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ISSN p 1221-7212

CONTENTS

I. GENETICS

1. ELEMENTS OF RISK ASSESSMENT AND GENETIC COUNSELING IN CANCER

Maria Puiu, Dorina Stoicanescu3

2. THE PRENATAL RISK ASSESSMENT OF TRISOMY 21 (DOWN SYNDROME)

Demetra Socolov, R Socolov, Julieta Maria Puiu8

II. NEONATOLOGY

3. INFECTIONS PATHOLOGY INCIDENCE TO NEWBORNS WITH CONGENITAL MALFORMATIONS

Daniela Iacob, V Boțiu, Marioara Boia, RE Iacob, Aniko Manea12

4. HYDROCEPHALY AT INFANTS AND CHILDREN

Nicoleta Pavel, A Pavel, Marioara Boia, ES Boia, Maria Trăilescu15

III. PEDIATRICS

6. ENTERIC COATED MINIMICROSPHERE IN THE TREATMENT OF PANCREATIC FAILURE FROM CYSTIC FIBROSIS

L Pop, I Popa, Zagorca Popa, Ioana Popa23

7. EMPTY SELLA SYNDROME A CAUSE FOR GROWTH HORMONE DEFICIENCY (GHD) OR JUST A COINCIDENT ASSOCIATION?

Corina Paul, I Popa, I Velea, Maria Mogoșeanu, Ana-Maria Vesa25

8. PULMONARY ATELECTASIS ON INFANCY: CLINICAL AND RADIOLOGICAL EVOLUTIONAL OBSERVATIONS

Lucretia Cristoi, I Sabau, I Simedrea, Oana Belei, Camelia Daescu, Mihaela Linu, Daniela Icma27

IV. PEDIATRIC SURGERY

9. OUR EXPERIENCE IN SACROCOCCYGEAL TERATOMAS

ES Boia, C Popoiu, RE Iacob, Ioana Lazar, Marioara Boia, Julieta Puiu30

10. MODIFICATIONS OF THE HORMONAL TABLE IN THE UNDESCENDED TESTICLE

RE Iacob, ES Boia, Aurora Milos, F Miclea, Daniela Iacob33

11. ECHINOCOCCIASIS OF THE SPLEEN

ES Boia, RE Iacob, V Gîrlă, Marioara Boia42

V. PSYCHOLOGY

12. GAME AND ART AT CHILDREN

V Botiu45

VI. RADIOLOGY

13. PARTICULAR CASES OF SYMPTOMATIC JUVENILE EPILEPSY OF CEREBRAL VASCULAR CAUSE

M Popescu, E Lazăr, H Prundeanu49

MANUSCRIPT REQUIREMENTS54

I. GENETICS

ELEMENTS OF RISK ASSESSMENT AND GENETIC COUNSELING IN CANCER

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Abstract

People who have been diagnosed with cancer at an atypically young age, which have a rare cancer, childhood adrenal carcinoma, right-sided colon cancer, multiple primary cancers, cancers associated with birth defects and people with a strong family history of cancer are usually considered to be candidates for genetic counseling.

Key words: cancer, genetic counseling

Introduction

People are usually considered to be candidates for genetic counseling if they have a strong family history of cancer. In general, this means a family history that includes several affected relatives, with at least some affected at atypically early ages. The definition of a strong family history, however, varies for different cancers.

People who have been diagnosed with cancer at an atypically young age; have a rare cancer, e.g., childhood adrenal carcinoma; unusual presentation, e.g., right-sided colon cancer; multiple primary cancers; cancers associated with birth defects; or, in some cases, have extreme cancer anxiety, even in the absence of risk, may also be candidates for genetic counseling.

Individuals who are candidates for genetic testing receive genetic counseling prior to undergoing testing to facilitate decision making. This gives them time to fully understand both the various medical uncertainties and psychosocial risks and benefits of this information (1).

Certain components are common to the genetic counseling process, including those focused on cancer risk. These include medical, genetic and counseling components such as constructing and evaluating a pedigree; eliciting and evaluating personal and family medical history and providing information about genetic risk. When testing is needed, genetic counseling incorporates pretest counseling, testing, post-test counseling, and follow-up. This may include discussing, ordering and interpreting clinical genetic laboratory tests. Much preparation time outside the appointment is spent obtaining and reviewing medical records, seeking information about diagnoses in the differential diagnosis list, finding support groups and patient resources, communicating with other specialists, and case documentation.

In some instances, physical findings may be important in determining whether or not a cancer syndrome is present; this requires a targeted physical examination by

a medical professional for physical findings specific to a genetic syndrome.

Cancer Risk Counseling

Genetic counseling has been defined as “a communication process which deals with the human problems associated with the occurrence, or risk of occurrence, of a genetic disorder in a family”. The process involves an attempt by one or more appropriately trained persons to help the individual or family to:

1. comprehend the medical facts including the diagnosis, probable course of the disorder, and the available management;
2. appreciate the way that heredity contributes to the disorder, and to the risk of recurrence (occurrence), in specific relatives;
3. understand the alternatives for dealing with the risk of recurrence (occurrence);
4. choose a course of action which seems to them appropriate in view of their risk, their family goals, and their ethical and religious standards and act in accordance with that decision; and
5. make the best possible adjustment to the disorder in an affected family member and/or to the risk of recurrence (occurrence) of that disorder.

Central to genetic counseling philosophy and practice are the principles of voluntary utilization of services, informed decision making, attention to psychosocial and affective dimensions of coping with genetic risk, and protection of patient confidentiality and privacy (2).

An important objective of genetic counseling is to provide an opportunity for shared decision making when the medical benefits of one course of action are not demonstrably superior to another.

The relationship between availability of effective medical treatment for mutation carriers and clinical validity of a given test affects the degree to which personal choice or physician recommendation is supported in counseling at-risk individuals. Genetic counseling generally involves some combination of rapport-building and information gathering; establishing or verifying diagnoses; risk assessment and calculation of quantitative occurrence/recurrence risks; education and informed consent processes; psychosocial assessment, support and

counseling appropriate to a family's culture and ethnicity; and other relevant background variables.

In the past decade, genetic counseling has expanded to include discussion of genetic testing for cancer risk as more genes associated with inherited cancer susceptibility have been discovered. Cancer genetic counseling often involves a multidisciplinary team, which may include a genetic counselor, genetic advanced practice nurse, or medical geneticist, mental health professional, and medical expert such as an oncologist, surgeon, or internist. The process of counseling may require a number of visits in order to address the medical, genetic testing, and psychosocial support issues. Even when cancer risk counseling is initiated by an individual, inherited cancer risk has implications for the entire family.

Because genetic risk affects biological relatives, contact with these relatives is often essential to collect an accurate family and medical history. Cancer genetic counseling may involve several family members, some of whom may have had cancer, and others who have not.

Certain features of genetic disease susceptibility highlight the importance of genetic counseling. Specifically, an accurate assessment depends on detailed family history and, conversely, information about one individual has implications for others in the family. The purpose of risk counseling is to provide information about an individual's empiric risk of cancer.

If the assessment indicates an increased cancer risk, counseling may include discussion of cancer risk management strategies or of options for genetic testing (3). Risk counseling may also lead to reassurance if cancer risk is found not to be greater than the average, or substantially less than the person had anticipated. In some cases, the purpose of counseling includes helping the individual to explore feelings about his/her personal risk status and to make a healthy adjustment to that risk status. Either alone, or in consultation with a mental health provider, professionals offering cancer genetic counseling attempt to assess whether the individual's expectations of counseling are realistic and whether there are factors suggesting unusual risk of adverse psychological outcomes following disclosure of risk and/or genetic status. Sometimes, referral for psychotherapeutic treatment prior to or in lieu of testing may be recommended.

There have been some studies of patient satisfaction with cancer genetic counseling services. For example, one survey of participants after the first year of operation of a cancer genetics program reported that the clinical services met the needs and expectations of most people.

Patients reported that the best parts of the experience were having personalized summary letters and family pedigrees, learning that cancer risk was either lower than expected, or realizing that one had been justified in suspecting the inheritance of cancer in one's family, allowing for cleansing of one's conscience of burdensome guilty feelings, as well as simply having a chance to talk to someone about cancer concerns (4).

Follow-up is often multidisciplinary, with input from, and referral to, professionals trained in genetic

counseling, nursing, social work, psychology, preventive medicine, public health, occupational health, and mental health, and as needed to other medical specialties such as surgery, gastroenterology, gynecology, or oncology. Because inherited cancers affect more than the individual, the entire family may become involved.

Taking a Family History

It is essential to summarize family history information in the form of a pedigree. A pedigree, or family tree, is a standardized graphic representation of family relationships, in which patterns of disease transmission are tracked. A graphic illustration facilitates identification of patterns of transmission, recognition of specific hereditary cancer syndromes, and assists in determining the best methods for risk assessment.

Factors suggesting inherited cancer risk include the following:

- Clustering of the same type of cancer in close relatives.
- Unusually early age of cancer onset.
- Two or more primary cancers in a single relative.
- Evidence of autosomal dominant inheritance.
- Bilaterality in paired organs.
- Patterns of cancer in the family that are associated with a known cancer syndrome.

A cancer family history typically includes the following:

- Both maternal and paternal relatives. Hereditary cancer syndromes can be inherited from either the mother or the father.
- Notation of nonpaternity, consanguinity, and use of assisted reproductive technology (e.g., donor egg or sperm).
- Race, ancestry and ethnicity information for all grandparents. This may influence decisions about genetic testing, because specific mutations may occur with increased frequency in selected populations.
- Seemingly unrelated conditions such as birth defects or other nonmalignant conditions of children and adults as they may aid in the diagnosis of a cancer susceptibility syndrome.
- A minimum of 3 generations. This will help identify inheritance patterns since cancer is often an adult-onset disease.

For any relative with cancer, collect the following information:

- Type of each primary cancer.
- Age of diagnosis for each primary cancer.
- Where the relative was diagnosed and/or treated.
- If the individual is still living, current age; if deceased, age at death and cause of death.
- Carcinogenic exposures (e.g., tobacco use, radiation exposure).
- Other significant health problems.

For any relative not affected with cancer, collect the following information:

- Current age or age at death.
- If deceased, cause of death.
- Any surgeries that reduce the risk for cancer.

- Whether routinely screened for cancer.
- Any nonmalignant features of the syndrome in question.
- Carcinogenic exposures.
- Other significant health problems.

People often have incomplete or inaccurate information about the cancer history in their family (e.g., because of adoption, loss of contact with relatives, small family size, or deaths at an early age from unrelated conditions).

Family histories change over time; therefore, it is useful to update pedigrees periodically. Self-reported family history may contain errors. Verification of medical diagnoses through medical records, tumor registries, or death certificates may improve the risk assessment.

Analysis of the Family History

Since a family history of cancer is one of the important predictors of cancer risk, analysis of the pedigree constitutes one important aspect of risk assessment.

The index of suspicion should be raised by:

- Multiple cancers in close relatives, particularly in multiple generations.
- Early age of onset, before 40 to 50 years for adult onset cancers.
- Multiple cancers in a single individual.
- Bilateral cancer in paired organs (e.g., breast, kidney).
- Recognition of the known association between etiologically related cancers in the family.
- Presence of congenital anomalies or precursor lesions that are known to be associated with increased cancer risk (e.g., presence of atypical nevi and risk of malignant melanoma).
- Recognizable Mendelian inheritance pattern.

There are hundreds of inherited conditions associated with an increased risk of cancer. Diagnostic criteria for different hereditary syndromes incorporate different features depending on the original purpose of those defining the syndrome, e.g., for gene mapping, genotype-phenotype studies, epidemiological investigations, population screening, or clinical service.

Thus, a syndrome such as hereditary nonpolyposis colorectal cancer (HNPCC) can be defined for research purposes by the Amsterdam Criteria as having 3 individuals with colorectal cancer, 2 generations, of which 1 person is less than 50 years of age, better known as the 3-2-1 rule. These criteria have limitations in the clinical setting, however, in that they ignore endometrial and other extracolonic tumors known to be important features of HNPCC.

Risk Perception

A person's subjective view of risk may differ from his/her estimated statistical risk. The individual's perception of their cancer risk, however, may be the most important factor in determining decisions about screening or other risk reduction strategies.

Thus, it is important to begin a risk assessment process by eliciting the person's perception of their risk as well as how concerned they are about the risk and how this has affected their day to day life.

The Option of Genetic Testing

Factors to take into consideration in offering testing

1. Pedigree suggesting an inherited cancer syndrome.

Experts recommend offering genetic testing only when a pedigree analysis suggests the presence of an inherited cancer syndrome for which specific mutations have been identified. American Society of Clinical Oncology (ASCO) guidelines propose that genetic testing should be offered when:

- An individual has a personal or family history suggestive of a genetic cancer susceptibility syndrome.
- The results of the test can be interpreted.
- Testing will influence medical management.

2. Value of testing an affected family member first.

Genetic susceptibility testing generally yields the most useful information when a living family member affected with the cancer of concern is tested first to determine if a genetic basis for the cancer in the family can be established. If a mutation previously associated with cancer risk is demonstrated in the affected family member, other family members may be tested for the presence or absence of this specific mutation. If no mutation is found in an affected family member, testing is considered uninformative regarding the possible inherited basis for cancer in that family, and thus there is no basis for testing unaffected relatives (5, 6).

Where there is no close, living, affected relative, other options may be discussed with the patient and the testing laboratory. These generally involve weighing a decision to test stored tissue on a deceased relative or to test an unaffected person without prior testing of an affected family member. Tests done on stored tissue are technically difficult and may not yield a definitive result. Testing an unaffected person without prior testing of an affected relative often is uninformative, because a negative test does not rule out the presence of a cancer susceptibility gene in the family or the subject. In addition, counseling needs to take into account the risk and consequences of a false positive test.

Determining the test to be used

Genetic testing is highly specialized. Any given test is usually performed in only a small number of laboratories. There are also multiple molecular testing methods available, each with its own costs, strengths, and weaknesses. Depending on the method employed and the extent of the analysis, different tests for the same gene will have varying levels of sensitivity and specificity. Even

assuming high analytic validity, genetic heterogeneity makes test selection challenging.

A number of different genetic syndromes may underlie the development of a particular cancer type. Thus, hereditary colon cancer may be due to having HNPCC, Peutz-Jegher syndrome (PJS), juvenile polyposis syndrome (JPS), or other syndromes. Each of these has a different genetic basis. In addition, different genes may be responsible for the same condition, e.g., HNPCC can be due to mutations in 1 of at least 6 mismatch repair genes. There is also allelic heterogeneity, i.e., different mutations within the same gene can confer different risks or be associated with a different phenotype.

Thus, selection of the appropriate genetic test for a given individual requires considerable knowledge of genetic diagnostic methods, correlation between clinical and molecular findings and access to information about rapidly changing testing options.

All individuals considering genetic testing should be informed that they have several options even after the genetic testing has been completed. They may decide to receive the results at the post-test meeting, decide to delay result notification, or decide not to receive the results of testing (7).

Importance of Pretest Counseling

The complexity of genetic testing for cancer susceptibility has led experts to suggest that careful, in-depth counseling should precede any decision about the use of testing in keeping with the accepted principles for the use of genetic testing. The clinician who opts to take on this responsibility must provide the depth of content and time required to ensure that the patient can make an informed testing choice.

Qualitative and quantitative research studies indicate that families hold a variety of beliefs about the inheritance of characteristics within families; some of these beliefs are congruent with current scientific understanding while others are not. These beliefs may be influenced by education, personal and family experiences, and cultural background. Since behavior is likely to be influenced by these beliefs, the usefulness of genetic information may depend on recognizing and addressing the individual's pre-existing cognitions. This process begins with initial discussion and continues throughout the genetic counseling process.

Psychological Impact of Genetic Information/Test Results on the Individual

An accurate assessment of psychosocial functioning, and of emotional factors related to testing motivation and potential impact and utilization, is an important part of pretest counseling. Generally, a provider inquires about a person's emotional response to the family history of cancer and also about a person's response to his/her own risk of developing cancer. People have various

coping strategies for dealing with stressful circumstances such as genetic risk. Identifying these strategies and ascertaining how well or poorly they work will have implications for the support necessary during post-test counseling, and will help personalize the discussion of anticipated risks and benefits of testing.

Taking a brief history of past and current psychiatric symptoms (depression, extreme anxiety, suicidality) will allow for an assessment of whether or not this individual is at particular risk of adverse effects following disclosure of results. In such cases, further psychological assessment may be indicated.

In addition, cognitive deficits in the person may significantly limit understanding of the genetic information provided and hinder the ability to give informed consent, and may also require further psychological assessment. Emotional responses to cancer risk may also affect overall mood and functioning in other areas of life such as home or work. Education and genetic counseling sessions provide an opportunity for ongoing informal assessment of the affective as well as cognitive aspects of the health communication process. Since behavioral factors influence adherence to screening and surveillance recommendations, consideration of emotional barriers is important in helping a person to choose prevention strategies as well as in discussing the potential utility of genetic testing.

Psychological Impact of Genetic Information/Test Results on the Family

In addition to making an assessment of the family history of cancer, the family as a social system may also be assessed as part of the process of cancer genetic counseling. Hereditary susceptibility to cancer may affect social interactions and attitudes toward the family.

The practitioner may use the above framework to guide inquiries about the relationship of the individual to 1) the affected members of the family, or 2) others who are considering or deciding against the consideration of genetic counseling or testing. Inquiries about how the family shares (or does not share) information about health, illness, and genetic susceptibility may establish whether the individual feels under pressure from other family members or anticipates difficulty in sharing genetic information obtained from counseling or testing.

Inquiries about the present health (new diagnoses or deaths from cancer) or relationship status (divorce, marriage, grieving) of family members may inform the provider about the timing of the individual's participation in counseling or testing and may also reveal possible contraindications for testing at present.

Many individuals benefit from follow-up counseling and consultation with medical specialists after disclosure of test results to allow an opportunity for further discussion of their feelings about their risk status, their options for risk management to incorporate screening and detection procedures, and implications of the test result for other family members.

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THE PRENATAL RISK ASSESSMENT OF TRISOMY 21 (DOWN SYNDROME)

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Abstract

The chromosomal abnormalities (aneuploidies) have a frequency of 1 in 250 live new borns, and 1/3 of them are represented by the Down syndrome (1).

This syndrome was described the first time in 1866 by Langdon Down, and one of the elements his description underlined was the thickened skin ("the skin seems too large for their bodies"). In 1966, 100 years after the original essay of Down, it became possible to diagnose the trisomy 21 prenatally by the karyotype of cultured amniotic fluid cells. Therefore, it was demonstrated that the syndrome is produced when either a whole or a part of the long arm of chromosome 21 is present in three copies instead of two. This can occur as a result of three separate mechanisms: non-dysjunction (95% cases), translocation and mosaicism.

As this aneuploidy not only is the most frequent, but also it causes one third of the severe mental retardation in children, its' screening became of outmost importance. But, as an amniocentesis in every pregnancy would not have the economic efficiency, as well as ethical and medical support, the question of individualising a risk group arises.

This paper tries to evaluate different risk factors, in the perspective of their importance in the clinical decision.

Key words: chromosomal abnormalities (aneuploidies), trisomy 21, mosaicism

1. The basal risk factors

The risk of trisomy 21 increases with the maternal age, as shown by Snijders (2). For example, the risk of a 20 year old woman to give birth to a children with trisomy 21 is 1 in 1527 (1/1527), while a woman over 40 years will have a Down syndrome offspring in 97 cases (1/97). This risk is also related to the gestational age, as fetuses with trisomy 21 are more likely to die in utero than normal ones. Snijders (3, 4) calculated that the in utero death rate was 36% until 10 weeks, 30% at 12 weeks, and 21% at 16 weeks- that means that the estimated risk decreases with the gestational age. In the example above, the risk in a 20 year old woman is 1/983 at 10 weeks, respectively 1/1527 at term, while for a 40 year old woman the risk is 1/62 at 10 weeks and 1/97 at term.

This risk estimation imposed the recommendation adopted by some countries, that a caryotype for trisomy 21 should be performed in all pregnant patients over 38 years (and even 35 years) (5). For 35 year cut-off point, which

represents 5% of the pregnant population, there are 30% of trisomy 21 included.

It is important however to remind that, statistically speaking, the number of pregnancies in women over 35 is snaller than the one in younger women. Therefore, using only the maternal age (even correlated with gestational age criteria) could result in missing about 75% of trisomies 21.

Other risk factors, like previous affected pregnancies, modify the age related risk, with an increase of 0.75%. For example, a woman of 35 years, with a basal risk of 0.4% at 12 weeks, would be estimated at 1.15% if a previous Down syndrome case child exists.

2. Ultrasound risk factors

Trisomy 21 is associated with several fetal defects, and some of them could be described by ultrasound prenatal examination.

In the first trimester (upto 14 weeks), the most important ultrasound element for the Down syndrome is the nuchal translucency. It is the school of Nikolaides that showed for the first time the association between the increased nuchal translucency in the first three months of pregnancy (and more precisely, between 11-14 weeks) and Down syndrome. (6) Possible mechanisms for this sign include cardiac failure, venous congestion in the head and neck due to superior mediastinal compression, altered composition of the extracellular matrix, abnormal development of the lymphatic system, failure of lymphatic drainage due to impaired fetal movements, fetal anemia and congenital infection.

