMENT OF COMPLEMENTAL BIOMARKERS IN IMPRINTING DESORDERS (Prader Willi and Angelman Syndromes)

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The clue for searching new epigenetic approaches for deciphering the molecular mechanism of rare diseases, unexplained frequently by mutations or genetic modifications at DNA level, is to consider chromatin as the genetic mammalian material, which may be biochemically modified at both DNA and histone levels, without changing the nucleotide sequence. Until recently, such epigenetic modifications were merely neglected, but 30 years of research in epigenetic domain proved their tremendous impact on gene expression and chromosomal stability.

Our project is therefore targeting new molecular methods for the investigation of the 15 chromosome critical region (15q.11-13q) in order to detect certain altered epigenetic patterns such as histone and DNA methylation in connection with the genetic analyses,

such as FISH microdeletion detection. Moreover, a consideration of the transgenerational effect of certain environmental factors linked with parents' and grandparents' diet as part of their lifestyle is a novelty of our project, as these are presently associated with epigenetic factors too.

Epigenetic specific methods such as methylation specific PCR mediated by mutagenesis through bisulfate treatment with specific primers for certain critical regions of 15 chromosome will be used together with RT-PCR estimation of the involved sequences expression in order to obtain answers regarding the alteration in imprinting center region that resulted in altered imprinting process and even aberrant chromosomal deletions.

11. COMMUNICATION, COGNITIVE DEVELOPMENT AND BEHAVIOR FOR CHILDREN WITH PWS

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The goal of this project is to approach communication on insuring the child's and the family's mental health through the perspective of the neuropsychiatrist who works in the clinic with crisis situations, as well as through the lens of the team supervisor, who must insure the professional formation of clinician specialists.

The attitudes of the medical service staff in the fields of genetics, obstetrics and gynecology has an initial impact on the family when they “discover that the fetus and latter the newborn could be ‘different’ in physical appearance or mental predisposition.” Relaying medical information or simply medical suppositions on the child's diagnostic unleashes a cascade of emotional reactions that can be translated in nonverbal symbolic indicators for the family, which may in turn have positive or catastrophic implications

on the acceptance of the situation, on the inclusion of the child and on its accessing the warmth and tenderness of the daily family life. These early reactions may determine not only the family's predisposition to integrate the special need child but may settle on a path that could lead to neglect and abandonment. Mental health prevention of potential neglect presupposes a holistic, systematic understanding of the family and the community's values and reactions. This work must be based on scientific data gathered from multidisciplinary studies. The concepts of cognitive and behavioral development are used here address not just the child but also its family and are throughout used in relation to the formation of clinical specialists... so that their involvement at different life stages be done through the prism of individual needs and through the use of

scientific methods and knowledge developed up to that moment. It is imperative that we develop an algorithm of social intervention and systemic strategies centered

on the community from the perspective of the child's rights.

12. PSYCHOLOGICAL APPROACH TO CHILD AND ADULT WITH PRADER WILLI SYNDROME

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Aim: The lecture is aimed at revealing the main psychological problems in children and adults with Prader Willi Syndrome. Prader Willi Syndrome is a complex medical condition that affects boys and girls equally. It is characterized by neurological impairments causing altered pattern of growth and development. People with Prader Willi Syndrome have a compulsion to eat which can lead to further problems such as obesity with premature death.

Description: The focus of the course is to point out behavioral characteristics of the children and adults with Prader Willi Syndrome in order to obtain a clearer view of the problems confronting a wide range of people: patients, parents, practitioners, social-workers, etc. Children with Prader Willi Syndrome may undergo problems ranging from those related to physical aspects to those concerning the psycho-behavioral ones such as: short stature; small hands and feet; hypotonia, mild to moderate global developmental delay; learning difficulties; preservative

thinking; delayed or incomplete puberty is also common. In adolescents we can find a more prominent manifestation of some of the problems mentioned above such as: emotional instability, difficulties of socialization and depression. In adults the behavioral phenotype may include: a preoccupation with food; mood instability; impulsiveness; inactivity, repetitive speech patterns; lack of social skills and adaptive behavior; excessive sleepiness, etc.

We also want to emphasize the role played by the early management strategies and interventions such as: psychotherapy, speech therapy, occupational therapy as well as prevention and management of obesity in the ameliorative process of the disease.

Conclusions: Appropriate interventions, ongoing support and a holistic approach to care (effective communication between patient, family, social network, educators, etc) improve the life quality of people with Prader Willi Syndrome.

13. WORKING AT EUROPEAN LEVEL IN RD AS A NECESSITY

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Rare diseases are considered as a priority in the EU health and research programs. EU law and funding for R&D projects aim to promote the development of orphan drugs for patients with rare diseases. The EU is promoting through their programs adequate prevention, diagnosis and treatment of rare diseases by creating networks, sharing experience and training, and disseminating knowledge.

According to DG SANCO [The Health & Consumer Protection Directorate-General], the main objectives are:

The *Community action program on rare diseases*, including genetic diseases, was adopted for the period 1 January 1999 to 31 December 2003. Program' main aim was to contribute, in co-ordination with other Community measures, to ensure a high level of health protection in relation to rare diseases. As a first EU effort in this area, specific attention was given to

improving knowledge and facilitating access to information about these diseases.

In the *second program of Community action in the field of health (2008-13)*, rare diseases are now one of the priorities of EC. According to the DG SANCO Work Plans for the implementation of the Public Health Programme, the two main lines of action are the **exchange of information** through European information networks on rare diseases, and the **development of strategies and mechanisms for information exchange and co-ordination at EU level** to stimulate international co-operation.

The European Commission adopted the 11 November 2008 the *Commission Communication COMM(2008)*

679 final to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions on Rare Diseases: Europe's challenges and a proposal for a Council Recommendation on a European Action in the field of Rare Diseases setting out an overall Community strategy to support Member States in diagnosing, treating and caring for the 36 million EU citizens with rare diseases.

Conclusions: The limited number of patients affected by one certain rare diseases and the fragmentation of expertise about them across the European Union makes rare diseases a prime example of where working at European level is necessary and beneficial.

14. GENERAL HEALTH IN ADULTS WITH PRADER-WILLI SYNDROME (PWS)

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Prader-Willi Syndrome (PWS) is a well described genetic condition. Adults with PWS still have many of the typical symptoms seen during childhood and adolescence, but new clinical symptoms will typically arise. Thanks to more knowledge about PWS many more survive the childhood years, and the population of adults with PWS is growing worldwide.

The presentation focuses on the various possible medical symptoms in adults with PWS. The most apparent symptoms most often met are overweight, hypogonadism, edema of legs, problems in joints and teeth. Additional symptoms can be overlooked, such as osteoporosis, heart and lung diseases, diabetes type II,

side effects of some medications, altered temperature sensation and regulation and high pain threshold. The latter leading to difficulties in diagnosing fractures and severe episodes of sometimes fatal stomach distension. Also psychiatric diseases can be overlooked or misdiagnosed. The important day to day treatment is carried out by the family, professional caretakers or both. The importance of guidelines or checklists for the continuous care of the patient's general health is stressed. These guidelines can help the families, medical persons and other professionals, in securing the most optimal treatment and quality of life for adults with PWS.