The normal nuchal translucency increases with gestation (and with its' most relevant biometric element in this period- the crown-rump length CRL). The Nikolaides ultrasound school demonstrated that the optimal gestational age for this measurement to be accurate and allow risk calculation is 11-13 weeks, with a success rate of 98-100% (corresponding to 45-84 mm CRL). There are several requirements for a correct measurement, but as the experience of that school has shown, a good training makes the procedure entirely reproducible. There are also tables that correlate the nuchal translucency with the CRL, which has been shown to be more accurate than the simple threshold of 3 mm- with a single detection rate of 72%.

The other important alarm sign in the first trimester ultrasound scan is the absence of fetal nasal bone. A recent article (7) shows that 69% of fetuses with trisomy 21 have no nasal bone, while only 0,4% of normal fetuses have this abnormality.

Other signs that were associated with trisomy 21 in different articles are described in table 1.

Tabel 1. Significant ultrasonographic findings in trisomy 21

parameter	gestational age	likelihood ratio for trisomy 21
increased heart rate (over 180/min) (8)	at 14 weeks	NC- 26% of trisomy 21
nuchal edema (> 6 mm)	2 nd trimester	19
echogenic foci in the heart (9)	2 nd trimester	4
short limbs with femural length < 2 SD (foot/femur>1.1, BIP/femur>1.55)	2 nd trimester	2-4
echogenic bowel	2 nd trimester	3
mild hydronephrosis (10)	2 nd trimester	1.5
choroid plexus cyst	2 nd trimester	1.5
nasal bone hypoplasia (under 2 mm, normal > 7 mm)	> 22 weeks	NC- 69% of trisomy 21
facial dysmorphism- flat profile	2 nd trimester	NC- in 67% of trisomy 21
iliac bone angle (if >90) (11)	2 nd trimester	NC- 60% of trsomy 21
smaller ear length (normal >17 mm)	>22 weeks	NC- 21% of trisomy 21
atrioventricular septal defects	14-24 weeks	NC- 10 to 30% trisomy 21
clinodactily or mid phalanx hypoplasia of the 5 th finger	2 nd trimester	NC- 4 % of trisomy 21

NC- likelihood ratio not communicated

Polyhydramnios, separation of the amnios and the placenta, and other abnormalities have little specificity for trisomy 21.

Finally these abnormalities have a higher significance if associated, but many of them have low specificity. Therefore, the need of an earlier examination, with the appreciation of the nuchal translucency is obvious.

3. The serum markers

Since the 1980s, several studies answered the need for a screening test for Down syndrome using biochemical markers. Their values, expressed as multiple of median (MoM), have proven to have different significance for the risk of this pathology.

- *human chorionic gonadotrophin* (hCG) is a trophoblastic glycoprotein. In 1987, Bogart (12) showed that in trisomy 21, this evolution is modified, and the serum concentration remains elevated after 16-18 weeks. Although not extremely specific, a level higher than normal at this stage of pregnancy, correlated with other risk factors (increased maternal age, abnormal nuchal translucency) can be significant for this aneuploidy.
- More specific than the total hCG, the *free beta-hCG* is elevated until 9 weeks, then decreases. In trisomy 21, the level is stable at higher than normal level even after 12 weeks.

- The non-conjugated estriol is lower than normal in trisomy 21, as shown by Canick in 1988 (13). However, the specificity of this marker for this aneuploidy is quite low.
- Alpha feto protein (AFP) is an alpha globuline produced during the embryo development. A higher value is met in multiple pregnancies, intrauterine growth restriction, neural tube defect, anencephaly, and intrauterine death. Merkatz in 1984 (14) proposed it as a marker for trisomy 21, as its' value is decreased in this aneuploidy- as well as in diabetes.
- The pregnancy associated plasma protein A (PAPP-A) is a trophoblastic protein, which can be evaluated between 7 and 12 weeks. In Down syndrome, it is decreased.
- The inhibines (A and B) are produced by the placenta, with increasing values upto 10 weeks, and then a constant level between 15 and 25 weeks. Their values increases in trisomy 21, and it is strongly correlated with the hCG.
- The specific pregnancy b-1 glycoprotein (SP-1) is also decreased in Down syndrome.

As shown in the table, adapted from Uzan 1998 (1), there are only few markers which have significant variations in trisomy 21 (values > 2 MoM, or less than 0.5 MoM- significantly increased or decreased):

Table 2. Serum markers for Down syndrome screening (1)

Marker	Origins	Maximal concentration	Optimal screening period	Concentration (MoM)
hCG	Trophoblast	9 weeks	15-18 weeks	2.1
Free beta hCG	Trophoblast	9 weeks	11-18 weeks	2.4
PAPP-A	Trophoblast	20 weeks	7-12 weeks	0.3-0.5
AFP	Fetal	30 weeks	15-18 weeks	0.7
E3	Fetal, placental	37 weeks	15-18	0.73

If available, the best markers are therefore free hCG and PAPP-A, and they can be determined even earlier in the pregnancy- up to 14-15 weeks. The previous “classical” triple markers (AFP, hCG and E3) were determined at 16-18 weeks, and therefore needed a longer waiting period after the first risk assessment, at 12-14 weeks by the maternal age and nuchal translucency.

The other markers (for example, inhibine A or B) have concordant values with the main ones above, and

therefore are not suitable for a multiple testing, as they will be similar in most of cases.

4. Integrating the different elements for the risk calculation

The first estimation of risk, done by statistical studies, regarded only the maternal age, corrected after the gestational age (table 3). Yet, the risks associated with amniocentesis (6% fetal loss) or chorionic trophoblastic biopsy (7.6% fetal loss) required a further limitation for the risk groups. (15)

Table 3. The risk for trisomy 21, depending on maternal and gestational age, adapted from (2)

Maternal/ gestational age	12 weeks (1 in ... cases)	16 weeks (1 in ... cases)	20 weeks (1 in ... cases)	40 weeks (1 in ... cases)
20	1068	1200	1295	1527
25	946	1062	1147	1352
30	626	703	759	895
35	249	280	302	356
36	196	220	238	280
37	152	171	185	218
38	117	131	142	167
39	89	100	108	128
40	68	76	82	97
41	51	57	62	73
42	51	57	62	73
43	29	32	35	41
44	21	24	26	30
45	16	18	19	23

Depending on the national health policies, availability of caryotyping for aneuploidy, and the desire of the patient, a chorionic villus sampling or amniocentesis could be proposed. In France for example, the risk threshold is 1/250 since 1997 (16).

The risk factor associated with ultrasound markers- especially the nuchal translucency at 12-14 weeks, is also depending on the gestational age (or crown-rump length- CRL). If we decide upon a cut-off value (2.5 mm at 12 weeks, or 3 mm at 14 weeks were proposed by most of the authors), the risk ratio will be increased 3.5 times if the difference is 1 mm, 10 times if 1.5 mm, 30 times if 2 mm and 55 times if 2.5 mm. (17, 18).

There are two different approaches towards the integrated use of markers:

1). nuchal translucency with immediate biochemical assessment (of free beta hCG and PAPP-A) at 12-14 weeks. This has the advantage of shortening the “waiting” period, with less trauma for the patient. Unfortunately, not everywhere these tests are available. The rate of detection is 90% of affected fetuses, and the further development of analysis allow a short 30 min interval results, practically as one-step clinic for assessment of risk (also called OSCAR) (19)

2). nuchal translucency at 12-14 weeks, and biochemical markers at 16-18 weeks. It is the most common methodology, multiplying the basal maternal age risk with

the likelihood ratio for these 2 elements. For the biochemistry markers, the estimated detection rates are 50-70%, for a false positive rate of 5%. As nuchal translucency will detect almost 90% of trisomy 21 at 12-14 weeks, the efficiency of the 2nd trimester markers is 6% (60% of the remaining 10%). Also, in interpreting the results, we should be careful as 1 trisomy in 3 will have normal serum markers (1).

In women who had the 1st trimester screening by ultrasound plus biochemical markers, the 2nd trimester testing could be avoided, as recommended by Bizot and Nicolaides (20), because:

- the sensitivities of the 1st and 2nd trimester biochemical screening are similar

the main component of the 2nd trimester screening is beta hCG, and there is a good correlation between first and second trimester maternal hCG levels.

After calculating the integrated risk, by multiplying the risk (or dividing the coefficient described above as in relation to the maternal age), one can therefore decide what is the next step- amniocentesis or chorionic villi sampling, depending on the gestational age. Then, it could be up to the specialist and the parents if another serum marker is used, or if one could wait for a reevaluation at 22 weeks for the minor ultrasound signs cited before.

Conclusion

Ten years ago, the English ultrasound school provided the specialists with an important element in their struggle to screen for the most common aneuploidy- the nuchal translucency. This way the ultrasound scan at 11-14 weeks of pregnancy became an extremely important exam, justifying the recommendation for three ultrasound scans during the pregnancy.

Since then, the screening for trisomy 21 re-evaluated the biochemical markers, and we should now be able to integrate the different elements into a risk assessment strategy, able to detect therefore most of the Down syndromes in time to allow an informed parental decision and medical care.

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II. NEONATOLOGY

INFECTIONS PATHOLOGY INCIDENCE TO NEWBORNS WITH CONGENITAL MALFORMATIONS

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Abstract

This study wants to establish the correlation between congenital malformations of the newborns and the infections pathology they developed.

Key words: newborns, congenital malformations, infections pathology

Introduction

Birth defects are being diagnosed in an increasing number of infants during the prenatal and neonatal period because of improved diagnostic technology, especially ultrasonography.

Because of this, it is even more important for the neonatologist to be knowledgeable about congenital malformations. There are various causes of birth defects, including genetic abnormalities, dysmorphogenesis, and environmental affects on the fetus.

Congenital malformations represent a fundamental pathology problem correlated to incidence (3-5%), etiology, pathology and medical and social implications.

Objectives

This study wants to establish:

- the incidence of congenital malformations at newborns
- the types of congenital malformations
- the incidence of congenital malformations according to gender and social background
- the maternal risk factors
- the correlation between congenital malformations of the newborns and the infections pathology they developed

Material and methods

The necessary data to elaborate this study were collected by analyzing the observation files and laboratory records of the newborns hospitalized in Neonatology and Health Care Clinic Timisoara between 01.01.2001 and 31.12.2002.

Results and discussions

From a total number of 1044 cases, 72 (6,89%) newborns presented congenital malformations.

Distribution of cases related to sex indicated:

- 35 (49%) male
- 37 (51%) female (Fig. 1).

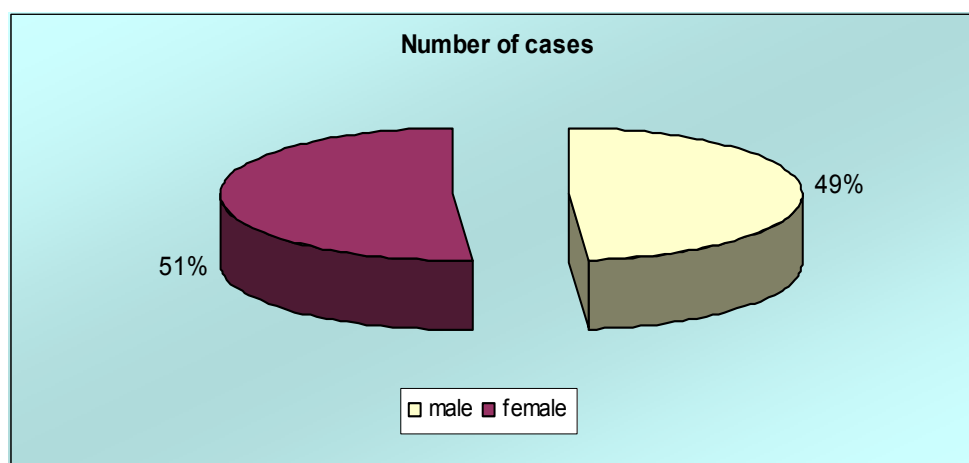


Fig. 1. Sex ratio.

The social background of the newborns indicated that 39 (54,16%) cases were from the urban area and 33 (45,84%) cases – from the rural area (Table 1).

Social background	Number of cases
urban area	39 (54,16%)
rural area	33 (45,84%)

Tab. 1. Repartition of cases related to social background

The types of malformations were:

- 29 (40,27%) cases with osseous malformations
- 28 (38,89%) cases with cardiovascular malformations
- 4 (5,55%) cases with penile hypospadias
- 4 (5,55%) cases with central nervous system malformations (3 cases with meningocele and 1 case with cerebral atrophy associated with left anophthalmia – Fig. 2)
- 3 (4,16%) cases with gastrointestinal malformations
- 3 (4,16%) cases with cleft lip and palate (Fig. 3)
- 1 (1,39%) case with chromosomopathy at 9 chromosome associated with cardiac malformation and congenital clubfoot



Fig. 2. Left anophthalmia



Fig. 3. Cleft lip and palate.

The infectious pathology of the newborns was:

- ❖ 42 (58,33%) skin and mucous infections
- ❖ 38 (52,78%) respiratory infections

- ❖ 12 (16,67%) bacteremia
- ❖ 9 (12,5%) urinary infections (Table 2)

Tab. 2. Distribution of cases according to type of infection

Infection type	Number of cases
skin and mucous infections	42 (58,33%)
respiratory infections	38 (52,78%)
bacteremia	12 (16,67%)
urinary infections	9 (12,5%)

Cultures from pharynx, nasal secretion, umbilicus, conjunctiva, skin wounds, urine, blood and meconium were made in attempt to identify the type of bacterial agent.

Of a total number of 131 positive cultures we found:

- staphylococcus aureus - 86 (65,65%) cases
- e. coli - 24 (18,32%) cases

- enterobacter - 9 (6,87%) cases
- klebsiella - 4 (3,05%) cases
- staphylococcus - R 4 (3,05%) cases
- pseudomonas aeruginosa - 3 (2,29%) cases
- staphylococcus epidermidis - 1 (0,76%) case (Fig. 4)

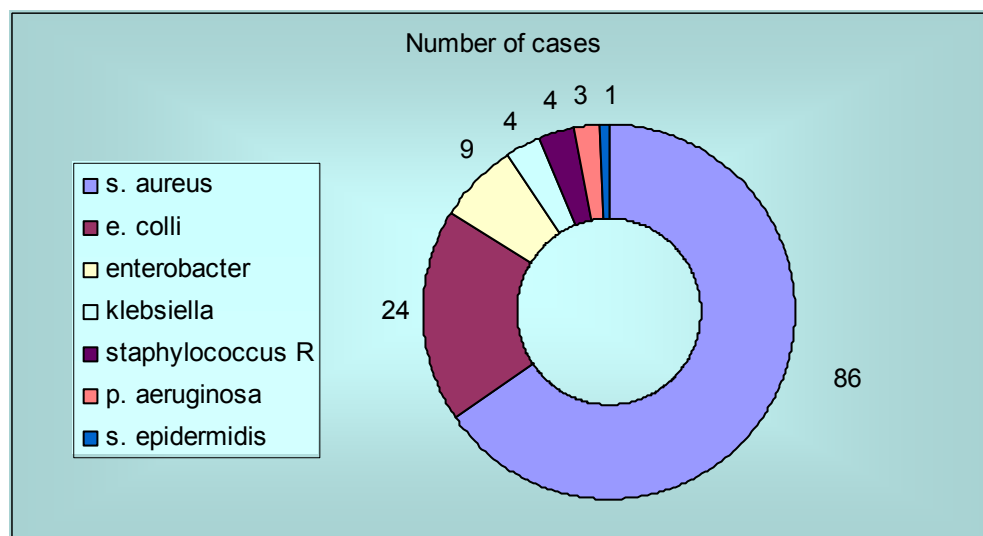


Fig. 4. Distribution of cases according to germ type

Maternal infections circumstances were found in 59 (74,68%) cases:

- the premature rupture of the amniotic membranes - 16 (22,22%) cases

- dystocia 7 (9,72%) cases
- green amniotic fluid 22 (30,55%) cases
- maternal infections - 14 (19,44%) cases (Table 3)

Tab. 3. Distribution of cases related to maternal infections circumstances.

Maternal infections circumstances	Number of cases
the premature rupture of the amniotic membranes	16 (22,22%)
dystocia	7 (9,72%)
green amniotic fluid	22 (30,55%)
maternal infections	14 (19,44%)

Conclusions

1. congenital malformations are more frequent to males and to newborns from the urban area
2. the most frequent malformations appear at the osseous system followed by the cardiovascular system
3. because of the immaturity of the imunitary system at newborns with congenital malformations, the infections pathology is more frequent
4. the most frequent infectious pathology is represented by skin and mucous infections and respiratory infections
5. the most frequent bacterial agents are staphylococcus aureus and e. colli
6. maternal infections circumstances are implicated in almost $\frac{3}{4}$ of cases

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HYDROCEPHALY AT INFANTS AND CHILDREN

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Abstract

The paperwork discusses about anatomy, physiology, classification, etiology, physiopathology, clinical aspects, paraclinical investigations, differential diagnosis, evolution, prognostic, therapeutical aspects of hydrocephaly.

Keywords: hydrocephaly.

By hydrocephaly of the infants we understand an increase in the volume of the skull due to an increase of the quantity CSF (cerebrospinal fluid) and its being accumulated, under pressure, in the preformed anatomical intraskulled cavities, which has for consequence an expansion of these liquid cavities because of the cerebral substance. As the quantity of CSF in the intracerebral spaces increases under pressure, so does the volume of the skull, while the global volume of the cerebral parenchyma decreases.

The hydrocephaly of the child involves an active increase of the quantity of CSF in the cerebral ventricles, under pressure without the increase of the skull perimeter, already finalized.

As far as the mechanism of production is concerned, we have to differentiate between the active hydrocephaly described above, and the passive hydrocephaly which follows the reduction of the cerebral parenchyma by cerebral atrophy, during which the CSF, being under normal pressure comes to fill in the empty space (ex vacuo). In the case of passive hydrocephaly, the skull has normal dimension.

The anatomy of liquid spaces

The anatomic spaces that normally contain the CSF, in the liquid spaces, include two compartments:

1-The spaces derived from the primitive neural tube, disposed inside the CNS (central nervous system), contains the cerebral ventricles (at the level of the encephalon) continued by the ependymal canal (at the level of the spinal cord).

At the level of the encephalon, there are the four ventricles: the lateral ventricles (2) (telencephalic), the third ventricle (diencephalic) and the fourth ventricle (rhombencephalic). These ventricles communicates with one another through the Monro foramen (which ties the lateral ventricles to the third ventricle) and through the Sylvius aqueduct (which links the third and the fourth ventricle).

The cerebral ventricles are lined with the ependym (nevroglial membrane) except the choroid plexus.

The ependymal canal (the central canal of the spinal cord) crosses longitudinally the spinal cord at the level of the grey commissure.

2-Subarachnoidian spaces form between arachnoid and pia matter. Subarachnoidian intracranial space communicates with intrarachidian space by cisternae systems (cisterna magna, cisterna pontomedullaris).

The connection between these two compartments (liquidian spaces derived from the primitive neural tube and subarachnoidian space) is done at the fourth ventricle level, through three foramens:

- Magendie foramen (connects fourth ventricle and cisterna magna);
- Luschka foramens (two) (that achieves the connection with cisterna pontomedullaris).

Physiology of CSF

The amount of CSF at infants is 40-60 ml, and after five years old reach 100ml.

The production of CSF was considering belonging to the choroids plexus of the ventricles, but new studies shows that nervous tissue has a role in CSF production.

There is two types of CSF circulation:

- longitudinal circulation – the CSF outflow is directed from choroids plexus toward arachnoid granulations (main place of CSF resorbtion);

- transversal circulation (transependymar and transspinal) - there is a continuous exchange between spaces filled with CSF and extracellular space of nervous system.

CSF resorbtion is an active process, which is in a dynamic balance with the active process of secretion of CSF. The main place of CSF resorbtion is Pacchioni's arachnoid granulation which allowed the passing of CSF outflow from subarachnoid space into the venous and lymphatic systems. Another resorbtion are as are: capillary - venous system of leptomeninges, perivascular and perineural slits. Resorbtion of CSF is controlled by the endocranial venous pressure.

The classification of hydrocephaly

The old classification used to divide hydrocephalies in to: congenital and gained.

Nowadays there are different classifications according to the etiology, morphology, clinical aspect, evolution etc.

The most used classification are:

1-Dandy's classification (1918) based on physiopathological criterion:

- the obstructive hydrocephaly: caused by a blocking of the circulation ways of CSF.

- the communicating hydrocephaly: caused by hypersecretion or hyporesorbtion of the CSF (the circulation ways are free).

2-Matson's classification (1963) based on clinical criterions and therapeutic importance:

- progressive hydrocephaly: with progressive signs but without proofs of irreversible cerebral lesions;
- extremely progressive hydrocephaly: with longtime persisting hydrocephaly and with irreversible cerebral lesions, having yet therapeutic importance;
- stabilized hydrocephaly when a cease of evolution exists, but which needs periodical control because it can often became progressive again;

3-Lazorthes's classification (1954):

- active hydrocephaly: when there is a disorder or a blockage of the CSF circulation (corresponding to Dandy's obstructive hydrocephaly);
- functional hydrocephaly: there is a disproportion between the CSF production and resorbtion (corresponding to Dandy's communicating hydrocephaly);
- passive hydrocephaly: following the reduction of the cerebral parenchyma through cerebral atrophy (it doesn't belong to the infant's and child's hydrocephaly).

4-Carnier's classification (1969):

- communicating hydrocephaly;
- noncommunicating hydrocephaly.

Etiopathogenesis

There are a lot of factors responsible for the formation of the hydrocephaly, which can be grouped in this way:

1. Congenital malformation. The hydrocephaly through congenital malformation can manifest itself at birth, but not obligatory, sometime it can be discovered after a few months from the birth.

During the intrauterine development there is a stage/phase of physiological hydrocephaly during the first 5 months, initially obstructive (through the unpermeabilisation of the Magendie and Luschka forams) then communicating (through the permeabilisation of the same forams) which normally up to the fifth month sets off. So, some forms of hydrocephaly do not represent a new phase, but the pathological persistence of a stage which is normal for the fetal life.

The hydrocephaly may be produced by the following congenital malformation:

- a. Disgenesis of the Sylvius's aqueduct produces through obstructive mechanisms a triventricular hydrocephaly accompanied by important cerebral lesions.
- b. The Dandy-Walker syndrome or the atresia of the Magendie and Lushka holes accompanied by agenesis of inferior vermis; realizes a quadriventricular hydrocephaly with an enormous pseudocystical dilatation of the IV th ventricle.
- c. The Arnold - Chiari malformation is characterized by the descent (herniation) of the cerebellum and the bulb in the medullary cervical duct produces the hydrocephaly as a result of the deformation which exists at the level of the IV th ventricle.

d. Spina bifida, the mielomeningoceles and the meningoencephalocoles are very frequently associated with the hydrocephaly (70-80 %). The belief that the surgical cure creates a liquids maladjusted followed by hydrocephaly is not true. It was proved through preoperative and postoperative ventriculography (Lorber 1961) that the hydrocephaly is present before the operation, and postoperative the hydrocephaly does not appear to those to whom the ventricular system was normal before the operation. It appears that the bag of the mielomeningocele acts as auxiliary to the normal mechanism of pulsate absorbtion of the spinal sheath; the ablation can produce a partial loss of this mechanism and can contribute to a ventricular dilatation. It has been noticed the frequent association of the mielomeningecele with cranio-vertebral junctions malformation and with the Arnold-Chiari malformation.

e. Other malformations: congenital arachnoidal cysts, bones malformations localized at the level of the cranio-vertebral junctions (the basilar impression, the platybasia) or generalized (achondroplasia, Hurler's polydistrophy).

2. Intracranial expansive processes

- a. The cerebral tumors are rare at the infant and at the child. They may produce hydrocephaly especially by an obstructive mechanism, affecting directly the flow of CSF: tumors of the IV ventricle, tumors of the posterior cranial fossa, tumors of the brain stem, and tumors of the pineal area. The papillomas of the choroidal plexus by the hypersecretion of CSF produce the communicating hydrocephaly.
- b. Cerebral abscesses;
- c. Subdural overflows.

3. Meningo-cerebral inflammatory processes

They include infectious processes, which generate a hydrocephaly of bacterial, viral or parasitic origin.

- a. Ependymitis (in case of inflammation, the ependyma produces an increased quantity of CSF);
- b. In ependymitis the hydrocephaly may be:
 - communicative, if the inflammation is limited to the lateral ventricles;
 - obstructive, if the inflammation expands secondary to the aqueduct.
- c. The meningitis produce obstructive hydrocephaly by the formation of adherences which prevent the CSF circulation;
- d. The toxoplasmic encephalitis produces an obstructive hydrocephaly, the presence of the classical triad of the congenital toxoplasmosis (hydrocephaly + intracranialcalcifications + corioretinitis) allows the suspicion of the toxoplasma as etiology of the hydrocephaly.

4. The hemorrhage of the meninx produces obstructive hydrocephaly by fibrous lying which causes fibroadhesive leptomenigitis, especially at the base and at the fissures of the cerebral hemisphere, accompanied by the blocking of the resorbtion.

Small quantities of blood can be found in the CSF at almost all new-born babies, with more severe bleeding in the case of prematurity ones. In the developing of a hydrocephaly, only severe bleeding in the CSF comes into consideration. After subarachnoid hemorrhage, the meninx fibrosis appears, especially if the blood had persisted for at least 10 days; this is the reason why the lumbar puncture are necessary and efficient in order to evacuate the blood and to prevent the installation of hydrocephaly.

5. Vascular disorders:

- thrombosis of the superior longitudinal sinus;
 - malformation of the great Galen's cerebral vein;
- In both cases, the hydrocephaly is obstructive because of the diminution of the CSF resorption causing by stasis and hypertension in venous sinuous.

6. CSF hypersecretion

- hypersecretative papillomas of the choroids plexus;
- -A hypervitaminosis and hypovitaminosis (they are benign and do not need treatment).

7. Hydrocephaly with normal pressure (HPN) - is rare in the case of children. The clinical signs consist of: mental retardation, equilibrium and behavioral disorder, personality changes, disorder of the sphincters. In all cases, the intraventricular pressure is not high; but drainage with automatic valve with low pressure is a must for diminishing the quantity of intracranial CSF which may become active as a result of cranio-cerebral trauma, sunstroke, etc.

8. Hydrocephaly of indeterminate origin

– it must be insisted both anamnestic and paraclinical investigations in order to detect the cause of this hydrocephalyes.

Physiopathology

Generally, in the pathogenesis of hydrocephaly the following three factors may occur:

a) CSF hyperproduction usually accompanies the evolution of a papilloma of the choroids plexus this is a rare possibility;

b) Insufficiency of CSF resorption.

In occur separately, this two factors did not cause progressive hydrocephaly.

c) An obstruction in CSF circulation can produce a chronic obstructive hydrocephaly by unbalance in secretion and absorption of CSF. Experimentally was established that absorption diminish with almost 80% in first hours after obstruction and remain low for 10-15 days. Concomitant CSF secretion decrease progressively and it will begin balance with absorption from 21-th day. This unbalance, determine a rise of ventricular volume. Initially cerebral substance remain unimpaired, but because of repeated episodes of high intracranial pressure lesion of cerebral structure appear.

An increase in ventricular volume determine a diminish in reserve functional space of CSF resorption by compression of subarachnoid space, cisterns and venous system. All this factors contribute to hydrocephaly development. Exceedingly ventricular dilatation cause

stretching of corticospinal nervous tracts, cerebellum compression and appearance of associated clinical signs.

Clinical aspect

1. A large neurocranium is the main sign. Because of enlargement of neurocranium, viscerocranium appears small in comparison.
2. Bulging and large anterior fontanel is a result of high intracranial pressure. A persistent bulging anterior fontanel is a proof of hydrocephaly even if perimeter is normal.
3. Dilatation of scalp's veins, which is very well visible at frontoparietal region.
4. The eyeballs are orientated downwards, with pupilla partial covered by eyelid.
5. The palpation find: cranial suture are dehiscent, anterior fontanel is large (8-10 cm or more), bulging.
6. The percussion of the head demonstrate a "broken pot" (Macewin sign)
7. Mental and motor retardation.
8. Psychico-motor agitation (because of CSF's high pressure)
9. In advanced stages there are present: slow spontaneous movements; spasticity of inferior limbs, than superior limbs; bilateral Babinski sign; strabismus; modification of retina, even optic atrophy with absence of pupillary reflexes and blindness; disorders of consciousness state that may advance to coma.

Clinical aspects in child's hydrocephaly is same as infant's with exception of: increase of cranial perimeter, bulging anterior fontanella and dehiscent of cranial sutures.

Diagnosis – is easy in advanced hydrocephaly, when all clinical signs are present, but is difficult in incipient stages, when paraclinical investigation is needed to confirm the diagnosis.

Paraclinical investigation

1. The diagrams of head circumference increasing and anterior fontanella closing (periodic measurement every two weeks). The normal increasing rhythm of head circumference is: 2 cm by month in the first three months; 1 cm /months between 4-6 month; 1 cm every two months in next months.
2. Transfontanellar ultrasound shows ventricles dimension and cerebral parenchyma status.
3. Head-radiograph shows a cranium with balloon shape and disproportion between neurocranium, which is very big, and viscerocranium. The anterior fontanel is very large. The radiograph transparency of the cranium is high, with invisible sutures. If a subsequent X-ray shows a most evident sutures there is a proof of stabilization of hydrocephaly. In case of intracranial expansive process (tumors, subdural hematoma, abscesses, etc) there is a little increase of cranium volume and sutures of cranium are dehiscent, which is the main sign. In case of intracranial calcifications we must consider toxoplasmosis, choroids plexus, papilloma with calcifications or craniopharyngioma.

4. CT-scan is the main investigation in hydrocephaly. This method identifies periventricular edema ("perilucency") which proves CSF accumulation in parenchyma of the cerebrum. This edema indicates a serious damage of the parenchyma and in this case is this case is requiring an emergency CSF drainage. CT scan provides informers about stadialization of hydrocephaly. Evans index represents ratio between extreme interventricular distance and interparietal distance on horizontal section and is below 0,3 normally.

There are four stages of hydrocephaly:

- stage I (minor hydrocephalus): Evans index = 0,26–0,40
 - stage II (medium hydrocephalus): Evans index = 0,41–0,60
 - stage III (severe hydrocephalus): Evans index = 0,61–0,90
 - stage IV (extreme hydrocephalus): Evans index = 0,91–1,00
5. MRI– is not obligatory if CT-scan was done. MRI advantage are major in discover of concomitant malformations which product obstructive hydrocephaly.
6. CSF examen

Two elements is important for hydrocephaly: total proteins of CSF and cytology of CSF which may indicates an inflammatory, tumoral or hemorrhagic etiology. A high level of proteins contraindicates the interventions for ventricular drainage.

7. Pneumoencephalography and ventriculography may be useful for estimate of: CSF cavities morphology, level of obstruction of CSF flow and to guide in surgical interventions.
8. Radioactives isotopes may provide dates about CSF flow, speed of circulation and CSF resorbtion.
9. Cerebral angiography discovers vascular malformations.

Differential diagnosis

1. Congenital macrocephaly: usually have familial character; is nonpathologic, nevolutive and ventricles dimensions are normal.
2. Florid rickets: the cranium is large but squarer shape, anterior fontanel is normal and time evolution makes the difference CT scan is useful.
3. Subdural overflow with macrocephaly necessitates CT scan and eventually MRI to make the diagnosis.
4. Congenital arachnoid cysts in infants can manifest with increase in cranian dimension.
5. CT scan identify the diagnosis. Hydranencephaly – there is no cerebral substance at the level of temporal, parietal lobes, on convex surface of temporal and occipital lobes which means the territory of distribution of medium and anterior cerebral arteries (hydranencephaly is cause by an occlusion of internal carotid arteries).Only brain stem exist and survival is due this nervous structure. There is no indication to surgical intervention.
6. Hydranencephaly must differentiate from extreme severe hydrocephaly (stage IV), when ventricles are in maximum distension but cerebral parenchyma exists between endym and leptomeninx.

Evolution

There are four stages that coincide with CT scan stages:

- stage I: head circumference is normal, ventriculomegaly exists, CSF pressure is increase and there is no cerebral atrophy

This stage may remain stationary or may progress.

Management in this stage consist in clinical, ETF and CT scan follow-up

- stages II and III: there appears the distension of the osteomembranous space as a compensation of the increase of the CSF pressure, with a clinical aspects typical of hydrocephaly and starting to diminish the cerebral mantle. These stages may be stabilized spontaneously or may evolve to stage IV. Therapeutic indication: CSF drainage proceeding
- stage IV: a stop appears in the growth of the nervous tissue and the one already existing is subjected to more and more rapid destruction . The cerebral mantle is reduced progressively and becomes papyraceous. In this stage the spread hypertonicity is always present. Therapeutic indication: CSF drainage proceeding depending on the clinical neurological and ophtalmological state and on the modification noticed on the CT scan or MRI.

Some hydrocephalies get stabilized suddenly – the stabilized hydrocephaly non-progressive. This type of hydrocephaly may decompensate in some situations (cranio-cerebral traumatism, effort, sunstroke, intercurrent illness, lumbar puncture, and the pneumoencephalography) and become evolutionary with serious phenomena of intracranian hypertension. So to the compensated hydrocephalies the lumbar puncture and the pneumoencephalography are dangerous leading very easily to the decompensation of the stabilized hydrocephaly.

The evolution at infant and children with acute hydrocephaly (stage IV) is towards death in the first 6-12 months by cardio-respiratory insufficiency due to the compressed of the brain stem (of the bulb) by CSF through intracranian hypertension.

The evolution of those who treated their hydrocephaly surgically (stages II -III) is easily favorable in the case of a good functionality of the drainage system. Through the reduction of the CSF pressure on the cerebral parenchyma, there is an obvious improvement of all the SNC functions. The postoperative results must be observed in time neurologically, ophtalmologically, psychiatrically and by repeated CT scan.

Prognostic

The vital prognostic of the progressive (active) hydrocephaly is reserved, being more favorable to the cases, which suffered a surgical treatment than to those that didn't.

The vital prognostic depends on: repeated intercurrent affections; infections of the CNS, septicæmic condition, other severe infections (bronchopneumonia, acute endocarditis, etc.); prematurity; severe cranio-cerebral

traumatism; other organic or metabolic affections; the evolutive stage of the hydrocephaly (stage IV has a severe vital prognostic).

The functional prognostic (intellectual, cognitive functions, IQ, neurological focal deficit, the affectation of the cranial nerves) of the active, evolutive hidrocephaly depends on: the time elapsed from the beginning to the diagnosis, the cranial hypertension syndrome, the destruction of the cerebral parenchyma, the affectation of the visual function, the evolution stage of the hydrocephaly, the time elapsed up to the surgical intervention, the correct surgical intervention adapted to the stage of the hydrocephaly. The exact evaluation of the functional prognostic of the treated hydrocephalics may be performed only after 10-15 years from the application of the CSF drainage.

Treatment

I. The active, evolutive hydrocephaly is only treated surgically, the medical treatments (lumbar or ventricular punctures) being insufficient or having a limited, temporary effect.

An essential principle of the surgical indications is that the time elapsed from the beginning to the treating of the hydrocephaly be as short as possible.

The immediate purpose of the surgical treatment is: to remove the causes of the hydrocephaly and to stop its evolution; and, as a secondary purpose: to ensure a functional future for the child, family, and society.

The major contraindications of the surgical treatment are:

1. signs of severe neurological damage :blindness, hemiplegia, coma;
2. concomitant congenital malformations of the CNS or of the other organs;
3. hyperalbuminorahia $> 1\text{g/l}$ (a uni-shunt drainage can be applied where the automatic valve is not obturated);
4. the cerebral mantle $< 1\text{ cm}$ thick (stage IV);
5. the cranial perimeter exceed 60 cm ;
6. an accentuated dystrophy or a bad general mood;
7. when the hydrocephaly is not plainly evolutive;
8. internal hydrocephaly without tension;
9. serious infections of the nervous system (menyngoencephalitis, ventriculitis – bacterial or bacillar)or general (bronchopneumonia, sepsis state, endocarditis).

Of all these , an absolute contraindication is only the serious infection that can lead to generalization of the infection .the other contraindications are given by the weak postoperative results to witch we can expect , and concern especially the future of the child .

Surgical treatment concerns the reduction of the intaventricular pressure of the CSF which is realized through three types of procedures:

A. Procedures to decrease the CSF secretion: resection or coagulation of the choroids plexus in the lateral ventricles. There were not

satisfactory results, they were accompanied by increased mortality and morbidity.

B. Intracranial drainage procedures of the ventricular CSF:

- 1.The perforation of the superoptic lame for ventriclestomia III.
- 2.Posterior ventriclecisternostomia type Torkildsen (1939)
- 3.Endoscopic ventriclecisternostomia.
- 4.The posterior endoscopic ventriclestomia of the ventricle III, with the opening of the Sylvius aqueduct: it has major efficiency, minimal complications, so it is recommended in conditions of neuroimagistic and actual endoscopy.

C. Extracranial drainage procedures of the CSF ventricular with the automatic valves: there are numerous possible variants: lomboperitoneal drainage, ventriclecardiac drainage, ventricleperitoneal drainage.

1. Lomboperitoneal drainage has been imagined in the communicant hydrocephalies for the deversation of CSF directly in the peritoneum on a much shorter path (Chuma and collab. 1993). The main complications are mechanical: hyperlordosis, scoliosis, the hernia of cerebellous amigdales (tonsils).
2. Ventriclecardiac (VC) drainage is a physiologic drainage, CSF in excess arriving directly to its destination medium (venous blood). Automatic drainage valves are used, type Holter-Codman, Hakim, Pudenz, Denver, Neurone, Heyer-Schulte, Chabra, etc., with a high-medium-low pressure dial or even with a much larger dial; these valves assure protection against the blood flow and also against the fast ventricular decompression.

The surgical procedure includes the application of three elements:

- intraventricular catheter with measurement of the intraventricular pressure;
- automatic valve adapted to the catheter, with a pressure dial perfectly adaptable to the intraventricular pressure;
- intra-atrial catheter (adapted by the facial vena, via the internal jugular vena, in the right atrium) connected to the automatic valve.

The advantages of the VC drainage consist in: simple surgical technique, minimal surgical trauma, good adaptability at infants, good tolerance, there are not water and electrolytes losses, it can be controlled radiologically, the surgical reintervention is relatively simple.

The complications of the VC drainage are mechanical and infectious. The mechanical complications are: the blocking of the tubules and of the valve, the tubes (the catheters) becomes too short as the child grows, the presence of the air in the valve or in the tubes hinders the CSF circulation, the disconnection of the tubes.

The infectious complications are major: infections of the nervous system (meningitis, ventriculitis), cardiopulmonary infections (bacterial endocarditis, bronchopneumonia), infections at distance (shunt glomerular nephritis), and sepsis state. Due to these

redoubtable infectious complications, in the last 20 years they passed gradually to the VC drainage

3. The ventriculoperitoneal drainage (VP) supposes the CSF ventricular drainage in the peritoneal cavity through a system of tubes (silicone catheters) and automatic valves.

The surgical procedure includes the application of four elements:

1. intraventricular catheter with measurement of the intraventricular pressure;
2. automatic valve with pressure dial adaptable to the intraventricular pressure, connected to the ventricular and to the distal catheter;
3. intermediary piece (connector) for the possibility of the effectuation of a MRI anytime;
4. intraperitoneal catheter of about 30 cm, allowing the sliding of the later along with the child's growing.

The advantages of the VP drainage are: the possibility of applying surgical techniques in the first week of life even the possibility of quick revising in case of mechanical complications, the infectious complications are much more reduced than in the VC drainage and with more efficient therapeutically possibilities.

The complications in VP drainage are frequent, being dominated by the mechanical ones.

The mechanical complications are: the disconnection of the tubes, the moving off of the tubes from the peritoneum, the moving off of the tubes from the cerebral ventricle (all possible with the child's growing), disconnections at the connector's level or between the tubes and the automatic valve. For the correct evaluation of the VP drainages and of the mechanical complications are imposed X-ray examinations, CT-scan abdominal and transfontanellar ultrasounds. For the mechanical complications we have two possible drainage tube revisions until puberty (Hirsch, 1992).

The infectious complications are more reduced than in the case of VC drainage and they consist of: infections of the nervous system (meningitis, ventriculitis), abdominal infections (peritonitis, septic abdominal cysts). The treatment protocol of the infectious complications is very strict and complex: the drainage system must be totally replaced, a temporary passage to the external CSF, the restoring of the VP drainage on the opposite side after having obtained 3 sterile CSF samples (Khanna & Co., 1995).

Other frequent complications of the VP drainages enclose: bilateral subdural overflowing, the premature closing of the cranial sutures, "slit-ventricle syndrome" (small ventricles on the median line), and "over-drainage" syndrome. The correction of these complications is made through: the checking of the intracranial pressure and the adjusting of the valves; Orbis-Sigma automatic valves with adjustable pressure according to the CSF pressure; Sophysa automatic valves with exterior adjustable pressure, with magnet.

The evaluation of the cases operated is obligatory for: the appreciation of the function of the VP drainage system, the decompression of the cerebral parenchyma, the

functionality of the nervous system (IQ). The protocol of evaluation is structured in this way:

1. in the first 3 post operator years :

-neurological, neuropsychiatric, ophthalmologic control at 2 months;

-CT-cerebral scan and the abdominal ultrasound at 3 months;

2. in the next 3 post operator years:

-neurological, neuropsychiatric and ophthalmologic control at 6 months;

-CT-cerebral scan and abdominal ultrasound at 4 months;

3. after 6 post operator years:

- neurological, neuropsychical and ophthalmologic control at 1 year;

- CT-cerebral scan and abdominal ultrasound at 1 year;

Any neuropsychical, ophthalmologic clinical modification must immediately be evaluated correctly and completed by a CT-scan examination. Also the post operator control (inclusively CT-scan) is obligatory in the case of possible decompositions of the hydrocephalic through: sunstrokes, undercurrent infections, TCC, abdominal surgery.

II The obstructive symptomatic hydrocephalic –benefit only by surgical treatment.

A. In these cases we must orientate firstly towards an ethiopathogenic surgical treatment that could solve the cause of obstruction.

In cerebral tumors, cerebral abscesses, subdural overflows it will be an attempt to their ablation.

In the arachnoidita of posterior cerebral fosses or the Arnold-Chiari malformation the intervention directly on these lesions has a temporary character because the arachnoidian adherences recovered very fast.

In the stenosis of aqueduct some authors propose the matter of repermeabilization of the aqueduct.

Because all these surgical interventions cause a great mortality, the ethiopathogenic treatment addresses to a limited number of hydrocephalus.