15. MULTIDISCIPLINARY APPROACH FOR THE MANAGEMENT OF INDIVIDUALS WITH PRADER-WILLI-SYNDROME

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Aim of the study. Prader- Willi syndrome is a complex neurobehavioral disorder affecting multiple systems with many manifestations relating to hypothalamic insufficiency. The phenotypic features include infantile hypotonia, developmental delay and

mental retardation, behavioral disorders, characteristic facial appearance, obesity, hypogonadism, and short stature. The obesity and the behavioral problems are the major causes of mortality. Besides learning ability, speech and language, self-esteem, emotional stability,

social perception, interpersonal functioning, and family dynamics may all be adversely affected by PWS. Since PWS is a complex disease, affected individuals need a multidisciplinary approach treatment by a team of professionals. We report our experience with a sample of PWS subjects.

Methods. The multidisciplinary team includes pediatrician, geneticist, neurologist, endocrinologist, dietitian, psychologist, pedagogist, social worker and, with regard to the habilitation aspects: educator, occupational therapist, psychomotor therapist, physical therapist, speech therapist. Protocol interventions are: diet, exercise, physical, psychomotor and occupational therapy, animation, educational and social support, psychological counseling and age-dependent parent training.

Cooperation between family and team members, during the phases of diagnosis and treatment, is needed to reach successful outcomes.

The above program is completed with a 45-day first term in our Institute where the PWS subjects and their families are trained, followed by a six-month term of home management. This cycle is repeated every six months.

Results. Our preliminary data show weight loss, improvements in: family's educational management, coordination of movements, self-management, and a reduction of anxiety, mood liability and self-injury.

Conclusions. The multidisciplinary approach is a valuable instrument to manage PWS individuals.

16. SELF INJURY AND PRADER-WILLI SINDROME

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Aim of study. Self Injury Behavior (SIB) is one of the signs frequently present in syndromes associated with intellectual disabilities (ID). SIB is defined as a behavior that produces immediately, or in time, physical damage to one's body. SIB is reported to occur in 80% of the Prader-Willi Syndrome cases (PWS). The most frequent behavior is skin picking, which can involve various areas of the body.

Methods: A specifically constructed card was developed for revealing self injurious behaviors and was administered in interview form to the families of PWS individuals under cure at the IRCCS Oasi Maria SS;

The sample is composed of 15 individuals with PWS and with ID of different levels.

Results: Data indicate that 73% of the sample presents a form of SIB. Age onset more frequent is in the range 0-6 years (91%).

The areas of the body principally involved are: the backs of the hands, the arms, the head, the legs,. The most common SIB in our sample are: nail tearing and scratching and skin picking.

Conclusions: The prevalence of SIBs in our sample, the types and localizations of these behaviors tend to confirm the data reported in literature. Besides, we have obtained good outcomes by cognitive-behavioral approach.

17. EFFECTS OF GH THERAPY IN TEN SUBJECTS WITH PRADER-WILLI SYNDROME

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Aim of the study: Recent reports have described improvements in alertness, activity level, extroversion,

personal relationship and body composition in a non Prader-Willi (PWS) population with GH deficiency.

We hypothesize that GH administration to children with the PWS, besides the stimulation of linear growth, would improve body composition, fat utilization and physical agility. However, the behavioral impact of GH treatment in this population remains incompletely reported

Our purpose is to measure the effects of GH administration on the same parameters; in addition we have evaluated the psychosocial burden, including emotional, behavioral, and cognitive disturbances.

Methods: We have studied 10 GH-deficient patients in treatment with GH. The evaluation has been made after 1 year.

Intelligence Quotient (IQ) was assessed by WISC-R scale, the attention deficit was monitored by computer attention assessments, and the adaptive profile by VABS.

The total body lean mass, fat mass and bone mineral density (BMD) were measured by DEXA.

Results: We have observed that the treatment with GH increases lean mass, improves weight maintenance, muscle tone and physical agility.

IQ remains stable, with little improvements in the adaptive profile.

Conclusions: Preliminary analysis suggests that GH-therapy improves the body composition and the behavioral phenotype.

18. ENDOCRINE APPROACH IN PRADER WILLI SYNDROME PATIENTS

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Prader Willi syndrome (PWS) is a genetic disorder with complex hormonal, metabolic and behavioral interrelations. The good prognosis is dependent upon a precocious diagnostic, ideally in the first years of life, in order to prevent the life threatening complications. The Holm's criteria are required for clinical diagnosis but definitive certification requires genetic assays for deletion of 15q11-13. Children with PWS requires endocrine evaluation since early childhood, due to excessive appetite, obesity, hypogonadism, delayed puberty and short stature. Later in life, morbid obesity leads to diabetes, hypogonadism - to osteoporosis, and central hypocorticism could be associated.

Growth axis is deficient, as shown by low GH in stimulation tests, low IGF1 and low IGFBP3. This correlates with beneficial effects of GH treatment in PWS children upon lean mass, stature and metabolic parameters, as shown by several authors. Excessive appetite and related obesity can be treated by Orlistat,

sibutramine or bariatric surgery, but none of the procedures proved enough safe and with significant improvement. Substitutive therapy for hypogonadism, in agreement with genetic and gonadic sex, is also beneficial for both metabolic and psychological reasons. Central hypocorticism can be evaluated and treated with limited results. Secondary diabetes and dyslipidemia often requires a metabolic approach and treatment. Psychological approach is useful for patient and families, with limited benefits concerning the food behavior.

In conclusion the endocrine evaluation and treatment is part of a multidisciplinary approach for the PWS patient. The knowledge of polymorphous features of PWS along the life is essential in preventing the development of complications by establishing a long-term management of hormonal, metabolic and mental problems.