B. Internal drainage of CSF: only in case of obstructive (noncommunicating) hydrocephaly and is vital for decrease of intracranial pressure cause by tumoral process. Can be used the "uni-shunt drainage" procedure (the absence of automatic valve) (Ciurea & co.1998). The major complications of this drainage is extradural hematoma or subdural overflow by over-drainage (control CT scan is necessary).

C. External drainage of CSF by a standard system with assessment of intraventricular pressure and CSF gathering. This system function for 48-72 hours and then must occur surgical intervention for obstructive hydrocephaly (maintain more than 72 hours may produce infections).

Results

Statistics about results of operates hydrocephalies vary and depending specially on duration of postoperative follow-up and less on valve type. Results depending very much on surgical indications which is made

on time and correctly. Long term results evaluation is made on the basis of mental and motor development criterions.

On an average, statistics with postoperative follow-up more than 8 years shows this results: excellent 20-25% of cases, good 40-50%, poor 20-25%, deaths 5-10 %, postoperative complications 25-35%.

In conclusion, functional outcome depend more on cerebral parenchyma damages than dimensions of hydrocephaly.

Conclusions

In last decades more progress in hydrocephaly's treatment was done, but wasn't found an ideal cure. The most used surgical procedure is ventriculoperitoneal drainage.

At present, since neuroimaging and endoscopy development, endoscopic posterior third ventricle ventriculosomy with Sylvius aqueduct opening is performing with very good results .

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III. PEDIATRICS

ENTERIC COATED MINIMICROSPHERE IN THE TREATMENT OF PANCREATIC FAILURE FROM CYSTIC FIBROSIS

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Abstract

Paper aim consists of a comparative retrospective evaluation of the pancreatic enzyme therapy with microsphere versus minimicrosphere. 25 children with mucoviscidosis, followed-up by the cystic fibrosis (CF) Centre Timisoara who benefit from both categories of enzymes represented study material. As a conclusion, using of enteric coated pancreatic minimicrosphere implies lower daily doses, decreases the risk for fibrosing colonopathy and reduces the therapy costs.

Key words: pancreatic enzyme therapy, microsphere, minimicrosphere, cystic fibrosis

Background

The pancreatic failure (PF) represents a major and characteristic aspect in cystic fibrosis (CF). More than 85-87% of the patients have varying degrees of PF. In fact the histological abnormalities started in utero (1).

Clinical manifestations connected to the deficiency of PF have a very large spectrum: meconial ileus or distal intestinal obstruction syndrome (DIOS), chronic diarrhoea with steatorrhea and failure to thrive, liposoluble vitamins deficiency, hemolytic anemia, hypoproteic edema, rectal prolapse (2, 3).

The most important treatment of PF consists of replacement with animal origin enzymes (3). During history, the main question was: how to produce replacement enzymes that in a small volume, could ensure both a sufficient enzymatic supply and a large digestive surface and to be protected by the gastric acids in the same time. The answer to these problems came after the introduction of the enteric coated pancreatic microsphere in '80. However, there were frequent clinical situations, when no improvement in steatorrhea has been observed, and, as a result, higher doses of enzymes have been used because: medical recommendation were more or less documented, the patients were familiar to take large amount of drugs, commercial products with up to 50 000 IU lipase were offered by pharmaceutical industry representatives, irrational interpretation of therapeutic scheme. Because of these problems, in the latest years had appeared a new complication of CF – fibrosing colonopathy (4,5). Fibrosing

colonopathy consists of severe fibrosis at the submucosal level in the upper colon, with secondary obstruction (6). In this context, the lower dose of enzyme could be compensated by ensuring a larger digestive surface. This problem was resolved after the introduction of the minimicrospheres in the treatment of CF.

Aim of the study

The aim of this study was a comparative retrospective evaluation of the pancreatic enzyme therapy with microsphere versus minimicrosphere.

Material and method

The studied lot: 25 children with CF, followed-up by the CF Centre Timisoara, who benefit from both categories of pancreatic enzymes.

Criteria for including patients in the study were: stable clinical status; digested stools, the absence of other clinical aspects related to PF (rectal prolapse, DIOS); minimal doses of enzyme in microspheres, at least 2000 IU lipase /Kg body/lunch, respectively 800IU/Kg body/snack (drugs with 25 000 IU lipase /ampoule).

We have administered minimicrospheres in varying doses, between 800-2000 IU lipase /Kg body/lunch, respectively 500-800 IU lipase /Kg body/ snack, so that the initial parameters remain similar with those for included criteria. We used minimicrospheres of 10 000 IU lipase /ampoule.

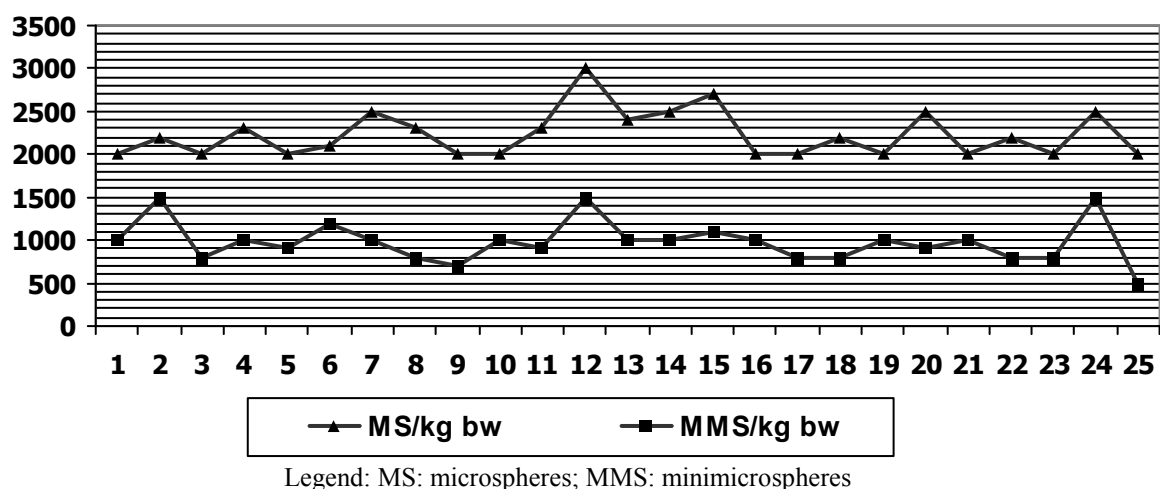
Results and discussions

Replacement therapy with minimicrospheres was introduced in our services more than 10 years ago (red cross helping) and it was generalized approximately 5 years ago when the specific types of drugs were available in Romania (7). Present recommendation for the dosage of pancreatic enzymes are (8):

- infant: 2000 – 4000 IU lipase /120 ml milk;
- 1-4 years: 1000 IU lipase /Kg bw/lunch, respectively 500 IU lipase /Kg bw/ snack;
- 4-15 years: 500 IU lipase /Kg bw/lunch, respectively 250 IU lipase /Kg bw/snack;
- teenager-adult: lower doses because of a lower lipid intake.

The comparative evaluation of the two types of pancreatic enzymes revealed a lower average amount for

minimicorpheres comparatively with standard | micorspheres. (see diagram).



The average amount for microspheres was 2128 IU lipase/Kg bw/lunch and for minimicorpheres the average amount was 916 IU lipase/Kg bw only. Results revealed that the enzyme average ratio/kg was lower with 12% in the case of minimicorphere than for microsphere. At the some time there were no cases with the fibrosing colonopaty observed in the study.

Conclusions

1. Using of enteric coated pancreatic minimicorpheres implies lower daily doses, decreases the risk for fibrosing colonopaty

2. The therapeutic regims elaborated by the CF Centre Timisoara as a coordinative institution at national level presents recommandations for such a treatment.

3. Using of enteric coated pancreatic minimicorpheres implies at the some time the reduces of therapy costs.

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EMPTY SELLA SYNDROME A CAUSE FOR GROWTH HORMONE DEFICIENCY (GHD) OR JUST A COINCIDENT ASSOCIATION?

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Abstract

The paper aims to establish a correlation between the computer tomographic finding of Empty Sella Syndrome and the growth hormone deficit (GHD) in children. The authors present 20 children with GHD evaluated and followed up in Clinic II Pediatrics Timișoara. The complete evaluation of children for GHD at diagnosis included, besides other investigations, hormonal dosage of GH and CT imaging of the pituitary. The study raises a question upon the involvement of the radiological empty sella syndrome in causing GHD, as the syndrome may represent the cause for the GHD in children but it may also be a coincident association with it.

Key words: empty sella syndrome, growth hormone deficit, computer tomography

Background

The empty sella syndrome occurs when the subarachnoid space extends into the sella turcica, partially filling it with cerebrospinal liquid. This process causes the remodeling and enlargement of the sella and also the compression and flattening of the pituitary. Thus, it is a morphological finding consisting in a descending of the arachnoid into the sella, so that the anterior pituitary tissue may not be seen (1,2).

Primary empty sella, resulting from a congenital incompetence of the diaphragma sellae, is most frequent in children, while the secondary form (after radiotherapy, surgery) is usually found in adults. The diagnosis is confirmed by computer tomography (CT) or magnetic resonance imaging (MRI) of the hypothalamic-pituitary region, showing more than 4 mm air or liquid above the diaphragmatic line, leaving most of the sellar cavity empty (1,3).

This radiological abnormality may be associated with deficiencies of anterior pituitary hormones including the growth hormone deficit (GHD), but may also be found accidentally coexisting with a normal pituitary function (4).

The authors tried to evaluate the frequency of empty sella syndrome (ESS) and its relationship with the growth hormone deficiency (GHD) in the child.

Material and method

We studied 20 children (13 males and 7 females) aged between 5⁶/₁₂-16 years admitted in Clinic II Pediatrics Timișoara for short stature and diagnosed with GHD after a complex clinical and biological evaluation.

The diagnostic criteria for GHD included:

- Clinical and auxological criteria
 - short stature (height more than 3SD below the mean for age and sex);
 - decreased growth velocity (< 25th percentile for age and sex);
 - delayed bone age;
- subnormal GH response at two provocative tests (RIA method). We used the GH stimulation test with intravenous insulin (0,1-0,15 i.u./kg) and considered a GHD at cut-off level of 3 ng/ml (total GHD) and 7 ng/ml (partial GHD).

Besides the investigations mentioned, a complete set of usual laboratory evaluation was performed in all cases and, also, some specific investigations (hormonal dosages) in selected cases:

- thyroid hormones (TSH, FT4, TT4, TT3);
- serum cortisol;
- serum prolactin;
- gonadotropins and sex steroids – in pubertal patients.

The imagistic evaluation of the pituitary consisted in:

- Radiography of the sella turcica;
- CT scan of the hypothalamic pituitary region.

Results

All children were diagnosed with GHD according to the clinical, auxological and hormonal evaluation. Depending on the GH peak at the insulin tolerance test, we found 11 patients with total GHD and 9 patients with partial GHD; 9 of 20 (45%) patients with GHD, were diagnosed with primary empty sella syndrome on CT scan (no history of cranial trauma, infection or radiation was revealed). None of the subjects presented any modifications of the sella turcica on the standard cranial radiography.



Fig nr.1. CT scan – Empty Sella Syndrome

The distribution of the cases with primary empty sella syndrome depending on gender, revealed a predominance of males (6 cases) with a sex ratio of 2/1 = male/female. Analyzing the relationship between the empty sella syndrome and the peak of growth hormone after stimulation, of the 9 patients with empty sella syndrome we found 8 patients with total GHD (peak GH below 3 ng/ml) and 1 patient with partial GHD.

The patients showing normal aspect of the hypothalamic pituitary region at the CT evaluation (11 cases) presented total GHD in 3 cases and partial GHD in 8 cases.

Discussions

The literature data mention that this radiological abnormality due to an incompetent sellar diaphragm, may be associated with deficiencies of the anterior pituitary hormones but when found as an incidental finding, it is most likely that normal pituitary function will be demonstrated (4,5,6,7). Also, it is mentioned that the syndrome is more frequently associated with hypothalamic pituitary abnormalities in childhood than in adult (8).

This entity was found in our patients on the occasion of the imagistic CT evaluation of hypothalamic pituitary region for the suspicion of growth hormone deficiency.

Keeping in mind the etiology of the syndrome, we presume that the compression of the somatotrophic cells by the arahnoidocel might be able to induce a cellular dysfunction leading to a decrease in the GH secretion. Some other studies that have also found an association between empty sella syndrome and growth hormone or other pituitary hormone deficits (7, 8) sustain our hypothesis.

We consider that the growth hormone deficiency could be the consequence of the empty sella syndrome as

much as it may also be a simple coincident association. The finding of 11 cases with normal CT aspect, along with 9 patients with empty sella syndrome between the 20 GHD children investigated, sustains this hypothesis. Also our results showing the association of total GHD in 8 of 9 cases of empty sella syndrome, sustain the possible involvement of the syndrome in the etiopathogenesis of GHD. The relation remains hypothetical for the moment.

Anyway, the relatively high frequency of the association between the empty sella syndrome and the GHD - resulting from our study - raises a question sign concerning the involvement of the syndrome in the pathogenesis of GHD in the child.

All cases benefited of substitutive treatment with recombinant growth hormone (rhGH) (Norditropin and later Norditropin SimpleXx, Novo Nordisk A/S) 0,025-0,035 mg/kg/day, administered daily, at bedtime. The outcomes of the treatment were comparable with those mentioned in the literature.

Conclusions

1. Although classically the ESS has been rarely mentioned as a cause for clinical manifestations or abnormal tests of the anterior pituitary function, our study shows that the syndrome seems to be quite frequent in the children with GHD.
2. The CT or MRI evaluation of the hypothalamic pituitary region should be performed in all children with growth hormone or other pituitary deficiencies.
3. Remains uncertain if the empty sella syndrome represents the cause for the GH deficiency in our patients or is just a pure association with it, as long as we couldn't find any other cause for the GH deficiency.

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PULMONARY ATELECTASIS ON INFANCY: CLINICAL AND RADIOLOGICAL EVOLUTIONAL OBSERVATIONS

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Summary

Pulmonary atelectasis is a rare disease in the neonatal period and infancy up to 1 year old. The confirmation is radiological by standing out the following elements: mediastinal shift – towards lesion, compensatory hyperinflation of other lobes, elevated diaphragm on the same side and variable air bronchogram. Pulmonary CT-scan brings new details.

The promoting factors are immunodeficiency, dystrophy, prematurity and anemic syndrome. Pulsoxymetry is a non-invasive method of estimating the respiratory distress syndrome.

Keywords: atelectasis (segmental collapse), pulsoxymetry, thymus hypertrophy

Introduction

Pulmonary atelectasis is a syndrome determined by a ventilation defect on the pulmonary zone but with maintaining blood perfusion. The prime cause is the bronchial obstruction on various etiologies (tumors, adenopathy, foreign bodies). The clinical examination shows a condensate syndrome with obstruction of the bronchi.

Causes of the atelectasis:

Newborn period:

- Respiratory distress syndrome
- Pneumonia
- Meconial aspiration
- Pneumothorax, lobar emphysema, tumors
- Ascites

Infancy period until 1 year old:

- Pneumonia, recurrent aspiration syndrome, immunodeficiency, immotile cilia syndrome
- Pertussis
- Bronchopulmonary dysplasia
- Rare causes: cystic fibrosis, bronchiolites obliterans
- Intubation/ after extubation
- Tracheal/ bronchi stenosis, hypoplastic air way
- Hilar adenopathy, cysts, tumors
- Rare causes: vascular ring, congenital hard disease with enlarged of left atrium

Infancy period up to 1 year old:

- Pneumonia
- Cystic fibrosis, bronchiectasis

- Pulmonary tuberculosis
- After surgery
- Neuromuscular disease, immobility
- Foreign bodies.

Case presentation

We present the case of a child SA, female, 5 months old, coming from rural area, premature birth with birth weight 1500 g, transferred in our clinic with the diagnosis: Interstitial pneumonia. Suspect right hilar adenopathy.

We haven't data about the family or the infant medical history, the child being a social case.

In the hospital of Sanicolaul Mare the child presented: fever 39,4 °C, productive cough, psychomotor agitation and respirator functional syndrome. Although the treatment (Zinacef, Gentamicin, Celeston), the health status didn't improve.

Weight: 5600 g, height: 61 cm, temperature: 36, 2°C. The infant presents: alteration of health status, pale skin, nasal obstruction, productive cough. Subcostal and intercostal retraction, wheezing, tachypnea, symmetric breath sound and evidence of adventitial breaths sounds: rales and rhonchi, prevalent in the third right superior area. Normal hearth sounds, tachycardia: 140/min. Hepatomegaly and splenomegaly. No signs of meningeal irritation.

Presumptive diagnosis:

Right superior lobe unspecified pneumonia.

Biological investigation:

- Acute-phase reactants: leukemoid reaction or reactive leukocytosis (12000/mm³) with neutrophilia, ESR (128 →75 mm/h), CRP (positive), increase serum α_2 globulin fractions (15.2%).
 - Anemia: decrease of hemoglobin (9.3g/dL), red cells count: 3500000/mm³
 - Arterial blood gas: pH=7.43, pCO₂=32.2 mmHg, BE=-1.2 mmol/l, HCO₃= 21.2 mmol/l PaO₂ = 41 mmHg, SaO₂ = 78,3%
 - Cultures of blood, urine, stool, nasopharyngeal are sterile
 - Negative sweat test
 - Negative tuberculin skin test, cultures of gastric lavage for Koch bacillus are sterile
- Face and profile, anterior-posterior and lateral/lateral chest roentgenogram: mediastinum, on apical right lung with inferior delimitation by elevated horizontal scissors,

with a retractile character on trachea and mediastinum towards right side. Right basal emphysema is present. This

opacification and emphysema are retro tracheal and inferior.

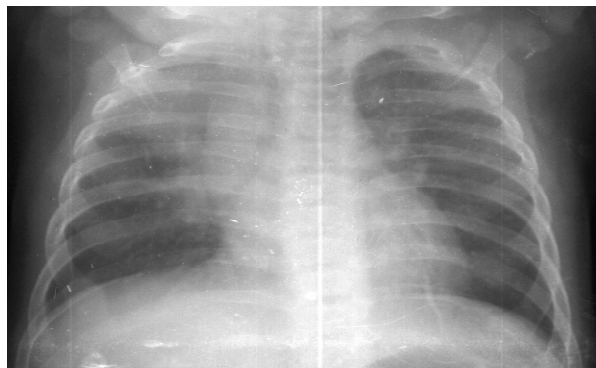


Fig. 1 Face chest roentgenogram

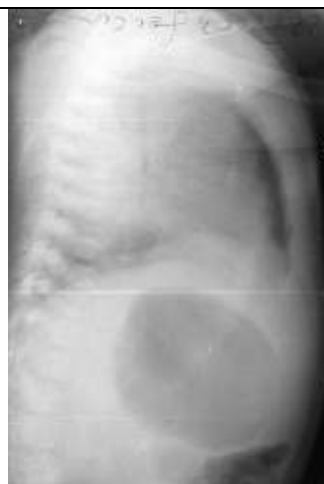


Fig. 2 Profile chest roentgenogram

Mediastinal computer tomography scanning shows: triangular opacification, inhomogeneous structures in the right superior lobe. Vertically, this image extends

from apical right lung until the trachea bifurcation. Mediastinum pushes on right side.

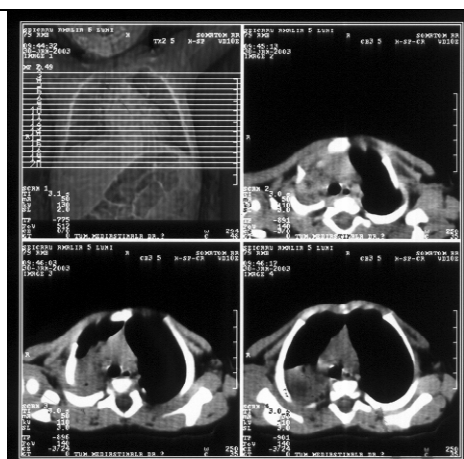


Fig. 3 Mediastinal computer tomogram

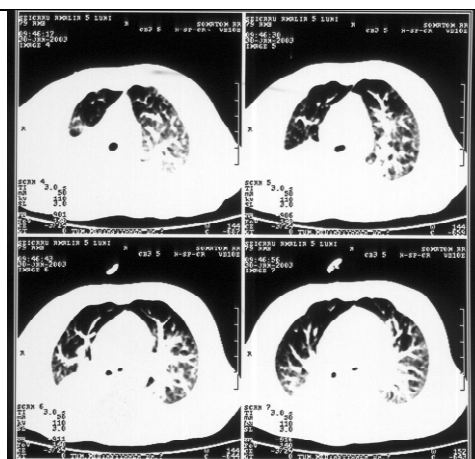


Fig. 4 Mediastinal computer tomogram

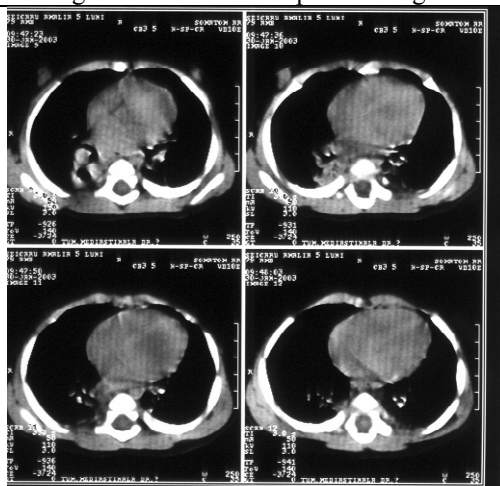


Fig. 5 Mediastinal computer tomogram



Fig. 6 Mediastinal computer tomogram

Echocardiogram: Ao = 10,1 mm; LA = 14,1 mm; RA = 15,5 mm; LV = 13,2/20,2 mm; EF = 0,67; SF = 34,78 %; RV = 13,4 mm; IVS = 3,36 mm, IAS in its integrity, PPLV = 3,33mm, normal valves, no pericardial effusions

Positive diagnostic:

1. Right lung atelectasis.
2. Thymus hypertrophy
3. Intrainfectious anemia
4. Dystrophy std. II by prematurity and disease.

Differential diagnosis:

- Pulmonary abscess
- Right apical pneumonia
- Cystic fibrosis
- α_1 antitrypsin deficiency
- Immotile cilia syndrome
- Pleurisy
- Mediastinum formation

Treatment

Curative treatment:

1. Hygienic treatment and diet:

- Isolation in incubator, individual small wards
- Change of the position in bed every 1-2 hours
- Lateral right decubitus to 30°
- Ingestion of liquids was adapted to the digestive tolerance and to the degree of respiratory distress
- Diet diversification

2. Medical therapy:

- Etiological: antibiotic treatment with: Ceftriaxone 0.5 g/day and Amikacin 0.08 g/day
- Pathogenic: steroidal anti-inflammatory agents: Dexamethasone 0.003 g/day, expectorant: Bromhexin 3x10 drops/day, aerosol with Fluimucil 0.5 ml and 4 ml 0.9% saline solution, Ventolin 3x1 puffs/day, respiratory kinesiterapy
- Symptomatic: Pseudoephedrine nose drops, fever treatment
- Administration of vitamins

Evolution

The evolution was slow but favorable, during 20 days hospitalization. Respiratory and inflammatory syndrome remit.

This patient left hospital with good health status, no fever, appetent; weight increase at a steady rate, and

respiratory status: symmetric breath sound and no evidence of adventitial breath sounds.

Evolution of biological investigation:

- Acute-phase reactants: white cells count: 13400/mm³ with Ly = 50,9 %, Mo = 5,6%, Gra = 43,5%, ESR: 10 mm/h
- Correction of anemia, except treatment: hemoglobin: 10.3g/dL, red cells count: 4780000/mm³
- SaO₂ = 87% → 96%
- Chest roentgenogram: emphasis of the interstitial space of the lung, normal cord

The child has been transferred in Sanicolaul Mare Hospital for continuation of the treatment.

Possible complications on long term are: pulmonary bacterial infection – pleuropneumonia, pulmonary abscess, pneumothorax, pneumomediastinum and mediastinitis.

The prognostic of this patient is good and depends on the appearance of the relapse.

The particularity of the case:

The child is dystrophic, by prematurity std. II and disease: anemia, rickets. He presents pneumonia upon pulmonary distelectasis which evolved with atelectasis. The pulmonary distelectasis is characteristic for an infant with dystrophy and immunodeficiency through the thymus hypertrophy. The main elements of pathology are the ventilation-perfusion mismatch and the absence of the clinical manifestations.

Conclusions:

1. The face and profile chest roentgenogram, the retractile character of the process and the presence of the basal emphysema have been important to establish the positive diagnosis: Atelectasis.
2. The mediastinal computer tomography scanning has confirmed the diagnosis, and brought important information for the exclusion of the other diseases.
3. Pulsoxymetry is a non-invasive method of estimate the respiratory distress syndrome
4. We consider that the appearance of atelectasis is a complication of the pneumonia and of the bronchial obstruction with suprainfection.
5. The pulmonary suprainfection due to the pulmonary distelectasis is characteristic for an infant with immunodeficiency with dystrophy and thymus hypertrophy.
6. The antibiotics, the respiratory kinesiterapy and the aerosol with mucolytic have determined the reversibility of the atelectatic process.

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IV. PEDIATRIC SURGERY

OUR EXPERIENCE IN SACROCOCCYGEAL TERATOMAS

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Abstract

The sacrococcygeal teratomas are tumors with relatively low incidence, but with a high risk of malign transformation with age.

We have included in our retrospective study a number of 39 cases of sacrococcygeal teratomas hospitalized in Pediatric Surgery Department from Timisoara in the last twenty five years. The necessary data were obtained by using retrospective statistical methods.

We analyzed in the study the frequency of sacrococcygeal teratomas in the period 1979 – 2004, the distribution of cases with regard to gender (F/M ratio) and the affected group. Using the histopatological results we were able to establish the benign/malign rate at newborn. Also we diagnosed the percentage of malign transformation in cases of sacrococcygeal teratomas ad addressed after the age of 2 months.

Results: the female patients were more affected than males. Benign forms of the disease were prevalent in the neonatal period. Patients diagnosed after 2 months of age had a high frequency of malign sacrococcygeal teratomas.

Surgical treatment before the age of 2 months leads to a decrease of malign transformation and relapse.

Key words: sacrococcygeal teratomas, benign, malign, neonatal period.

Introduction:

Sacrococcygeal teratomas are tumors which contain elements derived from all the three embryonic layers: ectoderm, mesoderm and endoderm. The common components of teratomas are skin, teeth, central nervous system tissue, respiratory and alimentary mucosae, cartilage and bone. At the newborns teratomas are generally localized at the sacrococcygeal level.

From the clinical point of view they are a tumoral mass in the sacrococcygeal region. Sometimes the localization can be in the presacral space or in the retroperitoneal space.

The diagnosis is sustained by the localization and the clinical aspect of the tumor, the abdominal extension being evident after the rectal examination. The confirmation of the diagnosis is obtained trough histopatological exam.

At birth the benign/malign rapport is 9/1. After the age of 2 months the rapport inclines towards malignity. Taking into account this aspect the surgical intervention, consisting in removing the tumor, is imposed as an emergency therapeutic measure.

Material and method:

It is presented a clinical and statistical analysis of the cases of sacrococcygeal teratomas operated in Pediatric Surgery and Orthopedics Clinic Timisoara, in the period 1.01.1979 – 1.02.2004, the data used being extracted of the surgical protocols and histopatological exams.

Objectives:

The study presents:

1. the variation of the incidence of sacrococcygeal teratomas in children in the last 25 years,
2. the sex ratio,
3. the repartition of cases based on age groups,
4. the incidence of the malignancy at the moment of diagnosis at newborn,
5. the variation of the rapport benign/malign according to age.

Results and discussions:

In the last 25 years 46 surgical interventions have been effectuated in our clinic for the treatment of sacrococcygeal teratomas, 7 being reinterventions occurring to relapses (Fig. 1).

	39 surgical interventions
Total number of cases 46	
	7 reinterventions

Fig. 1. Surgical treatment of the sacrococcygeal teratomas

Of the 39 cases 3 didn't have histopatological confirmation, the next results being obtained through the study of a lot of 36 cases. Comparing the number of

cases/year in the period 1979-2004, we've obtained a maximum incidence of these in the interval 1990-1994 (Fig. 2.).

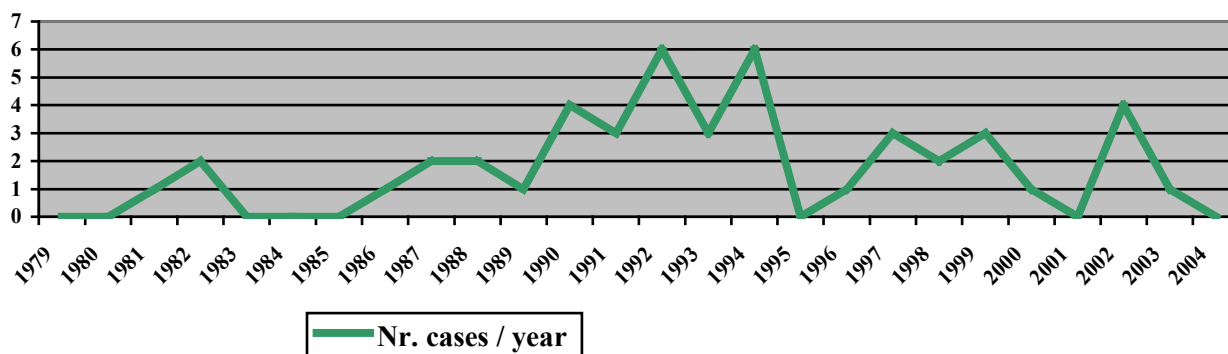


Fig. 2. The variation of incidence of the sacrococcygeal teratomas in children in the last 25 years.

The next table presents the distribution of cases according to age groups.

Age (months)	0 - 1	1 - 2	2 - 3	3 - 4	4 - 5	5 - 6	6 - 7	7 - 8	8 - 9	9 - 10	10 - 11	11 - 12	> 12
Nr. of cases	18	4	1	0	0	0	3	0	1	0	1	1	8

It can be observed that the biggest number of cases/age groups is that in the neonatal period (18 cases of 39), (Fig. 3.).

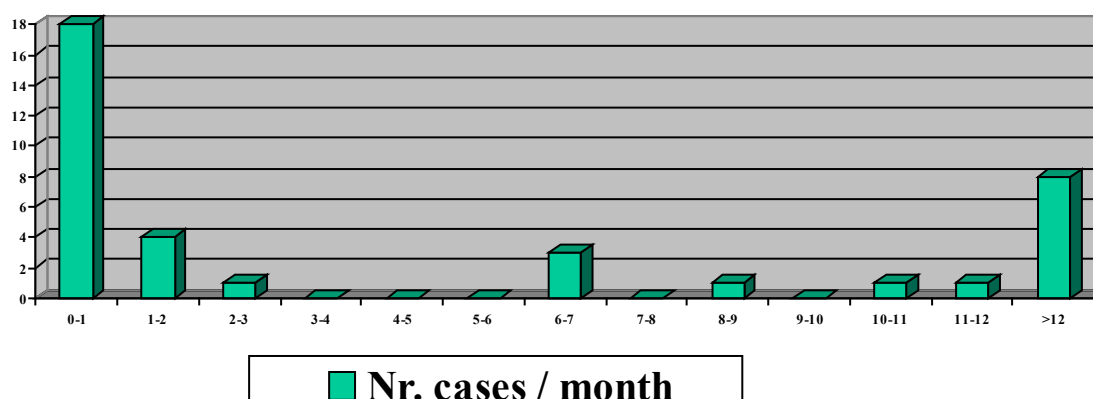


Fig. 3. Distribution of cases according to the age groups.

The repartition of cases according to the sex shows a high frequency of the disease at the female. Out of 36 cases,

25 were of female and 11 male, the final rapport F/M = 2,27/1 (Fig. 4.).

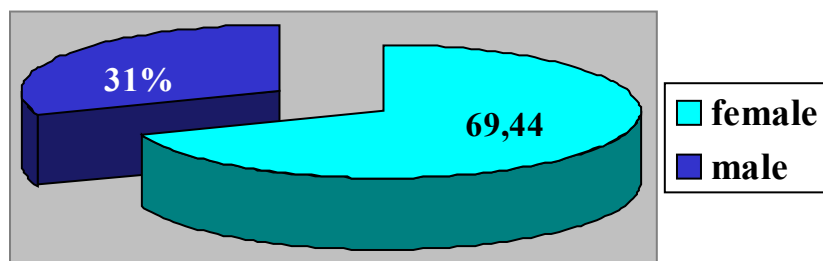


Fig. 4. Sex ratio.

In the decision of the malignity characteristics the histopatological exam was decisive. Of the 36 cases 8 were lost from our evidence, the next results referring to a

number of 28 cases. We've analyzed the benign/malign rapport by dividing the cases in 2 groups, having as a reference point the age of 2 months (Fig. 5.).

	Diagnosed and operated cases Age 0 – 2 months	Diagnosed and operated cases Age 2 – 12 months
Number of cases	16	12
Benign tumors	14	4
Malign tumors	2	8

- benign/malign rapport at age 0-2 months = 7/1
- benign/malign rapport at age 2-12 months = 1/2

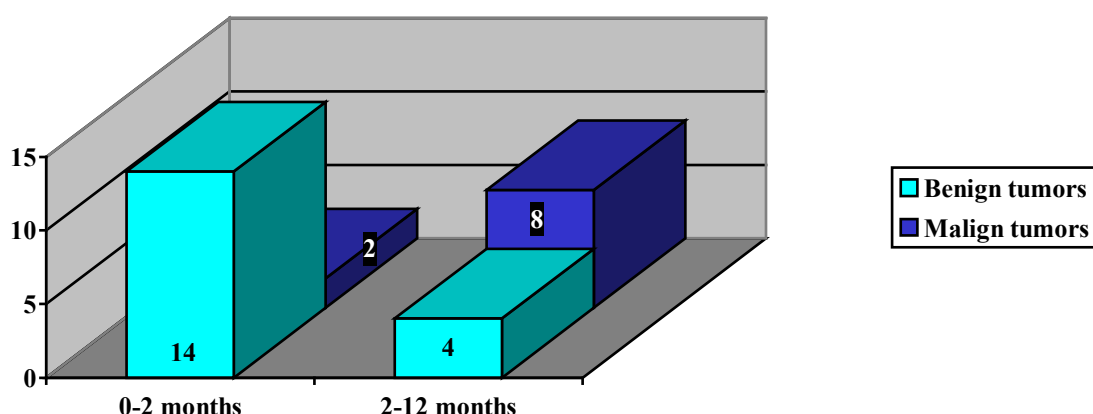


Fig. 5. Benign/malign rapport.

Conclusions:

- the maximum of incidence of the sacrococcygeal teratomas in the period of the 25 studied years is between 1990-1994;
- the disease is more frequent at female;
- the most affected age group is the neonatal period;

- the benign character prevails in the first 2 months of life and the malign transformation grows with age;
- after the radical surgical treatment the cases are usually cured, only a small number of cases having relapses.

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MODIFICATIONS OF THE HORMONAL TABLE IN THE UNDESCENDED TESTICLE

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Abstract

A special role in the descend of the masculine gonad is due to testicular hormones (the inhibition factor of Müller ducts and testosterone). Many authors have been preoccupied of the modifications of the hormonal table and fertility at patients treated formerly of cryptorchidism. This paper work describes the role of the testicular hormones in testicular migration and the modifications which take place in cryptorchidism.

Key words: testicular hormones, testicular migration, fertility, cryptorchidism.

The anomalies of testicular migration have preoccupied doctors from ancient times and they have tried to solve this problem and all its levels of manifestation: biological, psychological, social. Although the testicular descend has been described in the specialty literature for over 200 years and numerous studies have been dedicated to the understanding of the phenomenon, the processes and the factors which cause it are still incompletely elucidated problems.

It is known that a special role in the descend of the masculine gonad is due to testicular hormones (the inhibition factor of Müller ducts and testosterone).

The inhibition factor of Müller ducts

The first event of masculine differentiation is the regression of Müller ducts under the influence of the antimüllerian hormone – AMH (the inhibition factor of Müller ducts).

AMH is a glycoprotein with a molecular weight of 140.000, secreted by the Sertoli cells immediately after the constitution of the testicular cordons. By secreting AMH each testicle determines the regression of the Müller ducts on the same side with its position, without influencing the contralaterally Müller duct, so that, at real hermaphrodites, on the testicular side, the Müller ducts can be absent, while on the ovarian side they are normally developed.

In the case of testicular failure of secreting AMH or of the Müller ducts defect of responding to these, the virilism of the genital organs and of the Wolff ducts is normal, but the organs from the Müller ducts are present (men with uterus and uterine tubes) with the appearance of

the syndrome of Müller ducts persistence – a type of masculine pseudohermaphroditism with an autosomal recessive or X-linked recessive transmission.

Testosterone

Testosterone is the 2nd genitalia organizer testicular hormonal factor. At humans the gonadal testosterone secretion starts in the 8th week post conception, at the same time with the appearance of the Leydig cells in the testicular interstitial space. In all the genetic defects of testosterone synthesis the virilism of the genital tract is incomplete (in different degrees, in accordance to the severity of the enzymes defects) there being no doubt as to the major role of this hormone in the determination of sexual dimorphism.

Testosterone synthesis

Testosterone synthesis in Leydig cells approximately 20% of the testicular mass) takes place through the same intermediary reactions as the corticosteroids synthesis. The limited speed stage is the split of the lateral chain of cholesterol and the formation of the pregnenolone (Fig. 1.). Testosterone synthesis starts of the level of the internal membrane of the mitochondria in the presence of P450 cytochrome through cholesterol conversion from the plasma or synthesized by Acetyl CoA in pregnenolone. To get to the enzymatic conversion system cholesterol has to pass through the external mitochondria membrane, this being the slow enzymatic step, limiting the synthesis rate of the steroid and probably regulated through LH (*luteinizing hormone*).

The enzymes realize the conversion of the pregnenolone to testosterone in two different ways.

At human the main way of testosterone formation is through progesterone. Dehydrotestosterone is formed in the testicle or in the peripheral tissues by the action of a 5 α -reductase.

The daily secretion of testosterone (7 mg/day/adult person) predominated over the other 2 testicular hormones (dehydrotestosterone – DHT and androstendione) and that is why it is considered the main androgen hormone although a small part is converted at tissue level with 5 α -

steroid reductase participation into DHT, which is more active. The plasmatic concentration of testicular hormones

is 200-300 ng/dl until puberty and 600-700 ng/dl at adults (testosterone = 590 ng/dl).

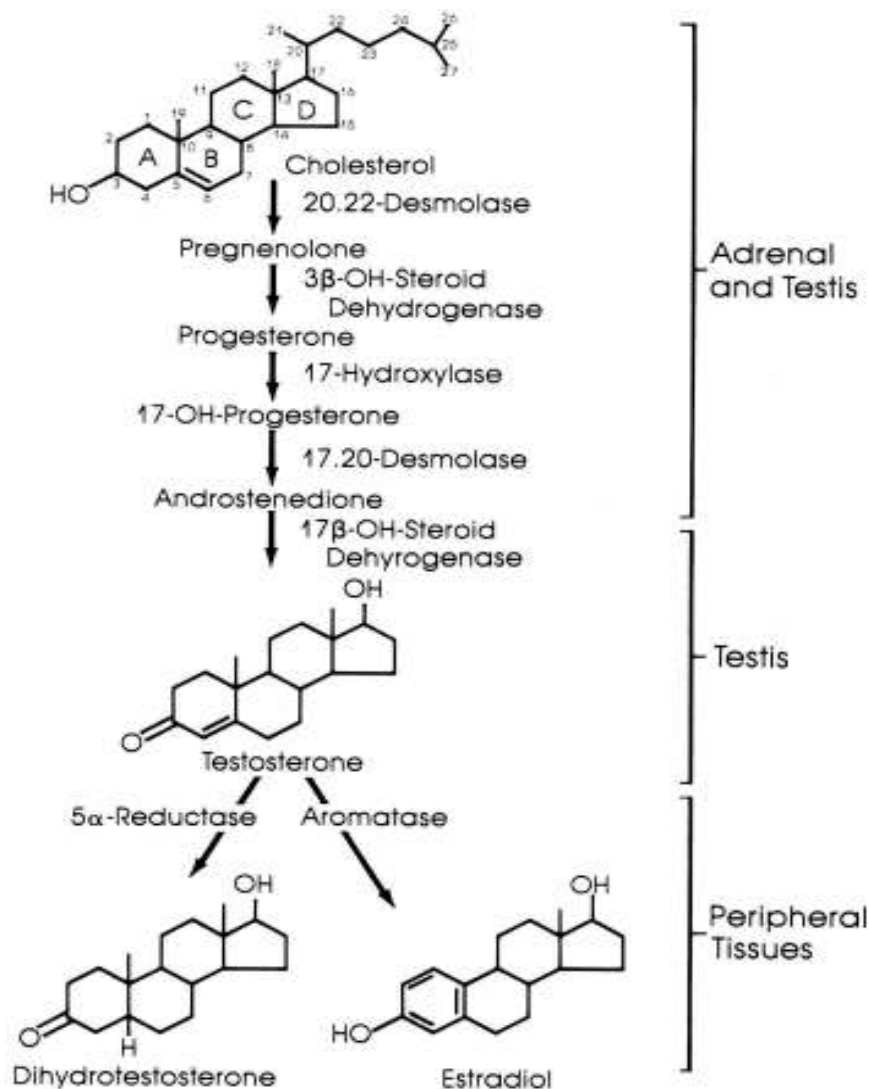


Fig. 1. Androgen synthesis in the testis

Secretion control

The development and the secretion function of the masculine sexual organs are controlled through a mechanism of negative feedback to which the pituitary gonadotropins LH, FSH (*follicle-stimulating hormone*), GnRH (*gonadotropin realising hormone*) and the circulatory testosterone participate.