19. GENOTYPE-PHENOTYPE CORRELATION IN PRADER WILLI SYNDROME - AN OVERVIEW OF THE LITERATURE

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Prader-Willi syndrome (PWS) is a contiguous gene syndrome caused by the loss of function of genes situated within the 15q11-q13 region. The molecular events underlying the disorder include interstitial deletions (70%), uniparental disomy (UPD) (25%), imprinting center defects (<5%), and rarely chromosomal translocations (<1%). Distinct differences have been reported between individuals with Prader-Willi syndrome resulting from deletion compared with uniparental maternal disomy 15 in physical, cognitive, and behavioral parameters. The goal of this paper is to summarize the most recent studies regarding the genotype-phenotype correlation in Prader Willi syndrome. Adaptive behavior, obsessive-compulsive behaviors, reading, math, and visual-motor integration assessments were generally poorer in individuals with Prader-Willi syndrome and the T1 deletion (big) compared with subjects with Prader-Willi syndrome with the T2 deletion (small) or uniparental maternal disomy 15. Four genes have been identified in the critical chromosomal region being implicated in compulsive behavior and lower intellectual ability observed in individuals with Prader-Willi syndrome with T1 versus T2 deletions. The presence of hypopigmentation is more frequent in patients with a deletion than in patients without, and

the average birth weight is lower in patients with a deletion than in patients without. Some data confirm an increased maternal age in the non-deletion group. Patients with maternal uniparental disomy (UPD) are at greater risk for autistic symptomatology than those with paternal deletions of 15q11-q13. Despite the positive correlation between the body-mass index and apnea-hypopnea index, the type and severity of sleep disordered breathing were not predictable based on underlying genetic defect. Scoliosis prevalence was not affected by the genotype or by growth-hormone treatment. Lately, studies have shown there is no significant gender or genotype pattern differences among the height, weight, body mass index before and after GH treatment. The high percentage of central adrenal insufficiency in PWS patients might explain, in the recent past, the high rate of sudden death, particularly during infection-related stress. There was no significant difference reported in age, gender, genotype, and body mass index score between patients with central adrenal insufficiency and those without. It is important to confirm the clinical diagnosis and to establish the genetic mechanism responsible for PWS, considering their important consequences regarding the prognosis and genetic counseling.

20. ORTHOPEDIC AND SURGICAL APPROACH IN PRADER WILLI SYNDROME PATIENTS

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Prader-Willi syndrome (PWS) is a congenital chromosomal disorder with an incidence of 1 in 25,000–30,000. Usually PWS is not diagnosed until rapid weight gain leading to obesity. Features in persons with PWS suggest a hypothalamic dysfunction: hyperphagia, sleep disorders, deficient growth hormone secretion, and hypogonadism. PWS patients suffer from various medical conditions that

require the attention of many professionals. This presentation focuses on the possible medical condition that requires the involvement of a surgeon. Genital hypoplasia and cryptorchidism are constant findings in PWS boys and the justification for and timing of surgical exploration and orchiopexy are controversial. Musculoskeletal disorders like scoliosis are also universal features of PWS and consultation with an

experienced orthopedist is essential. Gastrointestinal pathology is the most important feature of PWS. Generalized hypotonia in the neonate with PWS leading to weak suck reflex often require nasogastric tube-feeding even gastrostomy. Gastric dilatation, abdominal and rectal pain, rectal fissures, hemorrhoids, and rectal bleeding (bright red blood) may occur and require treatment in surgical compartment. Obesity is the major feature of PWS. The primary health issues in PWS are exacerbated by obesity and related findings. Obesity can become life-

threatening if not controlled. Surgical options for weight management are not generally recommended in PWS but bariatric surgery should be considered in severe cases. Despite that experience with bariatric surgery in PWS is limited there are some reports of relatively long-term successes in selected patients. A multidisciplinary approach is needed to treat individuals with PWS. Primary care physicians should be able to treat most patients with PWS but there are several medical conditions in PWS patients for which consultation with a surgeon is mandatory.

21. THE ASSOCIATED OF MORBID OBESITY, SHORT STATURE AND MENTAL RETARDATION – CONSIDERATION IN A PRADER WILLY SYNDROMES - CASE PRESENTATION

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Introduction: Prader-Willi syndrome is characterized by short stature obesity done by continuous appetite, caused by a defect in the hypothalamus. The disease is genetic conditioned.

Aim: To sensible the community about the disease by present the clinical picture and laboratory dates.

Case presentation: GA, 14 years old girl, admitted in our Hospital in 2006 for persistent cefaleea, insatiable hunger, compulsive eating, obesity, earning disabilities. She is carry by her grandmother. Clinical examination reveals: height 140cm (the height according to age 150), SDS- 1.5, weight 88Kg (the weight according to the height 54Kg), BMI 44.89kg/m², dimorphic faces (Almond-shaped and misalignment eyes, thin upper lip, narrow forehead, down-turned mouth), acneea, no puberty, delay in motor skill development and cognitive delay. The labs data's show Normal proteic and lipid metabolism, OGTT with 75g of glucose shows impaired glucose tolerance (glycaemia at 2h 142mg%), normal

insulinemia (14.5UI/ml) , HOMA 5, LH = 02 mIU/ml, FSH = 0.7 mIU/ml, E₂ = 7pg/ml). Cardiac exams reveal integrity of the septum, valvulas and pericardium. The psychological evaluation shows behavior problems, such as anger and inflexibility inadaptability with the children in school. MRI of the cranium - showed a reduction in pituitary.

The cariotype deletion on the chromosome region 15q11. The child do not received Growth hormone therapy because the poor family don't followed the medical instructions and they didn't came to control.

Conclusions:

1. All obsesses children with particularly phenotype must be suspected to be PWS.
2. It is necessary to educate the society, school teachers etc, about this syndrome.
3. The children with PWS may benefit also in our country of the treatment with GH.

22. PWS' QUALITY OF LIFE: SOCIAL ADJUSTMENT AND COGNITIVE SKILLS

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Prader Willy syndrome is characterized by learning disability and behavior problems of genetic origin related to hypothalamic hypofunction.

We study the relationship among cognitive profile, social skills and behavior problems in PWs and evaluate them according to diagnostic criteria for autism (problems in social interactions, communication and stereotyped behaviors).

Method: 15 children, aged 7–11 years, assessed through: Wechsler Intelligence Scale WISC-r, Peabody, test created for Emotional States Identification, Gilliam Autism Rating Scale (GARS) for parents, Social Skills Rating System (SSRS) for parents and teachers.

Results: mean IQ: 62 (range 47-80), Autism Quotient: 68,86 (range 55-83) lower than diagnosis criteria (90). All showed greater ability in recognizing the emotional states of the characters than in understanding their interpersonal relationships. Negative correlations: Autism Quotient and Verbal IQ (Information). Autism

Quotient and Emotional States Identification, Autism scales of Socialization and Assertivity SSRS, Internalizing and Performance IQ. Positive correlation: Iperattivity and Externalizing (SSRS parent form). Significant difference between parents and teachers in Assertion skills.

Conclusion: PWS show some behavior problems similar to autistic without reaching the diagnosis. PWS, having difficulties to understand the behavior or emotional states because of learning disabilities, show inadequate -internal and or external- responses. Cognitive deficits and specific behavior problems worsen the risk of isolation and depression. Teachers perceived more social problems than parents. Interacting with peers, due to PWS social and cognitive deficits, seems to be a source of particular stress in the classroom. PWs need specific precocious treatment in order to improve their social skills and self-esteem.

23. SLEEP APNEA SYNDROME: PATHOGENY, DIAGNOSTIC, TREATMENT

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Sleep Apnea Syndrome (SAS) is defined as a cessation of breathing characterized by repetitive episodes of airway obstruction caused by collapse of the upper airway during sleep. The prevalence is approximately 20 % if defined as an apnea-hypopnea index (AHI, the number of apneas plus hypopneas per hour of sleep) greater than five events per hour. Risk factors include obesity and craniofacial or upper airway soft tissue abnormalities (abnormal maxillary or mandibular position or size, tonsillar and adenoid hypertrophy, narrow nasal cavities), while potential risk factors include heredity, smoking, and nasal congestion. Approximately one-fourth has a genetic multifactorial basis. Diagnostic. Classic features include excessive daytime sleepiness, loud snoring, fatigue, obesity.

There is a strong association between obstructive sleep apnea syndrome and cardiovascular diseases including systemic hypertension, congestive heart failure, arrhythmias, stroke, angina pectoris. Associated conditions include adenotonsillar hypertrophy, nasal obstruction, hypothyroidism, acromegaly, Down syndrome, micro - retrognathia. Severity is assessed by polysomnography which includes an electroencephalogram for sleep staging, bilateral electro-oculograms, submental electromyogram, nasal and oral air flow, respiratory muscle movement, oxygen saturation, electrocardiogram, anterior tibialis electromyogram and sleep position.

Treatment. The options include lifestyle modifications (weight loss, smoking cessation, avoiding sleeping in

the supine position), continuous positive airway pressure (CPAP, the gold standard for treatment), oral appliances, surgery. Tonsillectomy and adenoidectomy is the preferred treatment for SAS in children. Proper

patient selection and long-term follow up may increase the effectiveness of the therapies and decrease the morbidity and mortality associated with the syndrome.

24. NEW TECHNIQUES OF DIAGNOSIS IN PWS

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Prader Willi syndrome is a genetic disorder produced by different abnormalities of the 15q11-q13 region. Clinical picture is defined by severe hypotonia and feeding difficulties in early infancy. After the age of 2 years, a marked increase of appetite appears and leads to severe obesity. Dysmorphic face, small extremities, hypogonadism and developmental delay are frequently associated. Genetic causes vary from chromosomal deletions, to microdeletions and imprinting defects. The classic investigation protocol includes: karyotype (to detect deletions), FISH analysis (for microdeletions) and methylation analysis (for imprinting defects). The main inconvenient of this

protocol is represented by the cost of the investigation (especially FISH). We present the introduction of the MLPA (Multiplex Ligation Probe Amplification) technique as a screening test for microdeletions. MLPA is a cheap and reliable method that can be used as a screening test after performing the karyotype. By using this strategy only abnormal cases have to be confirmed with FISH, with a major decrease of the investigation global cost. A comprehensive presentation of the genetic causes and corresponding genetic tests (with advantages and disadvantages) will be included.

25. IMPLICATION OF NGO IN EDUCATION OF PATIENTS WITH RARE DISEASES AND GENERAL POPULATION

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Vicepresident - Save the Children Romania

Introduction. In the absence of a governmental strategy for rare diseases in the 10 years after 2000, the most neglected group of disease in Romania, the social inclusion of these children remains to the private initiative of NGO's. The health-sector reforms include reduced direct state involvement and searched for alternative sources of funding with a wider participation of the non-governmental sector. Aim of our paper is to focus on the changes in life quality of children with these diseases, after teamwork and a multidisciplinary approach. **Material.** In our NGO partnership (a branch of a national NGO – Save the children Romania and another local one) we worked together with 32 children and youngsters affected with different rare diseases. They participate from 1999 in a Club organized by young volunteers from our organizations. **Results.** Children have interacted with

volunteers and benefited by becoming more assertive and by achieving more developmental targets. Assessment of their progress might establish the exact role of communication among the Club (parents, volunteers, other children). The parents have witnessed important cognitive and behavioral changes in their children, facts that at this moment are our method of evaluating their progress. **Conclusions.** The health of people with disability and the social integration can be improved if they have every opportunity to enjoy family life, education, friendship, access to public facilities and freedom of movement. Action should be aimed at counteracting helplessness and stigmatization. We provide expertise and experience in a community organization, which the government services do not possess, as well as increase the delivery of community-based primary health care.

26. VOLUNTARY ACTIVITY, STUDENTS AT FACULTY OF MEDICINE FOR RARE DISEASES PROMOTION

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Introduction. A *rare disease* is considered that one which affects less than 1 of 2000 persons. Today doesn't exist a treatment proper for the 8000 rare diseases which were identified (75% of them are affecting the children). Although, the diseases are rare, there are many patients. Statistically, 6-8% of the population suffers from a rare disease, which means that there are 1,3 millions suffering people in Romania. The rare diseases are chronic, progressive, degenerated, infirming, most of them genetic and in most cases threaten the life, with high levels of complexity and suffering. Realizing how important is the efficiency of a team of students at *university of medicine* willing to apply for activities that are having as a goal the improvement of the life quality of the children affected from rare diseases through activities which have in view: counseling and supporting the parents of these children, but also the sensitizing and informing the community regarding to this subject.

Materials. People with rare diseases have often similar problems, like tardy diagnostic, the absence of the information quality, the absence of the *adequate health care* and the inequality in the access of medical treatment and care. The medical students come to action in such cases performing activities for counseling, informing, supporting the parents of these children to become efficient partners of the medical

staff in taking care of the *children with special needs*. It is essential also the acquisition of the materials and instruments necessary to gain the beneficiary confidence, to exceed the embarrassing, distrusting, conjecture, guiltiness feelings of the family and to be able to create a favorable communication between patients, their parents and medical students. **Results.** Development of the modes of life at the children with disabilities produced by genetic rare diseases. The increasing of the professional grade of human resources involved in providing specialized medical services. Development of the practical skills to communicate and collaborate with the parents of the persons affected from rare diseases. **Conclusion.** The first step that medical students do for the future of their career, but also realizing that they were very efficient and useful only offering a part of their free time to these families which have children with rare diseases. Implementation of some programs and realizing some projects in which to be active involved medical students will always be efficient for parents who have children suffering from rare diseases. For the students, volunteering it might be an outlet for their natural talents, a road-test for their new career.

Keywords: rare disease, volunteering, family, community, children, medical student, informing, development

27. THE EDUCATORS INSTRUCTION IN INCLUSIVE METHODS

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Aim: The aim of the workshop is to reveal the special needs of education in people with Prader Willi Syndrome. It is a well-known fact that Prader Willi Syndrome includes learning disabilities, poor social, emotional skills and weakness in math and writing. At the same time, some type of skill were noted which are considered as strengths. These are reading and art skills. **Description:** The topics of the workshop will focus on: the pedagogical principles of the education for children with Prader Willi Syndrome, the different methods and techniques used in speech therapy, in

recuperation of the language processing, memory and the special rules in the organization of the appropriate physical and social environment to facilitate learning. We will also present some examples of good-practice when working with people with Prader Willi Syndrome at different age stages. **Conclusion:** Early intervention, supported change and choice of appropriate lessons and activities, acknowledged efforts contribute to motivating the children to persevere in accomplishing the learning and life skills.