Unlike spermatogenesis, which depends on the regulatory activity of FSH, the endocrine secretion of the testicles is under the stimulating influence of LH level. This is also called ICSH (*interstitial cell stimulating hormone*), because it stimulates the interstitial cells described by

Leydig. This functions according to the principle of inverse connection establishing relations of positive and negative feedback, with the participation of testicular hormones on one side and the hypothalamic factor which liberates LHRH (*luteinizing hormone releasing hormone*), on the other side. Hypothalamus represents the final common way at men and women. Although the pituitary secretes 2 gonadotropins, hypothalamus liberates them with the help of a single neurohormon called improperly LHRH. This stimulates LH secretion which, in turn, provokes the hyperplasia of Leydig cells in the testicle and the increased production of testicular hormones from puberty to old age. Testosterone secretion, as the main androgen hormone, is directly

proportional to the quantity of circulating LH. Prolactin intensifies the stimulating effect of LH on the production and secretion of testosterone. During gestation placenta releases great quantities of chorionic gonadotropin with a structure almost identical to LH and with a stimulating effect on foetus' Leydig cells, in order to produce the testosterone necessary to the development of the masculine sexual organs.

The excess of circulatory testosterone inhibits the secretion of LH directly and indirectly through LHRH. So testosterone limits its own secretion through its feedback relation to the hypothalamic-pituitary complex. When the concentration of the circulatory testosterone is low, the lack of hypothalamic inhibition leads to its normal secretion (Fig. 2.).

Puberty occurs with the secretion activity of the hypothalamus of LHRH. During childhood hypothalamus

does not release factors that start to produce and release LHRH at puberty. LHRH secretion does not appear when the interneuronal connections between hypothalamus and the surrounding nervous formations are not intact. Although the intimate mechanism of puberty is not completely clarified, it seems that this is a process of maturation of the neuronal connections between hypothalamus secreting LHRH and the temporal lobe. The functional unity which exists between the hypothalamus, the pituitary and Leydig cells assures the normal concentration of testosterone in blood, with low daily variations (20-25% higher at 8 o'clock in the morning than at 18 in the afternoon).

At the reciprocal inhibition between the pituitary gonadotropins and the testicular hormones, estradiol participates in a certain degree, as the metabolite of the testosterone.

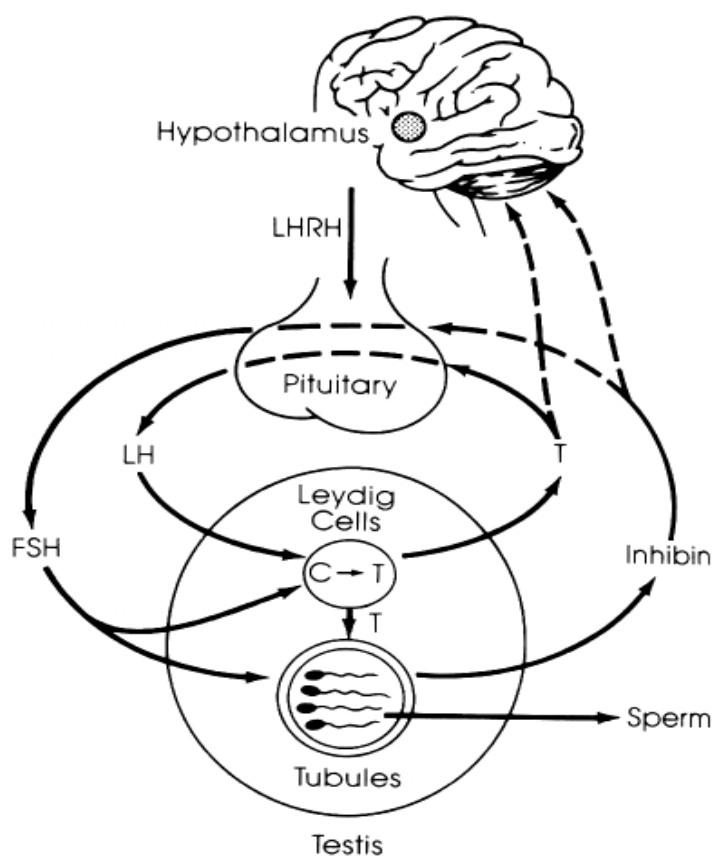


Fig. 2. Regulation of testosterone and sperm production by LH and FSH (C – cholesterol, T – testosterone).

Transport

After its release testosterone is found linked to albumin or a serum globulin for 15-30 minutes.

The hormone is released into blood as it is formed. There are no storage forms. The plasmatic transport is done by a protein which links testosterone and estrogens – SHBG (*sex hormone-binding globulin*) or TEBG (*testosterone-estrogen-binding globulin*). The protein links better to testosterone than to estrogens. SHBG is synthesized by the liver and its production is influenced by

a series of factors. The estrogens increase the synthesis of this protein, the thyroid hormones lower it.

Testosterone enters free into the cells and in some tissues it is transformed into dehydrotestosterone. These 2 hormones interact with the same type of intracellular receptors. The complex hormone-receptor interacts with chromatin and activates the transcription of some genes. The synthesized proteins mediate the biological effects of the hormone. It is not known if all the actions of the testosterone are the expression of a synthesis of all specific proteins.

Action mechanism

After going through the membrane of the target cell, testosterone or its metabolites, resulted from local conversion, exercise their specific action after interacting with nuclear chromatin. In a first phase the steroids are fixed by the specific receptors. Through modifications of the tertiary and quaternary structure of the steroid receptor complex activated complex results, which is fixed at the level of sites of the nuclear membrane and then it is transferred intranuclear. The steroid receptor complex continues to interact, for a limited period, with certain chromatin areas, raising the activity of transcription DNA (*deoxyribonucleic acid*) → RNA (*ribonucleic acid*) and the protein synthesis. In certain tissues (for example the masculine reproductory glands) the interaction of the complex steroid receptor with nuclear chromatin induces DNA and histone synthesis and cells proliferation.

The effects of androgens actions

Androgens are hormones which exercise major influences on the differentiation development and morphofunctional conservation of the genital system and of the sexual characteristics which are secondary masculine, and on the behaviour corresponding to the masculine role in reproduction.

The effects of the action of the testicular steroids on the target organs can be of organization / development or of action. The organizations appear after the exposure at sexual hormones in a critical period of development (usually the prenatal period) and they become permanent, appearing at early stages or only after reaching sexual maturity. The activation effects are the result of the postnatal interaction between gonadal steroids and the target organs and they are reversible and repeatable. A series of organizing effects induced by the sexual hormones prenatal or neonatal manifest themselves at puberty or at adults only in the activating presence of sexual hormones.

Testosterone, together with AMH, cancels the implied tendency of differentiation of the genital system

into a feminine one. The androgen makes the genital tract virile, no matter of the genetic sex of the embryo. Each event of the genital differentiation appears after the interaction of the steroid with the target organ in a limited period specific for its development.

At the level of the Wolff duct of the human embryo testosterone conversion in 5 α -DHT appears after the 12th week, so after this has become virile. At the urogenital sinus level and the external genital organs 5 α -reductase is present before the 6th week. Wolff's ducts virilism would be achieved by testosterone, while the masculine organization of the urogenital sinus and the external genital organs would be the consequence of 5 α -DHT action, resulted from the local metabolism of testosterone.

This hypothesis is demonstrated by the fact that, in the deficit of 5 α - reductase, individuals, genetically male, with testicles, have external genital organs closer to the fem sex, while the Wolff structures are normally virile.

If the virilism of the urogenital sinus and of the external genital organs are achieved through androgens present in the general circulation, the masculine organization of Wolff duct seems to need higher local testosterone concentrations. When the testicle is unilateral it makes virile completely only the Wolff duct on the same side, the contralateral Wolff duct virilism being absent or rudimentary (as in some cases of real hermaphrodites). The high concentration of testosterone is achieved either from the local diffusion of the hormone or through its secretion in the external ductal system of the testicle.

Testosterone controls the fundamental processes necessary for the development and function of the sexual organs, the appearance and maintenance of the secondary sexual characteristics, spermatogenesis.

Androgens stimulate the protein synthesis, a powerful action at puberty, which leads to the development of bones and skeleton muscles. The effect of the testicle steroids on growth and development of the genital and extragenitale structures at puberty is known (Fig. 3.).

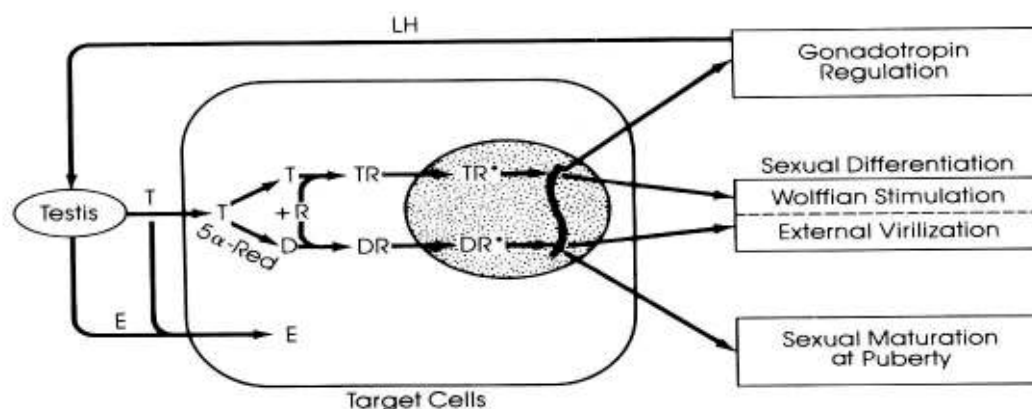


Fig. 3. Current concepts of androgen action (T – testosterone, D – dehydrotestosterone, E – estradiol, R – receptor protein, R* - transformed receptor protein, LH – luteinizing hormone, 5 α -Red - 5 α -reductase).

Although ovarian estrogens condition the distribution of the fatty tissue and the conformation of the pelvis at women, the major role in determining the sexual and somatic dimorphism at puberty is that of testosterone. The growth of the muscular mass, the modification of the vocal timbre, the growth of the skeleton, hyperpigmentation of the scrotum, the growth of the penis (paradoxically, as during the intrauterine life the phenomenon is mediated by 5α -DHT) are effects conditioned directly by testosterone. It is also the steroid which controls spermatogenesis. The growth in volume of the prostate, acne, the masculine distribution of facial and body hair, retraction of the temporal hair line are mediated by 5α -DHT.

The endocrine role has been researched with the help of orchiectomy. The consequences of orchiectomy differ, according to age. Before puberty orchiectomy stops the development of the sexual organs and stops the

appearance of the secondary characteristics and of the sexual instinct. At adults the effects of orchiectomy are less evident, limited to the involution of the sexual organs and the reduction of virility. The administration of total extracts or androgens hormones eliminates the functional and metabolic consequence of orchiectomy or of the testicular insufficiency both before puberty and at adults.

Testosterone functions are closely linked to the development of the primary and secondary sexual characteristics at man. If during foetal life and in the weeks after birth testosterone secretion is stimulated by chorionic gonadotropin, then the testosterone secretion stops, until puberty, under the influence of the pituitary gonadotropin. After the age of 50 it drops rapidly reaching 20% of its maximum value at the age of 80 (Fig. 4.).

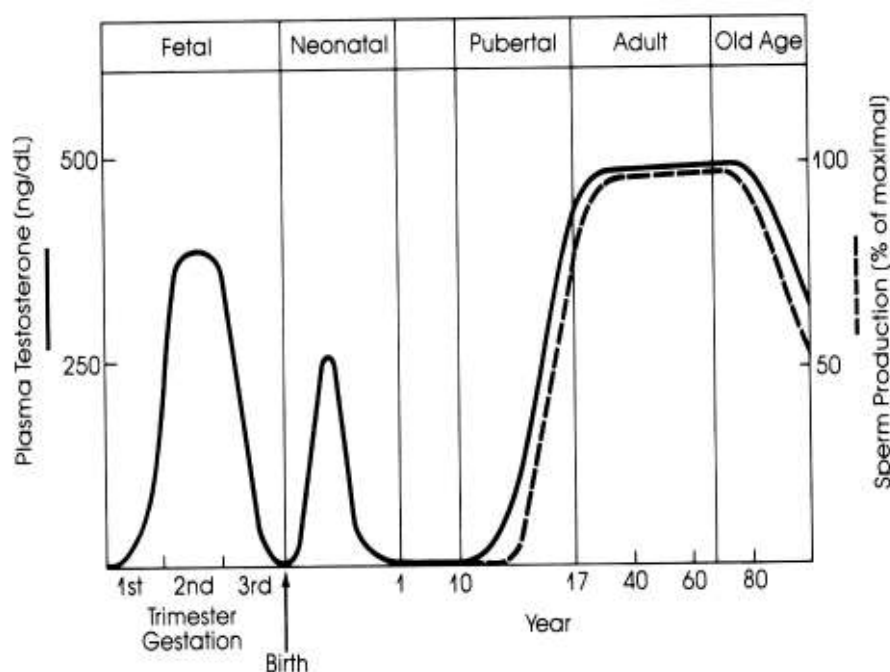


Fig. 4. Testosterone level variation during on the men's life.

During foetal development testosterone helps the growth of the genital organs and the descend of the testicles in scrotum in the last 2 months of gestation. In the case in which the descend did not take place before birth the administration of testosterone or of pituitary gonadotropin will help the descend take place in the days or weeks that follow.

At puberty testosterone secretion stimulates the development of the genital organs until the age of 20 and of the secondary sexual characteristics (pubian hair, chest and facial hair, thickening of voice and skin, development of the muscles of the skeleton). The cutaneous stimulating properties seldom determine the appearance of acne at puberty.

The biological effects of the testicular hormones can be classified according to the place and way of action in androgenic and anabolic effects.

In turn the androgenic effects are partially defined in the case of testosterone and dehydrotestosterone both in the foetal period and also at puberty. While testosterone stimulates, in the foetal period, the differentiated development of epididim, deferent ducts and seminal vesicles dehydrotestosterone assures the formation of the penis, urethra, scrotum and prostate. During puberty testosterone stimulates especially the spermatogenesis and the development of the penis, the seminal vesicles, the larynx and the muscles of the skeleton, while dehydrotestosterone has an action on the prostate, the scrotum and the secretion of the prostate. On a behavioural

level testosterone stimulates potency and libido. At adults the androgens effects of the both testicular hormones have as consequences baldness, skin thickening and contain particularities of anabolic effects.

Anabolic effects assure growth, maturity and puberty virilism in general, as a consequence of activating the protein synthesis and the phosphor and calcium metabolism at the level of different tissues and organs (skeleton muscles, bone matrix, bone marrow, and nervous tissue) and especially of those involved in the reproduction function. At the cellular level testicular hormones are fixed on a common receptor which moves them in the nucleus to action upon a chromosomal DNA stimulating RNA-polymerase and the formation of RNA as the main place of protein synthesis. Through such a mechanism of intensifying the protein synthesis, the growth of muscular mass during puberty is achieved and the anabolic effects of the testicular hormones at adults and old people, improving vigour and muscular force. Testicular hormones have an action of intensification of osteosynthesis and growth in length of the bones during puberty, as a consequence of bone matter growth. At the same time with bone thickening, in the post puberty period, the ossification of the growth cartilage and the stop of stature development are produced. At adults testosterone provokes sodium and water retention trough the mechanism of activating the processes of tubular resorption. The high quantities of testosterone lead to the growth of basal metabolism and of the number of red blood cells with 10-20%.

Metabolism

At the level of the peripheral structures testosterone is metabolized, being a prohormone for a series of other steroids. Depending on the target tissue testosterone is converted into more active androgens, estrogens or steroids without action on the genital system. As a consequence testosterone effects (or other androgens) are specific for certain organs (different for diverse organs).

One of the important ways of testosterone metabolism is the conversion to 5 α -DHT at the level of genital organs, skin and brain. The androgen effect of 5 α -DHT on the genital organs is 2,5 more powerful than testosterone.

At adults the daily production of 5 α -DHT is 300-400 μ g, and the plasmatic 5 α -DHT/T rapport is 1/10 at men and 1/3-1/4 at women.

The metabolites of the 5 β -testosterone, resulted trough the conversion of the hormone at the level of liver or bone marrow, are responsible of the anabolic action of the androgens at the level of these organs.

Testosterone is also a major prohormone for the circulatory estrogens. At man 20% of the daily synthesis of estradiol (65 μ g for a healthy adult) is of testicular origin, the rest resulting from the peripheral metabolism of testosterone.

Metabolites are eliminated in the urine. Women's urine also contains metabolites of androgen hormones which are produced by the ovaries and from adrenal cortex.

Men's urine also contains estrogens, secreted by Sertoli and Leydig cells as metabolic products which come from testosterone. Only 20% of the urinary corticosteroids come from testicular testosterone.

Approximately 1% of testosterone is eliminated as testosterone-17 and androstendione-glucuronid (these steroids come from the testicular testosterone).

Modifications of the hormonal table in the undescended testicle

Because of the implications of the hormonal placenta dysfunctions or hypothalamic dysfunctions in the aetiology of testicular migrations disorders as well as of the possible role of hypogonadism along a raise in temperature, the study of the serum values of gonadotropins and testosterone in diseases were of a real interest.

During prepuberty the low serum levels of these hormones make it difficult to determine the basal hormonal values. With the debut of puberty the basal values of gonadotropins and testosterone, and those resulted after stimulation, increase quickly.

The postnatal testosterone increase is at the normal superior limit at newborns with cryptorchidism, at whom the testicle descends spontaneously in the scrotum in the first 4 months and is low or absent at those without descended testicles and after 120 days the differences between the two groups disappear. At a serum testosterone level > 3 ng/ml all testicles descend.

The post natal testosterone increase is correlated positively to the LH serum levels, gonadotropins values being low at those with untreated cryptorchidism, FSH level being identical at the two groups (treated or not) and the serum levels of testosterone and gonadotropins are similar in bilateral and unilateral cryptorchidism.

Many authors have been preoccupied of the modifications of the hormonal table and fertility at patients treated formerly of cryptorchidism. Although there are many contradictory opinions, I'll present the most important studies in a chronological order.

Scheiber K and collaborators determined testicular volumes and exocrine testicular function in 82 men who had undergone orchidopexy (36 bilateral, 46 unilateral) at 5-18 years of age in 1981. The testicular volumes at patients with unilateral and bilateral orchidopexy correspond to those on normal mature males. Semen analyses in unilateral cryptorchidism were normal in 13, doubtful in 23 and pathological in 10 patients. Out of a total of 36 patients who have undergone bilateral orchidopexy, 3 patients were found to have normal, 7 patients doubtful and 26 patients' pathological sperm analyses. Endocrine evaluation in bilateral cryptorchidism (at pre puberty, puberty and post puberty) showed no differences in testosterone levels compared to control groups. Some post puberty patients with pathological sperm analyses were found to have elevated LH and FSH levels; 22 post puberty patients with pathological sperm analyses showed hypergonadotropism with markedly elevated LH and FSH levels after GnRH.

Kawada T and collaborators measured immunoreactive inhibin, FSH, LH, and testosterone in 17 patients after orchidopexy in 1995. FSH was extremely high (20 mIU/ml or above) in 3 patients. The inhibin level was significantly lower in these 3 patients than in the other 14 patients. All 3 high-FSH patients had azoospermia. Testosterone and LH were normal in one of them. Even considering problems involved in the inhibin assay, the high FSH levels are considered to reflect reductions in the blood inhibin level due to Sertoli cell dysfunction. These findings suggest that inhibin plays an important role in the suppression of FSH at least in some patients after orchidopexy.

Taskinen and collaborators evaluated the effect of patient age at treatment of cryptorchidism in relation to subsequent semen quality in 1996. Semen analyses and hormonal evaluations were performed in 51 men who were treated for cryptorchidism at ages 10 months to 12 years. Sperm concentration was normal in 90% of the patients with unilateral and 50% with bilateral cryptorchidism. No patient treated before age 4 years had severe sperm defects. Elevated follicle-stimulating hormone levels indicated severe testicular damage. Fertility was better in patients with bilateral cryptorchidism if treated before age 4 years. Age at treatment did not have a significant effect on semen quality in patients with unilateral cryptorchidism.

In 1997 Lenzi A and collaborators studied 71 patients with unilateral cryptorchidism who underwent orchidopexy in prepubertal age (6.4 +/- 2.8 years), followed up as adults (20.0 +/- 2.8 years). Patients underwent testicular examination and hormonal evaluation, 49 of these had semen analysis and antisperm antibody tests. Semen results were compared with those of two age-matched control groups: a group of 20 healthy, randomly selected subjects and a group of 20 patients operated on in postpubertal age for cryptorchidism. Unilateral reduced testis size was found in 30.1% of patients, eight patients had a low LH level, eight had a low T level, and none had abnormal FSH values. Antisperm antibodies were found in 1 of 49 cases. Cluster analysis of sperm parameters showed that the mean values of patients were worse than those of the healthy controls but better than those of the subjects operated on in postpubertal age. This study indicates that prepubertal orchidopexy can give better results than postpubertal correction.

Crespo Chozas and collaborators studied 20 postpubertal males with a mean age of 17.35 years (range: 15-21 years) and treated for cryptorchidism during childhood were evaluated for pubertal development and gonadal function in 1999. A hormonal study which included basal determinations of testosterone, luteinizing hormone (LH) and follicle-stimulating hormone (FSH), and semen analysis was performed on each patient. Complete virilism was observed in all patients. The start and development of puberty were normal in all cases (except one patient that started puberty at 10 years of age). Basal studies in all patients showed normal levels of LH and testosterone. FSH levels were increased in 3 patients and normal in the other 17 patients. Fourteen patients achieved normal spermatogenesis with more than 20 million

spermatozooids/ml. In the other 7 patients (35%), 5 with unilateral cryptorchidism and 2 with bilateral cryptorchidism, the sperm count remained below 20 million with a range of 0.8 to 18.4 x 10⁶ spermatozooids/ml. The three males with elevated levels of FSH also presented oligospermia. The results showed that pubertal development is normal after cryptorchidism. Impaired spermatogenesis was a major factor in undescended testes. Basal FSH levels can be useful in predicting germinal damage secondary to cryptorchidism.