28. THE MANAGEMENT OF SLEEP APNEA SYNDROME IN PRADER - WILLI SYNDROME

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Prader Willy Syndrome (PWS) is a rare genetic disorder distinguished by the high prevalence of sleep-breathing disorders, mostly obstructive sleep apnea syndrome (OSAS) with repetitive upper airway collapse during sleep resulting in hypoxia and sleep fragmentation and central hypoventilation apnea (CHA). Craniofacial characteristic such as narrow bifrontal diameter, almond-shaped palpebral fissures, narrow nasal bridge, and down-turned mouth. The largest problem associated with PWS is severe obesity. Patients with PWS have hyperphagia and require restricted access to foods to minimize weight gain. Binge-eating episodes may predispose patients to development of food poisoning and acute gastric dilation. A program of a well-balanced, low-calorie diet, regular exercise, and close supervision to minimize food stealing should be instituted to prevent obesity and its consequences. Disturbed sleep in

children and adults should prompt a sleep study, as treatment may be available. OSA is diagnosed with polysomnography and treatment depends on the cause and may include tonsillectomy and adenoidectomy and/or continuous positive airway pressure (CPAP). Efficiency is almost 100% and compliance at 5 years is 50-80%. Untreated OSA can have serious cardiovascular complications including death. Central hypoventilation is a disorder of decreased breathing in sleep which causes daytime sleepiness, frequent in PWS due to decreased muscle tone and mass, excessive obesity and decreased drive for breathing. In CHA bi-level positive airway pressure (BiPAP) is alternative treatment. To assure appropriateness of exercise program and diet, monitor height, weight, and BMI monthly in infancy, every six months in the first decade of life, at least annually thereafter.

29. NATIONAL PLAN FOR RARE DISEASES IN ROMANIA

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Objectives of the National Plan for Rare Diseases:

I. Defining an institutional setting to assure the progress of the problems that rare diseases cause.

Activities:

1. Creating an institutional setting to assure the development of services to prevent diagnosis and rehabilitation of patients with rare diseases.

Founding the National Committee for the Persons with Rare Diseases- NCPRD.

II. The development of regional centers of reference – there are 3 regional centers within the system currently in 2008 concentrating on university centers, collaborating with centers of expertise, all taking place within the European Referencing system.
- plan to have 5 regional centers by 2013

Aim of the referencing centers.

- To facilitate the diagnosis and to define a strategy of therapeutic and psychological care, also to help with social problems.
- To elaborate on how people are cared for with MS and ASP
- Epidemiological research and development.
- To provide training and information for the professionals working in this domain and also for patients and their families.
- Coordinating and providing medical and social care.

- To act as a mediator between ministers and the associations for patients.

Evaluating the criteria for the nomination of centers.

- Activity (number of patients)
- Organizing the medical management process.
- Multi-disciplined, expertise
- Prescription and following of other expensive medical products
- Technological platform (highly specialized biological testing, molecular biology)
- Coordination of the system
- Informing/training (patients, help and care professionals about systems)

Research

- Promoting
- Clinical projects and financed research
- Providing a good quality guide
- Looking after development
- Following epidemiology, to develop relevant indicators of health
- Following the development of activities

III Defining therapeutic, psychological and social strategy

- Creating recommended guide or protocol for care
- Diagnosis and promoting a good model of practice, following the patient and his family
- Collaboration of patients associations where there exists research and epidemiological surveillance
- Evaluating practices

IV Permanent implementation of a national plan in reference to people with rare genetic diseases in accordance with European Legislation and in partnership with EURODIS, the national alliance and consul. This is done through the Europlan project, financed by the European Commission/ DC Sanco, following the recommendation given by CE about rare diseases. A public debate was raised at the Lisbon Conference about the European Commission of rare disease/ announced under 14.02.2008.

V Creating a national register for rare diseases.

5.1 Founding the rare disease register, epidemiological supervision organized for genetic rare disease through the current political sphere.

5.2 Founding a register for people with rare disease, to be treated with Orfane medicine

5.3 Defining a communication strategy between local, regional and national levels of responsibility.

- Structuring and coordination of medical and social care including health insurance, education and job location.
- Training and informing the health care professionals, patients and their families.

VI Developing good quality services for patients with rare diseases

6.1 Improving the access to information about rare disease, sustaining the information centers, helplines and tel-verde.

To proceed with awareness campaigns to combat stereotyping and prejudice and to make them sensitive to the needs of people suffering from rare diseases; to sustain and be receptive to others rights.

Cooperation and financial support in organizing national campaigns for example

RARE DAY FOR RARE DISEASES

29.02.2008 in years to come this day will be celebrated on 29th February.

6.2 Developing preventative services for rare diseases (i.e. implementing screening at a national level for phenylketonuria and hypothyroidism, and to improve access to genetical diagnosis services. Extending groups for which screening is used for diagnosis.

6.3 Developing continuous services, including rehabilitation for patients for rare disease. Founding and sustaining rehabilitation centers specialized in different disabilities produced by rare genetic diseases.

Sustaining activities, counseling and information by centers.

- Establishing protocol for diagnosis and care with experts' approval because of a lack of scientific proof
- Process of 12-18 months
- Creating emergency cards and personal care. The possibility of reimbursing treatments without market authorization; if the first treatment was given by the reference center.

VII Developing human resources

7.1 Training programs for specialists from different rare disease domains.

Example- Cooperation in partnership with developing the human resources program with the minister of work, families and equality of opportunity.

7.2 Assuring personal specialist hired to attend the people with rare disease in relation to all social and medical services; genetics, specialist doctors, biologists, medical assistants, laboratory workers, social assistants, physiologists, ergo therapy trainers, kinetotherapy, speech therapy, special needs teachers, support teachers, special educators.

- training courses, adapting university curriculum.

VIII Intensifying the efforts in favor of orfane drugs,

8.1 Assuring the availability of orfane drugs and compensating the cost/compensation of Orfane drugs through the health insurance system.

- Evaluation of the added therapeutic value of all orfane drugs by the ministry of health and national agency for medicine.
- Production costs of orphan drugs will be supported in the social budget of social insurance from the budgets of hospitals or referencing centers.
- The establishment of protocols for diagnosis and care by the ministry of health and referencing centers. Financing without marketing authorization, nutritional supplements, creams and bandages, special dental care, clothes, (example for skin diseases) according to models of good practice and patients' needs.

8.2 The supplementation of number and types included in health insurance, contracts and the diversification of assistance devices, prosthetics, hearing aids, lenses, magnifying glass, devices, technical aid mobility devices.

IX Stimulating research in the domain of rare disease management

9.1 Improving capacity to access research projects about rare disease utilizing international partnerships.

- Course and instructions
- Joining networks in the European Countries particularly in epidemiology, diagnostics, information and research.

9.2 Stimulating scientific research, tackling rare diseases in Romania.

Examples : - FP7 Program, etc. (rare diseases is a priority)

-strategic orientation for research

-addressing patients' needs other than medical care.

Conclusions:

A partnership agreement has been signed on 29th of February 2008 with the Ministry of Health Romania and some objectives have been achieved partially (a list of orphan drugs, a budget in the national programs for health, etc.).

Only a large partnership among all the stakeholders will ensure a better life for people with rare diseases in Romania.

II. ABSTRACT POSTERS

1. WHY DO WE NEED AN EU PRADER WILLI SYNDROME REGISTRY?

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Prader-Willi syndrome (PWS) is a rare multi-systemic genetic disease leading to severe complications mainly related to obesity. The need for an EU registry of this disease was born from the lack information on the natural history of this complex disease and on what factors are involved in its evolution and its outcome. One of the main objectives of all Prader Willi Associations in the near future is to set-up a registry in order to make the inventory of Prader-Willi syndrome cases.

The main reasons for creating this registry are:

- To enable the reliable and lawful collection, management and analysis of data across many countries thereby having sufficient number of people with PWS to answer specific questions;
- For comparing the influence of different educational, health and social care policies on the lives of people with PWS to be investigated, in different countries;
- To establish a critical mass of inter-disciplinary clinical expertise to focus on a

rare disorder and the development of best practice across the EU

The benefits in creating such a registry are many:

- It brings together different research groups from all EU countries;
- It brings together clinical and basic science perspectives;
- It focuses for national PWS Associations across the EU;
- It will be the basis for future EU wide collaborations.

The registry will have to include medical data of children and adolescents with Prader-Willi syndrome, details about their management, socio-demographic data on their families, psychological data and quality of life of the parents. This registry covering all the aspects of PWS clinical, psychological and social profiles will be a powerful tool for retrospective studies concerning this complex and multi factorial disease and could be a basis for the design of future prospective multicentric studies.

2. A CASE WITH PRADER-WILLI SYNDROME. IS GROWTH HORMONE THERAPY A GOOD CHOICE?

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Introduction: As a group, patients with Prader-Willi syndrome (PWS) have growth hormone deficiency, though its degree may vary from mild to severe insufficiency. Recently, treatment with growth hormone in PWS has been approved in USA, Japan and some European countries. **Objective:** The authors presented a case with PWS and tried to establish whether growth hormone therapy is a good choice for this particular patient. **Material and method:** A 16

years old girl admitted in the Endocrinology Department, 1st Pediatric Clinic of „Louis Țurcanu” Emergency Hospital for Children and diagnosed with PWS. The approach of this case was complex: clinical, anthropometric, metabolic and hormonal evaluation, as well as multiple interdisciplinary consults. **Results:** Diagnosis was based on clinical and anthropometric criteria and on the neuropsychiatric consult and psychological profile. Laboratory studies and

interdisciplinary consults revealed complications due to the obesity associated with PWS, the most important being type 2 diabetes. The values of protein, lipid, and hormonal metabolism markers were in normal range. In addition to dietary measures, the growth hormone therapy could decrease fat mass and increase muscle mass. Unfortunately, the final height cannot be influenced due to the closure of growth

cartilages. The effects of growth hormone on glucose homeostasis is another reason that makes therapy in this case not suitable. Conclusions: Early diagnosis of PWS it's a must for an efficient growth hormone therapy. Whether hormonal treatment is a good choice should be discussed for each case, taking into consideration both favorable and side effects.

3. ORAL DISEASES IN A PATIENT WITH PRADER-WILLI SYNDROME

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A case of Prader-Willi syndrome (PWS) in a 22-year-old girl is reported. The patient presents systemic and oral manifestations of the disease: **distinctive facial features** obesity, hypotonia, mental retardation, small hands, prominent forehead, strabismus, hypoplastic teeth, poor oral hygiene, caries, oral candidiasis and thick, sticky saliva.

This case is reported to underline the importance of the oral and dental problems of these patients. Caries and oral candidiasis are correlated with the reduced secretion of saliva and with poor oral hygiene. The role of pediatric dentistry is considered to be necessary for the prevention of oral complications of this syndrome. Treatment of the dentition was established by minimal invasive and adhesive dentistry.

4. ORO-FACIAL ANOMALIES IN A COMPLEX ASSOCIATION WITHIN MOHR MAJEWSKI SPECTRUM

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The oral-facial-digital syndromes are a heterogeneous group of disorders that result from the pleiotropic effect of a morphogenetic error affecting the mouth, face and digits. Different other organs can be involved, defining specific types of oral-facial-digital syndromes. Based on the characteristic clinical manifestations, 13 types have been distinguished. We present the case of a female infant born from unrelated parents, who already had three abortions, all males with agenesis of corpus callosum. Clinical examination of the infant revealed hypertelorism, broad nasal bridge, cleft palate, bifid tongue, microretrognathia, hypoplasia of the mandibula, malformed and low-set

ears, mesomelic shortening of limbs, absence of phalanges in both hands, bilateral simian creases. Radiological findings were narrow thorax, with the same diameter over all its length, non-ventilated right lung and short ribs. Transfontanellar ultrasound revealed semilobar holoprosencephaly. On the basis of the clinical score, the case was classified within Mohr Majewski spectrum. The clinical features show overlaps with type I and II oral-facial-digital syndromes, but syndactily specific for type I is not present in our case, nor is polydactily that is specific for type II.

5. POSTAXIAL HYPOPLASIA OF THE LOWER EXTREMITY IN CHILDREN – CASE REPORT

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Background: Postaxial hypoplasia of the lower extremity is a rare, congenital disorder characterized by partial or total absence of the fibula. It occurs in about 7 to 20 per million living birth. Males are twice affected as females. It has variable expression, ranging from mild to severe deformity and associated anomalies of the foot. **Material and methods:** We present a 14 months old male toddler, product of a non-consanguineous marriage, born at term, after an uncomplicated pregnancy. The patient presents mild shortening of the left lower extremity and foot deformity: syndactyly of the first and second toe and absence of the fifth toe. Evaluation was made by history data, clinical and genetic examination,

laboratory and imaging studies. **Results:** No familial incidence of malformations, congenital infections or teratogenic factors were noticed. Completely absent left fibula and associated anomalies: tibiotalar valgus, tarsal coalition with 3-ray foot aspect; limb-length discrepancy of 2,5 cm were diagnosed. Observation and nonoperative management are appropriate in this case. Special shoes are prescribed to enable the child to gain maximal function. **Conclusions:** The diagnosis was made by the absence of the left fibula with associated skeletal anomalies. The functional, social and psychological state of the child will be considered. The patient must be monitored throughout his growth.