Lee PA and collaborators studied 84 men with a history of unilateral cryptorchidism in 1999. They found that age at orchidopexy significantly correlated inversely with inhibin B and positively correlated with FSH. Comparison of mean hormone levels and sperm density by analysis of variance for linear trend revealed a significant relationship between age at surgery with inhibin B and testosterone, while sperm density, FSH and luteinizing hormone were not significantly related. Men who previously had unilateral cryptorchidism and who underwent orchidopexy by age 2 years have higher inhibin B and lower FSH profiles than those who underwent surgery later in life. This finding suggests an overall beneficial effect of early orchidopexy in boys born with unilateral cryptorchidism.

The same authors compared sperm counts and gonadotropin levels before and after gonadotropin-releasing hormone stimulation between formerly unilaterally cryptorchid men and controls that had completed a detailed questionnaire on fertility and other pertinent paternity information. These parameters were also compared between the subsets of formerly cryptorchid men who reported paternity and unsuccessful attempts at paternity. Sperm density and total count, and basal and gonadotropin-releasing hormone stimulated follicle-stimulating hormone (FSH) levels were different in the cryptorchidism and control groups. Higher FSH levels and lower sperm counts correlated inversely in the cryptorchidism group, while luteinizing hormone, testosterone and other results of semen analysis did not differ. Furthermore, FSH levels were higher and sperm counts were lower in the subset who reported unsuccessful attempts at paternity compared with those reporting paternity. Other measured parameters did not differ between these groups. They concluded that FSH levels are significantly higher and sperm counts are significantly lower in formerly cryptorchid men than in controls. In the cryptorchidism group the same differences are found in fertile and infertile men. Thus, elevated FSH and low sperm counts may be considered risks for infertility in formerly cryptorchid men.

In 2000, the same authors, determined differences in paternity and levels of the hormones inhibin B, follicle-stimulating hormone, luteinizing hormone, testosterone and free testosterone based on the preoperative location of the undescended testis in men with previous unilateral cryptorchidism. In 103 cases they performed semen analysis and measured the levels of the hormones inhibin B, luteinizing hormone, follicle-stimulating hormone, testosterone and free testosterone. Paternity, sperm count and hormonal parameters were compared with cryptorchid

testicular location. Logistic regression was done to analyze pre-treatment testicular location as a risk factor for infertility. Paternity, duration of attempted conception in men who achieved paternity, sperm count and hormone levels did not differ based on abdominal, internal ring, inguinal canal, external ring, upper scrotum or ectopic testicular location. The overall paternity rate was 90% with the lowest rate of 83.3% in the abdominal group. More than 12 months were required to achieve conception in 28.9% of the study group overall and in 39.4% of the abdominal group. Varicocele and a partner with fertility problems were risk factors for infertility, while abdominal testicular location caused borderline significant risk. They concluded that preoperative testicular location in men with previous unilateral cryptorchidism is not a major determinant of fertility according to paternity, sperm count or hormone levels.

In 2001, in Italy, Vinardi S and collaborators evaluated testicular volume, serum luteinizing hormone (LH), follicle-stimulating hormone (FSH), and testosterone as well as semen specimens, in 57 men (mean age, 19 years; range, 18 to 27 years) treated in childhood for unilateral (n = 47) and bilateral (n = 10) cryptorchidism. In 3 unilateral cases monorchidism was found. Thirty-seven patients underwent orchidopexy after hormonal treatment (luteinizing hormone releasing factor, 1.2 mg/d for 28 days followed by human chorionic gonadotropin, 500 IU intramuscularly 3 times a week for 3 weeks). The remainder underwent surgery. Mean age at surgical treatment was 5.4 years (range, 2 to 12 years). These patients were examined again after a mean period of 13.3 years (range, 10 to 19 years). Reduced testicular volume (<12 mL) was found in 6 of 64 testes (9.3%). LH, FSH, and testosterone levels were found within the normal range in all patients. With linear regression, inverse relations were found between FSH and, respectively, testicular volume, sperm concentration, sperm motility, and normally shaped sperms. There were direct relations between testicular volume and sperm concentration, sperm motility, and normally shaped sperms. They did not find any statistical

correlation between age at surgery and semen quality. Significantly better results in terms of sperm counts were found in patients directly operated on in comparison to those treated with hormones before orchidopexy.

Cortes D and collaborators studied 135 patients with cryptorchidism (70 bilateral and 65 unilateral) in 2003, who had a simultaneous biopsy taken at orchidopexy in childhood, and in adulthood had analyses of semen and FSH. In adulthood 42 formerly bilateral cryptorchid boys had repeat testicular biopsies taken. Infertility was suspected in men with < 5 million sperm/mL in the best sample of semen and concomitant poor sperm motility, and who were classified by follicle-stimulating hormone (FSH) values. At orchidopexy the number of spermatogonia/tubule and the germ cell differentiation were measured. In adulthood the percentage of tubules with complete spermatogenesis, spermatogenic arrest and Sertoli-cell only status was assessed. Infertility was suspected in 38 of 70 (54%) of formerly bilateral and six of 65 (9%) formerly unilateral cryptorchid patients. High FSH values were expected in these suspected infertile patients, but 15 of 38 (59%) formerly bilateral and five of six formerly unilateral cryptorchid patients had normal FSH values. These patients were identified in childhood at orchidopexy; those with bilateral cryptorchidism generally presented with germ cells, but the mean number of spermatogonia per tubule was < 30% of the lowest normal value, and the germ cells were seldom normally differentiated, whereas those with unilateral cryptorchidism generally lacked germ cells in the biopsies. No patients had a decreased FSH value.

By analyzing these studies the conclusion is that the level of testosterone and LH, in the majority of the cases of undescended testicle, is in normal limits, while FSH levels modifies in connection to fertility. So, while oligospermia is high, FSH values are high too. The infertility rate is 50% in some studies, when the disease is bilateral and 10% when it is unilateral. There are no major influences regarding the initial position of the undescended testicle, but the best results were obtained in the case of orchidopexy until the age of 2 years.

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ECHINOCOCCIASIS OF THE SPLEEN

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Abstract

Echinococcosis is a tissue infection caused by the *Echinococcus granulosus* worm. The human body (an intermediary host) become infected when the child swallow the worm's eggs. It is more frequent in the rural area. We present the case of a patient, with spleen echinococcosis, hospitalized in our clinic. Lagrot cystectomy was performed with very good results.

Key words: spleen echinococcosis, Lagrot cystectomy.

Introduction

Echinococcosis is a tissue infection caused by the *Echinococcus granulosus* worm. Alternative names: hydatidosis, hydatid disease, hydatid cyst disease. The risk factors include exposure to canines, cattle, sheep, and the human body, which represent an intermediary host. Children become infected when they swallow eggs in contaminated food. The embryos escape from the eggs, penetrate the intestinal mucosa and enter the portal circulation. The infection is carried to the liver or to the lungs, where cysts form. Cysts can also form in the brain, bones, skeletal muscles, kidney, *spleen*, and other tissues^{1,2,3}.

Echinococcosis is common in southern South America, the Mediterranean, the Middle East, Central Asia and Africa and is more frequent in the rural area. It can be prevented by health education⁴.

In our clinic we operated 5-6 cases every year and the incidence is higher in the last years.

Diagnosis: In the spleen localization the symptoms are usually present when the cyst is large enough to be felt by physical examination which are: abdominal pain in the upper left quadrant with the presence of palpable mass, fever and fatigability.

Tests to determine the presence and location of the cysts are:

- a chest and an abdominal X-ray
- a thoracic and an abdominal CT or ultrasound
- tests for antibodies to echinococcus⁵
- liver function tests

Treatment: In early diagnosis many cysts can be successfully treated with albendazole or mebendazole, which must often be used up to three months. If the cyst is too large, the definitive treatment is to remove them surgically if the patient's condition permits the procedure⁶.

The Lagrot procedure is used with very good results in our clinic¹.

Complications: The large cysts may produce tissue damage by mechanical means. The resulting symptoms are related

to the site, type and rate of the growth of the cyst. The cysts may rupture and cause severe illnesses, including fever, low blood pressure and shock, the cysts may also disperse and cause widespread disease.

CASE REPORT

This is the case of a girl, V. L., 12 years old, coming from an urban area, who was hospitalized in our clinic with the following symptoms: a slight abdominal pain in the upper left quadrant, minor dyspeptic syndrome, and tumor in the upper left quadrant of about 10/8 cm, having a solid consistency, relatively stable, slightly sensitive and painful.

History of the illness:

She had an abdominal trauma 2 months ago. She presented a pain in the upper left quadrant, minor dyspeptic syndrome. An abdominal ultrasound was done, which showed a tumor in the upper left quadrant. She was hospitalized in our clinic for establishing the diagnosis and the treatment.

Diagnosis:

- **anamnesis:** - without any elements concerning the etiology of the disease.
- **clinical findings:** - abdominal pain in the upper left quadrant and the presence of a tumor of about 10/8 cm, having a solid consistency, relatively stable, slightly sensitive and painful; lack of appetite
- **paraclinical:**
 1. laboratory data: - high number of leucocytes
 - positive tests for antibodies to echinococcus
 - the other analyses were normal
 2. imaging data
 - a. ultrasound - transonic tumor of 74/70/115 mm, V = 317cc³, situated near the pancreas, the hilum of the spleen, and the left liver lobe, appearing to be a pancreatic cyst or a hidatid cyst (Fig. 1.).

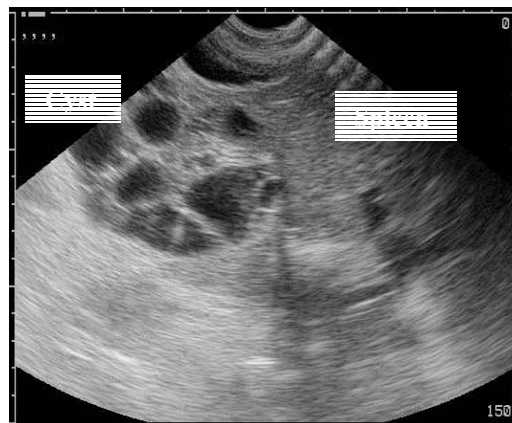


Fig. 1 Ultrasound aspect of the cyst.

b. X-ray - the thoracic and abdominal x-ray and the urography do not offer information for establishing the diagnosis.

c. CT – cystic tumor, well established, which is originated in the spleen, of 9,6/8,2 cm

Treatment

Preoperative care - complete biological investigation within normal limits.

Surgery – consist in following steps:

- median abdominal incision

- exposing the cyst in the superior part of the spleen (Fig. 2)
- puncture of the cavity of the cyst and aspiration of the clear liquid (Fig. 3)
- lavage of the cyst with NaCl 20%
- extraction of the germinal layer (Fig. 4 and 5)
- the partial excision of the external laminated cuticula of the cyst (Fig. 6) and the drainage of the remaining cavity (LAGROT procedure)
- double drainage of the abdominal cavity, suture of the abdominal wall



Fig. 2. Exposing the cyst in the superior part of the spleen

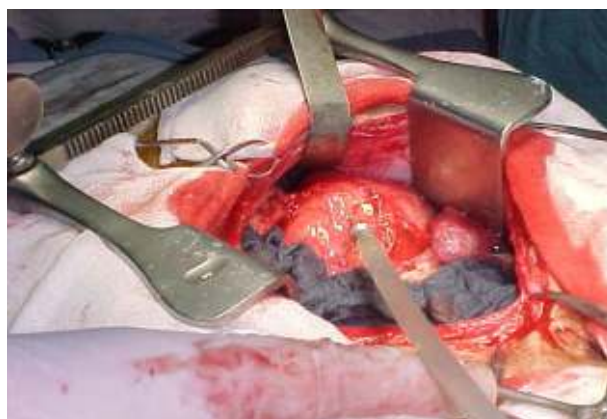


Fig. 3. Puncture of the cyst and aspiration of the clear liquid



Fig. 4. Extraction of the germinal layer



Fig. 5. The aspect and size of the germinal layer

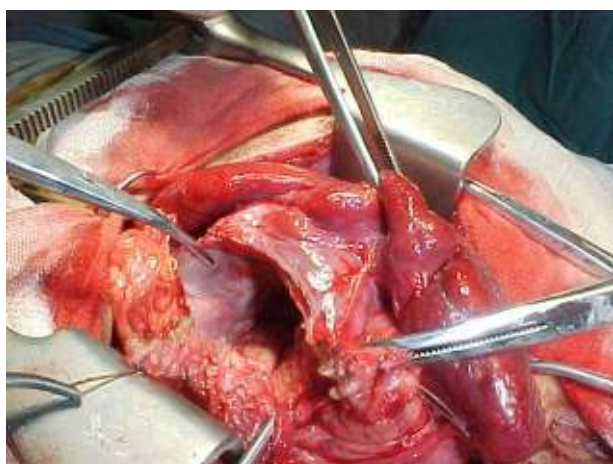


Fig. 6 The partial excision of the external laminated cuticula of the cyst

The postoperative care was done in the Intensive Care Unit in the first 4 days and after in the Surgery Compartment and it consisted of antibiotics (G Penicillin 4 x 1 mil. iu/day for 12 days, and after Amoxiklav 2x2 cp/day), electrolytes, vitamins.

The evolution was favorable, without complications. After 10 days stitches were removed, peritoneal drainage was interrupted after 12 days, and, at 14 days, the drainage of the cyst was interrupted too.

The patient was cured after 17 days.

Conclusions

1. The child's hydatidosis is sometimes localized at the level of the spleen.
2. The disease is asymptomatic for a long time and in this case it was diagnosed accidentally.
3. The Lagrot cystectomy has good results in this case, too.

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V. PSYCHOLOGY

GAME AND ART AT CHILDREN

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Abstract

Psychological development can't take place by itself, it must be the result of inborn forces, acquired through inheritance by the child. As instrument for realizing this he instinctively uses games and imitation. Imagination has a huge role in the child's life, being present in all his activities. Esthetic feeling is developed by practicing lots of games. Game is the first step towards art.

Key words: psychological development, games, art.

Psychological development can't take place by itself, it must be the result of inborn forces, acquired through inheritance by the child. As instrument for realizing this he instinctively uses games and imitation.

The game represents the child's first activity, after a few month of life imitation also occurs.

There are several game categories:

- ◆ games that exercise general mental life processes as: perception, motrition, ideation, feeling;
- ◆ games that are addressed to special functions: fighting, hunting, socializing, imitating, loving.

Each of them has its own importance.

Intellectual games are based on comparisons and reconnaissance, associations (given rhymes), judgment, thinking, inventivity and creative imagination.

Imagination has a huge role in the child's life, being present in all his activities. Occupying an important place in the child's mental life, it has to be used from very early. Creative imagination permits man to group natural elements in new combination. It supposes independence between the object itself and its representation.

Another category of intellectual games are addressed to curiosity defined as an intellectual testing or a game based on attention (Gross). Nature has offered man the wish and way to gain knowledge. The ways to realize it are observation, testing, searching of the mechanism of the happenings. Infantile curiosity represents a preparing exercise for this instinct. It is very useful for the child's development, because it stresses all the new things for him. The consequence of it is represented by the enrichment of attention and knowledge.

Esthetic feeling is developed by practicing lots of games as: drawing, painting, modeling, music. The

child may be put in the possession of his function that will be necessary in his future human existence in three ways: inheritance, personal experience and imitation. To imitate - visual and hearing perception and limbs movement skill (or of the larynx if sounds are imitated) - is needed. Evocation implies the presence of the association between perception and the motor images that lead the moves.

The majority of motrico-senzorial associations are not offered by heredity, each human being must create them himself.

Each of the various ways of imitating has its role and significance. Voluntary imitation (the child that purposeful imitates movements in order to reach a purpose) is characteristical to judgmental education that has the major role in mans life.

Art that has such an important role in the field of human preoccupation is a phenomenon that is part of the game category, which resulted through an evolutive process.

Friedrich Schiller, the great German poet, assimilated already then in his poem "Letters concerning esthetical education" art with game and presented a conception that was afterwards resumed by Spencer. Esthetical pleasure is based on a kind of interior imitation that is only a game. As games, art implies a self-illusion, being an enrichment of the human being, a satisfaction of profound inclination, a relief of all the compulsions of the real existence. Artistic production is very related to game, although it is less close to it than esthetical pleasure.

For K. Lange is just a special case in the large category of the game phenomenons.

The Finish scholar Yrjo Him admits that any art can, in a way, be called game, although the art phenomenon has its own specific characteristics that exceed the frame of the game. Every game gets an artistic character if it is perfectly realized.

Other manifestation, more or less linked with art, can be reported to games. So is fashion - its function, as Rakik says, is that to exert our tendency for changes.

Myths, symbolic creation of popular knowledge have, also, a lot in common with games.

Graffiti - wall paintings and inscriptions are games that mean to express wishes, feelings (often sensual ones), we can find here, as in games and art the tendency for self-expression, one of the profound characteristics of human nature.

Even religion may be considered a ludic phenomenon. As games, religion is preparing for a more complex life that is based on freedom, on the lack of compulsion. Many of religion related manifestations as ceremonies, habits have a ludic character, clearly visible at primitive religions (dances and ritual orgies).

Friedrich Schiller speaks about art as game, not only as spending the energy excess through these activities but mainly referring to harmony, interior tendencies, freedom of contemplation. Schiller has made a distinction between the significance of activity consumption and total harmonious activity, but he named them with the same word, showing that "the forces natural game", the consumption of superflu energy lets us understand the passage from "natural state" to "esthetic state". So we owe Schiller the plurality of senses he offered the word game, that made possible to define art, with the condition of not offering just an interior significance.

Psychology and pedagogy mixes sometimes games as spontaneous developmental activity up with amusement games. When we see an infant playing with his voice, or limbs, moving his finger or touching his feet, actually a function structuring takes place. In these situations the child tries to conquer the language or the body, without making energy consumption, only with a well directed activity amplifying motric answers.

Different forms of games are well suited to each step in the human beings orientation, developing, which are left behind in time. The type of the game depends at the same time of the momentary needs of the child, his interests, gifts, taste and his mental and organic development.

In the frame of the game the child's personality develops in his interest. The child presents himself as what he is and what he would like to be, he offers himself what he would like to have. Through the game the child creates a world, he acts dreaming, and the illusion is stimulated by convention, by the other partners' agreement, by the concentrate character of the game and the symbolic character of the infantile spirit. The child who plays creates a world, without being conscious that he is the one who creates it, he lives between his images and is conquered by his own invention.

The game of the child means taking into possession the world and running away in front of it, wanting to know and to conquer it, he at the same time escapes from it, he overlaps another which offers the illusion of power.

Progressing in age, the purely physical games seem to prevail and psychical games are much less extended as both sexes. The bigger child finds much more pleasure in coordinating difficult movements. While organizing the games they are socialized and put under well established rules, movements are also disciplined. Small children enjoy toys as stimulants and as symbols of the games. The child who prefers to play alone needs his game and toys. He is at first pleased with what he is offered or what he finds, giving the chosen object the necessary significance. Later the skillful child tries to build exactly the suited toys.

Through the game, reverie is mixed into the child's life. The child lives in a fog of dream; the reality is lost in dream. The dream changes in a strange way the reality. The reality gives the playing child just the starting and locating points.

The reverie state admits numerous steps: from the simple proposing of the topic to the plunging in the imaginary life, through permissive uncertainties and active consent.

Reverie completes life, representing the developing of the refused tendencies and of unsatisfied virtualities. Reverie which is the game of imagination builds - as the game - "another world". Without any doubt art recalls reverie, as certain form of reverie, is orientated towards art.

Sometimes, during the game, the social assent interferes. When children play together their consent concerning the reality of the game is very important. We know that drawings of small children are more symbolic than realistic. They are pleased with a single sign which they take for the object itself. The same is true for their way of observation: they catch some features and become blind for the whole rest.

Wundt was right to observe that if plastical art doesn't appear at all at small children it is because imagination makes it useless, giving objects the wished significance.

The child's game supposes the need to translate an inside image, and performing it, as it happens, consolidates and settles the tendency which offers life performance.

The child tends to reproduce in the first place everything that is characteristic for him, he selects and schematizes. The image is enriched and developed at the same time with his talent; painting is dramatized and gets shades. The simple symbolic sign is transformed in a picturesque image.

In passing from dream to reality we have to stress the role of the language. The child thinks with loud voice before his own actions - expressing an interior necessity, he speaks while acting. He uses words to obtain what the action itself couldn't realize alone. From here confabulation which consists in creating a reality through words and magic language, which consists in action

through words or as Piaget said "the word can become an order given to reality". In profound games every impression of reality, voluntary illusion, oscillation between dream and reality disappears.

During the game, the child looks somehow alike to an actor who invented step by step his role from the moment he wishes to play it. He represents what is exactly in that moment and he is what he represents. He lives his part before building it for a certain public. His role is mainly simple and improvised; it doesn't necessitate counting, organizing or special efforts. The child is also the actor who creates his part, plays it, he let himself be caught by it and he mystifies himself.

Emotion showed on stage pass through a double symbolism, that of the authors style and that of the actors performance. The images representing passion in the theater are not real images, are arranged portraits submitted to convention, the reality in the theater is submission and convention.