6. PRENATAL DIAGNOSIS IN A DMD FAMILY AT RISK

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Case Report: A 23-year-old pregnant woman is the sister of a patient who is affected by Duchenne muscular dystrophy (DMD). Her brother, an 18-year-old male, was detected to have a novel mutation in exon 6 of DMD gene (c.587delAT). She asked for prenatal diagnosis to detect whether her unborn child has DMD or not. A prenatal diagnosis by chorionic

villi sampling (CVS) has performed at 10 weeks of pregnancy. Analysis consisted of PCR amplification followed by direct sequencing of the entire coding region of the DMD gene. The fetus showed a normal male karyotype (46,XY) and no abnormality of dystrophin gene. In this case, prenatal diagnosis by CVS was able to exclude DMD in the unborn child.

7. THERAPEUTIC METHODS USED IN INFANTILE AUTISM

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Aim: The aim of the present paper is to reveal the role played by some therapeutic methods of improving the intellectual and emotional deficit in infantile autism.

The treatment of autism is concentrated on a multifaceted approach, a central tenet of which is the

collaboration between practitioner, psychologist, educator and parents.

Description: In keeping with the psychoanalytic findings, Francoise Dolto (1985) considers that autism occurs as a reactive adaptation process of the child in an identity-achieving attempt. In her conception autism does not exist at birth. The purpose of educational techniques is to help the autistic child to deal with the

environment as best (s)he can. The behavioral therapy sets out to improve communication and discourage such forms of destructive behavior as aggression.

Conclusion: So far data have shown that autism cannot be cured, but trying to ameliorate the behavioral disorders can give the subjects greater acceptance in relation with the people around them and with themselves.

8. PLURIMALFORMATIVE SYNDROME – CASE REPORT

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Complete situs inversus is a genetic disorder with autosomal dominant, autosomal recessive or x-linked transmission, part of the group of ciliopathies and the subgroup of primary ciliary dyskinesias. We present the case of a 3 years and 8 month old girl, who associates complete situs inversus to chronic renal failure – left vesicoureteric reflux with secondary hydronephrosis, hypoplastic ectopic right kidney, hydrocephaly, bilateral varus equin foot and failure to thrive. She was first admitted in our hospital at 3 weeks of age and followed-up since then, necessitating complex medical and surgical therapy: treatment of recurrent urinary

tract infections, surgical treatment of the VUR - terminal ureterostomy at 9 month, surgical treatment of the hydrocephaly – Medtronic – Delta valve – at 1 year and 6 month, surgical treatment of the varus equin foot at 3 years, nutritional and neurological recovery. The particularity of this case resents in the association of multiple malformations with a bad prognosis, because of progression of the renal failure and of the neurological impairment. She needs a complex follow-up with the collaboration of the pediatric nephrologist, pediatric surgeon, pediatric neurologist, brain surgeon and family doctor.

9. CHALLENGES OF GSTP1, AS A BIOMARKER IN THE MOLECULAR DIAGNOSIS OF PROSTATE CANCER

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In recent years the discovery of cancer biomarkers has become a major focus in the field of cancer research. Biomarkers are used for diagnosis, monitoring disease progression, predicting disease recurrence and therapeutic treatment efficacy.

Cancer of the prostate is nearly universal with advanced age. Promoter hypermethylation is a common epigenetic alteration that affects cancer-related genes.

New biomarkers are needed with higher specificity and sensitivity to accurately diagnose prostate cancer, to predict outcomes, and to categorize prostate cancer into subtypes for personalized treatment.

GSTP1 is the most frequently methylated gene in prostate cancer.

Studies have demonstrated that GSTP1 hypermethylation can be used as a biomarker for prostate cancer screening and for the early diagnosis of prostate cancer.

10. BIOMARKERS AND THEIR ROLE IN CANCER DETECTION

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Cancer remains the leading cause of death. Biomarkers are useful for diagnosis, monitoring disease progression, predicting disease recurrence and therapeutic treatment efficacy. They should be easy to detect, measurable across populations, and useful for

detection of cancer at an early stage, identification of high-risk individuals, detection of recurrence, or monitoring endpoints in intervention studies.

Key words: cancer, biomarkers

11. PRENATAL DIAGNOSIS OF TRISOMY 13 WITH SEMILOBAR HOLOPROSENCEPHALY AND PROBOSCIS

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We report a congenital anomalous fetus with semilobar holoprosencephaly, cyclopy, protruding proboscis, cardiac defects (atrial septal defect, hypoplastic left heart, anomalous communication between right ventricle and aorta) prenatally diagnosed by sonography at the twenty-sixth week during the gestational period. Chromosome analysis by amniocentesis revealed trisomy 13 (47,XY,+13). The newborn died just after delivery. The diagnosis was confirmed by autopsy. The right foot showed polydactylia with wide separation of the fifth and sixth toes. The mother was 33 years old and had no significant medical history. No pathological findings were noticed for the usual pregnancy test during. In the

medical literature there are numerous reports of similar cases: alobar holoprosencephaly associated with mobile proboscis and trisomy 13 in a fetus with maternal gestational diabetes mellitus, holoprosencephaly and trisomy 13, with maternal early gestational abuse of amphetamine. Conclusion The teratogenic effect of different substances during embryofetal development seems to determine complex developmental anomalies. For this reason it is of great importance the periodic ultrasonography surveillance during pregnancy and when is needed to perform appropriate chromosome analysis by amniocentesis. In this way proper measures could be taken to avoid further suffering.

12. NEPHROLOGICAL APPROACH OF 5 CASES WITH NEURAL TUBE DEFECTS

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Introduction: Neural tube defects result from the failed closure of the neural tube between the 3rd and 4th week of in utero development. Myelomeningocele represents the most severe form of dysraphism involving the vertebral column. Objective: The evaluation of prognosis and renal-urinary

complications in children with myelomeningocele. Material and method: Authors present 5 cases with myelomeningocele and neuropathic bladder admitted in “Louis Turcanu” Pediatric Emergency Hospital Timisoara. We evaluated clinical aspects, pathogenesis, evolution, complications and the

treatment of these cases. Results: In all cases the defect was surgically corrected. In two cases shunting procedure for hydrocephalus followed, while the other cases present spontaneous stabilization of hydrocephalus. Mental retardation was sever (1 patient), moderate (1 patient) and mild (3 patients). Urinary anomalies consisted of neuropathic bladder (5 cases), massive bilateral hydronephrosis (4 patients) and horseshoe kidney (1 patient). The patients presented urinary incontinence, urinary infections (1 case deceased from sepsis) and renal failure. The immobilization, urinary and fecal incontinence

represent a sever handicap for these patients and their family. Social integration is difficult. Patients' prognosis is unfavorable: 1 case deceased at six years of age, two cases already with renal failure and the recurrence of urinary tract infections followed, probably, by renal failure for the other two patients. Conclusions: The association of genitourinary system pathology determined an unfavorable evolution and a negative prognosis for these cases. Folic acid supplementation should be initiated before conception and continued until at least 12th wk of gestation in order to prevent the neural tube defects.

13. CELL DENSITY OF COSTAL CARTILAGE IN CHILDREN WITH PECTUS EXCAVATUM

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Aim: Despite large variety of treatment options for Pectus Excavatum (PE) the cause for the disease remains unclear. Several studies indicated that the disturbance of the costal cartilages is responsible for the deformity. In the majority of the patients the depression becomes apparent in pubertal growth spurt. The aim of this study is to analyze the relation between age of the patient and costal cartilages cell density in children with Pectus Excavatum.

Methods: Costal cartilage samples were obtained during opened surgical intervention for PE from 17 patients. Patient's age ranged between 5 and 18 years, mean 11.3 years. For each patient three samples were prepared, stained with Hematoxylin and Eosin and analyzed in light microscopy (10X). Area and

microdensity of cartilage lacunae were measured using NIS-elements BR software for Windows version 2.30.

Results: Density of the lacunae varies from 1.7 to 6.4/10000 μm^2 , mean 4/ 10000 μm^2 . In 10 and 14 years old children the density was up to three times higher than the rest ($p=0.18$). Between 0.4% and 6.7% (mean 2.7%) of cartilage area was occupied by lacunae, with the largest lacunae area in the 14 and 15 years old children ($p=0.05$).

Conclusions: Density and area occupied by the costal cartilages cells is higher in the prepubertal children with Pectus Excavatum in relation with the growth spurt characteristic for this age suggesting that the costal cartilage overgrowth is responsible for the disease.

14. GENETIC FACTORS EFFECT ON THE DEVELOPMENT OF THE LANGUAGE IN THE INFANTILE AUTISM

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Purpose: The paper aims identifying the role of the genetic factors on the language skills development in autism children.

After the organogenetic theories of A. Van Krevelen, Anthony, L. Bander, autism is the result of some biochemical organic dysfunctions or insufficient

development of the brain; owing to this cause the child cannot reach the normal parameters of the psychic activity. Consequently, speaking can develop later or never.

Methods: Therefore, to identify various aspects connected to language deficiency, one can use the "speak to pictures" vocabulary tests (Lege și Dagne, Boehm, Lelord), the communication development scale (ESCS), which analyzes three types of activities: social interaction, simultaneously attention, behavior adjustment.

Teaching methods: For the treatment and recovery of the autism child it is necessary an exact diagnose of the disease. And poor communication (solilocv

language, stereotypical, late echolalia, poor language, voice deficit, intonation, flexibility) should be a problem for us. As correction methods in the development of speaking, one can use the following techniques: the Hanen method, D.T.T. (Discrete Trial Training), P.E.C.S. (Picture Exchange Communication System).

Conclusions: Infantile autism is a major problem in psychology and contemporary psychiatry, as it is characterized by a wide range of manifestations.. Even though we cannot speak today about the cure of autism, partial recovery in some cases, using an intervention plan, may be an encouraging certitude.

15. THE STUDENT'S INVOLVEMENT IN VOLUNTEERING ACTIVITIES FOR RARE DISEASES

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Introduction. Volunteering is the activity carried on of one's own accord, through which any person offers his time, knowledge, talents and energy to help others without thinking at any financial rewards. Promotion of the idea of volunteering and increasing the number of involved and trained volunteers, prevention and limitation of vulnerable and difficulty situations, that can cause social marginalization or exclusion of the persons with special needs, increasing the level of informing and developing of a civic attitude toward these persons. **Materials/Methods.** Together with numerous wonderful people we succeeded to realize two projects: „Together for rare people”, „Volunteers for rare diseases” in which were active involved volunteers that are students at the university of medicine and young specialists. So that projects to go on following the planned trajectory, it was necessary a passing through three consecutive stages: training of the volunteers, weekly meetings with the manager of

the projects and the volunteer's coordinator, the activities with the persons that are suffering from rare diseases. **Results.** The knowledge store during the training sessions of the volunteers turned out to be useful both in working with children suffering from rare diseases and for developing the general knowledge of each of the persons involved in these projects (volunteer, specialist, beneficiary). We met different persons longing to learn more things about this subject debated by us, because in their environment (family, work, friends) there are persons suffering from rare diseases but which didn't had the chance to get help from others. **Discussions./** Because the volunteers and the young specialists showed that they were longing to work also in the future with these patients, there is the possibility of activities to go on after the projects are finished. For the students volunteering may be an outlet for their natural talents, a road-test for their new career.

16. USE GENETIC TESTS IN HUMAN PATHOLOGY

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Genetic tests can be used to look for possible predisposition to disease as well as to confirm a suspected mutation in an individual or family.

The most widespread type of genetic testing is *newborn screening*. Each year in the World, many millions newborn infants have blood samples tested for abnormal or missing gene products. Some tests look for abnormal arrangements of the chemical bases in the gene itself, while other tests detect *inborn errors of metabolism* (for example, *phenylketonuria*) by verifying the absence of a protein that the cell needs to function normally.

Carrier testing can be used to help couples to learn if they carry - and thus risk passing to their children - a recessive allele for inherited disorders such as cystic fibrosis, sickle-cell anemia, or *Tay-Sachs disease* (a lethal disorder of lipid metabolism). Genetic tests - biochemical, chromosomal, and DNA-based - also are widely available for the *prenatal diagnosis* of conditions such as Down syndrome.

In clinical research programs, doctors make use of genetic tests to identify telltale DNA changes in cancer or precancer cells. Such tests can be helpful in several areas: early detection (*familial adenomatous polyposis* genes prompt close surveillance for colon cancer); diagnosis (different types of *leukemia* can be distinguished); prognosis (the product of a mutated *p53 tumor-suppressor gene* flags cancers that are likely to grow aggressively); and treatment (antibodies block a gene product that promotes the growth of breast cancer).

Much of the current excitement in gene testing, however, centers on *predictive gene testing*: tests that identify people who are at risk of getting a disease, before any symptoms appear. Tests are already available in research programs for some two dozen such diseases, and as more disease genes are discovered, more gene tests can be expected.

17. DE NOVO DELETION DEL (5)(P14→TER) – A REPORT CASE

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This report presents a baby girl with a small terminal deletion of the short arm of chromosome 5, del (5)(p14→pter). Cri-du-chat syndrome, also known as Cat Cry Syndrome is a rare genetic disorder associated with deletion of a part of the short arm of chromosome 5. The patient was a two week old baby girl with characteristic high pitched cry at birth. She presented some of the clinical characteristics, such as microcephaly, dysmorphic face, hypertelorism, low-set ears, preauricular tags, macrostomia low birth

weight, poor muscle tonus, and medical complications such as feeding difficulties. The chromosomal analysis in lymphocyte culture showed 46,XX,del(5)(p14→ter) in 100% of cells. Majority of deletions arise as new mutations, as in the present case, due to the normal parental karyotype. Postnatal recognition of the syndrome requires genetic counseling of parents and supportive multidisciplinary treatment.