The actor, as all those who have the mission to directly act upon a crowd, has an double role - as an artist he has to perform and verify, and as a sort of abstract creature he has to stay nearby, observing the active human being and the public being capable of combinations, new shades and resources - with other words - a judge.

The actor, as the child has at his disposal the action and the dream. His means are composing the character and plastic materializing.

The game appears to us as an activity that is practiced ignoring the compulsion of the reality and which creates in accordance to the interests and the mental level of the subject, the necessary topics and objects for its performance. The game conquers the world and creates another world. It is natural that some people thought of it in order to explain art.

Art does not descend from game, sooner from every human activity. Art is one of the ways in which the mans total activity is used and consumed.

The game is almost insensitive in front of its matter. The person who plays uses the toy as a mean to reach his purpose.

The artists on the contrary begin to love the matter in itself and for itself, independently of what could help him to significate. The artist - viewer and creator - has an elective sensibility for a certain category of feeling.

In art there isn't anymore a game of images and feelings. It is a choice of images and beautiful, expressive feelings capable to be arranged in harmonious symbols.

Art supposes a more complex activity than game. It is a joy of creation, like the game but it creates a harmonious reality; it builds a world that imposes through its tidiness and laws on the spirits. It doesn't mean anymore the fugitive momentary creation that is lost in ephemeral emanation.

Dessoir puts the following problem: "we could believe that art is related to game that great artists have played a lot in their youth". Study shows that it is not the case, Beethoven and Mozart, for example, have given their whole attention to music from their very youth.

Art expresses a more complex and solid activity than game. It is possible that game has contribution to its preparation, because it has something liberal, and the person who plays - adult or child - liberates himself from the immediate necessity. Game becomes art just at a spiritual human being that is on the highest summit of spirituality. Game becomes art just if the person who plays is an artist. Game is an inferior step in liberation, created by an elementary life enough for itself. Art penetrates deeper through unfettering, through this liberation.

Any perfect, completed esthetic pleasure is the synthesis between a sensorial pleasure, a formal pleasure and a pleasure in a proper affective sense. Sensation is the beginning of art. The pleasant stimulation of the sense organs is the sine qua non condition of every beauty.

Music accords sounds and feelings, it composes them to forms, accords these sonorous forms with feelings and with the inexpressible life that is behind them.

The musical pleasure reunites and accords sensorial pleasure and sensorio-motor pleasure of the sounds and movements, the architectural pleasure of sonorous forms, the pleasure of the feelings and of the confused and precise world that stirs beyond them.

"Poetry is a music in which idea has become feeling" (Suares). Poetry uses plastical and musical, logical and affective elements. There is no poetry without the interaction and synthesis of ideas, feelings, the verbal images of music and poetic form. For the poet as for all artist thinking exists just when it falls under the senses.

"Any painting is a thing that is part of the intellect", said Leonardo da Vinci. We can say the same about all arts. Art is creation and not the copy of a reality. We must not let ourselves fooled by realism, neither by that of transcendental data nor by that of empirical data. Nature is never servile copied and without appealing to the artists imagination. The artist always appeals to the means nature posses in order to translate impressions and emotions rousen in him by the nature.

Every work of art is always the expression of an ideal. Without significance, value, the esthetic pleasure remains poor. We ask from a painting, from a poem, from a symphony to be more than just a nice arrangement of lines, colors, words, sounds and to symbolize a state of the soul. There exist well build, agreeable works but they present no interest, there are empty. Another

possibility is that works are overloaded with good intention, but they don't reach the adequate expression.

Game is the first step towards art. It is the art of the muscles and that is why it seldom makes a whole with concert, painting and poetry.

Often the sport games may reach shades and subtleness, that brings them close to art, but this alternative can't be imagine without the correlation between physical and psychical performance.

The proximity between game and art is realized based on a common element: both induce pleasure.

The distance between game and art consists in the fact that art consistently outruns the level of recreative, immediate needs having as a purpose the establishing of a psycho-sensorial advice on the way enlightening the individual and the society.

Despite all these, game is necessary because it stimulates somatic acuity and that of the sense organs, it shelters them from atrophying.

In the end we can understand the true meaning of Schiller's words: "The man is complete just when he plays" and as the poet Rambert said "If the perfect game would be in the power of man, would he be God and would heaven be on earth?"

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VI. RADIOLOGY

PARTICULAR CASES OF SYMPTOMATIC JUVENILE EPILEPSY OF CEREBRAL VASCULAR CAUSE

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Summary

The work presents two particular cases of symptomatic juvenile (adolescent) epilepsy of vascular cause: dural venous malformation and ischemic CVA (lacunary infarct) underlined the importance of the imagistic investigations (classical cranial radiography, CT native and with contrast substance, cerebral angiography) for establishing the incriminated anatomical substratum.

Key words: - symptomatic juvenile epilepsy of cerebral vascular cause; the diagnostical and etiopathogenical importance of the imagistic investigations

Introduction

Epilepsy represents a cerebral suffering symptom caused by extremely various factors and characterized by the appearance of some paroxysm (accesses and attacks) of sensitive, sensorial, vegetative or psychical order, sometimes preceded (in the generalized forms) by the loss of conscience. The mechanism of the epileptical attacks cause the clinical form of the suffering: the generalized epilepsy with "grand mal" attacks, the motor, sensitive and sensorial focal epilepsy (cortical), the diencephalic or striated subcortical epilepsy, hysteroepilepsy etc.

Among the incriminated causing factors there are the cerebral vascular pathology, cerebral vascular anomalies through fatal disembrionplasy (the encephalotrigeminal angiomatosis), perinatal vascular accidents (cerebral epileptogene hematoma) or postnatal (aneurismal breakage, cerebral lacunary infarct, cerebral atherosclerosis, cerebral embolisms, cerebral vasospasms, hemopathies and coagulopathies of different causes.

At children with epileptic attacks must be taken into consideration the possibility of incrimination of the cerebral vascular pathology for whose diognostication the progressive and adequate imagistic investigations are absolutely necessary.

Material and method

In the present work have been selected two particular cases of symptomatic epilepsy; the first case is the one of a 15 years old child, who when she was 3 had her first attack of absence type and whose symptoms persisted, appearing in alternating degrees (sporadic attacks or absences associated with motor automatisms); the second case is the one of a child with the same age as the first one

who presented hemiparesis on the left side (frustum form associated with left partially convulsive attacks).

For the clearing of the etiopathogenic cause, the two patients were clinically, paraclinically and through different imagistic methods investigated (standard cranial radiography, native and with contrast substance computerized tomograph investigations and cerebral angiography). In the first case, thus was diognosticated a dural venous malformation, while in the second case was discovered a lacunary infarct at the right putamen.

Results

Case no. 1

The patient B.F., a female, hospitalized in the Neuropsychiatry Stationery for children in Timișoara, presents a neuropsychiatric history starting when she was 3 years old under the form of a first absence type attack. Despite the different treatments applied, the neurological symptoms persist, alternating only under the aspect of their importance: sporadic absence type attacks associated with motor automatisms.

In 1997, at the age of 15, the cranial radiography made in the anteroposterior incidence reveals an evident asymmetry of the dural lateral sinus in the favor of the left side sinus. (Fig. 1).



Fig.1. Asymmetry of the dural lateral sinus in the favor of the left side sinus.

This aspect entails the recommendation for a cerebral angiography. This investigation made by the Cardiology Centre in Timișoara underlines – in the venous time – a significant stenosis of the superior sagittal sinus

(with 75%) in the region proximal to the confluence of sinuses (dural Herophile crossroad), as well as a pronounced diminution (with 50%) in the diameter of the right transverse sinus (Fig. 2 and Fig. 3) in its distal half.



Fig. 2 and 3. Cerebral angiography – a significant stenosis of the superior sagittal sinus.

The classic radiography examination as well as the venous time of the cerebral angiography reveals the presence of a dural venous malformation. To clear the etiopathogeny of the absence attacks associated with motor automatisms was made the native cerebral CT exam that

revealed normal aspects (Fig. 4 and 5), thus excluding the other types of cerebral pathology (hydrocephalus, cerebral tumour etc.) which could explain the above symptomatology.

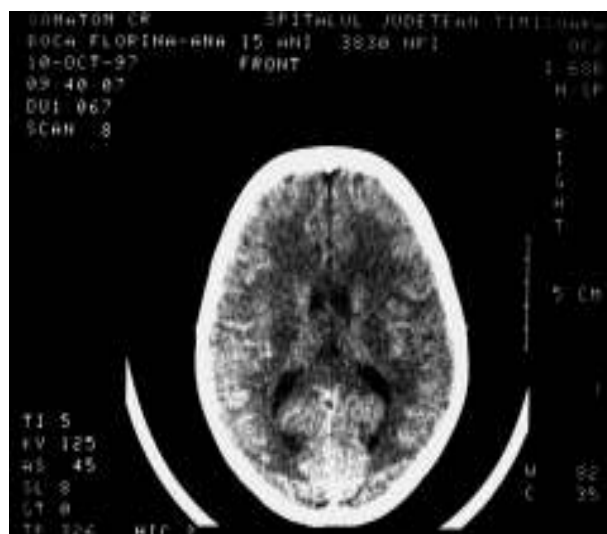


Fig. 4 and 5. Native cerebral CT exam that revealed normal aspects.

Case no. 2

The patient S.I., a female of 16, hospitalized in the Neuropsychiatry Stationery for children in Timișoara, with the neurologic diagnosis of left hemiparesis (frustum form) presented left partially convulsive attacks. In 2001, when she was 14, in order to establish the cause that generated

this clinical situation, the doctors made a native CT exam and with contrast substance in the middle of an acute access. This examination underlined an irregular hypodensity of 3/2/1,5 cm, visible on the medium transventricular sections at the right side putamen, near the insula (Fig. 6 and Fig. 7).

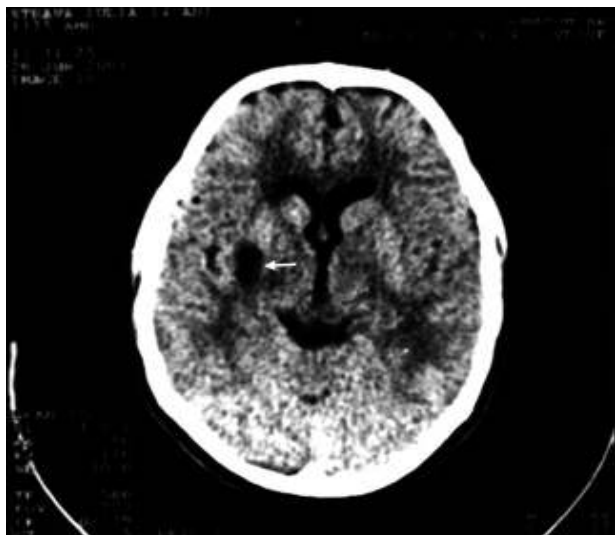


Fig. 6. Native CT exam.

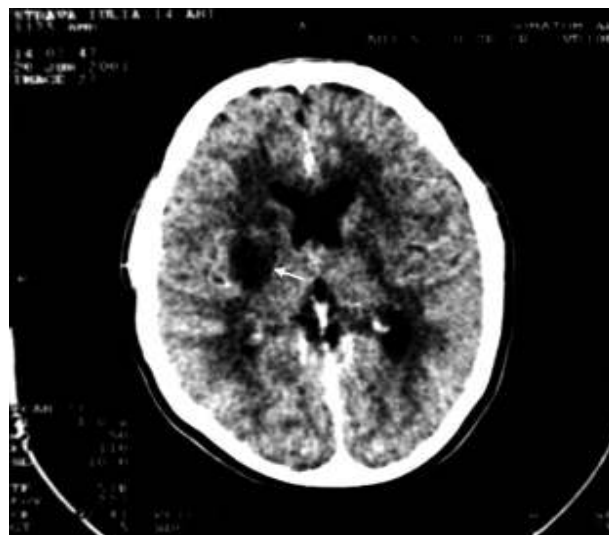


Fig. 7. CT exam with contrast substance.

After administrating the contrast substance (50 ml Ultravist) it appeared a discrete diminution of the hypodense area. The CT image establishes the cause of the previous mentioned clinical aspects, by installing an ischemic vascular accident supervened on an artery of a reduced diameter. At an interval of about 6 months after the

first examination, was made a CT of control, pointing out a hypodense image of net diminished size (Fig. 8 and Fig. 9), of liquid aspect, resembling cerebrospinal fluid. It is thus confirmed the typical evolution of a cerebral lacunary infarct – term used by T. Pop for the arteriolar infarct of reduced dimensions.

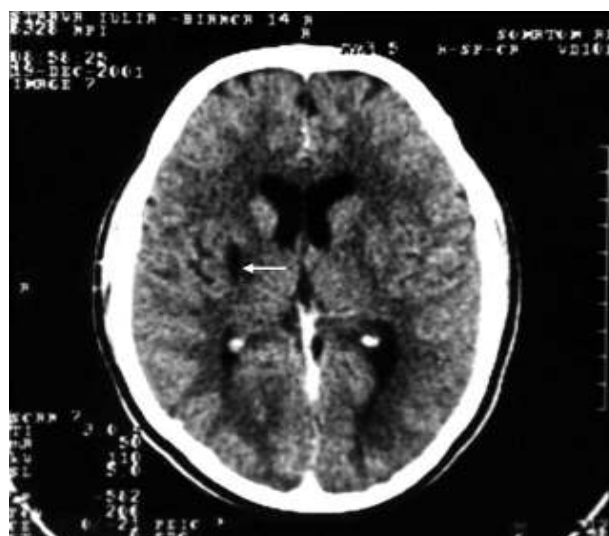
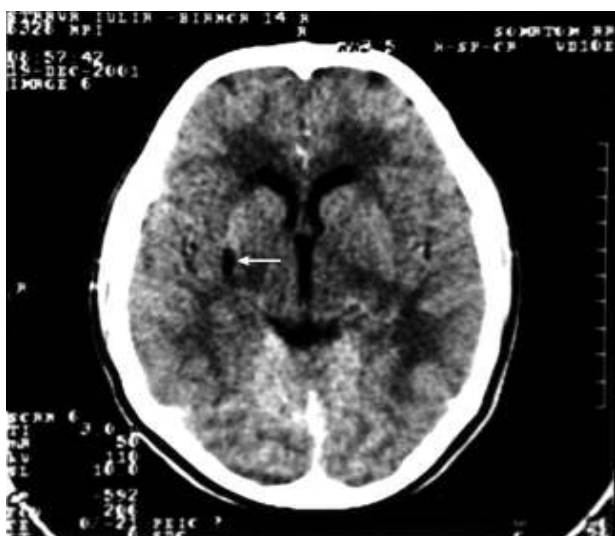


Fig. 8 and Fig. 9. CT control exam 6 months after the first examination.

Discussions

In the first case, the precocious clinical debut (at the age of 3) and long lasting persistence under treatment of neurologic symptoms, as well as angiographic aspects of stenosis (aspect in clepsydra) of the superior sagittal sinus as well as of the right transverse sinus near the confluence of sinuses (dural Herophile crossroad) plead for a congenital cerebral vascular anomaly (dural venous malformation of posterior fossa).

The dural venous malformations are rare. On the other hand, the changes in diameter of the dural sinuses evidenced by imagistic methods must be correctly evaluated to be differentiated from the anatomical variants which are normal situations and do not provoke craniocerebral venous drainage disorders of clinical response.

The position and duality of the stenotic injury in the proximal area of the confluence of sinuses (dural Herophile crossroad) shows the importance of the obstruction which, by impeding the cerebral venous drainage may explain the physiopathology of the absence attacks accompanied by the motor automatisms.

The second case presented refers to a very rare situation at children, namely the cerebral vascular accident (CVA). The ischemic CVA etiology knows (according to Solomon and the associates quoted by C. Aldescu) as more frequent causes: cerebral atherosclerosis, cerebral embolisms (cardiac, fat etc.), inflammatory and non-inflammatory arteriopathies, vasospasms (cerebral posthemorrhage, migraineous, etc.), hemopathies, coagulopathies, other various causes – traumatical, anoxical, iatrogenical (cerebral postangiography, after interventions of the internal carotid artery etc.). In the presented case, the lab exams had excluded the incrimination of the above causes and the age of the patient excluded the cerebral atherosclerosis. In this context was taken into consideration the possibility of the vascular malformative etiopathogeny.

Paturet, Lazorthes, D. Sutton and other authors describe at the level of the putamen the lenticulostriate arteries group (Fig. 10).

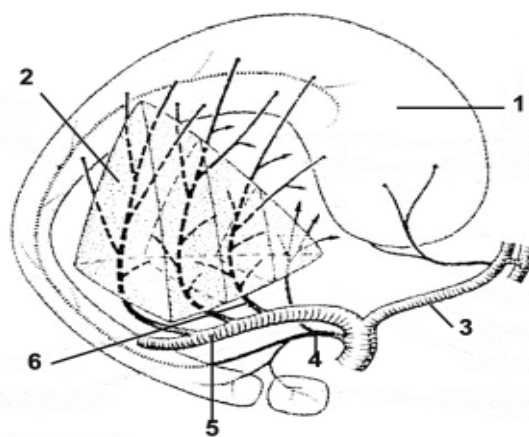


Fig.10. Arterial supply of corpus striatum (after G.Lazorthes) 1.nucleus caudatus; 2.nucleus lentiformis; 3.a. cerebri anterior; 4.a. choroidea anterior; 5.a. cerebri media; 6. rr. striati (lenticulostriate arteries)

The reduced size of these arteries as well as their terminal character explains the diminished size of the ischemic injuries. One ramus, usually the largest, was termed by Charcot the "artery of cerebral haemorrhage". Classic authors (Paturet, etc.) consider that some of these arteries touch the superior portion of the lateral nucleus of the thalamus (Fig. 11) under the name of lenticulooptic arteries, contested fact by the majority of neurosurgeons (Lazorthes and others) by the study of the cerebral arterial theories through modern imagistic methods (cerebral CT with contrast substance) (Fig. 12) as well as by the above presented case.

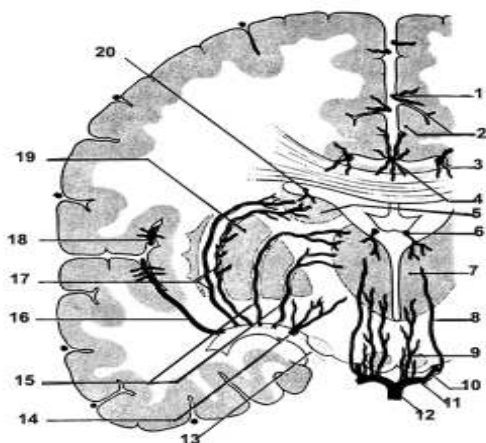
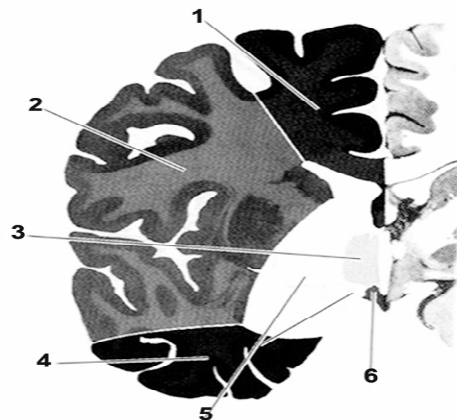


Fig. 11. Deep cerebral arterial supply (after G.Paturet): 1.r. sulci cinguli (a. cerebri anterior); 2.sulcus cinguli et gyrus cinguli; 3.a. cerebri anterior; 4.a. cerebri anterior mediana; 5.nucleus caudatus; 6.a. choroidea anterior; 7.thalamus; 8.r. thalami (a. communicans posterior); 9.r. thalami dorsolateralis; 10.a. communicans posterior; 11.a. cerebri posterior; 12.a. basilaris; 13.a. cerebri media; 14.a. choroidea anterior; 15.lenticulooptic arteries (a. cerebri media); 16.a. cerebri media; 17.lenticulostriate arteries (a. cerebri media); 18.r. sulci lateralis (a. cerebri media); 19.putamen (nucleus lentiformis); 20.a. choroidea media.

Fig. 12. Arterial cerebral territories (cerebral CT with contrast substance): 1.a. cerebri anterior; 2.a. cerebri media; 3.A. communicans posterior; 4.a. cerebri posterior; 5.a. choroidea anterior; 6.a. cerebri posterior.



Conclusions

1. The work presents two cases of children with cerebral vascular anomalies that, through cerebral circulatory disorders can cause different symptoms, such as epileptic attacks.
2. The etiopathogenic clearing of such cases needs the corroboration of clinical and biological aspects with the results of imagistic investigations.
3. The simple classical radiographic examination may draw the attention over possible cerebral vascular

anomalies, requiring the use of modern imagistic methods (cerebral angiography, cerebral CT, RMN, etc.) for the exact clearing of the situation and for establishing the presence, topography and of spreading of possible cerebral injuries.

4. A complexe investigation of such cases is due to the paediatrician, to the neurologist and to the radiologist work in a team, who must choose the type and the order of the optimum investigations needed to a correct diagnosis step.

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MANUSCRIPT REQUIREMENTS

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

The article should be organized in the following format: Title, Names of all authors (first name initial, surname), Names of institutions in which work was done (use the Arabic numerals, superscript), Abstract, Keywords, Text (Introduction, Purpose,